

Evidence of effectiveness for popular herbal medicines

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Summary

Herbal dietary supplements are among the most popular treatment options, used by about 12 to 34% of respondents. Market analyses indicate that the size of the herbal market increased from approximately \$1.6 billion in 1994 to \$4 billion in the US in 1998. In 1999, the total US supplement market including vitamins, minerals, herbal and homeopathic remedies was evaluated at \$14.5 billion, while the respective figure for Europe is about \$12.3 billion. The objective of this assessment was to evaluate the evidence from systematic reviews and meta-analyses of the effectiveness of popular herbal medicines for selected conditions.

Key words: Ginkgo biloba, dementia, intermittent claudication, Allium sativum, hypercholesterolemia, Echinacea spp., common cold, Serenoa repens, benign prostatic hyperplasia, depression, Crataegus spp., chronic heart failure

INTRODUCTION

Complementary/alternative medicine can be defined as 'diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine' [1]. A high level of use of complementary treatment options has been reported in many countries [eg. 2-4]. Prevalence data for the UK, for instance, indicate that about 20 to 28% of the general population use complementary therapies annually [5, 6] and that one in two GP practices offers access to complementary therapies [7]. In the US, the 1-year prevalence currently amounts to about 62% including prayer [8]. The majority of the data suggest that herbal dietary supplements are among the most popular treatment options, used by about 12 to 34% of respondents [2, 5]. Market analyses sup-

port these findings indicating that the size of the herbal market increased from approximately \$1.6 billion in 1994 to \$4 billion in the US in 1998 [9, 10]. In 1999, the total US supplement market including vitamins, minerals, herbal and homeopathic remedies was evaluated at \$14.5 billion, while the respective figure for Europe is about \$12.3 billion [11]. The US Food and Drug Administration notes that this industry has grown rapidly and will continue to do so in the near future [12]. The objective of this assessment was to evaluate the evidence from systematic reviews and meta-analyses of the effectiveness of popular herbal medicines for selected conditions.

METHODS

Herbal medicines were identified from a recent market analysis [13]. The four top selling herbal medicines in the US in 2004 – *Ginkgo biloba*, *Allium sativum*, *Echinacea spp.* and *Serenoa repens* were chosen and complemented by data for *Hypericum perforatum* and *Crataegus spp.* Systematic literature searches were conducted to identify systematic reviews and meta-analyses for selected conditions. The following databases were searched from its inception until July 2004: Medline, Embase, Amed, and The Cochrane Library. Hand-searches included the bibliographies of all retrieved articles. There were no restrictions regarding the language of publication. Systematic reviews and meta-analyses were included if their findings were based on the results of RCTs. Systematic reviews and meta-analyses, which did not report on separate analyses for RCTs were excluded.

RESULTS

Ginkgo biloba

Dementia

An updated Cochrane review of *Ginkgo biloba* for treating dementia identified 33 double-blind placebo controlled RCTs [14]. The methodological quality was formally assessed using the system developed by Jadad and colleagues and ranged between 2 to 5 of a possible maximum score of 5. Meta-analyses were performed using data from patients treated with up to 200 mg daily for up to 12 weeks and from patients treated with 240 mg for 24 weeks. The Clinical Global Impression Scale was the main outcome measure and the results suggest significant effects in favour of ginkgo compared with placebo (odds ratio 15.3, 95% confidence interval 5.9 to 39.8, n=126; OR 2.2, 1.1 to 4.2, n=156 respectively).

Intermittent claudication

A meta-analysis assessed the effectiveness for treating patients with intermittent claudication [15]. Twelve double-blind, placebo-controlled RCTs were identi-

fied of which 8 met all inclusion criteria and were reviewed. Patients were treated with 120 to 160 mg daily for 12 to 24 weeks. The common outcome measure was the painfree walking distance. Meta-analysis indicates a significant beneficial effect in favour of ginkgo compared with placebo (weighted mean difference 34 m, 95% confidence interval 26 m to 46 m). Six of the 8 trials also assessed maximal walking distance. All trials report a significant increase in this outcome measure compared with placebo. The increase in maximal walking distance ranged between 36 to 189 metres.

Allium sativum

Hypercholesterolemia

Many earlier studies reported that *Allium sativum* reduces total cholesterol levels. However, newer studies came to different conclusions and seem to contradict the notion that garlic extract is effective for this condition. In a meta-analysis of garlic for treating hypercholesterolemia we included 13 double-blind RCTs [16]. The common endpoint was the total cholesterol reduction and the meta-analysis indicated a significant but relatively small effect of 0.4 mmol/l (95% confidence interval 0.7 to 0.2 mmol/l). A sensitivity analysis of trials using 900 mg daily for 8 to 24 weeks showed no significant effect (weighted mean difference 0.2, 95% confidence interval 0.4 to -0.01). There were no effects on LDL and HDL levels. Since this meta-analysis three new trials were published. The inclusion of these data diminished the overall effect to 0.3 mmol/l (95% confidence interval 0.6 to 0.2, n=971) [17].

Echinacea spp.

Common cold

Echinacea extracts are widely used by patients for preventing and treating the common cold. On the German market, for instance, there are at present more than 200 preparations available which contain extracts of echinacea alone or in combination with other plant extracts. The Cochrane review included 5 placebo-controlled trials on the prevention of the common cold and 8 placebo-controlled trials for treating the common cold [18]. The methodological quality in these trials was described by the authors as insufficient. According to the investigators, the results indicate that there is not enough evidence to recommend a specific echinacea preparation for preventing or treating the common cold.

Serenoa repens

Benign prostatic hyperplasia

Convincing data are available for *Serenoa repens* for treating benign prostatic hyperplasia. Fifteen placebo-controlled RCTs were identified in a Cochrane review [19]. Six of these assessed the self-rating of urinary tract symptoms. Meta-analysis indicates a significant beneficial effect in favour of saw palmetto compared with placebo (risk ratio 1.8, 95% confidence interval 1.2 to 2.5, n=659). Nine

trials assessed peak urinary flow. Meta-analysis suggests significant differences compared with placebo (weighted mean difference 1.9 ml/sec, 95% confidence interval 0.6 to 3.1, n=723). In addition, two trials including a total of almost 1500 patients compared saw palmetto with finasteride on the International Prostate Symptom Scale. There were no significant differences between these two treatments (weighted mean difference 0.4, 95% confidence interval -0.5 to 1.2). Little evidence, however, is available for its long-term effectiveness. A specific brand (Permixon) was assessed in a further meta-analysis [20] which provides additional evidence suggesting that saw palmetto is effective over and above placebo for treating patients with benign prostatic hyperplasia.

Hypericum perforatum

Mild to moderate depression

St John's Wort belongs to one of the best-investigated plant extracts. The Cochrane review included 37 RCTs [21]. Patients were treated with 0.24 g to 1.8 g daily for 4 to 12 weeks. The common endpoint was the responder rate ratio. Responders were defined as those patients with a score of less than 10 on the Hamilton Depression Scale at the end of the trial or a 50% reduction compared with baseline scores. The analysis suggests superiority of St John's Wort over placebo (responder rate ratio 1.6, 95% confidence interval 1.4 to 1.7, n=2752). Compared with selective serotonin reuptake inhibitors the difference was not significant (responder rate ratio 1.0, 95% confidence interval 0.9 to 1.1, n=813).

Crataegus spp.

Chronic heart failure

Extract of *Crataegus spp.* is used as an adjunctive treatment for chronic heart failure (CHF) and the German Commission E approved its use for CHF stage I to II New York Heart Association (NYHA). For this meta-analysis 8 double-blind RCTs provided data suitable for statistical pooling [22]. Seven trials used standardised extract from the same German manufacturer. All trials used the NYHA classification to categorize patients in chronic heart failure stages I to III. Patients who received hawthorn extract experienced on average an increase of their maximal workload by 7 watt over placebo (95% confidence interval 3 to 11, n=310). This is an increase of about 9% from baseline values compared with placebo. Sensitivity analyses included only those trials which explicitly stated that the patients received concomitant medication during treatment with hawthorn and trials in which it was unclear if the patients received any concomitant medication. Both analyses suggest significant beneficial effects in favour of hawthorn compared with placebo and strengthen the overall findings (weighted mean difference 5 watt 95% confidence interval 0.2 to 10; 12 watt 4 to 21, respectively).

CONCLUSION

Some popular herbal medicines are backed by evidence of effectiveness for specific indications. More research, particularly on safety issues is needed for full risk-benefit assessments. In cases of favourable safety profiles herbal medicines may provide treatment options worthy of consideration.

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DOWODY SKUTECZNOŚCI POPULARNYCH SPECYFIKÓW ZIOŁOWYCH

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Streszczenie

Ziołowe produkty uzupełniające dietę są jednym z najbardziej popularnych specyfików leczniczych. Sięga po nie od 12% do 34% badanych. Analizy rynku dowodzą, że w Stanach Zjednoczonych obroty uzyskiwane ze sprzedaży produktów zielarskich wzrosły z 1,6 mld USD w 1994 r. do 4 mld USD w 1998 r. W 1999 r. obroty na całym amerykańskim rynku produktów uzupełniających dietę – włącznie z witaminami, związkami mineralnymi oraz środkami ziołowymi i homeopatycznymi – oszacowano na 14,5 mld USD. Celem tej pracy jest ocena dowodów podawanych w systematycznie publikowanych przeglądach oraz analiz skuteczności popularnych specyfików ziołowych w wybranych warunkach.

Słowa kluczowe: Ginkgo biloba, dementia, chromanie przestankowe, Allium sativum, podwyższony poziom cholesterolu, Echinacea spp., przeziębienie, Serenoa repens, niezłośliwy przerost prostaty, depresja, Crataegus spp., chroniczna niedoczynność serca