



DESIGN PHILOSOPHY:

Menopause Essentials

Perspective

- Menopause is a significant risk factor for cardiovascular disease, which is the primary cause of mortality for women¹⁻²
- Changes in modern diets and activity levels have significantly increased the rates of insulin resistance in the population at large, as well as comorbidities such as hypertension; 50% of adult women in the U.S. have either hypertension or prehypertension³
- Insulin resistance and hypertension are significant comorbidities⁴
- During perimenopause and menopause, rates of insulin resistance increase significantly, as does hypertension⁵⁻⁶
- Decline in estrogen levels has been linked with increased rates of cardiometabolic disease, as well as reduced bone density and risk for osteoporosis during aging⁷
- Menopause is a risk factor for metabolic syndrome⁸
- Menopausal symptoms are worse in women with insulin resistance⁹
- Phytoestrogens, especially isoflavones, have been linked to improved experiences during menopause¹⁰
- Phytoestrogens, especially isoflavones, have a good underlying safety profile for long-term consumption, even in women with a family history of breast cancer¹¹⁻¹²
- Isoflavone consumption has been linked with improved health outcomes including reduced cardiovascular disease risk¹³⁻¹⁵
- Women are at a significantly higher risk for osteopenia and osteoporosis, and menopause significantly accelerates bone-density loss⁷



- By the time women are in their 70s, their rate of bone-density loss is more than twice that of men, and they lose an average of 1% of bone density per year¹⁶
- RCT interventions with isoflavones in peri-/post-menopausal women have shown significant reduction in bone loss relative to placebo¹⁷⁻¹⁸

What Menopause Essentials Is Not

- **Not alternative medicine.** Menopause Essentials is grounded in science and medicine. It relies on clinical data, and it is designed to be supported by rigorous clinical trials.
- **Not a cure.** Menopause Essentials does not cure diseases, and will not claim to, but rather provides support for individuals undergoing menopause and is designed to support this transition.
- **Not a quick fix.** Changes to diet, environment, and exercise are the best approaches to promote a healthy lifestyle, and Menopause Essentials is designed to be a supportive addition to lifestyle changes.

Menopause Essentials shows it is possible to rationally design a product that supports multiple physiological factors linked with an improved menopause transition and that does so in a safe manner. Menopause Essentials is designed to support hormonal and metabolic health during perimenopause and beyond.

Product Profile for Menopause Essentials

Design Objectives

- Provide isoflavones at levels that are supported by epidemiological studies and RCTs to reduce symptoms of menopause and promote long-term health (red clover extract)
- Support cardiometabolic health through the use of plant extracts supported by epidemiological studies and RCTs (red clover, bergamot, and olive extracts)
- Provide micronutrients from dietary sources shown to support metabolic and cardiac health, which are additive to American diets (olive extract)

Semaine Health Co. Philosophy

- Rooted in a patient- and advocacy-focused approach with deep relationships with advocates and patient groups
- Focused on continuous engagement with medical professionals to guide product development and provide useful information to customers
- Committed to using clinical trials to validate claims

Product Formulation

Red Clover Extract

Rationale:

- Isoflavone usage has been linked with improved menopausal symptoms in RCTs and epidemiological studies¹⁹
- Isoflavones are selective estrogen receptor modulators, with significantly higher affinity for ER β over ER α ²⁰
- This selective binding affinity is linked to the improved cancer outcomes, lower risk of isoflavone usage, and improved health outcomes²¹⁻²²
- Red clover contains four isoflavones (genistein, daidzein, biochanin A, and formononetin)

- Biochanin A and formononetin are methylated forms of genistein and daidzein with improved absorption and bioavailability

Safety:

Well tolerated; it is recommended that women with estrogen-sensitive breast cancer not exceed isoflavone dosages of 100 mg²¹

Form and Dosage:

- 250 mg of red clover extract standardized to 20% isoflavones (50 mg of isoflavones)
- RCT showing improvements in bone density used 44 mg of red clover-derived isoflavones¹⁷

- Sourced from Spain (Natac Biotech) to ensure reduced pesticide usage

Olive Extract

Rationale:

- Olive polyphenols and olive oil have been shown to protect heart and brain function and reduce cancer risk in large-scale epidemiological studies²³⁻²⁴
- Intervention studies with olive polyphenols have shown improvement in blood lipid profiles and osteopenia during aging²⁵
- Olives and olive oil are consumed at much lower rates in the U.S. relative to Mediterranean countries; additionally, the olive oil consumed in the U.S. tends to be older and has a lower polyphenol content than that consumed in the Mediterranean²⁴⁻²⁶
- In the U.S., consumption of olive oil above ½ tbsp per day is associated with a 19% reduction in all-cause mortality²⁷
- Olive polyphenols will be protective for long-term aging and an additive to the standard U.S. diet

Safety:

Excellent

Form and Dosage:

- 50 mg of olive fruit extract; this is equivalent to 1–2 tbsp per day of high-polyphenol olive oil, which is

above the amount recommended by the American College of Cardiology for reduced CVD risk

- Opextan® from Indena, an extract double standardized relative to the polyphenols in the olive fruit

Bergamot

Rationale:

- In patients with metabolic syndrome, multiple well-designed RCTs have shown bergamot polyphenols improve lipid profile, reduce blood sugar, reduce visceral fat, and improve triglyceride levels²⁸⁻²⁹
- Decreasing estrogen levels during perimenopause and postmenopause are a risk factor for metabolic syndrome and cardiometabolic disease⁵
- Bergamot polyphenols are rarely consumed in the U.S. and will be additive to most diets

Safety:

Excellent

Form and Dosage:

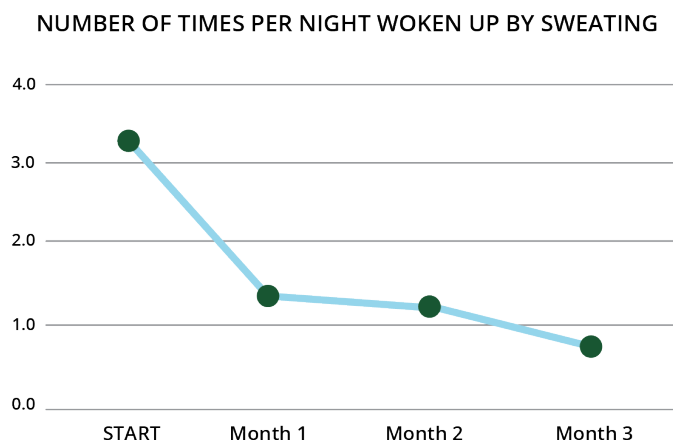
- 40 mg of bergamot polyphenolic fraction from Italian bergamot (from 100 mg bergamot phytosome)
- Bergamot polyphenols that have been optimized for bioavailability by enclosing them in a fat and protein structure; this increases bioavailability ~2.5X on a molar level

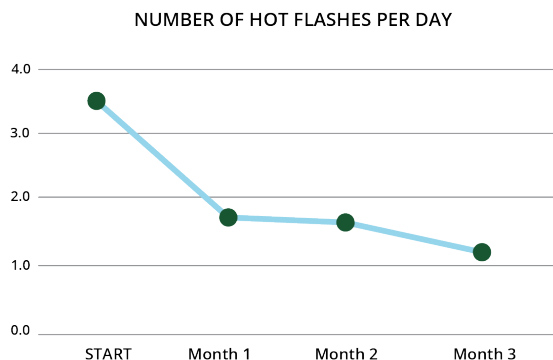
Pilot Clinical Trial

To help determine the efficacy of the product, an independent third-party-conducted trial was designed and registered at clinicaltrials.gov (NCT05617287). This was an observational open-label trial. All participants (n=42) experienced a three-month intervention.

Participants were recruited between ages 40-57 and if they experienced 3 or more hot flashes per day. All participants completed a baseline survey using the validated Menopause Rating Scale, and then completed the survey at the end of each month.

The severity of every reported menopause symptom was significantly decreased ($p < 0.001$) and number of hot flashes and night sweats decreased by 69% and 80% respectively.





93% Had Improved Hair
(less hair loss, brittleness, etc)



93% Had Higher Sexual
Satisfaction



90% Had Improved Mood
and Less Irritability

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