semaine

DESIGN PHILOSOPHY:

PMS & Period Support

Perspective

- Period pain "is one of the most common complaints encountered in medicine"[1]
- There are limited solutions available for health-care professionals to provide patients or for patients to pursue
- 1/5 patients with dysmenorrhea find "little or no" relief when using NSAIDs[2]
- Patients are increasingly reluctant to use high doses of NSAIDs[3]
- Patients increasingly rely on wellness or naturopathic products that can vary significantly in quality, design strategy, and methodology[4]
- Without engagement and options, patients will continue to rely on these products, frequently to their detriment, and thus better options are needed
- Inflammation increase before and during menstruation is not well understood by the general public, resulting in non-optimal usage of OTC painkillers[5]
- Significant evidence exists linking nutritional deficiencies and pain during menstruation[6]
- Many people with periods are extremely interested in the wellness space
- Natural products have well-studied mechanisms of action and some well-designed RCTs for period pain

Semaine Health Co. Philosophy

- Rooted in a patient- and advocacy-focused approach with deep relationships especially in the endometriosis community.
- 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. Results from the pilot study are included in this report.

Semaine PMS & Period Support shows it is possible to rationally design a product that address multiple physiological factors linked with period pain and that does so in a safe and efficacious manner.

What Semaine PMS & Period Support Is Not

- **Not alternative medicine.** PMS & Period Support 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.** PMS & Period Support will not cure a disease (endometriosis, fibroids, etc.), and does not claim to. Semaine Health uses a rigorous design process centered on alleviating menstrual discomfort (mental and physical), but it will always advocate for customers to engage with and pursue expert medical opinions.
- **Not a quick fix.** Relying on natural products reduces the speed and strength of inhibition (relative to optimized pharmacological interventions), so PMS & Period Support is designed to be taken over multiple days.

Product Profile for PMS & Period Support

Intended purpose/indication:

A broad-spectrum nutritional supplement designed to address key nutritional deficiencies linked to dysmenorrhea and provide multiple anti-inflammatory benefits.

Customer population:

People with recurring period pain. People who experience limited relief from NSAIDs or are interested in nutritional approaches to period-pain management.

Mechanism of action (MOA):

Reduction in nutritional deficiencies (magnesium and vitamin D3), anti-oxidant support (direct scavenging, increases in glutathione, SOD, Nrf2 activity), reduction in prostaglandin levels (NF-kB inhibition, cyclooxygenase inhibition, mPGE inhibition), reduction in leukotriene levels (lipoxygenase inhibition), increased GABAA signaling.

Performance/benefit:

Reduced cramping, bloating, and pelvic pain. Improved mood.

Precautions:

Minimal concern due to dosage levels and duration of treatment (3–7 days). Concern for patients on blood-thinning medication due to potential interaction.

Product usage and regimen:

Take as needed, up to 4 times a day. For best results start immediately upon menstruation, or a day prior. Continue to take as needed.

Evidentiary support:

RCTs performed with different key ingredients addressing dysmenorrhea or significant comorbidities. Rational design integrating ingredient MOA and underlying physiological causes of dysmenorrhea, PMDD, or related comorbidities (i.e., IBS). An observational trial for current product/formulation has been completed; an RCT is planned.

Formulation and Design

Ingredient Dosage: Keep raw extracts as low as possible. Excess loads that are not absorbed are frequently associated with negative side effects (primarily gastric or intestinal distress). For example, poorly absorbed magnesium can act as a laxative. Important to maximize the bioavailability of the ingredients to ensure minimal GI disruption.

Ingredient Synergy: Leverage known MOAs to combine supplements and increase efficacy as a result of addressing multiple inflammatory pathways.

Safety: Ingredient evaluation, dosage evaluation, and potential interaction evaluation.

MOA: Quantity and quality of evidence regarding specific MOA and potential roles.

Clinical Trials: What relevant (disease adjacent) clinical trials have been conducted with the ingredients? Outcomes of trials and determination of trial quality.

Design Objectives

- Address nutritional deficiencies that have been linked to increased period pain[9-11]
- Address IBS, a key comorbidity with dysmenorrhea[12]
- Address oxidative stress (endometriosis and dysmenorrhea)[13--14]
- Address prostaglandin synthesis (cramping and pain)[15]
- Address leukotriene levels (implicated in patients with dysmenorrhea who fail to respond to NSAIDs)[16]
- Address mast-cell stability (emerging treatment option for dysmenorrhea and endometriosis pain)[17-20]
- Address mood and emotional aspects linked with menstruation[21]

Product Concept

Idea: A supplement designed to anticipate the increase in inflammation coupled with entry into the menstrual cycle and reduce discomfort.

Simple: Only administered around menstruation when subjects are already altering their lifestyles and thinking about additional habits (pads/tampons/cups).

Straightforward: Limited duration to increase ease of use and compliance. Most people are reactive to pain/discomfort and want something to take only when they are in discomfort or anticipating it.

Synergistic: Natural products are less effective at inhibiting key anti-inflammatory enzymes (compared with pharmaceutical compounds), so Semaine uses ingredients to target multiple pathways and different stages of inflammatory pathways.

Potential Safety Implications: Reduced inhibitory efficacy could improve safety profile. For example, the strong COX inhibition of NSAIDs can result in issues for asthmatics as a result of accumulation of arachidonic acid.[7-8]

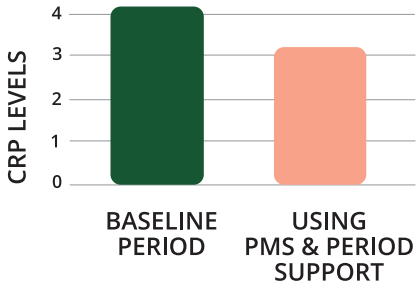
Pilot Clinical Trial

To help determine the efficacy of the product, an independent third-party-conducted trial was designed and registered at clincaltrials.gov (NCT05019924). This was an observational, open-label, cross-over trial. All participants (n=48) experienced a baseline menstrual cycle and an intervention.

Designed to mimic real-world use cases, participants were asked to take the supplement only around/during their period. This is the first test of a supplement for rapid intervention as opposed to a continuous dosing regimen.

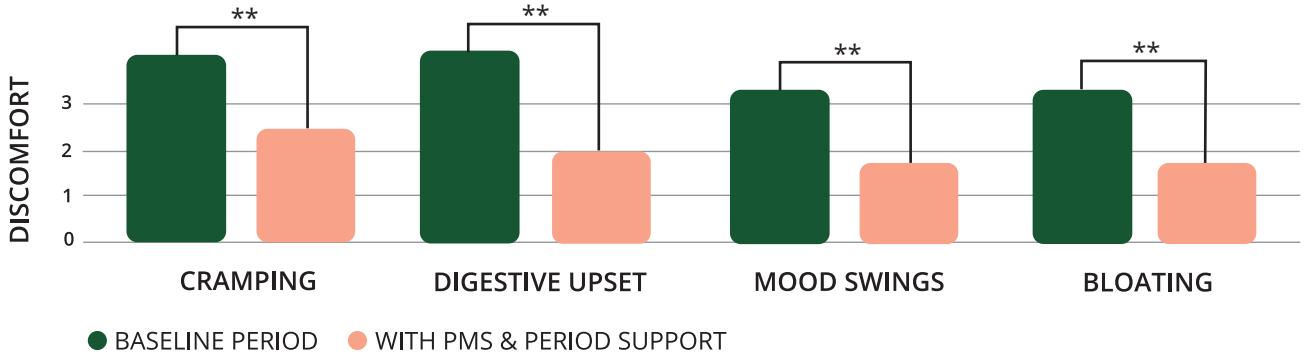
Participants completed the same survey asking questions about the level of perceived discomfort for common PMS and period symptoms. There was a significant reduction ($p<0.01$) seen on every symptom surveyed. Several key results are shown here, and the full report is available on our website.

On day four of menstruation, study participants used an at-home dried-blood-spot collection kit to measure hs-CRP levels. CRP levels have been shown to fluctuate throughout the menstrual cycle, and have also been shown to correlate with higher levels of discomfort. The measured CRP levels moved in the hypothesized direction, but not significantly ($p>0.01$).



Conclusion:

This pilot study provides strong evidence for the perceived benefits of the intervention, and it is also strongly suggestive of activity that reduces inflammation. Follow-up studies are warranted.



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