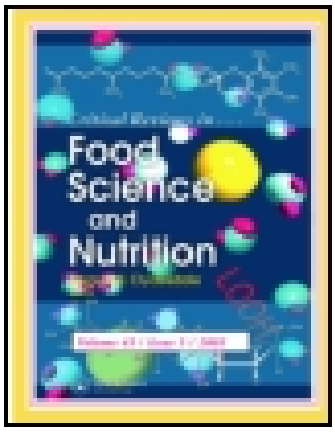

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Omega-3 Fatty Acids - A Review of Existing and Innovative Delivery Methods

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Omega-3 fatty acids – a review of existing and innovative delivery methods.

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Key words

Omega-3 intakes, delivery vehicles, bioavailability, health

Abstract

Omega-3 fatty acids are generally under consumed in Western diets; a factor that may largely be attributed to low intakes of oily fish. Although supplementation strategies offer one approach in terms of improving blood fatty acid levels, rates of compliance are generally low, due to difficulties swallowing capsules, or unfavourable aftertastes. Consequently, new approaches, including food-based strategies may be an alternative approach to improving omega-3 status and the health of public sectors. This paper sets out to discuss and review how the use of novel food

vehicle and delivery advancements may be used to improve omega-3 status, which may have wider benefits for public health and well-being.

Introduction

Evidence from dietary surveys show that intakes of oily fish tend to fall short of recommended guidelines in Western regions (Nelson et al., 2007, Elmadfa and Freisling, 2009, Bates et al., 2014, Swanson et al., 2012). Dietary guidelines advise that at least two portions of fish (approximately 140 grams per portion) should be consumed weekly, with one portion ideally being oily fish (Scientific Advisory Committee on Nutrition, 2004). This, in turn, has wider implications for habitual omega-3 (*n*-3) intakes, which have been found to be approximately 5-times lower in Western regions when compared with Japanese intakes (Meyer, 2011). Vegetarians and vegans are another population group whose diets are particularly low in *n*-3 fatty acids, with vegetarian diets including dairy foods and eggs still only providing around 0.02 g/d of docosahexaenoic acid (DHA). This may have broader, long-term pathophysiological implications, although this remains to yet be studied (Sanders, 2009).

Presently, supplements are the main alternative choice to dietary sources of *n*-3 fatty acids for those with a dislike for fish, or who cannot meet the recommended requirements from food sources alone (Ruxton and Derbyshire, 2009, Givens and Gibbs, 2008). However, data from the latest National Diet and Nutrition Survey (NDNS) clearly demonstrates that only around 11 per cent of UK adults aged 19-64 years use fish oil supplements, such as cod liver oil (Bates et al., 2014). For vegetarians and vegans the use of gelatine as the main encapsulation material for most supplements, unfortunately makes them an unsuitable choice for most vegetarians, vegans and certain religious groups (Jain et al., 2012).

Another commonly reported problem associated with capsule ingestion is the tendency to produce an unpleasant reflux. Oils have a lower density than gastric fluids and the burst of capsules in the stomach can result in high concentrations of lipids in the upper layers of gastric juices causing a fishy reflux (Fetterman and Zdanowicz, 2009). Subsequently, signs of gastrointestinal upset, fishy aftertastes and repetition symptoms have also been linked to the use of fish oil supplements (Fetterman and Zdanowicz, 2009, Kris-Etherton et al., 2002, Sacks et al., 1995, Wallace et al., 2000).

While capsule ingestion may be tolerated by some individuals and does have an important role in helping to improve *n*-3 status, this paper sets out to discuss and review the role of alternative methods of *n*-3 delivery, focusing namely on food fortification, nanoemulsion techniques and the topical delivery of *n*-3 fatty acids. The article first provides some background in terms of existing *n*-3 sources and then goes on to discuss emerging modes of *n*-3 delivery.

Food sources of *n*-3 fatty acids

Fish sources

As shown in Table 1 fish and fish oils are currently the most prevalent sources of fatty acids DHA and eicosapentaenoic acid (EPA) (Bourre, 2007). Fish oils obtained from the flesh of oily fish and the offal of white fish contain a large number of long-chain *n*-3 polyunsaturated fatty acids and an array of different fatty acids within their triglyceride structures (Gunstone, 2006). The flesh of oily fish such as mackerel, salmon, sardines, anchovies and pilchards is particularly rich in EPA and DHA (Bailey, 2009).

Krill oil represents a rich source of EPA and DHA containing 34.1 grams of long-chain *n*-3 polyunsaturated fatty acids per 100 grams (Ulven et al., 2011). However, as with other marine-based sources the sustainability of krill oil production cannot be guaranteed (Surette, 2013, Trivelpiece et al., 2011). Recent studies suggest a link between krill abundance and global warming. An absence of winter sea ice from krill habitats means that krill abundance may be reduced (Trivelpiece et al., 2011).

Animal sources

Meat and poultry also provide an important source of *n*-3 fatty acids, as shown in Table 2. However, it should be considered that the *n*-3 content of meat from animal sources per 100 grams is considerably lower than that found in fish and particularly oily fish (Howe et al., 2006). Data from the latest NDNS shows that UK adults generally consume around 83 grams per day of red and 61 grams per day of white meat (Bates et al., 2014). Poultry meat also contributes small but worthwhile amounts of EPA and DHA (Givens et al., 2006), with some evidence from dietary surveys showing that meat, poultry and game can provide around 43 per cent of the *n*-3 intake of non-vegetarians (Howe et al., 2006).

Other studies have examined the enrichment of animal derived foods with EPA and DHA using fish-oil supplemented feeds. There are, however, concerns that the continued and possibly increased use of fish oils in animals' diets is not a suitable cost-effective or sustainable long-term approach (Givens and Gibbs, 2008).

Vegetarian sources

Alpha-linolenic acid (ALA) is currently the most predominant dietary source of *n*-3, found in the lipid portions of leafy green plants and some seeds.

Flaxseed oil (also known as linseed oil) is currently the main vegetarian source of ALA and can contain up to 56 per cent ALA when cold pressed (Harper et al., 2006). Other vegetarian sources of long-chain *n*-3 polyunsaturated fatty acids include echium, perilla seed, walnut and blackcurrant seed oil (Breivik, 2007).

Echium oil is a non-genetically modified vegetable oil, which is obtained from the seeds of the *Echium plantagineum* plant. It contains significant amounts of the long-chain *n*-3 fatty acid, also known as stearidonic acid (18:4*n*-3; SDA). Echium seed oil consists of up to 47.1 per cent of long-chain *n*-3 polyunsaturated fatty acids, comprised of around 36.6 per cent ALA and 10.5 per cent SDA (Kuhnt et al., 2012). Perilla seed oil is obtained from the seed of the *Perilla frutescens* plant and is another rich source of *n*-3 containing up to 54 per cent ALA (Asif, 2011) while blackcurrant seed oil is rich in both *n*-3 and *n*-6 fatty acids with the main source of long-chain *n*-3 polyunsaturated fatty acids being ALA and SDA (Linnamaa et al., 2010)

Current *n*-3 fatty acid delivery methods

A summary of n-3 fatty acid delivery methods can be found in table 4.

Food fortification

Enriched or functional foods containing *n*-3 fatty acids may offer an alternative dietary source to naturally rich foods and supplements. Functional foods are generally defined as whole, fortified,

enriched or enhanced foods that provide additional health benefits (Buttriss, 2010). As the body of scientific evidence continues to support inter-relationships between certain foods and improved health, the market for functional foods has developed rapidly (Reglero et al., 2008). For example, the European market for functional foods is estimated to be valued in excess of 2 billion US dollars (Menrad, 2003) while the UK functional food industry was worth £785 million in 2010 and is estimated to increase in value to £1195 million by 2016 (Mintel, 2011).

From a research and development perspective, functional foods represent an area where the expertise of medical doctors, nutritionists and food technologists should be combined to develop innovative products, whilst maintaining the sensory qualities of traditional foods (Fogliano and Vitaglione, 2005). Consumers perceive products that are intrinsically healthy such as yogurt, cereals and juice, as preferable and credible carriers of functional foods (Annunziata and Vecchio, 2011). Jacobsen, (2009) examined consumer acceptance of various *n*-3 enriched foods including mayonnaise, salad dressings, milk products, yogurt products and fitness bars. Of these, yogurt was found to be less susceptible to lipid oxidation compared with milk and mayonnaise products, possible due to the anti-oxidative peptides created during manufacturing (Jacobsen, 2009).

Over the last 10 years, several studies have investigated the feasibility and possible health effects associated with *n*-3 food fortification. For example, recently Hughes *et al.* (2012) developed oat and soy-nutrition bars fortified with nonencapsulated, nonemulsified fish oil. Scientists found that replacing 20 per cent of canola oil with fish oil (6g per 600g), equating to 178mg EPA and

DHA per 35g serving was most successful in terms of being oxidatively stable and acceptable to consumers. Similarly, another study investigating the addition of flax to bagels found that bagels made with 23 per cent milled flaxseed providing 6g ALA were acceptable to consumers without causing gastrointestinal distress (Aliani et al., 2011).

McCowen *et al.* (2010) developed a stable DHA emulsion that was added to yoghurt, containing 600mg DHA per daily serving. This study also investigated the effects of long-term consumption of the DHA yoghurt emulsion with plasma phospholipid levels found to increase by 32 per cent after 12 weeks of daily ingestion. Work by Garg *et al.* (2007) has tested the effects of ingesting an *n*-3 enriched dip which was consumed by diabetic patients daily over 6 weeks and found to significantly improve the *n*-3 blood fatty acid profile. Equally, Mardones *et al.* (2008) found that mean birth weight of Chilean infants increased when mothers were provided with a milk product containing micronutrients and *n*-3 fatty acids during their pregnancy, when compared with the pregnancy outcomes of women receiving regular powdered milk.

It should also be considered that certain claims may be applied to foods containing *n*-3 fatty acids, provided that these are at the correct levels. For example, for a food product to claim that it is ‘a source’ of *n*-3 fatty acids the product should contain at least 0.3g ALA per 100g and per 100kccal, or at least 40mg of the sum of EPA and DHA per 100g and per 100kcal. In addition, for a claim that a food is ‘high in’ *n*-3 fatty acids the product should contain at least 0.6g ALA per 100g or per 100kcal, or at least 80mg of the sum of EPA and DHA per 100g and per 100kcal (European Commission, 2012). Table 3 also shows a list of health claims approved by the

European Food Safety Authority, although the conditions of the claims should be carefully noted and applied before the claim could be used in practice.

Encapsulation

Encapsulation involves the spray drying of emulsion systems to create a powder that can used to enrich food matrixes (Rubilar et al., 2012). The encapsulation of source oils may be used to mask the undesirable taste and odour of *n*-3 fatty acids and stabilise them against degradation and oxidation (Sanguansri *et al*., 2013). Barrow *et al*, (2009) demonstrated that a microencapsulated fish oil powder was bioequivalent to soft gel capsules of the same oil formulation in a randomised crossover trial using fourteen participants. Earnest et al. (2009) examined the absorption of commercially available products fortified with microencapsulated fish oil as part of a breakfast meal. Fortified foods were found to increase plasma *n*-3 concentrations and positively modulate triacylglycerols in the two week study, which used 20 participants in total.

Nanoemulsion techniques

One major focus of current nanotechnology applications in food is the development of nanostructured food ingredients and delivery systems for nutrients and supplements (Chaudhry et al., 2008). Nanoemulsions are typically defined as systems with an extremely small droplet size (Gutiérrez et al., 2008) with materials at the nanometre scale generally being around 10^{-9} m (Silva et al., 2011, Rao and McClements, 2011). The incorporation of nutrients into foods using

nano-technology has the potential to improve bioavailability due to small particle sizes and high surface to surface volume ratio (Acosta, 2009).

Jafari *et al*, (2006) states that nanoemulsion droplet sizes cover the size range of 20 to 200nm if transparent or up to 500nm with a milky appearance. A further definition by Anton and Vandamme (2009) identifies nanoemulsions as systems with lipid particles smaller than 300 nm. Nanoemulsions, like conventional emulsions can be classified in accordance with the relative spatial organisation of their oil and water phases.

A system consisting of oil droplets dispersed within an aqueous base is referred to as an oil in water nanoemulsion and aqueous droplets distributed in an oil/lipid base is referred to as a water in oil nanoemulsion (McClements and Rao, 2011).

Oil in water nanoemulsions offer the potential to improve the bioavailability of lipid based nutrients including *n*-3 polyunsaturated fatty acids (Dey et al., 2012, Acosta, 2009). Small droplets of nutrients can easily be transported in the body through cell membranes giving increased blood plasma and erythrocyte concentrations (Huang et al., 2010).

Presently, few studies have investigated the human bioavailability of *n*-3 nanoemulsions. One randomised crossover trial recruited eleven adults, asking them to ingest treatments: 1) Yogurt drink containing algae oil and water nanoemulsion, providing 1264mg (DHA), or 2) Formulated strawberry yogurt drink containing bulk algae oil providing the same amount of DHA (control). Fingertip blood sampling took place at baseline, 2, 4, 6, 24 and 48 hours. The validated Omega Blood Count test kit™ (Bell et al., 2011) was used for blood percentage fatty acid analysis.

Study findings showed that the absorption of *n*-3 long-chain polyunsaturated fatty acids peaked 4 hours after ingestion, for both treatments, with the baseline adjusted incremental area under the curve being statistically significantly higher for the nanoemulsion from 2-4 and 4-6 hours following ingestion compared with the bulk oil (p = 0.020 and p = 0.03 respectively). A comparison of the treatments at all times demonstrated that the ratio of omega-6 to *n*-3 was significantly more decreased for the nanoemulsion treatment (p = 0.028), which may offer long term health benefits (Simopoulos, 2011). Larger and longer trials are needed but this preliminary trial indicates that nanoemulsion of vegetarian *n*-3 oils may help to improve *n*-3 status (Lane et al., 2014).

Topical Delivery

As dietary supplementation with *n*-3 fatty acids is not always effective there has been increased interest in the local (skin) application of *n*-3 fatty acids rich oils for specific conditions (Puglia et al., 2005).

Topical delivery methods involve direct application to the skin and have previously been used to provide targeted delivery in the treatment of localised inflammatory conditions such as arthritis and psoriasis (Zulfakar et al., 2007).

In one study Puglia *et al*, (2005) evaluated the *in vitro* percutaneous absorption of EPA and DHA from fish oil using excised human skin. Results suggested that long-chain *n*-3 rich oils may be used as ingredients for topical pharmaceutical and cosmetic products targeted at the treatment of skin inflammation. Zulfakar *et al*, (2007) also found that EPA in particular has a potential role in

the treatment of the skin condition psoriasis. Overall, this provisional work indicates that EPA offers beneficial effects, particularly as a topical treatment, either as an active anti-inflammatory agent by itself, or as a dual action permeation enhancer for other anti-psoriatic treatments.

A further study by Kumar et al, (2014) used *in vitro* skin permeation to evaluate the bioavailability of omega-3 enriched nanoemulsion of thiocolchicoside (TCC) a therapeutic agent for orthopaedic, traumatic and rheumatologic disorders. Nanoemulsions of TCC and omega-3 source oils were formulated successfully and the optimised omega-3 enriched nanoemulsion formulation showed significantly improved *in vitro* permeation compared to the control.

Discussion

It is now well established that *n*-3 status is directly associated with health benefits throughout life, including foetal development, cardiovascular function, and supporting cognitive function (Swanson et al., 2012). Although *n*-3 fatty acids may be obtained directly from food sources, low intakes and a general dislike of oily fish means that these are generally under consumed habitually; a trend common across Western regions (Bates et al., 2014, Elmadfa and Freisling, 2009, Nelson et al., 2007). While poultry and red meat are important sources of *n*-3 fatty acids, their *n*-3 content per 100 grams is considerably lower than levels present in oily fish (Howe et al., 2006). Considering this, most individuals need to top up dietary intakes either with supplement sources, or as we have discussed in this review functional foods containing *n*-3 fatty acids.

We have considered how supplement compliance is generally low, due to the need to swallow large capsules and the aftertaste that is commonly associated with taking these. Equally, while fortifying foods also appears to be an innovative and alternative way forward, the chemical structure of *n*-3 fatty acids also makes them particularly susceptible to the effects of lipid oxidation (Jacobsen, 2009). Lipid oxidation can cause three main problems; firstly, it reduces the nutritional value of foods containing lipids. Secondly, free radicals, which are formed during oxidation may contribute to the development of atherosclerosis, posing a potential health risk to consumers and, finally, it can give rise to objectionable 'off' flavours (Jacobsen, 1999). Consequently, these issues can affect sensory characteristics; a problem that appears to be further exacerbated by integrating nanoemulsion techniques, although this has the added benefit of improving bioavailability (Lane et al., 2013a, Lane et al., 2012, Lane et al., 2013b).

With further regard to nanoemulsions and flavour, some authors have found that the use of oil-soluble flavours, vitamins and nutraceuticals can help to reinforce their sensory properties (McClements, 2011). However, this unfortunately does not appear to be the case in relation to *n*-3 nanoemulsion oils, and further work is required to improve this. For example, Lane et al, (2013b) found that the addition of a high DHA algal oil nanoemulsion to a strawberry yogurt product had significant and adverse effects on the aroma, flavour, texture, aftertaste and overall acceptability. While the appearance was unaffected and the product consistency was slightly improved, this was not to levels of statistical significance when compared with the controls.

During the creation and storage of oil in water emulsion systems, it is also possible that the number of free radicals generated per droplet increases as the droplet concentration decreases

(Osborn and Akoh, 2004). Additionally, with higher oil concentrations, more unsaturated fatty acids may move to the interior of oil droplets, becoming less accessible to direct interaction with the pro-oxidants in the aqueous phase (McClements and Decker, 2000). This demonstrates that, where possible, nanoemulsions systems with higher oil loads (in the range of 30 to 50 per cent) are likely to remain more stable to oxidation when compared with lower oil concentrations. Further consideration should also be given to how the reduction of oil droplets to nanoscale proportions may affect their biological fate in the human body and potential toxicity issues (McClements and Rao, 2011). These aspects warrant additional consideration when deciphering oil loads and undertaking future nanoemulsion work.

As identified in this paper, the topical application of *n*-3 fatty acids appears to be a promising and growing area of research, particularly for conditions such as psoriasis management. However, significantly more work is needed to study the potential benefits of such nanomedicines. Teething problems such as stability issues and vulnerability to degradation due to lipid oxidation and inconsistent bioavailability (an issue relevant to both oral and topical administration) are yet to be ironed out (Rahman et al., 2013). Certainly, before these can be used in a broader, health or medical context more work is needed to improve stability and identify consistent improvements in terms of bioavailability. However, if this can be achieved, nanomedicine techniques offer a unique solution to patients that may benefit from direct application of *n*-3 fatty acids, or who have problems tolerating the ingestion of *n*-3 fatty acids orally.

In summary, when using nanoemulsion of *n*-3 oils, it is necessary to achieve a balance between positive increases in *n*-3 bioavailability compared with potential unfavourable sensory attributes. As discussed, reducing the dose of nanoemulsified oils could be one way forward, while the use of masking agents or flavour enhancers could be another solution. It should also be considered that while there are advantages of using nanoemulsions i.e. to improve the bioavailability of lipophilic substances there may also be some risks associated with their oral ingestion, including their ability to change the biological fate of bioactive components within the gastrointestinal tract and the potential toxicity of some of the components used in their fabrication (McClements, 2011). Clearly, all of these issues need to be targeted before nanoemulsions can have a wider use. The direct, topical application of *n*-3 nanoemulsions could be one way to overcome some of the sensory problems, but again more work is needed to study their stability, bioavailability and effects in relation to the longer-term use of these.

Conclusions

In conclusion, while dietary sources, namely in the form of oily fish provide an important source of *n*-3 fatty acids these are generally under consumed by the lay population. Supplements offer one alternative approach in terms of helping to improve *n*-3 status but poor compliance and unfavourable aftertastes often act as barriers to their use. As discussed in this article, fortification may offer an alternative potential strategy but this itself has limitations, including overcoming the process of lipid oxidation which can impact on sensory characteristics and shelf-life. Finally, work on nanoemulsions looks particularly promising in terms of the treatment of exogenous skin conditions; it may also provide an alternative approach to those who cannot

tolerate the ingestion of oral *n*-3 fatty acids. That said, there remains to be a great deal of work that needs to be done to advance this area.

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Table 1. Long-chain *n*-3 polyunsaturated fatty acid content of dietary fish species.

Fish species	**EPA+DHA content g/100 g of fish**
Atlantic herring	2.01
Atlantic salmon	1.28–2.15
Sardines	1.15–2.00
Rainbow trout	1.15
Mackerel	0.40–1.85
Halibut	0.47–1.18
Tuna	0.28–1.51
Oyster	0.44
Flounder or sole	0.40
Shrimp	0.32
Tuna (canned)	0.31
Cod	0.28
Haddock	0.24
Catfish	0.18
Krill	1.02
Scallop	0.20

Adapted from Wall *et al*,(2010); Ulven *et al*, (2011) and Kolakowska *et al*, (1994)

Table 2. *n*-3 content of dietary meats

Animal species	mg/100g of muscle tissue		
	ALA	**EPA**	**DHA**
Beef	26.00	9.95	1.63
Lamb	65.80	0.00	7.20
Pork	20.60	6.51	8.33
Poultry (white meat)	4.50	6.30	16.20
Poultry (dark meat)	15.50	13.30	22.00

Adapted from Enser *et al*, (1996) and Rymer and Givens (2005)

Table 3. Approved health claims for *n*-3 fatty acids

Nutrients/ingredients	Authorised claim	Condition of claim
ALA	ALA contributes to the maintenance of normal blood cholesterol levels	The claim may be used only for food which is at least a source of ALA as referred to in the claim SOURCE OF OMEGA 3 FATTY ACIDS as listed in the Annex to Regulation (EC) No 1924/2006. Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 2 g of ALA.
DHA	DHA contributes to maintenance of normal brain function	May only be used for food which contains at least 40mg DHA per 100g and per 100 kcal. To bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 250 mg of DHA.
DHA	DHA contributes to the maintenance of normal vision	The claim may be used only for food which contains at least 40 mg of DHA per 100 g and per 100 kcal. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 250 mg of DHA.
Eicosapentaenoic acid and docosahexaenoic acid (EPA/DHA)	EPA and DHA contribute to the normal function of the heart	The claim may be used only for food which is at least a source of EPA and DHA as referred to in the claim SOURCE OF OMEGA 3 FATTY ACIDS as listed in the Annex to Regulation (EC) No 1924/2006. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 250 mg of EPA and DHA.

Source: European Commission (2012).

Table 4 Summary of *n*-3 fatty acid delivery methods

Author	Study Design	Delivery method	*n*-3 source and amount	Main findings
Food fortification (Hughes et al., 2012)	The assessment of the oxidative stability and consumer acceptance of oat and soy based nutrition bars fortified with fish oil compared to a canola oil control product	Enriched foods in the form of oat and soy based nutrition bar treatments	Tocopherol enriched non-emulsified fish oil at 4 levels (0, 1, 2, 3g respectively) Providing 0, 17.7, 41.5, and 61.1mg EPA and 159.8, 392.1 and 392.1g DHA per serving respectively	Enriched bars provided up to 721.6mg EPA and DHA per serving without affecting oxidative stability. The lowest level of enrichment did not affect consumer acceptance compared to the non-enriched control
(Aliani et al., 2011)	Sensory evaluation of the flavour profile of different muffin and snack bar formulations with and without milled flaxseed. Three snack bar formulations and two muffin formulations with and without flaxseed evaluated by trained assessors respectively.	Enriched foods in the form of snack bars and muffins	Flaxseed oil to provide 6g ALA per day	Flaxseed enriched products had significantly lower sweetness, vanilla aroma and flavour intensities. Flax aroma, flavour and bitter taste were also significantly higher in the enriched products
(McCowen et al., 2010)	To supplement yogurt with DHA and assess incorporation into plasma lipids using 12 healthy human subjects	Food enrichment. Enriched yogurt product using a	DHA algal oil to provide 600mg DHA per	Significant increases in plasma DHA ($p <$ 0.01) were evident in

			stable emulsion system	272g serving of yogurt	volunteers after 3 weeks of ingestion. Preliminary results suggest that algal oil can successfully be incorporated into everyday foods such as yogurt
(Garg et al., 2007)	The use of micro emulsification technology to fortify foods with LC3PUFA without the undesirable fishy odours and taste and reasonable shelf life. The effect of supplementing people with type II diabetes was examined		Micro emulsification. 13 participants with diabetes given 100g/d of a jalapeno or olive flavoured enriched humus type dip	Fish oil to provide 1.3 to 1.4g LC3PUFA per 100g of humus dip	Short term consumption (6 weeks) of a LC3PUFA enriched dip product allowed incorporation of LC3PUFA into plasma lipids and exhibited known lipid modifying effects
(Mardones et al., 2008)	To determine whether maternal food fortification	Food enrichment. Pregnant women received	ALA, 0.9g per 100g of milk. Participants consumed 66g per day to		The intervention resulted in

	with *n*-3 fatty acids and multiple macronutrients increases birth weight and gestation duration	powdered milk during health check-ups. The treatment group received a milk product with multiple micronutrients and *n*-3. The control group received non fortified powdered milk	provide a dose of 0.6g/d	significant increases to gestational duration and infant length ($p = 0.034$ and 0.019 respectively
Encapsulation (Rubilar et al., 2012)	The development of an optimised formulation of a soup powder enriched with *n*-3 fatty acids.	Food enrichment and microencapsulation. The development of an *n*-3 enriched soup powder.	Linseed oil, ALA, 316mg per serving of soup	The successful development of an ALA enriched soup product that was highly acceptable to consumers.
(Sanguansri et al., 2013)	The development of 3 encapsulant matrixes which were tested for degradation and oxidation of fatty acids. In vitro digestion	Encapsulation of spray dried emulsions to form powders suitable to be added to food matrixes	Tuna oil DHA 5.12 to 6.19g/100g powder, EPA 1.16 to 1.45g/100g powder	Bioactive mixtures of tuna oil, tributyrin and reservatrol can be produced into stable powdere

				d formats. Further human in vitro trials are necessary to confirm the bioavailability of these bioactives
(Barrow et al., 2009)	Randomised crossover study to compare the bioavailability of microencapsulated *n*-3 fish oil and standard fish oil soft gel capsules	A crossover study using 14 male participants. A milkshake product was used as a delivery vehicle	Fish oil, 30/20 ethyl ester containing 297mg/g EPA and 218mg.g DHA either as capsules or microencapsulated . Each 1g capsule contained 200mg DHA and 272g EPA. Participants asked to ingest 4 x 1g capsule per day giving a dose of 800mg DHA and 1088mg EPA.	*n*-3 fatty acids have equivalent bioavailability when delivered as microencapsulated complex coacervates or as soft-gel capsules
(Earnest et al., 2009)	A randomised placebo controlled trial using 20 participants who were asked to consume a breakfast meal	Breakfast meals contained milk, yogurt and bread products fortified with MicroN3 microencapsulated fish oil. Hens eggs from hens fed	Fish oil, total EPA/DHA ranged from 450-500mg/meal. The placebo group	A large volume of *n*-3 can be administered with the alteration of one daily meal.

		ALA incorporated as hens are able to derive ALA from flax to DHA	consumed similar non enriched breakfast foods	Foods fortified with MicroN3 can serve as an effective vehicle for the delivery of *n*-3 fatty acids
Nanoemulsion technologies (Lane et al., 2014)	A randomised crossover trial using 11 participants who were asked to consume a yogurt drink	Participants ingested 2 yogurt drink products. The first fortified with a high DHA algal oil nanoemulsion, the second fortified with the same untreated oil	DHA from algal oil providing a dose of 1264mg DHA	When compared to a bulk oil enriched yogurt, the consumption of a yogurt with an added nanoemulsion of algae oil offers an enhanced rate and extent of absorption of DHA ($p \leq 0.05$) and total LC3PUFA ($p \leq 0.05$) levels with a decline in ARA:EPA levels ($p = 0.028$), which may broaden health benefits
Topical delivery (Puglia et al., 2005)	Part 1, *in vitro* evaluation of percutaneous absorption of EPA and DHA from 3 oily extracts using excised human skin. Part 2, *in vitro* permeation of *n*-3 studied to establish inhibiting qualities *in vivo* UVB	*In vitro* and *in vivo* percutaneous absorption methods	Oil extracted from sardine, horse mackerel and mackerel entrails. DHA/EPA 1.99, 1.4, 0.9 respectively. Oil in water sardine emulsions used for *in vivo* tests	*In vitro* experiments showed that sardine oil significantly higher steady state refluxes through human skin ($p < 0.01$) *In vivo* testing revealed anti-inflammatory activity against UVB induced

	induced skin erythema			erythema in human volunteers
(Kumar et al., 2014)	*In vitro* skin permeation study to evaluate the bioavailability of omega-3 enriched nanoemulsion of thiocolchicoside (TCC) a therapeutic agent for orthopaedic, traumatic and rheumatologic disorders	Water in oil nanoemulsion systems applied to porcine skin	Linseed oil used in differing ratios for its anti-inflammatory properties .	Nanoemulsions of TCC and omega-3 source oils were successfully formulated. The optimised formulation showed significantly improved *in vitro* permeation compared to the control ($p < 0.05$)