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ω-3 Polyunsaturated Fatty Acids and Eicosanoids: Sources, Biochemistry and Functions in Physiological Conditions and in Cardiovascular Disease: Current Status

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■SUMMARY. The ω-3 and ω-6 polyunsaturated fatty acids (PUFA) are important components of animal and plant membranes. Amongst these PUFA, eicosapentaenoic acid (EPA, 20:3ω-3) and docosahexaenoic acid (DHA, 22:6ω-3) are nearly exclusively derived from marine sources. Dietary PUFA are incorporated into cell membranes esterified to phospholipids, where they affect membrane characteristics and give rise to biologically active compounds. Compounds that serve as signals for eicosanoids production bind to cell membrane receptors and activate phospholipases that cleave the polyunsaturated fatty acids from cell membrane phospolipids. EPA is metabolised to TXA_3 in platelets, LTB_5 in leukocytes and PGI_3 in endothelial cells. These products derived from EPA are called eicosanoids. DHA is probably not metabolised in mammalian cells to products of biological significance, but DHA may directly influence cellular functions and can be retroconverted to EPA. ω-3 PUFA reduce fasting and postprandial triglycerides, decrease the reactivity of platelets (decrease of platelet aggregation: competition between arachidonic acid and EPA for the cyclo-oxygenase reduce platelet formation of TXA_2) and leukocyte reactivity (conversion of EPA to LTB_5 through the 5-lipoxygenase pathway and decrease of LTB_4 formation from arachidonic acid), increase erythrocyte deformability, and may slightly decrease blood pressure, ω-3 PUFA may also beneficially influence vessel wall characteristics and blood rheology (decrease of blood viscosity). Furthermore, these compounds may impair fibrinolysis and could lead to increased oxidation of lipoproteins. Many clinical studies show that the effects of ω-3 PUFA on serum lipids depend on the type of patient and whether the amount of saturated fatty acids in the diet is held constant. In patients with hypercholesterolaemia very high dosages of ω-3 PUFA (above 10 g/day) may modestly decrease LDL cholesterol. Dietary ω-3 PUFA reduce plasma triglycerides in patients with hypertriglyceridaemia in a dose-dependent

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way. In patients with familial combined hyperlipi- daemia, dietary ω-3 PUFA reduce plasma triglycerides, but have no effect on LDL cholesterol or HDL cholesterol, ω-3 PUFA dose-dependently lower blood pressure in hypertensive patients. Changes of lipid metabolism, reduced erythrocyte deformability, increased platelet aggregation and high blood pressure often found in subjects with diabetes meilitus are all favourably influenced by the administration of EPA and DHA. In non-insu- lin-dependent patients supplementation with ω-3 PUFA usually worsens the glycaemic control; this may be a dose-related phenomenon and is reversed after discontinuation of the supplementation. Potential adverse effects of ω-3 PUFA must not be neglected, but should be viewed in light of their beneficial effects.

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