DOI: 10.6060/ivkkt.20236608.6782

УДК: 546.93:546.97:577.114:615.281.9

МЕХАНИЧЕСКИЕ, АНТИБАКТЕРИАЛЬНЫЕ И АНТИПРОЛИФЕРАТИВНЫЕ СВОЙСТВА ИРИДИЙ- И РОДИЙСОДЕРЖАЩИХ ХИТОЗАНОВЫХ ПЛЕНОК

А.А. Годзишевская, Е.П. Лопашинова, М.Н. Курасова, А.С. Критченков, О.И. Андреева

Анастасия Андреевна Годзишевская (ORCID 0000-0002-0197-6799)*, Елизавета Петровна Лопашинова (ORCID 0009-0000-6929-6290), Маргарита Николаевна Курасова (ORCID 0000-0002-9107-5264), Андрей Сергеевич Криченков (ORCID 0000-0002-6411-5988), Ольга Ивановна Андреева (ORCID 0000-0003-4097-7599)

Кафедра неорганической химии, Факультет физико-математических и естественных наук, Российский университет дружбы народов, ул. Миклухо-Маклая, 6, Москва, Российская Федерация, 117198
E-mail: kovalevskaya2804@mail.ru*

В последние десятилетия наиболее актуальными стали исследования в области химии природных полимеров, а также производных на их основе. Данные соединения включают в свой состав катионы металлов, что открывает новые возможности для применения этих соединений в химической, пищевой и фармацевтической промышленности. Развивающимся направлением является определение антипролиферативной активности полученных соединений и материалов. Эти исследования открывают новые горизонты для разработки селективных препаратов борьбы с делением и развитием атипичных клеток в организмах. Получены родий- и иридийсодержащие пленки на основе природного полимера хитозана, пластифицированные глицерином. В этой работе проведен комплексный анализ полученных материалов методами рентгенофазового анализа (РФА), рентгеноспектрального анализа (РСА), сканирующей электронной микроскопии (СЭМ), также изучены механические характеристики и биологические свойства (антибактериальная и антипролиферативная активность) полученных пленок. Равномерное распределение катионов металлов в полимерной матрице контролировалось рентгеноспектральным анализом. Результаты рентгенофазового анализа подтверждают незначительное изменение структуры получаемых материалов. С помощью СЭМ была охарактеризована морфология поверхности металлсодержащих хитозановых пленок. Анализ механических свойств пленок показал, что иридийсодержащие образцы характеризуются более высокими показателями предела кратковременной прочности и относительного удлинения до разрыва, чем родийсодержащие образцы. Таким образом, можно сделать вывод о том, что природа металлоцентра влияет на механические свойства пленок. Иридиевые пленки обладают большей антибактериальной активностью, чем соответствующие родиевые пленки. Антипролиферативная активность исследуемых образцов обусловлена содержанием родия(III) и иридия(IV) и практически не зависит от природы вводимых катионов металлов.

Ключевые слова: хитозановые пленки, родий, иридий, механические свойства, антибактериальная активность, антипролиферативная активность

Для цитирования:
Годзишевская А.А., Лопашинова Е.П., Курасова М.Н., Критченков А.С., Андреева О.И. Механические, антибактериальные и антипролиферативные свойства иридий- и родийсодержащих хитозановых пленок. *Изв. вузов. Химия и хим. технология*. 2023. Т. 66. Вып. 8 С. 92–98. DOI: 10.6060/ivkkt.20236608.6782.

For citation:
Godzishevskaya A.A., Lopashinova E.P., Kurasova M.N., Kritchenkov A.S., Andreeva O.I. Mechanical, antibacterial and antiproliferative properties of iridium- and rhodium-containing chitosan films. *ChemChemTech* [*Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol*.]. 2023. V. 66. N 8. P. 92–98. DOI: 10.6060/ivkkt.20236608.6782.

MECHANICAL, ANTIBACTERIAL AND ANTIPROLIFERATIVE PROPERTIES OF IRIDIUM- AND RHODIUM-CONTAINING CHITOSAN FILMS

A.A. Godzishevskaya, E.P. Lopashinova, M.N. Kurasova, A.S. Kritchenkov, O.I. Andreeva

Anastasia A. Godzishevskaya (ORCID 0000-0002-0197-6799)*, Elizaveta P. Lopashinova (ORCID 0009-0000-6929-6290), Margarita N. Kurasova (ORCID 0000-0002-9107-5264), Andreii S. Kritchenkov (ORCID 0000-0002-6411-5988), Olga I. Andreeva (ORCID 0000-0003-4097-7599)

Department of Inorganic Chemistry, Faculty of Physical, Mathematical and Natural Sciences, Peoples' Friendship University of Russia, Miklukho-Maklaya st., 6, Moscow, 117198, Russia
E-mail: kovalevskaya2804@mail.ru*

Over the last decades, the research in the chemistry of natural polymers as well as derivatives based on them has become most relevant. These compounds include metal cations in their composition, which opens up new opportunities for the application of these compounds in the chemical, food processing and pharmaceutical industries. A developing area is the determination of the antiproliferative activity of the resulting compounds and materials, which provides opportunities for the development of selective anti-cancer drugs. Rhodium- and iridium-containing films based on the natural polymer of chitosan plasticized with glycerol have been obtained. In this work, a comprehensive analysis of the materials obtained by X-ray phase analysis (XRD), X-ray spectral analysis (XRD), scanning electron microscopy (SEM) was carried out, and the mechanical characteristics and biological properties (antibacterial and antiproliferative activity) of the obtained films were also studied. An analysis of the mechanical properties of the films showed that iridium-containing samples are characterized by higher mechanical properties than rhodium-containing samples. Thus, we can conclude that the nature of the metal center affects the mechanical properties of the films. Iridium films have greater antibacterial activity than the corresponding rhodium films. The antiproliferative activity of the studied samples is due to the content of rhodium(III) and iridium(IV) and is practically independent of the nature of the introduced metal cations.

Key words: chitosan films, rhodium, iridium, mechanical properties, antibacterial activity, antiproliferative activity

INTRODUCTION

Chitosan is biodegradable natural aminopolysaccharide. Chitosan is used as matrix for nanoparticles, biodegradable films production, antitumor medications, etc [1, 2].

In the past several years complexes of chitosan and platinum (II), hybrid platform based on graphene oxide/chitosan and xyloglucan are being widely studied for their effect on the tumor cells. These compounds have ultra-small sizes, which contribute to the deep penetration in the tumor cells, as well as enhance the effect of chemotherapeutic agents, therefore reducing the rate of tumor growth [3, 4].

The production of films is one of the most perspective tendency in the chemistry of chitosan. Moreover, nowadays the interest for this field of science is increasing. Depending on their structure and composition, the films have a wide range of properties. Chitosan films have an impact on psychrotrophic strains Pseudomonas fluorescens and Listeria innocua as well as on mesophilic strains Escherichia coli and Staphylococcus aureus. Bacterial growth under the chitosan discs were surpressed which confirms the strong antimicrobal effect [5, 6].

The group of Chinese scientists [7] produced nanocomposite film based on sodium alginate and chitosan with copper oxide (CuO) and zinc oxide (ZnO) nanoparticles. In case of nanocomposite films application the result of antibacterial researches indicates the growth suppression of E. coli and S. Aureus on more than 60% in the dark and more than 90% with light radiation. It's worth mentioning, that these films exhibit the excellent mechanical (smoothness, flexibility and fragility), barrier and optical (transmission and fluorescence) properties. The inclusion of the Ag^{+}- and Co^{3+}-based composites in the films led to inactivation of more than 99,6% against *S. aureus* and *E. coli* within 10 min. Moreover, nanocomposites are considered non-cytotoxic for mammals [8].

Modern technology makes it possible to test new chemicals against different types of pathogens and oncogenic cancer cell lines [9, 10]. Chitosan-based compounds with the addition of metals not only affect bacterial cell growth but also exhibit high antiproliferative properties [11]. The incorporation of metals into

chitosan matrices has been shown to have a general cytotoxic effect on cells [12].

One of the most interesting and rather promising branch of science is the study of the antitumor properties of new compounds, as well as their biological compatibility with living organisms. In this paper, we have made an assumption that chitosan films based on Rh(III) and Ir(IV) cations have potential to suppress cellular growth and possess a range of biological properties.

METHODOLOGY

Preparation films

The method of casting from a solution in which the formation of intermolecular bonds leads to a cross- linked three- dimensional structure is the one of the most widepread and convinient methods of obtaining chithosan-based food films and cover [13-16].

0.4 g of chitosan was dissolved under stirring at 70 °C for 30 min in 10 ml of 1% acetic acid. Thereafter 0.33 glycerin, 0.1M solution of rhodium(III) chloride or sodium hexachloroiridate(IV) in volume ratios chitosan solution/salt solution 1:1; 1:0.5; 1:0.2; 1:0.1; were added to the obtained chitosan solutions. The resulting solutions were poured in Petri dishes, placed in dust-free storage for 3-4 days at 20-25 °C. After drying smooth flexible films with different composition were obtained.

The thickness of the resultant films was 0.052±0.002 mm (measured by Inforce 06-11-44 Digital Micrometer 0-25mm/0-1). Moisture percentage of the films was 7±0.5% (detected by thermogravimetric analysis using T.A.Instruments, SDT Q600 apparatus).

Antiproliferative activity

Cucumber C. sativus seeds were placed 50 pieces at a time in Petri dishes on a layer of water (chitosan – control, the rest according to code numbers – experiment) in 3 replicates. Incubation took place at a stable temperature of 20-22 °C. The seeds were checked daily for germination. Root length was measured and the number of lateral roots of cucumber was counted on the fourth day after germination. In total, at least 35 cucumber seedlings from each Petri dish were analyzed. Statistical processing was performed using standard methods using Microsoft Excel software. Significance was accepted at $p < 0.05$ [17].

Methods of analysis

X-ray phase analysis were conducted on the diffractometer DRON-7 with monochromatic CuK_α radiation at rate of ¼ deg/min in the range of 5° – 50° ($\lambda_{CuK\alpha}$= 1.5405 Å). The diffractograms were taken in discrete mode ($\Delta\delta = 0.02°$, exposure time $\tau = 3$ s).

The results of X-ray spectral analysis confirmed the individuality of synthesized compounds (energy dispersive X-ray fluorescence spectrometer CLEVER C-31 (40.0kV, 100.0mA, F: Cu, 0.05mm, 100 s)).

SEM images were obtained using a JEOL JSM - 6490LV electron microscope (voltage 15 kV, SEM detector, electron beam 30, in high vacuum). The tested samples were applied to a platinum substrate with width of 20 nm (40 s at current of 40 mA) using an automatic attachment for applying thin films JEOL JFC - 1600.

The tensile tests were conducted using an automatic tensile tester (XLW-PC PARAM, China) equipped with a 500 N load sensor. The measurements were carried out at a deformation rate of 300 mm/min at 25 °C.

The antibacterial activity of the resulting films against gram-positive bacteria *Staphylococcus aureus* (RCMB 010027) and gram-negative bacteria *Escherichia coli* (RCMB 010051) were carried out by method of disk analysis of the inhibition zone [18]. Molten agar (10 ml) was inoculated with 200 µl of bacterial culture containing approximately 108 CFU/ml of bacteria. The films test discs were placed on bacterial lawns. The tablets were incubated at 37 °C for 24 h. The diameter of the inhibition zone was measured with a caliper.

RESULTS AND DISCUSSION

X-ray phase analysis

The spectrum of the chitosan sample shows one main broad reflex of crystalline chitosan at $2\theta = 19.27°$. After adding glycerol to the initial chitosan and obtaining the film, small diffraction peaks at $2\theta = 11.24, 19.18, 20.82$ were observed. The investigated films based on chitosan and rhodium(III) chloride are characterized by broadening and smoothing of the reflex ($2\theta = 19.27$) and its shift to the right, which indicates molecular miscibility and interaction between the components.

The films based on chitosan and sodium(IV) hexachloroaridate are X-ray amorphous. On the diffractograms of metal-containing samples we can note the broadening of the reflex present in the diffractogram of the original chitosan. The appearance of a small peak in the region of $2\theta = 8.55$ is also registered, which indicates a slight change in the structure.

3.2 X-ray spectral analysis

The radiation intensity of the rhodium tube in the idle experiment is 1.78 cu. When conducting analyses on rhodium-containing samples, the intensity of peaks increases sharply, which allows us to conclude that Rh^{3+} cations are present in all the obtained films.

X-ray spectral analysis of samples of chitosan/rhodium(III) and chitosan/iridium(IV) films

made it possible to determine the presence of metal and chlorine atoms in the film. The results are presented in Table 1.

Table 1

Results of X-ray spectral analysis. Quantitative content of metal and chlorine in the studied films

Таблица 1. **Результаты рентген-спектрального анализа. Количественное содержание металла и хлора в исследованных пленках**

Code	Element	C, %	Intensity
BX3GlyRh0,1:1	Cl	98.89	65.86
	Rh	1.11	11.16
BX3GlyRh0,2:1	Cl	98.52	124.66
	Rh	1.48	27.92
BX3GlyRh0,5:1	Cl	95.79	205.42
	Rh	4.21	122.14
BX3GlyRh1:1	Cl	96.96	338.00
	Rh	3.04	149.56
BX3GlyIr0,1:1	Cl	79.61	87.20
	Ir	20.39	477.48
BX3GlyIr0,2:1	Cl	78.62	88.84
	Ir	21.38	518.65
BX3GlyIr0,5:1	Cl	83.47	291.89
	Ir	16.53	1204.66
BX3GlyIr1:1	Cl	73.56	209.06
	Ir	26.44	1655.49

According to the results of X-ray fluorescence analysis, the intensity of peaks corresponding to Rh(III) and Ir(IV) increases with an increase in the concentration of metals in the synthesized films.

The results of X-ray fluorescence analysis confirm a uniform distribution of metal ions over the surface of the film.

Scanning electron microscopy (SEM)

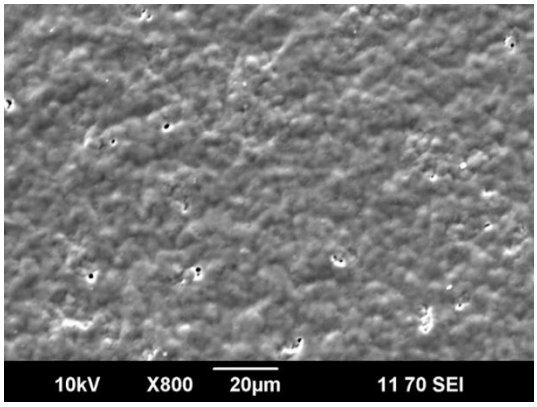

Fig. 1. SEM rhodium-containing sample in the volume ratios $RhCl_3$ /chitosan 0,1:1

Рис. 1. Микрофотографии родийсодержащих пленок в объемных соотношениях $RhCl_3$ /chitosan 0.1:1

An example of scanning electron microscopy results of Rh-containing films is shown in Fig. 1. Two defects in the film structure can be distinguished in the synthesised films: holes (pores) and ridges (wavy changes in the film structure). It should be noted that holes are mostly absent in all rhodium-containing films. The highest number of holes is characteristic of rhodium-containing samples at RhCl3/chitosan volume ratios of 0.1:1. Samples with Rh(III)/chitosan volume ratios of 0.2:1 and 0.5:1 do not contain the described defect. Films in 1:1 volume ratios contain insignificant changes, but the number and size of holes is smaller than in the sample in Fig. 1. Thus, a correlation is obtained between the decrease in the number of pores in the samples with an increase in Rh(III) concentration, except for the sample in volumetric ratios of metal/chitosan 1:1. An increase in porosity occurred in a series of volume ratios: 0.2:1; 0.5:1; 1:1; 0.1:1.

Ridges can be observed on all samples of the films presented. The sample in Fig. 1 has a pronounced lumpy surface where the ridges are large and flat. The SEM of the rhodium-containing sample at a $RhCl_3$/chitosan volume ratio of 0.2:1 shows a film with fine and sharp ridges. Films with the highest metal concentrations contain a large number of ridges and, although they are not planar, have a distinct cliff structure.

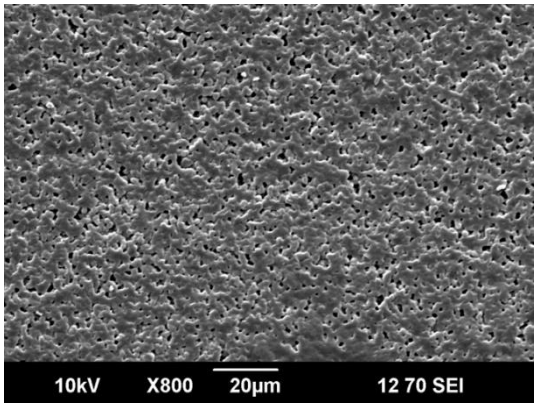

Fig. 2. SEM iridium-containing sample in the volume ratios $Na_2[IrCl_6]$/chitosan 0,5:1

Рис. 2. Микрофотографии иридийсодержащих пленок в объемных соотношениях $Na_2[IrCl_6]$/chitosan 0.5:1

Micrographs of the front side of the films showed that changing the concentration of the added iridium(IV) salt created some porosity in the resulting samples. However, no definite pattern of pore formation was detected. As the concentration of iridium increased, the number of pores in the obtained films also increased. It was recorded that the iridium-containing sample at a $Na_2[IrCl_6]$/chitosan volume ratio of 0.1:1 contained a small number of pores. Doubling the

metal concentration resulted in a film with large pores unevenly distributed over the surface of the sample; in addition, the number of ridges in this film is rather small and those ridges that were observed are unstable and small compared to the size of the sample. The sample in Fig. 2 has the highest porosity of all those presented, and small, precarious volume ridges distributed over the entire surface of the sample. The film with a $Na_2[IrCl_6]$/chitosan volume ratio of 1:1 has neither holes nor ridges and is characterised by a smooth surface. An increase in porosity occurred in the series of volume ratios: 1:1; 0.1:1; 0.2:1; 0.5:1.

Mechanical properties of films

Table 2

Mechanical properties of films

***Таблица 2.* Механические свойства пленок**

Code	σ_b (MPa)	ε_b (%)
BX3GlyRh0,1:1	38.36±1.35	37.12±1.11
BX3GlyRh0,2:1	33.23±1.16	31.10±1.01
BX3GlyRh0,5:1	26.61±1.03	25.14±1.07
BX3GlyRh1:1	20.70±1.10	21.22±1.01
BX3GlyIr0,1:1	45.21±1.55	44.73±1.13
BX3GlyIr0,2:1	42.17±1.14	39.03±1.17
BX3GlyIr0,5:1	36.52±1.21	34.39±1.35
BX3GlyIr1:1	28.43±1.22	28.11±1.12
BX3Gly	48.35±1.54	94.12±1.26

Mechanical properties of films were evaluated with respect to two parameters: the ultimate tensile strength (σ_b (MPa)) and the relative strain of the film before rupture (ε_b (%)). For the samples investigated, both values decrease linearly with increasing metal concentration in the film, which may occure due to a decrease in polymer (chitosan) concentration in the given samples. It's worth mentioning, that iridium-containing samples are characterized by higher mechanical properties than rhodium-containing samples, which indicates the influence of the metal center nature on the mechanical properties of the films.

Antibacterial activity

Table 3

Antibackterial activity of films

***Таблица 3.* Антибактериальная активность пленок**

Code	*S. aureus*	*E. coli*
	Zone of inhibition, mm	
BX3GlyRh0,1:1	13.2±0.1	9.1±0.2
BX3GlyRh0,2:1	14.1±0.2	9.4±0.1
BX3GlyRh0,5:1	17.7±0.2	11.3±0.1
BX3GlyRh1:1	20.9±0.2	12.7±0.1
BX3GlyIr0,1:1	14.1±0.1	9.3±0.2
BX3GlyIr0,2:1	18.0±0.3	12.5±0.2
BX3GlyIr0,5:1	21.7 ±0.1	14.8±0.2
BX3GlyIr1:1	25.6±0.2	18.5±0.1
BX3Gly	8.7±0.1	7.1±0.1

Rhodium(III) and iridium(IV) containing films has been reported to exhibit antibacterial activity. With the increase in the metal concentration the antibacterial activity increases naturally. However, the inhibition diameter of iridium(IV)-based films is approximately 1,2 (*Staphylococcus aureus*) and 1,3 (*Escherichia coli, exept at 0.01:1 concentration*) times larger than that of the corresponding rhodium(III)-based film samples. Iridium films therefore have greater antibacterial activity than the corresponding rhodium films.

Antiproliferative activity

Table 4

Antiproliferative activity of films

***Таблица 4*. Антипролиферативная активность пленок**

Code	*l*, cm	*n*, pcs
BX3GlyRh0,1:1	8.3	15.2
BX3GlyRh0,2:1	6.2	11.0
BX3GlyRh0,5:1	5.0	8.1
BX3GlyRh1:1	3.3	4.2
BX3GlyIr0,1:1	8.0	15.1
BX3GlyIr0,2:1	6.4	11.6
BX3GlyIr0,5:1	5.6	7.8
BX3GlyIr1:1	2.9	5.5
Control	8.2	15.4

Quantitative measures such as the length of the main root *l* and the number of lateral roots *n* were investigated in the experiment. The lower the values mentioned, the more effective antiproliferative activity of the test sample. As shown in Table 4, the antiproliferative activity of the metal-containing films is clearly dependent on the metal concentration and is approximately the same for both rhodium(III) and iridium(IV). The samples with the highest metal concentration (BX3GlyRh1:1 and BX3GlyIr1:1) exhibit the maximum of antiproliferative activity, which decreases with decreasing metal concentration. The samples with the lowest metal concentration (BX3GlyRh1:0.1 and BX3GlyIr1:0.1) do not exibit antiproliferative activity, because in their case the effect on the main root length *l* and number of lateral roots *n* is almost the same as that for the chitosan film sample without metal. It has been proven that the antiproliferative activity of the tested samples is determined by the rhodium(III) and iridium(IV) concentrations and is not depends on the nature of the metal centre.

CONCLUSION

Metal:chitosan ratios of 0.2:1 (for rhodium(III)) and 1:1 (for iridium(IV)) produce smooth elastic films with improved mechanical properties (when glycerine is used as plasticiser). Rhodium(III) and iridium(IV)-containing films based on chitosan

are characterised by a number of valuable biological properties:

- low toxixity *in vitro*;
- high antibacterial activity *in vitro*;
- distinct antiproliferative activity *in vitro*.

The results of antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* of copper, silver and cobalt-containing films presented in literature revealed lower effect as compared with rhodium and iridium-containing films presented in the current study [19-21]. To the best of our knowledge, there are not examples in the literature of antiproliferative activity studies of chitosan films with other metal cations. Thus, the elaborated rhodium and iridium-containing antiproliferative films are promising for further research *in vivo*, and this project is underway in our group.

The authors declare the absence a conflict of interest warranting disclosure in this article.

Авторы заявляют об отсутствии конфликта интересов, требующего раскрытия в данной статье.

ЛИТЕРАТУРА

1. **El Kadib A.** // *ChemSusChem*. 2015. V. 8. N 2. P. 217-244. DOI: 10.1002/cssc.201402718.
2. **Ailincai D., Bercea M., Tartau L.M., Marin L.** // *Carbohyd. Polym.* 2022. V. 298. P. 120071. DOI: 10.1016/j.carbpol.2022.120071.
3. **Kankala R.K., Liu C., Yang D., Wang S., Chen A.** // *Chem. Eng. J.* 2020. V. 383. P. 123138. DOI: 10.1016/j.cej.2019.123138.
4. **Kesavan S., Meena K.S., Dhakshinamoorthy R.** // *Biointerface Res. Appl. Chem.* 2022. V. 12. N 3. P. 3429-3445. DOI: 10.33263/BRIAC123.34293445.
5. **Malinowska-Pańczyk E., Staroszczyk H., Gottfried K., Kołodziejska I., Wojtasz-Pająk A.** // *Polym. J. Chem., Technol. Polym. Proc.* 2015. V. 60. N 11-12. P. 735-741. DOI: 10.14314/polimery.2015.735.
6. **Yuan D., Hao X., Liu G., Yue Y., Duan J.** // *Food Chem.* 2022. V. 385. P. 132647. DOI: 10.1016/j.foodchem.2022.132647.
7. **Guan G., Zhang L., Zhu J., Wu H., Li W., Sun Q.** // *J. Hazard. Mater.* 2021. V. 402. P. 123542. DOI: 10.1016/j.jhazmat.2020.123542.
8. **Han H., Xu X., Kan H., Tang Y., Liu C., Wen H., Wang F.** // *J. Colloid. Interface Sci.* 2022. V. 616. P. 304-315. DOI: 10.1016/j.jcis.2022.02.068.
9. **Adhikari H.S., Garai A., Manandhar K.D., Yadav P.N.** // *ACS omega*. 2022. V. 7. N 35. P. 30978-30988. DOI: 10.1021/acsomega.2c02966.
10. **Gojo I., Tidwell M.L., Greer J., Takebe N., Seiter K., Pochron M.F., Johnson B., Sznol M., Karp J.E.** // *Leuk. Res*. 2007. V. 7. N 31. P. 1165–1173. DOI: 10.1016/j.leukres.2007.01.004.
11. **Rao V.A., Klein S.R., Agama K.K., Toyoda E., Adachi N., Pommier Y., Shacter E.B.** // *Cancer Res.* 2009. V. 69. N 3. P. 948– 957. DOI: 10.1158/0008-5472.can-08-1437.
12. **Malarz K., Mrozek-Wilczkiewicz A., Serda M., Rejmund M., Polanski J., Musiol R.** // *Oncotarget*. 2018. V. 9. N 25. P. 17689– 17710. DOI: 10.18632/oncotarget.24844.
13. **El-Hefian E.A., Nasef M.M., Yahaya A.H.** // *E-J. Chem.* 2010. V. 7. N 4. P. 1212-1219. DOI: 10.1155/2010/626235.
14. **Muxika A., Etxabide A., Uranga J., Guerrero P., De La Caba K.** // *Int. J. Biolog. Macromol.* 2017. V. 105. N 2. P. 1358-1368. DOI: 10.1016/j.ijbiomac.2017.07.087.
15. **Suhag R., Kumar N., Trajkovska Petkoska A., Upadhyay A.** // *Food Res. Int.* 2020. V 136. P. 109582. DOI: 10.1016/j.foodres.2020.109582.

REFERENCES

1. **El Kadib A.** // *ChemSusChem*. 2015. V. 8. N 2. P. 217-244. DOI: 10.1002/cssc.201402718.
2. **Ailincai D., Bercea M., Tartau L.M., Marin L.** // *Carbohyd. Polym.* 2022. V. 298. P. 120071. DOI: 10.1016/j.carbpol.2022.120071.
3. **Kankala R.K., Liu C., Yang D., Wang S., Chen A.** // *Chem. Eng. J.* 2020. V. 383. P. 123138. DOI: 10.1016/j.cej.2019.123138.
4. **Kesavan S., Meena K.S., Dhakshinamoorthy R.** // *Biointerface Res. Appl. Chem.* 2022. V. 12. N 3. P. 3429-3445. DOI: 10.33263/BRIAC123.34293445.
5. **Malinowska-Pańczyk E., Staroszczyk H., Gottfried K., Kołodziejska I., Wojtasz-Pająk A.** // *Polym. J. Chem., Technol. Polym. Proc.* 2015. V. 60. N 11-12. P. 735-741. DOI: 10.14314/polimery.2015.735.
6. **Yuan D., Hao X., Liu G., Yue Y., Duan J.** // *Food Chem.* 2022. V. 385. P. 132647. DOI: 10.1016/j.foodchem.2022.132647.
7. **Guan G., Zhang L., Zhu J., Wu H., Li W., Sun Q.** // *J. Hazard. Mater.* 2021. V. 402. P. 123542. DOI: 10.1016/j.jhazmat.2020.123542.
8. **Han H., Xu X., Kan H., Tang Y., Liu C., Wen H., Wang F.** // *J. Colloid. Interface Sci.* 2022. V. 616. P. 304-315. DOI: 10.1016/j.jcis.2022.02.068.
9. **Adhikari H.S., Garai A., Manandhar K.D., Yadav P.N.** // *ACS omega*. 2022. V. 7. N 35. P. 30978-30988. DOI: 10.1021/acsomega.2c02966.
10. **Gojo I., Tidwell M.L., Greer J., Takebe N., Seiter K., Pochron M.F., Johnson B., Sznol M., Karp J.E.** // *Leuk. Res.* 2007. V. 7. N 31. P. 1165–1173. DOI: 10.1016/j.leukres.2007.01.004.
11. **Rao V.A., Klein S.R., Agama K.K., Toyoda E., Adachi N., Pommier Y., Shacter E.B.** // *Cancer Res.* 2009. V. 69. N 3. P. 948– 957. DOI: 10.1158/0008-5472.can-08-1437.
12. **Malarz K., Mrozek-Wilczkiewicz A., Serda M., Rejmund M., Polanski J., Musiol R.** // *Oncotarget*. 2018. V. 9. N 25. P. 17689– 17710. DOI: 10.18632/oncotarget.24844.
13. **El-Hefian E.A., Nasef M.M., Yahaya A.H.** // *E-J. Chem.* 2010. V. 7. N 4. P. 1212-1219. DOI: 10.1155/2010/626235.
14. **Muxika A., Etxabide A., Uranga J., Guerrero P., De La Caba K.** // *Int. J. Biolog. Macromol.* 2017. V. 105. N 2. P. 1358-1368. DOI: 10.1016/j.ijbiomac.2017.07.087.
15. **Suhag R., Kumar N., Trajkovska Petkoska A., Upadhyay A.** // *Food Res. Int.* 2020. V 136. P. 109582. DOI: 10.1016/j.foodres.2020.109582.

16. **Лебедева О.А., Седелкин В.М., Потехина Л.Н.** // *Изв. вузов. Химия и хим. технология.* 2022. Т. 65. Вып. 1. С. 58-65. DOI: 10.6060/ivkkt.20226501.6340.
17. **Иванов В.Б.** // *Физиология растений*. 2011. Т. 58. № 6. С. 944-952. DOI: 10.1134/S1021443711060082.
18. **Rahman A.-U., Choudhary M.I., Thomson J.** Techniques for Drug Development. London: CRC Press. 2001. DOI: 10.3109/9780203304532.
19. **Tripathi S., Mehrotra G.K., Dutta P.K.** // *Bull. Mater. Sci.* 2011. V. 34. P. 29-35. DOI: 10.1007/s12034-011-0032-5.
20. **Wichai S., Chuysinuan P., Chaiarwut S., Ekabutr P., Supaphol P.** // *J. Drug Delivery Sci. Technol.* 2019. V. 51. P. 662-671. DOI: 10.1016/j.jddst.2019.03.043.
21. **El-Shahawy A.A., El-Ela F.I.A., Mohamed N.A., Eldine Z.E., El Rouby W.M.** // Mater. Sci. Eng. 2018. V. 91. P. 361-371. DOI: 10.1016/j.msec.2018.05.042.

16. **Lebedeva O.A., Sedelkin V.M., Potekhina L.N.** // *ChemChemTech [Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.]*. 2022. V. 65. N 1. P. 58-65 (in Russian). DOI: 10.6060/ivkkt.20226501.6340.
17. **Ivanov V.B.** // *Fiziolog. Rasteniy.* 2011. V. 58. N 6. P. 944-952. DOI: 10.1134/S1021443711060082.
18. **Rahman A.-U., Choudhary M.I., Thomson J.** Techniques for Drug Development. London: CRC Press. 2001. DOI: 10.3109/9780203304532.
19. **Tripathi S., Mehrotra G.K., Dutta P.K.** // *Bull. Mater. Sci.* 2011. V. 34. P. 29-35. DOI: 10.1007/s12034-011-0032-5.
20. **Wichai S., Chuysinuan P., Chaiarwut S., Ekabutr P., Supaphol P.** // *J. Drug Delivery Sci. Technol.* 2019. V. 51. P. 662-671. DOI: 10.1016/j.jddst.2019.03.043.
21. **El-Shahawy A.A., El-Ela F.I.A., Mohamed N.A., Eldine Z.E., El Rouby W.M.** // Mater. Sci. Eng. 2018. V. 91. P. 361-371. DOI: 10.1016/j.msec.2018.05.042.

Поступила в редакцию 12.12.2022
Принята к опубликованию 27.03.2023

Received 12.12.2022
Accepted 27.03.2023