ANTIATHEROGENIC ACTION OF CORN OIL IN EXPERIMENTAL ATHEROSCLEROSIS

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The attention of many research workers seeking ways of preventing and treating atherosclerosis has been drawn in recent years to the study of the effect of polyunsaturated fatty acids (PUFA) of the ω-3 series, which are found predominantly in fish oil fat (16-19%), but which are almost completely absent from vegetable oils [5, 13]. Increased consumption of these acids has an antiatherogenic action, whose mechanism is associated mainly with the effect of specific prostaglandins [5]. Meanwhile, another mechanism of action of PUFA is associated with their liquefying action on biomembranes and lipid regions of lipoproteins (LP), restoring many metabolic processes to normal [3, 12]. This effect and, in particular, a fall in the cholesterol level in apoB-containing LP and in the aorta has also been observed under the influence of PUFA of the ω-6 series (with the first double bond at the sixth, not the third carbon atom) in the composition of various vegetable oils [1, 4-6, 9, 10, 13]. Meanwhile, the experiments in these studies were set up in such a way that it was not the therapeutic, but rather the prophylactic action of oils with ω-6 PUFA that was investigated, for they were administered to the animal while at the same time it was fed on cholesterol. Besides, in most studies only the hypocholesterolemic effect of these oils was examined, without any attempt to assess their effect on the state of the aorta. At the same time, however, it is this effect, and not simply a fall in the cholesterol level, that is the final aim of antiatherogenic therapy.

In the investigation described below the effect of a diet containing corn oil on regression of experimental atherosclerosis was studied in rabbits.

EXPERIMENTAL METHOD

Experiments were carried out on 20 Chinchilla rabbits. For 12 weeks the rabbits were given cholesterol (0.25 g/kg), after which they were kept for 4 weeks on a standard diet. Before the beginning of treatment the animals were divided into two equivalent groups, each of which included the same number of animals with a very high (800-1000 mg/dl), average (700-550 mg/dl), and relatively low (350-500 mg/dl) plasma cholesterol level. One group received 1.5-2 ml/kg corn oil, with the usual fatty acid composition [5, 13], for 30 days: the predominant acids were linoleic (65.4%) and oleic (23.2%), the content of linolenic acid ($C_{18:3}$) was 0.2%.* Blood for testing was taken at intervals of 10 days, and concentrations of cholesterol, triglycerides and cholesterol of high-density LP (HDL) were determined on a "Centrifichem-400" automatic analyzer. After sacrifice of the animals the degree of involvement of the aorta was estimated [14]. The results were subjected to statistical analysis by Student's test.

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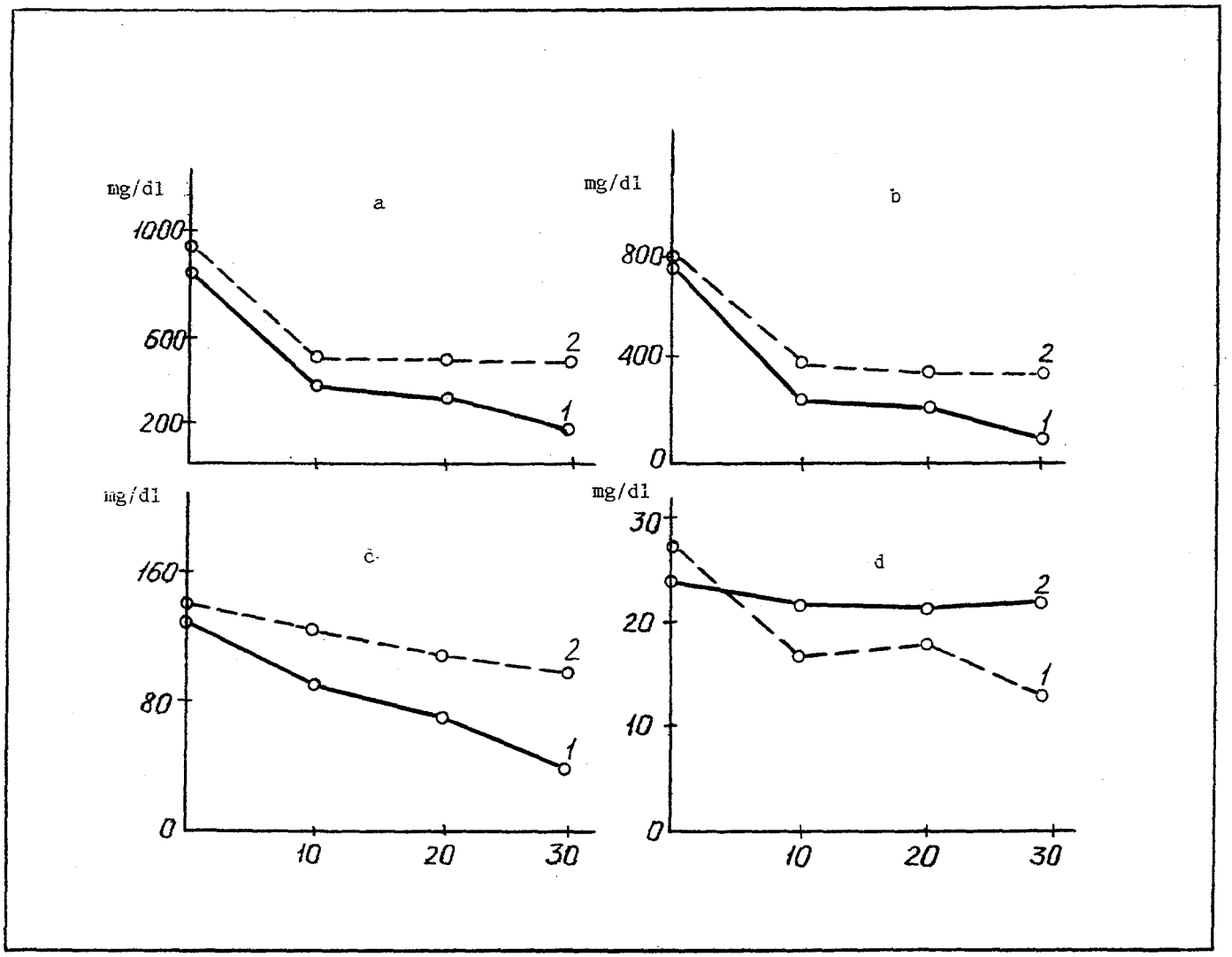

Fig. 1. Concentration of blood plasma lipids of rabbits receiving corn oil (1) and existing under conditions of spontaneous regression (2). Abscissa, time of experiment (in days); ordinate, concentration (in mg/dl); a) total cholesterol, b) cholesterol of apoB-containing lipoproteins, c) triglycerides; d) HDL cholesterol.

EXPERIMENTAL RESULTS

The fall in the plasma cholesterol concentration of the rabbits during feeding on corn oil and during spontaneous regression is demonstrated in Fig. 1a. Clearly, although the fall in its plasma concentration which began after cessation of cholesterol feeding gradually became slower at the 300-400 mg/dl level, on the addition of corn oil to the diet, cholesterol excretion took place more rapidly, and by the end of the experiment its plasma level was only one-third of that in the "control" and, judging by the nature of the curve, it continued to fall even later. Fractionation of lipoproteins by sedimentation followed by assay of individual cholesterol fractions showed that this decrease was due to a change in the level of apoB-containing lipoproteins (Fig. 1b). A similar tendency also was observed with the degree of lowering of the plasma triglyceride level (Fig. 1c) – it also fell more rapidly during feeding with corn oil. This fact deserves special attention for triglycerides – mainly esterified with linoleic acid – constitute 90-95% of the total in corn oil, just as in other vegetable oils. Contrary to expectation, therefore, the observed fall in their level points to predominance of an activating effect of corn oil on the elimination of very low density LP from the plasma, possibly by activation of lipolysis. The total reduction of the fraction of apoBcontaining LP observed under these circumstances may be connected with the fact that linoleic acid prevents the cholesterol-induced depression of LDL-receptor activity in the liver [12] – these recent results also explain the data reported previously showing enhance-

TABLE 1. Aortic Lesions in Rabbits Receiving Corn Oil

Group of animals	Number	Percentage involvement of the aorta
Rabbits receiving corn oil	10	4,8±0,5
Rabbits during spontaneous regression	10	52,9±19,9

ment of the "cholesterol-excretory function" [1] or the fat-adsorbing capacity [10] of the liver under the influence of corn oil. One result of this rapid uptake by the liver may probably be the absence of an increase in the HDL cholesterol level (Fig. 1d).

The most important results were obtained during morphological investigation of the aorta. As Table 1 shows, in rabbits not receiving treatment the degree of atherosclerotic damage to the aorta at the end of the experiment was 52.9%, whereas in rabbits receiving corn oil for 30 days it was only 4.8%.

Thus both the hypocholesterolemic and the antiatherosclerotic effects of corn oil were observed in rabbits with experimental atherosclerosis. Unlike in the other existing studies, in this case it was not the prophylactic, but the therapeutic action of the oil that was demonstrated.

The positive action of corn oil was observed by other investigators [4] in patients with hypercholesterolemia, who explained its effect on LDL metabolism, by contrast with phospholipids, which act through an increase in HDL cholesterol [4]. Meanwhile, in another study [10], the effect of corn oil different depending on its dose, and the need for further research to determine the optimal amounts of PUFA was emphasized. Some workers [5] used a diet containing corn oil as the control for fish fat, and observed a ratio of PUFA ω-6/ω-3 in lipids of the intestinal mucosa and a tendency for the formation of prostaglandin PGE_2 to fall. The action of corn oil and olive oil was studied in rabbits with a specially selected equal plasma cholesterol level, and it has been shown that the antiatherogenic effect of corn oil, i.e., its effect on the fall in the cholesterol content in the aorta, is manifested even in the absence of a hypocholesterolemic effect [9]. The fact that the antiatherogenic action exceeds the hypocholesterolemic action was demonstrated previously in pigs [6] and monkeys [14]. One possible explanation of this finding could be the change observed [13] in the composition and properties of HDL under the influence of a diet containing PUFA. Although in this study, in which other oils also were used, the maximal liquefying effect was achieved through the use of olive oil, which is rich in oleic acid (79%), corn oil also had a beneficial action on the structure of HDL, lowering the percentages of free and esterified cholesterol in them and increasing the proportion of protein [13].

Meanwhile, in a series of investigations [7, 8] several natural oils, including corn oil, were used to obtain experimental atherosclerosis without cholesterol administration – through the prolonged addition of 14% of oil to the rabbits' diet. Although butter had the maximal atherogenic effect in this case, in the group of animals receiving corn oil a mild degree of hypercholesterolemia also was observed, although admittedly with minimal lipoidosis of the aorta [7]. These results, together with those mentioned above pointing to some degree of fatty infiltration of the liver and elevation of its cholesterol concentration in rats, receiving very large doses of corn oil [10], and also reports of mild inhibition of apoprotein A biosynthesis under the influence of PUFA [11], show that the question of the antiatherogenic use of oils containing PUFA requires special study from the modern point of view, in the context of identification of the optimal dosage and mechanism of action.

Taking these factors into consideration, vegetable oils containing ω-6 PUFA and, in particular, corn oil, can be regarded as the potential basis for the development of accessible antiatherogenic or, at least, prophylactic preparations, as the results of the present investigation indicate.

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