

## INFLUENCE OF SALYUZID ON INTEROCEPTOR REFLEXES

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Salyuzid, one of the new synthetic preparations, possesses high chemotherapeutic activity in relation to tuberculosis and is of only low toxicity.

According to the findings of the Department of Chemotherapy of the All-Union Scientific Chemical-Pharmaceutical Research Institute, various types of laboratory animals tolerate large doses of salyuzid (up to 2g/kg) administered parenterally without any perceptible change in general condition.

In the present investigation we sought to establish what influence salyuzid exerts on the reflexes, arising when the receptors of some internal organs are stimulated. We studied the reflex reactions on blood pressure and breathing arising from the chemoreceptors of the small intestine and the mechanoreceptors of the urinal bladder.

### EXPERIMENTAL METHOD

The experiments were conducted on 19 cats. Narcosis was induced in the animals by urethane. We studied the reflexes of the chemoreceptors of the small intestine according to the method of perfusion of the small intestine, isolated from the general blood circulation, the link with the organism being maintained only by means of the mesenteric nerves. The intensity of the blood pressure and respiratory reflexes produced by introducing acetylcholine in a concentration of  $1:10^{-4}$  and  $1:10^{-3}$  into the perfusate served as an index of the excitability of the intestinal chemoreceptors. In order to obtain the reflexes of the mechanoreceptors of the urinal bladder the wall of the organ was distended with air at a pressure of 70-80 mm mercury.

We recorded the blood pressure in the common carotid artery by means of a mercury manometer and respiration was recorded by means of a Marey's drum. The findings obtained were registered on the smoked drum the kymograph.

### EXPERIMENTAL RESULTS

In the first group of experiments a study was made of the influence of different concentrations of salyuzid on the excitability of the chemoreceptors of the small intestine when direct contact between them was established for a short duration.

We tested the solutions of salyuzid, prepared extemporaneously by dissolving 0.6 g and 1.2 g in 10 ml distilled water (0% and 12% solutions) and introducing them into the perfusate. We usually introduced

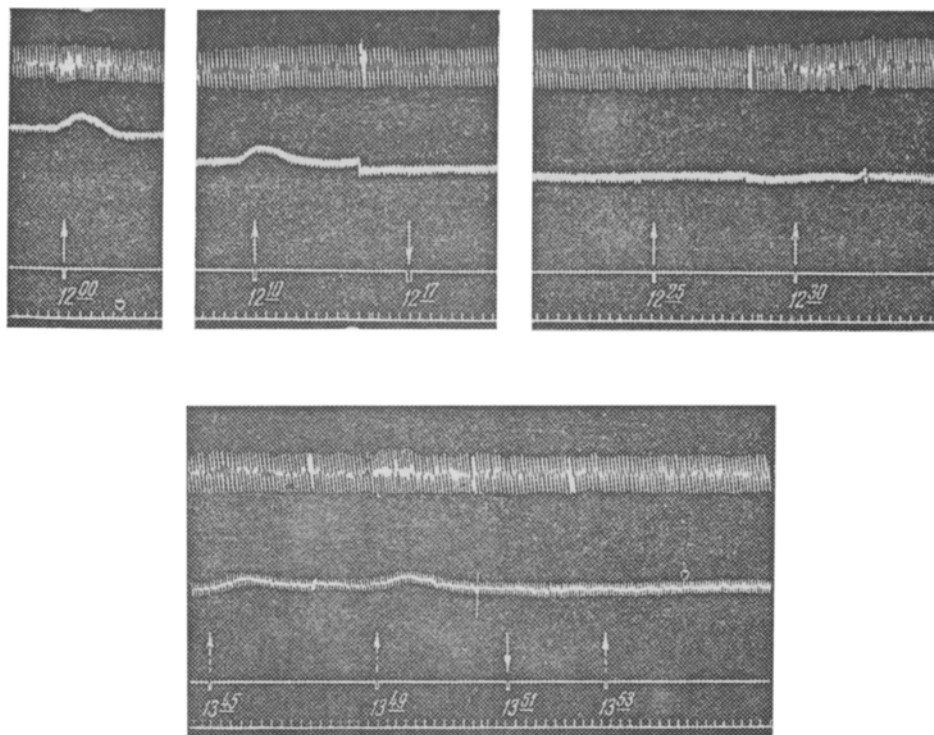


Fig. 1. Influence of short-duration contact of 12% salyuzid solution ( $\downarrow$ ) with the chemoreceptors of the small intestine on their reflexes associated with blood pressure and respiration.

Significance of tracings (reading top to bottom): respiration, blood pressure, indication of stimulation, time interval (5 seconds),  $\uparrow$ -moment of introduction of acetylcholine ( $1 : 10^{-4}$  and  $1 : 10^{-3}$ ).

Fig. 2. Influence of short duration contact of diethylamine ( $1 : 10^{-3}$ ) with the chemoreceptors of the small intestine on their reflexes associated with blood pressure and respiration.

Denotation as in Fig. 1.

$\downarrow$ -moment of introduction of diethylamine;

$\uparrow$ -moment of introduction of acetylcholine.

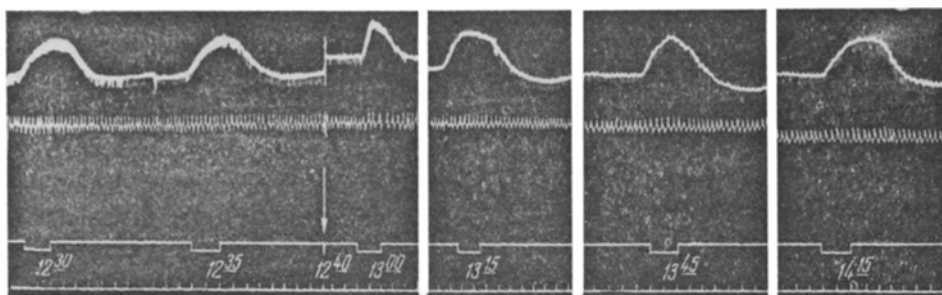


Fig. 3 Absence of changes in blood pressure and respiratory reflexes arising in the mechanoreceptors of the urinary bladder after intramuscular injection of salyuzid (0.5 g/kg). Denotation as in Fig. 1.

not more than 2 ml of this solution, that is, 0.12 g and 0.24 g of dry salyuzid into the perfusate.

At the commencement of the experiment, for the purpose of establishing the original excitability of the chemoreceptors, a check was made on the reflexes of the intestine to acetylcholine. Then, the salyuzid was introduced into the perfusate. Introduction of the preparation did not produce any reflex changes in blood pressure and respiratory movements. However, the excitability of the chemoreceptors to the acetylcholine, introduced immediately after salyuzid (1- 1.5 minutes) was sharply reduced, compared with the original. Failure to induce a reflex to acetylcholine after administration of salyuzid was generally recorded in a number of experiments. 10-15 minutes later in the course of which the intestine was washed with Tyrode solution, the excitability of the chemoreceptors to acetylcholine was restored, reaching the original level in a series of tests. On subsequent administration of the same amounts of salyuzid the observed effect usually recurred (Fig. 1).

In the second group of experiments the salyuzid was introduced intramuscularly in the ratio of 0.3-10 mg, in a 20% solution per kg body weight.

As in the earlier group of experiments, the initial excitability of the chemoreceptors of the intestine to acetylcholine was first established, and only after this was the cat given the preparation. By the nature of the method, salyuzid could not exert a direct influence on the chemoreceptors of the experimental segment of the small intestine. However, usually within only 15-20 minutes of introduction of the salyuzid, the vasculomotor reflexes significantly diminished or became protracted and the respiratory reflexes were completely suppressed. In all the experiments of this group a fall in blood pressure, reaching 50-60% of the original level, was observed after administration of the preparation.

In the third group of experiments we tested one of the component groupings of salyuzid-distilled diethylamine. This preparation, according to our findings, in a concentration of 1:10 and in higher concentrations exercised a toxic effect on the intestinal tissue: administration of 1 ml diethylamine in the concentration mentioned caused a sharp and irreversible spasm of the smooth musculature of the experimental segment of the intestine. It was natural that in these conditions the perfusion fully ceased. A higher attenuation of the preparation (1:10<sup>-3</sup> and 1:10<sup>-4</sup>) did not evoke spasm of the intestine and did not disturb the course of perfusion. The very introduction in the perfusate of the preparation in the given concentrations brought about a manifestation of blood pressure and respiratory reflexes. However, the excitability of the chemoreceptors to acetylcholine after being in contact with the test preparation was fully suppressed (Fig. 2).

In the study of the influence of salyuzid on the reflexes of the mechanoreceptors of the urinal bladder (fourth group of tests) we gave an intramuscular injection at a dosage of 0.3-0.5 g per kg body weight. As in the above-described investigations the original blood pressure and respiratory reflexes were initially tested, the preparation was then administered and the reflexes again tested every 15-20 minutes for 1-1½ hours.

In these tests we did not notice suppression or even an insignificant diminution of the blood pressure reflexes on introduction of salyuzid; on the contrary, towards the end of the investigation the blood pressure reflexes in a series of tests even increased somewhat. Respiratory reflex reaction to stimulation of the mechanoreceptors of the urinal bladder was not expressed in every test either before or after administration of the preparation. In

those cases in which this reaction occurred it was expressed in the form of an insignificant increase in the amplitude of the respiratory movements with no change after administration of salyuzid (Fig. 3).

The results obtained testify to the fact that salyuzid exerts a depressant influence on the reflexes arising from the chemoreceptors, both on direct contact with the cells of the chemoreceptors (included in their metabolism) and with intramuscular administration. With intramuscular administration of salyuzid the chemoreceptors themselves (by the nature of the method) were not subject to its influence and depression of the reflexes took place as a result of the direct influence of salyuzid on the centers of the corresponding reflex arc, starting at the periphery of the chemoreceptors. The blood pressure and respiratory reflexes arising from the mechanoreceptors in our tests proved to be more resistant in relation to salyuzid and did not decrease after its administration.