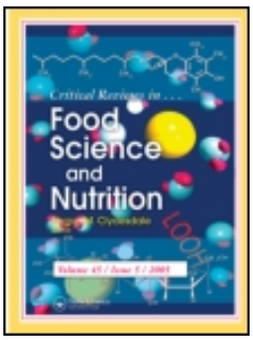

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Bioavailability and Potential Uses of Vegetarian Sources of Omega-3 Fatty Acids: A Review of the Literature

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Presently alpha-linolenic acid (ALA) is the most widely used vegetarian LC3PUFA, but only marginal amounts are converted into eicosapentaenoic (EPA) and docosahexaenoic acid (DHA); both of which are strongly related to human health. Currently, fish oils represent the most prominent dietary sources of EPA and DHA; however, these are unsuitable for vegetarians. Alternative sources include flaxseed, echium, walnut, and algal oil but their conversion to EPA and DHA must be considered. The present systematic review sets out to collate information from intervention studies examining the bioavailability of alternative vegetarian long chain omega-3 (n-3) polyunsaturated fatty acids (LC3PUFA) sources. Ten key papers published over the last 10 years were identified with seven intervention studies reporting that ALA from nut and seed oils was not converted to DHA at all. Three studies showed that ingestion of micro-algae oil led to significant increases in blood erythrocyte and plasma DHA. Further work is now needed to identify optimal doses of alternative vegetarian LC3PUFAs and how these can be integrated within daily diets. The potential role of algal oils appears to be particularly promising and an area in which further research is warranted.

Keywords LC3PUFA, vegetarians, EPA, DHA, flaxseed oil, walnut oil, echium oil, algae oil

INTRODUCTION

A large number of studies have been carried out to investigate the potential health benefits of long chain omega-3 (*n*-3) polyunsaturated fatty acids (LC3PUFA) (Metcalf et al., 2003; Koch and Heller, 2005; Gogus and Smith, 2010). LCPUFA are defined as fatty acids that typically comprise of 20 or more carbon atoms (Scientific Advisory Committee on Nutrition (SACN), 2004). Eicosapentaenoic acid (20:5*n*-3; EPA) and docosahexaenoic acid (22:6*n*-3; DHA) are dietary forms of LC3PUFA usually obtained from fish or fish oils. They are also the end products of the *n*-3 metabolic pathway (refer to Fig. 1), with the vegetarian-based parent fatty acid being alpha-linolenic acid (18:3*n*-3; ALA). A further major metabolic pathway of LCPUFA's is the omega-6 (*n-6*) pathway in which arachidonic acid (20:4*n*-6; AA) is the end product from the parent linoleic acid (18:2*n*-6; LA) (Derbyshire, 2009).

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So far, research has identified that vegetarians/vegans, non-fish eaters and pregnant mothers may not consume adequate quantities of LC3PUFA's (Davis and Kris-Etherton, 2003; Derbyshire, 2009; Welch et al., 2010). A vegan diet is completely devoid of DHA and vegetarian diets contain smaller amounts of DHA than that of meat and particularly fish eaters (Sanders, 2009). Clinical studies suggest that tissue levels of LC3PUFA's are at low levels in vegetarians and particularly low in vegans (Davis and Kris-Etherton, 2003). Currently, the most significant vegetarian dietary form of *n*-3 is ALA. Abundant ALA commodities include flaxseed, walnut, and echium seed oils (Kurowska et al., 2003; DeFilippis and Sperling, 2006).

Most vegetarian diets are rich in LA, (Davis and Kris-Etherton, 2003) a dietary source of *n*-6 which can be converted to the longer chain AA in the *n*-6 metabolic pathway (DeFilippis and Sperling, 2006). The increasing popularity of vegetable oils such as corn, sunflower, and safflower has lead to a rise in *n*-6 fatty acid intakes in US and Western diets (Simopoulos, 2002), whilst intakes of *n*-3 have declined (Bailey, 2009). In the metabolic pathway *n*-3 and *n*-6 fatty acids compete for the enzyme that is able to convert them (Davis and

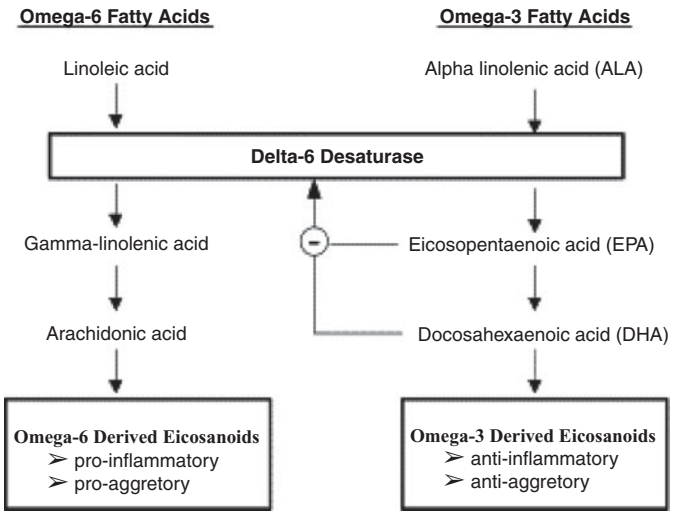

Figure 1 Metabolic pathway of omega-6 and omega-3 fatty acids. (Defilippis and Sperling, 2005).

Kris-Etherton, 2003). Diets with a high ratio of LA:ALA can suppress DHA synthesis in favor of docosapentenoic acid (22:5*n-6*; DPA) which takes the place of DHA in the retinal and neural tissues (Sanders, 2009). Delta-6 desaturase is the enzyme responsible for synthesizing LCPUFA's from ALA and LA. The activity of this enzyme can be reduced by aging, stress, diabetes, eczema, and some types of infection. Various dietary and lifestyle factors can impair LCPUFA synthesis including high intakes of saturated, hydrogenated or "trans"-fatty acids, a lack of vitamin and mineral cofactors and lifestyle choices such as smoking and the use of alcohol and caffeine (Bailey, 2009). Therefore, usually, very little ALA is converted to EPA and even less, if any to DHA (Sanderson et al., 2002).

Consequently, non-fish eaters could represent a portion of the population who may be at risk from the health consequences of a decreased LC3PUFA status. The National Diet and Nutrition Survey reports that average oily fish consumption is only around eight grams per day (Bates et al., 2010). Welch et al. (2010) also found that EPA and DHA intakes in non-fish eaters including vegetarians and meat eaters were significantly lower than fish eaters in the EPIC-Norfolk cohort. Recent UK recommendations state that two portions of fish should be consumed per week, one of which should be oily fish (Scientific Advisory Committee on Nutrition (SACN), 2004) but in reality only 27% of individuals consume any oil-rich sources of fish (Bentley, 2007).

There is now strong scientific evidence highlighting that an adequate LC3PUFA status is a key factor in the maintenance of health and can reduce the risk of chronic and inflammatory diseases (Welch et al., 2010). EPA is antithrombotic and is thought to confer cardiovascular protection (Metcalf et al., 2007). DHA has been linked to eye and brain development and is important for ongoing visual, cognitive, and cardiovascular health (Arterburn et al., 2007). Research suggests *n*-3 fats may protect against cardiovascular disease (CVD) by lowering blood pressure and heart rate; reducing serum triglycerides, inflammation, and arrhythmias. Further protection is thought to be given by the ability of *n*-3 to improve endothelial function, insulin sensitivity, and plaque stability (DeFilippis and Sperling, 2006; (Hooper et al., 2006; Lee et al., 2008).

In terms of cardiovascular health, one meta-analysis undertaken by Mozaffarian et al. (2005) concluded that EPA and DHA in fish oils may reduce heart rates in humans, particularly in those with a higher baseline heart rate or with treatment durations of 12 weeks or more. It was thought that this time period, i.e., longer than 12 weeks as an intervention was needed for EPA and DHA to be incorporated into effective tissues, producing a greater affect than short term intakes. Bucher et al. (2002) also concluded that a diet rich in LC3PUFA may decrease mortality in a meta-analysis of 11 coronary heart disease (CHD) randomized controlled trials (RCT).

HEALTH BENEFITS

To elaborate on the previous section LC3PUFAs have been found to confer several health benefits. The anti-inflammatory properties of LC3PUFA's have been used successfully in the treatment of CVD, CHD, inflammatory diseases, eczema, psoriasis, and rheumatoid arthritis (Gogus and Smith, 2010). Several studies have shown that *n*-3 consumption is inversely associated with CVD, particularly sudden cardiac death (DeFilippis and Sperling, 2006). In recent years, a large number of trials have demonstrated a positive correlation between dietary LC3PUFA intake and heart health. A literature review by Harris et al. (2008) suggests that CHD risk factors may be affected by LC3PUFA status, the authors recommended a direct intake of EPA and DHA for optimal for CHD risk reduction. A meta-analysis of LC3PUFA's and CHD completed by Bucher et al. (2002) concluded that dietary intakes of LC3PUFA's reduce overall mortality, mortality due to myocardinal infarction and sudden death in patients with CHD. An *n*-3-based formula has also been approved by the Food and Drug administration for use to reduce very high triglyceride levels (>500 mg/dl) in adults (DeFilippis and Sperling, 2006).

Over the past decade some studies have suggested that DHA may be more active than EPA in certain disorders and that DHA is required for normal brain function (McCann and Ames, 2005; Breivik, 2007). A review by McCann and Ames (2005) concluded that brain concentrations of DHA are positively associated with changes in cognitive and behavioral performance. Earlier research also indicated that DHA levels in serum/plasma phospholipids may be inversely correlated with CVD (Conquer and Holub, 1997), this might suggest that individuals with lower levels of DHA could have a higher risk of developing CVD.

Most intervention studies carried out in this field have used marine sources of LC3PUFA. This, in turn, has other environmental and health perturbations. Certain types of fish are more likely to contain high levels of methyl-mercury, creating a risk of mercury poisoning (Verbeke et al., 2005). Environmental pollutants such as dioxins and polychlorinated biphenyls have been found in fish oils, which may dissuade the use of supplementation (Eckert et al., 2010). In addition, the depletion of marine fish sources has repeatedly been highlighted. This has resulted

Table 1 *n*-3 content of vegetarian oils

Source oil	% ALA	% EPA	% DHA
Flaxseed	50	—	—
Walnut	10	—	—
Echium	33	—	—
Algae	0.11	0.29	46

Sources: (Kurowska et al., 2003; Zhao et al., 2004; Geppert et al., 2006; Breivik, 2007).

in a UN resolution on restoring fisheries and marine ecosystems to sustainable levels (Domergue et al., 2005).

There has been rising media attention regarding levels of contaminants in fish (Greiner et al., 2010). Intensive fish farming may also heighten concerns regarding contamination (Lobstein, 2002). Oils obtained from wild or feral fish can be used as a feed supplement to improve the LC3PUFA status of farmed fish. These oils represent the main source of contamination in farmed fish (Berntssen et al., 2010). Consequently, this has led to consumers becoming more aware of the content and effect of harmful substances than the nutrients offered by fish (Verbeke et al., 2005). Therefore, alternative sources of LC3PUFA could be one way to address these issues while improving human health and allaying fear of fish stock collapse and risk of contamination.

ALTERNATIVE OPTIONS

A number of alternative sources of LC3PUFA are available (see Table 1). ALA rich oils would be appropriate supplements for vegetarians and vegans. Although supplements do not appear to be a popular choice with consumers, Bates et al. (2010) found that only 12% of the British population use any type of supplements. In addition, fish oil supplements are not suitable for vegetarians and conversion of ALA is limited, as discussed earlier in this review.

Recent advances in processing techniques within the food industry now mean that traditional oils such as soybean and canola may be genetically modified to give enriched quantities of LC3PUFA's (Gillingham et al., 2010; Lemke et al., 2010). However, there have been no official recommendations or guidance in relation to these alternative sources from food agencies (Ruxton and Derbyshire, 2009). Also due to recent adverse publicity, consumers may be particularly wary of products containing genetically modified organisms.

FUNCTIONAL FOODS

Functional foods may be whole, fortified, enriched, or enhanced foods that provide health benefits beyond the provision of essential nutrients (Hasler, 2002; Berntssen et al., 2010). The European market for functional foods is estimated to be valued in excess of 2 billion US dollars (Menrad, 2003). Enriched or functional foods containing LC3PUFA from plant origin may offer an alternative to supplementation for vegetarians who account for around 6% of the population (Food Standards Agency, 2008). Consumer choice and expectation may favor an enriched food option over supplementation as approximately two thirds of consumers prefer to eat functional foods instead of taking supplements (Mintel, 2009). Consumer expectations are usually influenced by marketing communication, although healthiness appears to be one choice factor among some others including price, pleasantness, and convenience (Urala and Lähteenmäki, 2006). Research indicates that consumers are willing to pay between 30% and 50% extra to obtain the perceived health benefits that could be offered by functional foods in comparison to conventional products (Menrad, 2003).

The aim of this review is to evaluate some of the most recent, key up to date papers that have assessed the bioavailability of vegetarian *n*-3 and to highlight the most efficient vegetarian LC3PUFA sources in terms of conversion and bioavailability of EPA and DHA in the *n*-3 metabolic pathway.

METHODS

Pubmed was searched to obtain English-language, peer reviewed intervention studies published during the last 10 years. Search limits including human species, clinical trial, RCT, and dietary supplement were applied. A total of 73 articles were identified using search terms such as "bioavailability" and "supplement" in combination with ALA or "α-linolenic acid" or "alpha-linolenic acid" along with the current richest sources "flaxseed," "walnut," "echium," and "algae." From these papers high quality interventions and RCTs were chosen, including studies which investigated the bioavailability of *n*-3 from flaxseed, walnut, echium, or algae oils as supplement sources. Human intervention and RCT studies that measured bioavailability with suitable blood analytes (blood plasma and/or erythrocytes) were selected. Papers with mixed or single genders, with supplement periods of one to six months were included. Studies that examined only the compliance with intervention or supplementation were excluded as were studies analyzing *n*-6: *n*-3 fatty acid ratios.

Further inclusion criteria were that studies:

1) Investigated plasma lipid and/or erythrocyte bioavailability of *n*-3 from vegetarian sourced *n*-3 oils in dietary supplements or fortified foods.
2) Clearly stated the supplement source and dose.
3) Did not use genetically modified plant sources.
4) Included research utilizing vegetarian *n*-3 oils with or without antioxidants but with no other additional supplements.
5) Analyzed differences in *n*-3 blood fatty acid status at baseline and at the end of the intervention period.

The literature search identified 10 key studies that have investigated the bioavailability of vegetarian sources of *n*-3. Ten intervention trials are summarized in Table 2.

Table 2 Studies using vegetarian *n*-3 sources

Author	Study design	Source and dose	No./type of subjects	Time period	*n*-3 changes after intervention (X = not measured; − = decreased; + = increased; N/S = Not significant)					
					PL ALA	PL EPA	PL DHA	RBC ALA	RBC EPA	RBC DHA
Barcelo-Coblijn et al. (2008) Canada	RCT with six groups of fire-fighters. One placebo group given sunflower oil, others flaxseed oil or fish oil in three different doses, blood drawn twice weekly	Flaxseed oil 1.2–3.6 g/d	62 M and F	12 weeks	+	+	N/S	+	+	N/S
Francois et al. (2003) Oregon, USA	Intervention (no placebo), breast-feeding mothers between 2 and 11 months postpartum asked to take flaxseed oil, blood taken at weeks 0, 2, and 4	Flaxseed oil 20 g (10.7 g ALA)	7 F	4 weeks	+	+	N/S	+	+	N/S
Cao et al. (2006) Minneapolis USA	SB–RCT parallel study to compare the effects of flaxseed and fish oil supplementation using healthy subjects blood taken twice weekly	Flaxseed oil (3.5 g/d ALA)	20 M and F	8 weeks	+ (N/S)	+ (N/S)	N/S	N/S	+	N/S
Harper et al. (2006) Atlanta, USA	DB-RCT. Subjects asked to take a supplement of flaxseed or olive oil, bloods taken at weeks 0, 12, and 26	Flaxseed oil 5.2 g/d, 3 g/d ALA	49 M and F ill health	26 weeks	+	+	N/S	X	X	X
Kaul et al. (2008) Canada	DB-RCT control trial with a placebo group comparing flaxseed oil supplementation with fish oil and hempseed oil, bloods taken at weeks 0, 6, and 12	Flaxseed oil 2 g/d (1 g/d ALA)	86 M and F	12 weeks	+	N/S	N/S	X	X	X
Surette et al. (2004) Canada	A single centre open-label study to investigate dietary echium oil in subjects with mild to moderately high cholesterol bloods taken 2 weekly	Echium seed oil 15 g/d	11 M and F	4 weeks	+	+	N/S	X	X	X
Zhao et al. (2004) Pennsylvania, USA	RCT 3-diet crossover study in healthy subjects with elevated cholesterol levels, bloods taken at weeks 0 and 6	Walnut oil 15 g/d	23 M and F	6 weeks (per diet)	+	+	N/S	X	X	X
Arterburn et al. (2007) Columbia USA	RCT bioequivalence of *n*-3 measured in a parallel group study, bloods taken at weeks 0, 2, and 4	Algae DHA oil up to 1 g/d (DHA)	96 M and F	4 weeks	X	+ (N/S)	+	X	+ (N/S)	+
Sanders et al. (2006) London, UK	DB-RCT. Examines bioavailability of algal sources of *n*-3 DHA and *n*-6 DPA, bloods taken at baseline, day 28 and 29	Algae DHA oil 1.5 g/d (DHA)	79 M and F	4 weeks	X	X	+	X	X	+
Geppert et al. (2006) Munich, Germany	RCT-DB. Investigates the effects of DHA rich algae oil in healthy vegetarians, bloods taken at weeks 0 and 8	Algae DHA oil 2.28 g/d (0.94 g/d DHA)	106 M and F vegetarians	8 weeks	X	+	+	X	+	+

RCT = randomized control trial, SB = single blinded, DB = double blinded, M = male, F = female, PL = plasma, RBC = red blood cells.

FLAXSEED OIL

Flaxseed oil is also known as linseed oil and can contain up to 50% ALA when cold pressed (Breivik, 2007). The majority of studies identified in the review examined the bioavailability of flaxseed oil using high (Francois et al., 2003) and low doses (Cao et al., 2006; Harper et al., 2007; Barcelo-Coblijn et al., 2008; Kaul et al., 2008). Doses as low as 2 g/d flaxseed were found to increase plasma ALA levels by Kaul et al. (2008), although other studies concluded that higher doses were necessary to increase plasma and erythrocyte EPA levels.

Male and female Canadian fire-fighters ($n = 62$) were randomized into six groups by Barcelo-Coblijn et al. (2008) with the aim of ascertaining dosages of ALA required for optimal elongation and desaturation in the *n*-3 metabolic pathway. Three of the groups consumed 1.2, 2.4, or 3.6 g/d flaxseed oil respectively, two other groups consumed fish oil and the control group were given sunflower oil. Flaxseed doses of 2.4 and 3.6 g/d were found to significantly elevate erythrocyte ALA and EPA levels by 0.23 and 0.42 (mol%), respectively ($p < 0.05$ for both), although no significant changes were noted in DHA levels. The authors concluded that the amounts of ALA required to give effective conversion to EPA were easily achievable in the general population through dietary modification.

Harper et al. (2006) and Cao et al. (2006) investigated flaxseed supplementation which equated to 3 and 3.5 g/d ALA, respectively. No significant rises in plasma ALA, EPA, or DHA were noted in the eight-week study by Cao et al. (2006), although small but significant increases were observed in erythrocyte EPA levels. It was concluded that intake of ALA had little effect on EPA and DHA blood concentrations and that fish oil supplements gave optimal levels of erythrocyte EPA and DHA. However, the longer term study with similar doses by Harper et al. (2006) found supplementation with 5.2 g/d flaxseed oil (3 g/d ALA) significantly increased plasma and erythrocyte levels of ALA and EPA ($p = 0.04$ and $p = 0.03$, respectively) in men and women with chronic illnesses including hypertension (55%) and type II diabetes (12%).

Finally, Francois et al. (2003) used large doses (20 g) of flaxseed oil to supplement breast feeding mothers ($n = 7$) over a four-week period. Plasma lipid levels of ALA and EPA were significantly elevated in comparison to baseline values. After two weeks, ALA and EPA levels rose by 2.2 and 0.8%, respectively, then continued to rise to 3.4 and 1.6%, respectively, at the end of the study. Breast milk EPA levels were also significantly higher than baseline levels. However, blood and breast milk DHA levels remained unchanged and it was concluded that flaxseed oil supplementation was not an effective way to increase DHA concentrations in maternal breast milk.

ECHIUM SEED OIL

Extracted from the seeds of the *Echium plantagineum* plant, echium oil contains around 33 per cent ALA and up to 12.5% stearidonic acid (18:4, *n*-3, SDA), (Breivik, 2007). SDA follows ALA in the *n*-3 metabolic pathway (Bailey, 2009). Surette et al. (2004) utilized a single centre open labeled study to investigate the effect of large doses (15 g/d) of echium oil. The trial took place over a four-week period, using male and female participants ($n = 11$) with elevated cholesterol levels. The authors hypothesized that consumption of echium oil may lead to enrichment of tissues with LC3PUFA's such as EPA and DHA. Once completed, significant increases were noted in EPA blood plasma levels (0.97 μmol/L), although there were no significant rises in levels of DHA. It was concluded that oils rich in SDA appear to possess some of the properties typically associated with fish oils. More research was considered necessary to investigate the extent of tissue enrichment required to impart various physiological benefits.

WALNUT OIL

Walnut oil contains up to 10.4% ALA (Simopoulos, 2002) the lowest proportion of the seed/nut oils examined in this study. Therefore, a relatively high dose of 15 g/d was given to male and female overweight/obese participants with elevated cholesterol levels over a six-week intervention period by Zhao et al. (2004). The subjects were otherwise healthy, nonsmokers and were not taking any medication or dietary supplements. Participants were randomized to receive one of three diets, the first a typical American diet, high in saturated and monounsaturated fats, the second high in *n*-6 LA, and the third high in ALA. Those who received the ALA diet, which incorporated the walnut oil, demonstrated a significant rise in plasma ALA and EPA ($p < 0.05$, exact amounts not specified) levels along with a decrease in lipid lipoprotein.

The study concluded that a diet high in PUFA, especially ALA from walnuts and walnut oil produced a cardio-protective effect by eliciting vascular anti-inflammatory outcomes. However, there was no evidence that ALA from walnut oil was converted to DHA in the *n*-3 metabolic pathway as DHA levels were not significantly different from baseline values. Further research was recommended to investigate the underlying mechanisms of the cardio-protective effects.

ALGAE OIL

Algae oils are a relatively recent innovation in the food industry. Produced in tightly controlled, closed fermentation facilities they are entirely vegetarian and never come into contact with oceanic contaminants (Breivik, 2007). Capable of providing large amounts of DHA algae are also the primary source of DHA in the food chain (Arterburn et al., 2007) and are available for use in fortification of foods and infant formulas along with dietary supplements. Algae oils provide Kosher, halal, and vegetarian sources of LC3PUFA (Breivik, 2007). Three of the

studies examined by the review investigated the bioavailability of LC3PUFA from algae oils over reasonably short time periods.

The studies by Arterburn et al. (2007), Sanders et al. (2006) and Geppert et al. (2006) used relatively small dosages of between 0.6 and 1.5 g/d (DHA) and noted significant increases in the plasma DHA levels of participants. Arterburn et al. (2007) found that DHA increased by 3.03 g per 100 g of fatty acids, Sanders et al. (2006) observed erythrocyte phospholipid DHA increases of 27% and Geppert et al. (2006) noted that DHA supplementation decreased plasma triacylglycerol levels by 23%.

All of the algae oil studies examined small supplement doses over short time periods. Trials over four weeks were sufficient to give significant rises in blood and plasma DHA levels, this did not occur in any of the nut/seed oil trials. Therefore, it appears there is further potential for research to examine the integration of LC3PUFA's from algal oils into functional foods and this may help improve habitual intakes.

DISCUSSION

A number of organizations have made recommendations for the dietary intake of LC3PUFA's. The International Society for the Study of Fatty Acids and Lipids (ISSFAL), (2004) recommends 2 and 0.7% of energy per day should come from LA and ALA, respectively, in healthy adults. The Institute of Medicine of the National Academies, (2002) states the recommended nutrient intake for ALA is 1.6 and 1.1 g/d for men and women aged 19 to > 70 years, respectively. The most recent UK recommendations state that people should consume 0.2 g/day LC3PUFA (Bates et al., 2010). Currently, there are no official *n*-3 recommendations for vegetarians and vegans although some experts suggest vegetarians and those receiving no direct dietary sources of EPA and DHA should at least double the recommended intake of ALA (Davis and Kris-Etherton, 2003).

A considerable amount of research has examined the LC3PUFA status of humans after supplementation with ALA rich oils. All of the studies included in this review have shown that LC3PUFA's can successfully be used to increase blood levels of ALA but conversion of ALA to its longer chain relatives EPA and DHA is limited within the *n*-3 metabolic pathway. Overall, findings indicate that vegetarian sources of *n*-3 oils such as flaxseed, echium, and walnut may elicit similar results to marine sources of LC3PUFA, although further research is necessary to indicate optimal levels of supplementation. The conversion process can be affected by several factors such as current LC3PUFA status and consumption of *n*-6 fatty acids as shown in Fig. 1. None of the ALA papers reviewed made any significant findings in relation to plasma or erythrocyte DHA increases.

As discussed earlier in this paper, DHA may provide superior health benefits over EPA, (Breivik, 2007). Harris et al. (2008) recommend a direct intake of the longer chain *n*-3 fatty acids EPA and DHA, although this may be difficult for non-fish eaters. Therefore, it seems logical that a direct vegetarian source such as marine-algae oils could offer a solution. Oils produced from marine-algae sources are vegetarian, kosher, halal, and suitable for vegans; they are contaminant free and could be used to provide a direct, vegetarian source of DHA (Conquer and Holub, 1997).

Unlike the other vegetarian sources identified in this review, increases were noted in plasma and erythrocyte DHA levels using relatively small doses of algal oils. Geppert et al. (2006) found significant increases in the EPA and DHA levels of vegetarians with doses of 0.94 g/d DHA. It was not clear if baseline LC3PUFA levels were depressed in the study participants, although the uptake of DHA may have been increased in line with findings by Cao et al. (2006) who concluded that individuals with higher DHA concentrations at baseline tended to take up additional DHA at a slower rate than those with lower baseline levels. Increases in plasma and erythrocyte EPA levels found by Geppert et al. (2006) concur with findings in an earlier paper by Conquer and Holub (1997) who examined dietary supplementation with algal DHA as a source of EPA for vegetarians and omnivores. Retro-conversion of DHA to EPA was found to be 9.4%, which suggested that dietary DHA could be used as a source of EPA via retro-conversion.

With regards to toxicity signs, participants in all algae oil intervention trials were closely monitored for side-effects and symptoms. All three of the studies found that low doses of algae oils were well tolerated and represented a safe bioavailable source of DHA for humans. Adverse event monitoring in all of the studies revealed an excellent safety and tolerability profile.

As algae oils do not occur in regular foods, a nutritional vehicle would be necessary to incorporate them into the diet. As discussed earlier in this review, supplements are not widely used within the general population. Consumers are more likely to dismiss supplements in favor of a healthy diet, making functional foods better suited to consumer lifestyles (Mintel, 2009). Of the 10 papers evaluated in this review, only one (Arterburn et al., 2007) made use of *n*-3 functional foods. A cereal bar was enriched with 465 mg algae oil and participants asked to consume a bar each day for four weeks. One of the oils tested in capsule form gave similar DHA levels to the cereal bar at higher supplement doses of 600 mg/d after four weeks. This would suggest that DHA from algae sources may be more bioavailable from enriched foods than supplements, although more research is necessary to ascertain that this would be the case.

RECOMMENDATIONS

In view of the relatively short study periods in previous research, further long-term studies may be needed to assess the bioavailability of LC3PUFA when using echium seed, walnut, and particularly algae oil supplements. The majority of studies examined in this review recruited male and female participants. Additional interventions analyzing the potential differences in bioavailability of vegetarian LC3PUFA's in males and females within single sex cohorts may be beneficial.

Further research relating to bioavailability of LC3PUFA's from marine-algae based oils is necessary. In future, research should be carried out over longer study periods to investigate the suitability and safety of algae oils as a replacement for marine/fish sources of LC3PUFA. Further intervention type studies should be undertaken to identify the optimum doses required to give maximum bioavailability of LC3PUFA from algae oils. Research is also needed to establish the effectiveness of microalgae supplementation for the at risk groups identified in this review. Finally, suitable foods appropriate for fortification or enrichment with LC3PUFA's particularly from algae oils need to be identified and evaluated.

CONCLUSIONS

Non-fish sources of *n*-3 are particularly important for vegetarians, non-fish eaters and pregnant mothers. Flaxseed oil is a rich source of *n*-3 and has been proven to have good bioavailability when used in bulk or emulsion in several studies. Consumption of walnuts or walnut oils and echium seed oil also improved levels of *n*-3 and LC3PUFA's in study participants. However, research has shown that conversion of the essential fatty acid ALA to DHA from foods or supplements has been ineffective, leading scientists to seek further DHA sources in the form of algae oils and genetic engineering. Interventions using algae oil have been extremely successful in terms of the safety and bioavailability of algal DHA, although further research is necessary to evaluate optimal doses and suitability for fortification of enriched/functional foods.

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