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ANTITUMOR ACTIVITY OF ACTINOBACTERIA

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Abstract. *Actinomycetes are the most powerful source for the production of secondary metabolites, antibiotics and other bioactive compounds. Analysis of the literature showed that marine actinomycetes have a significant effect on the proliferative activity of tumor cells and can be potential sources of new anticancer drugs.*

Keywords: *marine actinobacteria, exometabolites, antitumor activity.*

Introduction. The annual increase in the level of oncological morbidity in the world, and in particular in Ukraine, prompts scientists to search for new and effective solutions for the treatment of oncological diseases. Today, actinobacteria are a promising source of clinically useful anticancer drugs.

The purpose of the work was to analyze the literature devoted to the study of the antitumor activity of actinobacteria.

Results and discussion. Actinobacteria represent one of the largest groups of prokaryotic microorganisms, which includes gram-positive bacteria with a content of more than fifty-five percent guanine and cytosine, aerobic or anaerobic, filamentous, spore-forming bacteria that are widely distributed in aquatic and terrestrial environments. Actinomycetes are the most powerful source for the production of secondary metabolites, antibiotics and other bioactive compounds. Analysis of the literature showed that actinomycetes are potential sources of new anticancer drugs [1].

Recently, much attention has been paid to the isolation of rare actinomycetes from various extreme environments. It was established that each strain of actinomycetes has the ability to produce up to 20 secondary metabolites. Along with significant antimicrobial activity, secondary metabolites of marine actinobacteria also exhibit cytotoxic effects. For example, exometabolites of Black Sea strains of actinobacteria *Streptomyces* sp. Lim 9.2 and *Streptomyces* sp. Lim 10 at a concentration of 25.0 - 500.0 µg/ml showed a pronounced cytotoxic antiproliferative effect on tumor cultures of human cells - rhabdomyosarcoma (RD) and adenocarcinoma of the larynx (Hep-2). The antitumor activity of marine bacteria can be associated with campechic acid,

cyanophycin and mirabilite found in the metabolome. Campechic acid belongs to antitumor agents and is an inhibitor of tumor cell metastasis. Cyanophycin, due to its ability to inhibit the growth of tumors, has attracted attention for a long time, since one type of cyanobacterial compounds, dolastatin, has already proven itself well in clinical practice. Cytotoxic activity of exometabolites of *Streptomyces* sp. Lim 10 can be explained by the action of the apoptosis inducer staurosporine together with its structural homologues [1].

The actinomycete strain *S. bingchenggensis* ULS14 isolated from the Lagos lagoon showed cytotoxic activity. Two purified bioactive compounds were isolated from it - ULDF4 and ULDF5. The antitumor activity of ULDF5 against the HeLa cell line was higher than that of ULDF4. Cytotoxicity of 5-(2,4-dimethylbenzyl)pyrrolidin-2-one (DMBPO) extracted from marine bacteria *Streptomyces* VITSVK5 spp. was established on Hep G2 and HEP-2 cell lines. isolated from samples collected on the Marakkanam coast of the Bay of Bengal [2].

Cytostatic compounds of marine origin are extremely diverse in chemical structure. Among them are known alkaloids, terpenes, amino carbohydrates, polyketides, non-ribosomal peptides and nucleoside compounds, etc. [3]. A number of metabolites of representatives of marine microbiota are unique in their structure. In the strain *Streptomyces* sp. KMM 9048 revealed specific variants of antitumor antibiotics of the aureolic acid group [4].

A representative of the genus *Streptomonospora* from the group of "rare actinomycetes" from the littoral of the Wadden Sea revealed new cytotoxic bacteriocins from the group of thiopeptides - litoralimycins [5]. Among microbial exometabolites of marine origin, they are unique not only in structure, but also in mechanism of action. For example, polyketide compounds of the salinisporamide group are known for representatives of the genus *Salinispora*, native to the sea, which are capable of antitumor action through specific inhibition of the proteasome. In the polyketides of the group of manumycins, produced by marine representatives of the genus *Streptomyces*, an extremely rare mechanism of action based on the type of "molecular glue" was found. They act by forming a covalent bridge between UBR7 ligase molecules and an abnormal variant of the TP53 protein characteristic of breast cancer cells, which leads to tumor cell apoptosis [6].

Conclusions. According to the literature, exometabolites of marine actinobacteria show antitumor activity in in vitro experiments and may be promising for the development of medicinal antitumor drugs.

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ПРОТИПУХЛИННА АКТИВНІСТЬ АКТИНОБАКТЕРІЙ

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Анотація. *Актиноміцети є найпотужнішим джерелом вторинних метаболітів, антибіотиків та інших біологічно активних речовин. Аналіз літературних даних показав, що морські актиноміцети мають значні ефекти на проліферативну активність пухлинних клітин і можуть бути потенційними продуцентами нових протипухлинних препаратів.*

Ключові слова: *морські актинобактерії, екзометаболіти, протипухлинна активність.*

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