SIMPOSIO / SYMPOSIA 6

Coordinadora Dra. Caroline Weinstein-Oppenheimer. Simposio Prof. Dra María Eugenia Letelier: "Natural products that promote tissue regeneration".
Expositores: C. Weinstein (UV), T. Bahamondez (UV), A. Muller (UO).

ENSAYOS PRECLÍNICOS PARA MATPATCH™, UN PARCHE FITOTERAPÉUTICO PARA EL TRATAMIENTO DE ÚLCERAS CUTÁNEAS ISQUÉMICAS EN ADULTOS MAYORES. PRECLINICAL ASSAYS FOR MATPATCH™, A PHYTOTHERAPEUTICAL PATCH FOR THE TREATMENT OF ISCHEMIC SKIN ULCERS IN THE ELDERLY

Aging predisposes to skin ulcers, and once formed, they are hard to treat with the available strategies, supporting the need to explore novel treatments. Thus, Matpatch™ emerges, a phytotherapeutic patch that combines a polymeric scaffold with a standardized matico (Budleja globosa Hope) extract (BG-126). The aim of this research was to evaluate Matpatch™ at the preclinical level. For this, the biocompatibility of Matpatch™ with human dermal fibroblasts was determined by the measurement of cell viability through the resazurin assay and by the quantification of cytokines and trophic factors with commercial kits. In addition, histochemical, immune-histochemical and scanning electronic microscopy techniques were used to evaluate the cellular viability of the normal human fibroblasts grown on the scaffold. Finally, the product´s safety was studied on an ischemic wound model on aged rats, applying a Latin square experimental design. The viability assay and the histochemistry showed that the cell population seeded on top of Matpatch™ grew over time. In addition, the chemokine CXCL-12 and the trophic factor VEGF were detected in the supernatants of the fibroblasts cultured on the patch. The immune-histochemical analysis of the patch corroborated VEGF expression. The examination of the biopsies from the wounds treated with Matpatch™, showed vWF expression, an angiogenesis expression marker, and from this analysis it was also observed that wounds treated with our product, exhibited a lower proportion of hyperplasic scars, compared with controls with no treatment, BG-126 or scaffold alone. It is concluded that Matpatch™ is biocompatible both in vitro as in vivo, promotes the secretion of trophic factors and chemokines relevant to a better wound healing.

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FORMULACIÓN DE EXTRACTOS SOLUBLES EN AGUA DE BUDDLEJA GLOBOSA HOPE Y SUS PROPIEDADES ANTIMICROBIANAS CONTRA PSEUDOMONAS AERUGINOSA. FORMULATION OF WATER SOLUBLE BUDDLEJA GLOBOSA HOPE EXTRACTS AND THEIR ANTIMICROBIAL PROPERTIES AGAINST PSEUDOMONAS AERUGINOSA.

Buddleja globosa Hope (BG) extracts are traditionally used to treat skin and gastric ulcers due to their healing properties. Non-aqueous solvents such as ethanol and DMSO are usually used to extract naturally occurring compounds. However, the cytotoxicity of these solvents and the low water-solubility of the extracted compounds can hinder their biomedical applications. To overcome the limited solubility of the BG extracts, we aimed to enhance the solubility by processing a standardized hydroalcoholic extract (BG-126) through spray drying (SD), with and without two solubility enhancers. Spray dried BG extract (BG-SD) and spray dried BG extracts plus polyvinylpyrrolidone (BG-SD PVP) and Soluplus® (BG-SD SP) were developed starting from BG-126 (containing 53% ethanol). These four formulations were characterized by total phenolic content, water solubility at 25 and 37 °C, and antimicrobial properties against Pseudomonas aeruginosa. All the SD formulations presented a solubility that allowed to reach maximum concentrations of 1024 µg/mL catechin for BG-SD and 2048 µg/mL catechin for BG-SD PVP and BG-SD SP for antimicrobial testing. BG-SD showed the highest antimicrobial potency with a minimum inhibitory concentration (MIC) of 512 µg/mL catechin, followed by BG-126 with a MIC of 1024 µg/mL catechin and SP. BG-126 also showed to inhibit biofilm formation as well as the excipients PVP and SP. Spray dried BG extract (BG-SD) represents a promising natural active with enhanced antimicrobial properties against P. aeruginosa for further research and development of novel phytopharmaceuticals.

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PRODUCTOS NATURALES PARA CICATRIZACIÓN DE HERIDAS EN MEDICINA VETERINARIA. NATURAL PRODUCTS FOR WOUND HEALING IN VETERINARY MEDICINE.

Wound healing in veterinary medicine is a mixture of processes including inflammation, cell proliferation and, in most cases, microbial infection due to the characteristics of the animals' skin. Natural products from different sources, whether animal or plant, have antioxidant, anti-inflammatory, antibacterial and pro-regenerative activities that aid in wound healing. Honey and herbal extracts are natural products that have many health benefits, both human and animal, including their effect on wound healing. Honey is a highly concentrated viscous solution of floral sugars, proteins and enzymes derived from bee crops. Herbal extracts are liquid solutions made from dried or fresh plants extracted with alcohol and/or water. The active compounds of natural products depend on their biological origin, but both (honey and herbal extracts) contain several compounds that act additively or synergistically. Among these compounds, we can mention polyphenols which are considered the most important antioxidants and can be easily quantified. They also help in the elimination of inflammation products. The antibacterial effect is usually a combination of different mechanisms of action due to the different compounds present. Since these compounds may have redundant activity, the occurrence of resistance is less frequent with these products than with commonly used antibiotics with only one active compound. We should not forget that there is concern about antibiotic resistance after use, so natural products provide an alternative approach to skin infections and wound healing in animals. Finally, they also promote the proliferation of cellular components (fibroblasts and keratinocytes) involved in the regeneration mechanism. Despite the beneficial effects on wound healing, efficacy and safety data supporting the use of natural products in animals is limited and further research is needed.

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SIMPOSIO / SYMPOSIA 7

Coordinador Dr. Mario Herrera (Uch), "Pharmacological opportunities targeting long-term metabolic deficits induced by perinatal asphyxia".
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PARTO, UNA INSTANCIA DE REPROGRAMACION METABOLICA CON UN INCIERTO RESULTADO. DELIVERY, A METABOLIC REPROGRAMMING HUB LEADING TO AN UNCERTAIN OUTCOME: CLINICAL AND EXPERIMENTAL CONSIDERATIONS.

Labour and delivery imply a complex and sequential metabolic and physiologic cascade, culminating in a successful childbirth in most circumstances. Delivery can, however, be risky, whenever oxygen supply is interrupted, producing perinatal asphyxia (PA). PA causes an energy failure, leading to cell dysfunction and death when re-oxygenation is not promptly restored. Re-oxygenation induces a long-term energetic crisis affecting metabolism and the repairing machinery required for proper development, making the neonate vulnerable to recurrent metabolic insults. The consequences of PA depend upon the length of the oxygen-deprivation period, resuscitation/re-oxygenation manoeuvres, and developmental stages of the affected brain regions, mesencephalon and hippocampus being highly vulnerable regions. With a model of PA in rat, we identified relevant targets responsible for the metabolic cascades linked to neurodevelopmental impairments. Severe PA induced a sustained effect on redox homeostasis, increasing oxidative stress, decreasing metabolic and tissue antioxidant capacity in vulnerable brain regions, even weeks after the insult. Catalase activity was decreased in mesencephalon and hippocampus from PA-exposed, compared to control neonates, in parallel with increased cleaved-caspase-3 levels, associated with decreased glutathione reductase and glutathione peroxidase activity, a shift towards the TIGAR-dependent pentose phosphate pathway, and delayed calpain-dependent cell death. The brain damage continued long after the re-oxygenation period, extending for weeks after PA, affecting neurons and glial cells, including myelination in grey and white matter. The resulting vulnerability was investigated with organotypic cultures built from PA and control neonates, finding that substantia nigra TH-dopamine-positive cells from PA neonates were more vulnerable to 1 mM of H2O2 than the controls. Several therapeutic strategies have been investigated, including hypothermia, nicotinamide, and intranasally administered mesenchymal stem cell secretomes, promising clinical translation.

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