

# Alternative treatments for menopausal symptoms

## *Systematic review of scientific and lay literature*

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### ABSTRACT

**OBJECTIVE** To review the scientific literature on common alternative remedies for treatment of symptoms attributed to menopause and to contrast this with available lay literature.

**QUALITY OF EVIDENCE** Scientific articles were identified by searching MEDLINE, CINAHL, and HEALTH databases from 1966 to mid-1997 for English-language articles. More than 200 references were reviewed; 85 were selected for citation based on specific reference to alternative medicine for symptoms commonly attributed to menopause (eg, hot flashes), to the effects of changing estrogen levels (eg, irregular menses, vaginal dryness), and to reported side effects of the treatments.

**MAIN FINDINGS** The scientific literature was categorized under the headings nutritional supplements, herbal remedies, homeopathic remedies, and physical approaches. Some scientific evidence of the safety and efficacy of alternative treatments during menopause was uncovered, with the strongest evidence emerging in favour of phytoestrogens, which occur in high concentrations as isoflavones in soy products.

**CONCLUSIONS** In available controlled studies, the strongest data support phytoestrogens for their role in diminishing menopausal symptoms related to estrogen deficiency and for possible protective effects on bones and the cardiovascular system. Randomized controlled trials, standardization of dosage, and accurate safety and efficacy labeling are required to ensure proper use of alternative remedies.

### RÉSUMÉ

**OBJECTIF** Analyser les ouvrages scientifiques sur les médecines douces communément utilisées dans le traitement des symptômes de la ménopause et en comparer le contenu avec celui des publications populaires disponibles.

**QUALITÉ DES DONNÉES** La sélection d'articles scientifiques en anglais s'est faite au moyen d'une recherche dans les bases de données MEDLINE, CINAHL et HEALTH, entre 1966 et le milieu de 1997. Plus de 200 articles ont été examinés, dont 85 ont été retenus aux fins de citation en raison des références précises sur les thérapies d'appoint pour traiter les symptômes associés communément à la ménopause (comme les bouffées de chaleur), sur les effets des changements du taux d'œstrogène (comme l'irrégularité des menstruations, l'assèchement des muqueuses vaginales) et sur les effets secondaires rapportés à la suite des traitements.

**PRINCIPALES CONCLUSIONS** Les ouvrages scientifiques ont été classés sous les rubriques suivantes: suppléments nutritionnels, plantes médicinales, remèdes homéopathiques et approches physiques. On a dégagé certaines preuves scientifiques de la sécurité et de l'efficacité des thérapies d'appoint durant la ménopause, la plus probante étant en faveur des phytoestrogènes qui se trouvent en fortes concentrations sous forme d'isoflavones dans les produits du soja.

**CONCLUSIONS** Dans les essais contrôlés disponibles, les données les plus probantes sont favorables aux phytoestrogènes en raison du rôle qu'elles jouent dans l'atténuation des symptômes de la ménopause associés à la carence en œstrogène et de ses effets possibles de protection des os et du système cardiovasculaire. Des essais aléatoires contrôlés, la normalisation des dosages et l'étiquetage exact en matière de sécurité et d'efficacité sont nécessaires pour assurer un usage approprié des médecines douces.

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## CME

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### Alternative treatments for menopausal symptoms

**M**anagement of menopause has received increased attention in recent years, as a consequence both of the growing interest in women's health and of the greater number of women entering the menopausal years.<sup>1</sup> Fear and dislike of possible side effects and long-term risks of hormone replacement therapy (HRT), disenchantment with conventional medicine, and belief in the safety of "natural" products are factors that have contributed to increased use and acceptance of alternative and complementary medicine.<sup>2,3\*</sup>

According to Health Canada's recent National Health Survey,<sup>4</sup> at least 15% of Canadians aged 15 and older have sought alternative medical health care. Despite the wide use of alternative medicine, little is known about the safety and efficacy of alternative treatments.

This review examines evidence from controlled studies of use of alternative therapies by women experiencing symptoms attributed to menopause. Its purpose is to familiarize family physicians with scientific support for the alternative therapies their patients are using, with the information their patients are exposed to in the lay literature, and with the topics that require further clinical trials.

Despite evidence supporting the benefits of HRT, only 11% to 15% of Canadian postmenopausal women currently use HRT.<sup>5</sup> Of those who begin HRT, less than 50% continue beyond 1 year.<sup>6</sup> Although evidence supports the benefits of estrogen in reducing the risk of osteoporosis<sup>7</sup> and coronary vascular disease,<sup>8</sup> using HRT for prevention does not appear to be a high priority for women.<sup>9</sup> Most women use it only for relief of vasomotor symptoms attributed to menopause.<sup>5</sup>

Review of 7000 letters received by the menopause information and support publication, *A Friend Indeed*, revealed reasons women elect not to take HRT. These included regarding menopause as a natural transition, not perceiving osteoporosis or cardiovas-

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*References originating from non-academic books and non-peer-reviewed journals and magazines are identified by \* throughout.*

cular disease as a personal threat, unwillingness to tolerate side effects (such as vaginal bleeding), belief that estrogen is not safe, and fear of cancer.<sup>10\*</sup> A study of women's perceptions of HRT also revealed that women do not want to commit to its long-term use and that unsatisfactory communication with physicians results in a lack of confidence in HRT.<sup>11</sup> Reasons for discontinuing HRT include return of unacceptable vaginal bleeding, other side effects, fear of long-term complications, cost, and lack of encouragement from physicians to try various HRT regimens for a "better fit."<sup>12,13\*</sup>

Interest in use of complementary and alternative remedies for managing menopausal symptoms has increased exponentially in the last 5 years.<sup>10\*,11,14</sup> This interest is fueled by growing media coverage and lay literature on the topic and by claims often made without scientific evidence.<sup>11,15\*</sup> Providers of complementary medicine are perceived to offer a more personalized and user-friendly service.<sup>16</sup>

## METHODS

Data were obtained by searching the MEDLINE, CINAHL (Nursing and Allied Health), and HEALTH (Health Planning and Administration) databases from 1966 to mid-1997. Lay literature was obtained through the Health Reference Centre, a consumer database in the Metropolitan Toronto Reference Library, as well as from recent articles and books referenced in the Toronto public library system and recommended by alternative health care providers.

Articles with reference to symptoms commonly attributed to menopause (eg, hot flashes) or to topics related to changing estrogen levels (eg, irregular menses, vaginal dryness) were included. A preliminary search involved combining the key word "menopause" with "alternative medicine," "complementary medicine," "plants—medicinal," "herbs," "medicine—herbal," "medicine—traditional," "phytosterols," "phytoestrogens," "isoflavones," "diet," "nutrition," "vitamins," "minerals," "homeopathy," "naturopathy," "acupuncture," "electroacupuncture," "acupressure," "chiropractic," "massage," "massage therapy," "relaxation techniques," and "exercise." Additional articles were obtained through references cited in articles previously identified. The search was restricted to English literature. The lay literature was also searched to determine what women are reading on alternative therapies for menopause and to compare this with the available scientific literature.

## RESULTS

Alternative methods for coping with symptoms attributed to menopause cluster into nutritional supplements, herbal remedies, homeopathic remedies, and physical approaches.

### Nutritional supplements

Following national dietary guidelines should ensure that women in the menopausal years receive adequate nutrients.<sup>17</sup> This includes choosing a variety of foods and getting adequate calcium; choosing high-fibre and low-fat foods for their protective effects against cardiovascular disease and cancer; and limiting intake of salt, alcohol, and caffeine.<sup>18</sup> Additional calcium and vitamin D might have osteoprotective effects for menopausal women, especially those at high risk for osteoporosis.<sup>19</sup>

Phytoestrogens, naturally occurring compounds found in many foods (including cereals, legumes, and grasses), deserve special mention due to evidence of their estrogenic effect in postmenopausal women.<sup>20</sup> Phytoestrogens are defined as plant substances that are functionally similar to 17 $\beta$ -estradiol or that produce estrogenic effects. There are several classes, including isoflavones, lignins, coumestans, and resorcylic acid lactones.<sup>20</sup> Isoflavones generally occur in legumes, with the highest concentrations in soybeans and soy products.<sup>20</sup>

The estrogenic effect of phytoestrogens on postmenopausal women was established in a study that observed the maturation of the vaginal epithelia of 25 women after 6 weeks' supplementation with soya (isoflavones) and linseed (lignins).<sup>21</sup> A subsequent randomized, double-blind study of 58 postmenopausal women given daily supplements of either 45 g of soy flour or 45 g of wheat flour for 12 weeks showed that soy flour produced a more rapid and continuous reduction (40%) in hot flashes compared with wheat flour (25%) ( $P < .001$  for both).<sup>22</sup> A study of isoflavonoid and endogenous estrogen levels in Japanese, American, and Finnish women's urine found that the Japanese women excreted far more isoflavonoids in their urine than the other two groups did, and that isoflavonoid estrogens were excreted in 100-fold to 1000-fold greater amounts by the Japanese women than endogenous estrogen was excreted by all groups.<sup>23</sup> The authors suggested that the Japanese women's high levels of dietary isoflavonoid phytoestrogens might partly explain why hot flashes and other menopausal symptoms are much less frequent among the Japanese.<sup>24</sup>

The biologic effects of isoflavonoid phytoestrogens can vary with age because of their proposed mechanism of action.<sup>25</sup> The relative potency of phytoestrogens is, at most, only 2% that of estradiol (E2).<sup>26</sup> Thus, in premenopausal women with high concentrations of circulating estrogens, isoflavonoids must compete for sites on estrogen receptors.<sup>25</sup> Since most of these sites are occupied by estrogen, when isoflavonoids do bind there is a net weakly antiestrogenic effect because their activity is much lower than that of estrogen. In postmenopausal women with much lower endogenous circulating estrogen, isoflavonoids can occupy more estrogen receptor sites, and since they have some estrogenic activity, they increase total estrogens in these women.

The estrogenic effects of phytoestrogens might decrease risk of osteoporosis and fracture.<sup>27</sup> Genistein, one of the important isoflavones, was recently reported to have identical effects to conjugated equine estrogens in maintaining bone mass in ovariectomized rats.<sup>28</sup> Ipriflavone, a synthetic isoflavone, was also found to maintain bone density in premenopausal women given gonadotropin-releasing hormone agonists,<sup>29</sup> and to maintain or increase bone density in postmenopausal women.<sup>30</sup>

The cardioprotective effects of phytoestrogens have recently been under study also. A meta-analysis of the effects of soy consumption on lipid levels concluded that total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels can be significantly reduced by three servings of soy products daily, with phytoestrogens accounting for 60% to 70% of the effects.<sup>31</sup>

Although studies on the safety of phytoestrogens are few, phytoestrogen consumption through legumes is assumed to be safe as part of a balanced diet, since legumes have provided humans with their main source of protein for thousands of years.<sup>32</sup> The scientific literature most frequently attributes phytoestrogenic properties to soybeans and soy products. In addition to soy products, the lay literature identifies several herbs as containing phytoestrogens, including dong quai and black cohosh.<sup>33\*</sup> We were unable to find any studies that confirmed this.

**Table 1**<sup>34-61</sup> shows some of the more popular nutritional supplements used by women in the climacteric. Despite abundant popular claims, randomized placebo-controlled studies are required to demonstrate the efficacy of bioflavonoids in menopause. Vitamin E and evening primrose oil were found to have no benefit over placebo.

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**Alternative treatments  
for menopausal symptoms****Herbal remedies**

About \$15 million of the \$400 to \$500 million profits earned annually by the Canadian health food industry come from the sale of herbal medicines.<sup>62</sup> Because herbal medicines are legally classified as foods in North America, only limited scientific literature is required or available on their action, safety, and interactions with other drugs.<sup>60</sup> While some herbs might be pharmacologically and clinically effective, they are not necessarily free from toxicity

and side effects nor can we be sure that they will not interact with prescription medications.<sup>63</sup> Health problems from herbs can also result from contamination, adulteration, and misidentification of products.<sup>64</sup> Herbs can have nonspecific chronic effects, such as hepatitis, that are hard to associate with the cause.<sup>65</sup> Because of the reputed estrogenlike activity of some herbs, menopausal women might be exposing themselves to unpredictable amounts of unopposed estrogen.<sup>66\*</sup>

**Table 1. Nutritional supplements used to alleviate menopausal symptoms**

SUPPLEMENT	SCIENTIFIC LITERATURE	WHAT YOUR PATIENTS MIGHT BE READING
Bioflavonoids	<p>No known nutritional or medical need for bioflavonoids.<sup>34</sup></p> <p>Randomized crossover study of eight ovariectomized women showed that grapefruit juice (containing three bioflavonoids) might increase bioavailability of administered 17<math>\beta</math>-estradiol and estrone.<sup>35</sup></p> <p>In vitro, chalcones, flavonones, and flavones bind to and activate nuclear estrogen receptors in cell-free extracts.<sup>36</sup></p> <p>In vitro evidence of flavonoid prevention of LDL oxidation.<sup>37</sup></p> <p>Cross-cultural correlational study suggests average flavonoid intake partly contributes to differences in coronary heart disease mortality across populations<sup>38</sup>; randomized clinical trial needed to support claims that flavonoids protect against atherosclerosis.<sup>39</sup></p>	<p>Bioflavonoids are recommended for hot flashes,<sup>40*,41*</sup> mood swings,<sup>41*,42*</sup> insomnia,<sup>41*</sup> vaginal dryness,<sup>42-44*</sup> and heavy vaginal bleeding.<sup>42*</sup></p>
Vitamin E (tocopherol)	<p>Uncontrolled studies in 1940s found vitamin E effective for hot flashes<sup>45,46</sup>; later placebo-controlled study found no efficacy.<sup>47</sup></p> <p>Reported side effects are dermatitis, vaginal bleeding, hemorrhagic luteal cyst.<sup>46</sup></p>	<p>Vitamin E is recommended for hot flashes,<sup>40*,41*,42*,48*</sup> mood swings,<sup>41*</sup> vaginal dryness<sup>41*,42*</sup>; reputed to enhance effect of estrogen.<sup>43*,49*</sup></p>
Evening primrose oil (EPO) (Oil of <i>Oenothera biennis</i> )	<p>Randomized, double-blind, placebo-controlled study of 56 menopausal women with hot flashes found no benefit over placebo in treating menopausal flushing.<sup>50</sup> Meta-analysis found five randomized placebo-controlled trials for treatment of premenstrual syndrome, but no evidence of efficacy.<sup>51</sup></p> <p>Recommended for premenstrual syndrome (PMS),<sup>52,53</sup> including cyclical mastalgia<sup>54</sup>; earlier trials reported success with PMS treatment,<sup>55</sup> but recently no differences were found between EPO and placebo in crossover trial of 38 women with PMS.<sup>56</sup></p> <p>Contains gamma linolenic acid, precursor of prostaglandin PGE<sub>1</sub>.<sup>50</sup></p> <p>Reported side effects are inflammation, thrombosis, immunosuppression,<sup>57</sup> nausea,<sup>50,58</sup> diarrhea.<sup>58</sup> Contraindications are epilepsy,<sup>59</sup> mania,<sup>59</sup> anticoagulants,<sup>59</sup> phenothiazines.<sup>60</sup></p>	<p>Oil from seeds relieves PMS<sup>61*</sup> and hot flashes.<sup>49*</sup></p>

**Table 2**<sup>40,41,43,44,48,49,52,67-69,70-97</sup> lists some of the more popular herbs used for menopausal symptoms, as well as their known effects and safety considerations. No randomized placebo-controlled studies have been reported in the available English literature to support any of the many claims of herbal treatments for menopausal symptoms.

### Homeopathic remedies

According to the theory on which homeopathy is based, illness can be cured by very small doses of drugs that would in large doses produce symptoms in healthy people similar to those of the disease.<sup>98</sup> The effect of the drug is believed to be enhanced by repeated mechanical shock at each stage of preparation in a series of dilutions.<sup>99</sup> Some homeopathic remedies are attenuated beyond Avogadro's number, so that in theory none of the original substance remains. Despite such minute quantities of reputedly active substance, homeopathic products are considered drugs in Canada under the Food and Drugs Act; each remedy requires a Drug Identification Number.<sup>98</sup> Since homeopathic remedies are considered non-toxic and generally free of side effects, homeopathy is currently an unregulated profession that can be practised by naturopaths, other health care providers, or lay people designating themselves as "homeopaths."<sup>98</sup>

Homeopathy views menopausal problems as long-term imbalances that require constitutional treatment.<sup>100\*</sup> The three most commonly prescribed homeopathic remedies for menopausal symptoms are lachesis (derived from South American bushmaster snake venom), pulsatilla (derived from the perennial windflower, *Anemone pulsatilla*), and sepia (derived from cuttlefish ink).<sup>40\*,41\*,100-102\*</sup>

Due to lack of known mechanism for homeopathic remedies,<sup>103</sup> numerous studies have been conducted to determine whether the effects of homeopathy are placebo responses.<sup>99,104</sup> We found no double-blind, placebo-controlled evidence to show homeopathic drugs as more effective than placebo.

### Physical approaches

Although properly randomized controlled clinical trials have not yet been conducted to assess the effectiveness of physical ways of obtaining relief from menopausal symptoms, treatments such as exercise, acupuncture, massage therapy, and chiropractic are often used.<sup>5</sup> Exercise has an important role in enhancing well-being, promoting

mobility, preventing and treating a variety of diseases,<sup>105-106</sup> and providing osteoprotection and cardioprotection.<sup>107</sup> One study of the effects of exercise on the frequency of postmenopausal hot flashes found that moderate to severe hot flashes occurred in 21.5% of a group of postmenopausal women belonging to an athletic club compared with 43.8% of women in a large control group who did not exercise in a structured manner.<sup>108</sup> This study, however, used a questionnaire completed by a self-selected group without controls for socioeconomic status and other variables.

Numerous anecdotes report the effectiveness of exercise in alleviating menopausal symptoms. Another limited questionnaire study did not find any demonstrable effect of energy expenditure on hot flashes.<sup>109</sup> The only study examining the effects of acupuncture on menopausal symptoms was found in a Swedish journal.<sup>110</sup> According to the English translation, both superficial needle position and electrostimulated acupuncture resulted in a decrease in hot flashes in both groups; however, without a placebo group, the results of the study are meaningless. Chiropractic, massage therapy, acupressure, and relaxation techniques might be effective in stress management,<sup>5</sup> but we could find no studies examining their effects on menopausal symptoms. Further study is required to determine whether specific physical approaches are effective in alleviating symptoms attributed to menopause.

### Conclusion

Many alternative remedies, including nutritional, herbal, homeopathic, and physical, for treating menopausal symptoms were reviewed to identify the scientific evidence on their efficacy and safety. The strongest evidence emerged in favour of phytoestrogens for their role in diminishing menopausal symptoms related to estrogen deficiency and for their possible osteoprotective and cardioprotective effects. Long-term effects of increased phytoestrogen intake, however, are unknown.

While anecdotal information about the effectiveness of herbal remedies in alleviating menopausal symptoms is plentiful in the lay literature, scientific data are usually lacking, and there are risks for side effects and drug interactions. Homeopathy is growing in popularity as anecdotal success stories abound in the lay literature and media; but scientific data are insufficient to indicate that these

**Table 2. Herbal remedies commonly used for relief of menopausal symptoms**

HERB	SCIENTIFIC LITERATURE	WHAT YOUR PATIENTS MIGHT BE READING
Black cohosh ( <i>Cimicifuga racemosa</i> )	Luteinizing hormone-suppressive effects observed in menopausal women and ovariectomized rats. <sup>67</sup>  No evidence of estrogenic effect in study of uterine growth in immature mice and vaginal cornification in ovariectomized rats. <sup>68</sup>	Recommended for hot flashes, <sup>40*,44*,69*,70*</sup> excessive vaginal bleeding, <sup>41*</sup> depression, <sup>69*</sup> nervous tension, <sup>71*</sup> menstrual pain, and irregularity. <sup>44*,48*,70*</sup>  May result in endometrial hyperplasia if unopposed with progesterone. <sup>48*</sup>
Blue cohosh ( <i>Caulophyllum thalictroides</i> )	Alkaloids (eg, methylcysteine) and glycosides (eg, caulosaponin) appear to contribute to its physiologic activity. <sup>52</sup>  Reported side effects are methylcysteine elevates blood pressure and stimulates respiration and intestinal motility, and caulosaponin constricts coronary blood vessels and induces intestinal spasms in animals. <sup>52</sup>	Blue cohosh is recommended for hot flashes, <sup>40*</sup> spasms, <sup>48*</sup> and as a menstrual inducer. <sup>48*</sup>
Chasteberry ( <i>Vitex agnus castus</i> )	Found to have a dopaminergic effect and to be effective for hyperprolactinemia. <sup>72,73</sup>  A case report described one woman having symptoms of mild ovarian hyperstimulation syndrome in the luteal phase following ingestion. <sup>74</sup>  Reported side effect was an itchy rash. <sup>75</sup>	Chasteberry is recommended for hot flashes, <sup>40*,41*,44*,49*</sup> dry vagina, <sup>44*</sup> depression. <sup>70*</sup>
Dong quai ( <i>Angelica sinensis</i> )	Seven different coumarins (acting as vasodilators and antispasmodics) have been identified; insufficient clinical evidence to support effectiveness as an estrogenic or therapeutic agent. <sup>52</sup>  Decreased prothrombin time following cotreatment of rabbits with warfarin and dong quai indicates need for precautionary advice for patients who self-medicate with dong quai while taking chronic warfarin treatment. <sup>76</sup>  A double-blind, randomized, placebo-controlled trial of 71 women indicated that dong quai is no more helpful than placebo in relieving menopausal symptoms and does not alter endometrial thickness, vaginal maturation, or estrogen levels. <sup>77</sup>  Ferulic acid, phenolic compound in dong quai, showed inhibitory effect on spontaneous movement of rat uteri in situ. <sup>78</sup>	Dong quai is recommended for hot flashes, <sup>40*,41*,44*,67*,79*</sup> and for uterine spasm, dry vagina, and palpitations. <sup>44*</sup>  Reputed to have estrogenic effects. <sup>48*,70*</sup>  Reputed side effects are breast enlargement and tenderness <sup>44*,80*</sup> and menstrual flooding. <sup>44*,48*</sup>  Dong quai is not recommended for women with fibroids, <sup>44*</sup> fever, <sup>81*</sup> excessive menstrual flow, <sup>44*,81*</sup> and women using ASA or blood thinners regularly. <sup>44*</sup>
Ginseng ( <i>Panax ginseng</i> )	Active ingredients are triterpenoid saponins. <sup>52</sup>  Estrogenic activity uncertain <sup>52,82</sup> ; possible estrogenic effect due to chemical similarity of ginsenosides to estrogens. <sup>83</sup>  Case report of postmenopausal bleeding attributed to vaginal application of ginseng cream's estrogenlike effect. <sup>84</sup>  Double-blind, non-placebo-controlled study of a multivitamin complex supplemented with and without ginseng extract demonstrated significant improvement in quality of life in ginseng group, as reported in a questionnaire. <sup>85</sup>	Ginseng is reputed to increase energy levels, <sup>49*</sup> metabolic rate, <sup>49*</sup> estrogen production, <sup>70*,79*</sup> and immune function. <sup>49*,70*</sup>  Recommended for hot flashes, <sup>44*,49*</sup> stress, <sup>44*,49*</sup> and headaches. <sup>44*</sup>  Reported side effects are hypertension, <sup>44*,86*</sup> vaginal bleeding. <sup>44*</sup>  Contraindications include asthma or emphysema due to histamine-liberating action, <sup>87*</sup> hypertension, <sup>70*</sup> difficulty sleeping. <sup>44*</sup>
Hops ( <i>Humulus lupulus</i> )	Belong to Cannabinaceae Hemp family, closely related to marijuana; known as a neurosedative. <sup>88</sup>  Reported to relax smooth muscle and possess estrogenic and antiandrogenic activity <sup>88</sup> (no clinical study in English found).  Reported side effects are central nervous system effects on brewery workers. <sup>88</sup>	Hops are recommended for water retention, <sup>44*,89*,90*</sup> insomnia, <sup>40*,91*</sup> suppressed or painful periods, <sup>89*</sup> relaxation. <sup>90*</sup>  Reputed to contain estrogen precursors. <sup>89*,90*</sup>  Reported side effects include decreased libido <sup>90*</sup> and skin irritation. <sup>90*</sup>
Licorice ( <i>Glycyrrhiza glabra</i> )	Glycyrrhizin in licorice has structure and physiologic effects similar to aldosterone and desoxycortisone. <sup>52</sup>  Reported side effects are increased serum sodium, decreased serum potassium, raised arterial and venous pulse pressures, <sup>92</sup> and headaches. <sup>52</sup>  Negative effects of licorice found to be dose-related and more frequent in women. <sup>93</sup>	Licorice is recommended as a hormone balancer and anti-inflammatory agent. <sup>44*</sup>  Reputed to have estrogenic activity. <sup>70*,94*</sup>  Contraindications include hypertension, <sup>70*,95*</sup> and kidney disease. <sup>91*</sup>
Wild yam ( <i>Dioscorea villosa</i> )	Does not contain natural progesterone, but a chemical procedure converts components of Mexican wild yam into progesterone. <sup>96</sup>	Recommended for hot flashes, <sup>41*</sup> excessive vaginal bleeding, <sup>41*,70*</sup> inflammation. <sup>70*</sup>  Progesterone can be extracted as an alternative to HRT. <sup>43*,70*,79*</sup>  May increase libido. <sup>97*</sup>

**Key points**

Despite widespread use of alternative treatments for menopausal symptoms, good scientific evidence supporting their safety and efficacy is sparse. In published controlled trials, phytoestrogens, which occur in soy products, seem to have the greatest evidence for a role in diminishing menopausal symptoms.

remedies are superior to placebo. Well-controlled studies are needed to prove that specific physical approaches to obtaining relief from menopausal symptoms are safe and effective. Although some scientific evidence about the safety and efficacy of alternative treatments was found in this review, that evidence was usually inconclusive.

There are obvious limitations to this search, which could not review all lay literature on the topic, studies or abstracts in foreign languages, and unpublished data. Further searches of European and other databases might provide additional scientific evidence supporting alternative therapies and warning of specific adverse effects.

The role of alternative and complementary remedies as placebo, defined as any treatment deliberately used for nonspecific psychological and psychophysiological effect,<sup>111</sup> and regarded as a form of treatment without demonstrable substance,<sup>112</sup> must be considered when evaluating their effectiveness. Researchers suggest that the extent of the true placebo effect depends on, among other factors, the attitude of health care providers toward treatment of patients, patients' suggestibility, and the type of treatment.<sup>113</sup>

An American survey uncovered the fact that 72% of patients using alternative therapies did not tell their physicians.<sup>114</sup> While most physicians are not trained in alternative medicine, it is important that they ask patients about alternative remedies to check for possible side effects, toxic effects, and incompatibility with pharmacologic treatment.<sup>60,115\*</sup>

This review indicates that, despite widespread use of alternative treatments, scientific evidence supporting the efficacy and safety of most complementary treatments for relief of menopausal symptoms is sparse. Double-blind, randomized placebo-controlled trials demonstrating the short- and long-term effects of these treatments are needed. In addition, regulation of content, standardization of dosage, and accurate labeling of safety and efficacy are required to increase professional and public confidence in these products. ♣

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**References**

1. Hulka BS, Meirik O. Research on the menopause. *Maturitas* 1996;23:109-12.
2. Marwick C. Growing use of botanicals forces assessment by drug regulators. *JAMA* 1995;273:607-9.
- 3\*. Skelly A. The blooming of botanicals. *Nutr Post* 1996:13-4.
4. Milka WJ. Use of alternative health care practitioners by Canadians. *Can J Public Health* 1997;88:154-8.
5. Society of Obstetricians and Gynaecologists of Canada. Canadian Menopause Consensus Conference. *Journal SOGC* 1994;16:1645-97.
6. Ryan PJ, Harrison R, Blake GM. Compliance with hormone replacement therapy after screening for postmenopausal osteoporosis. *Br J Obstet Gynaecol* 1992;99:325-8.
7. Consensus Development Conference. Prophylaxis and treatment of osteoporosis. *Am J Med* 1991;90:107-10.
8. Barrett-Connor E, Bush TL. Estrogen and coronary heart disease in women. *JAMA* 1991;265:1861-7.
9. Griffiths F. Women's health concerns: is the promotion of HRT for prevention important to women? *Fam Pract* 1995;12:54-9.
- 10\*. O'Leary CJ. Why women choose not to take hormone therapy. *A Friend Indeed* 1993;10:1-3.
11. Wind Wardell D, Engebretson JC. Women's anticipation of hormonal replacement therapy. *Maturitas* 1995;22:177-83.
12. Wren BG, Brown L. Compliance with hormonal replacement therapy. *Maturitas* 1991;13:17-21.
- 13\*. Faculty of Medicine, University of Toronto. Menopausal hormone replacement: yes or no? *Health News* 1995;13:1-4.
14. Notelovitz M. Non-hormonal management of menopause. In: Berg G, Hammar M, editors. *The modern management of the menopause: a perspective for the 21st century*. New York: Parthenon Publishing Group Ltd; 1994. p. 513-24
- 15\*. National Women's Health Network. *Current uses of hormone therapy. Taking hormones and women's health: choices, risks and benefits*. Washington: National Women's Health Network; 1995.
16. Buckman R, Sabbagh K. *Magic or medicine?* London: Macmillan; 1993.
17. Health and Welfare Canada. *Canada's food guide to healthy eating*. Ottawa: Health and Welfare Canada; 1992.
18. Health and Welfare Canada. *Using the food guide*. Ottawa: Health and Welfare Canada; 1992.

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.....**Alternative treatments  
for menopausal symptoms**

19. Reide IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Effect of calcium supplementation on bone loss in postmenopausal women. *N Engl J Med* 1993;328:460-4.
20. Knight DC, Eden JA. Phytoestrogens—a short review. *Maturitas* 1995;22:167-75.
21. Wilcox G, Wahlqvist ML, Burger HG, Medley G. Oestrogenic effects of plant foods in postmenopausal women. *BMJ* 1990;301:905-6.
22. Murkies AL, Lombard C, Strauss BJG, Wilcox G, Burger HG, Morton MS. Dietary flour supplementation decreases post-menopausal hot flushes: effect of soy and wheat. *Maturitas* 1995;21:189-95.
23. Adlercreutz H, Hamalainen E, Gorbach S, Goldin B. Dietary phytoestrogens and the menopause in Japan. *Lancet* 1992;339:1233.
24. Lock M. Contested meanings of the menopause. *Lancet* 1991;337:1270-2.
25. Dwyer JT, Goldin BR, Saul N, Gualtieri L, Barakat S, Adlercreutz H. Tofu and soy drinks contain phytoestrogens. *J Am Diet Assoc* 1994;92:739-43.
26. Tamaya T. Inhibition by plant herb extracts of steroid bindings in uterus, liver and serum of the rabbit. *Acta Obstet Gynecol Scand* 1986;65:839-42.
27. Knight DC, Eden JA. A review of the clinical effects of phytoestrogens. *Obstet Gynecol* 1996;87:897-904.
28. Anderson J, Ambrose WW, Garner SC. Orally dosed genistein from soy and prevention of cancellous bone loss in two ovariectomized rats [abstract]. *J Nutr* 1995;125(Suppl 3):799S.
29. Gambacciani M, Spinetti A, Piaggese L. Ipriflavone prevents bone mass reduction in premenopausal women treated with gonadotropin hormone-releasing hormone agonists. *Bone Miner* 1994;26:19-26.
30. Valente M, Buflaino L, Castiglione GN. Effects of 1-year treatment with ipriflavone on bone in postmenopausal women with low bone mass. *Calcif Tissue Int* 1994;54:377-80.
31. Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995;333:276-82.
32. Desplande SS. Food legumes in human nutrition: a personal perspective. *Crit Rev Food Sci Nutr* 1992;32:333-63.
- 33\*. Marti JE. *The alternative health and medicine encyclopedia*. Detroit: Visible Ink Press; 1995.
34. Wardlaw GM, Insel PM. *Perspectives in nutrition*. Toronto: Times Mirror and Mosby College Publishing; 1990.
35. Schubert W, Cullberg G, Edgar B, Hedner T. Inhibition of 17 beta-estradiol metabolism by grapefruit juice in ovariectomized women. *Maturitas* 1994;20:155-63.
36. Miksicek R. Commonly occurring plant flavonoids have estrogenic activity. *Mol Pharmacol* 1993;44:37-43.
37. Viana M, Barbas C, Bonet B, Bonet MV, Castro M, Fraile MV, et al. In vitro effects of a flavonoid-rich extract on LDL oxidation. *Atherosclerosis* 1996;123:83-91.
38. Hertog MG, Kromhout D, Aravanis C, Blackburn H, Buzina R, Fidanza F, et al. Flavonoid intake and long-term risk of coronary heart disease and cancer in seven countries of study. *Arch Intern Med* 1995;155:381-6.
39. Katan MB. Flavonoids and heart disease. *Am J Clin Nutr* 1997;65:1542-3.
- 40\*. Langer S. Nutrition for menopause. *Better Nutrition for Today's Living* 1995;57:44-7.
- 41\*. Molvig D. 41 ways to cope with menopause naturally. *Natural Health* 1995;May/June:88-94.
- 42\*. Lark SM. Vitamins and minerals for menopause. *Ontario's Common Ground Magazine* 1992;Winter:10-4.
- 43\*. Ojeda L. *Menopause without medicine*. Salt Lake City, Utah: Publishers Press; 1995.
- 44\*. Weed S. *Menopausal years: the wise woman way*. Woodstock: Ashtree Publishing; 1992.
45. Christy CJ. Vitamin E in the menopause. *Am J Obstet Gynecol* 1945;50:84-7.
46. McLaren HC. Vitamin E in the menopause. *BMJ* 1949; 2:1378-82.
47. Blatt MHG, Weisbader H, Kupperman HS. Vitamin E and climacteric syndrome. *Arch Intern Med* 1953;91:792-9.
- 48\*. Kamen B. *Hormone replacement therapy: yes or no?* Novato, Calif: Nutrition Encounter; 1995.
- 49\*. DeMarco C. Menopause: trusting the body mind wisdom. *Health Naturally* 1995;6-9.
50. Chenoy R, Hussain S, Tayob Y, O'Brien PMS, Moss MY, Morse PF. Effect of oral gamolenic acid from evening primrose oil on menopausal flushing. *BMJ* 1994;308:501-3.
51. Budeiri D, Li Wan Po A, Dornan JC. Is evening primrose oil of value in the treatment of premenstrual syndrome? *Control Clin Trials* 1996;17:60-9.
52. Tyler VE. *The honest herbal*. New York: Pharmaceutical Products Press; 1993.
53. Brush MG. Efamol (evening primrose oil) in the treatment of the premenstrual syndrome. In: Horrobin DF, editor. *Clinical uses for essential fatty acids*. Montreal: Eden Press; 1982. p. 155-61.
54. Pye JK, Mansel RE, Hughes LE. Clinical experience of drug treatments for mastalgia. *Lancet* 1985;2:373-6.
55. O'Brien P, Massil H. Premenstrual syndrome: clinical studies on essential fatty acids. In: Horrobin DF, editor. *Omega-6 essential fatty acids: pathophysiology and roles in clinical medicine*. New York: Wiley-Liss; 1990. p. 523-45.
56. Khoo SK, Munro C, Battistutta D. Evening primrose oil and treatment of PMS. *Med J Aust* 1990;153:189-92.
57. Kleijnen J. Evening primrose oil. *BMJ* 1994;309:824-5.
58. Briggs CJ. Herbal medicine: evening primrose. *Can Pharm J* 1986;119:249-54.
59. Barber AJ. Evening primrose oil—a panacea? *Pharm J* 1988;240:723-5.
60. Institute for Clinical Evaluative Sciences in Ontario. Getting acquainted with herbs. *Informed* 1996;2:1-10.



- 61\*. Field D. Healing plants. *Toronto Star* 1995 Jan 8; FYI sect. B:1.
62. Dundass H. The herbal niche. *Can Pharm J* 1993;126:293-5, 311.
63. Chandler RF. Traditional remedies still valued in modern pharmacy. *Can Pharm J* 1985;118:419.
64. Huxtable RJ, Awang DV. Pyrrolizidine poisoning. *Am J Med* 1990;89:547-8.
65. Huxtable RJ. The myth of beneficent nature. *Ann Intern Med* 1992;117:165-6.
- 66\*. Frisch M. *Stay cool through the menopause*. New York: The Putnam Publishing Group; 1993.
67. Duker EM, Kopanski L, Jarry H, Wuttke W. Effects of extracts of *Cimicifuga racemosa* on gonadotropin release in menopausal women and ovariectomized rats [abstract]. *Planta Med* 1991;57:420-4.
68. Einer-Jensen N, Ahao J, Andersen KP, Kristoffersen K. *Cimicifuga* and *Melbrosia* lack oestrogenic effects in mice and rats. *Maturitas* 1996;25:149-53.
- 69\*. Murray F. Get by with a little help... women's nutritional care plan. *Better Nutrition for Today's Living*. 1995; June:50-6.
- 70\*. Cabot S. *Smart medicine for menopause*. New York: Avery Publishing Group; 1995.
- 71\*. Gottlieb B. *New choices in natural healing*. Emmaus, Pa: Rodale Press Inc; 1995.
72. Milewicz A, Gejdel E, Sworen H, Sienkiewicz K, Jedrezejak J, Tuecher T, et al. Vitex *Agnus castus* extract in treatment of luteal phase defects due to latent hyperprolactinemia [abstract]. *Arzneimittelforschung* 1993; 43:752-6.
73. Sliutz G, Speiser P, Schultz AM, Spona J, Zeillinger R. *Agnus castus* extracts inhibit prolactin secretion of rat pituitary cells [abstract]. *Horm Metab Res* 1993;25:253-5.
74. Cahill DJ, Fox R, Wardle PG, Harlow CR. Multiple follicular development associated with herbal medicine. *Hum Reprod* 1994;9:1469-70.
75. Tyler VE. *Herbs of choice: the therapeutic use of phytomedicines*. New York: Haworth Press Inc; 1994.
76. Lo AC, Chan K, Yeung JH, Woo KS. Danggui (*Angelica sinensis*) affects the pharmacodynamics but not the pharmacokinetics of warfarin in rabbits. *Eur J Drug Metab Pharmacokin* 1995;20:55-60.
77. Hiruta JD, Swierz LM, Zell B, Small R, Ettinger B. Does dong quai have estrogenic effects in postmenopausal women? A double-blind, placebo-controlled trial. *Fertil Steril* 1997; 68:981-6.
78. Ozaki Y, Ma JP. Inhibitory effects of tetramethylpyrazine and ferulic acid on spontaneous movement of rat uterus in situ. *Chem Pharm Bull* 1990;38:1620-3.
- 79\*. Brown E, Walker L. *Breezing through the change: managing menopause naturally*. Berkeley, Calif: Frog Ltd; 1994.
- 80\*. Royal PC. *Herbally yours*. Hurricane, Utah: Sound Nutrition; 1991.
- 81\*. Heinerman J. *Heinerman's encyclopedia of healthy herbs and spices*. New York: Parker Publishing Co; 1986.
82. Punnonen R, Lukola A. Oestrogen-like effect of ginseng. *BMJ* 1980;281:1110.
83. Chandler RF. Herbal medicine: ginseng—an aphrodisiac? *Can Pharm J* 1988;121:36-8.
84. Hopkins MP, Androff L, Benninghoff AS. Ginseng face cream and unexplained vaginal bleeding. *Am J Obstet Gynecol* 1988;159:1121-2.
85. Caso Marasco A, Vargas Ruiz R, Salas Villgomez A, Begona Infante C. Double-blind study of a multivitamin complex supplemented with ginseng extract. *Drugs Exp Clin Res* 1996;22:323-9.
- 86\*. Cameron I. Herbal remedies: big risks, few benefits? *Med Post* 1995;October 10:14.
- 87\*. O'Leary CJ. *Understanding menopause*. Toronto: Key Porter Books; 1988.
88. Salvador RL. Hops. *Can Pharm J* 1994;127:203-4.
- 89\*. McIntyre A. *The complete woman's herbal*. New York: Henry Holt Company; 1995.
- 90\*. Scott J, Scott S. *Natural medicine for women*. New York: Avon Books; 1991.
- 91\*. Burton Goldberg Group. *Alternative medicine—the definitive guide*. Fife, Washington: Future Medicine Publishing Inc; 1995.
92. Chandler RF. Licorice, more than just a flower. *Can Pharm J* 1985;118:421-4.
93. Bernardi M, D'Intinto PE, Trevisani F, Cantelli-Forti G, Raggi MA, Turchetto E, et al. Effects of prolonged ingestion of graded doses of licorice by healthy volunteers. *Life Sci* 1994;55:863-72.
- 94\*. Leung AY. *Encyclopedia of common natural ingredients used in food, drugs and cosmetics*. Toronto: John Wiley and Sons; 1980.
- 95\*. Wright K. Menopause, naturally. *Health* 1996;10:74-80.
96. Briggs CJ. Herbal medicine: *Dioscorea*. *Can Pharm J* 1990; 123:413-5.
- 97\*. Lee J. *Natural progesterone: the multiple roles of a remarkable hormone*. Sebastopol, Calif: BLL Publishing; 1994.
98. Berube B. Homeopathy. *Can Pharm J* 1994;127:278-81.
99. Reilly DT, Taylor MA, McSharry C, Aitchison T. Is homeopathy a placebo response? *Lancet* 1986;2:881-5.
- 100\*. Lockie A, Geddes N. *The women's guide to homeopathy*. London: The Penguin Group; 1992.
- 101\*. Barbach L. *The pause*. Toronto: Penguin Books Canada Ltd; 1994.
- 102\*. MacEoin B. *Homeopathy for women*. London: Hodder and Stroughton; 1996.
103. Buckman R, Lewith G. What does homeopathy do and how? *BMJ* 1994;309:103-6.

