

Compounded and 'bioidentical' hormone therapy — claims and uncertainties¹⁻⁷

What is claimed	What is known
<ul style="list-style-type: none"> 'Bioidentical' hormones are promoted as being identical to those produced by a woman's body (e.g. oestriol), rather than 'synthetic'. 	<p>Bioidentical hormones may contain oestradiol, oestriol, oestrone, progesterone, testosterone and dehydroepiandrosterone (DHEA), formulated in various combinations in buccal trouches, lozenges and topical creams. The formulations 'triest' and 'biest' are commonly used, in which oestriol is the principal component.</p> <p>In reality 'bioidentical hormones' may be from plant, animal or synthetic sources.</p>
<ul style="list-style-type: none"> Compounded bioidentical hormone therapy can be 'tailored' or 'customised' to the woman's hormone needs, sometimes using salivary measures of hormone levels. 	<p>There are no peer-reviewed data of appropriate salivary levels required for a clinical response, and salivary measures are unreliable hormone assays.⁴</p>
<ul style="list-style-type: none"> Promoted as being safer, gentler and more natural than pharmaceutical HRT. 	<p>Some substances used in bioidentical hormone therapy are available in conventional HRT; for example, many conventional HRT products contain oestradiol, an oestrogen that naturally occurs in the body.</p> <p>Any oestrogenic compound with similar benefits to those of conventional HRT may also have the same risks. There is a further risk of inadequate endometrial protection, with 3 reported cases of endometrial cancer in women taking bioidentical hormones (including progesterone, dose unknown) for several years.⁵ Testosterone and DHEA 'bioidenticals' may cause high testosterone levels, with unknown safety.⁶</p>
<ul style="list-style-type: none"> Claim to be supported by evidence. 	<p>Compounded products have not been shown to be effective in randomised trials.</p> <p>Safety claims are based on animal studies and trials with oestriol using inadequate doses.⁷</p> <p>There are medicolegal concerns about the prescription of unproven, non-TGA-approved bioidentical hormones.</p>

Evidence for efficacy and safety of complementary medicines available for menopausal symptoms

Efficacy for hot flushes and menopausal symptoms	Safety
Black cohosh — equivocal, inconsistent evidence of benefit	
<ul style="list-style-type: none"> 3 of 6 trials reported improvements on a menopausal symptom severity score.^{8,9} The best quality 1-year publicly funded study found no benefit.^{10,11} The extract in this study was a non-proprietary product, similar to marketed products. Women were aged 45–55, with an average of 6.5 hot flushes per day.^{10,11} 	<ul style="list-style-type: none"> Hepatotoxicity has occurred.¹² Advise people to report liver symptoms. No short-term adverse effects identified in small studies up to 1 year. Gastrointestinal upset may occur rarely. Effects on breast have not been studied¹³ No endometrial thickening seen after 3 months¹³ No long-term data
<p>Quality of evidence[†]</p> <p>Evidence reviewed: systematic reviews of 6 trials, in 1170 peri- or postmenopausal women. 217 women with breast cancer risk or history.⁸</p> <p>Quality: fair–poor, with only one good-quality study.⁸ Average duration: 3 months, one 12-month study.</p>	
Phytoestrogens/isoflavones	
Red clover extract — treatment effects range from small to none in systematic reviews¹⁴⁻¹⁶	
<ul style="list-style-type: none"> At best, 1 fewer hot flush per day in women experiencing 5–9 flushes per day.¹⁶ A good-quality 12-week study in mostly postmenopausal women found no benefit.¹⁷ In this study, symptoms were reduced by 35% to 40% in both placebo and 2 red clover study groups (Promensil and Rimostil). Despite this, women in all three groups were still experiencing more than 5 hot flushes per day after 12 weeks.¹⁷ 	<ul style="list-style-type: none"> No serious short-term adverse effects were identified. No effects on breast density, lipids, endometrial thickness or bone were found in a 3-year study in women with a family history of breast cancer. 320 of the 401 women were premenopausal; may not generalise to postmenopausal women.¹⁸ 2 trials reported no effect on endometrial thickness, 2 reported a decrease in endometrial thickness.¹⁴ Red clover extracts may contain coumarins and can affect INR.
<p>Quality of evidence</p> <p>Evidence reviewed: systematic reviews of 6 placebo-controlled trials, all of the brand Promensil; including about 300 women.¹³ Average duration: 12-16 weeks.</p> <p>Quality: fair–poor, with 1 good-quality study.^{8,14}</p>	

(Continued overleaf)



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Evidence for efficacy and safety of complementary medicines available for menopausal symptoms (continued)

Efficacy for hot flushes and menopausal symptoms	Safety
Soy isoflavones	
Dietary soy (flour, powder or beverages) — no evidence of an effect on hot flush frequency or severity^{14,15}	
<ul style="list-style-type: none"> • 7 of 9 studies found no differences in hot flushes.¹⁴ • 1 good-quality trial found no difference from placebo after 12 weeks 90 mg/day.⁸ 	<ul style="list-style-type: none"> • Short-term effects include unpleasant taste and gastrointestinal effects (bloating, weight gain). • No data to assess longer term adverse effects.
<p>Quality of evidence</p> <p>Evidence reviewed: systematic reviews of 10–11 trials.^{8,14} Average duration: 12–24 weeks, 1 trial of 96 weeks.⁸ Quality: most poor to fair. 1 good-quality trial.⁸</p>	
Soy isoflavone extracts (usually tablets) — mixed results, with no consistent evidence of benefit, in mostly poor-quality trials	
<ul style="list-style-type: none"> • 5 of 9 trials reported significant differences in frequency or severity of hot flushes¹⁴ • At best, 1 less hot flush per day.¹⁵ 	<ul style="list-style-type: none"> • 5 trials evaluated endometrial thickness and found no difference during course of trial (longest trial 1 year).¹⁵ • Short term effects include bloating, nausea, weight gain, concerns about bowel function.¹⁴ • Studies measuring effects on vaginal pH and vaginal maturation indices had mixed results.¹⁴ • One poor quality trial found increased endometrial hyperplasia in older postmenopausal women taking a soy extract for 5 years compared with placebo.¹⁹
<p>Quality of evidence</p> <p>Evidence reviewed: 3 systematic reviews of 9–11 trials^{14,15,16}, including around 1200 women. 1 systematic review included around 600 women with breast cancer.¹⁵ Average duration: 12–24 weeks, one 2-year study. Quality: Fair–poor.^{14,15}</p>	
Other interventions	
Dong quai — no effect on number of hot flushes or the Kupperman Index^{20†}	
	<ul style="list-style-type: none"> • May have oestrogenic effects and has shown in-vitro proliferation of breast-cancer cells — do not use in breast cancer and other oestrogen-sensitive conditions.²¹ • One small trial found no effect on endometrial thickness, or vaginal maturation indices. • Contains coumarins and can increase INR.²¹ • Has antiplatelet and anticoagulant effects.
<p>Quality of evidence: 1 poor-quality trial of 71 postmenopausal women.²⁰</p>	
Wild yam, progesterone topical creams — no effect on hot flushes⁸	
	<ul style="list-style-type: none"> • Wild yam is incorrectly believed to be a natural progesterone, but it cannot be converted to progesterone in the body and does not oppose oestrogen.²² • Do not use as the progestogen component of HRT.²²
<p>Quality of evidence: 2 poor-quality trials in 80 women using wild yam for 12 weeks.⁸</p>	
Ginseng — no effect on menopausal symptoms including mood, psychological wellbeing and cognition	
	<ul style="list-style-type: none"> • May interact with warfarin to reduce INR.²³
<p>Quality of evidence: 2 trials (6–16 weeks); 1 trial used a standardised ginseng extract, the other panax ginseng with ginkgo.²³</p>	
Vitamin E — no differences in hot flushes or severity with 800 units daily⁸	
	<ul style="list-style-type: none"> • Doses of vitamin E > 400 units per day have been associated with increased mortality in observational data.¹³
<p>Quality of evidence: 1 fair-quality trial in 125 women with previous breast cancer⁸</p>	

* In randomised, blinded clinical trials

† Indicators of quality were adequacy of randomisation, allocation concealment, blinding, power, intention-to-treat analysis (the least-biased, most conservative method; results are analysed according to randomisation regardless of dropouts).^{8,14}

‡ A scale rating severity of symptoms, including hot flushes, numbness/tingling, insomnia, arthralgia, nervousness, weakness, depression, vertigo, headache, palpitations and formication.²³

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