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**OBTAINING AND RESEARCH OF THE SUPRAMOLECULAR  
COMPLEXES OF ALKALOID SALSOLEINE WITH  
CYCLODEXTRINS BY NMR SPECTROSCOPY**

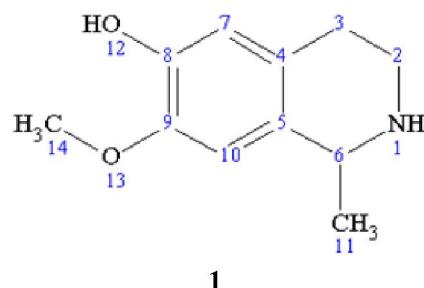
**Abstract.** One-dimensional NMR  $^1\text{H}$ ,  $^{13}\text{C}$  and DEPT and two-dimensional spectroscopy COSY ( $^1\text{H}-^1\text{H}$ ),  $^1\text{H}-^1\text{H}$  TOCSY,  $^1\text{H}-^1\text{H}$  ROESY, HMQC ( $^1\text{H}-^{13}\text{C}$ ) and  $^1\text{H}-^{13}\text{C}$  HMBC were used to study the alkaloid salsoline, as well as its supramolecular components, and the supramolecular components of the HMBC spectroscopy polysaccharides  $\alpha$ - and  $\gamma$ -cyclodextrins. Schemes of proton correlation with protons through three carbon atoms ( $^1\text{H}-^1\text{H}$ ) and HMQC ( $^1\text{H}-^{13}\text{C}$ ) in the initial state of the alkaloid under study. The use of the possibilities of two-dimensional spectroscopy COSY ( $^1\text{H}-^1\text{H}$ ),  $^1\text{H}-^1\text{H}$  TOCSY,  $^1\text{H}-^1\text{H}$  ROESY, HMQC ( $^1\text{H}-^{13}\text{C}$ ) and  $^1\text{H}-^{13}\text{C}$  HMBC when studying the alkaloid under study correctly and uniquely identify the structure of the substrate of supramolecular self-assembly with cyclic fields. Homonuclear and heteronuclear correlation NMR COSY ( $^1\text{H}-^1\text{H}$ ) and HMQC ( $^1\text{H}-^{13}\text{C}$ ) are also used to confirm the structure and structure of the cyclic polysaccharides of  $\alpha$ - and  $\gamma$ -cyclodextrins. The chemical shifts of the aliphatic and hydroxyl protons of the inner and outer surfaces of the receptors were determined. A comparative analysis of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of salsoline,  $\alpha$ - and  $\gamma$ -cyclodextrins and their supramolecular complexes was carried out. Certain changes have the chemical shifts of  $^1\text{H}$  and  $^{13}\text{C}$  nucleus of salsoline, as well as  $\alpha$ - and  $\gamma$ -cyclodextrins in supramolecular complexes. The proton integral intensities of the substrate and receptors in the  $^1\text{H}$  NMR spectra were definitely that the supramolecular self-assembly with alpha and  $\gamma$ -cyclodextrins occurs with the formation of complexes without including (external) due to the intermolecular interaction of hydroxyl groups from both the alkaloids and cyclodextrins. The water-soluble aggregates formed during this process are capable of solubilizing the required substrate through non-inclusive complexation.

**Keywords:** alkaloid salsoline, cyclodextrins, supramolecular complexes.

**Introduction**

Supramolecular self-assembly of alkaloids complexes with cyclodextrins (CD) allows to increase the solubility of a substance in water, to improve their bioavailability and physical and chemical stability, to protect against biodegradation and to reduce toxicity [1-5]. CDDs are relatively affordable compounds, produced from renewable raw materials - starch. The most common are  $\alpha$ -,  $\beta$ -,  $\gamma$ -CDA-containing, containing, respectively, 6, 7 and 8 glucopyranose units. The increased interest in CD-us is due to their cyclic structure and the ability, due to the internal hydrophobic cavity, to form supramolecular inclusion complexes of the host-guest type (receptor-substrate) in an aqueous medium [6-8].

The choice of salsoline 1 as a substrate for the supramolecular self-assembly of complexes with  $\alpha$ - and  $\gamma$ -CD is determined by the presence of a wide spectrum of biological activity of the alkaloid and its poor solubility in water [9-12].



Supramolecular complexes 1 with  $\alpha$ - and  $\gamma$ -CD were obtained by interaction of equimolecular amounts of substrate 1 with  $\alpha$ - and  $\gamma$ -CD receptors in ethanol solutions of the reactants at 65–70°C for 7 hours, followed by separation of the supra complexes by drying.

### Results and discussion

The NMR spectroscopic study of supramolecular inclusion complexes 1, obtained on the basis of CDs, is based on determining the difference in the chemical shifts of the  $^1\text{H}$  and  $^{13}\text{C}$  substrates (1) and receptors (CDs) in the free state and in the complexes as a result of intermolecular interaction. In terms of the magnitude of the change in chemical shifts of internal or external protons of CDDs, it is possible to judge the formation of internal (inclusion complexes) or external (without inclusion) complexes, respectively. The change in the chemical shifts of  $^1\text{H}$  and  $^{13}\text{C}$  in the spectra of the substrate makes it possible to determine the direction of the latter's entry into the cavity of the CDs [1–8].

The structure of compound 1 was established on the basis of the results of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy obtained in DMSO-d<sub>6</sub> (Tables 1 and 2). The correctness of the assignment of one-dimensional  $^1\text{H}$  and  $^{13}\text{C}$  1 NMR spectra was confirmed by the data of two-dimensional correlations of the  $^1\text{H}$ - $^1\text{H}$  TOCSY NMR spectra,  $^1\text{H}$ - $^1\text{H}$  ROESY,  $^1\text{H}$ - $^{13}\text{C}$  HMQC and  $^1\text{H}$ - $^{13}\text{C}$  HMBC.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of  $\alpha$ - and  $\gamma$ -CDA in the free state and the supramolecular complexes based on them with 1, obtained in DMSO-d<sub>6</sub>, are presented in Tables 1 and 2.

Table 1 – Chemicalshifts  $^1\text{H}$  and  $^{13}\text{C}$  NMR of compound 1 and  $\alpha$ -CD-na in the free state ( $\delta_0$ ) and in the composition of the supramolecular complex ( $\delta$ )

Atomnumber C	Group	$\delta_0$ , ppm		$\delta$ , ppm		$\Delta\delta=\delta-\delta_0$ , ppm	
		$^1\text{H}$	$^{13}\text{C}$	$^1\text{H}$	$^{13}\text{C}$	$^1\text{H}$	$^{13}\text{C}$
<b>Connections 1</b>							
2	CH <sub>ax</sub> CH <sub>eq</sub>	2.76 2.83	38.85	2.76 2.81	38.94	0 -0.01	0.09
3	CH <sub>ax</sub> CH <sub>eq</sub>	3.14 3.28	24.87	3.15 3.23	24.97	0.01 -0.05	0.10
4	C		124.28		124.28		0
5	C		124.87		124.97		0.10
6	CH	4.32	50.46	4.34	50.58	0.02	0.12
7	CH	6.55	115.51	6.54	115.55	-0.01	0.04
8	C		146.47		146.48		0.01
9	C		147.22		147.25		0.03
10	CH	6.75	110.36	6.74	110.39	-0.01	0.03
11	CH <sub>3</sub>	1.53	19.74	1.52	19.81	-0.01	0.64
14	CH <sub>3</sub>	3.69	56.31	3.70	56.35	0.01	0.04
12	OH	9.17		9.09		-0.08	
<b><math>\alpha</math>-Cyclodextrin</b>							
1	CH	4.76	102.48	4.76	102.46	0	-0.02
2	CH	3.24	72.64	3.23	72.60	-0.01	-0.04
3	CH	3.73	73.78	3.73	73.78	0	0
4	CH	3.34	82.59	3.34	82.60	0	0.01
5	CH	3.53	72.64	3.54	72.60	0.01	-0.04
6	CH <sub>2</sub>	3.60	60.55	3.60	60.50	0	-0.05
2	OH	5.44		5.49		0.05	
3	OH	5.38		5.41		0.03	
6	OH	4.42		4.47		0.05	

Table 2 – Chemical shifts  $^1\text{H}$  and  $^{13}\text{C}$  NMR of compound 1 and  $\gamma$ -CD-na in the free state ( $\delta_0$ ) and in the supramolecular complex ( $\delta$ )

Atomnumber C	Group	$\delta_0$ , ppm		$\delta$ , ppm		$\Delta\delta=\delta-\delta_0$ , ppm	
		$^1\text{H}$	$^{13}\text{C}$	$^1\text{H}$	$^{13}\text{C}$	$^1\text{H}$	$^{13}\text{C}$
<b>Connections1</b>							
2	CH <sub>ax</sub> CH <sub>eq</sub>	2.76 2.83	38.85	2.77 2.82	38.93	0.01 -0.01	0.08
3	CH <sub>ax</sub> CH <sub>eq</sub>	3.14 3.28	24.87	3.16 3.28	24.95	0.01 0	0.08
4	C		124.28		124.28		0
5	C		124.87		124.93		0.06
6	CH	4.32	50.46	4.34	50.58	0.02	0.12
7	CH	6.55	115.51	6.54	115.55	-0.01	0.04
8	C		146.47		146.49		0.02
9	C		147.22		147.25		0.03
10	CH	6.75	110.36	6.74	110.39	-0.01	0.03
11	CH <sub>3</sub>	1.53	19.17	1.52	19.80	-0.01	0.63
14	CH <sub>3</sub>	3.69	56.31	3.70	56.35	-0.01	0.04
12	OH	9.17		9.09		-0.08	
<b><math>\gamma</math>-Cyclodextrin</b>							
1	CH	4.83	102.20	4.85	102.18	0.02	-0.02
2	CH	3.28	73.11	3.28	73.10	0	-0.01
3	CH	3.54	73.44	3.54	73.44	0	0
4	CH	3.30	81.46	3.31	81.41	0.01	-0.05
5	CH	3.47	72.69	3.48	72.68	0.01	-0.01
6	CH <sub>2</sub>	3.58	60.53	3.58	60.48	0	-0.05
2	OH	5.69		5.75		0.06	
3	OH	5.66		5.72		0.06	
6	OH	4.46		4.51		0.05	

Comparison of the integral intensities of the  $^1\text{H}$  NMR signals of the salsoline molecule with  $\alpha$ - and  $\gamma$ -CDA in supramolecular complexes showed that alkaloid 1 with both CDA forms 1: 1 complexes.

During the formation of supramolecular complexes 1 with  $\alpha$ - and  $\gamma$ -CD, we observe insignificant changes in proton chemical shifts  $\Delta\delta$  in cyclodextrin molecules to the same extent both for internal hydrophobic protons H-5 and H-6 that are closest to the edge of the cylindrical rim, and for located in the outer hydrophilic surface of protons H-1, H-2 and H-4. In both CD-new molecules, there is no change in the chemical shift of  $^1\text{H}$  NMR of the internal hydrophobic proton H-3. The greatest change in the proton spectra of cyclodextrins occurs in hydroxyl protons 2-OH, 3-OH and 6-OH. In the alkaloid molecule 1, the change in the proton spectra is also insignificant. The greatest change in the proton spectra is observed at the hydroxyl proton H-12. These results indicate that the supramolecular self-assembly of salsoline with CD-nam leads to the formation of complexes without the inclusion of (external) [3, 13] due to the intermolecular interaction of hydroxyl groups from both the alkaloid and the CD-n (Fig. 1). The water-soluble aggregates formed during this process are able to solubilize the substrate molecule through non-inclusive complexation [14].

As a result of a comparative analysis of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of salsoline,  $\alpha$ - and  $\gamma$ -cyclodextrins and their supramolecular complexes, as well as by the value of the proton integrated intensities of the substrate and receptors in the  $^1\text{H}$  NMR spectra, it was determined that supramolecular self-assembly of salsoline with  $\alpha$ - and  $\gamma$ -cyclodextrins occurs with the formation of complexes without the inclusion of (external) due to the intermolecular interaction of hydroxyl groups from both the alkaloid and cyclodextrins. The water-soluble aggregates formed during this process are capable of solubilizing the substrate molecule through non-inclusive complexation. This allows you to increase the solubility of the substrate in water. The resulting salsoline supra complexes are essentially nanocomplexes of the latter and can be used in nanomedicine in the future.

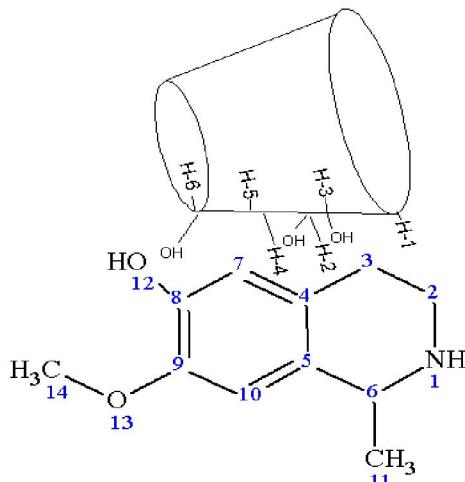


Figure 1 – Estimated supramolecular complexes without the inclusion of molecule 1 with  $\alpha$ - and  $\gamma$ -CD-us

### Experimental part

$\alpha$ - and  $\gamma$ -CDs were used by Fluka, 99% pure. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Jeol JNM-ECA 400 spectrometer (399.78 and 100.53 MHz on  $^1\text{H}$  and  $^{13}\text{C}$  cores, respectively) in a  $\text{DMSO-d}_6$  solution at room temperature. Chemical shifts are measured relative to the residual signals of protons or carbon atoms  $\text{DMSO-d}_6$ .

Obtaining the inclusion complexes of salsoline alkaloid with  $\alpha$ - and  $\gamma$ -cyclodextrins. We have chosen the coprecipitation method, since this method allows to obtain a very pure preparation of the inclusion complex in crystalline form. To a concentrated solution of salsoline alkaloid in ethanol in the ratio of 1: 1 a saturated solution of cyclodextrin in water was added dropwise. Then stirred with a magnetic stirrer at a temperature of 65-70 ° C. The individuality of the proposed complexes was checked by thin layer chromatography on Silufol UV-254 plates in the system of isopropyl alcohol - 25% ammonia-water solution 7:2:1. The final product must be dried at a temperature of 60°C in a vacuum dryer at an atmospheric pressure of 0.4 kgf / cm<sup>2</sup>. The inclusion complexes of salsoline with cyclodextrins were obtained in the form of a powder.

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### ЯМР СПЕКТРОСКОПИЯСЫ ӘДІСІМЕН ЦИКЛОДЕКСТРИНДЕРМЕН САЛЬСОЛИН АЛКАЛОИДТАРЫНЫҢ СУПРАМОЛЕКУЛЯРЛЫ КЕШЕНДЕРІН АЛУ ЖӘНЕ ЗЕРТТЕУ

**Аннотация.**  $^1\text{H}$ ,  $^{13}\text{C}$  және DEPT бір өлшемді ЯМР және COSY ( $^1\text{H}-^1\text{H}$ ),  $^1\text{H}-^1\text{H}$  TOCSY,  $^1\text{H}-^1\text{H}$  ROESY, HMQC ( $^1\text{H}-^{13}\text{C}$ ) және  $^1\text{H}-^{13}\text{C}$  HMBC әдістерімен алкалоид сальсолиннің оның циклдық полисахарид  $\alpha$ -және  $\gamma$ -цикодекстриндермен супрамолекулярлық кешендері зерттелді. Зерттелетін алкалоид молекуласында COSY ( $^1\text{H}-^1\text{H}$ ) және HMQC ( $^1\text{H}-^{13}\text{C}$ ) бір байланыс арқылы көміртекті атомдармен протондар корреляциясының, сондай-ақ үш байланыс арқылы протондары бар протондар корреляциясының схемалары ұсынылған. Зерттелетін алкалоидты сәйкестендіру кезінде COSY ( $^1\text{H}-^1\text{H}$ ),  $^1\text{H}-^1\text{H}$  TOCSY,  $^1\text{H}-^1\text{H}$  ROESY, HMQC ( $^1\text{H}-^{13}\text{C}$ ) және  $^1\text{H}-^{13}\text{C}$  HMBC екі өлшемді спектроскопия мүмкіндіктерін пайдалану циклдік полисахаридті рецепторлармен супрамолекулярлық өздігінен жинаудың субстратының құрылымын дұрыс және бір мәнді сәйкестендіруге мүмкіндік берді. Гомоядерлік және гетероядролық корреляция ЯМР COSY ( $^1\text{H}-^1\text{H}$ ) және HMQC ( $^1\text{H}-^{13}\text{C}$ )  $\alpha$ - және  $\gamma$ -цикодекстриндердің циклдық полисахаридтерінің құрылымы мен құрамын сәйкестендіру және растау мақсатында колданылды. Рецепторлардың ішкі және сыртқы бетінің алифатикалық және гидроксильді протондарының химиялық өзгерістері анықталды. Сальсолиннің  $^1\text{H}$  және

$^{13}\text{C}$  ЯМР спектрлеріне,  $\alpha$ - және  $\gamma$ -циклодекстриндерге және олардың супрамолекулярлық кешендеріне салыстырмалы талдау жүргізілді. Сальсолиннің  $^1\text{H}$  және  $^{13}\text{C}$  ядроларының химиялық ығысуы мәндерінің, сондай-ақ супрамолекулярлық кешендердегі  $\alpha$ -және  $\gamma$ -циклодекстриндердің өзгеруі анықталды. Субстрат пен рецепторлардың ЯМР  $^1\text{H}$  спектріндегі протонды интегралды қарқындылығының шамасы бойынша  $\alpha$ - және  $\gamma$ -циклодекстриндермен сальсолиннің супрамолекулалық өздігінен жинауы алкалоид жағынан да, циклодекстриндер жағынан да гидроксильді топтардың молекулааралық өзара әрекеттесуі (сырткы) әсерлердің көмегінсіз-ақ, кешендердің пайда болуымен жүреді. Бұл ретте түзілетін суда еритін агрегаттар субстрат молекуласын инклузивтік емес кешен құру арқылы солюбилизациялауға қабілетті.

**Кілт сөздер:** сальсолин алкалоиды, циклодекстриндер, супрамолекулярлық кешендер.

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## **ПОЛУЧЕНИЕ И ИССЛЕДОВАНИЕ СУПРАМОЛЕКУЛЯРНЫХ КОМПЛЕКСОВ АЛКАЛОИДА САЛЬСОЛИНА С ЦИКЛОДЕКСТРИНАМИ МЕТОДОМ СПЕКТРОСКОПИИ ЯМР**

**Аннотация.** Методами ЯМР одномерной  $^1\text{H}$ ,  $^{13}\text{C}$  и DEPT и двумерной спектроскопии COSY( $^1\text{H}-^1\text{H}$ ),  $^1\text{H}-^1\text{H}$  TOCSY,  $^1\text{H}-^1\text{H}$  ROESY, HMQC ( $^1\text{H}-^{13}\text{C}$ ) и  $^1\text{H}-^{13}\text{C}$ HMBC исследованы алкалоид сальсолин, а также его супрамолекулярные комплексы с циклическими полисахаридами  $\alpha$ - и  $\gamma$ -циклодекстринами. Представлены схемы корреляций протонов с протонами через три связи и схемы корреляций протонов с углеродными атомами через одну связь COSY( $^1\text{H}-^1\text{H}$ ) и HMQC ( $^1\text{H}-^{13}\text{C}$ ) в молекуле исследуемого алкалоида. Использование при идентификации изучаемого алкалоида возможностей двумерной спектроскопии COSY( $^1\text{H}-^1\text{H}$ ),  $^1\text{H}-^1\text{H}$  TOCSY,  $^1\text{H}-^1\text{H}$  ROESY, HMQC ( $^1\text{H}-^{13}\text{C}$ ) и  $^1\text{H}-^{13}\text{C}$ HMBC позволило правильно и однозначно идентифицировать строение субстрата супрамолекулярной самосборки с циклическими полисахаридными рецепторами. Гомоядерная и гетероядерная корреляция ЯМР COSY( $^1\text{H}-^1\text{H}$ ) и HMQC ( $^1\text{H}-^{13}\text{C}$ ) применена также для идентификации и подтверждения строения и структуры циклических полисахаридов  $\alpha$ - и  $\gamma$ -циклодекстринов. Были определены химические сдвиги алифатических и гидроксильных протонов внутренней и внешней поверхности рецепторов. Проведен сравнительный анализ спектров ЯМР  $^1\text{H}$  и  $^{13}\text{C}$  сальсолина,  $\alpha$ - и  $\gamma$ -циклодекстринов и их супрамолекулярных комплексов. Определены изменения значений химических сдвигов ядер  $^1\text{H}$  и  $^{13}\text{C}$  сальсолина, а также  $\alpha$ - и  $\gamma$ -циклодекстринов в супрамолекулярных комплексах. По величине протонных интегральных интенсивностей субстрата и рецепторов в спектрах  $^1\text{H}$  ЯМР было определено, что супрамолекулярная самосборка сальсолина с  $\alpha$ - и  $\gamma$ -циклодекстринами происходит с образованием комплексов без включения (внешних) за счет межмолекулярного взаимодействия гидроксильных групп как со стороны алкалоида, так и со стороны циклодекстринов. Образуемые при этом водорастворимые агрегаты способны солюбилизировать молекулу субстрата через неинклузивное комплексообразование.

**Ключевые слова:** алкалоид сальсолин, циклодекстрины, супрамолекулярные комплексы.

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**REFERENCES**

- [1] Hadaruga D.I., Hadaruga N.G., Butnaru G., Tatu C., Gruia A. Bioactive microparticles (10): thermal and oxidative stability of nicotine and its complex with  $\beta$ -cyclodextrin // J. Incl. Phenom. Macrocycl. Chem. **2010**. Vol. 68. P. 155-164.
- [2] Ivanova B., Spitteler M. Novel pyrrolo-quinazolino-quinoline analogues of the natural alkaloids and their inclusion molecular complexes in the native cyclodextrins: experimental versus theoretical study // J. Incl. Phenom. Macrocycl. Chem. **2013**. Vol. 76. P. 87-98.
- [3] Hazra S., Hossain M., Kumar G.S. Studies on  $\alpha$ -,  $\beta$ -, and  $\gamma$ -cyclodextrin inclusion complexes of isoquinoline alkaloids berberine, palmatine and coralyne // J. Incl. Phenom. Macrocycl. Chem. **2014**. Vol. 78. P. 311-323.
- [4] Rekharsky M.V., Goldberg R.N., Schwarz F.P., Tewari Y.B., Ross P.D., Yamashoji Y., Inoue Y. Thermodynamic and Nuclear Magnetic Resonance Study of the  $\alpha$ Interactions of  $\alpha$ - and  $\beta$ -Cyclodextrin with Model Substances: Phenethylamine, Ephedrines, and Related Substances // J. Am. Chem. Soc. **1995**. Vol. 117. P. 8830-8840.
- [5] Seilkhanov T.M., Nurkenov O.A., Isaeva A.Zh., Nazarenko L.A., Seilkhanov O.T. Preparation and NMR spectroscopic studies of the supramolecular inclusion complex of anabasine and  $\beta$ -cyclodextrin // Chem. Nat. Compd. **2016**. Vol. 52, № 6. P. 1066-1068.
- [6] Szejtli J. Cyclodextrins and Their Inclusion Complexes. Budapest: Akademiai Kiado, **1982**. 296 p.
- [7] Uekama K., Hirayama F., Irie T. Cyclodextrins Drug Carrier Systems // Chem. Rev. **1998**. Vol. 98, № 5. P. 2045-2076.
- [8] Rasheed A., Kumar A.S.K., Sravanti V.V. Cyclodextrins as Drug Carrier Molecule: A Review // Sci. Pharm. **2008**. Vol. 76, issue 4. P. 567-598.
- [9] Mashkovsky M.D. Drugs: in 2 t. M.: New Wave, **2012**. 1216p.
- [10] Orekhov A.P. Chemistry of alkaloids. M.: ed. USSR ACADEMY OF SCIENCES, **1955**. 672 p.
- [11] Henry T.A. Chemistry of vegetable alkaloids. M.: Goskhimizdat, **1956**. 669 p.
- [12] Lurie Y.Y. Handbook of analytical chemistry. M.: Chemistry, **1979**. 312p.
- [13] Demarco P.V., Thakkar A.I. Cyclohepta-amilose Inclusion Complexes. A ProtonMagnetic Resonanse Study // J. Chem. Soc., Chem. Commun. **1970**. Issue 1. P. 2-4.
- [14] Loftsson T., Masson M., Brewster M.E. Self-association of cyclodextrins and cyclodextrin complexes // J. Pharm. Sci. **2004**. Vol. 93, Issue 5. P. 1091-1099.
- [15] Nurkenov O.A., Fazylov S.D., Issayeva A.Zh., Seilkhanov T.M., Zhivotova T.S., Shulgau Z.T., Kozhina Zh.M. Complexes of inclusion of functionally-substituted hydrazones of isonicotinic acid with cyclodextrines and their antiradical activity // News of the NAS RK. Series of chemistry and technology. -2018. №6. P.57-66.<https://doi.org/10.32014/2018.2518-1491.26>.