MODERN STATE IN THE RESEARCH AND APPLICATION OF PROTEOLYTIC ENZYMES OF FUNGI

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Proteolytic enzymes are studied as tools for understanding protein structure and the mechanisms of enzymatic catalysis, or as well as bioactive substances applied in medicine, agriculture and industry.

The growing needs of biotechnology, changes in environmental and radiation backgrounds, widespread usage of drugs encourages the search for a new, effective, safe species and strains of fungi which could be the base for new probiotics production and serve in biotransformations of food products. In brewing, alcohol production, winemaking the proteases are used to remove various types of protein turbidity and accelerate filtration; in bakery industry they are applied to reduce the duration of batches in the production of custard bread; in cheese and curd making the proteases of *Cryphonectria parasitica* help in acceleration of its ripening. The milk-clotting enzyme of *C. parasitica* enhances hydrolysis of β-CN groups during storage of Mozzarella cheese in comparison to veal rennet or the milk-clotting enzyme of the fungus *Rhizomucor miehei*. The modern approach to replacement the enzyme of animal origin with fungal proteases is much more productive and profitably. Processing and softening meat, fish and their products are also under the proteolytic enzymes that facilitate and accelerate processing of intermediates, improves quality of end product (pronase preparations). Besides, alkaline and neutral proteases of the fungi *Aspergillus flavus* and *A. parasiticus* play a key role in soya sauce fermentation. Proteases are used in the food concentrate and canning industries for production of concentrates from hard-to-boil cereals, beans and peas.

Proteases found their application in chemical and light industries. In the textile industry, the process of tissue treatment with enzyme preparations of fungal proteases is speeded in 7-10 times. The same enzymes are used for sericin removal from unwinding cocoons of the mulberry silkworm during natural silk production. In the chemical industry proteases are added to detergents, besides, some proteases together with glucose oxidase and catalase used as components of toothpaste for antimicrobial action and prevention of caries.

The search of medicinal proteases producers should be done amongst the fungi as only the bacterium *Bacillus mesentericus* is applied for coating wounds nowadays. In medical practice, for treatment of burns is used the coating "Elastotherase immobilized" (as gauze napkins or bandages) based on the bacterial proteases. They fasten the healing of burns of II-IV degrees, trophic ulcers, bedsores and purulent wounds. In general, proteolytic enzymes of microorganisms can be used in medicine for treatment of liver diseases, frostbites, trophic ulcers and for acceleration of dead

tissues rejection and for cleaning purulent-necrotic plaques. Proteolytic complexes are also essential in antibacterial chemicals for processing surgical instruments and cleaning medical surfaces.

Proteases are tools in struggle with several serious diseases. Fungi of the genus *Candida albicans* (SAPS) are secreting asparagine proteinases. It was found that inhibitors of this protease, directed against asparagine proteinase of the viral origin are used in the treatment of HIV infection, could also inhibit *Candida* SAPS and reduced the incidence of candidiasis in such patients. So, the asparagine proteinases are an important target for development of new medicinal preparations based on protease inhibitors for the treatment of candidiasis. The other example is serine protease and its role in treatment of allergies. It is known that proteins from catalytic type of serine are allergens. The secreted alkaline serine protease of *A. fumigatus* has been shown to help avoid the host immune response by degrading human complement proteins and is, therefore, a good target for further development of anti-allergic drugs. Besides, associated with proteases metabolites of fungi could be used in cancer treatment. The thiol-protease specific inhibitor, E-64, originally isolated from the fungus *A. japonicus*, is being studied extensively as a potential antitumor agent in cell culture.

Thus, fungi are an important source of proteases and their inhibitors which are diverse in their structure and mechanisms of action. Proteases found numerous applications in medicine, industry and biotechnology. Variety of chemical and biological processes in which proteases have key importance encourages the search of new compounds and protease producers for biotechnology.

References

1. Braga-Silva L.A., Santos A.L. Aspartic protease inhibitors as potential anti-*Candida albicans* drugs: impacts on fungal biology, virulence and pathogenesis. *Curr Med Chem*. 2011. Vol.18 (16). P. 2401-19.

2. Ghosh A.K., Osswald H.L., Prato G. Recent Progress in the developent of HIV-1 protease inhibitors for the treatment of HIV/AIDS. *Journal of medicinal chemistry*. 2016. Vol. 59 (11). P. 5172–5208.

3. Kim S.Y., Gunasekaran S., Olson N.F. Combined use of chymosin and protease from *Cryphonectria parasitica* for control of meltability and firmness of cheddar cheese. *J Dairy Sci.* 2004. Vol. 87(2). P. 274-83. URL: doi: 10.3168/jds.S0022-0302(04)73166-5.

4. Suwannarach N., Kumla J., Sujarit K. *et al*. Natural bioactive compounds from fungi as potential candidates for protease inhibitors and immunomodulators to apply for coronaviruses. *Molecules*. 2020. Vol. (25 (8). P.1800.

5. Варбанець Л.Д., Мацелюх О.В. Протеолітичні ферменти мікроорганізмів та методи їх дослідження: монографія. Київ. 2008. 108 с.