SHORT COMMUNICATIONS Japan. J. Pharmacol. 21, 829 (1971)

The present experiments indicate that 4-MU has a somewhat weak but definite papaverine-like action on the isolated guinea-pig’s gallbladder. Fontaine et al. (3) reported that this compound did not affect acetylcholine-induced contraction in the same preparation. They tested 4-MU only with a concentration of $10^{-4}$ g/ml. The atropine-like action of benadryl was confirmed in acetylcholine-induced contractions. However, unlike atropine, benadryl had an antagonistic action against barium as well.

REFERENCES
1) Fontaine, L., Grand, M., Molho, D., Chabert, J. and Boschetti, E.: Thérapie 23, 51 (1968);
3) Fontaine, L., Grand, M., Molho, D., Chabert, J. and Boschetti, E.: Thérapie 23, 63 (1968);

RELATIONSHIPS BETWEEN 5-HYDROXYTRYPTAMINE AND VAGAL RELAXATION IN THE DOG STOMACH

Yoshikazu NAKAZATO and Akira OHGA

Department of Pharmacology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo

Received for publication July 5, 1971

It has been reported that after treatment with atropine, stimulation of the vagus nerve causes a relaxation of the stomach which is possibly mediated by a non-adrenergic inhibitory mechanism (1-4). Bülbring and Gershon (5) proposed that 5-HT, with acetylcholine, seemed to be a neurotransmitter substance in the vagal inhibitory pathways of the guinea-pig stomach. According to them, in the presence of hyoscine, 5-HT causes a similar relaxation of the stomach to that produced by vagal stimulation, and the 5-HT and vagal responses are similarly affected by the same antagonists. In the present experiment, the possible contribution of tryptaminergic nerve mechanisms to the vagally induced relaxation of the dog stomach has been examined.

The experiments were performed on adult dogs. The animals were anesthetized with pentobarbital sodium (25-30 mg/kg i.v.). The dorsal vagal trunk and the perivascular nerve attached to the coeliac artery were stimulated for 10-30 seconds with a supramaximal pulse of 1 millisecond duration at a frequency of 20 Hz. The mechanical activity of the stomach was displayed on a recording paper through a mechano-electronic transducer system as a volume change in a water balloon introduced into the fundus or body. Further details of the experimental methods have been described in the previous paper (4).

5-HT injected into the gastric artery always caused a contraction of the stomach. The threshold dose was about 0.1 μg. With an increase of the dose, amplitude of the contraction
was increased until attaining a maximum at about 1 \( \mu \)g. The 5-HT contraction was reduced by treatment with atropine and it was further decreased by subsequently administered phenoxybenzamine (Fig. 1). However, these treatments did not convert the contractile response into a relaxation. On the other hand, as reported in the previous papers (4, 6), stimulation of the vagus nerve consistently caused a pure relaxation after treatment with either atropine or atropine plus phenoxybenzamine.

It has been shown that the biguanides stimulate neural excitatory and inhibitory receptors for 5-HT and then in the presence of hyoscine the drug causes relaxation of the guinea-pig stomach (5) and of the mouse small intestine (7). In the present experiment, however, intraarterially injected phenylbiguanide invariably caused a contraction of the stomach even in the dog which was pretreated with atropine plus phenoxybenzamine.

It is well known that reserpine depletes catecholamine and 5-HT contents in various tissues (8, 9). Bulbring and Gershon (5) have described that the vagal inhibitory response of the isolated guinea-pig stomach in which the sympathetic response has already been abolished by chronic treatment with reserpine, is weaker and is much more susceptible to fatigue than in the normal preparation. Acute inhibitory effects of reserpine on the responses to stimulation of the sympathetic nerves have previously been reported by Day and Warren (10) in the isolated rabbit ileum and by Euler (11) in the guinea-pig vas deferens. Recently, we demonstrated that the sympathetically induced response of the dog stomach was selectively inhibited by a single large dose of reserpine in a relatively short period in vivo (12). If a tryptaminergic nervous mechanism is involved in the initiation of the vagal relaxation of the
FIG. 2. Effects of reserpine on the relaxation caused by long-lasting vagal stimulation (V.P.S) and by stimulation of the perivascular nerve (Peri. S) in the dogs pretreated with atropine plus phenoxybenzamine.

A, Control, B, 4 hours after reserpine 5 mg/kg i.v. Traces from above downwards are time markers, responses of the stomach (G.R) and systemic arterial pressure (B.P). The vagus nerve is stimulated for 5 minutes. Stimulating periods are indicated by arrows (→) and half blanks of the time marker. Note that even after the relaxation caused by perivascular nerve stimulation is almost abolished by reserpine, vagally induced relaxation remained without any significant change.

dog stomach, it is expected that the relaxation is also inhibited by reserpine in a similar manner to the sympathetic response.

Reserpine 5 mg/kg was administered intravenously to the dogs pretreated with atropine plus phenoxybenzamine after the control responses to stimulation of the vagus and perivascular nerves were recorded. The sympathetically induced response was markedly reduced or abolished 4-5 hours after the administration of reserpine. On the other hand, vagal relaxation remained almost unchanged. Furthermore, when the stimulating period of the vagus nerve was lengthened from the usual 30 seconds up to 5 minutes, the relaxation persisted during stimulation without any significant reduction (Fig. 2).

The results obtained in the present experiment are in disagreement with those observed by Bülbring and Gershon (5) in the guinea-pig stomach. This discrepancy might be attributed to the difference between species of the animal used. In any case, at least in the dog, it cannot be said that 5-HT is involved in the vagally induced relaxation of the stomach as a neuro-transmitter substance.

REFERENCES
THE THERAPEUTIC EFFECT OF FM100, A FRACTION OF LICORICE ROOT, ON ACETIC ACID ULCER IN RATS

Keiijiro TAKAGI, Susumu OKABE, Koichiro KAWASHIMA
and Toshiki HIRAI

Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences,
University of Tokyo, Bunkyo-ku, Tokyo

Received for publication July 17, 1971

Extracts of licorice root have long been used for the treatment of peptic ulcer though active principles have not yet determined. A new fraction of licorice root, FM100, showed a protective effect on ulceration in pylorus ligated rats (Shay rats) and gastric antisecretory activity in rats and dogs in spite of being devoid of anticholinergic properties (1–3). In the present investigation, the therapeutic effect of FM100 on chronic gastric ulcer in rats induced by the injection of acetic acid into gastric wall was examined.

The detail of the experimental procedure of acetic acid ulcer was described in our previous paper (4). Male Donryu rats weighing about 200 g were laparotomized under ether anesthesia and 0.05 ml of 10% acetic acid solution was injected into subserosal layer in the glandular stomach. Then the abdomen was closed and the animals were housed in colony cages and fed on commercial rat pellets. FM100 suspended in 0.5% C.M.C. solution was administered orally twice a day. The control animals were treated with the vehicle alone. The animals were sacrificed by exsanguination 10 days after operation and the healing process of the ulcer was observed. The ulcer index was defined as the sum of the area of ulcers, which was calculated by multiplying the length by the width of each ulcer (mm²). As seasonal variation of experimental results was expected, the experiments were designed to carry out several times at various time.

The results are shown in Table 1. At each experiment, FM100 showed a significant repairing effect on the acetic acid ulcer at doses of 200 and 400 mg/kg. The mean curative ratios of FM100 by 10 days administration were 44.3% and 41.0%, at doses of 200 and 400 mg/kg, respectively. There was no significant difference in curative ratio between doses of FM100. As standard drugs, several conventional drugs used for peptic ulcer were also