LIPINOVA®

SPECIALIZED PRO-RESOLVING LIPID MEDIATORS

Unique immune-nutrition solutions for Inflammation management

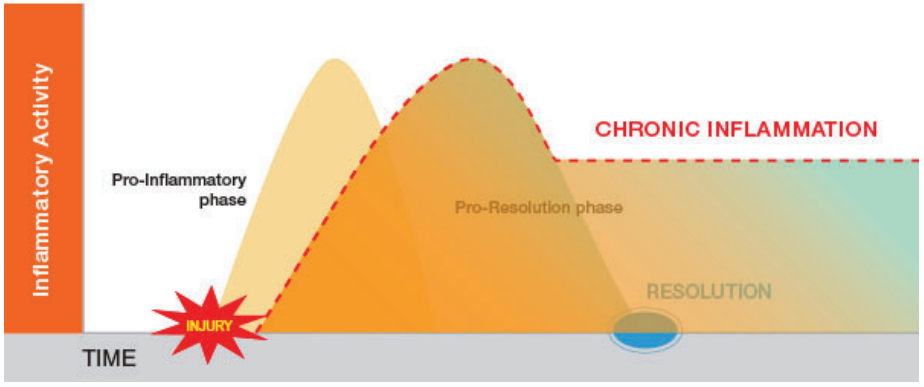
Inflammation is critical for healing, but excessive or uncontrolled inflammation is linked with disease[1].

In modern day life, lifestyle choices such as poor nutrition along with alcohol and tobacco consumption give rise to chronic disease including cardiovascular disease, atherosclerosis or metabolic syndrome, and others. These illnesses are caused or exacerbated by unresolved or uncontrolled inflammation and have a deficit of 'Specialized Pro-resolving Mediators' (SPMs), or an imbalance in the mediators of the inflammatory response.

stress...tobacco...alcohol...deficient diets...inadequate physical exercise...

Obesity	Atheroschlerosis, PAD	Cancer
Diabetes	Hypertriglyceridemia	Gastrointestinal inflammation
Cardiovascular Disease	Fatty liver	Arthritis

The inflammatory response – Resolution vs Chronicity



An acute inflammatory response is protective for the host, and a sign that the immune system is responding to infection or tissue injury. Yet when uncontrolled or inappropriately activated, acute inflammation can lead to persistent chronic inflammation that is unresolved and can promote organ fibrosis and dysfunction[1-2].

Specialized Pro-Resolving Mediators

The inflammatory response is mainly orchestrated by Lipid Mediators and it is naturally programmed to be resolved through SPMs actions, which enable tissue healing and a return to previous normal condition[2].

SPMs are active metabolites of EPA and DHA produced endogenously that modulate the natural immune response favoring the resolution of inflammation.

SPMs are a large family of Lipid Mediators, including the monohydroxilated 18-HEPE, 17-HDHA, 14-HDHA, and Lipixins, Resolvins, Protectins and Maresins. that all work together to resolve inflammation.

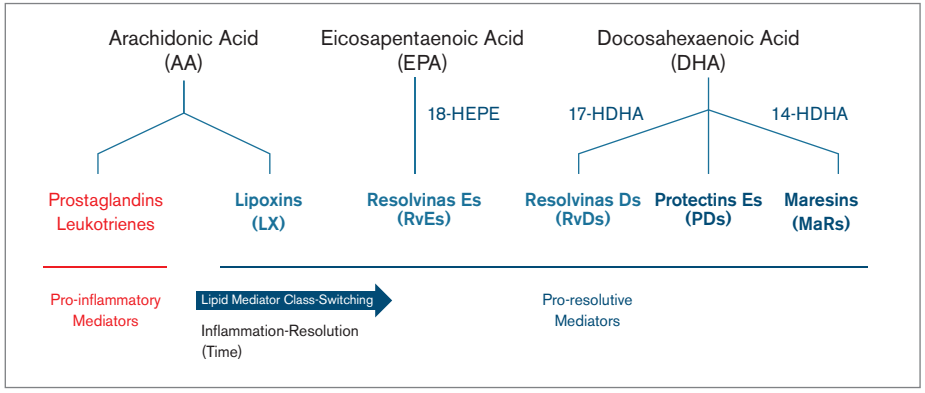


Figure: SPM family and their sustrates: AA, EPA y DHA.
Graphic adapted from Biochim Biophys Acta. 2015; 1851(4):397–413

How do SPMs resolve inflammation?[2]

SPMs act as stop signals in the inflammatory response, counter-regulate pro-inflammatory mediators and promote the phagocytosis of pathogens and cellular debris by immune cells generated during the process, clearing up the medium and enhancing tissue regeneration.

Phagocitosis by macrophage is insturmental in the process of terminating inflammation.

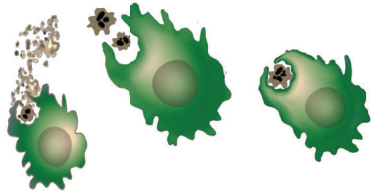


Figure: Macrophages phagocyting apoptotic cells and cell debris.

SPMs are essential to promoting resolution of the inflammatory process and a return to homeostasis (body's equilibrium) [2]

LIPINOVA® SPMs is a unique, IP-protected ingredient concentrated in 'specialized pro-resolving mediators', or SPMs, to support the body's natural capacity to resolve inflammation.

Unique SPM content
IP-protected ingredient containing standardized levels of SPMs: 18-HEPE, 17-HDHA & 14-HDHA

Specifically designed for pro-resolving activity
The only ingredient available concentrated in SPMs with characterized bioactivity.

Scientifically Proven
A non-toxic, data-based SPM solution demonstrated to be safe and effective.

Non-immunosuppressive
Resolves inflammation without compromising host defenses or suppressing the immune response.

NON-GMO and Gluten-free
Shelf Life: 24 months

Exclusive Delivery Forms
Oil available in different delivery forms including an IP protected nano-emulsion providing 1.5g in a single 15ml dose/sachet.

Fish Sourced
A unique combination of fractionation and purification techniques applied to fish oil through a proprietary and extensive enrichment process.

Environmentally Friendly Process
Sustainably sourced, gently processed and respects the product's natural properties at all times during the enrichment process.

GRAS status
LIPINOVA is Generally Recognized as Safe by the FDA.

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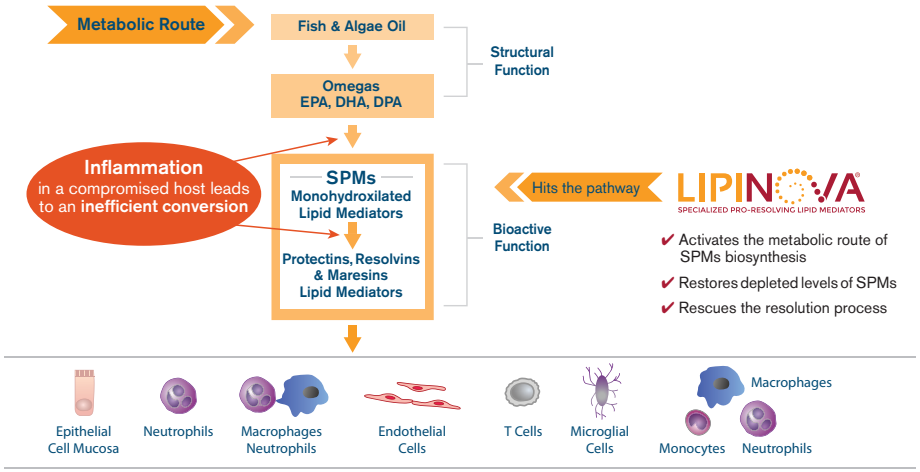


A data-based SPM ingredient scientifically proven to be safe and effective.

LIPINOVA® safety and efficacy is proven in several published studies.
Results after supplementation with LIPINOVA indicated:[3-5]

- An increased concentration of SPMs in blood
- A modulation of the immnune system towards resolution
- An improvement in outcomes such as pain
- No side effects

A randomized, double-blind, placebo-controlled study[3] completed with healthy patients demonstrated that LIPINOVA supplementation leads to:

- A dose-and time-dependent increase of plasma SPM concentrations
- The increase in SPM concentrations correlates with changes in platelet and leukocyte responses including diurnal activation and bacterial phagocytosis
- Supplementation reprograms the circulating leukocyte transcriptome

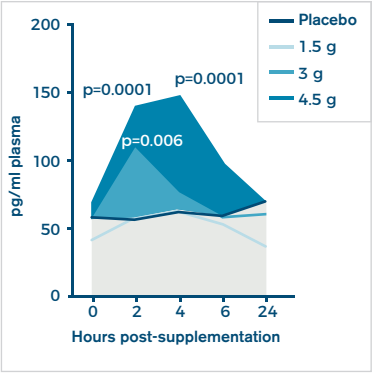


Figure: Cumulative SPM concentration post-supplementation
Graphic adapted from Circulation Research. 2020;126:75–90.

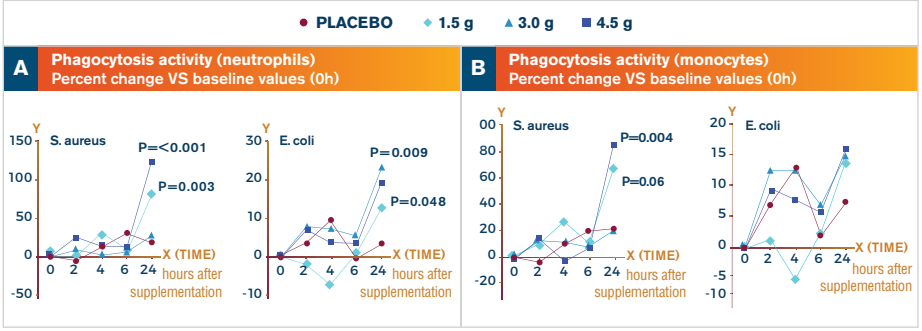


Figure: Increase in the bacterial phagocytosis by neutrophils and monocytes from peripheral blood (blood from patients incubated with S.aureius and E.Coli) following supplementation with Placebo, 1.5g, 3g and 4.5g of LIPINOVA. *Graphic adapted from Circulation Research. 2020;126:75–90.*

Study results and conclusions

A study conducted in patients with Peripheral Artery Disease (PAD), an inflammatory health condition with high cardiovascular risk, showed that supplementation with LIPINOVA® increases SPM concentrations and induces a less inflammatory and more pro-resolutive phenotype in circulating leukocytes and monocyte-derived macrophages[4].

LIPINOVA modulates the immune response after supplementation in patients with PAD, promoting an improvement in inflammatory status.

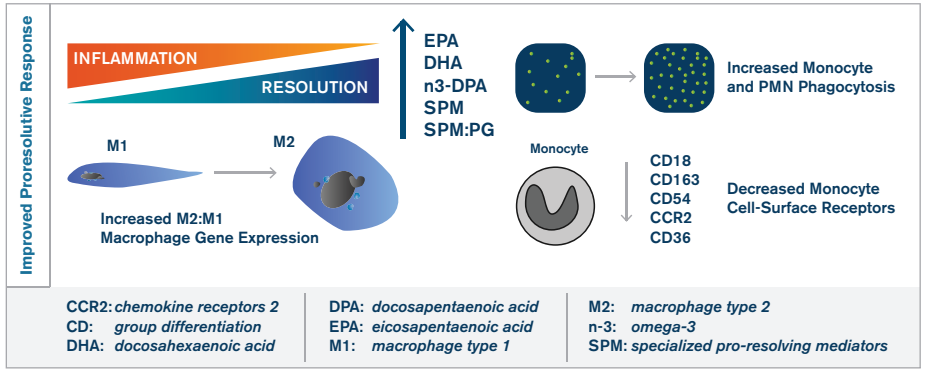


Figure: Improvements in the pro-resolution response and biochemical changes mediated by SPMs in monocytes and macrophages in patients with PAD after supplementation with LIPINOVA.
Graphic adapted from Journal of the American Heart Association, 2020; 9 (15), 120.016113.

LIPINOVA vs Omega-3 in patients with PAD

Two studies[6-7] developed with patients suffering PAD (Peripheral Artery Disease) taking Omega-3s (EPA and DHA) to test improvements in vascular function and lipid profiles, followed by a third study conducted with LIPINOVA emulsion[4], showed that:

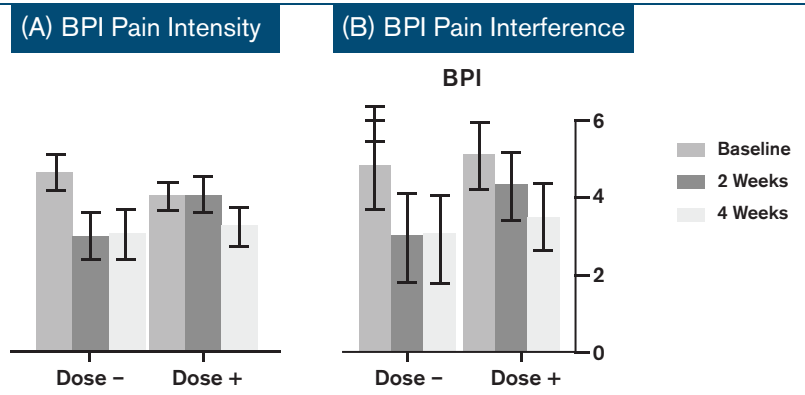
- LIPINOVA decreases inflammatory markers and increases pro-resolving markers significantly in patients with PAD with a concentration 22 times lower of EPA and DHA in the formula than that the ones utilized in the two previous studies where the results were not significant.
- LIPINOVA showed efficacy in just 1 month whereas the studies conducted with omegas lasted 3 months obtaining no significant improvements.
- Supplementation with Omega-3s increased the omega-3 index but no increase in their metabolites SPMs were detected

LIPINOVA supplementation significantly improved lipid profiles and proresolution parameters.

Pain is triggerd by inflammation. LIPINOVA® SPMs have shown positive effects in patients suffering from chronic pain by modulating the inflammatory response and therefore reducing pain and improving their quality of life[5].

The study was conducted in patients with chronic pain consuming between 1g to 2g of LIPINOVA depending on the pain intensity and the evolution in the tested period[5].

The study in adults with chronic pain, concluded that supplementation with LIPINOVA improved quality of life, reduced pain intensity and interference, resulting in an improvement in mood within 4 weeks.



Figures: Reduction in Pain Intensity (A) and Pain interference (B) measured by Brief Pain Inventory (BPI), long form. *Graphic adapted from Journal of Translational Medicine (2020) 18:401.*

'Pain relief' corroborates the overall association between LIPINOVA SPMs supplementation and a decrease in pain intensity.

Conclusion

A balance in Lipid Mediators together with an optimal response from the immune cells and mechanisms involved in the resolution of inflammation are key for maintaining an individual resolution capacity.

LIPINOVA enables safe and efficient immune-nutrition solutions targeted towards specific inflammatory health conditions and pain.

HDAS Platform – Analysis, Tracking & Segmentation Tool

A unique, analytical platform to track the evolution and severity of inflammatory-based diseases based on SPM profiles. The platform is capable of measuring biomarkers of the immune response and its evolution to identify the resolutive or immunosuppressed status of an individual, as well as the severity and progression of disease.

1. Biochim Biophys Acta. 2015 April ; 1851(4): 397–413. doi:10.1016/j.bbalip.2014.08.006.
2. Mol Aspects Med. 2017 December ; 58: 1–11. doi:10.1016/j.mam.2017.03.001.
3. Circulation Research. 2020;126:75–90. DOI: 10.1161/CIRCRESAHA.119.315506
4. J Am Heart Assoc. 2020;9:e016113. DOI: 10.1161/JAHA.120.016113
5. J Transl Med (2020) 18:401. DOI: 10.1186/s12967-020-02569-5
6. J Am Heart Assoc. 2015;4:e002034 DOI: 10.1161/JAHA.115.002034
7. Journal of Surgical Research, Volume 238, 164 – 174. DOI:10.1016/j.jss.2019.01.038

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