MODIFICATION OF FATTY ACIDS

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Abstract: Within freshwater fish, fatty acids arising from the diet or by endogenous synthesis are potential substrates for a variety of enzyme systems. Although the activities of these systems are present in all fish their relative activities can vary with species and the nutritional or physiological status of the fish.

Keywords: Fatty acids, enzymes, triacylglycerols, glycerol-3-phosphate

Fatty acids are not usually found to any great extent in fish tissues as free fatty acids but exist mainly in their esterified form as components of saponifiable lipids (Henderson and Tocher, 1987). Thus, fatty acids arising from both the diet and endogenous synthesis are definite substrates for the enzymes of esterification. Although these enzymes have not been characterised in fish, it is thought that fatty acids are incorporated into triacylglycerols and phospholipids as in mammals via the micro somal glycerol-3-phosphate pathway, details of which can be found elsewhere (Gurr and Harwood, 1991) (Fig 2). It is assumed that the fatty acids are first activated to their CoA derivatives before being used as substrates for the acyltransferase enzymes involved in this pathway. In addition to the enzymes necessary for the synthesis of phosphatidylcholine de novo (Holub et al, 1975), the microsomes of the trout liver are also known to contain acyl CoA: l-acyl-sn-glycero-S-phosphorylcholine acyltransferase which is responsible for the reacylation of lysophosphatidylcholine to phosphatidylcholine during phospholipid turnover (Holub et al, 1976). Thus, fatty acids can be incorporated into completely new phospholipid molecules or they can be esterified itno existing phospholipid molecules during turnover. Following the digestion of dietary lipid in mammals, fatty acids are absorbed into intestinal enterocytes along with 2-monoacylglycerols as the products of the lipolytic degradation of triacylglycerols by pancreatic lipase

(Gurr and Harwood, 1991). Experimental evidence suggests that the same process also occurs in fish (Henderson and Tocher, 1987; Sheridan, 1988), including carp (Iijima et al., 1990a). Within the intestinal cell, the fatty acids are re-esterified onto the monoacylglycerol to reform triacylglycerols which are carried from the intestine in the blood as components of chylomicrons to adipose tissues and muscle for deposition. Before they can be assimilated by muscle and adipose tissues the triacylglycerols of chylomicrons are first hydrolysed by lipoprotein lipase. The resulting fatty acids are absorbed by the adipose or muscle cells and re-esterified within the cell into triacylglycerols. In mammals triacylglycerols synthesised within the liver using endogenously-synthesised fatty acids or fatty acids derived originally from the diet, are transported as components of very low density lipoprotein to the extrahepatic tissues where they are assimilated by the same mechanisms which act upon chylomicron triacylglycerols (Gurr and Harwood, 1991). The presence of chylomicrons in trout plasma indicates that the mechanisms just described operate in this species (Rogie and Skinner, 1985; Sheridan, 1988). However, the situation regarding the plasma transport of lipids in carp is less clear since chylomicrons have not been detected although the other classes of lipoproteins do occur and may be involved in the transport of absorbed dietary lipid from the intestine (Iijima et al, 1990 a, b). The absorption and esterification of dietary fatty acids directly into the muscle and adipose triacylglycerols explains the strong influence of dietary fatty acid composition on that of flesh and adipose tissue triacylglycerols. However, the fatty acid composition of body triacylglycerols is never identical to those of the diet since, in addition to those obtained directly from the diet, the fatty acids deposited in triacylglycerols include fatty acids synthesised de novo and dietary fatty acids which have been modified by desaturation and elongation, presumably in the liver, as outlined below. This latter process of modification is particularly true of the phospholipids which generally contain a higher level of polyunsaturated fatty acids than triacylglycerols. The importance of the enzymes of fatty acid esterification have been largely overlooked, particularly with respect to how they control the specific fatty acid

composition of phospholipids in tissues. It is well established that the neural tissues of trout contain phospholipids which are enriched in 22:6(n-3). Particularly noticeable are the high proportions of the di-22:6(n-3) molecular species of phosphatidylethanolamine which occur in retina and brain (Bell and Tocher, 1989). The recent finding of high levels of di-22:6 phosphatidylethanolamine in the pineal organ of trout (Henderson et al, unpublished data) as well as the retina suggests a specific presence of this highly unsaturated species of phospholipid in photoreceptor cells. However, although this unique fatty acid composition is of critical importance in the fish, the acyltransferase enzymes which are responsible for bringing it about remain unstudied. In the reduction process, a fatty acid (usually a saturated or monounsaturated fatty acid) is first converted to its CoA derivative and this is then the substrate for the enzyme acylCoA reductase which employs NADH or NADPH as reducing agent to produce a fatty alcohol (Griffith et al., 1981; Kayama et al., 1979). Only trace amounts of free fatty alcohol are found in fish tissues as fatty alcohol produced by the acylCoA reductase is quickly esterified into other lipid classes (Fig. 3). For example, the fatty alcohol may be esterified with dihydroxyacetone phosphate and used to produce plasmalogens which are found in small amounts in many fish tissues such as brain (Bell and Dick, 1993). The fatty alcohols can also be esterified with another fatty acyl CoA to form wax esters which occur in the eggs of a few freshwater species, most notably the gourami (Sand et al., 1969). The hepatopancreas of the carp also has the capacity to reduce fatty acids to fatty alcohols (Kayama et al., 1979) Several studies have shown that when freshwater fish are injected with radiolabelled acetate radioactivity is recovered in a wide range of liver fatty acids including saturated, monounsaturated and polyunsaturated fatty acids (Table 1). As discussed above, the products of the fatty acid synthetase system in fish are saturated fatty acids. Although in a study with pike most of the label from l4C-acetate was actually recovered in 16:0 other fatty acids most notably 16:1 and 18:1 also contained considerable proportions of the incorporated radioactivity (Kluytmans and Zandee, 1974). Similarly with tilapia, 16:0 in phospholipids was well labelled

but in neutral lipids 16:1 and 18:1 and contained most of the radioactivity (Kanazawa et al., 1980). When I4Cacetate was injected to carp and trout 16:0, 18:0 and 18:1 (n-9) were all well labelled and several polyunsaturated fatty acids contained smaller amounts of radioactivity (Farkas and Csengeri, 1976). The extensive incorporation of acetate into 16:1 and 18:1 indicates that freshwater fish can convert the saturated fatty acids produced de novo to monounsaturated fatty acids. Eukaryotic organisms possess a desaturase enzyme which can insert a double bond 9 carbons removed from the carboxy terminal of a saturated fatty acids i.e. the A9 position (Gurr and Harwood, 1991). The action of this A9 desaturase on 16:0 and 18:0 produces 16:l(n-7) and 18:l(n-9), respectively. The recovery of large amounts of radioactivity from acetate in these two fatty acids when fish were injected with this substrate is consistent with the existence of an active A9 desaturase in freshwater fish. Although freshwater fish can synthesise 18:1 (n-9), in common with all animals, they lack both the A12 desaturase enzyme which can desaturate 18:l(n-9) to 18:2(n-6) and the A15 desaturase which can convert 18:2(n-6) to 18:3(n-3). Consequently, fish are unable to synthesise polyunsaturated fatty acids completely de novo from non-lipid precursors. In fish, as in all animals, polyunsaturated fatty acids play essential roles in cellular function. Since the fish is unable to make them de novo, polyunsaturated faty acids must therefore be obtained performed in the diet. Differences exist between marine and freshwater fish in terms of their qualitative and quantitative requirements for essential fatty acids. Evidence to date suggests that freshwater fish require 18:2(n-6) and 18:3(n-3) whereas marine fish have a dietary requirement for the longer chain and more highly unsaturated 20:5(n-3) and 22:6(n-3), and possiby, 20:4(n-6). The essential fatty acid requirements of carp are the subject of another paper in this workshop. The recovery of radioactivity from injected I4C-acetate in polyunsaturated fatty acids is in part a reflection of the ability of freshwater fish to modify dietary polyunsaturated fatty acids by the combined processes of desaturation and elongation. In addition to the A9 desaturase, freshwater fish are believed to contain A6, A5 and A4 desaturases (Henderson and Tocher, 1987). The

sequential operation of these three enzyme systems together with enzymes of elongation would permit the formation of 22:6(n-3), one of the most characteristic fatty acids of fish lipids, from dietary 18:3(n-3). The pathway of formation which has frequently been postulated is illustrated in Fig. 4. In this scheme, 18:3 obtained in the diet can be acted upon by a A6 desaturase to from 18:4 which is elongated to 20:4. This PUFA is then further desaturated by A5 desaturation to 20:5 which can be elongated to 22:5. A final desaturation by what is traditionally thought to be a A4 desaturase yields 22:6(n-3). The same enzymes acting on 18:2(n-6) would generate 22:5(n-6) as the end product. The addition of two-carbon units in the elongation steps would explain why in fish injected with 14C acetate radioactivity is recovered in the long chain polyunsaturated fatty acids. Evidence for the operation of these pathways of polyunsaturated fatty acid metabolism in freshwater fish has been obtained from the results of nutritional studies with salmon and trout in which feeding 18:2(n-6) or 18:3(n-3) as the only dietary polyunsaturated fatty acid corresponded with appearance of (n-6) and (n-3) C20 and C22 polyunsaturated fatty acids in the fishes' polar lipids (Takeuchi an Watanabe, 1982; Watnabe et al., 1974). In an early analytical study, Kayama et al. (1963) found that the lipid of adult guppies contained 17% 22:6(n-3) when reared on Artemia whose lipid contained only 20:5(n-3) and no 22:6(n-3). This demonstrates the ability of this fish to convert 20:5(n-3) to 22:6(n-3).

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