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IN VITRO STUDY OF THE BIOLOGICAL ACTIVITY OF COMPLEX COMPOUNDS SYNTHESIZED BASED ON LEVOFLOXACIN

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Abstract. This study investigates the antibacterial activity of novel metal complexes synthesized using levofloxacin (LEV) as a ligand. The in vitro antimicrobial effects of these complexes were evaluated against three clinically significant bacterial strains: *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*. The synthesized copper(II), cobalt(II), and nickel(II) complexes of levofloxacin were tested using the agar well diffusion method at a fixed concentration of 35 µg/mL. The diameter of the bacterial growth inhibition zones was measured and compared to those produced by free levofloxacin and the corresponding metal salts. Results demonstrated that the metal complexes exhibited significantly enhanced antibacterial activity compared to levofloxacin alone, with the copper complex showing the highest efficacy. These findings suggest that metal complexation with levofloxacin can improve its antimicrobial potency and may serve as a promising strategy for developing more effective antibacterial agents..

Keywords: Levofloxacin, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa bacteria**.**

Introduction. Currently, due to global climate change, increasing pollution of the atmosphere and environment with various wastes has led to the rise of harmful microorganisms and the diseases they cause. This situation increases the need for antibiotics, which imposes on scientists in the fields of chemistry, biology, and pharmaceutical medicine the task of creating new and effective drugs, reducing their concentration, and increasing the scope of action [1]. Levofloxacin (LEV) [2-3] is one of the most effective fluoroquinolones, a biologically active compound that is used in medical practice as a drug, and is included in the group of broad-spectrum fluoroquinolones. It is used in the clinical treatment of many infections, such as chronic prostatitis, skin and soft tissue infections, lung and urinary tract infections [4-5]. It is known from the literature that in many cases, metallocomplex compounds of a particular drug are active relative to the free ligand [6]. From the research, metallocomplexes of LEV containing a pyridine ring, which have certain bioactive properties, have been synthesized and studied [7-8]. Therefore, the synthesis of LEV-based metal complexes and the investigation of their bioactivity remain pressing research areas.

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Research methodology. Chemicals, instruments and calculations. In this study, the antibacterial properties of levofloxacin and its synthesized metal complexes were evaluated in vitro on strains of Bacillus subtilis-5, Escherichia coli-221, Pseudomonas aeruginosa-225, Staphylococcus aureus-91, Candida albicans-247 obtained from the microbial culture collection at the Institute of Microbiology, Academy of Sciences of the Republic of Uzbekistan (ASRUz) [9].

Experimental part. Antibiotic resistance of microorganisms is currently emerging as a serious global medical problem. Antibiotic resistance of microorganisms significantly complicates the treatment of infections. Resistant strains place an excessive burden on the health system, increase the risk of mortality, and reduce the effectiveness of medical procedures such as surgery and cancer treatment. Therefore, it is necessary to develop effective antimicrobial therapies, as well as optimize existing antibiotics using chelation processes [10].

The antibacterial properties of levofloxacin and the synthesized complexes (labeled as Compounds 1-3) were tested in the laboratory of the "Collection of Microorganisms" of the Institute of Microbiology of the ASRUz. The experiments were conducted in vitro on strains of Bacillus subtilis, Escherichia coli, and Pseudomonas aeruginosa.

In the experiments, the antimicrobial activity of LEV, Cu-complex, Co-complex and Ni-complexes was evaluated using the "agar well diffusion" method. LEV, Cu-complex, Co-complex and Ni-complexes were used in the tests at the same concentration of 35 µg/ml. Levofloxacin was chosen as the control. Microorganisms were incubated at 28°C for 2 days, and then the inhibitory effect of synthetic compounds and antibiotics was evaluated by measuring the growth inhibition zone. All experiments were repeated five times, and statistical analysis was conducted with a significance level of P=0.05. In the study, standard strains of Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa were obtained from the collection of the Institute of Microbiology in Tashkent.

Antibacterial activity tests of the synthesized Cu-complex showed that the biological effect of the complex was significantly enhanced against LEV (Table 1, Figure 1). According to the data obtained, the activity of the complex against gram-negative Escherichia coli bacteria was 45% higher than that of levofloxacin.

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Antimicrobial activity of levofloxacin (LEV) and complex compounds synthesized on its basis (3-5 days)

№	Sample	Antagonistic activity d (growth inhibition zone), mm		
		Escherichia coli	*Bacillus subtilis*	*Pseudomonas aeruginosa*
0001	LEV (control)	20 ± 0,43	18 ± 0,41	16 ± 0,35
0002	$CuSO_4 \cdot 5H_2O$	16 ± 0,35	15 ± 0,65	15 ± 0,84
0003	$[LEVH_3]_2[Cu_3Cl_9(H_2O)_2]Cl$	29 ± 0,62	27 ± 0,26	26 ± 0,75
0001	LEV (control)	20 ± 0,43	18 ± 0,41	16 ± 0,35
0004	$CoCl_2 \cdot 2H_2O$	08 ± 0,25	07 ± 0,25	07 ± 0,15
0005	$[LEVH_2]_2 \cdot [CoCl_4] \cdot 2H_2O$	27 ± 0,41	24 ± 0,15	23 ± 0,65

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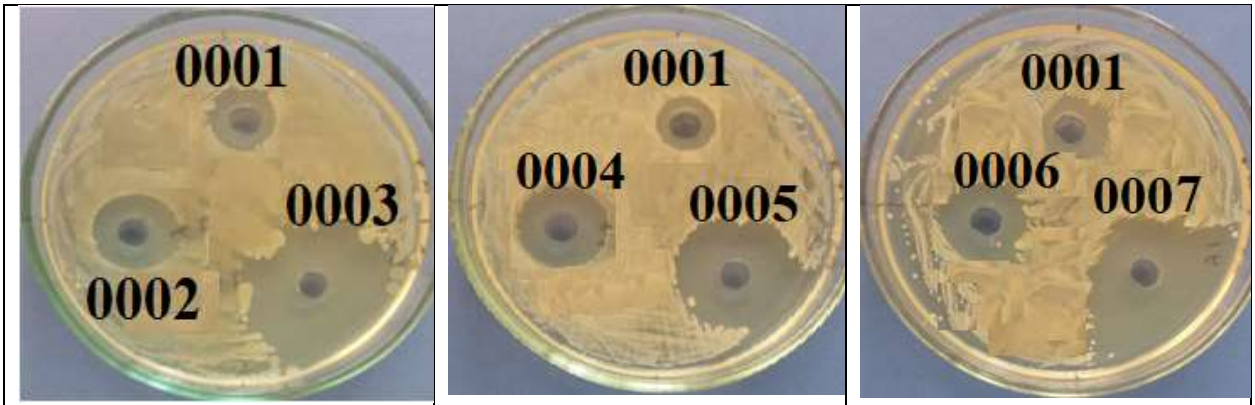
0001	LEV (control)	20 ± 0,43	18 ± 0,41	16 ± 0,35
0006	$NiSO_4 \cdot 7H_2O$	12 ± 0,36	10 ± 0,23	9 ± 0,95
0007	$[Ni(LEV)_2EDA] \cdot 7H_2O$	28 ± 0,55	26 ± 0,91	24 ± 0,10

In this study, Levofloxacin was selected as the control substance. At the same time, the results of the desired metal salts and complex compounds were studied together and compared. Metal salts showed a very poor result compared to LEV. However, our complex compounds showed a better result compared to LEV. For example: The activity results obtained for complexes with copper, cobalt and nickel metals against the gram-negative bacterium Escherichia coli were improved by 45%, 35% and 40% compared to the activity of levofloxacin, respectively. The activity of these complexes against Bacillus subtilis was improved by 50%, 33.3% and 44.4% compared to the activity of the ligand (LEV), respectively, while the activity against Pseudomonas aeruginosa was improved by 62.5%, 43.75% and 50% compared to the activity of the ligand (LEV). These findings confirm that the antibacterial activity of organic compounds can be enhanced through metal complexation.



Escherichia coli | *Bacillus subtilis* | *Pseudomonas aeruginosa*

Figure 1. Antibacterial activity of the cobalt complex against *Bacillus subtilis, Escherichia coli, and Pseudomonas aeruginosa.*

Although the antimicrobial effect of the Cu complex is similar to that of the Co complex and Ni complex, the result suggests that the presence of metal ions contributes significantly to the enhanced antimicrobial properties of the complexes..

The results obtained indicate that the antibacterial activity of the metal complexes is higher than that of levofloxacin. The activity of the copper complex against the bacteria Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa is significantly higher than that of the cobalt and nickel complexes.

The antibacterial activity of Cu, Co, and Ni complexes, respectively, is higher than that of levofloxacin, indicating that they may be more effective than traditional antibiotics in treating infections caused by various microbes.

Conclusion. As a result of the studies conducted, Levofloxacin was selected as the control substance and the results of the desired metal salts and complex compounds were compared. Metal

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salts showed very poor results compared to LEV, but our complex compounds showed better results compared to LEV.

It can be concluded that the antibacterial activity of the synthesized metal complexes exceeds that of levofloxacin alone, indicating that they may be more effective than traditional antibiotics in treating infections caused by various microbes.

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