THE PHARMACOLOGY OF SOME HIGH-MOLECULAR POLYSACCHARIDES

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The bacterial polysaccharides possess a wide range of activity against the animal body. Since these compounds have only recently attracted attention, however, many of their properties remain undiscovered.

In a previous communication [2] we published the first data concerning the pharmocological properties of a bacterial polysaccharide obtained from Proteus vulgaris. In subsequent work we have carried out experiments to study the pharmacological properties both of polysaccharides from Proteus vulgaris (preparation PP9) and of a bacterial polysaccharide recently obtained in the laboratory under the direction of Prof. M. V. Svyatukhin from Bacillus pyocyaneus (preparation PST).* The results of these investigations are described in the present article.

METHOD AND RESULTS

The general action and toxicity of the pyrogenic polysaccharide from B. pyocyaneus were studied in sexually mature male white mice weighing 21 ± 2 g. The preparation was injected intraperitoneally in physiological saline, prepared in double-distilled pyrogen-free water.

In a dose of 25,000 μg/kg, the preparation caused slight depression of the animals which passed off without trace after a few days. With an increase in the dose, the degree of depression was intensified, and at a dose of 50,000 μg/kg several animals died. A dose of 100,000 μg/kg, however, did not cause death of all animals.

The preparation had no local irritant effect, whether injected subcutaneously or applied to the mucous membranes.

The pyrogenic action of the polysaccharide from B. pyocyaneus was studied in experiments on 50 white rats and 10 rabbits.

These experiments showed that in white rats, after receiving injections of this preparation intraperitoneally, in a dose of 1-100 μg/kg, the pyrogenic effect was less clearly shown than in the case of the polysaccharide from P. vulgaris; in some experiments the temperature rose by 0.5-1.8°, and in others no increase in the rectal temperature was observed.

In intact rabbits, the pyrogenic action was more constant: the temperature began to rise between 15 and 30 minutes after intravenous injection of the preparation in a dose of 1-20 μg/kg, reached its maximum after 1-2 hours, and then gradually fell in the course of the next 4-6 hours to its initial figures. As in the case of injection of the polysaccharide from P. vulgaris, no regular relationship was observed between the degree of rise of temperature and the dose of the preparation.

By injection of procaine into the blood stream, the development of the temperature reaction could be appreciably delayed, and the subcutaneous injection of amidopyrin in a dose of 100 mg/kg (in the form of a 6% solution) almost completely abolished it (Fig. 1).

It must be pointed out that the injection of pyrogen from B. pyocyaneus into irradiated rabbits produced a paradoxical reaction on individual days: instead of a rise of temperature, a fall was observed (Fig. 2).

A similar reaction of irradiated animals to pyrogen was also observed by N. A. Volokhova [5]. We consider that this author rightly regards the observed changes in the reaction to pyrogen as the result of the liability and asthenia of the thermoregulatory center developing under the influence of ionizing radiation.

In addition to studying the temperature reaction to the injection of the pyrogens, we studied the intensity of metabolism, as shown by the quantitative oxygen consumption. We used P. N. Veselkin's (1955) modification of the method of Renier and Reise† for this purpose. The experiments with the preparation from P. vulgaris were carried out on rabbits and rats, and those with the preparation from B. pyocyaneus on rats alone. These experiments showed that during the first 1½-3 hours after injection of the pyrogens, the observed fall in temperature by 0.5-1.8° was accompanied, as a rule, by a decrease in the oxygen consumption by 9-18% by comparison with the initial values. The decrease which we found in the

* The preparations are individual substances; the first is obtained from Gram-positive, and the second from Gram-negative bacteria. The method of their production is identical and is described in the article by A. A. Bodarev and M. V. Svyatukhin [1].

† Transliterated from Russian.

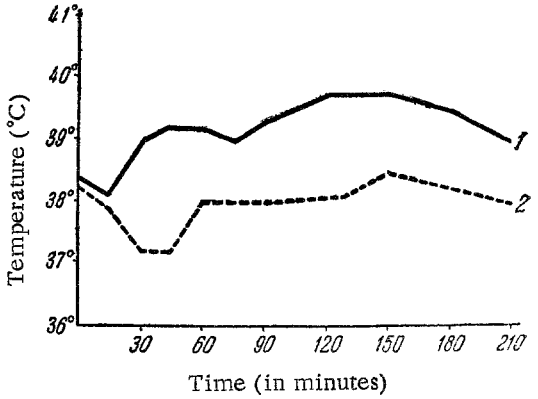

Fig. 1. Temperature reaction to injection of 10μg/kg pyrogen from B. pyocyaneus into an intact rabbit (1) and into a rabbit receiving amidopyrin (2).

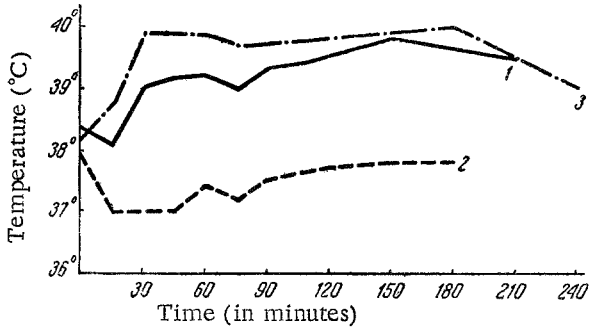

Fig. 2. Effect of irradiation on the character of the temperature reaction in a rabbit caused by intravenous injection of pyrogen from B. pyocyaneus in a dose of 10 μg/kg. 1) before irradiation; 2) on the first day after irradiation; 3) on the ninth day after irradiation.

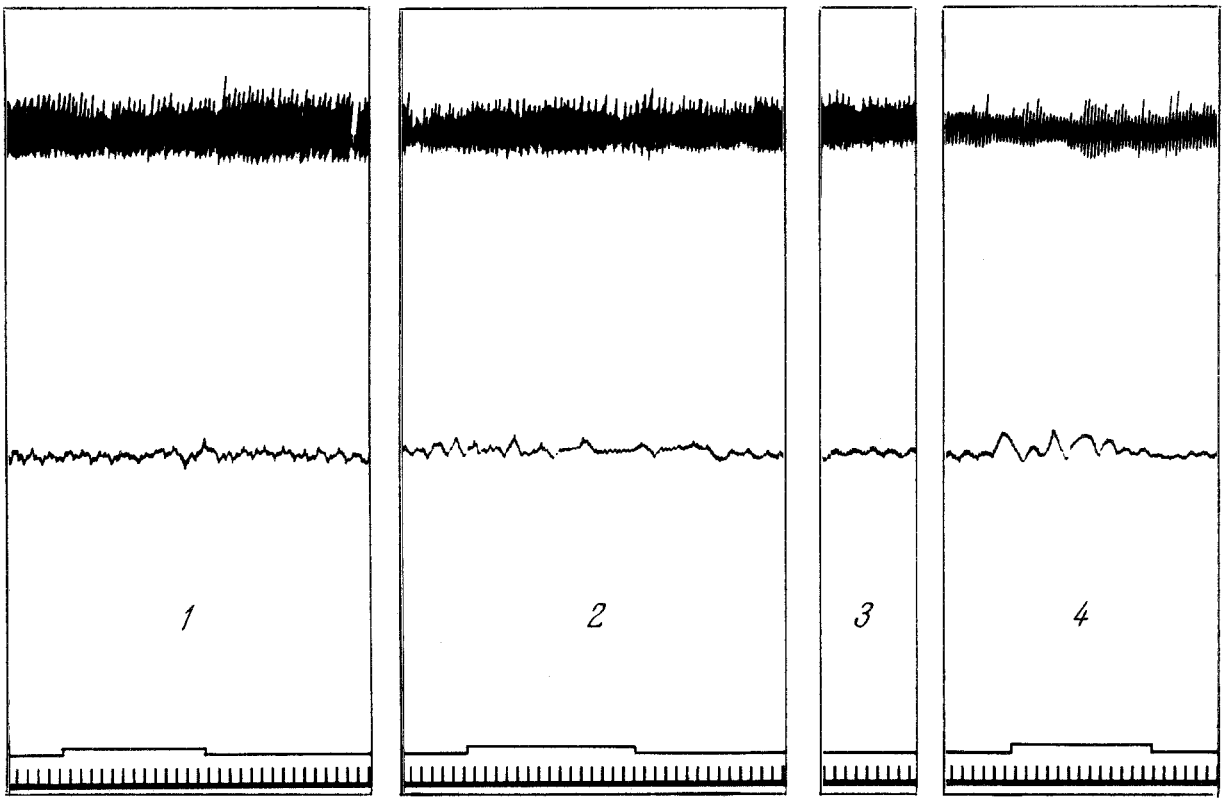

Fig. 3. Effect of the pyrogenic polysaccharide of B. pyocyaneus in a dose of 100 μg/kg on the arterial pressure and respiration. Significance of the curves (from above down): respiration, arterial pressure, marker of injection of the preparation, time marker (2 seconds); 1) physiological saline (4.5 ml); 2) pyrogen solution (4.5 ml); 3) 10 minutes after injection; 4) repeated injection of 4.5 ml of pyrogen 30 minutes after the first.

oxygen consumption will arouse no surprise, for at different stages of development of the pyrexial reaction the level of oxidative processes can fluctuate sharply both on the side of increase or decrease [3, 8, 10].

The anti-inflammatory properties of the bacterial polysaccharide from B. pyocyaneus, determined by the method of I. A. Oivin and K. N. Monakova [9], were less evident in our investigations than those of the pyrogen from P. vulgaris [2].

Acute experiments on anesthetized (urethane in a dose of 1 g/kg intravenously) and unanesthetized rabbits showed that neither a single nor repeated injections of the polysaccharide from B. pyocyaneus in doses from 10 to 1200 μg/g caused any appreciable changes in the arterial pressure and respiration (Fig. 3). Similar results have been described after injection of other polysaccharides [2, 3].

During the study of the action of this polysaccharide on the isolated heart by Straub's method(concentrations of $1 \cdot 10^{-5}$ to $1 \cdot 10^{-3}$), on the smooth muscle of the small intestine by Magnus' method (concentrations of $3 \cdot 10^{-5}$ to $5 \cdot 10^{-4}$) and on the diuresis by Gibbs' method it was found that no essential changes took place in the functions of these organs and systems.

In order to study the influence of bacterial polysaccharides on the central nervous system, we carried out experiments on white mice by E. N. Guseva's method [6], and also on rabbits in which the latent period of the flexor reflex was determined by V. V. Zakusov'smethod (1947).

In the experiments on mice (10 animals in the group) the preparation from B. pyocyaneus was injected intraperitoneally in a dose of 10 μg/kg, 30 minutes before the beginning of swimming. At the same time the control animals received an injection of an equal volume of sterile physiological saline. The average swimming time of the control mice was 181.5± 16.4 minutes, and that of the experimental mice 159.3± 11.6 minutes. Statistical treatment, however, showed that this difference was not significant, for the degree of probability T = 1.11.

Likewise,in the experiments on rabbits,no changes in the duration of the latent period of the flexor reflex could be observed in the 3 hours immediately after intravenous injection of 10 μg /kg of the preparation (V. E. Belai).

The bacterial polysaccharides obtained from both P. vulgaris and B. pyocyaneus, when injected parenterally in doses of 1 μg/kg or over, thus caused a marked hyperthermic reaction. The rise of temperature could, however, be greatly diminished by the preliminary intravenous injection of procaine, and it could be completely abolished by amidopyrin.

SUMMARY

The author presents data on the pharmacology of bacterial polysaccharides obtained from Proteus vulgaris and B. pyocyaneus. Within the first 2-3 hours after injection both preparations provoke pyrexia, reduce the oxygen intake and the vascular permeability. In doses tested they exercise no effect upon diuresis, smooth intestinal musculature and functional condition of the central nervous system. The arterial polysaccharide obtained from B. pyocyaneus fails to produce any changes in the arterial blood pressure and the rate and depth of respiration.

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‡ Original Russian pagination. See C.B. translation.