

Effect of Sodium Polyanhydromannuronic Acid Sulfate on Incidence of Ulcers in the Shay Rat.* (22502)

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It was shown by Babkin and Komarov(1) that chondroitin sulfate would reduce the proteolytic action of dog gastric juice. Later, Zaus and Fosdick(2) reported that chondroitin sulfate decreased the rate of digestion of gelatin sheets by commercial pepsin. More recently, Levey and Sheinfeld(3) noted that sulfated polysaccharides inhibit the proteolytic action of pepsin *in vitro*. Heparin, chondroitin sulfate and Paritol C, a clinical grade of sodium polyanhydromannuronic acid sulfate, were used in their studies. In addition, they found that chondroitin sulfate markedly reduced the incidence of ulcers in the Shay rat. In view of this more recent communication, we instituted a study in Shay rats to determine whether oral administration of sodium polyanhydromannuronic acid sulfate (Manuronate®) would reduce the incidence of gastric ulcers and whether sodium polyanhydromannuronic acid sulfate added to alumina gel (Amphojel®) would enhance the ulcer prevention properties of alumina gel.

Method. The method employed in this study is essentially that of Shay *et al.*(4). Male, Wistar rats ranging in weight from 120 to 170 g were fasted for 48 hours and the pylorus of each animal was ligated under ether anesthesia by the conventional technic. Immediately after ligation, the stomach was flushed with 4.0 ml saline and 2.0 ml of the proper medication was administered by stomach tube. No food or water was allowed during the remainder of the experiment. Nineteen hours after drug administration, each rat was sacrificed with ether, the stomach removed, opened and examined for ulcers under a dissecting microscope (7 X magnification). The protective action against ulcers, of sodium polyanhydromannuronic acid sulfate solution, various concentrations of alumina gel

(expressed as Al_2O_3 equivalent) and mixtures of the two were observed.

Twenty to 25 animals were used at any one time. Five of these were saline controls and the remainder were used 5 or 10 to a group, usually 5, for the various test substances. The groups of animals for any one test substance were spaced as much as possible throughout the duration of the study. Two systems of ulcer gradation were used. The first consisted of 5 categories: (1) No ulcers; (2) < 10 ulcers—none perforated; (3) > 10 ulcers—none perforated; (4) Perforated ulcers—animal living; (5) Perforated ulcers—animal dead. These gradings for each drug at each dose level were plotted on a graph. The second system consisted of an arbitrary gradation of the severity of ulceration, taking into account all the above factors plus the distribution and size of ulcers. Seven categories were included here: 0 to 4+ ranging from negative to many large ulcers approaching perforation; 5+ perforated ulcers—animal living; 6+ perforated ulcers—animal dead. The sum of plus values divided by number of animals used is called the "ulcer index." On occasion, a rat was found dead which on careful examination showed no ulceration. It was assumed in these cases that death was due to other causes and the animal was discarded.

Results. The results obtained in this study are shown in Fig. 1. Alumina gel in a concentration equivalent to 0.25% Al_2O_3 resulted in a somewhat lesser degree of ulceration than seen in the saline control animals. The concentrations equivalent to 0.5 and 2.0% Al_2O_3 reduced ulcer incidence appreciably. Alumina gel in a concentration of 1.0% Al_2O_3 , did not, in this series of experiments, fall in line with the usual reduction in ulcer formation. We have no explanation for this.

Sodium polyanhydromannuronic acid sulfate when added to 0.25% alumina gel in con-

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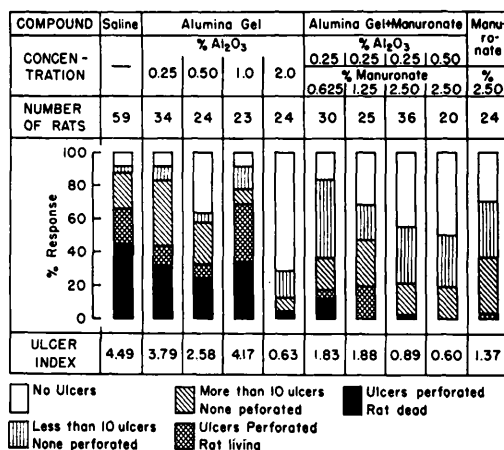


FIG. 1. Effect of alumina gel and Manuronate on incidence of ulcers in the Shay rat.

centrations of 0.625 and 1.25%, both greatly reduced ulcer incidence, the 2 showing approximately equal potency. An increase of sodium polyanhydromannuronic acid to 2.5% in 0.25% Al₂O₃ further decreased ulcer formation. Sodium polyanhydromannuronic acid sulfate, 2.5% in 0.5% alumina gel reduced ulcer formation still more.

A 2.5% solution of sodium polyanhydro-

mannuronic acid sulfate without alumina gel, also reduced ulcer formation, the efficacy being approximately mid-way between 1.25 and 2.50% sodium polyanhydromannuronic acid sulfate in 0.25% alumina gel.

Summary. 1) A study has been made of the effects of sodium polyanhydromannuronic acid sulfate, alumina gel, and mixtures of the two, on incidence of ulcers in the Shay rat. 2) Each provided significant protection from ulcers and mixtures of the two reduced ulcer formation to a greater degree than either alone.

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Relation of Sodium, Potassium, and Chloride Intake to Cortisone Action During Food Restriction. (22503)

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In a recent study(1), it was reported that the increase in renal size noted in rats on potassium low diets containing NaCl is not observed if the NaCl is replaced by NaHCO₃. It seemed desirable to extend these studies to include observations of food and water intake and to investigate the relation of cortisone to these functions on account of its importance for salt excretion. As on previous occasions, it seemed expedient to carry out the studies on rats whose weights were kept constant by restricted feeding.

Materials and methods. Male albino rats weighing approximately 100 g were kept individually in cages with wire bottoms and were provided with bottles suitable for the determination of water intake. They were weighed daily and supplied with enough food to keep their weight constant within ± 2 g. The requirements were eventually calculated as calories per gram body weight per week. Details of the procedures will be reported elsewhere(2). The basic experimental diet consisted of 30% test casein, 10% commer-