Anti-inflammatory and chondro-protective effects of Rose hip powder and its constituent galactolipid GOPO

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Introduction
Cartilage erosion and rebuilding are highly complex biological processes that reflect interactions of cells and mediators produced by different cell types. These might efficiently be modulated by the concomitant action of a variety of constituents such as those occurring in natural extracts and substances that provide relief for joint diseases like osteoarthritis (OA). Indeed, a rose hip powder (RHP) has been found to have beneficial effects in the treatment of OA as shown in several randomized controlled clinical trials. The rose hip powder tested was produced by Hyben Vial, Denmark, and standardized process ensuring the preservation of its active constituents and is commercially available in Europe as Litizin™ and in the rest of the world as i-flex™. A constituent of RH, the galactolipid GOPO inhibits chemotaxis of neutrophils and is thus one of several bioactives contained in RH powder, that has a putative chondroprotective and/or cartilage-regenerating effect in OA.

We present experimental approaches for identifying RH bioactives. The anti-inflammatory and chondroprotective effects of GOPO have been evaluated at different levels in vitro in three relevant cellular systems.

RHP and GOPO inhibit the production of nitric oxide (NO) and prostaglandin E2 (PGE2) in murine macrophages (RAW264.7 cells)

RAW264.7 cells were activated with lipopolysaccharide (LPS) in the presence or absence of RHP and GOPO for 24 hours. The amount of PGE2 and NO was measured in the cultured supernatants.

RHP and GOPO inhibit the production of inflammatory mediators in murine macrophages
RAW264.7 cells were activated with lipopolysaccharide (LPS) in the presence or absence of RHP and GOPO for 24 hours. The production of chemokines, interleukins and cytokines was measured in the supernatants by multiparametric analysis (Luminex technology).

RHP and GOPO decrease the expression of inflammatory genes in murine macrophages
RAW264.7 cells were activated with LPS in the presence or absence of RHP and GOPO for 4 hours. The gene expression was measured by quantitative RT-PCR.

RHP and GOPO inhibit the secretion of chemokines and interleukins in human peripheral blood leukocytes (PBL)
PBLs were activated with lipopolysaccharide (LPS) / Interferon-gamma (IFN-γ) in the presence or absence of RHP and GOPO for 24 hours. The production of chemokines, interleukins and cytokines was measured in the cultured supernatants by multiparametric analysis (Luminex technology).

Summary and conclusions:
Bioactives have been identified in RH extracts initially by using anti-inflammatory parameters and subsequently multi-parametric profiling in three cellular systems. Murine macrophages were convenient for identifying first effects, while the heterogeneous PBL populations (containing mononuclear and polymorphonuclear cells) permitted to monitor more diverse effects. GOPO has been identified as a potent and pleiotropic effector molecule that modulates various facets of the inflammatory processes and cell migration mediated by chemokines. Its importance in cartilage protection has been evidenced by its effect on the chemokine production by chondrocytes and the expression of catabolic and anabolic genes by human articular chondrocytes. Although RH contains significant quantities of GOPO (<0.1%), the contents cannot account for the whole biological activity of RH. Consequently, other constituents contribute to, and might act in concert to reduce the erosion of the extracellular matrix in joints or favor the rebuilding of cartilage.

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