

THE EFFECT OF A SULPHATED POLYSACCHARIDE ON THE ACIDITY AND VOLUME OF HISTAMINE-STIMULATED GASTRIC SECRETION IN THE GUINEA-PIG

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Degraded carrageenan administered in aqueous solution via an oesophageal tube to guinea-pigs twice daily and also freely available as drinking fluid, for 8 to 14 days, causes a 50 per cent reduction in the volume and acidity of histamine-stimulated gastric juice. This could be an important factor in the protection afforded by carrageenan against histamine-induced duodenal ulceration.

DEGRADED carrageenan, a sulphated polysaccharide, forms a complex with the mucoprotein of acidified gastric mucus. *In vitro*, experiments have shown that this material retards the diffusion of pepsin through the mucus layer (Anderson, 1961). The possibility that the mucoprotein complex or even degraded carrageenan itself might reduce gastric secretion arose during the course of clinical investigations on this substance. Preliminary studies in the guinea-pig indicated that degraded carrageenan administered over a 36 hr. period caused a 40 to 50 per cent reduction in the acidity of histamine-stimulated gastric juice. We have now administered degraded carrageenan over a longer period, and have studied the effects on both the volume and acidity of histamine-stimulated secretion.

METHODS

Animals were maintained on an ordinary cube and cabbage diet. Drinking fluid was supplied freely at all times, control animals receiving water, experimental animals receiving a 3 per cent aqueous solution of degraded carrageenan which was readily accepted. Degraded carrageenan (20 per cent solution) was also given at intervals via an oesophageal tube, the final dose coinciding with the removal of all food from the cages some 15 hr. before administering histamine and collecting the gastric juices. The histamine preparation used was the acid phosphate suspended in a beeswax : arachis oil vehicle (10 mg. histamine acid phosphate per ml.). Injections were given intramuscularly usually at 9 a.m. in doses of 10 mg. histamine acid phosphate per kg. One and a half hr. later, a stomach-tube was introduced via the oesophagus, the gastric contents were removed, the volumes recorded and the free and total acidities measured by titration with 0.04N NaOH, using Topfer's reagent and phenolphthalein as indicators.

In the first experiment, 11 small female guinea-pigs (350 g. body weight) were given 5 ml. of 20 per cent degraded carrageenan twice daily by stomach tube for 8 days, in addition to free access to a 3 per cent solution as drinking fluid. The volume and acidity of the histamine-stimulated

gastric juices were examined at the start of the experiment, at the end of the 8 days treatment and finally after a further 14 days during which time no degraded carrageenan was given. Four animals were killed for histological examination of the stomach.

In the second experiment, 8 male Albino guinea-pigs of larger size (600 g.) were used. After obtaining control histamine-stimulated gastric juices, the animals received the same treatment as in the first experiment but over 14 days. Histamine-stimulated juices were then collected from 4 animals in the group, and from the remainder at the end of a further 7 days, during which time no degraded carrageenan was given.

RESULTS

The results are shown in Tables I and II. After administering degraded carrageenan for 8 days there was approximately a 50 per cent reduction both in the volume and acidity of the gastric juices. At the end of 2

TABLE I

EFFECT OF 8 AND 14 DAYS ADMINISTRATION OF DEGRADED CARRAGEENAN ON HISTAMINE-STIMULATED GASTRIC SECRETION

	Gastric acidity (ml. 0.1N HCl/100 ml.)				Volume of juice (ml.)	
	No. of guinea- pigs	Range Free acid (FA)	Range Total acid (TA)	Average FA/TA	Total	Average per animal
<i>Experiment I—Small animals (350 g.)</i>						
Before carrageenan	11	99-143	110-152	124/134	50.7	4.6
After 8 days carrageenan ..	9	24-97	42-109	58/72	19.3	2.1
After 2 weeks off carrageenan ..	7	100-128	115-150	110/129	33.5	4.8
<i>Experiment II—Large animals (600 g.)</i>						
Before carrageenan	8	47-129	90-136	105/117	69.5	8.6
After 14 days carrageenan ..	4	38-80	50-98	58/81	14.4	3.6
After 14 days carrageenan and off for 7 days	4	116-123	126-131	119/128	42.5	10.6

weeks, during which time the animals received no further amounts of degraded carrageenan, the volume and acidity of the histamine-stimulated juices had returned to normal control values. When carrageenan was given over 14 days to larger animals, secreting larger volumes of juice, a similar reduction in the histamine-stimulated juices was obtained. A return to normal values took place when the animals had been 7 days without carrageenan. No histological changes were noted in the gastric mucosa after 8 or 14 days treatment with carrageenan.

DISCUSSION

Recently it has been shown that degraded carrageenan imparts some protection against histamine-induced gastro-duodenal ulceration in both the dog (Houck, Bayana and Lee, 1960) and guinea-pig (Anderson and Watt, 1959). Factors believed to be concerned in the protective mechanism and so far studied are the inhibition of peptic digestion and the enhancing of the protective function of the mucus lining the mucosa.

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The above findings isolate another factor and indicate that degraded carrageenan, either by itself or in complexed form, may reduce both the volume and acidity of the gastric secretion by as much as 50 per cent.

TABLE II
RESULTS FOR INDIVIDUAL ANIMALS IN THE GROUP OF 4 BEFORE AND AFTER RECEIVING CARRAGEENAN FOR 14 DAYS

	Volume (ml.)		Histamine-stimulated gastric juice Free Acid/Total Acid (ml. 0.1N HCl/100 ml. of gastric juice)	
	Before	After	Before	After
	19	4.5	128/135	67/85
	13	5.4	129/136	80/92
	2	3.5	84/95	48/98
	8	1.0	126/133	38/50
Totals	42	14.4	—	—
Mean per animal	10.5	3.6	117/125	58/81

This is likely to be an important factor in the prevention of histamine-induced ulceration, particularly duodenal ulceration which is frequently associated with, and attributed to, the hypersecretion of highly acid gastric juice.

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