

## ФАРМАЦЕВТИЧЕСКИЕ НАУКИ

### RESEARCH ON THE CHOICE OF ANTIMICROBIAL PRESERVATIVE IN THE SPRAY

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*Currently, special attention is paid to the quality and safety of medicines entering the consumer market. A necessary and most important indicator of medicines is mandatory quality control and microbiological purity during the manufacturer's stated shelf life. Studies to determine the optimal concentration of the preservative in the spray solution, which ensures the microbiological purity of the dosage form, were conducted.*

**Key words:** preservative, microbiological purity, benzalkonium chloride, nasal spray

Currently, special attention is paid to the quality and safety of medicines entering the consumer market. In this regard, the most important indicator is the microbiological purity throughout the entire shelf life and repeated use of the drug.

The developed spray is intended for application to the nasal mucosa, which implies a high probability of contamination of the primary packaging and penetration of microorganisms into the drug solution. To prevent microbial contamination and growth of microorganisms inside the spray solution, it is advisable to introduce an antimicrobial agent into its composition.

The effective concentration of the preservative in the finished drug form should be lower than the dose that is toxic to humans. Preservatives are considered effective if their use reduces the number of bacterial cells in accordance with the criteria of the Pharmacopoeia article of the State Pharmacopoeia of the Russian Federation, and the number of yeast and mold cells should not increase during the shelf life of the drug.

Nasal sprays belong to the second category of drugs containing preservatives-non-sterile, applied topically, for administration into the nasal cavity, including the mucous membranes [1].

After reviewing the State register of medicines of Russia, found that in the development

of liquid dosage forms using a wide range of antimicrobial agents: chlorhexidine bigluconate, boric acid, benzoic acid, chlorbutanolhydrate (chlorate), sodium benzoate, sodium pyrosulfite, naphine and most widely – benzalkonium chloride. Due to the wide range of antibacterial activity and low toxic effect on the human body, benzalkonium chloride (BC) is often used in various dosage forms.

BC has a bacteriostatic and bactericidal effect against gram-positive and gram-negative aerobic and anaerobic microorganisms: *Staphylococcus spp.*, *Streptococcus spp.*, *Escherichia coli*, *Klebsiella spp.*, *Proteus spp.*, *Pseudomonas aeruginosa*, *Clostridium spp.*, *Bacillus subtilis*. BC *in vitro* is active against *Neisseria gonorrhoeae*, *Chlamydia spp.*, *Trichomonas vaginalis*, *Human herpesvirus 2*, *Staphylococcus aureus*. Benzalkonium chloride also has a fungistatic and fungicidal effect on pathogenic fungi, in particular on yeast-like *Candida* fungi [3].

Taking into account the literature data and extensive successful experience in the use of BC in medical practice, we selected this antimicrobial preservative in order to introduce it into the composition of the developed spray to ensure its microbiological stability during the entire shelf life and use.

Studies were conducted to determine the

concentration of benzalkonium chloride in the spray solution, which ensures the microbiological purity of the dosage form.

BC was injected into the spray samples in concentrations: 0,005%, 0,01%, 0,015%, 0,02%. To

quantify the microbiological content in 1 g (ml) of contaminated spray samples, a modified depth method was used in accordance with the requirements of the Russian state Pharmacopoeia.

The results are presented in table 1.

Test-strain	Recommended requirements	BC concentration, %			
		0,005	0,01	0,015	0,02
Number of anaerobic microorganism	No more than $10^2$ CFM	$1,2 \cdot 10^2$	$0,4 \cdot 10^2$	$0,4 \cdot 10^2$	$0,4 \cdot 10^2$
<i>Pseudomonas aeruginosa</i>	Absence	Absence	Absence	Absence	Absence
<i>Staphylococcus aureus</i>	Absence	Absence	Absence	Absence	Absence

From the results of research, it follows that the microbiological purity of the spray is pro-

vided by the minimum concentration of benzalkonium chloride-0.01%.

## REFERENCES

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3. Yaremchuk A.A., Hishova O.M., Polovko N.P. Microbiological justification of the use of benzalkonium chloride in a mild dosage form for external use. Bulletin of pharmacy. № 2(56). 2012. P. 39-45.

## ИССЛЕДОВАНИЯ ПО ВЫБОРУ АНТИМИКРОБНОГО КОНСЕРВАНТА В СОСТАВЕ СПРЕЯ

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*В настоящее время уделяется особое внимание качеству и безопасности лекарственных препаратов (ЛП), поступающих на потребительский рынок. Необходимым и самым главным показателем лекарственных препаратов является обязательный контроль качества и микробиологической чистоты в течение заявленного производителем срока годности. Были проведены исследования по установлению оптимальной концентрации консерванта в составе раствора спрея, обеспечивающей микробиологическую чистоту лекарственной формы.*

**Ключевые слова:** консервант, микробиологическая чистота, бензалкония хлорид, спрей назальный.