Rhapontic Rhubarb Root Extract:
Herbal Alternative for Menopause Symptoms

Menopause, or the final menstrual period, is a natural event in a woman's life that generally occurs between ages 45 and 55.[1] Prior to menopause, women experience changes in the length and regularity of their periods during perimenopause, which may last as long as four to eight years.[2]

The symptoms experienced before and after menopause vary greatly and include hot flashes, vaginal dryness, weight gain, bladder/urinary problems, and disturbances in sleep, mood, and memory.[1,3]

Hot flashes are the most common menopausal complaint with up to three out of four women experiencing them, and, for 30% of women, hot flashes are frequent and severe, causing a profound impact on their quality of life.[2-4]

Hormones are widely prescribed for women still having a period, but if they are not an option, then other classes of medication (certain antidepressants, antiepileptics, and blood pressure medications) may be prescribed to treat hot flashes.[3]

Although hormone therapy is effective at relieving the symptoms of menopause, it carries an increased risk of breast and uterine cancer and blood clots, so many women turn to alternative treatments.[4,5]

One alternative option for addressing hot flashes is made from a dry extract of rhapontic rhubarb roots (extract *Rheum rhaponticum*).[5]

A standardized version of this extract, was originally registered in Germany in 1993 and was sold only by prescription until 2005 when it became nonprescription but only available in pharmacies. It became available as a dietary supplement in the U.S. in 2009.[6]

One study showed that by the end of 12 weeks of treatment, 83.3% of women taking rhapontic rhubarb root extract had significant improvement in 11 menopause symptoms, including a clear decrease in the number and severity of hot flashes, as opposed to 1.8% of women taking placebo where no change was seen.[4]

A two-year study of rhapontic rhubarb root extract also showed significant and sustained improvement in menopause symptoms along with no safety concerns.[7]

Estrogen Receptors and Menopause Treatment

For over 50 years menopause symptoms have been treated using hormone replacement therapy (HRT) with either estrogen alone or estrogen and progestin.[8]

Estrogen compounds exert their effect mainly through two types of estrogen receptor subtypes, alpha (ERα) and beta (ERβ). Both of these receptor subtypes are found in many cells and tissues throughout the body. They control important functions in specific tissues and in organ systems.[8]

ERα has a more prominent role in the breast and uterus. ERβ's effects are more pronounced in the central nervous and immune systems, and it counteracts excessive cell growth from ERα in both breast and uterine tissue.[8]

Estrogen Receptors in the Body

Hormone replacement targets both ERα and ERβ. Due to the actions in their targeted tissues and organ systems, menopausal women taking them may be at an increased risk of breast and uterine cancers along with increased blood clotting and strokes.[8]

Selective estrogen receptor modulators, or SERMs, are also known as estrogen agonists/antagonists because they activate (agonist effect) or block (antagonist effect) estrogen receptors, but only in certain areas of the body.[8,9] These compounds can be used to prevent and/or treat a number of diseases including breast cancer, weakening of the bones (osteoporosis), and vaginal thinning/dryness due to menopause.[9]

There are currently no single-agent SERMs approved to treat hot flashes, but a SERM in combination with conjugated estrogens is approved to treat hot flashes and prevent osteoporosis in women who still have a uterus.[8]

How Does Rhapontic Rhubarb Root Extract Work?

Rhapontic rhubarb has been used for decades to treat menopausal symptoms, and its mechanism of action further demonstrates its safety.[10]

In 2007, results from two *in vitro* studies evaluating rhapontic rhubarb root extract's selectivity toward ERα and ERβ were published.[10,11] The studies used two human cell culture models that were representative for endometrium (uterine tissue) and bone.[11]

There were two very important findings from these studies. First, rhapontic rhubarb root extract caused ERβ activation in both cell lines, and that effect was eliminated by an anti-estrogen agent. Second, rhapontic rhubarb root extract produced only a very weak stimulation of ERα in the bone model. Taken together, it indicated that rhapontic rhubarb root extract selectively activates ERβ.[11]

A subsequent *in vivo* study was undertaken in rats that had their ovaries taken out. The study assessed the effect of rhapontic rhubarb root extract, either alone or in combination with estradiol, on the growth and proliferation of uterine tissue. This study supported the ERβ selectivity results of the *in vitro* studies and provided additional support for the safety of rhapontic rhubarb root extract on the uterus and endometrium seen in clinical trials.[11]

Although rhapontic rhubarb root extract is not a SERM, it selectively activates ERβ similar to some of the SERMs.

Estrogen Receptor Subtype Selectivity

Medical Research on Rhapontic Rhubarb Root Extract

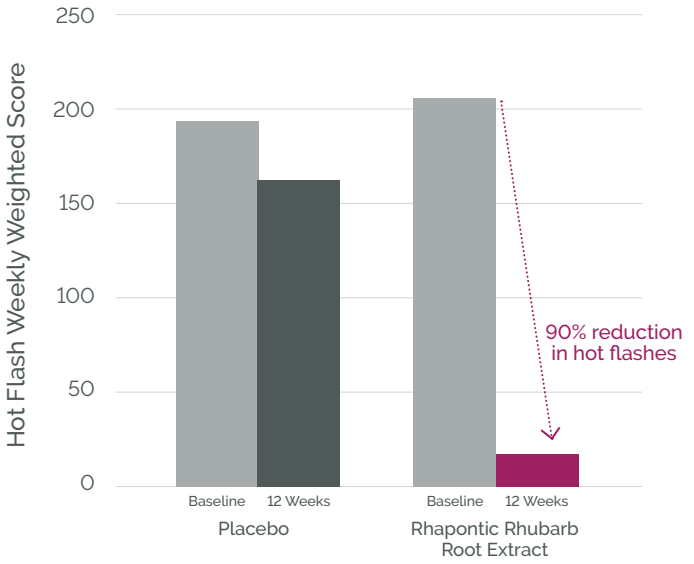
Researchers have conducted both short-term and long-term studies in women to establish the safety and effectiveness of rhapontic rhubarb root extract.

Clinical Studies

Three 12-week studies were conducted to evaluate the safety and effectiveness of rhapontic rhubarb root extract compared to placebo.[4,12,13]

The first study was conducted in 109 perimenopausal women.[4] A rating scale of 11 menopause symptoms (MRS II) showed significant decreases in all individual symptoms for 83.3% of women taking rhapontic rhubarb root extract compared to 1.8% of those taking placebo.[4] Lower scores indicate improvement in symptoms.[4] A score of weekly hot flashes (HFWWS), where hot flashes are scored on frequency and severity, showed a 90% reduction in hot flashes.[4,7] Rhapontic rhubarb root extract was well tolerated, and no safety concerns were identified.[4] A long-term observational follow-up of this study was conducted and is discussed in the next section.

12-Week Study of Rhapontic Rhubarb Root Extract vs. Placebo: Reduction in Hot Flashes



Improvement in Hot Flashes from Baseline to 12 Weeks (Mean)

A second publication focused on anxiety, health state, and general well-being. At four weeks, anxiety scores were significantly reduced in the women taking rhapontic rhubarb root extract compared to those taking placebo. At the end of 12 weeks, further reductions in anxiety scores were seen with rhapontic rhubarb root extract. General well-being assessments were also substantially higher at 12 weeks in women taking rhapontic rhubarb root extract. As with the previous study, no safety concerns were noted.[12]

The third study was conducted in 112 perimenopausal women to confirm that treatment with rhapontic rhubarb root extract was superior to placebo for menopausal symptoms. This study confirmed the previous Menopause Rating Scale results. It also showed an 83% reduction in the number of hot flashes for women taking rhapontic rhubarb root extract; hot flashes went from a median of 12 at study start down to two at the end of the study. As with the other short-term studies, no safety issues were identified.[13]

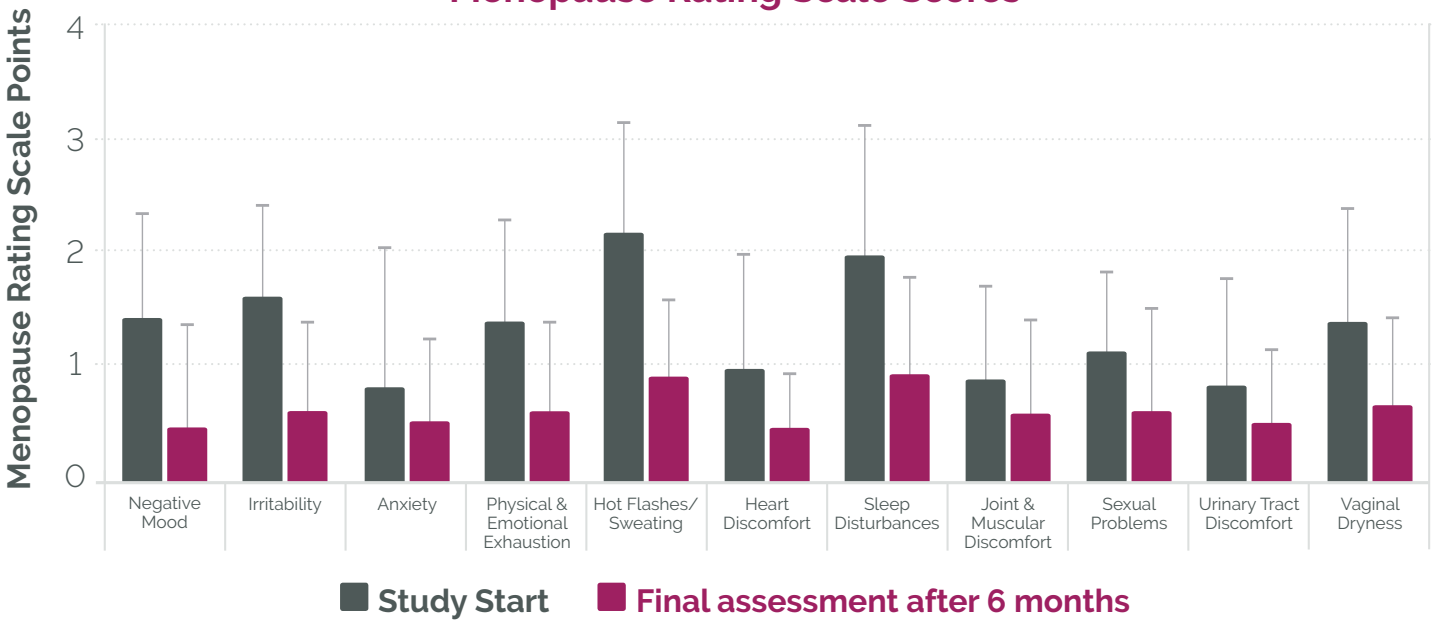
Long-Term Studies

Two long-term observational studies, one for six months and one for two years, were conducted to evaluate the safety and effectiveness of rhapontic rhubarb root extract.[7,14]

The six-month study evaluated 252 perimenopausal and postmenopausal women. At the end of the study, a significant decrease in the Menopause Rating Scale total score was demonstrated with all symptoms. No safety concerns were identified, and 90% of women rated rhapontic rhubarb root extract tolerability as good or very good.[14]

Women completing the first 12-week rhapontic rhubarb root extract/placebo study were asked to participate in a long-term (two years including the original study) study to assess the safety, tolerability, and sustained effectiveness of rhapontic rhubarb root extract. The MRS II symptom scores decreased by 83%, showing marked improvement in symptoms, by the end of 48 weeks of the long-term study and remained there until the end of the study. Rhapontic rhubarb root extract was well tolerated, and no side effects from its use were noted.[7]

Six-Month Study of Rhapontic Rhubarb Root Extract: Menopause Rating Scale Scores



Additional Safety Data

All products approved for pharmaceutical use must track and report adverse events to health authorities after approval. Although dietary supplements do not have the same direct reporting requirements, in the regions where rhapontic rhubarb root extract is used, manufacturers are required to forward reports of adverse events to the appropriate health authorities.[6]

One post-marketing safety analysis evaluated all of the available data from 1993 to 2014 for rhapontic rhubarb root extract in Germany, and from the product launch until 2014 in the U.S., Canada, and South Africa.[6]

Out of 153 million doses sold of products containing rhapontic rhubarb root extract, only 294 adverse events have been reported, most of which were not serious. The low rate of occurrence demonstrates that rhapontic rhubarb root extract is safe for consumption.[6]

Summary

Menopausal symptoms can be present during perimenopause and after menopause.

Menopausal symptoms vary greatly in women, with hot flashes being the most common in up to three out of four women.

Although hormone therapy is widely prescribed to treat menopausal symptoms, it can carry an increased risk of breast and uterine cancers, increased blood clotting, and stroke, leading some women to seek alternative therapies.

A standardized extract from rhapontic rhubarb roots has been used for decades as an alternative to hormone therapy in the treatment of menopausal symptoms.

Rhapontic rhubarb root extract exerts its effect selectively on ERβ receptors, similar to the way some SERMs work.

A number of short- and long-term studies have shown that rhapontic rhubarb root extract is safe and effective when taken for up to two years to treat a variety of menopausal symptoms.

REFERENCES

1 Menopause FAQs: Understanding the Symptoms. The North American Menopause Society website. http://www.menopause.org/for-women/expert-answers-to-frequently-asked-questions-about-menopause/menopause-faqs-understanding-the-symptoms. Accessed June 03, 2020.

2 Menopause 101: A primer for the perimenopausal. The North American Menopause Society website. http://www.menopause.org/for-women/menopauseflashes/menopause-symptoms-and-treatments/menopause-101-a-primer-for-the-perimenopausal. Accessed June 03, 2020.

3 Menopause Symptoms and Relief. U.S. Department of Health & Human Services womenshealth.gov website. https://www.womenshealth.gov/menopause/menopause-symptoms-and-relief. Updated May 22, 2018. Accessed June 03, 2020.

4 Heger M, Ventskovskiy BM, Borzenko I, Kneis KC, Rettenberger R, Kaszkin-Bettag M, et al *Menopause*. 2006;13(5):744-759.

5 Vollmer G, Papke A, Zierau O. *Chin Med*. 2010;5:7. doi: 10.1186/1749-8546-5-7.

6 Chang JL, Montalto MB, Heger PW, Thiemann E, Rettenberger R, Wacker J. 2016;15(3):34-39.

7 Hasper I, Ventskovskiy BM, Rettenberger R, Heger PW, Riley DS, Kaszkin-Bettag M. 2009;16(1):117-131.

8 Paterni I, Granchi C, Katzenallenbogen JA, Minutolo F.. *Steroids*. 2014;0:13-29.

9 SERMs FAQ. The North American Menopause Society website. http://www.menopause.org/docs/default-source/for-women/serms-faqs.pdf. Accessed June 03, 2020.

10 Möller F, Zierau O, Jandausch A, Rettenberger R, Kaszkin-Bettag M, Vollmer G.. *Phytomedicine*. 2007;14(11):716-726.

11 Papke A, Kretzschmar G, Zierau O, Kaszkin-Bettag M, Vollmer G. *J Steroid Biochem Mol Biol*. 2009;117(4-5):176-184.

12 Kaszkin-Bettag M, Ventskovskiy BM, Kravchenko A, Rettenberger R, Richardson A, Heger PW, et al. *Menopause*. 2007;14(2):270-283.

13 Kaszkin-Bettag M, Ventskovskiy BM, Solskyy S, Beck S, Hasper I, Kravchenko A, et al. *Altern Ther Health Med*. 2009;15(1):24-34.

14 Kaszkin-Bettag M, Beck S, Richardson A, Heger PW, Beer A-M. *Altern Ther Health Med*. 2008;14(6):32-38.