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Welcome

On behalf of the Organising Committee and the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists we are delighted to invite you to the 20th World Congress of Basic and Clinical Pharmacology – WCP2026.

From 13th – 18th July 2026 we will welcome the world's pharmacology and therapeutics community to the Melbourne Convention Centre in Melbourne, Australia. We look forward to celebrating the diversity of this community including students, early career pharmacologists, global leaders in clinical pharmacology, and innovators at the cutting edge of drug discovery and development, innovation and engagement with the pharmaceutical industry and academic sectors.

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The WCP2026 leadership group and local organising committee recognize that the diversity and inclusivity within the global pharmacology community is a strength. As such, the composition of our committees, scientific programmes and the make-up of its attendees, will be guided by our Equity Diversity and Inclusion (EDI) policy. We will actively collect and report on EDI metrics as we develop the program and deliver the conference. We look forward to welcoming speakers and chairs, and attendees across the world at our six-day congress.

We look forward to welcoming you to Australia, a vast country with significant diversity and natural landscapes, adventures, food, culture, sporting culture and many other opportunities. Book some time either side of the Congress to explore some of the amazing tourist and cultural opportunities in Victoria and Australia.

We hope this website provides essential information you need to start planning your WCP2026 experience.



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Congress Chair


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ARTÍCULOS / ARTICLES

- PRESCRIPTION OF DRUGS THAT INHIBIT GASTRIC SECRETION IN A PUBLIC TEACHING HOSPITAL IN URUGUAY: A DESCRIPTIVE CROSS-SECTIONAL STUDY.
  Maite Inthamoussu, Stefano Fabbiani, María José Vergara, Natalia Cuña, Agustina Deffes, Milenka del Pino, Camila Ferreira, Virginia Gurbindo, Rodrigo Monroy, Noelia Speranza

ARTÍCULO DE INVESTIGACIÓN CLÍNICA / CLINICAL RESEARCH ARTICLE

PRESCRIPCIÓN DE FÁRMACOS INHIBIDORES DE LA SECRECIÓN GÁSTRICA EN UN HOSPITAL UNIVERSITARIO DE URUGUAY: ESTUDIO OBSERVACIONAL DESCRIPTIVO. Prescription of drugs that inhibit gastric secretion in a public teaching Hospital in Uruguay: a descriptive cross-sectional study.

Maite Inthamoussu [1], Stefano Fabbiani [1], María José Vergara [2], Natalia Cuña [3], Agustina Deffes [3], Milenka del Pino [3], Camila Ferreira [3], Virginia Gurbindo [3], Rodrigo Monroy [3], Noelia Speranza [1].

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ABSTRACT

Introduction. *Proton pump inhibitors (PPIs) and H2 receptor antagonists are highly prescribed drugs for the treatment and prophylaxis of diseases related to gastric acid secretion. However, irrational prescription is a global problem.*
Objectives. *To describe the prescription characteristics of PPIs and H2 receptor antagonists in hospitalized patients at a public teaching Hospital of Uruguay.*
Methods. *An observational, cross-sectional, descriptive study was carried out in the "Hospital de Clínicas". Patients hospitalized in selected wards who had a prescription of anti-ulcer drugs between July and August of 2023 were included. We analyzed the prevalence of prescription, characteristics of the utilization and reasons for receiving them (prophylaxis or therapeutic). We also established if the prescriptions were according to recommendations made in 2016 by experts of the Hospital.*
Results. *297 patients were included. The median age was 59 years. The prevalence of prescription was 46%. The most prevalent risk factor was intensive care unit hospitalization for more than 7 days (36%), followed by non-steroidal anti-inflammatory drug (NSAID) consumption more than three times a week (25%), and gastritis (20%). 38% received anticoagulants, 26% NSAIDs, and 15% antiplatelet agents. Most patients received omeprazole (78%), mainly administered orally, similar to ranitidine. 94% had formal indications to receive these drugs prophylactically, 45% of them were according to the recommendations of the hospital.*
Conclusions. *The prevalence of PPI prescription was lower than that found in an institutional study in 2006 (46% versus 66%). Most patients received omeprazole, the most effective drug for the prophylaxis and treatment of these pathologies. However, compliance with institutional recommendations does not exceed 50%, and a large percentage presents unjustified use, exposing patients to drug interactions and adverse effects. Due to the methodology of this study, there could be information bias related to under-reporting data in medical records.*

Keywords: *Anti-ulcer agents; Proton pump inhibitors; Histamine H_2 antagonists; Drug utilization review.*

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1) INTRODUCCIÓN

Los inhibidores de la bomba de protones (IBP) y los antihistamínicos H2 son inhibidores de la secreción gástrica (ISG) ampliamente utilizados en la práctica clínica, considerados pasibles de usos inapropiados y aumento del riesgo de reacciones adversas e interacciones medicamentosas [(1)]. Ambos tienen el efecto de inhibir la secreción ácida por parte de la célula parietal gástrica.

Es frecuente el uso irracional de estos grupos terapéuticos tanto porque se indican en situaciones clínicas inapropiadas como por la baja percepción de riesgo con respecto a su perfil de efectos adversos. Sin embargo, la farmacovigilancia ha permitido identificar reacciones adversas derivadas principalmente de su uso crónico. Por ejemplo, los IBP se han asociado con riesgo de hipomagnesemia o aumento del riesgo de fractura, relacionado con la pérdida de masa, aparición o progresión de enfermedad renal crónica y presencia de lupus eritematoso cutáneo sistémico [(2)]. Con los antihistamínicos, se ha observado que el uso continuado genera tolerancia con disminución de la efectividad, ginecomastia, hiperprolactinemia, alteraciones en la libido e impotencia [(3)].

La hospitalización es un factor de riesgo para la prescripción inadecuada, y además la prolongación del tratamiento al alta puede derivar en duraciones de tratamiento innecesariamente prolongados [(4)]. Estudios realizados en España y Latinoamérica han observado un aumento en la prescripción de IBP en los últimos años, principalmente en adultos mayores con múltiples comorbilidades y polifarmacia. Aproximadamente entre 25% y 70% de las prescripciones son inadecuadas, ya sea en la indicación, dosificación o duración del tratamiento [(5-8)].

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En Uruguay los datos son escasos. La última investigación realizada en el Hospital de Clínicas, el principal hospital universitario, de tercer nivel de atención y referencia a nivel nacional, con sede en Montevideo se llevó a cabo en 2006, evidenciando una alta frecuencia en el uso de ranitidina (62%) y la falta de indicación en presencia de factores de riesgo por comedicación (21%) [1]. Parte de esta información sirvió como base para el desarrollo de una guía con recomendaciones sobre las indicaciones, el uso y la administración de los ISG en el Hospital [9]. Desde esa fecha no se han realizado nuevas recomendaciones institucionales de uso de ISG en pacientes hospitalizados. En 2014 se realizó un estudio similar en el Hospital Maciel, uno de los principales hospitales públicos de Montevideo que también tiene un perfil universitario, y se observó que 84% recibieron fármacos ISG, de los cuales 78,2% se trataban de prescripciones incorrectas [10].

A nivel nacional, no existen recomendaciones estandarizadas a seguir, más allá de las recomendaciones de uso del Hospital de Clínicas mencionadas previamente.
El objetivo del presente trabajo fue describir las características de la prescripción de IBP y antihistamínicos H2 en una población de pacientes hospitalizados en el Hospital de Clínicas Dr. Manuel Quintela durante el mes de agosto del año 2023.

2) MATERIALES Y MÉTODOS

2.1) Diseño del estudio

Se realizó un estudio observacional, transversal de tipo descriptivo, de pacientes a los que se les indicó fármacos ISG durante su internación en el Hospital de Clínicas Dr. Manuel Quintela. La muestra fue seleccionada por conveniencia. Se incluyeron los y las pacientes mayores de 18 años con indicación de un ISG durante el mes del estudio y que consintieron participar del mismo.

2.2) Pacientes

Los participantes se identificaron desde las prescripciones electrónicas de ISG de salas que contaban con sistema de prescripción electrónica y posteriormente se solicitó consentimiento para acceder a su historia clínica para extraer datos sobre las demás variables de estudio. Se incluyeron pacientes de un total de 177 camas distribuidas en salas de medicina, cirugía, hematología, nefrología, cardiología y cuidados intermedios. Se le solicitó a los pacientes hospitalizados consentimiento informado verbal y escrito para participar del estudio. El estudio contó con el aval del Comité de Ética del Hospital de Clínicas Dr. Manuel Quintela y fue registrado en el Ministerio de Salud Pública de Uruguay.

2.3) Protocolo Experimental

Se elaboró un protocolo de recolección de datos para homogeneizar la extracción, considerando además que esta tarea estuvo a cargo de estudiantes de la carrera Doctor en Medicina de la Facultad de Medicina de la Universidad de la República. Los mismos se entrenaron previamente al inicio de la recolección.
Los fármacos ISG evaluados fueron omeprazol y ranitidina, dado que son los que se encuentran incluidos en el Listado de Medicamentos Esenciales (LIME) del Hospital de Clínicas. Omeprazol se encuentra disponible en comprimidos de 20 mg de administración por vía oral y ampollas de 40 mg de administración intravenosa. En el caso de ranitidina, se encuentra en ampollas de 50 mg para administración intravenosa y en comprimidos de administración vía oral de 150 mg.
La prevalencia de pacientes que recibieron ISG se calculó con el número de prescripciones de estos fármacos sobre el total de pacientes ingresados en los servicios mencionados en el período estudiado.

Para caracterizar la prescripción se consideró la edad, sexo, diagnostico al ingreso, sala de internación, comorbilidades, fármacos concomitantes, factores de riesgo para enfermedad ulcerosa péptica, tipo de ISG y pauta posológica (dosis, intervalo interdosis, vía de administración y forma farmacéutica).
Para determinar si las prescripciones se adecuaban a las recomendaciones del Hospital de Clínicas, se definió tratamiento cuando se constató como motivo de ingreso algunas de las siguientes patologías: hemorragia digestiva, úlcera gastroduodenal, enfermedad por reflujo gastroesofágico (ERGE), dispepsia funcional o no estudiada o gastroduodenitis. A su vez, también se consideró como tratamiento cuando existía registro en la historia clínica de indicación de estos fármacos previo al ingreso por alguna de las patologías mencionadas. Cuando la fecha de prescripción e ingreso eran diferentes, se buscó en la historia clínica si la prescripción coincidía con un nuevo diagnóstico de estas patologías y se clasificó la prescripción como tratamiento. El resto de las prescripciones se clasificaron como profilaxis.
Para evaluar el cumplimiento de las recomendaciones profilácticas mencionadas, se categorizó a las mismas en 2 grupos: gastroprotección por consumo de antiinflamatorios no esteroideos (AINE) y lesiones agudas por estrés, considerándose para cada uno los factores de riesgo mencionados en el marco teórico.

2.4) Análisis estadístico

Las variables cualitativas se presentaron con frecuencias absolutas y relativas. La variable cuantitativa edad se presentó con mediana y rango intercuartílico, por presentar una distribución no normal. Para evaluar la normalidad se analizó la relación entre la media y la mediana, la distribución de la variable en el histograma, los valores de skewness y kurtosis y se utilizó el test de Shapiro-Wilk.
Para el análisis de los datos se utilizó el programa Excel®.

3) RESULTADOS

Durante el período del 28 de julio al 28 de agosto de 2023 fueron hospitalizados 870 pacientes en las salas incluidas para participar del estudio, de los cuales 404 tenían prescripción de ISG. La prevalencia de prescripción de ISG fue 46%.
De los pacientes elegibles, 107 no fueron incluidos en el análisis posterior planteado en la investigación, por lo que la caracterización de los pacientes y la prescripción se hizo en un total de 297 pacientes. En la figura 1 se muestran los motivos de exclusión.
La mediana de edad fue de 59 años y 52% pertenecía al sexo masculino. La mayoría de los pacientes se encontraban ingresados en salas de medicina interna (58%); y el resto en otros servicios. El resto de las características generales de la población se describen en la tabla 1.

Figura 1

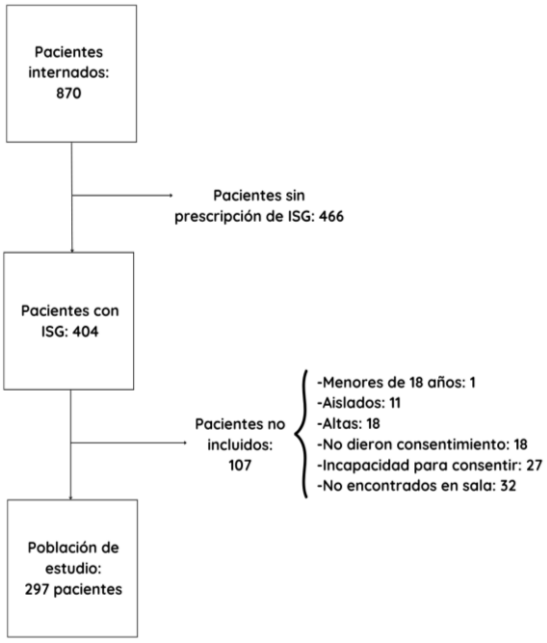


Figura 1: Diagrama de flujo de la población estudiada. ISG: inhibidores de la secreción gástrica

Respecto a las comorbilidades, 38% de los pacientes presentaban insuficiencia cardíaca, 26% enfermedad renal crónica, 12% enfermedad autoinmune y otro 12% depresión mayor (Tabla 1).

Sobre los factores de riesgo para el desarrollo de enfermedad úlcera péptica gastroduodenal, 36% de los pacientes tuvo una permanencia mayor a una semana en cuidados intensivos, 25% presentaban consumo de AINE mayor a tres veces por semana, 20% tenían gastritis, 12% presentaban insuficiencia hepática aguda y 7% contaba con un antecedente de úlcera gastroduodenal previo (Figura 2).

Con respecto a los fármacos concomitantes, 38% de los pacientes recibían anticoagulantes, 26% AINE, 15% antiagregantes, 13% glucocorticoides sistémicos y 8% antidepresivos. Del total de pacientes 78% recibió omeprazol y 22% ranitidina. Se destaca que 2 pacientes recibieron ambos fármacos concomitantemente. En la tabla 2 se muestran las características de la prescripción de ambos fármacos. En cuanto la prescripción de omeprazol, la mayoría recibió 20 mg diarios (85%), seguido por 40 mg diarios (12%). En la mayoría (88%) el intervalo interdosis fue de 24 horas, en 11% de 12 horas y en 1% de 8 horas. La forma farmacéutica empleada en el 95% de los casos fue en comprimido vía oral y el resto por vía intravenosa. En cuanto a la prescripción de ranitidina, 68% recibió 300 mg diarios, seguido por 150 mg diarios (30%). En la mayoría (71%) el intervalo interdosis fue de 12 horas, 15% de 24 horas y 14% fue de 8 horas. Las formas farmacéuticas utilizadas fueron un 76% comprimidos vía oral y 24% en ampollas intravenosas.

Tabla 1

Edad** en años - **Md (RIC)	59 (46-69)
Género	***n (%)***
Masculino	153 (52)
Femenino	140 (47)
No binario	4 (1)
Diagnóstico al ingreso	***n (%)***
Cardiovascular	83 (28)
Cáncer	41 (14)
Patología renal	29 (10)
Patología respiratoria	22 (7)
Infección de piel y partes blandas	18 (6)
Patología del aparato digestivo	16 (5¿)
Otros	88 (30)
Comorbilidades	***n (%)***
Insuficiencia cardíaca	78 (38)
Enfermedad renal crónica	53 (26)
Enfermedad autoinmune	25 (12)
Depresión mayor	24 (12)
Prótesis de válvula cardíaca	9 (4)
Enfermedad hepática crónica	8 (4)
Coagulopatías	6 (3)
ERGE[1]	2 (1)

Tabla 1: Características de la población con prescripción de inhibidores de la secreción gástrica, Hospital de Clínicas, agosto 2023. 1- Enfermedad por reflujo gastroesofágico.

Figura 2

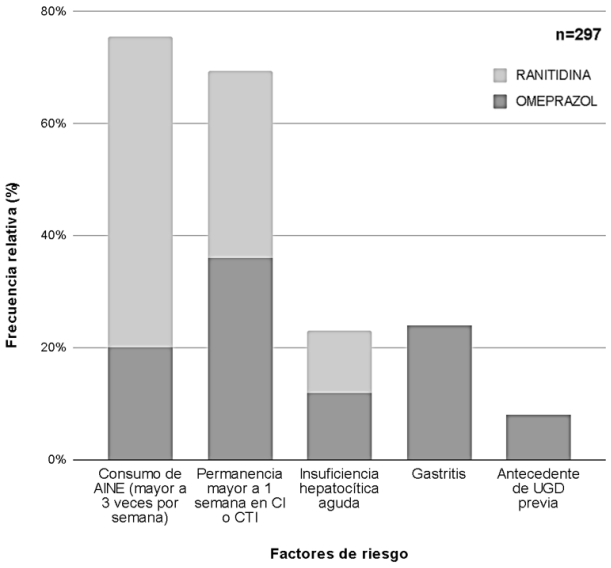


Figura 2: Factores de riesgo de la población con prescripción de inhibidores de secreción gástrica, Hospital de Clínicas, agosto 2023. AINE: antiinflamatorios no esteroideos / CI: cuidados intermedios / CTI: centro de terapia intensiva / UGD: úlcera gastroduodenal.

De la población de estudio 94% recibió ISG con fines profilácticos, mientras que 6% tenía indicación de tratamiento, correspondiendo a gastritis (63%), hemorragia digestiva (16%), ERGE (11%) y consumo de AINE (11%). Del total de los pacientes que recibieron ISG de forma profiláctica, 45% lo recibió de acuerdo a las recomendaciones institucionales (32% por consumo de AINE, 13% por profilaxis de lesiones agudas por estrés). Se destaca que en el 55% restante no constaba en la historia clínicas factores de riesgo que justificaran su uso profiláctico.

Tabla 2

OMEPRAZOL		RANITIDINA	
Dosis (mg) en 24 horas	*n (%)*	*Dosis (mg) en 24 horas*	*n (%)*
20	198 (85)	100	2 (3)
40	28 (12)	150	19 (29)
80	5 (2)	300	45 (68)
120	2 (1)		
Intervalo en 24 horas	*n (%)*	*Intervalo en 24 horas*	*n (%)*
8	2 (1)	*8*	9 (14)
12	26 (11)	*12*	47 (71)
24	205 (88)	24	10 (15)

Tabla 2: Caracterización de la prescripción de inhibidores de la secreción gástrica, Hospital de Clínicas, agosto 2023

De las prescripciones por consumo de AINE, la mayoría (93%) tenían prescripción de omeprazol. De las prescripciones por profilaxis de lesiones, la mayoría también tenía prescripción de omeprazol (84%). De los pacientes que recibieron ranitidina, solamente 1 de 6 pacientes lo recibió por vía intravenosa. De las prescripciones por tratamiento, en aquellos que la indicación era gastritis, 92% recibió omeprazol. En cuanto a la indicación por ERGE y hemorragia digestiva, la totalidad recibió omeprazol.

4) DISCUSIÓN

La prevalencia de prescripción de ISG en el presente estudio fue de 46%, menor a la observada en el trabajo realizado en el año 2006 en el Hospital de Clínicas de similares características (66%) [1]. Por lo tanto, podría interpretarse que la prescripción de estos fármacos se encuentra en descenso, dado que a partir de dicho estudio se elaboraron las recomendaciones institucionales mencionadas; la utilización de las mismas podría explicar esta reducción en la prescripción.

El fármaco más utilizado fue omeprazol. La administración fue predominantemente por vía oral, y en una única administración diaria, lo que se adecua a las recomendaciones. Dichos hallazgos concuerdan con los observados en el estudio de Vallejos y cols. [7]. Sin embargo, este hallazgo contrasta con el estudio previo del Hospital de Clínicas en dónde ranitidina fue más prescrita. Este cambio puede deberse a la adherencia a las recomendaciones locales mencionadas, su mayor disponibilidad en el Hospital y a que ha demostrado ser más eficaz que los antihistamínicos H2 [3]. Un número reducido de pacientes recibieron varias dosis diarias de omeprazol, cuyas indicaciones no cumplían los criterios de las recomendaciones. Desde el punto de vista farmacológico, podría considerarse una práctica irracional dado que con una única dosis se inhibe alrededor del 90% de las bombas de protones [11].

La prescripción con ranitidina se vio disminuida en más de la mitad en comparación al uso observado en el estudio de Vázquez et al [1]. Como se mencionó previamente, este cambio podría deberse a mayor disponibilidad de omeprazol en el Hospital de Clínicas, su menor eficacia comparada con éste, mayor adherencia a las recomendaciones, a lo que se suma recientes alertas en cuanto a su riesgo por la liberación del metabolito NDMA, un compuesto probablemente carcinógeno [12, 13]. Este fármaco fue utilizado principalmente por vía oral, administrado en dos dosis diarias, de acuerdo a las recomendaciones. Sin embargo, se observó un uso mayor por vía intravenosa que con omeprazol. Si bien en las recomendaciones esta indicación es sugerida frente a la imposibilidad de administrar IBP por vía oral [9], con los datos analizados no es posible determinar la causa de esta diferencia.

Entre los pacientes con prescripción de ranitidina el factor de riesgo más prevalente fue el consumo de AINE. Un reducido número de pacientes tenía indicación de profilaxis de gastropatías por AINE por lo que debían recibir omeprazol según las recomendaciones, pero recibieron ranitidina. Dos pacientes contaban con una doble prescripción de omeprazol vía oral y ranitidina por vía intravenosa. Esta práctica no solo no se adecua a las recomendaciones, sino que es irracional desde el punto de vista farmacológico y terapéutico. En el estudio previo de Vázquez y cols. [1] se había observado una situación similar. Esto podría deberse a un error en la transcripción de las prescripciones, o a intentar reducir la acidez gástrica mediante dos mecanismos diferentes. Sin embargo, la evidencia sobre el beneficio clínico de esta práctica es escasa y podría implicar riesgos para los pacientes.

En este estudio aproximadamente la mitad de los pacientes incluidos tenían prescripciones que se adecuaban con las recomendaciones institucionales. Este hallazgo podría explicarse debido a que el motivo de ingreso más frecuente fueron patologías cardiovasculares (28%) cuyos pacientes suelen recibir con frecuencia anticoagulantes o antiagregantes, entre otros fármacos. El uso de estos fármacos y la polifarmacia determina habitualmente la profilaxis con ISG de forma sistemática, un hecho que se repite en la literatura. Esta práctica es irracional ya que no se ha demostrado que la polifarmacia aumente el riesgo de sangrado digestivo [14]. Además, este resultado concuerda con lo observado en el boletín de la Fundación Catalana de Farmacología que describió que la principal causa de prescripción de ISG no son patologías digestivas [2].

La mayoría de los pacientes que recibió ISG de forma profiláctica no presentaba indicación documentada. Cabe destacar que podría existir

un sesgo de información, dado que la recolección de datos fue a partir de historias clínicas y no fue posible verificar esta falta de justificación del motivo del uso (por lo menos en las situaciones en las que se revisó el dato: ingreso, comorbilidades y fármacos concomitantes), lo que correspondería a un infraregistro de estos datos. Es un aspecto clave, considerando a la historia clínica como un documento médico legal que se registre el porqué de las conductas terapéuticas que se implementan, sobre todo si se hacen fuera de las recomendaciones más reconocidas de los ISG.

5) CONCLUSIÓN

El presente estudio cuenta con varias fortalezas como el número elevado de pacientes que accedieron a participar. La utilización de un programa electrónico proporcionó todos los datos necesarios para evaluar la prescripción de los fármacos con una información completa y legible. Este es un sistema relativamente nuevo dentro del Hospital, y este tipo de usos muestra que su utilidad excede el de la asistencia y favorece también la investigación y la calidad de los datos.

Como limitaciones, la metodología mediante la revisión de historias clínicas tiene como debilidad la falta de registro de información, sesgos por parte de los médicos tratantes y la necesidad de interpretación de las mismas por parte de los investigadores. Esto imposibilita que se catalogue como un verdadero estudio de indicación-prescripción y que solo sea una aproximación a los motivos de uso de los ISG. Esto determina que se deba recurrir a inferencias para determinar las indicaciones de estos fármacos en las y los pacientes incluidos. Otra limitante fue la imposibilidad de obtener consentimiento informado de algunos pacientes dado que no se permitía el ingreso de personal fuera del sector, incapacidad de consentir o por la transferencia a otros sectores del hospital sin historia clínica electrónica. A su vez, la recolección de datos fue por un tiempo limitado (1 mes) por lo que tal vez no refleje la prevalencia real de prescripción en el Hospital, si bien no parece que la estacionalidad pueda determinar una variación importante en la frecuencia de la misma.

Se requiere realizar estudios de forma sistemática para monitorizar la adecuación a las recomendaciones y también analizar las causas de estos incumplimientos. Para ello sería ideal contar con información más completa en las historias clínicas y con el sistema de prescripción instalado en todo el Hospital para conocer en una medida más real la prevalencia de la prescripción. Sería importante trabajar en facilitar el acceso a la información a investigadoras/es desde el punto de vista institucional.

Se destaca la importancia de contar con recomendaciones institucionales actualizadas y basadas en la mejor evidencia disponible para colaborar con el uso racional de los medicamentos.
Es necesario reforzar las estrategias para evitar prácticas injustificadas como las evidenciadas en este estudio. Entre ellas las actividades de educación permanente y de difusión de las recomendaciones existentes colaboran con promover mayor adherencia a las mismas y al uso racional, evitando situaciones de uso inadecuado como la polifarmacia y aparición de efectos adversos.

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Comité de ética:
El protocolo de investigación fue avalado por el Comité de ética Institucional del Hospital de Clínicas Dr. Manuel Quintela.

6) REFERENCIAS

1. Vazquez M, Iade B, Duré C, Boronat A, González N, Tchekmedeyian A, et al. Estudio de utilización de omeprazol y ranitidina en el Hospital Universitario de Uruguay. Revista de la OFIL. 2009;19(4):47-54.
2. Inhibidores de la bomba de protones: no son “protectores”, son fármacos. Butlletí Groc. marzo de 2016;29(1):1-4.
3. Flórez J, Armijo JA, Mediavilla Á. Farmacología humana. 6.ª ed. Barcelona, España: Elsevier; 708-722 p.
4. Inhibidores de la bomba de protones (IBP): recomendaciones de uso. INFAC [revista de Internet]. 2016;24(08):45-51. Disponible en: https://www.osakidetza.euskadi.eus/contenidos/informacion/cevime_infac_2016/es_def/adjuntos/INFAC_24_n_8_%20IBP%20recomendaciones.pdf
5. Saiz Ladera GM, Pejenaute Labari ME, García Pascual JN. Actualización en la prescripción de inhibidores de la bomba de protones. Qué hacer y qué no hacer. Medicina de Familia- SEMERGEN. 2021;47(4):267-79.
6. Posada Bustos S, De León Fernández N, González Morales R, Tihanyi Feldman J, Vera Chamorro JF. Prevalencia de prescripción inapropiada de terapia supresora de ácido en adultos hospitalizados en un hospital general en Bogotá. Rev Colomb Gastroenterol. 2018;33(1):16.
7. Vallejos Á, Maldonado L, Calvache JC, Hernandez W, Torres S, Diaz D. Descripción del uso de medicamentos gastroprotectores en pacientes con polifarmacia en una población colombiana, a partir de bases de datos transaccionales. Rev Colomb Gastroenterol. 2017;31(2):102.
8. Bustamante Robles Katherine Yelenia, Ticse Aguirre Ray, Cánepa Rondo Italo Francisco, Costta Herrera Carmela Giuliana, Vasquez Kunze Sergio, Soto Arquiñigo Leslie et al . Frecuencia de la prescripción de los inhibidores de bomba de protones basada en guías de práctica clínica en pacientes hospitalizados en dos hospitales docentes de Lima - Perú. Rev. gastroenterol. Perú [Internet]. 2012 Ene [citado 2024 Mar 19] ; 32(1): 44-49. Disponible en: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1022-51292012000100006&lng=es.
9. Vazquez M, Caligaris L, Maldonado C, Duré C, Boronat A, Oteiza D, et al. Resumen de las recomendaciones sobre indicaciones y uso-administración de los inhibidores de la secreción ácida en el Hospital de Clínicas [Internet]. Montevideo, Uruguay: Hospital de Clínicas; Disponible en: https://www.comitedeterapeutica.hc.edu.uy/images/resumen-aines.pdf/
10. Braz J, Macadam JP, Pirez J, Noel M, Fernández A, Facal J, et al. “Prevalencia de prescripción-indicación de fármacos inhibidores de la secreción gástrica en pacientes ingresados en un hospital de tercer nivel de Montevideo Uruguay”. Udelar, FM [Internet]. 2014; Disponible en: https://www.colibri.udelar.edu.uy/jspui/handle/20.500.12008/32418
11. Katzung, Bertram. Katzung, Bertram. (2022). Farmacología básica y clínica. McGraw Hill. McGraw Hill; 2022.
12. Retirada del mercado de medicamentos que contienen ranitidina vía oral [Internet]. Agencia Española de Medicamentos y Productos Sanitarios. AEMPS; 2019 oct. Disponible en: https://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/calidad/2019/docs/NI-ICM-CONT-14-2019-nitrosaminas.pdf
13. Pension J, Wormsley KG. Adverse Reactions and Interactions with H2-Receptor Antagonists. Medical Toxicology. 1986;1(3):192-216.
14. Martín-Echevarría E, Pereira A, Torralba A, Arriola G, Martín P, Mateos J, et al. Evaluación del uso de los inhibidores de la bomba de protones en un servicio de medicina interna. Revista Española de enfermedades digestivas. 2008;100(2):76-81.

XLV CONGRESO ANUAL
SOCIEDAD DE FARMACOLOGÍA DE CHILE



WELCOME

Dear Participants,

As President of the Chilean Society of Pharmacology (SOFARCHI), it is a great honor to warmly welcome you to the 45th Congress of the Chilean Society of Pharmacology, held in the beautiful and peaceful city of Viña del Mar. We are delighted to host undergraduate and doctoral students, as well as national and international researchers, whose presence greatly enriches this academic gathering.

We extend our deepest thanks to all those who contribute to this congress: the students who bring their enthusiasm and eagerness to learn, the researchers who share their knowledge and findings, and the keynote speakers and presenters who have prepared their talks with dedication. Your hard work and commitment contribute significantly to advancing and strengthening research in pharmacology, allowing us to explore and discuss the forefront of science in this field.

This congress is not only an opportunity to immerse ourselves in the latest advancements in pharmacology but also to carry forward the commitment to the ABCs of pharmacology, ensuring that our knowledge and understanding of the field continue to deepen the link between our neighborhood countries.

We would also like to express our sincere gratitude to the sponsors and collaborators, whose support has made this congress possible. Their contributions allow us to promote science and build a network of knowledge that transcends borders.

I hope that this congress becomes an enriching professional experience, fostering the exchange of ideas and strengthening bonds among colleagues and friends. May each of you find here an environment conducive to dialogue, learning, and collaboration, and may you enjoy a wonderful time in this serene and beautiful city.
Welcome to the 45th SOFARCHI Congress!



Sincerely,

Guillermo Antonio Díaz-Araya
President
SOFARCHI

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CONFERENCIAS / LECTURES



Dr. Mauro Teixeira.
Department of Biochemistry and Immunology, Federal University of Minas Gerais (UFMG), Brazil.

RESOLUTION PHARMACOLOGY – FROM CHRONIC INFLAMMATION TO INFECTION. Farmacología de la Resolución -desde inflamación crónica a infección.

Resúmen:
Inflammation is elicited by the host in response to microbes, and is believed to be essential for protection against infection. In contrast, chronic and uncontrolled inflammation may cause tissue damage and is implicated in the pathogenesis of various chronic diseases in humans. When infection is controlled or an initiating stimulus is removed, the inflammatory response is followed by a resolution phase and return to homeostasis. In the last few years, a significant amount of research has revealed that the resolution of inflammation is an active process driven by pro-resolving molecules which trigger a series of actions in tissues that results in return to homeostasis. I will review the major pro-resolving molecules, the biological responses triggered by these mediators and their potential impact on chronic inflammation. Recent proof of concept studies and the clinical use of steroids during COVID-19 have provided major evidence to show that targeting inflammation may be beneficial during infection. I will review our studies showing that pro-resolving molecules are beneficial in the context of viral and bacterial infection and may serve as valuable adjunct therapies alongside antimicrobial agents in treating infectious diseases.

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Dr. Denise Belsham
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THE AMAZING MOLECULAR DIVERSITY OF HYPOTHALAMIC NEURONS: TACKLING MECHANISMS ONE NEURON AT A TIME. La asombrosa diversidad molecular de las neuronas hipotalámicas: abordando los mecanismos una neurona a la vez.

Resúmen:
Abstract: The hypothalamus maintains whole-body homeostasis by integrating information from circulating hormones, nutrients and signaling molecules. Distinct neuronal subpopulations that express and secrete unique neuropeptides execute the individual functions of the hypothalamus, including, but not limited to, the regulation of energy homeostasis, reproduction, and circadian rhythms. Alterations at the hypothalamic level can lead to a myriad of diseases, such as type 2 diabetes mellitus, obesity, and infertility. The excessive consumption of saturated fatty acids can induce neuroinflammation, endoplasmic reticulum stress, and resistance to peripheral signals, ultimately leading to hyperphagia, obesity, impaired reproductive function, and disturbed circadian rhythms. This lecture focuses on the how the changes in the underlying molecular mechanisms caused by palmitate exposure, the most commonly consumed saturated fatty acid, and the potential involvement of microRNAs, a class of non-coding RNA molecules that regulate gene expression post- transcriptionally, can result in detrimental alterations in protein expression and content. Studying the involvement of microRNAs in hypothalamic function holds immense potential, as these molecular markers are quickly proving to be valuable tools in the diagnosis and treatment of metabolic disease.

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Socio Patrocinante: Rafael Barra Pezo



Dr. Samia Joca.
Department of Biomedicine, Health Faculty, Aarhus University, Denmark.
Editor-in-Chief of Pharmacological Research – Reports, Elsevier.

DEMYSTIFYING PUBLISHING IN PHARMACOLOGY: A CONVERSATION WITH THE EDITOR. desmitificando la publicación en farmacología: una conversación con el editor.

Resúmen:
This talk is designed to guide researchers in enhancing their chances of publication in high quality Pharmacological journals, with a especial focus on the Pharmacological Research family (Elsevier). The participants will benefit from an insider perspective on how to shape their submissions for success, focusing on crucial elements like robust experimental design, clear novelty, and comprehensive in vitro and in vivo validation. Through direct guidance and open discussion, the editor will address common challenges that lead to desk rejections and offer tips on crafting compelling abstracts, choosing effective titles, and responding to reviewerfeedback. Attendees will gain a clearer understanding of the journal's commitment to transparent and author-friendly practices. Additionally, we will discuss the concept of sound-science and its relevance for building a reliable knowledge base and advancing scientific understanding in a systematic and reproducible way. Overall, this session aims to empower participants seeking opportunities to communicate their findings to a broad and highly qualified audience especialized in pharmacological research.

Autores: Dr Sâmia Joca, Editor-in-Chief of Pharmacological Research – Reports (on site). Prof. Emilio Clementi, Editor-in-Chief of Pharmacological Research (online).
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Dr. Jenny L. Fiedler
Departamento de Bioquímica y Biología Molecular, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile, Chile.

SEX SPECIFIC EFFECTS OF STRESS ON HIPPOCAMPUS: NEW OPPORTUNITIES OF PHARMACOLOGICAL INTERVENTIONS. Efectos sexo específicos del estrés en el hipocampo: nuevas oportunidades de intervenciones farmacológicas.

Resúmen:
The research highlights significant sex differences in the prevalence and severity of psychiatric disorders, particularly anxiety and depression, which are more common in women and linked to psychosocial stress. The primary aim is to investigate how these sex differences in rats influence the effects of chronic stress on synaptic function in the hippocampus, a brain region crucial for memory and emotional regulation. The studies have identified key factors that regulate hippocampal function and the varying responses of susceptibility and resilience to stress. By exploring the molecular basis of these differences, the research seeks to uncover potential molecular targets for developing more effective therapies for mood disorders. Preliminary findings indicate that the hippocampal transcriptome exhibits differential responses to stress based on biological sex, with ongoing studies focusing on local transcriptomic changes in somatic and dendritic regions of the dorsal hippocampus in male and female rats.

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GATHERING CHEMISTRY, PHYSICS, BIOLOGY AND PHARMACOLOGY AROUND POLYMERIC BIOMATERIALS FOR WOUND HEALING. La reunión de la química, la física, la biología y la farmacología alrededor de los biomateriales poliméricos para la cicatrización de heridas

Resúmen:
Introduction. Wound healing is a process that might be hindered by sustained inflammation, which may be multifactorial, including underlying chronic diseases and bacterial infection. Tissue engineering, a discipline that gathers chemistry, physics, biology, and pharmacology around polymeric materials searches for solutions to this problem. Aim. The aim of this talk is to show several polymeric tissue engineering devices we have developed and their physicochemical, biological, and pharmacodynamic properties. Methods. The scaffolds were produced by freeze-drying raw materials solutions of chitosan, hyaluronic acid, gelatin, and/or grounded Durvillaea Antarctica with or without crosslinking. The scaffolds were seeded with mesenchymal stem cells, Buddleja globosa Hope extract or Pannexin inhibitors (PNX inhs). The evaluated outcomes included bending resistance, humidity and swelling capacity. In addition, biocompatibility with dermal human fibroblasts through the resarzurin assay, determination of trophic factors secretion by ELISA, antibacterial and antibiofilm activities against pathogenic microorganisms and fibroblasts migration assays were determined. Also, some scaffolds were evaluated for their in vivo performance in ischemic and normal full-thickness wounds. Results. Most of the scaffolds exhibit mechanical resistance, humidity and noticeable water absorption capacity. All of the scaffolds were biocompatible and secrete VEGF. The incorporation of Buddleja globose extract was associated with antibacterial and pro-regenerative activities, both in vitro and in vivo. PNX inhs-constructed devices promoted both in vitro and in vivo healing and showed pain-relieving capacity in an ischemic aged rat wound healing model. Finally, scaffolds made of gelatin/ Durvillaea Antarctica showed promising in vitro wound healing properties. Discussion and Conclusion. Wound healing is an unsolved medical need. We have developed several platforms that might be used for wound heal.

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Dr. Mario Herrera-Marschitz
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A SIGHTSEEING TOUR ALONG A LIFE DEVOTED TO PHARMACOLOGY: HARD WORK, OUTSTANDING TEACHERS, SOME HIGHLIGHTS AND MANY FRIENDS. Un recorrido turístico por una vida dedicada a la farmacología: trabajo duro, profesores destacados, algunos momentos destacados y muchos amigos.

Resúmen:
While staying in Bratislava in1973, I was invited to apply for an academic career leading to a PhD, fulfilled in 1978, letting me to apply for a scholarship at the Karolinska Institutet (KI), Stockholm, received by Urban Ungerstedt, Dept. of Histology, just before he was nominated Professor at the Dept. of Pharmacology, KI, 1978. A lucky, but challenging opportunity, to start again, but now from the bottom in a top-class Lab, pioneering research on the pharmacology of dopamine and other neurotransmitters. The decision implied hard work, to be integrated into a highly demanding scientific and technological environment, also an opportunity to meet outstanding scientists. The hard work was rewarded by finishing a Doctoral Thesis, defended on June 5th, 1986, demonstrating the heterogeneity of basal ganglia regarding dopamine receptors, conveying the neuronal flow through D1 and D2 pathways. The studies led to a functional characterization of monoamine, aminoacid and neuropeptide pathways, a topic for several thesis. Awarded by the Swedish Medical Research Council, I spent a Sabbatical period at the Dept. of Anatomy & Neurobiology, UT, Memphis, USA, learning about organotypic cultures, a model that I transferred to the KI and then to Chile. At the KI, we developed and characterised an experimental model for studying perinatal asphyxia (PA), a relevant clinical issue. This line of research involved a wide international network of collaboration, leading to several thesis, in Europe and in Chile. We are now studying the effect of PA on mitochondrial metabolism, using a Seahorse platform. The studies have revealed long-term mitochondrial impairments induced by PA, affecting oxygen consumption (OCR) and extracellular acidification (ECAR) rate.

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SIMPOSIO / SYMPOSIUM

NEUROPSYCHOPHARMACOLOGY

Symposium Neuropsychopharmacology «Inaugural Symposium of the **Master in Physiology and Pharmacology**: New frontiers in nucleus accumbens pharmacology».
Chair: **Dr. Ramón Sotomayor-Zárate**

MODULATING THE REWARD SYSTEM: VASOPRESSIN'S IMPACT ON AMPHETAMINE ADDICTION IN MALE AND FEMALE RATS VIA THE LATERAL SEPTUM. Modulación del sistema de recompensa: impacto de la vasopresina en la adicción a anfetamina en ratas macho y hembra a través del septum lateral.

Resúmen:
Drug addiction is a chronic brain disease characterized by compulsive use of drugs. Amphetamine (AMPH) is a psychoactive substance commonly used as a recreational drug by young people, and there is a lack of effective medications for the treatment of AMPH or other psychostimulant addiction. Recent studies have shown that the vasopressin (AVP) system plays a significant role in drug addiction, making it an interesting therapeutic target. The lateral septum (LS) is a brain structure implicated in addictive behaviors, regulating the activation of dopamine (DA) neurons in the ventral tegmental area (VTA), therefore modulating the reward system. Extended amygdala vasopressin (AVP) projections to LS are sexually dimorphic and could be responsible for the vulnerability to addiction in a sex-dependent manner. Our work aimed to study the effect of LS AVP system modulation on AMPH-induced behavioral and neurochemical responses in female and male rats. We showed that AVP microinjection in LS reduces the expression of AMPH-induced conditioned place preference (CPP) in male and female rats. However, this behavior is only associated with lower nucleus accumbens (NAc) DA release in male rats. Also, intra-LS AVP administration increases LS GABA release and decreases VTA DA release only in male rats. Interestingly, our data demonstrate that intra-LS AVP reduces AMPH-induced CPP in rats of both sexes; however, at the neurochemical level, we observed sex differences. This research contributes to the knowledge about sex differences in the role of AVP in LS in regulating the reward circuit and addictive-like behaviors.

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IDENTIFICATION OF SPECIFIC RESIDUES WITHIN THE C-TERMINUS OF DOPAMINE TRANSPORTER INVOLVED IN AMPHETAMINE-MEDIATED DOPAMINE EFFLUX. Identificación de residuos específicos dentro del extremo C-terminal del transportador de dopamina involucrados en el eflujo de dopamina mediado por anfetamina.

Resúmen:
The dopamine transporter (DAT) plays a crucial role in the regulation of brain dopamine (DA) homeostasis through the re-uptake of DA back into the presynaptic terminal. In addition to re-uptake, DAT is also able to release DA through a process referred to as DAT-mediated DA efflux. This is the mechanism by which potent and highly addictive psychostimulants, such as amphetamine (AMPH) and its analogues, increase extracellular DA levels in motivational and reward areas of the brain. Recently, we discovered that G protein βγ subunits (Gβγ) binds to the DAT, and that activation of Gβγ results in DAT-mediated efflux – a similar mechanism as AMPH. Previously, we have shown that Gβγ binds directly to a stretch of 15 residues within the intracellular carboxy terminus of DAT (residues 582–596). Additionally, a TAT peptide containing residues 582 to 596 of DAT was able to block the Gβγ-induced DA efflux through DAT. Here, we use a combination of computational biology, mutagenesis, biochemical, and functional assays to identify the amino acid residues within the 582–596 sequence of the DAT carboxy terminus involved in the DAT-Gβγ interaction and Gβγ-induced DA efflux. Our in-silico protein-protein docking analysis predicted the importance of F587 and R588 residues in a network of interactions with residues in Gβγ. In addition, we observed that mutating R588 to alanine residue resulted in a mutant DAT which exhibited attenuated DA efflux induced by Gβγ activation. We demonstrate that R588, and to a lesser extent F5837, located within the carboxy terminus of DAT play a critical role in the DAT-Gβγ physical interaction and promotion of DA efflux. These results identify a potential new pharmacological target for the treatment of neuropsychiatric conditions in which DAT functionality is implicated including ADHD and substance use disorder.

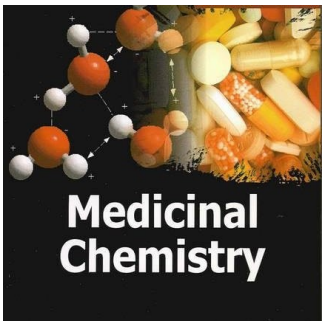
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SEXUAL DIMORPHISMS IN ADDICTION AND SOCIAL BEHAVIOURS OF RATS EXPOSED TO ANTIBIOTICS EARLY IN LIFE. Dimorfismos sexuales en adicción y comportamientos sociales de ratas expuestas a antibióticos en etapas tempranas de la vida.

Resúmen:
Neonatal gut colonization begins as the newborn passes through the birth canal and later comes into contact with the mother (e.g., through breastfeeding). Alterations in the maternal gut microbiota, such as those induced by antibiotic use during the perinatal period, can affect the infant's microbiota. Moreover, it has been shown that changes in the gut microbiota influence human and animal behaviour. In Sprague-Dawley rats, early life exposure to antibiotics (ELEA) has been demonstrated to modify the mesocorticolimbic circuit in a sex-dependent manner, promoting addiction-like behaviours in adult male rats but not in females, while inducing neurochemical alterations in females but not in males. One possible explanation for these differences involves sex hormones. Research has shown that oestrogen in females regulates brain dopamine levels and release, and oestrogen circulation is, in turn, regulated by the gut microbiota, contributing to the observed effects on the brain. This presentation will highlight the effects of ELEA on addiction-like and social behaviours, as well as the role of sex hormones in these outcomes. To explore this further, we performed gonadectomies on the offspring of Sprague-Dawley dams exposed to antibiotics and analysed their social behaviour, revealing only a few sex-specific behavioural traits, which will be discussed in this presentation. Overall, findings from our group suggest that the gut microbiota contributes to some of the behavioural changes observed in dopamine-related neuropsychiatric conditions, opening possibilities for novel pharmacological and/or nutritional interventions

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SIMPOSIO / SYMPOSIUM



Symposium Medicinal Chemistry «Medicinal Chemistry in Chile: From design to experimental pharmacology".
Chair: Dr. Patricio Iturriaga-Vásquez

MEDICINAL CHEMISTRY IN CHILE: FROM DESIGN TO EXPERIMENTAL PHARMACOLOGY. Química Medicinal en Chile: Desde el diseño a la Farmacologia Experimental

Resúmen:
Medicinal chemistry is an interdisciplinary discipline that combines principles of chemistry, biology, and pharmacology for the design, synthesis, and development of new drugs. Its main objective is to create compounds that interact specifically with biological targets, such as proteins or nucleic acids, to treat different pathologies. The drug discovery process begins with identifying a therapeutic target, which may be a protein involved in a pathological process. From there, studies are carried out to design molecules that modulate the activity of this target. This design may involve computational chemistry methods, which allow the interaction between the compound and its target to be predicted. In addition, medicinal chemistry is influenced by advances in areas such as structural biology and biotechnology, which facilitate the understanding of how molecules work at the molecular level. This has allowed the development of more targeted and effective therapies. In short, medicinal chemistry is essential for the creation of new treatments, contributing significantly to the improvement of human health and the treatment of complex diseases. Its interdisciplinary approach makes it a dynamic and constantly evolving field. In this symposium, we present the work of three prominent Chilean Medicinal Chemistry Researchers and their work on the design and synthesis of new substances with biological activity. Dr. Carlos D. Pessoa-Mahana, Benzimidazole: A suitable framework for synthetic cannabinoids, Dr. Christian Espinosa-Bustos, Synthesis of histamine 3 receptor ligands: our six-year journey and Dr. Cristian Salas, Purine as a privileged scaffold for designing new Bcr-Abl inhibitors as potential leukemia drugs.

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BENZIMIDAZOLE: A SUITABLE FRAMEWORK FOR SYNTHETIC CANNABINOIDS. Benzoimidazol: Un heterociclo dúctil para la construcción de moduladorers cannabinoides.

Resúmen:
The endocannabinoid system (ECS) constitutes a broad-spectrum modulator of homeostasis in mammals, providing therapeutic opportunities for several pathologies. Its two main receptors, cannabinoid type 1 (CB1) and type 2 (CB2) receptors, mediate anti-inflammatory responses and their different patterns of expression make the development of selective ligands therapeutically attractive. The benzimidazole ring can be considered a privileged scaffold in drug discovery and has demonstrated its versatility in the development of molecules with varied pharmacologic properties. Here, we present a summary of the main results obtained in our laboratory where we focuse on the synthesis of benzimidazole derivatives and their application as suitable chemical modulators of the ECS. Our initial efforts focused on the study of the benzimidazole system as a useful framework to develop novel high-affinity CB1R synthetic cannabinoids. We then extended our investigation to the CB2R and worked to obtain benzimidazole derivatives with selective CB2R agonist activity. Additionally, we have explored the endocannabinoid degrading enzyme FAAH target through the synthesis and 3D-QSAR studies of FAAH inhibitors.
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Socio Patrocinante: Patricio Iturriaga-Vásquez

SYNTHESIS OF HISTAMINE 3 RECEPTOR LIGANDS: OUR SIX-YEAR JOURNEY. Síntesis de ligandos del receptor de histamina 3: nuestro recorrido en estos 6 años

Resúmen:
Histamine is released predominantly from the tuberomammillary nucleus of the hypothalamus in the central nervous system (CNS) and acts as a neurotransmitter. H3 receptors as presynaptic autoreceptors on histaminergic nerve terminals, they are unique members of the histaminergic receptor family (H1-H4) and show higher densities in the CNS in comparison to peripheral tissues (e.g, basal ganglia, globus pallidus, cortex and hippocampus) and are involved in the modulation of a wide range of physiological effects (e.g. neurotransmitter release, regulation of cognitive processes, attention and/or arousal, appetite, food and water intake and many hypothalamic functions). As H3 receptors are negatively coupled to adenylyl cyclase via Gi/o proteins, their activation results in the inhibition of cAMP production, leading to a wide range of signalling events. Due to their constitutively active nature in vitro and in vivo, H3 receptors tonicly inhibit histaminergic (and possibly other) neuronal activity. Therefore, antagonism/inverse agonism of the H3 receptor increases histaminergic neuronal activity and CNS histamine levels, which in turn stimulate neurotransmitter release and contribute to the overall physiological effects of H3 blockade. The anatomical localisation and favourable properties of H3 receptors make them a viable target for CNS-related drug discovery. In view of the above, our research group has focused in recent years on the design, synthesis and evaluation of heterocyclic compounds as H3R ligands. Therefore, in this symposium we will show our main results in terms of affinity for this receptor as well as results of the search for multi-target ligands directed against H3R and other therapeutic targets involved in neurodegenerative diseases.

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PURINE AS A PRIVILEGED SCAFFOLD FOR DESIGNING NEW BCR-ABL INHIBITORS AS POTENTIAL LEUKEMIA DRUGS. Purina un privilegde scaffold para el diseño de nuevos inhibidores de Bcr-Abl como potenciales fármacos contra la leucemia

Resúmen:
Bcr-Abl is an oncoprotein with aberrant tyrosine kinase activity involved in the progression of chronic myeloid leukemia (CML) and has been targeted by inhibitors such as imatinib and nilotinib. Despite their efficacy in the treatment of CML, a mechanism of resistance to these drugs associated with mutations in the kinase region has emerged. Since the most potent inhibitors of Bcr-Abl are those that bind directly to the ATP-binding site, the purine core has been chosen as a privileged scaffold in the development of new inhibitors of this kinase. In this address, we have been working on the design and synthesis of new 2,6,9-trisubstituted purine derivatives as Bcr-Abl inhibitors. From our most promising results, we identified several purines that showed enhanced inhibition with IC50 values of 4.6 – 14 nM and were more potent than imatinib and nilotinib (IC50 = 327 and 47 nM). Structure-activity relationships and in silico studies were able to explain the differences in potency and selectivity between some kinases by our compounds. Likewise, our Bcr-Abl inhibitors exhibited low micromolar cytotoxicity in CML-cancer cell lines (KCl22, K562, KBM5, and BV173) and decreased the phosphorylation of downstream proteins in the signaling pathways of Bcr-Abl in K562 cells at lower concentrations than imatinib. In addition, some purine derivatives have shown antiproliferative effects in a panel of subclones of KCL22 cells expressing different mutations in Bcr-Abl. Finally, one compound is being considered for in vivo testing. Therefore, we demonstrated that certain purine derivatives are promising compounds for the development of new drugs for CML treatment.

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SIMPOSIO / SYMPOSIUM

Symposium Argentina-Brazil-Chile (ABC) Pharmacology «The ABC of South American Pharmacology: Addiction Research".
Chair: Dr. Mario Rivera-Meza

COCAINE INDUCED HIPPOCAMPAL NEUROADAPTATIONS: UNRAVELLING THE ROLE OF PHOSPHODESTERASE 5 INHIBITORS IN THE VULNERABILITY TO SUBSTANCE USE DISORDERS. Cambios neuroadaptativos inducidos por cocaina en el hipocampo: develando la influencia de los inhibidores de la fosfodiesterasa 5 en la vulnerabilidad a los trastornos por consumo de sustancias.

Resúmen:
Behavioral sensitization to the hyperlocomotion effect of psychostimulants is a useful model for studying addiction, the most severe form of substance-use-disorders-SUD. The hippocampus-HP and prefrontal cortex-mPFC participate in the neuropathological mechanisms underlying addiction. Nitric oxide-NO is involved in neuronal excitability, synaptic plasticity, and sensitization to psychostimulants. Phosphodiesterase-5 inhibitors-PDE5i potentiate NO-activated signaling pathways. Our work aims to characterize the role of NO in development and expression of cocaine-COC sensitization, the brain areas involved and the effect of sildenafil-SILD on sensitization. Behavioral procedures were performed in male Wistar rats to observe COC sensitization in presence of inhibitors or activators of the NOS1/NO/sGC/cGMP signaling pathway. Electrophysiological tools were used to determine HP synaptic plasticity and mPFC-neuronal activity ex-vivo. The effects of SILD upon the dopamine-DA system were determined by amperometry ex-vivo and of-silico methods. Systemic administration of NO signaling pathway inhibitors reduced the proportion of sensitized rats and the increased neuronal activity in HP and mPFC. Conversely, its activation by sildenafil-SILD increased the proportion of sensitized animals and HP synaptic plasticity. Inhibition of NO signaling within the HP, but not mPFC, reversed COC sensitization. On the other hand, reduced function of DAT was observed in HP and nucleus accumbens of SILD-treated animals. Furthermore, molecular docking, dynamics and free-energy of binding analyses showed that SILD binds to the DAT allosteric regulatory site. We can conclude that upregulation of NO signaling pathway in HP may initiate or exacerbate SUD in humans. Considering the widespread prescription and misuse of PDE5i, we demonstrated here that they may increase susceptibility to drug abuse, describing a novel mechanism of action for SILD via direct action on the DA system.

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Socio Patrocinante: Mario Rivera-Meza

PREVENTING DEFICITS FROM PRENATAL ALCOHOL EXPOSURE THROUGH ENVIRONMENTAL ENRICHMENT DURING PREGNANCY: THE POTENTIAL ROLE OF OXYTOCINERGIC MECHANISMS. Prevención de déficits por exposición prenatal al alcohol mediante enriquecimiento ambiental durante el embarazo: el potencial rol de los mecanismos oxitocinérgicos

Resúmen:
Fetal Alcohol Spectrum Disorders (FASD) encompass a range of conditions arising from prenatal alcohol exposure, impacting physical, cognitive, and behavioral development. The severity of FASD varies with the timing, frequency, and amount of alcohol exposure, as well as environmental factors like stress. Early diagnosis and intervention are crucial for improving outcomes. Prenatal alcohol exposure disrupts oxytocin (OT) system development, leading to FASD-related deficits in social interaction, anxiety, and depression. Environmental enrichment (EE) offers diverse stimuli that enhance social, cognitive, and physical activity. Previous findings indicate that EE modulates the oxytocinergic system by increasing OT levels and mRNA expression in the hypothalamus and reducing OT receptor binding and phospholipase C (PLC) activity in specific brain regions. In this study, pregnant mice exposed to ethanol were housed in EE or standard conditions (SC). Ethanol exposure impaired maternal behaviors in SC, while EE mitigated these deficits, with increased OT-immunoreactive cells in the paraventricular nucleus (PVN) and elevated OT gene expression. Offspring from ethanol-exposed dams in SC showed delayed physical and reflex development, reduced social interaction, and heightened anxiety, regardless of sex. Female offspring displayed increased ethanol consumption and reduced maternal aggression, while males showed increased aggression compared to their EE-exposed counterparts. Gestational EE exposure attenuated these ethanol-induced impairments.These findings underscore the complex interplay between environmental factors and prenatal ethanol exposure, highlighting EE's potential to counteract the detrimental effects of alcohol during gestation. Additionally, they identify the OT system as central in FASD pathophysiology, suggesting OT modulation as a promising therapeutic approach.

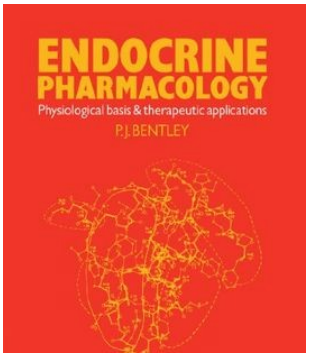
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HCN ION CHANNELS AS A POTENTIAL PHARMACOLOGICAL TARGET TO REDUCE THE ADDICTIVE EFFECTS OF ETHANOL. Canales iónicos HCN como un potencial blanco farmacológico para reducir los efectos adictivos del etanol

Resúmen:
A key target for the addictive properties of ethanol is the dopaminergic circuitry within the ventral tegmental area (VTA). Ethanol enhances the activity of VTA dopamine neurons, leading to increased dopamine release in the nucleus accumbens (NAc). The excitability of these neurons is primarily regulated by hyperpolarization-activated cyclic nucleotide-gated (HCN) ionic channels. In vitro studies indicate that ethanol can activate HCN channels, and blocking these channels inhibits ethanol's effects. Among the four HCN channel genes (HCN1-4), HCN2 is the most prevalent in the VTA. Our research demonstrated that overexpressing HCN2 in the VTA significantly increases ethanol consumption and amplifies ethanol-induced locomotor activity, dopamine release, and place preference compared to control rats. Conversely, reducing HCN2 expression in the VTA resulted in a substantial decrease in voluntary ethanol intake. Recent experiments showed that administering various HCN blockers—ZD7288 (non-selective), MEL55A (moderately selective for HCN2), and 4e (highly selective for HCN2)—to rats led to a significant dose-dependent reduction in ethanol-induced dopamine release in the NAc, with 4e exhibiting the highest potency. These neurochemical changes correlated with a notable decline in voluntary ethanol consumption among the animals. These findings suggest that HCN2 channels may serve as a promising molecular target for addressing the rewarding effects of ethanol.

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SIMPOSIO / SYMPOSIUM



Symposium Endocrine Pharmacology and Metabolism «From Obesity to Diabetes: Pathophysiological Mechanisms and Therapeutic Options».
Chair: Dr. Rafael Barra

NUTRITIONAL PROGRAMMING OF HYPERTENSION. CENTRAL ROLE OF THE HYPOTHALAMIC PVN. Programacion nutricional de la hipertension. Rol central del nucleo paraventricular del hipotalamo.

Resúmen:
The literature supports that undernourishment is one of the leading nutritional issues remaining in the world. Prenatal exposition to undernourishment has permanent and severe effects on the adult health of the offspring. In this context, chronic hypertension has been described as one of the most relevant conditions manifested. Our research groups have characterized a higher neuronal activity in the Paraventricular Nucleus of the hypothalamus (PVN) through electrophysiological recordings and using pharmacological manipulations to blockade and activate excitatory and inhibitory control on the neuronal activity of the PVN. Mainly, the noradrenergic connections from the Locus Coeruleus (LC) are excitatory and reciprocal with the PVN, and the connections from the Subiculum ventral (vSUB) are inhibitory for the neuronal activity of the PVN. We have demonstrated a chronic increase of the Noradrenergic input from the LC to the PVN and its subsequent effect on blood pressure control. Additionally, we found coherent changes in the expression levels of glucocorticoid receptors in the PVN. Our research allows us to identify the status of neuronal excitatory and inhibitory controls over the PVN and correlate them with cardiovascular parameters, like blood pressure and Heart frequency. The research associated with this prenatal nutritional impairment model will allow the development of better pharmacological and therapeutic strategies for diminishing the harmful effects of prenatal nutritional programming and help to unravel the pathognomonic of persistent hypertension in prenatal malnutrition.

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Socio Patrocinante: Dr. Rafael Barra Pezo

STUDY OF NEW PHARMACOLOGICAL TARGETS IN THE CONTEXT OF CARDIAC FIBROSIS INDUCED BY DIABETES AND OBESITY. Estudio de nuevos blancos farmacológicos en el contexto de la fibrosis cardiaca inducida por diabetes y obesidad

Resúmen:
Cardiac fibrosis is a pathological condition characterized by excessive extracellular matrix (ECM) that slowly replaces functional tissue, decreasing the heart's contractile, relaxation, and conduction capacity, leading to cardiac dysfunction. Many diseases progress to cardiac fibrosis, from hypertension to myocardial infarction. Lately, interest has been focused on metabolic diseases, such as diabetes, dyslipidemia, and obesity, as essential promoters of cardiac fibrosis and myocardial dysfunction. However, the cellular and molecular targets for cardiac fibrosis promoted by these last pathologies are not yet fully known. Cardiac fibroblasts (CF) are mesenchymal cells responsible for synthesizing, secretion, and degradation of ECM components, such as collagen I and III. Under normal conditions, CF have minimal basal activity, while pathological stimuli such as high glucose (HG) or hypoxia increase their ECM secretory activity, leading to cardiac fibrosis. Fibrotic and inflammatory activation of CFs induced by metabolic stimuli has not been extensively studied. Our results have determined that members of the FoxO family are critical for HG-induced CF activation, where FoxO1 promotes fibrosis and inflammation, whereas FoxO3a demonstrates antifibrotic effects. On the other hand, SGK1, an aldosterone-activated kinase involved in renal and cardiac inflammatory pathologies, is activated in CFs, inducing fibrosis and inflammation of CF by inhibiting FoxO3a, and its gene targets SOD2 and catalase. Finally, through an in vitro obesity model, we demonstrated that conditioned medium obtained from adipocytes induces fibrosis and CF inflammation of CFs by activating SGK1 and inhibiting FoxO3a. Similarly, similar results were obtained in an in vivo obesity model. The heart of obese animals presents a higher expression of fibrotic markers and SGK1 than control mice. In comparison, a lower expression of FoxO3a was observed. Our results point to SGK1 and FoxO3a as novel antifibrotic.

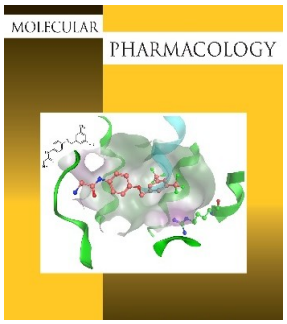
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ROLE OF THE NLRP3 INFLAMMASOME AND CHOLESTEROL IN SKELETAL MUSCLE DURING OBESITY-INDUCED INSULIN RESISTANCE. Papel del inflamasoma NLRP3 y del colesterol en el músculo esquelético durante la resistencia a la insulina inducida por la obesidad.

Resúmen:
Chronic inflammation is a critical factor in the development of insulin resistance (IR), a key precursor to type 2 diabetes mellitus. The NLRP3 inflammasome, which regulates the release of pro-inflammatory myokines IL-1β and IL-18, has been implicated in the impairment of insulin sensitivity associated with IR. Skeletal muscle is the primary site for insulin-stimulated glucose uptake via GLUT4, a process predominantly occurring in transverse tubules (TT). However, in the context of IR, the translocation of GLUT4 to TT is disrupted. Insulin-resistant animals exhibit elevated cholesterol levels and reduced expression of the ATP-binding cassette transporter A1 (ABCA1) in TT. Nevertheless, the specific role of cholesterol accumulation in activating the NLRP3 inflammasome - and its contribution to low-grade inflammation and impaired glucose homeostasis during the progression of IR- remains poorly understood. We investigated the effects of cholesterol dysregulation on low-grade inflammation and the development of IR in skeletal muscle. Compared to chow-fed mice (NCD-fed), high-fat diet-fed mice (HFD-fed) displayed significantly reduced ABCA1 expression and increased cholesterol content in flexor digitorum brevis (FDB) muscle. Elevated levels of NLRP3, ASC, caspase-1, and IL-1β were observed in homogenized FDB muscle from HFD-fed mice. Importantly, pre-incubation with T0901317, a selective liver X receptor (LXR) agonist, enhanced ABCA1 expression, reduced membrane cholesterol, and improved insulin-mediated glucose uptake. This treatment also decreased NLRP3 inflammasome components in muscle fibers from HFD-fed mice. In conclusion, these findings indicate that targeting cholesterol accumulation and NLRP3 inflammasome activation may provide promising therapeutic strategies for mitigating insulin resistance and type 2 diabetes mellitus.

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Socio Patrocinante: Dr. Rafael Barra Pezo

SIMPOSIO / SYMPOSIUM



Symposium Molecular Pharmacology «The problem of the 3 elements: receptor, ligand and AI. Pharmacological approaches in purinergic transmission». **Chair: Dr. Jorge Fuentealba**

ROLE OF THE P2X2 RECEPTOR IN THE CELLULAR MECHANISMS OF NEUROGENERATION, THE EXAMPLE OF ALZHEIMER'S DISEASE. Papel del RECEPTOR P2X2 en los mecanismos celulares de neurogeneración, el ejemplo de la Enfermedad de Alzheimer.

Resúmen:
One of the main toxic agents in Alzheimer's Disease (AD) are the soluble oligomers of the Aβ peptide (AβOs). In our laboratory, we have demonstrated that AβOs induce an intracellular Ca2+ increase, ATP leakage, changing the modulation of ionotropic purinergic receptors (P2XR). We have also shown that AβOs induce an increase the expression of P2X2, further reinforcing the Ca2+ overload in the cytoplasm that modulate several proteins and pathways, including the AMP-activated protein kinase (AMPK), CALP-1, TG2, which plays diverse roles in protein, energy, and mitochondrial metabolism. In our hands, We have shown that in AD, overexpression of the P2X2 receptor generates the activation of a vicious circle that enhances the generation of the amyloid beta peptide, alters mitochondrial functionality and dynamics, altering its interaction with the ER and promoting an alteration of calcium homeostasis that results in synaptic failure in the excitatory terminals. The main findings of this project are corroborated in human samples, providing the first confirmed evidence of the role of this receptor in the disease, which opens a new space for pharmacological development for AD.

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PURINERGIC AND GLUTAMATERGIC CROSSTLAK IN THE NEURAL TUVE FORMATION. DECIPHERING THE ROLE OF ANTISEIZURE MEDICATION (ASM). Interacción purinérgica y glutamatérgica en la formación del tubo neural. Descifrando el papel de los medicamentos anticonvulsivos.

Resúmen:
Neurulation is crucial for the central nervous system (CNS) formation, which initiates with the folding and fusion of the neural plate generating the Neural Tube and subsequently the brain and spinal cord. Paracrine signals like FGF participate in Neurulation wherein others signals such us purinergic (ATP) and glutamate has been recently described, which are required for the cellular responses like migration and proliferation necessary for the process. Environmental factors like anti-seizure medications (ASM) alter Neurulation promoting Neural Tube Defects (NTDs) and others latter alterations of neural function. Our group investigate the pharmacological modification of purinergic and glutamate signaling analyzing their synthesis, release and P2X4/NMDAR activity during Xenopus laevis Neurulation, evaluating the phenotypic and the cellular and molecular consequences. We found the presence and functionality of glutamate synthesis enzyme, GLS1 and even though expression levels remains constant, its catalytic activity increases significantly (~66%) between early and middle to late stages of Neurulation. We increased the appearance of NTDs reducing GLS activity (~36%) using the competitive inhibitor 6-diazo-5-oxo-L-norleucine. Related to purinergic signaling, we demonstrate the expression and functionality of connexin hemichannels (HCs), including Cx46, which are associated with the release of ATP. Furthermore, applications of FGF2 and/or changes in intracellular redox potentials (DTT), well known HCs-Cxs modulators, transiently regulated the ATP release in our model. Importantly, the blockade of HCs-Cxs by carbenoxolone (CBX) and enoxolone (ENX) reduced ATP release and increases NTDs. Additionally, the potentiation of P2X4 with ivermectin during Neurulation generates NTD with a significantly reduced motor behavior associated with a neuromuscular junction alteration. All together could contribute to a comprehensive view of how ASM affects the neural development.

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MODELLING THE ACTIVE SITE OF PURINERGIC RECEPTORS. Modelando el sitio activo de receptores purinérgicos

Resúmen:
Purinergic P2X receptors (P2XRs) are a family of ligand-gated ion channels (LGICs) composed of seven different subunits that can assemble into homo- or heterotrimeric channels activated by ATP. Each subunit consists of an extracellular loop, two transmembrane domains (TM1-2), and intracellular N- and C-termini. Three ATP-binding sites are located at the interfaces between subunits; however, two ATP molecules are sufficient to activate the channel and allow the passage of cations. P2XRs have been implicated in neurological disorders, including Alzheimer's disease, where overexpression of P2X2, P2X4, and P2X7, along with their activation by ATP released into the extracellular medium, have been reported. Despite the therapeutic potential, efforts to develop modulators targeting P2XRs have yielded limited success, with only a few receptor structures and specific modulators described to date. The structures of human P2X2 (hP2X2) and P2X4 (hP2X4) receptors are not yet available, complicating the design of more selective and effective modulators. To address this, we generated models of both receptors through comparative modeling and performed structure-based virtual screening to identify potential modulators. For protein-ligand docking, interaction grids were created at the ATP-binding sites, and ligand were obtained from the Molport database. Resulting complexes were analyzed and ranked by docking scores and delta Gbind. Promising candidates with values comparable to ATP were selected from various chemical families for in vitro testing. Electrophysiological evaluations revealed active molecules capable of modulating the P2X2 and P2X4 receptors expressed in HEK293 cells. In conclusion, our in-silico approach demonstrates a valuable strategy for characterizing interactions between P2X receptors and ATP and for screening novel, selective compounds with potential modulatory activity.

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DEVELOPING SELECTIVE DRUG BY NANO IMPRESION – NANOMIPS – THE NEXT GENERATION. Desarrollo de fármacos selectivos mediante nanoimpresión – NanoMIPs – la próxima generación

Resúmen:
The advancement of nanotechnology has opened the way for innovative approaches in drug development, particularly through the use of nano-imprinted materials known as nanoMIPs (Nano Molecularly Imprinted Polymers). This study highlights the potential of nanoMIPs as the next generation of selective drugs, emphasizing their ability to replicate biological recognition processes with high specificity and efficiency. By employing nano-imprinting techniques, we can create customized molecular recognition sites that enhance drug targeting and minimize side effects. It is also a review on the synthesis, characterization, and application of nanoMIPs in the pharmaceutical field, highlighting their advantages over traditional drug delivery systems. The findings suggest that nanoMIPs can significantly improve diagnosis and therapeutic outcomes by enabling precise drug interactions at the molecular level, ultimately contributing to the development of more effective and safer therapeutic agents. Future directions include exploring the scalability of this technology and its integration into clinical practices for personalized medicine.

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SIMPOSIO / SYMPOSIUM



Symposium «Women in Pharmacology» **Chair: Dr. Mabel Catalán**

CARDIAC FUNCTION AND REMODELING DURING SIMULATED MICROGRAVITY: INVESTIGATING THE HIPPO PATHWAY AND THERAPEUTIC POTENTIAL OF VERTEPORFIN. Función y remodelamiento cardiaco durante la microgravedad simulada: Investigando la vía Hippo y el potencial terapéutico de la Verteporfina

Resúmen:

Changes in hydrostatic pressure due to prolonged bed rest and microgravity conditions, such as those experienced during spaceflight, have profound effects on cardiovascular function and structure. These effects include reduced cardiac workload, myocardial atrophy, and impaired contractile function, ultimately leading to significant cardiac remodeling. Despite advances in understanding these phenomena, the molecular mechanisms driving these changes remain unclear. The Hippo signaling pathway, a key regulator of organ size, has recently emerged as a critical player in cardiac remodeling. Under physiological conditions, the Hippo pathway helps maintain cardiac homeostasis and normal cardiac function. However, its role in response to microgravity-induced cardiac stress remains unexplored. We are studying the impact of simulated microgravity and prolonged bed rest on cardiac function and remodeling, with a specific focus on changes in cardiac T-tubules and the Hippo pathway. Using a preclinical model of hindlimb suspension unloading (HSU), we evaluate the molecular and structural changes in the myocardium. Additionally, we assess the therapeutic potential of Verteporfin, a drug known to inhibit the transcriptional co-activators YAP/TAZ, which are downstream effectors of the Hippo pathway. By targeting YAP/TAZ, we aim to mitigate the deleterious effects of Hippo pathway dysregulation in microgravity-induced cardiac remodeling. Our findings will contribute to a better understanding of the molecular pathways of cardiac remodeling during spaceflight and prolonged physical inactivity. Furthermore, this study explores the potential of Verteporfin as a therapeutic intervention, which may lead to the development of new strategies to protect cardiovascular health in astronauts and bedridden patients.

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MIRO1: AT THE HEART OF EMERGING MITOCHONDRIAL PHARMACOLOGICAL TARGETS. Miro1: en el corazón de los nuevos blancos farmacológicos dirigidos a la mitocondria.

Resúmen:

Mitochondrial dynamics, including fission and fusion processes, are vital for maintaining cellular homeostasis, particularly in high-energy-demanding cells like cardiomyocytes. These dynamic processes allow mitochondria to adapt to changing energy needs, repair damaged regions, and remove dysfunctional mitochondria through mitophagy. In the heart, where continuous energy production is essential for contractile function, disruptions in mitochondrial dynamics can lead to severe cardiac dysfunction. Recent studies have highlighted the mitochondrial Rho GTPase 1 (Miro1) as a critical regulator of mitochondrial movement and positioning within cells, particularly in neurons. However, emerging evidence indicates that Miro1 also plays a significant role in cardiac pathophysiology, especially under conditions of stress and injury. This presentation will explore the functions of Miro1 in cardiomyocytes, focusing on its involvement in cardiomyocyte hypertrophy and its contributions to mitochondrial dynamics and localization. Our research demonstrates that Miro1 expression is upregulated in hypertrophic cardiomyocytes, suggesting a potential role in the pathological remodeling of the heart. Beyond its established influence on mitochondrial fission, Miro1 appears to affect the spatial distribution of mitochondria within cardiomyocytes, which is crucial for efficient energy distribution. By investigating Miro1's dual role in mitochondrial dynamics and positioning, we aim to uncover novel pathophysiological mechanisms underlying cardiac diseases, ultimately paving the way for innovative therapeutic strategies targeting Miro1 and mitochondrial function.

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MICROFLUIDICS AS A NANOTECHNOLOGICAL TOOL FOR EARLY CANCER DIAGNOSIS. La microfluídica como herramienta nanotecnológica para el diagnóstico temprano del cáncer.

Resúmen:
Tumor-derived extracellular vesicles (EVs) are emerging as crucial biomarkers for cancer diagnosis, prognosis, and therapeutic monitoring. These nanoscale particles, secreted by cancer cells, facilitate cell-to-cell communication, making their detection in body fluids a promising tool for non-invasive diagnostics. However, capturing and analyzing EVs, especially in early disease stages, is challenging due to their small size and low abundance. Traditional methods like ultracentrifugation and Western blotting are labor-intensive, time-consuming, and require large sample volumes, often yielding low sensitivity. To address these issues, we developed a 3D self-assembled nanostructured SiO_2 microfluidic chip, designed to enhance EV capture efficiency. This chip was functionalized with antibodies targeting exosomal markers CD63 and CD81 and tested using conditioned media from breast cancer cell lines (MCF7, MDA-MB-231, and MCF10A). Results showed that the 3D SiO_2 nanostructured chip successfully captured EVs from the conditioned media with high sensitivity and specificity. Fluorescence microscopy revealed a significant increase in the detection of EVs expressing CD63 and CD81 compared to conventional methods. The chip demonstrated a detection limit capable of identifying even low-abundance EVs, which is critical for early cancer diagnosis. Additionally, the platform required minimal sample volumes and allowed for rapid analysis, making it suitable for high-throughput applications. These findings highlight the platform's potential as a liquid biopsy tool for cancer detection, providing a faster, more efficient, and non-invasive alternative to traditional biopsy methods. This technology could significantly improve early cancer detection and patient outcomes by enabling real-time monitoring of tumor-derived EVs.

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Socio Patrocinante: Dra. Mabel Catalán

OBESITY AND CANCER: THE LINK THROUGH THE MITOCHONDRIAL MODULATION. Obesidad y cáncer: El link a través de la modulación mitocondrial

Resúmen:
Chronic conditions such as cardiovascular diseases, obesity, and cancer are prevalent in the world. In this context, pharmacological research has progressively focused on providing novel alternatives for managing these diseases, with the awareness of solving these health problems with increasing effectiveness and safety. From the pharmacology point of view, cancer and obesity have been struggling with novel and effective alternatives to be included as part of the treatment. Both situations involve the search for novel therapeutic targets. In this context, the mitochondrion emerges as an attractive target from the pharmacological perspective, given the distinctive characteristics that allow different pharmacophores to be directed into this organelle. Additionally, both obesity and cancer have a similar background of mitochondrial dysfunction; thus, restoring function or taking advantage of this abnormality could result in a novel therapeutic strategy for the treatment of these pathologies. In this sense, we have studied different lipophilic cations derived from polyphenols that have been shown as antineoplastic agents in many cancer cellular models without evident toxicity in normal cells and tissues. Additionally, these new drugs could improve the functioning of adipocytes in vitro and in vivo models, making them metabolically active. Different concentrations of these new lipophilic cations can modulate cellular effects. In conclusion, our background in designing, synthesizing, and evaluating novel mitochondrial agents could offer an alternative as a therapeutic for mitochondrial dysfunction in prevalent diseases.

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SIMPOSIO / SYMPOSIUM



Inaugural Symposium of the Master in Physiology and Pharmacology: «Empowering Science by Women in Valparaíso» **Chair: Dr. Marcela Julio-Pieper**

ROLE OF DYNAMINS IN CENTRAL EXCITATORY SYNAPTIC TRANSMISSION: A POTENTIAL NEW THERAPEUTIC TARGET IN THE SYNAPTOPATHY OF ALZHEIMER´S DISEASE. Rol de las dinaminas en la transmision sinaptica excitatoria central: un potencial nuevo blanco terapeutico en la sinaptopatia de la Enfermedad de Alzheimer.

Resúmen:

Dynamins are large GTP-ases implicated in membrane and cytoskeleton remodeling in different cell types. They are expressed in the Central Nervous System (CNS), playing key functions at pre and post-synapses. At presynapses dynamins modulate the endocytic recycling of synaptic vesicles; at post-synapses dynamins regulate the insertion and turnover of neurotransmitter receptors. We recently demonstrated that dynamin-2, the only ubiquitous dynamin´s isoform, is critical for neuronal morphology, synaptic transmission and plasticity. In neurons that express pathogenic mutations in dynamin-2 that impair its catalytic activity, dendritic arborization and formation of dendritic spines are significantly impaired, leading to synaptic and cognitive defects in mice. These results suggest that dynamin´s dysfunction at the CNS might lead to neurological disorders. It has been demonstrated that dynamin´s expression is reduced in postmortem brains of Alzheimer´s disease (AD) patients, suggesting that dynamins are involved in the pathogenesis of AD, the most prevalent for of dementia in elderly. Our in-progress work has been aimed to evaluate the impact of the pharmacological and genetic modulation of dynamins on the neuronal morphology, and functional synapses in neurons from APP/PS1 and 3xTg mice, murine models of AD. Additionally, we have also evaluated the impact of the pharmacological modulation of dynamin´s activity on cognitive functions in adult APP/PS1, 3xTg and wildtype (WT) mice. Our data suggest that promoting dynamin´s GTPase activity enhances dendritic arborization and dendritic spine formation in hippocampal neurons, preventing the loss of spatial and recognition memory in mouse models of AD. Our work contributes to positioning dynamins as new actors, and potential therapeutic target in Alzheimer´s disease.

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IMPACT OF DOPAMINE D2 RECEPTORS AND DOPAMINE LEVELS IN COMPULSIVE BEHAVIOR. Impacto del receptor D2 y los niveles de dopamina sobre la conducta compulsiva

Resúmen:
The repeated administration of Quinpirole (QNP), a dopamine D2 receptor (D2R) agonist, induces locomotor sensitization, a sustained increase in locomotor activity. Although QNP-induced locomotor sensitization is very robust in rats, this effect is poorly observed in mice. The mesolimbic dopamine system, composed of ventral tegmental (VTA) dopamine neurons projecting to the Nucleus Accumbens (NAc), underlies the induction of locomotor sensitization. QNP activates D2R in medium spiny and dopamine neurons, promoting locomotion and decreasing dopamine release. Previously, we found that rats showing QNP locomotor sensitization have decreased basal dopamine release in the NAc. We hypothesize that the chronic reduction of extracellular dopamine levels facilitates QNP-induced locomotor sensitization. To induce a chronic decrease of NAc dopamine levels independently of D2R activation, we expressed the inhibitory DREADD, hM4Di, selectively in the mesolimbic dopamine pathway in mice and repeatedly administered its agonist C-21. In these mice, we found increased sensitivity of D2R inhibition of DA release measured by fast-scan cyclic voltammetry, suggesting sensitized D2R presynaptic function. Then, we assessed whether repeated QNP administration affects locomotion in our hands. Interestingly, mice repeatedly treated with QNP did not develop locomotor sensitization. However, QNP administration in mice with previous chemogenetic inhibition of mesolimbic DA activity induced a sustained and enhanced locomotion, suggesting that chronic reduction of tonic dopamine in the NAc facilitates QNP-induced locomotor sensitization. We are assessing whether this chronic inhibition impacts D2R levels in the VTA and NAc. We intend to contribute to understanding the mechanisms that underlie compulsivity by studying the involvement of D2R in dopamine neurons.

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RESOLUTION OF VASCULAR INFLAMMATION: EXPLORING THE IMPACT OF SPECIALIZED PRO-RESOLVING MEDIATORS. resolucion de la inflamación vascular: explorando el impacto de los mediadores especializados proresolutorios

Resúmen:
Cardiovascular diseases are the leading cause of death in Chile and worldwide, placing a significant burden on healthcare systems. These conditions, such as hypertension and atherosclerosis, are characterized by vascular deterioration driven by high levels of angiotensin II, vasoconstriction, and chronic inflammation, which lead to the formation of atherosclerotic plaques. Conventional therapies focus on reducing cholesterol and the effects of angiotensin but do not address chronic inflammation. Endogenous pro-resolving mediators of inflammation and chronic damage, such as resolvins, maresins, lipoxins and protectins, have been identified as being reduced in patients with cardiovascular damage, suggesting their therapeutic potential. However, it remains unclear whether their exogenous administration in combination or sequence is more effective and whether they involve the NF-κB and NLRP3 pathways, which are key in chronic inflammation. This study evaluated the effects of RvE1, RvD2, and MaR1, administered alone, in sequence, or in combination, on inflammation and vascular damage using in vitro models of multicellular spheroids and in vivo models of vascular damage induced by angiotensin II. RvE1 and its combination significantly reduced neutrophil adhesion and pro-inflammatory cytokines, while RvD2 decreased the proliferation of muscle cells. A reduction in the expression of p65 was observed, but its localization in the nucleus was minimal. All conditions, except for RvD2, reduced the expression of NLRP3, correlating with decreased levels of IL-1β and IL-18. In vivo results indicated that the mediators decreased arterial hypertrophy, edema, and leukocyte infiltration, as well as serum levels of MCP-1, IL-1β, IL-6, VEGF, and TGF-β. These findings highlight the potential of pro-resolving mediators to resolve inflammation and promote vascular repair, suggesting their use in chronic inflammatory diseases.

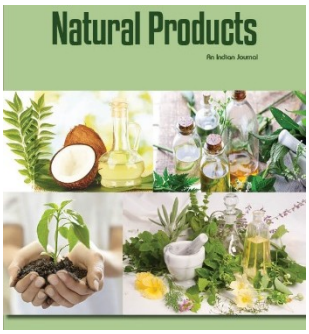
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THE GUT NEUROCHEMICAL CODE AND PLASTICITY AS INSIGHTFUL THERAPEUTIC TARGETS FOR GASTROINTESTINAL DISORDERS. El código neuroquímico y la plasticidad entérica como blancos terapéuticos de interés para desórdenes gastrointestinales.

Resúmen:
Current gastrointestinal drugs are directed against a variety of cell types and molecular targets, but traditionally, they modify gastrointestinal motility and liquid absorption and many of them act on effector cells. More recently, the possibility of targeting regulatory –rather than effector– cells within the gut has received increasing attention. This is how enteric neurons, glia, immune cells and microbial communities have been shown to provide a wide array of molecular targets that are worth investigating. The gut submucosal plexus is a notoriously plastic tissue, located at the interphase of mucosal and muscular layers, with access to signals from the luminal compartment, the lymphatic vasculature and the bloodstream. The type of signalling molecules and receptors expressed by neurons in the submucosal plexus, also known as their neurochemical code, readily adapt to their microenvironment. We and others have described the responses and involvement of colonic submucosal neurons in the context of both physiological processes and pathological conditions. This talk will address some of the features that make submucosal neurons as well as their mechanisms, targets of interest for developing pharmacological strategies to treat gastrointestinal related disorders.

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SIMPOSIO / SYMPOSIUM



Symposium Natural Products «Medicinal and Food Plants in Chile: Status, Opportunities and challenges"
Chair: Dr. Raquel Bridi

ANTI-INFLAMMATORY PROPERTIES AND CHEMICAL COMPOSITION OF NATURAL PRODUCTS: INFLUENCE OF GENOTYPE AND DRYING. Propiedades 34nti-inflamatorias y composición química de productos naturales: influencia del genotipo y el secado.

Resúmen:
A wide range of factors can influence the production of bioactive compounds in natural products and, consequently, the pharmacological activities of the resulting extracts. Key factors include the plant genotype and the drying process of the plant material used to produce extracts. Regarding genotype, studies on Chilean endemic plants, such as Ugni molinae Turcz. (commonly known as murtilla), conducted by our research group, have evaluated the anti-inflammatory activity and chemical composition of extracts from the leaves and fruits of 10 different murtilla genotypes (INIA), all cultivated under the same edaphoclimatic conditions. Significant differences were observed in the profile of phenolic compounds and pentacyclic triterpenes, quantified by HPLC-UV/MS, as well as in the anti-inflammatory activity, assessed in an in vivo mouse ear edema model. Among the genotypes studied, genotype 19-1ha stood out with higher anti-inflammatory activity and greater bioactive compound content (1,2). Regarding the drying process, research conducted by our group in collaboration with researchers from the University of La Serena and the University of Chile has demonstrated that the content of active compounds and pharmacological properties, such as in vitro antioxidant and in vivo anti-inflammatory activities, can vary depending on the drying method used. In plant species such as Ugni molinae, Aristotelia chilensis, and Fuchsia magellanica, among others, freeze-drying, vacuum drying, and low-temperature vacuum drying have proven superior in preserving bioactive compounds compared to convection or infrared drying methods. These results highlight the importance of selecting an appropriate drying method for plant material intended for medicinal use (3,4).
References (DOI/LINK): 1. 10.1016/j.foodchem.2016.07.159 2. https://www.redalyc.org/articulo.oa?id=85647558001 3. 10.3389/fpls.2023.1095179 4. 10.3390/foods13193162

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UNRAVELING THE HEALTH-PROMOTING AND DISEASE-PREVENTATIVE BENEFITS OF TRADITIONAL FERMENTED BEVERAGES FROM CHILE. Desentrañando los beneficios para la salud y la prevención de enfermedades de las bebidas fermentadas tradicionales de Chile.

Resúmen:
Ethnohistorical and ethnographic information in Chile has shown that fermented beverages have an important role beyond the social or ritual use linked to their function as alcoholic beverages. This is evident, based on the extensive documentation of their use as foods and medicines. In South America, especially in the Andean regions, indigenous communities prepared chicha based on practically all plant materials, including fruits, grains, starchy tubers, and even mushrooms. As food, chicha has been used as an energy source providing calories, proteins, vitamins, minerals, and different bioactive compounds. Among the health-beneficial properties reported are: diuretic, treatment of respiratory and digestive infectious diseases, anti-inflammatory, antineuralgic, to treat extreme fatigue and thinness, to relieve menstrual pain, to treat hemorrhoids, as a tonic, astringent, emollient, and to improve appetite. The notion that consuming fermented beverages is associated with health benefits is widespread and even survives to the present day. However, health claims are mostly based on ethnographic reports and traditional knowledge, while the experimental evidence is still incomplete. Yet, besides the limited scientific information, the existing research on plant-raw materials, phenolic compounds, in general, and fermented beverages of different plant-raw materials, indicate that Chilean traditional fermented beverages may possess a promising potential yet to be investigated and fully exploited. This talk provides scientific evidence that permits validation that fermentation results in changes in the chemical profile of the initial plant raw materials and that these modifications are associated with an increase in antioxidant capacity, bioaccessibility, bioavailability, and pharmacological activities against metabolic syndrome and gastrointestinal cancers.

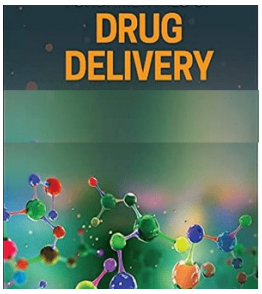
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HEPATOPROTECTIVE POTENTIAL OF IRIDOIDS AND POLYPHENOLS. Potencial hepatoprotector de iridoides y polifenoles

Resúmen:
Liver disease accounts for approximately 2 million deaths per year worldwide. Regular usage of medicines, increased consumption of western-type diets (high in fructose, lipids, and cholesterol), alcohol, and also exposure to radiation, viral infections, lipid peroxidation products, and other toxic chemicals are considered to be the main causative factors to liver disorders. Since currently available synthetic drugs may not be effective and may have limitations due to their negative side effects, there is a vast need for new and alternative approaches to find novel hepatoprotective agents. Accordingly, much attention is focused on developing novel drugs for treating liver diseases derived from medicinal plants. Active extracts, fractions, or isolated compounds of plants may prove very effective drugs for liver diseases. Some secondary metabolites like polyphenols and iridoids showed hepatoprotective activity. Iridoids are secondary metabolites recognized by their intense bitter taste. Several plants containing iridoids are used as hepatoprotective agents, and some studies confirmed this effect. On the other hand, polyphenols from a wide range of foods and medicinal plants have demonstrated therapeutic effects in a range of liver diseases. The hepatoprotective effect of iridoids and polyphenols is mainly attributed to their antioxidant activity. Our studies using extracts rich in these compounds obtained from medicinal plants, legumes, and bee products showed protection in hepatic cells against oxidative damage triggered by AAPH-derived free radicals. This effect can be credited to the ability of the iridoids and phenolic compounds present in the extracts to protect the liver cells from chemical-induced injury, which might be correlated to their free radical scavenging potential. Additionally, some extracts reduce lipid accumulation in a cellular model of steatosis.

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SIMPOSIO / SYMPOSIUM



Symposium Drug Delivery "Breaking Barriers for Drug Delivery"
Chair: Dr. Tania Bahamondez

DRUG DELIVERY STRATEGIES THROUGH MUCOSAL MEMBRANES. Estrategias de entrega de activos a través de membranas mucosas

Resúmen:
Mucosal membranes form a barrier between the body's internal systems and the environment. This route offers several advantages over traditional routes of administration, such as rapid absorption due to their rich blood supply, resulting in a faster onset of action and avoiding first-pass metabolism. Mucosal delivery is typically non-invasive, improving patient compliance. Furthermore, mucosal delivery allows localized treatment using formulations such as sprays, gels, and films, targeting specific tissues such as the respiratory or gastrointestinal tracts. This can be particularly beneficial for managing localized infections while minimizing systemic side effects since these membranes provide a moist, nutrient-rich environment for pathogens. In susceptible patients, bacteria can adhere and grow into biofilms—structured communities encased in a protective matrix that resists antibiotics and immune defenses. However, this route poses unique challenges, including limited permeability, rapid clearance, and risk of degradation by mucosal enzymes. Overcoming these barriers is crucial for effective treatment. Recent strategies focus on integrating bioactive compounds, such as essential oils, due to their ability to perfuse through these membranes, exert antimicrobial, antioxidant, and antifungal effects, and improve mucociliary clearance. Essential oils can disrupt biofilm structure and inhibit bacterial growth. Additionally, oxygen delivery agents, such as perfluorooctyl bromide (PFOB), are being explored to enhance oxygenation in lung tissues. PFOB can dissolve significant volumes of oxygen, making them suitable for addressing the hypoxic conditions typical within biofilm environments. By improving oxygen levels, PFOB promotes tissue regeneration and boosts the effectiveness of antimicrobial agents, which often require oxygen to function optimally. These combined approaches help overcome the challenges of mucosal drug delivery in managing chronic mucosal infections.

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THE IDEAL FILTER DOES EXIST: OVERCOMING MECHANICAL, CHEMICAL, AND AERODYNAMIC OBSTACLES IN RESPIRATORY DOSING. El filtro ideal sí existe: Superando obstáculos mecánicos, químicos y aerodinámicos en la dosificación respiratoria

Resúmen:
This presentation explores the delivery of drugs to the lungs, highlighting the advantages and challenges associated with this route compared to traditional oral administration. In terms of benefits, pulmonary drug delivery allows for rapid absorption and bypasses hepatic first-pass metabolism, making it an ideal route for drugs intended to act locally within the lungs. It also requires lower dosages than oral administration for local pulmonary action, potentially minimizing systemic side effects. However, significant biological and aerodynamic barriers challenge the effective delivery of drugs to the lungs. Key obstacles include the branching structure of the respiratory tract, which affects particle distribution and aerodynamics; inertial impact within the oropharyngeal region, where many particles are lost before reaching the lungs; and lung barriers, such as mucociliary escalator action and macrophage activity, which effectively remove foreign particles, including respirable drugs, from the lungs. These barriers act as "ideal filters," presenting hurdles to achieving efficient pulmonary dosing. This presentation will discuss strategies designed to overcome these natural lung barriers, aiming to enhance drug deposition in the lungs and improve therapeutic outcomes in respiratory dosing.

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NANOCARRIER DESIGN FOR INTACT BARRIER PERMEATION FOLLOWED BY TARGETING. Diseño de nanocarriers para la permeación intacta a través de barreras seguida de direccionamiento.

Resúmen:
Nanocarrier development for targeted drug delivery has advanced considerably, with promising strides in lipid-core micelles (LCMs) tailored to permeate biological barriers and respond to disease-specific biomarkers. Our recent work highlights the potential of MMP-9-responsive LCMs designed to release therapeutic payloads upon encountering elevated enzyme levels typical in cardiovascular pathologies, followed by specific cardiomyocyte targeting. Extending this strategy, our ongoing research investigates buccal administration as a non-invasive route for peptide-loaded nanocarriers, designed to bypass gastrointestinal and hepatic barriers, thus enhancing systemic bioavailability of labile biomolecules. Utilizing inkjet-printed mucoadhesive films, we are exploring intact nanocarrier permeation through the buccal epithelium, focusing on the role of film polymer hydration in modulating permeability and achieving controlled release. Preliminary data shows that optimized inkjet-printed films loaded with nanostructured lipid carriers can achieve stable permeation, as confirmed by NTA and TEM imaging. This research is exploring physicochemical parameters such as particle size, zeta potential, and deformability, alongside the impact of permeation enhancers, including bile salts, in promoting intact nanocarrier passage. Findings aim to delineate the synergy between nanocarrier design and buccal film hydration dynamics, establishing a robust platform for targeted and sustained peptide delivery via buccal administration. This presentation will cover the integration of bioresponsive nanocarriers with non-invasive delivery platforms, showcasing how advanced formulation and characterization techniques pave the way for more efficient and patient-conscious targeted drug delivery systems.

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ORAL COMMUNICATIONS

Day 2, 12:35 – 13:35 h, november 12, 2024 (tuesday)



1. IBUPROFEN OR PREGABALIN REDUCE THE HUMAN SPINAL CORD NEUROVASCULAR COUPLING RECORDED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (fNIRS). El ibuprofeno o la pregabalina reducen el acoplamiento neurovascular de la médula espinal humana registrada mediante espectroscopía funcional de infrarrojos cercanos (fNIRS).

Resúmen:
Neurovascular response (NVR) a vital coupling between neural activity and local blood flow is supposed to depends on neuronal Ca++ channels activation and glial prostaglandin release. Recently, fNIRS was applied for functional diagnosis of the spinal cord evaluating perispinal NVR triggered by peripheral nerve electrical stimulation. Here, pregabalin (PGL), an alpha2delta subunit blocker of the Ca++ channel, or Ibuprofen (IBU) a non-specific COX inhibitor was tested in healthy volunteers assigned to the IBU (n=38) or PGL (n=32) groups. Spinal NVR triggered by median nerve electrical stimulation was recorded by fNIRS optodes (750/850 nm) placed at cervical and lumbar level during basal condition and 60 minutes after a single oral dose of IBU 10 mg·Kg-1 or 75 mg PGL. Mann-Whitney and Kruskal-Wallis test were used at $p<0.05$. IBU decreases both NVR amplitude and rise time at the cervical (-45.2% and -17.1% respectively). However, more than 60.5% of the volunteers show lower lumbar NVR amplitudes and rise times after IBU. The NVR duration was reduced by IBU at both cervical (-24.4%) and lumbar (-18.3%) sites ($p<0.05$). PGL decreases NVR amplitude at cervical (-69.7%) but not at lumbar recording site. However, 84.4% of the volunteers of this group show lower lumbar NVR amplitudes and rise times respectively after IBU. The NVR duration was reduced by IBU at both cervical (-14.0%) and lumbar (-18.6%) sites ($p<0.05$). The resulting reduction of the NVR was probably due to the blocking of the Ca++ channel by PGL thus reducing neuronal excitability and prostaglandins release. The IBU non-specific COX synthesis inhibition results in a strongly NVR reduction. Additionally, fNIRS was able to monitor the pharmacological effects of these drugs.

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Socio Patrocinante: N/A

2. IDENTIFYING ALTERNATIVE CONCEPTIONS IN UNDERGRADUATE'S PHARMACOLOGY STUDENTS. Identificando concepciones alternativas en Farmacología de estudiantes universitarios.

Resúmen:
Introduction: One of the many challenges that affect students when learning sciences, is the presence of alternative conceptions (prior knowledge, preconceptions) about the content that will be taught. These ideas show characteristics that have been classified by neuroscience, sociology, history and education. Furthermore, they are deeply rooted in students' cultural heritage, significantly hindering the conceptual change necessary for effective science education. Thus, studies have shown that pharmacological concepts are often not fully understood by students, posing serious risks in health education. For this reason, many experts have emphasized the need to adjust the pharmacology curriculum without adequately considering students' prior knowledge, which is essential for effective learning. Aim: To identify the most common prior knowledge about pharmacokinetics and pharmacodynamics core concepts among Chilean undergraduate students. Methods: Observational study with a cross-sectional design and primarily quantitative approach for a multiple-choice questionnaire on pharmacological concepts that will be applied to 150 Chilean students from three different universities and fields of study. Results: Although in the first pilot the reliability parameter was insufficient for the dimensions considered (Cronbach's alpha < 0.7), within the preliminarily measurement scales responses were obtained that suggest the existence of several strong prior ideas. Among these are those related to the excretion (72%), antibiotic resistance (70%) and the mechanism of action of widely used drugs (78%). Conclusion: Even though there is abundant literature regarding alternative conceptions in science teaching, very little of it systematically addresses prior ideas about pharmacology among university students. We believe that the instrument we will develop can be useful as a foundation for future research aimed at clarifying the preconceptions that students hold most firmly in this domain.

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Socio Patrocinante: Javier A. Bravo, Ph.D.

3. ALZYFINDER: AN ML-DRIVEN PLATFORM FOR LIGAND-BASED VIRTUAL SCREENING AND NETWORK PHARMACOLOGY. AlzyFinder: Una plataforma impulsada por ML para el cribado virtual basado en ligandos y farmacología de redes

Resúmen:
Neurodegenerative diseases, such as Alzheimer's disease (AD), are characterized by progressive cognitive, emotional, and behavioral losses, impacting daily activities. Central to these disorders is neuronal degeneration, which affects essential brain functions. AD, the most common form of dementia, primarily affects the elderly. Key pathological features include amyloid plaques from amyloid-β (Aβ) aggregation and neurofibrillary tangles (NFTs) from tau hyperphosphorylation. Neurodegeneration begins 10-20 years before noticeable cognitive decline. Despite advances, AD remains a significant challenge for the elderly. To address this, research in AD drug discovery must focus on therapies targeting multiple pathological mechanisms. In response, the Alzyfinder Platform was developed. This web-based tool employs machine learning models to virtually screen over 80 key targets linked to AD. Alzyfinder offers a user-friendly interface for ligand-based drug design and presents results through drug-protein interaction networks (DPIs), illustrating how potential therapies interact with AD-related targets. As the first open-access platform of its kind, Alzyfinder's models have been rigorously tested for accuracy in virtual screening. The platform not only predicts interactions between candidate molecules and key targets but also identifies multitarget ligands, offering insights into their therapeutic potential. Alzyfinder Platform represents a crucial advancement in AD drug research by addressing multiple pathological mechanisms. This tool has the potential to improve patient outcomes and is freely accessible at www.alzyfinder-platform.udec.cl, with all necessary resources available in its GitHub repository.

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4. IMPACT OF EXPOSURE TO AN OBESOGENIC DIET AND SUBSEQUENT WEIGHT LOSS ON THE GLP-1 SYSTEM IN THE LATERAL SEPTUM AND RE-FEEDING BEHAVIOR. Impacto de la exposición a una dieta obesogénica y posterior bajada de peso sobre el sistema GLP-1 en septum lateral y comportamiento de re-alimentación.

Resúmen:
Feeding control is regulated at the central level by hypothalamic and extra-hypothalamic areas such as the lateral septum (LS). Last years, the Glucagon-like peptide-1 (GLP-1) system has taken great relevance in controlling food intake, and LS expresses the GLP-1 receptor (GLP-1R). However, the potential alterations in the GLP-1 system in obesity, its effects on feeding behavior, and whether these changes can be reversed after weight loss remain unknown. To test this, we induced obesity by exposing Sprague Dawley rats at post-natal day (PND) 21 to a high-fat diet (HFD) plus 5% sucrose solution for six weeks. Then, we performed a dietary and pharmacological treatment for 10 days where all groups were fed with chow food plus water and were injected with saline (1 mL/kg/day), liraglutide (0.05 mg/kg/day), or phentermine (30 mg/kg/day). Re-feeding test and Westen Blot analysis were performed before and after the treatment, to evaluate GLP-1R levels in LS. The exposure to the obesogenic diet reduces GLP-1R levels in LS of males but not females, and the change in diet was sufficient to reverse this effect. Liraglutide and phentermine treatments did not alter GLP-1R levels in LS of obese males, however, these drugs led to an increased in the HFD consumption during the re-feeding test. In conclusion, chronic exposure to obesogenic diet affects GLP-1 system in LS and re-feeding behavior, and anorectic treatments do not impact GLP-1R levels but induce a preference for HFD during re-feeding, which could lead to weigh regain.

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5. DEVELOPMENT OF A PLATFORM FOR THE EVALUATION OF MOLECULES WITH ACTIVITY AGAINST CASTRATION-RESISTANT PROSTATE CANCER AND ABIRATERONE-RESISTANT CÁNCER. Desarrollo de una plataforma de evaluación de moléculas con actividad frente al cáncer de próstata resistente a la castración y resistente a Abiraterona.

Resúmen:
Castration-resistant prostate cancer (CRPC) is a significant public health problem, especially when patients develop resistance to Abiraterone, a last-line drug in the treatment of this disease. This thesis presents the development of a platform for evaluating compounds with potential therapeutic activity against Abiraterone-resistant CRPC (AbiR). Two Abiraterone-resistant cellular models were generated using the C4-2B and 22RV1 cell lines, by chronic treatment with increasing concentrations of Abiraterone. These models were validated through real-time proliferation and cell death assays, which demonstrated that the resistant cells exhibited greater survival and proliferation in response to the drug compared to the parental cells. Additionally, traditional crystal violet staining methods were compared with automated real-time analysis, revealing that the latter offers advantages in terms of accuracy, amount of data, and reduced experimental bias. Five compounds with potential activity were evaluated using an automated robotic platform that allowed for real-time cytotoxicity and cell proliferation assays. The results showed significant differences in the activity of these compounds against the AbiR models, providing crucial data to identify candidates that could reverse resistance or have therapeutic activity against this type of cancer. This platform represents a breakthrough in the development of tools for researching new therapies against Abiraterone-resistant CRPC, improving the evaluation process of potential new treatments.

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ORAL COMMUNICATIONS

Day 3, 12:35 - 13:35, november 13, 2024 (wednesday)



1. INVOLVEMENT OF TREK AND BKCA CHANNELS IN PROTEIN-PROTEIN INTERACTION NETWORK ASSOCIATED WITH PAIN. Participación de los de los canales TREK y BKCa en la red de interacción proteína-proteína asociada al dolor.

Resúmen:
Large-conductance calcium-activated potassium (K+) channels (BKCa channels) and TWIK-related K+ channels (TREK-1 and TREK-2) are present in nociceptive primary sensory neurons. Novel molecules that increase TREK or BKCa activity have been suggested as potential treatments for pain. In this study, a graph database was constructed to map the pain interactome (or protein-protein interaction network) and its modulating drugs, with a focus on TREK and BKCa channels as nodes in the graph. The graph was analyzed using centrality parameters such as degree, eccentricity, and radiality. These topological parameters, along with the pharmacology of TREK and BKCa channels, were compared to other relevant pharmacological targets like different ion channels, GPCRs, and kinases. Additionally, a functional enrichment analysis was performed for the first- and second-neighbor networks of TREK and BKCa channels to understand the biological processes and metabolic pathways involving these proteins. This study contributes to understanding the pain interactome, providing a framework for designing multitarget pain therapies that regulate TREK and BKCa channels.

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Socio Patrocinante: Wendy González

2. IDENTIFICATION OF DRUGGABLE BINDING SITES AND SMALL MOLECULES AS MODULATORS OF TMC1. Identificación de sitios de unión a fármacos y pequeñas moléculas moduladoras de TMC1

Resúmen:
Inner ear sensory hair cells use mechano-electrical transducer (MET) channels, formed by TMC1/2 proteins, to convert mechanical stimuli into electrical signals essential for hearing and balance. The non-selective cationic channels allow the permeation of ototoxic drugs into hair cells. Recently, the FDA approved sodium thiosulfate to reduce the risk of cisplastin-induced ototoxicity. Its mechanism of action is not fully understood and does not protect against aminoglycoside-induced damage. This underscores the need for structure-guided search for novel otoprotectants compunds to prevent hearing loss. Also, multiple studies have aimed to identify or modify compounds as potential otoprotectants against ototoxic drugs. Despite the understanding of the interaction mechanisms between these modulators and TMCs remains limited. In this study, we used computational and experimental methods to identify novel TMC1 modulators and developed the first in silico pipeline using a structure-based screening approach, integrating molecular pharmacophore modeling, molecular docking and free-energy estimations analysis coupled with AM1-43 loading as a screening pipeline. Our 3D pharmacophore model contains structural features necessary for ligands to bind and modulate TMC1 activity. Molecular docking and free-energy estimations identified three potential drug binding sites within the TMC1 pore, phospholipids and highlighted key amino acids for ligand interaction. This approach successfully identified several FDA and non-FDA compounds that demonstrated MET modulation activity by reducing dye uptake in cultured cochlear explants. Additionally, the computational methods provide a deeper understanding of the key structural elements and moieties required for hit-to-lead optimization with enhanced biological activities. Finally, our pipeline offers a broad application to discover small molecule modulators for a wide spectrum of mechanosensitive ion channels.

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Socio Patrocinante: Ramírez D.

3. IMPACT OF QUERCETIN ON CELL PROLIFERATION AND ENZALUTAMIDE SENSITIVITY IN CASTRATION-RESISTANT PROSTATE CANCER. Impacto de quercetina en la proliferación celular y la sensibilidad a la enzalutamida en el cáncer de próstata resistente a la castración.

Resúmen:
Castration-resistant prostate cancer (CRPC) is a condition where prostate cancer continues to progress despite castration-level androgen levels. One of the drugs used to treat CRPC is the androgen receptor antagonist enzalutamide. A key pathway in CRPC progression is the PI3K/AKT pathway, which leads to increased expression of androgen receptor (AR) and prostate-specific antigen (PSA), both critical in resistance and desensitization to enzalutamide. Currently, the search for molecules that could serve as adjuvants to chemotherapeutic agents has gained prominence in cancer research. Quercetin, a secondary metabolite with antioxidant activity, has shown antiproliferative effects in various cancer types. Here, we propose that quercetin could enhance sensitivity to enzalutamide by inactivating AKT and reducing the expression and activation of AR and PSA. To test this, quercetin treatments were conducted on CRPC cell lines C4-2B and 22RV1. AKT activation was analyzed through Ser473 phosphorylation via Western blot, and AR and PSA levels were assessed using Western blot and RT-qPCR. Finally, cytotoxicity and cell proliferation assays were performed using increasing doses of quercetin combined with enzalutamide doses of 20 µM and 40 µM (for C4-2B) and 40 µM and 80 µM (for 22RV1), monitored through the Incucyte cell-by-cell system. Our results show that quercetin inhibits cell proliferation, prevents AKT activation, and reduces AR and PSA expression and activation. Additionally, quercetin increased the sensitivity of these cells when combined with enzalutamide.

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Socio Patrocinante:

4. METABOLIC PROFILE AND BIOACTIVE EVALUATION OF Berberis microphylla G. FORST (CALAFATE) LEAF INFUSION. Perfil metabólico y evaluación bioactiva de la infusión de hojas de Berberis microphylla G. FORST (CALAFATE).

Resúmen:
Berberis microphylla G. Forst (Calafate) fruit have been used in traditional medicine since pre-Hispanic times in Patagonia, its consumption provides health benefits, particularly in protecting against various metabolic diseases[1]. However, the bioactive properties of the leaves, have been poorly studied. Recently, 108 compounds, mainly hydroxycinnamic acids, flavonols, and berberine, were identified in a methanolic extract of the leaves[2]. Based on this, we evaluated the bioactive capacity of a Calafate leaf infusion prepared in hot water. For this, the chemical characterization of the infusion was performed using HPLC-Q-TOF. Bioactivity was assessed through antioxidant capacity, cell cytotoxicity, and cell oxidative stress assays. The inhibition of Aβ aggregation for Alzheimer's disease and gastrointestinal enzymes for metabolic syndromes were also evaluated. The results show that the infusion is rich in hydroxycinnamic acids and other bioactive compounds. The infusion does not exhibit cytotoxic activity. Additionally, it can reduce intracellular reactive oxygen species in HUVEC cells and showed a reduction in Aβ aggregation. Finally, the infusion exhibited in vitro hypoglycemic and hypolipidemic effects. These results support the use of Calafate infusion as a new functional beverage.

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Socio Patrocinante: Jorge Fuentealba

ORAL COMMUNICATIONS

Day 4, 12:35 - 13:35, november 13, 2024 (thursday)



INCORPORACIONES / INCORPORATIONS

1. GENETIC VARIANTS AND CLINICAL FACTORS AFFECTING THE RESPONSE TO 5-FLUOROURACIL-BASED TREATMENT IN CHILEAN PATIENTS WITH ADVANCED COLORECTAL CANCER. Variantes genéticas y factores clínicos afectan la respuesta al tratamiento basado en 5-fluorouracilo en pacientes chilenos con cáncer colorrectal avanzado

Resúmen:

Colorectal cáncer (CRC) is the second most common cancer in Chile, with late diagnoses leading to about 25% of patients presenting with metastatic disease and a five-year survival rate around 14%. Standard treatment involves tumor resection and adjuvant chemotherapy, primarily 5-fluorouracil (5-FU) combined with oxaliplatin or irinotecan. However, responses to 5-FU vary significantly due to genetic polymorphisms in enzymes like thymidylate synthase (TYMS) and dihydropyrimidine dehydrogenase (DPD), influencing drug metabolism. Polymorphisms in genes related to oxaliplatin's efficacy also contribute, yet the relationship between genetic variants and treatment outcomes is often population- and stage-dependent. Notably, a comprehensive model to predict chemotherapy safety for Chilean CRC patients has not been established. This study aimed to identify relevant genetic variants in TYMS, TYMP, DPYD, GSTP1, MTHFR, ERCC2, ABCB1, ABCC2, ABCC4, and ABCG2 that, alongside clinical variables, could help create a predictive model for the safety of 5-FU-based chemotherapy in advanced CRC patients. A retrospective nested case-control study analyzed 82 advanced CRC patients and 16 genetic variants to assess their influence on adverse reactions (ADRs). Key findings included that the G allele of GSTP1 (rs1695) was protective against neuropathy but increased the risk of mucositis. The C allele of DPYD (rs1801265) raised neuropathy risk, while TYMS deletion (rs151264360) was protective against skin and hematological ADRs. Two multivariate models predicted anemia and pain development. This study is a step toward developing predictive models for ADRs related to 5-FU, potentially aiding in pharmacogenetic-based dose adjustments for Chilean patients.

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Socio Patrocinante: Dr. Luis Quiñones Sepúlveda, PhD

2. MODELING AND DYNAMICS OF THE MINERALOCORTICOID RECEPTOR IN ITS INACTIVE STATE: DEVELOPMENT OF A PHARMACOPHORE MODEL AND SCREENING OF NOVEL ANTAGONISTS. Modelado y Dinámica del Receptor de Mineralocorticoides en su Estado Inactivo: Desarrollo de un Modelo Farmacofórico y Búsqueda de Nuevos Antagonistas

Resúmen:

The mineralocorticoid receptor (MR) is a critical therapeutic target in cardiovascular and renal diseases. However, structural data on its inactive conformation remain limited. In this study, we employed molecular modeling to complete the recently published, yet incomplete, crystallographic structure of the MR-Esaxerenone complex, enabling the exploration of MR in its inactive state. To characterize binding patterns and derive a pharmacophore model of pure MR antagonists, molecular dynamics simulations were conducted. Clustering strategies were applied to identify prevalent binding modes and pinpoint key residues in the protein-ligand interactions. This analysis revealed critical anchoring points that determine antagonist affinity and specificity for MR. We conducted a virtual screening campaign of approximately 100 million compounds using the most representative binding mode. This effort led to the identification of several novel chemotypes with potential selective antagonist activity for MR. These compounds represent promising candidates for MR-targeted therapies, providing new opportunities in modulating this receptor for potential clinical applications. Through molecular modeling and dynamics, we generated a detailed model of MR's inactive state, identifying novel chemotypes for MR antagonists. This work underscores the potential of virtual screening and computational modeling in drug discovery for diseases modulated by MR.

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Socio Patrocinante: Dr. David Ramirez

PANEL COMMUNICATIONS

Day 1, 19°°-21°°, november 11, 2024 (monday)



1. P2X2R/CALPAIN-1 ACTIVATION AXIS ENHANCES THE AMYLOIDOGENIC PATHWAY AND BETA-AMYLOID PEPTIDE FORMATION IN ALZHEIMER'S DISEASE. El eje de activación P2X2R/calpaína-1 potencia la vía amiloidogénica y la formación del péptido beta-amiloide en la Enfermedad de Alzheimer.

Resúmen:

The key event in the pathogenesis of Alzheimer's disease (AD) is the accumulation of beta-amyloid peptide (AB), which produces intracellular Ca2+ dyshomeostasis. In our hands, AB was found to induce a specific increase in P2X2 purinergic receptor (P2X2R) levels, which has a high Ca2+ conductance. Ca2+ activates calpain cytosolic proteases, that produce a p35 protein cleavage, generating the p25 fragment (an activator of Cdk5). Cdk5 phosphorylates to the STAT3 transcription factor to upregulate BACE1 expression. Here, we study the calpains activity after P2X2R activation to determine its impact on the amyloidogenic pathway and AB formation. Using western blot and/or immunocytochemistry techniques, PC-12 cells showed that both activation of P2X2R with ATP or with optogenetic tools (light) increased calpain-1 levels, while calpain-2 and calpastatin (endogenous calpain inhibitor) did not present variations in its expression. Calpain protease activity was also increased due to the degradation of its main substrates: spectrin and p35, and the fluorescent calpain substrate Ac-LLY-AFC. Furthermore, PC-12 cells showed an increase in the pSTAT3/STAT3 ratio and in the BACE1 expression, which correlated with an increase in AB peptide generation, while co-incubation with MDL28170 calpain inhibitor maintained these levels close to control. Elevated levels of P2X2R and calpain-1 were also found in the hippocampus of APP/PS1 transgenic mice and in presynaptic membranes of prefrontal cortex of AD patients. Considering that chronic exposure to AB increases P2X2R expression, our data point to positive feedback, where AB peptide increases P2X2R expression to reinforce AB production through a calpain-1-mediated mechanism. Our results represent a novel, unexplored pathway in Alzheimer's disease, opening a new space to develop pharmacological strategies to treat AD.

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Agradecimientos: This research has been funded by FONDECYT 1200908 (JF) and ANID 21200612 (JG). We thank to Ixia Cid, Jocelin González and CMA Bio-Bio for their technical assistance.

Socio Patrocinante: Jorge Fuentealba Arcos

2. THE EXPRESSION OF THE GPR158 RECEPTOR IN THE SPINAL CORD AND ITS POTENTIAL AS A THERAPEUTIC TARGET FOR PAIN. Expresión del receptor GPR158 en la médula espinal y su potencial como blanco terapéutico para el dolor.

Resúmen:

The GPR158 receptor has recently been identified as the first G protein-coupled receptor (GPCR) activated by the neurotransmitter glycine. GPR158 belongs to the type C family of GPCRs, and its activation leads to a reduction in intracellular cAMP levels. Evidence increasingly supports the role of GPR158 in regulating brain function. However, its expression and potential roles in the spinal cord remain unexplored. Furthermore, apart from glycine, little is known about the pharmacology of GPR158, and no synthetic modulators have yet been discovered. To begin investigating GPR158 expression in the spinal cord, we analyzed transcript levels using RT-qPCR and protein expression via western blot and immunostaining techniques. We also assessed potential changes in GPR158 expression in mouse spinal tissue under chronic pain conditions using behavioral models. In addition, to identify possible synthetic modulators, we used in silico methods to screen the interactions of 3447 drugs (ZINC Database) with the orthosteric site of GPR158. Our results demonstrate that GPR158 is expressed in the adult mouse spinal cord, with enhanced immunoreactivity detected in dorsal horn neurons. Behavioral assays revealed a significant reduction in spinal GPR158 transcript expression in a model of peripheral inflammation. Finally, molecular docking and free energy binding calculations identified promising drugs that may modulate GPR158 activity. Collectively, these findings suggest that spinal GPR158 may play a role in pain signaling. Furthermore, our in silico screening suggests that several existing drugs could act as GPR158 modulators, underscoring its pharmacological potential. Future studies will provide more definitive evidence regarding the role of spinal GPR158 signaling in chronic pain and its potential as a therapeutic target.

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Socio Patrocinante: Yévenes G. E.

3. INVESTIGATING GLYCINERGIC NEUROTRANSMISSION IN THE PERIAQUEDUCTAL GRAY. Investigando la neurotransmision glicinergica en la sustancia gris periacueductal.

Resúmen:
Glycine receptors (GlyRs) are anion-permeable pentameric ligand-gated ion channels. Their activation leads to membrane hyperpolarization, providing dynamic control over neuronal excitability. Glycinergic dysfunction in the spinal cord is a key factor associated with chronic pain. However, it remains unknown whether GlyRs expressed in supraspinal structures involved in pain modulation, such as the periaqueductal grey (PAG), contribute to chronic pain states. The inhibitory control of PAG neurons is crucial for regulating the activity of descending pain pathways to the spinal cord and plays a critical role in opioid-mediated analgesia. Despite this, the expression, function, and pharmacological modulation of GlyRs in the PAG have not been thoroughly explored. To address this, we initiated studies aimed at characterizing glycinergic neurotransmission in the PAG of adult mice using electrophysiology and RT-qPCR. Whole-cell recordings showed that applying exogenous glycine to PAG neurons elicited chloride-evoked currents in all neurons tested. Additionally, a subpopulation of PAG neurons (4/13) exhibited spontaneous glycinergic post-synaptic currents. RT-qPCR assays from PAG tissue confirmed the presence of GlyR subunit transcripts, with a predominance of the alpha1 and alpha3 subunits. These results provide a preliminary characterization of glycinergic neurotransmission in the PAG. Ongoing experiments are evaluating the sensitivity of PAG-expressed GlyRs to allosteric modulators and will further define their subunit composition. In the long term, we aim to elucidate the role of the glycinergic system in the PAG in chronic pain and its potential in analgesic development.

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4. THE ENTACTOGEN MDMA (3,4-METHYLENEDIOXYMETHAMPHETAMINE) INCREASES LONG-TERM POTENTIATION OF TRANSCALLOSAL RESPONSES IN THE ANTERIOR CINGULATE CORTEX: POSSIBLE ROLE IN MDMA-MEDIATED EFFECTS ON HELPING BEHAVIOUR IN RATS. MDMA (3,4-metilendioximetanfetamina) aumenta la potenciación de largo plazo en la corteza cingulada anterior: posible papel en la conducta de ayuda en ratas.

Resúmen:
Helping behaviour is an empathy-based prosocial behaviour expressed as non-stereotyped complex responses in rats. In contrast to classic social interaction, subtoxic doses of the entactogen MDMA (3,4-methylenedioxymethamphetamine, “ecstasy”) seem to disrupt helping behaviour through an unknown mechanism, possibly combining an evocation of the willingness to help with the activation of key central nuclei associated with cognitive capabilities. In this regard, helping behaviour has been proposed to rely on the activity of mirror neurons located in the anterior cingulate cortex (ACC), and some studies have showed functional neural plasticity in the ACC associated with emotions. Given the role of MDMA in empathy-based behaviours, combined neuroplasticity may play a relevant role in remembering prosocial decisions and actions. In this work, the effects of MDMA (10 mg/kg i.p.) on long-term synaptic potentiation (LTP) evoked in vivo in the ACC has been studied in rats. Animals were anesthetized with urethane (1.5 g/kg i.p.), tracheostomized and placed in a stereotaxic frame under artificial ventilation. Field potentials were evoked in the ACC by electrical stimulation of the contralateral ACC. Transcallosal LTP-like plasticity was elicited by applying an already reported protocol consisting of two consecutive pulse trains of 100 Hz each at double strength. The results obtained showed that train-stimulation of the contralateral ACC of saline treated rats produced a long-lasting increase in peak-to-peak amplitude of transcallosal responses in the ACC. Following MDMA administration, a significant LTP increase could be recorded from the ACC, as compared with saline rats. These data suggest that transcallosal LTP was increased by serotonin released in the ACC after MDMA treatment, which might be related to an eventual effect of MDMA on remembering helping behaviour execution.

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Agradecimientos: FUNDING SUPPORT: DICYT-USACH GRANT 022401SB.
Socio Patrocinante: Alejandro Hernández Kunstmann

5. PRIOR KNOWLEDGE BETWEEN CAGE COMPANIONS MODULATE THE EFFECT OF A SUBTOXIC DOSE OF THE ENTACTOGEN MDMA (3,4-METHYLENEDIOXYMETHAMPHETAMINE, “ECSTASY”) ON HELPING BEHAVIOR IN SPRAGUE-DAWLEY RATS. El conocimiento previo entre compañeros de jaula modula el efecto de una dosis subtóxica de MDMA (3,4-metilendioximetanfetamina) sobre la conducta de ayuda en ratas Sprague-Dawley

Resúmen:
In humans, empathy is expressed through a variety of prosocial behaviours between individuals that are enhanced after intake of the entactogen MDMA (3,4-methylenedioxymethamphetamine, “Ecstasy”). Empathy-like behaviours may also occur in rodents, including social interaction and helping behaviour. In this regard, whereas social interaction has been reported to be enhanced by MDMA, the administration of subtoxic doses of the drug (1 mg/kg – 10 mg/kg) seems to disrupt helping behaviour between isolated mates that do not know each other. Besides, previous knowledge between congeners is known to favour its occurrence. In the present work, the effects of MDMA (5 mg/kg i.p.) on helping behaviour between rats that do know each other has been studied using a modified water-trap model developed ad hoc. Male Sprague-Dawley rats previously housed in pairs for at least one week (assigned as “helper” rat or “soaked” rat) were placed separately in a box divided in 2 compartments (“wet”/“dry”) by a transparent, acrylic wall with a circular door to go across the wall. 12 days-administration/training cycles lasting 5 minutes each were carried out to evaluate each drug dose level. Similar cycles were also carried out after interchanging roles (“helper” versus “soaked”). Helping behaviour was verified when the helper rat opened the door to rescue the soaked rat from the water-trap. The results obtained indicated that, unlike isolated animals, MDMA did not disrupt helping behavior (even after interchanging roles), as the occurrence of door openings were indistinguishable from controls. These data suggest that prior knowledge between congeners may prevent the disruption induced by MDMA on helping behaviour, highlighting the prevalence of the willingness to help over a disruption mediated by serotonin in isolated animals.

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Socio Patrocinante: Patricio Sáez Briones

6. MORPHOLOGICAL MODIFICATIONS OF MICROGLIA IN THE SRD NUCLEUS IN MALE AND FEMALE FIBROMYALGIA RAT MODEL. Modificaciones morfológicas de la microglia en el nucleo SRD en ratas macho y hembra sometidas a un modelo de fibromialgia.

Resúmen:

Introduction: Fibromyalgia (FM) is a persistent chronic musculoskeletal pain syndrome without organic injury. The dorsalis reticularis subnucleus (DRS) in the brainstem (BS) regulates the inhibitory modulation of pain, known as diffuse nociceptive inhibitors (DNIC), where its alterations are implicated in the maintenance of chronic pain. We studied the cellular mechanisms of hyperalgesia in FM induced by neonatal stress (NLB). Aim: Characterize morphological modifications in SRD microglia and their relationship with algesimetric changes in rats with FM/NLB. Methods: In BS sections from male and female control, NLB, and NLB/Minocycline (NLB/MC) rats, we performed Fractal (DF) and Sholl analysis. Hyperalgesia was evaluated using the Randall-Sellito algesimetric test. Minocycline (MC) was administered intraperitoneally (50 mg/kg/12days). Statistical analyses were performed using one-way ANOVA test, $p<0.05$. Results: Male NLB rats showed an increase in Iba1 cells (21.56±1.08) compared to controls (17.67±0.96). NLB/MC rats did not show significant differences compared to NLB rats. We obtained significant differences in the Sholl branch decay coefficient (K). In male and female NLB rats, K increased significantly (1.228±0.101 and 1.471±0.137, respectively), in contrast to control (0.268±0.067 and 0.7147±0.057). NLB/MC rats showed a decrease compared to NLB, similar to control (male/MC 0.171±0.028; female/MC 0.141±0.008). The algesimetric test indicated a decrease in NLB rats (male: 133.5±7.2g/cm²; female: 114±3.2g/cm²) versus controls (males: 224±7.5g/cm²; females: 176.8±8.3g/cm²), reversed by MC (male/MC 222.0±12.00g/cm²; female/MC 247.5±1.50g/cm²). Conclusions: Male and female NLB rats show morphological changes in Iba1+ cells related to heterogeneity/branching, suggesting a role of microglial reactivity in the plastic changes in SRD, leading to FM, which is reversed by Minocycline.

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Agradecimientos: Luis Constandil was supported by grant 1231042 from Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT)
Socio Patrocinante: Luis Constandil

7. ETHANOL INCREASES THE BOTTOM-DWELLING ON THE NOVEL TANK TEST AND PRODUCES CONDITIONING ON CPP, THAT CAN REVERT BY UFR2709 ON ADULT ZEBRAFISH. El etanol aumenta la permanencia en el fondo en la prueba de tanque nuevo y produce condicionamiento en CPP, que puede revertirse mediante UFR2709 en peces cebra adultos.

Resúmen:

There are different animal models to demonstrate the behavioral properties of addictive drugs. Murine models are the most popular and common however in the last decade, the zebrafish has been positioning itself over murine models due in principle to the high similarity between his genome and the human genome, their active behavior, ease of acclimation to new environments, ease of manipulation, low maintenance cost, and rapid reproductive cycle. Zebrafish is a useful model for researching human pathologies and is an efficient model for drug discovery and drug screening because it has a high sensitivity to psychotropic substances. The Novel Tank Diving Test (NTT) and the Conditioned Place Preference (CPP) paradigms have become powerful tools for the study of drugs of abuse, measuring how their preferences change in the choice of areas compared to other fish that have not interacted with the drug. Alcohol is a substance that can induce dependence, with 3.7% of the world's population in 2019 being dependent on alcohol and an estimated 3 million deaths per year. In our lab, we have performed assays using alcohol as a drug of abuse in the zebrafish model. Our results show that ethanol increases the time spent at the bottom of the NTT and induces conditioning on the CPP paradigm. Additionally, we tested the effect of UFR2709 to revert the conditioning evoked by ethanol, our results demonstrated that the conditioning could be reverted by the nicotinic antagonist UFR2709 in this paradigm of addiction.

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Socio Patrocinante: Patricio Iturriaga Vasquez

8. EFFECTS OF INTRAHIPPOCAMPAL VASOPRESSIN ADMINISTRATION AND AMPHETAMINE-INDUCED ADDICTIVE-LIKE BEHAVIOR. Efecto de la administración de vasopresina intrahipocampal y la conducta de tipo adictiva inducida por anfetamina

Resúmen:

Addiction to substances such as amphetamine (AMPH) has a significant impact on the brain and behavior, and there are currently no effective pharmacological treatments available. AMPH increases dopamine (DA) levels in the nucleus accumbens (NAc), which is associated with addictive behaviors that develop in response to certain contexts. In this process, the hippocampus, particularly the dorsal CA3 region (CA3d), plays a key role through a circuit involving the lateral septum (LS) and the ventral tegmental area (VTA). The LS, a GABAergic nucleus, is modulated by vasopressin (AVP) via the V1A receptor, influencing reward perception and mood. It has been demonstrated that the administration of AVP in the LS reduces AMPH-related addictive-like behaviors in male rats, an effect mediated by an increase in GABA levels in the LS and a decrease in DA levels in the NAc. To further investigate these findings, the effect of AVP in the CA3d region on the reward system was studied, showing that this administration reduces the conditioned response to AMPH in both male and female rats. Additionally, GABA and glutamate levels were measured in the LS and NAc, and DA levels in the NAc when AVP was administered in the CA3d. On the one hand, DA decreased significantly in the NAc of male rats, whereas Glutamate decreased significantly in the NAc of female rats. These results reveal sexually dimorphic effects of AVP on the neurochemical mechanisms present in the NAc. Despite this major neurochemical sexual dimorphism in the NAc, significant differences were not observed in the addictive-like behavior of the rats, which suggests that AVP could be a promising therapeutic option for the treatment of AMPH addiction.

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Agradecimientos: DICYT Regular Nº 022101RSSA; Rol of vasopressin in the hippocampus in sex differences of addictive-like behaviors. DICYT Ayudante; 022301RG_Ayudante; Role of vasopressin in the hippocampo-septal pathway modulation: Implications for sex differences observed in addictive-like behaviors.
Socio Patrocinante: Dra. Georgina Renard

9. LIRAGLUTIDE MODULATES TYROSINE HYDROXYLASE EXPRESSION IN SUBSTANTIA NIGRA OF A HIGH-FAT DIET ANIMAL MODEL. Liraglutida modula la expresión de tirosina hidroxilasa en sustancia nigra de un modelo animal de dieta alta en grasa

Resúmen:
Obesity is a chronic disease characterized by an excessive accumulation of adipose tissue caused by an energy imbalance, which has increased due to sedentary lifestyles and high-fat diets (HFD) consumption. It is associated with comorbidities that can worsen the individual's health, such as insulin resistance, type 2 diabetes, cardiovascular diseases, among others. Moreover, in recent years research on the effects of high-fat diets on the central nervous system has demonstrated their ability to modulate the dopaminergic pathways. Traditional strategies to treat this disease consist of changes in the patient's diet and lifestyle, but pharmacological strategies have been added. In this context, liraglutide, a glucagon-like peptide 1 receptor (GLP-1R) agonist used for the treatment of type 2 diabetes, has proven to be effective in reducing body weight and controlling appetite. In the present study we demonstrated the capacity of liraglutide treatment to counteract the effects of HFD on the expression of tyrosine hydroxylase (TH) in the substantia nigra (SN). The results indicate that a HFD for 6 weeks increases TH levels in SN of male Sprague-Dawley rats, measured by western blot, while liraglutide treatment for 10 days reverses this effect. These findings contribute to the understanding of the effects of HFD on dopaminergic circuits and provide new evidence of the neuroprotective potential of liraglutide.

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10. EVALUATION OF BEHAVIORAL, NEUROCHEMICAL AND MOLECULAR CHANGES ASSOCIATED WITH CRFERGIC NEUROTRANSMISSION IN LATERAL SEPTUM RATS EXPOSED FOR 6 WEEKS TO AN OBESOGENIC DIET. Evaluación de cambios conductuales, neuroquímicos y moleculares asociados a la neurotransmisión crférgica en septum lateral de ratas expuestas durante 6 semanas a una dieta obesogénica.

Resúmen:
Obesity is a pandemic that has been associated with changes in people's lifestyle, such as the intake of obesogenic foods. In this sense, brain areas of both homeostatic and hedonic control of feeding have been related and studied using models of diet induced obesity. As mentioned, the main brain areas involved in the regulation of feeding are the hypothalamic areas such as the lateral hypothalamus (LH), while at the hedonic level the ventral tegmental area (VTA) and the nucleus accumbens play an important role. Interestingly, both feeding control systems are regulated by the lateral septum (LS), a GABAergic nucleus that acts as a relay station, projecting GABAergic efferents to the LH and VTA. On the other hand, the CRF system at the level of the LS has been studied in motivated behaviors associated with drug abuse and the generation of anxiogenic responses; however, its role in the regulation of feeding or whether exposure to obesogenic diets deregulates has not been studied. In this context, the aim of this research was to study the effects of chronic exposure to an obesogenic diet on the neurophysiological function of the LS, specifically on the role of the CRFergic system in feeding regulation, using a model of exposure to high fat diet (HFD) for 6 weeks. The results indicate an increase in the expression of genes for D1, D2 and CRF1 receptors in females exposed to HFD and with respect to CRF peptide levels, we observed a significant increase in HFD exposed males.

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11. FISHING INSIDE THE GLP-1 RECEPTOR BIBDING SITE, A CHALLENGE IN RATIONAL DRUG DESING. Pescando dentro del sitio de unión del receptor GLP-1, un desafío en el diseño racional de fármacos.

Resúmen:
Obesity has become a severe public health problem, as its prevalence has increased significantly over the last few decades. According to the World Health Organization, the percentage of obese adults rose from 7% to 16% between 1990 and 2022 (WHO, 2024). The primary cause of obesity is an imbalance between caloric intake and energy expenditure, contributing to sedentary lifestyles, hormonal alterations, and the consumption of highly caloric diets. In addition, high obesity prevalence is associated with the industrialization of food production, which has promoted ultra-processed food intake rich in macronutrients such as fat and sugar, which are highly caloric and palatable. The lateral septum (LS) is an important brain area involved in physiological functions such as reward, stress, and autonomic regulation. LS is one of the brain areas with the highest expression of the glucagon-like peptide 1 receptor (GLP-1R), and the pharmacological modulation of GLP-1R in LS affects food intake. However, if obesity development is associated with LS dysregulations of GLP-1/GLP-1R, it has practically not been studied. Our study is focused on the different crystal structure of GLP-1R available on the PDB website 6X1A, 6X19,7S15, 7X8R, 7X8S, and the principal amino acids residues and their interaction with the co-crystalized ligands looking for the common residues interactions that allow us to recognize the GLP-1R binding site and design/search new drugs to treat obesity.

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12. LONG NONCODING RNA KCNQ1OT1 IS INVOLVED IN CISPLATIN-INDUCED NEPHROTOXICITY. RNA largo no codificante kcnq1ot1 está involucrado en la nefropatía inducida por cisplatino.

Resúmen:
Cisplatin (cis-diamminedichloroplatinum (II), DDP) is an antineoplastic agent widely used in the treatment of solid tumors because of its extensive cytotoxic activity. One of the main treatment adverse reactions is nephrotoxicity, for which there is currently no adequate specific and sensitive biomarker. Recent studies have reported the role of non-coding RNAs (microRNAs and lncRNAs) in the cisplatin-induced nephrotoxicity. Among the lncRNAs, KCNQ1OT1, the KCNQ1 opposite strand/antisense transcript 1, is capable of interacting with miRNAs, RNAs and proteins, thereby affecting gene expression and various cell functions. In addition, KCNQ1OT1 is dysregulated in a wide range of diseases, and it is speculated to act as a therapeutic target for treating various human diseases. Nevertheless, there are no studies to date that show their role in cisplatin-induced nephrotoxicity. Thus, the aim of this study was to assess the levels of expression of lncRNA KCNQ1OT1 in two cellular models of nephrotoxicity induced by cisplatin. Human kidney cell lines HEK-293 and HK-2 were cultured and treated with different concentrations of cisplatin for 24 hours to induce nephrotoxicity. Cell viability was determined using the MTS assay to establish the cisplatin concentration that results in 50% cell death (CI50= 14.66 µM). The expression of lncRNA KCNQ1OT1 was assessed in HEK-293 and HK-2 cells lines by RT-qPCR. It was observed that treatment with cisplatin induces overexpression of LncRNA KCNQ1OT1 in both cellular models when compared to control cells ($p<0.05$). Moreover, in HEK-293 cells, KCNQ1OT1 expression was higher than in HK-2 cells. These findings provide relevant information on the potential role of lncRNA KCNQ1OT1 in renal toxicity and open new perspectives for the development of therapies based on the regulation of lncRNA to mitigate the adverse effects of cisplatin.

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13. EFFECT OF DOXYCYCLINE ON MITOCHONDRIAL UNFOLDED PROTEIN RESPONSE IN HEART AND CARDIAC FIBROBLASTS. Efecto de doxiciclina sobre la respuesta mitocondrial a proteínas desplegadas en corazón y fibroblastos cardiacos

Resúmen:
Introduction: Cardiac fibrosis leads to the accumulation of extracellular matrix proteins. The primary cell involved in this process is the cardiac fibroblast (CF). The mitochondrial unfolded protein response (UPRmt) is a potential new pharmacological target for the treatment of cardiac fibrosis. Doxycycline (DOXI) is a known inducer of UPRmt. However, it is unclear whether UPRmt is induced by doxycycline in the heart and in CFs. Methodology: C57BL/6 mice were treated with DOXI at 6 mg/kg/day or vehicle via i.p. injection for 6 days. Cardiac function parameters and UPRmt markers (ATF5, HSP60, and LONP1) were evaluated using western blot. Adult rat CFs were stimulated with DOXI at various doses for 48 hours. LDH and UPRmt markers (ATF5, HSP60, and LONP1) were assessed via western blot. Additionally, UPRmt markers were measured in CFs pre-treated with angiotensin II (Ang II) at 1 µM for 24 hours and subsequently treated with DOXI at 25 µM for 48 hours. Results: No alterations in heart size or cardiac function parameters were observed in DOXI-treated mice; however, there was an increase in the protein expression of ATF5, HSP60, and LONP1. In CFs, DOXI exhibited toxicity at doses above 50 µM, and no increase in protein expression of ATF5, HSP60 or LONP1 was detected. Pre-treatment with Ang II did not modify UPRmt. Conclusion: DOXI increases the protein expression of UPRmt markers without altering cardiac function parameters in the hearts of mice; meanwhile, it does not induce UPRmt in CFs.

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14 INHIBITION OF Src KINASE IMPAIRS KININ-INDUCED MIGRATION AND INVASION IN BREAST CANCER CELL. La Inhibición de la quinasa Src disminuye la migración e invasión inducidas por las cininas en células de cáncer de mama

Resúmen:
Kinin receptors B1 and B2 are involved in migration and invasion in gastric, glioma, and cervical cancer cells, among others. Our previous work showed that kinins, Lys-des[Arg9]bradykinin (LDBK), and Bradykinin (BK) enhance proliferation, migration, and invasion in cancer cells, such as MDA-MB-231, MCF-7, and T47D. However, the role of kinin receptors in breast cancer cells has been poorly studied. We explored signaling pathways downstream of kinin receptors. The Src kinase plays a crucial role in cell adhesion and migration in cancer cells. Because of this, we evaluated the impact of Src inhibition on migration and invasion induced by kinins on breast cancer cells. To assess this, MDA-MB-231, MCF-7, or T47D cells were treated with the specific Src inhibitor, PP2. Cells were incubated with PP2 combined with LDBK or BK to test migration and invasion by transwell and matrigel assay, respectively. Additionally, we evaluated the phosphorylation of Src in response to LDBK and BK by western blot assay. Treatment with PP2, combined with LDBK or BK as appropriate, demonstrated that PP2 could effectively block the increase in migration and invasion induced by LDBK and BK in MDA-MB-231, T47D, and MCF-7 cells. Additionally, the inhibitor of Src also impaired the invasion promoted by kinin nonapeptides, indicating that their treatment reversed the effects of kinins. The treatment of cells with LDBK or BK increases the levels of phosphorylation of Src in a concentration-dependent manner. In conclusion, the increase in migration and invasion induced by LDBK and BK is mediated through Src activation signaling.

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15. MARESIN 1, AS A HEPATOPROTECTIVE AGENT BY DOWNREGULATING THE MAPK PATHWAY ALLOWING THE RORA NUCLEAR TRANSLOCATION IN A MODEL OF METABOLIC DAMAGE ASSOCIATED WITH LIVER FIBROSIS. Maresina 1 actúa como agente hepatoprotector al regula negativamente la via MAPK y permite la translocación de RORa al núcleo en un modelo de daño metabólico asociado a fibrosis hepática.

Resúmen:
Chronic liver diseases account for approximately two million deaths annually worldwide. Within this spectrum, the inflammation plays a critical role in advancing to complications, particularly in the transition to extensive fibrosis and subsequent cirrhosis. Fibrosis is key in the development of the disease as it represents the liver's response to continuous response due to persistent injury, leading to the replacement of functional liver parenchyma with extensive connective tissue, resulting in hepatic dysfunction. Maresin 1 (MaR1), a derivative of docosahexaenoic acid (DHA) polyunsaturated fatty acids of the omega-3 family, has demonstrated potential to promote a protective state against inflammatory diseases. Its properties suggest it is a promising therapeutic agent targeting liver injury, oxidative stress, and inflammatory modulation. The objective of this study was to determine the MaR1 hepatoprotective effects by negatively regulating the MAPK pathway and facilitating the translocation of the nuclear factor RORa to the nucleus, reducing inflammation in the liver fibrosis model. Fibrosis was induced in male Sprague Dawley through administration of diethylnitrosamine (DEN, 50 mg/kg), and MaR1 (4 ng/g) was administered as a hepatoprotective agent. Liver function was assessed via AST/ALT profile and gene expression levels of ERK-1, p33, JNK, AKT/p7056k, as well as RORa protein localization. The results demonstrated that MaR1 reduce MAPK expression and promotes RORa nuclear translocation, suggesting that MaR1 induces a hepatoprotective state against metabolic damage associated with liver fibrosis in this murine model. These findings highlight the anti-fibrotic potential of MaR1, mediated through the regulation of the RORa receptor, making it an interesting candidate for future research.
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16. DEVELOPMENT OF HSC70:LAMP-2A INTERACTION INHIBITORS FOR THE DEVELOPMENT OF A SELECTIVE ANTI-CANCER THERAPY. Desarrollo de Inhibidores de la interacción HSC70:LMP2-A para el desarrollo de una terapia selectiva contra el cáncer

Resúmen:
Chaperone-Mediated Autophagy (CMA) is a selective lysosomal degradation process in which proteins bearing the KFERQ motif are recognized by the chaperone HSC70 and translocated across the lysosomal membrane via LAMP-2A, a transmembrane protein. This process is crucial for cellular homeostasis but is frequently upregulated in cancer cells, aiding their survival under stress conditions like hypoxia and nutrient deprivation. Inhibition of CMA has been linked to reduced tumor growth and metastatic potential, making it a promising target in cancer therapy. In this study, we aimed to develop novel inhibitors of the HSC70:LAMP-2A complex to block CMA selectively in cancer cells. Using comparative modeling and molecular dynamics simulations, we constructed models of HSC70 and LAMP-2A and predicted their interaction through protein-protein docking. The resulting complex was embedded in a lysosomal membrane model and subjected to molecular dynamics simulations in GROMACS, confirming the stability of the interaction site for inhibitor targeting. We screened over 3 million compounds from the MCULE and NCI databases for high binding affinity to the HSC70 interaction region. After filtering for ADME properties and structural diversity, several compounds were identified as potential inhibitors. Among these, three exhibited micromolar IC50 values in viability assays against several breast, prostate and lung cancer cell lines, while showing around 10-fold reduced toxicity in non-cancerous cells, demonstrating their potential as selective CMA inhibitors for cancer treatment. This work introduces CMA inhibition as a novel therapeutic approach, with specific compounds advancing as candidates for further analog development and preclinical evaluation.
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17. SYNTHESIS OF A TETRAHYDROISOQUINOLINE WITH MIGRASTATIC EFFECT ON TRIPLE-NEGATIVE BREAST CANCER CELLS. Síntesis de una Tetrahidroisoquinolina con Efecto Migrastático en Células de Cáncer de Mama Triple Negativo

Resúmen:
Breast cancer is the leading cause of cancer-related death among Chilean women. Among its subtypes, triple-negative breast cancer is one of the most aggressive, with a high tendency to develop metastasis in various organs. Current treatments focus on reducing tumor size but are ineffective at inhibiting the production of metastases. This study focuses on the search for compounds that inhibit tumor cell migration without being cytotoxic. In this context, a methodology was developed to obtain a tetrahydroisoquinoline core featuring an intramolecular hydrogen bond, a structural characteristic that allows compounds to be directed to the mitochondria. This organelle has proven to be relevant in the metabolic changes that promote cancer cell migration and invasion. The synthesis of a first example of tetrahydroisoquinoline was carried out from a carboxylic acid through a series of tandem reactions. Preliminary results show that the tetrahydroisoquinoline exhibits a selective migrastatic effect on triple-negative breast cancer cells (MDA-MB-231) and affects mitochondrial NADH levels, which may produce alterations in mitochondrial bioenergetics, leading to changes in the migratory capacities observed in these cells.
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18. SYNTHESIS OF B-KETO AMIDES AND THEIR EVALUATION FOR INHIBITING BREAST CANCER METASTASIS. SÍNTESIS de β-cetoamidas y su evaluación para inhibir la metástasis del cáncer de mama

Resúmen:
In 2017, a new approach in cancer medicinal chemistry introduced the concept of "migrastatic" drugs—compounds that, rather than killing cancer cells, selectively and potently inhibit their ability to metastasize. In Chile, 54,227 new cancer cases were recorded in 2020, with breast cancer being the leading cause of cancer-related deaths among Chilean women, primarily due to metastasis. Among the subtypes, triple-negative breast cancer (TNBC) is the most aggressive, showing a strong tendency for metastasis to the lungs, liver, and brain compared to other forms. The current standard treatment for TNBC is cytotoxic chemotherapy, which is often limited by its severe side effects and lack of effectiveness. Recent studies suggest that mitochondrial bioenergetics play a crucial role in supporting various stages of metastasis, making mitochondria an interesting target for developing migrastatic drugs. Several mitochondrial uncouplers contain an amide moiety, which led us to explore these compounds as potential migrastatic agents. A particularly unexplored class of mitochondrial-targeting compounds to β-keto amides. In this study, we synthesized a series of beta-keto amides, evaluated their cytotoxicity in normal (MCF10F) and TNBC (MDA-MB-231) cells, and investigated their effects on the migration of TNBC (MDA-MB-231) cells.

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19. Free space

20. NEW TETRAHYDROBETACARBOLINE DERIVATIVES WITH CYTOTOXIC PROPERTIES. Nuevos derivados de tetrahidrobetacarbolinas con propiedades citotóxicas.

Resúmen:
This research focuses on the development of synthetic derivatives of tetrahydrobetacarboline, recognised as a privileged scaffold in the design of therapeutic agents. Six derivatives (6a-f) of tetrahydrobetacarboline were synthesised in high yields and their cytotoxic activity was evaluated in different cancer cell lines. The results show a marked selectivity of these compounds for liver cancer cells: HepG2 (IC50 = 4.8 – 9.3 uM) and Huh7 (IC50 = 2.3 – 7.0 uM), as well as the cervical cancer line: HeLa (IC50 = 2.1 – 8.5 uM). In addition, derivative 3c showed, in addition to the above activity, a broad spectrum profile, also exhibiting activity in the triple negative breast cancer cell line: MDA-MB-231 (IC50 = 3.0 uM)) and acute myeloid leukaemia (HL60 (IC50 = 2.1 uM)). With this simple initial screening, this series stands out for its promising cytotoxic properties and we intend to investigate its pharmacological implications with a view to developing a lead molecule for preclinical studies.

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21. rs1799971 AS A NOVEL BIOMARKER OF PREDICTION AND RESPONSE TO ONCOLOGIC PAIN IN PATIENTS WITH ADVANCED-STAGE COLORECTAL CANCER: A CROSS-SECTIONAL STUDY. rs1799971 como nuevo biomarcador de predicción y respuesta al dolor oncológico en pacientes con cáncer colorrectal estadio avanzado: Un estudio transversal

Resúmen:
Moderate to severe oncologic pain is present in 75 to 90% of patients when they reach advanced stages, when opioid treatment is the gold standard. It is proposed that carriers of certain single nucleotide polymorphisms (SNP) of the OPRM1 gene have greater sensitivity to pain and an altered response to opioids. Furthermore, this same gene, together with TLR4, are proposed as modulators of the degree of oxaliplatin-induced peripheral neuropathy (OIPN), which has a prevalence of approximately 90%. Therefore, through an association between SNPs of the OPRM1 (rs1799971, rs510769) and TLR4 (rs4986790, rs4986791) genes, together with other variables, we seek to address the high variability in pain experienced by patients with advanced colorectal cancer (CRC). A total of 96 patients were genotyped using the qPCR technique associated with TaqMan® probes. Among the results, patients carrying the A/G genotype for rs1799971 tend to have a higher risk of severe oxaliplatin-induced peripheral neuropathy (OIPN) compared to those with mild to moderate OIPN (OR= 5.57; 95%CI=0.88-35.1; p=0.062). In addition, three regression equations were obtained that include as explanatory variables demographic, clinical aspects and the SNP rs1799971, with which the maximum VAS reported by patients (adjusted R2 = 0.160; p= 0.0057), the dose of morphine equivalents (adjusted R2 = 0.473; p= 0.0097) and the degree of OIPN (adjusted R2 = 0.099; p= 0.034) can be predicted. Thus, frequent genetic changes in the population may modulate pain management in CRC, a useful avenue in the future to deliver more effective analgesic treatments or to take preventive measures to avoid the development of more accentuated pain.

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22. ASSOCIATION OF THE rs6021191 VARIANT IN NFATC2 WITH L-ASPARAGINASE HYPERSENSITIVITY IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA. Asociación de la variante rs6021191 en NFATC2 con la hipersensibilidad a L-asparaginasa en pacientes pediátricos con leucemia linfoblástica aguda

Resúmen:
Acute lymphoblastic leukemia (ALL) is the most common type of cancer in children (. The standard treatment includes L-asparaginase (L-ASP), but hypersensitivity reaction to L-ASP (HSR) compromises treatment efficacy and is difficult to predict. Previous studies suggest that the rs6021191 genetic variant in NFATC2 could predict this event. Objective: To evaluate the association between the rs6021191 genetic variant in NFATC2 and HSR in pediatric patients with ALL. Methodology: Multicenter cohort study in pediatric ALL patients between 2013 and 2023 treated with L-ASP. Genotyping was performed via rt-PCR from buccal swab samples. The association between HSR and genotypes was assessed using the chi-square and Fisher's exact tests. The strength of the association was evaluated with the relative risk (RR) and its 95% confidence interval (95% CI). Results: A total of 169 patients were included, with a mean age at diagnosis of 5.3 years. Of these, 54% (91) were male. The protocols analyzed were 1A (n=139), 1A' (n=27), and augmented 1B (n=17), with an overall group from all protocols (n=168). The RR associated with the variant for all protocols was 1.29, 95% CI (0.70-2.38), p=0.426; for the IA and IA' protocols, 2.07, 95% CI (0.93-4.60), p=0.162; and for the augmented 1B protocol, 1.36, 95% CI (1.01-1.85), p=1.00. Conclusion: The rs6021191 variant in NFATC2 is associated with an increased risk of HSR in the studied protocols. A more detailed definition of the event will help establish a better relationship. These findings could be used to prevent HSR in ALL patients.

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23. ACTIVIDAD VASODILATADORA BIFUNCIONAL DE UNA CHALCONA SINTETIZADA A PARTIR DE UN METABOLITO DE SENECIO NUTANS EN LA AORTA DE RATAS ESPONTÁNEAMENTE HIPERTENSAS. Actividad vasodilatadora bifuncional de una chalcona sintetizada a partir de un metabolito de Senecio nutans en la aorta de ratas espontáneamente hipertensas

Resúmen:
In recent years, the antihypertensive and vasodilatory effects of Senecio nutans (chachacoma) have been attributed to the presence of benzophenone derivatives. In this study, we have synthesized a series of chalcones (CHAL1, 2, 3 and 4) from 4-hydroxy-3-(3-methyl-2-butenyl)acetophenone, a metabolite present in Senecio nutans and from another commercial acetophenone, to investigate the relationship between structure and activity. The vascular effects of the synthesized compounds are evaluated by vascular reactivity assays in the aorta of spontaneously hypertensive rats (SHR). In addition, the effect on nitric oxide (NO) and intracellular Ca2+ levels were studied by fluorescence microscopy. The use of animals was approved by the Ethics Committee of the University of Antofagasta (CEIC-275/2020). Initially, CHAL1 was determined to be the most active compound and showed that the absence of endothelium and blockade of the eNOS-NO-sGC-cGMP signalling pathway did not affect vasorelaxation. It was then observed that CHAL1 could block the voltage-gated Ca2+ channel (VGCC), given its ability to reduce contraction mediated by extracellular Ca2+ influx. The reduction of the intracellular Ca2+ increase induced by 60 mM KCl in a primary culture of vascular smooth muscle cells loaded with Fluo-4 AM (5 µM) and the lack of effect of the CaV1.2 agonist (Bay-K8644) on SHR aortic rings confirmed that CHAL1 reduced Ca2+ influx by blocking the CaV1.2 channel. Likewise, the findings also showed that activation of KCa channels and, to a lesser extent, KV, followed by a subsequent activation mechanism of the Na+/K+−ATPase pump, was essential to mediate the vasorelaxant effect of CHAL1. CHAL1 acts as a bifunctional vasodilator that activates KCa channels and reduces Ca2+ influx by blocking CaV1.2 in the aorta of SHR.

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24. WHITE STRAWBERRY POLYPHENOLS ALLEVIATE NONALCOHOLIC FATTY LIVER DISEASE. Polifenoles de frutilla blanca alivian la Enfermedad hepática no-alcohólica.

Resúmen:
While strawberry (WS) is a native Chilean berry commonly found on southern with high content of polyphenols. WS polyphenolic extract showed in vitro simulated digestion and by using cell models an interesting antioxidant potential and ability to inhibit digestive enzymes, which could help on management of obesity related disorders. We aimed to evaluate the impact of a WS extract on liver disorders in obese mice model. We used 4 experimental groups: Control; Control + WS; High fat diet (HFD); HFD + WS. At postnatal day 21, all the animals received control diet or HFD during 12 weeks. After, the groups received vehicle or WS for 4 weeks. The animals were sacrificed and tissues were collected to determine liver histology and genes expression of factors related to lipogenesis de novo. Histology was measured by hematoxylin and eosin, while liver gene expression were measured by qPCR. A significant reduction on liver drop accumulation was observed in the group with HFD+WS compared to HFD. Improvement on gene expression of PPAR-alpha, ChREBP and SREBP-1c were observed in the group HFD+WS. WS can be a good source of polyphenols with biological effect that must be in deep investigated to prevent and treat chronic disease associated to obesity.

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25. SURVIVAL OF PATIENTS WITH HEAD AND NECK CARCINOMA TREATED WITH NIMOTUZUMAB. Supervivencia de pacientes con carcinoma de cabeza y cuello tratados con nimotuzumab

Resúmen:
Nimotuzumab is a humanized monoclonal antibody against epidermal growth factor receptor, highly expressed protein in malignant tumors of epithelial origin. There is little evidence of its effectiveness in standard clinical practice. Objective: to characterize the survival of patients with recurrent and/or metastatic diagnostic head and neck carcinoma treated with nimotuzumab. Methods: Retrospective study in patients, from the "Hospital Conrado Benítez García" of Santiago de Cuba, with head and neck carcinoma treated with nimotuzumab from 2016 to 2020. The Kaplan Meier method was used for overall survival analysis and the Log-Rank test for curve comparison. A multivariate analysis and the Cox regression method were used to identify the risk of the variables analyzed for survival. A statistical significance level of 0.05 was used for all test performed. Results: The data consisted of 52 patients, who experienced an overall survival rate of 76.9%, 65.4%, and 51.9% at 12, 24, and 36 months respectively, and a mean value of 58.2 months (95% CI:47.1-69.4). There was an increased risk of death in ex-smokers [HR= 13.26 (95 % CI:2.01-87.39), p=0.007] and underweight patients [HR=9.31 (95 % CI: 1.39-62.19), p=0.021]; while mixed/black skin color had a protective effect on survival [HR=0.058 (95 % CI:0.08-0.38), p=0.003]. Progression-free survival at 12, 24 and 36 months was 67.3 %, 53.9 % and 42.3 %, respectively. Median progression-free survival was 52 months, (95 % CI:40.4-63.6) and median 44 months Conclusions: Overall and progression-free survival of patients with recurrent and/or metastatic head and neck carcinoma treated with nimotuzumab were superior to those reported with the exclusive use of conventional treatments.

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26. PROGNOSTIC FACTORS DETERMINING CLINICALLY SIGNIFICANT PHARMACOLOGICAL INTERACTIONS IN HOSPITALIZED PATIENTS WITH ISCHEMIC STROKE OR TRANSIENT ISCHEMIC ATTACK UNDERGOING COMBINED THERAPY WITH ACETYLSALICYLIC ACID AND CLOPIDOGREL. Factores pronósticos que determinan interacciones farmacológicas clínicamente significativas en pacientes hospitalizados con ataque cerebrovascular isquémico o ataque isquémico transitorio sometidos a terapia combinada de ácido acetilsalicílico y clopidogrel.

Resúmen:
Stroke is a neurological deficit caused by interrupted blood flow to the brain and is the second leading cause of mortality worldwide. Managing modifiable risk factors and using dual antiplatelet therapy (DAPT) with acetylsalicylic acid (ASA) and clopidogrel are primary strategies for preventing recurrence. Both medications may have potential pharmacological interactions (PPIs) with other drugs during hospitalization. This study aimed to characterize clinically relevant PPIs in patients with ischemic stroke or transient ischemic attack who received DAPT from April to June 2024 at Carlos Van Buren Hospital. Additionally, sociodemographic, clinical, and pharmacological factors associated with progressing from a PPI to a clinically relevant interaction (CRI) were evaluated. This single-center, cross-sectional study collected data from medical records and patient or caregiver interviews (CEC-FAR 02/2024 approval). Lexicomp® and Micromedex® databases were used to identify PPIs related to DAPT, focusing on frequent interactions with D or X risk ratings, high/prominent/contraindicated severity, and 'good' or 'excellent' documentation levels. The study identified 363 PPIs associated with DAPT, with 57.14% of patients having more than 10 PPIs. About 10% of all PPIs were clinically relevant. Two patients (5.71%) experienced upper gastrointestinal bleeding as a negative outcome linked to an interaction, leading to the death of one. Interactions fell into risk category C (indicating significant interaction potential), with 'major' severity and pharmacodynamic type. The most frequent clinically relevant PPI was clopidogrel-omeprazole, affecting 13 patients. Hospitalization duration and prescribed medication count were identified as prognostic factors for clinically significant interactions. The findings highlight active pharmacovigilance's importance in detecting PPIs and predictive factors that may impact patient outcomes.

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27. DESIGN OF NANOSYSTEMS FOR THE ENCAPSULATION OF IMMUNOMODULATORS IN THE DEVELOPMENT OF VACCINES. Diseño de nanosistemas para la encapsulación de inmunomoduladores en el desarrollo de vacunas

Resúmen:
Vaccines have been positioned as a powerful health tool in combating various viral and bacterial infections, saving 2-3 million lives each year. Despite the program immunization, there is still a gap in access, and around 20 million children worldwide do not receive adequate coverage of basic vaccines. Since the first vaccine, a huge arsenal of formulations has been developed to treat or prevent diseases associated with pathogens like polio, measles, tetanus, rubella, influenza, and recently SARS-CoV-2. Despite the new vaccines are being developed to be safer, they are less immunogenic, so it is necessary to have formulations capable of activating the immune system or carrying molecules that are capable of activating it. One strategy is to have particles with similar sizes to viruses, like nanoparticules. For that reason, in the present investigation, we designed a new lipid-based nanosystem that encapsulates resiquimod, a Toll-like receptor agonist molecule, to reduce its dose, increase its solubility, and protect it from ambient conditions. The newly designed nanosystem has nanometric size, monomodal distribution, and positive zeta potential. In addition, this lipid nanosystem encapsulates resiquimod with high efficacy (~100%) and can release it in a fashion first order following kinetics. This system presents high stability under physiological and storage conditions and a good safety profile in the Raw 264.7 cell line. These excellent results show that the lipid system could be used as a future platform to associate an antigen to generate a future immunization system.

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28. SELF-ASSEMBLY COARSE-GRAINED PHOSPHOLIPIDS COATING AROUND THE FULLERENE C60 NANOPARTICLES. Recubrimiento de fosfolípidos de grano grueso autoensamblado alrededor de las nanopartículas de Fullerene C60

Resúmen:

Fullerene C60 nanoparticles, with their spherical structure, high chemical stability, and functionalization capability, offer promising applications in biomedicine. These structural properties allow them to play a crucial role in targeted drug delivery, making them an important target for research into their functionalization with phospholipids. In this study, we will use the GROMACS 2023.3 simulation engine and the Martini 2 force field to carry out our protocol based on lipid self-assembly in two models of fullerene C60 nanoparticles, named F216 and F576, according to their carbon numbers. The nanoparticles were placed at the center of 15x15x15 nm periodic boxes, which were solvated and ionized according to the specific conditions of each system, and were supplemented with 50, 100, 150, and 200 POPC and POPS lipids in separate systems. Unbiased molecular dynamics simulations were conducted for 1 µs for each system (a total of 8 systems), during which the compactness of the nanoparticles was observed over time. F216 nanoparticles functionalized with POPC and POPS lipids demonstrated better compactness, as assessed by their radial distribution function, making these models suitable for free energy sampling using umbrella sampling in a mammalian-type membrane. This setup will involve positioning a collective variable that ranges from 0 to 6.5 nm, considering the centers of mass of both bodies, which will be subjected to a constant force pulling. We will perform umbrella sampling with 600 ns windows to accurately sample the free energy landscape. With the obtained data, we will calculate the energy differences in a mammalian-type membrane model, which has shown that the affinity of fullerene nanoparticles with POPC lipids is superior to that with POPS in mammalian membranes, which is promising for advancing the development of new targeted therapies and biomedical applications.

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29. HUMANIZED L-ASPARAGINASE: A NOVEL CHIMERIC ENZYME FOR ALL TREATMENT. L-Asparaginasa Humanizada: Una enzima quimérica novedosa para el tratamiento de LLA

Resúmen:

Acute lymphoblastic leukemia (ALL) is the most common cancer among children worldwide, characterized by an overproduction of undifferentiated lymphoblasts in the bone marrow. The treatment of choice for this disease is the enzyme L-asparaginase (ASNase) from bacterial sources. ASNase hydrolyzes circulating L-asparagine in plasma, leading to starvation of leukemic cells. The ASNase formulations of E. coli and E. chrysanthemi present notorious adverse effects, especially the immunogenicity they generate, which undermine both their effectiveness as drugs and patient safety. In this study, we developed a humanized chimeric enzyme from E. coli L-asparaginase which would reduce the immunological problems associated with current L-asparaginase therapy. For these, the immunogenic epitopes of E. coli L-asparaginase (PDB: 3ECA) were determined and replaced with those of the less immunogenic Homo sapiens asparaginase (PDB:4O0H). The structures were modeled using the Pymol software and the chimeric enzyme was modeled using the SWISS-MODEL service. A humanized chimeric enzyme with four subunits similar to the template structure was obtained, and the presence of asparaginase enzymatic activity was predicted by protein–ligand docking.

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30. FORMULATION OF A BONE GRAFT FROM DURVILLAEA ANTARCTICA (COCHAYUYO). FORMULACIÓN DE UN INJERTO ÓSEO A PARTIR DE DURVILLAEA ANTARCTICA (COCHAYUYO)

Resúmen:

Bone fractures are an increasing clinical challenge, particularly in aging and sedentary populations. Tissue engineering offers an innovative approach to address these issues, with marine algae like Durvillaea antarctica, rich in sulfated polysaccharides, emerging as promising biomaterials for biomedical applications. Objective: To evaluate the biocompatibility and osteogenic differentiation potential of a bone graft formulated with Durvillaea antarctica, fibrin, gelatin, and hydroxyapatite. Methods: Four matrices were prepared; the first included 3% cochayuyo powder (C) and 1.5% gelatin (G), while the others contained 3% C, 1.5% G, and increasing hydroxyapatite concentrations (1%, 5%, and 10%, respectively). The matrices were stabilized using freeze-drying and an EDC/NHS crosslinking protocol. They were characterized by swelling percentage and degradation rate. Human Bone marrow-derived mesenchymal stem cells (HBMSCs) viability on the matrices was assessed using a resazurin assay, and ELISA measured VEGF expression. Results: The matrices exhibited 600–1400% swelling and remained intact in a saline medium for two weeks. HBMSCs viability increased by the third day of culture. The highest VEGF expression was observed in the matrix with 10% hydroxyapatite and the fibrin clot. Conclusions: The formulated matrices demonstrated favorable properties, supporting their potential application in bone tissue engineering.

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31. HEPATOPROTECTION OR HERB-INDUCED LIVER DISEASE, THE DUAL FACETS OF NATURAL COMPOUNDS USE – A CASE STUDY ON AZORELLA COMPACTA. Hepatoprotección o hepatotoxicidad inducida por hierbas, las dos caras del uso de compuestos naturales: un estudio de caso sobre Azorella compacta

Resúmen:
Azorella compacta (A. compacta) is a shrub enriched in diterpenoids, endemic to the Andean Altiplano, including regions of Chile, where it has been traditionally used in folk medicine for several disorders such as diabetes, hepatic and inflammatory diseases. While its hypoglycemic properties have been documented, its potential effects on liver disease have yet to be thoroughly explored. This study aimed to investigate the hepatoprotective capacity of A. compacta organic extract in a model of high-fat diet (HFD)-induced liver diseases. Male C57BL/6 mice were fed with a 45% high-fat diet (HFD) to induce liver steatosis and received A. compacta fractions (collected in the El Tatio geysers area) in drinking water for two weeks (13,4 g each). After this treatment, hepatic parameters were evaluated. The A. compacta extract did not mitigate hyperglycemia; instead, it exacerbated hepatic dysfunction, as evidenced by increased serum levels of hepatic transaminases (AST and ALT), reduced albumin, and elevated bilirubin, indicating hepatic damage. The histopathological analysis further revealed that the herb failed to ameliorate HFD-induced liver damage, including steatosis, inflammation, and necrosis. These findings suggest that A. compacta may induce herb-induced liver disease (HILI). Caution is warranted in its use until further studies can clarify its safety profile in hepatic disease settings.

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32. CHEMICAL CHARACTERIZATION OF ULVAN POLYSACCHARIDE AND EVALUATION OF ITS POTENTIAL ACTIVITY AS A VACCINE ADJUVANT. Caracterización química del polisacárido ulvano y evaluación de su potencial actividad como adyuvante de vacunas.

Resúmen:
Ulvan is a sulfated heteropolysaccharide that can stimulate and activate the immune response in vitro. The objective of this research was to characterize and evaluate in a human cell model the immunostimulant properties of ulvan extracted from Ulva spp collected in Algarrobo, Chile. Ulvan characterized by spectrophotometric methods showed that it is composed of 47.6% of total sugars, 14.3% of which corresponds to uronic acids, 8.9% of sulfates and an average molecular weight of 40000. As for FTIR, the stretching and vibration bands at 3340.3 cm-1 correspond to uronic acids, at 2943.4 cm-1 to rhamnose and at 1244.2 cm-1 and 847.3 cm-1 to sulfate groups. GC-MS confirmed the presence of rhamnose, xylose, glucose and galactose in the ulvan composition. HL60 cells differentiated to macrophages were cultured with three concentrations of ulvan (25, 50 and 100 µg/mL) and cell viability was greater than 90% at the lower ulvan concentrations. The immunostimulatory action indicated that ulvan is able to activate the co-stimulatory molecules CD86, promote the release of cytokines IL-6, IL-10 and IL-4 and nitric oxide. The results indicate that ulvan is non-toxic at any concentration and is a precursor of inflammation, so it is able to activate inflammatory pathways that would allow a controlled activation of the immune system, being a possible candidate for studies as a vaccine adjuvant.

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Socio Patrocinante: Caroline R.Weinstein-Oppenheimer

33. EFFECT OF MITOCHONDRIAL REACTIVE OXYGEN SPECIES PRODUCTION ON THE EXPRESSION OF PROINFLAMMATORY MEDIATORS IN BOVINE FIBROBLAST-LIKE SYNOVIOCYTES. Efecto de la producción de especies reactivas de oxígeno mitocondriales sobre la expresión de mediadores proinflamatorios en sinoviocitos tipo fibroblasto bovinos.

Resúmen:
Lameness in cattle is a major cause of animal discomfort and dairy productivity loss, impacting both animal welfare and economic outcomes. Joint inflammation, a common factor in lameness, involves significant production of inflammatory mediators largely attributed to fibroblast-like synoviocytes (FLS), which express IL-1β, IL-6, IL-8, and COX-2. This inflammatory process is associated with increased production of reactive oxygen species (ROS), primarily mitochondrial ROS (mtROS), which may act as signaling agents during inflammation. This study aimed to assess the impact of mtROS on the expression of these mediators in bovine FLS stimulated by bovine TNF-α. Bovine FLS were isolated from carpometacarpal joints and cultured in a controlled environment. Cells were treated with rotenone, antimycin A, oligomycin A, or bTNF-α to assess mtROS production via MitoSOX staining and flow cytometry, with additional treatments using antioxidants N-acetylcysteine (NAC) and Mito-Tempo. The expression of proinflammatory mediators was analyzed by RT-qPCR after bTNF-α stimulation. Statistical analysis used ANOVA and Tukey or Kruskal-Wallis tests, considering $p < 0.05$ as significant. Results showed that NAC and Mito-Tempo significantly reduced the bTNF-α-induced expression of IL-6, IL-8, pro-IL-1β, and COX-2, suggesting a role for ROS in modulating inflammation in bovine FLS. However, bTNF-α did not significantly increase mtROS production. Inhibition of electron transport chain complexes I, III, and V did increase mtROS production, with varied responses depending on antioxidant presence. The findings suggest mtROS may contribute to the inflammatory response, however cytoplasmic ROS, possibly from NADPH oxidase, could play a more prominent role. Further studies are needed to explore ROS origin and mitochondrial interactions in ruminant joint pathologies.

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34. β-HYDROXYBUTYRATE DISRUPTS THE GLYCOLYTIC METABOLISM OF BOVINE NEUTROPHILS AND IMPAIRS THEIR PHAGOCYTIC CAPACITY AGAINST Staphylococcus aureus. β-hidroxibutirato perturba el metabolismo glicolítico de los neutrófilos bovinos y desmejora su capacidad fagocítica contra Staphylococcus aureus.

Resúmen:
In the early lactation, high-producing dairy cows suffer a marked negative energy balance with excessive adipose tissue mobilization and hyperketonemia, which has been strongly associated with mammary and reproductive infections and linked to neutrophil dysfunction. Bovine neutrophils express TLR2 and the signaling through heterodimer TLR2/1 is pivotal for the recognition and response against Staphylococcus aureus (S. aureus). Since neutrophils rely almost exclusively on glycolytic metabolism for energy, fueling it with exogenous glucose and glycogen stores, we hypothesize that beta-hydroxybutyrate (BOHB), the major ketone body in the blood of ketotic cows, may alter the glycolytic metabolism of neutrophils and limit their phagocytic ability against Gram-positive bacteria. The effect of BOHB over metabolic and signaling mechanisms were assessed by stimulating neutrophils with the TLR2/1 agonist Pam3CSK4. By metabolic flux analysis we demonstrated that BOHB decreases the glycolysis and ATP rate production in unstimulated neutrophils. Furthermore, BOHB also truncates the TLR2/1 agonist-induced glycolytic reprogramming of neutrophils, leading to a lower ATP production during proinflammatory stimulation. Along with the above, BOHB downregulated the Pam3CSK4-induced overexpression of the glycolytic enzymes hexokinase 2 and 3 (HK2, HK3), pyruvate kinase M2 (PKM2) and lactate dehydrogenase A (LDHA). Interestingly, BOHB also decreased GLUT1 and GLUT3 translocation and extracellular glucose uptake, while reversing the Pam3CSK4-induced drop in glycogen stores. Finally, preincubation of neutrophils with BOHB, as well as with the pharmacological inhibitors of glycolysis 2-DG and 3PO, and the glycogenolysis inhibitor CP91,149, decreased in vitro phagocytosis of S. aureus. These results suggest that BOHB disrupts the glycolytic reprogramming of neutrophils during the proinflammatory challenge and subsequently reduces their ability to phagocytose Gram-positive bacteria.

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35. IMPORTANCE OF THE DETERMINATION OF BASIC QUALITY PARAMETERS IN NATURAL PRODUCTS: EXAMPLE OF HONEY AS A VETERINARY THERAPEUTIC AGENT. Importancia de la determinación de parámetros básicos de calidad en productos naturales: ejemplo de la miel como agente terapéutico veterinario

Resúmen:
Honey is a highly concentrated viscous solution of flower sugars and proteins, enzymes and amino acids derived from bee crops. In addition to its nutritional properties, honey has many health benefits and therapeutic effects. However, as honey is a naturally occurring product, it is necessary to standardize it to make it a medical grade product. Standardization involves the determination of different basic quality parameters such as: pH, humidity, electrical conductivity, sugars, color, diastatic activity, hydroxymethylfurfural (HMF) content, antioxidant capacity, total polyphenol content, melissopalynological analysis and chromatographic profile. In addition, we must confirm the absence of contaminating agents or spore-producing pathogens. By determining these basic parameters, we have found that some of them remain stable over time and in the different samples tested. However, there are some that allow us to identify if the honeys were adulterated or if they have lost their therapeutic properties. In this sense, the concentration of sugars, diastatic activity and HMF content can show whether the honeys were adulterated and therefore do not comply with their basic characteristics. In addition, we have noticed that after performing a PCR-RT molecular analysis of the origin of the honeys, these results do not agree with the traditional melissopalynological analysis (microscopic observation of the pollen). Finally, we must not forget that the parameters usually used to determine the quality of honeys must be associated with efficacy and safety tests, carried out firstly in vitro, according to the therapeutic use of honey, and secondly in vivo, to confirm the beneficial effect.

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36. HIGH-POTASSIUM DIET REDUCES THE DIABETES EFFECTS AT THE VASCULAR ENDOTHELIUM LEVEL. Una dieta rica en potasio reduce los efectos de la diabetes a nivel del endotelio vascular.

Resúmen:
Previous studies from our laboratory showed that nitric oxide (NO) donors induced dilatation in rat vascular mesentery of streptozotocin (STZ)-induced diabetes is reduced. In turn, studies in hypertensive Dahl rats showed that a high-potassium diet increases vascular relaxation mediated by NO in carotid arteries. We evaluated the effect of a high-potassium diet in STZ-diabetic rats, and determined: 1. The plasma levels of the endogenous eNOS inhibitor asymmetric dimethyl arginine (ADMA). 2. The exogenous ATP induced NO production through selective NO fluorophore DAF-FM in endothelial cell cultures. 3. The release of ATP and its metabolites elicited by mechanical stimuli in endothelial cell cultures from STZ-diabetic rats treated with high potassium diet. ADMA and its symmetric dimethyl arginine (SDMA) analogue, ATP/metabolites were determined by fluorescence detection. ADMA plasma levels were increased in STZ-diabetic rats (1.38 ± 0.13 (9) to 1.85 ± 0.18 (4) µM, $p<0.05$); the high potassium diet reduced these levels (0.97 ± 0.24 (4) µM, $p<0.05$). 100 µM ATP induced an increase of NO in endothelial cells, an effect reversed by pre-incubation with 100 µM ADMA. Endothelial cells from STZ-diabetic rats have increased basal ATP release (39.9 ± 3.8 (96) vs 56.8 ± 7.3 (53)), value reduced in cells treated with a high potassium diet (18.9 ± 3.8 (24) pmol/mg protein, $p < 0.05$). The ATP released by mechanical stimulation was similar in control and STZ-diabetic rats (182.0 ± 17.2 (36) vs 143.8 ± 23.3(19) pmol/mg protein). Cells from STZ-diabetic rats fed with a high potassium diet released less ATP (68.8 ± 16.7 (8) pmol/mg protein, $p < 0.05$). Thereafter, we conclude that dietary potassium is beneficial to decrease vascular alteration induced by diabetes.

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37. ALDOSTERONE CAUSES DUAL RAPID VASCULAR EFFECTS, BIOMEDICAL IMPLICATIONS. Efectos vasculares rápidos duales de aldosterona, implicaciones biomédicas

Resúmen:
Aldosterone (A) exerts biological effects not associated with the classical nuclear mineralocorticoid receptor (MR), which require a lag time of hours to days. A series of A effects are observed in the minute range, in resemblance of estrogen actions referred to as rapid effects. To ascertain rapid vascular effects of A in the vascular system, the rat arterial mesenteric bed was perfused with A (0.1-100 nM) in tissues precontracted with 50 µM noradrenaline, a condition which favors vasodilation. Using this preparation, we ascertained: 1. The EC50 value of A expressed as percentage of the noradrenaline contracture. 2. The endothelium requirement and 3. The role of eNOS. In addition, direct measurements of NO production in isolated endothelial cells were also examined. Results indicate that: the EC 50 is 0.41nM, a value compatible with circulating A levels; the maximal vasodilation observed was 32.5 ± 2.1%, effect significantly reduced by 5 µM spironolactone or 2uM eplerenone treatment. Endothelial denudation following 55 sec saponin 0.1% perfusion, the A-induced vasodilation was reduced (30-80%) in 5/5 cases followed by a brief vasoconstriction that lasted 1-2 min, an indication of dual rapid vascular effects of A. eNOS inhibition by perfusion with 300 µM L-NAME, significantly reduced the vasodilation, in all preparations vasocontractile responses were attained with varying A concentrations. Significant NO production within 5 min was observed in cultured endothelial cells treated with 1-10 nM A, compatible with the vasodilatation. We conclude that A causes eNOS activation in endothelial cells while contraction of the vascular smooth muscle cells, especially evident following endothelium removal. Vascular effects are counter balanced limiting the magnitude of the endothelial vasodilation.

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38. RATIONAL DESIGN OF PEPTIDE IMITATOR OF RUTHENIUM RED INHIBITOR AS A MODULATOR OF THE TASK-1 ION CANNEL. Diseño Racional de un péptidido imitador del Inihibidor Rojo de Rutenio como modulador del canal iónico TASK-1

Resúmen:
Potassium channels are membrane proteins that enable selective K+ ion flow. These channels fall into three main families: Kv (voltage-gated), Kir (inward rectifying), and K2P (two-pore). K2P channels are involved in key physiological processes like action potential propagation, heart rate regulation, and pain sensation. The TASK subfamily of K2P channels includes TASK-1 (KCNK3), TASK-3 (KCNK9), and TASK-5 (KCNK15). TASK-1 and TASK-3 share 58.9% sequence identity, and TASK-5 shares 51.4% and 55.1% identity with TASK-1 and TASK-3, respectively. These channels are emerging therapeutic targets for conditions such as atrial fibrillation and pulmonary hypertension. A notable feature of K2P channels is the extracellular cap, which directs ion flow through tunnel-like extracellular ion pathways (EIPs) into the selectivity filter. Ruthenium Red (RuR) inhibits TASK-3 by interacting with the EIP but fails to inhibit TASK-1 due to an unfavorable interaction with residue K70. However, a K70E mutation in TASK-1 renders it sensitive to RuR inhibition. Targeting the EIP of TASK-1 offers a strategic approach to developing selective inhibitors. In this study, we designed a peptide to interact with key EIP residues in TASK-1. Molecular dynamics simulations, performed in a POPC lipid bilayer under physiological conditions, showed that the peptide interacts with K70 of each TASK-1 monomer, mimicking Ruthenium Red's inhibition mechanism. This highlights the peptide's potential as a TASK-1 channel inhibitor.

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39. 17-β-ESTRADIOL AND DAIDZEIN INDUCE NO PRODUCTION IN ENDOTHELIAL CELLS THROUGH THE PI3K, PKA, AND EGF PATHWAYS. El 17-β-estradiol y la daidzeina indicen producción de NO en células endoteliales a través de las vías PI3K, PKA y EGF.

Resúmen:
Endothelial cells express receptors that mediate rapid estrogen responses coupled to GPER a G protein-coupled receptor. We investigated whether 17-β-estradiol (E2) and daidzein (DAI), a natural phytoestrogen, activate similarly GPER to elicit nitric oxide (NO) production, a potent vasodilatator. We hypothesized that E2 and DAI trigger NO production through different intracellular signaling pathways. E2 and DAI NO production in individual endothelial cells was quantified following DAF-FM incubation, a NO-selective fluorophore. Fluorescence elicited by ligands was quantified using confocal microscopy. Both E2 and DAI-induced within minutes NO production; NO-DAF signals were blocked by G-36 (a selective GPER antagonist) or fulvestrant (nuclear estrogen receptor antagonist), and by the combination of both antagonists, indicating several E2 receptors in these cells. PI3K inhibitors (wortmannin or LY-294002) blocked more E2-induced NO production than that elicited by DAI. In contrast, desmethylxestospongin-B, an IP3 receptor antagonist abolished NO production by both ligands, supporting intracellular calcium release to a same extent by either ligand. H-89 blocked to a larger extent DAI-induced NO production compared to E2 ($P<0.0001$). Epidermal growth factor (EGF)-induced signals and treatment with AG-1478, an EGF receptor kinase inhibitor, decreased the DAI-induced response by 90% ($P<0.0001$), whereas the E2-induced NO production was decreased only by 53% ($P<0.0001$). It is concluded that E2 and DAI activate GPER estrogen receptors, through the activation of PI3K, PKA and EGF which trigger rapid NO synthesis, consonant with non-nuclear receptor activation. It follows that the intracellular pathways activated by E2 and DAI are distinct, a finding attributed to functional selectivity.

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40. STUDY OF THE CARDIOPROTECTIVE EFFICACY OF ENDOTHELIAL EXTRACELLULAR VESICLES CONTAINING PHARMACOLOGICALLY ACTIVATED ANGIOTENSIN CONVERTING ENZYME 2 (ACE2). Estudio de la eficacia cardioprotectora de vesículas extracelulares endoteliales que contienen enzima convertidora de angiotensina (ECA2) activada farmacológicamente

Resúmen:
Introduction: Endothelial extracellular vesicles are cardioprotective against ischemia/reperfusion injury. However, the mechanism mediating this effect and whether this effect could be enhanced through pharmacological activation of Angiotensin Converting Enzyme 2, using diminazene aceturate, remains to be elucidated. ACE2 is a protein with known cardioprotective functions, but its role in the protective effects of endothelial EVs is still unknown Objectives: Evaluate the cardioprotective effect of endothelial EVs, the role of ACE2 in this effect and whether this could be enhanced through pharmacological activation of ACE2 Methods: HUVEC were treated with different concentrations of DIZE. Cytotoxicity was determined using an LDHassay. Activity of ACE2 was determined by a fluorometric reaction. Expression of ACE2 was determined by ELISA. HUVEC were treated with 1µM of DIZE and EVs were isolated from HUVECs using size exclusion chromatography. Size and concentration of EVs was obtained by NanoSight, whereas morphology by Electronic Microscopy. Cardioprotection of EVs was evaluated by determination of infarct size using adult C57BL/6 mice hearts in ex vivo ischemia/reperfusion (CICUA-CQyF2023-53). Data is presented as mean ± SEM and analyzed using One Way ANOVA test with Dunn's multiple comparison analysis Results: No concentration of DIZE had cytotoxic effects on HUVECs. Activity of ACE2 was detectable under every condition studied. Treatment of HUVEC with DIZE at all concentrations causes a significant increase in ACE2 protein levels, reaching its maximum at 1µM and 10µM. Treatment with 1µM DIZE does not alter the size, concentration, or morphology of EVs. EVs presented a cup-shaped form and the expression of ACE2. EVs from HUVECs treated with 1µM DIZE reduced infarct size Conclusion: DIZE is not cytotoxic to HUVECs, increases ACE2 protein levels and does not alter size, concentration, or morphology of EVs. EVs from HUVEC treated with 1µM DIZE reduced infarct size.

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41. DEVELOPMENT OF A CHRONIC CARDIOTOXICITY MODEL INDUCED BY DOXORUBICIN IN FEMALE C57BL/6 MICE. Desarrollo de un modelo de cardiotoxicidad inducida por Doxorrubicina en ratones hembra C57BL/6

Resúmen:
Introduction: Cancer is one of the major public health challenges worldwide, with breast cancer being the most prevalent type among women. Cardiotoxicity caused by antineoplastic treatments remains a significant limitation to the use of agents like Doxorubicin (DOX). Given that female sex is a risk factor for cardiotoxicity and preclinical research predominantly relies on male models, our group aimed to develop a female animal model that reflects the pathophysiological characteristics of clinical cardiotoxicity. This model will allow us to test various hypotheses regarding the molecular basis of this condition. Methods: Female C57BL/6 mice, aged 10-12 weeks, were subjected to weekly injections of DOX (intraperitoneally), reaching a cumulative dose of 30 mg/kg by the fifth week, followed by a 5-week observation period. Cardiotoxicity was assessed through: (1) structural alterations in the heart (heart weight to tibia length ratio, HW/TL, n=11), (2) hemodynamics (echocardiography, n=8), and (3) mRNA expression profiles from the left ventricle (RNA-seq, n=4). CBA#1173 FMUCH. Results: The DOX-treated animals exhibited two response patterns: premature death during follow-up (PD) and normal death by euthanasia after completing the follow-up (ND). Both subgroups, PD (4.74 ± 0.63) and ND (6.01 ± 0.12), showed a significant reduction (ANOVA, $p<0.0003$) in HW/TL compared to the control group (CT, 6.69 ± 0.56). In terms of hemodynamics, the ND group (77.36 ± 6.82%) developed a reduced ejection fraction (Student's t-test, $p<0.0026$) compared to CT (87.27 ± 4.78%). Both ND and PD groups displayed distinct mRNA expression profiles compared to CT, such as DNA break repair pathways in ND (GO:0010792 & GO:0045002) and cytoplasmic stress granule pathways in PD (GO:0010494). Conclusion: Our developed animal model successfully recapitulates clinically relevant characteristics, including the subgroups of cardiotoxicity observed in humans.

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42. MaR1 ENHANCES IN SITU PROLIFERATION OF RESIDENT MACROPHAGES IN A MURINE MODEL OF EARLY DIABETIC CARDIOMYOPATHY. MaR1 aumenta la proliferación in situ de macrófagos residentes en un modelo murino de cardiomiopatía diabética temprana

Resúmen:
Clinical and experimental studies have demonstrated the existence of a specific diabetic cardiomyopathy, where different pathophysiological processes contribute to inflammation, fibrosis, hypertrophy, cardiomyocyte death and finally systolic and diastolic dysfunction. Specialized proresolving mediators (SPMs) are agonists with the potential to stimulate key cellular events in the resolution of inflammation. Evidence suggests that maresin1 (MaR1), an omega-3-fatty acid derived SPM, promotes resolution of inflammation and exerts cytoprotective effects by inhibiting neutrophil infiltration and proinflammatory cytokines and promoting polarization to M2 macrophages. Our objective was to evaluate the effects of MaR1 on morphophysiological parameters of cardiac injury and on the density of cardiac macrophage subpopulations. Diabetes was induced in male C57BL/6 mice by treatment with streptozotocin (50 mg/Kg) 5 days. After 4 weeks, mice were treated either with daily i.p. injections of MaR1 (4 ng/g) or vehicle for 4 weeks. A group of normoglycemic mice was used as control (n=4-6 each group). Cardiac hypertrophy and fibrosis were analyzed histologically, functional parameters by echocardiography and leucocytes populations by flow cytometry. Data is presented as average ± SD and was analyzed by one-way ANOVA. Diabetic mice treated with MaR1 presented reduced the area of cardiac fibrosis (%): 4.9±2.8 control, 6.7±5.1 diabetic and 4.4±2.7 diabetic+MaR1, $p<0.05$, but increased myocyte diameter (µm): 16.0±5.2 control, 22.6±4.3 diabetic and 34.8±11 diabetic+MaR1, $p<0.05$. Ejection fraction and fractional shortening were not different among groups ($p>0.05$). MaR1 treatment re-established the reduced levels of resident cardiac macrophages (%): 5.1±2.1% control, 1.7±1.3% diabetic and 5.5±2.5% diabetic+MaR1 ($p<0.05$). These results suggest that MaR1 reduces the fibrotic process in the early stage of DCM, along with restoring the population of resident macrophages of embryonic origin.

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43. RHO ASSOCIATED KINASE (ROCK) 1 AND 2 MEDIATE ENDOTHELIAL INFLAMMATION CAUSED BY TRYPANOSOMA CRUZI, IN IN VITRO MODELS OF HUMAN VASCULAR ENDOTHELIUM. Las kinasas dependientes de Rho (ROCK) 1 y 2 median la inflamación endotelial provocada por Trypanosoma cruzi en modelos in vitro de endotelio vascular.

Resúmen:
Chronic Chagasic cardiomyopathy (CCC), caused by the parasite protozoan Trypanosoma cruzi (T. cruzi) is the most severe manifestation of Chagas Disease. The major determinant of the pathophysiology is a sustained inflammation, caused by the persistence of the parasite in myocardical tissue. CCC involves an inflammatory vasculopathy. Although it is known that this endothelial inflammation is mediated through the activation of the transcriptional factor NF-κB, the exact mechanism is not completely elucidated. Rho A is a small GTPases that, through their main effector proteins called Rho-associated kinase (ROCK) 1 and 2, regulate the actomyosin cytoskeleton. Recently, it was shown that ROCK activation by T. cruzi mediates NF-κB activation via RhoA/TLR4 in human macrophages. Thus, this work aims to identify the effect of the pharmacological inhibition of ROCK by Y-27632 in the endothelial inflammation caused by T. cruzi. For that purpose, human HMVEC-C and EAHy926 cells were pre-incubated with the ROCK inhibitor (Y-27632; 10 µM) or vehicle (DMSO 0,1%) for 1 hour, and then incubated with T. cruzi DM28 (1:1) for 6, 12 and 24 h. The expression of adhesion molecules was evaluated by RT-qPCR, the pro-inflammatory cytokine secretion by LUMINEX and the human U937 monocyte adhesion by microscopy. It was shown that the inhibition of ROCK by Y-27632 significantly decreases the expression of cell adhesion molecules, the pro-inflammatory cytokine secretion, and the adhesion of U937 monocytes to the endothelium, in the presence of T. cruzi at all time. These results suggest that ROCK inhibition is a potential pharmacological target to prevent endothelial inflammation caused by T. cruzi in CCC.

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44. SCAVENGERS RECEPTORS IN CASTRATION RESISTANT PROSTATE CANCER. Receptores Scavenger en el cáncer de próstata resistente a la castración.

Resúmen:
Introduction: Scavenger receptors are known to enhance various tumor progression parameters, including angiogenesis, invasion, and cell proliferation. This effect has been observed in multiple cancer types and may play a significant role in castration-resistant prostate cancer (CRPC), the most lethal form of prostate cancer. Objective: This study aims to assess the expression of scavenger receptors in CRPC and castration-sensitive cells. Additionally, it investigates the impact of oxidized LDL (oxLDL) treatment on scavenger receptor expression and endocytosis under androgen-deprivation conditions in vitro. Methodology: Expression and endocytosis analyses were conducted using RT-qPCR, Western blot, and immunocytochemistry on the LNCaP and C4-2B cell lines for various scavenger receptors, including CD36, CD68, COLEC12, CXCL16, MSR1, SRB1, SCARF1, LOX-1, and LDLR. The experiments included androgen deprivation and dihydrotestosterone (DHT) treatments, as well as oxLDL incubation to examine receptor expression and endocytosis. Results: The findings revealed higher scavenger receptor expression in the C4-2B cell line compared to LNCaP, as demonstrated by RT-qPCR, Western blot, and immunocytochemistry. Additional replicates and further studies are necessary to confirm these observations. Conclusion: The results suggest that oxLDL and scavenger receptors may play a significant role in the progression of androgen deprivation in CRPC in C4-2B and LNCaP cell lines. However, further research is needed to validate these findings.

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45. OXIDIZED LOW-DENSITY LIPOPROTEIN REDUCES TAXANE CYTOTOXICITY IN CASTRATION RESISTANT PROSTATE CANCER CELLS VIA NF-ΚB ACTIVATION AND UPREGULATION OF RESISTANCE MARKERS TUBB3 AND MDR1. La lipoproteína de baja densidad oxidada reduce la citotoxicidad de los taxanos en células de cáncer de próstata resistente a la castración mediante la activación de NF-κB y la sobreexpresión de los marcadores de resistencia TUBB3 y MDR1

Resúmen:
The treatment of advanced prostate cancer typically begins with androgen deprivation therapy (ADT). However, many patients develop resistance, progressing to castration-resistant prostate cancer (CRPC), which is then treated with Docetaxel. Some patients also develop resistance to Docetaxel, requiring the use of Cabazitaxel; however, the effectiveness of this drug is limited due to the rapid emergence of resistance in a significant number of patients. The NF-κB signaling pathway, known to be involved in Docetaxel resistance, may also contribute to Cabazitaxel resistance by promoting the expression of resistance genes such as ABCB1 and TUBB3. Additionally, oxidized low-density lipoprotein (oxLDL) is elevated in the plasma of patients with CRPC, and it has been shown to promote NF-κB activation in other pathologies, although its role in chemotherapy resistance remains unclear. We hypothesize that NF-κB signaling activation by oxLDL induces resistance to Docetaxel and Cabazitaxel through the overexpression of therapy resistance markers, such as MDR1 and TUBB3, in CRPC cell models. Results showed an increase in NF-κB p65 and p52 expression, as well as TUBB3 and MDR1, along with greater cell survival in oxLDL-treated lines exposed to Docetaxel or Cabazitaxel. We also observed overexpression of scavenger receptors for oxLDL at different disease stages, which may contribute to the observed effects via oxLDL interaction. We conclude that NF-κB activation mediated by oxLDL induces taxane resistance through the overexpression of MDR1 and TUBB3 in the CRPC cell models studied.

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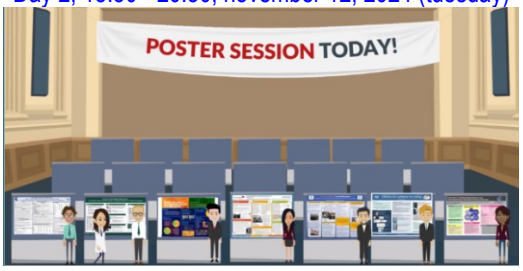
46. EFFECTS OF BOLDINE, LAUROLITSINE, LAUROTETANINE, OR N-METHYL-LAURETETANINE FROM PEUMUS BOLDUS ON THE MODULATION OF THE IMMUNE-INFLAMMATORY RESPONSE AND INHIBITION OF BONE RESORPTION DURING EXPERIMENTAL PERIODONTITIS. Efectos de boldina, laurolitsina, laurotetanina o N-metillaurotetanina de Peumus boldus en la modulación de la respuesta inmuno-inflamatoria e inhibición de la resorción ósea durante la periodontitis experimental.

Resúmen:
Periodontitis originates from dysbiotic changes in subgingival microbial communities, causing immune system dysregulation and disruption of alveolar bone balance. This increases RANKL production, which activates osteoclasts and promotes bone resorption. The imbalance between Th17 and Treg lymphocytes favors inflammation and RANKL expression. M1 macrophages promote the differentiation of Th1 and Th17 lymphocytes, while M2 macrophages promote the differentiation of Th2 and Treg cells. Boldine has inhibited bone resorption in previous animal models. This study evaluated four structurally related alkaloids from Peumus boldus Molina—boldine, laurolitsine, laurotetanine, and N-methyllaurotetanine—in modulating the immune-inflammatory response and alveolar bone resorption during experimental periodontitis. Periodontitis was induced in 6-8-week-old C57BL/6 mice by ligation. After ligation, an oral dose of 20 mg/kg of each alkaloid was administered daily for 10 days. Alveolar bone loss was quantified based on anatomical parameters. Cytokine expression levels and transcription factors in periodontal tissues were measured by RT-qPCR. The proportion of Treg lymphocytes in cervical lymph nodes was assessed by flow cytometry, and periodontal osteoclasts were evaluated by TRAP+ staining. Boldine and laurolitsine reduced alveolar bone loss. All alkaloids reduced the expression of RANKL, OPG, and FOXP3. Laurolitsine decreased IL-17A, while N-methyllaurotetanine increased IL-10. No differences were observed in lymphocyte subpopulations in the analyzed cervical lymph nodes. Boldine and laurolitsine reduce alveolar bone loss, and all alkaloids modulated the immune-inflammatory response, suggesting their potential as treatments for periodontitis.

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PANEL COMMUNICATIONS

Day 2, 18:30 - 20:30, november 12, 2024 (tuesday)



1. CONTRIBUTION OF DYNAMINS TO CYTOSKELETON-DEPENDENT SPINOGENESIS IN HIPPOCAMPAL NEURONS OF 3XTG MICE, A MURINE MODEL OF ALZHEIMER'S DISEASE. Contribucion de las dinaminas a la espinogenesis dependeinte del citoesqueleto en neuronas hipocampales de ratones 3xtg, modelo murino de la Enfermedad de Alzheimer.

Resúmen:

Alzheimer's disease (AD) is the most common dementia in elderly. It is characterized by loss of synapses and dendritic spines, major sites of synaptic contact in the mammalian brain. The spine loss correlate with the onset of cognitive decline in AD. Dendritic spines are highly dynamic structures that depend on cytoskeleton organization and remodeling; therefore, it is feasible that promoting cytoskeleton remodeling could prevent dendritic spine and synaptic loss in AD. As a direct modulation of cytoskeleton is potentially cytotoxic, an alternative is to modulate cytoskeleton-regulatory proteins. Here we evaluated whether pharmacological and genetic modulation of dynamins, large GTP-ases that remodel actin and microtubule cytoskeleton in different cells, could prevent spine loss in the context of AD. Hippocampal neurons, were primarily cultured from wildtype (WT) and 3XTg mice, a murine model of AD. Dynamins were pharmacologically modulated using the experimental drug BIST23, a promoter of dynamin´s GTPase activity. Additionally, we transfected neurons with gain- and loss-of-function mutants of dynamin-2 (Dyn2), the only ubiquitous isoform of dynamin, to evaluate dendritic spine density. Besides, subcellular localization of endogenous Dyn2, was analyzed by colocalization with the presynaptic marker v-GLUT and the postsynaptic marker PSD95. Our results showed that BIST23 increases dendritic spine density in WT and 3xTg neurons both under resting conditions and in response to the induction of synaptic plasticity (LTP). In 3xTg neurons the postsynaptic localization of Dyn2 was significantly decreased and dendritic spine density reduced compared to WT neurons. However, the expression of gain-of-function-Dyn2 prevented this loss. Altogether, these results suggest that promoting dynamin´s activity, either by genetic or pharmacological approaches, could be a promising therapeutic approach to prevent synapse loss in AD.

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Agradecimientos: Fondecyt Regular 1231511

Socio Patrocinante: ANDREA TAPIA-BUSTOS

2. MODULATION OF LOCOMOTOR BEHAVIOR IN ZEBRAFISH BY NICOTINE AND MODAFINIL. Modulación del Comportamiento Locomotor en Peces Cebra por Nicotina y Modafinilo.

Resúmen:

It has been shown that nicotine, despite its addictive effects, enhances cognitive function and memory in various animal models due to the modulation of nicotinic acetylcholine receptors (nAChRs) in dopamine release and metabolism, as well as chromatin modification through the inhibition of histone deacetylases. Modafinil, on the other hand, increases synaptic monoamine concentrations, specifically dopamine, by inhibiting its transporter (DAT). Previous studies suggest that modafinil can improve working memory performance in a dose-dependent manner. Both substances have been shown to enhance zebrafish performance in the T-maze paradigm. In our study, we focused on analyzing how different doses of modafinil and nicotine modify the locomotor profile of zebrafish, using the open field and novel tank diving paradigms. We evaluated parameters such as swim speed, total distance traveled, and zone preference. The results indicate that, under the evaluated doses, both nicotine and modafinil significantly alter zebrafish behavior in both tests. Nicotine, especially at higher concentrations, caused a decrease in distance traveled and an increase in time spent in the center of the tank, suggesting an altered locomotor profile. In contrast, modafinil increased the distance traveled, suggesting a more exploratory behavior. These findings reveal differentiated effects of these substances on locomotor activity and exploration in this animal model.

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Socio Patrocinante: Patricio Iturriaga Vásquez

3. OBESITY-INDUCED NEUROINFLAMMATION ROLE IN THE HIPPOCAMPAL-LATERAL SEPTUM-LATERAL HYPOTHALAMUS PATHWAY IN RATS. Rol de la neuroinflamación inducida por la obesidad en la vía hipocampal-septum lateral-hipotálamo lateral en ratas.

Resúmen:
Obesity-induced neuroinflammation is a chronic aseptic central nervous system inflammation associated with increased pro-inflammatory cytokines, reactive astrogliosis, and activation of NLRP3 inflammasome. Obesity is associated with an excessive intake of obesogenic foods and decreased physical activity. Brain areas such as the lateral hypothalamus (LH), lateral septum (LS), ventral tegmental area, and nucleus accumbens participate in the homeostatic and hedonic control of feeding. Chronic lipid intake triggers neuroinflammation in several brain regions, such as the hypothalamus, hippocampus, and amygdala. This work aimed to study the effects of the exposure to a high-fat diet (HFD) for six weeks on the neuroinflammation of the Lateral-Hippocampal- Lateral Septum- Hypothalamus Pathway through the NLRP3 inflammasome gene expression and Iba-1 and GFAP gene expression and protein content. The results reveal an increase of Asc gene expression in male HFD rats in the Ventral Hippocampus, compared to control and HDF female rats. In the LS, HFD males showed higher expression levels of Asc and Caspase-1 transcripts compared to the control group and to HFD females, and an increase of Nlrp3 in males HFD compared with male control and female HFD. In the lateral hypothalamus, Iba-1 transcript expression was increased in HFD females compared to both the control group and HFD males, while HFD males showed an increase in Asc and Caspase-1 transcripts relative to the control, and Nlrp3 transcript increase in female HFD compared to control. Finally, GFAP protein content increased in the dorsal hippocampus of HFD males compared to the control group and HFD females.

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Socio Patrocinante: Dr. Ramón Sotomayor-Zárate

4. microRNA 17-5p MODULATES HEDONIC AND ANXIETY-LIKE BEHAVIORS: RELEVANCE OF SYNAPTIC TRANSCRIPTOME AND PROTEOME IN THE VENTRAL HIPPOCAMPUS. microRNA 17-5p Modula Conductas de tipo Hedónicas y Ansiosas: Relevancia del Transcriptoma y Proteoma Sinápticos en el Hipocampo Ventral.

Resúmen:
The hippocampus plays an important role in acquiring memory, a function attributed to the dorsal pole. The ventral hippocampus is linked to anxiety behavior and the processing of emotional experiences through its interaction with other limbic areas, such as the amygdala, and the prefrontal cortex. We have previously shown that chronic restraint stress induces anxious-like and depressive-like behaviors in rats, which mirror the transcriptomic variations induced by stress in the ventral hippocampus. Since microRNAs can finely modulate gene expression, we sought to understand how they participate in behavioral alterations. In that line, we found an increase in the levels of miR-17-5p in the ventral hippocampus of male rats exposed to chronic restraint stress. Interestingly, miR-17-5p is part of the miR-17-92 cluster, which plays a key role in neurogenesis and participates in anxiety-like and depression-like behaviors in mice. Research addressing the impact of individual members such as miR-17-5p is controversial. While some evidence supports a decrease in the levels of all members of the cluster, chronic unpredictable mild stress increases the levels of hippocampal miR-17-5p in rodents. However, there have been no reports evaluating the direct impact of miR-17-5p on anxiety-like and depression-like behaviors. Here, we evaluated the effect of administering a miR-17-5p mimic into the ventral hippocampus of naive adult male rats. Surprisingly, miR-17-5p exerts hedonic and anxiolytic effects. Furthermore, transcriptomic and proteomic analyses in whole homogenates and synaptic fractions of the ventral hippocampus revealed that miR-17-5p alters canonical pathways relevant to specific neurotransmission systems. Thus, this evidence identifies miR-17-5p as a potential therapeutic target for the treatment of mood disorders.

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Agradecimientos: This work was supported by the Agencia Nacional de Investigación y Desarrollo (ANID, Chile), through grants of the Fondo Nacional de Ciencia y Tecnología (FONDECYT) awarded to JLF (# 119 0899 and # 123 0471), Beca de Doctorado Nacional awarded to FO (# 21200296), and Fondo de Equipamiento Científico y Tecnológico (FONDEQUIP) awarded to CAV (# 190142).
Socio Patrocinante: Jenny L. Fiedler

5. ANALYSIS OF PHARMACOLOGICAL INTERACTIONS IN PATIENTS UNDERGOING DUAL ANTIPLATELET THERAPY FOR SECONDARY PREVENTION: AN OUTPATIENT MEDICATION PERSPECTIVE. Análisis de Interacciones Farmacológicas en Pacientes que Reciben Terapia Antiplaquetaria Dual para Prevención Secundaria: Una Perspectiva de Medicamentos Ambulatorio.

Resúmen:
Stroke is one of the leading causes of global mortality, ranking as the second most common cause of death in Chile. Dual antiplatelet therapy (DAPT), combining acetylsalicylic acid and clopidogrel, prevents ischemic events. However, it is susceptible to potential pharmacological interactions (PPI) that may reduce its efficacy or safety. This single-center, cross-sectional observational study assessed the prevalence and clinical impact of PPI in patients with stroke or transient ischemic attack on DAPT, considering their chronic pre-admission medication. Lexicomp® and Micromedex® databases were used to identify and characterize PPIs, alongside evaluations of sociodemographic, clinical, and pharmacological factors, based on patient medical records and interviews with patients, caregivers, or legal guardians (with CEC-FAR 02/2024 approval). A total of 170 PPIs were identified, with the most common being clopidogrel-atorvastatin (7.34%) and acetylsalicylic acid-metformin (3.08%), with risk category C interactions predominating (82.31%). Of the PPIs, 26.29% were clinically relevant, particularly clopidogrel-atorvastatin, clopidogrel-amlodipine, and clopidogrel-omeprazole, which reduce clopidogrel concentrations, warranting clinical or biochemical monitoring (VerifyNow system). The use of herbs and supplements, such as garlic (20.63%), ginger (9.52%), and grapefruit juice (6.35%), was also noted as they interact with DAPT. The first two interactions (garlic and ginger) enhance the antiplatelet effect, while grapefruit juice reduces clopidogrel plasma concentration, potentially diminishing its efficacy. Outpatient treatment adherence, assessed via the MMAS-8 scale and AVIS platform, showed low adherence, with approximately 40% and 60% non-adherence, respectively. These results highlight the need to manage PPIs and educate patients to improve therapeutic adherence and prevent treatment failure.

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Socio Patrocinante: Dra. Andrea Tapia Bustos

6. ROLE OF DYNAMIN´S CATALYTIC ACTIVITY ON MITOCHONDRIAL DYNAMICS IN HIPPOCAMPAL NEURONS OF 3XTG MICE, A MURINE MODEL OF ALZHEIMER'S DISEASE. Rol de la actividad catalítica de las dinaminas en la dinámica mitocondrial en neuronas del hipocámpano de ratones 3xtg, un modelo murino de Enfermedad de Alzheimer

Resúmen:
Alzheimer's disease (AD), the most prevalent neurodegenerative disorder in elderly, is characterized by progressive decline in cognitive functions. An understudied mechanism in AD is mitocondrial-dynamics, which includes mitochondrial fusion/fission. Defects in mitocondrial-dynamics are associated with impaired neuronal-bioenergetics, loss of neuronal function and neurodegeneration. To date, there are no therapies aimed to modulate mitochondrial dynamics in AD. Dynamins are enzymes with GTPase activity that participate in mitocondrial dynamics, by controling fission/fusion. Particularly, the classic isoform dynamin-2 and dynamin-related proteins regulate mitochondrial fragmentation in neurons, suggesting their potential as pharmacological targets in AD. Here, we evaluated the role of dynamins on mitochondrial dynamics in the hippocampus of 3xTg mice, a murine model of AD. Hippocampal neurons were cultured from wildtype (WT) or 3xTg mice and were acutely treated during 30 min with 20 uM Dynasore or Bis-T-23, dynamin´s inhibitor and enhancer respectively. Mitochondria number, size and morphology were quantified in neurons stained with mitotracker. In addition, ATP-production and reactive-oxygen-species-(ROS) were quantified in ex vivo brain tissue of WT and 3xTg mice. Our data show that 3xTg neurons exhibit fewer, smaller and more “circular” mitochondria than WT neurons. The acute treatment with BIST23 increased mitocondria´s size, without modifying the amount of mitochondria. We did not observe differences in the ROS-antioxidant capability between experimental conditions. Interestingly, 3xTg exhibited a lower ATP-production compared to WT brains, and tretment with BIST23 trend to prevent this difference. Dynasore had no significant effects on any of the analyzed parameters. Together, these results could suggest that dynamins are key modulators of neuronal mitocondrial function in the context of AD. Future studies could help to provide insights of dynamin-based therap.

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Socio Patrocinante: Andra Tapia Bustos

7. COMPUTATIONAL STRATEGY FOR THE IDENTIFICATION OF MULTITARGET COMPOUNDS: APPLICATIONS IN ALZHEIMER'S DISEASE. Estrategia Computacional para la Identificación de Compuestos Multiobjetivo: Aplicaciones en la Enfermedad de Alzheimer.

Resúmen:
Neurodegenerative diseases, such as Alzheimer's, represent a growing challenge in medicine due to their high incidence and significant impact on patients' quality of life. These conditions are characterized by the progressive loss of neurons in the central nervous system, leading to cognitive and motor decline. Although various pathophysiological theories have been proposed, such as the accumulation of misfolded proteins (beta-amyloid and tau) and decreased cholinergic activity, no effective therapies have been found to halt their progression. Current treatments, such as acetylcholinesterase inhibitors, offer only symptomatic relief, and their efficacy diminishes as the disease advances. Therefore, it is essential to explore new therapeutic strategies that comprehensively address these pathologies. In this context, advanced approaches in computer-aided drug design were adopted. Polypharmacology emerged as a promising solution, enabling the development of compounds that act on multiple therapeutic targets simultaneously. Several key therapeutic targets were selected for the study: acetylcholinesterase, glycogen synthase kinase 3 beta, nicotinic acetylcholine receptor alpha 7, beta-secretase, cannabinoid receptor type 2, and monoamine oxidase A. Virtual screening techniques were employed, including Ligand-Based Virtual Screening (LBVS) and Structure-Based Virtual Screening (SBVS). Additionally, free energy calculations using MM-GBSA were performed to predict the binding affinity of the compounds obtained in the final stage of SBVS. These methodologies allowed the identification of 21 promising compounds, which will be subjected to experimental assays to evaluate their biological activity and antioxidant capacity on acetylcholinesterase. This approach aims to find multitarget ligands that can address the various pathological features of Alzheimer's disease.

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Socio Patrocinante: David Ramirez

8. CHLOROGENIC ACID PREVENTS THE TOXIC EFFECTS OF 27-HYDROXYCHOLESTEROL IN DANIO RERIO EMBRYOS. El ácido clorogénico previene los efectos tóxicos del 27-hidroxicolesterol en embriones de Danio rerio.

Resúmen:
Polyphenols have been described as neuroprotective agents, which have been shown to prevent and mitigate 27-hydorxycholesterol (27-OHC) induced neuroinflammation. Chlorogenic acid (CGA) is a polyphenol, but its neuroprotective properties have yet to be determined. Therefore, in order to evaluate the potential neuroprotective effects of CGA, Danio rerio (zebrafish) embryos were exposed to 27-OHC, and assessed if CGA was able to prevent the damage induced by this cholesterol metabolite. Wild-type zebrafish embryos were exposed to 50μM of 27-OHC at 24 hours post-fecundation either alone or in combination with 0.1mg/ml of CGA. Embryos were maintained in these conditions for up to 7 days, with daily media changes. An untreated group was used as control. Zebrafish embryos exposed to 27-OHC had lower survival rates than those exposed to CGA, suggesting that 27-OHC is indeed toxic. CGA exposure prevented 27-OHC induced toxicity. However, it is uncertain whether the toxicity observed is due to 27-OHC alone, or partly due to the ethanol present in the preparation of the stock solution. The damage on the embryos is so harsh that no tissue was viable for molecular screening and comparison. No damage is observed in CGA treated embryos. Therefore, CGA prevents 27-OHC induced damage in zebrafish embryos, which strongly suggests that CGA might be a good candidate for neuroprotection.

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Socio Patrocinante: Caroline Weinstein Oppenheimer

9. EARLY-LIFE EXPOSURE TO ANTIBIOTICS SHAPES SOCIAL BEHAVIOURS AND INTESTINAL BETA-GLUCURONIDASE ACTIVITY IN JUVENILE RATS. La exposición temprana a antibióticos da forma a los comportamientos sociales y a la atividad beta-glucuronidasa en ratas juveniles

Resúmen:
There is a difference in addiction and social behaviours between males and females (men and women). Early life exposure to antibiotics (ELEA) induces addiction-like behaviours in adult male Sprague-Dawley (SD) rats, but not in females, while changing dopamine neurochemistry in females but not in males (doi: 10.3389/fphar.2022.837652). Female oestrogen regulates brain dopamine levels and release, while oestrogen circulation is influenced by gut microbes through intestinal β-glucuronidase activity, which further contributes to oestrogen's impact on the brain. Since dopamine has been linked to social behaviours, and its function is related to oestradiol concentrations, we asked whether ELEA impacts these behaviours later in life, and if changes in intestinal gut beta-glucuronidase activity relate to these changes. ELEA was achieved by oral administration of bacitracin, neomycin, vancomycin (100 mg/kg each) and pimaricin (5μg/kg) to pregnant SD dams from embryonic day 18 to postnatal day (PND) 7. Vehicle-treated pregnant SD dams served as controls. Behavioural analysis was conducted on male and female offspring from PND 35 to 37. Half of the subjects underwent gonadectomy (GDX) to remove the influence of sex steroids. ELEA prevented weight loss associated to behavioural testing in males. Three-way ANOVA revealed a main effect of ELEA, reducing pinning, pouncing, total time of social play and social grooming. In GDX males, ELEA diminished entries to the interaction zone in the presence of an unknown rat. Beta-glucuronidase activity was reduced in females by ELEA and GDX. ELEA reduces some social behaviours in a sex-independent manner, while sex-dependently lowering intestinal beta-glucuronidase activity, suggesting that early-life gut symbiont acquisition influences social coping strategies and intestinal oestradiol metabolism later in life.

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Socio Patrocinante: Javier A. Bravo Ph. D.

10. IMPACT OF BIST-23, A PHARMACOLOGICAL PROMOTOR OF DYNAMIN´S GTP-ASE ACTIVITY, ON THE COGNITIVE FUNCTION AND ACTIN ORGANIZATION IN A MURINE MODEL OF ALZHEIMER'S DISEASE. Impacto de la potenciación farmacológica de las dinaminas con BIST-23, sobre la función cognitiva, organización de actina y densidad de espinas dendríticas en un modelo murino de la Enfermedad de Alzheimer.

Resúmen:
Alzheimer's disease (AD) is the leading cause of dementia in elderly. The onset of cognitive defects in AD correlates with synapses-loss. Defective actin organization and remodeling is a major cause of synapses-loss in AD, impairing neuronal structure and altering synaptic transmission/plasticity. Therefore, actin-dynamics has emerged in recent years as a potential therapeutic target in AD; however, a direct actin-cytoskeleton´s intervention is potentially cytotoxic, making it necessary to search alternatives, by modulating actin-regulatory proteins. One potential candidate is dynamin superfamily (DSF). These are large GTP-ases critical for multiple cellular processes including actin remodeling. Remarkably, DSF expression is reduced in the context of AD, suggesting their involvement in the pathological mechanisms of the disease. In the current work we evaluated the impact of pharmacologically promoting DSF-activity on cognitive functions, and actin cytoskeleton organization in brains of APP/PS1 mice, a murine model of AD. Six month- old APP/PS1 mice and their wild-type littermates were treated for 14 days with a daily dose of 10 mg/kg BIST-23, an enhancer of dynamin´s activity, or with its vehicle DMSO. Cognitive functions were analyzed by behavioral tasks to assess recognition and spatial memory, and actin organization was analyzed by quantifying the relative amounts of filamentous(F-) and monomeric(G-)-actin in hippocampal-tissue. Our data showed that APP/PS1 mice exhibit impaired recognition and spatial memory compared to WT littermates and that the BIST-23-treatment significantly prevent these differences. In addition, APP/PS1-hippocampi exhibited significantly lower F/G-actin-ratio than WT, and BIST23 prevented this difference. Together, these data strongly suggest that dynamin´s activity could be considered as a new therapeutic target to intervene the molecular mechanisms that lead to cognitive dysfunction in AD.

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11. IMPAIRED MITOCHONDRIAL RESPIRATION FOLLOWING PERINATAL ASPHYXIA IN RATS: INSIGHTS FROM REAL TIME ANALYSIS WITH SEAHORSE XF TECHNOLOGY INTEGRATION. Deterioro de la respiración mitocondrial después de la asfixia perinatal en ratas: perspectivas del análisis en tiempo real con la integración de la tecnología Seahorse XF.

Resúmen:
Perinatal asphyxia (PA) is a leading cause of neonatal morbidity and mortality, linked to long-term neurological impairments. Mitochondrial dysfunction is a pivotal factor on the cellular damage caused by PA. Since mitochondria are essential for energy production and apoptosis regulation, particularly vulnerable to disrupted oxygen supply, its disruption impairs oxidative phosphorylation, increasing reactive oxygen species (ROS), inducing mitochondrial permeability transition pore (mPTP) opening, affecting the viability basal ganglia circuits. The long-term mitochondrial impairments in the brain following PA reduce the CNS resilience to future stressors, affecting development. Although previous research has implicated mitochondrial dysfunction in the lasting effects of PA, direct evidence has been limited by challenges in monitoring mitochondrial function in tissue from asphyxia-exposed animals. This study describes for a first time a methodology for evaluating changes in mitochondrial respiration from isolated organotypic cultures of PA-exposed rats. Using a real time platform, involving Seahorse XFe96/Cytation5 integration (Agilent Technologies, USA), we hypothesized that PA would impair mitochondrial respiration. Cultures from asphyxia-treated rats were compared to controls, while oxygen consumption rate (OCR) was analysed under basal respiration, ATP production, and maximal electron transport flux conditions. It was found a significant decrease in ATP-linked respiration and spare respiratory capacity in asphyxia-treated rats, suggesting compromised mitochondrial efficiency and adaptive capacity. These findings highlight the impact of PA on mitochondrial integrity and could guide therapeutic approaches to mitigate mitochondrial dysfunction following hypoxic injury.

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12. EFFECT OF ASTAXANTHIN ON NLRP3 AND MITOCHONDRIAL FUNCTION IN A MOUSE HIPPOCAMPAL CELL LINE. El efecto de astaxantina en NLRP3 y la funcion mitocondrial en una linea hipocampal de raton

Resúmen:
Astaxanthin (ASX) is an antioxidant and neuroprotective carotenoid pigment capable of crossing the blood-brain barrier, preventing excessive reactive oxygen species (ROS) formation, calcium overload, and mitochondrial dysfunction in various cellular models of excitotoxicity and neurodegenerative diseases. Previous studies have shown that ASX enhances mitochondrial function by reducing cell death in oxidative stress cellular models. Additionally, unpublished data from our laboratory demonstrate that ASX decreases the nuclear translocation of nuclear factor kB (NF-kB) in aged rats, suggesting that ASX may act as an anti-inflammatory agent. In this study, we investigated the effect of ASX on mitochondrial function and inflammatory response using an oxidative stress model induced by hydrogen peroxide in immortalized hippocampal HT22 cells. We found that hydrogen peroxide reduced mitochondrial function as measured by the MTT assay, which was associated with an increased number of small-volume objects detected with Mitotracker and ImageJ, suggesting that hydrogen peroxide induces mitochondrial fragmentation. Hydrogen peroxide also induced the expression of a key inflammasome component, the NLRP3 protein, suggesting the activation of the cellular inflammatory response. Incubation with ASX improved mitochondrial function and decreased the number of mitochondria and NLRP3 expression in HT22 cells treated with hydrogen peroxide. Interestingly, incubation with ASX alone increased the number of mitochondria, but with a similar volume to controls, suggesting that ASX induces mitochondrial biogenesis.

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13 EFFECTS OF INTRANASAL VASOPRESSIN ADMINISTRATION ON AMPHETAMINE RELAPSE AND VTA NEUROTRANSMITTERS CONTENT IN MALE AND FEMALE ADOLESCENT RATS. Efectos de la administración intranasal de vasopresina sobre la recaída a anfetamina y el contenido de neurotransmisores en VTA en ratas adolescentes macho y hembra.

Resúmen:
Adolescence is a vulnerable period for drug abuse and the development of drug dependence or addiction. Amphetamine (AMPH) is a psychoactive substance usually used as a recreational drug by young people, which, to date, does not have effective medications that can treat addiction to AMPH or other psychostimulants. Recent studies have shown that the vasopressin (AVP) system has a crucial role in drug addiction, transforming it into an attractive therapeutic target. Hence, this research aims to study the effect of intranasal AVP administration during the conditioned place preference (CPP) extinction phase on AMPH-induced reinstatement. Male and female adolescent Sprague-Dawley rats (43-45 postnatal days) were conditioned with AMPH (1.5 mg/kg i.p.) or saline for 5 days. After 5 days of extinction, in which the animals received intranasal treatment with AVP (20 µg/kg) or saline, the animals received an injection of AMPH inducing reinstatement. Additionally, glutamate, GABA, and dopamine levels were quantified in the ventral tegmental area (VTA), a nucleus that forms an important part of the reward system. The results suggest that intranasal AVP administration during the extinction phase partially reverts drug-seeking behavior after the AMPH challenge only in male rats and increases glutamate and GABA tissue levels in the VTA. On the other hand, the effect observed in males was not observed in female rats, both in behavior and neurotransmitter content in VTA. In conclusion, in males, AVP may act by inhibiting glutamate release in the VTA through increased GABAergic tone of VTA interneurons. Therefore, intranasal AVP produces sex-dependent effects on behavior and neurotransmitter levels.

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14. EFFECT OF THE CHEMOGENETIC INHIBITION OF DA NEURONS IN THE FUNCTION AND LEVELS OF D2R IN THE MOUSE NUCLEUS ACCUMBENS. Efecto de la Inhibición Quimiogenética de las Neuronas DA en la Función y Niveles de D2R en el Núcleo Accumbens de Ratón.

Resúmen:
Repeated administration of quinpirole (QNP), a dopamine D2 receptor (D2R) agonist, elicits compulsive behaviors and locomotor sensitization. The induction of locomotor sensitization is related to the mesolimbic dopaminergic system, consisting of dopamine (DA) neurons from the ventral tegmental area (VTA) projecting to the nucleus accumbens (NAc). QNP activates D2 receptors (D2R) on indirect medium spiny neurons and DA terminals of the NAc, promoting locomotion and reducing DA release. QNP-treated animals have lower basal DA levels and increased D2R presynaptic function measured by Fast Scan Cyclic Voltammetry (FSCV). How does D2R-induced chronic inhibition of mesolimbic DA activity modify D2R function and levels, and how is it related to locomotor sensitization? We propose that chronic inhibition of mesolimbic DA activity contributes to the appearance of compulsive behaviors by modifying the expression and function of D2R in the NAc. To investigate this hypothesis, mesolimbic DA neurons were chronically inhibited by chemogenetically expressing the inhibitory DREADD hM4D in TH-Cre mice. To activate the DREADD, its agonist (compound 21) was injected for 5 days, with locomotor activity assessed after each injection. The repeated inhibition of DA neurons did not modify locomotor activity. However, we found an increased D2R presynaptic inhibition of DA release in the NAc in mice with chemogenetic inhibition of mesolimbic DA activity. Moreover, the repeated QNP induced locomotor sensitization only in mice with chemogenetic inhibition of DA neurons. Suggesting that chronic inhibition of DA sensitizes D2R in dopamine terminals and NAc MSNs. Currently, we are evaluating the levels of D1R and D2R in the NAc using Western blot and immunofluorescence techniques. We aim to contribute to understanding the mechanisms underlying OCD by studying the involvement of D2R in DA neurons.

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15. CHARACTERIZATION OF NEUROSPHERES OBTAINED FROM HUMAN DERMAL FIBROBLASTS. Caracterización de Neuroesferas Obtenidas a partir de Fibroblastos Dérmicos Humanos

Resúmen:
Neurodegenerative diseases have risen significantly, primarily due to the aging population. Currently, there is no effective cure for these diseases. However, treatment using mesenchymal stem cells (MSCs) offers a promising therapeutic alternative. MSCs can be used to generate neurons and glial cells. Since dermal fibroblasts share key characteristics with MSCs, we propose dermal fibroblasts as a viable source for generating neural progenitors. Methods: Neurospheres were generated from human neonatal dermal fibroblasts over 7 days, followed by an additional 7-day differentiation phase to produce neurons and glial cells. Neurospheres, neurons, and glial cells were characterized using qRT-PCR to assess semiquantitative mRNA expression of CD105 (MSC marker), GFAP (marker for NSCs and astrocytes), NeuN (neuronal marker), and CD206 (anti-inflammatory glial marker). Results: Neurospheres were obtained, expressing CD105, GFAP, and NeuN. A decrease in GFAP and NeuN expression was observed upon differentiation, while CD206 expression was undetected under all conditions tested. Conclusion: Neurospheres expressing neuroglial markers were successfully generated from human neonatal foreskin-derived dermal fibroblasts. However, differentiated neurospheres exhibited reduced expression of neuronal and glial markers.

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16. STUDY OF THE DISTRIBUTION OF GRK-2 IN THE MOUSE MESOLIMBIC SYSTEM. Estudio de la distribución de GRK2 en el sistema mesolímbico del ratón

Resúmen:
Dopamine (DA) in the mesolimbic dopaminergic circuit is crucial in executing motivated behaviors. This system comprises dopaminergic neurons that project from the ventral tegmental area (VTA) to the nucleus accumbens (NAc). DA binds to G protein-coupled receptor (GPCR). DA release in the NAc favors motor behavior by binding to D1R and D2R located in the direct and indirect Medium Spiny Neurons (MSNs). D2R receptors are also found in DA neurons' terminals and somatodendritic compartments, where they inhibit DA release. Chronic administration of quinpirole (QNP), a D2R agonist, induces locomotor sensitization, compulsive-like behaviors and decreases basal DA levels of the NAc. However, the downstream cellular mechanisms are still unknown. One of the possible candidates may be proteins that modify D2R trafficking and endocytosis. The GRK2 kinase, a member of the GPCR family of kinases, is involved in agonist-induced desensitization and signaling of D2R. GRK2 regulates D2R trafficking by phosphorylation of the C-terminal domain of the receptor. Although research exists on the functions of GRK2, its distribution in the mesolimbic DA system of mice, as well as the effect of repeated D2R activation on its levels, has been poorly described. This work aims to characterize the distribution and levels of GRK2 in the mesolimbic DA system of mice. We have established an immunofluorescence protocol for GRK2 and TH as a marker of DA neurons. We have shown that GRK2 is highly located on the somatodendritic compartments of DA neurons from the VTA and less in NAc MSNs. Quantifications of the colocalization of GRK2 and TH are under development. In the future, we will characterize whether QNP repeated treatment affects GRK2 distribution and levels.
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17. RV D1 DOES NOT PREVENT THE INCREASE OF SOD2/ATF5/PGC-1α IN ANGIOTENSIN II-STIMULATED CARDIAC FIBROBLAST. RV D1 no previene el aumento de sod2/atf5/pgc-1α en fibroblastos cardíacos estimulados con angiotensina ii.

Resúmen:
Introduction: In cardiac fibroblasts, angiotensin II (Ang II) increases the secretion of extracellular matrix proteins and pro-inflammatory cytokines, as well as cellular senescence. However, its effect on mitochondrial function markers remains unclear. Additionally, in Ang II-stimulated cardiac fibroblasts (CFs), resolvin D1 (Rv D1) has been shown to reduce both senescence and pro-inflammatory markers. The aim of this study was to determine whether Ang II induces mitochondrial-level changes and whether these effects could be prevented by Rv D1. Methodology: Adult rat CFs were stimulated with 1 µM Ang II for 24, 48, and 72 hours. Reactive oxygen species (ROS) production was measured by fluorimetry, and the expression of SOD2/ATF5/PGC-1α proteins was assessed by western blot. We also evaluated whether pretreatment with 100 nM Rv D1 could modify the effects of 1 µM Ang II. Results: Ang II treatment in CFs caused an early increase in ROS production, which was significant at 48 hours. Additionally, an increase in SOD2/ATF5/PGC-1α protein expression was observed at 24 hours. Pretreatment with N-acetyl cysteine (NAC) prevented the Ang II-induced increase in ROS; however, NAC could not prevent the Ang II-induced increase in SOD2/ATF5/PGC-1α proteins. Similarly, pretreatment with Rv D1 failed to prevent the effects of Ang II on ROS or SOD2/ATF5/PGC-1α protein levels. Conclusion: Ang II increases ROS production in CFs, an effect countered by NAC pretreatment. However, neither NAC nor Rv D1 prevented the Ang II-induced increase in the studied proteins.
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18. CYTOTOXIC EFFECT OF AUTOPHAGY INHIBITION WITH FERROQUINE ON ORAL SQUAMOUS CELL CARCINOMA. Efecto citotóxico de la inhibición de la autofagia con ferroquine sobre carcinoma oral de células escamosas.

Resúmen:
Oral squamous cell carcinoma (OSCC) is the most prevalent oral cancer, and has a high rate of resistance to conventional therapy. Ferroquine (FQ), an antimalarial agent, is an autophagy inhibitor that can produce cytotoxic effects on tumor cells. Objective: To evaluate the effect on cell cytotoxicity of ferroquine on 2D and 3D cultures of OSCC. For 2D cultures, CAL-27, SCC-25 and SCC-180 lines were used. 20,000 cells per well were incubated for 24 hours with increasing concentrations of CF. Cell viability was assessed at 48 and 72 h by MTT assay by determining IC50 values. In 3D cultures, 4000 SCC-25 cells were seeded in 96-well plates. After 72 h of incubation, the cultures were treated with increasing concentrations of CF. Cell viability at 72 h was assessed by resazurin assay by determining IC50 values through 4-parameter dose-response curves with variable slope using Graphpad Prism® 8.0.2 software. Results: The average IC50 in uM of CF for 2D cell culture at 48 hours for CAL-27,SCC-25 and SCC-180 was 72.56, 51.67, 91.77 respectively, and at 72 hours for CAL-27,SCC-25 and SCC-180 was 59.93, 58.85, 150.96, respectively; from 3 independent experiments. As a preliminary study, an IC50 in uM in 3D cell culture of approximately 193.2 was obtained. In conclusion, we were able to evaluate the cytotoxic effect of ferroquine on CAL-27, SCC-25 and SCC-180, both in 2D and 3D (preliminarily), observing that it is a promising drug in oral cancer.
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19. EVALUATION OF THE ANTIFIBROTIC EFFECT OF BOLDINE IN HUMAN LUNG FIBROBLASTS. Evaluar efecto antifibrótico de boldina en fibroblastos de pulmón humano.

Resúmen:
Introduction: Idiopathic pulmonary fibrosis (IPF) is a progressive chronic interstitial lung disease of unknown etiology with high mortality, characterized by an abnormal reparative response to repetitive alveolar damage in genetically susceptible individuals, progressively decreasing lung function. Treatment options for IPF are limited and mainly palliative with essential side effects; randomized clinical trials have failed to demonstrate the benefits of new drugs. A particular condition of IPF is inflammation of lung fibroblasts. Boldine is an alkaloid isolated from Boldo (Peumus boldus), an endemic tree of Chile, recognized in national folklore by its supposed beneficial health properties; several in vitro and in vivo studies have demonstrated anti-inflammatory, antioxidant, antiproliferative, and antiatherogenic effects. However, its benefits in pulmonary pathologies have not been studied. Objectives: To demonstrate the anti-inflammatory effect of Boldin on human lung fibroblasts (HLF). Methods and Materials: HLF were stimulated with LPS 1 µg/mL at 1, 3, and 6 h. Subsequently, levels of the total and phosphorylated form of NF-κB, p-ser536-NF-κB, were determined by western blot as a marker of HLF inflammation. Once the inflammation time was determined, HLF were stimulated with Boldine 100 µM one hour before LPS, assessing NF-κB phosphorylation to evaluate its anti-inflammatory capacity. DMSO was used as a Boldine vehicle. Results: LPS induced NF-κB activation at one hour of treatment compared to its control. Boldine reduced NF-κB phosphorylation compared to vehicles caused by LPS. Conclusions: Our results suggest that Boldine induces an anti-inflammatory effect in HLP, which could offer an alternative of natural origin as a possible treatment of one of the factors that condition the progression of IPF.

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20. ELECTROPHYSIOLOGICAL AND COMPUTATIONAL STUDY OF TREK CHANNELS MODULATION BY CHARGED MOLECULES. Estudio electrofisiológico y computacional de la modulación de canales TREK por moléculas cargadas

Resúmen:
Pain remains a major medical problem with limited treatments, increasing the demand for non-opioid alternatives due to the opioid crisis. Two-pore domain potassium (K2P) channels, in particular TREK-2, play a crucial role in stabilizing the resting membrane potential in primary sensory neurons and are involved in pain modulation, including mechanical allodynia and hyperalgesia. Small molecules such as BL-1249, a negatively charged activator (NCA), potentiate TREK-2 mediated currents, decreasing the resting membrane potential and consequently decreasing pain perception. On the other hand, norfluoxetine (NFX), a positively charged inhibitor, shares the binding site with NCAs but has the opposite effect. However, its inhibitory effect is not due to its positive charge, since the neutral derivative desamino-chloro fluoxetine also inhibits the TREK-2 channel. Therefore, its effects are expected to be at the level of the selectivity filter. The project investigates the modulation of TREK-1 and TREK-2 channels by computational and electrophysiological approaches. Special attention is paid to acid NFX, a putative NCA. Atomistic molecular dynamics simulations, free energy calculations, and mutagenesis are employed to assess how these modulators affect ion flux through the channels. The research aims to characterize the energetic landscape of the ionic flow in TREK-2 with the WTM-eABF method in the presence of charged molecules. On the other hand, it is intended to determine the binding site of the putative NCA molecule, acid NFX, by Two Electrode Voltage Clamp in TREK-1 channel mutants. Finally, this study aims to contribute to developing new pain therapies targeting TREK-1 and TREK-2 channels.

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21. CHARACTERIZING CCO-TX3 TOXIN BINDING SITE IN HNAV1.5 CHANNEL. Caracterización del sitio de unión de la toxina Cco-Tx3 en el canal hNaV1.5

Resúmen:
Voltage-gated sodium channels (VGSCs) are membrane proteins found in excitable cells such as neurons and cardiomyocytes. NaV1.5 channel is the most abundant sodium channel expressed in myocardial cells, and mutations in its sequence can lead to various cardiac diseases, including atrial fibrillation and Brugada syndrome. Consequently, hNaV1.5 has become an attractive target for treating related channelopathies. Toxin peptides isolated from scorpions and tarantulas are natural ligands of VGSCs. Cco-Tx3 is a peptide toxin derived from the straight-horned baboon tarantula, which selectively targets hNaV1.5 with a moderate IC50 of 447 nM. Cco-Tx3 does not block other VGSCs such as hNaV1.1- hNaV1.4. However, Cco-Tx3 blocks 45% of the peak current in hNaV1.8 at a concentration of 2 µM. The toxin structure has not been determined, and it is believed to target hNaV1.5VSDII in its closed state. Additionally, no published structure exists for hNaV1.5 in the closed state. We generated a toxin model using AlphaFold and created a homology model of hNaV1.5VSDII in its closed state using MODELLER, based on the NaV1.7VSDII closed-state template (PDB: 7K48). Docking with HADDOCK2.4 yielded a binding pose similar to that obtained through Cryo-EM between 3m-HwTx4 and a chimera of NaVAb-NaV1.7VSDII in the closed state. Identifying the potential binding site for the interaction between Cco-Tx3 and hNaV1.5 was further validated using a combination of site-directed mutagenesis of hNaV1.5 neurotoxin site 4 and two-electrode voltage clamp measurements. The results showed that S743, E746, E747, R800, and S802 are hotspots for toxin binding, inhibiting channel activation. Understanding the molecular basis of Cco-Tx3 selectivity for hNaV1.5 and identifying the specific binding sites for the toxin could aid in developing biobetters that selectively target the cardiac ion channel with greater potency, offering promising prospects for treating cardiac diseases.

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22. AMINOALKYLOXICHALCONES LIGANDS TARGETING HISTAMINE 3 RECEPTOR AND MAO-B FOR TREATMENT OF PARKINSON'S DISEASE. Aminoalkyloxichalcones dirigidas al receptor de histamina 3 y MAO-B para el tratamiento de la enfermedad de Parkinson.

Resúmen:
Parkinson's disease (PD) is the second most common neurodegenerative disorder affecting old-age people worldwide. It characterized of a progressive loss of dopaminergic neurons mainly in the substantia nigra, leading to a decrease in dopamine amounts available in the Central Nervous System (CNS). The current treatment for PD is based on symptomatology relieve, without targeting pathogenic mechanisms, which is known to be very complex. For this reason, the study for new therapy has lately focused on the design of multitarget ligands enable to modulate more than one receptor/enzyme which can offer diverse advantages. Monoaminoxidase B (MAO-B) enzyme is one of the approved targets for PD since its inhibition can lead to an increase in dopamine levels in CNS because of the resulting decrease of its degradation. On the other hand, histamine H3 receptor (H3R) antagonists/inverse agonists are also known to increase dopamine levels, since they can counteract the decrease of dopamine, and other neurotransmitters, due to the presynaptic activation of this heteroreceptor. With all the above mentioned, our group of study has been working on dual ligands targeting both, the MAO-B enzyme and H3R. Sixteen new derivatives were synthesized, all of them with a MAO-B inhibitor scaffold consisting in a chalcone-containing pharmacophore and an aminoalkyloxi moiety, the typical and accepted fragment of structure in H3R antagonists/inverse agonists. The compounds were synthesized in three steps obtaining moderate to good yields and biological assays were carried out. All compounds presented H3R affinity values in the nanomolar range (Ki 35-551 nM) and great inhibition (more than 70% at 10 µM in some derivatives) on MAO-B.
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23 DESIGN AND SYNTHESIS OF NEW LIGANDS WITH ACTIVITY ON ACHE AND AFFINITY ON SERT. Diseño y Sintesis de nuevos ligandos con actividad en AChE y afinidad en SERT.

Resúmen:
Alzheimer's disease (AD) is an irreversible neurodegenerative disorder that primarily affects older individuals, characterized by cognitive decline, memory loss, and neuropsychiatric symptoms such as depression. Acetylcholinesterase (AChE) is a crucial therapeutic target, as the loss of cholinergic neurons contributes to cognitive deterioration. Current treatments, including AChE inhibitors like tacrine and donepezil, provide symptomatic relief but do not prevent disease progression. Moreover, increasing the dosage can cause side effects, leading to treatment discontinuation. Additionally, 50% of AD patients experience depression, which worsens cognitive decline and accelerates disease progression. To manage this, selective serotonin reuptake inhibitors (SSRIs) are commonly used. The limited effectiveness of current treatments highlights the need for new therapeutic alternatives that combine both pharmacological targets. This study presents the synthesis of new compounds derived from 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline of 4-benzylpiperidine and 4-benzoylpyridine, along with new phenylacetate and 2-naphthoate derivatives of 1-benzylpiperidine (figure 1). In vitro AChE inhibition assays and SERT binding studies were conducted for these synthesized compounds. Additionally, in silico docking studies of these compounds were performed on AChE and SERT. The pharmacological results revealed that compounds 1, 2, 3, and 4 inhibited AChE without affecting SERT. Compounds 6, 9 and 10 inhibited SERT but showed poor inhibitory activity on AChE, while compounds 12 and 15 inhibited AChE and exhibited low affinity for SERT.
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24. DESIGN OF PROHIBITIN 2 LIGANDS FOR MITOPHAGY ACTIVATION IN SENESCENT CELLS: MODULATION OF THE PHB2/LC3/P62 PATHWAY. Diseño de ligandos de Prohibitin 2 para la activación de la mitofagia en células senescentes: modulación de la vía PHB2/LC3/P62.

Resúmen:
As cells age, their ability to clear out defective mitochondria declines, leading to increased oxidative stress and metabolic dysfunctions1. This reduction in mitophagy, which is crucial for mitochondrial health, results in the buildup of dysfunctional mitochondria, impairing ATP production and exacerbating cellular damage. Factors such as elevated p53 levels and reduced PINK12 hinder mitophagy, contributing to tissue aging and degradation. Although the PHB2/LC3/P62 pathway remains active, excessive mTORC1 activation and lysosomal overload compromise this process3. Exploring PHB2 ligands that could reactivate this pathway may be key to enhancing mitophagy in senescent cells. In this study, the Prohibitin 2 (PHB2) structure was explored to identify potential binding sites with the sequestrosome and the LC3 protein. The conformations that could trigger mitophagy were analysed, highlighting the most important amino acids involved in this process. Furthermore, twenty-four analogues of Prohibitin 2, arranged in three series, were studied by molecular docking with said protein. The ΔG values obtained ranged between -7.00 kcal/mol and -8.24 kcal/mol, being similar to the control (YL-939/Prohibitin 24), with a value of -7.74 kcal/mol. The results obtained suggest that the investigated compounds may be promising candidates for biological evaluation.
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25. EVALUATION OF CELL VIABILITY IN GES-1 CELL CULTURE EXPOSED TO SEQUENTIAL EXTRACTS MADE FROM INFLORESCENCES OF THE PALO NEGRO PLANT (Leptocarpha rivularis). Evaluación de viabilidad celular en cultivo celular GES-1 expuesto a extractos secuenciales elaborados a base de inflorescencias de la planta Palo Negro (*Leptocarpha rivularis*).

Resúmen:
Introduction: Some pharmacological treatments can cause side effects, and therapies derived from medicinal plants can be a solution to avoid them. In 2005, Alvarez et al. studied infusions of palo negro as a hypoglycemic agent, demonstrating its effect, which could be due to compounds such as leptocarpine, quercetin, chlorogenic acid and other sesquiterpene lactones, identified and quantified by Montenegro et al. in 2020. Objective: To evaluate cell viability in GES-1 cell culture exposed to sequential extracts from Palo Negro plant inflorescences. Methodology: Sequential extracts were obtained and an adapted cell viability assay protocol was applied to each one with sulforhodamine B in the GES-1 cell line, using decreasing concentrations (500-3,125 ppm). Treatments were carried out for 72 hours, using 0.1% DMSO solvent as a control. Results: The lowest cell viability value was 10.3% in the extract obtained with dichloromethane at 500 ppm and the highest value was with ethyl acetate at 3,125 ppm. The extract that generated more cytotoxicity at various concentrations was with ethyl acetate solvent at 125 ppm (21.8%), 250 ppm (23.5%) and 500 ppm (15.4%). For all extracts at 250 ppm concentration, there is cell viability from 23.5% to 96.0% and at 500 ppm, there is cell viability from 10.8% to 75.8%. Discussions and conclusions: the least cytotoxic extract was the one obtained with vegetable oil and the most cytotoxic was ethyl acetate. For all the extracts used, from 3.125 to 62.5 ppm, viability was greater than 80%; therefore, the extracts elaborated from Leptocarpha rivularis inflorescences are safe for normal human gastric epithelium (GES-1).

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26. FUNCTIONAL SELECTIVITY, OR BIASED AGONISM, A NOVEL CONCEPT AND ITS PHARMACODYNAMICAL IMPLICATIONS. El novedoso concepto de la selectividad funcional e implicaciones farmacodinámicas

Resúmen:
Recent structural biology advances of G protein coupled receptors (GPCRs) evidence that multiple conformational changes occur following ligand interactions, both agonists or antagonists. GPCRs have two intracellular essential signaling routes: 1 through trimeric G proteins (Gs, Gq, Gi, Go) and 2 associated with β-arrestin signaling. While the first pathway leads to signaling responses attributed to cAMP, IP3/DAG or calcium mobilizastion, the β- arrestin cascade is related to the phosphorylation of several intracellular proteins like EKK1/2 or MAPK kinases. These kinases in turn phosphorylate other kinases and may eventually modify gene expression. This concept may certainly modify the Fergusson proposal of intrinsic activity for agonists and antagonists, including partial agonists. The emerging idea is that ligands, either agonists, partial agonists or even antagonists produce responses through multiple receptor conformational changes which will eventually cause intracellular messengers responsible for the ongoing pharmacological response. Therefore, the new drug classification calls for ligands that preferentially activate either the GPCR route or the β-arrestin cascade, such as antagonists. Partial agonists may preferentially activate either pathways. Morphine, for example is classified as a balanced agonist since it may essentially actívate both the G proteins or the β-arrestin pathway, which is not the case for codeine or naloxone as an antagonist prototype. On the other hand, cardevilol a non-selective β-adrenergic antagonist causing preferential a β-arrestin mediated signaling profile is also a balanced β-arrestin GPCR ligand. This novel concept predicts that new GPCR ligands should prove more selective for one of the pathways involved clearing efficacy and safety. This principle discovered initially with GPCR ligands may be extended to other receptors including nuclear or tyrosine kinase activated receptors.

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27. ASSOCIATION BETWEEN GENETIC VARIANTS OF DNA REPAIR ENZYMES AND COLORECTAL CANCER PATIENT'S GLOBAL SURVIVAL UNDER 5-FU BASED TREATMENT. Asociación entre variantes genéticas de enzimas de reparación del ADN y sobrevida global de pacientes con cáncer colorrectal avanzado bajo tratamiento basado en 5-FU.

Resúmen:
Colorectal cancer is the second most common cancer in Chile, reaching up to 11.3% of total cases in both sexes. The main treatment is chirurgic removal of the tumor, which can be paired with chemotherapy depending on the cancer stage. The antineoplastic treatment used in Chile is based on 5-Fluorouracil (5-FU). This molecule has three targets, the enzyme thymidylate synthase, RNA transcription, and DNA replication or reparation. 5-FU inserts itself onto the DNA molecule, damaging its structural integrity, and thus activating the DNA repair response mechanisms. These mechanisms will try to repair the damage and recover the integrity of the DNA, but low-activity enzymes in these mechanisms (ERCC1, ERCC2, XRCC1, or XRCC3) will impair the recovery of the DNA, thus aiding in the antineoplastic treatment. This study aimed to identify relevant genetic variants in ERCC1, ERCC2, XRCC1, and XRCC3 that could help create a tool to predict 5-FU effectiveness. A retrospective study of 6 genetic variants in 75 patients under 5-FU based treatment, analyzed the global survival using Kaplan-Meier estimator, log-rank test, and Cox model regression. Preliminary results indicate that the G allele of ERCC1 (rs11615) variant and the A allele of the ERCC1 (rs3212986) variant may have clinical significance (p-values of 0.250 and 0.172, respectively) on predicting colorectal cancer patients' survival as a risk factor, though these analyses were not done with the information of all patients, so more variants of significance could still be added.

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28. ASSOCIATION BETWEEN TMPT GENETIC VARIANTS (rs 1142345 AND rs1800460) AND HEMATOLOGICAL ALTERATIONS IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA UNDERGOING INDUCTION TREATMENT WITH 6-MP. Asociación entre variantes genéticas de TMPT (rs1142345 y rs1800460) y alteraciones hematológicas en pacientes pediátricos con leucemia linfoblástica aguda en tratamiento con 6-MP.

Resúmen:
Introduction: 6-mercaptopurine (6-MP) is a key treatment for acute lymphoblastic leukemia (ALL) in children, but its use is often complicated by hematological toxicity, including anemia, neutropenia, and thrombocytopenia. Aim: This study investigates the association of genetic variants rs1142345 and rs1800460 in thiopurine methyltransferase (TMPT) with the occurrence of hematological adverse reactions in pediatric ALL patients. Methodology: We conducted a retrospective multicenter cohort study involving patients diagnosed with ALL between 2014 and 2023 at hospitals in the Metropolitan region. DNA was extracted from buccal swab samples, and genotyping was performed using RT-PCR. Patient medical records were analyzed, and the association between hematological reactions and genotypes was evaluated using χ^2 and Fisher's exact tests. Results: A total of 97 patients were included. Our findings revealed that the presence of either variant was significantly associated with anemia ($p = 0.0429$), red blood cell transfusions ($p = 0.0232$), and thrombocytopenia ($p = 0.0320$). Conclusion: These results indicate that variants rs1142345 and rs1800460, which are linked to poor metabolism of 6-MP, are associated with an increased risk of anemia, thrombocytopenia, and the need for red blood cell transfusions in pediatric ALL patients. This research highlights the importance of genetic screening for TMPT variants to better predict hematological toxicity in children undergoing treatment with 6-MP.

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29. ASSOCIATION BETWEEN THE rs1045642 VARIANT IN ABCB1 AND rs11045879 IN OATP1B1 AND THE ONSET OF MUCOSITIS IN INTERMEDIATE RISK PEDIATRIC ALL PATIENTS UNDERGOING CONSOLIDATION PROTOCOL WITH METHOTREXATE. Asociación entre variantes genéticas de ABCB1 (rs1045642) y OATP1B1 (rs11045879) y aparición de mucositis en pacientes pediátricos con LLA de riesgo intermedio en tratamiento de consolidación con metotrexato.

Resúmen:
Childhood Acute lymphoblastic leukemia (ALL) is the most frecuent type of cancer in pediatric population. The treatment includes methotrexate. This drug can cause mucositis. The variability in mucositis onset could be explained by genetics. The aim of this study is to associate the presence of rs1045642 variant in ABCB1 and rs11045879 variant in OATP1B1 with the occurrence of mucositis. A cohort was carried out in patients diagnosed between 2014 and 2023 in three hospitals. They were asked for bucal swab from which DNA was extracted. The analyzes were carried out with real time-PCR. The clinical records of the patients were collected in REDCap. The association between mucositis and the genotypes was assessed by relative risk (RR) and its 95% confidence interval (95%CI) 47 patients were included, with an average age of 5.4 ± 3.5 years, 53,2% of the patients were female and 46.8% were male. An analysis of the RR was carried out for each variant, analyzing the dominant and recessive model. The RR associated with the rs1045642 variant was 0.84 95% CI [0.37 – 1.94] and with the rs11045879 variant was 0.83 95% CI [0.36 – 1.92]. The OR was evaluated with Fisher's exact test. The OR associated with the rs1045642 variant was 0.76 95%CI [0.15 – 3.45] and with the rs11045879 variant was 0.73 95% CI [0.13 – 4.35]. The rs1045642 and rs11045879 variants could be associated with a higher risk of presenting mucositis. A more robust statistical analysis could achieve a statistically significant association. These findings can be used for prevention of mucositis in pediatric patients with ALL.

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30. CYTOTOXIC ACTIVITY OF INCOMPTINE A THROUGH DOWNREGULATION OF HEXOKINASE II IN BREAST CANCER CELL LINES. Actividad citotóxica de la incomptina a mediante la regulación negativa de hexocinasa ii en líneas celulares de cáncer de mama.

Resúmen:

Introduction: Treatments for breast cancer are limited by the cancer subtype and its selectivity towards tumor cells, hence the importance of finding compounds that increase the survival of healthy cells and target any subtype. Incomptine A (IA) is a sesquiterpene lactone isolated from Decachaeta incompta that has cytotoxic activity and alters the expression of proteins involved in glucose metabolism.1,2 With respect to the previous information, we consider it of utmost importance to evaluate the cytotoxic effect of IA in breast cancer cells and analyze its effect on glycolytic proteins. Objective: Determine the cytotoxic effect of IA against different subtypes of breast cancer and analyze its effect on the expression of proteins of the glycolytic pathway. Methodology: The cytotoxicity of IA was evaluated in the cell lines 4T1, MDA-MB-231, SK-BR-3, T-47D, MCF7 and in the non-tumorigenic line MCF10A using the WST-8 viability kit. The relative expression of glycolytic pathway proteins was measured by Western blot. Finally, IA molecular docking studies were carried out. Results: IA has similar cytotoxic activity among breast cancer cell lines, damaging non-tumorigenic cells to a lesser extent. IA decreased only the expression of hexokinase II (HKII). In silico studies suggests that IA binds to HKII.

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31. CYTOTOXIC ACTIVITY OF EXTRACTS FROM FLOWERS OF THE TRIBE HELIANTHEAE EVALUATED IN NEOPLASTIC CELL LINES. Actividad citotóxica de extractos de flores de la tribu heliantheae evaluada en líneas celulares neoplásicas.

Resúmen:

Introduction: The plants Leptocarpha rivularis, Podanthus mitique and Podanthus ovatifolius commonly known as palo negro, are endemic to Chile,ranging from Coquimbo to Concepción (P. mitique), from the Maule region to the Lakes region (L. rivularis). Traditionally, it has been used by the medicine of the Mapuche people and other ethnic groups to treat ailments related to the urinary tract, stomach and kidneys, as well as being used as a remedy for diabetes. Objective: Sequential extracts of P. mitique, P. ovatifolius and L. rivularis are shown to reduce cell viability of MCF-7 (breast adenocarcinoma), HT-29 (colorectal adenocarcinoma) and PC-3 (prostate adenocarcinoma) cell lines, suggesting their potential as an adjunct in the treatment of these diseases. Methodology: Sequential extracts (n-hex, DCM, ACOEt and ETOH) were obtained from flowers of these three species and cell viability was evaluated by the Sulforhodamine-B method in cell lines, using decreasing concentrations (50-12.5µg/mL). The treatments were carried out for 72 hours, using 0.1% DMSO as solvent control. Results: The n-hexane and DCM extract showed the highest cytotoxicity for the three species studied in the different cell lines at the different concentrations used. The DCM extract was shown to be cytotoxic in the different cell lines at the different concentrations used except for the species P. ovatifolia. The ethanol extract is the least cytotoxic for all three species and in all cell lines studied. The extracts of P. ovatifolia species in general are the least cytotoxic of the three species.

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32. DETERMINANTS OF ADHERENCE TO ANTIRETROVIRAL TREATMENT IN HIV PATIENTS: AN ASSESSMENT FROM THE PERSPECTIVE OF A SPECIALIZED NATIONAL ADVISORY PANEL. Determinantes de la adherencia al tratamiento antirretroviral en pacientes con VIH: evaluación desde la perspectiva de un panel consultivo especializado a nivel nacional.

Resúmen:

The introduction of antiretroviral (ARV) drugs has been essential in extending life and reducing mortality in people living with HIV. However, adherence to antiretroviral therapy (ART) continues to face significant challenges. The objective of this study was to categorize the priority variables that may impact ART adherence failure through the collection and analysis of healthcare personnel opinions who work in HIV/AIDS patient care programs. In the first phase of this research, a questionnaire titled "Categorization of Variables Affecting Adherence in ART Patients" was validated. This questionnaire assessed factors hindering adherence in HIV patients, including sociodemographic and economic factors and elements related to healthcare teams, the disease, treatment, and the patient. A numerical scale from 1 to 5 was used to obtain quantifiable responses, where 1 indicates the low determination of adherence failure, and 5 indicates the high determination of adherence failure. The questionnaire was administered to a specialized advisory panel of 47 professionals from various regions, including Tarapacá, Antofagasta, Metropolitana, Valparaíso, Maule, Bío-Bío, Araucanía, and Los Lagos. Participants included pharmacists, nurses, doctors, psychologists, social workers, and midwives, who categorized variables based on their influence on adherence failure. After applying the Saaty hierarchy method, critical factors identified were “Patient refuses to accept diagnosis,” “History of adherence failure,” “Alcohol and/or recreational drug use,” “Psychiatric comorbidities,” and “Lack of information about the illness.” A subsequent literature review proposed strategies to address these priority factors, highlighting text message reminders and peer support as practical approaches. Both methods have shown effectiveness in improving adherence, which is crucial to reducing morbidity and mortality and preventing HIV transmission.

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33. ALGORITHMS BASED ON INTERNATIONAL CRITERIA FOR PHARMACOVIGILANCE ALERTS IN ELDERLY PEOPLE AND APPLIED TO THE HISTORICAL DATABASE OF DESAM VALDIVIA. algoritmos basados en criterios internacionales para alertas de farmacovigilancia en ancianos y aplicados a la base de datos histórica de desam valdivia.

Resúmen:
This project aims to improve medication safety in elderly people, through the development and implementation of pharmacovigilance algorithms based on international criteria and their application in the historical database from primary healtcare electronic clinical record, proportionated by the DESAM-Valdivia. A retrospective cohort methodology will be performed on anonymized prescription data from 2017 to 2022 of the 11 primary healthcare centers in the commune of Valdivia obtained by the HASFa innovation core carrying over 5 millions medical prescriptions. The international criteria to build the algorithm were "Versión en español de los criterios STOPP/START 3.", "American Geriatrics Society 2023 updated AGS Beers Criteria®" and "CRIDECO Anticholinergic Load Scale", focused on people over 60 years old. The implementation of the algorithm was carried out using Python programming language and Jupiter notebook free software tool. This research expects to reduce the number of drug-related problems from the alerts created. reducing the time required for the pharmaceutical validations on medical prescriptions, as a support to the pharmacist decisions.

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34. ROLE OF PANNEXIN 1 CHANNELS IN BFGF -INDUCED DERMAL FIBROBLAST RESPONSE. Rol de los canales de Panexina 1 en la respuesta de fibroblastos dérmicos inducida por βFGF

Resúmen:
As the body's largest organ, the skin is highly susceptible to environmental damage but has an intrinsic healing capacity. Dermal fibroblasts play a central role in wound healing through signaling molecules like the basic Fibroblast Growth Factor (βFGF), which stimulates proliferation, migration, and extracellular matrix deposition, critical processes in repair. Our studies indicate that Pannexin 1 (Panx1) channels are involved in cutaneous repair, though how the Panx1 channel modulates the fibroblast response to βFGF signaling remains unclear. Methodology: Human neonatal dermal fibroblasts were treated with βFGF (10 ng/mL), and Panx1 channel activity was blocked using Probenecid and 10Panx. ATP levels were measured to assess Panx1 functionality, and Panx1 expression was evaluated using qRT-PCR and western blot. Cell proliferation, migration, and Vascular Endothelial Growth Factor (VEGF) expressions in fibroblasts treated with βFGF were assessed through a proliferation assay, scratch wound assay, and qRT-PCR. Additionally, wound healing time in rat skin treated with FGF and 10Panx was evaluated. Results: Panx1 functionality in fibroblasts treated with βFGF (10 ng/mL) for 7 and 24 hours reduced extracellular ATP concentration, similar to the effect observed with Panx1 blockers. βFGF did not alter Panx1 expression but increased fibroblast migration independently of Panx1 activity. Combined treatment with βFGF and Panx1 blockers enhanced proliferation, while Probenecid treatment elevated VEGF expression. No significant differences in wound closure were observed between βFGF only and βFGF plus 10Panx treatments. Conclusion: Panx1 channels modulate βFGF related activities in cell proliferation and VEGF expression in dermal fibroblasts.

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35. EFFECT OF INDOLE-BASED ARYL HYDROCARBON RECEPTOR LIGANDS ON CELL VIABILITY OF HUMAN CEREBRAL MICROVASCULAR ENDOTHELIAL CELLS. Efecto de ligandos indólicos del receptor de aril hidrocarburos sobre la viabilidad celular de células endoteliales cerebrales humanas.

Resúmen:
Tryptophan-derived indole compounds, produced by gut microbiota and diet, play crucial roles in homeostasis and are recognized as ligands of the aryl hydrocarbon receptor (AhR). This study examines the cytotoxic effects of specific indole derivatives on human cerebral microvascular endothelial cells (hCMEC/D3 cell line), a model of the blood-brain barrier (BBB) that expresses AhR. We evaluated the effects of the agonists FICZ, indoxyl sulfate (a renal toxin and chronic kidney disease marker), indole-3-acetate, indole-3-propionate, indole-3-pyruvate, indole-3-carbinol, and the AhR antagonist CH223191. Cell viability was assessed after 48-hour treatments using the neutral red assay, both with agonists alone and in co-treatments with the antagonist. Results revealed that only indole-3-carbinol exhibited significant cytotoxicity, reducing cell viability below 90% at concentrations of 50 and 100 micromolar while co-treatment with CH 223191 reversed its cytotoxic effect in a concentration-dependent manner. The other indole ligands did not affect cell viability under similar conditions. These findings might support the hypothesis that activation of AhR by specific ligands disrupt endothelial integrity, through reactive oxygen species (ROS) generated by the up-regulation of CYP1A1 and CYP1B1, two key enzymes involved in oxidative stress and regulated by ligand-mediated AhR activation.

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36. ANTITUMOR MECHANISMS INDUCED BY A NOVEL FULLY HUMAN ANTIBODY TARGETING THE MICA PROTEIN. Mecanismos antitumorales inducidos por un nuevo anticuerpo completamente humano dirigido contra la proteína mica.

Resúmen:
The use of monoclonal antibodies for cancer treatment has become a major immunotherapeutic strategy due to their high affinity, antigenic specificity and their ability to interact with receptors on immune cells through the crystallizable fragment (Fc). Upon binding to their target, the Fc of the antibody interacts with Fc gamma receptors on immune cells, activating mechanisms such as antibody-dependent cellular phagocytosis (ADCP) and antibody-dependent cellular cytotoxicity (ADCC). These mechanisms are involved in the selective elimination of tumor cells that express surface molecules, which are recognition signals for effector cells. MICA, is a target protein expressed on the surface of various tumor cells. The aim of this work is to evaluate antitumor effector mechanisms mediated by a novel fully human anti-MICA IgG1 antibody, across different MICA-expressing cell lines. To achieve it, NK cell-enriched PBMCs were isolated from healthy donors and co-cultured with K562 target cells in the presence of anti-MICA, isotype control antibody, or PBS (vehicle). ADCC was evaluated by measuring immune cell degranulation and IFN-gamma production by flow cytometry. To evaluate ADCP, monocytic U937 cells expressing EGFP were differentiated into macrophages using PMA. The gastric human cell line GES1, which expresses MICA, was labeled with TFL4 and treated as described above, followed by co-incubation with macrophages. Phagocytic activity was assessed by flow cytometry and confocal microscopy. Our results showed increased CD107a, a degranulation marker in NK cells (CD3-CD56+), and increased IFN-gamma production in groups treated with anti-MICA compared to controls. Compared to vehicle and isotype controls, enhanced macrophage-mediated phagocytosis of GES1 cells was also observed with anti-MICA. Our anti-MICA IgG1 antibody enhances ADCC and ADCP, indicating its potential for immunotherapy against MICA-expressing cells.

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37. DEVELOPMENT OF ANTI-MICA FUNCTIONALIZED GOLD NANOSPHERES FOR ENHANCING PHAGOCYTOSIS OF MICA-EXPRESSING CELLS: TOWARDS GASTRIC CANCER APPLICATIONS. Desarrollo de nanoesferas de oro funcionalizadas con anti-MICA para potenciar la fagocitosis de células que expresan MICA: hacia aplicaciones en cáncer gástrico.

Resúmen:
Introduction: Overexpression of the Major Histocompatibility Complex Class I Chain-Related Protein A (MICA) in certain cell types can contribute to immune evasion and disease progression. Targeting MICA may enhance the immune system's ability to clear abnormal cells. Gold nanoparticles (AuNPs) offer a promising platform for developing targeted immunotherapies, with potential applications in gastric cancer treatment. Objective: To develop and characterize a nanosystem of gold nanospheres functionalized with anti-MICA monoclonal antibodies and evaluate its capacity to enhance antibody-dependent cellular phagocytosis (ADCP) of MICA-expressing cells. Methods: Gold nanospheres (40 nm) were synthesized using a seed-mediated growth method and functionalized with anti-MICA antibodies through cooperative adsorption, forming the AuNP/anti-MICA/BSA nanosystem. Characterization was performed using UV-Vis spectroscopy, dynamic light scattering, zeta potential measurements, and immunodot blot assays. ADCP was assessed in vitro by co-culturing GES-1 cells with U937-derived macrophages expressing EGFP. Phagocytic activity was measured and compared between treatments with soluble antibodies and the nanosystem. Results: Functionalization of AuNPs with anti-MICA antibodies was confirmed by an increase in hydrodynamic diameter (100 nm), a red shift in the surface plasmon resonance peak (3 nm), and positive immunodot blot results. Approximately 90 antibodies were conjugated per nanoparticle. The AuNP/anti-MICA/BSA nanosystem enhanced phagocytosis of MICA-expressing GES-1 cells by macrophages compared to the negative controls. Conclusion: The AuNP/anti-MICA/BSA nanosystem effectively enhances macrophage-mediated phagocytosis of MICA-expressing cells in vitro, particularly when compared to negative controls. These findings suggest the potential of this nanosystem to boost immune clearance of MICA-overexpressing cells, but further studies using gastric cancer cell models are necessary.

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38. EFFECT OF A NUTRITIONAL INTERVENTION WITH KEFIR ON THE INTESTINAL MICROBIOTA AND METABOLIC PARAMETERS OF ADULTS WITH METFORMIN TREATED TYPE 2 DIABETES. Efecto de una intervención nutricional con kéfir sobre la microbiota intestinal y parámetros metabólicos de personas con diabetes mellitus tipo 2 tratados con metformina

Resúmen:
Cambios en la microbiota intestinal se asocian a patologías metabólicas como diabetes mellitus tipo 2 (DM2). Probióticos, como el kéfir, podrían restituir la composición de la microbiota intestinal e introducir funciones beneficiosas para las comunidades microbianas intestinales, ayudando de esta forma a mantener un buen control metabólico. El presente estudio busca determinar el efecto del consumo de kéfir en la composición de la microbiota intestinal, el control metabólico y la salud digestiva en sujetos con DM2 en tratamiento con metformina. Para esto se realizó un ensayo clínico controlado de ciego simple en 20 individuos con DM2 los cuales fueron asignados a dos grupos: intervención y control donde recibieron 150 g/d de kéfir o yogurt natural comercial, respectivamente, durante ocho semanas. Para cada grupo se evaluaron parámetros metabólicos y gastrointestinales pre/post intervención. El efecto sobre la composición de la microbiota intestinal se analizó en cinco sujetos que consumieron kéfir mediante la secuenciación metagenómica de la región V4 del ARNr 16S a partir de muestras fecales pre/post intervención de 2 semanas. Los resultados indican que dos semanas de consumo del probiótico aumentó la abundancia relativa de los phyla Firmicutes y Actinobacteria mientras que produjo una disminución de Bacteroidetes y Proteobacteria. A nivel de géneros bacterianos, el consumo de kéfir generó un aumento de géneros productores de butirato Coprococcus y Lachnospira, junto con Leuconostoc. Adicionalmente, el consumo de kéfir durante ocho semanas disminuyó significativamente los triglicéridos plasmáticos, hinchazón, acidez, gases, frecuencia y dificultad evacuatoria. Estos resultados indican que la intervención con kéfir contribuye a modular la microbiota intestinal hacia un normotipo, además de disminuir los triglicéridos sanguíneos y mejorar síntomas gastrointestinales.

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39. 3-NITROTYROSINE AND NLRP3 AS MARKERS OF ATRIAL FIBRILLATION FOLLOWING CARDIAC SURGERY: POTENTIAL PHARMACOLOGICAL TARGETS IN CARDIAC ARRYTHMIAS. 3-Nitrotirosina y NLRP3 como marcadores de fibrilación auricular posterior a una cirugía cardíaca: potenciales blancos farmacológicos en arritmias cardíacas

Resúmen:
Background: Cardiopulmonary bypass (CPB) determines cardiac injury in which oxidative stress (OS) plays a critical role in the induction of postoperative atrial fibrillation (AF). The hypothesis tested is that preoperative reduced left ventricular ejection fraction (rLVEF) is associated with higher levels of 3-nitrotyrosine in atrial tissue and plasma of AF patients; Material and Methods: Fifty-two patients (45 – 79 years old) were admitted to the Surgery Thorax Service at Instituto Nacional del Thorax, Santiago, Chile, between March 2022 and December 2023. Patients were divided by LVEF: pLVEF >40%, n=27 and rLVEF≤40%, n=25. Atrial tissue and plasma samples were obtained at the surgical time for NLRP3, 3-nitrotyrosine, 3-NT; 8-Isoprostanes, malondialdehyde, MDA; and thiobarbituric acid reaction, TBARS levels; in addition, measurement of the total plasma antioxidant capacity and nuclear factor erythroid 2-related factor 2, NRF2 in atrial tissue were measured; Results: Higher 3-nitrotyrosine and MDA levels in plasma and atrial tissue from rLVEF patients compared with pLVEF patients were measured. Patients who developed AF (29/52) showed higher levels of plasma and atrial tissue NLRP3, 3-NT, lipid peroxidation levels as MDA and TBARS, with respect to patients in sinus rhythm (SR) (23/52). Also, nitrotyrosine plasma and atrial tissue levels showed a negative correlation with LV function in both groups and a positive with NLRP3 tissue levels. Conclusions: 3-NT plasma levels preoperatively and at surgical time could predict oxidative injury and NLRP3 activation in atrial tissue in rLVEF patients who develop AF. This pilot trial will determine a potential target with non-traditional antiarrhythmic drugs in heart failure, such as NLRP3 pathways.

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40. ASSESSING OF THE PRO-RESOLVING EFFECTS OF RvD2, MaR1 AND RvE1: THE ROLE OF NF-κB-NLRP3 PATHWAY IN A 3D VASCULAR INFLAMMATION MODEL. Evaluación del efecto pro-resolutorio de rvd2, mar1 y rve1: ROL DE LA VÍA NF-κB−NLRP3 en un modelo 3d de inflamación vascular.

Resúmen:

Inflammation is a central factor in diseases that affect the heart and blood vessels, including hypertension and atherosclerosis. These are characterized by high circulating levels of angiotensin II, vasoconstriction and chronic inflammation. Current treatment focuses on acute processes, but none addresses chronic inflammation or vascular damage. The resolution phase is the one that promotes the reparation of the damage through the action of specialized pro-resolution mediators. Previous studies have identified that patients with cardiovascular disease have low levels of these bioactive compounds. On the other hand, it has been identified that NF-κ B-NLRP3 pathways are involved in chronic inflammation, but it has not been clarified whether pro-resolving mediators regulate these pathways to exert their effect. This study evaluated whether the administration of RvE1, RvD2 and MaR1, alone or in combination, act on the NF-κ B-NLRP3 pathway and its effects on inflammation resolution in a spheroidal 3D model. The inflammatory response in the vascular spheroid was induced with angiotensin II and its cellular organization was characterized. The endothelial cells are located on the periphery and the muscle cells in the center of the spheroid. RvE1 significantly reduced the adhesion of neutrophils and proinflammatory cytokines, RvD2 the proliferation of muscle cells. Angiotensin II induces a surge in p65 expression, although poor localization of this in nucleus and the conditions of SPMs except RvD2 induce a decrease in NLRP3. These findings support the significant effect of RvE1 on inflammatory markers and suggest that SPMs may be involved in the NF-kB-NLRP3 pathway, although their effect on NF-kB is unclear; however, a more defined influence on NLRP3 is observed.

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41. GUT-BRAIN AXIS ALTERATIONS AND CIRCADIAN CHANGES IN SALIVARY CORTISOL: A PILOT STUDY IN UNIVERSITY STUDENTS FROM VALPARAISO. Alteraciones del eje intestino-cerebro y cambios circadianos en cortisol salival: un estudio piloto en universitarios de Valparaíso

Resúmen:

BACKGROUND AND AIM: Gastrointestinal alterations are highly comorbid with stress-associated disorders. In order to improve the chances for timely treatment in occupational settings with a high workload, we are investigating the predictive value of self-reported gastrointestinal data for the detection of stress-related mental health disorders. EXPERIMENTAL DESIGN AND METHODS: This pilot study was performed in university students from the program of Education in Biology at Pontificia Universidad Católica de Valparaíso. All the participants (n=6) were carrying out their final professional practice, and answered questionnaires regarding quality of life, burnout syndrome, depression, anxiety and stress, and gastrointestinal health. Additionally, they provided saliva samples collected at four times during the same day (upon awakening, 30 minutes post-awakening, at noon and just before bedtime), from which cortisol levels were quantified by EIA. RESULTS: Cortisol levels showed AM-PM variation, but there was no additional value in evaluating four samples versus only two samples (i.e. only at awakening and bedtime). Due to small sample size and high data dispersion, no correlation was found between the survey results and cortisol data. However, there were insightful associations between survey components, including an inverse correlation between stress and gastrointestinal quality of life. CONCLUSION: This pilot study is the prelude for a full-size investigation that will focus on practicing educators. Understanding how components of gut-brain axis relate in a stressful occupational setting will help to find and adapt predictive tools, in order to recognize a decline in the mental and physical -particularly gastrointestinal- health of educators, a relevant step to ensure opportune access to therapy.

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42. GLUT4 AND GLYCOSIDIC METABOLISM: METFORMIN AS A POTENTIAL THERAPEUTIC ALTERNATIVE IN AUTOSOMAL DOMINANT CENTRONUCLEAR MYOPATHY (AD-CNM). GLUT4 y metabolismo glicosídico: Metformina como potencial alternativa terapéutica en la miopatía centronuclear autosómica dominante (MCN-AD).

Resúmen:

Autosomal Dominant centronuclear myopathy (AD-CNM) is an early-onset inherited muscle disease that affects skeletal muscle structure and function. Clinically it manifests with myalgia, hypotonia, muscle weakness and defects in voluntary movements. AD-CNM is caused by mutations in the DNM2 gene, which encodes dynamin-2, a GTP-ase required in several cellular processes including membrane and cytoskeleton remodeling. AD-CNM-causing mutations in DNM2 affect catalytic activity of dynamin-2, causing defects in membrane protein trafficking in muscle cells. Particularly important for muscle metabolism and functions, AD-CNM-causing mutations in dynamin-2 disrupt the glucose transporter GLUT4 trafficking from intracellular stores to the surface membranes. Consequently, it is feasible to assume that a treatment modifying GLUT4-trafficking could positively impact on the myopathic signs in the context of AD-CNM. Here, we evaluated the effect of metformin, a hypoglycemic drug that promotes GLUT4- trafficking in a murine model of AD-CNM and their healthy wild-type (WT) littermates. Both were treated with a daily dose of 50 mg/kg of metformin for 14 days. We evaluated the impact of this treatment on the muscle mass, grip strength, histological signs of atrophy and surface-membrane expression of GLUT4 in the tibialis anterior (TA) muscle, one of the most affected in patients and animal models of AD-CNM. Our results show that the AD-CNM mice treated with metformin exhibit similar values of grip-strength, muscle fiber diameter and GLUT4 surface expression compared to their WT littermates. Although preliminary, these data suggest a positive effect of metformin on the myopathic signs in the AD-CNM model, and they could pave the way for considering a new use for metformin, as a possible therapeutic alternative in the treatment of AD-MCN.

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43. MORPHOLOGICAL CHANGES OF COLONIC SUBMUCOSAL NPY NEURONS AT DIFFERENT DEVELOPMENTAL STAGES. Cambios morfológicos de las neuronas NPY de la submucosa colónica en diferentes etapas del desarrollo.

Resúmen:
BACKGROUND: Neuropeptide Y (NPY) is a neuroimmune regulator of physiological processes, such as food intake, and is involved in inflammatory conditions, including obesity. Considering that obesity, a disorder linking inflammation, dysmetabolism and aberrant enteric ecology, can arise during infancy or childhood, there is little information on NPY colonic neuron dynamics or their involvement at inflammatory processes, during early life. The interaction between NPY and the metabolic environment during growth may also influence susceptibility to inflammatory disorders, which emphasizes the importance of understanding these changes to develop preventive and therapeutic strategies. AIM: To analyze and describe the chemical code and morphology of colon submucosal neurons from young female rats. METHODS: Colon (n=6) was collected at postnatal days 21, 35 and 45, representing infancy, puberty and adolescence, respectively. The submucosal plexus was used in immunofluorescence assays to detect total (PGP9.5+) and NPY neurons. RESULTS: A decrease in total neuron density and in NPY neurons percentage/ganglion, as well as an increase in NPY projections percentage/ganglion was observed as rats aged, although without significant differences. On the other hand, there was a significant age-associated increase in the number of neurons and projections per ganglion, as well as an increase in the size of total and NPY-neuron soma. Finally, ganglion density significantly decreased with age. CONCLUSION: there are morphological differences in colon submucosal neurons (including NPY-positive ones) between infant and juvenile female rats. DISCUSSION: his data, together with future functional experiments, will contribute significantly to the search for new pharmacological targets for inflammatory pathologies of the gastrointestinal tract. Research on the early role of enteric NPY could provide information on the mechanisms linking growth, inflammation and obesity risk in adulthood.

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44. CATIONIC TRIPHENYLPHOSPHONIUM COMPOUNDS AS H3R LIGANDS WITH ANTIOXIDANT PROPERTIES. Compuestos derivados del cation de trifenilfosfina como ligandos H3R con actividad antioxidante.

Resúmen:
Neurodegenerative diseases represent a major public health challenge due to the aging population and their complex pathology, searching for new therapeutic alternatives is crucial. In response to this, a series of six 1-(3-phenoxypropyl)piperidines, alkyl-linked to a triphenylphosphonium cation, designed as H3R ligands with antioxidant properties to mitigate excessive mitochondrial oxidative stress were synthesized. These compounds are aimed at contributing to the development of potential new therapies for neurodegenerative diseases. Radioligand displacement assays demonstrated high affinity for the histamine 3 receptor (H3R), with Ki values ranging from 14.1 nM to 67.4 nM, comparable to pitolisant, a well-known H3R inverse agonist. The antioxidant properties of the compounds were evaluated using the ORAC assay, where all derivatives showed low to moderate radical scavenging activity. Cytotoxicity studies conducted on SH-SY5Y neuroblastoma cells using the alamar blue assay revealed significant effects on cell viability, with a clear structure-toxicity relationship emerging. Furthermore, docking and molecular simulations were performed to understand the binding form of the H3R, which will guide further modifications to the compounds. These modifications aim to refine the structure-activity relationship and identify a lead compound with therapeutic potential for neurodegenerative diseases.

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45. CHEMICAL CHARACTERIZATION AND ANTIOXIDANT CAPACITY OF THE HYDROALCOHOLIC EXTRACT OF LAMPAYO MEDICINALIS F. PHIL (VERBENACEAE). Caracterización química y capacidad antioxidante del extracto hidroalcohólico de Lampayo medicinalis f. Phil (Verbenaceae).

Resúmen:
Lampayo (Lampayo medicinalis F. Phil) is a high Andean shrub traditionally used in infusions to treat kidney and liver ailments. Lampayo research has indicated that antioxidant molecules such as flavonoids and terpenes stand out in chemical composition. The objective of this research was to chemically characterize the hydroalcoholic extract of L. medicinalis leaves and to determine its antioxidant capacity. For this purpose, a phytochemical screening, the quantification of alkaloids by the bromocresol blue method, the application of Banford's systematic march to determine the alkaloid groups and the Folin-Ciocalteu and complex formation methods with AlCl3 for the polyphenol and flavonoid content, respectively, were carried out. In addition, antioxidant capacity was evaluated using the DPPH and ORAC methods. Hydroalcoholic extraction resulted in a yield of 40.5% and phytochemical screening confirmed the presence of secondary metabolites such as alkaloids, flavonoids, glycosides, quinones, phenols, saponins, terpenes and triterpenes. The content of total polyphenols by Folin-Ciocalteu method was 14 ± 0.3 mg EAG/g ES, the content of total flavonoids by AlCl3 method was 10.3 ± 0.5 mg EQ/g ES. The results of quantitative antioxidant effect by DPPH at 20 min was 12.8 ± 4.97% and the evaluation of antioxidants present by ORAC was 93.98 ± 2.62 µmol eq Trolox/g ES. The results indicate a significant antioxidant potential of the extract, suggesting its possible application in the formulation of natural antioxidants with therapeutic properties to combat oxidative stress in the human body.

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Socio Patrocinante: no aplica

46. FORMULATION OF AN ULVAN-BASED POLYMERIC MATRIX FROM ULVA RIGIDA AND GELATIN FOR POTENTIAL USE IN CUTANEOUS WOUND TREATMENT. Formulación de una matriz polimérica en base de ulvano extraído de Ulva rígida y gelatina con potencial uso para el tratamiento de heridas cutáneas.

Resúmen:
Chronic wounds affect between 1% and 2% of the global population, particularly impacting the elderly and individuals with conditions such as diabetes and vascular disease. These wounds exhibit impaired healing, which diminishes the quality of life and increases the risk of infections and amputations, highlighting the need for new treatments. In this context, ulvan, a polysaccharide extracted from green algae with antioxidant, antimicrobial, and anti-inflammatory properties combined with gelatin, is known for its wound-healing properties; both could be a promising alternative for developing biocompatible matrices that optimize wound healing. This study aims to formulate a polymeric matrix based on ulvan extracted from Ulva rigida and gelatin compatible with human dermal fibroblasts. Methods: Four polymeric matrices were formulated with ulvan (from Ulva rigida) concentrations of 1%, 3%, 6%, 10% (w/v), and 1.5% gelatin. Cell viability was assessed using the resazurin assay, glucose uptake, and cell proliferation measurements in human neonatal dermal fibroblasts cultured in these matrices. Finally, VEGF production in fibroblast culture supernatants was quantified by ELISA. Results: All matrices exhibited a swelling capacity exceeding 2000%. The combination of 1% ulvan and 1.5% gelatin showed no apparent degradation and achieved the best results for cell viability, glucose uptake, cell proliferation, and VEGF production. Conclusion: The polymeric matrix composed of ulvan and gelatin demonstrates biocompatibility with dermal fibroblasts, suggesting its potential to support the development of new treatments for wound healing.
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47. EFFECT OF A HIGH-FAT DIET ON OXIDATIVE STRESS AND RELATIVE ABUNDANCE OF ANTIBIOTIC RESISTANCE GENES IN THE GUT MICROBIOTA. Efecto de una dieta alta en grasas sobre el estrés oxidativo y la abundancia relativa de genes de resistencia a los antibióticos en la microbiota intestinal.

Resúmen:
Introducción: La resistencia a los antibióticos es un problema de salud pública global que causa 1,27 millones de muertes anuales. Es por esto que es de suma importancia identificar los factores que contribuyen a este fenómeno. En la actualidad se ha establecido que diversas comunidad microbianas, incluida la microbiota intestinal (MI), pueden actuar como reservorio de genes de resistencia. Este trabajo busca estudiar el efecto de la dieta alta en grasas, sobre el estrés oxidativo a nivel intestinal y su potencial impacto sobre la resistencia a antibióticos en la MI. Metodología: El efecto de la dieta alta en grasa (HFD) sobre el estrés oxidativo sistémico e intestinal y la resistencia a antibióticos se determinó en ratas macho Sprague-Dawley sometidas a diet HFD por 12 semanas. Como control se sometió un grupo de animales a dieta control por el mismo tiempo. Para determinar el estrés oxidativo a nivel sistémico e intestinal se cuantificaron, en suero y tejido intestinal, los siguientes marcadores: malondialdehído (MDA), superóxido dismutasa (SOD) y el ratio glutatión oxidado/reducido (GSH/GSSG). El perfil de resistencia a los antibióticos se evaluó mediante shotgun metagenomic sequencing y posterior análisis bioinformático de la microbiota intestinal del ciego. Resultados: Los resultados obtenidos muestran que la dieta alta en grasa produce un aumento en el estrés oxidativo en el tejido intestinal del ciego, medido por las concentraciones de MDA, SOD y GSH/GSSG pero no en suero tras 12 semanas de exposición. Así mismo, la exposición a dieta alta se asocia directamente a la identificación de dos genes de resistencia, cblA y aad9, que confieren actividad betalactamasa y resistencia a espectinomicina, respectivamente.
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48. ALDOSTERONE EFFECTS ON HEPATIC AND RENAL CELLS: ACTIVATION OF THE UNFOLDED PROTEIN RESPONSE VIA IRE1 AND PERK PATHWAYS In Vitro. Efectos de la Aldosterona en Células Hepáticas y Renales: Activación de la Respuesta a Proteínas Malplegadas a través de las Vías de IRE1 y PERK In Vitro

Resúmen:
Aldosterone, a key mineralocorticoid hormone for electrolyte balance, is increasingly recognized for roles beyond its classical targets, particularly in cellular stress responses in non-traditional tissues. This study investigates aldosterone's effects on the unfolded protein response (UPR) in hepatic (HepG2) and renal epithelial (HEK293) cells, focusing on two main UPR signaling pathways: IRE1 and PERK, which are critical for managing cellular stress. Using in vitro models, we treated cells with physiological and supraphysiological concentrations of aldosterone, assessing UPR activation through fluorescent reporters for XBP1 and ATF4, key markers of IRE1 and PERK pathway activation, respectively. Results reveal that aldosterone induces cell type-specific UPR activation, with notable differences between hepatic and renal cells. Importantly, prolonged exposure to high aldosterone levels activates a PERK-mediated stress response, potentially leading to cellular damage. These findings broaden our understanding of aldosterone's non-classical functions, suggesting its involvement in the pathogenesis of stress-related disorders in hepatic and renal tissues. The observed link between aldosterone and cellular stress responses indicates that targeting UPR pathways activated by this hormone could offer novel therapeutic strategies for mitigating mineralocorticoid-induced cellular stress. Overall, this study highlights aldosterone's influence on cellular stress mechanisms, suggesting new research directions to further explore its role in various pathophysiological conditions.
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49. EVALUATION OF THE ASSOCIATION BETWEEN GENETIC VARIANTS IN ENZYMES INVOLVED IN THE METABOLISM OF FLUOROPYRIMIDINES AND ADVERSE REACTIONS LINKED TO TREATMENT WITH 5-FU OR CAPECITABINE IN PATIENTS WITH ADVANCED COLORECTAL CANCER. Evaluación de la asociación entre variantes genéticas en enzimas implicadas en la metabolización de fluoropirimidinas y reacciones adversas vinculadas al tratamientos con 5-FU o Capecitabina, en pacientes con cáncer colorrectal avanzado.

Resúmen:
Colorectal cancer is a significant public health issue in Chile, with 3,330 deaths recorded in 2022. The most used treatments involve antineoplastic drugs such as 5-FU and capecitabine in chemotherapy regimens, which, while effective, can lead to severe adverse drug reactions (ADRs) in some patients, necessitating cautious administration. Classic pharmacological studies have attributed this variability in responses to factors like age, drug interactions, sex, cancer stage, among other. However, more recent research highlights genetic variants as a crucial factor. Some of the variants associated with the development of ADRs correspond to enzymes (Dihydropyrimidine dehydrogenase DPYD, Cytidine deaminase CDA, Thymidine phosphorylase TYMP and Thymidylate synthase TYMS) involved in the metabolic pathways of these drugs. This study aims to investigate the association between genetic variants of DPYD (rs3918290), CDA (rs532545), TYMP (rs11479), and TYMS (rs2853741) and the development of severe ADRs in Chilean patients with advanced colorectal cancer. A total of 87 patients were recruited from Hospital Clínico de la Universidad de Chile, Fundación Arturo López Pérez, and Instituto Nacional del Cáncer for a case-control study (43 controls and 44 cases), based on the severity of the ADR (Grade 2 or higher considered a case). DNA was extracted from blood samples and tumor tissue, with genotypes determined using Real-Time PCR and TaqMan® probes. The most frequently reported ADRs were nausea, diarrhea, and fatigue. No significant associations were found for the studied SNPs, though p-values of 0.063 for TYMS and 0.070 for TYMP suggest that larger sample sizes and further analysis are needed to establish associations between the SNPs studied and ADRs in the Chilean population.

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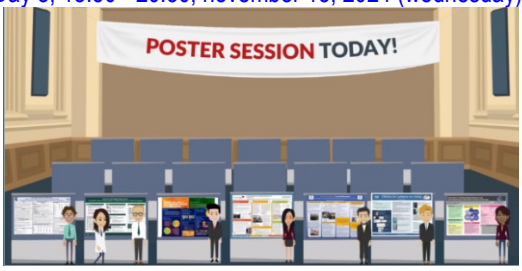
50 ASSOCIATION BETWEEN GENETIC POLYMORPHISMS OF COMT, OPRD1 AND OPRM1 AND OPIOID SAFETY IN ADVANCED STAGE COLORECTAL CANCER PATIENTS. Asociación entre polimorfismos genéticos en COMT, OPRD1 y OPRM1 y la seguridad de tratamientos analgésicos con opioides en pacientes con cáncer colorrectal de etapa avanzada.

Resúmen:
Colorectal cancer was the second most frequent and the third most lethal cancer in Chile in 2022. Pain is a common symptom in these patients, often requiring pharmacological management with non-opioids, opioids and adjuvants. Opioids are widely used because of their efficacy and safety, but the intensity of the pain experience, the dose requirement to achieve analgesia and the incidence of adverse drug reaction (ADR), can be explained by interindividual factors which include the presence of genetic variants. The most common opioid induced ADRs are related to gastrointestinal, neurologic and respiratory systems. The study aims to investigate the association between the presence of genetic variants of COMT (rs4680), OPRD1 (rs2236861) and OPRM1 (rs9479797) and the risk opioid-induced ADRs in Chilean advanced stage colorectal cancer patients. A total of 114 colorectal cancer patients were recruited from Hospital Clinico de la Universidad de Chile (HCUCH) and Instituto Nacional del Cancer (INC) for a case-control study. The DNA extraction was realized from blood samples with the E.Z.N.A.® Blood DNA Mini Kit and the genotypes were determined with the AriaMx® Real-Time PCR System. The Hardy-Weinberg equilibrium was determined through the SNPStats website. A total of 30 patients who experienced opioid-induced ADRs were included in an odds ratio analysis. No significant associations were found for the studied SNPs. The most frequent ADRs reported were nausea, constipation and vomits, while the most frequent opioids administered were tramadol, morphine and fentanyl. Larger sample sizes and further analysis are needed to establish the association between the SNPs studied and opioid-related ADRs in the Chilean population.

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PANEL COMMUNICATIONS

Day 3, 18:30 - 20:30, november 13, 2024 (wednesday)



1. DESIGN OF SELECTIVE POSITIVE ALLOSTERIC MODULATOR AFFECTING THE FUNCTION OF THE HYPEREKPLEXIC GLYCINE RECEPTOR CARRYING THE R271Q MUTATION. Diseño de moléculas alostéricas selectivas que modulen la función del receptor de glicina que porta la mutación R271Q causante de la enfermedad hiperekplexia

Resúmen:
Hyperplexia is a rare neurological disorder characterized by an exaggerated startle response and severe, generalized or intermittent muscle rigidity. This condition is caused by mutations in various genes encoding the different subunits of the glycine receptor (GlyR). The GlyR is an ion channel belonging to the family of pentameric ligand-gated ion channels (pLGICs), which plays a critical role in regulating neuronal excitability. To date, mutations causing hyperplexia have mainly been described in the GLRA1 gene, which encodes the alpha 1 subunit of the GlyR (GlyRa1). In this context, the mutation in residue R271 is the most well-characterized mutation, resulting in a hypofunctional receptor. Biochemical and electrophysiological studies have shown that the R271Q mutation stabilizes the closed conformation of the channel, a phenotype that is reversed by the intravenous general anesthetic propofol. However, propofol's specificity has limited its use as a therapeutic agent for hyperplexia. Therefore, this study aims to rationally search for new molecules that act as positive allosteric modulators of the receptor bearing the R271Q mutation. Using the structural model of GlyRa1 with the R271Q mutation, we have rationally designed de novo molecules capable of interacting with the binding pocket described for propofol. Subsequently, we conducted a screening of existing molecules in databases using a shape-based screening protocol to identify molecules similar to those designed in the previous stage. The resulting set of molecules was validated using molecular docking and free energy binding predictions. The 6 molecules with the best binding parameters were selected. These will be evaluated through functional assays using electrophysiology in subsequent studies.

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Socio Patrocinante: David Ramírez y Gustavo Moraga

2. ACTIVATION OF SOMATOSTATIN-EXPRESSING INTERNEURONS IN THE DENTATE GYRUS ENHANCES STRUCTURAL PLASTICITY AND MEMORY IN AGED MICE. La activación de interneuronas que expresan somatostatina en el giro dentado mejora la plasticidad estructural y la memoria en ratones de edad avanzada.

Resúmen:
Aging is a natural process that affects our brain. The hippocampus, a key brain region for learning and memory, undergoes changes during aging, such as a decrease in the number of synapses, making it difficult to form new memories. The balance between excitatory and inhibitory neurotransmission is crucial for the formation of new memories, and interneurons (INs) are essential for controlling this activity. Among them, interneurons expressing somatostatin (INs-SST), especially in the region of the dentate gyrus (DG), where they are in higher proportion. In the hilus, INs-SSTs synapse with granule cells (GC) in the outer layer. A decrement in the inhibitory neurotransmission in aged subject is related to deficit in new memory formation. In this work we propose that activation of INs-SSTs in the DG improves structural plasticity and memory, decreasing the cognitive deficit observed in aged subjects. Our results showed that the number of INs-SST decreases in the hippocampus of aged mice. In addition, aged SST-cre transgenic male mice were injected in the hilus of the DG with AAV-hSyn-DIO- hM3Gq virus or AAV-hSyn-DIO- hM4Gi virus to stimulate or inhibit the SST-INs activity and AAV-CamKII-GFP to visualize the GC. Behavioral tests were performed to assess different types of memory. Intraperitoneal administration of CB21 one hour before training allowed to modulate the activity of INs-SST population in the hilum of the DG. Behavioral analysis showed that stimulation of SST-INs increases in working memory but decreases the spatial memory. While the inhibition of SST-INs reduces working memory. Moreover, the morphological analysis of GFP positive cells revealed an increase in the density of dendritic spines, and also the increment of excitatory postsynaptic markers as GluN2B subunits of the glutamatergic type-NMDA receptor. These differences reflect differential modulation of the levels of inhibitory and excitatory synapse components by SST-INs modulations.

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3. THE RELATIONSHIP BETWEEN THE ORAL MICROBIOTA AND OBSESSIVE-COMPULSIVE DISORDER: A SCOPING REVIEW. La relación entre la microbiota oral y el trastorno obsesivo compulsivo: Un Scoping Review.

Resúmen:
The oral microbiome (OM), the ecosystem of around 700 species of microorganisms residing in the oral cavity, has drawn increasing attention in recent years for its emerging role in overall health. Recent studies have demonstrated a connection between the dysbiosis of the OM and neurodegenerative diseases like Alzheimer's and Parkinson's. Moreover, investigations have suggested a link between OM and psychiatric disorders and conditions, including anxiety, depression, and autism. This work reviewed recent literature to explore whether the scientific evidence available can indicate an interplay between the dysbiosis of OM and Obsessive-Compulsive Disorder (OCD). Since literature exploring this relationship is scarce, we developed a scoping review following JBI guidelines in PubMed, Scielo, Web of Science, and Scopus databases to identify studies published from 2018 to December 2023 that explored this link. The search resulted in 140 records; 22 papers were included in the present review after exclusions. The objectives were to explore dysbiosis and specific changes in the normal oral microbiome in patients with OCD or animal models, examine possible pathological pathways involved, and identify biomarkers associated with OCD. Our findings show specific changes in the normal oral microbiome in patients with OCD or animal models, where Actinobacter, Firmicutes, and Fusobacteria were identified. Altered biomarkers in OCD include IL-6, TNF-α, IL-1ß. Treg and OXTR with most studies indicating biomarkers of the humoral pathway involved. Much research has established a relationship between oral diseases and neurodegenerative and psychiatric disorders, highlighting the significance of elucidating the specific changes in oral dysbiosis and its dynamics modulating normal pathways in the oral–brain and gut–brain axes. These dynamics could be involved in other neurological disorders like OCD with associated oral biomarkers.

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4. THE INTERFERENCE IN REELIN SIGNALING REACTIVATES PLASTICITY IN MATURE CORTICAL NEURONS la interferencia en la señalización de Reelina reactiva la plasticidad en neuronas corticales maduras.

Resúmen:
Neural plasticity refers to the brain's capacity to adapt both functionally and structurally in response to experiences or injury. In mature neurons, the extracellular matrix (ECM) plays a crucial role in restricting plasticity by limiting axonal and dendritic growth and preventing synaptic reactivation. This indicates that the ECM contributes to the stabilization of neuronal circuits in mature neurons. Components of the ECM, such as Reelin, are essential for synaptic maturation, learning, and memory. Reelin is secreted by GABAergic interneurons and regulates synaptic maturation by signaling through the ApoER2 receptor, which promotes the maturation of glutamatergic synapses by binding to NMDA receptors. Previous studies have shown that interference with Reelin signaling—using an antibody to neutralize Reelin—reactivates dendritogenesis and shifts synapses toward a more immature, plastic phenotype in vitro and in vivo. This suggests that modulation of ECM can reactivate neural plasticity. Therefore, we designed a peptide (RA01) to interfere with Reelin signaling and promote neuronal plasticity in mature neurons. We determined the optimal concentration of RA01 for binding Reelin through in vitro assays. Primary cultures of mature cortical neurons (20 DIV) were incubated for one hour with the peptide (200 nM) to analyze its effects on Reelin signaling, synaptic composition and morphology. Immunofluorescence analysis revealed that RA01 administration in neurons interferes with Reelin signaling, evidenced by decreased fluorescence intensity of p-Dab1, p-CREB and Erk1/2. Additionally, we observed that RA01 treatment reduced the levels of the synaptic marker Synapsin-1 in the dendrites of mature cortical neurons, while increasing dendritic complexity. These results suggest that RA01 effectively reactivates structural plasticity in mature neurons, highlighting its potential therapeutic effects in treating synaptic pathologies associated with reduced plasticity.

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Socio Patrocinante:

5. PROBENECID ORAL ADMINISTRATION MITIGATES COGNITIVE IMPAIRMENTS AND GLIAL ACTIVATION IN A MURINE MODEL OF ALZHEIMER'S DISEASE. La administración vía oral de Probenecid mitiga los defectos cognitivos y la activación glial en un modelo murino de la enfermedad de Alzheimer

Resúmen:
Probenecid (PBN) is a drug used for gout treatment and to reduce the renal excretion of antibiotics. Evidence has also shown neuroprotective and anti-inflammatory effects in several conditions affecting the central nervous system. However, its direct impact on Alzheimer's disease has not been investigated yet. PBN is a known blocker for Pannexin-1 (Panx1) channels, a membrane protein that modulates the induction of excitatory synaptic plasticity under physiological contexts but also contributes to neuronal death under inflammatory conditions, such as Alzheimer's disease (AD). In this study, we investigated the impact of the treatment with PBN on the Panx1 channel activity, morphological changes of microglia and astrocytes, and cognitive function in a murine model of AD. Our data show that the treatment with PBN prevented the defects in recognition and spatial memory observed in APP/PS1 mice, reduced the pro-inflammatory morphological changes in glial cells, and decreased the number of pyknotic cells in the CA1 region of APP/PS1 mice. These findings suggest that a "neuroprotective" effect of PBN could rely on the blockade of Panx1 channels in a murine model of AD.
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Socio Patrocinante: Andrea Tapia Bustos

6. DESIGN OF SULFONAMIDES WITH TETRAHYDROQUINOLINE RINGS AS POTENTIAL POSITIVE ALLOSTERIC MODULATORS OF THE GLYCINE RECEPTOR ALPHA 3. Diseño de sulfonamidas con anillos de tetrahidroquinolinas como posibles moduladores alostéricos positivos del receptor de glicina alfa 3.

Resúmen:
The glycine receptor (GlyRs) is a chloride-permeable ion channel that plays a critical role in controlling key neurophysiological functions. The importance of GlyR function is further highlighted by the presence of abnormal glycinergic inhibition in many pathological states, such as hyperekplexia, epilepsy, autism, and chronic pain. In this context, previous studies have shown that functional inhibition mediated by phosphorylation events in GlyRs containing the alpha-3 subunit is a key mechanism in pain hypersensitivity. Biochemical and electrophysiological studies have described that phosphorylation of GlyR alpha-3 leads to a reduction in receptor function, resulting in chronic pain states. Currently, there are no drugs aimed at restoring the function of this hypofunctional receptor, thus hindering the development of effective therapies. Therefore, the aim of this work is to design new molecules, using the AM-3607 compound as a lead molecule, previously described as a potent positive allosteric modulator (PAM) of GlyR alpha-3. A library of 621 sulfonamides with tetrahydroquinoline rings derived from AM-3607 was generated. These molecules were energetically evaluated using binding free energy calculations, allowing the identification of 17 molecules with a high affinity for GlyR alpha-3. These results positioned these sulfonamides as promising candidates. This set of molecules was subsequently characterized by 500 ns molecular dynamics simulations under NPT conditions and a pH of 7.4. It was observed that sulfonamides with the best energetic profiles formed stable complexes with GlyR alpha-3, showing significant stability in receptor-ligand interaction over the simulation time. The results obtained provide a solid basis for the development of new therapies for chronic pain, highlighting the potential of the designed sulfonamides to restore GlyR alpha-3 function.
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Agradecimientos: I'm especially grateful to my advisors for their constant guidance and support throughout the planning and execution of the project.
Socio Patrocinante: David Mauricio Ramírez Sanchez and Gustavo Alonso Moraga Cid

7. EFFECT OF ASTAXANTHIN ON NUCLEAR CALCIUM SIGNALING, TRANSCRIPTION FACTOR ACTIVATION AND NEUROINFLAMATION USING AN EXCITOXIC MODEL IN CULTURED HIPPOCAMPIAL NEURONS. Efecto de la astaxantina sobre la señal de calcio nuclear, la activación de factores de transcripción y la neuroinflamación usando un modelo excitóxico en neuronas hipocampiales cultivadas.

Resúmen:
Calcium influx through synaptic NMDARs evokes an increase in calcium both in the cytoplasm and in the nucleus, promoting CREB-dependent gene expression. However, Ca2+ overload caused by NMDAR overactivation trigger subsequent cytotoxic events including generation of reactive oxygen species (ROS), aberrant increases in calcium, mitochondrial dysfunction, CREB shut-off and activation of the inflammatory response that ultimately leads to neuronal death. Astaxanthin (ASX) is an antioxidant carotenoid and neuroprotective agent capable of crossing the blood-brain barrier, it has demonstrated effectiveness in preventing oxidative stress and inflammation in cellular models of excitotoxicity and neurodegenerative diseases. This study aims to examine the ASX effects on nuclear calcium signal, CREB shut-off, NFkB activation (ROS- activated transcription factor related to inflammation) and the inflammatory response in NMDA-stimulated hippocampal neuron cultures. To this end, we used viral constructs expressing genetically encoded nuclear calcium sensors and immunofluorescence to assess activation of the transcription factor CREB, as well as nuclear translocation of NF-κB, along with changes in microglial morphology. We found that ASX decreased nuclear calcium signaling, NFkB translocation, and inflammatory responses associated with changes in microglial processes. On the other hand, ASX produced robust phosphorylation at Ser133 of CREB. Our data suggest that ASX activates survival and synaptic plasticity mechanisms and inhibits the inflammatory response by a putative nuclear calcium-dependent mechanism.
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8. EFFECT OF ASTAXANTHIN ON RECOGNITION MEMORY, HIPPOCAMPAL SYNAPTIC PLASTICITY, OXIDATIVE STRESS AND NEURO-INFLAMMATORY RESPONSE IN AGED RATS. Efecto de la astaxantina sobre la memoria de reconocimiento, la plasticidad sináptica hipocampal, el estrés oxidativo y la respuesta neuroinflamatoria en ratas envejecidas.

Resúmen:
Brain aging leads to a progressive decline in cognitive functions as well as hippocampus-dependent synaptic plasticity and memory. Aging brain is associated with an increase in oxidative stress and neuroinflammatory response. Previous studies indicate that Astaxanthin (ASX), an antioxidant and carotenoid pigment capable of crossing the blood-brain barrier, reduces oxidative damage and normalizes gene expression in neuronal excitotoxicity models; and also shows potential as a regulator of synaptic plasticity. These findings suggest ASX as a potent anti-inflammatory agent to combat aging brain. In this study, the effect of ASX was evaluated in recognition memory, synaptic plasticity, oxidative stress and neuroinflammation in aged Sprague Dawley rats fed with diet supplemented with ASX. To assess recognition memory, we used the spontaneous object recognition test, finding that ASX improves recognition memory. ASX effect on inflammatory response was analyzed by immunofluorescence of the nuclear translocation of NF-κB in the hippocampal area CA3-CA1, observing that ASX inhibits NF-κB translocation in aged rats. ASX Using PCR we demonstrated that ASX produces an increase in the expression of antioxidant response gene NQO1. Finally, long-term potentiation (LTP) and long-term depression (LTD), two synaptic plasticity types, was assessed by electrophysiological experiments in acute hippocampal slices obtained from aged rats fed with normal diet supplemented with or without ASX, revealing significant variations between the treated and control groups. Taken together, these findings suggest that ASX has therapeutic potential for the prevention of cognitive decline associated with aging, although further research is required to fully clarify its mechanisms of action.

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9. SEXUAL DIMORPHISM IN THE DISTRIBUTION AND DENSITY OF SOMATOSTATIN INTERNEURONS IN THE DENTATE GYRUS. Dimorfismo sexual en la distribución y densidad de interneuronas de somatostatina en el giro dentado

Resúmen:
Memory and learning are essential processes for life, with the hippocampus playing a crucial role in spatial and episodic memory. Within this structure, interneurons, particularly somatostatin (SST) interneurons located in the dentate gyrus, are fundamental for regulating cognitive processes. Aging is associated with a decline in the ability to form new memories, which includes a reduction in synaptic connections within the hippocampus. Somatostatin interneurons (INs-SST) in the dentate gyrus play a crucial role in modulating excitatory and inhibitory neural network activity, significantly influencing memory formation. Previous studies have demonstrated that the density of SST interneurons is reduced with age in male mice; however, whether this phenomenon occurs in aged female mice remains largely unexplored. This study aims to investigate sexual dimorphism in the distribution of interneurons, specifically somatostatin (SST), parvalbumin (PV), and calretinin (CLR), in the hippocampus of mice at 6 and 12 months of age. Additionally, we will analyze whether stimulation of SST interneurons differentially affects learning and memory processes in aged female and male mice. Utilizing stereotaxic surgery to deliver the AAV-hSyn-DIO-hM3Gq virus into the hippocampus, we activated or inhibited INs-SST through administration of the CB21agonist and subsequently conducted behavioral tests to assess spatial memory, working memory, and recognition memory. The results indicated significant sexual differences in the INs distribution and responses to modulation of activity. In females, activation led to an improvement in spatial memory, whereas males showed slight enhancements in working memory but reduced the spatial memory. This research underscores the importance of considering sexual dimorphism in aging neuroscience studies for future therapeutic approaches aimed at enhancing memory and learning.

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10. SEX-BIASED PSEUDOURIDYLATION LANDSCAPE INDUCED BY CHRONIC STRESS IN THE RAT DORSAL HIPPOCAMPUS: A POTENTIAL THERAPEUTIC TARGET FOR NEUROPSYCHIATRIC DISORDERS. Paisaje de pseudouridilación sesgado por sexo e inducido por estrés crónico en el hipocampo dorsal de rata: un potencial blanco terapéutico para trastornos neuropsiquiátricos.

Resúmen:
RNA modifications are essential for RNA stability, processing, and translation, enabling cellular adaptation to diverse stimuli in normal and pathological contexts that promote brain dysfunction. Among these, pseudouridine (Ψ) is highly abundant across RNA types, impacting various biological processes. This study proposes that pseudouridylation in the dorsal hippocampus—key for cognitive functions such as memory and learning—may be modulated under external stimuli. Using Nanopore direct RNA-sequencing (DRS), we evaluated whether Ψ deposited in mRNA coding regions is altered in the rat hippocampus by chronic stress exposure and whether this modification is sensitive to biological sex. To explore this, we used a depressive-like paradigm (chronic restraint stress, 2.5 h per day for 14 days) on adult male and female Sprague-Dawley rats (n=5 per condition and sex) to evaluate stress-induced and sex-biased changes in dorsal hippocampus epitranscriptomic profiles. Nanopore DRS and RT-qPCR were used to assess the Ψ landscape and the pseudouridylation machinery presence. Analysis showed a predominance of pseudouridylation sites in male mRNAs compared to females, with the largest difference in the 3' UTR region. Additionally, males exhibited more pseudouridylated sites and pseudouridine-modified transcripts than females, suggesting a sex-specific epitranscriptomic adaptation to chronic stress. Functional enrichment analysis highlighted stress-induced pathway modulation, including Endoplasmic reticulum processing, Autophagy, Endocytosis, and pathways related to neuronal plasticity. RT-qPCR confirmed the presence of pseudouridylation machinery (Pusl1 and Rpusd2), supporting Ψ's role in stress response. These findings suggest pseudouridylation as a potential biomarker and therapeutic target for stress-related cognitive dysfunction, with sex-biased modifications indicating its role in neuroplasticity, offering opportunities for interventions in neuropsychiatric disorders.

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11. IMPACT OF TNF-A ON PANNEXIN 1 CHANNELS ACTIVATION AND ITS ROLE IN DYSFUNCTION OF MOUSE BRAIN ENDOTHELIAL CELLS. Impacto de TNF-α en la Activación de los canales de Panexina 1 y su rol en la disfunción de Células Endoteliales Cerebrales de ratón.

Resúmen:
Tumor necrosis factor α (TNF-α) plays a crucial role in both acute and chronic inflammatory responses. Dysregulation of TNF-α has been linked to brain dysfunctions, including alterations in the formation and function of the blood-brain barrier (BBB). This study explores how TNF-α influences the activation of Pannexin 1 channels (Panx1) channels and its impact on cerebrovascular development. To address this objective, mouse brain endothelial cell (BEC) cultures were treated with TNF-α (10 ng/ml) for 1, 5, and 24 hours, establishing an inflammation model in the presence and absence of Panx1 blockers. Our findings show that membrane protein biotinylation followed by immunoblotting revealed a significant increase in both total Panx1 and phosphorylated Panx1 (Y198) levels after 5 and 24 hours of TNF-α treatment, compared to control. Furthermore, to evaluate Panx1 activity, BECs treated with siRNA-Panx1 and Probenecid (PBN) exhibited a significant reduction in DAPI uptake. Additionally, PBN treatment restored occludens-1 redistribution to the cell membrane and reorganized F-actin content, suggesting a protective effect on endothelial structure. Finally, following 5 and 24 hours of TNF-α treatment, Angiogenic Cellular Activity Assay and migration in BECs were reduced. In contrast, PBN improved these parameters. In summary, this study underscores the role of TNF-α in endothelial dysfunction and suggests that Panx1 inhibition may serve as a potential therapeutic strategy to prevent cerebrovascular damage linked to inflammatory processes.

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12. IMPAIRED SYNAPTIC TRANSMISSION IN CULTURED ACCUMBAL NEURONS OF AN ALZHEIMER DISEASE MOUSE MODEL. Transmisión sináptica alterada en neuronas acumbales cultivadas de un modelo murino de enfermedad de Alzheimer.

Resúmen:
Alzheimer's disease (AD) is a neurodegenerative pathology that affects brain areas such as the cortex and hippocampus. In advanced stages, this disease leads to cognitive impairment, primarily caused by the accumulation of beta-amyloid peptide (Aβ) and the formation of neurofibrillary tangles. However, a series of non-cognitive symptoms have recently been reported in the early stages of AD, which have been associated with alterations in deep nuclei, including the nucleus accumbens (nAc). Interestingly, in a transgenic mouse model of AD, recent studies demonstrated changes in the excitability and synaptic transmission in neurons of this area. To further investigate how neurons in this region are affected in AD, our laboratory has developed a primary culture of nAc derived from the 2xTg APP/PS1 mouse model. We observed a progressive accumulation of Aβ peptide. However, the consequences on the neuronal physiology of the culture were unknown. This study demonstrates that the accumulation of Aβ peptide causes an increase in AMPAergic transmission in accumbal neurons from the APP/PS1 model compared to wild-type (WT). Interestingly, this increase is significantly reduced by the presence of NASPM, an antagonist of calcium-permeable AMPA receptors (CP-AMPAR). Additionally, changes in the sensitivity of GABAA receptors were observed, as reflected in the shift of the EC50 in concentration-response curves. These results help us understand how physiological neurotransmission in accumbal neurons is affected by the presence of Aβ peptide, providing new insights into how nucleus accumbens may be impaired in AD.

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13. PROBENECID, THE DRUG THAT BLOCKS PANX1 CHANNELS, ENHANCES GLUTAMATERGIC SIGNALING IN HIPPOCAMPAL NEURONS OF ALZHEIMER'S DISEASE. Probenecid, el fármaco que bloquea los canales panx1, incrementa la señalización glutamatérgica en neuronas hipocampales de Enfermedad de Alzheimer.

Resúmen:
Alzheimer's disease (AD) is a is a progressive neurodegenerative disorder characterized by gradual memory loss and dementia. These cognitive deficits are partly due to a reduction in synaptic plasticity (SP), which is linked to decreased levels of AMPA glutamate receptors (AMPARs) in the postsynaptic membranes of hippocampal neurons and reduced glutamate release from the presynaptic compartment. Pannexin 1 (Panx1), a transmembrane protein, plays a role in memory and hippocampal SP, particularly concerning long-term depression (LTD). Notably, increased Panx1 expression and activity have been observed in the hippocampus of adult murine models of AD (APP/PS1). On the other hand, Probenecid (PBN), a drug previously approved by the FDA for gout disease, has been shown to block Panx1 channels, and its acute blockade restore SP to normal levels in the APP/PS1 adult hippocampus. However, the mechanism underlying the blockade of Panx1 with PBN in modulating AMPAR-mediated glutamatergic signaling in AD remains unclear. In this study, we explored the contribution of Panx1 activity to AMPAR expression in hippocampal neurons from postnatal APP/PS1 mice at DIV 14. Our findings revealed that APP/PS1 neurons exhibited higher Panx1 expression and activity than wild-type (WT) neurons. Interestingly, treatment with PBN increased GluR1 and VGluT1 levels in APP/PS1 and WT neurons under basal conditions. Furthermore, PBN also enhanced GluR1 insertion into the membrane following the induction of chemical potentiation. These results provide new evidence for the contribution of Pannexin channels to PS through the modulation of glutamatergic signaling and further support PBN as a potential drug with a new use for AD.

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14. MOLECULAR INTERACTIONS OF GELSEMIUM COMPOUNDS WITH GLYCINE RECEPTORS. Interacciones moleculares de compuestos de Gelsemium con receptores de glicina.

Resúmen:
Glycine receptors (GlyRs) are essential ion channels in the central nervous system that play a critical role in synaptic inhibition. Among the GlyR subtypes, the alpha-1 and alpha-3 subunits have been implicated in neurological disorders such as chronic pain and hyperekplexia. Gelsemium plant species, despite their inherent toxicity, have been traditionally used for pain management and other medical conditions. Recent electrophysiological studies show that the two major Gelsemium alkaloids, gelsemine and koumine, modulate GlyR function. Molecular modeling and site-directed mutagenesis suggest that these alkaloids interact with the orthosteric site of GlyRs. However, our understanding of Gelsemium compounds' effects on GlyRs remains limited, particularly considering that Gelsemium alkaloids comprise over 200 molecules. In this study, we aim to characterize the interactions of six classes of Gelsemium alkaloids—gelsemine, koumine, gelsedine, sarpagine, yohimbane, and humantenine—with the orthosteric site of alpha-1 and alpha-3 GlyRs using in silico methods. By analyzing nearly 100 compounds, our molecular docking and free energy binding calculations reveal promising interaction profiles, particularly for koumine, sarpagine, and gelsedine derivatives. These findings suggest stable binding at the GlyR orthosteric site, highlighting the potential for modulating glycinergic signaling. Ongoing research will provide a comprehensive interaction profile of the more than Gelsemium 170 compounds, identifying candidates for further electrophysiological testing.
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15. COMPUTATIONAL MODELING AND DESIGN OF TUBULIN-BINDING PEPTIDES FOR POTENTIAL ANTIMITOTIC ACTIVITY. Modelado computacional y diseño de péptidos de unión a Tubulina con potencial actividad antimitótica

Resúmen:
Microtubules are one of the most important targets for anticancer compounds due to their crucial role in the mitotic process. They have a cylindrical structure with ~25 nm diameter and are formed by the polymerization of protein monomers called tubulin. Tubulin is a highly conserved globular protein being α- and β- types found in the cell in greater proportion as a heterodimer assembly in long fibers known as protofilaments. Over the years, drug-like tubulin-binding agents have been widely employed in different types of cancer with effective results in blocking the uncontrolled division of the cells but including critical problems in clinical use. Recently, therapeutic peptides have taken great relevance in medicine, showing advantages and development highlights such as low immunogenicity, low production costs, high specificity, and good capability to inhibit large surface PPIs. The discovery of new efficient chemical compounds is a significant challenge of this area, where the design of peptides that interfere with the internal protein-protein interactions (PPIs) of the microtubules could help to obtain new results with the available structures and new computational tools, aiming to reduce undesirable effects and optimize the chemical properties that hinder their effectiveness. In this work, a computational search and design of potential tubulin-binding peptides was carried out using multiple computational tools, such as deep learning, docking, molecular dynamics and MM-GBSA calculations. As a result, 10 peptides are proposed, which demonstrated significant stability when interacting with tubulin dimers, evaluated through classical molecular dynamics simulations. The knowledge obtained in this work will help to find new peptides and get a better understanding of how these molecules interact with tubulin promoting the efficient rational design of antimitotic therapeutic peptides.
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16. MaR1 AS A PHARMACOLOGICAL TARGET FOR INFLAMMATION RESOLUTION AND HEPATOPROTECTION IN MAFLD: SOLVING FROM MOLECULAR DYNAMICS. MaR1 como target farmacológico para la resolución de la inflamación y la hepatoprotección en MAFLD: solución a partir de la dinámica molecular.

Resúmen:
Chronic liver diseases related to metabolic dysfunction-associated fatty liver disease (MAFLD, formerly NAFLD), affect 35% of the adult population, with a prevalence ranging from 17% to 46% worldwide. MAFLD is characterized by the accumulation of lipids in hepatocytes (steatosis), a key factor in its pathogenesis and in the development of conditions such as type 2 diabetes mellitus (DM2), creating a synergy that significantly increases worldwide health challenges. Maresin 1 (MaR1), a derivative of docosahexaenoic acid (DHA, an omega-3 fatty acid), has demonstrated remarkable pro-resolving and anti-inflammatory properties, and promotion of tissue regeneration. This study aimed to explore the molecular interactions of MaR1 with nuclear receptors (NRs) that are key in regulating lipid metabolism, adipogenesis, energy balance, and inflammation. Specifically, peroxisome proliferator-activated receptors alpha and gamma (PPAR a and y), and retinoic acid-related orphan receptor alpha (RORa). We performed a robust in-silico analysis, including molecular dynamics simulations and molecular mechanics/generalized Born surface area (MM-GBSA) binding free energy calculations. MaR1 was found to have highly favorable affinities: MaR1/PPARy (-76.95 Kcal/mol) > MaR1/PPARa (-76.49 Kcal/mol) > MaR1/RORa (-69.30 Kcal/mol), with Van der Waals forces and lipophilic interactions being key to the stability of the complexes. An in vivo MAFLD model was developed in Sprague-Dawley rats, where 4ng/g MaR1 improved plasma lipids parameters, reduced steatosis, and preserved liver cytoarchitecture. These results suggest that the MaR1-NR pathway could be a promising pharmacological target for inflammation resolution and hepatoprotection.
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17. MARESIN 1, AS A HEPATOPROTECTIVE AGENT, HAS AN ANTI-INFLAMMATORY ROLE OVER METABOLIC DAMAGE ASSOCIATED WITH TYPE 2 DIABETES MELLITUS. La maresina 1, como agente hepatoprotector, tiene un papel antiinflamatorio sobre el daño metabólico asociado a la diabetes mellitus tipo 2.

Resúmen:
The liver is responsible for maintaining homeostasis. When it is altered, various pathologies can arise. An important factor that alters hormonal balance is type 2 diabetes mellitus (DM-2), caused by insulin resistance, which generates weight gain and, consequently, the accumulation of triglycerides in hepatocytes. This increases the risk of developing metabolic-associated fatty liver disease (MAFLD). Studies suggest that consuming polyunsaturated fatty acids, particularly omega-3, can protect the liver through an anti-inflammatory response and promote resolution. Maresin 1 (MaR1), an omega-3 derivative, modulates the expression of IKBα, a negative regulator of NF-κB, thus promoting a decrease in inflammation exacerbation. This modulation could reduce inflammation and mitigate the progression of MAFLD associated with DM-2. This study aimed to evaluate the hepatoprotection role of Maresin 1 over metabolic damage associated with type 2 diabetes mellitus. Male Sprague Dawley rats were fed with a high-fat diet (HFD) for metabolic damage and streptozotocin (STZ) (50 mg/kg) for diabetes induction. MaR1 (4 ng/g) was administrated as a hepatoprotective agent. After treatment, lipid profile, histopathological techniques to analyze the morphology of hepatocytes, and expression of cytokines were assayed to clarify the anti-inflammatory role of MaR1. Treatment with MaR1 decreased the expression of pro-inflammatory cytokines, restoring liver morphology towards cytoarchitecture normalization and decreasing the necrosis foci generated by HFD/DM2-induced liver damage. MaR1 wouldave hepatoprotective effects through an anti-inflammatory pathway and prevent the generation of metabolic damage associated with MAFLD/DM-2.

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18. TRISUBSTITUTED PYRIMIDINES AS AUTOPHAGY INHIBITORS. Pirimidinas Trisustituidas como inhibidores de autofagia

Resúmen:
Autophagy is a conserved process in which the cytosolic materials are degraded and eventually recycled for cellular metabolism to maintain homeostasis. The dichotomous role of autophagy in pathogenesis is complicated . It is well known that autophagy pathway is a major contributor to tumour cell survival and as a result it is considered a target for cancer therapy. To date, only a small number of autophagy modulators have been described, with the majority of studies focused on inhibition of the lysosomal degradation stage of autophagy, using agents such as hydroxychloroquine (HCQ) or the lysosomal autophagy inhibitor LYS05 . In this context, this investigation presents a homologue series of 12 compounds that produce autophagy inhibition at 5 uM on C2C12 and 10 uM on U2OS cells. On both cases an MTT assay was performed to determine the cytotoxicity of the compounds. Subsequently, for C2C12 LC3 I/II and P62 proteins were analyzed by western blot to determine if there was an inhibition of the autophagy after 24h of exposure. On the other hand, for U2OS autophagy inhibition was analyzed by immunofluorescence after 24h of exposure. The results showed that the compounds are not toxic presenting over 95% cell survival for all compounds at 2 uM for C2C12 and 10 uM for U2OS. Compounds 1, 7 and 12 showed LC3 II/I and P62 accumulation on C2C12 and compounds 1, 5, 7 and 10 showed an accumulation of autophagosomes on U2OS. Further experiments as autophagic flux should be performed to confirm autophagy inhibition on both cell lines.

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19. IMPLEMENTATION OF AN INTEGRATED SCREENING PLATFORM FOR THERAPEUTIC DISCOVERY AND INNOVATION IN BIOMEDICAL RESEARCH CENTERS OF CENTRAL CHILEAN MACROZONE. implementacion de una plataforma de screening integrado para el descubrimiento e innovacion terapeutica para centros de innovacion biomedica.

Resúmen:
Current drug discovery and development, including chemical drugs and biopharmaceuticals; as well as the discovery of new therapeutic targets, has been greatly accelerated using equipment that can perform multiple screening assays rapidly and reliably using automated robotic and high sensitive analytic technologies. The screening of libraries of small molecules and biologics including antibodies, RNAs, peptides, etc. on purified targets, cells, tissues, and even whole small organisms is now a validated approach to identifying drug candidates. Indeed, at least 69% of FDA-approved drugs in the past decades were discovered using screening approaches. Screening technologies also make it possible to identify therapeutic compounds from complex biological mixtures, such as cell-derived secretome or natural extracts. Additionally, screening assays accelerate downstream hit-to-lead development processes and further medicinal chemistry refinements with their ability to test in parallel small molecule analogs and derivatives. Demonstration of molecular binding of a compound to a given purified target; however, is not a guarantee of a functional outcome in cells or vice versa. For this reason, exhaustive pharmacodynamic characterization, including target engagement and mechanism of action validation at molecular and cellular levels are important to predict on-target and off-target effects. The Drug Discovery and Screening Center of Universidad del Desarrollo (Fondequip Mayor EQY230019) offers to the scientific community and the industry a platform of equipment and services for the discovery of new drugs and biopharmaceuticals through molecular and phenotypic screening methods and to validate drug-target engagement. The platform is supported by a scientific data management system and a management and service model that ensures remote access, flexibility, data security and documentation quality under GLP standards that facilitates IP generation and technology transfer.

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20. MetaDrug: AN AI-DRIVEN TOOL FOR ACCELERATED MOLECULE OPTIMIZATION IN HIT-TO-LEAD DRUG DEVELOPMENT. MetaDrug: Una herramienta basada en IA para la optimización acelerada de moléculas en el desarrollo hit-to-lead de fármacos

Resúmen:

Computer-Aided Drug Design (CADD) is indispensable in modern drug development, enabling researchers to optimize potential therapeutic compounds with greater speed and accuracy. The integration of Artificial Intelligence (AI) has transformed CADD by allowing rapid exploration of chemical space and targeted optimization of molecular properties. MetaDrug is an AI-based platform developed to accelerate molecular optimization during the Hit-to-Lead phase in drug development. Using a Junctional Tree Variational Autoencoder (JT-VAE) framework that was trained on a 4.5 million compound diverse dataset from the ZINC database, a unique graph-based molecular representation of the target molecule is transformed into an embedding in the latent space. The embedding then undergoes iterative modifications via a genetic algorithm whose role is the optimization of specific properties that are predicted using fitness functions. Currently, our fitness functions cover synthetic accessibility, solubility, half-life and toxicity. All of them are derived either from experimental data obtained from public databases or from calculated properties. MetaDrug's genetic algorithm operates directly on the latent space, bypassing repeated molecular reconversion and significantly reducing processing time. Once a convergence criteria has been met, the embedding is decoded into a molecule once again. Initial validation of generated molecules has shown promising in silico results, affirming MetaDrug's potential to minimize costly and time-consuming traditional optimization steps that require chemist-led modifications. We're currently capable of generating families of molecules with enough structural similarity to be part of an analog program. With its capacity for rapid, robust optimization, MetaDrug is designed to complement existing in silico tools and holds particular appeal for academic research and pharmabiotech companies seeking scalable, AI-driven solutions to advance drug development pipelines.

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21. DARK AND LIGHT-INDUCED ACTIVITIES OF RHENIUM (I) AND MANGANESE (I) BASED PHOTOACTIVATABLE CO-RELEASING COMPLEXES WITH P,N-BIDENTATE LIGAND. Actividades inducidas por la oscuridad y la luz de complejos fotoactivables liberadores de CO basados en renio (I) y manganeso (I) con ligando P,N-bidentado

Resúmen:

This study presents the photochemical characterization of monometallic complexes with P,N-bidentate ligands using UV-Vis, FTIR, and NMR techniques, highlighting their potential as photoinduced carbon monoxide-releasing molecules (photoCORMs). The primary objective was to evaluate their phototoxic potentials, both in darkness and after photoactivation, on MCF-7 breast cancer cells. For this purpose, photoactivation was performed using blue light irradiation (450 nm) for 1 hour, with a negative control group that was not exposed to the compound. Subsequently, the antiproliferative activity was assessed through cell viability assays using the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) method. Preliminary results from the phototoxicity assay suggest that these compounds offer new perspectives on the development of light-controlled therapies based on CO release.

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22. AMINOQUINAZOLINE HYBRIDS: A STRATEGY IN AGR2 MODULATION FOR THE REGULATION OF SECRETORY MUCINS. Híbridos Aminoquinazolina: Una estrategia en la Modulación de AGR2 para la Regulación de Mucinas de secreción.

Resúmen:

The present study is aimed at the design and synthesis of aminoquinazoline compounds with the potential to modulate the activity of the AGR2 protein, which plays a critical role in the production of secretion mucins such as MUC5AC in the context of muco-obstructive respiratory pathologies and some types of neoplasms. In silico analysis identified the key amino acids in the dimerization site of AGR2, the substituents favoring ligand-protein binding, and the nature of the predominant interactions. Their synthesis was carried out by means of an organic cyclocondensation reaction and a three-component catalysis with iodine to obtain allylamine derivatives, and by means of an Fmoc protection strategy, the addition of L-amino acids was carried out, optimizing the generation of aminoquinazoline hybrids of high purity, with good yield and high regioselectivity. This work represents an advance in the characterization of AGR2 and lays the foundation for the development of compounds with biological activity in future experimental studies in in vitro and in vivo models and the development of new pharmacological therapies.

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23. DEVELOPMENT OF AN ANALYTICAL METHOD USING UV SPECTROSCOPY TO DETERMINE FLUOXETINE AND METHYLATED FLUOXETINE AFTER SIMULATED IN VITRO DIGESTION CONDITIONS IN MONOGASTRIC ANIMALS. Desarrollo de un método analítico por espectroscopía UV para determinar fluoxetina y fluoxetina metilada tras condiciones simuladas de digestión in vitro en animales monogástricos.

Resúmen:
The selective serotonin reuptake inhibitor (SSRI) fluoxetine (FLX) is a widely used antidepressant. It has effects beyond the central nervous system (CNS). Notably it also influences the gastrointestinal system, where most of the 5-hydroxytryptamine (5-HT) is produced. Upon oral administration, there is a small fraction of FLX that travels through the intestinal lumen, suggesting that this SSRI might have an extra CNS effect. To test this, we have synthesized a methylated form of FLX (FLX+), which, due to its positive charge, is not absorbed by the intestinal barrier and does not produce antidepressant effects when administered intraperitoneally. Although FLX+ has a higher IC50, it retains SSRI-like activity as by binding to Danio rerio SERT protein. The primary objective of this study is to develop and validate an analytical method using UV spectroscopy for quantifying FLX+ and to assess its stability under conditions simulating digestion in monogastric animals. Decomposition kinetics of FLX+ were analysed in simulated gastric fluid at acidic pH and in simulated intestinal fluid containing bile salts and pancreatic enzymes, comparing its degradation to that of FLX. The results show that UV spectroscopy is robust and enables reliable quantification of FLX+ in various simulated media. Furthermore, FLX+ did not show significant stability loss under conditions similar to those of the intestine, suggesting that it may progress to in vivo evaluations. This advancement opens the possibility of considering the intestinal lumen as a therapeutic target in depression treatment, with FLX+ as a potential candidate for further studies.

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24. INDIVIDUALIZED VANCOMYCIN DOSING: EVALUATION OF TDMX AND PRECISEPK® TO OPTIMIZE ANTIBIOTIC THERAPY IN A UNIVERSITY HOSPITAL. Dosificación individualizada de Vancomicina: Evaluación de TDMx y PrecisePK® para optimizar terapia antibiótica en un hospital universitario.

Resúmen:
Vancomycin is an essential antibiotic for treatment of severe infections; however, its use requires precise monitoring due to its narrow therapeutic range and potential toxicity. Therapeutic drug monitoring (TDM) guided by model-informed precision dosing (MIPD) offers an innovative approach to optimize vancomycin's safety and efficacy through personalized dosing adjustments.This study evaluated the performance of two MIPD programs, PrecisePK® and TDMx, within a routine clinical setting for vancomycin TDM. Patients treated with vancomycin were included, and two consecutive plasma concentrations were measured to allow comparison of both software tools in terms of predictive performance (bias, relative bias [rBias]), and relative root mean squared error [rRMSE] and diagnostic accuracy (sensitivity, specificity, positive predictive value [PPV], and ROC curve analysis). Additionally, the standard TDM strategy was compared with the MIPD-guided TDM approach.A total of 92 patients contributed 184 plasma vancomycin levels. The mean bias and relative bias were -0.50 mg/L and 2.70%, respectively, for PrecisePK®, and 0.13 mg/L and 6.38% for TDMx. The rRMSE was 44.32% for PrecisePK® and 40.28% for TDMx. Both software programs demonstrated the same sensitivity (88.40%) in identifying patients requiring dose adjustments, with PPVs of 81.33% for PrecisePK® and 80.26% for TDMx.Only 25% of patients achieved therapeutic exposure by the second measurement, suggesting that MIPD-guided TDM may be a valuable strategy for optimizing vancomycin therapy, with clinical interchangeability between TDMx and PrecisePK®. Larger-scale prospective studies are warranted to confirm these findings.

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25. THE NIFEDIPINE-LIKE EFFECT INDUCED BY DRIMYS WINTERI SEED EXTRACT ON INTRACELLULAR CA2+ SIGNALS: MODULATION OF L-TYPE CA2+ CHANNEL. Efecto similar a nifedipino inducido por el extracto de semilla de Drimys winteri sobre las señales de Ca2+ intracelular: modulación del canal de Ca2+ tipo L.

Resúmen:
Drimys winteri seeds (DwS) are characterized by strong pungency, mediated by drimane-type compounds which have been poorly characterized. This study aimed to characterize the effects of compounds present in DwS extracts (DwSE). The chromatographic analysis allowed the investigation of 14 sesquiterpene compounds, of which 71.5% were identified, highlighting Polygodial (33.11%) and Drimenin (31.73%). Using The MTT assay we observed that the DwSE lack of cytotoxicity in PC12 cells and the primary culture of mouse cortical neurons. On the other hand, intracellular Ca2+ levels were studied by microfluorometry. In PC12 cells, 10µg/mL DwSE pre-treatment blocked the increase in the intracellular Ca2+ triggered by high K+ external solution [90 mM] compared to control (69.90%±4.725, p<0.001), while Nifedipine, elicit 25.69%±1.812, p<0.001. DwSE was shown to be 16 times less potent than nifedipine to block the L-type Ca2+ channel (IC50 29.80µg/mL, 1.836 µM, respectively). Also, it was determined that 10µg/mL DwSE modulates the amplitude of Ca2+ transients in mouse cortical neurons (10µg/mL, 54.67%±4.709, p<0.001). Likewise, 10µM of Nifedipine decreased the amplitude (23.55%±4.770, p<0.001). Different experimental strategies for applying the blockers suggest that the effects of DwSE did not exert a potentiation of the effects of nifedipine. Our results suggest that the DwSE could use or block the site of action of Nifedipine, without cooperative effects, opening the possibility to develop new pharmacological tools to modulate L-type Ca2+ channel with more selective effects. Taken together our studies provide novel information on the chemical composition of DwS and explore their possible effects and neuronal function. Therefore, our results suggest that we have a novel family of molecules that could act as modulators of the L-type VGCC, which could potentially add value to Dw seeds as a source of neuroprotective active ingredients.

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26. DETERMINATION OF TOTAL PHENOLIC AND FLAVONOID CONTENT AND EVALUATION OF ANTIOXIDANT AND ANTIMICROBIAL PROPERTIES OF ETHANOLIC EXTRACTS FROM LEAVES AND FLOWERS OF Fuchsia magellanica Lam. Determinación del contenido de fenoles totales, flavonoides y evaluación de propiedades antioxidantes y antimicrobianas de extractos etanólicos de hojas y flores de Fuchsia magellanica Lam.

Resúmen:
Fuchsia magellanica Lam. is a native Chilean species of the Onagraceae family, characterized by its bright pink bell-shaped flowers. Information on Fuchsia magellanica is limited, and to date there are no studies that deepen in its pharmacological properties, despite being a plant widely used in Chilean folk medicine (1). The aim of this study is to contribute to the literature on the antioxidant and antimicrobial profile of extracts of leaves and flowers of Fuchsia magellanica. Fuchsia flowers and leaves were collected and treated to obtain an ethanolic extract of each organ separately. Characterization of phenolic compounds and flavonoids was performed by Folin-Ciocalteau method and AlCl3 colorimetric assay. FRAP and ABTS assays were performed to measure their antioxidant activity, having Fe+2 and Trolox as standards, respectively (2). The minimum inhibitory concentration (MIC) and inhibition halo were measured in cultures of clinical isolates of E. coli, S. aureus and C. albicans, to determine their antimicrobial activity (3). The results show that leaves have a higher content of total phenols and flavonoids, compared to flowers. The highest antioxidant activity was found in leaves. Inhibition halo was observed in clinical isolates of C. albicans, and a remarkable MIC for E. coli. This study constitutes the first advances in the understanding of the antioxidant and antimicrobial profile of Fuchsia magellanica LAM., and further assays are planned to obtain a fuller profile of this plant. References (1) SHAWKY et al. (2021). Journal of Ethnopharmacology, 281;114450. (2) OYARZÚN et al. (2020). Molecules, 26(1); 6. (3) CLINICAL AND LABORATORY STANDARDS INSTITUTE (2016). "M100S. Performance Standards for Antimicrobial Disk Susceptibility Testing".

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27. EVALUATION OF CARDIOVASCULAR RISK AND METABOLIC DISORDERS IN HIV/AIDS PATIENTS UNDERGOING ANTIRETROVIRAL THERAPY. Evaluación del Riesgo Cardiovascular y Trastornos Metabólicos en Pacientes con VIH/SIDA en Terapia Antirretroviral.

Resúmen:
The diagnosis of Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS is made in individuals with HIV infection. While antiretroviral therapy (ART) has improved the life expectancy of these patients, it has been associated with metabolic disorders that increase the risk of cardiovascular diseases. This study evaluated cardiovascular risk (CVR) in patients from the HIV program at CRSCO Peñalolén, with 167 individuals seen between January 2019 and March 2023. Sociodemographic, clinical, and pharmacological data, as well as cardiovascular risk factors (CVRF), were collected using the Framingham scale adapted to the Chilean population, the PAHO/WHO CVR calculator, and the 2021 guidelines of the European Society of Cardiology (ESC). The study was conducted with the approval of the Scientific Ethics Committee for Adults of the Metropolitan Health Service East (CEC-SSMO). In the study population, 81.44% presented low CVR, with men (74.25%) being predominant and a mean age of 36.63. A total of 43.12% of patients began therapy with the TAF/FTC/EVT/COBI regimen (50 mg/200 mg/150 mg/150 mg), followed by ABC/3TC/DDTG (600 mg/300 mg/50 mg) with 22.16%, and TDF/FTC/RPV (300 mg/200 mg/25 mg) with 9.58% of patients. Of the patients, 13.79% showed moderate CVR and 4.79% high CVR, with factors such as family history of premature cardiovascular disease (CVD) and being male over 45 years in higher-risk groups. Among modifiable CVRFs, smoking and dyslipidemia were most common, along with a sedentary lifestyle and elevated triglyceride levels. Pearson's Chi-square test showed a significant association ($p<0.005$) between various CVRFs and CVR, highlighting the impact of hypertension and diabetes mellitus on risk. The study emphasizes the importance of stratifying CVR in HIV patients to adapt treatment strategies, combining pharmacological interventions and lifestyle changes according to individual needs.

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28. CHARACTERIZATION STUDY OF CLOZAPINE DOSAGE IN PATIENTS AT FÉLIX BULNES HOSPITAL. Estudio de caracterización de la dosificación de clozapina en pacientes del Hospital Félix Bulnes.

Resúmen:
Clozapine is an effective atypical antipsychotic for treating schizophrenia, noted for reducing extrapyramidal effects by blocking dopaminergic receptors and affecting other receptors as well. Monitoring its plasma levels is crucial due to associated adverse effects, although this measurement, typically performed via HPLC, is not frequently requested. The aim of this study was to characterize patients undergoing clozapine treatment to identify a dosing regimen that optimizes clinical response while minimizing toxicity from accumulation. Data were collected through the internal Dashboard system at Félix Bulnes Hospital and analyzed using the SPSS statistical software. Initial characterization revealed that 21.4% of patients had subtherapeutic levels, 34.7% therapeutic levels, and 43.9% supratherapeutic and/or toxic levels. Additionally, 46.3% of patients did not adhere to the recommended dosing regimen. Dosing was directly related to elevated clozapine blood levels ($p = 0.027$), and regimen adherence was significantly associated with both the dose administered ($p = 0.028$) and dosing frequency ($p = 0.01$). Regarding hematological reactions, a significant reduction in neutrophil counts was observed in patients with toxic levels ($p = 0.030$). This study demonstrates that, under current dosing practices, clozapine plasma levels are often outside the optimal therapeutic range, underscoring the need for careful monitoring to ensure both efficacy and safety.

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29. ANALYSIS OF PSYCHOTROPIC DRUG PRESCRIPTIONS IN PRIMARY HEALTH CARE USING DATA SCIENCE. Análisis de prescripciones de psicofármacos en Atención Primaria de Salud utilizando ciencia de datos.

Resúmen:
Psychotropic drugs are intended to influence the central nervous system and are used to address complex mental health disorders, which are often associated with multimorbidity. This, in turn, can lead to polypharmacy, with its associated risks and consequences. We conducted a descriptive, retrospective study on the use of psychotropic drugs to identify the factors that predispose patients to polypharmacy. The study focused on users with an ICD-10 F diagnosis for anxiety and depressive disorders in the primary health care network of Valdivia in 2022. DESAM-Valdivia provided the anonymized database, based on Rayen electronic clinical records. Results: A total of 5,813 users were identified, with 212,900 prescriptions in total. The majority were women (72.6%), elderly individuals, particularly those over 65 years of age, and people with low educational attainment. Polypharmacy was observed in 19.28% of patients, who were prescribed between 5 and 8 concomitant medications for a period exceeding 6 months, with an accumulated anticholinergic burden in the range of 3-6. Additionally, 46.5% of clonazepam users were treated for more than two months ($\overline{x}$ = 6.30 ± 3.00). 26.5% of psychotropic drug users had potentially risky prescriptions. Conclusion: Chilean real-world data (RWD) are valuable for pharmacovigilance processes, especially concerning key issues such as polypharmacy, long-term benzodiazepine use, and the anticholinergic burden from psychotropic medications.

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30. INHIBITORY EFFECTS OF ACETAMIDE CORE COMPOUNDS ON hACE2/Omicron SPIKE PROTEIN INTERACTION. Efectos inhibidores de compuestos con un núcleo de acetamida en la interacción entre hACE2 y la proteína Spike de Omicron.

Resúmen:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), causes a highly infectious disease characterized by fever, acute respiratory illness, and pneumonia. Recognition and binding to the host cell receptor is the initial step of virus entry into the host cell. Cryo-EM structural studies have revealed that angiotensin-converting enzyme 2 (ACE2) can only interact with the RBD (receptor-binding domain) of Spike glycoprotein trimer when is in active RBD states. Most studies with ACE2 receptor receptors have used the ACE2 ectodomain, although a cryo-EM structure of the full-length ACE2 protein bound to the receptor-binding domain (RBD) of the SARS-CoV-2 Spike was reported. Therefore, the aim of this study wasthis study aimed to evaluate infection using Omicron variant pseudovirus in a stable HEK-293T cell line expressing human ACE2 (HEK293/ACE2), in the presence of inhibitory compounds. First, the presence of the hACE2 receptor in the stable line was demonstrated by immunofluorescence and Wertern blot. Next, a battery of Compounds compounds were selected by cytotoxicity assays. Subsequently, the effect of infection was determined using Omicron pseudoviruses, with which include the the Spike protein in addition to incorporating the reporter genes for GFP and luciferase. Infection was assessed by determining the level of fluorescence or luciferase activity. Compounds LA52, LA42, LA45, LA15, LA5, LA10, LA16, LA44 presented a cell viability greater than 50%. Compound LA5 presented a decrease in infection over a 50%.

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31. DEVELOPMENT OF AN ANTIVIRAL FORMULATION, BASED ON DURVILLAEA ANTARCTICA EXTRACTS, TO TREAT SKIN LESIONS CAUSED BY HERPES SIMPLEX VIRUS. Desarrollo de una formulación antiviral, a base de extractos de Durvillaea antarctica, para tratar lesiones cutáneas causadas por el virus del herpes simple.

Resúmen:
Herpes simplex virus (HSV) is a highly prevalent microorganism that causes lifelong infections with recurrent clinical manifestations in humans, such as herpes labialis, herpetic keratitis, and herpetic encephalitis, among others. To date, various therapies exist for treating HSV infections, most of which are nucleoside analogs targeting the viral polymerase, such as acyclovir. However, these drugs are often ineffective for treating skin lesions caused by HSV infections due to their low penetration capability and the emergence of resistant strains. Therefore, there is a need for new and effective drugs to treat herpetic skin lesions. Previous reports have demonstrated the antiviral effects of botanical compounds against HSV skin lesions, such as the marine alga Durvillaea antarctica. In this study, we evaluated the antiherpetic effect of Durvillaea antarctica extract produced under Good Manufacturing Practices (GMP) in vitro on epithelial models and its efficacy in treating skin lesions in mice. We demonstrate that Durvillaea antarctica extracts are highly effective in reducing viral loads in a dose-dependent manner in both cell types tested. Furthermore, GMP-produced ointments were found to be highly effective in reducing the clinical score and duration of skin lesions in two mouse strains.

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32. BROMHEXINE HYDROCHLORIDE DECREASES THE INFECTION OF OMICRON PSEUDOVIRUS IN A STABLE HEK293/ACE2 CELL LINE. Clorhidrato de bromhexina disminuye la infección del pseudovirus Omicron en una línea celular estable HEK293/ACE2

Resúmen:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causes a highly infectious disease characterized by fever, acute respiratory illness, and pneumonia, coronavirus disease 2019 (COVID-19). The SARS-CoV-2 virus infects the host cells through the interaction of its Spike glycoprotein with human angiotensin-converting enzyme 2 (hACE-2), and Cryo-EM structural studies have revealed that hACE2 can only interact with the RBD (receptor-binding domain) of Spike glycoprotein. High binding affinity between the viral Spike glycoprotein and host cells hACE-2 receptor has been reported to enhance the viral infection. Thus, the disruption of this molecular interaction will lead to reduction in viral infectivity. This study, therefore, aimed to evaluate infection using Omicron variant pseudovirus in a stable HEK-293T cell line expressing human ACE2 (HEK293/ACE2), in the presence of mucolytic drug Bromhexine hydrochloride. First, the presence of the hACE2 receptor in the stable line was demonstrated by immunofluorescence and Wertern blot. Next, Bromhexine hydrochloride concentrations for treatments were determined by cytotoxicity assays. Subsequently, the effect of infection was determined using Omicron pseudoviruses, which include the reporter genes GFP and luciferase. Infection was assessed by determining the level of fluorescence or luciferase activity. All the evaluated concentrations of Bromhexine hydrochloride (100 µM, 10 µM, 1 µM, 0.1 µM, and 0.01 µM) presented a cell viability more significant than 50%. Bromhexine hydrochloride at 100 µM showed a decrease in infection over a 50%. The findings from this study suggest the Bromehexine hydrochloride reduces the infection of Omicron SARS-CoV-2, via inhibit viral attachment and entry.

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33. DESIGN OF DNA APTAMERS AS A PHARMACOLOGICAL TOOL TO MODULATE THE HCN2 ION CHANNEL ACTIVITY. diseño de aptámeros de adn como herramienta farmacológica para modular la actividad del canal iónico hcn2

Resúmen:
Hyperpolarization-activated and cyclic nucleotide-gated (HCN) channels form a family of non-selective ion channels composed of four isoform, HCN1-HCN4. HCN2 is highly expressed in somatosensory neurons and plays a central role in inflammatory and neuropathic pain. Dysfunction of this channel is linked to chronic pain, a condition that represents one of the leading causes of suffering worldwide and lacks effective, specific, and safe treatment. This makes HCN2 a key therapeutic target for the development of new drugs. In this context, aptamers—single-stranded DNA (ssDNA) sequences—have been explored as therapeutic agents due to their high specificity, low production cost, and safety in the human body. This study focuses on the design of aptamers capable of interacting with and modulating the function of HCN2 channels, intending to contribute to the development of drugs targeting this receptor. To achieve this, 10,000 random ssDNA sequences were designed using Python programming language, which were processed with RNAFold to predict their secondary structure. Subsequently, the three-dimensional structures were generated using RNAComposer software and energy minimized using NAMD. The 100 structures with the lowest energy after minimization were selected. On the other hand, the structure of the HCN2 channel was modeled using ColabFold, taking the HCN4 structure as a template. Finally, a molecular docking study was performed between the aptamers and the HCN2 channel, selecting the 15 sequences with the lowest interaction energy, with values ranging from -8.9 to -7.9 kcal/mol. These results identify promising sequences that will be evaluated in electrophysiological experiments to determine their effect on HCN2 channel function, potentially paving the way for new therapies for chronic pain.

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34. EFFECT OF TRYPTOPHAN-DERIVED INDOLIC ARYL HYDROCARBON RECEPTOR (AhR) AGONISTS ON CELL VIABILITY OF HUMAN NEURAL CELLS. Efecto de derivados indólicos del triptófano agonistas del receptor de aril hidrocarbonos (AhR) sobre la viabilidad celular de células neurales humanas.

Resúmen:
El receptor de aril hidrocarburos (AhR) es un factor de transcripción nuclear ampliamente conocido por su rol en el metabolismo de xenobióticos por medio del aumento de la expresión de enzimas CYP450, CYP1A1 y CYP1B1, sin embargo este también presenta ligandos de origen endógeno como los derivados indólicos del triptófano provenientes de la microbiota intestinal. Los efectos biológicos de estos catabolitos en células neurales han recibido un creciente interés. En este trabajo se utilizó la línea celular SH-SY5Y de neuroblastoma humano, diferenciada con ácido retinóico, para indagar el efecto de estos compuestos indólicos sobre la viabilidad celular, usando el ensayo de Rojo Neutral. La expresión de AhR se determinó a través de RT-PCR. En los rangos de concentración estudiados, durante una exposición por 72 h, se observa una reducción significativa en la viabilidad celular a concentraciones crecientes de los ligandos de AhR indol-3-carbinol e indol-3-piruvato, mientras que los ligandos FICZ, indol-3-acetato, indol-3-propionato e indoxil sulfato no afectaron de forma significativa la viabilidad celular. Los resultados obtenidos permitirán determinar las concentraciones de trabajo para ensayos de expresión de enzimas CYP450 como CYP1A1 y CYP1B1, así como ensayos funcionales de actividad.

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35. EFFECTS OF TIME RESTRICTED FEEDING IN MACROPHAGE PHENOTYPE AFTER HIGH FAT DIET. Efectos de la alimentación restringida en el tiempo en el fenotipo de los macrófagos tras una dieta rica en grasas

Resúmen:
In skeletal muscle, macrophages are known to be involved in tissue homeostasis, repair, immunity and pathophysiology. In recent years, the metabolic reprogramming of macrophages has been studied, proposing that the M1 phenotype relies primarily on glycolysis for energy, whereas M2 macrophages obtain their energy through enhanced oxidative metabolism, triggering proinflammatory and anti-inflammatory properties, respectively. In chronic inflammatory states such as insulin resistance and obesity, an imbalance of the M1/M2 ratio has been described. Preliminary results from our laboratory show that time-restricted feeding has positive effects on muscle function and physical performance, without modifying body weight in a mouse model. With this in mind, we propose to use obese mice subjected to time-restricted feeding (TRF) to evaluate the immunometabolism of bone marrow-derived macrophages, as well as the impact of this intervention on skeletal muscle and physiological aspects. Bone marrow-derived macrophages (BMDM) were obtained from control and high-fat diet (HFD) mice subjected or not to time-restricted feeding, and their phenotype was determined by flow cytometry. Additionally, mitochondrial mass and potential were measured using the same technique. Physiological measurements of the mice were recorded, such as weight, strength, maximum speed reached and glycemia measurement. Physiologically, no differences in weight are observed in HFD diet mice subjected to TRF, although, it avoids significant differences in blood glucose, respect to HFD diet mice without TRF. No phenotypic differences of BMDM subpopulations are observed, however, there are significant differences between the potential and mitochondrial mass of macrophages derived from HFD AL mice, with respect to the HFD condition subjected to TRF. This might suggest that although there is a change in cellular metabolism, there may not be a marked phenotypic change between BMDMs.

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36. CHARACTERIZATION OF BONE MARROW DERIVED MACROPHAGES FROM C57BL6 MICE WITH SARCOPENIC OBESITY TREATED WITH NAHS. Caracterización de macrófagos derivados de medula ósea de ratones C57BL6 con obesidad sarcopénica tratados con NaHS

Resúmen:
H2S is a gasotransmitter that has been in the spotlight for more than a decade, with promising effects shown in literature. One of them includes the reversal of the pro-inflammatory phenotype found in macrophages in a state of low-grade chronic inflammation. This state is produced in individuals that suffer from the physiopathological condition known as sarcopenic obesity, in which an excess of adipose tissue and a decrease of muscle mass and function is present. To elucidate the effect of this gasotransmitter in sarcopenic obese individuals, we injected the sodium salt of H2S, NaHS, intraperitoneally to CB57Bl6 mice fed with a high-fat diet or to 12-month-old mice to study its effect in bone marrow derived macrophages (BMDMs), which were later analyzed using flow cytometry. The growth media was analyzed with an ELISA test for differences in cytokine secretion. Additionally, skeletal muscle proteins were analyzed using western blot to elucidate the effect of diet, age and NaHS injection in the mitochondria, which is known to play a role in sarcopenia and obesity. Our results showed that BMDMs from mice treated with NaHS tend to polarize more towards a pro-inflammatory phenotype when treated with LPS and that 12-month mice BMDMs tend to secrete higher levels of anti-inflammatory cytokines and lower levels of pro-inflammatory cytokines when treated with NaHS. Western blot results indicate that the presence of mitochondrial UPR (UPRmt) proteins such as CLPP and HSP60 is increased in the skeletal muscle of obese mice treated with NaHS. Together, these results show that NaHS plays a role in the polarization of macrophages and in the skeletal muscle UPRmt, however further investigation is necessary to corroborate our hypothesis.

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37. ANTIFIBROTIC EFFECTS OF HCN CHANNEL BLOCKADE ON CARDIAC FIBROBLAST ACTIVATION FOLLOWING SIMULATED ISCHEMIA/REPERFUSION. Efectos Antifibróticos del Bloqueo de los Canales HCN en la Activación de Fibroblastos Cardíacos tras Isquemia/Reperfusión Simulada.

Resúmen:
Background: Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels, particularly HCN2 and HCN4, contribute to cardiac automaticity, and their blockade with ivabradine (IVA) has shown potential antifibrotic effects. Cardiac fibroblasts (CFs) play a central role in myocardial fibrosis post-ischemia/reperfusion (I/R) injury by activating the NLRP3 inflammasome, which releases profibrotic cytokines. Aim: To evaluate the effects of IVA-mediated HCN channel inhibition on the fibrotic activity of CFs through modulation of inflammasome activation. Methods: CFs isolated from neonatal rat hearts were subjected to simulated I/R conditions (6 hours ischemia, 16 hours reperfusion) with or without IVA (10 μM). NLRP3 inflammasome components were assessed by RT-qPCR and western blot. Positive controls for inflammasome activation included LPS (10 μM) and ATP (100 μM). Results: IVA treatment significantly reduced NLRP3 inflammasome activation, as evidenced by decreased expression of NLRP3 and caspase-1, compared to untreated I/R groups. HCN2 and HCN4 expression was notably upregulated under ischemic conditions but was prevented by IVA pretreatment. Additionally, IVA reduced alpha-SMA expression, indicating an inhibition of CF differentiation into myofibroblasts. Conclusion: HCN channel blockade with IVA attenuates the profibrotic response in CFs, possibly through downregulation of inflammasome activation. This highlights IVA's potential as a therapeutic strategy to mitigate adverse cardiac remodeling and fibrosis post-I/R injury.
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38.

39. LONG NON-CODING RNAS: PROMISING BIOMARKERS FOR EARLY DETECTION OF CISPLATIN-INDUCED NEPHROTOXICITY. ARN largos no codificantes: biomarcadores promisorios para la detección temprana de nefrotoxicidad por cisplatino

Resúmen:
Introduction: Cisplatin is widely used agent effective against various cancers. However, its clinical application is often hampered by drug resistance and significant adverse effects, particularly nephrotoxicity, which affects approximately 20% of patients and contributes to considerable morbidity and mortality. Current treatment strategies have proven inadequate due to the complex interplay of genetic and epigenetic involved in cisplatin-induced nephrotoxicity. Therefore, identifying reliable biomarkers for early detection of this adverse effect is crucial. Notably, the role of long non-coding RNAs (lncRNA) in this context remains underexplored. This study investigates the differential expression of three specific long non-coding RNAs– XLOC_032768, GAS5 and HOTAIR in an in vitro model of cisplatin-induced nephrotoxicity. Methods: Human kidney cell lines HEK-293 and HK-2 were cultured and exposed to varying concentrations of cisplatin for 24 hours to induce nephrotoxicity. Cell viability was assessed using the MTS assay to ascertain the concentrations resulting in 25%(IC25), 50%(IC50), and 75% (IC75) cell death. Following RNA extraction, RT-qPCR was employed to evaluate the expression levels of XLOC_032768, GAS5, and HOTAIR. Results: Cisplatin induced cell death in renal cells, with IC_{25}, IC_{50}, and IC_{75} values of 8.8 μM, 15.43 μM, and 27 μM for HEK-293 cells, and 8.1 μM, 13.57 μM, and 22.8 μM for HK-2 cells, respectively. The analysis revealed that lncRNA expression was amplified across all conditions. Notably, HOTAIR and XLOC_032768 exhibited significantly reduced expression levels in response to cisplatin treatment, whereas GAS5 expression remained stable at baseline levels. Conclusions: The findings suggest that HOTAIR and XLOC_032768 may serve as potential biomarkers for early detection of cisplatin-induced nephrotoxicity. Further research is warranted to validate these lncRNAs as diagnostic tools in clinical settings.
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Socio Patrocinante: Salazar L.A

40. PHAGE DISPLAY-IDENTIFIED CYCLIC PEPTIDE INHIBITORS OF TASK-1 POTASSIUM CHANNELS.
Indentificación de péptidos cíclicos inhibidores de canales de potasio TASK-1 mediante Phage Display

Resúmen:
Ion channels are transmembrane proteins facilitating ion flow across cellular membranes via passive diffusion. Specific types, including sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-) channels, exhibit ion selectivity. K^+ channels, for instance, establish outward potassium currents from the cytoplasm to the extracellular medium. TASK-1, a two-pore domain K^+ channel, is part of the TASK subfamily of acid-sensitive channels (TASK-1, TASK-3, TASK-5) and is overexpressed in the human atrium, where it affects atrial action potential duration. Atrial fibrillation (AF), a prevalent chronic arrhythmia, is associated with abnormal K^+ channel function, and inhibition of TASK-1 has been shown to counteract AF-related action potential shortening, positioning TASK-1 as a promising pharmacological target. Based on this premise, we hypothesized that "Short peptides can inhibit the TASK-1 potassium channel activity associated with persistent atrial fibrillation". This study aimed to evaluate the inhibitory effect of short peptides on TASK-1 channel activity, generated through Phage Display. A peptide library was generated and transformed into phages, and candidate peptides were selected via biopanning. Two peptides, each 14 amino acids long and differing by a single residue, were obtained as potential TASK-1 inhibitors, expected to counteract action potential shortening. Inhibitory effects will be assessed through Patch-Clamp electrophysiology and in silico ligand-protein models.
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41. COMPUTATIONAL ANALYSIS OF THE SSDNA APTAMER-LACTADHERIN INTERACTION AS A STRATEGY TO INHIBIT ITS ACTIVITY DURING BREAST CANCER PROGRESSION. Análisis computacional de la interacción aptámero de ssDNA-Lactadherina como una estrategia para inhibir su actividad durante la progresión del cáncer de mama

Resúmen:
Lactadherin is a glycoprotein involved in crucial processes such as the clearance of apoptotic cells, immunity, and regulation of blood coagulation. Pathologically, lactadherin promotes proliferation, migration, invasion, and metastasis in breast cancer when present in extracellular vesicles (EVs) secreted by tumor cells. This protein consists of 387 amino acids distributed across three domains: C1, C2, and EGF-like, whose dysfunction contributes to the progression of certain types of cancer. Previously, our laboratory analyzed the effect of two aptamers (apta2 and apta4) specific to lactadherin, which inhibit the migration of breast cancer cells when incubated with EVs from metastatic cells. However, although we have determined the inhibitor effect of both aptamers, it is necessary to characterize how they interact with lactadherin. Here, we propose to identify the domains of lactadherin potentially relevant for the union of the aptamers, analyzing the interactions generated in the aptamer-lactadherin complex, through the implementation of computational strategies based on homology modeling and molecular docking using mFOLD, RNA-Composer, VMD, PyMOL, HDOCK, and PLIP tools. Our results indicate that the C1 and C2 domains of lactadherin are potential binding sites for the studied aptamers. The number of intermolecular interactions for the apta2-lactadherin and apta4-lactadherin complexes was 21 and 15 interactions, respectively. The types of interactions identified included hydrogen bonds, hydrophobic interactions, and salt bridges. These interactions occur between amino acid residues and nucleotides that appear to be relevant for the affinity between aptamers of ssDNA and lactadherin.
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42. THE CURRENT STATE OF OPIOID PHARMACOGENETICS IN LATIN AMERICA: A REVIEW. El estado actual de la farmacogenética de opioides en Latinoamérica: una revisión

Resúmen:
INTRODUCTION: Opioid consumption in Latin America remains moderate relative to other regions; however, usage trends have increased significantly over the last two decades, with some countries reporting a tenfold increase. In this context, opioid pharmacogenetics is an interesting and important field of study, with several studies worldwide analyzing different genes that influence the pharmacodynamics or pharmacokinetics of opioid drugs. Despite this, opioid pharmacogenetics in Latin America is relatively unexplored. AIM: This study investigates the current state of opioid pharmacogenetics in Latin America, analyzing existing research and highlighting genes potentially involved in opioid pharmacogenetics. METHODOLOGY: A literature research was conducted in PubMed, SCOPUS, Web of Science, LILACS and Scielo with specific search queries. The search returned 9964 results, that were analyzed according to selecting criteria. RESULTS: The search identified only three studies exploring correlations between specific genes and the pharmacokinetics or pharmacodynamics of specific opioids. The genes analyzed included CYP2D6, CYP2B6, CYP3A4, COMT, OPRM1 and OPRK1. Despite the limited number of studies founded, some correlations were statistically significant, and findings are discussed in the context of relevant implications from other opioid pharmacogenetics studies. CONCLUSION: Limited research on opioid pharmacogenetics in Latin America populations has identified some correlations, providing the base for understanding genetic factors that influence interindividual variability in opioid responses. Further investigations across Latin American countries are needed to assess the broader impact of pharmacogenetics on opioid use in this region.
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43. ASSOCIATION BETWEEN THE GENETIC VARIANT RS4696480 IN TLR2 AND THE RISK OF INFECTIONS IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA. Asociación entre la variante genética rs4696480 en TLR2 y el riesgo de infecciones en pacientes pediátricos con Leucemia Linfoblástica Aguda

Resúmen:
Introduction: Acute lymphoblastic leukemia (ALL) is the most frequent hematological neoplasm in children. It severely affects the immune system, increasing susceptibility to infections. Genetic factors, such as the rs4696480 polymorphism in Toll-like receptor-2 (TLR2) could explain the event. Objective: To evaluate the association between the rs4696480 variant in TLR2 and the incidence of infections in pediatric patients with ALL. Methodology: A retrospective cohort study was performed in patients with ALL between 2014 and 2023 in the three Chilean hospitals. Buccal swab samples were collected, whose DNA was extracted. Genotypes were analyzed using the rt-PCR technique with TaqMan probes. The clinical records of the patients were compiled in the REDCap platform, where the presence or absence of infections in protocols IA and IB were identified. The association between infections and variants was evaluated with the chi2 test. Results: 108 patients were included with an average age at diagnosis of 4.9 years, 52% (n=56) of the patients were male, the protocols analyzed were 1A (n=90), 1A' (n=18), 1B (n=104) and 1B' (n=5). Of the patients, 29,91% (n=32) reported febrile neutropenia and 33,03% reported infection (n=36), the rs4696480 variant was not associated to infection (p = 0,230) nor febrile neutropenia (p =0,117) Conclusions: The rs4696480 variant in TLR2 is not associated with the risk of infections or febrile neutropenia in the studied regimens. A more detailed definition of the event will help to establish a better relationship. These findings could be used to prevent infections in patients with ALL.
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44. IMMUNOMODULATORY EFFECT OF DELPHINIDINE ON THE PRODUCTION OF REACTIVE OXYGEN SPECIES, METALLOPROTEINASE 9 AND EXTRACELLULAR TRAPS OF CANINE NEUTROPHILS. Efecto inmunomodulador de delfinidina sobre la producción de especies reactivas de oxígeno, metaloproteinasa 9 y trampas extracelulares de neutrófilos caninos

Resúmen:
Introduction Neutrophils are the first line of defense of the organism, being able to release reactive oxygen species (ROS), metalloproteinases 9 (MMP9) and neutrophil extracellular traps (NET). Delphinidin is a compound that is part of fruits endemic to the region and has anti-inflammatory effects in vitro and in laboratory animals and humans. Therefore, we want to know the effect of delphinidin on the immune response in vitro of canine neutrophils. Objectives To determine the effect of delphinidin on the inflammatory response of canine neutrophils, through the quantification of ROS, MMP9 activity, NET quantification by measuring cell-free DNA production. Material and methods The randomized study used 20 clinically healthy dogs, 1 to 6 years of age, from which a venous blood sample was obtained from which neutrophils were isolated by gradient centrifugation. ROS production was quantified by the luminometric method of luminol. MMP9 activity was determined by zymography. NET quantification was determined by cell-free DNA production with Picogreen. Results Delphinidin decreased ROS production, metalloproteinase 9 activity, and NET production Conclusion Delphinidin has an immunomodulatory effect as it decreases the inflammatory response of canine neutrophils. This research is the beginning of the study of the effect of delphinidin on the immune response in dogs, projecting its use as a nutritional supplement.

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45. ASSOCIATION BETWEEN NUDT15 GENE POLYMORPHISM AND THROMBOCYTOPENIA IN ALL PATIENTS TREATED WITH 6-MERCAPTOPURINE. Asociación entre polimorfismo en gen NUDT15 y trombocitopenia en pacientes con LLA en tratamiento con 6-Mercaptopurina.

Resúmen:
Acute lymphoblastic leukemia (ALL) is one of the most common neoplasms in childhood. 6-Mercaptopurine is a key drug in the treatment of ALL; however, its use is limited by hematological complications, such as thrombocytopenia, which in severe cases requires platelet transfusions. Previous research has suggested that the NUDT15 polymorphism (rs116855232) may be associated with an increased likelihood of developing these complications. The aim of this study is to determine whether the NUDT15 rs116855232 variant is associated with thrombocytopenia levels below 100,000, 50,000, and 10,000 platelets, and its relationship with the need for platelet transfusions. A retrospective cohort study was conducted in 178 pediatric patients diagnosed with ALL and treated with the PINDA 2009 1A and 1B protocols at the Roberto del Río, Calvo Mackenna, and Exequiel González hospitals. Buccal swab samples were collected for genotyping, and were analyzed by rt-PCR using Taqman probes. Of the 178 patients, 97 were male and 81 female, all diagnosed before the age of 15. The frequency of the C allele was 96.33% and the variant T allele was 3.64%. A significant association was observed between the T variant and severe thrombocytopenia: less than 100,000 (p=0.0107), less than 50,000 (p=0.0102), and less than 10,000 (p=0.0008). In conclusion, the NUDT15 rs116855232 variant may be associated with a higher probability of developing severe thrombocytopenia and, consequently, the need for platelet transfusions in pediatric patients with ALL treated with 6-Mercaptopurine.

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Socio Patrocinante: Martínez F. M.

46. TAMOXIFEN PRODUCES A REDUCTION IN NEUTROPHIL FUNCTION IN OBESE IN ASTHMA-AFFECTED HORSES. El tamoxifeno produce una reducción en la función neutrofílica en caballos obesos afectados por asma

Resúmen:
Equine asthma, which develops in horses exposed to dusty environments, leads to bronchoconstriction, neutrophilic inflammation, and airway hyper-responsiveness. This condition serves as a valuable model for studying neutrophilic asthma in humans. Research indicates that obese individuals with asthma suffer from more severe symptoms, have poorer asthma control, and exhibit a diminished response to treatment. Drawing from these parallels, it is hypothesized that obese horses with asthma may similarly present more severe symptoms and compromised lung function compared to lean horses. Previous findings suggest that tamoxifen may modulate neutrophil functionality in this context. To explore this potential, in vitro studies are planned, utilizing peripheral blood neutrophils from naturally obese and non-obese horses affected by asthma. These studies will focus on evaluating the effect of tamoxifen on key components of the innate immune response. Results to date demonstrate that tamoxifen can effectively reduce reactive oxygen species (ROS) production in neutrophils stimulated with opsonized zymosan. Additionally, tamoxifen has shown the capacity to decrease inflammasome complex activation, which is associated with a corresponding reduction in IL-1β levels. Therefore, it can be concluded that tamoxifen has the potential to reduce specific elements of the innate immune response in peripheral blood neutrophils of obese horses with asthma.

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Socio Patrocinante: N/A

CRONOGRAMA / SCHEDULE



XLV Congreso Anual

SOCIEDAD DE FARMACOLOGÍA DE CHILE

11 al 14 noviembre 2024

Lugar:

Hotel Novotel
6 Norte 745
Viña del Mar
Chile

registration time

Schedule	Monday 11th November 2024	Schedule	Tuesday 12th November 2024	Wednesday 13th November 2024	Thursday 14th November 2024
09:00	**Symposium Neuropsychopharmacology** "Inaugural Symposium of the Master in Physiology and Pharmacology: New frontiers in nucleus accumbens pharmacology" **Chair: Dr. Sotomayor-Zárate**	09:00	**Symposium Endocrine Pharmacology and Metabolism** "From Obesity to Diabetes: Pathophysiological Mechanisms and Therapeutic Options" **Chair: Dr. Barra**	**Symposium** "Women in Pharmacology" **Chair: Dr. Catalán**	**Symposium Natural Products** "Medicinal and Food Plants in Chile: Status, Opportunities and challenges" **Chair: Dr. Bridi**
11:00		11:00			
11:00 - 11:30	SOFARCHI Coffee break	11:00 - 11:30	SOFARCHI Coffee break	SOFARCHI Coffee break	SOFARCHI Coffee break
11:30	**Symposium Medicinal Chemistry** "Medicinal Chemistry in Chile: From design to experimental pharmacology" **Chair: Dr. Iturriaga-Vásquez**	11:30	**Lecture Nº 2 Professor Denise Belsham (Canada)** "The amazing molecular diversity of hypothalamic neurons: Tackling mechanisms one neuron at a time" **Chair: Dr. Barra**	**Lecture Nº 4 Professor Dr. Jenny L. Fiedler (Chile)** "Sex specific effects of stress on hippocampus: New opportunities of pharmacological interventions" **Chair: Dr. Bravo**	**Lecture** To be announced soon
		12:30			
13:30		12:35 13:30	Oral Communications and Incorporations	Oral Communications and Incorporations	Prof. Letelier Award
13:30 - 15:00	Free Lunch break	13:30 - 15:00	Free Lunch break	Free Lunch break	Free Lunch break
15:00	**Symposium ABC Pharmacology** "The ABC of South American Pharmacology: Addiction Research" **Chair: Dr. Rivera-Meza**	15:00	**Symposium Nº5 Molecular Pharmacology** "The problem of the 3 elements: receptor, ligand and Al. Pharmacological approaches in purinergic transmission". **Chair: Dr. J. Fuentealba**	**Symposium** "Inaugural Symposium of the Master in Physiology and Pharmacology: Empowering Science by Women in Valparaíso" **Chair: Dr. Julio-Pieper**	**Symposium Drug Delivery** "Breaking Barriers for Drug Delivery" **Chair: Dr. Bahamondez**
17:00		17:00			
17:00 - 17:30	SOFARCHI Coffee break	17:00 - 17:30	SOFARCHI Coffee break	SOFARCHI Coffee break	SOFARCHI Coffee break
17:30	**Opening Lecture Professor Dr. Mauro Teixeira (Brazil)** "Resolution pharmacology - from chronic inflammation to infection" **Chair: Dr. Diaz-Araya**	17:30	**Lecture Nº 3 Professor Dr. Samia Joca (Denmark)** "Demystifying Publishing in Pharmacology: A Conversation with the Editor" **Chair: Dr. Reyes-Parada**	**Lecture Nº 5 Professor Dr. Caroline Weinstein (Chile)** "Gathering chemistry, physics, biology and pharmacology around polymeric biomaterials for wound healing" **Chair: Dr. Sotomayor-Zárate**	**Closing Lecture Professor Dr. Mario Herrera-Marschitz (Chile)** "A sightseeing tour along a life devoted to Pharmacology: Hard work on the lab bench; outstanding teachers; some highlights, and many friends" **Chair: Dr. Diaz-Araya**
18:30		18:30			
18:30 - 19:00	Opening ceremony	18:30 - 20:30	Poster session No. 2	Poster session No. 3	Closing ceremony
19:00 - 21:00	Poster session No. 1				Dinner with tickets

INTRUCCIONES PARA LOS AUTORES

i) Tipos de Manuscritos:

(a) Investigaciones Originales (*Full papers*): Trabajos que reportan investigaciones originales realizadas con procedimientos experimentales adecuados y según las guías nacionales e internacionales para el uso de sujetos de experimentación serán revisados para eventual publicación en la revista (ver preparación del manuscrito).
(b) Comunicaciones Cortas (*Short Communications*): Reportes científicos originales cuyo tamaño debe ser de 1000 a 4000 palabras como máximo de extensión, incluyendo la leyenda de la figura (no se incluyen las referencias). Estos trabajos solo pueden incluir 1 figura y 1 tabla de resultados. En situaciones especiales se consideraran 2 figuras o 2 tablas. No deben ser usadas más de 15 referencias en el manuscrito
(c) Revisiones (*Reviews*): Revisiones sobre temas relevantes de la Farmacología serán solicitados por el Editor en jefe o el comité editorial, a través de invitación escrita. Estas revisiones no requerirán una exhaustiva revisión editorial y serán publicadas en volúmenes temáticos de la Revista de Farmacología de Chile.
(d) Columnas de Opinión u otras Publicaciones: Columnas de opinión sobre temas de contingencia nacional que involucren políticas públicas de medicamentos, correcto uso de medicamentos por parte de la población o la aparición y/o retirada de medicamentos en el mercado nacional, serán solicitadas por el Editor en jefe o el comité editorial, a través de invitación escrita.

ii) Detalles para el envío de Manuscritos:

El envío de manuscritos a la Revista de Farmacología de Chile para revisión (*Full papers*, *Short Communications o Reviews*) o solicitudes de columnas de opinión deben ser enviados a los siguientes correos electrónicos (ramon.sotomayor@uv.cl cc: pjarapicas@gmail.com cc geormrenard@gmail.com). Se solicita colocar en el asunto del correo electrónico la siguiente frase: Manuscrito para Rev.Farmacol.Chile

iii) Preparación del Manuscrito:

* Se recomienda el uso del programa para procesar texto Word de Microsoft Office. Cuando guarde el manuscrito que ha elaborado se solicita que la opción de guardado sea: Guardar como: "Documento de Word 97-2003".
* El manuscrito debe ser escrito en formato "Times New Roman" tamaño 12, doble espacio y a una columna. Las páginas del manuscrito deben ser enumeradas en el borde inferior derecho con números arábigos.
* Cualquier figura inserta en el manuscrito debe ser en formato TIFF, JPEG o BMP de alta resolución (600 dpi) y en caso de usar tablas se debe usar la opción insertar tablas de Word. No se recomiendan tablas hechas con la opción de insertar líneas.
* Fotografías y gráficos a color son aceptadas para la versión digital, sin embargo en la versión impresa de la revista se utilizará la impresión en escala de grises. Además se recomienda verificar la calidad de la figura reduciéndola al tamaño de 1 columna de ancho, es decir 8 cm.
* La Revista de Farmacología de Chile acepta trabajos en español, sin embargo previa autorización del comité editorial se podrán revisar trabajos en inglés o portugués.

iv) Estructura del Artículo:

iv.1) Investigaciones Originales y Comunicaciones Cortas:

Cada una de las secciones del manuscrito debe ser enumerada con números arábigos y cada subdivisión con la nomenclatura (X.1). No se considera en la enumeración el resumen (abstract).

Primera página:

- Titulo: El título del trabajo debe ser conciso e informativo. No se recomiendan abreviaciones de palabras en el titulo. Se debe incluir el título del trabajo en inglés.
- Nombre de los autores y Filiación: Se solicita indicar el nombre de cada autor y su apellido. Se acepta incluir la inicial del segundo nombre, aunque no es obligatorio. Al término de cada apellido se solicita colocar un número arábigo en superíndice que relacionará al autor con su respectiva filiación.
- Autor Correspondiente: Se debe indicar claramente al autor correspondiente del trabajo, incluyendo: Nombre, Dirección Postal, Teléfono, Fax y Correo Electrónico.

Segunda página:

- Resumen (Abstract): La extensión máxima del resumen es de 300 palabras y debe describir claramente el propósito de la investigación, los principales resultados y principal conclusión del trabajo. El resumen debe ser escrito en español e inglés.
- Palabras Claves: Se deben incluir palabras claves que permitan identificar los aspectos más importantes del trabajo. No incluir más de 10 palabras claves. Las palabras claves deben ser escritas en español e inglés.

Tercera y más páginas:

- Introducción: La introducción al tema a discutir en el trabajo no debe tener una extensión superior a las 750 palabras.
- Materiales y Métodos: Se debe detallar claramente todos los materiales y metodologías utilizadas en el desarrollo del trabajo. Además se debe explicitar en consentimiento bioético de la institución donde fue realizada la investigación. Los trabajos realizados en humanos deben incluir el apego experimental a la Declaración de Helsinki de la Asociación Medica Mundial, considerando consentimiendo informado y aprobación de comité de ética.
- Resultados: Se debe incluir en detalle los principales resultados obtenidos, con sus respectivos análisis estadísticos. No se aceptarán trabajos para publicar que no tengan un adecuado tratamiento estadístico. La expresión gráfica de resultados puede ser realizada a través de gráficos de 1 columna de ancho (8 cm) o agrupaciones de gráficos con un ancho máximo de dos columnas (16 cm). También se pueden incluir tablas que detallen resultados relevantes para el trabajo, incluyendo número de casos y valor de la significancia *p.*
- Discusión de los Resultados: La discusión de resultados debe ser objetiva y se debe evitar una excesiva discusión bibliográfica que reste valor a los resultados presentados en el manuscrito. Es recomendado una conclusión final que indique las proyecciones de la investigación.
- Agradecimientos: Se pueden incluir las fuentes de financiamiento que permitieron el desarrollo del trabajo, indicando claramente a que autor corresponde la fuente de financiamiento. También se pueden incluir agradecimientos a personas que prestaron ayuda técnica o de revisión del manuscrito. En esta sección se debe declarar si existió conflicto de interés. En caso de no haber conflicto de interés se debe mencionar esta situación. Se recomienda consultar la siguiente dirección URL http://zl.elsevier.es/es/revista/neurologia-295/conflicto-intereses-publicaciones-cientificas-90101004-editorial-2012 para aclarar en concepto y situaciones de conflicto de interés.
- Referencias: En el texto se deben citar las referencias con el apellido del primer autor, sus iniciales y el año de la publicación. En la sección de referencias se deben ordenar las mismas por orden alfabético. Se recomienda utilizar algún programa de manejo de referencias como EndNote con el formato de referencias de Journal of Neurochemistry.

Ejemplos:

Semenova M. M., Maki-Hokkonen A. M., Cao J., Komarovski V., Forsberg K. M., Koistinaho M., Coffey E. T. and Courtney M. J. (2007) Rho mediates calcium-dependent activation of p38alpha and subsequent excitotoxic cell death. Nat. Neurosci. 10, 436-443.

La abreviación de los títulos de las revistas debe de acuerdo a el listado de revistas indexadas en *Index Medicus* (Superintendent of Documents, US Government Printing Office, Washington, DC 20402, USA, DHEW Publication No. 95-267). Ejemplo: Acta Neurol. Scand. Acta Physiol. Scand. Anal. Biochem. Arch. Biochem. Biophys. Biochem. J. Biochem. Pharmacol. Biochim. Biophys. Acta Biol. Chem. Hoppe Seyler Br. J. Pharmacol. Eur. J. Pharmacol. Experientia J. Biol. Chem. J. Cell Biol. J. Mol. Biol. J. Pharmacol. Exp. Ther. J. Physiol. (Lond.) Mol. Pharmacol. Nature Proc. Natl Acad. Sci. USA Proc. Soc. Exp. Biol. Med. Science

iv.2) Revisiones:

Las revisiones de unidades temáticas serán solicitadas por el editor en jefe o por el co-editor, sin embargo para aquellas unidades temáticas específicas oficiara como co-editor algún miembro del comité editorial que sea especialista en el tema

Primera página:

- Titulo: El título del trabajo debe ser conciso e informativo. No se recomiendan abreviaciones de palabras en el titulo. Se debe incluir el título del trabajo en inglés.
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Tercera y más páginas:

- Introducción: La introducción al tema a discutir en el trabajo no debe tener una extensión superior a las 750 palabras.
- Temas a Desarrollar: Por cada tema que se pretenda desarrollar se debe entregar una visión objetiva que destaque los avances más importantes en la investigación científica. Se pueden desarrollar subtemas, destacando claramente a que unidad temática corresponde. Se recomienda si se revisa algún procedimiento experimental mencionar las ventajas y desventajas de su aplicación. Es recomendado una conclusión final que integre la información entregada en la revisión.
- Agradecimientos: Se pueden incluir las fuentes de financiamiento que permitieron el desarrollo del trabajo, indicando claramente a que autor corresponde la fuente de financiamiento. También se pueden incluir agradecimientos a personas que prestaron ayuda técnica o de revisión del manuscrito. En esta sección se debe declarar si existió conflicto de interés. En caso de no haber conflicto de interés se debe mencionar esta situación. Se recomienda consultar la siguiente dirección URL http://zl.elsevier.es/es/revista/neurologia-295/conflicto-intereses-publicaciones-cientificas-90101004-editorial-2012 para aclarar en concepto y situaciones de conflicto de interés.
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Leyendas para las Figuras: Los títulos y leyendas de las Figuras deben presentarse en forma clara y corta. Se debe identificar y explicar todo símbolo, como flecha, número o letra que haya empleado para señalar alguna parte de las ilustraciones. En la reproducción de preparaciones microscópicas, explicite la ampliación y los métodos de tinción empleados.

Unidades de Medida y Nomenclaturas: Use unidades correspondientes al sistema métrico decimal. Las abreviaturas deben ser definidas la primera vez que aparecen en el texto. El listado de abreviaturas debe ser de acuerdo a la siguiente publicación Biochem. J. (1978) 169, 1-27. Al finalizar este instructivo se mencionan las abreviaturas que no deberían ser definidas (el listado esta en idioma inglés). La nomenclatura que se refiere a drogas y sustancias químicas no terapéuticas deben nombrarse de acuerdo a la nomenclatura IUPAC (International Union of Pure and Applied Chemistry). Mientras que para fármacos solo se acepta el nombre genérico INN (DCI). Respecto a los nombres de fantasía solo pueden ser nombrados entre paréntesis con el signo ® siempre que esté registrada la patente y que no exista un conflicto de interés evidente con el laboratorio fabricante del fármaco.

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- Los artículos originales de investigación que no se agrupen en unidades temáticas específicas y que sean aceptados para publicación, serán publicados en el volumen y número del congreso anual de la Sociedad de Farmacología de Chile. La fecha aproximada de publicación será comunicada a los autores con suficiente antelación.
- Respecto a la revisión de artículos originales los revisores enviarán al Editor en Jefe, los cambios propuestos, sus opiniones, sus proposiciones, rechazos, etcétera, las cuales serán comunicadas a los autores con absoluta confidencia.
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Abreviaciones Permitidas sin necesidad de definición en el texto:

ADP, CDP, GDP, IDP, UDP, 5(pyro)-diphosphates of adenosine, cytidine, guanosine, inosine, and uridine AMP, etc.-5-phosphates of adenosine, etc. ANOVA, analysis of variance ATP, etc.-5`(pyro)-triphosphates of adenosine, etc. ATPase, adenosine triphosphatase bp, base pair Ci, curie CoA and acyl-CoA-coenzyme A and its acyl derivatives (e.g., acetyl-CoA) cpm, counts per minute CNS, central nervous systemCSF, cerebrospinal fluid Cyclic AMP, 3,5-cyclic adenosine monophosphate Cyclic GMP-3,5-cyclic guanosine monophosphate DNA, deoxyribonucleic acid DNase, deoxyribonuclease DOPA, 3,4-dihydroxyphenylalanine dpm, dps-disintegrations per minute, disintegrations per second EDTA, ethylene-diaminetetraacetate EEG, electroencephalogramEGTA, ethyleneglycol bis(aminoethylether)tetraacetate ELISA, enzyme-linked immunosorbent assay FAD, FADH2, flavin-adenine dinucleotide and its reduced form FMN, flavin mononucleotide g, average gravity GABA, gamma-aminobutyric acid (not Gaba) GLC, gas-liquid chromatography GSSG, GSH, glutathione, oxidized and reduced forms h, hour HEPES, N-2-hydroxyethylpiperazine-N-2-ethanesulfonic acid HPLC, high performance liquid chromatography Ig, immunoglobulin IR, infrared kb, kilobase kDa, kilodalton im, micron min, minute MPP+, 1-methyl-4-phenylpyridinium MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine NAD+, NADH-oxidized and reduced forms of nicotin-amide-adenine dinucleotide NADP+, NADPH-oxidized and reduced forms of nicotin-amide-adenine dinucleotide phosphate NAD, NADP may be used when the oxidation state need not be indicated NMDA, N-methyl-D-aspartate NMN, nicotinamide mononucleotide NMR, nuclear magnetic resonance PCR, polymerase chain reaction Pi, orthophosphate (inorganic) PNS, peripheral nervous system PPi, pyrophosphate (inorganic) rpm, revolutions per minute RNA, ribonucleic acid RNase, ribonuclease RT, reverse transcription s, second SEM, standard error of mean SD, standard deviation TLC, thin-layer chromatography Tris, 2-amino-2-hydroxymethylpropane-1,3-diol UV, ultraviolet