

## **Polyunsaturated fatty acids and inflammatory processes – Mechanisms of action and therapeutic possibilities**

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Most interest in the influence of fatty acids on inflammatory processes has centered on the frequently opposing actions of n-6 and n-3 polyunsaturated fatty acids. The n-6 arachidonic acid gives rise to the eicosanoid family of inflammatory mediators (prostaglandins, leukotrienes and related metabolites) and through these regulates the activities of inflammatory cells, and the production of damaging inflammatory cytokines, matrix metalloproteinases etc. Arachidonic acid metabolism is a well known target for pharmacologic control of inflammation. However, arachidonic acid metabolism is also subject to dietary control. Consumption of long chain n-3 fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) found in oily fish and in fish oils decreases the amount of arachidonic acid in inflammatory cell membranes and so available for eicosanoid production. Thus, consumption of long chain n-3 fatty acids results in decreased production of eicosanoids from arachidonic acid. EPA acts as an alternative substrate for eicosanoid synthesis giving rise to mediators that are often less potent than the analogues produced from arachidonic acid. EPA and DHA give rise to newly discovered families of mediators termed E- and D-resolvins, respectively, which have very potent anti-inflammatory and inflammation resolving actions in cell culture and animal model systems. In addition to this range of effects on lipid mediators, long chain n-3 fatty acids also decrease production of some peptide mediators of inflammation including the classic inflammatory cytokines. These effects appear to involve a reduction in gene expression through mechanisms currently being elucidated. These anti-inflammatory actions suggest that long chain n-3 fatty acids could be useful to protect against and to treat inflammatory conditions. A number of clinical trials have been conducted using these fatty acids, usually in the form of fish oil. Trials in rheumatoid arthritis have been the most successful. Anti-inflammatory actions may also contribute to the widely recognized protective effect of long chain n-3 fatty acids towards cardiovascular disease and may also contribute to a reduction in occurrence and severity of cardiovascular events.