

Challenges for phytopharmacovigilance

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It is important that the safety of herbal medicines is scientifically addressed

Throughout history, plants have been used for medicinal purposes and, during the last three decades, we have witnessed a most remarkable revival of herbal medicine.¹ Germany is the country with the largest per head consumption of herbal medicines. In 2002, the 100 best selling products achieved a total turnover of 420 million Euros.² This high level of popularity means, among other things, that we ought to ensure that no harm is done. Even though the media frequently try to persuade us otherwise, not all herbal medicines are free of adverse effects (table 1).²⁻⁵ Phytopharmacovigilance—that is, the systematic research of the safety of herbal medicines—has therefore become an important topic. In this article, I will briefly outline some of the challenges encountered in this area.

Herbal medicines are usually not patentable. Therefore, keen commercial impetus for systematic research rarely exists. Consequently there is a lack of hard data on herbal safety.³ Much of the available evidence is either built on non-clinical investigations⁴ or on incomplete

and thus inconclusive clinical data.⁵ Depending on the circumstances, both under-reporting⁶ and over-reporting⁷ of herbal adverse effects have been suspected, and the unduly strong influence of the press in this area is a well recognised aggravating factor.⁸ Users of herbal medicines often do not inform their doctor, and conventional health-care professionals sometimes lack sufficient knowledge of herbal medicine to advise their patients responsibly. As a consequence, the evidence regarding the nature and incidence of adverse effects caused by herbal medicines is woefully incomplete.

In most countries, herbal medicines are not regulated as medicines but marketed as dietary supplements. The quality of some products has repeatedly been shown to be suboptimal,⁹ some of the most extreme examples include Asian herbal mixtures which can be contaminated (for example with heavy metals, micro-organisms, pesticides) or adulterated with powerful prescription drugs.¹⁰ Even top quality herbal medicines suffer from a degree of product

variability. This may not be altogether avoidable, considering that the raw material for herbal medicines obviously varies according to factors such as climate, soil, and season, method of harvesting, drying, storing, or extraction. Product quality will thus always be a considerable challenge to phytopharmacovigilance.

Product identification can be a further obstacle. Many commercially available products contain multiple ingredients. For instance, Sinupret (Bionorica, Germany), the best selling herbal medicinal product in Germany (total sales in 2002 were 22.6 million Euros), contains five different medicinal plants.² Asian herbal mixtures typically contain about twice that amount. In such cases, it is often impossible to discover which ingredient caused a reported health problem. Brand names and sometimes even plant nomenclature suffer from a babylonian confusion.⁹ One herbal extract can be contained in dozens of different brands, and not infrequently identical brand names contain different mixtures of plants. Labelling of commercial products is often less than sufficient. Associations between one herbal ingredient and a reported adverse effect can therefore be difficult, sometimes impossible to establish.

Consumers of herbal medicines tend to be affluent, middle aged, and chronically ill.¹ They are thus likely to combine herbal medicines with prescriptive drugs. Herb-drug interactions have thus become an important subject.^{3, 5, 9} The list of herbal medicines with potential for such interactions seems endless.¹¹ Yet only relatively few clinical cases of herb-drug interactions have been documented in the medical literature.¹² It is unclear whether this indicates that, in clinical practice, interactions occur only rarely or whether it suggests that not looking for such events means not recognising them.

In conclusion, phytopharmacovigilance is a new area of scientific inquiry. Because of the current popularity of herbal medicines, it has become important for public health. Phytopharmacovigilance faces numerous challenges. In the interest of the consumer we should address them with scientific rigour.

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Table 1 Examples of popular herbal medicines* and associated risks

Common name	Latin name	Indication	Adverse effects	Potential interactions with
Garlic	<i>Allium sativum</i>	Raised blood cholesterol	Allergic reactions, nausea, heartburn	Anticoagulants, antidiabetics
Hawthorn	<i>Crataegus</i> spp	Heart failure	Nausea, dizziness, fatigue	Cardiac glycosides, antihypertensives, nitrates
Horse chestnut	<i>Aesculus hippocastanum</i>	Varicose veins	Pruritus, nausea, gastrointestinal symptoms	Anticoagulants
Kava	<i>Piper methysticum</i> Forster	Anxiety	Liver damage	Drugs acting on CNS
Maidenhair tree	<i>Ginkgo biloba</i>	Dementia, peripheral vascular disease	Gastrointestinal symptoms, diarrhoea, vomiting, allergic reactions	Anticoagulants
Saw palmetto	<i>Serenoa repens</i> Bartram	Benign prostate hyperplasia	Gastrointestinal complaints, dysuria, decreased libido	Hormonal drugs
St John's wort	<i>Hypericum perforatum</i>	Mild/moderate depression	Gastrointestinal symptoms, allergic reactions, fatigue	All drugs metabolised by cytochrome P450 enzyme system

*All examples are of well documented efficacy (data extracted from Ernst *et al*).

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