

**REVIEW  
ARTICLE**

# The efficacy of herbal medicine – an overview

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edzard.ernst@pms.ac.uk**ABSTRACT**

Herbal medicine has become a popular form of healthcare. Even though several differences exist between herbal and conventional pharmacological treatments, herbal medicine can be tested for efficacy using conventional trial methodology. Several specific herbal extracts have been demonstrated to be efficacious for specific conditions. Even though the public is often misled to believe that all natural treatments are inherently safe, herbal medicines do carry risks. Ultimately, we need to know which herbal remedies do more harm than good for which condition. Because of the current popularity of herbal medicine, research in this area should be intensified.

**INTRODUCTION**

Many of today's synthetic drugs originated from the plant kingdom, and only about 200 years ago our pharmacopoeia was dominated by herbal medicines. Medical herbalism (i.e. the medicinal use of preparations that contain exclusively plant material) went into rapid decline when pharmacology established itself as a leading branch of therapeutics. In much of the English-speaking world, herbalism virtually vanished from the therapeutic map about a century ago. In contrast, many developing countries never abandoned medical herbalism (e.g. Ayurvedic medicine in India, Kampo medicine in Japan, and Chinese herbalism in China) and in other countries, e.g. Germany and France, medical herbalism continued to co-exist with modern pharmacology, albeit at an increasingly lower level [1].

In recent years, this situation has started to change again. The usage of herbal medicines by the general US population, for instance, increased by 380% (from a 1-year prevalence of 2.5–12.1%) between 1990 and 1997 [2]. A more recent US survey suggested that 16.4% of all patients attending an internal medicine clinic were current users of herbal medicines [3]. According to these and other survey data, medical herbalism was most

commonly employed for allergies, insomnia, respiratory problems, and digestive problems. The total out-of-pocket expenditure amounted in 1997 to \$5.1 billion [2]. *Table 1* lists the 10 best-selling herbal medicines in the US [4].

The aim of this article is to provide a general introduction to herbal medicine using three examples. While my focus is on efficacy and safety, this is not a systematic review of the existing data.

**GENERAL CHARACTERISTICS**

Herbal medicines usually contain a range of pharmacologically active compounds; in some cases it is not known which ingredients are important for the therapeutic effect [5]. Many herbalists believe that isolated ingredients have weaker clinical effects than whole plant extracts, a notion that would obviously require proof in each case. The multi-ingredient character of herbal medicines can render efficacy testing more complex than with synthetic drugs. One approach is to view the entire herbal extract as the active principle. To optimize the reproducibility of such studies, extracts need to be sufficiently characterized. This is often attempted through standardization according to a key constituent of the extract (e.g. a pharmacologically active ingredient or, if such an ingredient is

**Table I** The 10 best-selling herbal medicines (US, 2001).

Rank	Herb	Retail sales <sup>a</sup>
1	Ginkgo biloba <sup>b</sup>	46
2	Echinacea	40
3	Garlic <sup>b</sup>	35
4	Ginseng <sup>b</sup>	31
5	Soy	28
6	Saw palmetto	25
7	St John's wort	24
8	Valerian	12
9	Cranberry	10
10	Black cohosh	10

<sup>a</sup>Million US\$ in rounded figures.

<sup>b</sup>Herbal medicines discussed in detail in this review.

not known, a marker suitable substance) [5]. Standardization can, however, only cover one or two ingredients; thus variation of other ingredients may still remain, and it is possible that this could influence both efficacy and safety of the product. Full product characterization and quality control are therefore essential for the reproducibility of scientific tests of herbal remedies.

Given these caveats, clinical trials of herbal medicines are feasible much in the same way as for other drugs. Numerous randomized clinical trials (RCTs) of herbal medicines have been published and systematic reviews/meta-analyses of these studies have become available [6,7]. *Table II* provides examples of such articles [8–12].

Their conclusions are often limited by the low methodological quality of the primary studies. Research funds in this area are scarce, not least because plants are not patentable.

Generalizations about the efficacy of herbal medicines are clearly not possible. Each herbal medicine has to be judged on its own merits; some have been demonstrated to be efficacious for certain indications, others may not be efficacious and by far most of them have not been submitted to extensive clinical testing [6,13].

## EFFICACY

Given the multitude of herbal medicines, it is obviously not possible to discuss all of them in this review. The following will therefore provide a detailed evaluation of three relatively well-researched examples. In addition, *Table II* provides brief overviews of several further, well-researched herbal medicines.

### Garlic (*Allium sativum* L.)

Fresh garlic bulb dried and powdered or oil extracted from the bulb are used for medicinal purposes. The active constituents include alliin, allinase, diallyl-disulphide, ajoens and others. Alliin is enzymatically converted to allicin which is responsible for the characteristic, sulphur-like smell. The pharmacological actions of garlic are multifold: anti-bacterial, anti-viral,

**Table II** Examples of systematic reviews and meta-analyses of herbal remedies.

Common (Latin) name [reference]	Pharmacologically active ingredients <sup>a</sup>	Indications	No. of trials included	Average methodological quality of		
				primary studies	Efficacy	Main result
<i>Echinacea</i> [8]	Polysaccharides, glycoproteins, alkamides, flavonoids	Upper respiratory tract infections	16	Good	Likely	Six of eight prevention trials reported positive results
Feverfew ( <i>Tanacetum parthenium</i> ) [9]	Parthenolide	Migraine prevention	5	Good	Likely	Three trials were positive, two were negative
Hawthorn ( <i>Crataegus</i> ) [10]	Proanthocyanides, flavonoids	Congestive heart failure	13	Good	Certain	Meta-analysis showed that maximal workload decreased by 7 W
Horse chestnut seed extract ( <i>Aesculus hippocastanum</i> ) [11]	Triterpene saponins	Chronic versus venous insufficiency	13	Good	Likely	Active treatment more effective than placebo and equally effective as reference treatments
Peppermint oil ( <i>Mentha × Piperia</i> L.) [12]	Menthol	Symptoms of irritable bowel syndrome	8	Food	Likely	Positive effect of peppermint oil compared with placebo

<sup>a</sup>Examples only.

anti-fungal, anti-hypertensive, blood-glucose-lowering anti-thrombotic, anti-mutagenic and anti-platelet activities have been described. Its best-researched clinical effect is that of lowering total serum cholesterol levels, probably through inhibition of hepatic cholesterol synthesis [6].

Numerous RCTs demonstrated a significant reduction of total cholesterol and low-density lipoprotein. Several systematic reviews of these data arrived at positive overall conclusions. More recently, however, a number of negative RCTs have emerged. An updated meta-analysis of all 13 rigorous RCTs produced only a marginally positive result (average reduction = 0.41 mmol/L). It generated a non-significant effect on total cholesterol when only the high quality RCTs were analysed [14].

The cumulative trial data on its blood pressure-lowering effects show a significant, albeit small, anti-hypertensive effect [15] whether it is clinically relevant seems debatable. Some interesting, though not compelling data [16] suggest that, due to its broad-ranging effects on the above-mentioned and other cardiovascular risk factors, the regular intake of garlic might prevent or delay the development of arteriosclerosis [16]. Epidemiological data indicate that the regular consumption of garlic might convey a protective effect for malignancies, in particular intestinal cancers [17]. A recent RCT implies that high-dose garlic consumption reduces the frequency of tick bites in a tick-endemic area [18]. All other claimed health effects, particularly those related to garlic's anti-microbial activities *in vivo*, are not supported by compelling evidence.

The recommended dosage is about 4 g of fresh garlic daily, equivalent to approximately 8 mg garlic oil or 600–900 mg garlic powder preparations standardized to 1.3% alliin content. Patients with bleeding abnormalities should be cautioned about the uncontrolled use of garlic supplements. It is recommended that garlic supplements should be discontinued before major surgery. Adverse effects of garlic are usually mild and transient; they include breath and body odour, allergic reactions, nausea, heartburn, flatulence [6].

As a result of its effects on platelet function, garlic can increase the effect of anti-coagulants. Theoretically it could also enhance the hypoglycaemic effects of anti-diabetic medications [6]. *Table III* summarizes all possible interactions based on a recent review of the secondary literature [19]. The primary literature tells us little about interactions. Published case reports tend to be poorly documented [20].

**Table III** Potential interactions of garlic, ginger and ginkgo.

Name	Potential interactions
Garlic	Increased risk of bleeding with anti-coagulants Decreased serum levels of drugs metabolized via the cytochrome P450 system Increased hepatotoxicity with acetaminophen Decreased effectiveness of antacids Increased effect of hypotensives Hypoglycaemia with anti-diabetics Increased chronotropic and inotropic effects with isoprenaline Decreased serum levels of saquinavir
Ginkgo	Increased risk of bleeding with anti-coagulants Increased anti-cancer effects of fluorouracil Increased serum levels of drugs metabolized by the CYP2D6 isoenzyme Increased effects with cyclosporin Decreased cardiotoxicity of doxorubicin Reversal of effects on libido of fluoxetine Decreased nephrotoxicity of gentamicin Enhanced efficacy of haloperidol in schizophrenia
<i>Panax ginseng</i>	Increased effects of anti-hypertensive drugs Additive effects with benzodiazepines Increased effect of cardiac glycosides Decreased effect of immunosuppressants Increased effect of anti-diabetic drugs Potentiation of adverse effects of MAO inhibitors Increased effectiveness of kanamycin and monomycin Additive effects with stimulants

Data extracted from ref. [19] and based mostly on indirect evidence.

### **Ginkgo (*Ginkgo biloba* L.)**

Medicinal ginkgo products are made from the leaves of this ancient tree. Their main pharmacological constituents include ginkgolides A, B, C, J, bilobalide, flavonoids. Ginkgo leads to an increase of microcirculatory blood flow, inhibition of erythrocyte aggregation, platelet-activating factor antagonism, free radical scavenging, oedema protection. These actions suggest that there is no single mechanism of action but a complex interaction of a multitude of effects.

A meta-analysis of ginkgo for intermittent claudication assessed eight double-blind RCTs and suggested a significant but modest increase of pain-free walking distance compared with placebo [21]. The majority of these studies also implied a significant increase in maximal walking distance. Another systematic review identified nine double-blind placebo-controlled RCTs of ginkgo for the symptomatic treatment of dementia and suggested that it is effective in delaying the clinical deterioration of patients or in bringing about symptomatic improvement [22]. Whether ginkgo also improves

cognitive function in healthy individuals is uncertain [23]. Ginkgo extract is also often recommended for the treatment of tinnitus. A systematic review identified five RCTs and concluded that the evidence is favourable, but methodological limitations prevent firm conclusions [24].

The recommended dosage of an oral standardized dry extract of ginkgo (24% ginkgo flavonol glycosides, 6% terpenolactones) is 120–240 mg daily. Adverse effects include gastrointestinal disturbances, diarrhoea, vomiting, allergic reactions, pruritus, headache, dizziness, nose bleeds. The most frequently reported interaction is the potentiation of anti-coagulants [6]. This is biologically plausible considering the documented anti-platelet effects of ginkgo. It is recommended that ginkgo be discontinued before major surgery. *Table III* provides a full list of potential interactions [19]. The primary literature holds four case reports of suspected interactions with aspirin, thiazide, trazodone and warfarin [25]. Causality was deemed possible but cannot be considered proved on the basis of the existing data.

#### Asian ginseng (*Panax ginseng* C.A. Meyer)

There is considerable confusion about terminology of ginseng: Asian ginseng is also called Chinese ginseng, Korean ginseng, ninjin (Japanese) or true ginseng. It is often confused with Siberian ginseng (*Eleutherococcus senticosus* Maxim) which belongs to the same family (Araliaceae) but is a different genus. Asian ginseng, which we discuss here and is the main form of ginseng, is also called *Panax ginseng*.

Its dried roots are used for medicinal purposes and its main constituents are triterpene saponins known as ginsenosides or panaxosides. The pharmacologic actions of ginseng include immunomodulatory, anti-inflammatory, anti-tumour, smooth muscle relaxation, stimulant and hypoglycaemic effects.

The evidence from all double-blind RCTs of Asian ginseng for any indication was evaluated in a systematic review [26]. The trials related to physical performance, psychomotor performance and cognitive function, immunomodulation, type II diabetes mellitus and herpes simplex type II infections. It was concluded that the effectiveness of Asian ginseng root extract is not established for any indication. With regard to improving physical performance, this finding is largely corroborated by a more recent, non-systematic but reasonably comprehensive review [27].

The recommended dosage is 200 mg daily of standardized extract (4% total ginsenosides). Patients

suffering from hypertension, cardiovascular disease, hypotension or diabetes and patients receiving steroid therapy should use ginseng only with caution, i.e. under medical supervision.

Adverse effects, which have been reported include insomnia, diarrhoea, vaginal bleeding, mastalgia, swollen tender breasts, increased libido, manic episodes, a possible cause of Stevens–Johnson syndrome [6]. A ‘Ginseng abuse syndrome’ (dosage approximately 3 g daily) has been described with symptoms such as hypertension, sleeplessness, skin eruptions, morning diarrhoea, agitation. Doses of more than 15 g daily were associated with depersonalization, confusion and depression [6]. Our own systematic review of the totality of the safety data concluded that adverse effects are rare, mild and transient [28].

The most frequently reported interactions are those with monoamine oxidase (MAO) inhibitors and anti-diabetic drugs [6]. *Table III* provides a list of further theoretically possible interactions [19]. The primary literature contains four case reports of alleged interactions [25,28,29]. As the above-mentioned confusion about terminology extends to these case reports, we cannot be sure that all of these interactions are related to *Panax ginseng*. Any conclusions about causality seem therefore premature.

#### COMMENT

Despite the complexity of herbal products, investigations of their efficacy are feasible and desirable, particularly vis-a-vis their popularity. For some but by no means all herbal medicines, efficacy data are now emerging [6]. *Table IV* summarizes the efficacy data on the three herbal medicines used as examples in this overview and *Table II* provides additional information on other, well-researched herbal treatments. They show that some herbal medicines are efficacious for certain indications. All herbal medicines are associated with safety issues which are often complex [30,31].

Generally speaking, research into herbal medicines is much less active than research into conventional drugs. Lack of commercial impetus due to lack of patent protection is one obvious reason. Another reason may lie in the legal status of herbal medicines: as dietary supplements (their legal status in most countries) they are not under any formal obligation to prove efficacy.

Based on the data available today, it is impossible to draw general conclusions about the therapeutic value of herbal medicines. Healthcare professionals have therefore been cautious in recommending herbal medicines.

**Table IV** Efficacy data on three selected herbal medicines.

Herbal medicine	Indication	Strength of evidence
Garlic	Hypercholesterolaemia	Statistically significant effect, debatable clinical relevance
	Hypertension	Small effect size
	Cancer prevention	No trial data available
Ginkgo	Intermittent claudication	Positive effect comparable with conventional drugs
	Dementia	Delay in deterioration
	Tinnitus	Uncertain efficacy
<i>Panax</i>	Physical performance	Uncertain efficacy
<i>ginseng</i>	Psychomotor performance	Uncertain efficacy
	Cognitive function	Uncertain efficacy
	Immunomodulation	Uncertain efficacy
	Diabetes	Uncertain efficacy
	Herpes simplex	Uncertain efficacy

'Clinicians should not prescribe or recommend herbal remedies without well established efficacy...' [30]. But they also have an obligation to be sufficiently well informed to advise their patients responsibly.

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