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# Modern chemistry of medicines

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# MODERN CHEMISTRY OF MEDICINES

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Збірник містить матеріали Міжнародної Internet-конференції «Modern chemistry of medicines» (18 травня 2023 р., м. Харків) присвячені висвітленню сучасних тенденцій створення оригінальних АФІ синтетичного та рослинного походження, фармацевтичної розробки, забезпечення якості лікарських засобів.

Для широкого кола наукових та практичних фахівців у галузі фармації та медицини, магістрантів, аспірантів, докторантів, співробітників фармацевтичних підприємств, викладачів закладів вищої освіти.



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## ЗМІСТ

# ANTIBACTERIAL ACTIVITY OF AMMONIUM HEXAFLUOROSILICATES: SOLVENT EFFECT ANALYSIS

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**Introduction**. One of the ten global problems of modern medicine behind the tribute of the World Health Organization is the growing antibiotic resistance (ABR) and the growing number of multi-resistant strains of bacteria. So, for the rest of the estimates in 2019, 1.27 million deaths in the whole world were directly related to infections resistant to drug diseases. For forecasts up to 2050, the ABR may predict up to 10 million deaths on a random basis. If you don't make any attempts to fight back from the ABR, you could end up wasting $3.4 trillion in US GDP on the river and throwing another 24 million people into extreme poverty in the coming decade.

It is urgent to search for new compounds that can have an antibacterial effect on bacteria, especially multi-resistant strains that pose a threat to human health and safety, among which are *E.coli, K.pneumonia, P.aeruginosa.*

Promising in this direction are chemical compounds - derivatives of ammonium hexafluorosilicate (AHFS).

**Aim** – study of antibacterial activity of AHFS against multiresistant strains of bacteria.

**Materials and methods.** Hexafluorosilicates I-XI were synthesized according to previously described methods. Hexafluorosilicates I-XI are I – octenidine; II – 2-pyridinepropionic acid hexafluorosilicate; III – 3-pyridinepropionic acid hexafluorosilicate; IV – 4-pyridinepropionic acid hexafluorosilicate; V – 2-aminoorenylacetic acid hexafluorosilicate; VI – 3-aminoorenylacetic acid hexafluorosilicate; VII – 4-aminoorenylacetic acid hexafluorosilicate; VIII – 3-hydroxymethylpyridinium hexafluorosilicate monohydrate; IX – 4-carboxymethylpyridinium hexafluorosilicate; X – 3-carboxymethylpyridinium hexafluorosilicate; XI – 4-hydroxymethylpyridinium hexafluorosilicate.

Methanol, ethanol and distilled water were used as solvents.

All chemical compounds with different solvents were tested against the following pathogens: wild-type ST307 (PBIO2003) (*E.coli*) compared to the mutants with nonspecific porin modifications (PBIO1806 and PBIO1807) – by performing the disk diffusion test. The disk diffusion test was performed as follows. Test discs (diameter 6 mm) were impregnated with 1 mg of each test substance by transferring 20 μl of solution (5 mg per 100 μl of solvent). The test disks were kept for 24 hours to evaporate the solvent. As a control, test discs impregnated with the same amount of the appropriate solvent were used. Petri dishes with appropriate nutrient medium and bacterial inoculum were prepared separately. After inoculation of bacteria in Petri dishes, soaked test discs were applied to agar. Then it was incubated for 24 hours at t 37 °C, after which the zone of inhibition of bacterial growth was measured. Each experiment was performed in 3 replicates.

**Results.** According to the results of the disc diffusion test, the following data were obtained.

For *ST307 (PBIO2003)* were obtained following data. The average value of inhibition bacterial growth (mm) for *methanolic solutions* of the investigated AGFS was: I – 17±1; II – 12±2; III – 6,3±0,57; IV – 11±1; V – 6±0; VI – 11,33±1,15; VII – 14,67±1,15; VIII – 8,67±1,15; IX – 7,67±1,53; X – 6±0; XI – 11,33±0,6.

The average value of bacterial growth delay for the *ethanol solutions* of the investigated AGFS was: I – 14,67±1,15; II – 7,67±0,58; III – 11±1; IV – 6,67±1,15; V – 19,33±1,15; VI – 14,33±1,53; VII – 11,67±0,58; VIII – 9,33±0,58; IX – 17,33±0,58; X – 7,33±1,15; XI – 15±1.

The average value of inhibition bacterial growth for *aqueous solutions* of the investigated AGFS was: I – 10±0; II – 16,33±1,53; III – 16±0; IV – 16,67±1,15; V – 6±0; VI – 15,67±1,15; VII – 14,67±1,15; VIII – 13,67±0,6; IX – 14,33±1,53; X – 14,33±1,15; XI – 13,33±0,6.

For *PBIO1806* were obtained following data. The average value of inhibition bacterial growth (mm) for *methanolic solutions* of the investigated AGFS was: I – 14±0; II – 8±1; III – 12±0; IV – 12,67±1,15; V – 6,67±1,15; VI – 13,33±1,16; VII – 13,33±0,6; VIII – 7±1; IX – 11±1; X – 6±0; XI – 13,33±0,6.

The average value of bacterial growth delay for the *ethanol solutions* of the investigated AGFS was: I – 15,67±1,15; II – 20,33±1,53; III – 16,67±1,15; IV – 16,67±1,15; V – 14,67±1,15; VI – 22±2; VII – 11±1; VIII – 9,3±0,6; IX – 9±0; X – 6±0; XI – 6±0.

The average value of inhibition bacterial growth for *aqueous solutions* of the investigated AGFS was: I – 11,67±0,6; II – 20,67±1,15; III – 18±0; IV – 20±0; V – 6,67±1,15; VI – 15,67±0,6; VII – 16,33±1,15; VIII – 17,33±0,6; IX – 18±0; X – 14±0; XI – 12,67±0,6.

For PBIO1807 were obtained following data. The average value of inhibition bacterial growth (mm) for *methanolic solutions* of the investigated AGFS was: I – 11,67±0,6; II – 6,67±0,6; III – 6±0; IV – 6±0; V – 6,33±0,6; VI – 12,33±0,6; VII – 13±1; VIII – 8,33±0,6; IX – 6±0; X – 6±0; XI – 8,33±0,6.

The average value of bacterial growth delay for the *ethanol solutions* of the investigated AGFS was: I – 12±0; II – 6±0; III – 11,33±1,15; IV – 6±0; V – 6±0; VI – 12±0; VII – 12,3±0,6; VIII – 6±0; IX – 6±0; X – 9,67±0,6; XI – 6,3±0,6.

The average value of inhibition bacterial growth for *aqueous solutions* of the investigated AGFS was: I –10,67±0,6; II – 18,67±1,15; III – 16±0; IV – 15,67±0,6; V – 6±0; VI – 14,67±0,6; VII – 11,67±0,6; VIII – 16,33±1,15; IX – 14,67±1,15; X – 16±0; XI – 8±0.

**Conclusions.** The results of the conducted studies indicate that almost all derivatives of aminohexafluorosilicates have antibacterial activity both against the wild strain and against mutant strains. However, even against the same bacterial strain, the activity of the same compound can vary significantly, which we attribute to the solvent used.

Therefore, the strongest antibacterial activity is found in aqueous solutions of the investigated AHFS, which, in our opinion, is related to the influence of the nature of the solvent on the efficiency of the release of fluoride ions, which provide the antibacterial effect, as a result of the hydrolysis of the $SiF_6^{2-}$ anion. In aqueous solutions, the degree of hydrolysis of the $SiF_6^{2-}$ anion is high and, accordingly, the maximum antibacterial effect of AGFS is observed, while in alcoholic solutions, hydrolysis is significantly suppressed.