Measurement of Organochlorines in Commercial Over-the-Counter Fish Oil Preparations

Implications for Dietary and Therapeutic Recommendations for Omega-3 Fatty Acids and a Review of the Literature

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• ***Context.*—The consumption of fish high in omega-3 fatty acids is advocated by the American Heart Association to decrease the risk of coronary artery disease. However, fish contain environmental toxins such as mercury, polychlorinated biphenyls, and organochlorine pesticides, which may negate the beneficial cardiovascular effects of fish meals. Toxin levels vary depending on both the fish source and the specific toxin, and neither farm-raised nor wild fish are toxin free. Fish oil supplements also prevent the progression of coronary artery disease and reduce cardiovascular mortality. However, only sparse data exist on the level of toxins in fish oil. In a previous study we showed that the amount of mercury in 5 over-the-counter brands of fish oil was negligible.**

***Objective.*—To determine the concentrations of polychlorinated biphenyls and other organochlorines in 5 over-the-counter preparations of fish oil.**

***Design.*—The contents of 5 commercial fish oil brands were sent for organochlorine analysis.**

***Results.*—The levels of polychlorinated biphenyls and organochlorines were all below the detectable limit.**

***Conclusions.*—Fish oil supplements are more healthful than the consumption of fish high in organochlorines. Fish oils provide the benefits of omega-3 fatty acids without the risk of toxicity. In addition, fish oil supplements have been helpful in a variety of diseases, including bipolar disorder and depression.**

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Fish possess antiatherogenic properties, presumably because of their high content of essential omega-3 polyunsaturated fatty acids (ie, eicosapentaenoic acid or docosahexaenoic acid). Several studies demonstrate the benefits of fish consumption in patients with cardiac disease, including a decreased mortality following myocardial infarction.[1–6] In addition, regular fish intake is recommended to decrease the risk of coronary artery disease.[6] On the other hand, many studies have illustrated that certain fish contain high levels of environmental toxins, such as mercury, polychlorinated biphenyls (PCBs), organochlorine (OC) pesticides, and related compounds.[6,7] Some of these toxins may negate the cardiovascular health advantages of fish meals.[6]

Concentrated omega-3 fatty acids are found in fish oil supplements and may provide benefits similar to fish without the exposure to harmful environmental toxins.[1] Daily fish oil ingestion slows the progression of coronary artery disease.[5] Furthermore, fish oil supplements have been shown to stabilize mood in bipolar disorder, relieve depression in pregnancy, and decrease inflammation in some autoimmune diseases.[8–15] In a previous study, we showed that several over-the-counter brands of fish oil supplements contained negligible amounts of mercury compared with fish and suggested that the consumption of fish oils may be preferable to eating fish.[16] However, mercury is not the only toxin potentially in fish oil supplements.

Organochlorines have at least 1 aromatic ring and include PCBs, which have 2 aromatic rings. Organochlorines can be divided into pesticide OCs (ie, dichlorodiphenyltrichloroethane [DDT]) and nonpesticide OCs (ie, PCBs). PCBs are unwanted byproducts of a variety of industrial processes and are still found in transformers and capacitors that were manufactured before PCBs were banned in 1977. PCBs persist in the environment because of their resistance to degradation, and they bioconcentrate in fish along the food chain. PCBs and related compounds have adverse dermatologic, reproductive, developmental, endocrine, hepatic, and immunologic effects.[17–19] DDT is the best-known OC pesticide. Similar to PCBs, OC pesticides such as DDT are resistant to degradation and accumulate in fish and in the environment. Exposure to OC pesticides may cause neurotoxicity and cardiac and pulmonary dysfunction.[17,18,20]

The levels of PCBs, OC pesticides, and related compounds in fish have received considerable attention in the

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Selected Environmental Toxin Content of 5 Preparations of Fish Oil		
Brand Name	Polychlorinated Biphenyls, ppb	Organochlorine, ppb
CVS	None detected	None detected
Kirkland	None detected	None detected
Natrol	None detected	None detected
Omega Brite	None detected	None detected
Sundown	None detected	None detected

press recently.[21,22] Articles warn the public about the hazards of toxins in certain fish and discuss the use of fish oil as an alternative. Commercially available fish are either farm raised or wild. Researchers have addressed concerns about the source of fish and its associated contaminants. A recent *Wall Street Journal* article stated that farm-raised salmon had higher levels of certain toxins than wild salmon. Consequently, people who regularly consume farm-raised salmon may have an increased risk of cancer later in life. On the other hand, toxins such as mercury are detected at equal or higher concentrations in wild fish, so neither farm-raised nor wild fish appear superior.[17,23–27] In this study, we examined the levels of a common group of environmental toxins, organochlorines, in 5 over-the-counter fish oil preparations to further evaluate whether advocating fish oil over fish is potentially warranted.

MATERIALS AND METHODS

Five commercial over-the-counter brands of fish oil supplements were purchased from retail or Internet sources. The brands included Omega Brite (Waltham, Mass), Natrol (Chatsworth, Calif), Sundown (Boca Raton, Fla), Kirkland (Houston, Tex), and CVS (Woonsocket, RI). The capsules were punctured, and approximately 5 mL of the liquid contents were sent in a citrate tube to National Medical Services (Willow Grove, Pa) for OC analysis (α-chlordane, 1,1-dichloro-2,2-bis(*p*-chlorphenyl)ethane [DDD], dichlorodiphenyldichloroethene [DDE], DDT, dieldrin, γ-chlordane, heptachlor, heptachlorepoxide, hexachlorobenzene, lindane, methoxychlor, oxychlordane, polybrominated biphenyls (PBBs), PCBs, *trans*-nonachlor). The OC levels were measured by gas chromatography with electron capture detection. This methodology has been described previously.[28–30] The lower limits for detection of PCBs and other OCs in this assay are 400 parts per billion (ppb) and 200 ppb, respectively.

RESULTS

The results of the analysis are shown in the Table. None of the 5 brands contained detectable amounts of PCBs or OCs. We previously tested the mercury levels in 5 over-the-counter preparations of fish oil. None of the 5 brands contained significant amounts of mercury. No mercury (less than 6 μg/L) was detected in the Nordic Ultimate, Sundown, and Kirkland brands. The Omega Brite brand had 12 μg/L of mercury, and the CVS brand contained 10 μg/L.[16]

COMMENT

Organochlorines are a group of toxic chemicals that can be divided into OC pesticides (chlordane, dieldrin, DDT, aldrin, endrin, heptachlor, hexachlorobenzene, mirex, toxaphene) and OC nonpesticides (PCBs, PBB, polychlorinated dibenzofurans and polychlorinated dibenzodioxins). DDT and PCBs will be discussed as representatives from each category.[17]

Polychlorinated biphenyls are a family of 209 congeners with 2 linked phenyl rings and variable chlorination. PCBs are colorless and odorless chemicals that were widely used in electrical equipment such as transformers and capacitors before 1977. Of the PCBs produced in the United States before 1976, 1.2 billion pounds ended up in rivers, lakes, and ultimately the oceans, where they accumulate in wildlife. Bottom-feeding fish ingest PCBs, and the PCBs become more concentrated higher up on the food chain (0.6–20 parts per million [ppm] in edible fish high in the food chain).[18,31–33] A higher degree of chlorination correlates with an increased resistance to biodegradation. Some properties that made PCBs and other OCs so useful in industrial applications, such as stability and nonflammability, enable them to persist in the environment for long periods (environmental half-lives as long as 5 years). These toxins can still be found in older x-ray equipment, refrigerators, televisions, and fluorescent lighting fixtures.[17]

Polychlorinated biphenyls have been responsible for widespread environmental contamination affecting both animals and humans. In 1988, PCBs were linked to the death of 20 000 European harbor and gray seals, which represented 60% of the local population. The seals died after a viral outbreak of *Morbillivirus*, presumably because the PCBs diminished the seals' immune response to viral infections. Humans have also been affected. Rice oil contaminated with PCBs was the culprit in both the Yusho incident in 1968 and the Yucheng incident in 1979.[34] In 1968, approximately 1000 people were poisoned. Follow-up of a subset of children in this population showed growth retardation, movement disorders, generalized slowness, and a substantial IQ deficit (average 70). In the 1979 incident, approximately 2000 people in Taiwan were exposed to contaminated rice oil. Babies born to the exposed mothers showed a small but systematic lower IQ and higher scores for behavioral disorders.[34]

Acute high levels of PCB exposure occurred in industrial accidents before 1977, when PCBs were still manufactured. Exposed subjects experienced eye irritation, headache, fatigue, skin eruptions, nausea and vomiting, digestive disturbances, and liver dysfunction.[17] More commonly, people are chronically exposed to PCBs from the consumption of tainted fish. PCBs are readily absorbed into the body but are only slowly metabolized and excreted. Half-lives range from 1 to 460 days, depending on the level of chlorination. The liver is the primary site of metabolism where hydroxylation and conjugation occur, but metabolism is slow, and most PCBs accumulate in adipose tissue. Chronic effects include dermatologic manifestations, developmental deficits with exposure in utero, disruption of thyroid or female sex hormones, elevation of liver enzymes (overt hepatotoxicity uncommon), decreased immunity, impaired memory and learning in adults and children, and carcinogenesis.[19,27,35,36]

Polychlorinated biphenyls are complete carcinogens, acting as initiators and promoters.[19] The most susceptible tissues are liver, biliary tract, and intestines, followed by stomach, lip, and skin. PCBs pass to babies during pregnancy and breast-feeding, and studies illustrate their detrimental effects on the immune system[37] and neurodevelopment.[27,34,36,38] In a Michigan cohort, 313 women were exposed to PCBs from Lake Michigan fish. Prenatal exposure was associated with decreased IQ and intellectual impairment in children examined from birth to age 11 years.[38] In a North Carolina cohort, 880 pregnant women

were selected from the general population. PCB exposure was associated with decreased muscle tone, lower activity levels, hyporeflexia, and lower psychomotor scores in children from birth to 5 years.[38]

PCBs are present in all categories of food as well as in the environment.[18] Because of baseline environmental and nutritional exposure, humans have an average of 1.4 ppb of PCBs in their serum.[17,39,40] Because PCBs concentrate in fatty tissue, the levels can be 300 times higher in adipose tissue[39,41,42] or breast milk.[43,44] Studies on the detrimental effects of PCBs prompted regulations on the allowable levels of PCBs in food and warnings about dangerous toxins in fish. The US Food and Drug Administration (FDA) allows 0.1 to 3.0 ppm of PCBs for all foods. Recently, concern about the levels of PCBs in fish has increased. In 1984 the FDA lowered the limit to 2.0 ppm for edible fish.[18]

Organochlorine pesticides are the second type of OCs. Pesticide OCs are diphenyl aliphatics previously used to control insect vector infections. During their production, OC pesticides entered the air, water, and soil when they were sprayed on crops and forests. They bound to particles in the water, settled, and deposited in sediment. Organochlorine pesticides remain in sediment for a very long time because of their resistance to degradation (half-lives of months to years), and so they are still taken up by small organisms and fish even today. Similar to PCBs, OC pesticides concentrate over 1000-fold in fish and marine mammals. In the 1990s, DDT and its metabolites were detected in 94% of whole fish samples.[18,20]

Because of their neurotoxic properties, OC pesticides were banned in 1973. DDT is the best-known OC pesticide. It can be absorbed through the respiratory system, gastrointestinal tract, or the skin. DDT and other OC pesticides impair nerve impulse conductions. Exposure to large amounts (ie, grams) of DDT over a short time causes tremors, seizures, sweating, headaches, nausea, vomiting, and dizziness. Chronic toxicity has reproductive, developmental, neurologic, hepatic, and carcinogenic effects. The US Environmental Protection Agency determined that DDT is a probable human carcinogen. In addition, children can be exposed to DDT by eating fish or drinking breast milk contaminated with these compounds. In the United States between 1985 and 1991, the average 8.5-month-old infant consumed 4 times more DDT for each pound of body weight than the average adult. Exposure to DDT during development in children may affect the reproductive and nervous systems.

Exposure to OCs has been monitored, and regulatory limits are currently mandated. Monitoring indicates that 99.5% of the population has an average of 1.8 to 12.6 ppb of DDT in their serum from persistent nutritional and environmental exposure.[17,40] DDT and its metabolite DDE concentrate in adipose tissue and breast milk at levels of 123 to 567 ppb and 24 to 202 ppb, respectively.[41,43] DDT is found in all types of food, including fish. Fish contain 37 to 373 ppb of DDT and DDE, constituting a significant contribution to a person's daily intake. The FDA set a limit of 5 ppm of DDT for edible fish to avoid detrimental health effects.[17,18,45]

Evidence suggests that consumption of fish containing unsaturated omega-3 fatty acids, such as salmon, swordfish, trout, and mackerel, provides protection against cardiovascular disease. The consumption of 200 to 400 g of oily fish each week has been recommended. However, recommending regular fish intake for its health benefits presents potential problems, particularly in certain populations, such as children and pregnant women. In 1994, the levels of PCBs in the San Francisco Bay ranged from a low of 21 ppb to as high as 638 ppb. In the Great Lakes, PCBs and OC pesticides were 753 ppb and 633 ppb, respectively.[33] Herring from the Baltic Sea and several edible marine organisms from the Adriatic Sea were analyzed for their PCB and OC pesticide content.[31,32] The levels of PCBs and OC pesticides were high in both seas, and concentrations increased with the age of the fish.[31] Anchovy, mackerel, cod, and red mullet showed the highest OC pesticide and PCB content. Calamari, cob-fish, and mussel had intermediate concentrations, and sole, cuttle, frog-fish, scampi, and hen clam had the lowest concentrations.[32]

Although consuming fish provides health benefits, these benefits may be outweighed by the levels of toxins in fish.[6] Cold-water fish contain high levels of PCBs, OC pesticides, and mercury. Pregnant women and children are specifically urged to restrict their fish intake to prevent adverse outcomes. Some debate exists over the possibility that eating wild fish as opposed to farm-raised fish reduces exposure to toxins. Several studies have also examined the differences in toxin levels in farmed versus wild salmon, and the data have been discussed in the press.[24] Farm-raised salmon have significantly higher levels of PCBs, as well as fat and cholesterol, than wild salmon and can lead to PCB intake higher than the allowable limit.[25,26] The increased level of certain toxins in farm-raised fish presumably results from the salmon feeds, antibiotics, and chemicals, which contain concentrated amounts of PCBs and OC pesticides. Mercury, on the other hand, is found in equal concentrations in wild fish.[23] In short, neither farm-raised nor wild fish are toxin free, and neither source can be advocated.

Fish oil supplements, which provide concentrated essential omega-3 fatty acids, may be a safe alternative to fish meals. A limited number of studies, primarily done in Europe, examined the levels of PCBs and OC pesticides in fish oils. In Greece, Tyrpenou and Tsigouri[30] determined that fish oils contain 2% of the provisional intake of PCBs and other OCs for adults and 12% of the provisional level for children. These quantities are small but may be considered a long-term hazardous risk, especially for children. Similar studies from Europe also found small but detectable levels of PCBs and OCs in fish oil.[28,46] Hilbert et al[29] suggested that the procedure used to manufacture fish oil causes a moderate reduction in the levels of toxins.

The sparse evidence on the levels of PCBs, PBBs, and OC pesticides in fish oil and the current media hype over toxins in fish prompted our study on the content of PCBs, PBBs, and OC pesticides in fish oil. Our study illustrated that none of the 5 over-the-counter brands of fish oil contained detectable levels of PCBs or other OCs. We also found negligible levels of mercury in fish oil in our previous study. The lower limits of detection for PCBs, PBBs, and other OCs in this study were 400 ppb, 400 ppb, and 200 ppb, respectively. This method is less sensitive than some other methods, which can detect as low as 50 parts per trillion. However, our data and limits are sufficient to show that (1) fish oil contains at least 5 times less PCB and 25 times less DDT than the FDA daily recommended limits, and (2) fish oil contains less OC than fish high in the food chain. For example, regular consumption of fish from the Great Lakes (400 g of fish per week, with PCB

levels of 0.753 μg/g, would amount to 301 μg of PCBs per week) would expose humans to at least 70 times more PCBs than routine doses of fish oil (1.5 g/d, that is, 10.5 g/wk, with PCB levels of 0.4 μg/g, would amount to 4.2 μg of PCBs per week). A similar calculation illustrates that fish from the Great Lakes have 120 times more OC pesticides than fish oil supplements.

Fish oils provide the advantages of omega-3 fatty acids with minimal toxic risks. Our data suggest that even large amounts of fish oil can be consumed without risk of toxicity. This is particularly important because high doses of fish oil supplements are currently being used to treat hypertriglyceridemia and to augment antidepressive therapy in patients with bipolar disorder and unipolar depression.[10,11,13] Our data concerning the levels of OCs suggest that fish oil supplements may be preferable to fish consumption as a dietary guideline for the general population and as a therapeutic source of omega-3 fatty acids in patients with cardiovascular disease and depression.

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