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Towards sustainable sources for omega-3 fatty acids production

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Omega-3 fatty acids eicosapentaenoic acid (EPA) and docohexaenoic acid (DHA), provide significant health benefits for brain function/development and cardiovascular conditions. However, most EPA and DHA for human consumption is sourced from small fatty fish caught in coastal waters and, with depleting global fish stocks, recent research has been directed towards more sustainable sources. These include aquaculture with plant-based feeds, krill, marine microalgae, microalgae-like protists and genetically-modified plants. To meet the increasing demand for EPA and DHA, further developments are needed towards land-based sources. In particular large-scale cultivation of microalgae and plants is likely to become a reality with expected reductions in production costs, yield increasese and the adequate addressing of genetically modified food acceptance issues.

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Introduction

On the basis of their proven health benefits, global demand for omega-3 fatty acids has significantly increased over the last two decades, but there is mounting concern about the sustainability of sourcing these compounds from wild fish. Figure 1 presents an overview of different sources of omega-3 fatty acids and how they link to the food and supply chain. In this review, we present alternative sources of omega-3 fatty acids and discuss recent developments towards their sustainable production.

Very long chain polyunsaturated fatty acids (VLC-PUFAs), are fatty acids (FAs) of ≥20 carbons in length and at least two conjugated double bonds in the *cis* position. VLC-PUFAs are divided into two main groups, omega-3 (ω-3) and omega-6 (ω-6), which are distinguished by the first double bond position counted from the methyl end at carbon 3 and 6, respectively [1]. Nutritionally, C20:5 eicosapentaenoic acid (EPA) and C22:6 docohexaenoic acid (DHA) are the most important VLC-PUFAs belonging to the ω-3 family. Out of the ω-6 family, C18:1 alfa linoleic acid (ALA) [2] and C20:4 arachidonic acid (AA) [3] have also been shown to have health benefits. There is a considerable amount of research that supports the beneficial health properties of VLC-PUFAs, particularly the ω-3 FAs [4].

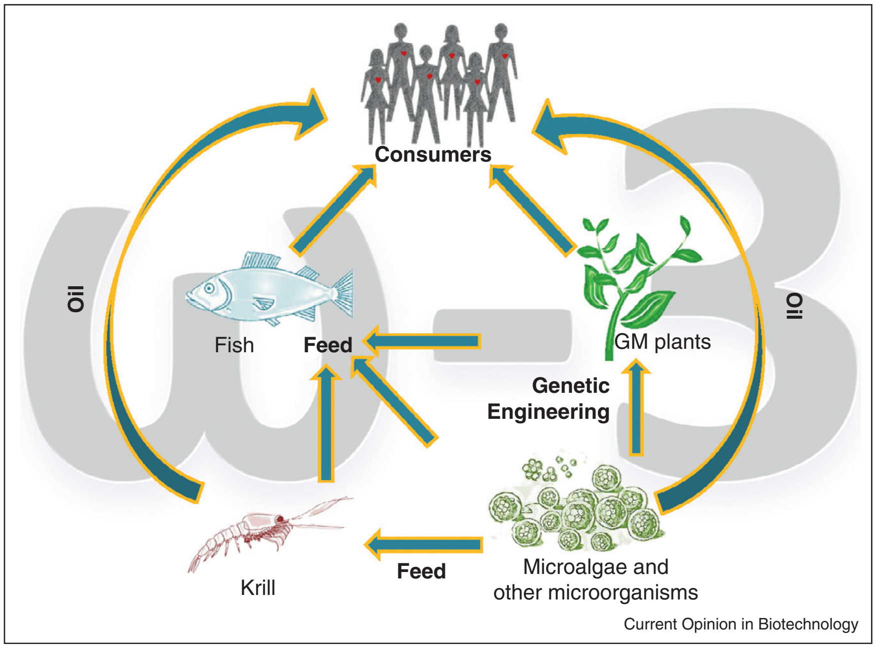
VLC-PUFAs are essential constituents of higher vertebrate membranes, particularly neuronal cells in humans [5]. The consumption of EPA and DHA has been reported to prevent and support cardiovascular, nervous systems and inflammatory conditions. Regarding cardiovascular benefits by regular consumption of ω-3, hypertension risk, cardiac arrhythmia, myocardial infarction and thrombosis can be reduced [4]. They exhibit positive effects on brain function [6], healthy development of the fetal brain [7] and as such are commonly included in infant formula. They have also been related with alleviation of depression symptoms [8] and post natal depression [9]. Contributions to the immune-modulatory effects, such as treating Crohn's disease, psoriasis, rheumatoid arthritis, ulcerative colitis, cystic fibrosis and lupus have also been made [10•].

However, present average daily intakes of EPA and DHA for most people is well below the recommended doses and there is growing concern about the sources that are often viewed as unsustainable and unable to meet future demands [11]. Wild fish has been the most common source of EPA and DHA for human consumption in the last decades [12] and is at great risk of being overfished [13]. The global demand for wild fish is now much larger than the oceans can sustain [14]. The Food and Agriculture Organization (FAO) reported in 2008 that nearly 53% of marine fish stocks were close to be entirely exploited, 28% overexploited and 3% depleted or recuperating from depletion (1%) [15]. Populations of some fish have been deflated to only 10% and over 100 species have been already confirmed extinct in the ocean [16]. Worldwide fish stocks could be depleted within 40 years if harvests continue at the current rate [4]. Concern about the ability and sustainability of wild fisheries to meet increasing demand of VLC-PUFAs has moved efforts towards land-based production, including farmed fish, genetically modified plants, and large-scale production of microalgae [1] (Figure 1). The estimated market value of packaged products containing omega-3 has been estimated to reach $34.7 billion by 2016 [17••].

Aquaculture

Aquaculture is currently the fastest growing food production industry, with an annual average of 8.3% increase

Figure 1



Food and supply chain of different sources of omega-3 fatty acids.

since the 1970s [18•]. Farming seafood and fish has been one of the strategies to reduce over-fishing in wild populations, yet this practise is heavily reliant on addition of formulated feeds composed of wild caught fish to enhance fish VLC-PUFAs content. Fish typically require diet supplementation of FA for improved EPA and DHA synthesis when being farmed [1]. Fishmeal and fish oil are the main ingredients of formulated feeds used to supply protein and FA requirements, but plant-based additives from soybean, canola, wheat, linseed, flaxseeds, including crude palm oil for freshwater fish [19], as well as some marine organisms such as krill and microalgae [1] (Figure 1), presented mostly positive effects on growth performance and nutritional content of aquaculture-farmed animals.

Bioengineered plants

Plants and plant seeds have been widely used as a direct source of PUFA. However, higher plants lack the natural capacity to synthesize VLC-PUFA such as EPA and DHA [1]. The predominant ω-6 and ω-3 found in most seed oils are C18 FAs including linoleic acid (LA 18:2 Δ-9,12) and α-linoleic acid (ALA C18:3 Δ-9,12,15) [1]. These are associated with prevention of vision and brain function impairments, as well as stroke occurrence [20]. The conversion of native plant FAs such as LA and ALA to VLC-PUFA requires several FA elongases and desaturases that are not present in higher plants [21]. Considerable efforts have been made to improve the composition of vegetable oil, and tremendous progress has been made by developing the seed VLC-PUFA biosynthesis pathway by producing the required enzymes in plants [1]. The production of EPA and DHA in plants is currently implemented by utilizing algal, bacterial and yeast genes involved in the PUFA biosynthetic pathway.

There are two predominant pathways for VLC-PUFA synthesis in nature: (1) the conventional (aerobic) fatty acid desaturation/elongation pathway, and (2) the anaerobic polyketide synthase pathway (PKS) [22•]. The PKS pathway has been found in numerous marine bacteria (e.g. actinobacteria, cyanobacteria and proteobacteria) and eukaryotes (e.g. the fungus *Schizochytrium*) where it often coexists with the conventional pathway [5]. The aerobic pathway for producing VLC-PUFA has been introduced into *Arabidopsis*, soybean and canola [1,21]. The genes encoding the enzymes Δ6-desaturase [35], Δ6/Δ5-desaturase, and Δ6-elongase from the fungus *Mortierella alpine*, which are involved in the conventional pathway have been successfully expressed in soybean [23]. Additionally, the expression of different desaturases from zebrafish and *Caenorhabditis elegans* to generate EPA has been documented. DHA biosynthesis was then conferred by an elongase and a desaturase from *Trypanosoma brucei* and *Thraustochytrium* sp. respectively [24]. A similar study reported the synthesis of DHA in *Arabidopsis* plants using the anaerobic PKS-like pathway derived from *Schizochytrium* together with a phosphopantetheinyl transferase from *Nostoc*, essential for activating the acyl carrier protein domains of the DHA synthase PKS [21]. Substantial