

BIOLOGICAL ACTIVITY OF LIPIDS AND POLYSACCHARIDES OF YEAST-LIKE FUNGI

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During recent years the problem of moniliasis has attracted the serious attention of investigators in various specialties. The overwhelming majority of their researches have been concerned with the ecology and pathogenicity of yeast-like fungi of the genus *Candida* and with the changes which they produce in the organism. Little work has been done on the study of the biochemistry of these fungi and, in particular, of their biological activity. We have studied the polysaccharides and lipids isolated from some species of *Candida*.

An important place in the structure of the cells of the yeast-like fungi is occupied by polysaccharides, which constitute the determinant group of the antigens of these microorganisms. They account on the average for 2.5-4% of the dry weight. The polysaccharide preparations obtained by hydrolysis of the cells with β -naphthol [1] consist of a white powder, odorless and soluble in water and physiological saline. Chemical analysis shows that the polysaccharides from *Candida* cells are mainly mannans [2].

In immunological reactions the polysaccharides behave as haptens of high activity and of marked specificity. In the precipitation reaction, for example, their titers may reach 1:100,000-1:2,000,000, and in the complement fixation reaction—1:1,000,000-1:100,000,000. The optimal dilution for the intradermal tests was 1:1000.

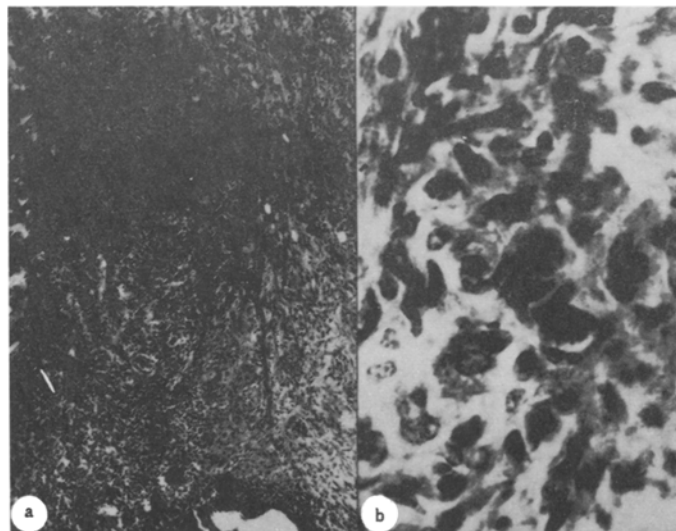
A pharmacological investigation of the polysaccharide preparation from *Candida albicans* [4] showed that it is practically nontoxic and has no side action on the arterial pressure and respiration.

METHOD

To elucidate the character of the reaction of the host's tissues, two series of experiments were carried out on 32 guinea pigs receiving subcutaneous injections of polysaccharides obtained from *Candida albicans*. These substances were injected on a cotton thread, 0.41-0.45 mm thick, preliminarily soaked in a thick suspension of the polysaccharides in physiological saline. The thread was introduced into the lumen of a long injection needle, so that none of the test substance should be lost during passage through the animal's tissues.

RESULTS

A focus of inflammation developed immediately after the beginning of the experiment at the sites of injection of the polysaccharides. A few small groups of leukocytes were observed after 3-5 h. Sometimes a few isolated Gram-negative particles could be seen, staining pink with Shabadash's method. In size and shape they resembled yeast-like fungi. After 1-2 days the groups of leukocytes were still present in these areas, but they were now intermingled with a small number of macrophages. After 4 days foci of proliferation of polyblasts, elongated in shape, and individual giant cells of foreign-body type were observed. A few leukocytes were present here, too, especially in the center of the foci. In the later stages the inflammatory foci gradually disappeared. In the animals in the second series of experiments the changes were more marked than in the animals in the first series. Histological



Focus of inflammation developing on the 7th day around a thread soaked with lipids of *Candida albicans*. a) General appearance, 70 \times ; b) detail of preparation: granulation tissue rich in endothelioid cells, 770 \times . Photomicrograph. Shabadash's stain.

examinations were carried out only after the inflammatory process had attained its maximum, i.e., on the 7th day. A thick exudate was present in these guinea pigs close to and inside the thread, consisting mainly of disintegrating leukocytes. Nearer to the periphery large mononuclear cells with lightly stained cytoplasm began to predominate, and when stained by Shabadash's method red inclusions were often seen in their cytoplasm. In some places small areas of proliferation of young granulation tissue were seen.

The lipid content of the cells of the yeast-like fungi is dependent on the species of the microorganism; its average value is 5-7% of the dry weight, of which 1.25-2.44% of the dry weight is accounted for by free lipids. They are dark yellow substances with a peculiar odor, and solid or semisolid in consistency at room temperature. Chemical analysis showed that the lipids of *Candida albicans*, *C. tropicalis*, and *C. pseudotropicalis* are composed of stearic, palmitic, lauric, petroselenic, and linoleic acids. The lipids of *C. krusei* also contain linolenic acid but not stearic acid.

The lipids of the yeast-like fungi do not possess antigenic properties and have no effect on the results of serological reactions in vitro [3].

These lipids are toxic. Intravenous injection of an emulsion containing 5 mg of the substance into mice causes instantaneous death; a dose of 2.5 mg causes convulsions in mice, with difficulty in breathing. Intraperitoneal injection of lipids in doses of 5 and 10 mg per mouse causes death of the animals 24-48 h after injection. In control experiments in which sunflower oil was injected in the same dose and by the same method, the mice remained alive.

The lipids of *Candida* influence the phagocytosis of homologous organisms. This effect is dependent on the concentration of the lipid and on its degree of dispersion. With a small concentration of lipids (0.02%) the process of phagocytosis is activated. This action is nonspecific and is dependent on the surface activity of the lipids. This is confirmed by control experiments carried out with vegetable oils.

The reaction of the host to injection of the lipids was next investigated. Experiments were carried out on the same number of guinea pigs, by the same method as was used to study the polysaccharides, with the exception that the thread was soaked differently: the lipids were first dissolved in a mixture of ethyl alcohol and ether, and the thread was dried after it had been soaked.

The changes observed during histological examination were qualitatively similar to those described above, although a definite quantitative difference was noted. This most clearly seen in the experiments of the second series, in which the foci in the transverse sections on the 7th day after injection of the lipids measured $3.5-4 \times 1-2$ mm

compared with $2-3 \times 1-2$ mm at the site of injection of the polysaccharides and 0.6×0.7 mm around the control thread. Another difference was the much more marked zone of granulation tissue surrounding the central areas, where there were dense masses composed of disintegrating granulocytes. This zone was about 0.25 mm wide. Microscopic examination showed that it was rich in cells of epithelioid type (see figure), and sometimes giant cells were found here, resembling cells of Langhans, and not only foreign-body cells.

LITERATURE CITED

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
