



Review article

## Supplementing with DHA and ARA for infant's brain and vision development

Rajesh D Ahire\*, Rakesh S Dhole

Ahinsa Institute of Pharmacy, Dondaicha, Dhule, Maharashtra India.

**Corresponding author:** ahirerajesh11@gmail.com, **Orcid Id:** <https://orcid.org/0009-0008-6610-8475>

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### ABSTRACT

In new borns, docosahexaenoic acid (DHA) is essential for both the growth and functional development of the brain. Maintaining proper brain function requires DHA. While insufficient DHA in the diet is linked to learning and visual development impairments in babies, DHA in the diet enhances learning capacity. Natural sources of DHA and arachidonic acid (ARA) are widely available in diets, as well as through fortified meals, drinks, and supplements. DHA can also be found in meat and eggs, albeit in little amounts. The first two years of life and pregnancy are when the baby's brain grows the most. New born babies have the highest need for docosahexaenoic acid (DHA) throughout these periods. It is a crucial vitamin for supporting brain growth. Docosahexaenoic acid (DHA) and arachidonic acid (ARA) enriched new born food showed enhanced brain development and improved visual acuity.

**Keywords:** Dietary source, Visual acuity, DHA, and ARA.

### INTRODUCTION

The polyunsaturated omega-3 fatty acid (PUFA) docosahexaenoic acid, or DHA, is present throughout the body. It is a significant structural fat that makes up to 96% of all omega-3 fats in the brain and up to 94% of omega-3 fats in the retina, a specific area of the eye.<sup>[1]</sup> DHA has three key roles in the brain: it protects the structure, aids in message transmission between nerve cells, and keeps the brain flexible. DHA is also necessary for vision and is a membrane component of the eye's photoreceptor cells. Infants' developing brains are significantly influenced by the polyunsaturated fatty acid arachidonic acid (ARA). Human milk contains both of these fatty acids, arachidonic acid (ARA) and docosahexaenoic acid (DHA).<sup>[2]</sup> The composition and function of human tissues, including the development of the brain and retina during pregnancy, are significantly influenced by DHA and ARA supplements.<sup>[3]</sup>

### The arcade of DHA and ARA

The long-chain, highly unsaturated omega-3 (n-3) fatty acid docosahexaenoic acid (DHA) has six double

bonds in the cis (Z) configuration and 22 carbon atoms in its acyl chain. Chemically speaking, it is known as all-cis 4, 7,10,13,16, and 19-docosahexaenoic acid. The numbers 4, 7, 10, 13, 16, and 19 correspond to the carbon atoms in the acyl chain that have double bonds, while number 1 represents the carboxyl or  $\alpha$ -carbon. Because DHA's acyl chain has six cis double bonds, it gets very twisted, giving it special physical properties and a melting point that is extremely low ( $-44^{\circ}\text{C}$ ).<sup>[4]</sup>

The fatty acid Arachidonic acid (ARA) is a 20-carbon chain that contains four methylene-interrupted cis double bonds. The first of these, referred to as omega, x, or n, is situated between carbon 6 and. As a result, ARA is classified as an omega-6 (n-6) polyunsaturated fatty acid (PUFA), with the biochemical nomenclature all-cis-5, 8, 11, 14-eicosatetraenoic acid.<sup>[5]</sup>

### ARA and DHA sources

Arachidonic acid is mainly found in the flesh of lean red meat and chicken, in egg yolks or milk and DHA

are synthesized in abundance by using marine algae and found concentrated in fish and marine oils, specifically the oil compartments of cold water fish. Eggs are also an important source of DHA especially for non-fish eaters.<sup>[6]</sup>

### **The sources of DHA found in food are:**

#### **Algae**

DHA is naturally found in certain types of algae. *Schizochytrium sp.*, *Cryptocodinium cohnii*, and other species are among them. Fish are a high source of omega-3 fatty acids because of the algae in their food chain. Numerous foods, drinks, and dietary supplements made from algae are available.

#### **Fish and oils**

It's a great place to get DHA. The greatest sources of fatty acids are found in a variety of fish, such as salmon, tuna, herring, mackerel, anchovies, and halibut.

#### **Meat and egg**

Meat and eggs also contain small amounts of DHA, but newly enriched eggs can have as much as 56 mg of DHA per egg.

#### **Others products**

It consists of foods, drinks, and supplements enhanced with DHA.

### **The Dietary sources of ARA are**

Fish oil, algae, egg yolks, and red meat. The liver, muscles, and brain all contain a lot of it.

Additional dietary supplements, such as X-FACTOR (Arachidonic Acid) and ARASYNTM.<sup>[7]</sup>

### **Biosynthesis and metabolism of DHA and ARA**

The DHA and ARA share the same metabolic route. A series of desaturation and elongation events convert linoleic acid and ALA into ARA and EPA, respectively. The EPA-to-DHA conversion process entails elongating EPA to 24:6(n-3) in steps, then utilizing a single  $\beta$ -oxidation reaction to produce DHA.<sup>[8]</sup> An aid in the production of ARA is linoleic acid. Delta 6-desaturase easily oxidizes linoleic acid to c-linolenic acid (18:3-n6), gamma linolenic elongation step to dihomo-c-linolenic acid (20:3-n6), and delta-5 desaturase further oxidizes it to ARA.<sup>[9]</sup>

### **Role in brain development**

The mental health of the infants who were given Formula enriched with DHA and ARA showed some improvement. The entire body is made up of DHA Omega-3 fatty acids, and the amount that is passed from the mother to the fetus relies on placental function.<sup>[10]</sup>

Increased fatty acid levels in the fetal circulation, particularly docosahexaenoic acid, are indicative of the

third trimester of development, particularly to support brain and visual development.<sup>[11]</sup> When DHA is administered throughout the third trimester of pregnancy, the mother's DHA level improves, as shown by the makeup of fatty acids in the mother's erythrocyte membrane.<sup>[12]</sup>

In the developing brain, DHA has a unique function that helps astrocytes carry out some basic tasks. DHA is essential for the healthy development of the human brain. Consuming considerable amounts of DHA-containing sources has been linked to both a higher birth weight and an extended gestational age.<sup>[13]</sup> DHA's impact on the endothelium is linked to its effects on fetal weight and development. In young adults, DHA increases blood flow by vasodilatation and activates membrane receptors.<sup>[14]</sup>

An insufficiency of DHA impairs memory and IQ. DHA supplements have a number of advantages, including improved neurological and motor development. Communication skills, language, and interpersonal conduct.<sup>[15]</sup>

One of the most prevalent fatty acids in the brain, ARA is essential for the structural integrity of neuronal cells membranes.<sup>[16]</sup> ARA is essential for brain development because it is involved in signaling and cell division. ARA quickly builds up in the brain throughout development, which occurs between the start of the third trimester of pregnancy and roughly the age of two.<sup>[17]</sup>

Despite having relatively little presence in brain lipids, ARA and LA may be able to get through the blood-brain barrier. LA and ARA are changed by the brain.<sup>[18]</sup> There is increased brain ARA activity. The biological significance of ARA in human milk stems from its continuous provision of preformed ARA during a critical period of brain growth and development. Maternal reserves of ARA are the primary source of ARA in human milk.<sup>[19]</sup>

ARA serves a number of purposes in the brain. Long-term potentiation and neuronal firing signals are facilitated by ARA. Additionally, by activating the peroxisome proliferator-activated receptor gamma

(PPAR $\gamma$ ), ARA protects the brain from oxidative stress in the hippocampus and aids in the production of new proteins in tissue. It also helps preserve membrane organization and hippocampal plasticity. The role of ARA metabolism as an in vivo direct precursor for adrenic acid is possibly crucial. The third most prevalent polyunsaturated fatty acid (PUFA) in the brain, adrenic acid is largely present

in myelin lipids. Adrenic acid, like ARA, accumulates quickly in an infant's early postnatal stage of brain development. One key process for using ARA is its conversion to adrenic acid. Autism is caused by a lower blood level of ARA. [20]

### Role in visual development

Not only do DHA and ARA support brain growth, but they also enhance the development of vision. DHA is a substance found in retinal cells, which aids in preserving the size and structure of these light-sensitive cells in the retina. This helps to preserve visual functions. The formula with added DHA and ARA aids in enhancing visual acuity. The baby's red blood cells have a high concentration of DHA, which improves visual acuity. [21] Improved neurophysiological processes include enhanced visual evoked potential, electroretinogram, and visual acuity. Improved visual acuity is achieved in babies when DHA supplements, at 0.32% of total fatty acids, are given. DHA is a crucial component of cortical gray matter and retinal photoreceptors. Pregnancy-related DHA supplements can enhance visual acuity. [22].

ARA was advised to promote the integrity of the neurovascular membrane in order to control damage to the central nervous system, as well as visual and auditory impairment in premature newborns. The levels of DHA and ARA in the different formulae have a significant influence on visual acuity during the first two years of life. DHA affects how infants develop their vision. The visual system is extremely underdeveloped in newborns, especially preterm infants, and it rapidly matures in the first year of life. Early life exposure to the right fatty acid supply has been linked to improved visual development. [23].

An acuity card referential gazing test conducted at two and four months of age showed that preterm infants treated with marine oil, a high source of DHA, had superior visual acuity than the control group. These findings were reported in a 1993 first study. Electroretinography and the visual evoked potential (VEP) measure improved retinal function when DHA and ARA supplements were used. The retina's lipid makeup affects rhodopsin's capacity to produce a visual nerve impulse. The increased concentration of DHA and ARA in the retinal membrane helps to regulate the proper transmission of visual signals. [24].

### Infant formula of DHA and ARA

Breast milk or term formulas with added DHA and ARA can provide infants with the right amount of these fats. Different DHA and ARA formulas have been created by numerous organizations and foundations. In the US, the majority of formula manufacturers add DHA and ARA as supplements to infant formula. Based on global averages for the amounts of ARA and DHA in human milk, infant formulae normally contain 140 mg of ARA and 100 mg of DHA per day, respectively. As a result, baby formula provides ARA and DHA at levels comparable to those in human milk.

**Table 1:** Organizations and foundations on the addition of DHA and ARA to infant formulas

Organization or Foundation	Percent Fatty Acids DHA	Percent Fatty Acids ARA
British Nutrition Foundation	0.4	0.4
Food and Agricultural Organization of the United Nations/World Health Organization expert panel	0.35	0.7
Expert panel convened by the International Society for the Study of Fatty Acids and Lipids	0.35	0.5

### CONCLUSION

DHA and ARA supplements and their sources support early language development, brain and cognitive growth, learning capacity, and IQ assessment in both adults and infants. Worldwide, baby formulae have included DHA and ARA for more than a decade in an effort to mimic the nutritional profile and functional advantages of human milk. Numerous studies have demonstrated the safety of combining ARA and DHA in newborn formulae for millions of babies worldwide. Formulas with added DHA and ARA also help to strengthen the retina's cells, which greatly enhances visual acuity and visual-motor function. In conclusion, adding DHA and ARA to baby formulae promotes the development of their eyes and brains.

### REFERENCES

1. Innis SM., 2003. Perinatal biochemistry and physiology of long-chain polyunsaturated fatty acids. *J Pediatr.* 143(4), Pages 1-8 Doi: 10.1067/s0022-3476(03)00396-2.
2. Pankaj Garg, Ranjan Kumar Pejaver, Manpreet Sukhija, et al, 2017. Role of DHA, ARA, & phospholipids in brain development. An Indian perspective *Clinical Epidemiology and Global Health* 5 Doi: <https://doi.org/10.1016/j.cegh.2017.09.003>.
3. Hadley, K.B., Ryan, A.S., et al, 2016. The essentiality of arachidonic acid in infant development. *Nutrients.* 8(4), Pages 216. Doi: 10.3390/nu8040216.
4. Innis, S., 2008. Dietary omega 3 fatty acids and the developing brain. *Brain Res.* 1237: 35–43

Doi:10.1016/j.brainres.2008.08.078.

5. Molendi-Coste O, Legry V, Leclercq I A., 2011. Why and How Meet n-3 PUFA Dietary Recommendations? *Gastroenterol Res Pract.* 3640406. Doi: 10.1155/2011/364040.
6. Cetin I., Alvino G., Cardelluccio M., 2009. Long chain fatty acids and dietary fats in fetal nutrition. *J. Physiol.* 587(14), Pages 3441–3451. Doi: 10.1113/jphysiol.2009.173062.
7. Joardar A., Sen A.K., Das S., 2006. Docosahexaenoic acid facilitates cell maturation and  $\beta$ -adrenergic transmission in astrocytes. *J. Lipid Res.* 47(3), Pages 571–581. Doi: 10.1194/jlr.M500415-JLR200.
8. Judge MP, Harel O, Lammi-Keefe CJ, 2007. A docosahexaenoic acid-functional food during pregnancy benefits infant visual acuity at four months of age. *Lipids* 42(4), Pages 117–122. Doi: 10.1007/s11745-006-3007-3.
9. Birch EE, Castaneda YS, Wheaton DH, et al, 2005. Visual maturation of term infants fed long-chain polyunsaturated fatty acid-supplemented or control formula for 12 mo. *Am J Clin Nutr.* 81(5), Pages 871–879 Doi:10.1093/ajcn/81.4.871.
10. Meldrum S, Simmer K., 2016 Docosahexaenoic acid and neurodevelopmental outcomes of term infants. *Ann Nutr Metab.* 69 (1), Pages 22–28. Doi: 10.1159/000448271.
11. Birch EE, Carlson SE, Hoffman DR, et al, 2010. The diamond (DHA intake and measurement of neural development) study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. *Am J Clin Nutr.* 91(4), Pages 848–859. Doi:10.3945/ajcn.2009.28557.
12. Strokin M, Sergeeva M, Reiser G, 2004. Role of Ca<sup>2+</sup>-independent phospholipase A2 and n-3 polyunsaturated fatty acid docosahexaenoic acid in prostanoid production in brain: perspectives for protection in neuroinflammation. *Int J Dev Neurosci.* 22(7), Pages 551–557. Doi:10.1016/j.ijdevneu.2004.07.002.
13. Auestad N, Scott DT, Janowsky JS, et al, 2003. cognitive, and language assessments at 39 months: a follow-up study of children fed formulas containing long-chain polyunsaturated fatty acids to 1 year of age. *Paediatrics.* Sep; 112(3), Pages 177-183. Doi: 10.1542/peds.112.3.e177.
14. Calder, P. C., 2016. Docosahexaenoic Acid. *Annals of Nutrition and Metabolism,* 69(1), Pages 8–21 Doi: 10.1159/000448262.
15. Forsyth, S., Gautier, S., & Salem, N., 2017. The importance of dietary DHA and ARA in early life: a public health perspective. *Proceedings of the Nutrition Society,* 76(04), Pages 568–573. Doi: 10.1017/s0029665117000313.
16. Martinez M. 1992. Tissue levels of polyunsaturated fatty acids during early human development. *J Pediatr.* 120(2), Pages 129-138. Doi: 10.1016/s0022-3476(05)81247-8.
17. Oken E, Kleinman KP, Berland WE, et al, 2003. Decline in fish consumption among pregnant women after a national mercury advisory. *Obstet Gynecol.* 102(2), Pages 346-351. Doi: 10.1016/s0029-7844(03)00484-8.
18. Welch, A.A.; Shakya-Shrestha, S.; et al, 2010. Dietary intake and status of n-3 polyunsaturated fatty acids in a population of fish-eating and non-fish-eating meat-eaters, vegetarians, and vegans and the precursor-product ratio of -linolenic acid to long-chain n-3 polyunsaturated fatty acids: Results from the EPIC-Norfolk cohort. *Am. J. Clin. Nutr.* 92(4), Pages 1040–1051 Doi: 10.3390/nu14010128.
19. Whelan, J.; Jahns, L.; Kavanagh, et al, 2009. Docosahexaenoic acid: Measurements in food and dietary exposure. *Prostaglandins Leukot. Essent. Fatty Acids* 81(5), Pages 133–136. Doi: <https://doi.org/10.1016/j.plefa.2009.05.008>.
20. Crawford, M.A.; Bloom, M.; Cunnane, S.; et al, 2001. Docosahexaenoic acid and cerebral evolution. *World Rev. Nutr. Diet.* 88(6), Pages 6–17. Doi: 10.1159/000059743.
21. Koletzko B, Carlson SE, van Goudoever JB. 2015. Should infant formula provide both omega-3 DHA and omega-6 arachidonic acid? *Ann Nutr Metab.* 66(5), Pages 137–138. Doi:10.1093/ajcn/nqz252.
22. Lauritzen L, Fewtrell M, Agostoni C., 2015. Dietary arachidonic acid in perinatal nutrition: a commentary. *Pediatr Res.* 77(2), Pages 263–269. Doi: 10.1038/pr.2014.166.
23. Tiwari A, Dwivedi D, Shukla AK, et al, 2022. Understanding the Role of  $\omega$ -3 polyunsaturated fatty acids on autoimmunity AAP Advances in Nutraceuticals. CRC press Taylor & Francisgroup. Pages 145-155. Doi:10.1080/14737140.2018.1524299.
24. Sandeep Arya, Sreevani Rentala, 2021. Mental status examination: an assessment key to rehabilitation with implication in nursing. *Jour. of Med. P'ceutical & Alli. Sci.* 10(3), Pages 2753-2757. Doi: 10.22270/jmpas.V10I3.1111.