Hypocholesterolemic Effects of Marine Oils

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By

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This circular excerpts only a little more than 15 percent of the text from the original article. Some of the long sections in the original version that are not included here are: Cholesterol and cardiovascular diseases; Hypocholesterolemic effects of polyunsaturated oils; hypocholesterolemic effects of marine oils; Hypocholesterolemic factors in marine oils; Effects of marine oil fatty acid ester fractions; Lipid imbalances of diabetes treated with marine oils; and Tissue fatty acid patterns following marine oil treatments. The entire bibliographical literature cited section with more than 200 references has been retained here. Most of these will not be mentioned in this abbreviated text.

Hypocholesterolemic Effects of Marine Oils

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INTRODUCTION

The nutritive values of fish and fish products can be greatly influenced by the chemical nature of their fats and other lipid components. In recent years the dietary effects of fish oils have attracted attention because of the numbers of reports which have described their ability to lower the blood cholesterol levels of both man and experimental animals. Although other factors may be involved, this effect of marine oils and other polyunsaturated oils appears to be largely due to their abundant supplies of polyunsaturated fatty acids. The important role which polyunsaturated oils could play in the treatments of hypercholesterolemias of man was emphasized by the original reports of Kinsell et al. (1952, 1953, 1954). In these initial studies, only a few polyunsaturated oils of plant origin were tested, but further investigations by Bronte-Stewart et al. (1956) and Malmros and Wigand (1957) soon revealed that the oils from marine animals could also be used to reduce the blood cholesterol levels of man. Hegsted et al. (1957A) also observed that various polyunsaturated oils, including sardine oil, would alleviate the induced hypercholesterolemic condition of rats. During the last decade there has been a continuing series of reports about the effectiveness of fish and fish oils as hypocholesterolemic agents. It is this property of the marine oils and specific polyunsaturated acids which will be reviewed in this chapter. Also discussed are some of the reported interrelationships between cardiovascular diseases, hypercholesterolemias, and polyunsaturated oil treatments.

THE EFFECTS OF EATING FISH

Although the relatively low blood cholesterol levels of the native Japanese have been correlated with their low intakes of fat, it is tempting to speculate that this is partially due to their high consumptions of fish products containing marine oils. However, it does not necessarily follow that hypocholesterolemic effects of polyunsaturated oils will be duplicated by dietary intakes of foodstuffs containing such oils. The blood and tissue cholesterol levels of man and experimental animals have been reported to be altered by a number of non-lipid components including the type and levels of proteins in the diet, the sources of carbohydrates, the dietary levels of nicotinic acid and pyridoxine, and by mineral imbalances. For this reason, we tested the effects of

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four different types of fish and their component oils on the hyper-cholesterolemia of rats (Peifer et al., 1962). Freeze-dried preparation of menhaden (Brevoortia tyrannus), silver salmon (Oncorhyncus kisutch), mullet (Mugil cephalus), and ocean perch (Sebastes marinus) promote significant depressions in the blood cholesterol levels of the rats, a effect which was duplicated by treatments with equivalent amounts o the oils present in these fish products (see Table 40). Furthermore both the fish and their oils promoted significant reductions in the cho-lesterol and phospholipid levels of the livers in these animals. Althoug earlier studies had suggested that essential fatty acids were necessar for mobilizing cholesterol from the liver, it was now apparent that suc an effect could also be induced by the linolenate hemologues of marin oils. It was also apparent that both "oily" and "lean" types of fish coul be used to elicit such hypocholesterolemic responses.

Miller et al. (1962) have also reported that whole sardines have a hypocholesterolemic effect in rats and that this treatment inhibited th onset of the artherosclerotic syndrome in these animals. Imaichi et al. (1963) and Harlow and Morton (1962) have commented on some pre-liminary studies with human subjects who were encouraged to eat more fish or combinations of fish and fish oils. Although the available data from these studies do not permit any final conclusions, it seems likely that increased intake of fish would prove to be a practical and palatable method of introducing the linolenate homologues of marine oils into the diet.

Unlike many fish oils, the body lipids of crustaceans, such as the shrimp, contain appreciable amounts of cholesterol dispersed in the body oils. Connor et al. (1963) have reported that high intakes of shrimp promoted the onset of a hypercholesterolemia and atherosclerosis in rabbits, a species of animals which is particularly susceptible to the effects of dietary cholesterol. However, more information will be re-quired to evaluate the effects of such "shellfish" on the blood and cardio-vascular tissues of other species, including man, who are less sus-ceptible to the effects of exogenous cholesterol. In the rat, mouse, and chicken, dietary intakes of cholesterol as high, or higher, than those present in the shrimp diets were found to be counteracted by the in-fluences of the polyunsaturated acids of fish oils. Kingsbury et al. (1961) also obtained some of their results by merely adding small amounts of cod-liver oil polyunsaturated acids to the normal diets of students; such diets would certainly have included significant amounts of cho-lesterol. Nevertheless, such observations do emphasize the need for more experimental data concerning the relative amounts of specific types of polyunsaturated acids needed to minimize the effects of cho-lesterol and/or other atherogenic factors which may be present in the diets of man and various species of experimental animals.

HYPOCHOLESTEROLEMIC RESPONSES WITH MINIMAL INTAKES OF MARINE OILS

Both clinical and experimental animal studies have suggested that the effects of the polyunsaturated oils must be related to their ability to partially correct for specific fatty acid imbalances arising in the individual. However, our present knowledge does not permit any con-clusions as to the exact amounts of oils required to reestablish and maintain normal tissue levels of cholesterol. Supplements of oils at levels of 40% or more, of the total caloric intakes have often been used in the treatments of hypercholesterolemic patients. However, Kingsbury et al. (1961) reported that less than one-quarter of this level of

TABLE 40

EFFECTS OF FISH AND THEIR COMPONENT OILS[1]

Treatments	Fish Oil in Diets, Gm./100 Gm.	Marine Oil-PUFA,[2] in Dietary Fat, %	Plasma Lipids, Mg./100 Ml and %-Change			Liver Lipids, Gm./100 Gm.	
			Mg./100 Ml.	TC %	TC/Pl	TC	TC/Pl
Tallow controls	—	—	507	—	2.2	11.3	4.2
Menhaden							
Whole fish	4.9	13	250	−51	1.3	8.5	3.1
Fish oils	4.9	13	223	−56	1.2	8.2	2.7
NL-solids	0.0	0	510	0	2.2	10.9	4.1
Silver salmon							
Whole fish	5.3	12	193	−62	1.1	8.1	2.8
Fish oil	5.3	12	162	−68	1.1	10.9	3.4
NL-solids	0.0	0	614	+20	2.3	11.7	4.6
Mullet							
Whole fish	3.8	7	359	−49	1.4	7.0	2.5
Fish oil	3.8	7	263	−48	1.3	9.2	3.3
NL-solids	0.0	0	563	+12	2.4	10.3	4.1
Ocean perch							
Whole fish	2.5	5	398	−61	1.3	8.8	2.8
Fish oils	2.5	5	190	−63	1.1	9.9	3.6
NL-solids	0.0	0	552	+9	2.2	10.3	3.7

[1] Peifer *et al.* (1962).
[2] Diets contained 15% fat, most of which was supplied as tallow.
NL-solids = residual solids after removal of total lipids; PUFA = polyunsaturated fatty acids; Pl = phospholipids; TC = total cholesterol.

arachidonate or cod-liver oil polyunsaturated acids was sufficient to reduce the blood cholesterol levels of medical students. Such changes were evident even when the subjects received 3 to 10 times as much of their fat from the animal and dairy products in their normal diets. Hypocholesterolemic responses have also been obtained when ocean perch oil accounted for less than four percent of the total fat calories in the diets of rats (Peifer et al., 1965; Peifer, 1966A). Howe and Bosshardt (1962A, B) observed that minimal intakes of marine oil polyunsaturated acids were sufficient to promote significant hypocholesterolemic responses in mice. A cod-liver oil concentrate appeared to be nearly ten times as effective as corn oil in the treatments of the hypercholesterolemias of their mice. Such observations suggest that minimal alterations in the compositions of dietary fats may be sufficient to establish normocholesterol levels in the tissues when arachidonate or marine oil polyunsaturated acids are included in the diet. The ingestion of excessive amounts of any type of polyunsaturated oil seems to be unwarranted and possibly contraindicated. The fatty acid patterns in cardiovascular tissue suggest that the integrity of tissues depends upon a proper balance of saturated, monounsaturated and polyunsaturated acids of both the linoleate and linolenate families of acids (see Table 43). There is little supporting evidence that such a balance could be achieved by excessive caloric intakes of either the linoleate or linolenate family of acids. It seems more probably that the ingestion of mixed acids from animal, plant, and fish products would supply the wide range of fatty acid homologues which are possibly required for the integrity of lipoproteins and cell wall components of vital tissues including those of the cardiovascular system.

SUMMARY

Both clinical and experimental animal studies suggest that a sustained hypercholesterolemic condition is accompanied by the onset of serious cardiovascular diseases in man and experimental animals.

Isocaloric substitution of polyunsaturated oils, including marine oils, for more saturated acids in the diets has proved to be an effective treatment for the hypercholesterolemias of man and various experimental animals.

Many different types of marine oils have been shown to have similar hypocholesterolemic activities.

Marine oils, or concentrates of their polyunsaturated acids, have often been found to be more effective hypocholesterolemic agents than oils which contain only linoleate as the polyunsaturated acid component.

The polyunsaturated acid components of marine oils appear to be primarily responsible for their abilities to lower blood and tissue cholesterol levels of hypercholesterolemic subjects.

The hypertriglyceridemia of man has also been successfully treated by dietary intakes of menhaden oil.

The relative hypocholesterolemic activities of vegetable and marine oils are not readily predictable on the basis of such criteria as their total unsaturation, total contents of polyunsaturated acids, or their relative contents of saturated and monounsaturated acids. The dietary effects of saturated fats may be largely due to their myristate component.

Minimal intakes of marine oil polyunsaturated acids have been sufficient to promote significant hypocholesterolemic responses in man

Table 43

FATTY ACID PATTERNS IN TISSUE LIPIDS AND MARINE OILS[1]

	Brain		Pit.	Testis	Liver	Heart	Plasma	Plasma Pl[5]	Marine Oils			
	Pig	Rat	Rat					Man	Menhaden	Tuna	Salmon	O. Perch
Saturated												
16:0	15	20	27	26	17	11	18	31	18	18	22	23
18:0	22	19	9	4	11	9	8	14	3	4	4	4
22:0	+	+	2	+	+	1	1	—	—	2	4	9
Monoenoic acids												
16:1	1	1	4	2	4	1	6	1	12	5	5	4
18:1	30	16	16	16	14	13	25	12	12	15	24	19
20:1	—	—	—	—	—	—	—	—	—	—	5	7
Linoleic acid family[2]												
18:2	0.5	0.8	5	6	6	13	7	26	2	1	1	2
20:4	9	14	20	20	26	33	19	4	1	2	+	+
22:5	5	4	1	15	2	5	3	2	1	1	—	—
Linolenic acid family[2]												
18:3	2	2	+	+	—	—	+	1	3	3	1	—
20:5	+	+	2	+	2	1	1	2	19	10	11	8
22:5	—	—	4	2	+	1	1	—	3	2	3	+
22:6	10	17	4	2	10	8	3	5	14	30	13	14
Other acids[3]												
	5	6	8	9	8	5	9	2	14	7	7	10

[1] Tissues from animals receiving tallow, corn oil, or mixtures of corn oil and tallow. Normocholesterolemic animals were source of tissue lipids and none of the animals were receiving linolenate homologues as dietary supplements.
[2] Linoleic acid family, the essential fatty acids, have their first two double bonds at the 6,9 positions from the terminal methyl end of the fatty acids. The linolenate homologues have their first three double bonds at the 3,6,9 positions from the terminal methyl end of the acids.
[3] Other acids not indicated in the above table are 14:0, 15:0, 20:3, etc. These represent minor components in most of the tissues and marine oils.
[4] Pit = pituitary gland.
[5] Pl = phospholipid.

and experimental animals. This has been true even when 3 to 25 times as much saturated fat was included in the diet.

Increased metabolic requirements caused by thyrotoxicosis can be partially alleviated by the linolenate homologues of marine oils and by oils rich in linoleate.

The hypocholesterolemic effects of marine oils have been observed in diabetic men and women and in hypothyroid animals.

Significantly lower levels of cholesterol have been found in the liver and other tissues of experimental animals treated with marine oils.

The high levels of circulating polyunsaturated acids which result from treatments with marine and vegetable oils appear to have little influence on the brain and reproductive tissues of adult animals.

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