References

1. *Ivanchina E.D., Ivashkina E.N., Dolganova I.O., Platonov V.V. Vliyanie termodinamicheskoj ustojchivosti vysokomolekulyarnyh aromaticheskih uglevodorodov na aktivnost' HF-katalizatora processa alkilirovaniya benzola olefinami S9–S14 // Neftekhimiya, 2014.– V.54.– №6.– P.1–8. [In Russian]*
2. *Dolganova I.O. Diss. kand. tekhn. nauk.– Tomsk: TPU, 2014.– 155 p. [In Russian].*

INFLUENCE OF GRAMICIDIN S AND β-CYCLODEXTRIN COMPLEXATION TECHNIQUES ON THE DRUG RELEASE

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Gramicidin S is an antimicrobial peptide known worldwide since 1942 and clinically applied since 1944 [1].

Recently proved mechanism of the antimicrobial activity of Gramicidin S reveals its benefit comparing to the conventional antibiotics which reflects in low inhibitory and bactericidal concentrations.

The discovered mechanism also explains the long clinical practice with a lack of resistance to the antibiotic among most known microorganisms [2].

Besides its high effectiveness against gram-positive microorganisms, Gramicidin S demonstrates high antimicrobial activity towards to gram-negative bacteria and also some fungi which makes it possible to be applied for infection treatment [3].

However, due to its high hemotoxicity, the antibiotic is only administered orally or topically and manufactured predominantly in solid dosage form as tablet, which limits peptide effectiveness due to low bioavailability caused by low water solubility of the drug.

In present work the attempt had been made to increase the solubility of gramicidin S via complex formation with β-cyclodextrin using different complexation techniques.

Cyclodextrins are the starch derivatives discovered in 1891 and widely used in pharmaceutical industry in many purposes, which is possible due to the specific structure of cyclodextrins.

The manufacturing technology provides polysaccharides with the cone shape with a hydrophobic inner cavity and hydrophilic surface. This type of structure lets cyclodextrins incorporate hydrophobic molecules or the most hydrophobic parts of those [4].

That specific property of cyclodextrins is widely applied in pharmacy to modify the drug release, mask negative organoleptic properties as well as to improve its solubility in water.

Among those, β-cyclodextrin is the most used agent due to its low price, availability on the market and regulatory status: it is described in EP, USP and JP monographs.

β-cyclodextrin had been studied clinically and finds its application as drug excipient for different dosage forms either via inclusion complex formation or in an uncomplexed state [5].

The aim of the present work was to study the influence of β-cyclodextrin on gramicidin S properties via inclusion complex formation as following.

Antibiotic inclusion complexes were formed applying different methods of complex formation such as: co-precipitation, paste complexation and dry mixing.

The Gramicidin S:β-cyclodextrin ratio was taken as 1 : 10. The resulting powders were dried in convector to remove the residual solvent and uniformed to reach the particle size not more than 0.8 mm.

The *in vitro* release studies were performed in different pH (2.0, 4.3, 6.8) at 37 °C and the drug concentration in buffer solution was detected using HPLC method.

It was found that gramicidin S complexation with β-cyclodextrin increases the drug solubility in water and provides sustained release of the peptide at pH = 4.3 for at least 48 h.

However, there was almost no release at higher pH level while at pH = 2.0 the burst release had been

observed which makes it possible to make some advice regarding Gramicidin S administration.

Additionally, some technological parameters were evaluated for each mixture and compared to the unloaded β-cyclodextrin to reveal its potential or industrial application in solid dosage form production.

Particle size distribution, bulk density, flowability and slope angle were determined according to the European pharmacopoeia procedures [6].

As a result, it was found that Gramicidin S complexation with β-cyclodextrin applying any technique modifies its technological properties as well as the drug release parameters.

References

1. *Gause G.F., Brazhnikova M.G. // Nature, 1944.– V.154.– №3918.– P.703.*
2. *Wenzel M. et al. // MBio., 2018.– V.9.– №5.– P.802–818.*
3. *Wan Y. et al. // European journal of medicinal chemistry, 2018.– V.149.– P.122–128.*
4. *Del Valle E.M.M. // Process biochemistry, 2004.– V.39.– №9.– P.1033–1046.*
5. *Challa R. et al. // AapsPharmscitech, 2005.– V.6.– №2.– P.329–357.*
6. *European Pharmacopoeia (Ph. Eur.) 9th Edition, 2017.*

A STUDY OF THE GRAPHENE OXIDE INFLUENCE ON THE MORPHOLOGY AND CRYSTALLINE STRUCTURE OF PIEZOELECTRIC BIODEGRADABLE ELECTROSPUN POLY (L-LACTIC ACID)-BASED SCAFFOLDS

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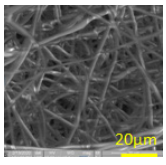
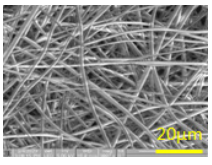
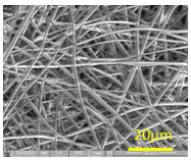
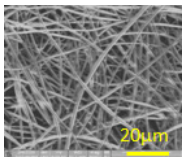
Introduction. Tissue engineering and regenerative medicine (TERM) aim to the regeneration or replacement of damaged or diseased tissues/organs using artificial materials, especially biodegradable. Moreover, a bioactive charged surface can provide enhanced cell adhesion and proliferation [1]. Poly (l-lactic acid) (PLLA) polymer is studied for diverse biomedical applications as a biocompatible and biodegradable material [2]. Compared to piezoelectric ceramics or non-biodegradable polymers, PLLA scaffolds demonstrate a weak mechanical and piezoelectric performance that can limit their successful use in TERM. However, some nanofillers, such dielectric graphene oxide (GO), can improve mechanical and piezoelectric properties of hybrid polymers [3]. Moreover, GO possesses unique physicochemical properties, flexibility and biocompatibility [4]. Thus, the present study aims to fabricate and analyze the morphology and structure of hybrid piezoelectric biodegradable composites based on PLLA and GO.

Results and discussion. Scanning electron microscope (SEM) was used to examine the morphology of the prepared PLLA-GO scaffolds (Table 1).

The addition of GO led to the formation of defect-free scaffolds (e.g. without beads), thereby resulting in GO homogenous distribution within fibers. Furthermore, it was found that a high concentration of GO led to the formation of thinner fibers. The decrease of the fiber diameter could be attribut-

Table 1. SEM images of PLLA-GO scaffolds with corresponding average diameters (D)

Scaffolds			
Pure PLLA	PLLA-0.2% GO	PLLA-0.7% GO	PLLA-1% GO
			
D = 1.64±0.36 (μm)	D = 1.35±0.37 (μm)	D = 1.26±0.37 (μm)	D = 1.12±0.25 (μm)