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Antitumor and antimicrobial activity of exometabolites of Black Sea actinobacteria

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Background/Aim. In connection with the growing incidence of cancer in the world and in Ukraine [1], in search of compounds with antitumour and antimicrobial activity, scientists have turned their attention to the world's oceans, since marine actinobacteria produce unique types of secondary metabolites [2]. The **aim** is to determine the biotechnological potential of marine actinobacteria in order to assess the prospects for their use as producers of antibiotics and antitumour compounds in the biotechnology of new drugs. **Methods.** Secondary exometabolites of the strains *Streptomyces* sp. Lim9.2 and *Streptomyces* sp. Lim10, isolated from mussel fouling collected in the Odessa Bay of the Black Sea, were used as material for the study. To obtain exometabolites, actinobacterial cultures were grown on a rotary shaker in tryptic soy broth for 72 h at 28 °C and in soy-glucose medium for 7 days until the stationary phase of growth was reached. The culture fluid was separated from the cell mass by centrifugation. The exometabolites were extracted with ethyl acetate with stirring for 2 h, separated from the culture fluid and evaporated. Stock solutions of the extracts were prepared in dimethylsulfoxide and working solutions were prepared on cell culture medium. Sterilisation was performed using membrane filters with a pore diameter of 0.22 μm [3]. The cytotoxic properties of the exometabolites were investigated in a model of human tumour cell cultures — laryngeal carcinoma Hep-2 and rhabdomyosarcoma RD. To determine the antimicrobial activity, 7 test strains of bacteria were used: *S. aureus* ATCC25923, *E. coli* ATCC25922, *P. vulgaris* ATCC6896, *S. enterica* NCTC6017, *P. aeruginosa* ATCC27853, *P. putida* KT2440, *C. albicans* ATCC18804. **Results.** Exometabolites of strains Lim9.2 and Lim10 showed antitumor potential in a wide range of concentrations (from 25 to 500 μg/ml) against Hep-2 and RD tumor cells. Metabolomic analysis showed that strains Lim9.2 and Lim10 produce staurosporine, apoptosis inducers, and cytotoxic compounds of marinoquinoline. Exometabolites of actinobacteria possessed antimicrobial potential against opportunistic bacteria. Exometabolites of the Lim10 strain, a producer of organic peroxides of the manadodioxane group, inhibited *P. aeruginosa* ATCC27853, *P. putida* KT2440 and *P. vulgaris* ATCC6896 more than exometabolites of the Lim9.2 strain. **Conclusions.** The Black Sea strains of actinobacteria Lim9.2 and Lim10 are promising producers of antitumor compounds and antibiotics and can be recommended for use in the biotechnology of new drugs.

K e y w o r d s: marine streptomycetes, exometabolites, antimicrobial and cytotoxic activity, tumour cell cultures.

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