Medical Nutrition
Whitepaper | January 2020

Nutritional lipids in medical nutrition solutions

dsm-firmenich

Contents

Omega-3 DHA and EPA for better patient and senior care

Life expectancy is increasing on a global scale and the prevalence of age and lifestyle-related noncommunicable diseases (NCDs), such as cancer, Alzheimer's disease, diabetes and cardiovascular conditions, is rising. This has led to patients worldwide presenting with more complex needs, putting significant pressure on healthcare systems globally. To address and manage the nutritional and physiological challenges often associated with these conditions, and to reduce the risk of and improve recovery from disease, there is a growing need for targeted medical nutrition solutions.

While nutritional lipids, such as the long-chain omega-3 fatty acids (n-3 LCPUFAs), docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are well-known to play a vital role in human health and overall wellbeing, their relevance in medical nutrition is becoming more and more apparent. Mounting evidence now indicates the benefits of DHA and EPA in reducing medical complications and supporting the management of specific medical needs in areas such as oncology, perioperative care and brain health. Furthermore, research indicates that solutions containing DHA and EPA may also provide cognitive and mobility health benefits for the elderly; contributing to improved quality of life. This whitepaper outlines the latest science on nutritional lipids, containing DHA and EPA, for medical nutrition solutions, with a focus on the specific patient groups that would benefit most from DHA and EPA intervention.

Why is n-3 LCPUFA nutritional lipid intake and status important?

Omega-3 LCPUFAs are one of the most researched nutrients in the world. Indeed, there are more than 36,000 scientific papers, including more than 4,000 human clinical trials, dedicated to the research of the role of omega-3 fatty acids in heart, brain and eye health, and also specific benefits during pregnancy and infancy.[1] DHA and EPA, in particular, are essential to maintaining overall health, with studies indicating that they support the development and maintenance of proper brain function, the visual process, immune and inflammatory responses and the production of hormone-like molecules.

Moreover, the European Food Safety Authority (EFSA) recognizes that DHA and EPA have cardiovascular health benefits, with well-researched links to healthy blood pressure and healthy heart function.[2]

As additional human studies are published, the importance of obtaining an adequate intake of n-3 LCPUFAs in the diet, via fish or microalgal sources, becomes more evident. However, despite the significance of omega-3 fatty acids in human health, DHA and EPA status is considered low in many populations globally, particularly in the Western world, and intake is often below the recommended levels of 250-500 mg/day.[3] Moreover, some patients and the elderly may experience difficulties swallowing or lose their appetite as they age, widening the nutrient gap even further. Given the significant health benefits that DHA and EPA provide throughout life and also their increasingly recognized role in disease prevention, this indicates the need for increased DHA and EPA levels through innovative nutritional solutions.

How DHA and EPA work in the human body

The search for the molecular and cellular mechanisms by which omega-3 fatty acids affect (patho)-physiological pathways has led to a large body of evidence which suggests that these nutritional lipids modulate numerous processes, including brain and visual development, inflammatory reactions, thrombosis and carcinogenesis. But how can these nutrients affect so many seemingly unrelated functions in different cell types and tissues?

Following consumption, omega-3 fatty acids are incorporated into cell membranes in all tissues of the body. Whether the source of DHA and EPA was from fish, fish-oil supplements or microalgae, measurable changes in cellular membrane content occur within days of increasing the daily consumption of these fatty acids. Cellular membranes from some tissues, like the retina and brain, are particularly enriched with these fatty acids. The high concentrations of DHA and EPA in these tissues suggests that they may play a significant role in maintaining healthy cell function.

With regards to their effect on cells, DHA and EPA act via overlapping but distinct mechanisms that are mainly membrane-mediated and modify cell function to benefit overall health and wellbeing, as well as reduce the risk and severity of disease (Figure 1). This happens because DHA and EPA are incorporated into the phospholipid bilayer of cell membranes and exposed to many different extracellular and intracellular signaling molecules (lipids and proteins). The interactions between these nutrients and other components of cell membranes can affect the cell membrane structure – fluidity, flexibility, permeability and the activity of membrane-bound enzymes – and hence the cell function. Moreover, omega-3 fatty acids are shown to play an important role in cell signaling and neurotransmission, cell division, gene expression and lipid mediator production. For instance, DHA and EPA can affect the formation of lipid rafts – a microdomain in the plasma membrane involved in cell signaling – leading to changes in gene expression and protein synthesis.[4]

In addition, the inflammation resolving effects of long-chain omega-3 fatty acids have also been established in many animal and clinical studies.[5,6,7] This is significant when you consider that many human diseases and conditions involve chronic inflammation, including arthritis, asthma, cancer, obesity and type-2 diabetes, as well as wasting disorders like cancer cachexia and sarcopenia. The possible application of DHA and EPA as inflammation resolving agents is therefore promising in terms of the potential prevention of the disease and supporting disease treatment.

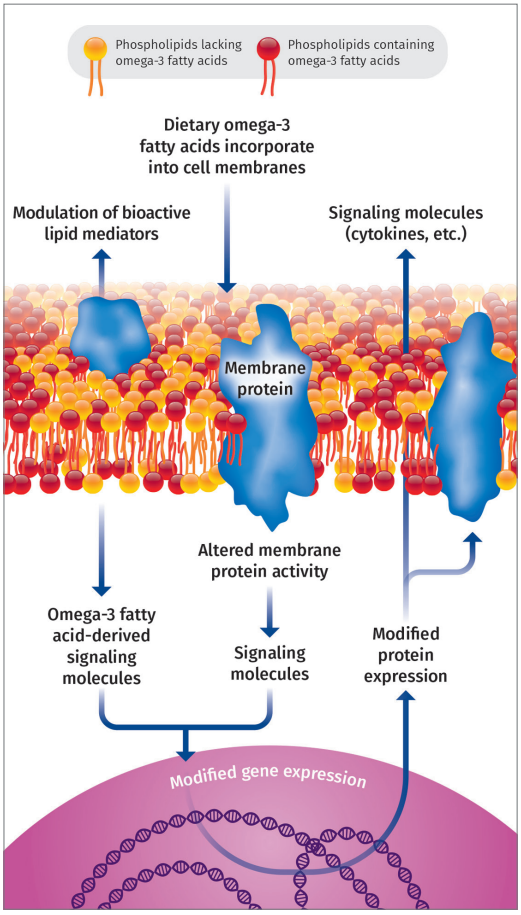


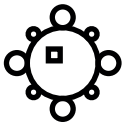
Figure 1: Cell membrane showing omega-3 fatty acids incorporated into the phospholipid bilayer. Omega-3 fatty acids can modify gene and protein expression, modulate membrane protein activity and act as a reservoir for bioactive molecules[8]

Nutritional care to counter immunosenescence

As patients and senior adults are more vulnerable to risk of infection and disease, nutritional support is extra critical in clinical settings.

In fact, the right nutrition has been widely demonstrated to improve patient outcomes and overall wellbeing. Mounting evidence now indicates that long-chain omega-3 fatty acids play a role in reducing medical complications, can manage the distinct nutritional needs in certain areas such as oncology, perioperative care and brain health and also support independence, subsequently lowering healthcare costs in these specific therapeutic areas.

Below, listed in more detail, are the areas where DHA and EPA-rich nutritional lipids are known to have positive effects on patient outcomes:

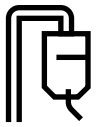


1 Cancer cachexia

Cancer is a major cause of morbidity and mortality worldwide, with incidence of the disease and associated healthcare costs expected to continue to rise significantly in the coming decades. While recent advancements in the field have improved outcomes for patients, the frequent presence of malnutrition in cancer patients and unwanted weight and muscle loss – known as cancer cachexia –can limit their response to therapies.9 Currently cachexia is often not addressed quickly enough, but this is expected to change in coming years as major oncological societies recognize the role of early supportive care and patients become more aware of the benefits of proper nutrition. Moreover, it is estimated that only 50% of drugs approved by the Food and Drug Administration (FDA) are effective.[10] Nutrition may have an important role to play in improving the efficacy of treatment, as well-nourished patients tend to react better to therapy, as well as reducing the impact of side effects associated with cancer treatments.

For example, cachexia correlates with an increased inflammatory response in patients.[11] Nutrients that exhibit anti-inflammatory properties, such as DHA and EPA, appear to be promising adjuncts to therapeutic treatment as part of a multimodal approach to cancer care.[12] Although results have varied, in some clinical settings, DHA and EPA have been shown to improve the immune response of patients, help individuals fight infection, support the effects of cancer therapies, maintain lean body mass and prevent cachexia; giving patients better treatment outcomes and quality of life.[13,14,15]

Despite increasing awareness of DHA and EPA intervention, many oncologists are yet to be convinced by the benefits of nutritional lipids for cancer patients. The reason for this is that nutritional interventions are often given in combination with drug treatments, making it difficult to determine the effect attributable to the nutrition intervention. Moreover, the benefits of DHA and EPA in patient care might be masked by clinical trial inconsistencies due to poor study design, rather than lack of effect. Many oncologists therefore only recommend drug therapies in most cases, although long-chain omega-3 fatty acids intervention, in conjunction with treatment, might be more suitable and promote more positive outcomes. To overcome this challenge, education courses are a great opportunity to increase awareness and support the use of long-chain omega-3 fatty acids in medical nutrition, and nutrition support teams will continue to play a significant role in nutritional care for cancer patients.



2 Nutrition pre- and post-surgery

Many patients, when admitted to hospital, present with malnutrition, which is a serious risk factor for surgical complications. Malnourished patients are more likely to experience longer hospital stays, increased risk of infection and higher mortality rates.[16,17,18] Elderly individuals, for example, are a high-risk patient group for surgery, at least partially because their nutritional status is often poor when entering the hospital due to a range of factors including so-called 'anorexia of aging'.

To reduce the risk of complications, the Enhanced Recovery After Surgery (ERAS) concept promotes perioperative clinical nutrition, i.e. integration of nutrition into the overall management of the patient, avoidance of long periods of pre-operative fasting and the re-establishment of oral feeding as early as possible after surgery.[19] Studies indicate that preoperative and perioperative DHA and EPA supplementation can help to reduce inflammation and risk of infection when provided in conjunction with arginine, sometimes glutamine, nucleotides and various vitamins and trace minerals.[20,21,22,23] Known as immuno-nutrition, due to the benefits of this nutrient composition on the immune system, this type of nutritional rehabilitation promotes improved healing, reduces complications, and shortens recovery time and length of hospital stays.[24]

However, the clinical outcomes appear to be inconsistent and more well-designed trials are required to give strong recommendations for immuno-nutrition use in surgery patients. Despite this, immuno-nutrition containing DHA and EPA is increasingly recommended by experts for patients at risk of or are malnourished in the perioperative period.[25,26,27]

3 Sarcopenia in the elderly population

As individuals age, achieving adequate intake of essential nutrients becomes even more difficult because of changing hormone levels, slower metabolism, decreased activity levels and lower bioavailability, which leads to reduced energy requirements and nutritional frailty.[28] Moreover, older individuals frequently fail to ingest adequate amounts of food to meet their essential energy and nutrient requirements. A major contributing factor to under-nutrition and adverse health outcomes in the geriatric population, 'anorexia of aging' is defined by a decrease in appetite and/or food intake in old age. In addition, commonly used medications for chronic conditions can alter nutrient requirements by interacting in ways that may affect absorption or metabolism. This means that older individuals need foods or nutritional solutions that provide higher nutrient density to achieve adequate intakes, however, nutritional shortfalls or even deficiencies are often overlooked.

Currently, it is estimated that up to 40% of people worldwide suffer from age-related degenerative loss of skeletal muscle mass, quality and function, also known as sarcopenia (depending on the definition used).[29] However, reports suggest that the total population diagnosed with sarcopenia will grow to 500 million by 2050, due to increasing life expectancy.[30] The disease has multi-factorial causes, resulting in decreased quality of life, surgical outcomes and immune function, as well as increased mortality, healthcare costs and length of hospital stays; emphasizing the need for preventative and treatment strategies to address the condition.[31,32]

Age-related chronic low-grade inflammation may be an important contributor for sarcopenia, with studies showing that the disease is associated with higher serum inflammatory parameters. Highly inflammatory cytokines are negatively related to muscle strength and mass, for instance, and have demonstrated to prompt muscle wasting and suppress muscle synthesis.[33] Exercise and protein supplementation can help to slow down sarcopenia, however long-chain omega-3s may also have a key role to play. The anti-inflammatory effects of DHA and EPA, for example, could be beneficial in mitigating the loss of muscle strength and physical performance associated with aging by targeting the age-related low-grade inflammation that contributes to the development of the disease. Moreover, n-3 LCPUFAs may modulate muscle protein synthesis, promoting muscle strength and function.[34] To improve the quality of life of the senior population, long-term DHA and EPA supplementation is therefore of great interest as it is simple to administer, safe and low cost.

4 Brain health

With a growing aging population, cognitive performance and mental wellbeing are two of the biggest health and wellbeing challenges. For instance, there are currently 50 million individuals living with dementia globally – a leading cause of disability, malnutrition and decreased independence among older people.[35] With this number expected to treble to more than 152 million by 2050, and no treatment currently available, the development of innovative medical nutrition solutions that will offer preventative measures and support brain and cognitive health is critical.

Research has indicated risk factors for cognitive decline; one of which is low intake of long-chain omega-3 fatty acids. Some studies, for example, have observed lower DHA and EPA concentrations in individuals with mild cognitive impairment or dementia compared to subjects not impaired.[36,37,38] In fact, 22% of dementia cases may have developed as a result of inadequate omega-3 consumption.[39]

The link between DHA and brain health is clear when considering that DHA represents the majority of fatty acids in the brain and is an important component in the membranes of the brain and eyes. Research also shows that omega-3 fatty acids are associated with decreased brain inflammation and preservation of brain function.[40] Furthermore, several clinical studies have confirmed that DHA supplementation in older adults may support cognitive outcomes, with more recent studies and reviews underlying the benefits of DHA status and cognitive function, cognitive decline or dementia.[41,42]

However, research outcomes to date have varied, which is likely due to inconsistencies such as trial duration, intervention dosage, interactions between omega-3 fatty acids and medications or other nutrients, such as B vitamins, and baseline assessments of omega-3 levels not being determined before the research commenced.[43] Despite this, and because the positive evidence is strong, some experts recommend that omega-3 supplementation is given to individuals with mild cognitive impairment to help slow progression of the disease.[44]

Adapting nutrition to specific medical needs

Evidently, the specific patient groups mentioned could benefit from medical nutrition products containing omega-3 fatty acids. In combination with drug therapies and exercise, solutions containing DHA and EPA could boost the quality of life and clinical outcomes of patients globally, and lower healthcare costs. However, research also indicates the potential beneficial role that DHA and EPA nutritional intervention could have for other patients too, such as those with diabetes or chronic kidney disease.[45,46,47]

With each condition presenting different and complex nutritional and clinical needs, the development of tailored nutrition solutions that can be targeted to specific conditions, are appealing to consume and work on an individual level is critical. Furthermore, despite the available observational and preclinical evidence signaling the beneficial effects of DHA and EPA in clinical settings, a major roadblock for the widespread acceptance and use of DHA and EPA in medical nutrition is the lack of consistent clinical data from well-designed and randomized controlled trials.

Only continued in-depth scientific research and patient insights will help to improve our understanding of the malnutrition challenge and the impact of specific ingredients on the quality of life of patients and elderly. In turn, this data will inspire the creation of more appealing, palatable delivery formats that overcome compliance issues and promote overall health. To further bridge knowledge gaps and innovate in the field of medical nutrition for specific therapeutic areas, experts highlight the importance of more well-designed trials to explore the effects of omega-3 fatty acids in specific conditions, as well as the optimal ratio for treatment, to give strong recommendations for DHA and EPA use. Moreover, with advances in reliable and precise diagnostics, new medical nutrition solutions entering the market have the potential to be better tailored towards individual patient needs. With this in mind, nutrition experts recommend that DHA and EPA are integrated into multimodal interventions combined with additional nutrients and exercise, where relevant, to optimize medical care in specific therapeutic conditions.[48]

dsm-firmenich: your preferred partner for medical nutrition

dsm-firmenich is a global purpose-led, science-based company active in Nutrition, Health and Sustainable Living. We offer high quality ingredients, customized premixes and expert services for medical nutrition solutions to solve challenges we face in keeping the world's growing population healthy and improving quality of life for patients and the elderly.

With unparalleled scientific heritage, our unique understanding of the nutritional needs for specific conditions and a human-centric approach, we create advanced medical nutrition solutions.
The combination of our high quality ingredients and application expertise ensures elevated product features and compliance. We partner and innovate to shape a favorable market environment and deliver improved patient and elderly care.

We provide a broad range of proven nutritional ingredients that meet the highest safety and quality requirements. From vitamin straights as individual ingredients, including vitamins as active pharmaceutical ingredients (APIs) for parenteral nutrition, to nutrients such as omega-3 fatty acids — including DHA and EPA from marine and microalgae sources — our high-quality ingredients can be used in a range of medical nutrition formulations. Our global blending capabilities allow for the creation of fully customizable premixes, including nutrient blends of desired functional ingredients – vitamins, minerals, amino acids, hydrocolloids, nutraceuticals and more – in one single efficient homogenous premix. As well as a strong scientific heritage and diverse ingredients portfolio, we offer a broad range of expert services across our global network. These services support the development of medical nutrition solutions that successfully address the nutritional needs of patients and the elderly with specific conditions.

For more information on how dsm-firmenich can support you in the development of innovative and customized medical nutrition solutions, including those that contain omega-3s DHA and EPA, visit: www.dsm-medicalnutrition.com

References

1. GOED, 'About EPA and DHA' [website], https://goedomega3.com/about-epa-and-dha, accessed 11 December 2019.
2. EFSA Scientific Opinion on the substantiation of health claims related to eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), docosapentaenoic acid (EPA) and maintenance of normal cardiac function, EFSA Journal, vol. 8, no. 10, 2010.
3. K. D. Stark et al., 'Global survey of the omega-3 fatty acids, docosahexaenoic acid and eicosapentaenoic acid in the blood stream of healthy adults', ELSEVIER, vol. 63, pg. 132-152, 2016.
4. C. de Carvalho et al., 'The various roles of fatty acids', Molecules, vol. 23, no. 10, pg. 2583, 2018.
5. S. Dyall, 'Long-chain omega-3 fatty acids and the brain: a review of the independent and shared effects of EPA, DPA and DHA', Front Aging Neurosci., vol. 7, no. 52, 2015.
6. A. Molfino et al., 'Omega-3 polyunsaturated fatty acids in critical illness: anti-inflammatory, proresolving, or both?', Oxidative Medicine and Cellular Longevity, 2017.
7. P. Calder, 'Omega-3 polyunsaturated fatty acids and inflammatory processes: nutrition or pharmacology?', British Journal of Clinical Pharmacology, vol. 75, no. 3, 2012.
8. M. E. Surette, 'The science behind dietary omega-3 fatty acids', CMAJ, vol. 178, no. 2, pg. 177-180, 2008.
9. T. Aoyagi et al., 'Cancer cachexia, mechanism and treatment', World J Gastrointest Oncol., vol. 7, no. 4, pg. 17-29, 2015.
10. C. Davis et al., 'Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13', BMJ, 2017.
11. J. Onesti et al., 'Inflammation based regulation of cancer cachexia', Biomed Research International, 2014.
12. R. Freitas et al., 'Protective effects of omega-3 fatty acids in cancer-related complications', Nutrients, vol. 11, no. 5, pg. 945, 2019.
13. E. Bruera et al., 'Effect of fish oil on appetite and other symptoms in patients with advanced cancer and anorexia/cachexia: a double-blind, placebo-controlled study', J Clin Oncol., vol. 21, pg. 129-134, 2003.
14. M. D. Barber et al., 'Fish oil-enriched nutritional supplement attenuates progression of the acute-phase response in weight-losing patients with advanced pancreatic cancer', J Nutr., vol. 21, pg. 1120-1125, 1999.
15. P. Bougnoux et al., 'Improving outcome of chemotherapy of metastatic breast cancer by docosahexanoic acid: a phase II trial', Br J Cancer, vol. 101, no. 12, pg. 1978-1985, 2009.
16. J. D. Williams et al., 'Assessment of perioperative nutrition practices and attitudes – a national survey of colorectal and GI surgical oncology programs', American Journal of Surgery, vol. 213, no. 6, pg. 1010-1018, 2016.
17. S. Awad et al., 'What's new in perioperative nutritional support? Current opinion in anesthesiology', Curr. Opin. Anaesthesiol, vol. 24, no. 3, pg. 339-348, 2011.
18. T. Philipson et al., 'Impact of oral nutritional supplementation on hospital outcomes', American Journal of Managed Care, vol. 19, pg. 121-128, 2013.
19. O. Ljungqvist et al., 'Enhanced recovery after surgery', JAMA Surg., vol. 152, no. 3, pg. 292-298, 2017.
20. A. Weimann et al., 'ESPEN guideline: clinical nutrition in surgery', Clinical Nutrition, vol. 36, pg. 623-650, 2017.
21. S. Bisch et al., 'Impact of nutrition on enhanced recovery after surgery (ERAS) in gynecologic oncology', Nutrients, vol. 11, no. 5, 2019.
22. N. Johnson, 'Enhanced recovery after surgery: the role of nutrition', BSNA, no. 130, pg. 19-22, 2018.
23. J. Xu et al., 'Immunonutrition in surgical patients', Curr Drug Targets, vol. 10, no. 8, pg. 771-777, 2009.
24. P. Calder, 'Immunonutrition may have beneficial effects in surgical patients', BMJ, vol. 327, no. 7407, pg. 117-118, 2003.
25. P. E. Wischmeyer et al., 'American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Nutrition Screening and Therapy Within a Surgical Enhanced Recovery Pathway', Anesth Analg., vol. 126, no. 6, pg. 1883-1895, 2018.
26. A. Weimann et al., 'ESPEN guideline: Clinical nutrition in surgery', Clinical Nutrition, vol. 36, no. 3, pg. 623-650, 2017.
27. S. A. McClave et al., 'Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)', JPEN, vol. 40, no. 2, pg. 159-211, 2016.
28. D. Remond et al., 'Understanding the gastrointestinal tract of the elderly to develop dietary solutions that prevent malnutrition', Oncotarget, vol. 6, no. 16, pg. 13,858-98, 2015.
29. A. J. Mayhew et al., 'The prevalence of sarcopenia in community-dwelling older adults, an exploration of differences between studies and within definitions: a systematic review and meta-analysis', Age Ageing, vol. 48, no. 1, pg. 48-56, 2019.
30. T. Hida et al., 'Managing sarcopenia and its related-fractures to improve quality of life in geriatric populations', Aging Dis., vol. 5, no.4, pg. 226-237, 2014.
31. J. Friedman et al., 'Implications of sarcopenia in major surgery', Nutr Clin Pract., vol. 30, no. 2, pg. 175-179, 2015.
32. S. L. Bokshan et al., 'Sarcopenia in orthopedic-surgery', Orthopedics, vol. 39, no. 2, pg. 295-300, 2016.
33. J. Wang et al., 'Inflammation and age-associated skeletal muscle deterioration (sarcopenia)', Journal of Orthopaedic Translation, vol. 10, pg. 94-101, 2017.
34. J. Dupont et al., 'The role of omega-3 in the prevention and treatment of sarcopenia', Aging Clin Exp Res., vol. 31, no. 6, pg. 825-836, 2019.
35. WHO, Dementia factsheet, https://www.who.int/news-room/fact-sheets/detail/dementia, accessed 19 September 2019.
36. S. C. Cunnane et al., 'Docosahexaenoic acid homeostasis, brain aging and Alzheimer's disease: can we reconcile the evidence', Prostaglandins Leukot. Essent. Fatty Acids, vol. 88, no. 1, pg. 61-70, 2013.
37. S. S. Lopes et al., 'Plasma nutrient status of patients with Alzheimer's disease: systematic revew and meta-analysis', Alzheimer's Dement., vol. 10, no. 4, pg. 485-502, 2014.
38. M. C. de Wilde et al., 'Lower brain and blood nutrient status in Alzheimer's disease: results from meta-analyses', Alzheimer's Dement. vol. 3, no. 3, pg. 416-431, 2017.
39. M. Beydoun et al., 'Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis', BMC Public Health, vol. 14, no. 643, 2014.
40. C. Janssen et al., 'Long-chain polyunsaturated fatty acids (LCPUFA) from genesis to senescence: the influence of LCPUFA on neural development, aging and neurodegeneration', Prog. Lipid Res., vol. 53, pg. 1-17, 2014.
41. S. Canhada et al., 'Omega-3 fatty acids' supplementation in Alzheimer's disease: a systematic review', Nutr. Neurosci., vol. 21, no. 8, pg. 529-538, 2018.
42. Y. Zhang et al., 'Intakes of fish and polyunsaturated fatty acids and mild-to-severe cognitive impairment risks: a dose-response meta-analysis of 21 cohort studies', Am J Clin Nutr., vol. 103, no. 2, pg. 330-340, 2016.
43. A. Oulhaj et al., 'Omega-3 fatty acid status enhances the prevention of cognitive decline by B vitamins in mild cognitive impairment', Journal of Alzheimer's Disease, vol. 50, no. 2, pg. 547-557, 2016.
44. ESPEN Congress, dsm-firmenich expert roundtable: Emerging benefits of EPA and DHA in medical nutrition concepts, 31 Aug–3 September 2019.
45. J. Bosch et al., 'ORIGIN Trial Investigators: n-3 fatty acids and cardiovascular outcomes in patients with dysglycemia', N Engl J Med., vol. 367 pg. 309-18, 2012.
46. J. Hu et al., 'Omega-3 fatty acid supplementation as an adjunctive therapy in the treatment of chronic kidney disease: a meta-analysis', Clinics (Sao Paulo), vol. 72, no. 1, pg. 58-64, 2017.
47. ESPEN 'Nutrition management in chronic kidney diseases and after transplantation', 32nd ESPEN Congress, 2010.
48. (Op. Cit. ESPEN 2019).

dsm-firmenich