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Docosahexaenoic acid-enriched canola oil increases adiponectin concentrations: A randomized crossover controlled intervention trial

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Abstract *Background and aims:* Little is known about the effect of various dietary fatty acids on pro- and anti-inflammatory processes. We investigated the effect of 5 oils containing various amounts of alpha-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA) and docosahexaenoic acid (DHA) on plasma inflammatory biomarkers and expression levels of key inflammatory genes and transcription factors in whole blood cells.
Methods and results: In a randomized, crossover controlled nutrition intervention, 114 adult men and women with abdominal obesity and at least one other criterion for the metabolic syndrome consumed 5 experimental isoenergetic diets for 4 weeks each, separated by 4-week washout periods. Each diet provided 60 g/3000 kcal of different oils: 1) control corn/safflower oil blend (CornSaff; LA-rich), 2) flax/safflower oil blend (FlaxSaff; ALA-rich), 3) conventional canola oil (Canola; OA-rich), 4) high oleic canola oil (CanolaOleic; highest OA content), 5) DHA-enriched high oleic canola oil (CanolaDHA; OA- and DHA-rich). Gene expression in whole blood cells was assessed in a subset of 62 subjects. CanolaDHA increased plasma adiponectin concentrations compared with the control CornSaff oil treatment (+4.5%, $P = 0.04$) and FlaxSaff (+6.9%, $P = 0.0008$). CanolaDHA also reduced relative expression levels of interleukin (*IL*)*1B* compared with CornSaff and Canola (−11% and −13%, respectively, both $P = 0.03$). High-sensitivity C-reactive protein concentrations were lower after Canola than after FlaxSaff (−17.8%, $P = 0.047$).

Acronyms: ALA, alpha-linolenic acid; BMI, body mass index; BP, blood pressure; *CCL2*, chemokine (C–C motif) ligand 2; cDNA, complementary deoxyribonucleic acid; COMIT, Canola Oil Multicenter Intervention Trial; CRP, C-reactive protein; CV, coefficient of variation; Ct, cycle threshold; CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; *G6PD*, glucose-6-phosphate dehydrogenase; *GAPDH*, glyceraldehyde-3-phosphate dehydrogenase; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity CRP; IDF, International Diabetes Federation; IL, interleukin; LA, linoleic acid; LDL-C, low-density lipoprotein cholesterol; MetSyn, metabolic syndrome; MUFA, monounsaturated fatty acids; *NFKB1*, nuclear factor kappa-B subunit 1; *NPR3*, natriuretic peptide receptor C; OA, oleic acid; PPAR, peroxisome proliferator-activated receptor; *PPARA*, PPAR alpha; PUFA, polyunsaturated fatty acids; RNA, ribonucleic acid; SD, standard deviation; SFA, saturated fatty acids; *SREBF2*, sterol regulatory element-binding transcription factor 2; TG, triglycerides; *TNF*, tumor necrosis factor; *TRAF3*, TNF receptor-associated factor 3.

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Conclusion: DHA-enriched canola oil exerts anti-inflammatory effects compared with polyunsaturated fatty acids from plant sources.

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Introduction

Pro-inflammatory biomarkers such as C-reactive protein (CRP) and interleukin (IL)-6 have been associated with an increased risk of all-cause mortality and cardiovascular events [1,2]. Conversely, adiponectin is an adipose tissue-derived hormone recognized for its anti-atherosclerotic and anti-inflammatory properties [3].

Convincing evidence now suggests that diet significantly affects pro- and anti-inflammatory processes [4]. However, confusion remains about the effects that various dietary fatty acids have on inflammation. Saturated fatty acids are believed to have pro-inflammatory properties [4]. While observational studies have quite consistently reported inverse associations between consumption of *n*-3 polyunsaturated fatty acids (PUFA) from marine sources (eicosapentaenoic acid, EPA; docosahexaenoic, DHA) and inflammation [5,6], results from randomized controlled trials have been inconsistent [5,7]. Data from intervention studies on the effect of the plant-based essential *n*-3 PUFA alpha-linolenic acid (ALA) on inflammation are also conflicting [5,8,9]. Contrary to some beliefs, a recent systematic review of randomized controlled nutrition intervention studies has shown that consumption of the *n*-6 PUFA linoleic acid (LA) actually exerts no deleterious effect on inflammatory markers [10]. Finally, the effect of monounsaturated fatty acids (MUFA), specifically oleic acid (OA), on inflammation is poorly understood since most previous studies were conducted in the context of experimental diets that included changes beyond just MUFA, such as the Mediterranean diet or inclusion of MUFA-rich foods such as nuts [11,12].

The objective of this study was to evaluate the effects of oils containing various amounts of ALA, LA, OA and DHA in the context of a low SFA diet [13,14] on plasma high-sensitivity (hs)-CRP, IL-6, and adiponectin concentrations in subjects with abdominal obesity and at least one other criterion for the metabolic syndrome. Consistent with previous extensive review of the literature on diet and inflammation [4], we hypothesized that the oil containing DHA exerts the greatest benefit on inflammatory markers. In exploratory analyses, we also investigated how consumption of the different oil blends modified the expression of inflammatory genes and transcription factors in whole blood cells.

Methods

Study population

COMIT (Canola Oil Multicenter Intervention Trial) was a multicenter trial designed to study the effect of various forms of canola and flax oils on vascular function and biomarkers of CVD risk. Methods have been described in detail elsewhere [13,14]. Recruitment took place at the University of Manitoba in Winnipeg (Canada), Laval University in Québec City (Canada) and Pennsylvania State University (Penn State) in University Park, Pennsylvania (USA). Inclusion criteria were: age between 18 and 65 years, abdominal obesity defined by a waist circumference $\geq$94 cm for men, and $\geq$80 cm for women [15], and at least one of the four following metabolic abnormalities according to the International Diabetes Federation (IDF) criteria for metabolic syndrome [15]: fasting glucose $\geq$ 5.6 mmol/L, triglycerides (TG) $\geq$ 1.7 mmol/L, systolic and diastolic blood pressures $\geq$ 130/85 mmHg, and high-density lipoprotein cholesterol (HDL-C) $\leq$ 1.0 mmol/L for men and $\leq$1.3 mmol/L for women. Otherwise subjects had to be healthy; exclusion criteria have been described previously [13,14]. Written consent was obtained from all subjects at the beginning of the study. The protocol was approved by Institutional Ethics Boards at all centers.

Experimental design

The study was designed as a double-blind, randomized crossover intervention that utilized a controlled feeding design with five experimental 4-week phases each separated by a 2–4-week washout period [13,14]. All foods were provided to participants during the five experimental dietary phases to maximize control over each experimental diet effect, as well as every subject's energy needs. Daily energy requirements were estimated at study onset using the Mifflin equation [16] and the Harris–Benedict equation [17] with adjustment for subjects' level of physical activity. Further details on the feeding protocol during the experimental phases are given in Ref. [13] and Supplemental File 1.

Diet and oils

Table 1 presents the fatty acid composition of the five oil blends. Experimental oils (60 g/3000 kcal) were incorporated into shakes made with non-fat milk, sorbet and fruits that were consumed twice a day, typically at breakfast and dinner. The 7-day cycle menu was identical for each of the five experimental diets at all centers and only the experimental oils provided in the shakes differed. The macronutrient content of the diets was 15% from protein, 50% from carbohydrate and 35% from lipids (Table 2).