COMPARATIVE INVESTIGATION OF THE BIOLOGICAL ACTIVITY OF CERTAIN MICROBIAL POLYSACCHARIDES

(UDC 576.0.098.345.8:612.017.1)

G. E. Vaisberg

Chair of Microbiology, Central Institute for the Advanced Training of Physicians, Moscow
(Presented by Member of the Acad. Med. Sci. USSR, Z. V. Ermol'eva)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 61, No. 4, pp. 39-41, April, 1966
Original article submitted May 14, 1964

The polysaccharide complexes of a number of microorganisms can sharply stimulate the protective-adaptive responses of the organism. This ability is quite pronounced, in particular, in acetoxan A, acetoxan B, and prodigiosan —polysaccharide complexes isolated from nonpathogenic organisms in the laboratory headed by Z. V. Ermol'eva [1-3]. It was of interest to establish whether the manifestations of the biological activity of polysaccharide complexes isolated from various microorganisms are the same, and consequently, whether they differ in composition and structure.

In a comparison of the action of acetoxan A and prodigiosan in experimental sepsis, induced by various microorganisms, it was established that acetoxan A in definite doses causes a more or less uniform increase in the resistance, independent of the causative agent used. In contrast to this, prodigiosan increased the resistance to sepsis induced by E. coli to a far greater degree than to sepsis induced by other organisms [3].

The same irregularity in the increase in resistance to various infections is noted as a result of an investigation of the action of typhoid endotoxin on the resistance of mice to infections induced by intestinal and thyphoid bacilli and Bacillus pyocyaneus, as well as Proteus [5].

Considering the fact that in sepsis the death of animals is determined to a definite degree by the action of the bacterial toxin, in this work we investigated the influence of acetoxan A and prodigiosan upon the resistance of animals to the effects of endotoxin.

EXPERIMENTAL PROCEDURE AND RESULTS

The experiments were conducted with dysentery endotoxin, since acetoxan A and prodigiosan, in the doses used, increased the resistance of mice to dysentery sepsis. The work was conducted on more than 200 experimental and control mice.

The results of experimental series I are presented in Table 1.

From Table 1, it is evident that prodigiosan increases the resistance to endotoxin to a lesser degree than acetoxan A. On the basis of the combination of these data, it was assumed that acetoxan A and prodigiosan act differently upon individual components of the complex of protective-adaptive reactions.

TABLE 1. Influence of Acetoxan A (200 μg per animal) and Prodigiosan (5 μg per animal) on the Survival Rate of Mice after Injection of Dysentery Endotoxin

Day after adminis. of preparation	Survival (in %)			
	acetoxan A		prodigiosan	
	exptl.	control	exptl.	control
1st	80	30	35	6
3rd	79	6	30	0.6
5th	79	6	30	0

From the literature data and our observations, it is known that the response of animals to the injection of microbial polysaccharides is two-phase in character. In the first place, there is a transitory inhibition of the protective responses, which is especially noticeable when polysaccharide is administered simultaneously with infection of the animal.

The administration of polysaccharide on the eve of the infection prevents the inhibition of the protective functions that sets in when the same polysaccharide is administered again on the follow-day, simultaneously with infection.

TABLE 2. Survival of Mice in Experimental and Control Groups (in %)

Preparation administered on the eve of infection	Dose (in μg)	Preparation administered simultaneously with infection			
		acetoxan A (200 μg)	acetoxan B (200 μg)	prodigiosan (2 μg)	physiological saline (0.2 ml)
Acetoxan A	–	5	–	–	–
The same	200	42	68	69	82
Acetoxan B	–	–	1	–	–
The same	300	3	60	80	82
Prodigiosan	–	–	–	8	–
The same	2	4	1	62	82
Physiological saline (in ml)	0.2	8	8	8	–

In view of the above, the following assumption was made. If the investigated polysaccharides activate the protective responses to an equal degree, then it does not matter for the experimental results whether the same polysaccharide is administered on the day before as on the following day, simultaneously with infection, or whether a different polysaccharide is used. If their action differs, then the administration of one polysaccharide on the eve of the infection, and the other on the following day, simultaneously with infection, will affect the experimental results.

To verify this hypothesis, we conducted the following series of experiments. On the eve of the infection, the first group of mice received acetoxan A, the second acetoxan B, and the third prodigiosan. The polysaccharides were administered in doses equally effective in the case of sepsis induced by E. coli. The control animals simultaneously received an equal volume of physiological saline. On the following day, each of the groups was divided into three subgroups. The first of them received the same polysaccharide as on the day before, simultaneously with the infection, while the other two received different polysaccharides. The results of these experiments, conducted on more than 600 mice, are presented in Table 2.

In all the groups in which the animals received acetoxan A on the eve of the infection, their survival rate was high (from 42 to 82%). This is evidence that acetoxan A, administered on the eve of the infection, activates the protective responses of the animals to such a degree that it eliminates their inhibition, which sets in after infection simultaneously with the injection of prodigiosan or acetoxan B. Neither prodigiosan nor acetoxan B, administered to the mice on the day before, eliminates the inhibition of the protective functions induced by the administration of acetoxan A simultaneously with infection, and the survival rate of the mice in these groups proves low. However, the inhibition of the protective functions, which sets in when the mice are infected simultaneously with the administration of acetoxan B or prodigiosan, is eliminated by the administration of acetoxan B on the day before.

Prodigiosan, administered on the eve of the infection, eliminates the inhibiting effect of the same polysaccharide, administered to the animals simultaneously with the infection. In the case of the administration of acetoxan A or B simultaneously with infection, prodigiosan administered on the day before does not increase the survival rate of the animals.

In the following group of experiments, the dose of prodigiosan, administered on the day before, was increased five-fold, while the dose of acetoxan A or B, administered on the following day simultaneously with infection, was halved. In this experiment, the survival rate of the mice was high—69 and 56%.

From the data obtained it followed that when the dose of prodigiosan administered on the day before is increased, the protective-adaptive responses are stimulated to a sufficient degree so as to eliminate their inhibition, which sets in when the mice are infected simultaneously with the injection of acetoxan A or B. However, it was sufficient to administer the usual effective dose of acetoxan A (200 μg) or prodigiosan (2 μg) to the animals on the day before infection, in order to guarantee high survival rate of mice infected simultaneously with the administration of an increased dose of prodigiosan (10 μg), i.e., to eliminate the inhibition of the protective responses, noted under these conditions without preliminary injection of prodigiosan.

The results obtained may be explained by the fact that acetoxan A stimulates a broader complex of protective responses, related to the resistance of the animals to bacterial sepsis, and to a greater degree than the other two polysaccharides. Acetoxan B stimulates only part of them, and to a lesser degree, while prodigiosan evidently acts upon them even less.

The difference in the action of the acetoxans and prodigiosan is not limited to the examples cited above. It was established that acetoxan A, acetoxan B, and glucan, which increase the resistance of animals to infections, also promote a normalization of the permeability of the blood vessels, increased under the influence of irritants that induce an inflammatory reaction [1]. At the same time, polyglucin exerts the same effect, in spite of the fact that it does not increase the resistance of the animals to infections, while polysaccharide K-12, which extremely actively increases the resistance to infections, not only does not normalize the permeability of the vessels, but rather intensifies the effect of the irritant, increasing the necrotic degeneration of the irritated portion of the tissue, like levan [6]. The indicated differences in the effects of individual biologically active polysaccharides are evidently due to a difference in their structure.

A further decipherment of the dependence of the nature of the effects of individual polysaccharides upon their chemical structure is of great importance, both from the theoretical standpoint, and for the development of indications for their practical application.

LITERATURE CITED

1. A. I. Braude, G. E. Vaisberg, T. I. Afanas'eva, et al., Antibiotiki, No. 6 (1960), p. 91.
2. G. E. Vaisberg, T. I. Afanas'eva, and N. I. Givental', in book: Carbohydrates and Carbohydrate Metabolism [in Russian], Moscow (1962), p. 270.
3. G. E. Vaisberg, T. I. Afanas'eva, N. I. Givental', et al., Dokl. AN SSSR, 146, No. 5 (1962), p. 1233.
4. Z. V. Ermol'eva, G. E. Vaisberg, T. I. Afanas'eva, et al., Antibiotiki, No. 6 (1958), p. 46.
5. M. Landy and I. Pillemer, J. Exp. Med., 104 (1956), p. 383.
6. M. Shilo and B. Wolman, J. Exp. Path., 39 (1958), p. 652.