Universität Basel

Research Project

Herbal safety in the pregnancy – Treatment options for nonpsychotic mental diseases

Third-party funded project

Project title Herbal safety in the pregnancy – Treatment options for nonpsychotic mental diseases
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Pregnancy is a critical period for medical care, well-being of both the woman and the embryo/foetus are to be considered. This is particularly relevant in the management of nonpsychotic mental disorders (NMD), since treatment with CNS-active drugs, but also untreated NMD may have negative effects. Some herbal preparations (phytopharmaceuticals) possess sedative, anxiolytic, or antidepressant properties. Since these preparations are often perceived as safe, their consumption during pregnancy might be high even though only a few studies have been conducted. Assessment of safety issues with phytopharmaceuticals is highly challenging.ă The active ingredients are multi-component mixtures of compounds, many of which undergo metabolisation by the intestinal microbiota upon oral administration, and metabolisation in the liver once reaching systemic blood circulation. Moreover, some of these compounds might be toxic and reach the embryo/foetus via the placenta.

The project strives for characterising the safety of commonly used herbal medications for the treatment of NMD during pregnancy. Well-known herbal medications for these diseases are valerian, hops, golden poppy, lavender, and St. John's wort. Major aims of the project are: (1) characterisation of the use of herbal preparations during pregnancy, (2) analyses of their metabolisation by the intestinal flora and in the liver; (3) assessment of cytotoxicity and genotoxicity in vitro of these extracts and of critical compounds in extracts before and after metabolisation; (4) characterisation of intestinal absorption of the various compounds; (5) prediction of their hormone-disrupting effects and possible drug interactions; (6) assessment of effects on the function of immunocompetent cells and; (7) of placenta cell cultures; (8) investigation of their permeation across the placenta barrier.

Whether the herbal preparations are commonly being used during pregnancy will be addressed with a survey in aim 1 (Zurich/A.P. Simões-Wüst, in collaboration with M. Puhan). To accomplish aim 2, the chemical composition of herbal preparations will be characterised before and after being metabolised by intestinal flora and liver microsomes (Basel/M. Hamburger, O. Potterat, in collaboration with C. Lacroix). Extracts and compounds (unmetabolised and metabolised) will be then submitted to cytotoxicity and genotoxicity assessment, in comparison with two synthetic CNS-active drugs that are frequently given during pregnancy, namely diazepamă and citalopram. Cytotoxicity and genotoxicity will be tested in sensitive immunocompetent cells and in a placenta cell line (Freiburg/C. Gründemann). Hormone disruptive effects and possible drug interactions will be assessed in silico (Basel/M. Hamburger, O. Potterat, in collaboration with M. Smieško).ă Further experiments should clarify the impact of the herbal preparations on functional properties of immunocompetent cells (Freiburg/C. Gründemann), and of placenta

cells (gene expression, Zurich/A.P. Simões-Wüst). At the same time, permeation across the placenta barrier will be assessed in a transwell model, and effects on functional properties in a placenta perfusion system (Zurich/A.P. Simões-Wüst, analytical support in Basel/M. Hamburger, O. Potterat).
Knowing whether herbal preparations can be considered safe for use during pregnancy will provide a rational basis for decisions on the treatment of NMD during pregnancy. Taking into account the intestinal and hepatic metabolism is an entirely novel approach in the risk assessment of phytopharmaceuticals. The general approach, and the methodology developed in the project will be generically applicable to pharmacological and safety studies with phytomedicines.

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Published results

4683907, Winker, Moritz; Chauveau, Antoine; Smieško, Martin; Potterat, Olivier; Areesanan, Alexander; Zimmermann-Klemd, Amy; Gründemann, Carsten, Immunological evaluation of herbal extracts commonly used for treatment of mental diseases during pregnancy, 2045-2322, Scientific Reports, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

4645372, Spiess, Deborah; Winker, Moritz; Dolder Behna, Alexandra; Gründemann, Carsten; Simões-Wüst, Ana Paula, Advanced in Vitro Safety Assessment of Herbal Medicines for the Treatment of Non-Psychotic Mental Disorders in Pregnancy, 1663-9812, Frontiers in Pharmacology, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

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