Clinical Studies on Black Cohosh (*Actaea racemosa* L., syn. *Cimicifuga racemosa*)

Gynecology

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Jacobson *et al*., 2001	Menopausal symptoms: Hot flashes in women with history of breast cancer	R, DB, PC n=69 (randomized based on current tamoxifen use)	2 months	One, 20 mg tablet, 2 x daily with meals	Remifemin®	Although both treatment and placebo groups self-reported declines in number and intensity of hot flashes, black cohosh was not found to be statistically more harmful or beneficial than placebo in treating menopausal symptoms. Sweating was the only symptom that did show significantly greater improvement over placebo in the black cohosh group (p=0.4). Subset analysis showing effects on patients taking tamoxifen was not reported.
Liske *et al*., 2002	Menopause complaints; comparison of standard safety and efficacy and high dose	R, DB, C, PG n=116 (women ages 42–60 with climacteric complaints)	6 months	40 mg/day (crude drug) vs. 127 mg/day (crude drug)	Remifemin®	Decrease in the Kupperman-Menopause Index (KPI) (values ~31 at the beginning) was observable after 2 weeks of Remifemin® therapy. Median scores dropped to 8 (standard dosage) and 7 (high dosage) after 12 weeks. Similar results in safety and efficacy were observed for both dosages. After 6 months, a positive response (KPI<15) was seen in ~90% of patients. No detectable changes were seen in hormone levels of LH, FSH, SHBG, prolactin, or estradiol. Remifemin® did not influence vaginal cytological parameters (degree of proliferation). The authors concluded that Remifemin may act as a selective estrogen receptor modulator ("Phyto-SERM").
Düker *et al*., 1991	FSH and LH levels during menopause	PC n=110 female patients with menopausal-complaints who have received no hormonal therapy for at least 6 months (mean age=52)	2 months	8 mg/day extract vs. placebo	Remifemin® tablet vs. placebo	Remifemin® showed an estrogen-like mode of action with selective LH suppression in menopausal women. No significant change in FSH was observed. Mean LH levels significantly reduced compared to placebo (p<0.05).
Lehmann-Willenbrock and Riedel, 1988	Menopause complaints	R, Cm n=60 randomized into 4 treatment groups (Estriol, conjugated estrogen, estrogen gestation, black cohosh)	6 months	1 mg tablet/day Ovestin® or 1.25 mg tablet/day Presomen® or 1 tablet/day Trisequens® or 48–140 mg/day Remi-femin®	Ovestin®, Estriol alone; Presomen®, conjugated estrogens; Trisequens®, combined estrogen-gestagen theapy; Remifemin® tablet	Remifemin® extract was shown to produce a decline in modified KPI and improvement of complaints associated with postoperative ovarian function deficiencies. No significant differences were noted among treatment groups. No differences in LH or FSH levels were observed.
Pethö, 1987	Menopause complaints	O n=50 (female patients converting from hormone injections to black cohosh over 6 months)	6 months	48–140 mg/day	Remifemin® tablet	Hormone replacement therapy (Gynodian, injection) may be switched to black cohosh extract with equivalent success. Of the patients, 82% reported black cohosh preparation good or very good; 56% of patients did not require additional hormone injections. No side effects were noted. Significant improvement in mean menopausal index after 2 months (p<0.001).

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

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Gynecology (cont.)

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Stoll, 1987	Menopause complaints	R, DB, PC, Cm n=80 female patients (ages 46 to 56)	12 weeks	48–140 mg/day or 0.625 mg CE/day plus 3 placebo tablets/day on days 1–21, then 2 placebo tablets 2x/day on days 22–28 or 2 placebo tablets 2x/day	Remifemin® tablet or conjugated estrogens (CE) or placebo	Patients treated with Remifemin® showed significant increase in proliferation status of vaginal epithelium compared to those patients treated with estrogens or placebo ($p<0.001$) and significant improvements in somatic and psychological parameters ($p<0.001$) (measured by KPI and Hamilton Anxiety (HAMA) scales). The number of hot flashes dropped from average of 4.9 daily to < 1 in black cohosh group; estrogen group, dropped from 5.2 to 3.2 average daily; and placebo dropped from 5.1 to 3.1 average daily occurrences. Improvements in vaginal lining were so significant, author suggests that black cohosh extract is suited as a remedy of first choice to treat menopausal symptoms, particularly if HRT is contraindicated or not desired by patient. Significant improvement of proliferation of vaginal epithelium with Remifemin®, compared to other groups ($p<0.001$).
Warnecke, 1985	Menopause complaints	O, C, Cm n=60 female patients with menopausal complaints (average age 54 years)	12 weeks	48–140 mg/day or 0.6 mg/day or 2 mg/day	Remifemin® drops or Conjugated estrogens or diazepam	Patients showed similar cytological responses (measured by proliferation and maturation of vaginal epithelial cells) to Remifemin® and estrogens. Patients receiving diazepam had no observable cytological changes. Comparable improvements in neurovegetative and psychological symptoms (measured by Self-Assessment Depression scale,HAMA, and Clinical Global Impressions (CGI) scale) were seen in all 3 treatment groups.
Vorberg, 1984	Menopause complaints	O n=50 menopausal women (39 patients showed contraindications to HRT, and 11 refused hormone treatment)	12 weeks	48–140 mg/day	Remifemin® drops	Improvements in psychological symptoms, KPI ($p<0.001$), Profile of Mood States (POMS) ($p<0.001$), and CGI ($p<0.001$) were all significant to highly significant in treatment group. No serious side effects were observed. Only mild gastrointestinal disturbances, which did not require discontinuation of treatment, were observed.
Daiber, 1983	Menopause complaints	O n=36 menopausal women; hormone replacement therapy was refused or contraindicated for these subjects (ages 45–62 years)	12 weeks	48–140 mg/day	Remifemin® drops	Highly significant decreases in KPI were observed, as was improvement in psychological symptoms including decreases in weariness and despondency, and increases in motivation and positive mood. A positive response in the CGI scale was also observed. No side effects or incompatibility reactions were observed during the 12 weeks of administration. Reduction of hot flashes ($p<0.001$), nervousness ($p<0.001$), depressive psychosis ($p<0.01$).
Stolze, 1982	Menopause complaints	O, MC n=704 female patients, 629 evaluated (mean age 51 years)	6 to 8 weeks	48–140 mg/day	Remifemin® drops	Significant improvements in neurovegetative complaints and psychological disturbances were experienced by 3 of 4 patients after 4 weeks of Remifemin® therapy. After 6 to 8 weeks, 40–50% of patients experienced complete relief from symptoms and another 30–40% of patients reported marked improvement in symptoms. The Remifemin® was well-tolerated, with no discontinuation of therapy. Only 7% of patients reported mild, transitory nonspecific complaints. In 72% of cases, physicians observed advantages of Remifemin® over previous hormonal treatment. In 54.3% of the cases, physicians stated advantages of Remifemin® compared to previous treatment with psychoactive drugs. No statistics provided.

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