hearts of animals previously treated with reserpine, and by the unpublished observations of Gascon & Cloutier, which showed a significant increase in the noradrenaline content of the seminal vesicles in animals so treated.

This work was supported by the Medical Research Council of Canada; Grants: MA–3084 and MA–3130.

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Ulcerative colitis in rabbits fed degraded carrageenan

We recently described the occurrence of ulcerative colitis in guinea-pigs fed orally in their drinking water degraded and undegraded carrageenan derived from the red seaweed *Eucheuma spinosum* (Watt & Marcus, 1969). The lesions produced by degraded carrageenan were severe and involved the whole length of the colon.

We have found that degraded carrageenan derived from the same seaweed also causes severe damage to the colon of the rabbit. In this communication we report on the incidence of ulcerative lesions found in rabbits fed various concentrations of the degraded product.

Twenty male Californian rabbits of 2950 g average body weight were housed in separate cages and fed a standard cube diet (S.G.1). Three experimental groups, 5 rabbits in each group, received as drinking fluid 5, 1 and 0·1% respectively aqueous solutions of degraded carrageenan derived from *Eucheuma spinosum.** The solutions of degraded carrageenan were freshly prepared daily, stored at 4°, and supplied *ad lib* in drinking bottles which were cleaned each day. The volume of fluid consumed per animal per day was measured throughout the 6 to 12 week period of the experiment. Control animals received water *ad lib* but without added carrageenan. At weekly intervals, the animals were weighed and their faeces examined for occult blood using the Haematest method. At the end of the experiment, the animals were killed with pentobarbitone. At post-mortem examination, the colon was removed, emptied of faeces and examined for the presence of ulcerative lesions.

Animals fed degraded carrageenan at the 5% concentration in their drinking water received on average a daily dose of 1·4 g/kg weight over a 6 week period. Diarrhoea associated with visible and occult blood in the faeces developed by the end of 7 days and persisted. The animals rapidly lost weight, the average loss at the end of the

experiment being 976 g. All animals in this group showed severe ulceration of the colon.

Animals fed degraded carrageenan at the 1% concentration received on average a daily dose of 0·8 g/kg weight over a 7 week period. Only 1 animal developed diarrhoea; occult blood was present in the faeces in all of the animals after 2 weeks. The average weight loss in the group was 190 g. All of the animals showed ulceration of the colon of moderate severity.

Animals fed degraded carrageenan at the 0·1% concentration received on average a daily dose of 0·07 g/kg over a 12 week period. Diarrhoea did not occur but occult blood in the faeces was demonstrable in 3 of the animals by the end of 10 weeks. One animal lost 30 g in weight; the remainder gained weight, the average weight gain in the group being 238 g. Multiple ulcers in the colon were found in 3 of the 5 rabbits.

Control animals drank on average 370 ml water per day over a 12 week period. There was no diarrhoea or occult blood in the faeces at any time. The average gain was 1218 g. No ulcerative lesions were found in the colon in any of the control animals.

The results indicate that degraded carrageenan at doses of 0·07 g/kg per day will produce ulcerative lesions in the colon in 3 out of 5 rabbits when given orally in the drinking fluid over a period of 3 months. It is possible that an even higher incidence of lesions may have been found had the feeding experiment been prolonged.

In this country, degraded carrageenan derived from *Eucheuma spinosum* has been used only in clinical trials in the treatment of chronic peptic ulcer (Evans, Lowell & Thomas, 1965). On the continent, however, the product in tablet form is widely used to reduce peptic activity and gastric acidity in gastro-duodenal disorders (Bonfils, 1968). The maximal dose recommended per day is about the same (0·07 g/kg) as produces ulcerative lesions in the colon of the rabbit.

In the light of these findings, together with our results in three other animal species (Marcus & Watt, 1969), it seems that the continued use of degraded carrageenan as a drug in the treatment of peptic ulcer may not be without risk.

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October 17, 1969

* Carrageenan degraded by mild acid hydrolysis and retaining about 29% sulphate was kindly supplied by Laboratoires Glaxo, Paris.

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