HYPOLIPIDEMIC EFFECT OF PHENOLIC ANTIOXIDANTS

Yu. K. Vasilenko, L. I. Lisevitskaya, and L. M. Frolova

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Recognition of the essential role of lipid peroxidation in the pathogenesis of atherosclerosis has aroused considerable interest in the study of the antiatherogenic action of antioxidants and in the search for antioxidants with marked hypolipidemic properties [2-6, 8, 9, 11, 12].

This paper describes a study of the effect of antioxidants — ionol, and the lithium, potassium, and sodium salts of phenosan (ionol is a methyldi-tert-butylphenol in its structure, phenosan is di-tert-butylhydroxyphenylpropionic acid), obtained at the Institute of Chemical Physics, Academy of Sciences of the USSR and generously supplied by Professor E. B. Burlakova, on lipid parameters in noninbred albino rats with experimental hyperlipidemia.

EXPERIMENTAL METHOD

Hyperlipidemia was induced in the animals by the method in [13] in our modification by peroral administration of 2 ml of a mixture of alcoholic and oily solutions of vitamin D_2, in a dose of 80,000 Units/100 g body weight, and cholesterol in a dose of 200 mg/kg daily for 4 days. The substances for testing were given perorally together with cholesterol and vitamin D_2 in a dose of 25 mg/kg. To assess the hypolipidemic activity of the antioxidants their effect was compared with the action of the official antiatherosclerotic drugs polysponin, miscleron, and nicotinic acid in a dose of 25 mg/kg under the same experimental conditions.

TABLE 1. Effect of Antioxidants on Parameters of Lipid Metabolism (in mg%) in Albino Rats with Hyperlipidemia (M ± m)

Experimental conditions	Number of animals	Blood cholesterol	Blood β-lipoproteins	Blood triglycerides	Cholesterol in aorta
Intact animals	13	63,0±5,8	89,0±12,8	54,0±7,9	165,0±3,8
Control	11	172,3±23,1	369,0±51,6	147,0±16,0	276,0±14,6
Ionol	5	127,0±9,3	167,0±32,0**	108,0±7,8****	300,0±19,0
Lithium phenosan	6	148,0±6,0	178,0±27,8**	96,0±20,5****	370,0±24,0**
Potassium phenosan	10	102,0±11,5***	170,0±20,0**	107,0±10,7****	412,0±11,0*
Control	12	126,0±3,8	253,0±23,1	174,0±17,6	250,0±9,0
Sodium phenosan	15	79,0±3,7*	120,0±8,9*	105,0±18,2****	195,0±3,0*
Miscleron	15	66,0±4,5*	138,0±11,9*	71,0±9,6*	203,0±7,6*
Control	15	144,6±2,0	271,0±18,5	163,0±11,7	276,0±14,6
Nicotinic acid	15	88,4±4,0*	122,0±8,7*	54,0±7,8*	135,0±7,0*
Polysponin	6	90,0±5,7*	316,0±42,0	196,0±21,7	205,0±3,0*

Legend. *P < 0.001, **P < 0.01, ***P < 0.02, ****P < 0.05 compared with control.

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Results obtained on animals with experimental hyperlipidemia not subjected to other factors served as the control. The lipid parameters were studied first in intact animals.

The animals were decapitated on the 5th day of the experiment. Total cholesterol in the blood was determined by Ikles' method, triglycerides by the method of Carlson and Ignatovskaya, and β-lipoproteins by Burstein's method [7]. Total cholesterol in tissues of the aorta was determined by the Liebermann–Burchardt test in a chloroform–methanol extract by the method in [10]. The experimental results were subjected to statistical analysis [1].

EXPERIMENTAL RESULTS

It will be clear from Table 1 that both the official antiatherosclerotic drugs and the antioxidants had an appreciable hypolipidemic action on the experimental animals. Of the official preparations the most effective were nicotinic acid and miscleron. Among the antioxidants, the strongest hypocholesterolemic effect, equal to that of nicotinic acid, was exhibited by potassium and sodium phenosans. Sodium and lithium phenosans had the strongest hypotriglyceridemic action, but it was weaker than the effect of nicotinic acid and miscleron. The hypo-β-lipoproteinemic effect of the antioxidants and of miscleron and nicotinic acid was at about the same level. A different picture was observed in the aorta. Only sodium phenosan reduced the cholesterol content in the aorta. This reduction was more marked than in the experiments with miscleron but less marked than in those with nicotinic acid.

The results of these experiments thus demonstrate that the most promising antioxidant, capable of significantly lowering lipid levels both in the blood and in tissues of the aorta in animals with experimental hyperlipidemia, is sodium phenosan. Its activity is comparable with that of the most effective official antiatherosclerotic agents.

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