Antilipemic Activity of an Extract of Hog Gastric Mucosa

By Aurelio Cantone, M.D., Vincenzo Rulli, M.D., and Baldo Rossi, M.D.

In recent years numerous studies have been made on the clearing effect exerted by heparin on hyperlipemic plasma, specially in connection with the problem of atherogenesis. The present paper deals with investigations, carried out on both animals and men, concerning the hypocholesteremic, plasma-clearing, and lipotropic effects, as well as the inhibitory action on the electrocardiographic changes associated with alimentary hyperlipemia, exerted by orally active extracts of gastric juice and hog gastric mucosa.

Following Hahn's observation that heparin administered parenterally exerts a clearing effect on lipemic plasma, Korn and Anfinson demonstrated that this effect is due to the action of a lipase, called lipoprotein lipase, because it causes hydrolysis of the triglycerides bound to beta-lipoproteins and chylomicrons. Korn stated that the lipoprotein lipase is a mucoprotein which probably contains a polysaccharide component similar to that of heparin. In all likelihood administered heparin has the function of activating this lipolytic ferment present in the tissues and of releasing it into the blood stream.

In addition to the clearing effect exerted by heparin through enzymic mechanisms, other clearing effects of a nonenzymic nature have been reported. These can be produced, though indirectly, by bacterial polysaccharides and probably also by polysaccharide derivatives existing in the gastric mucosa. In the course of a series of researches on the properties of a mucin compound obtained from the gastric juice of normal men, some of us found that in the rabbit the oral administration of this compound is followed by a mild and fleeting but significant increase of the plasma-clearing action, determined in vitro on the plasma-lipemic substrate system. The oral administration of this mucin compound to rabbits rendered hyperlipemic by the intravenous injection of an emulsion of vegetable oil (Ediol Schenley) produces a decrease of the optical density of the plasma. In addition, this compound has a protective effect against fatty liver of alimentary origin in rats.

Subsequently a fraction was precipitated from the gastric juice with cetyltrimethylammonium bromide (Schuchardt); this fraction has the same properties as the crude mucin compound (fig. 1). The fact that it forms a precipitate with the quaternary ammonium derivative used and stains metachromatically with toluidine blue suggests that the material contains an acid aminopolysaccharide.

A physically homogeneous substance was isolated from hog gastric mucosa which is probably a nonsulfurated acid aminopolysaccharide, because of its high hexuronic acid and hexosamine content and the absence of sulfur. This substance has an average molecular weight of about 5,000, shows a marked anodic mobility, is precipitated by cetyltrimethylammonium bromide, and stains metachromatically with toluidine blue. When administered by mouth, it exerts an in vivo clearing effect in rabbits rendered hyperlipemic by injecting a lipidic emulsion (fig. 2) and a lipotropic action in fatty liver of dietary origin in rats. Furthermore, experiments involving prolonged treatment with this substance show that it has an hypocholesteremic effect in rabbits fed a diet rich in cholesterol (table 1).

A crude extract of hog gastric mucosa with a 10 per cent aminopolysaccharide content showed an antilipemic action (cholesterol, fatty acids) in a group of elderly persons. Other authors also reported that this extract exerts an hypocholesteremic effect in...
TABLE 1.—Effect of the Oral Administration of the Hog Gastric Mucin Extract (5 mg./Kg./Day) in Hyperlipemic Rabbits

<table>
<thead>
<tr>
<th></th>
<th>No. of rabbits</th>
<th>Controls</th>
<th>Mean value ±S.E.</th>
<th>Treated with gastric mucin extract</th>
<th>Mean value ±S.E.</th>
<th>t</th>
<th>N</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes of total fatty acids</td>
<td>6</td>
<td>395.3 ±11.7</td>
<td>6</td>
<td>290.7 ±12.4</td>
<td>6.07</td>
<td>10</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Changes of total cholesterol</td>
<td>6</td>
<td>327.4 ±8.7</td>
<td>6</td>
<td>246.7 ±9.1</td>
<td>6.38</td>
<td>10</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Changes of esterified cholesterol</td>
<td>6</td>
<td>241.6 ±14.9</td>
<td>6</td>
<td>162.5 ±8.4</td>
<td>4.85</td>
<td>10</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&amp;/α ratio</td>
<td>6</td>
<td>6.38 ±0.57</td>
<td>6</td>
<td>3.99 ±0.32</td>
<td>3.66</td>
<td>10</td>
<td>0.01&gt;p&gt;0.001</td>
<td></td>
</tr>
<tr>
<td>Total lipids (aorta)</td>
<td>5</td>
<td>8.26 ±0.68</td>
<td>5</td>
<td>4.60 ±0.31</td>
<td>4.41</td>
<td>8</td>
<td>0.01&gt;p&gt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

*The values of the changes of total fatty acids, and of total and esterified cholesterol are in mg./100 ml. of plasma. The mean values of total lipids of the thoracic aorta are in mg./10 Gm. of dry thoracic aorta.

t=t of Student. N=number of degrees of freedom. P=significance. S.E.=standard error.

Fig. 1 Left. Mean values and standard error of the optical density (Beckman DU spectrophotometer: λ = 540 mp) of the plasma of rabbits treated with 0.5 ml./Kg. of lipidic emulsion intravenously (o—o) and of the plasma of rabbits treated with 0.5 ml./Kg. of lipidic emulsion intravenously as well as with 5 mg./Kg. by mouth of the fraction precipitated with cetrimethylammonium bromide from the gastric juice mucine extract (*—*). This fraction was given 15 minutes after the lipidic emulsion.

Fig. 2 Right. Mean values and standard error of the optical density (Beckman DU spectrophotometer: λ = 540 mp) of the plasma of rabbits treated with 0.5 ml./Kg. of lipidic emulsion intravenously (o—o) and of the plasma of rabbits treated with 0.5 ml./Kg. of lipidic emulsion intravenously as well as with 3.75 mg./Kg. by mouth of the acid amino-polysaccharide fraction obtained from the mucin extract of hog gastric mucosa (*—*). In this experiment the fraction was given at the same time as the lipidic emulsion.
pathologic hyperlipidemic states. In an investigation carried out both on young people clinically free from atherosclerosis, and on patients presumed to be atherosclerotic because of histories of myocardial infarction and/or definite evidence of coronary insufficiency, we have found that under basal conditions the oral administration of crude gastric mucin from hog stomach is able to decrease the plasma optical density (as determined by the Leitz-Rouy photometer). The average decreases in the two groups were 30 and 26 per cent respectively. This difference in the average decrease of plasma optical density between the two groups is not significant.

The clearing effect exerted by gastric mucin under basal conditions is even more striking when the mucin is administered to "atherosclerotic" patients fed a fat meal. In such patients the marked hyperlipemia induced by a fat meal in control experiments was always greatly reduced when gastric mucin was given at the same time as the fat meal (about 3.5 mg./Kg. of body weight) (fig. 3). 19

Finally, in line with the results obtained in previous investigations with heparin, 21, 22 gastric mucin administered simultaneously with a fat meal prevented (either fully or in part), in 50 per cent of the anginal patients...

Fig. 3. Mean values of plasma optical density (Leitz-Rouy photometer: λ = 640 mμ) in a group of atherosclerotic patients fed a fat meal (200 Gm. of milk cream), without (solid line) and with (broken line) administration of crude gastric mucin (about 3.5 mg./Kg. of body weight). (Reproduced from figure 1 of an article by Dr. Rulli and Dr. Rossi, Circulation 18: 400, 1958.)

Fig. 4 Top. Showing the changes of the repolarization phase induced by a fat meal in the electrocardiogram of 2 anginal patients with old myocardial infarcts, and of their inhibition when crude gastric mucin is administered at the same time as the fat meal. The plasma optical density shows similar changes. Top, electrocardiogram recorded before the test: optical density 65. Middle, electrocardiogram recorded 3 hours after a fat meal: optical density 75. Bottom, electrocardiogram recorded 3 hours after a fat meal with the addition of gastric mucin: optical density 60.

Fig. 5 Bottom. Top, electrocardiogram recorded before the test: optical density 62. Middle, electrocardiogram recorded 3 hours after a fat meal: optical density 85. Bottom, electrocardiogram recorded 3 hours after a fat meal with the addition of gastric mucin: optical density 60. (Reproduced from figures 2 and 3 of an article by Dr. Rulli and Dr. Rossi, Circulation 18: 400, 1958.)
thus studied, the electrocardiographic changes associated with a fat meal, the conditions of the experiment being identical (figs. 4 and 5).

Concluding, we have the impression that the normal gastric juice of man contains an acid aminopolysaccharide fraction, which, when administered by mouth, acts indirectly on the state of dispersion of the plasma lipids, and which in all likelihood, in addition to other physiologic function, plays a role in the etiology of certain disease states.

**Summary**

A mucin compound obtained from the human gastric juice exerts a plasma-clearing effect in rabbits rendered hyperlipemic and has a prolonged effect against fatty liver of alimentary origin in rats.

An extract of hog gastric mucosa, which in all likelihood is chemically a nonsulfurated acid aminopolysaccharide, exerts a clearing effect in rabbits and men, an hypocholesteremic action, an antilipemic effect, a lipotropic action in fatty liver of dietary origin in rats, and inhibits the electrocardiographic changes associated with a fat meal in men.

It is possible that, in addition to their physiologic function, such mucins, which contain an aminopolysaccharide fraction, by acting on the state of dispersion of the plasma lipids, play a role in the etiology of certain disease states.

**SUMMARIO IN INTERLINGUA**

Un composito mucinic obtenite ab le succo gastrico de humanos exerce un effecto clarificatori super le plasma de conilios rendite hyperlipemic per medio di dietas experimentali. Illo exerce un effecto protectori contra le disveloppamento de un hepate adipose de origine alimentari in rattos.

Un extracto de porcin mucosa gastrico—le qual, in terminos chimic, es probabilissimemente un aminopolysaccharido de acido non-sulfurated—exerce un effecto clarificatori in conilios e humanos, un action hypocholesterolemic, un effecto antilipemic, e un action lipotropic in casos de hepate adipose de origine alimentari in rattos, e un effecto inhibitori contra le alteraciones electrocardiographic associate con le ingestion de repastos grasses in humanos.

Il es possibile que—a parte lor function physiologic—tal mucinas (que contine un fraction aminopolysaccharidic) es implicate—per ager super le stato di dispersion del lipidos del plasma—in le etiologia de certe conditiones pathologic.

**REFERENCES**

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