



SPECIALISED PRO-RESOLVING MEDIATORS - What is the Latest in Cardiovascular Health?

SPMs are unique derivatives of omega-3 polyunsaturated fatty acids (EPA and DHA) that represent a family of naturally occurring lipid mediators. They actively promote resolution or 'ending' of inflammation and a return to homeostasis. In essence they 'deactivate', or switch off, the inflammatory and immune response in an area once it is no longer needed, clear away the damaging by-products of inflammation and aid in tissue repair.¹

Cardiovascular Health

Fish oil supplementation for cardiovascular health benefits and overall risk reduction can be traced to an epidemiologic study of Eskimos in the 1940s. It was noticed that an Eskimo population in Greenland had exceedingly low rates of cardiovascular death. It was concluded that the Eskimo population consumed more fish, as compared to other Greenland inhabitants, who consumed more "Westernised" diets. The theory was that fish contained greater omega-3 fatty acids, which modified the inflammatory process resulting in reduced atherosclerosis. This study then led to an increase in research to identify the link between fish oil and cardiovascular health.²

Over the years many more clinical trials have confirmed a broad body of evidence demonstrating the beneficial effects of EPA and DHA supplementation for cardiovascular health and disease. There are many mechanisms by which fish oil may improve cardiovascular health including:³⁻⁶

- Antithrombotic / antiplatelet action.
- Significantly lowers triglycerides levels.
- Reduces synthesis of triglycerides.
- May reduce risk of atherosclerosis.
- Improves endothelial function.
- Vasodilatory effects.
- Reduces blood viscosity.
- Helps to regulate blood pressure and renal function.
- Stabilises heart rate; anti-arrhythmic properties.
- Antioxidant effects.

In-fact, The Australian Heart Foundation supports daily intake of omega-3 fatty acids (EPA/DHA) and recommends fish oil supplements for those who do not have sufficient dietary intake. 80% of Australians do not eat the recommended amount of fish per week according to survey data.⁶

However, not all research has shown a clear benefit for increased intake of EPA and DHA.¹ A meta-analysis in 2014, consisting of several large, randomised control trials (RCTs), did not identify a clear benefit in modifying cardiovascular health. The results of this meta-analysis, as well as other research, setback the theories regarding cardiovascular health and fish oil, even though the trials were not without faults: use of low-quality data, no evaluation of adequate dosing and ill-defined, objective outcome parameters.⁷

Fortunately, the discovery of new lipid mediators produced from EPA and DHA, called specialized pro-resolving mediators (SPMs), have once again given fish oil new hope for therapeutic benefit. SPMs are unique derivatives of omega-3 PUFAs (EPA, DHA and DPA) that serve to "resolve" host inflammation. SPMs' novel influence on host inflammation could potentially be the key to fish oils' benefits and their absence or low quantity could also be the reason why some of the trials have failed in the past.⁸⁻²¹

It is well known that cardiovascular disease and inflammation are linked. Cardiovascular diseases represent the most frequent causes of death worldwide, and persistent inflammation is a key aggravator in many cardiovascular diseases.^{2,21-25} Atherosclerosis is characterised by chronic unresolved inflammation, leading to plaque formation and progression.^{2,22} Vascular inflammation in arterial walls has also been identified as a key cause of coronary artery disease.²⁵

Evidence suggests that increased SPM concentration may assist in reducing cardiovascular risk by:^{2,21-25}

- Reducing vascular inflammation and regulating production of inflammatory mediators.
- Decreasing uptake of oxidized low-density lipoproteins (LDL).
- Upregulation of macrophage phagocytosis.
- Reprogramming and upregulating the ability of macrophages to clear apoptotic cells and bacteria.
- Reduced platelet aggregation.

Although the omega-3 fatty acids EPA, DHA and DPA are the building blocks for natural endogenous SPM biosynthesis, supplementation with conventional fish oils may not provide adequate amounts of the SPMs to meet the body's needs, especially where there is pre-existing chronic pathology or chronic inflammation, both of which increase endogenous demand, while also compromising natural SPM biosynthesis. An absence of adequate SPM bioactivity may result in unresolved inflammation. This can be a concern as chronic inflammation is known to underpin several disease states including cardiovascular, neurological and joint conditions.^{26,27}

Conversion of dietary or supplemental EPA, DHA and DPA to form SPMs is a complex, multi-step process. It is affected by a person's health status, with the rate and extent of conversion for each individual being variable and unpredictable. In addition, an individual may have elevated SPM requirements due to injury, trauma, chronic inflammation, chronic health conditions or suboptimal health.^{26,27}

Apart from inadequate intake of dietary omega-3 fatty acids and pre-existing health conditions, other factors that limit endogenous production of SPMs include aging, with SPM production decreasing with age, dietary factors, genetic predisposition, environmental toxin overload, physical stressors, overexertion, a sedentary lifestyle and insufficient or poor-quality sleep.^{26,27}

Furthermore, although conventional fish oil supplements may theoretically raise SPM levels, research suggests that you need a dose of at least 4000 mg EPA/DHA to result in measurable increases in SPM activity.²⁸ This dose is in excess of the usual recommended maximum dose of 3000 mg EPA/DHA daily for ongoing use, unless under medical supervision. Above this dose has been associated with a higher risk of adverse effects.³

Supplementation of SPM precursor PRMs overcomes barriers to natural SPM biosynthesis. This form is particularly beneficial in anyone with pre-existing health conditions that require increased SPM activity such as those with cardiovascular, joint or neurological health conditions, or in those with a compromised ability to produce SPMs, including the elderly. Supplemental intake of SPMs augments the actions of omega-3 fatty acids, providing a more comprehensive solution to patient care.²⁶

**References available on request.*