

EFFECT OF SOME NATURAL SUBSTANCES ON ULCERATION OF THE RAT STOMACH CAUSED BY ACETYSALICYLIC ACID

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The effect of two natural substances — quercetin and plantaglucide — on ulceration of the stomach induced by acetylsalicylic acid was investigated in experiments on rats. Both substances had a protective action against ulceration as manifested by a decrease in the number of animals with stomach lesions and a decrease in the intensity of hemorrhagic inflammation observed. The dominant factors in the mechanism of the protective effect of quercetin are presumably its capillary-strengthening and anti-inflammatory action; plantaglucide may possibly interact with the mucopolysaccharides of the gastric mucosa.

One of the chief disadvantages of acetylsalicylic acid (aspirin) is the damage which it causes to the gastrointestinal tract, manifested as the development of gastric erosions and ulcers and of gastrointestinal hemorrhages [2, 5, 10, 11]. Attempts to overcome or diminish these side-effects by improvements in the presentation or changes in the mode of administration of the drug have been described [13, 14].

The object of this investigation was to attempt to minimize or to completely abolish the side effects of acetylsalicylic acid on the stomach by using the flavonoid quercetin and the polysaccharide plantaglucide, both of which protect against toxico-degenerative lesions of the gastric mucosa [3, 4].

EXPERIMENTAL METHOD

Experiments were carried out on 74 rats weighing 150–180 g. All the substances were given by mouth, acetylsalicylic acid in a dose of 150 mg/kg twice a day, quercetin simultaneously with it in doses of 50 and 100 mg/kg, and plantaglucide 1 h before acetylsalicylic acid in doses of 100–1000 mg/kg. The animals were killed 17–18 h after the second dose of acetylsalicylic acid and the stomach was examined macro- and microscopically.

EXPERIMENTAL RESULTS AND DISCUSSION

At autopsy on most rats of the control group, hemorrhages, erosions, and ulcers of different sizes were found in the region of the lesser curvature, nearer to the pyloric end of the stomach. Histological examination revealed the characteristic changes of acute toxic desquamative gastritis. Multiple erosions extended through $\frac{1}{3}$ – $\frac{1}{2}$ of the thickness of the gastric mucosa.

Quercetin reduced the intensity of hemorrhagic inflammation and of ulceration by 1.7–4 times; its action was particularly marked in the larger dose.

Plantaglucide in a dose of 100 mg/kg gave a weak effect. When used in doses of 250–1000 mg/kg it reduced the number of rats with gastric lesions from 100% in the control to 40% and reduced the index of ulceration by 1.6–6.6 times. Histological investigation showed that plantaglucide protected a large part of

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the epithelium. The erosions were smaller and more superficial. They were surrounded by a leukocytic barrier demarcating the zone of damage from the healthy tissue. Evidence of edema and hyperemia was observed only in certain areas of the mucosa, and their intensity was much lower than in the control. The appearance and size of the chief and parietal cells indicated a state of hypersecretion. These results are evidence of the protective and anti-ulcerative action of quercetin and plantaglucide against gastric lesions induced by acetylsalicylic acid.

The substances tested presumably exert their anti-ulcerative effect by increasing the resistance of the gastric mucosa to the direct harmful effect of acetylsalicylic acid. Since quercetin has no effect on gastric secretory function [7] and plantaglucide stimulates it [4, 6], their effect on the secretion of gastric juice must be presumed not to play the decisive role in the mechanism of their protective action. This effect for quercetin depends on a reduction of capillary permeability, whereas for plantaglucide it is possibly due to the formation of a complex with the mucopolysaccharides of the gastric mucosa, forming a film permeable to small molecules of the HCl and NaCl type but impermeable to pepsin, as has been shown for other polysaccharides [8, 9, 12].

The results of these experiments suggest that administration of flavonoids and polysaccharides is a rational measure for abolishing the side effects of acetylsalicylic acid on the stomach.

LITERATURE CITED

1. I. L. Bilich and Kh. S. Bikbulatova, Abstracts of Proceedings of a Scientific Conference on the Physiology and Pathology of Digestion and Absorption [in Russian], Odessa (1961), p. 24.
2. A. I. Geller, *Klin. Med.*, No. 8, 20 (1967).
3. G. V. Obolentseva and Ya. I. Khadzhai, *Byull. Éksperim. Biol. i Med.*, No. 9, 86 (1964).
4. G. V. Obolentseva and Ya. I. Khadzhai, *Farmakol. i Toksikol.*, No. 4, 469 (1966).
5. G. Plevins'kii, *Klin. Med.*, No. 3, 89 (1963).
6. T. F. Podval'nyukova, *Vrach. Delo*, No. 4, 142 (1967).
7. Ya. I. Khadzhai and G. V. Obolentseva, in: *Phenol Compounds and Their Biological Functions* [in Russian], Moscow (1968), p. 365.
8. W. Anderson, *J. Pharm. Pharmacol.*, 13, 139 (1961).
9. P. S. Cammarata, R. G. Bianchi, and F. J. Fago, *Gastroenterology*, 61, 850 (1971).
10. A. R. Cooke, *Austr. Ann. Med.*, 3, 269 (1970).
11. D. N. Croft, *J. Pharm. Pharmacol.*, 18, 354 (1966).
12. I. W. Hillyard, J. Doczi, and P. B. Kiersan, *Proc. Soc. Exp. Biol. (New York)*, 115, 1108 (1964).
13. A. G. Mitchell, *Austr. J. Pharm.*, 48, 52 (1967).
14. D. A. Schlichting, *Am. J. Pharm.*, 142, 16 (1970).