Decreased Gastric Secretory Activity Following Injection of Lignin Sulfonates. (23289)

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We have been studying the effects of certain substances on gastric secretion in the pylorus-ligated rat and Heidenhain pouch dog. While it is premature to report our data for most of these substances, observations on the use of lignin sulfonates, dried and dialyzed pulp mill sulphite waste liquor(1), appear sufficiently definite and interesting to warrant a communication. Since some lignin sulfonate (LS) derivatives prepared here were among the compounds under investigation, we decided to use calcium LS itself in preliminary experiments, the results of which are recorded here.

Materials and methods. Sprague-Dawley rats, starved for 48 hours and deprived of water for the last 16 hours of this period, were lightly anesthetized with ether and the pylorus of each was ligated (The Shay preparation(2)). After ligation, the LS (Ca salt) in water solution was injected into the peritoneal cavity. The controls received an equal injection of water. After 24 hours, the animals were sacrificed and the stomachs removed, emptied and examined. Some of our LS was kindly supplied by Professor Holger Erdtman of the Royal Institute of Technology, Stockholm (S/OMe, 0.38). In most of our experiments, more highly sulfonated material has been used, (S/OMe, slightly less than 0.5) generously provided by Dr. Joseph L. McCarthy, Department of Chemical Engineering, Univ. of Washington.

Results. In the initial experiment, 6 Shay rats were each given 50 mg of LS (Ca salt) in 0.5 ml of water, as described. Six Shay rats served as controls. When sacrificed, the rumens of the control animals (one had died) were heavily ulcerated. Stomachs from the LS treated animals were without ulcers and had significantly less secretion than the controls. Table I summarizes this and subsequent experiments. An intraperitoneal dose of LS of approximately 10 mg per 100 g rat body weight was a borderline below which there was little 24-hour protection. Three-quarters of this dose at the time of ligation, followed by injection of an equal amount 8 hours later, afforded no protection. Results in the 10-20 mg per 100 g range were generally satisfactory, but for most of this work we used 20 mg per 100 g.

With LS injection 4 to 2 hours before ligation, the anticoagulant action of the LS(3) was so pronounced that many early deaths resulted. Progressively less protection was afforded as time increased between ligation and postoperative injection. With a 4 to 5 hours interval, stomachs 24 hours after ligation were indistinguishable from the controls. This follows from the fact that most of the secretion in the Shay rat occurs during the

TABLE I. Effect of 2 Dosages of LS on Ulcer Incidence and Gastric Secretion in the Shay Rat. Figures in parentheses (last 2 columns) show No. of stomachs represented by preceding avg. Ulcers in test groups were, almost without exception, very small and not bloody, in great contrast to most ulcers in control stomachs.

Rats	No.	Dose CaLS, mg/100 g rat body wt*	Ulcer incidence and description	Avg pH of secretion	Avg vol of secretion, ml†
Controls	11		100% (73% dead or/and perforated)	4.1 (5)	7.8 (3)
Test	14	10	29% (14% dead *without* ulcers)	4.6 (12)	6.7 (12)
Controls	15		93% (47% dead or/and perforated)	4.3 (8)	8.4 (8)
Test	39	20	18% (8% dead *without* ulcers)	4.2 (36)	4.7 (36)

* 100 mg LS/ml H_2O. † After centrifugation.

first few hours following ligation, and ulceration can often be detected within 4 to 5 hours.

In another experiment, 6 Shay rats were each given 0.2 g LS (Ca salt) in 1 ml water *per os* after ligation, and 6 controls were given 1 ml of water *per os*. The following day, although control stomachs were heavily ulcerated (an average of 12 ulcers per stomach was noted, many of them bloody), the stomachs of 4 of the treated animals were completely free of ulceration, one had 2, and one had 5 small ulcers (none bloody). The mechanism of this protection would appear to be different from that after injection of LS into the peritoneal cavity. The average volume of secretion in the stomachs of the treated animals was about the same as in the controls and the pH was more strongly acidic (compare Funk(4), but in this latter work it should be noted that while ox-bile protected against ulceration, it was also anti-secretory when given *per os* to the Shay rats).

Summary. Solutions of calcium lignin sulfonates injected immediately after ligation in the Shay rat (20 mg/100 g rat weight) afforded pronounced protection against ulceration as compared with controls. The same material given *per os* also protected Shay rats against ulceration, probably by a different mechanism.

We are grateful to Mr. Clifford L. Pitts for technical aid in carrying out these experiments and to the National Institutes of Health for a research grant which aided this work in part.

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Received April 24, 1957. P.S.E.B.M., 1957, v95.

Influence of Ascorbic Acid and Chlorpromazine on Body Temperature and Resistance of Mice to Drowning. (23290)

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Increased resistance to anoxia at low barometric pressure resulting from ascorbic acid has been recognized since the report of Gander(1) with Swiss ski troops. Comparable results have been reported with rabbits(2,3), and rats, mice and men(4,5). Because it is known that body temperature influences anoxic resistance to drowning a comparison of body temperature change following injections of ascorbic acid was made. Also injections of chlorpromazine, a hypothermic drug, were used.

Methods and materials. Adult mice of the RAP strain (75 males and 88 females) were divided into groups of 14 or 15. Controls were injected with distilled water of the same volume as that used with the experimentals. Ascorbic acid buffered to pH 7.3 with $NaHCO_3$ (10 mg in 0.5 ml of water) was injected intraperitoneally and after a lapse of 0, 30, 45, 60, 120 minutes the mice were drowned in water at 37.5°C. Drowning was accomplished by seizing the tip of the tail with a long hemostatic forceps and plunging the mouse under water. The last visible mandibular movement was taken as the criterion of death timed by an electric metronome and observed by at least 2 of the investigators simultaneously. Rectal temperatures were recorded by a L & N potentiometer using copper-constantan electrodes inserted to a marked depth each time. Chlorpromazine (Thorazine S.K.F.*), 25 mg/kg was injected i.p. for the second part of the experiment.

* Chlorpromazine (Thorazine) was kindly supplied by Dr. Edwin J. Fellows, Director of Biological Sciences, Smith, Kline & French Laboratories, Philadelphia, Pa.