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ANTAGONISTIC ACTIVITY OF ACTINOBACTERIA ISOLATED FROM SPONGES *HALICLONA* SPP. ODESA BAY

The marine ecosystem is a promising source for discovering the producers of totally new bioactive compounds. Among the significant biodiversity, actinobacteria also are known by huge antagonistic potential. ***Aim.*** *To study the antagonistic activity of actinobacteria isolated from marine sponges Haliclona spp. against the strains of indicator prokaryotic and eukaryotic microorganisms.* ***Methods.*** *Antagonistic activity of actinobacteria isolated from marine sponges Haliclona spp. against Staphylococcus aureus ATCC 25923, Micrococcus luteus ATCC 4698, Enterococcus faecalis ATCC 29212, Bacillus subtilis ATCC 6633, Kocuria rhizophila DSM 348, Escherichia coli ATCC 25922, Proteus vulgaris ATCC 6896, Salmonella enterica NCTC 6017, Klebsiella pneumoniae ATCC 10031, Pseudomonas aeruginosa ATCC 27853, Pseudomonas putida KT 2440 and Candida albicans ATCC 18804 were determined in vitro by the block method.* ***Results.*** *Thirteen from fourteen strains of actinobacteria inhibit the growth of at least one strain of the indicator microorganism. The most active strains of actinobacteria were Hal 2 and Hal 14, that significantly inhibit the growth of fifth strains of indicator microorganisms, the spectrum of which were differed. Strain Hal 2 has ability to inhibit the growth of S. aureus ATCC 25923, M. luteus ATCC 4698, E. faecalis ATCC 29212, K. rhizophila DSM 348, P. aeruginosa ATCC 27853 and C. albicans ATCC 18804, strain Hal 14 inhibit all Gram-positive bacteria, including B. subtilis ATCC 6633. K. rhizophila DSM 348, M. luteus ATCC 4698 and P. aeruginosa ATCC 27853 shown the impressive sensitivity to the studied strains of actinobacteria. The growth of P. aeruginosa was inhibited by ten strains of actinobacteria. Four strains of actinobacteria (Hal 2, Hal 4, Hal 5 and Hal 6) inhibit the growth of C. albicans ATCC 18804 with different intensity. All the indicators of the family Enterobacteriaceae and P. putida KT 2440 were resistant to the studied strains of actinobacteria.* ***Conclusions.*** *Strains of actinobacteria isolated from marine sponges Haliclona spp. inhibit the growth of indicator strains of prokaryotic and eukaryotic microorganisms. S. aureus ATCC 25923, M. luteus ATCC 4698, E. faecalis ATCC 29212, K. rhizophila DSM 348, P. aeruginosa ATCC 27853 and C. albicans ATCC 18804 are the most sensitive to the antagonistic action of actinobacteria. Strains of actinobacteria Hal 2, Hal 4 and Hal 14, which suppressed the ability to grow of-the large quantity of indicator microorganisms with significant zones of inhibition of the growth, were chosen for further studies of the spectrum and properties of their secondary metabolites.*

Key words: actinobacteria, antagonistic activity, indicator microorganisms, marine sponges Haliclona spp.

Discovering and "introduction" to the medical practice of new antibiotics and synthetic antibacterial and antiviral drugs remains one of the main problems of medicine, since infectious diseases occupy a leading place in human pathology [13]. Despite significant progress in medicine, diagnosis and treatment of infectious diseases, pathogenic microorganisms are still pose a serious threat to human health. This is happened due to the rapidly developing resistance to new antibiotics in the majority of both Gram-positive and Gram-negative pathogenic microorganisms [12]. Therefore, there is a problem of new antibiotic substances necessary to counteract and stop the spread of resistant pathogens. The strategy of creating new synthetic antibiotics by modifying existing natural ones does not "justify itself": as occurs, the pathogenic microorganisms are quickly adapts to the new drugs [9]. A number of promising strategies for the searching the new antibiotic substances are connected with the use of metabolic products of marine microorganisms [15].

Actinobacteria plays a significant role in the production of various antimicrobial agents. Actinobacteria have an ability to synthesized a wide range of biologically active compounds with various chemical structures. Today, actinobacteria are the producers of more than 65% of the antibiotics used in pharmacology [7]. The most producers were isolated from terrestrial ecosystems, while actinobacteria, from marine sources, have not been sufficiently studied in this aspect. The marine environment conditions differ significantly from the terrestrial environment, and marine actinobacteria, they have characteristics that differ from the terrestrial representatives. Therefore, there is good reason to believe that they may produce compounds with different chemical structures and mechanisms of action [6, 12]. In recent years, there have been quite a lot of publications about studding the secondary metabolites activity of actinobacteria isolated from the marine environment [5, 6, 7, 8, 12].

The aim of this work was to study the antagonistic activity of actinobacteria isolated from marine sponges *Haliclona* spp. against the strains of indicator prokaryotic and eukaryotic microorganisms.

Materials and Methods

Fourteen strains of actinobacteria were studied of their antagonistic activity. The strains were isolated from marine sponges *Haliclona* spp. (Class *Demospongiae*, Order *Haplosclerida*, Family *Chalinidae*), collected using scuba gear at a depth of 5–6 m in the Odesa Bay of the Black Sea (46°27′01′′N 30°46′14′′E) at a distance of 300–400 m from the shore by a PhD Kovtun O. O. in 2022.

The antagonistic activity of actinobacteria against indicator strains of prokaryotic and eukaryotic microorganisms was determined *in vitro* by the block method, which is based on the ability of the producer's metabolites to diffuse into agar media and inhibit the growth of sensitive microorganisms [1].

Actinobacteria were grown on Gause2 agar medium in Petri dishes for 12 days at 30 °C. Indicator strains of Gram-positive bacteria: *Staphylococcus aureus* ATCC 25923, *Micrococcus luteus* ATCC 4698, *Enterococcus faecalis* ATCC 29212, *Bacillus subtilis* ATCC 6633, *Kocuria rhizophila* DSM 348, Gram-negative bacteria: *Escherichia coli* ATCC 25922, *Proteus vulgaris* ATCC 6896, *Salmonella enterica* NCTC 6017, *Klebsiella pneumoniae* ATCC 10031, *Pseudomonas*

aeruginosa ATCC 27853*, Pseudomonas putida* KT 2440 and yeast-like fungus *Candida albicans* ATCC 18804 were used as test cultures. Indicator bacterial strains were grown in nutrient broth (GranuCult® Nutrient Broth, Merck KGaA, Darmstadt, Germany) at 37 °C, *Candida albicans* strain in liquid Sabouraud nutrient medium (NutriSelect® Plus Sabouraud-2% Dextrose Broth, Merck KGaA, Darmstadt, Germany) at 30 °C.

To prepare lawns of indicator microorganisms, 200 µl of daily culture (10^9 cells/ml) was added to 20 ml of molten semi-liquid medium nutrient agar (0.7% agar-agar) or, in the case of *C. albicans*, semi-liquid Sabouraud nutrient medium (with the same concentration of agar-agar), mixed and placed in a Petri dish. After solidification of the appropriate media with indicator microorganisms, agar blocks were cut from the 12-day cultures of actinobacteria and were placed on their surface. On each inoculated dish, 6 blocks of the studied actinobacteria were placed at the same distance from each other and from the edge of the Petri dish. As the controls the dishes inoculated with appropriate strains of indicator microorganisms without overlaying blocks with actinobacteria were used. The results were observing after cultivation at temperatures optimal for each group of microorganisms after 24 h (for bacteria) and 48 h (for *C. albicans*), every time checkoff the presence of inhibition zones of growth of the indicator strains [1, 2].

The experiment was carried out in triplicate. To analyze the results, descriptive statistics were carried out using the Microsoft Office Excel-2016 program.

Results and Discussion

One of the sources of new natural biologically active compounds can be sea sponges, which includes many microbes in their tissues. It is widely believed that a large number of bioactive compounds of sponges are the result of the joint action of symbiotic microorganisms, among which there are also actinobacteria [14].

The study of the antagonistic properties of 14 strains of actinobacteria (Hal 1 – Hal 14) isolated from sponges *Haliclona* spp., collected in the waters of the Odesa Bay of the Black Sea, showed that 13 studied strains inhibited the growth of at least one strain of indicator microorganisms. The growth of only one indicator microorganism was inhibited by 4 strains of actinobacteria, which accounted for 28.6% of all tested strains (Fig. 1).

Five (35.7%) strains prevented the growth of 3 indicators, two strains (14.3%) were the most active and prevented the growth of 5 strains of indicator microorganisms.

Not all studied strains of actinobacteria were equally active, which was visualized in the size of zones of no growth of sensitive indicator test-strains (Table).

As can be seen from the Table of the results, the sizes of the zones of inhibition of the growth of indicator microorganisms ranged from 11.3±0.1 mm (under the influence of the Hal 13 strain on *S. aureus* ATCC 25923) to 27.4±0.2 mm (under the influence of the Hal 2 strain on *P. aeruginosa* ATCC 27853).

The sizes of the zones of growth inhibition depended on the specific strain of both actinobacteria and the indicator microorganism. The most active against indicator microorganisms were Hal 2 and Hal 14 strains, which prevented the growth of 5 indicator microorganisms, the spectrum of which differed.

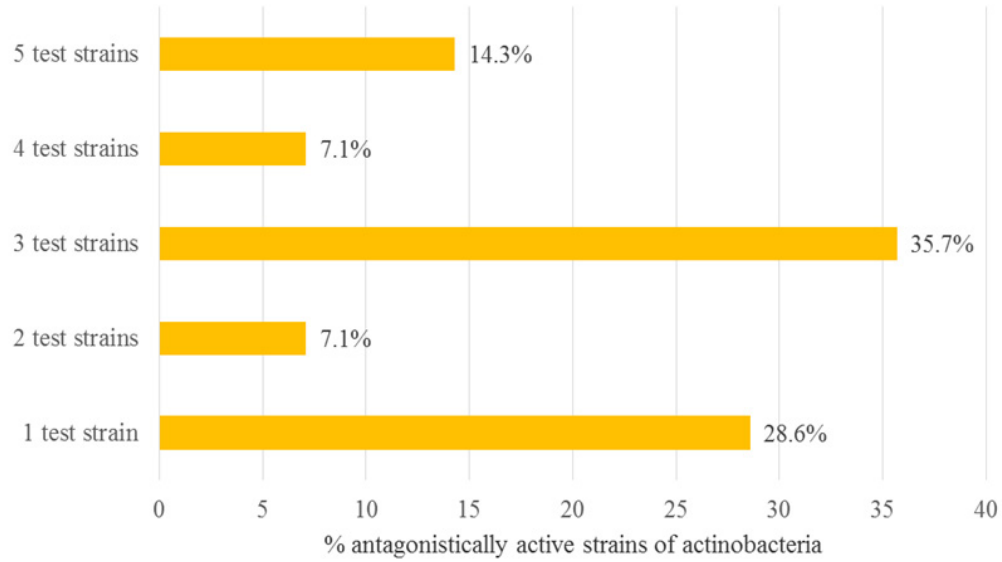

Fig. 1. The proportion of antagonistically active strains of actinobacteria isolated from marine sponges *Haliclona* spp.

So, if the Hal 2 strain suppressed the growth of Gram-positive (*S. aureus* ATCC 25923, *M. luteus* ATCC 4698, *E. faecalis* ATCC 29212, *K. rhizophila* DSM 348), Gram-negative (*P. aeruginosa* ATCC 27853) bacteria and yeast-like fungus *C. albicans* ATCC 18804, the Hal 14 strain inhibited only Gram-positive bacteria, including *B. subtilis* ATCC 6633. In addition, the zones of no growth of sensitive strains of indicator microorganisms under the action of these two strains of actinobacteria exceeded 17.0 mm, that is, these strains are quite antagonistically active. In addition to strains Hal 2 and Hal 14, the strains Hal 13 and Hal 7 attract attention, which inhibited the growth of *S. aureus* ATCC 25923 and *E. faecalis* ATCC 29212, respectively, as well as the Hal 4 strain, which inhibited the growth of 4 indicator microorganisms, including *P. aeruginosa* ATCC 27853 and *C. albicans* ATCC 18804.

Among the tested indicator microorganisms, *K. rhizophila* DSM 348, *M. luteus* ATCC 4698 and *P. aeruginosa* ATCC 27853 manifested the greatest sensitivity, the growth of which was inhibited with varying intensity by more than half of the investigated actinobacteria strains (Fig. 2).

The most sensitive occurred strain *P. aeruginosa* ATCC 27853, the growth of which was inhibited by 10 strains of actinobacteria, and the zones of absence of its growth ranged from 13.2±0.1 mm to 27.4±0.2 mm (Table). And if the detected antagonistic activity of actinobacteria against Gram-positive bacteria is quite predictable and is confirmed by the results of many publications [10, 11], the high sensitivity of *P. aeruginosa* ATCC 27853 is to some extent an unexpected and encouraging result and may be indirectly may indicate the synthesis of new bioactive compounds by actinobacteria isolated from marine sponges. Our assumptions are confirmed in relevant publications. In particular, in their research, Goel N. et al. (2023) showed that secondary metabolites of a rare halophilic

Table

Zones of nongrowth of indicator microorganisms (mm) under the action of actinobacteria isolated from marine sponges *Haliclona* spp.

Strain of actinobacteria	*B. subtilis* ATCC 6633	*E. faecalis* ATCC 29212	*K. rhizophila* DSM 348	*M. luteus* ATCC 4698	*S. aureus* ATCC 25923	*E. coli* ATCC 25922	*K. pneumoniae* ATCC 131	*P. vulgaris* ATCC 6896	*S. enterica* NCTC 6017	*P. aeruginosa* ATCC 27853	*P. putida* KT 2440	*C. albicans* ATCC 18804
Hal 1	0	0	20.6±0.2	21.8±0.2	0	0	0	0	0	20.5±0.2	0	0
Hal 2	0	0	22.8±0.2	25.5±0.2	17.2±0.1	0	0	0	0	27.4±0.2	0	23.4±0.2
Hal 3	0	0	0	0	0	0	0	0	0	24.5±0.2	0	0
Hal 4	0	0	16.2±0.2	22.1±0.2	0	0	0	0	0	18.5±0.1	0	23.2±0.2
Hal 5	0	0	0	13.7±0.1	0	0	0	0	0	17.3±0.2	0	18.4±0.1
Hal 6	0	0	0	0	0	0	0	0	0	18.8±0.2	0	13.2±0.1
Hal 7	0	23.8±0.2	0	0	0	0	0	0	0	0	0	0
Hal 8	0	0	0	0	0	0	0	0	0	0	0	0
Hal 9	0	0	11.4±0.1	19.2±0.1	0	0	0	0	0	24.5±0.2	0	0
Hal 10	0	0	0	0	0	0	0	0	0	26.1±0.2	0	0
Hal 11	0	0	0	0	0	0	0	0	0	25.9±0.2	0	0
Hal 12	0	0	18.8±0.1	24.7±0.2	0	0	0	0	0	13.2±0.1	0	0
Hal 13	0	0	20.2±0.2	19.4±0.1	11.3±0.1	0	0	0	0	0	0	0
Hal 14	19.6±0.2	20.9±0.3	24.6±0.2	27.0±0.2	19.5±0.1	0	0	0	0	0	0	0

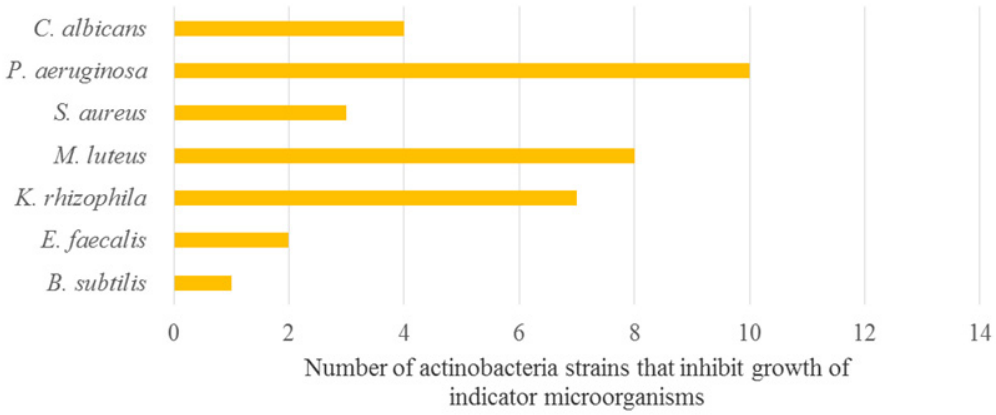

Fig. 2. The number of actinobacteria strains that shown the antagonistic effect against indicator microorganisms

actinobacterium, *Nocardiopsis lucentensis* EMB25, inhibited and destroyed biofilms of the *P. aeruginosa* PseA museum strain and clinical *P. aeruginosa* isolates [4]. The bioactivity of metabolites from actinobacteria isolated from the Red Sea against a wide range of microorganisms, including *P. aeruginosa* ATCC 9027, is discussed in the publication Osman M. E. et al. (2022) [10]. At the same time, another member of the family *Pseudomonadaceae*, *P. putida* KT 2440, was resistant to the investigated strains of actinobacteria. All representatives of the family *Enterobacteriaceae,* taken for the study, were also resistant (Table). Instead, the eukaryotic microorganism *C. albicans* ATCC 18804 turned out to be sensitive to the antagonistic action of actinobacterial strains Hal 2, Hal 4, Hal 5 and Hal 6. At the same time, the zones of absence of its growth due to the influence of strains Hal 2 and Hal 4 were quite large and amounted to 23.4 ± 0.2 mm and 23.2 ± 0.2 mm, respectively. Taking this into account, we can assume that there are the presence of metabolites with antibacterial and antifungal activities in the metabolic profile of the investigated strains of actinobacteria. The obtained data are combine with the results of Chakraborty B. et al. (2022), which detected significant antimicrobial activity in the *Streptomyces filamentosus* KS17 strain against a wide range of human pathogens, including *C. albicans*. This strain was isolated by the authors from a marine ecosystem in the Indian region [3]. In our previous studies on determining the antimicrobial potential of actinobacteria isolated from the biological fouling of natural shell rock and mussels of the Odesa Bay of the Black Sea, their significant activity against a wide range of indicator microorganisms was also established, especially in strains isolated from mussels [2].

Thus, taking into account the obtained results, the following conclusions can be made:

1. The investigated strains of actinobacteria, isolated from marine sponges *Haliclona* spp., are antagonistically active against indicator strains of prokaryotic and eukaryotic microorganisms.

2. Indicator strains of Gram-positive bacteria, as well as *P. aeruginosa* ATCC 27853 and C. *albicans* ATCC 18804, were most sensitive to the antagonistic effect of actinobacteria.

3. The most visualized antagonistic activity was identified in the strains of actinobacteria Hal 2, Hal 4 and Hal 14, which inhibited the growth of a large number of indicator microorganisms with significant zones of nongrowth. These three strains (Hal 2, Hal 4 and Hal 14) were chosen for further studies of the spectrum and properties of their secondary metabolites.

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АНТАГОНІСТИЧНА АКТИВНІСТЬ АКТИНОБАКТЕРІЙ, ВИДІЛЕНИХ ІЗ ГУБОК *HALICLONA* SPP. ОДЕСЬКОЇ ЗАТОКИ

Реферат

Морське середовище є перспективним джерелом для пошуку продуцентів нових біоактивних сполук. Серед значного біорізноманіття актинобактерії виділяються своїм метаболічним потенціалом. ***Мета.*** *Дослідити антагоністичну активність актинобактерій, виділених із морських губок Haliclona spp., щодо штамів індикаторних прокаріотичних і еукаріотичних мікроорганізмів.* ***Методи.*** *Антагоністичну активність актинобактерій, ізольованих з морських губок Haliclona spp. щодо Staphylococcus aureus ATCC 25923, Micrococcus luteus ATCC 4698, Enterococcus faecalis ATCC 29212, Bacillus subtilis ATCC 6633, Kocuria rhizophila DSM 348, Escherichia coli ATCC 25922, Proteus vulgaris ATCC 6896, Salmonella enterica NCTC 6017, Klebsiella pneumoniae ATCC 10031, Pseudomonas aeruginosa ATCC 27853, Pseudomonas putida KT 2440 та Candida albicans ATCC 18804 визначали in vitro методом блоків.* ***Результати.*** *Тринадцять із 14 досліджених штамів актинобактерій пригнічували ріст хоча б одного штаму індикаторного мікроорганізму. Найбільш активними були штами актинобактерій Hal 2 and Hal 14, які значно пригнічувати ріст 5 штамів індикаторних мікроорганізмів, спектр яких відрізнявся. Штам Hal 2 пригнічував ріст S. aureus ATCC 25923, M. luteus ATCC 4698, E. faecalis ATCC 29212, K. rhizophila DSM 348, P. aeruginosa ATCC 27853 та C. albicans ATCC 18804, штам Hal 14 пригнічував усі грампозитивні бактерії, у тому числі B. subtilis ATCC 6633. Найбільшу чутливість до досліджених штамів актинобакетрій виявили K. rhizophila DSM 348, M. luteus ATCC 4698 і P. aeruginosa ATCC 27853, ріст якого пригнічували 10 штамів актинобактерій. Чотири штами актинобактерій (Hal 2, Hal 4, Hal 5 та Hal 6) з різною інтенсивністю перешкоджали росту C. albicans ATCC 18804. Усі індикаторні представники родини Enterobacteriaceae та P. putida KT 2440 були нечутливі до дії досліджених штамів актинобактерій.* ***Висновки.*** *Штами актинобактерій, виділені із морських губок Haliclona sp., пригнічують ріст індикаторних штамів прокаріотичних та еукаріотичних мікроорганізмів. S. aureus ATCC 25923, M. luteus ATCC 4698, E. faecalis*

ATCC 29212, K. rhizophila DSM 348, P. aeruginosa ATCC 27853 і C. albicans ATCC 18804 є найбільш чутливими до антагоністичної дії актинобактерій. Штами актинобактерій Hal 2, Hal 4 і Hal 14, які пригнічували ріст великої кількості індикаторних мікроорганізмів зі значними зонами відсутності росту, відібрані для подальших досліджень спектру і властивостей їх вторинних метаболітів.

Ключові слова: актинобактерії, антагоністична активність, індикаторні мікроорганізми, морські губки Haliclona spp.

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