

newsletter

Herbal medicines (Phytopharmaca)

Herbal medicines are becoming more and more popular. Contrary to widespread opinion, however, many of these natural products can also have severe side effects. Examples are kava kava (*Piper methysticum*), which was taken off the market in 2002, and ephedrine (from the ephedra plant), which the FDA is planning to ban from use as a dietary supplement in the US in the first half of 2004.

Phytopharmaca, importance in Germany, USA

The use of herbal medicines (phytopharmaca) is becoming more and more widespread. According to a survey performed by the Institut für Demoskopie Allensbach in 2002, more than two thirds of the German population take natural medicines – and the trend is rising. Only about 30% of these products are prescribed by a doctor; the rest is sold "over the counter" (OTC). In all, Germans spent € 6.8 bn on non-prescription medicines in 2002, € 2.1 bn of this on phytopharmaca (source: IMS Health). Over 90% of the products are derived from about 250 to 300 medicinal plants. By contrast, only about 13% of the US population take phytopharmaca, although here, too, the trend is rising sharply. Many people prefer herbal medicines because they assume that, as opposed to synthetic pharmaceutical compounds, they are free from or exhibit only very weak unwanted side effects.

Applicable regulations in Germany and USA; traditional and rational phytopharmaca

Phytopharmaca contain pharmaceutically processed substances obtained from medicinal plants. Herbal medicines are manufactured from the active constituents of plants, plant components or preparations (eg tinctures, extracts). According to the German Pharmaceuticals Act (AMG), plants, plant components and plant constituents in their processed or unprocessed state are counted alongside chemical elements and compounds and their naturally occurring mixtures and solutions as substances intended for use on or in the human or animal body for the purposes of curing, relieving, preventing or diagnosing diseases, ailments, injuries, physical complaints or mental conditions. Manufacturers are required to apply to the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) for approval before marketing medicines or medical products. A distinction is made between traditional and rational phytopharmaca.

Traditional phytopharmaca:

The 5th (1994) amendment to the AMG simplified the approval procedure for traditional medicines with a long history of use. According to Art 109a AMG, the quality requirements are fulfilled if pharmaceutical documentation and the prescribed analytical expertises are available for a product and the producer makes a statutory declaration certifying that the product has been tested in line with the regulations governing the licensing of medicines and was found to exhibit the requisite quality.

Proof of efficacy may be provided in the form of time-honoured publications, pharmacological plausibility reviews, and as the lowest requirement, documentary evidence of traditional use. The description of the areas of application must be preceded by a qualifier such as "to strengthen or fortify..., to improve well-being ..., to enhance the function of..., to guard against..., as a mild-acting remedy for...". Further pre-requisites for recognition as traditional are that the medicine must fulfil the criteria for marketability that have been applicable since 1 January 1978, that the product must be free of risk, and that the dose must be at least ten percent of the recommended standard range given in the monographs of the cognisant commission.

Rational phytopharmaca:

The term "rational phytopharmaca" is applied to herbal medicines that claim "higher" therapeutic benefit than traditional phytopharmaca. In Germany, they have to fulfil the same requirements as synthetic medicines. In terms of quality, efficacy and safety, approved rational phytopharmaca that comply with the recommendations in the monographs are on a par with chemically defined medicines. For example, approval procedures prescribe the same level of clinical trials in accordance with scientific methods and standards.

In the USA, phytopharmaca are sold as dietary supplements and thus, unlike synthetic medicines, are not subject to FDA (Food and Drug Administration) regulations. The FDA can intervene only if it can prove that a product is a health hazard. However there are by now numerous documented cases in which phytopharmaca were contaminated with heavy metals, pesticides, synthetic medicines or bacteria.

A widespread problem in the case of herbal medicines is the lack of established quality and concentration standards, with the result that different products with the same active ingredients can not always be compared with each other. And last but not least, the efficacy of most products is attributable not to a single herbal ingredient but to the interaction of a number of constituents.

Side effects, interactions

In phytotherapy, as in the case of treatment with synthetic medicines, the following unwanted effects can occur:

- allergic reactions,
- toxic effects,
- unintended pharmacological effects,
- interactions with other medicines,
- effects caused by contamination.

Even if many herbal products exhibit a relatively mild range of side effects by comparison with synthetic medicines, attention should be paid to avoiding the aforesaid complications. However, it is doubtful whether this rule is always followed, especially in the case of OTC products.

Examples

Selected examples of phytopharmaca that have attracted attention due to severe side effects:

Kava kava (Piper methysticum)

Kava kava is the name of a member of the pepper family that grows on the islands of the South Pacific, where it is consumed for its psychedelic effects. Medical products contain extracts from its rootstock or its major ingredient, kavain, which is also manufactured synthetically. These extracts are used to treat various nervous anxiety and stress conditions.

There are over 40 case reports from Germany, most of them describing serious liver damage occurring in connection with the use of medicines containing kava kava or kavain. There is evidence to indicate that liver damage is relatively more frequent and more severe, the higher the doses taken. In six cases, liver failure was so complete as to necessitate a transplant. Three patients died as a result of liver damage. In several other cases, the liver was able to recover after intake of kava kava was discontinued. For this reason, kava kava was banned in Germany and the UK in 2002, and all products were taken off the market. In the USA, on the other hand, kava kava products are still freely available.

**Ephedra,
ephedrine**

Ephedrine is the principal alkaloid of the ephedra plant, also known as "mormon tea" or desert jointfir. Ephedrine is a strong bronchodilating substance and cough suppressant. Because of these properties, it is used in combination with other substances eg in cough medicines or to treat mild asthma conditions. It is widely abused as a doping agent in bodybuilding circles and, by virtue of its appetite-reducing effect, as a slimming aid. The substance is on the International Olympic Committee's (IOC) doping list. Ephedrine is sometimes also used as an additive by narcotics abusers, because taken in high doses it stimulates the central nervous system, elevates mood, masks fatigue and suppresses hunger. In the USA, ephedrine-based medicines are in high demand as OTC products. Especially if taken in overdoses, ephedrine products can cause sometimes severe side effects such as heart attack, stroke, high blood pressure and hallucinations. Since 1994, more than 800 cases of severe side effects have been notified to the FDA; there are also reports of fatalities in connection with the consumption of ephedrine. According to an FDA report dated 30 December 2003, dietary products containing ephedra are to be banned from over-the-counter sale in the US.

**Information for
the underwriter**

Phytopharmaca play a major role in our society as a treatment for or as an aid to preventing certain illnesses. The regulations to which they are subject vary widely from country to country, and as a result their quality characteristics also differ. From the insurance perspective, phytopharmaca should be treated just like classical synthetic medicines. The main exposures lie – as in the case of conventional synthetic products - in the area of products liability and product recall. For this reason, it is advisable to assess each herbal medicine product on its own merits in the light of the potential range of unwanted side effects and on the basis of the latest data available. This assessment should also pay attention to possible interactions with classical products (eg blood pressure regulators), how the product may be used (eg as a "lifestyle" drug), potential abuse (eg as doping agents) and accessibility (OTC versus prescription).

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