B011 Evaluation of chemical stability and skin irritation of lawsone methyl ether in oral base

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Lawsone methyl ether (2-methoxy-1,4-naphthoquinone) was first isolated from the dried flowers of *Impatiens bal - samina* L. (1). Its activities against *Trichophyton rubrum*, *T. mentagrophytes*, *Microsporum gypseum*, *Epider - mophyton floccosum* and *Candida albicans* have been reported. The values of both minimal inhibitory concentration (MIC) and minimal fungicidal concentration (MFC) of the naphthoquinone against *Trichophyton* and *Microsporum* were 2.50 µg/ml whereas values for both *Epidermophyton* and *Candida* were 1.25 µg/ml (2). Because of the antifungal activity of lawsone methyl ether, attempts were made to formulate an oral anticandidiasis preparation from semisynthesized lawsone methyl ether. Its acute toxicity, chemical stability and skin irritating property were also evaluated. In this study, lawsone methyl ether was semisynthesized by methylation of lawsone. It exhibited low acute toxicity with LD_{50} of 70.7 mg/kg upon intraperitoneal administration in mice. An oral preparation of 0.5% lawsone methyl ether in sodium carboxymethyl cellulose oral base, appeared to be stable under heating-cooling cycle test. Lawsone methyl ether in oral base did not cause any skin irritation under primary skin irritation test and cumulative skin irritation test. In contrast, the solution of lawsone methyl ether, potassium salt produced erythema with some papulosquamous in the cumulative skin irritation test.

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B012 Stability testing on typical flavonoid containing drugs

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Stability of herbal drug compounds is essential to guarantee a constant quality of herbal drugs and related finished products during the storage period. Up to now, only few investigations on the genuin herbal drug material exist. In most cases no data about stability of the pharmacological active components or marker substances are documented in the respective monographs.

The aim of the presented work is to examine possible changes in the flavonoid HPLC-fingerprint of the most common flavonoid containing herbal drugs, in order to provide detailed information about quality of the respective herbal drug material during long term and stress testing periods.

For long term testing, herbal drugs are stored at constant conditions of 25°C/60% rH (climatic zone II) according to the ICH-regulations over a 2 year period (1). To accelerate possible changes of the flavonoid pattern, birch leaves were exposed to increased temperatures of 70°C and 100°C. Typical stress conditions, in accordance with the ICH guideline (40°C/75% rH) are also tested (1).

During the storage period, the stability of flavonoids measured as the total flavonoid content by the current pharmacopoeial method (acid hydrolysis of flavonoid glycosides and photometric determination of an Al-chelate complex) is compared with HPLC-fingerprint chromatograms (2). Methanolic extracts of herbal drugs are directly injected in a HPLC system.

It is interesting to note that during long term testing, no significant changes in the flavonoid pattern can be detected. However, samples of birch leaves, stored at high temperatures, showed a decrease of most flavonoids and the total flavonoid content and an increase of the aglycone quercetine. Similar results were obtained for storage at 40°C/75% rH. It can be concluded, that under usual storage conditions, stability of these flavonoids is guaranteed over at least a 2 year period. Only extreme temperatures or humidity cause a significant reduction of the flavonoid content.

References: 1. EMEA (2001) ICH-Guideline: Note for guidance on quality of herbal medicinal products. **2.** Ph. Eur. Suppl. (1998) Monograph "Birch leaves".