

This information is provided as a medical and scientific educational resource for the use of physicians and other licensed health-care practitioners ("Practitioners"). This information is intended for Practitioners to use as a basis for determining whether to recommend these products to their patients. All recommendations regarding protocols, dosing, prescribing, and/or usage instructions should be tailored to the individual needs of the patient considering their medical history and concomitant therapies. This information is not intended for use by consumers.

SPM Supreme™ is a combination of three highly potent specialized pro-resolving mediators, 18-hydroxyeicosapentaenoic acid, 17-hydroxydocosahexaenoic acid, and 14-hydroxydocosahexaenoic acid. Specialized pro-resolving mediators (SPMs) are endogenously produced in human blood, milk, and brain tissue from naturally occurring omega-3 and omega-6 polyunsaturated fatty acids (PUFAs). These unique metabolites help support the body's innate immune response during the resolution phase of acute inflammation.¹ SPMs are a superfamily of bioactive mediators, including resolvins, maresins, protectins, and lipoxins, actively downregulating the inflammatory response without compromising the immune response.² SPMs are endogenously produced in the tissues surrounding the affected areas of inflammation or infection and are the end result of the complex multi-step conversion process from eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and arachidonic acid (AA).

The SPMs found in this product are delivered at 150 mcg, the highest concentration currently available.

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.³ SPM Supreme™ was designed to help support the body's natural ability and capacity to respond to physiological challenges and "resolve" the immune process. The "resolution" of inflammation is an active process controlled by specialized pro-resolving mediators. SPMs do this by targeting immune cells to stop actively responding to pro-inflammatory chemical mediators (i.e., shut down the immune response and inhibit inflammation). More specifically, SPMs can modify cellular behavior to promote resolution by binding to G-protein coupled receptors (GPCRs), a mechanism that mediates pro-inflammatory chemokine, cytokine, and adipokine regulation, microRNA transcription and translocation, and cell traffic. Furthermore, SPMs enhance macrophage phagocytosis of apoptotic neutrophils and clear out other damaging byproducts, microbes, and debris at the site of inflammation.⁴

Direct supplementation may help in facilitating the body's natural resolution process and response to inflammatory challenges caused by aging, physical stressors, pro-inflammatory/nutrient-poor diets, chronic or prolonged inflammation, and other insults.* Additionally, supplementation may be beneficial to those with genetic single nucleotide polymorphisms (SNPs), such as ALX/FPR2 receptor SNPs,⁵ for enzymes involved in SPM biosynthesis or dysfunctional SPM receptors, and for those with reduced dietary intake of omega-3 essential fatty acids. A diet enriched in n-3 PUFAs coupled with these functional lipid mediators has been shown to be a promising approach to reduce overall inflammation.⁶

Currently, there are no known side effects or interactions with other supplements or drugs.* SPMs have favorable profiles and lack the potential side effects associated with common anti-inflammatory drugs such as glucocorticoids, methotrexate, and aspirin. Additionally, SPMs do not suppress immune function as they are naturally produced and involved in the biological process of inflammatory resolution.

Healthy Pain Response

Specialized pro-resolving mediators may also help dampen the pain response caused by inflammation.* Evidence indicates that SPM production and concentrations are much lower in circulation and affected tissues among those with chronic inflammatory conditions.⁷ According to a randomized clinical trial of a chronic headache population, a dietary intervention of increased omega-3 and reduced omega-6 PUFAs raised serum SPM concentrations that significantly alleviated headache pain by increasing antinociceptive mediators, thus improving quality of life.⁸

In a mouse model of rheumatoid arthritis, there was a significant reduction of resolvin D3 mediators (members of the SPM family) in the experimental group compared with healthy controls.⁹ Moreover, the administration of resolvin mediators reduced leukocyte and inflammatory eicosanoid infiltration in joints, and edema, thereby, alleviating joint stiffness, inflammation, and pain in arthritic mice.⁹ Several human studies profiling synovial fluids showed increases in SPMs upon resolvin supplementation that correlated with reduced pain scores.¹

Benefits*

- Supports a normal pain response
- Promotes tissue repair
- Promotes a healthy inflammatory response
- Supports wound healing

60 softgels

Supplement Facts	
Serving Size 1 softgel	
Amount Per Serving	% Daily Value
Calories	5
Total Fat	0.5 g 1%*
Active Fractionated Marine Lipid Concentrate	300 mg †
[standardized to 150 mcg Total Pro-Resolving Mediators (PRMs) - 18-hydroxyeicosapentaenoic acid (18-HEPE), 17-hydroxydocosahexaenoic acid (17-HDHA) and 14-hydroxydocosahexaenoic acid (14-HDHA)]	

*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, squid, sardine, mackerel, and herring).

120 softgels

Supplement Facts	
Serving Size 1 softgel	
Amount Per Serving	% Daily Value
Calories	5
Total Fat	0.5 g 1%*
Active Fractionated Marine Lipid Concentrate	300 mg †
[standardized to 150 mcg Total Pro-Resolving Mediators (PRMs) - 18-hydroxyeicosapentaenoic acid (18-HEPE), 17-hydroxydocosahexaenoic acid (17-HDHA) and 14-hydroxydocosahexaenoic acid (14-HDHA)]	

*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, squid, sardine, mackerel, and herring).

Tissue Repair

Resolution mediators also aid in tissue remodeling and wound healing, which is essential in re-establishing function. In an in vitro animal model of peritonitis, the resolution interval reduced significantly from 20 hours to 10 hours when maresin lipid mediators were given and significantly increased neutrophilic phagocytosis of the *E. coli* and bacteria at the site of infection.¹⁰

Inflammation

Impaired resolution can contribute to pathological conditions such as atherosclerosis and obesity caused by persistent inflammation in the body. In a clinical trial of obese women, supplementation with omega-3 PUFAs significantly increased concentrations of DHA-derived resolvins, which activated peroxisome proliferator-activated receptors-alpha, NRF-2, and nuclear factor kappa B target genes. The crosstalk between these genetic pathways upregulated the antioxidant enzymes and lipid metabolism in these obese subjects.¹¹ A review of in vivo and in vitro human and animal studies found emerging evidence to support SPMs as candidates for chronic inflammation and infection in cystic fibrosis patients.⁵

Specialized Pro-Resolving Mediators (SPMs)

α-Linolenic Acid

Essential Fatty Acids
Must be acquired through diet

Inefficient, multi-step conversion

Conditionally essential fatty acids support

- Cell membrane integrity
- Brain and eye health
- Healthy triglycerides levels
- Heart health

EPA
↓
DHA

Multi-step process and production affected by certain health conditions*

SPMs

Unique role in supporting the resolution of the inflammation response necessary for healthy aging

- Neutrophil activity is curtailed
- Macrophages remove dead neutrophils, bacteria, and debris
- Tissue is remodeled
- Cellular return to homeostasis

Inefficient conversion to meet the needs in the face of inflammation, particularly in an already compromised host

Adapted from: Serhan CN. Pro-resolving lipid mediators are leads for resolution physiology. *Nature*. 2014;510:92-101.

Recommended Use: Take 1 softgel 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. Healthcare 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.

DeltaGold® is a registered trademark of American River Nutrition, LLC and protected by US Patent Number 8,586,109.

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

To contact Designs for Health, please call us at (860) 623-6314, or visit us on the web at www.designsforhealth.com.