

## DOCOSAHEXAENOIC ACID: WONDER DIETARY SUPPLEMENT

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### ABSTRACT

Docosahexaenoic acid (DHA) is an omega-3 fatty acid that is a primary structural component of the human brain and retina and is manufactured internally by  $\alpha$ -linolenic acid. Although  $\alpha$ -linolenic acid (ALA) does convert to DHA in humans, the process is inefficient and very limited even in healthy individuals. Most of the DHA in fish and complex organisms with access to cold-water oceanic foods originates in photosynthetic and heterotrophic microalgae (*Cryptocodinium cohnii*), and becomes increasingly concentrated in organisms, as they move up the food chain. Dietary DHA may reduce the risk of heart disease by reducing the level of blood triglycerides in humans. During the last 50 years, many infants have been fed formula diets lacking DHA and other omega-3 fatty acids. Its deficiencies are associated with foetal alcohol syndrome, attention deficit hyperactivity disorder, unipolar depression, heart disease, aggressive hostility. A new study found that higher intake of DHA was associated with slower rates of telomere shortening, which is a basic DNA-level marker of aging. Its decrease in the brain is associated with onset of sporadic Alzheimer disease. Epidemiological studies have shown a strong correlation between fish consumption and reduction in sudden death from myocardial infarction. The reduction is approximately 50% with 200 mg per day of DHA from fish. It is available as a supplement in two forms: Fish oil capsule (contains both DHA and EPA i.e. eicosapentaenoic acid) and DHA from algae (contains no EPA). Fish oil reduces triglycerides in the blood, decrease thrombosis, and prevents cardiac arrhythmias, rheumatoid arthritis, menstrual pain, Raynaud's syndrome, and lupus. Side effects such as loose stools, stomach upset,

and belching may be associated with use of fish oil capsule.

**Keywords:** Alpha linolenic acid, Fatty acid, Arachidonic acid, Eicosapentaenoic acid.

### INTRODUCTION

Docosahexaenoic acid (DHA) is an omega-3 fatty acid that is a primary structural component of the human brain cerebral cortex, sperm, testicles and retina. It can be synthesized from alpha-linolenic acid or obtained directly from fish oil.<sup>1,2,3</sup> Hence found in fish oil supplements, along with eicosapentaenoic acid (EPA). Vegetarian sources of DHA come from seaweed. Our body needs DHA for the proper functioning of brain as an adult, and for the development of nervous system and visual abilities during the first 6 months of life. In addition, omega-3 fatty acids are part of a healthy diet that helps lower risk of heart disease. Our bodies naturally produce small amounts of DHA, but we must get the amounts we need from our diet or supplements. Most people in the Western world do not get enough omega-3 fatty acids in their diet.

### SOURCES

#### Dietary source

DHA is found in cold water fatty fish, including salmon, tuna (blue fin tuna have up to five times more DHA than other types of tuna), sardines, shellfish, and herring. Although some of these fish contain low levels of mercury, the Food and Drug Administration has found that consuming several servings of fish each week poses no risk to healthy people and conveys many health benefits.

Women who are pregnant or planning to

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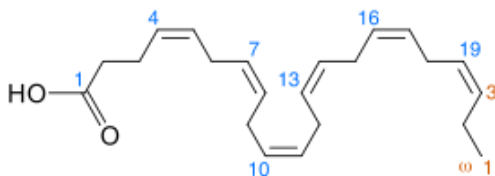
become pregnant should avoid king mackerel, shark, swordfish, and tilefish. They should also limit consumption of white albacore tuna to under 6 oz. per week.

High-quality fish oil supplements made by manufacturers who test for mercury and other toxins do not pose the same risk of mercury contamination. Read labels carefully and check for purity, or ask your doctor to help you find the best quality DHA supplement.

For infants, breast milk from a mother who eats a healthy diet contains significant amounts of DHA. Infant formula may or may not have any DHA. Read labels carefully to find a brand that does.

### BIOCHEMISTRY

In chemical structure, DHA is a carboxylic acid with a 22-carbon chain<sup>3</sup> and six *cis* double bonds; the first double bond is located at the third carbon from the omega end.<sup>4</sup> Its trivial name is Cervonic acid, its systematic name is *all-cis-docosa-4,7,10,13,16,19-hexa-enoic acid*, and its shorthand name is 22:6(n-3) in the nomenclature of fatty acids.



Molecular formula	C <sub>22</sub> H <sub>32</sub> O <sub>2</sub>
Molar mass	328.488 g/mol
Density	0.943 g/cm <sup>3</sup>
Melting point	-44 °C, 229 K, -47 °F
Boiling point	446.7 °C, 720 K, 836 °F

### MECHANISM OF ACTION

DHA leads to decreased production of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) metabolites, decreased thromboxanes A<sub>2</sub> which is a potent platelets aggregator and vasoconstrictor. It is a strong inhibitor of 5-lipoxygenase, whereby inhibits production of leukotriene B<sub>4</sub> (LTB<sub>4</sub>) from inflammatory cells, an inducer of inflammation and a powerful inducer of leukocyte chemotactic

and adherence. There occurs increase in thromboxane A<sub>3</sub>, a weak platelets aggregator and a weak vasoconstrictor and also increase in prostacyclin PGI<sub>3</sub>, leading to an overall increase in total prostacyclin by increasing PGI<sub>3</sub> without a decrease in PGI<sub>2</sub>. Both PGI<sub>2</sub> and PGI<sub>3</sub> are active vasodilators and inhibitors of platelets aggregation; and increase in leukotriene b<sub>5</sub>, a weak inducer of inflammation and a weak chemotactic agent.<sup>5</sup> Thus, DHA in high doses lowers cholesterol and has antithrombotic and anti-inflammatory properties.<sup>6</sup>

### CLINICAL INDICATIONS(USES)

#### Attention Deficit Hyperactivity Disorder (ADHD)

Research on DHA supplementation and Attention Deficit Hyperactivity Disorder (ADHD) have shown mixed results. One study of pure DHA supplementation on children with ADHD found no behavioral improvements,<sup>7</sup> while another study found fish oil containing both EPA and DHA did improve behavior,<sup>8</sup> though these studies and most others regarding the influence of DHA on behavior are confounded by not controlling for gender differences.<sup>9</sup>

#### Alzheimer's disease and decline of mental health

Preliminary studies indicated that DHA can slow the progression of Alzheimer's disease in mice,<sup>10, 11</sup> sparking interest in additional research. However, the first large-scale human trials showed that DHA did not slow decline of mental function in elderly people with mild to moderate Alzheimer's disease.<sup>12</sup> These trials were part of a large US National Institutes of Health (NIH) intervention study to evaluate DHA in Alzheimer's disease.<sup>13</sup>

Researchers from the National Institute on Aging-supported Alzheimer's Disease Cooperative Study conducted a double-blind, randomized, placebo-controlled clinical trial comparing DHA and placebo over 18 months in 402 people (average age=76) diagnosed with mild to moderate Alzheimer's at 51 sites. According to this study, treatment with DHA increased blood levels of DHA, and appeared to increase brain DHA levels, based on a measured increase of DHA in study participants' cerebrospinal fluid.

However, DHA treatment did not slow the rate of change on tests of mental function, global dementia severity status, activities of daily living, or behavioral symptoms in the study population as a whole. Treatment effects did not differ between the mild and moderate Alzheimer's patients, leading study authors to conclude that the results do not support the routine use of DHA for patients with Alzheimer's.

Animal studies in the TG3 transgenic mouse model of Alzheimer's disease had linked dietary DHA to decreases in amyloid plaques and tau. Animal studies also showed, when DHA was combined with arachidonic acid (also present in fish oil), plaque formation was greater with the arachidonic acid compared to DHA alone.

DHA deficiency likely plays a role in decline of mental function in healthy adults, which is indicated in a study from 2010 conducted at 19 U.S. clinical sites on 485 subjects aged 55 and older who met criteria for age-associated memory impairment. The study found algal DHA taken for six months decreased heart rate and improved memory and learning in healthy, older adults with mild memory complaints. These findings indicate the importance of early DHA intervention and provided a statistically significant benefit to cognitive function in individuals over 50 years of age.<sup>14</sup> Higher DHA levels in middle-aged adults is related to better performance on tests of nonverbal reasoning and mental flexibility, working memory, and vocabulary.<sup>15</sup>

### **Cancer**

DHA was found to inhibit growth of human colon carcinoma cells,<sup>16, 17</sup> more than other omega-3 PUFAs. The cytotoxic effect of DHA was not caused by increased lipid peroxidation or any other oxidative damage, but rather a decrease in cell growth regulators. However, different cancer lines handle PUFAs differently and display different sensitivities toward them. Such preliminary findings point to the need for further research, and are not proof DHA does or does not provide any benefit for intended treatment, cure, or mitigation of cancer. However, in 2008, DHA was shown to increase the efficacy of chemotherapy in prostate cancer cells,<sup>18</sup> and in 2009, a chemoprotective effect in a mouse model was

reported.<sup>19</sup> One large clinical trial, the "Prostate Cancer Prevention Trial", found that DHA was correlated with an increase in high-grade prostate cancer.<sup>20</sup>

### **Pregnancy and lactation**

DHA concentrations in breast milk range from 0.07% to greater than 1.0% of total fatty acids, with a mean of about 0.34%. DHA levels in breast milk are higher if a mother's diet is high in fish. The Food and Drug Administration has noted specific concerns for women who are pregnant or might become pregnant, nursing mothers, and young children regarding mercury levels in fish and shellfish.<sup>21</sup>

DHA has recently gained attention as a supplement for pregnant women, noting studies of improved attention and visual acuity. Given the recently gained attention, the majority of pregnant women in the U.S. fail to get the recommended amount of DHA in their diets.<sup>23</sup> One recent study indicated low levels of plasma and erythrocyte DHA were associated with poor retinal development, low visual acuity, and poor cognitive development. In that same study, alpha-linolenic acid was shown as a source of fetal DHA, but preformed DHA was more readily accredited. A working group from the International Society for the Study of Fatty Acids and Lipids recommended 300 mg/day of DHA for pregnant and lactating women, whereas the average consumption was between 45 mg and 115 mg per day of the women in the study. The March of Dimes recommends pregnant women consume at least 200 mg DHA per day.<sup>[23]</sup> Other requirements are available from other sources.<sup>24</sup>

Docosahexaenoic acid single-cell oil (DHASCO)<sup>25, 26</sup> has been an ingredient in several brands of premium infant formula sold in North America since 2001 after Mead Johnson, the first infant formula manufacturer to add DHASCO and arachidonic acid single-cell organism oil to its Enfamil Lipil product, received a "Generally Regarded As Safe" status by the Food and Drug Administration and Health Canada. Several past and recent studies indicate supplementation with arachidonic acid (omega-6) may be unsuitable for some infants and toddlers as it may potentiate the inflammatory response.<sup>27</sup>

DHASCO does not make infant formulas more like human milk than "conventional" formula containing alpha-linolenic acid and linoleic acid, which are precursors to DHA. Formula sold in North America uses lipids from microorganisms grown in bioreactors as sources of DHA.<sup>6, 28</sup> No scientific review studies show DHA additives benefit brain development of term infants, as formula makers claim in their advertisements, which has led some public interest groups to file complaints with the Federal Trade Commission of the United States, alleging false and misleading advertising.<sup>29</sup>

A study<sup>30</sup> found that preterm infants fed baby formulas fortified with DHASCO provided better developmental outcomes than formulas not containing the supplement.

A study sponsored by March of Dimes and National Institutes of Health suggests that women who take DHA supplements during pregnancy give their babies some degree of added protection against getting common colds.<sup>31</sup> The babies whose mothers had taken DHA supplements seemed to get over cold symptoms faster when they did get sick.

### **Infant Development**

DHA plays a crucial role in the growth and development of the central nervous system as well as visual functioning in infants.

### **Rheumatoid Arthritis**

Several small studies indicate that fish oil may help reduce symptoms and inflammation associated with rheumatoid arthritis. However, it does not stop joint damage from getting worse.

### **Menstrual Pain**

Fish oil appears to reduce the pain of menstrual cramps when taken on a regular basis (not just when menstruating).

### **Raynaud Syndrome**

Several studies show that high doses (12 g) of fish oil can reduce sensitivity to cold in the fingers and toes of people with Raynaud syndrome. Doses this high should be taken only under a doctor's supervision.

### **Lupus**

Two small studies suggested that fish oil reduced fatigue and joint pain associated with lupus.

### **PRECAUTIONS**

Fish oil capsules contain both DHA and EPA. Supplements containing EPA may not be recommended for infants or small children because they upset the balance between DHA and EPA during early development. Pregnant women should talk to their doctor before taking fish oil supplements.

Fish oil capsules may cause minor side effects, such as loose stools, stomach upset, and belching.

They may prolong bleeding time slightly. If you take blood-thinning medication, talk to your doctor before taking fish oil.

### **INTERACTIONS**

#### **Blood Pressure Medication**

DHA may lower blood pressure, so it could make the effects of prescription blood pressure medication stronger.<sup>4</sup>

#### **Anticoagulants (blood thinners)**

EPA in fish oil supplements may increase bleeding time, so fish oil could make the effects of these drugs stronger. The same does not appear to be true of DHA alone. Blood thinners include warfarin (Coumadin) and aspirin.

#### **Diabetes medications**

Theoretically, fish oil supplements may lower blood sugar levels and could make effects of diabetes drugs stronger. If you have diabetes, talk to your doctor before taking fish oil.

#### **Aspirin**

Combined with aspirin, fish oil could help treat some forms of heart disease. However, this combination may also increase the risk of bleeding. Talk to your doctor to see if this combination is right for you.

#### **Cyclosporine**

Omega-3 fatty acids may reduce some of the side effects of cyclosporine, which is often used to stop rejection in transplant recipients. Talk to your doctor before adding any new herbs or

supplements to the medication you already take.

### CURRENT RESEARCH FOCUS

Although most studies demonstrate positive effects of dietary DHA on human health, contrary results exist. For example, one study<sup>32</sup> found that the use of DHA-rich fish oil capsules did not reduce postpartum depression in mothers or improve cognitive and language development in their offspring during early childhood.

Additional studies confirmed DHA benefits for other nervous system functions, cardiovascular health, and potentially other organs. In one study, men who took DHA supplements for 6–12 weeks decreased the concentrations of several inflammatory markers in their blood by approximately 20%.<sup>33</sup> It has been shown that heart disease patients with higher intakes of DHA and EPA survived longer. A new study found that higher intake of DHA was associated with slower rates of telomere shortening, which is a basic DNA-level marker of aging.<sup>34</sup> Preliminary studies showed that a high intake of DHA was associated with reduced risk for developing Alzheimer's disease and Parkinson's Disease<sup>35</sup> consistent with DHA being the most abundant omega-3 fatty acid in the brain. It is now considered so important to brain and eye development that DHA is included in most infant formulas.<sup>36</sup> Lastly, in preliminary research, it was found that a diet rich in DHA might protect stroke victims from brain damage and disability and aid in a speedier recovery.<sup>37</sup>

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