Effect of Taurine, Glycine and \( \beta \)-Sitosterols on Serum and Tissue Cholesterol in the Rat and Rabbit

By Roy G. Herrmann, Ph.D.

Rats and rabbits were fed a hypercholesteremic diet until elevated serum cholesterol levels were observed in all animals. The animals were then divided into groups, one group remaining on the original diet and the others receiving the same hypercholesteremic diet fortified with either taurine, glycine, or \( \beta \)-sitosterols. In the rat, 4 per cent taurine in the diet significantly decreased the serum, liver, and aorta cholesterol concentration, but glycine was without significant effect. In the rabbit, 2 per cent \( \beta \)-sitosterol in the diet significantly reduced the serum, liver, and aorta cholesterol, while taurine or glycine produced no significant effect. Neither taurine, glycine, nor \( \beta \)-sitosterols produced any signs of toxicity.

CHOLESTEROL is eliminated mainly via biliary excretion in the form of bile acids.\(^1\)\(^{-3}\) Normally these acids are present in bile almost entirely in the conjugated form.\(^4\) In the rat conjugation occurs mainly with taurine, in the rabbit with glycine, and in man and monkey with either taurine or glycine.\(^4\)\(^,\)\(^5\) Feeding experiments\(^6\)\(^,\)\(^7\) have indicated that a diet deficient in sulfur containing amino acids and high in cholesterol produces a pronounced hypercholesteremia in the Cebus monkey, rat, and mouse. By supplementing this diet with cystine or methionine the hypercholesteremia was significantly reduced. Since it has been shown that cystine may be metabolized to taurine in the mammalian body\(^6\) and administered taurine can be utilized for bile acid conjugation,\(^9\) it was therefore of interest to test the effect of taurine on the serum and tissue cholesterol concentrations of cholesterol-fed animals. Glycine and \( \beta \)-sitosterols (obtained from Tall Oil) also were included in this study.

METHODS

Female rabbits (about 1.5 Kg.) and female albino rats (about 200 Gm.) were employed for this study. All animals were individually caged, and food consumption was measured. The rabbit diet consisted of laboratory rabbit pellets impregnated with the desired supplement. The supplement was dissolved in either chloroform or water, as required, and sprayed onto the food pellets with thorough mixing. The pellets were then air dried before use. The rat diet was prepared by grinding Purina laboratory chow together with the proper supplement to a relatively fine powder and then thoroughly mixing in a mechanical mixer.

The cholesterol, taurine, and glycine were obtained from Distillation Products Industries, a division of Eastman Kodak, and were of Eastman grade White Label purity; the cholic acid was obtained from Nutritional Biochemicals Corporation. The \( \beta \)-sitosterols preparation was obtained from our biochemical division; it contained not less than 95 per cent total sterol (sitosterol + dihydrositosterol).

At weekly intervals all animals were weighed and blood samples were taken—by heart puncture, under ether anesthesia, from the rat and from the marginal ear vein of the rabbit. At the end of the experiment all animals were killed and their tissues examined both grossly and microscopically for any pathological abnormality. The tissues examined included the heart, lungs, liver, pancreas, spleen, intestine, kidneys, adrenals, thymus, and thyroid. A small section of the liver and the entire aorta, cleaned from adhering fat and connective tissue, were quickly frozen between two blocks of dry ice and stored in the freezer, up to two weeks, until used for tissue cholesterol analysis. Cholesterol was determined by the method described previously.\(^10\)

RESULTS

Rat Experiment. Twenty-nine rats were divided into 3 groups. 12 rats in each of groups 1 and 2, and 5 rats in group 3. All animals were fed, ad libitum, diet 1 which was
TAURINE, GLYCINE, β-SITOSTEROLS

**TABLE 1.—The Effect of Taurine and Glycine on Serum Cholesterol, Weight Gain, and Food Consumption in the Rat (Group 1, Control; Group 2, Taurine; Group 3, Glycine)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Weeks on diet</th>
<th>Serum cholesterol (mg. %)</th>
<th>Av. wt. gain (Gm./rat)</th>
<th>Food consumption (Gm./day/Kg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1—3</td>
<td>4—7</td>
<td>8—11</td>
</tr>
<tr>
<td>1</td>
<td>72±4</td>
<td>249±40</td>
<td>312±41</td>
<td>319±28</td>
</tr>
<tr>
<td>2</td>
<td>70±2</td>
<td>237±40</td>
<td>202±21</td>
<td>180±21</td>
</tr>
<tr>
<td>3</td>
<td>74±4</td>
<td>307±61</td>
<td>293±52</td>
<td>279±45</td>
</tr>
</tbody>
</table>

**TABLE 2.—The Effect of Taurine on Liver and Aorta Cholesterol in the Rat**

<table>
<thead>
<tr>
<th>Group</th>
<th>Cholesterol concentration (mg./100 Gm. wet tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver</td>
</tr>
<tr>
<td>1 (no taurine)</td>
<td>6400 ± 780</td>
</tr>
<tr>
<td>2 (with taurine)</td>
<td>2260 ± 426</td>
</tr>
<tr>
<td>Normal rats</td>
<td>225 ± 9</td>
</tr>
</tbody>
</table>

designed to produce hypercholesteremia and was of the following composition: 97 per cent Purina laboratory chow, 2 per cent cholesterol, and 1 per cent cholic acid. After three weeks on this diet all rats had elevated serum cholesterol levels and a new dietary regimen was started as follows: group 1 remained on diet 1; group 2 received diet 2 which was of the same composition as diet 1 but contained 4 per cent taurine added at the expense of the Purina laboratory chow; group 3 received diet 3 which contained 4 per cent glycine in place of taurine. The experiment was terminated eight weeks later and the animals were killed for tissue cholesterol analysis and pathologic examinations.

The data obtained (table 1) clearly indicate that taurine (group 2) produced a significant lowering, about 50 per cent, of serum cholesterol as compared to the controls (group 1). Furthermore, the liver and aorta cholesterol concentration of group 2 was significantly lower than that of group 1 (table 2). The results obtained were not influenced by the amount of cholesterol consumed, since the food consumption of the 3 groups was not significantly different (table 1). Glycine (group 3) produced a slight but not significant decrease in serum cholesterol as compared to the controls.

Both gross and microscopic examination of the tissues showed no evidence of toxicity due to either taurine or glycine feeding. This was indicated indirectly by the comparable weight gain of the 3 groups (table 1).

**Rabbit Experiment.** Twenty-eight rabbits were fed ad libitum diet 4, consisting of 96 per cent rabbit pellets, 1 per cent cholesterol, and 3 per cent cottonseed oil. After 4 weeks on this diet the rabbits were divided into 4 groups of 7 animals each, and a new dietary regimen was started as follows: Group 1 remained on diet 4; group 2 received diet 5 which contained 2 per cent taurine added at the expense of the rabbit pellets; group 3 received diet 6 containing 2 per cent glycine in place of taurine; group 4 received diet 7 containing 2 per cent β-sitosterols in place of the taurine. The experiment was terminated nine weeks later and the animals were killed for tissue cholesterol determination and pathologic examination.

The serum cholesterol response in rabbits to cholesterol feeding was found to vary considerably, not only from one rabbit to another but also from one week to the next in the same animal. This resulted in rather large standard errors in most instances. Nevertheless, the results indicate that neither taurine nor glycine had any significant effect on serum or tissue cholesterol concentration (table 3). On the other hand, β-sitosterols (group 4) produced a lowering of serum cholesterol and also decreased the cholesterol concentration of both aorta and liver (table 4) as compared to the controls (group 1). This effect was not attributable to a decrease in food consumption, as shown in table 3. This is in agreement with the findings of others.
TABLE 3.—The Effect of Taurine, Glycine and β-Sitosterols on Serum Cholesterol, Weight Gain, and Food Consumption in the Rabbit (Group 1, Control; Group 2, Taurine; Group 3, Glycine; Group 4, β-Sitosterols)

<table>
<thead>
<tr>
<th>Group</th>
<th>Weeks on diet</th>
<th>Serum cholesterol (mg. %)</th>
<th>Av. wt. gain (Gm./rabbit)</th>
<th>Food consumption (Gm./day/Kg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1—4</td>
<td>5—8</td>
<td>9—13</td>
</tr>
<tr>
<td></td>
<td>Serum cholesterol (mg. %)</td>
<td>Av. wt. gain (Gm./rabbit)</td>
<td>Food consumption (Gm./day/Kg.)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>47±4</td>
<td>186±00</td>
<td>563</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>52±3</td>
<td>278±108</td>
<td>583</td>
<td>52</td>
</tr>
<tr>
<td>3</td>
<td>55±5</td>
<td>204±79</td>
<td>428</td>
<td>49</td>
</tr>
<tr>
<td>4</td>
<td>49±5</td>
<td>213±57</td>
<td>438</td>
<td>55</td>
</tr>
</tbody>
</table>

Some difference in weight gain was observed (table 3), with group 1 gaining the most and group 4 the least. The weight gain did not correlate with toxicity findings; no gross nor microscopic abnormalities were observed in any of the tissues studied other than those obviously due to the high fat, high cholesterol diet.

DISCUSSION

The results presented clearly show that taurine in the rat, and β-sitosterols in the rabbit, lowered serum and tissue cholesterol levels of the hypercholesteremic animal. Furthermore, none of the diet supplements investigated produced any signs of toxicity.

The lack of cholesterol-lowering effect of either taurine or glycine in the rabbit was unexpected. If taurine promoted cholic acid conjugation in the rat and thereby indirectly enhanced cholesterol elimination, one would expect glycine to produce a similar effect in the rabbit. Furthermore, if it is assumed that cholesterol esterase is involved in cholesterol absorption, a decrease in the bile of free cholic acid could be expected to decrease cholesterol absorption since it has been found that free cholic acid, and not conjugated cholic acid, is primarily required for cholesterol esterase activity.14 If the effect of taurine in the rat was due to some mechanism other than cholic acid conjugation, it might be expected to produce a similar action in the rabbit. Further studies are required to elucidate the mechanism of taurine action.

SUMMARY

Taurine significantly decreased the serum and tissue cholesterol levels of the hypercholesteremic rat. Glycine was without any significant effect. β-Sitosterols significantly decreased the serum and tissue cholesterol levels in the hypercholesteremic rabbit while glycine and taurine were without effect.

No signs of toxicity were observed, both grossly and microscopically, due to the feeding of taurine, glycine or β-sitosterols.

ACKNOWLEDGMENT

The author wishes to express his thanks and appreciation to Dr. P. N. Harris of our Laboratory for the pathological studies, and Mr. R. H. Tust for technical assistance.
TAURINE, GLYCINE, β-SITOSTEROLS

SUMARIO IN INTERLINGUA

Taurina reduceva significativamente le nivellos de cholesterol del sero e del histos in rattos con hypercholesterolemia. Glycina esseva sin effecto significative in iste respecto. β-Sitosteroles reduceva significativamente le nivellos de cholesterol del sero e del histos in conilios con hypercholesterolemia. Glycina e taurina esseva sin effecto in iste respecto.

Esseva observate nulle signos macroscopic o microscopic de un toxicitate resultante del administration de taurina, glycina, o β-sitosteroles.

REFERENCES
Effect of Taurine, Glycine and β-Sitosterols on Serum and Tissue Cholesterol in the Rat and Rabbit
ROY G. HERRMANN

Circ Res. 1959;7:224-227
doi: 10.1161/01.RES.7.2.224

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1959 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/7/2/224

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/