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Kinetics of omega-3 polyunsaturated fatty acids when co-administered with saturated or omega-6 fats

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ABSTRACT

Objective. Absorption of long chain omega-3 polyunsaturated fatty acids (LCn-3PUFA) has been shown to be potentiated when consumed with a high fat meal. However, the effect of different dietary fats on n-3PUFA absorption and postprandial kinetics has not been previously studied.

Method. In a randomized cross-over design intervention, postprandial incorporation of LCn-3PUFA into plasma lipids following consumption of a meal rich in either saturated fat or omega-6 polyunsaturated fatty acids (n-6PUFA) was investigated. Healthy adult male and female subjects (n = 26) were fed an isocaloric meal containing equivalent amount of either butter or sunflower seed oil supplemented with 1.8 grams of LCn-3PUFA (300 mg eicosapentaenoic acid, 20:5n-3 and 1500 mg docosahexaenoic acid, 22:6n-3).

Results. Postprandial plasma lipids were enriched with saturated fatty acids and linoleic acid (18:2n-6) following consumption of the butter and the sunflower oil containing meals respectively. The increase in plasma 20:5n-3 and 22:6n-3 levels over the 6 hour study period was similar in both the saturated and the n-6 fat groups.

Conclusion. These results suggest that the expected competition between LCn-3PUFA and n-6PUFA at the absorption level is unlikely; therefore competition at the enzymatic level should be primarily responsible for differences in their metabolic and clinical effects.
Trial registered with the Australia New Zealand Trial registry as ACTRN12612000654853.

1. Introduction

Long chain omega-3 polyunsaturated fatty acids (LCn-3PUFA) have been associated with decreased risk for chronic diseases, due to their anti-inflammatory, anti-aggregatory, anti-arrhythmic and lipid lowering potential [1–5]. It is known that consumption of LCn-3PUFA in combination with a high fat meal can improve LCn-3PUFA absorption and incorporation into

Abbreviations: LCn-3PUFA, long chain omega-3 polyunsaturated fatty acids; n-6PUFA, omega-6 polyunsaturated fatty acids; SFA, saturated fatty acids; 20:5n-3, eicosapentaenoic acid; 22:6n-3, docosahexaenoic acid; 20:4n-6, arachidonic acid; 18:3n-3, α-linolenic acid; AUC, area under the curve; iAUC, incremental area under the curve; 18:2n-6, linoleic acid; 22:5n-3, docosapentaenoic acid; 18:1n-9, oleic acid; 16:0, palmitic acid; 18:0, stearic acid; MUFA, monounsaturated fatty acids.

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plasma lipids [6] and tissue [7]. However, the effect of different dietary fats on LCn-3PUFA absorption and postprandial kinetics has not been previously studied.

Chronic feeding studies [8–13] have reported a competition between omega-6 polyunsaturated fatty acids (n-6PUFA) and LCn-3PUFA, as the same enzymes are involved in the metabolic pathways of both fatty acid groups. The increased consumption of n-6PUFA was shown to cause a decrease in LCn-3PUFA in blood and tissues [10,11,14]. Evidence to date suggests that an increase in n-6PUFA consumption may decrease activity of delta-6-desaturase [15,16], which is a key enzyme in the process of elongation and desaturation of LCn-3PUFA and n-6PUFA for the synthesis of longer chain n-3PUFA and n-6PUFA [17]. Thus, the relative synthesis of eicosapentaenoic acid (20:5n-3), docosahexaenoic acid (22:6n-3) and arachidonic acid (20:4n-6) can be influenced by the type of dietary fat (saturated, monounsaturated or n-6PUFA) consumed during LCn-3PUFA supplementation. Furthermore, the competition and imbalance between LCn-3PUFA and n-6PUFA has been demonstrated to affect eicosanoids formation [17,18] and cell membrane composition, fluidity and permeability [19]. However, whether any competition exists at the absorption level and incorporation into plasma lipids has never been studied. LCn-3PUFA and n-6PUFA could compete for re-acylation into chylomicron lipid species, reducing LCn-3PUFA incorporation into plasma lipids postprandially and consequently reducing LCn-3PUFA concentration in tissues.

It has been demonstrated, in animal studies, that consuming LCn-3PUFA combined with a saturated fatty acid (SFA) diet resulted in higher serum 20:5n-3 [20,21] and α-linolenic acid (18:3n-3) [20] concentrations when compared to a diet containing the same amount of LCn-3PUFA but combined with n-6PUFA. In addition, a combination of LCn-3PUFA with a SFA diet was more efficient in reducing blood triglyceride levels than the combination of LCn-3PUFA with n-6PUFA [22]. However no human studies have been conducted to establish whether similar effects are apparent in the short or long term.

Despite the well-established health benefits of LCn-3PUFA and ready availability of LCn-3PUFA enriched functional foods and supplements; saturated, monounsaturated and n-6PUFA will remain the major type of dietary fats consumed in human diets. Therefore, it is important to determine how the background dietary fats influence the absorption, transport and metabolism of LCn-3PUFA in order to optimize their health benefits. In the present study, we examined postprandial plasma fatty acid levels over a 6-hour period, when subjects consumed meals containing either saturated fat (butter) or n-6PUFA (sunflower oil) and supplemented with LCn-3PUFA.

2. Materials and Methods

2.1. Participants

Thirty five healthy adults aged between 18 and 65 years were recruited and 26 of them (18 females and 8 males) completed the intervention (Supplementary Material 1). Participants were excluded if they were using lipid-lowering drugs (e.g. statins); had consumed fish oil supplements regularly within the past month; had regular consumption of 2 or more fish meals a week over the past month; had any history of congestive heart failure, stroke, myocardial infarction, coronary artery bypass graft, or atherosclerotic cardiovascular disease; had history of diabetes; had history of gastrointestinal or liver disease; were smokers; or were pregnant or breast feeding. Participants were recruited from the community using media advertising and advertisements placed on noticeboards and distributed via departmental email lists at the University of Newcastle. They were also recruited using the Hunter Medical Research Institute (HMRI) Volunteer Register.

2.2. Study Design

The study was a randomized, cross-over, acute postprandial study. Following an overnight fast, participants visited the Nutraceuticals Research Clinic Facility at the University of Newcastle on two occasions and consumed one of two meals, consisting of 150 g mashed potato mixed with either 38 g butter (SFA meal) or 32 g sunflower oil (n-6PUFA meal). Two hundred milliliters of water and 3× 1 g fish oil capsules of LCn-3PUFA [100:500 mg eicosapentaenoic acid:docosahexaenoic acid (EPAX 1050TG, Norway)] providing 1.8 g of n-3PUFA were also consumed. The SFA meal contained 19 g carbohydrates, 3.8 g protein and 31.8 g fat and the n-6PUFA meal contained 18.8 g carbohydrates, 3.5 g protein and 32.2 g fat. Test meals were consumed within 15 minutes. Blood was collected after an overnight fast and 1, 3, 4 and 6 hours postmeal consumption. Following a minimum of one week washout period, the same procedure was repeated, after consumption of the alternate meal. The order in which the meals were consumed was randomly determined using computer generated random tables (www.randomization.com, seed 9511). A twenty four hour food recall was used to measure nutrient intake prior to the study meal. Plasma fatty acids were measured at each time point. All volunteers gave written informed consent before participation. The University of Newcastle Human Research Ethics Committee approved the study (protocol H-2012-0117), and the study was registered with the Australia New Zealand Trial registry as ACTRN12612000654853.

2.3. Plasma Fatty Acid Composition

Blood was collected in EDTA vacutainers and plasma was immediately separated from the erythrocytes by centrifugation (1000*g*, 15 minutes at 4 °C) and stored at −80 °C until analyzed. Incorporation of fatty acids into plasma was determined using gas chromatography following transesterification. Fatty acids were methylated according to the method by Lepage and Roy [23] with C:19 used as an internal standard. Methyl ester products were separated, identified and quantified using a 30 m × 0.25 mm (DB-225) fused carbon-silica column, coated with cyanopropylphenyl (J&W Scientific, Folsom, CA) and Hewlett Packard 6890A series gas chromatographer with Chemstations Version A.04.02 for gas chromatographic analysis [24]. Fatty acid peaks were identified by comparison with a standard mixture of fatty acid methyl esters (C4-C24 Unsaturates, Supelco) of known composition and concentration.