The Genotoxicity Guideline of HMPC

The “Guideline on the Assessment of Genotoxicity of Herbal Substances/Preparations” of HMPC, the Herbal Medicinal Product Committee of the European regulatory agency EMA, provides guidance on the assessment of genotoxicity of herbal medicinal substances/preparations (1). This guideline states that for many herbal substances/preparations, contained in well established or traditional herbal medicinal products (HMPs), an adequate safety profile may be confirmed by documented history of medicinal use. However, the complete lack of some specific non-clinical studies (e.g. on genotoxicity) may present a safety concern as important questions relating to product safety would remain unsolved. The guideline provides a pragmatic framework on how to assess potential genotoxicity of HMPs and to interpret the results, describing a step-wise test strategy, beginning with the Ames test, followed, in case of positive results, by a mammalian cell assay and, in case of a still positive result, by in vivo genotoxicity tests. If the respective step gives negative results, progression to the next test step is not required (Fig. 1). A further guideline on the selection of test materials for genotoxicity testing for HMPs supports limiting the number of tests (2).

Scope of the Project

In advance to the adoption and in accordance with this guideline (1), Kooperation Phytopharma, a German scientific organisation on HMPs, had started a model project for the screening of herbal medicinal preparations. The scope of this project is to offer an alternative to testing each individual preparation of a certain herb by a joint conduction of tests.

Material and Methods

Following a bracketing and matrixing approach, the project covers extracts from the whole range of polarity of extraction solvents (Fig. 2), allowing even the testing of medicinal drug powder preparations otherwise non-accessible by in vitro methods.

Material and Methods (continued)

Extracts, characterized according to their individual specifications, were provided by pharmaceutical companies. Tests were conducted in cooperation with GLP-conform laboratories according to current guidelines including those of OECD, ICH and EMA, including even validation of test results by independent testing in two laboratories. They were started with the Ames test in five bacterial strains, the first step of the test strategy.

Results

The project has until now produced data on several of the most important herbal drugs in Europe:

Fig. 3: Results from the AMES Test, showing data from two S. typhimurium strains (TA 98 and TA 100) and controls (P1= quercetin). These negative results have been validated by independent testing in two laboratories.

Conclusions

The project has broadened the knowledge of the safety of important herbal drugs used in Europe, and allowed to meet present regulatory requirements. Unexpectedly it also has shown that the safety profile of some herbal drugs previously having been under discussion (4) can be rerated. Thus, the project has turned out to be an important step in the continuous updating process of the safety profile of modern phytotherapy, which already now is well documented. For expanding the project to further drugs, cooperation partners are welcome.*

Acknowledgement

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References


Dedication to Prof. Dr. Hilke Winterhoff, Institute for Pharmacology and Toxicology, University of Münster, Germany, who passed away on May 9, 2010, in honour of her important services to Kooperation Phytopharma, as head of its scientific working group on efficacy and safety, and of her exemplary contributions to the study of the pharmacology and toxicology of herbal medicines.

Litterature


This contribution is dedicated to Prof. Dr. Hilke Winterhoff, Institute for Pharmacology and Toxicology, University of Münster, Germany, who passed away on May 9, 2010, in honour of her important services to Kooperatlon Phytopharma, as head of its scientific working group on efficacy and safety, and of her exemplary contributions to the study of the pharmacology and toxicology of herbal medicines.