Biotechnological method for production of 8-prenylnaringenin for application in treatment of inflammatory skin diseases

Aim of the work

The main aim of the work is the development of a novel biotechnological method for production of 8-prenylnaringenin from hops cones for application in treatment of inflammatory skin diseases. More specifically, the aims of the project are to investigate the supercritical fluid extraction (SFE) process of hop cones experimentally and numerically and to optimize it; to develop an efficient method for increasing the concentration of 8PN in the extract via chemical and biotechnological transformation, and – finally – to assess the potential of the resulting preparations for treatment of inflammatory skin diseases using three preclinical models.

Motivation

Supercritical fluids have found broad applications in various fields, such as chemical, food and pharmaceutical industry, as well as biotechnology. Due to their unique properties, combining advantageous features of liquids and gases, they constitute an attractive and more environmental-friendly alternative to liquid organic solvents, used in many industrial processes. One of the most widespread applications is the process of supercritical fluid extraction, in which a supercritical fluid is used to extract a particular substance from a raw material being a porous solid or a liquid. An effective and yet demanding application of supercritical fluid extraction is obtaining extracts from Hop cones (*Lupuli flos*), which are valuable products for the food, pharmaceutical and cosmetics industry. Hop extract ingredients, especially xanthohumol (XN), isoxanthohumol (IX) and 8-prenylnaringenin (8PN), exhibit favorable health effects in humans. Especially 8PN shows potential for application in treatment of skin diseases. For obtaining hop cone extracts containing XN, IX, and 8PN, SFE utilizing supercritical carbon dioxide can be applied. However, the process is challenging due to low concentrations of the key ingredients in the plant matrix, the necessity of using high pressures (up to 1000 bar), together with a high sensitivity of the process in terms of process conditions. The very low concentration of 8PN in the raw extract can be potentially increased by performing (bio)transformation of XN and IX to 8PN.

Description of the research

In the first part of the project, SFE of hop cones and extract fractionation will be investigated experimentally. The influence of various process parameters, such as temperature, pressure, extraction time, on extraction efficiency and kinetics will be assessed. Next, chemical processes and bioprocesses involving microorganisms, leading to the transformation of hp cones extract ingredients (especially XN and IX) to 8PN will be studied experimentally. Moreover, mathematical models of the SFE and extract fractionation processes will be developed in order to study the SFE process using computer simulations and to optimize the process, i.e. to determine of optimum process conditions, based on technical and economic criteria. In the second part of the project, biological testing of 8PN for the treatment of inflammatory skin diseases such as atopic dermatitis (AD) will be conducted. Analyses on cellular models of human keratinocytes and fibroblasts will be performed. The effects on chronic and acute cellular inflammation and wound healing will be investigated. Moreover, interactions with the skin microbiota of volunteers will be investigated and the effect of 8PN on microbiota biodiversity, as well as the effect of bacterial metabolism on the stability of the molecule will be carried out. Finally, the anti-inflammatory activity of 8PN in an in vivo model of AD in rats will be examined.

Expected effects of project realization

The primary effect of project realization will be the development of a novel method for production of hop cones extracts enriched with 8PN. The extensive experimental and numerical study of the SFE process will provide insight on mechanisms governing the process, identification of factors determining the process rate, evaluation of the impact of changing process conditions on its course, selection of the most favorable process conditions, and criteria for process scale-up. Moreover, the research hypothesis on the beneficial effect of 8PN-enriched hop cones extract in treatment of inflammatory skin diseases will be examined. A potential long-term effect of the project is the development of a novel hop-derived preparations for treatment of inflammatory skin diseases, produced using supercritical fluid extraction. This is particularly important, as application of supercritical fluids meets the principles of “Green Chemistry” and favors the realization of the idea of sustainable development, especially enables the limitation of consumption of natural resources, as well as reduction of the environmental burden.