THE PROTECTIVE ACTION OF PRODIGIOSAN IN EXPERIMENTAL INFECTION

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Numerous investigators have noted the ability of the polysaccharide complexes of various microorganisms to produce marked stimulation of the protective reactions of the living organism [3,7,11,14-17].

The object of the present investigation was to study the biological activity of prodigiosan, a polysaccharide complex isolated from Bacterium prodigiosum in the laboratory directed by Z. V. Ermol'eva, because during the last few years, the authors have made a systematic study of various substances (benzimidazole derivatives, antibiotics, vitamins, polysaccharide, etc.) exhibiting a prophylactic action in certain infections. It was also decided to study the combined action of prodigiosan and vitamins B_1, B_6, and B_{12}; according to some reports in the literature, the administration of these vitamins alone increases the resistance of the organism to infection [9,10,12,13,18], while according to other reports [6], the course of infections is aggravated.

EXPERIMENTAL METHOD

The experiments to study the effect of prodigiosan on infection caused by Salmonella typhimurium were carried out on 120 albino mice weighing 18-20 g. Before the beginning of the experiment, the animals received a single subcutaneous injection of prodigiosan (1 μg/g), prodigiosan together with vitamins B_1, B_6, and B_{12}, or the vitamins alone, after which all the animals were infected with 1 LD_{100} of S. typhimurium (4000 bacterial cells) subcutaneously in the region of the right inguinal gland. The index showing the effectiveness of the action of the preparations was the mean survival period of the mice. The animals which died were autopsied and material from their internal organs seeded on Endo's medium for bacteriological control purposes.

The humoral factors of natural immunity were investigated in 32 guinea pigs and 150 albino mice. In experiments on the former, the concentration of normal antibodies and the titer of complement were studied by the usual methods. The preventive activity of the blood serum of guinea pigs receiving prodigiosan (1 μg/g, subcutaneously) was also determined, for which the serum of these animals was injected intraperitoneally into albino mice. One hour after injection of the serum, these mice were infected intraperitoneally with 1 LD_{50} (50 million cells) of a culture of Bacterium pyocyaneum. The test sera were pooled in pairs and injected into mice in doses of 0.2 ml of a 1:2 dilution. Prodigiosan (batch 266), obtained from the laboratory directed by Z. V. Ermol'eva,was used in the experiment*.

EXPERIMENTAL RESULTS

The experimental results are given in the table, which shows that statistically significant differences in the increase of the survival period of the mice were observed in the group of animals receiving prodigiosan or prodigiosan together with vitamins. Combined administration of the preparations had no advantage over administration of prodigiosan alone. These results indicating the protective effects of prodigiosan in infections agreed with and supplemented findings reported in the literature [2,5].

The main points of the dynamics of the changes in the concentration of normal antibodies in the guinea pigs after receiving prodigiosan are illustrated in the figure. Injection of prodigiosan stimulated the production of normal typhoid and dysentery (Shigella flexneri C) agglutinins. The differences from the control were statistically significant. These results, together with those indicating an increase in the opsonic properties of the serum following administration of prodigiosan [4], may be useful for elucidation of the mechanism of nonspecific immunity.

Interesting results were obtained by the study of the preventive activity of guinea pigs' serum under the influence of prodigiosan. All seven pairs of sera from animals receiving a preliminary (three days beforehand) injection

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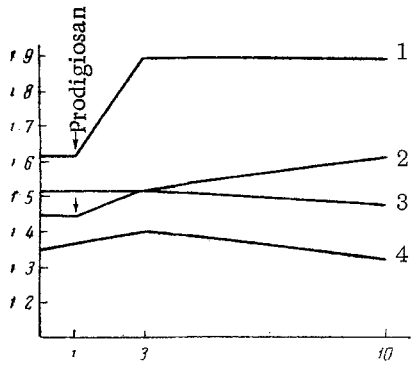

Effect of prodigiosan on production of normal agglutinins. Along the axis of abscissas — times of observation (in days). Along the axis of ordinates — titer of antibodies (geometrical mean). 1 and 3) typhoid antibodies (control and experiment, respectively); 2 and 4) S. flexneri antibodies (control and experiment, respectively).

Protective Action of Prodigiosan in Infection Caused by Injection of S. typhimurium into Albino Mice

No.	Preparation	No. of animals in group	Mean survival period (in days)	P
1	Physiological saline	30	4.5 ± 0.4	—
2	Prodigiosan	30	6.7 ± 0.4	<0.01
3	Prodigiosan + vitamins	30	6.5 ± 0.4	<0.01
4	Vitamins B_1, B_6, B_{12}	30	5.6 ± 0.4	>0.05

of prodigiosan gave 100% protective effect, whereas in the control animals only four pairs of sera from the seven studied acted in this way. A statistical analysis of these results using the criterion of signs [1] demonstrated that prodigiosan produced a significant increase in the preventive activity of the guinea pigs' sera during infection.

No regular pattern could be observed in the changes in the complement titer of the guinea pigs' serum under the influence of injections of prodigiosan.

It is concluded from these findings that the protective effect of prodigiosan may be explained to some extent by the increased preventive power of the serum, as revealed in experiments with infection of mice by B. pyocyaneum. It may fairly be asked what is responsible for the increase in the preventive properties of the serum of the guinea pigs receiving prodigiosan. Unfortunately, a complete answer to this question is not yet possible. A parallel investigation of the complement titer of the serum of the experimental animals ruled out the possibility that this humoral factor of immunity was of decisive importance in these experiments, because no significant changes in this index were observed. The stimulation of the production of agglutinins by prodigiosan, which was observed, could however be attributed to some extent to this factor, but since the question of the protective function of normal antibodies still remained unanswered [9], it does not seem possible to use this fact as a valid argument.

Hence, it may be concluded from the comparison of all the results obtained that the mechanism of the protective action of prodigiosan in infection is much more complex than is apparent at first glance, and for this reason further studies of prodigiosan must be carried out.

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