ABSTRACT&REFERENCES

DOI: 10.15587/2519-4852.2018.151447

STUDIES ON THE DESIGN OF A COMPOSITION OF GEL FOR THE TREATMENT OF INFLAMMATORY DISEASES OF THE JOINTS

p. 4-8

Liliia Vyshnevska, Doctor of Pharmaceutical Sciences, Professor, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: liliiavyshnevska@gmail.com
ORCID: *http://orcid.org/0000-0002-6887-3591*

Oksana Strilets, Doctor of Pharmaceutical Sciences, Professor, Department of Biotechnology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: biotechnology.nuph@gmail.com
ORCID: *http://orcid.org/0000-0003-0846-8663*

Vladyslav Postoy, Postgraduate Student, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: 19_vladik_91@ukr.net

The aim: *the aim of our work was to experimentally substantiate the effectiveness of antimicrobial preservatives in the design of the composition of the combined gel for the treatment of acute and chronic inflammation of the joints.*
Methods: *biological pharmacopoeial method of research was used (research of the effectiveness of antimicrobial preservatives).*
Results. *All drugs must meet the requirements of regulatory documents on indicators "Microbiological purity." To ensure the microbiological stability of the preparations, it is necessary to eliminate the factors associated with microbial contamination, therefore we carried out experimental studies on the choice of preservative and its concentration for the developed gel. According to the results of experimental studies on the effectiveness of antimicrobial preservatives in gel samples, the following data were obtained. Samples of the studied gel with sodium preservatives benzoate 0.5 % and nipagin 0.2 % meet the criterion "A" according to the requirements of SPHU for drugs for skin application. But, according to research results, the antimicrobial efficacy of the gel with the preservative nipagin 0.2 % was slightly higher (lg reduction in the number of viable Staphylococcus aureus ATCC 6538 cells was 3.32 and 4.81; Pseudomonas aeruginosa ATCC 9027 – 3.28 and 4.66 ; Candida albicans ATCC 885-653 – 3.50 and 4.09; Aspergillus brasiliensis ATCC 16404 – 3.10 and 4.00 (2 and 7 days, respectively) and the spectrum of antimicrobial action is wider, which will contribute to the quality of the rotated gel also during storage. Therefore, for further research, we will use nipagin 0.2 % as a preservative.*
Conclusions: *The expediency of using nipagin 0.2 % as a part of a combined gel for the treatment of acute and chronic joint inflammation has been theoretically proved and experimentally proved*
Keywords: *combined gel, composition, preservatives, antimicrobial activity, nipagin, technology, inflammation of the joints*

References

1. Akao, T., Yoshino, T., Kobashi, K., Hattori, M. (2002). Evaluation of Salicin as an Antipyretic Prodrug that does not Cause Gastric Injury. Planta Medica, 68 (8), 714–718. doi: http://doi.org/10.1055/s-2002-33792

2. Bisset, N. G. (2004). Herbal Drugs and Phytopharmaceuticals. Stuttgart: Medpharm Scientific Publishers, 534–536.

3. Meier, F. M., Frerix, M., Hermann, W., Müller-Ladner, U. (2013). Current immunotherapy in rheumatoid arthritis. Immunotherapy, 5 (9), 955–974. doi: http://doi.org/10.2217/imt.13.94

4. Klimes, J., Vocelka, M., Sedova, L., Dolezal, T., Mlcoch, T., Petrikova, A., Vlcek, J. (2014). Medical and Productivity Costs of Rheumatoid Arthritis in The Czech Republic: Cost-of-Illness Study Based on Disease Severity. Value in Health Regional Issues, 4, 75–81. doi: http://doi.org/10.1016/j.vhri.2014.07.004

5. Postoi, V. V., Vyshnevska, L. I. (2017). Doslidzhennia z rozrobky skladu heliu dlia likuvannia revmatoidnoho artrytu. Kyiv, 2, 143.

6. Postoi, V. V., Vyshnevska, L. I. (2018). The marketing research of the Ukrainian market of drugs for the treatment of arthritis. News of Pharmacy, 1 (93), 38–42. doi: http://doi.org/10.24959/nphj.18.2198

7. Derzhavna Farmakopeia Ukrainy (2011). Kharkiv: Derzhavne pidpryiemstvo «Naukovo-ekspertnyi farmakopeinyi tsentr», RIREH, 536.

8. Derzhavna Farmakopeia Ukrainy Kharkiv. Vol. 1 (2015). Kharkiv: Derzhavne pidpryiemstvo «Ukrainskyi naukovyi farmakopeinyi tsentr yakosti likarskykh zasobiv», 1128.

9. Mirsonbol, S. Z., Issazadeh, K., Pahlaviani, M., Momeni, N. (2014). Antimicrobial efficacy of the methylparaben and benzoate sodium against selected standard microorganisms, clinical and environmental isolates in vitro. Indian Jornal of Fundamental and Applied Life Sciences, 4 (S4), 363–367.

10. Stanojevic, D. C. (2009). Antimicrobial effects of Sodium benzoate, Soium nitrate and Potassium sorbate and Their synergistic action in vitro. Bulgarian Journal of Agricultural Science, 15 (4), 307–311.

DOI: 10.15587/2519-4852.2018.151428

STUDY OF ANTHELMINTIC ACTIVITY AND ACUTE TOXICITY OF MEDICINE OF COMBINED COMPOSITION

p. 8-12

Kateryna Semchenko, PhD, Associate Professor, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: tolochko.kv@gmail.com
ORCID: *http://orcid.org/0000-0003-3824-8899*

Liliia Vyshnevska, Doctor of Pharmaceutical Sciences, Professor, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: atl@nuph.edu.ua
ORCID: *http://orcid.org/0000-0002-6887-3591*

Natalia Polovko, Doctor of Pharmaceutical Sciences, Professor, Head of Department, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: atl@nuph.edu.ua
ORCID: *http://orcid.org/0000-0002-1224-1739*

Aim. *The aim of the work is to investigate the anthelmintic activity and acute toxicity of the drug containing albendazole and praziquantel in the ratio (1:4) in relation to pathogens of ascariasis in pigs, toxocarosis and dipylidiosis in dogs. These pathogens belong to the class of nematodosis (ascariasis, toxocarosis) and cestodoses (dipylidiosis).*

Materials and methods. *The studies were carried out in the coproscopic laboratory of the parasitology department of Kharkov State Zooveterinary Academy and by the standardized method of Füllbourne and the 'Method for the quantitative determination of helminth eggs' (patent No. 9265). Samples for the study in dogs were obtained in the CP "Center for Animal Welfare". In order to study the degree of toxicity of the proposed combination of albendazole and praziquantel, blood samples of pigs before and in 24 hours and 72 hours after the drug administration were taken for carrying out morphological and biochemical studies.*

Results. *The results obtained indicate the presence of anthelminthic activity of the studied drug in relation to pathogens of ascariasis, toxocarosis and dipylidiosis. The parameters of hematological studies in pigs free from intestinal helminthes before and after 24 and 72 hours after intake the drug were within the limits of the physiological norm. Findings of the clinical examination of the animals of the two experimental groups showed that the behavior of the animals did not change (natural), the intake of food and water was normal, the visible mucous membranes were pale pink, the skin was intact, without damage and elastic.*

Conclusion. *Thus, the proposed drug shows high level of anthelminthic activity in relation to pathogens of ascariasis, toxocarosis and dipylidiosis. The degree of its toxicity corresponds to "low toxic". The obtained results indicate the advisability of the further research*

Keywords: *anthelmintic drugs, albendazole, praziquantel, nematodosis, cestodosis, pharmacological studies*

References

1. Dudnik, V. M., Izumets, O. I., Layko, L. I. et. al. (2011). Diagnostika i patogenetichni aspekti likuvannya gel'mintoziv [Diagnostics and pathogenetic aspects of treatment of helminthiasis]. Modern pediatrics, 4 (38), 70–72.

2. Ershova, I. B., Osichnyuk, L. M., Mochalova, G. O. (2013). Gel'mintozi u ditei [Helminthiasis in children]. Perinatology and pediatrics, 2 (54), 125–131.

3. Samura, B. A., Babak, O. Ya., Kolesnik Yu. M. et. al.; Samura, B. A. (Ed.) (2010). Farmakoterapiya [Pharmacotherapy]. Kharkiv: Golden Pages, 800.

4. Shadrin, O. G., Koval'chuk, A. A., Dyukareva, S. V., Polkovnichenko, L. M. (2015). Stan shlunkovo-kishkovogo traktu ta shlyahi korektsii iogo porushen' pry hel′mintozakh u ditei [State of the gastrointestinal tract and ways of correction of its disorders in helminthiasis in children]. Modern pediatrics, 8 (72), 88–91.

5. Avdyukhina, T. I., Konstantinova, T. N., Prokosheva, M. N. (2011). Sovremennyy vzglyad na problemu gel'mintozov u detey i effektivnyye puti ee resheniya [Modern view on the problem of helminthiases in children and effective ways to solve it]. Modern pediatrics, 1 (35), 73–75.

6. Tolochko, K. V., Vishnevska, L. I. (2016). Basic approaches to pharmacotherapy of helminthiases and prospects of phytomedicines development for their treatment. Clinical pharmacy, 20 (4), 4–10.

7. Schekina, E. G. (2007). Gel'mintozy: sovremennyy vzglyad na problemu [Helminthiasis: a modern look at the problem]. Provisor, 12. Available at: http://www.provisor.com.ua/archive/2007/N12/gelmintoza.php?part_code=62&art_code=5986

8. Tolochko, K. V., Vyshnevska, L. I. (2017). Analysis of the domestic pharmaceutical market of anthelmintic medicines. News of Pharmacy, 1 (89), 56–60.

9. Abbas, A., Newsholme, W. (2011). Diagnosis and recommended treatment of helminth infections. Prescriber, 22 (19), 56–64. doi: http://doi.org/10.1002/psb.814

10. Kovalenko, L. M. (2014). Terapevtychna efektyvnist albendazolu pry helmintozakh svynei [Therapeutic Efficiency of Albendazole in Helminthiasis of Pigs]. Veterynarna medytsyna, 98, 144–146.

11. Prykhod′ko, Yu. O. (2001). Efektyvnist albendazolu pry helmintozakh sobak [The effectiveness of albendazole in helminthiasis of dogs]. Annotation of Sumy State Agrarian University, 6, 97–100.

12. Mazannyi, O. V., Byrka, V. I., Prykhodko, Yu. O. (2005). Pat. No. 9265 UA. Method of quantitative determination of helminths eggs. MPK 7, G01N 33/487. No. u200502006; declareted: 04.03.2005; published: 15.09.2005. Bul. No. 9, 6.

13. Kamyshnikov, V. S. (2013). Tekhnika laboratornykh rabot v meditsinskoy praktike [Technique of laboratory work in medical practice]. Moscow: MEDpress-inform, 344.

14. Herasymenko, S. S., Holovach, A. V., Yerina, A. M. et. al.; Herasymenko, S. S. (Ed.) (2000). Statistika [Statistics]. Kyiv: KNEU, 467.

15. Mostovii, G. I., Digtyar, A. O., Garkavii, V. K. et. al. (2002). Teoriya statistiki [Theory of statistics]. Kharkiv: Vyd-vo Khar RI UA DU «Mahistr», 300.

16. Prykhod′ko, Yu. O. (2000). Vyvchennia hostroi toksychnosti albendazolu na svyniakh [Study of Acute Toxicity of Albendazole in Pigs]. Veterynarna medytsyna, 77, 282–284.

DOI: 10.15587/2519-4852.2018.152837

DEVELOPMENT OF QUALITY CONTROL METHODS OF PROMISING ANTICONVULSANT

p. 13-21

Lina Perekhoda, Doctor of Pharmacy, Professor, Head of the Department, Head of department of Medicinal Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
ORCID: *http://orcid.org/0000-0002-8498-331X*

Igor Sych, Postgraduate Student, Department of Medicinal Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
ORCID: *http://orcid.org/0000-0002-1689-8260*

Irina Sych, PhD, Associate Professor, Department of Medicinal Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
ORCID: *http://orcid.org/0000-0001-9540-7038*

Bevz Natalia, PhD, Associate Professor, Department of Pharmaceutical Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
ORCID: *http://orcid.org/0000-0002-7259-8908*

Maryna Rakhimova, Assistant, Department of Medicinal Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
ORCID: *http://orcid.org/0000-0003-2454-7396*

Vitaliy Yaremenko, PhD, Associate Professor, Department of Medicinal Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
ORCID: *http://orcid.org/0000-0002-0850-1489*

In the previous studies, NUPh scientists proved that the search of potential anticonvulsants among derivatives of 1,3,4-thiadiazole is very perspective [1-3]. At the medicinal chemistry department of NUPh N-(5-ethyl-[1,3,4]-thiadiazole-2-yl)-2-nitrobenzamide was synthesized. This substance demonstrated high anticonvulsive activity on pentylentetrazole model of seizure compared to classic drug «Depakin». The substance is patented and proposed for further preclinical studies. One of the most important stages in the introduction of a new medicinal product or substance into medical practice is the development of quality control techniques.

The aim. *The aim of this work was to develop methods of identification, determination of impurities and quantitative determination of N-(5-ethyl-[1,3,4]-thiadiazole-2-yl)-2-nitrobenzamide for further application in standardization of the substance.*

Methods. *Chromatographically pure sample of N-(5-ethyl-[1,3,4] -thiadiazole-2-yl) -2-nitrobenzamide, methods of IR, UV and 1H NMR spectroscopy.*

Results*. The physical-chemical properties and spectral characteristics of N-(5-ethyl-[1,3,4]-thiadiazole-2-yl)-2-nitrobenzamide were studied, and chemical identification methods were proposed. The optimal conditions for the determination of the impurities by the method of thin-layer chromatography using the method of internal normalization are selected. The assay for N-(5-ethyl-[1,3,4]-thiadiazol-2-yl)-2-nitrobenzamide was carried out by absorption spectrophotometry in the alcohol solution at the wavelength of 282 nm with the absorption index 631. For application of methods such validation characteristics as robustness, linearity, correctness, stability of analytical solutions, precision, convergence, reproducibility, calculation of uncertainty of samples preparation were studied.*

Conclusions*. The methods of identification of N-(5-ethyl-[1,3,4]-thiadiazol-2-yl)-2-nitrobenzamide with the use of chemical reactions and spectral methods of analysis – IR and UV and ^{1}H NMR spectroscopy have been developed. To determine the concomitant impurities in the substance, the TLC method is recommended. Specific and nonspecific impurities were determined. The method of quantitative determination of substance by absorption spectrophotometry method in the ultraviolet region by the method of specific absorption index have been developed*

Keywords: *pharmaceutical analysis, identification, quantitative determination, impurity, spectroscopy, thin-layer chromatography, anticonvulsant*

References

1. Noolvi, M. N., Patel, H. M., Kamboj, S., Kaur, A., Mann, V. (2012). 2,6-Disubstituted imidazo[2,1-b][1,3,4]thiadiazoles: Search for anticancer agents. European Journal of Medicinal Chemistry, 56, 56–69. doi: http://doi.org/10.1016/j.ejmech.2012.08.012

2. Noolvi, M. N., Patel, H. M., Singh, N., Gadad, A. K., Cameotra, S. S., Badiger, A. (2011). Synthesis and anticancer evaluation of novel 2-cyclopropylimidazo[2,1-b][1,3,4]-thiadiazole derivatives. European Journal of Medicinal Chemistry, 46 (9), 4411–4418. doi: http://doi.org/10.1016/j.ejmech.2011.07.012

3. Yousif, E., Rentschler, E., Salih, N., Salimon, J., Hameed, A., Katan, M. (2014). Synthesis and antimicrobial screening of tetra Schiff bases of 1,2,4,5-tetra (5-amino-1,3,4-thiadiazole-2-yl) benzene. Journal of Saudi Chemical Society, 18 (3), 269–275. doi: http://doi.org/10.1016/j.jscs.2011.07.007

4. Alagawadi, K. R., Alegaon, S. G. (2011). Synthesis, characterization and antimicrobial activity evaluation of new 2,4-Thiazolidinediones bearing imidazo[2,1-b][1,3,4]thiadiazole moiety. Arabian Journal of Chemistry, 4 (4), 465–472. doi: http://doi.org/10.1016/j.arabjc.2010.07.012

5. Cressier, D., Prouillac, C., Hernandez, P., Amourette, C., Diserbo, M., Lion, C., Rima, G. (2009). Synthesis, antioxidant properties and radioprotective effects of new benzothiazoles and thiadiazoles. Bioorganic & Medicinal Chemistry, 17 (14), 5275–5284. doi: http://doi.org/10.1016/j.bmc.2009.05.039

6. Khan, I., Ali, S., Hameed, S., Rama, N. H., Hussain, M. T., Wadood, A. et. al. (2010). Synthesis, antioxidant activities and urease inhibition of some new 1,2,4-triazole and 1,3,4-thiadiazole derivatives. European Journal of Medicinal Chemistry, 45 (11), 5200–5207. doi: http://doi.org/10.1016/j.ejmech.2010.08.034

7. Kadi, A. A., Al-Abdullah, E. S., Shehata, I. A., Habib, E. E., Ibrahim, T. M., El-Emam, A. A. (2010). Synthesis, antimicrobial and anti-inflammatory activities of novel 5-(1-adamantyl)-1,3,4-thiadiazole derivatives. European Journal of Medicinal Chemistry, 45 (11), 5006–5011. doi: http://doi.org/10.1016/j.ejmech.2010.08.007

8. Hafez, H. N., Hegab, M. I., Ahmed-Farag, I. S., El-Gazzar, A. B. A. (2008). A facile regioselective synthesis of novel spiro-thioxanthene and spiro-xanthene-9′,2-[1,3,4]thiadiazole derivatives as potential analgesic and anti-inflammatory agents. Bioorganic & Medicinal Chemistry Letters, 18 (16), 4538–4543. doi: http://doi.org/10.1016/j.bmcl.2008.07.042

9. Jatav, V., Mishra, P., Kashaw, S., Stables, J. P. (2008). CNS depressant and anticonvulsant activities of some novel 3-[5-substituted 1,3,4-thiadiazole-2-yl]-2-styryl quinazoline-4(3H)-ones. European Journal of Medicinal Chemistry, 43 (9), 1945–1954. doi: http://doi.org/10.1016/j.ejmech.2007.12.003

10. Rzeski, W., Matysiak, J., Kandefer-Szerszeń, M. (2007). Anticancer, neuroprotective activities and computational studies of 2-amino-1,3,4-thiadiazole based compound. Bioorganic & Medicinal Chemistry, 15 (9), 3201–3207. doi: http://doi.org/10.1016/j.bmc.2007.02.041

11. Chen, C.-J., Song, B.-A., Yang, S., Xu, G.-F., Bhadury, P. S., Jin, L.-H. et. al. (2007). Synthesis and antifungal activities of 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-thiadiazole and 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-oxadiazole derivatives. Bioorganic & Medicinal Chemistry, 15 (12), 3981–3989. doi: http://doi.org/10.1016/j.bmc.2007.04.014

12. Liu, F., Luo, X.-Q., Song, B.-A., Bhadury, P. S., Yang, S., Jin, L.-H. et. al. (2008). Synthesis and antifungal activity of novel sulfoxide derivatives containing trimethoxyphenyl substituted 1,3,4-thiadiazole and 1,3,4-oxadiazole moiety. Bioorganic & Medicinal Chemistry, 16 (7), 3632–3640. doi: http://doi.org/10.1016/j.bmc.2008.02.006

13. Perekhoda, L. O., Sych, I. V., Shtrigol, S. Yu., Taran, A. V., Drapak, I. V. (2018). Pat. No. 110054 UA. N-(5-ethyl- [1,3,4] thiadiazol-2-yl) -2-nitrobenzamide, which exhibits anticonvulsant activity. MPK A61K 31/165, A61K 31/433, C07D 285/12. No. a 2016 02439; declared: 14.03.2016; published: 25.10.2018, No. 20.

14. Lyapunov, N. A., Soloviev, A. S., Stetsiv, V. V. et. al. (2012). Standartizatsiya farmatsevticheskoy produktsii – osnova razvitiya farmatsevticheskogo sektora Ukrainy [Standardization of pharmaceutical products is the basis of the development of the pharmaceutical sector of Ukraine]. Weekly Pharmacy, 826 (4).

15. Perekhoda, L. O. (2013). Molekulyarne modelyuvannya ta tsilespryamovaniy sintez protisudomnih zasobIv pohIdnih p'yatichlennih di(tri)azageterotsikliv [Molecular modeling and purposeful synthesis of anticonvulsants of derivatives of five-membered di (three) azaheterocycles]. National University of Pharmacy. Kharkiv, 46.

16. Sych, I. V., Perekhoda, L. A., Tsapko, T. O. (2016). Synthesis of 5-substituted 1,3,4-thiadiazol-2-yl-sulfanyl acetic acid derivatives. Scripta Scientifica Pharmaceutica, 2 (2), 53–59. doi: http://doi.org/10.14748/ssp.v2i2.1404

17. Perekhoda, L. O. (2013). Kolichestvennoe issledovanie vzaimosvyazi «struktura – protivosudorozhnaya aktivnost» v ryadah proizvodnyih 1,2,3-triazola(1N), 1,2,4-triazola(4N), 1,3,4-oksadiazola(1N) i 1,3,4–tiadiazola(1N) [Quantitative study of the relationship between "structure – anticonvulsant activity" in the series of derivatives of 1,2,3-triazole (1H), 1,2,4-triazole (4H), 1,3,4-oxadiazole (1H) and 1,3,4-Thiadiazole (1H)]. Him.-farmats. zhurnal, 47 (11), 42–44.

18. Sych, I. V., Perekhoda, L. O., Ieromina, Z. G., Grinevich, L. O., Kobzar, N. P., Drapak, I. V. (2016). The synthesis and physicochemical properties of new derivatives of 5-r-phenylamino-2-mercapto-1,3,4-thiadiazole. Visnik Farmacii, 1 (85), 24–28. doi: http://doi.org/10.24959/nphj.16.2074

19. Derzhavna Farmakopeya Ukrayini. Vol. 1 (2015). Kharkiv: DP «Ukrayinskiy naukoviy farmakopeyniy tsentr yakosti likarskih zasobiv», 1128.

20. Larkin, P. J. (2011) Infrared and raman spectroscopy: principles and spectral interpretation. Elsevier, 230.

21. Ivolgina, V. A., Chernov'yants, M. S. (2018). Spectroscopic and structural investigation of interaction of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt with molecular iodine. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 199, 315–321. doi: http://doi.org/10.1016/j.saa.2018.03.069

22. Mohamed, T. A., Soliman, U. A., Shaaban, I. A., Zoghaib, W. M., Wilson, L. D. (2015). Raman, infrared and NMR spectral analysis, normal coordinate analysis and theoretical calculations of 5-(methylthio)-1,3,4-thiadiazole-2(3H)-thione and its thiol tautomer. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 150, 339–349. doi: http://doi.org/10.1016/j.saa.2015.05.039

DOI: 10.15587/2519-4852.2018.153199

SEARCH OF THE PROMISING SPECIES OF SUBFAMILY *AMYGDALOIDEAE* AND *PYROIDEAE* USING THE CHEMOTAXONOMY

p. 21-25

Natalia Sydora, PhD, Associate Professor, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: sydora2005@gmail.com
ORCID: *http://orcid.org/0000-0002-3333-2250*

Alla Kovaleva, Doctor of Pharmaceutical Sciences, Professor, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: allapharm@yahoo.com
ORCID: *http://orcid.org/0000-0002-1758-1222*

Alexandr Goncharov, PhD, assistant, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: gnosy@nuph.edu.ua

World flora has more than 1000 species of the genus Crataegus L., more than 30 species belong to the subgenus Prunus L., genus Malus Mill. has 100 species, subgenus Cerasus Juss. includes more than 150 species. Despite the diversity of species and a sufficient resource base, only a few representatives of the genus sufficiently researched and found their use as sources of biologically active substances (BAS).

Aim of research. *To conduct a chemotaxonomic study of representatives of the genus Crataegus L., Prunus L., Malus Mill., Cerasus Juss.; to establish a promising sources of biologically active substances for the drugs production.*

Materials and methods. *Chemotaxonomic study was carried out using the method of the graph analysis. The chemomarkers were phenolic compounds and terpenoids, identified in the generative and vegetative organs of the representatives of the genus Crataegus L., Prunus L., Malus Mill., Cerasus Juss. The terpenoids and organic acids were identified by a chromatography-mass-spectrometric method on an Agilent Technology 6890N chromatograph with a 5973N mass-spectrometric detector. Flavonoids and hydroxycinnamic acids were detected by chromatography.*

Results. *The chemical profiles of vegetative and generative organs of 34 species of the genus Crataegus L. are established, 5 species of the genus Prunus L., 7 species of the genus Malus Mill., 4 species of the genus Cerasus Juss. The promising species of hawthorn, wich accumulated a general group BAS of genus was detected.*

Conclusion. *According to the results of a chemotaxonomic study of representatives of subgenus Amygdaloideae and Pyroideae was detected a promising sources of biologically active substances (BAS) among species of the genus Crataegus L., Prunus L., Malus Mill. and Cerasus Juss. The chemical profiles are forming flavonoids, terpenoids and aromatic acids. The promising species of hawthorn was added to the complex «Kratophyt»*

Keywords: *Rosaceae, hawthorn, apple, cherry, plum, leaves, flowers, fruits, taxon, chemotaxonomy*

References

1. Phipps, J. B., Robertson, K. R., Rohrer, J. R., Smith, P. G. (1991). Origins and Evolution of Subfam. Maloideae (Rosaceae). Systematic Botany, 16 (2), 303–332. doi: http://doi.org/10.2307/2419283

2. Talent, N., Dickinson, T. A. (2005). Polyploidy in Crataegus and Mespilus (Rosaceae, Maloideae): evolutionary inferences from flow cytometry of nuclear DNA amounts. Canadian Journal of Botany, 83 (10), 1268–1304. doi: http://doi.org/10.1139/b05-088

3. Goncharov, N. F., Kovaleva, A. M., Komissarenko, A. N. (2008). Fenol'nye soedineniya severoamerikanskikh vidov roda boyaryshnik. Rossiyskiy mediko-biologicheskiy vestnik imeni akademika Pavlova, 3, 150–154.

4. Kamelin, R. V. (2006). Rozotsvetnye (Rosaceae). Bornaul, 100.

5. Potter, D., Eriksson, T., Evans, R. C., Oh, S., Smedmark, J. E. E., Morgan, D. R. et. al. (2007). Phylogeny and classification of Rosaceae. Plant Systematics and Evolution, 266 (1-2), 5–43. doi: http://doi.org/10.1007/s00606-007-0539-9

6. Eremin, G. V. (2017). Genofond roda Prunus L. Trudy po prikladnoy botanike, genetike i selektsii, 164, 208–217.

7. Sydora, N. (2018). Morphological and taxonomic study of oxyacanthae Zbl. section of crataegus L. genus by vegetative characteristics. ScienceRise: Pharmaceutical Science, 1 (11), 36–41. doi: http://doi.org/10.15587/2519-4852.2018.124432

8. Chen, J., Song, S., He, J., Xu, S. (2008). A study of the chemical constituents of the leaves of Crataegus pinnatifida. Asian Journal of Traditional Medicines, 3, 80–83.

9. Hamahameen, B. A., Jamal, B. (2013). Determination of Flavonoids in the Leaves of Hawthorn (Crataegus Azarolus) of Iraqi Kurdistan Region by HPLCAnalysis. International Journal of Bioscience, Biochemistry and Bioinformatics, 3 (1), 67–70. doi: http://doi.org/10.7763/ijbbb.2013.v3.166

10. Lenchyk, L. V., Upyr, D. V., Ovezgeldiyev, D. (2016). Phytochemical investigation of bird cherry fruits. Der Pharmacia Lettre, 8 (6), 73–76.

11. Sydora, N., Kovalova, A., Komissarenko, A. (2016). Gas chromatographic-mass spectrometric studies of organic acids of Crataegus pedicelata Sarg leaves. Science and Education Studies, 2 (1 (17)), 769–774.

12. Bicchi, C., Brunelli, C., Cordero, C., Rubiolo, P., Galli, M., Sironi, A. (2016). Methods of the chromate-mass-spectrometric research. Journal of Chromatography A, 1-2, 195–207.

13. Kovaleva, A. M., Goncharov, N. F., Komissarenko, A. N., Sidora, N. V., Kovalev, S. V. (2009). GC/MS study of essential oil components from flowers of Crataegus jackii, C. robesoniana, and C. flabellata. Chemistry of Natural Compounds, 45 (4), 582–584. doi: http://doi.org/10.1007/s10600-009-9373-3

14. Sydora, N. V., Kovalova, A. M. (2016). Gas chromatographic-mass spectrometric studies the volatile compounds and organic acids the leaves of Crataegus macracantha Loud. American Journal of Science and Technologies, 3 (1 (21)), 1041–1045.

15. Lenchyk, L., Shapoval, O., Kyslychenko, V. (2016). Phytochemical study and determination of pharmacological activities of cherry shoots dry extract. ScienceRise: Pharmaceutical Science, 1 (1), 40–45. doi: http://doi.org/10.15587/2519-4852.2016.72746

16. Lenchyk, L. V. (2016). Determination of phenolic compounds in prunus domestica leaves extract. Scripta Scientifica Pharmaceutica, 2 (2), 31–35. doi: http://doi.org/10.14748/ssp.v2i2.1302

DOI: 10.15587/2519-4852.2018.153035

DEVELOPMENT AND VALIDATION OF HPLC/UV-PROCEDURES OF SECNIDAZOLE DETERMINATION IN BLOOD AND URINE

p. 26-34

Oksana Shovkova, Assistant, Department of Biological Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkov, Ukraine, 61002
E-mail: kseniashovkova@gmail.com

Lina Klimenko, Doctor of Pharmaceutical Sciences, Associate Professor, Department of Analytical Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkov, Ukraine, 61002
E-mail: lina_klimenko@nuph.edu.ua
ORCID: *http://orcid.org/0000-0002-4857-5706*

Zoia Shovkova, PhD, Associate Professor, Department of Drug and Analytical Toxicology, National University of Pharmacy, Pushkinska str., 53, Kharkov, Ukraine, 61002
E-mail: toxchem@nuph.edu.ua
ORCID: *http://orcid.org/0000-0003-1908-1237*

Olena Mykytenko, PhD, Associate Professor, Department of Analytical Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkov, Ukraine, 61002
E-mail: mikitenko-elena@ukr.net
ORCID: *http://orcid.org/0000-0003-3178-3418*

Aim. *The system of HPLC-analyzer MiLiChrome® A-02 is widely used in Ukrainian laboratories of forensic toxicology. The purpose is to apply the HPLC-analyzer system for secnidazole quantitative determination in biological liquids and carry out validation of the developed procedures.*

Methods. *Sample preparation of blood and urine was carried out in three ways:*

1) liquid-liquid extraction with organic solvents immiscible with water,

2) amphiphylic solvents extraction and salting-out with ammonium sulphate,

3) complex application of liquid-liquid extraction with organic solvents immiscible with water and amphiphylic solvents extraction with salting-out.

Chromatographic conditions: column – ∅2×75 mm, ProntoSIL 120-5-C18 AQ, 5 μm; temperature – 40 °C; flow rate – 100 μl/min; Eluent A – 0.2 M $LiClO_4$ – 0.005 M $HClO_4$; Eluent B – acetonitrile; elution mode – linear gradient; detection – UV, 277 nm; volume of injection – 2 μl.

Results. *Validation of all developed procedures has been carried out by such parameters as specificity, recovery, linearity, accuracy and precision in the variant of the method of standard. The results of analysis have shown the absence of peaks with the retention time, which is coincident with the secnidazole retention time, on the chromatograms of blank-samples for all variants of procedures of analyte isolation. All procedures of sample preparation show the high efficiency of secnidazole isolation both for blood and urine (at the level of 90 %). All examined procedures are characterized by the acceptable parameters of linearity, within-run and between-run accuracy and precision.*

Conclusions. *The set of HPLC-procedures of secnidazole quantitative determination in blood and urine has been developed. Validation of the developed procedures has been carried out; isopropanol application in the acid medium is optimal for biological liquids sample preparation*

Keywords: *secnidazole, high-performance liquid chromatography, blood, urine, sample preparation, validation, method of standard*

References

1. Brook, I. (2016). Spectrum and treatment of anaerobic infections. Journal of Infection and Chemotherapy, 22 (1), 1–13. doi: http://doi.org/10.1016/j.jiac.2015.10.010

2. Upcroft, P., Upcroft, J. A. (2001). Drug Targets and Mechanisms of Resistance in the Anaerobic Protozoa. Clinical Microbiology Reviews, 14 (1), 150–164. doi: http://doi.org/10.1128/cmr.14.1.150-164.2001

3. Rose, M. D., Bygrave, J., Sharman, M. (1999). Effect of cooking on veterinary drug residues in food Part 9 Nitroimidazoles. The Analyst, 124 (3), 289–294. doi: http://doi.org/10.1039/a809062i

4. Sobel, R., Sobel, J. D. (2015). Metronidazole for the treatment of vaginal infections. Expert Opinion on Pharmacotherapy, 16 (7), 1109–1115. doi: http://doi.org/10.1517/14656566.2015.1035255

5. Samuelson, J. (1999). Why Metronidazole Is Active against both Bacteria and Parasites. Antimicrobial Agents and Chemotherapy, 43 (7), 1533–1541. doi: http://doi.org/10.1128/aac.43.7.1533

6. Freeman, C. D., Klutman, N. E., Lamp, K. C. (1997). Metronidazole. A therapeutic review and update. Drugs, 54, 679–708. doi: http://doi.org/10.2165/00003495-199754050-00003

7. Commission Regulation (EU) No. 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin (2010). Official Journal of the European Union, L15, 1–72.

8. Lamp, K. C., Freeman, C. D., Klutman, N. E., Lacy, M. K. (1999). Pharmacokinetics and Pharmacodynamics of the Nitroimidazole Antimicrobials. Clinical Pharmacokinetics, 36 (5), 353–373. doi: http://doi.org/10.2165/00003088-199936050-00004

9. Gillis, J. C., Wiseman, L. R. (1996). Secnidazole. A review of its antimicrobial activity, pharmacokinetic properties and therapeutic use in the management of protozoal infections and bacterial vaginosis. Drugs, 51 (4), 621–638. doi: http://doi.org/10.2165/00003495-199651040-00007

10. El Walily, A. F. M., Abdine, H. H., Razak, O. A., Zamel, S. (2000). Spectrophotometric and HPLC determination of secnidazole in pharmaceutical tablets. Journal of Pharmaceutical and Biomedical Analysis, 22 (6), 887–897. doi: http://doi.org/10.1016/s0731-7085(99)00290-3

11. Sun, H. W., Wang, F. C., Ai, L. F. (2007). Simultaneous determination of seven nitroimidazole residues in meat by using HPLC-UV detection with solid-phase extraction. Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences, 857 (2), 296–300. doi: http://doi.org/10.1016/j.jchromb.2007.07.039

12. Ravi, S. K., Naidu, M. U. R., Sekhar, E. C., Rao, T. R. K., Shobha, J. C., Rani, P. U., Surya, K. J. (1997). Rapid and selective analysis of secnidazole in human plasma using high-performance liquid chromatography with ultraviolet detection. Journal of Chromatography B: Biomedical Sciences and Applications, 691 (1), 208–211. doi: http://doi.org/10.1016/s0378-4347(96)00419-7

13. Li, X., Sun, J., Wang, G., Zheng, Y., Yan, B., Xie, H. et. al. (2007). Determination of secnidazole in human plasma by high-performance liquid chromatography with UV detection and its application to the bioequivalence studies. Biomedical Chromatography, 21 (3), 304–309. doi: http://doi.org/10.1002/bmc.758

14. Zhu, D., Hu, K., Tao, W., Feng, L., Duan, H., Jiang, X., Chen, J. (2011). Evaluation of the Bioequivalence and Pharmacokinetics of Two Formulations of Secnidazole after Single Oral Administration in Healthy Volunteers. Arzneimittelforschung, 57 (11), 723–726. doi: http://doi.org/10.1055/s-0031-1296674

15. Tenenbaum, H., Cuisinier, F. J. G., Liboux, A., Pichard, E., Montay, G., Frydman, A. (1993). Secnidazole concentrations in plasma and crevicular fluid after a single oral dose. Journal of Clinical Periodontology, 20 (7), 505–508. doi: http://doi.org/10.1111/j.1600-051x.1993.tb00398.x

16. Mitrowska, K., Antczak, M. (2017). Development and validation of a liquid chromatography with tandem mass spectrometry method for the determination of nitroimidazole residues in beeswax. Journal of Separation Science, 40 (5), 1158–1166. doi: http://doi.org/10.1002/jssc.201600928

17. Rúbies, A., Sans, G., Kumar, P., Granados, M., Companyó, R., Centrich, F. (2015). High-throughput method for the determination of nitroimidazoles in muscle samples by liquid chromatography coupled to mass spectrometry. Analytical and Bioanalytical Chemistry, 407 (15), 4411–4421. doi: http://doi.org/10.1007/s00216-014-8436-x

18. Azarova, I. N., Baram, G. I. (2014). Primenenie perhlorata litiya v obraschenno-fazovoy vyisokoeffektivnoy zhidkostnoy hromatografii aminosoedineniy. Sorbtsionnyie i hromatograficheskie protsessyi, 14 (1), 858–867.

19. Shovkova, O. V., Klimenko, L. Yu., Shovkova, Z. V., Kostina, T. A. (2018). Development and validation of HPLC/UV-procedure of secnidazole determination. Journal of Organic and Pharmaceutical Chemistry, 16 (3 (63)), 30–38. doi: http://doi.org/10.24959/ophcj.18.948

20. Klimenko, L. Yu. (2016). The integrated approach to development and validation of the procedures of analytes quantification in biological fluids for chemical and toxicological analysis. Kharkiv, 816.

21. Moffat, A. C., Osselton, M. D., Widdop, B. (2011). Clarke's analysis of drugs and poisons in pharmaceuticals, body fluids and postmortem material: 4th ed. London: Pharmaceutical Press, 2609.

22. Klimenko, L. Yu. (2014). Development of approaches to determination of linearity, accuracy and precision of UV-spectrophotometric methods of quantitative determination by the method of standard in forensic and toxicological analysis. Farmatsyia Kazakhstana, 4 (155), 31–35.

23. Klimenko, L. Yu., Trut, S. M., Poluyan, S. M. (2014). Determination of validation characteristics of UV-spec-trophotometric method of doxylamine quantitative determination in blood in the variant of the method of standard. News of Pharmacy, 2 (78), 53–58. doi: http://doi.org/10.24959/nphj.14.1969

DOI: 10.15587/2519-4984.2018.153381

RESEARCH OF SOCIO-PSYCHOLOGICAL CHARACTERISTICS OF PHARMACY SPECIALISTS

p. 35-40

Rita Sahaidak-Nikitiuk, Doctor of Pharmaceutical Sciences, Head of Department, Department of Processes and Apparatuses of Chemical and Pharmaceutical Industries, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: sagaidak_rita@ukr.net

Marianna Harkusha, Postgraduate Student, Department of Processes and Apparatuses of Chemical and Pharmaceutical Industries, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: garkusham@ukr.net.

Nataliya Demchenko, PhD, Associate Professor, Department of Management and Administration, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: demchenata@ukr.net

*The **purpose** of the article is to study the socio-psychological characteristics of Ukrainian pharmacists.*
***Methods:** methods of psychodiagnostic analysis, expert assessments, analytical, comparative and logical. The survey involved 352 pharmacist practitioners from all regions of Ukraine.*
***Results.** In the context of introducing the proper pharmacy practices in pharmacies and aggravating the socio-economic situation in the country, pharmacy specialists face the issue of providing pharmaceutical assistance to pharmacy visitors at an appropriate professional level, for which they need a certain set of socio-psychological characteristics. Evaluation of these characteristics was carried out using the methods of diagnostics of systemic-characterological relations, resistance to conflicts, level of subjective control, MPI (G. Aysenck), SSB-98 (Self-regulation style of behavior), volitional qualities by N. Stambulova. The proposed methods allowed us to identify the inherent qualities of specialists, namely, the average level of indicators of self-control and endurance, initiative, creativity and independence. At the same time, pharmacy specialists overcome obstacles to achieve the goal, but show a certain softness, they are also not always confident in making decisions, they are prone to doubt. The willful sphere of the interviewed pharmacists is characterized by a tendency towards uncertainty and lack of initiative. Most pharmacists have poorly defined leadership qualities and an average level of conflict resistance. 22,03 % of pharmacy specialists have a high level of conflict, 8,48 % of respondents have a pronounced conflict level.*
***Conclusion.** The socio-psychological characteristics of pharmacy specialists were studied using psychodiagnostic methods. According to the test, the system-characterological relations of the individual determined that tactics, integrity, responsiveness, organization, diligence, self-criticism, self-confidence, accuracy, frugality and moderation in needs are characteristic of most pharmacy specialists, but there is a definite need to develop or improve these qualities. Pharmacy specialists are also characterized by an average value of the level of subjective control. The willful sphere of the interviewed pharmacists is characterized by partial uncertainty and lack of initiative*
***Keywords:** social and psychological characteristics, pharmacy specialist, psychodiagnostic methods, conflict resistance, tact, organization, hard work*

References

1. Dovidnyk kvalifikatsiinykh kharakterystyk profesii pratsivnykiv. Vypusk 78 "Okhorona zdorov'ia" (2002) Available at: http://consultant.parus.ua/?doc=0B7Y6D7812

2. Whitmarsh, S., Futter, B., Rouse, M., Bates, I., Anderson, C. (2010). A Case Study in Terminology: the FIP Pharmacy Education Taskforce. American Journal of Pharmaceutical Education, 74 (7), 134. doi: http://doi.org/10.5688/aj7407134

3. Galkovskaya, G. (2015). Farmatsevtycheskaia praktyka v Brytanyy y Hermanyy. Zakonodatel'stvo y tendentsyy. Ezhenedelnyk Apteka, 47. URL: http://www.apteka.ua/article/353365

4. Sternberg, R. J., Kaufman, J. C.; Sternberg, R. J., Kaufman, J. C. (Eds.) (2010). Constraints on Creativity: Obvious and Not So Obvious. The Cambridge Handbook of Creativity. Cambridge University Press, 467–482. doi: http://doi.org/10.1017/cbo9780511763205.029

5. Tolochko, V. M., Halyi, L. V. (2009). Model' kompetentsiy provizora apteki. Provyzor, 15, 7–9.

6. Halii, L. V. (2011). Theoretical and scientific-practical bases of definition of competencies in personnel management of pharmaceutical establishments. Kharkiv.

6. Pestun, I. V., Mnushko, Z. M. (2017). Ohliad suchasnykh tendentsij profesijnoi diial'nosti provizoriv (farmatsevtiv) v Ukraini ta za kordonom. Sotsial'na farmatsiia v okhoroni zdorov'ia, 1, 52–59.

7. Barnett, M., Frank, J., Wehring, H., Newland, B., Von-Muenster, S., Kumbera, P. et. al. (2009). Analysis of Pharmacist-Provided Medication Therapy Management(MTM) Services in Community Pharmacies Over 7 Years. Journal of Managed Care Pharmacy, 15 (1), 18–31. doi: http://doi.org/10.18553/jmcp.2009.15.1.18

9. Stupans, I., Atkinson, J., Meštrović, A., Nash, R., Rouse, M. (2016). A Shared Focus: Comparing the Australian, Canadian, United Kingdom and United States Pharmacy Learning Outcome Frameworks and the Global Competency Framework. Pharmacy, 4 (3), 26. doi: http://doi.org/10.3390/pharmacy4030026

10. Atemasova, O. A. (2010). Praktychna psykholohiia [Practical Psychology]. Kharkiv: Ranok, 160.

11. Pov'iakel, N. I. (2012). Psykhoprofilaktyka konfliktiv [Psychoprophylaxis of conflicts]. Kyiv: Shkilnyi svit, 122.

12. Raihorodskyi, D. (2017), Praktycheskaia psykhodyahnostyka [Practical psychodiagnostics]. Moscow: Bakhrakh-M, 672.

DOI: 10.15587/2519-4852.2018.153387

DEVELOPMENT OF HPLC METHOD FOR QUANTITATIVE DETERMINATION OF NEW PERSPECTIVE APhI WITH ANTI-ULCER ACTIVITY OF TRIAZOPRAZOL

p. 41-46

Narzullo Saidov, PhD, Associate Professor, Department of Pharmaceutical Chemistry, Tajik National University, Rudaki str., 17, Dushanbe, Tajikistan, 734025
E-mail: narzullos@mail.ru

Natalia Smelova, Director, Education and Research Training Center of Chromatographic Studies, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: smelova08@gmail.com
ORCID: *http://orcid.org/0000-0001-5878-5072*

Natalya Garna, PhD, Associate Professor, Department of Pharmaceutical Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: garnayan@ukr.net
ORCID: *http://orcid.org/0000-0003-2918-4985*

Oksana Koretnik, PhD, Assistant, Department of Pharmaceutical Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: oksanakoretnik@gmail.com
ORCID: *http://orcid.org/0000-0002-8943-8281*

Nataliia Khanina, Technician, Educational and Scientific Training Center for Chromatographic Studies, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: lucky820.ua@gmail.com
ORCID: *http://orcid.org/0000-0002-8400-2163*

Svetlana Gubar, PhD, Head of Laboratory, State Research Laboratory for Quality Control of Medicines, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: gubarsn@ukr.net
ORCID: *http://orcid.org/0000-0002-5434-9502*

Aim. *Development of optimal, high-precision, reproducible method of quantitative determination of triazoprazole in substance using the method of high performance liquid chromatography.*

Materials and methods. *Physico-chemical (high-performance liquid chromatography) and mathematical (statistical processing of results) methods of research were used to achieve this goal. Chromatography was performed on a liquid chromatograph Agilent 1290 Infinity II with diode-array (LC 1290) detector and quadrupole-time-of-flight (QTOF 6530) mass analyzer. Fixed phase: chromatographic column 100×2.1 mm, filled with silica gel octadecylsilyl for chromatography P Zorbax Eclipse Plus C18, with particle size 3,5 mkm. Mobile phase A: 0.1 % formic acid solution S in water S. Mobile phase B: 0,1 % formic acid solution S in acetonitrile S. Flow rate of the mobile phase: 0,6 ml/min. Temperature of the column: 30 ºC. Volume of the injection: 5 mkl. Detector – diode-array (DAD). Detecting: by wavelength 248 nm.*

Detector settings (Q-TOF): type of ionization: positive, electrospray (+ ESI); metering mode: scanning ion with a mass from 100 to 1000 u.; voltage on the fragmentator 100 V; nitrogen temperature 350 C; nitrogen consumption 10 ml/min; nebulizer pressure 35 PSI; voltage on the capillary 4 Kv. The chromatographic separation was carried out with gradient elution on column filled with silica gel octadecylsilyl.

Results. *Content of active ingredient in the substance of triazoprazole meets the requirements of regulated limits of quantitative content. Therefore, the proposed method can be used in the process of pharmaceutical development and standardization of the dosage form. Solvent and mobile phase do not interfere in conditions of the proposed method for determining the active substance. It testifies about specificity of the proposed method.*

Conclusions. *High-precision and reproducible method of quantitative determination of triazoprazole in substance using the method of high performance liquid chromatography was developed.*

Keywords. *1,2,4-triazole, triazoprazole, anti-ulcer activity, analysis, quantitative determination, HPLC method, diode-array detector.*

References

1. Kaur, P., Chawla, A. (2017). 1,2,4-Triazole: a review of pharmacological activities. International Research Journal of Pharmacy, 8 (7), 10–29. doi: http://doi.org/10.7897/2230-8407.087112

2. Namratha, B., Gaonkar, S. (2014). 1,2,4-triazoles: Synthetic strategies and pharmacological. International Journal of Pharmacy and Pharmaceutical Sciences, 6 (8), 73–80.

3. Felton, L. A. (Ed.) (2013). Remington – Essentials of Pharmaceutics. Pharmaceutical Press, 772.

4. Georgiyants, V., Perekhoda, L., Saidov, N., Kadamov, I. (2014). Synthesis, docking studies, and biological evaluation of anti-ulcer activity of 4-allyl-5-(4-R1)-phenylthiomethyl-1,2,4-triazole-3-ylmercaptoacetic acid derivatives. European Chemical Bulletin, 3 (5), 466–471.

5. Georgiyants, V., Severina, G., Drogovoz, S., Timofeev, M., Saidov, N., Kadamov, I., Saaod, Khaidar (2016). Pat. No. 112867 UA. Zastosuvannia alkilovanykh pokhidnykh 1,2,4-tryazol-3-tiolu ta 1-fenil-1n-tetrazol-5-tiolu yak zasobu protyvyrazkovoi dii. MPK: C07D 249/08 (2006.01), C07D 257/04, A61K 31/41, A61K 31/4196. No. u 2013 13290; declareted: 15.11.2013; published: 10.11.2016, Bul. No. 10.

6. Kenesov, B., Saylauhanulyi, E., Musrepov, B., Kaldarov, A. (2008). Opredelenie 1-methyl-1H-1,2,4-triazole v vodnyih obraztsah metodom vyisokoeffektivnoy zhidkostnoy hromatografii s diodno-matrichnyim detektirovaniem. Habarshyi vestnik. Seriya himicheskaya, 1 (49), 184–189.

7. Yegemova, S., Bakaikina, N. V., Kenessov, B., Koziel, J. A., Nauryzbayev, M. (2015). Determination of 1-methyl-1H-1,2,4-triazole in soils contaminated by rocket fuel using solid-phase microextraction, isotope dilution and gas chromatography–mass spectrometry. Talanta, 143, 226–233. doi: http://doi.org/10.1016/j.talanta.2015.05.045

8. Tatarczak-Michalewska, M., Flieger, J., Wujec, M., Swatko-Ossor, M. (2014). Isolation and Quantitative Determination of New Tuberculostatic 1,2,4-Triazole Derivative in Urine and Plasma Samples. Journal of Analytical & Bioanalytical Techniques, 5 (4). doi: http://doi.org/10.4172/2155-9872.1000206

9. Acanski, M., Perisic-Janjic, N., Dimova, V. (2003). Normal and reversed phase high performance liquid chromatography of some new 1, 2, 4-triazole derivatives. Acta Periodica Technologica, 34, 83–92. doi: http://doi.org/10.2298/apt0334083a

10. Hawryl, A., Kusmierz, E., Hawryl, M., Swieboda, R., Wujec, M. (2014). Determination of Lipophilicity of New Thiosemicarbazide and 1,2,4-triazole-3-thione Derivatives Using Reversed-Phase HPLC Method and Theoretical Calculations. Journal of Liquid Chromatography & Related Technologies, 38 (4), 430–437. doi: http://doi.org/10.1080/10826076.2014.913519

11. Varynskyi, B., Kaplaushenko, A. (2017). The development and validation of HPLC-DMD method for intermediate products impurities determination of morpholinium2-((4-(2-methoxyphenyl)-5-(pyridine-4-yl)-4H-1,2,4-triazole-3-yl)thio)acetate in bulk drug. Zaporozhye Medical Journal, 9 (3), 373–380. doi: http://doi.org/10.14739/2310-1210.2017.3.100947

12. Blondel, A., Krings, B., Ducat, N., Pigeon, O. (2018). Validation of an analytical method for 1,2,4-triazole in soil using liquid chromatography coupled to electrospray tandem mass spectrometry and monitoring of propiconazole degradation in a batch study. Journal of Chromatography A, 1562, 123–127. doi: http://doi.org/10.1016/j.chroma.2018.05.056

13. Sanagi, M., Heng, S., Ibrahim, W., Naim, A. (2004). High temperature high performance liquid chromatography of triazole fungicides on carbon-clad zirconia stationary phase. Malaysian Journal of Chemistry, 6 (1), 55–66.

14. Derzhavna Pharmakopeya Ukrayini. Vol. 1 (2015). DP «Naukovo-ekspertniy farmakopeyniy tsentr». Kharkiv: DP «Ukrayinskiy naukoviy farmakopeyniy tsentr yakosti likarskih zasobiv», 1128.

15. Saidov, N., Kadamov, I., Perehoda, L., Georgiyants, V. (2017). Razrabotka metodiki kolichestvennogo opredeleniya potentsialnogo AFI s protivoyazvennyim deystviem. Nauka i innovatsii, 4, 35–41.