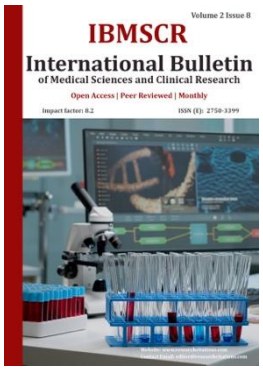

STUDY OF SPECIFIC ANTIMICROBIAL ACTIVITY OF FILM-COATED TABLETS OF CLARITHROMYCIN

Maksudova Firuza Khurshidovna
Nusratova Nozima Narzulloevna
Sultonova Rano Rakhimovna
Tashkent Pharmaceutical Institute
nozima9292@gmail.com
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Abstract. Research was conducted to assess the specific (antimicrobial) activity of film-coated tablets containing clarithromycin. The results showed that, according to the toxicity classification, this preparation is classified as low-toxic. It was ascertained that the preparation "Clarin" (250 mg and 500 mg) manufactured by Novugen Pharma LLC (Uzbekistan) has comparable specific activity compared to the similar preparation "Claricide" (250 mg and 500 mg) manufactured by Abbott Laboratories Ltd (Pakistan), indicating their biological equivalence.

Key words: clarithromycin, antibiotic, film-coated tablets, acute toxicity.

Introduction: Respiratory tract infections remain among the leading causes of morbidity and mortality worldwide. Clarithromycin, a semisynthetic, broad-spectrum macrolide antibiotic, occupies a significant place in modern antibacterial therapy. It is active against gram-positive and some gram-negative microorganisms, as well as atypical pathogens (Chlamydia pneumoniae, Mycoplasma pneumoniae, Legionella pneumophila) and Helicobacter pylori [1-3].

Clarithromycin is widely used in the treatment of community-acquired pneumonia, acute and chronic bronchitis, sinusitis, tonsillopharyngitis, and skin and soft tissue infections. It is also used in eradication regimens for gastric and duodenal ulcers. Its pharmacological action is based on the inhibition of protein synthesis in bacterial cells through reversible binding to the 50S subunit of the ribosome [2,3].

In recent years, increasing antibiotic resistance has been observed in microorganisms, necessitating the development of new clarithromycin dosage forms with improved pharmacokinetic properties, increased bioavailability, and better tolerability. Particular emphasis is placed on the development of film-coated tablets with extended or modified release [2,3,9].

According to the WHO, hundreds of millions of cases of bacterial respiratory infections are reported annually, with antibiotic resistance being a particularly pressing issue in low- and middle-income countries. Despite the widespread use of clarithromycin, improving its dosage forms to enhance therapeutic efficacy and reduce the risk of side effects remains a pressing issue.

In this regard, the Tashkent Pharmaceutical Institute, together with the manufacturing enterprise IP LLC Novugen Pharma, is conducting research on the development of film-coated tablets of clarithromycin in dosages of 250 mg and 500 mg [3,9].

One of the key stages in the pharmacological assessment of new antibiotic formulations is the study of their specific (antimicrobial) activity. This indicator reflects the preparation's ability to inhibit the growth and reproduction of susceptible microorganisms and is considered one of the main criteria for its therapeutic efficacy.

The aim of this stage of the study was to conduct a comparative analysis of the antimicrobial activity of the developed film-coated tablets of clarithromycin in doses of 250 mg and 500 mg compared with a standard sample of the substance and a reference preparation.

Materials and methods: The antimicrobial activity of the preparations was determined by the method of diffusion in agar on a dense nutrient medium, comparing the sizes of the inhibition zones of growth of test microorganisms formed under the influence of solutions of given concentrations of the standard sample and the preparation under study [4].

Sterile Petri dishes of uniform diameter with smooth, flat bottoms were used for the analysis. The dishes, placed horizontally, were inoculated with 20 ml of a nutrient medium of the specified composition, pre-inoculated with an 18-20-hour culture of test strains (Staphylococcus epidermidis, Escherichia coli, Bacillus subtilis, Pseudomonas aeruginosa). Appropriate nutrient media were used throughout the study to ensure optimal growth conditions for the microorganisms [5].

The inoculum was prepared using pure, 24-hour cultures of microorganisms grown on solid nutrient media. Several identical, clearly isolated colonies were selected, after which a small amount of material from their surface was transferred using a sterile loop into a test tube containing a sterile 0.9% NaCl solution. The density of the resulting suspension was adjusted to 0.5 according to the McFarland standard. The prepared inoculum was used within 15 minutes.

Conducting the analysis: three solutions of the standard sample (C1, C2, C3) from the preparation "Claricide" (250 mg and 500 mg, Abbott Laboratories Ltd) and three solutions of the test sample (I1, I2, I3) from the preparation "Clarin" (250 mg and 500 mg, FE OOO "Novugen Pharma") were prepared for the test. The concentrations of the solutions corresponding to the low, medium and high doses were in a multiple ratio of 1:2:4. Wells were formed on the solidified surface of the agar using a glass cylinder, into which solutions of the compared preparations in the specified concentrations were added. The experiment was carried out in five Petri dishes [6, 7].

Incubation: The dishes were placed in a thermostat at 36 ± 1°C for 18-24 hours. After incubation, the zones of inhibition of microorganism growth formed by the solutions of the comparison preparations were measured using a microbiological ruler with an accuracy of 1 mm. The antimicrobial activity of the preparations was assessed based on the zone sizes.

The obtained data were subjected to statistical processing using the STATISTICA program [8].

Research results: After incubation in a thermostat, the zones of microbial growth inhibition formed by the solutions of the compared preparations were measured using a microbiological ruler with an accuracy of 1 mm. The antimicrobial activity of the test samples was assessed based on the sizes of these zones. The obtained data showed that the diameters of the zones of microbial growth inhibition for the compared preparations were comparable. The experimental results are presented in Tables 1 and 2.

Table 1

Inhibition zones of microorganism growth under the influence of the preparations "Clarin" 250 mg produced by FE OOO Novugen Pharma (Uzbekistan) and "Claricide" 250 mg produced by Abbott Laboratories Ltd (Pakistan)

Preparations	Solution concentration	Microorganism growth inhibition zones, mm			
		St.epidermidis	E.coli,	Bacillus subtilis	Ps. aerugmosa
"Clarin" 250 mg manufactured by Novugen Pharma LLC (Uzbekistan)	I1	24.6±0.4	21.6 ± 0.4	21.6±0.4	17.6±0.4
	I2	22.6±0.4	19.8 ± 0.2	18.4±0.6	15.8±0.2
	I3	20.6±0.4	18.2 ± 0.8	17.2±0.8	15.0±0.1
Claricide 250 mg, manufactured by Abbott Laboratories Ltd (Pakistan)	C1	25.4±0.6	23.4 ± 0.6	23.4±0.6	19.2±0.8
	C2	23.6±0.4	20.6 ± 0.4	19.4±0.6	17.0±0.1
	C3	21.0±0.1	19.4 ± 0.4	17.8±0.2	15.6±0.6

Table 2

Inhibition zones of microorganism growth under the influence of the preparations "Clarin" 500 mg produced by FE OOO Novugen Pharma (Uzbekistan) and "Claricide" 500 mg produced by Abbott Laboratories Ltd (Pakistan)

Preparations	Solution concentration	Microorganism growth inhibition zones, mm			
		St.epidennidis	E. coli	Bacillus subtilis	Ps. aeruginosa
"Clarin" 250 mg manufactured by Novugen Pharma LLC (Uzbekistan)	I1	24.6±0.4	22.0 ± 0.1	22.4±0.6	17.6±0.4
	I2	22.4±0.6	20.6 ± 0.4	19.4±0.6	15.8±0.2
	I3	20.4±0.6	19.4 ± 0.6	18.4±0.6	15.0±0.1
Claricide 250 mg, manufactured by Abbott Laboratories Ltd (Pakistan)	C1	25.6±0.4	24.6 ± 0.4	23.6±0.4	19.4±0.6
	C2	24.6±0.4	22.4 ± 0.6	20.6±0.4	18.2±0.8
	C3	22.8±0.1	20.4 ± 0.6	19.0±0.1	16.0±0.1

Conclusions: Thus, the results of the study of the specific activity of the preparation "Clarin" (250 mg and 500 mg, manufactured by FE OOO "Novugen Pharma", Uzbekistan) in comparison with the analog preparation "Claricide" (250 mg and 500 mg, manufactured by "Abbott Laboratories Ltd", Pakistan) showed that the studied preparations have comparable antimicrobial activity and, therefore, are biologically equivalent in specific action

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