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Received June 17, 1954. P.S.E.B.M., 1954, v86.

## Effect of Dihydrocholesterol and Soy Bean Sterols on Elevated Tissue Cholesterol. (21173)

W. T. BEHER AND W. L. ANTHONY. (Introduced by O. H. Gaebler.)
*From the Edsel B. Ford Institute for Medical Research, Henry Ford Hospital, Detroit, Mich.*

Dihydrocholesterol and soy bean sterols have attracted attention because they prevent accumulation of cholesterol in blood and tissues of animals receiving high cholesterol diets. While the exact mechanism of action remains undetermined, it appears that the principal effect of these substances is to diminish absorption of ingested cholesterol(1,2). It seemed important to determine whether mobilization of cholesterol already deposited in tissues can be influenced at all by adding soy bean sterols or dihydrocholesterol to the diet. Rabbits and mice in which tissue cholesterol had been elevated were therefore maintained on diets shown to be effective in preventing accumulation of cholesterol(3), and compared at intervals with animals maintained on control diets.

*Experimental.* Webster strain female mice weighing 20 g were used. They were fed *ad lib.* a fat-free diet, the composition of which has been covered in detail(3). Their liver cholesterol concentrations were elevated by supplementing this diet with 1% cholesterol and 0.5% cholic acid. After a 2-week period, the animals were divided into 2 groups. One group, the controls, received the unsupplemented diet *ad lib.*; while the other group received the same diet with the addition of 2% dihydrocholesterol* and 0.5% cholic acid, in place of equal percentages of alphacel. This diet has been shown to be efficient in preventing cholesterol accumulation(3) in the mouse. At definite intervals mice were sacrificed from both groups and their liver cholesterol levels determined by a method described previously (3).

In the second experiment, male albino rabbits weighing about 2,000 g were employed. Their plasma cholesterol levels were elevated by feeding *ad lib.*, for a 2-week period, a diet consisting of ground Rockland rabbit chow supplemented with 1% cholesterol and 8% corn oil. The animals were divided into 2 groups. The control group received, *ad lib.*, ground Rockland rabbit chow supplemented with 8% corn oil. The experimental animals received ground Rockland rabbit chow supplemented with 4% soy bean sterols and 8% corn oil. The latter diet when tested proved to be efficient in preventing absorption of dietary cholesterol. At definite intervals blood samples were obtained from both groups and the plasmas analyzed for total cholesterol according to the method of Sperry and Webb (4). The mice in both groups consumed 3.5 $\pm$ 0.5 g of food per day; the rabbits 150 $\pm$ 25 g per day.

*Results.* Table I gives the results of the experiments designed to show whether dihydrocholesterol is effective in mobilizing accumulated mouse liver cholesterol. It is apparent that dihydrocholesterol did not cause any acceleration of cholesterol mobilization.

* Generously supplied by the Schering Corporation, Bloomfield, N. J.

TABLE I. Mobilization of Accumulated Mouse Liver Cholesterol by Dihydrocholesterol.

| No. of mice | Weeks on diet | Additions to cholesterol-free diet | | Total cholesterol remaining in liver | |
|---|---|---|---|---|---|
| | | Cholic acid | Dihydro-cholesterol | Per organ | Per body wt |
| | | % | % | mg | mg |
| 7 | 1 | — | — | 28.1 ± 8.0* | 1.3 ± .32* |
| 8 | 2 | — | — | 30.6 ± 6.1 | 1.5 ± .41 |
| 8 | 3 | — | — | 13.0 ± 3.9 | .63 ± .13 |
| 7 | 4 | — | — | 12.0 ± 4.2 | .61 ± .18 |
| 7 | 1 | .5 | 2.5 | 30.7 ± 7.3 | 1.6 ± .62 |
| 7 | 2 | .5 | 2.5 | 31.9 ± 7.1 | 1.8 ± .61 |
| 7 | 3 | .5 | 2.5 | 20.1 ± 5.1 | 1.04 ± .47 |
| 7 | 4 | .5 | 2.5 | 12.0 ± 4.5 | .60 ± .23 |

* Stand. dev.

Fig. 1 presents the data obtained in the experiments dealing with the rate of fall in elevated total plasma cholesterol in rabbits treated with dietary soy bean sterols and in control animals. Each curve represents the average total cholesterols of 7 animals at various time intervals. Inasmuch as the 2 curves are parallel throughout their entire range, it is clear that in this species the soy bean sterols do not accelerate the rate of decrease of plasma cholesterol levels.

*Discussion.* The lack of correlation between the results obtained in the prevention of cholesterol accumulation by the use of dietary soy bean sterols or dihydrocholesterol and the mobilization of accumulated tissue cholesterol is of interest. It has been demonstrated that these substances act by preventing the absorption of cholesterol from the intestinal lumen(1,2). Therefore, accumulated cholesterol in these species cannot be mobilized into the intestinal lumen as free cholesterol, or the rate of mobilization would be increased due to the prevention of recycling. It has been shown recently(5) that in the rat accumulated cholesterol is eliminated to a large extent as bile acid. If we assume these results apply in the mouse and rabbit, a possible explanation for our observations is obtained.

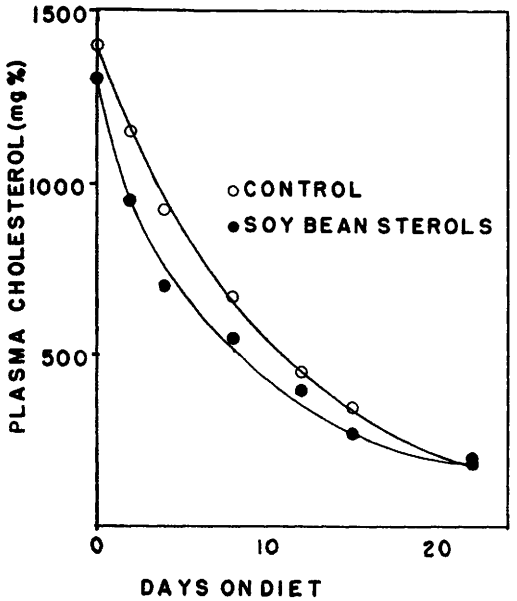


FIG. 1. Rate of decrease of elevated rabbit plasma cholesterol in control animals and animals fed a basal diet supplemented with 4% soy bean sterols.

*Summary.* 1. Feeding a diet containing dihydrocholesterol to mice with elevated liver cholesterol did not result in an increased rate of liver cholesterol mobilization. 2. Rabbits with elevated blood cholesterol levels were treated with dietary soy bean sterols. The rate of fall of plasma cholesterol was not increased above that observed in a control group.

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Received May 19, 1954. P.S.E.B.M., 1954, v86.