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ORIGINAL CONTRIBUTION

A short-term n-3 DPA supplementation study in humans

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Abstract
Purpose Despite the detailed knowledge of the absorption and incorporation of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) into plasma lipids and red blood cells (RBC) in humans, very little is known about docosapentaenoic acid (DPA, 22:5 n-3). The aim of this study was to investigate the uptake and incorporation of pure DPA and EPA into human plasma and RBC lipids.

Methods Ten female participants received 8 g of pure DPA or pure EPA in randomized crossover double-blinded manner over a 7-day period. The placebo treatment was olive oil. Blood samples were collected at days zero, four and seven, following which the plasma and RBC were separated and used for the analysis of fatty acids.

Results Supplementation with DPA significantly increased the proportions of DPA in the plasma phospholipids (PL) (by twofold) and triacylglycerol (TAG) fractions (by 2.3-fold, day 4). DPA supplementation also significantly increased the proportions of EPA in TAG (by 3.1-fold, day 4) and cholesterol ester (CE) fractions (by 2.0-fold, day 7) and of DHA in TAG fraction (by 3.1-fold, day 4). DPA proportions in RBC PL did not change following supplementation. Supplementation with EPA significantly increased the proportion of EPA in the plasma CE and PL fractions, (both by 2.7-fold, day 4 and day 7) and in the RBC PL (by 1.9-fold, day 4 and day 7). EPA supplementation did not alter the proportions of DPA or DHA in any lipid fraction. These results showed that within day 4 of supplementation, DPA and EPA demonstrated different and specific incorporation patterns.

Conclusion The results of this short-term study suggest that DPA may act as a reservoir of the major long-chain n-3 fatty acids (LC n-3 PUFA) in humans.

Keywords n-3 Polyunsaturated fatty acids (PUFA) · Docosapentaenoic acid (DPA) · Eicosapentaenoic acid (EPA) · Docosahexaenoic acid (DHA) · Fatty acid metabolism

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Introduction

A vast amount of information exists in relation to the beneficial cardiovascular [CV] health actions of long-chain

n-3 polyunsaturated fatty acids (LC n-3 PUFA), namely EPA and DHA [1, 2]. In contrast, very little is known about the regularly consumed intermediary product DPA (22:5 n-3). DPA is found in most fish and marine foods and is also present in lean red meat from ruminant animals [3, 4]. On average, the intake of DPA in adult Australian population is 71 mg/day, which represents approximately 29 % of total LC n-3 PUFA intake [5].

The available literature, based on in vitro, ex vivo and animal studies, suggests that n-3 DPA may exert beneficial CV health effects [6–8]. DPA has been shown to be the most potent inhibitor of platelet aggregation in rabbit platelets, compared with either EPA or DHA. Platelet aggregation is an early event in the development of thrombosis or blood clot formation and is initiated by thromboxane A_2 (TXA_2) [9]. DPA inhibits cyclooxygenase-1 which is required for the synthesis of TXA_2 thereby inhibiting platelet aggregation. In human subjects, DPA is equally effective as EPA and DHA in inhibiting platelet aggregation (ex vivo) in female subjects; however, in male subjects, only EPA inhibited platelet aggregation [10]. Furthermore, DPA exhibits additional physiological actions, including the ability to suppress the expression of lipogenic genes in cultured liver cells and in mice receiving DPA supplementation [7, 11]. Mechanistically, these actions may be due, in part, to the ability of DPA to also induce the expression of peroxisome proliferator–activated receptor (PPARα), which negatively regulates lipolysis in favour of increased fat oxidation [12]. In addition, DPA is involved in the reduction of the expression of inflammatory genes such as tumour necrosis factor (TNF-α) in cell culture models [13]. The beneficial role of DPA in CV health is also supported by the studies investigating the metabolism of DPA, which have shown that DPA is highly incorporated in heart phospholipids (PL) compared with EPA [14, 15]. In addition, there is evidence from in vitro [7] and in vivo [14] studies that DPA can be metabolized into DHA and retro-converted to EPA. Collectively, these studies suggest that DPA may provide an additional source of beneficial LC n-3 PUFA.

To date, there has only been one clinical study using a supplement rich in DPA, namely seal oil. However, this supplement also contained EPA and DHA in higher proportions than DPA [16]. Therefore, the benefits observed cannot be attributed purely to DPA rather than the EPA or DHA present. The present study was conducted to investigate the actions of a highly purified DPA source, relative to pure EPA, on the incorporation into plasma and RBC lipids, following a 7-day supplementation period. It was hypothesized that the pattern of incorporation of DPA into human blood lipids would be similar to EPA.

Materials and methods

Study population

Ten healthy lean females with a body mass index (BMI) of 20–25 kg/m^2, aged between 21 and 30 years were recruited for the study. Participants provided a written informed consent and completed a medical questionnaire and PUFA Food Frequency Questionnaire (FFQ). Participants were excluded if they consumed more than 500 mg of LC n-3 PUFA per day (based on results of PUFA FFQ [17–19]), were at high risk of any form of CVD (based upon family history information obtained from medical questionnaire) or were overweight as indicated by their BMI (>26 kg/m^2). Ethics approval was obtained from the Deakin University Human Research Ethics Committee (EC2011-023).

Daily supplements

Purified EPA (99.8 %; w/w) and DPA (99.8 %; w/w), both as free fatty acids, were sourced from Equateq Ltd, Breasclete, Callanish, Scotland. The study investigators had access to only 100 grams of pure EPA and DPA. To our knowledge, this is the first ever study using pure DPA because it has been very difficult to obtain the pure DPA, given the prohibitive costs, technical expertise and time required in its manufacture. Since DPA is in scarce supply, we chose to feed a high dose for a short time to determine into which lipids the DPA was incorporated, recognizing that the dose was well above what might be ingested through usual food sources of DPA.

The participants consumed the supplements for seven consecutive days, after which time the study concluded. The participants consumed 2 g of the supplement in question on the first day of the study and 1 g daily for the subsequent 6 days. The total DPA or EPA that was consumed per supplementation period per subject was 8 g. The initial dose was double that of the remaining doses in an attempt to boost the DPA or EPA levels from the beginning of the study.

Study design

Following screening, the participants received the olive oil placebo treatment first, and they were then randomized to receive the DPA or EPA supplements. The participants consumed a standardized dinner meal (containing pasta (dry 200 g), tomato stir through sauce (70 g) and a packet pudding the night before the start of the study and were given instructions to fast overnight for 10 h. On the first study day, a fasted blood sample (day 0) was drawn, and following this, the participants were asked to consume a meal of 180 g of instant mashed potato (Continental,

Deb™, Unilever Australasia) that contained the 2 g of DPA or EPA mixed with 18 ml of olive oil. The placebo group consumed 20 ml of olive oil in the 180 g of mashed potato. The participants consumed this 'breakfast' in 15 min.

For the next 6 days, participants were provided with six, 2 g aliquots of a 1:1 mixture of DPA or EPA in olive oil in 2 ml cryovials in a box (protecting the oils from exposure to light). Participants were provided with instructions to keep the supplements in the fridge and to consume them each morning. During the placebo period, the participants received six 2 g aliquots of olive oil. For days 1–6, the participants were asked to pour the contents of the cryovial into 200 ml of standard commercial orange juice to aid in palatability. On the mornings of day 4 and 7 of their supplementation week, participants attended the clinical facility to provide a fasting blood sample.

During the three supplementation weeks, participants were requested to refrain from consuming high LC n-3 PUFA products including fish, red meat and LC n-3 PUFA–fortified products (<2 marine and/or 2 red meat meals/week and <2 LC n-3 PUFA–fortified products/week), in order to prevent false increases in plasma-circulating LC n-3 PUFA. The participants were asked to give a recall of their diet 24 h before they came into provide blood samples at days 0, 4 and 7. It was found that the participants did not consume any fish during the study period, and consumption of red meat was <2 serves per week. Each supplementation period lasted 7 days with a 2-week washout period prior to crossover.

Plasma and red blood cell lipid analysis

Venous blood was collected into two 8-ml EDTA vacutainers. Samples were immediately centrifuged for 15 min at $591 \times g$ and 15 °C. Plasma at each time point was aliquoted and stored at −80 °C until further analysis. The RBC remaining after the removal of the plasma were washed twice with 0.9 % sodium chloride, centrifuged each time and after the removal of the upper saline solution, the washed red cells were aliquoted into storage vials and stored as the plasma.

Total plasma lipids were extracted from plasma as described by Sinclair et al. [20]. In brief, 850 µl of plasma was extracted using 15 ml of dichloromethane: methanol 2:1 (v/v) containing 0.01 mg butylated hydroxytoluene (BHT) and reference internal lipid standards, specifically TAG-17:0, CE-17:0 (NuChek Prep, Minnesota, USA) and phosphatidyl choline (PC)-17:0 (Avanti Polar Lipids, USA). The major neutral lipid classes were separated by thin layer chromatography (TLC), and the CE, TAG and PL fractions were scraped from the TLC plates and transmethylated with 5 % H_2SO_4 in methanol prior to GC. The resulting fatty acid methyl esters (FAME) were isolated and identified using an Agilent Technologies GC 7890A (Agilent Technologies, Santa Clara, California, USA) equipped with an Omegawax 250 capillary column (30 m × 0.25 µm internal diameter, 0.25 µm film thickness, Supelco, Bellefonte, PA, USA), a flame ionization detector (FID) and an Agilent Technologies 7,693 auto-sampler. Each of the FAME peak was identified relative to known external standards, a FAME mix of three PUFA, these being a marine source, animal source and menhaden oil (Supleco, Bellefonte, PA, USA). The resulting peaks were then corrected by the theoretical relative FID response factors and quantified relative to the internal standard used at the lipid extraction stage [21].

Total RBC lipids were extracted from 200 µl of RBC with dichloromethane/methanol (1:1 v/v, containing a known amount of PC-17:0 standard), similar to the Folch method [22], with modifications by Armstrong et al. [23]. The RBC lipids were separated by TLC, and the PL fraction was scraped from the TLC plates and transmethylated; the FAME were analysed as described above.

Plasma TAG concentration

Plasma TAG concentrations were measured on a Roche Cobas Integra 400 plus autoanalyser using a commercially available enzymatic colorimetric method using a commercially available kit (TRIGL) as per the manufacturer's instructions (Roche, Lavel, Quebec, Canada).

Statistical analysis

Data calculations and statistical analysis were performed using the Minitab Statistical Software (Minitab Version 15; Minitab Inc., USA). Data were analysed using two-way ANOVA repeated measures, and pairwise comparisons were made using Tukey's test. A value of $p < 0.05$ was taken as significant.

Results

Subject characteristics

The 10 healthy female participants had a mean age of 25.5 ± 3.3 years, with a BMI of 22.3 ± 1.6 kg/m^2; they were non-diabetic, not taking CVD medication and did not regularly consume fish oil capsules. All participants

completed a PUFA FFQ [17–19] and were found to consume 102 ± 66 mg LC n-3 PUFA/day.

Acceptability of the supplements

Participants who experienced any adverse reaction were requested to inform investigators immediately. Three cases of mild diarrhoea were reported by participants during the DPA and EPA supplementation periods, respectively, with severity ranging from very mild to moderate. These events were found to occur only during first 4 days of supplementation and were most commonly reported to occur within the first hour following supplement consumption. Participants received daily reminders in person or by e-mail to consume their supplement, and upon returning for the final blood collection, participants were requested to return the box containing all the vials; the supplements were provided in a way to ascertain compliance with consumption of the supplement. It was found that all returned vials were empty.

Plasma and red blood cell fatty acid composition

Plasma PL

The average baseline levels of LC n-3 PUFA in plasma PL were 0.8 % for EPA and DPA and 2.3 % for DHA (Fig. 1). For those consuming the DPA supplement, there was a significant increase in the proportion of DPA at day 4 (from 0.7 % to 1.4 %), compared with day 0 value ($p = 0.006$). Although, there was a trend for an increase in day 7 DPA levels, this was not statistically significant ($p = 0.076$). In

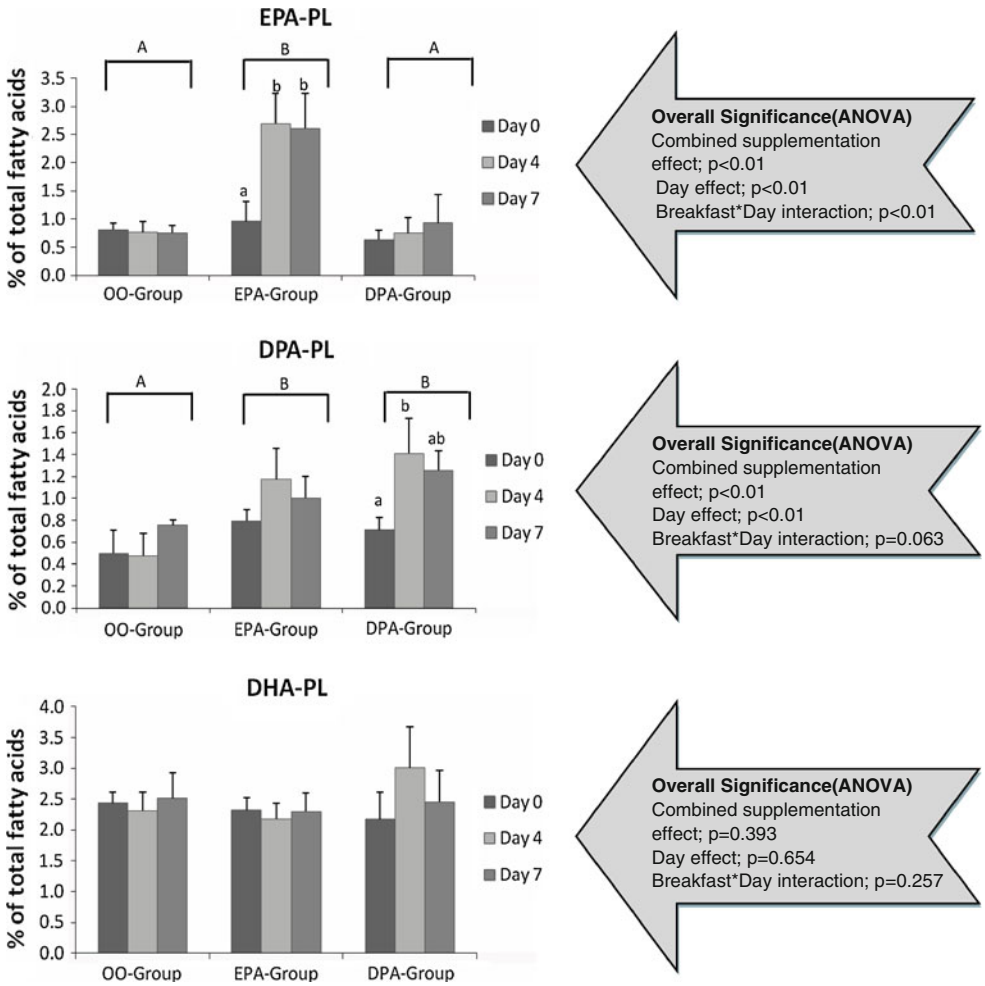

Fig. 1 Fatty acid composition of plasma phospholipids (PL) from human participants supplemented with olive oil, EPA or DPA with a dose of 2 g for the first day and 1 g for the subsequent 6 days. Results are expressed as percentage mean ± SEM ($n = 10$). Data were analysed using two-way ANOVA repeated measures, and pairwise comparisons were made using Tukey's test. The *superscripts* with capital *alphabets* represent a combined supplementation effect, and different *superscripts* represent values that are significantly different ($p < 0.05$). The *superscripts* with *small alphabets* represent time effect within each supplementation group, and different *superscripts* represent values that are significantly different ($p < 0.05$). The values with no *superscripts* show no significant differences. *OO* olive oil, *EPA* eicosapentaenoic acid, *DPA* docosapentaenoic acid, *DHA* docosahexaenoic acid

the EPA group, there was a significant increase in the proportion of EPA (from 1 to 2.7 %) relative to baseline at both days 4 and 7 ($p < 0.01$). There were no significant changes in the proportion of LC n-3 PUFA for participants consuming the olive oil placebo.

Plasma TAG

The average baseline levels of LC n-3 PUFA in plasma TAG were 0.3 % for EPA and DPA and 0.6 % for DHA (Fig. 2). After DPA supplementation, there was a significant rise in the proportion of DPA (from 0.5 to 1.2 %) at day 4 ($p = 0.027$), in the proportion of EPA (from 0.3 to 0.9 %) at day 4 ($p = 0.05$), as well as in the proportion of DHA (from 0.7 to 2.2 %) at day 4 ($p = 0.004$). There were no significant changes in the proportions of EPA, DPA or DHA in plasma TAG for participants consuming the EPA supplements or the olive oil placebo, compared with day 0.

Plasma CE

The average baseline levels of LC n-3 PUFA in plasma CE were 0.9 % for EPA, 0.8 % for DPA and 0.7 % for DHA (Fig. 3). As shown in Fig. 3, there were no significant changes in the proportion of LC n-3 PUFA caused by the olive oil supplementation. After DPA supplementation, there was a significant rise in EPA proportions at day 7 (from 0.9 to 1.7 %, $p = 0.027$) compared with day 0. After supplementation with EPA, there was a significant rise in the proportion of EPA at day 4 (from 0.9 to 2.4 %, $p < 0.01$) and day 7 (from 0.9 to 2 %, $p < 0.01$), compared with day 0.

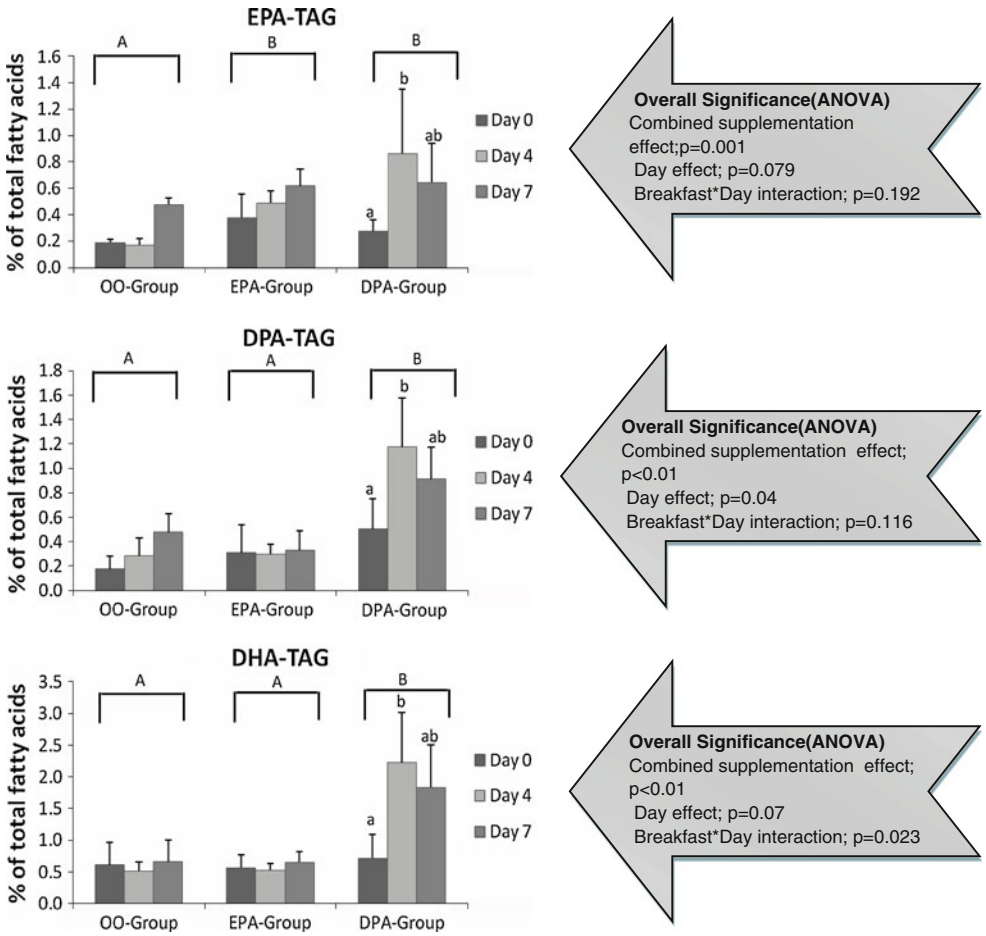

Fig. 2 Fatty acid composition of plasma triacylglycerides (TAG) from human participants supplemented with a dose of 2 g for the first day and 1 g for the subsequent 6 days. Results are expressed as percentage mean ± SEM ($n = 10$). Data were analysed using two-way ANOVA repeated measures, and pairwise comparisons were made using Tukey's test. The *superscripts* with capital alphabets represent over all supplementation effect, and different *superscripts* represent values that are significantly different ($p < 0.05$). The *superscripts* with small alphabets represent time effect within each supplementation group, and different *superscripts* represent values that are significantly different ($p < 0.05$). The values with no *superscripts* show no significant differences. *OO* olive oil, *EPA* eicosapentaenoic acid, *DPA* docosapentaenoic acid, *DHA* docosahexaenoic acid

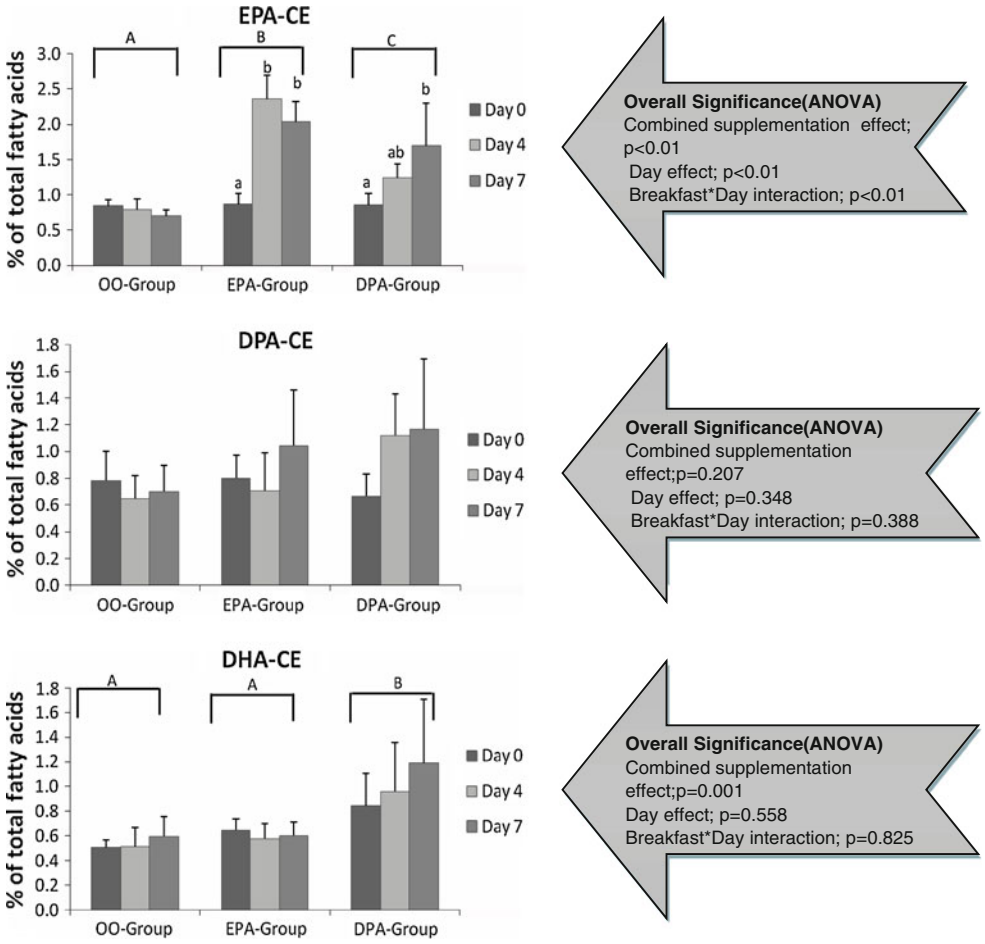

Fig. 3 Fatty acid composition of plasma cholesterol ester (CE) from human participants supplemented with olive oil, EPA or DPA with a dose of 2 g for the first day and 1 g for the subsequent 6 days. Results are expressed as percentage mean ± SEM ($n = 10$). Data were analysed using two-way ANOVA repeated measures, and pairwise comparisons were made using Tukey's test. The *superscripts* with capital alphabets represent over all supplementation effect, and different *superscripts* represent values that are significantly different ($p < 0.05$). The *superscripts* with small alphabets represent time effect within each supplementation group, and different *superscripts* represent values that are significantly different ($p < 0.05$). The values with no superscripts show no significant differences. *OO* olive oil, *EPA* eicosapentaenoic acid, *DPA* docosapentaenoic acid, *DHA* docosahexaenoic acid

RBC PL

The average baseline levels of EPA, DPA and DHA in RBC PL were 1.0, 2.2 and 6.7 %, respectively (Fig. 4). After the DPA supplementation, there was no significant change in the proportion of DPA in RBC PL. After the EPA supplementation, there was a significant increase in the proportion of EPA at both day 4 (from 1.1 to 2.0 %) and 7 (from 1.1 to 1.9 %), compared with the baseline value ($p < 0.01$). There were no significant changes in the proportions of DPA or DHA in any of the treatment groups.

Plasma TAG concentrations

There were no significant changes in the concentration of TAG in plasma samples between the control and LC n-3 PUFA supplement periods, or with time in any of the three groups (data not shown).

Discussion

The ingestion of LC n-3 PUFA–rich marine oils, either as fish or in purified oil supplements, is a widely accepted strategy for the reduction in plasma TAG levels [24–27]. This is supported by a considerable quantity of data on the effect of LC n-3 PUFA in cell models [28, 29], experimental animals [30, 31] and intervention clinical studies [32, 33]. DPA is one of the three major LC n-3 PUFA in marine oils; yet, there is no available data on the plasma lipid or RBC PL distribution of DPA following supplementation with pure DPA in humans. Therefore, the aim of

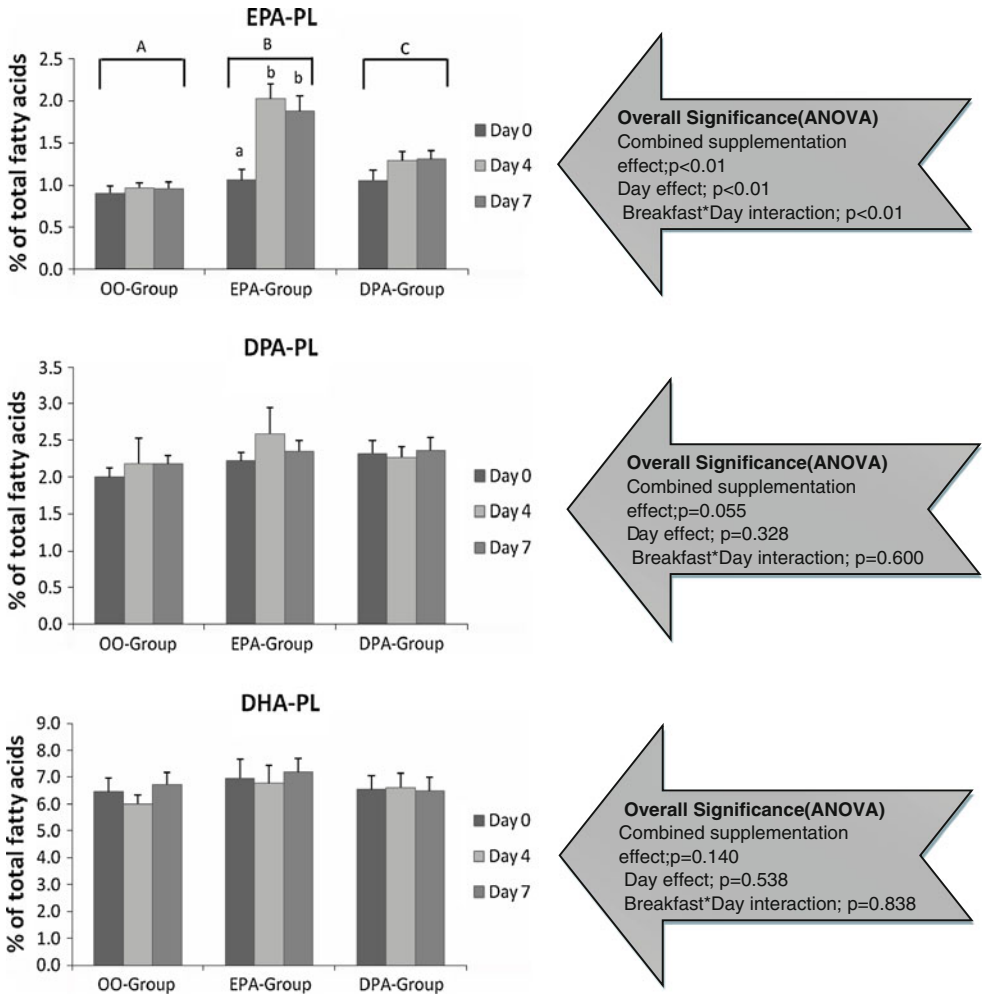

Fig. 4 Fatty acid composition of red blood cell phospholipids (PL) from human participants supplemented with olive oil, EPA or DPA with a dose of 2 g for the first day and 1 g for the subsequent 6 days. Results are expressed as percentage mean ± SEM ($n = 10$). Data were analysed using two-way ANOVA repeated measures, and pairwise comparisons were made using Tukey's test. The *superscripts* with capital alphabets represent over all supplementation effect, and different *superscripts* represent values that are significantly different ($p < 0.05$). The *superscripts* with small alphabets represent time effect within each supplementation group, and different *superscripts* represent values that are significantly different ($p < 0.05$). The values with no *superscripts* show no significant differences. *OO* olive oil, *EPA* eicosapentaenoic acid, *DPA* docosapentaenoic acid, *DHA* docosahexaenoic acid

this study was to investigate the partitioning of pure DPA into human plasma and red blood cell lipid fractions following a 7-day dietary supplementation period.

The most striking finding, contrary to expectations, was that DPA and EPA partitioned into different lipid fractions in both plasma and RBC phospholipids. In the steady state (baseline values), DPA and EPA were both present in RBC PL, plasma CE and plasma PL in higher proportions than in the plasma TAG fraction. With DPA supplementation, there was a significant increase in the proportions of DPA in the plasma TAG and PL fraction, but not in RBC PL or plasma CE fractions. Consistent with the steady state, EPA supplementation significantly increased the proportion of EPA in plasma CE and PL fractions and RBC PL, but not in the plasma TAG fraction. The failure of DPA to be incorporated into the plasma CE fraction and RBC PL fraction was unexpected and reveals in the time frame of this study a highly interesting difference between how DPA and EPA are processed in the body. This differential processing might occur perhaps at the level of incorporation of the PUFA into chylomicron TAG and/or at the level of the liver following the uptake of the PUFA from chylomicron remnants, subsequent processing into VLDL lipids and exchange between lipoproteins and red blood cell lipids.

The average baseline levels of LC n-3 PUFA in the plasma PL in our study were 0.8 % for both EPA and DPA and 2.3 % for DHA, which is consistent with previously reported data for Australian subjects [34, 35]. In our study, supplementation with DPA led to a significant increase in DPA levels (by twofold) in plasma PL which peaked by

4 days. Seal oil supplementation (which contains a higher proportion of DPA than other marine oils) led to a significant increase in DPA proportions in plasma PL [36]. No changes were observed in EPA levels in plasma PL as a result of DPA supplementation, which means any DPA that was retro-converted to EPA, say in the liver, was not incorporated into the plasma PL in the time frame of this study. In our study, supplementation with EPA significantly increased the EPA levels by approximately 2.7-fold in plasma PL. Similar findings have also been reported by Mori et al. [37] who fed 4 g/day of pure EPA to human subjects for 6 weeks and showed increases in EPA levels in plasma PL. In addition, Mori et al. showed an increase in the DPA level. In our study, although DPA levels in the EPA group were higher than baseline levels, this increase did not achieve statistical significance. It should be noted that the Mori et al.'s study was over an extended period (6 vs. 1 week in the present study). Studies utilizing fish oil supplements have also shown increased levels of all three LC n-3 PUFA in plasma PL after 6 weeks of supplementation [38].

The mean baseline values of LC n-3 PUFA in plasma TAG in our study were 0.3 % for EPA and DPA and 0.6 % for DHA, comparable to the previous reports [35]. In the present study, DPA supplementation significantly increased plasma TAG DPA, EPA and DHA levels at day 4. Previous studies have reported that high doses of EPA lead to the accumulation of EPA in the plasma TAG fraction [39]. The increases in all 3 major n-3 PUFA species indicate that DPA is both being retro-converted back to EPA and further elongated onto DHA. Retro-conversion involves both peroxisomal acyl-CoA oxidase and β-oxidation [40, 41]. Retro-conversion has been demonstrated in hepatocytes [12], and may also be present in endothelial cells [42] and fibroblasts [40, 43]. Recently, evidence of retro-conversion of DPA to EPA was found to be present in a wide variety of rat tissues including liver, heart and skeletal muscle [14, 15]. The current study demonstrated that in healthy female volunteers, 7 days of supplementation of DPA increased plasma TAG EPA, demonstrating retro-conversion and augmentation of this EPA pool. While we cannot be certain of the reason for the increase in DHA levels in plasma TAG fractions following DPA supplementation, this result demonstrates DPA can act as a source of DHA in the body. This increase in DHA levels is supported by animal studies with pure DPA supplementation by Kaur et al. [15], Holub et al. [14] and Gotoh et al. [11] who all reported increased DHA levels in liver tissue.

The mean baseline values for LC n-3 PUFA in plasma CE in our study were 0.9 % for EPA, 0.8 % for DPA and 0.7 % for DHA, consistent with previously published data [44]. In the current study, DPA supplementation trended towards an increased DPA and DHA levels in plasma CE; however, statistical significance was not achieved. It is possible that long-term supplementation might result in increased DPA and DHA levels in plasma CE. There was further evidence of DPA retro-conversion to EPA, since there was a significant increase in EPA in the plasma CE fraction (by twofold at day 8). This suggests that DPA can act as a source of EPA in the body. Our data show that EPA supplementation significantly increased plasma CE EPA levels by approximately 2.7- and 2.3-fold at day 4 and day 8, but did not impact on DPA levels. A previous long term study [44] has shown that an EPA-rich fish oil leads to significant increases in plasma CE proportions of EPA within 30 days of commencing the study (12-month study). The present study showed that EPA can be incorporated into plasma CE within 4 days of commencing the supplement.

The mean baseline values of LC n-3 PUFA in RBC PL in our study were 1.0 % for EPA, 2.2 % for DPA and 6.7 % for DHA, consistent with data published previously [38, 45]. In our study, there was no increase in DPA levels in RBC PL in any group. A seal oil supplementation study showed a considerable increase in EPA (0.8-fold) and DHA (onefold) levels in erythrocytes and an only modest increase in DPA (0.2-fold) [46]. Since seal oil also contains EPA along with DPA, the modest increases in DPA levels could be from the conversion of EPA into DPA, rather than direct incorporation of DPA itself.

Pure EPA supplementation for 6 weeks has been reported to increase EPA levels in RBC membrane [45]. Similarly, our data show that EPA supplementation for 1 week significantly increased RBC PL EPA levels at day 4. As RBC lifespan is approximately 120 days [44], incorporation of EPA into RBC PL is unlikely to be achieved through a process involving RBC turnover. Incorporation of EPA into the RBC is more likely achieved through exchange between plasma and RBC PL, as speculated previously [47–49].

It is recognized that the washout period between the EPA and DPA treatments was relatively short (2 weeks) and that this might have been insufficient time to allow for turnover of the LC n-3 PUFA in the RBC. Based on the literature, DHA appears to have the longest half life of all RBC omega 3 fatty acids [38]; however, in the present study, there were no changes (increases) in the DHA proportions in the RBC in any of the 3 groups. Furthermore, there were no changes in DPA or EPA proportions in the DPA group. The only significant change in RBC omega 3 PUFA proportions was that EPA was incorporated into the RBC lipids in the EPA group, and the EPA value at the start of the next treatment (DPA treatment) was not significantly different to the EPA value at the start of the EPA treatment ($p > 0.05$). Therefore, we believe that in this study, the 2-week washout period was sufficient length of

time to avoid carryover of raised LC n-3 PUFA from one treatment group to the next.

The metabolism of DPA has not been studied previously in humans. This short-term supplementation study in healthy volunteers demonstrated that DPA, along with EPA, were incorporated differentially into plasma and RBC lipid fractions. Future studies should examine the incorporation of DPA into chylomicrons, chylomicron remnants and VLD lipoproteins to help explain the differential metabolism of DPA and EPA. The most novel finding was that in the context of this short-term study, DPA showed the evidence of metabolism to both EPA and DHA. This suggests that DPA could function as a reservoir or buffer of the other LC n-3 PUFA.

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