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Stearidonic acid (18:4*n*-3): Metabolism, nutritional importance, medical uses and natural sources

Stearidonic acid (SA, 18:4*n*-3) is a polyunsaturated fatty acid (PUFA) that constitutes the first metabolite of α-linolenic acid (ALA, 18:3*n*-3) in the metabolic pathway leading to $C_{20–22}$ PUFA, such as eicosapentaenoic acid (EPA, 20:5*n*-3), and docosahexaenoic acid (DHA, 22:6*n*-3), which recently have received much attention because of their various physiological functions in the human body. Recently, several studies indicated that dietary SA increased EPA more efficiently than ALA. Thus, vegetable oils containing SA may become a dietary source of *n*-3 fatty acids that is more effective in increasing tissue *n*-3 PUFA concentrations than the current ALA-containing vegetable oils. Nevertheless, few SA sources occur in nature, although there are still a large number of species untested to date. SA has been detected in variable amounts in several species of algae, fungi and animals tissues, but the seeds of some plant families seem to be better sources of SA, especially *Echium* (Boraginaceae) species. This work reviews the nutritional significance, medical uses and natural occurrence of SA.

Keywords: Stearidonic acid, polyunsaturated fatty acids, essential fatty acids.

1 Introduction

Stearidonic acid [SA; moroctic acid; (6*Z*,9*Z*,12*Z*,15*Z*)-octadecatetraenoic acid; Δ6,9,12,15-octadecatetraenoic acid; all-*cis*-6,9,12,15-octadecatetraenoic acid] is a polyunsaturated fatty acid (PUFA) with an 18-carbon chain (C_{18} PUFA) (Fig. 1) and four double bonds in the acyl chain (Fig. 1). Its molecular weight is 276.4, and its melting point is –57 °C [1].

Among C_{18} PUFA, α-linolenic acid (ALA, 18:3*n*-3) and linoleic acid (LA, 18:2*n*-6) are considered essential fatty acids (EFA), whose absence in a normal diet has been described as responsible for the development of a wide range of diseases, such as cardiovascular disorders, inflammatory processes, viral infections, certain types of cancer, and autoimmune disorders [2, 3]. ALA and LA are the precursors of two families of PUFA. The first is the *n*-3 family which, besides SA and ALA, includes $C_{20,22}$ PUFA, such as eicosapentaenoic acid (EPA, 20:5*n*-3) and docosahexaenoic acid (DHA, 22:6*n*-3), which recently have received much attention because of their various physiological functions in the human body. The other one is the *n*-6 family which includes the above-mentioned LA, γ-linolenic acid (GLA, 18:3*n*-6), dihomo GLA (DGLA, 20:3*n*-6), and arachidonic acid (AA, 20:4*n*-6) [4].

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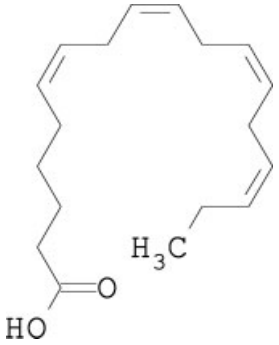

Fig. 1. Stearidonic acid: (6*Z*,9*Z*,12*Z*,15*Z*)-octadecatetraenoic acid.

C_{18} PUFA occur in several fish and plant species, but the seeds of higher plants constitute the richest source. This is because higher plants lack the metabolic pathways to produce PUFA with 20 or more carbons. Thus, LA, ALA, GLA and SA accumulate at variable amounts in plant tissues as terminal fatty acid (FA) metabolites [5]. Conversely, the majority of species of bacteria, microalgae and fungi have the ability to biosynthesize C_{20} and C_{22} *n*-3 and *n*-6 PUFA, such as EPA, AA, docosapentaenoic acid (DPA, 22:5*n*-3) and DHA [6].

Based on dietary estimates for fats and FA from the National Health and Nutrition Examination Survey (NHANES, 1999–2000), for the US population, the mean PUFA intake for men is 20.0 g/day and that for women is 16 g/day (age range 20–59 years), primarily from LA. For

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LA, the mean intake for men is 17.9 g/day and that for women is 13.5 g/day (20–59 years). In contrast, the mean intake of ALA is 1.7 g/day for men and 1.3 g/day for women (20–59 years). For EPA + DPA + DHA, the mean intake for men is 0.17 g/day and that for women is 0.11 g/day (20–59 years) [7]. SA daily intakes are not known. This can be attributed to the fact that the food contents of SA are not included in the food composition tables used to assess diets.

Actually, it is reported that the current "western diet", which is relatively high in *n*-6 and low in *n*-3 PUFA, may not supply the appropriate amounts of PUFA for proper biological functions [8, 9]. Thus, the current *n*-6/*n*-3 PUFA intake ratio may be undesirable, and a ratio more similar to the one our ancestors developed during the crucial evolutionary phase of the Pleistocene could be more appropriate. Therefore, the importance of *n*-3 PUFA in the diet has been recognized, by considering that the *n*-6/*n*-3 intake ratio during this pre-human phase has been estimated to range from 4:1 to 1:1. It seems that the current intake clearly differs from that of our ancestors: Pre-agricultural humans generally consumed ALA and LA in roughly equal amounts [10]. Thus, when considering both that ALA is a DHA precursor and also that DHA occurs largely in the human brain, it might be argued that the probable adequate intake of EFA of pre-humans contributed favorably to human encephalization. Nevertheless, DHA could be ingested directly from some foods. In this sense, there actually exists a controversy about the influence of fish consumption, as an adequate source of DHA, on the evolutionary encephalization process [11].

In any case, it seems that the bioconversion of ALA to EPA and DHA is very low –approximately 6% for EPA and 3.8% for DHA – for a diet rich in saturated fat. Furthermore, with a diet rich in *n*-6 PUFA, the bioconversion is reduced by 40 to 50%. Thus, an *n*-6/*n*-3 PUFA intake ratio lower than 4–6 seems to be reasonable [12]. Restricted conversion to DHA may be critical since evidence has been increasing that this long-chain metabolite has an autonomous function, *e.g.* in the brain, retina and spermatozoa, where it is the most prominent FA [12]. These findings indicate that future attention will have to focus on adequate provision of EPA and DHA, which can reliably be achieved only with their supply through the diet or perhaps with an increased supply of their precursors [12]. Considering the advantaged position of SA with respect to ALA in the metabolic pathway that leads to EPA and DHA, and also in considering its natural occurrence in some seed plants, it is possible that SA could be an adequate precursor of EPA and DHA.

Although the effects of the main *n*-3 PUFA (ALA, EPA, DHA) are fairly well known and have been reviewed elsewhere [13–16], the physiological importance of SA has begun to be recognized only recently. This work reviews the nutritional significance and natural occurrence of SA.

2 Structure and outline of the metabolism of SA in the context of *n*-3 and *n*-6 PUFA pathways

The *n*-6 and *n*-3 pathways for the synthesis of long-chain PUFA in eukaryotes are shown in Fig. 2. Both LA and ALA can be converted to AA and DHA, respectively, by the consecutive action of desaturases and elongases, either starting with an *n*-6 desaturation or with an *n*-9 desaturation. In mammals, the *n*-4 double bond in DHA is the result of a more complicated series of reactions that involve the elongation to a C_{24} FA, a second *n*-6 desaturation, and the final chain shortening in peroxisomes [17]. Both *n*-3 and *n*-6 PUFA are precursors of hormone-like compounds, the eicosanoids, which are involved in many important biological processes in the human body [4, 6]. The *n*-6 and *n*-3 FA are stored in cell membranes of tissues and have two primary functions: They are structural components of the membranes and serve as substrate for the enzymes cyclooxygenase (COX) and lipoxygenase (LO), which convert the *n*-6 and *n*-3 FA into the eicosanoids. The eicosanoids include prostaglandins (PG), thromboxanes (TX) and leukotrienes (LT). Eicosanoids influence several metabolic activities such as platelet aggregation, inflammation and immune function. The net effect of dietary PUFA can be largely attributed to a balance of actions resulting from the change in mediators derived from modifications in AA tissue content as well as the enzymatic pathways responsible for the liberation of AA and its conversion to bioactive eicosanoids. In addition, eicosanoids derived from AA are generally pro-inflammatory, whereas those derived from *n*-3 PUFA tend to inhibit platelet aggregation and to have anti-inflammatory activity [4]. On the other hand, the *n*-6 and *n*-3 pathways are linked in that they both compete for the same desaturase and elongase enzymes. However, these enzymes appear to give preference to the *n*-3 over the *n*-6 pathway [5].

Currently, ALA is the main *n*-3 FA available in vegetable oils [5, 6]. Although there may be cardiovascular benefits associated directly with ALA, there is poor conversion of ingested ALA to the longer-chain *n*-3 FA EPA and DHA [12]. A possible explanation for the low conversion of ALA to EPA is that the initial enzyme, Δ6 desaturase, is rate limiting in humans [18]. Thus, the ingestion of vegetable oils enriched in SA may be an efficient means of increas-

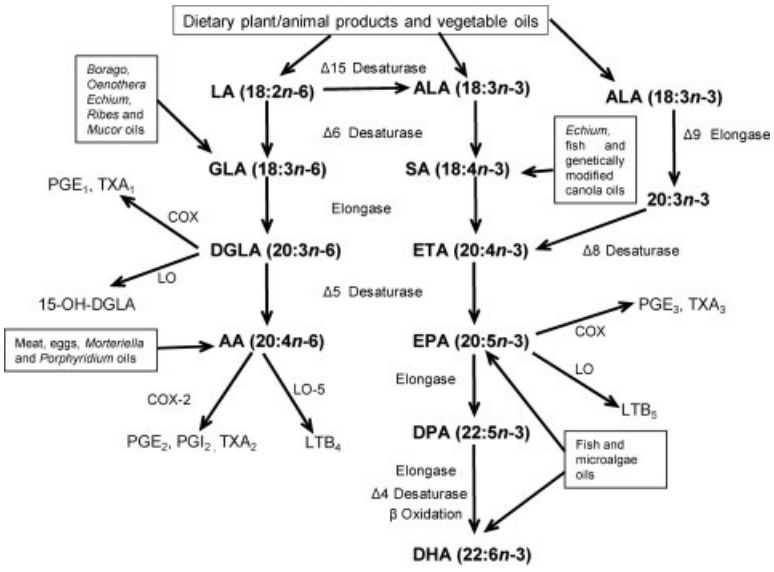

Fig. 2. LA and ALA, the parent compounds of the *n*-6 and *n*-3 PUFA families, are obtained primarily from vegetable oils, but are also found in foods of plant and animal origin. SA has been enriched in genetically modified canola oil. GLA can be found in specialized oils such as borage and evening primrose oils. AA is found only in meats and eggs, and some microbiological sources. EPA and DHA are obtained primarily from fish and microalgae oils. Eicosanoids are produced by COX, LO or cytochrome P450 monooxygenase (epoxygenase) enzymes, which are generally regulated at the level of gene transcription. Eicosanoids include prostaglandins (PG), thromboxanes (TX) and leukotrienes (LT), with opposed physiologic activities.

ing tissue EPA concentrations, even more effectively than *via* ALA [18–20]. This way, some workers pointed out that when a food source of SA is ingested, an increase of the plasma EPA level is observed. In this sense, the effect of the FA composition of the diet on liver lipid classes has been investigated in animal models (guinea pigs). It was found that feeding with black currant seed oil – a source of GLA and SA – resulted in significant increases of DGLA (attributed to the GLA content in the oil) in all liver lipid classes examined, whereas the levels of AA remained relatively stable. Also EPA increased when the diet contained decreased amounts of *n*-6 FA, especially if SA was present in the diet [21]. This effect has been also demonstrated in rats, in which the use of diets enriched with SA resulted in an increase in the EPA content in liver phospholipids, approximately 50% of that for EPA [22].

Other studies have focused on the ability of dietary SA to increase selected tissue concentrations – erythrocyte and plasma phospholipids – of EPA and DHA in healthy human subjects, and to compare the effectiveness of SA with that of ALA [20]. The results showed that dietary SA increased EPA more efficiently than ALA, with 1 g of dietary SA being established as equivalent to 300 mg of dietary EPA in terms of increasing tissue concentrations of EPA. Thus, vegetable oils containing SA could become a dietary source of *n*-3 FA that is more effective in increasing tissue EPA concentrations than the current ALA-containing vegetable oils. In addition, the use of SA-containing oils in food manufacture could provide a wide range of dietary alternatives to the current EPA-containing oils [20, 23].

On the other hand, when considering that global production of farmed fish has more than doubled in the last 15 years and that this expansion places an increasing demand on supplies of wild fish harvested to provide protein and oil as ingredients for aquafeeds, the replacement of oils for aquaculture with oils from commercial terrestrial plants might be desirable. In this sense, it has been demonstrated that Atlantic salmon can be grown on a diet in which fish oil is replaced with a plant oil containing 14% SA, without apparent detriment to fish growth or health or a reduction in the concentration of specific key FA, in particular EPA and DHA [24]. The same effect has been observed in cod (*Gadus morhua* L.) [25]. Thus, a new strategy to feed farmed fish with any SA terrestrial oil is starting now, which will provide unquestionable environmental benefits.

3 Medical uses of SA

3.1 Some cancer types

Several authors have reported that dietary AA potently increases the phospholipid AA content in some studied tissues, and these levels are positively correlated with tumor number [26]. Tissue AA levels are also positively correlated with PG levels, and PG levels are also positively correlated with tumor number [26]. Thus, inhibition of tumorigenesis by *n*-3 FA, including SA, may be due to competition with AA as substrate for the COX-2 and LO-5 pathway to produce PG (Fig. 2), which plays an important role as mediator in various disease processes [26–30].

In short, SA has been characterized as a potent inhibitor of cancer cell growth. To elucidate its therapeutic potential, several experiments have been performed. The incorporation and metabolism of oleic acid (OA), ALA and SA have been compared in cancer cells. In NIH-3T3 cells, it was found that over a 4-day period, the growth of the cells was slightly stimulated in the presence of ALA, but was strongly inhibited in the presence of SA at the same concentration. The authors concluded that this inhibition may be caused by enhanced lipid peroxidation as a result of the high levels of SA present [31].

In another experiment, SA and other PUFA were compared to attenuate tumor formation in animal models. The antitumorigenicity of several dietary FA was evaluated – ALA, SA, EPA, DHA, conjugated linoleic acid (CLA, 77% 18:2*n*-7) and GLA – and compared with OA, in the diets of $Apc^{Min/+}$ mice, a mouse line that is used as a genetic model of intestinal tumorigenesis. This study also tried to determine whether any alterations in tumorigenesis correspond to alterations in PG biosynthesis. It was noted that tumor multiplicity was significantly lower (by 50%) in mice fed with SA or EPA, compared with controls, whereas less pronounced effects were observed in mice fed with DHA. On the other hand, the remaining PUFA tested were ineffective at the tested doses. It was reported that, although lower tumor numbers coincided with significantly lower PG levels in SA- and EPA-fed mice, ALA and DHA supplementation resulted in equally low PG levels, despite proving less efficacious with regard to tumor number. Furthermore, the authors indicate that SA and EPA attenuate tumorigenesis in this model and that this effect may be related in part to alterations in PG biosynthesis [29]. Nevertheless, other authors suggest that the beneficial effect on carcinomas could be due to a generic effect of *n*-3 PUFA. This way, the effect of a mixture of *n*-3 FA added to the diet on a colon carcinoma *in vivo* in rat liver was examined. It was found that a diet rich in *n*-3 FA reduced the development of metastasis and prevented tumor growth. Furthermore, it was indicated that the mechanism of prevention is unclear, but suggesting an effect on apoptosis as a possible mechanism [32].

In any case, SA seems to be more effective as protecting agent in tumorigenesis than its metabolic precursor, ALA. In this sense, a comparison has been performed between SA and ALA on COX-2 enzyme expression and PGE_2 production and COX-2 protein levels in breast cancer cell cultures. It was found that both SA and ALA reduced the level of AA; however, SA was more effective than ALA in decreasing the ratio of *n*-6/*n*-3 PUFA in cells. In addition, SA was more potent than ALA in suppressing the expression of the COX-2 gene [33].

Another kind of tumorigenesis in which SA might provide health benefits in humans is prostate cancer, although clinical assays in humans have still not been performed. In this sense, it has been observed that men with higher endogenous 5α-reductase activity may have a higher prostate cancer risk [34]. To elucidate the relative inhibitory potencies of SA and other PUFA on 5α-reductase activity, it was measured in human and rat microsomal tissues. The relative inhibitory potencies of PUFA were, in decreasing order: GLA > DHA = SA = AA = ALA. Thus, SA and other PUFA may play an important role in regulating androgen action in target cells [35]. In addition, it seems that this tumor type could be modulated by another mechanism, by manipulating the *n*-6/*n*-3 ratio through diets enriched in SA. This way, it has been demonstrated that SA promotes apoptosis and decreases proliferation in mouse prostate cancer cells, causing a decrease in the prostate-specific antigen PSA doubling time, compared to *n*-6 LA [36].

In any case, the use of dietary SA as an antitumorigenic agent is promising because it is not dependent on the Δ6 desaturase reaction, the rate-limiting step in *de novo* biosynthesis of long-chain PUFA, which also indicates that SA may reduce the formation of AA-derived eicosanoids *in vitro* [30]. In addition, other studies indicate that the beneficial effects of SA could be attributed to an increase in immune function, based on the observation that SA, in combination with GLA, increased the proportion of EPA in peripheral blood mononuclear cells (lymphocytes and monocytes) [37]. This collective evidence, albeit limited, warrants investigation into the antitumorigenic potential of SA.

3.2 Antithrombotic activity

SA has an inhibitory effect on platelet aggregation and arachidonate oxygenation. This effect was established using fish oil and some plant oils, such as black currant seed oil, which were studied on human platelets. When added to platelets simultaneously with collagen, AA or the endoperoxide mimetic U46619, SA appeared as a weak inhibitor of platelet aggregation. In addition, SA did not alter the metabolism of exogenous AA. In contrast, when pre-incubated with platelets after precoating onto albumin, SA inhibited platelet aggregation induced by thrombin, collagen, AA or U46619, and was as potent as EPA tested under similar conditions. SA also altered the endogenous AA oxygenation stimulated by low doses of thrombin, but to a significantly lesser extent than did EPA. It seems therefore that, in addition to competing with the endogenous AA metabolism, SA may affect platelet aggregation by another mechanism [38].

3.3 Rheumatoid arthritis

Fish oil supplements containing PUFA are reported to have beneficial effects on the symptoms of rheumatoid arthritis whilst offering few, if any, side effects at the levels used [39]. It has been reported that modest clinical improvements usually emerge after 12 weeks of treatment and peak around 18–24 weeks [40]. Firstly, this effect was attributed to the EPA and DHA content in fish oil [39]. The levels of EPA and DHA required to produce a beneficial effect were established at around 90 mg per kg of body weight per day [41]. As exposed above, this effect is due to the competition of EPA with AA as a substrate for COX and 5-LO to produce PGE_3 and LTB_5, which are less inflammatory than the AA products PGE_2 and LTB_4 (Fig. 2). This way, the pro-inflammatory properties of LTB_5 are about 10% of those of LTB_4 [42]. Nevertheless, SA has demonstrated to be as effective as EPA in inhibiting 5-LO when tested *in vitro* [30]. Thus, the use of SA and/or SA-containing oils such as black currant and *Echium* oils, and certain fish oils in anti-inflammatory pharmaceuticals administered orally, rectally, enterally or parenterally is patented in the USA [43].

3.4 Acne

It has been noted that higher serum androgen levels, which depend on higher endogenous 5α-reductase activity, are associated with the presence of acne, especially in women [44]. In order to diminish this activity, the relative inhibitory potencies of SA and other PUFA on 5α-reductase were measured in human and rat microsomal tissues. The relative inhibitory potencies of PUFA were: GLA > DHA = SA = AA = ALA. Thus, SA as well as other PUFA may play an important role in regulating androgen action in target cells that could attenuate disorders associated with a high 5α-reductase activity [35].

3.5 Skin inflammation and atopic dermatitis

Leukotrienes have been shown to play an important role as mediators in various disease processes, including the inflammatory ones, and thus their synthesis is tightly regulated [30]. The major precursor of leukotrienes is AA (Fig. 2). Because of the structural similarity of SA with AA, a study was conducted to determine whether SA exerts an inhibitory effect on leukotriene synthesis. It was demonstrated that leukotrienes were reduced by SA at the same order as observed with EPA, and it was also found to be dose dependent [45].

In another experiment, the effects of dietary SA on inflammatory mediator release in whole blood and splenocytes in mice was investigated, and the effects were compared with those of two other *n*-3 PUFA, ALA and EPA. The release of PGE_2 and tumor necrosis factor (TNF) were measured in whole blood and splenocytes stimulated with lipopolysaccharide. In whole blood, the production of TNF was suppressed by all dietary *n*-3 PUFA as compared with the control diet, which contained triacylglycerols prepared from safflower oil. PGE_2 production was not significantly changed. It was also found that SA-containing diets induce an increase in eicosatetraenoic acid (ETA, 20:4*n*-3), EPA, and DHA in plasma and splenocytes [45].

It has been reported that patients with atopic dermatitis show a significant decrease in Δ6 desaturase activity and therefore an abnormal availability of eicosanoid precursors like DGLA, AA and EPA; an improvement for Δ6 desaturase patients has been described following dietary supplementation with evening primrose oil due to its GLA content, the first Δ6-desaturated metabolite of LA and a DGLA and AA precursor [46]. Thus black currant oil – source of both GLA and SA – in children affected with atopic dermatitis was tested. The authors concluded that the simultaneous administration of Δ6-desaturated *n*-6 and *n*-3 FA (like GLA and SA) could be a very useful atopic dermatitis treatment [46].

It is widely know that larger amounts of UV radiation cause sunburn, which is characterized by erythema, pain, swelling and blistering; in extreme cases, there is epidermal necrosis. Thus, new pharmaceutical formulations based on Δ6-desaturated *n*-6 and *n*-3 FA could be appropriate to treat skin inflammation. In this sense, the use of SA in inhibiting the COX pathway for treating skin inflammation is patented by CRODA, as a sunscreen composition comprising SA in combination with a UV-blocking and/or UV-absorbing material [47].

Echium oil, rich in SA, is used as a typical SA source. It has shown very useful properties when applied topically, which is of great interest for the Personal Care market. It has been described that, when applied topically to a skin model, *Echium* oil inhibited the release of PGE_2 by nearly two thirds, when compared to untreated tissue [48].

3.6 Hypertriglyceridemia

A wealth of evidence indicates that consumption of fish or dietary fish oils containing long-chain *n*-3 PUFA such as EPA and DHA is associated with cardiovascular benefits, including a reduction in circulating triacylglycerol concentrations and reduced mortality from coronary heart disease [49]. Nevertheless, it is established that shorter-chain dietary *n*-3 PUFA such as ALA from vegetable oils are inefficiently converted to EPA and DHA and do not possess the hypotriglyceridemic properties attributed to

fish oils [49]. A study was performed to investigate the effect of dietary *Echium* oil, a plant oil containing SA, on tissue FA content and serum triacylglycerol concentrations in hypertriglyceridemic humans. The results demonstrated that dietary plant oils rich in SA are metabolized to longer-chain, more unsaturated *n*-3 PUFA. Also, these oils appear to possess hypotriglyceridemic properties typically associated with fish oils [49]. Thus, a PUFA-containing composition – including SA – for treating hypertriglyceridemia and methods for its use have been patented by the above-mentioned authors [50].

4 Sources of SA

4.1 Algae

A selection of species of algae having SA in their oil is shown in Tab. 1. Micro- and macroalgae have considerable percentages of palmitic acid (PA, 16:0) and EPA, which are higher than the percentages of SA. Among the microalgae, *Isochrysis* seems to be a better source of SA. Macroalgae species, especially from the Phaeophyceae, such as *Scytosiphon lomentarius* and *Micelophycus simplex*, have SA percentages twice as high in their oil. Nevertheless, the saponifiable oil content in macroalgae is usually very low, although the majority of the consulted works lack any data about the oil content in macroalgae (Tab. 1). Other workers reported relatively high SA percentages in the oils of some macroalgae, but in considering the low oil content of these, they may not be useful SA sources [56]. On the other hand, an adequate strategy to upgrade the algal SA oils is effected through selective lipid fractionation. By this procedure, in the monogalactosyldiacylglycerol fraction, the macroalgae *Ulva fenestrata* accumulates SA at 24.3% based on the total lipid fraction, but yielding low FA amounts [57].

Tab. 1. Fatty acid content of selected algae species.

	Saponifiable oil (% of dry matter)	14:0	16:0	16:1	18:0	18:1	18:2*n*-6	18:3*n*-6	18:3*n*-3	18:4*n*-3 (SA)	20:4*n*-6	20:5*n*-3	22:6*n*-3
Microalgae													
Prymnesiophyceae													
Pavlova lutheri [51][a]	–	8.8	17.3	14.4	26.7	2.4	0.6	0.5	2.1	10.9	0.7	26.7	–
Isochrysis sp. [51][a]	10.0	18.4	9.3	5.0	3.7	7.6	3.7	2.0	5.7	26.8	0.1	0.8	–
Bacillariophyceae													
Phaeodactylum tricornutum [52]	10.5	5.4	15.5	17.3	0.3	0.5	2.2	0.6	0.3	0.4	3.4	29.8	0.8
Rhodophyceae													
Porphyridium cruentum [53]	4.1	1.9	26.6	1.8	0.8	1.0	6.2	–	1.0	0.5	23.0	23.9	0.2
Macroalgae													
Rhodophyceae													
Rhodomela confervoides [54]	–	3.0	21.9	2.4	0.9	12.8	3.1	0.5	5.8	9.8	11.9	24.8	–
Phaeophyceae													
Undaria pinnatifida [54]	–	3.6	23.9	1.2	1.7	9.7	9.9	0.5	5.8	10.8	15.5	12.5	–
Scytosiphon lomentarius [54]	–	4.2	14.4	1.0	0.4	9.0	5.6	1.1	6.2	18.8	12.0	24.2	
Micelophycus simples [54]	–	2.8	15.3	2.1	0.5	8.8	4.3	0.8	7.0	20.1	7.6	23.8	
Sargassum piluliferum [55]	–	4.0	31.8	6.5	1.36	7.0	2.4	0.22	4.51	4.50	9.45	4.68	–
Chlorophyceae													
Ulva lactuca [54]	–	1.1	24.8	0.4	0.3	7.5	4.6	0.8	20.5	17.9	0.0	1.3	–

On the other hand, PUFA profiles as well as oil percentages in microalgae can be improved by modifying some parameters in the photobioreactors, such as temperature, residence time, culture medium, *etc.* Thus, it is expected that microalgae could become a promising source of SA.

4.2 Fungi

SA is scarcely reported in fungi species. According to the current literature, it seems that studies about the FA composition of fungi have focused on taxonomical purposes. In this sense, the FA composition of *Thamnidium elegans*, a slightly psychrophilic fungus, has been determined and compared with other mucoraceous fungi [58]. It has been found that, in addition to the biosynthesis of ALA at low temperature, *T. elegans* shows an increase in the synthesis of SA, and also that the response to temperature has taxonomical value in relation to fungal phylogeny. Another studied species, from the genus *Morteriella*, showed low amounts of this PUFA [59].

4.3 Seed plants

Looking at the metabolic pathways that lead to SA biosynthesis (Fig. 2), it is comprehensible that both GLA and SA could appear jointly in the seed oil of some taxa. Thus, sometimes the literature about the FA distribution in seed plants shows data for both PUFA simultaneously. Normally, the data obtained from analyzed seed plants are indexed in the Seed Oil Fatty Acids (SOFA) database (http://www.bagkf.de/sofa/). Over many years, the Institute for Chemistry and Physics of Lipids in Munster (Germany) has collected seed oil FA composition data. This database permits searches for plant species, genera and families, for individual FA and combinations of FA in their seed oils, and for their proportional contents in form of FA composition tables. It also contains literature references and close to 1000 unpublished data from analyses carried out by GLC between 1986 and 2002 in the Institute for Chemistry and Physics of Lipids.

In the last years, the PUFA distribution in seed plants has been analyzed while looking for new and better sources. In addition, other sources have been investigated, such as fungi and microalgae. Nevertheless, seeds plants are intensively examined because this source has attractive advantages [5].

They constitute a natural and renewable material, whose by-products (forage, residues of seeds, *etc.*) can be easily recycled.

Genetic engineering possibilities, still not well known, seem to have a great future.

The agricultural techniques, which are easily applicable, have been well known for a long time.

Agriculture with non-alimentary purposes constitutes an alternative option to the traditional cultivation of lands, which sometimes is subsidized in the European Community.

Thus, according to the above exposed statements, seed plants seem to be the better option to produce SA oils. Unfortunately, to date, SA has been reported in only a small number of families: Aracauriaceae, Boraginaceae, Caryophillaceae, Cannabinaceae, Primulaceae, Saxifragaceae and Loasaceae.

Among the angiosperms, the Boraginaceae seemed to be the most appropriate family to continue the search for SA in nature. Nevertheless, after a vast search, only few plants from this family have shown SA amounts in their seed oils that could be useful for industrial extraction.

The FA percentages of the seed oils in which SA appears in noticeable amounts are shown in Tab. 2 (Boraginaceae) and Tab. 3 (other families). Notice that, usually, both GLA and SA are discovered at the same time when any new seed oil is characterized. This is because the occurrence of the $\Delta 6$ desaturase enzyme implies the biosynthesis of both GLA and SA (Fig. 2).

Among the Boraginaceae, *Echium*, *Lappula* and *Lithospermum* seem to be the better sources of SA. The high amount of ALA shown by all species that produce SA can be explained by considering the metabolic pathway that generates SA from ALA (Fig. 2). Other FA that appear in all species are PA, OA, LA and ALA.

The chemotaxonomic significance of the FA composition of the seed oil in the Boraginaceae is widely accepted. According to Tétényi [75], this family has different FA profiles at the tribal level. Velasco and Goffman [67] found that the subfamily Heliotropioideae is characterized by low levels of ALA, GLA and SA, and long-chain monounsaturated FA. The tribes Eritrichieae and Lithospermeae showed high concentrations of SA. The maximum levels of GLA were found in the tribe Borageneae, and the maximum concentrations of long-chain monounsaturated FA constitute a characteristic of the tribe Cynoglosseae. In this sense, important differences have been described between European and North-African *Echium* plants and Macaronesian *Echium* (endemic *Echium* from Macaronesia, a group of islands located in the Mid Northeast Atlantic: namely Canary, Madeira, Azores and Cape Verde Islands), consisting of an increase in the GLA content of the Macaronesian *Echium*

Tab. 2. Fatty acid content of selected species of Boraginaceae with SA >10% of the saponifiable oil.

	Saponifiable oil (% of dry matter)	16:0	18:0	18:1*n*-9	18:2*n*-6	18:3*n*-6	18:3*n*-3	18:4*n*-3 (SA)
Echium asperrimus [60]	18.7	7.7	2.8	14.7	16.3	9.6	35.3	11.1
Echium boissieri [60]	19.8	5.5	2.3	14.7	8.6	5.5	47.1	14.3
Echium creticum [60]	14.6	5.6	3.0	8.2	14.3	9.7	42.7	14.7
Echium italicum [61]	17.0	8.0	3.0	17.0	11.0	8.0	39.0	12.0
Echium lusitanicum [62]	20.6	6.7	2.5	16.4	16.4	10.9	33.3	12.3
Echium plantagineum [60]	30.0	7.0	4.0	17.0	15.0	10.0	34.0	13.0
Echium rubrum [63]	15.0	8.0	2.0	8.0	20.0	14.0	34.0	15.0
Echium russicum [62]	18.6	5.7	2.4	14.4	22.6	15.8	26.6	10.6
Echium sabulicola [60]	20.4	5.5	2.4	8.0	16.3	10.9	40.4	14.7
Echium fastuosum [64]	13.7	7.5	3.0	9.7	16.2	23.8	25.5	10.9
Hackelia americanum [65]	32.0	6.80	1.50	20.6	17.5	12.4	19.3	10.5
Lappula granulata [66]	12.7	5.3	1.9	16.1	11.7	6.9	32.6	17.7
Lappula intermedia [66]	4.6	5.1	1.5	13.8	13.4	7.1	35.4	17.7
Lappula myosotis [66]	18.0	5.9	1.9	13.3	12.9	6.7	34.9	17.2
Lappula squarrosa [67]	12.2	10.2	7.8	12.2	13.6	7.3	27.6	17.1
Lithospermum arvense [63]	16.1	7.0	5.6	10.9	10.6	5.2	41.5	17.4
Lithospermum incisum [60]	11.8	10.0	3.0	14.0	19.0	5.5	34.0	11.0
Moltkia aurea [59]	10.0	6.0	3.0	16.0	19.0	10.0	36.0	16.0
Rochelia disperma [63]	18.0	6.0	3.0	17.0	10.0	5.0	39.0	15.0
Rochelia stylaris [63]	21.0	6.0	2.0	18.0	12.0	5.0	40.0	14.0
Pectocarya platycarpa [68]	15.0	9.5	2.9	19	17.9	15.2	19.9	12.0

Tab. 3. Fatty acid content of seeds of selected species from other families.

	Saponifiable oil (% of dry matter)	16:0	18:0	18:1*n*-9	18:2*n*-6	18:3*n*-6	18:3*n*-3	18:4*n*-3 (SA)
Aracauriaceae								
Agathis robusta [69]	46.0	3.4	9.3	12.3	36.9	0.5	11.0	0.2
Cannabinaceae								
Cannabis sativa [70]	25.0	6.0	2.3	8.6	54.3	3.9	21.7	1.91
Primulaceae								
Aleuritia scotica [71]	–	7.7	0.4	10.3	26.9	2.2	29.0	22.5
Aleuritia farinosa [71]	–	9.1	0.4	7.3	29.9	1.8	29.2	17.5
Primula macrophylla [72]	–	9.9	1.1	18.2	7.3	0.8	55.4	17.0
Primula sikkimensis [73]	17.6	9.4	0.9	27.8	23.6	3.5	11.3	14.9
Saxifragaceae								
Ribes alpinum [74]	18.7	5.6	1.4	18.1	39.0	9.6	22.0	4.4
Ribes nigrum [74]	30.0	7.0	1.5	11.0	47.0	18.0	13.0	3.0
Ribes uva-crispa [74]	18.0	7.5	1.0	17.0	40.0	11.0	19.5	4.5

species – up to 100% as compared to the continental *Echium* – at the expense of a decrease in the ALA and SA amounts [64].

The seed oils of the Saxifragaceae (Tab. 3) are very similar to the Boraginaceae oils in that they contain both ALA and SA. *Ribes* species are commercially exploited to obtain GLA [76], but the amounts of SA in *Ribes* species are very low.

Primulaceae (*Primula* and *Aleuritia* species) (Tab. 3) show good amounts of SA. *Aleuritia scotica* seems to be the best source of SA found so far in nature. Nevertheless, some variables affecting the oil availability, such as seed size or cultivation viability, appear to be unreported. Hemp (Cannabis sativa L.) seed oil seems to be an exceptionally rich source of PUFA, specifically of LA and ALA [70]. There are now reports

of significant amounts of GLA and SA in the seed oil of this species.

In other families, SA appears sporadically at different taxon levels. For instance, *Nasa* is the only genus of the Loasaceae that shows both GLA and SA (at levels of 3.5–10% and 2–8.5%, respectively). As noted for the Boraginaceae [60], there is no obvious connection between the degree of unsaturation of the seed oil and the habitat of this species [77].

The genetic modification of oilseed crops provides an opportunity to tailor the composition of seed oils for optimal dietary or processing characteristics. Until recently, modifications of oil composition could only be achieved through traditional plant breeding, where the natural diversity within closely related species could be exploited, or through mutagenesis. Transgenic technology widens the scope of modifications achievable in oil composition by allowing the introduction of a wider range of genetic elements than is otherwise possible. This way, the production of GLA and SA in seeds of a marker-free transgenic soybean has been realized recently. Through a single desaturation step (Fig. 2), the *Borago officinalis* L. Δ6 desaturase can convert LA and ALA to GLA and SA, respectively. To this end, DNA sequences of the *B. officinalis* Δ6 desaturase gene were cloned downstream of the embryo-specific promoter β-conglycinin. In the transgenic soybean, the average GLA levels ranged from 3.4 up to 28.7%, while the SA levels varied from just under 0.6 to 4.2% [78].

Better results have been obtained by generating transgenic canola (*Brassica napus*) lines that expressed in seeds the Δ6 and Δ12 FA desaturases isolated from the commercially grown fungus *Mortierella alpina* and the Δ15 FA desaturase from canola. Seed oil from independent transformants accumulated SA, up to 23% of the oil by weight. Seed lipids were evaluated in the F1 and F2 generations from several independent crosses. In these progeny plants, SA accumulated to up to 23% of the F1 seed lipids. The total *n*-3 content in the seed lipids (ALA + SA) exceeded 55% of the seed lipids whereas the total *n*-6 FA content of the seed lipids (GLA + LA) was 22% [79].

4.4 Animal sources

Most fish oils show low percentages of SA. Thus, menhaden has 2.1, sardine 4.7, tuna 0.8, herring 3.0, mackerel 1.3 and salmon 1.4% SA based on total FA [80]. This means that fish oils are used mainly as sources of EPA or DHA instead of SA.

5 Conclusions

The Δ6 desaturated SA is reported as a PUFA that could be used in the treatment of several diseases. Nevertheless, new research about the physiological effects of SA on human health is needed, in which the physiological effects of this PUFA should be clearly distinguished from those of the other PUFA that usually are present in the same oil source.

Knowledge of SA in nature is increasing steadily; thus, a great number of SA producer species have recently been reported. Some of these new sources have interest, both for oil extraction to use as health food as well as for obtaining pure SA. Keeping in mind a possible future demand for SA oils, the use of new SA producer species could be a desirable option for agriculture. It is expected that new species containing higher amounts of SA than those described until now can still be found, by considering the high number of species untested to date.

Few oils are available as SA source. Marine oils show low SA percentages; thus it is mainly ingested through specialized seed oils. Among these, *Echium* oil seems to be a good option. Other marketed oils sources of SA are *Ribes* species and the novel hemp oil, but SA reaches low percentages in these oils.

Until today, references about possible adverse effects on health of this fatty acid have not been reported.

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References

[1] http://www.cyberlipid.org.

[2] WHO/FAO: Fats and oils in human nutrition. *FAO Food and Nutrition Paper*, Rome (Italy) 1994, **57**.

[3] WHO/FAO: Preparation and use of food-based dietary guidelines. *WHO Technical Report Series*, Rome (Italy) 1998, **880**.

[4] R. Charles, M. D. Harper, A. Terry, M. D. Jacobson: The fats of life. The role of omega-3 fatty acids in the prevention of coronary heart disease. *Arch Intern Med.* 2001, **161**, 2185–2192.

[5] J. L. Guil-Guerrero: Occurrence of gamma-linolenic acid. In: *Recent Progress in Medicinal Plants*. Vol. VIII. Eds. D. K. Majundar, J. N. Govil, V. K. Singh, Sci Tech Publishing LLC, Texas (USA) 2002, pp. 467–487.

[6] S. P. Singh, X. R. Zhou, Q. Liu, S. Stymne, A. G. Green: Metabolic engineering of new fatty acids in plants. *Curr Opin Plant Biol.* 2005, **8**, 197–203.

[7] R. B. Ervin, J. D. Wright, C. Y. Wang, J. Kennedy-Stephenson: Dietary intake of fats and fatty acids for the United States population: 1999–2000. *Adv Data* 2004, **8**, 1–6.

[8] Department of Health: Nutritional Aspects of Cardiovascular Disease: Report on Health and Social Subjects N° 46. HMSO, London (UK) 1997.

[9] A. Leaf, P. C. Weber: A new era for science in nutrition. *Am J Clin Nutr.* 1987, **745**, 1048–1053.

[10] S. Boyd Eaton, S. B. Eaton, E. J. Sinclair, L. Cordain, N. J. Mann: Dietary intake of long-chain polyunsaturated fatty acids during the Palaeolithic. *World Rev Nutr Diet.* 1988, **83**, 12–23.

[11] S. C. Cunnane, M. L. Plourde, K. Stewart, M. A. Crawford: Docosahexaenoic acid and shore-based diets in hominid encephalization: A rebuttal. *Am J Hum Biol.* 2007, **19**, 578–581.

[12] H. Gerster: Can adults adequately convert alpha-linolenic acid (18:3*n*-3) to eicosapentaenoic acid (20:5*n*-3) and docosahexaenoic acid (22:6*n*-3)? *Int J Vitam Nutr Res.* 1998, **68**, 159–173.

[13] R. Uauy,A Valenzuela: Marine oils: The health benefits of *n*-3 fatty acids. *Nutrition* 2000, **16**, 680–684.

[14] C. von Schacky: The role of omega-3 fatty acids in cardiovascular disease. *Curr Atherosc Reports* 2007, **5**, 139–145.

[15] D. S. Siscovick, T. E. Raghunathan, R. Lemaitre, I. King, L. A. Cobb: Long-chain *n*-3 polyunsaturated fatty acids and out-of-hospital primary cardiac arrest: Clinical and public health implications of observational studies and clinical trials. *Eur Heart J Suppl.* 2001, **3**, 70–74.

[16] M. F. McEntee, J. Whelan: Dossier: Polyunsaturated fatty acids in biology and diseases. Dietary polyunsaturated fatty acids and colorectal neoplasia. *Biomed Pharmacother.* 2002, **56**, 380–387.

[17] A. Meyer, H. Kirsch, F. Domergue, A. Abbadi, P. Sperling, J. Bauer, P. Cirpus, T. K. Zank, H. Moreau, T. J. Roscoe, U. Zähringer, E. Heinz: Novel fatty acid elongases and their use for the reconstitution of docosahexaenoic acid biosynthesis. *J Lipid Res.* 2004, **45**, 1899–1909.

[18] Y. S. Huang, R. S. Smith, P. R. Redden, R. C. Cantrill, D. F. Horrobin: Modification of liver fatty acid metabolism in mice by *n*-3 and *n*-6 Δ6-desaturase substrates and products. *Biochim Biophys Acta* 1991, **1082**, 319–327.

[19] K. Yamazaki, M. Fujikawa, T. Hamazaki, S. Yano, T. Shono: Comparison of the conversion rates of α-linolenic acid (18:3(*n*-3)) and stearidonic acid (18:4(*n*-3)) to longer polyunsaturated fatty acids in rats. *Biochim Biophys Acta* 1992, **1123**, 18–26.

[20] M. J. James, M. V. Ursin, L. G. Cleland: Metabolism of stearidonic acid in human subjects: Comparison with the metabolism of other *n*-3 fatty acids. *Am Clin Nutr.* 2003, **77**, 1140–1145.

[21] G. L. Crozier, M. Fleith, H. Traitler, P. A. Finot: Black currant seed oil feeding and fatty acids in liver lipid classes of guinea pigs. *Lipids* 1989, **24**, 460–466.

[22] J. Phipps, B. Enderson, L. Jones, J. Whelan, M. Karlstad: Enteral nutrition with stearidonic acid increases incorporation of antiinflammatory *n*-3 fatty acids in liver phospholipids in the rat. *J Surgical Res.* 2004, **121**, 330–331.

[23] E. S. Miles, T. Banerjee, P. C. Calder: The inuence of different combinations of γ-linolenic, stearidonic and eicosapentaenoic acids on the fatty acid composition of blood lipids and mononuclear cells in human volunteers. *Prostaglandins Leukoc Essent Fatty Acids* 2004, **70**, 529–538.

[24] M. R. Miller, P D. Nichols, C. G. Carter: Replacement of dietary fish oil for Atlantic salmon parr (*Salmo salar* L.) with a stearidonic acid containing oil has no effect on omega-3 long-chain polyunsaturated fatty acid concentrations. *Comp Biochem Phys Part B* 2007, **146**, 197–206.

[25] J. G. Bell, F. Strachan, J. E. Good, D. R. Tocher: Effect of dietary *Echium* oil on growth, fatty acid composition and metabolism, gill prostaglandin production and macrophage activity in Atlantic cod (*Gadus morhua* L.). *Aquac Res.* 2006, **37**, 606–617.

[26] J. Whelan, M. F. McEntee: Dietary (*n*-6) PUFA and intestinal tumorigenesis. *J Nutr.* 2004, **134**, 3421–3426.

[27] J. Whelan: Antagonistic effects of dietary arachidonic acid and *n*-3 polyunsaturated fatty acids. *J Nutr.* 1996, **126**, 1086–1091.

[28] M. B. Petrik, M. F. McEntee, C. H. Chiu, J. Whelan: Antagonism of arachidonic acid is linked to the antitumorigenic effect of dietary eicosapentaenoic acid in Apc(Min/+) mice. *J Nutr.* 2000, **130**, 1153–1158.

[29] M. B. Petrik, M. F. McEntee, B. T. Johnson, M. G. Obukowicz, J. Whelan: Highly unsaturated (*n*-3) fatty acids, but not α-linolenic, conjugated linoleic or γ-linolenic acids, reduce tumorigenesis in ApcMin/+ mice. *J Nutr.* 2000, **130**, 2434–2443.

[30] M. Guichardant, H. Traitler, D. Spielmann, H. Sprecher, P. A. Finot: Stearidonic acid, an inhibitor of the 5-lipoxygenase pathway. A comparison with timnodonic and dihomogammalinolenic acid. *Lipids* 1993, **28**, 321–324.

[31] R. C. Cantrill, Y. S. Huang, G. W. Ells, D. F. Horrobin: Comparison of the metabolism of alpha-linolenic acid and its delta 6 desaturation product, stearidonic acid, in cultured NIH-3T3 cells. *Lipids* 1993, **28**, 163–166.

[32] C. N. Gutt, L. Brinkmann, A. Mehrabi, H. Fonouni, B. P. Müller-Stich, G. Vetter, J. M. Stein, P. Schemmer, M. W. Büchler: Dietary omega-3-polyunsaturated fatty acids prevent the development of metastases of colon carcinoma in rat liver. *Eur J Nutr.* 2007, **46**, 279–285.

[33] E. Horia, B. Watkins: Comparison of stearidonic acid and α-linolenic acid on PGE production and COX-2 protein levels in MDA-MB-231 breast cancer cell cultures. *J Nutr Biochem.* 2005, **16**, 184–192.

[34] A. H. Wu, A. S. Whittemore, L. N. Kolonel, F. Z. Stanczyk, E. M. John, R. P. D. W. Gallagher: West lifestyle determinants of 5α-reductase metabolites in older African-American, white, and Asian-American men. *Cancer Epidemiol Biomarkers Prev.* 2001, **10**, 533–538.

[35] T. Liang, S. Liao: Inhibition of steroid 5 alpha-reductase by specific aliphatic unsaturated fatty acids. *Biochem J.* 1992, **15**, 557–562.

[36] U. P. Kelavkar, J. Hutzley, R. Dhir, P. Kim, K. G. D. Allen, K. McHugh: Prostate tumor growth and recurrence can be modulated by the omega 6:omega 3 ratio in diet: Athymic mouse xenograft model simulating radical prostatectomy. *Neoplasia* 2006, **8**, 112–124.

[37] E. A. Miles, T. Banerjee, M. M. B. W. Dooper, L. M'Rabet, Y. M. F. Graus, P. C. Calder: The influence of different combinations of gamma-linolenic acid, stearidonic acid and EPA on immune function in healthy young male subjects. *Br J Nutr.* 2004, **91**, 893–903.

[38] V. Kockmann, D. Spielmann, H. Traitler, M. Lagarde: Inhibitory effect of stearidonic acid (18:4*n*-3) on platelet aggregation and arachidonate oxygenation. *Lipids* 1989, **24**, 1004–1007.

[39] D. F. Horrobin: Medical roles of metabolites of precursor EFA. *Inform* 1995, **6**, 428–435.

[40] I. Newton: Meeting probes *n*-3 fatty acids' medical role. *Inform* 1997, **82**, 176–180.

[41] J. A. Nettleton: *Omega-3 Fatty Acids and Health*. Chapman & Hall, New York, NY (USA) 1995.

[42] P. M. Deborah, M. D. Symmons: Environmental factors and the outcome of rheumatoid arthritis. *Best Pract Res Clin Rheumatol.* 2003, **17**, 717–727.

[43] S. A. Nestec: *EEUU Patent US5158975* (1997).

[44] D. Thiboutota, H. Knaggsb, K. Gillilanda, G. Lina: Activity of 5-alpha-reductase and 17-beta-hydroxysteroid dehydrogenase in the infrainfundibulum of subjects with and without acne vulgaris. *Dermatology* 1998, **196**, 38–42.

[45] K. Ishihara, W. Komatsu, H. Saito, K. Shinohara: Comparison of the effects of dietary alpha-linolenic, stearidonic, and eicosapentaenoic acids on production of inflammatory mediators in mice. *Lipids* 2002, **37**, 481–486.

[46] F. Balli, G. Tarozzi, V. Barzanti, A. Dibiase, P. Bertolani, M. Cocchi: Omega-6 and omega-3-fatty-acids in children atopic-dermatitis. *Riv Ital Ped.* 1992, **18**, 639–643.

[47] K. Coupland, C. Packer, E. Claire: *Japanese Patent 07010736* (1995).

[48] K. Coupland, D. Coupland, J. A. Nichols: New sources of lipids containing stearidonic acid – powerful moderators of inflammation. *IFSCC 19th Congress*, 22–25 October 1996, Australia.

[49] M. E. Surette, M. Edens, F. H. Chilton, K. M. Tramposch: Dietary *Echium* oil increases plasma and neutrophil long-chain (*n*-3) fatty acids and lowers serum triacylglycerols in hypertriglyceridemic humans. *J Nutr.* 2004, **134**, 1406–1411.

[50] M. E. Surette: *EEUU Patent 6667064* (2003).

[51] G. A. Dunstan, J. K. Volkman, S. M. Barrett, C. D. Garland: Changes in the lipid composition and maximization of the polyunsaturated fatty acid content of three microalgae grown in mass culture. *J Appl Phycol.* 1993, **5**, 71–83.

[52] M. M. Rebolloso-Fuentes, A. Navarro-Pérez, J. J. Ramos-Miras, J. L. Guil-Guerrero: Biomass nutrients profiles of the microalga *Phaeodactylum tricornutum*. *J Food Biochem.* 2001, **25**, 57–76.

[53] M. M. Rebolloso-Fuentes, G. G. Acién-Fernández, J. A. Sánchez-Pérez, J. L. Guil-Guerrero: Biomass nutrient profiles of the microalga *Porphyridium cruentum*. *Food Chem.* 2000, **70**, 345–353.

[54] X. Li, X. Fan, L. Han, Q. Lou: Fatty acids of some algae from the Bohai Sea. *Phytochemistry* 2002, **59**, 157–161.

[55] E. A. Floreto, T. Teshima, S. Koshio: The effects of seaweed diets on the lipid and fatty acids of the Japanese disc abalone *Haliotis discus* hannai. *Fish Sci.* 1996, **62**, 582–588.

[56] L. D. Angelis, P. Rise, F. Giavarini, C. Galli, C. L. Bolis, M. L. Colombo: Marine macroalgae analyzed by mass spectrometry are rich sources of polyunsaturated fatty acids. *J Mass Spectrom.* 2005, **40**, 1605–1608.

[57] N. M. Sanina, N. Svetlana, E. Goncharova, Y. Kostetsky: Fatty acid composition of individual polar lipid classes from marine macrophytes. *Phytochemistry* 2004, **65**, 721–730.

[58] M. S. Manocha, C. D. Campbell: The effect of growth temperature on the fatty acid composition of *Thamnidium elegans* Link. *Can J Microbiol.* 1978, **24**, 670–674.

[59] Y. Shinmen, S. Shimizu, K. Akimoto, H. Kawashima, H. Yamada: Production of arachidonic acid by *Morteriella* fungi. Selection of a potent producer and optimization of culture conditions for large-scale production. *Appl Microbiol Biotechnol.* 1989, **31**, 11–16.

[60] J. L. Guil-Guerrero, F. F. García-Maroto, A. Giménez-Giménez: Fatty acid profiles from forty-nine plant species that are potential new sources of gamma-linolenic acid. *J Am Oil Chem Soc.* 2001, **78**, 677–684.

[61] R. Kleiman, F. R. Earle, I. A. Wolff: Search for new industrial oils. XI. Oils of Boraginaceae. *J Am Oil Chem Soc.* 1964, **41**, 459–460.

[62] J. L. Guil-Guerrero, F. García-Maroto, M. A. Vilches-Ferrón, D. López-Alonso: Gamma-linolenic acid from fourteen Boraginaceae species. *Ind Crops Prod.* 2003, **18**, 85–89.

[63] R. W. Miller, F. R. Earle, I. A. Wolff: Search for new seed oils. XV. Oils of Boraginaceae. *Lipids* 1968, **3**, 43–45.

[64] J. L. Guil-Guerrero, F. Gómez-Mercado, F. García-Maroto, P. Campra-Madrid: Occurrence and characterization of oils rich in γ-linolenic acid: (I) *Echium* seeds from Macaronesia. *Phytochemistry* 2000, **53**, 451–456.

[65] E. C. M. Coxworth: Oil and protein content, and oil composition of some plants of the Canadian prairiesa. *J Am Oil Chem Soc.* 1965, **42**, 891.

[66] N. Tsevegsüren, K. Aitzetmüller: γ-Linolenic and stearidonic acids in Mongolian Boraginaceae. *J Am Oil Chem Soc.* 1996, **73**, 1681–1684.

[67] L. Velasco, F. D. Goffman: Chemotaxonomic significance of fatty acids and tocopherols in Boraginaceae. *Phytochemistry* 1999, **52**, 423–426.

[68] R. B. Wolf, R. Kleiman, R. E. England: New sources of γ-linolenic acid. *J Am Oil Chem Soc.* 1983, **60**, 1858–1860.

[69] R. L. Wolff, W. W. Christie, F. Pedrono, A. M. Marpeau: Arachidonic, eicosapentaenoic, and biosynthetically related fatty acids in the seed lipids from a primitive gymnosperm, *Agathis robusta*. *Lipids* 1999, **34**, 1083–1097.

[70] J. C. Callaway, T. Tennilä, D. W. Pate: Occurrence of "omega-3" stearidonic acid (*cis*-6,9,12,15-octadecatetraenoic acid) in hemp (*Cannabis sativa* L.) seed. *J Int Hemp Assoc.* 1996, **3**, 61–63.

[71] O. Sayanova, J. A. Napier, P. R. Shewry: Δ6-Unsaturated fatty acids in species and tissues of the Primulaceae. *Phytochemistry* 1999, **52**, 419–422.

[72] V. D. Tsydendambaev, W. W. Christie, E. Y. Brechany, A. G. Vereshchagin: Identification of unusual fatty acids of four alpine plant species from the Pamirs. *Phytochemistry* 2004, **65**, 2695–2703.

[73] K. Aitzetmüller, G. Werner: Stearidonic acid (18:4omega3) in *Primula florindaee*. *Phytochemistry* 1991, **30**, 4011–4013.

[74] A. Johansson, P. Laako, H. Kallio: Characterization of seed oils of wild, edible Finnish berries. *Z Lebensm Unters Forsch A* 1997, **204**, 300–307.

[75] P. Tétényi: Données chimiotaxonomiques sur les Boraginacées. *Acta Bot Acad Sci Hung.* 1974, **20**, 159–167.

[76] H. Traitler, H. Winter, U. Richli, Y. Ingenbleek: Characterization of gamma-linolenic acid in *Ribes* seed. *Lipids* 1984, **19**, 923–928.

[77] M. Weigend, K. Aitzetmuller, L. Bruehl: The seeds of Loasaceae subfam. Loasoideae (Cornales). I. Seed release, seed numbers and fatty acid composition. *Flora* 2004, **199**, 424–436.

[78] Sato, A. Xing, X. Yec, B. Schweigerd, A. Kinneyd, G. Graefc, T. Clemente: Production of γ-linolenic acid and stearidonic acid in seeds of marker-free transgenic soybean. *Crop Sci.* 2004, **44**, 646–652.

[79] V. M. Ursin: Modification of plant lipids for human health: Development of functional land-based omega-3 fatty acids. *J Nutr.* 2003, **133**, 4271–4274.

[80] W. E. M. Lands: *Fish and Human Health*. 2nd Edn. Academic Press, Orlando, FL (USA) 2005.

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