SPM Supreme™

*Synergistic Blend of 3 Pro-Resolving Mediators**

designs for health®

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SPM Supreme™ is a combination of three highly potent specialized pro-resolving mediators (SPMs) and omega-3 fatty acids designed to help support the body's natural ability to respond to physical challenges and resolve the initial steps in the natural inflammatory process.* The resolution of a healthy inflammatory response is an active process controlled by these unique metabolites.

Formula Highlights

- The SPMs found in this product are standardized to deliver at 300 mcg
- Synergistic combination of three specialized pro-resolving mediators
- Omega-3 fatty acids are added to help support the body's normal healing process*
- Features a clinically relevant amount of SPMs standardized to 300 mcg
- Gluten-free, dairy-free, and soy protein-free
- Non-GMO

Benefits*

- Supports a normal inflammatory response[4-6,8,10,11,14,16,17]
- Promotes normal tissue repair[16,17]
- Promotes a normal pain response[5,11,14,15]
- May provide support for occasional muscle and joint discomfort[5,11,14,15]
- Helps support the body's normal healing process[4-6,8,14,16,17]

Supplement Facts

Serving Size 2 softgels
Servings Per Container 30

Amount Per Serving		% Daily Value
Calories	10	
Total Fat	1 g	1%*
Active Fractionated Marine Lipid Concentrate	600 mg	†
Total Omega-3 Fatty acids	360 mg	†
EPA (Eicosapentaenoic Acid)	150 mg	†
DHA (Docosahexaenoic Acid)	120 mg	†
Total Pro-Resolving Mediators (PRMs) [18-hydroxyeicosapentaenoic acid (18-HEPE), 17-hydroxydocosahexaenoic acid (17-HDHA), 14-hydroxydocosahexaenoic acid (14-HDHA)]	300 mcg	†

*Percent Daily Values are based on a 2,000 calorie diet.
†Daily Value not established.

Other Ingredients: Olive oil, bovine gelatin, glycerine, purified water, natural lemon flavor, DeltaGold® tocotrienols.
Contains fish (anchovy, sardine, mackerel, and herring).

SPM060-2

SPMs and the Inflammatory Response*

Emerging data from the past decade reveals that the resolution of inflammation is an active and elaborate process that involves several compounds and cell types.[1,2] Among them is a class of compounds derived from omega-3 and omega-6 fatty acids called specialized pro-resolving mediators (SPMs). SPMs' primary function is to help support a healthy inflammatory response with minimal damage to the surrounding tissues.[2] Until recently, the proposed mechanisms of how SPMs support healthy inflammatory responses remained controversial.[3,4] However, recent research has shown that SPMs, such as D-series resolvins, protectins, and maresins, exhibit their pro-resolving and healthy inflammatory responses through allosteric regulation of the E-type prostanoid receptor 4 (EP4) in both in vitro and in vivo models.[4] By activating G-protein coupled receptors (GPCRs), SPMs increase cyclic AMP (cAMP), which inhibits inflammatory signaling, ultimately resulting in catabasis, the resolution phase of inflammation.[4] Additionally, SPMs enhance macrophage phagocytosis of apoptotic neutrophils and clear out other damaging byproducts, microbes, and debris at the site of inflammation.[1]

SPMs are endogenously produced in the tissues surrounding the infected or inflamed areas through a complex multi-step conversion process from eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and arachidonic acid (AA). This multi-step process and production of SPMs may be negatively affected by certain health conditions or insufficient conversation of α-Linolenic acid to EPA/DHA. SPMs themselves do not stop or block the initial inflammation phase, which is a vital response to illness or injury, but rather, they aid in the process of resolving it and function as inflammation resolution agonists that send a signal to the immune system to accelerate a return to homeostasis.[2] SPMs drive this response by promoting five key processes: cellular debris removal, restoring tissue vascularity, tissue support, supporting normal body temperature, and promoting healthy inflammatory responses.[2] SPMs may help facilitate the body's innate resolution process and response to inflammatory challenges caused by aging, physical stressors, pro-inflammatory and nutrient-poor diets, and chronic or prolonged inflammation.[5]

There is a growing interest in using SPMs in clinical research, and the field continues to evolve.[6,7] In a randomized, double-blind, crossover study, the effects of EPA and DHA on systemic inflammation and plasma SPM amounts were investigated. Twenty-one participants (n = 9 men and 12 women) with chronic inflammation, as defined as an elevated (≥ 2 µg/mL) high-sensitivity C-reactive protein (hs-CRP), were given either a high dose (defined as three grams) of EPA or DHA for two phases each over ten-week periods.[8] No significant effect was observed for changes in serum cytokine amounts; however, when monocytes were stimulated ex vivo with lipopolysaccharide (LPS) and then given EPA and DHA, cytokine expression exhibited to be downregulated.[8] Notably, the monocytes that were given DHA, compared to EPA, exhibited a reduced expression of tumor necrosis factor-alpha (TNF-α; - 45%, $P < 0.001$), interleukin 6 (IL-6; -51%, $P < 0.02$), and monocyte chemoattractant protein 1 (MCP1; -28%, $P< 0.03$).[8] Furthermore, in the participants given EPA and DHA, the amounts of plasma SPMs exhibited a fivefold increase in 18-hydroxy-EPA and a threefold increase in 17-hydroxy-DHA and 14-hydroxy-DHA, respectively.[8]

SPM Function and Genetic Variability
To further explore how SPMs function in the body, studies on genetic variability, specifically single nucleotide polymorphisms (SNPs) in genes such as the formyl peptide receptor 2 (ALX/FPR2), have provided insight into individual differences. SNPs in this receptor, which encodes for enzymes involved in SPM function, may affect how well individuals respond to SPM supplementation.[9] Supplementation may also support those with reduced dietary intake of omega-3 essential fatty acids or those with genetic variations that affect SPM function.* A diet enriched in omega-3 PUFAs and SPMs may be a supportive approach to promoting healthy inflammatory responses in these individuals.[10,11]

SPMs and a Healthy Healing Process and Pain Response*
Evidence indicates that SPM production and amounts are much lower or below detectable limits in the circulation of affected tissues among those with chronic inflammatory conditions,[12,13] possibly indicating that higher amounts of SPMs may be able to support the body's healing process.* These findings have been elucidated in animal research. In a mouse model of rheumatoid arthritis, there was a significant reduction in the amounts of resolvin D3 mediators in the experimental group compared with healthy controls.[14] Moreover, arthritic mice given resolvin mediators exhibited reduced leukocyte and inflammatory eicosanoid infiltration in joints and edema, alleviating joint stiffness and pain and promoting healthy inflammatory responses.[14]

In clinical contexts, it has been observed that groups given SPMs exhibit a normalized pain response.* For example, patients with symptomatic knee osteoarthritis who were given resolvins exhibited reduced pain scores and increased SPMs in the synovial fluid of affected joints.[5] Further evidence to support this includes the findings from a randomized, double-blind, placebo-controlled study. Fifty-one adult participants (aged 18 to 68 years) who were diagnosed with symptomatic knee osteoarthritis (OA) were given four grams total of a softgel containing an SPM-enriched oil (n = 23) or placebo (n = 28; olive oil-containing softgel), divided morning and night evenly, with a meal.[15] After six weeks of taking four grams, the participants were instructed to take one softgel (500 mg each) morning and night after their meals for an additional six weeks (one gram total per day).[15]

The primary outcome was a change in pain assessed by the visual analog scale (VAS). In the group given the SPM-enriched oil, the participants exhibited a decreased VAS score compared to the placebo after eight weeks (4.2 ± 2.11 vs. 5.2 ± 1.6; $p < 0.039$), which reduced further after the next four weeks (3.4 ± 2.17 vs. 4.6 ± 1.79; $p = 0.031$).[15] When residual effects of SPMs were assessed at week 24 (12 weeks after the intervention was completed), the VAS score increased and was similar to the placebo group (4.5 ± 2.53 vs. 4.3 ± 1.77, respectively; $p = 0.372$), possibly indicating that sustained use may offer additional benefit.[15] One critical point is that similar findings were reported when a chronic headache population was instructed to increase food sources of omega-3 and decrease omega-6 dietary intakes, not specifically given SPM supplementation. The groups that increased their dietary intakes of omega-3 fatty acids from 47 mg to 1,482 mg and kept intakes of omega-6 fatty acids low (between 43 and 76 mg) over 12 weeks exhibited reductions in pain and improved quality of life.[11]

SPMs and Tissue Repair*
After tissue damage, resolution mediators, such as SPMs, may support tissue remodeling and wound healing, which is essential to restore function.* In an in vitro study, primary human epidermal keratinocytes (HPEKp) underwent a scratch assay in which the cells were scratched with the end of a pipette to induce tissue damage.[16] The primary outcome was to investigate the effects of novel SPMs (e.g., protectin conjugate in tissue regeneration 1 [PCTR1]) on keratinocyte cell migration after the scratch assay was performed.[16] Compared to untreated HPEKp, the HPEKp given ten nmol/L of PCTR1 exhibited an approximately 21% greater keratinocyte cell migration area 24 hours after wounding.[16] Additionally, a reduced bacterial presence was demonstrated in the wounds exposed to *Staphylococcus aureus* and given PCTR1.[16] After studying cell types involved in wound repair, monocytes and macrophages given PCTR1 exhibited a reduced presence compared to untreated wounds.[16] The authors speculate that these findings suggest a more regulated immune response, supporting reduced inflammation and potentially a faster healing time.[16] These findings are consistent with a prior study that shows tissues given PCTR1 exhibited enhanced macrophage phagocytosis of *Escherichia coli* at the site of peritonitis infection.[17]

Recommended Use: Take 2 softgels per day or as directed by your health-care practitioner.

For a list of references cited in this document, please visit:
https://www.designsforhealth.com/api/library-assets/literature-reference---spm-supreme-tech-sheet-references

Dosing recommendations are given for typical use based on an average 150-pound healthy adult. Health-care practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

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