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# Long-chain omega-3 PUFAs and their role in healthy ageing

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# Long-chain omega-3 PUFAs and their role in healthy ageing

## **Abstract**

The effects of various fat subtypes can have a profound influence on our health and performance, not only in the early years of life but also as we age. The long-chain omega-3s docosahexaenoic and eicosapentaenoic acid appear to have a positive role in our mental and physical health.

## **Keywords**

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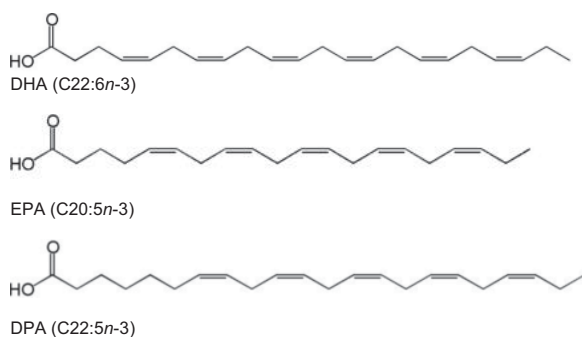
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# Long-chain omega-3 PUFAs and their role in healthy ageing

The effects of various fat subtypes can have a profound influence on our health and performance, not only in the early years of life but also as we age. The long-chain omega-3s docosahexaenoic and eicosapentaenoic acid appear to have a positive role in our mental and physical health.

The past century has seen significant changes in Western diets. Intake of saturated fatty acids and omega-6 polyunsaturated fatty acids (PUFAs) has increased, with a concomitant lowering of omega-3 PUFAs intakes, particularly the long-chain omega-3 PUFAs docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) (Fig. 1).

The importance of DHA and EPA in the development of important tissues such as the brain in early life has been acknowledged for many years. The inclusion of fish oil with a high DHA : EPA ratio in infant formula is common throughout the world because it resembles the fatty acid profile of human breast milk. More recently research into healthy ageing has shown that DHA and EPA may have health benefits in the areas of cardiovascular health, rheumatoid arthritis and other inflammatory conditions, cognitive and memory function, eye health, mental disorders such as depression, and in obesity and weight control.



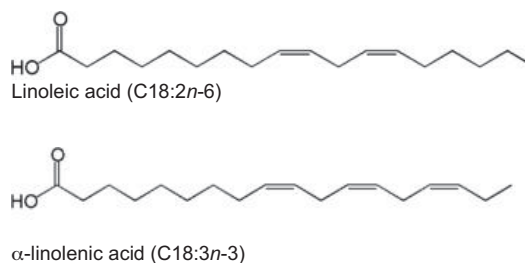
**Figure 1.** Chemical structures of docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA).

## Omega-3 structure and function

DHA and EPA can reverse omega-3 deficiency. The position of the double bonds within their hydrocarbon chain gives omega-3 PUFAs their name and their physical and physiological properties. For example, in omega-3s the terminal double bond (i.e. closest to the methyl end of the hydrocarbon chain) is on C3. In omega-6 PUFAs the terminal double bond is on C6. The omega-6 and omega-3 families of

PUFAs have a range of members, including linoleic acid and  $\alpha$ -linolenic acid (Fig. 2), both of which are plant-derived fatty acids. Although animals cannot produce these fatty acids, mammals have a requirement for them, and thus they are regarded as essential.

Mammalian cells cannot synthesise these fatty acids, but they can metabolise them by further saturation and elongation. Further metabolism of EPA to DHA is mediated by the formation of docosapentaenoic acid (DPA; see Fig. 1), then the addition of two carbons and desaturation at the  $\Delta 6$  position and finally  $\beta$ -oxidation to yield DHA.<sup>1</sup> It is important to note that recent studies have revealed that the conversion of  $\alpha$ -linolenic acid into its longer chain derivatives is not efficient in humans, and estimates for the conversion of  $\alpha$ -linolenic acid into EPA from stable isotope studies have varied between 0.2% and 8%.<sup>2</sup> The role of these fatty acids in the body, established through extensive nutritional and clinical research, is critical for human health and performance, although there appear to be significant differences in their physiological effects.



**Figure 2.** Chemical structures of linoleic acid and  $\alpha$ -linolenic acid.

## Heart health

The long-chain PUFAs DHA and EPA are thought to decrease the risk of coronary heart disease by several mechanisms. Animal and clinical studies have shown that they decrease triglycerides, inhibit inflammatory processes, increase high-density lipoproteins, improve heart rate variability, decrease

risk of thrombosis, slow progression of atherosclerotic plaques and reduce blood pressure, among other things.

It is the area of secondary prevention of heart disease that provides exciting evidence of the physiological effects of fish oils rich in DHA and EPA. The clinical effectiveness of fish oil was most strikingly demonstrated in an Italian secondary prevention study in 2002.<sup>3</sup> In this study, Marchioli and colleagues randomised 11 323 survivors of myocardial infarction to omega-3 supplements (885 mg of EPA + DHA/day), vitamin E (300 mg/day), both or neither (control). After 12 months, compared to the control group, the researchers demonstrated a reduction of cardiovascular deaths by 30% and a reduction of sudden death by 45% in the fish oil group, but not in the other groups. These findings were further supported earlier this year with release of results of the five-year heart failure study by the same group. Although this showed a moderate benefit (risk reduction for all-cause mortality was 1.8%) that was smaller than expected, the authors noted that it was obtained in a population already treated with recommended therapies and was consistent across all the predefined subgroups.<sup>4</sup>

The National Heart Foundation of Australia has long promoted the increased intake of long-chain omega-3s to improve cardiovascular health. Acknowledging the large body of evidence supporting regular consumption of DHA and EPA to improve heart health the foundation released a position paper<sup>5</sup> recommending the following long-chain omega-3 consumption levels:

- 500 mg per day of DHA and EPA to lower risk of coronary heart disease in Australian adults. This can be obtained from a combination of two to three serves of oily fish per week, fish oil capsules or liquid, and food and drinks enriched with long-chain omega-3s
- 1000 mg per day of DHA and EPA for people with established coronary heart disease.

### Anti-inflammatory properties

Early last year Goldberg and Katz published a meta-analysis on 17 randomised controlled trials assessing the effectiveness of omega-3s at alleviating rheumatoid arthritis and associated joint pain. The authors concluded that long-chain omega-3 PUFAs (> 2.7 g/day) are an attractive adjunctive treatment for joint pain associated with rheumatoid arthritis and other inflammatory diseases.<sup>6</sup> The ability of the omega-3 rich fish oils to suppress synthesis of inflammatory cytokines through competition with arachidonic acid for production of inflammatory eicosanoids appears to be fundamental to their action. Whether the ability to reduce pain is due to the suppression of the inflammation underlying



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inflammatory disease or direct effects on prostaglandins or possibly cytokines in the spinal cord dorsal horn remain to be fully elucidated.

### Preventing cognitive decline and depression

Adequate dietary availability of DHA and EPA is fundamental to brain function. DHA is the most important long-chain omega-3 PUFA for brain growth and development and the retention of cognitive and memory functions. Its importance in relation to reducing the effects of ageing on cognitive performance is now the subject of active research. Epidemiological studies indicate relatively high DHA and EPA intake is linked to lower relative risk of dementia incidence or progression.<sup>7</sup> In this longitudinal cohort study, 5386 participants aged 55 found that fish consumption was inversely related to dementia incidence, and more specifically to the risk of developing Alzheimer's disease. This was contrasted with a smaller study that found no association.<sup>8</sup> However, data from the latter study later confirmed an inverse linear relationship between DHA/EPA levels and cognitive decline.<sup>9</sup>

Seven double-blind randomised controlled trials of omega-3 fatty acids have been conducted for depression.<sup>10</sup> Of these, six studies reported clinically significant benefits of long-chain omega-3s in reducing the effects of depression. However, it remains unclear whether omega-3 supplementation is effective independent of antidepressant treatment for depressed patients in general or only those with abnormally low concentrations of these PUFAs. DHA is the most common fatty acid in the brain and the full range of actions within the brain is yet to be determined.

### Role in obesity and weight control

A positive energy balance (energy intake > energy expenditure), in which total fat intake plays an important role, is commonly regarded as a major factor contributing to obesity. New evidence is emerging showing the positive role that DHA and EPA have on appetite control. In a study published in *Appetite*, 112 subjects were provided with either low or high long-chain omega-3s for a period of two months. The authors concluded that long-chain omega-3 PUFA intake modulates postprandial satiety in overweight and obese volunteers during weight loss.<sup>11</sup> PUFAs are a major component of synaptic endings, are closely involved in the transport of appetite-regulating molecules such as dopamine and are related to receptor affinity.

### Improving dietary intakes of long-chain omega-3s

A good dietary source of long-chain omega-3 PUFAs is fish such as salmon, tuna, herring and mackerel. Essentially all

fish oil is high in long-chain omega-3 PUFAs, although the proportions of DHA, DPA and EPA can vary. Presently, people in most Western countries have diets with relatively low levels of fish. The consumption of omega-3 PUFAs, in particular DHA and EPA, has been shown to be suboptimal for all sections of the Australian population. It has been reported that 'the average omega-3 intake by Australians has been estimated at 246 mg/day comprising 75, 71 and 100 mg/day from EPA, DPA and DHA respectively'.<sup>12</sup> Compare this to the suggested intake of at least 500 mg per day promoted by most health authorities for cardiovascular health. Despite the body of evidence suggesting the importance of long-chain omega-3 PUFAs, dietary goals are difficult to achieve through the consumption of fish alone.<sup>13</sup> The National Heart Foundation of Australia also notes that people who do not consume enough long-chain omega-3 PUFAs from fish should use supplements and enriched foods. With advancements in microencapsulation technologies omega-3 PUFAs are now available in a wide range of food and beverages.

Long-chain omega-3 PUFAs are fundamentally important to healthy ageing as demonstrated by their health-promoting abilities across the wide range of age-related health problems. With the emergence of a wider variety of both food products enriched with marine oils and omega-3 supplements, which add to omega-3 intakes from fish, the potential to improve health and the quality of life throughout the ageing process is encouraging.

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