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Research review paper

Perspectives on the use of marine and freshwater hydrobiont oils for development of drug delivery systems

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ABSTRACT

Marine foods represent a unique source of poly-unsaturated fatty acids (PUFA) of the omega-3 (n-3) family. Today it is generally accepted that fish oil is important in a healthy and balanced omnivorous human diet. This favorable health perception of fish oil is however troubled by the high level of PUFA oxidation and low absorption in the gastro-intestinal tract. In this work we present and described various types of delivery systems which are used to improve PUFA and fish oil availability and oxidative stability.

Contents

1. Introduction

It has been proposed that the high consumption of marine oils, rich in the long-chain n-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid, could explain the low incidence of cardiovascular diseases in Greenland Inuits (Dyerberg et al., 1975; Bang et al., 1976; Dyerberg et al., 1978). In the past 3 decades, views of dietary polyunsaturated fatty acids (PUFA) have moved from speculation about their functions to solid evidence that they are not only essential nutrients but also may favorably modulate many diseases (Connor, 2000; Olsen et al., 2000). It is now well established that the long-chain n-3 PUFA interfere with eicosanoid production and lower plasma triglycerides, and that docosahexaenoic acid in particular is essential for optimal neural development (Sanders, 1993; Kinsella et al., 1990; Hansen, 1994; Harris et al., 1990; Crawford, 1993; Uauy et al., 1994; Carlson and Werkman, 1996). The strongest evidence of a relationship between n-3 fatty acids and disease is the inverse relation between the amount of n-3 fatty acids in the diet and in blood and tissues and the occurrence of coronary heart disease and its many complications. Effects of n-3 PUFA on coronary heart disease have been shown in hundreds of experiments in animals, humans, tissue culture studies, and even clinical trials (Hu and Willett, 2002; Laaksonen et al., 2005; Connor, 1994; Wang et al., 2006; Kris-Etherton et al., 2003). On the basis of epidemiological evidence and clinical studies, dietary intake of fish oils has been suggested to counteract atherosclerosis and perhaps even behavioral disorders and to have antithrombotic, and anti-arrhythmic effects (Goodnight et al., 1982; Connor, 2000; Albert et al., 2002; GISSI-Prevenzione Investigators, 1999). Moreover, PUFA are known as modulators of the immune response as they exhibit anti-inflammatory properties in many inflammatory diseases and

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decrease plasma lipids which are potential mediators of lipid-induced insulin resistance (Miles and Calder, 1998; Garnacho-Montero et al., 2002; Mayer et al., 2003; Calder, 1996, 1997; Gil, 2002; Lankinen et al., 2009). Thus, the nutritional and health benefits of consumption of marine fish and marine fish oil derived n-3 PUFA are beyond dispute.

Although free PUFA are essential to life, they show poor bioavailability when delivered by the oral route using traditional forms of administration, at least partly because of their oxidative lability in the gastrointestinal tract (Cansell et al., 2003). Therefore the development of the suitable fish oil and PUFA drug formulations is important task for the pharmaceutical and food industries.

2. Freshwater fish oil availability

It is popular to believe that freshwater fish intake is not so useful as a consequence of the lower n-3 PUFA concentration in freshwater fish oils. Polyunsaturated content has been used as the major distinction between 'marine' and 'freshwater' lipids for many years (Table 1) (Gruger et al., 1964; Ackman, 1967; Morris and Culkin, 1976; Sargent, 1976; Bayir et al., 2010). Most freshwater ecosystems comprise relatively small bodies of water which undergo considerable variation in temperature. This certainly applies to most freshwater ecosystems that have so far been studied with respect to their lipid chemistry. Therefore the membranes of marine organisms should to be able to function in permanently low temperatures and retain their fluidity. It has been suggested that the high levels of 20:5 and 22:6 fatty acids in marine lipids may reflect such an adaptation (Sargent, 1976; Morris, 1984). Environmental differences between the marine and freshwater habitats, of which salinity is the most obvious, have also been invoked. Membrane lipids of cells responsible for the ionic regulation of sea water might be expected to have different requirements in terms of fatty acid composition than equivalent lipids in the freshwater situation (Sargent, 1976). Indeed the brackish-water crustacean Gammarus has been found to increase the level of 20:5 and 22:6 fatty acids in its gill phospholipids during acclimatization to higher salinities (Morris et al., 1982).

It was usual to anticipate that the FA composition of fish tissue is a reflection of the FA composition of the diet (Gruger et al., 1964). And in the many feeding experiments where farmed fish are given diets with extreme, unnatural composition of the FAs was established (Xu and Kestemont 2002). There is no doubt that it in this manner is possible to obtain a shift in the tissue FAs towards the pattern of the diet FAs. However, this may be due to overriding of the enzyme system responsible for the metabolism of the lipids by large deviations in the FA composition in the experimental fodder compared to natural prey. Thus, it is revealed that in fish tissues, the composition of fatty acids of triacylglycerols (TAG), and to a lesser extent of phospholipids (PL), is determined by diet composition and lipid metabolism (Henderson and Tocher, 1987; Sargent et al., 1989; Linko et al., 1992; Sargent, 1995; Robin et al., 2003). In fact, incorporation of FA into tissues is modulated by various metabolic factors, and final composition will depend upon the initial FA content, cumulative intake of dietary fatty acids, growth rate and duration. Fish have the ability to synthesize the saturated fatty acids and monounsaturated fatty acids de novo, and also to selectively absorb and metabolize dietary fatty acids including dietary polyunsaturated fatty acids (PUFA) (Sargent et al., 1989; Bell et al., 1997) in order to obtain an optimal fatty acid composition (Ackman, 1980). This optimal fatty acid composition seems to be a characteristic for each species and even each strain, a so-called 'genotypic' composition (Viga and Grahl-Nielsen, 1990). In particular, the concentration of certain fatty acids in PL, as arachidonic acid (AA, 20:4n-6) or docosahexaenoic acid (DHA, 22:6n-3), seems largely determined by selective incorporation and could therefore be used to obtain systematic information, i.e. distinguishing between different strains or population types of the same species (Viga and Grahl-Nielsen, 1990; Pickova et al., 1999). The PUFA conversion capacity in fish varies among species and even races (Sargent, 1995).

Thus, some of the freshwater fish species are especially high in n-3 fatty acids. For instance, perch from Lake Baikal (Siberia, Russia) contains 7% EPA and 27% DHA in muscle lipids (Grahl-Nielsen et al., unpublished), the levels in wild perch from a Swedish lake was 9% EPA and 29% DHA (Ahlgren et al., 1994); in perch from Meuse River 9% EPA and 25% DHA (Blanchard et al., 2005); in perch from the Rhine River 13% EPA and 37% DHA and Lake Geneva 13% EPA and 32% DPA (Mairesse et al., 2006), 7% EPA and 17% DHA in perch from a lake in northern Poland (Jankowska et al., 2010), and 6% EPA and 18% DHA in perch from a lake in Italy (Orban et al., 2007).

The levels of EPA and DHA in the muscle lipids of Baikal pike were 7% and 31%, respectively (Grahl-Nielsen, unpublished). Pike from a Swedish lake had about the same levels, i.e. 9% EPA and 31% DHA (Ahlgren et al., 1994), and pike from a Polish lake had somewhat lower values, 6% EPA and 26% DHA (Zmijewski et al., 2006), as also was the case with pike from another lake in Poland, i.e. 7% EPA and 28% DHA (Jankowska et al., 2008). Much lower values, 5% EPA and 18% DHA have also been reprorted for pike (Kucska et al., 2006). Baikal roach had levels of 10% EPA and 20% DHA in the muscles (Grahl-Nielsen, unpublished), roach from two Swedish lakes had 12% EPA and 17% DA and 7% EPA and 25% DHA, respectively, (Ahlgren et al., 1994), and roach from a Turkish lake had 9% EPA and 6% DHA (Uysal et al., 2008).

Baikal grayling had higher muscle levels of EPA and DHA than graylings from other lakes, i.e. 9% EPA and DHA 41% (Grahl-Nielsen, unpublished). Reported levels for grayling from Sweden are 9% EPA and 30% DHA in males and 8% EPA and 16% DHA in females (Ahlgren et al., 1994), and grayling from Yenisei river had 11% EPA and 29% DHA (Sushchik et al., 2007).

Therefore some freshwater fish can be also considered as a prospective source of healthy n-3 PUFA.

3. Health benefits and potential risks related to consumption of fish

It should be mentioned the potential health risks related to fish consumption may be due to the presence of carcinogenic (e.g., DDT, dieldrin, heptachlor, PCBs, dioxin, etc.) and non-carcinogenic (e.g., methyl mercury) environmental contaminants that are stored in fish tissues. The fish species can concentrate the environmental contaminants by bioaccumulation and biomagnification. Fish consumption is a major source of human exposure to the above-mentioned environmental contaminants (Rissanen et al., 2000; Sidhu, 2003). The polychlorinated biphenyls and methyl mercury have long half lives in human bodies. Consequently, the contaminants in fish could attenuate all positive n-3 PUFA effects.

A recent international working group convened by the National Institutes of Health recognized the dietary importance and potential essentiality of n-3 FA (Simopoulos et al., 2000). Adequate intake of 650 mg/day of foods rich in n-3 FA was recommended. The American Heart Association (AHA) issued similar guidance, advocating 1 g of n-3 enriched foods daily. However, consistent supplementation may be difficult to maintain through dietary intake because of differences and awareness of n-3 FA content in different species of fish and food preparation techniques (Oh, 2005). Fish oil supplements provide the most consistent way of supplying higher doses of n-3 FA. Supplementation can be considered as an alternative to dietary intake for persons who are averse to a fish-enriched diet and can also be lower in mercury content and other environmental pollutants (Foran et al., 2003). Concentrated omega-3 fatty acids are found in fish oil supplements and may provide benefits similar to fish without the exposure to harmful environmental toxins (Melanson et al., 2005).