

15. Izutani Y. Aggregation property of glycyrrhizic acid and its interaction with cyclodextrins analyzed by dynamic light scattering, isothermal titration calorimetry, and NMR / Y. Izutani, K. Kanaori, M. Oda // *Carbohydr. Res.* – 2014. – Vol. 392. – P. 25–30.
16. Бабко А. К. Физико-химический анализ комплексных соединений в растворах / А. К. Бабко. – К.: Изд-во АН УССР, 1955. – 328 с.
17. Gluschenko O. Yu. NMR relaxation study of cholesterol binding with plant metabolites / O. Yu. Gluschenko, N. E. Polyakov, T. V. Leshina // *Appl. Magn. Reson.* – 2011. – Vol. 41, № 2. – P. 283–294.
18. Study of the interaction between monoammonium glycyrrhizinate and bovine serum albumin / Y.-J. Hu, Y. Liu, J.-B. Wang [et al.] // *J. Pharm. Biomed. Anal.* – 2004. – Vol. 36, № 4. – P. 915–919.
19. Комплексообразование глицирризиновой кислоты с 5-нитро-8-оксихинолином и тринитроглицерином / В. Н. Майстренко, В. Н. Гусаков, И. А. Русаков [и др.] // *Докл. Акад. наук.* – 1994. – Т. 335, № 3. – С. 329–331.

SUPRAMOLECULAR COMPLEX OF MONOAMMONIUM SALT OF GLYCYRRHIZIC ACID (GLYCYRAM) WITH TRYPTOPHAN

Yakovishin L. A.¹, Grishkovets V. I.²

¹*Sevastopol State University, Sevastopol, Russia*

²*V. I. Vernadsky Crimean Federal University, Simferopol, Crimea, Russian Federation*

E-mail: chemseventu@rambler.ru

A new supramolecular complex of triterpene glycoside glycyram (monoammonium salt of glycyrrhizic acid (3-*O*-β-*D*-glucuronopyranosyl-(1→2)-*O*-β-*D*-glucuronopyranoside of 18β-glycyrrhetic acid), GC) with hydrophobic essential amino acid *L*-tryptophan (Trp) was prepared.

The complexation of GC with Trp in aqueous solution at pH 7.2 (phosphate buffer Na₂HPO₄-NaH₂PO₄) was investigated by spectrophotometric method. Absorption spectrum of isomolar series for GC-Trp mixture has isobestic points at 232 and 274 nm. It was shown that GC and Trp forms a 1:1 complex, having a stability constant $K_{GC-Trp} = (4.8 \pm 0.2) \cdot 10^4 \text{ M}^{-1}$. In the previously obtained 1:1 complexes of glycyrrhizic acid and GC with biologically active molecules, stability constants were of the order of 10^3 – 10^5 M^{-1} . Molecular complex of GC with Trp was studied by IR spectroscopy. The changes in the IR spectra were indicated to presence of ionic interactions of the zwitter-ion Trp with GC (NH₃⁺ ⁻OOC) and hydrophobic contacts.

Keywords: triterpene glycosides, glycyrrhizic acid, glycyram, tryptophan, supramolecular complex, spectrophotometry, IR spectroscopy, stability constant.

References

1. Sandyk R., *L*-Tryptophan in neuropsychiatric disorders: a review, *Int. J. Neurosci.*, **67** (1-4), 127 (1992).
2. Korobov N. V., Bichenova K. A., Yavorsky A. N., Domestic innovative drugs: synthetic peptides prospects, *Med. technol. Assessment and choice*, 1, 98 (2011). (*in Russ.*).
3. Tolstikova T. G., Khvostov M. V., Bryzgalov A. O., The complexes of drugs with carbohydrate-containing plant metabolites as pharmacologically promising agents, *Mini Rev. Med. Chem.*, **9** (11), 1317 (2009).

4. Yakovishin L. A., Grishkovets V. I., Ivy and licorice triterpene glycosides: promising molecular containers for some drugs and biomolecules, in *Studies in natural products chemistry*, edited by Atta-ur-Rahman, **55**, 351 (Elsevier, Amsterdam, 2017).
5. Yakovishin L. A., Lekar A. V., Borisenko S. N., Vetrova E. V., Borisenko N. I., Grishkovets V. I., Molecular complexation of ivy saponins with *L*-tryptophan, *Khim. Rastit. Syr'ja*, **4**, 65 (2011). (in Russ.).
6. Yakovishin L. A., Grishkovets V. I., Epishina N. V., Kurtametov I. S., Molecular complexation of the triterpene glycosides with tryptophan in water solutions, *Sci. Not. Taurida V. I. Vernadsky Nat. Univ., ser. Biol. Chem.*, **23** (2), 270 (2010). (in Russ.).
7. Pilipenko V. V., Aksyonov S. A., Kalinkevich A. N., Sukhodub L. F., PDMS study of the steroid glycosides interaction with amino acids, *Biopolym. Cell*, **16** (3), 212 (2000). (in Ukr.).
8. Pilipenko V. V., Sukhodub L. F., Aksyonov S. A., Kalinkevich A. N., Kintia P. K., ²⁵²Cf Plasma desorption mass spectrometric study of interactions of steroid glycosides with amino acids, *Rapid Commun. Mass Spectrom.*, **14**, 819 (2000).
9. Gorchakova N. A., Samarskaya T. G., Samarsky V. A., Lezina G. G., Grischenko L. I., Babak V. V., Complexation of cardiac glycosides with amino acids and alkaline earth metals, *Eksp. Klin. Farmakol.*, **55** (2), 106 (1992). (in Russ.).
10. Yakovishin L. A., Korzh E. N., Degtyar A. D., Klimenko A. V., Spectrophotometry of the supramolecular complexes of ivy and licorice triterpene glycosides with laevomycetin (chloramphenicol), *Ukr. Bioorg. Acta*, **11** (1), 33 (2013). (in Ukr.).
11. Yakovishin L. A., Grishkovets V. I., Klimenko A. V., Degtyar A. D., Kuchmenko O. B., Molecular complexes of ivy and licorice triterpene glycosides with doxorubicin, *Khim.-Farm. Zhurn.*, **48** (6), 37 (2014). (in Russ.).
12. Tolstikov G. A., Baltina L. A., Murinov Yu. I., Davydova V. A., Tolstikova T. G., Bondarev A. I., Zarudin F. S., Lazareva D. N., Complexes of β -glycyrrhizinic acid with nonsteroidal antiinflammatory drugs as novel transport forms, *Khim.-Farm. Zhurn.*, **25** (2), 29 (1991). (in Russ.).
13. Dalimov D. N., Isaev Yu. T., Saiitkulov A. M., Molecular complexes of ammonium glycyrrhizate with certain medicinal agents and their interferon-inducing activity, *Khim. Prirod. Soedin.*, **2**, 132 (2001). (in Russ.).
14. Nafisi S., Manouchehri F., Bonsaii M., A comparative study of glycyrrhizin and glycyrrhetic acid complexes interactions with DNA and RNA, *Iranian J. Org. Chem.*, **4** (2), 841 (2012).
15. Izutani Y., Kanaori K., Oda M., Aggregation property of glycyrrhizic acid and its interaction with cyclodextrins analyzed by dynamic light scattering, isothermal titration calorimetry, and NMR, *Carbohydr. Res.*, **392**, 25 (2014).
16. Babko A. K., *Physico-chemical analysis of complex compounds in the solutions*, 328 (Izd-vo AN USSR, Kiev, 1955). (in Russ.).
17. Gluschenko O. Yu., Polyakov N. E., Leshina T. V., NMR relaxation study of cholesterol binding with plant metabolites, *Appl. Magn. Reson.*, **41** (2), 283 (2011).
18. Hu Y.-J., Liu Y., Wang J.-B., Xiao X.-H., Qu S.-S., Study of the interaction between monoammonium glycyrrhizinate and bovine serum albumin, *J. Pharm. Biomed. Anal.*, **36** (4), 915 (2004).
19. Maistrenko V. N., Gusakov V. N., Rusakov I. A., Murinov Yu. I., Tolstikov G. A., Complexation of glycyrrhizic acid with 5-nitro-8-hydroxyquinoline and trinitroglycerol, *Dokl. Akad. Nauk.*, **335** (3), 329 (1994). (in Russ.).