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Time Trend Investigation of PCBs, PBDEs, and Organochlorine Pesticides in Selected *n*−3 Polyunsaturated Fatty Acid Rich Dietary Fish Oil and Vegetable Oil Supplements; Nutritional Relevance for Human Essential *n*−3 Fatty Acid Requirements

MIRIAM N. JACOBS,*,† ADRIAN COVACI,§ ADRIANA GHEORGHE,# AND PAUL SCHEPENS§

School of Biomedical and Molecular Sciences, University of Surrey, Guildford GU2 7XH, United Kingdom; Department of Pathology and Infectious Diseases, The Royal Veterinary College, Hawkeshead Lane, North Mymms, Hatfield AL9 7TA, United Kingdom; Toxicological Center, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium; and Department of Analytical Chemistry, Faculty of Chemistry, University of Bucharest, Sos. Panduri 90-92, Bucharest, Romania

In addition to being used in the food and animal feed industry, fish oils have also been used traditionally as dietary supplements. Due to the presence of long-chain *n*−3 fatty acids, fish oils have therapeutic benefits in the prevention and treatment of cardiovascular, immunological, and arthritic diseases, as well as childhood deficiency diseases such as rickets, because of a high content of vitamin D. However, fish oils are also susceptible to contamination with lipophilic organic chemicals that are now ubiquitous contaminants of marine ecosystems. Many vegetable oils are sources of the shorter chain precursor forms of *n*−3 fatty acids, and in recent years the specialist dietary supplement market has expanded to include these oils in a variety of different formulations. This paper reports analytical results of selected contaminants, including polychlorinated biphenyls, organochlorine pesticides, and polybrominated diphenyl ethers, for a range of commercially available *n*−3 fatty acid rich fish and vegetable oil dietary supplements. Using principal component analysis, the values are compared with historic samples to elucidate time trends in contamination profiles. Levels of contaminants are discussed in relation to the nutritional benefits to the consumer of long- and short-chain forms of *n*−3 fatty acids.

KEYWORDS: Diet; fish oils; flaxseed/linseed oil; *n*−3 fatty acids; organochlorine pesticides; persistent organic pollutants; PCBs; PBDEs

INTRODUCTION

Fish oil is a byproduct of the fish meal manufacturing industry and comes from many different parts of the world. Fish oils are sold for dietary purposes due to the presence of long-chain *n*−3 polyunsaturated fatty acids (*n*−3 PUFA) such as eicosapentaenoic acid (EPA) and decosahexaenoic acid (DHA), which have certain health benefits and are essential to the human diet (*1*). Specific vegetable oils and foods are sources of the short-chain form α-linolenic acid (18:3*n*−3) (ALNA), the precursor to the long-chain form (22:6*n*−3) utilized in human metabolism. Essential fatty acids are needed for many metabolic functions, including growth, structural maintenance and repair of nervous tissue, cellular membrane phospholipid structure, the regulation of plasma lipid levels, and cardiovascular and immune function (*1*−*8*). The consumption of long-chain *n*−3 essential oils from fatty fish or concentrated sources such as fish oil supplements is thought to have associated benefits in reducing mortality from heart disease and improving symptoms of a number of diseases including multiple sclerosis, rheumatoid arthritis, and osteoporosis (*1*, *3*, *8*, *9*).

The 1990 Diet and Nutritional Survey of British Adults found that 17% of the women respondents took dietary supplements, commonly fish oil (*10*). In a more recent National Diet and Nutrition survey for young people aged 4−18 years, 20% of the respondents took dietary supplements (*11*). Fish oils have also been traditionally given to children to protect against vitamin D deficiency and rickets. However, oily fish and extracted fish oils are a major source of lipophilic persistent organic pollutants (POPs) entering the human food chain (*12*−*14*). Halogenated compounds, such as polychlorinated biphenyls (PCBs), organochlorinated pesticides (OCPs), and polybrominated diphenyl ethers (PBDEs), are persistent, accumulate in the lipid compartment of the animal, and thus accumulate in

* Corresponding author [telephone +44 (0)1483 876477; fax +44 (0)1483 300374; e-mail m.jacobs@surrey.ac.uk or mjacobs@rvc.ac.uk].
† University of Surrey and The Royal Veterinary College.
§ University of Antwerp.
# University of Bucharest.

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the food chain. Oil extracted from fish caught in polluted waters may be contaminated with these compounds. A wide range of toxicological and hormonal effects are stimulated by these environmental contaminants, from endocrine disruption in wildlife to associations with impaired development in children (*15*−*20*) and possible associations with hormone-dependent cancers (*21*−*24*). As quantities of fish oil consumed can vary enormously (*13*, *14*, *25*), it is important that close monitoring is undertaken to ensure contaminant levels are reduced as much as possible.

There is an extensive and growing body of data on the presence of POPs in the aquatic biota (*26*−*28*) and in some foods including margarine and vegetable oils (*29*, *30*). However, there are few data available in the public domain for PBDEs in fish oils and other essential *n*−3 fatty acid containing dietary oils.

This study reports the levels of selected PCBs, OCPs, and PBDEs in 21 *n*−3 rich dietary fish and vegetable oil supplements obtained through retail and wholesale outlets in London, U.K. A multivariate analytical comparison with previously reported dietary fish oil supplements available from the same sources and brands (*13*, *14*) is presented. Finally, dietary aspects and considerations on the simultaneous presence of POPs and *n*−3 fatty acids in the investigated dietary supplements are discussed.

MATERIALS AND METHODS

Sample Description. Twenty-one (S1−S21) dietary supplements rich in *n*−3 fatty acids (7 cod liver oils, 7 whole body fish oils, 3 vegetable and fish oil combinations, and 4 vegetable oils) were obtained from retail and practitioner suppliers of the U.K. market in December 2001 and January 2002. (Sample descriptions are given in **Table 1**.) Samples were chosen to cover the products available to the U.K. consumer, including a neighborhood pharmacy, a national retail chain pharmacy, whole food retailers, and dietary supplement companies selling directly to nutritional therapists. Although the samples cover the leading brands available on the London/U.K. market, this was not a comprehensive survey of all brands available.

Sample Preparation. The samples were logged and prepared in duplicate prewashed glass vials. They were kept at room temperature in the dark. All samples were analyzed for 28 PCB congeners (no. 18, 28, 31, 52, 74, 95, 99, 101, 105, 110, 118, 128, 132, 138, 149, 153, 156, 163, 167, 170, 174, 177, 180, 183, 187, 194, 196, and 199), for hexachlorocyclohexane isomers (α-, β-, and γ-HCH), for hexachlorobenzene (HCB), for trichlorobis(*p*-chlorophenyl)ethane (DDT) and metabolites (5 *o*,*p*- and *p*,*p*-isomers), and for 7 PBDE congeners (no. 28, 47, 99, 100, 153, 154, and 183). These congeners were selected on the basis of their relative abundance and presence in fish oils and in the marine environment in general. Analytical procedures have been described in detail previously (*28*), and a brief description is presented below. An aliquot of 0.5−0.7 g of oil was solubilized in 3 mL of *n*-hexane, internal standards (10 ng of PCBs 46 and 143, 5 ng of ϵ-HCH, and 1 ng of BB 80, BB 103, and BB 155) were added, and the mixture was equilibrated in an ultrasonic bath for 5 min. The extract was applied to an *n*-hexane prewashed cartridge filled with 5 g of acidified silica and was eluted with 15 mL of *n*-hexane and 10 mL of dichloromethane. The final eluate was concentrated with a rotary evaporator under nitrogen to ∼100 μL.

PCB and OCP Determination. One microliter of cleaned extract was injected in pulsed splitless mode into a gas chromatograph−electron capture detector (GC-μECD) equipped with a 50 m × 0.22 mm × 0.25 μm, HT-8 capillary column (SGE, Zulte, Belgium). For confirmation, 1 μL was injected in pulsed splitless mode into a gas chromatograph−mass spectrometer (GC-MS) equipped with a 25 m × 0.22 mm × 0.25 μm, HT-8 capillary column. The MS was operated in electron impact ionization and selected ion monitoring (SIM) mode. The two most abundant ions were monitored for each level of chlorination for PCBs or for each pesticide. Method limits of determination for individual compounds ranged between 0.1 and 0.2 ng/g of oil. Recoveries of internal standards were satisfactory, ranging between 75 and 85% (recoveries within the range of 70−110% are acceptable).

PBDE Determination. One microliter of extract was injected in cold splitless mode into a GC−negative chemical ionization (NCI)−MS equipped with a 10 m × 0.10 × 0.10 μm, HT-8 capillary column. The MS was operated in negative chemical ionization in SIM mode (*m*/*z* 79 and 81). Method limits of determination ranged between 0.05 and 0.1 ng/g of oil for individual PBDE congeners. Internal standards for PBDEs were BB 80, BB 103, and BB 155. Recoveries for PBBs were between 92 and 101%.

Quality Control. All samples were analyzed with GC-μECD and GC-MS systems. The lowest result for each compound obtained in both systems was considered for further calculations. The procedure was validated through regular analyses of procedural blanks and certified material CRM 350 (PCBs and organochlorine pesticides in mackerel oil) and through successful participation in Quasimeme interlaboratory studies (PCB determination in sediment and fish). For PBDEs, external quality control was ensured through successful participation in the second interlaboratory study for brominated flame retardants (*31*).

Oil Density. Densities of oils were determined gravimetrically and were between 0.87 and 0.90 g/mL. Thus, direct comparisons of concentrations given in micrograms per liter with those given in microgram per kilogram or nanograms per gram should allow for an approximate 10% underestimate of concentrations expressed on a volumetric basis.

Statistical Analysis. Principal component analysis (PCA) software (Umetrics SIMCA v. 10) was utilized for further time trend analysis of the data compared to that generated for *n*−3 fatty acid rich dietary supplements obtained from the same sources 7−8 years previously.

RESULTS AND DISCUSSION

Levels of POPs in *n*−3 Rich Dietary Supplements. Summary results are presented in **Table 1**, with total sum (Σ) values given using the LOD equal to zero where there were no detections. The full results are available in the supplementary information (SI) Table SI-1 and Figures SI-1−3.

All fish oil samples contained detectable residues of organohalogenated contaminants, with cod liver oil (samples S1−S7) having levels similar to those previously reported (*12*−*14*) and the greatest levels of POPs compared to the other supplement groups in this study. The oils with higher concentrations of PCBs presented low levels of volatile compounds (such as HCB, HCHs, and low chlorinated PCBs), an indication of solvent extraction and thermal distillation (*32*−*34*). The PCB profile was dominated by hexa- and pentacongeners followed by heptacongeners, with some variation in percentages of different PCB congeners depending upon the type of fish oil and sample formulation. Fish and vegetable oil mixtures (samples S14−S17) had lower levels than the whole fish body oils, whereas no PCBs were detected in the vegetable oils (samples S18−S21). The predominant pesticides were DDTs, present in all but one sample (sample S21, a vegetable oil mix from Canada). HCHs and HCB levels were very low; only the α- and γ-HCH isomers were detected. In the fish oils, higher levels of DDTs were correlated with higher PCB concentrations ($r^2 = 0.78$) as shown in **Figure 1**. PCB concentrations in the fish oil samples were between ND and 90.9 ng/g of lipid. These concentrations are generally of the same order of magnitude but are not as high as those previously reported based on ICES 7 PCBs (*14*).

The PBDE levels in cod liver oils ranged from 14.6 to 34.2 ng/g of lipid and were greater than the range of ND−12.7 ng/g of lipid reported for fish oil samples used in aquaculture feeds ($n = 4$) collected in 1999 (*28*). The fish and fish/vegetable formulations showed PBDEs levels that were an order of magnitude lower than the cod liver oils, and three of four fish/

Table 1. Summary Concentrations (Nanograms per Gram of Lipid Adjusted) of PCBs, PBDEs, and OCPs in Fish and Vegetable Oil *n*–3 PUFA Rich Dietary Supplements[a]

sample	further information	country of origin	sample wt (g)*	PCBs																	*p,p′*-DDT/ ΣDDT
				Σ tri	Σ tetra	Σ penta	Σ hexa	Σ hepta	Σ octa	Σ PCBs[b] (ND = 0)	Σ 7 marker PCBs[c]	Σ 7 PBDEs	HCB	γ-HCH	Σ HCHs	*p,p′*-DDE	*p,p′*-DDT	*p,p′*-DDD	Σ DDTs	
cod liver oils																					
S1	enriched with FO	U.K.	0.54	ND	2.2	39.0	90.3	27.6	1.6	160.7	92.1	14.9	ND	ND	ND	56.4	22.7	44.1	137.7	0.17
S2	pure CL	U.K.	0.60	ND	0.7	36.9	102.7	31.4	2.0	173.7	96.6	20.0	ND	ND	ND	56.7	26.0	55.1	155.9	0.17
S3	CL, soybean oil	NA	0.62	2.8	4.9	69.5	79.0	18.6	0.5	175.4	86.7	14.6	9.1	5.1	9.0	44.9	12.0	32.9	99.6	0.12
S4	pure CL	U.K.	0.66	2.9	6.7	120.9	183.7	43.6	2.4	360.1	201.9	34.2	2.9	0.9	1.8	106.3	28.3	73.7	224.1	0.13
S5	pure CL	U.K.	0.62	8.3	4.2	73.1	96.9	27.1	0.8	210.4	110.9	20.3	7.3	1.2	5.4	62.0	7.9	36.8	116.7	0.07
S6	enriched with FO	NA	0.61	6.9	4.3	78.4	93.3	26.4	1.1	210.3	107.7	15.6	4.9	1.3	3.2	50.5	7.4	38.7	104.9	0.07
S7	CL + taste masks	NA	0.61	0.2	3.8	54.1	120.5	44.0	2.5	225.1	133.3	22.3	ND	ND	ND	75.3	34.2	65.2	193.3	0.18
fish oils																					
S8	salmon oil	Norway/U.S.	0.62	ND	ND	ND	ND	ND	ND	ND	ND	0.8	ND	ND	ND	1.6	1.9	1.3	4.8	0.40
S9	MLC	NA	0.60	ND	2.1	28.6	34.4	9.9	ND	75	38.7	0.8	3.4	ND	0.5	14.5	5.6	10.2	30.3	0.19
S10	fish body oil	NA	0.60	ND	ND	32.9	24.8	2.5	ND	60.3	35.1	1.4	0.2	ND	ND	10.5	4.5	11.4	31.4	0.14
S11	fish body oil	NA	0.61	ND	ND	13.4	28.6	8.1	ND	50.1	27.8	2.6	ND	ND	ND	10.3	6.3	7.6	35.9	0.18
S12	FO concentrate	NA	0.62	0.2	ND	17.1	32.5	8.1	ND	57.9	32.0	1.9	ND	ND	ND	6.3	7.1	1.9	15.4	0.46
S13	pure FO	U.K.	0.60	0.2	3.8	38.5	40.4	8.0	ND	90.9	49.0	2.7	0.8	0.3	0.8	20.8	8.1	12.7	47.1	0.17
fish + veg oils																					
S14	EPO, tuna fish oil	NA	0.60	ND	ND	ND	ND	ND	ND	ND	ND	0.3	ND	0.2	0.2	12.3	2.2	2.7	21.4	0.10
S15	EPO, marine FO	NL	0.60	1.0	2.5	15.4	28.8	3.5	ND	51.2	28.9	1.9	4.2	0.7	1.7	14.4	6.2	11.7	39.8	0.16
S16	FO + garlic, vit/min, lecithin	NA	0.55	ND	ND	13.6	20.0	0.7	ND	34.4	18.7	1.1	ND	ND	0.4	48.6	77.8	10.2	142.9	0.55
S17	EPO, marine FO	NA	0.64	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.5	2.5	0.5	ND	0.6	1.1	-
veg oils																					
S18	unrefined LO	NA	0.61	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	5.9	5.9	0.7	5.4	0.8	8.2	0.66
S19	organic FSO	NA	0.61	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.3	1.3	0.5	2.3	0.5	3.9	0.59
S20	organic CP LO	Germany	0.60	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.6	0.6	0.3	ND	0.7	1.0	-
S21	FSO plus SSO, SeSO, MCT, EPO, RO, OO	Canada	0.61	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.3	0.3	ND	ND	ND	ND	-

[a] Abbreviations: CL, cod liver oil; CP, cold pressed; EPO, evening primrose oil; FO, fish oil; LO, linseed oil; FSO, flax seed oil; MCT, medium-chain triglycerides; MLC, marine lipid concentrate; NA, not available; SSO, sunflower seed oil; SeSO, sesame seed oil; RO, rice bran and rice germ oils; OO, oat bran and oat germ oils; veg, vegetable; vit/min, vitamins and minerals; *, sample wt taken for analyses; ND, nondetects (treated as 0 for Σ calculations). [b] 28 PCB congeners, IUPAC no.: 18, 28, 31, 52, 74, 95, 99, 101, 105, 110, 118, 128/174, 132, 138, 149, 153, 156, 163, 167, 170, 177, 180, 183, 187, 194, 196, 199. [c] ICES 7 marker PCBs: IUPAC no.: 28, 52, 101, 118, 138, 153, 180.

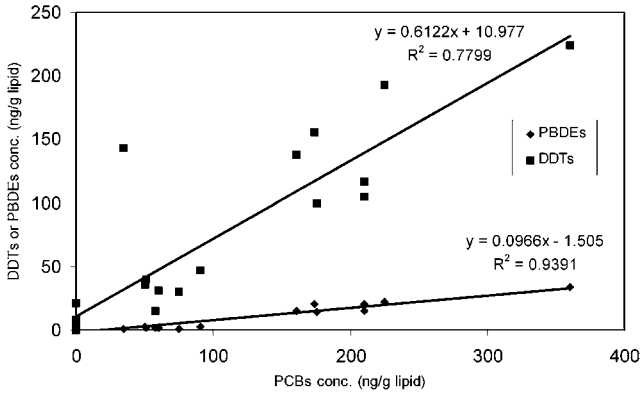

Figure 1. Correlation between concentrations of PCBs versus DDT and PBDEs in *n*–3 PUFA rich dietary supplements.

vegetable oil samples had detectable levels of PBDEs. No PBDEs were detected in the pure vegetable oils (samples S18−S21). BDE 47, the most abundant congener, was detected at concentrations comparable to PCB 118. PBDEs showed the same trend as PCBs ($r^2 = 0.94$) (**Figure 1**), in contrast to our previous data on PBDE and PCB contaminants in fish oils used in aquaculture feed formulations (*28*). These results are in good agreement with the levels of congener specific PCBs reported by the U.K. Food Standards Agency and the Irish Food Safety Authority for fish liver oils (*12*, *35*, *36*) but with higher levels of PBDEs than those recently reported (*28*). A more detailed comparison with other studies is hampered by the lack of congener specific data (*37*) or because different contaminants, such as dioxins and dioxin-like PCBs, were analyzed and reported in recent studies (*35*, *36*).

Time Trends in the Levels of POPs in *n*−3 Rich Dietary Supplements. Generally, the oil samples (S1−S21), particularly the fish oils (S8−S13), showed less contamination on a congener specific basis with similar or the same brands as those analyzed in a study conducted 8 years ago. The old data set consisted of 22 dietary supplements rich in *n*−3 fatty acids obtained from the same outlets and suppliers in late 1994/early 1995, including 9 cod liver oil supplements, 10 whole body fish oil based supplements, 2 probable cod liver oils, and 1 vegetable oil (*13*, *14*).

The time-related differences in selected organochlorine contaminant levels and patterns for these dietary supplements were examined using PCA, as the datasets are multivariate ($n = 22$ old samples, $n = 21$ recent samples; 13 PCBs and organochlorine contaminants measured in both studies), and there is a large variation within some of the variables. A three-component PCA model was constructed ($R^2X = 0.76$, $Q^2 = 0.44$, where R^2X accounts for the explained variation and Q^2 is the cross-validated R^2, a measure of predictability). Although the recent oil samples (S1−S21), particularly the fish oils (S8−S13), showed less contamination compared with past reports (old1−old21) (see **Figures 2** and **3** showing the primary variables and loading and score scatter plots), the cod liver oils (S1−S7) had the greatest levels of contaminants compared to the other supplement groups (see **Figure 3** and, for greater clarity, the score subplot shown in **Figure 4A**). Apart from a recent salmon oil sample (S8), fish and vegetable oil mixtures had lower levels (S14−S17) than the whole fish body oils (S9−S13) (see **Figures 3** and **4B**), whereas no PCBs were detected in the vegetable oils (S18−S21) as observed previously (old22), but HCHs were detected (see **Figure 3** and the score subplot in **Figure 4C**). With most PCBs detected a clear reduction in PCB contaminants was observed, except for PCB 52 (which had a high detection limit of 18 ng/mL for the old samples) and the pesticides HCHs and DDT, which were dissimilar in pattern (**Figures 2** and **3**). The comparative increase in DDT in the recent samples may be due to the poor recoveries for DDT for the old samples (*13*). The difference in the HCH patterns may be partly due to the greater proportion of vegetable oils analyzed in the recent study, which were not subjected to the same treatment processes as observed in the fish oils. Sample old9 (salmon oil), one of the most contaminated supplements, is clustered with the more contaminated fish oil supplements (top right, **Figures 3B** and **4D**), whereas the present-day equivalent from the same manufacturer (S8) is clustered with the least contaminated supplements (left, **Figures 3B** and **4D**).

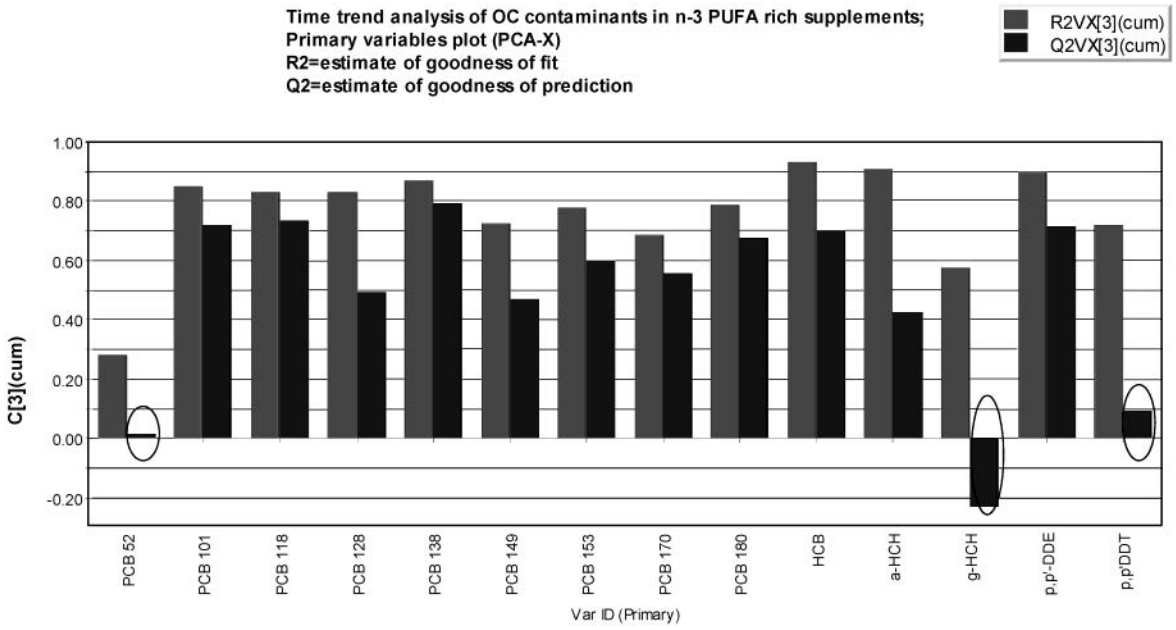

Figure 2. Time trend principal component analysis: organochlorine contaminants in *n*–3 PUFA rich dietary supplements: The primary variables plot for the three-component PCA model ($R^2X = 0.76$, $Q^2 = 0.44$).

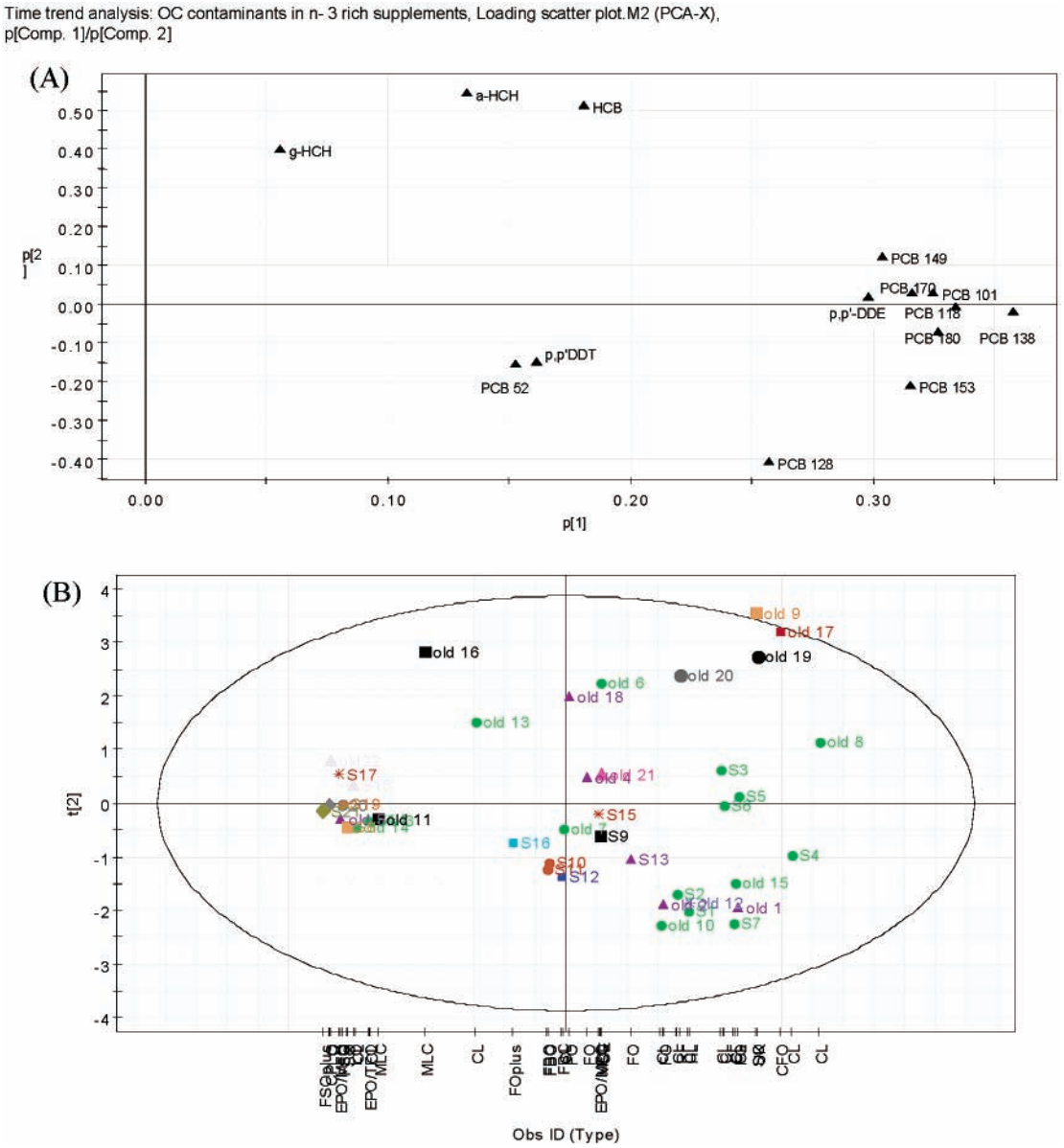

Figure 3. Time trend principal component analysis; organochlorine contaminants in *n*–3 PUFA rich dietary supplements: (**A**) loading scatter plot; (**B**) score scatter plot (colored according to sample type). Abbreviations in addition to those given for **Table 1**: FBO, fish body oil; FBC, fish body concentrate; RF, redfish oil; SO, salmon oil; TFO, tuna fish oil; UK, unknown.

The samples showed less contamination compared with past reports (*12*−*14*). Most fish oil samples showed evidence of steam distillation, and this probably contributed to the reduction in contaminant levels (*32*−*34*), in accordance with Good Manufacturing Practice guidelines and EC legislation. Comparisons with unrefined fish oils would indicate whether a real reduction in the steady state of PCBs has occurred (*38*, *39*). Apart from improvements in refining processes, further reasons for the reduction in contaminant levels include improved sourcing and nutritional profile development to create specific "optimum" essential fatty acid balances. Both this study and the U.K. Food Standards Agency (*35*) found that the fish oils available to the consumer were often diluted (usually with vegetable oils) to provide "optimum" essential fatty acid supplements compared with the pre-2000 fish oils analyses in the public domain. On a weight for weight basis these approaches appear to improve supplement quality for the consumer.

National extrapolations for levels and time trends of PCB contaminants in fish oils available on the U.K. market could be suggested on the basis of these studies in addition to other recent publications (*35*−*37*) but not for the other target contaminants, due to the small sample size and lack of available comparative data.

Nutritional Relevance of *n*−3 PUFA Rich Dietary Supplements for Human Metabolism. Although fish are a significant source of POPs in the diet, fish and fish oil consumption are associated with numerous health benefits due to the long-chain *n*−3 essential fatty acids. There are alternative dietary sources of *n*−3 fatty acids (*n*−3 PUFA) with evident lower contamination levels. ALNA (abundant in rapeseed and flax/linseed oil) is the short-chain natural precursor found in the vegetable oil based dietary supplements analyzed in this study. These sources offer an abundant and accessible source of dietary *n*−3 PUFA that can be further elongated and unsaturated in vivo, to contribute to the health benefits associated with a reduction in the *n*−6:*n*−3 ratio, which is currently considered to be too high in typical Western diets (*8*). There is growing (*40*), but still limited and sometimes conflicting, epidemiological evidence (*41*) of the nutritional benefits of dietary ALNA, raising

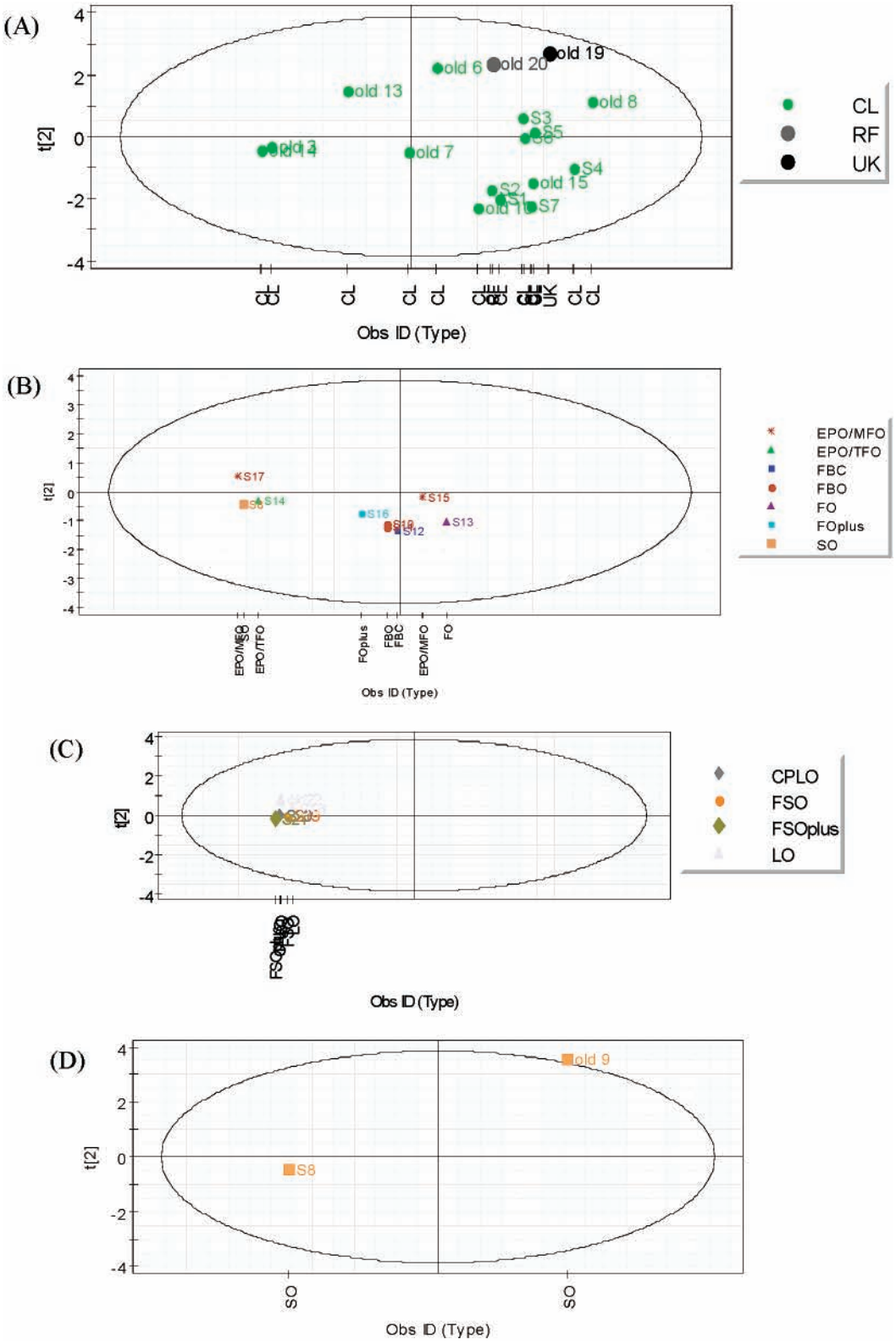

Figure 4. Time trend principal component analysis; organochlorine contaminants in *n*–3 PUFA rich dietary supplements; score scatter subplots: (**A**) cod liver oil samples; (**B**) fish and vegetable oil combinations and whole fish body oils (recent samples); (**C**) *n*–3 rich vegetable oil supplements; (**D**) salmon oil samples.

questions about the extent and efficiency of its long-chain conversion, especially its conversion to DHA. A number of human clinical studies have demonstrated good conversion of ALNA to the metabolically active EPA in infants and adults, increasing phospholipid EPA levels. However, DHA synthesis is reported to be much lower (*41*−*48*). The ALNA long-chain conversion rate is known to vary according to dietary ALNA and linoleic acid (LA) intake, and LA (*n*−6 PUFA) inhibits the conversion. Indeed, stable isotope studies show that ALNA can serve as a significant source of EPA, with a very approximate equivalence of 10:1 with dietary EPA, in subjects where the conversion is optimized by a low *n*−6:*n*−3 ratio (*48*).

In that study U^{13}C ALNA was given orally to a small cohort of normal, healthy male subjects. The subjects received either a diet enriched with flaxseed oil (high ALNA, $n = 6$) or a diet enriched with sunflower oil (high $n-6$ diet, $n = 5$) and the conversion to EPA and DHA was measured over a 2 week period from their ^{13}C enrichments in phosphatidylcholine fractions isolated from plasma and erythrocytes. Extensive and rapid conversion of ALNA to EPA was observed, and in contrast to the compositional data which showed no detectable increase in phospholipid DHA, the isotopic results showed that some DHA formation did occur in all subjects, albeit at a comparatively lower rate. Significant enrichment was observed at 24 h in plasma DHA on both diets and after 7 days in red blood cell DHA in all subjects. The 14 day mean total ^{13}C distributions between ALNA, EPA, docosapentanoic acid (DPA) and DHA, were 28, 52, 16, and 4%, respectively, with no differences between the two diets. Millward and Griffin (*48*) report an interesting observation, with respect to conversion efficiency, that in one subject studied after a fish oil diet conversion was very much reduced. Such stable isotope studies are limited due to the high cost involved but are generating very useful data for public health purposes. In the past 10 years there has been a clear shift in accepted wisdom from the traditional position that humans do not synthesize long-chain fatty acids efficiently to the current situation, where robust scientific evidence suggests that efficient conversion to EPA can and does occur.

At the bottom of the food chain, DHA is originally synthesized by phytoplankton and krill (*Euphausia pacifica*) (*49*). Species further along the food chain preferentially accumulate DHA, but appear to be unable to synthesize it effectively. DHA is of nutritional importance in fetal development, so nutritional sources of DHA are often promoted for pregnant and breast-feeding women. However, dietary DHA is not necessarily essential throughout life; it appears that DHA turns over very slowly, much more slowly than EPA, which is consistent with its low rate of conversion to eicosanoids. DHA synthesis may be regulated through additional pathways or independently from EPA. Metabolic demands for DHA appear to be very low, especially once tissue pools are sufficient. Indeed, existing metabolic levels of DHA probably represent what is appropriate for normal healthy metabolism, with levels rising when metabolic demands for DHA may be increased such as infection and pregnancy. Preliminary data suggest that women are able to convert ALNA to DHA with greater efficency than that observered in male subjects. Several studies have reported that arachidonic acid and DHA can be biosynthesized from their 18-carbon precursors in term and preterm human infants (*46*, *50*, *51*).

DHA has been shown to be toxic in vivo in advanced age. Supplementation with DHA resulted in oxidative DNA damage in the bone marrow of aged rats (*52*). Taken together, these studies suggest that if DHA is not found to be synthesized to any significant degree in the studies conducted so far, perhaps this is because it is not required in significant amounts for the general population's healthy metabolism and is produced only when required.

In terms of risk assessment, whereas fish and fish oil consumption is associated with numerous health benefits due to the long-chain $n-3$ essential fatty acids, the potential contribution to the human diet of POPs from $n-3$ PUFA food sources increases if sourced from fish, particularly cod liver. There are further metabolic and dose considerations. Supplementation with fish oils may impair a person's subsequent metabolic ability to convert EPA from vegetable sources of ALNA [as observed for one of the subjects observed in the Millward and Griffin study (*48*)]. Such effects may be transient, but are pertinent for reliable risk−benefit calculations.

Although the vegetable oils studied here presented little or no POPs contamination, ~8−10 times as much needs to be consumed to provide comparative levels of EPA, as delivered by fish oil (and the vegetable oils do not appear to provide an effective metabolic source of DHA for the average consumer). Therefore, when comparative dietary intakes of POPs contaminants from different sources that provide these essential fats are calculated, differences in recommended dose/consumption should be factored into the calculations.

Conclusion. This analysis strongly supports the need for ongoing monitoring of POPs in fish oils designated both as nutritional supplements for consumers and as animal feed ingredients. Furthermore, in the public interest, newer pollutants such as PBDEs need to be included in national and international POPs contaminant monitoring programs. This analysis also illustrates the value of multivariate analytical techniques for assessing contamination patterns and trends. An adequate risk−benefit analysis of fish oil and especially cod liver oil supplements would need to be multifactoral and consider the following: the range of dietary sources and currently available supplement formulations of short- and long-chain $n-3$ fatty acids; human variability in synthesis, metabolism, and utilization of the long-chain forms, at different times of life and in relation to other dietary fat intake; and knowledge of critical windows of developmental exposure to POPs, together with fetal and infant nutritional requirements for DHA, particularly with respect to brain and retinal development.

ABBREVIATIONS USED

ALNA, α-linolenic acid, DDT, trichlorobis(*p*-chlorophenyl)-ethane; DHA, decosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; OCP, organochlorine pesticide; PBDE, polybrominated diphenyl ether; PCB, polychlorinated biphenyl; POPs, persistent organic pollutants; PUFA, polyunsaturated fatty acids

Supporting Information Available: Congener specific concentrations (ng/g lipid adjusted) of PCBs, PBDEs, and OCPs in fish and vegetable oil $n-3$ PUFA rich dietary supplements (Table SI-1) and distribution of OCPs (A), PCBs (B), and PBDEs (C) in $n-3$ PUFA rich dietary supplements (Figure SI-1). This material is available free of charge via the Internet at http://pubs.acs.org.

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