ABSTRACT&REFERENCES

DOI: 10.15587/2519-4852.2017.119279

CYCLOALKANECARBALDEHYDES IN SYNTHESIS OF NOVEL 1,2-BENZOXATHIIN-4(3*H*)-ON 2,2-DIOXIDE DERIVATIVES AND STUDY OF THE ANTIMICROBIAL ACTIVITY OF SYNTHESIZED COMPOUNDS

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Purpose: *This paper is dedicated to the investigation of cycloalkanecarbaldehydes, 1,2-benzoxathiin-4(3H)-on 2,2-dioxide and active methylene nitriles interaction and to studying antimicrobial properties of the obtained compounds.*

Methods: *As initial products were used cycloalkanecarbaldehydes 1,2-benzoxathiin-4(3H)-on 2,2-dioxide and active methylene nitriles. During the course of the research were applied the methods of organic synthesis. The structures of the obtained compounds were confirmed by elemental analysis and ^{1}H NMR spectroscopy. The antimicrobial activity was measured with the agar "well" diffusion method.*

Results: *New 2-amino-4H-pyrans were synthesized by three-component reaction of cycloalkanecarbaldehydes, 1,2-benzoxathiin-4(3H)-on 2,2-dioxide and malononitrile. The replacement of the latter with ethylcyanoacetate in the case of cyclohexanecarbaldehyde led to the isolation of triethylammonium3-[(4-hydroxy-2,2-dioxido-2,1-benzoxathiin-3-yl)(cyclohexyl)methyl]-2,1-benzoxathiin-5-olat 2,2-dioxide. Based on this result and considering originality of such ammonium salts the latter were purposefully synthesized with two-component approach using a range of secondary and tertiary amines. The synthesized compounds demonstrated higher antimicrobial activity than the reference drugs against the gram-positive strains.*

Conclusions: *The current research showed the prospective pathway for the expanding of the existing 2-amino-4H-pyrans diversity by utilizing in their synthesis such enolnucleophile and carbonyl compounds as 1,2-benzoxathiin-4(3H)-one 2,2-dioxide and cycloalkanecarbaldehydes respectively. The revealed antimicrobial activity of the obtained compounds against gram-positive microorganisms gives the opportunity for further investigations of narrow spectrum antibiotics among this group*

Keywords: *1,2-benzoxathiin-4(3H)-one 2,2-dioxide, 2-amino-4H-pyran, multicomponent reaction, cycloalkanecarbaldehyde, ammonium salt, antimicrobial activity*

References

1. CAS REGISTRY 100 Millionth Fun Facts (2015). American Chemical Society. Available at: https://www.cas.org/content/chemical-substances/cas-registry-100-millionth-fun-facts

2. Mungra, D. C., Patel, M. P., Rajani, D. P., Patel, R. G. (2011). Synthesis and identification of β-aryloxyquinolines and their pyrano[3,2-c]chromene derivatives as a new class of antimicrobial and antituberculosis agents. European Journal of Medicinal Chemistry, 46 (9), 4192–4200. doi: 10.1016/j.ejmech.2011.06.022

3. Amr, A.-G. E., Mohamed, A. M., Mohamed, S. F., Abdel-Hafez, N. A., Hammam, A. E.-F. G. (2006). Anticancer activities of some newly synthesized pyridine, pyrane, and pyrimidine derivatives. Bioorganic & Medicinal Chemistry, 14 (16), 5481–5488. doi: 10.1016/j.bmc.2006.04.045

4. Litvinov, Y. M., Shestopalov, A. M.; Katritzky, A. (Ed.) (2011). Synthesis, Structure, Chemical Reactivity, and Practical Significance of 2-Amino-4H-pyrans. Advances in Heterocyclic Chemistry. Vol. 103. Boston: Academic Press, 175–273. doi: 10.1016/b978-0-12-386011-8.00003-4

5. Lega, D. A., Gorobets, N. Y., Chernykh, V. P., Shishkina, S. V., Shemchuk, L. A. (2016). Peculiarities of 2-amino-3-R-4-aryl-4H-pyranes multicomponent synthesis derived from 1H-2,1-benzothiazin-4(3H)-one 2,2-dioxide. RSC Advances, 6 (19), 16087–16099. doi: 10.1039/c5ra24566d

6. Lega, D. A., Chernykh, V. P., Zaprutko, L., Gzella, A. K., Shemchuk, L. A. (2017). Synthesis of 1-ethyl-1H-2,1-benzothiazine 2,2-dioxide derivatives using cycloalkanecarbaldehydes and evaluation of their antimicrobial activity. Chemistry of Heterocyclic Compounds, 53 (2), 219–229. doi: 10.1007/s10593-017-2043-7

7. Filimonova, N. I., Lega, D. O., Zupanets, I. A. et. al. (2016). Antimicrobial, anti-inflammatory and analgesic activities of 2-amino-6-ethyl-4,6-dihydropyrano[3,2-c][2,1]benzothiazine 5,5-dioxides and triethylammonium 3-[1-(4-hydroxy-1-ethyl-2,2-dioxido-1H-2,1-benzothiazin-3-yl)-3-(het)arylmethyl]-1-ethyl-1H-2,1-benzothiazin-4-olat 2,2-dioxides. News of Pharmacy, 3 (87), 61–69.

8. Coyle, M. B. (2005). Manual of Antimicrobial Susceptibility Testing. American Society for Microbiology. Washington: American Society for Microbiology, 236.

9. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement. Document M100-S22 (2012). Wayne: CLSI, 32 (3), 188.

10. McFarland, J. (1907). Nephelometer: An Instrument for Estimating the Number of Bacteria in Suspensions Used for Calculating the Opsonic Index and for Vaccines. Journal of the American Medical Association, 49 (14), 1176–1178. doi: 10.1001/jama.1907.25320140022001f

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DOI: 10.15587/2519-4852.2017.118169

IDENTIFICATION AND QUANTITATIVE DETERMINATION OF STEROIDAL COMPOUNDS IN THE PLANT MATERIAL OF CABBAGE

p. 10-16

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Vegetable crops are inexhaustible source of biologically active compounds. Cabbage (Brassica oleracea L.) is a plant that has been extensively used in folk medicine of different countries of the world for the treatment of various disorders, and has anti-inflammatory, expectorant, broncholytic, diuretic, and general tonic effect. The plant material of cabbage in not officinal in Ukraine, thus it requires a complex pharmacognostic research to be carried out.

The aim of the research. *Identification and quantitative determination of steroidal compounds in the leaves, seeds and stumps of cabbage.*

Materials and methods. *Identification of steroidal compounds and determination of their quantity in the plant material of cabbage was carried out using gas chromatography/mass-spectrometry (GC/MS) method.*

The results of the study and their discussion*. As a result of the carried out experiment 3 compounds of steroidal nature were identified in the leaves of cabbage of "Snow-white" variety, and 4 – of "Ukrainian autumn" and "Yaroslavna" varieties, 4 compounds in the seeds of cabbage of "Snow-white" variety, 3 – of "Ukrainian autumn" and "Yaroslavna" varieties, and 3 steroidal compounds in the stumps of cabbage of all the varieties. β-Sitosterol was the dominating compound by the content in all studied samples. Its highest content was found in the leaves (2499 mg/kg) and seeds (1728 mg/kg) of cabbage of "Yaroslavna" variety, as well as in the stumps (1148 mg/kg) of cabbage of "Ukrainian autumn" variety.*

Conclusion*. Results of the experiment can be used at the quality control methods for the cabbage plant material development as well as obtaining prospective biologically active substances from the studied plant material*

Keywords*: cabbage, leaves, seeds, stumps, steroidal compounds, gas chromatography, mass-spectrometry*

References

1. Arnoldi, A. (2004). Functional foods, cardiovascular disease and diabetes. Cambridge: Woodhead Publishing, 488. doi: 10.1201/9781439823385

2. De Stefani, E., Boffetta, P., Ronco, A. L., Brennan, P., Deneo-Pellegrini, H., Carzoglio, J. C., Mendilaharsu, M. (2000). Plant Sterols and Risk of Stomach Cancer: A Case-Control Study in Uruguay. Nutrition and Cancer, 37 (2), 140–144. doi: 10.1207/s15327914nc372_4

3. Lockwood, B. (2007). Nutraceuticals: A quide for healthcare professionals. Vol. 5. London: Pharmaceutical Press, 426.

4. Hall, R. D., de Vos, R. C. H., Ward, J. L. (2010). Plant metabolomics applications in the brassicaceae: added value for science and industry. Acta Horticulturae, 867, 191–206. doi: 10.17660/actahortic.2010.867.24

5. Jesch, E. D., Carr, T. P. (2017). Food Ingredients That Inhibit Cholesterol Absorption. Preventive Nutrition and Food Science, 22 (2), 67–80.

6. Ostlund, R. E., Racette, S. B., Stenson, W. F. (2003). Inhibition of cholesterol absorption by phytosterol-replete wheat germ compared with phytosterol-depleted wheat germ. The American Journal of Clinical Nutrition, 77 (6), 1385–1589.

7. Valsta, L. M., Lemstrom, A., Ovaskainen, M.-L., Lampi, A.-M., Toivo, J., Korhonen, T., Piironen, V. (2004). Estimation of plant sterol and cholesterol intake in Finland: quality of new values and their effect on intake. British Journal of Nutrition, 92 (4), 671–678. doi: 10.1079/bjn20041234

8. Gunstone, F. D. (1996). Fatty Acid and Lipid Chemistry. Boston: Springer US, 252–253. doi: 10.1007/978-1-4615-4131-8

9. Li, T., Beveridge, T., Drover, J. (2007). Phytosterol content of sea buckthorn (Hippophae rhamnoides L.) seed oil: Extraction and identification. Food Chemistry, 101 (4), 1633–1639. doi: 10.1016/j.foodchem.2006.04.033

10. Samec, D., Pavlovic, I., Salopek-Sondi, B. (2016). White cabbage (Brassica oleracea var. capitata f. alba): botanical, phytochemical and pharmacological overview. Phytochemistry Reviews, 16 (1), 117–135. doi: 10.1007/s11101-016-9454-4

11. Singh, J., Upadhyay, A. K., Bahadur, A., Singh, B., Singh, K. P., Rai, M. (2006). Antioxidant phytochemicals in cabbage (Brassica oleracea L. var. capitata). Scientia Horticulturae, 108 (3), 233–237. doi: 10.1016/j.scienta.2006.01.017

12. Park, S., Valan Arasu, M., Lee, M.-K., Chun, J.-H., Seo, J. M., Lee, S.-W. et. al. (2014). Quantification of glucosinolates, anthocyanins, free amino acids, and vitamin C in inbred lines of cabbage (Brassica oleracea L.). Food Chemistry, 145, 77–85. doi: 10.1016/j.foodchem.2013.08.010

13. Barnes, P. J., Adcock, I., Spedding, M., Vanhoutte, P. M. (1993). Anti-inflammatory actions of steroids: molecular mechanisms. Trends in Pharmacological Sciences, 14 (12), 436–441. doi: 10.1016/0165-6147(93)90184-l

14. Dovhal, Ye. O., Gurieva, I. G., Kyslychenko, V. S., Zhuravel, I. O. (2016). Identification and assay of steroid compounds in narrow-leaved catoptric raw material. ScienceRise: Pharmaceutical Science, 3 (3), 4–7. doi: 10.15587/2519-4852.2016.79473

DOI: 10.15587/2519-4852.2017.119091

ANALYSIS OF INNOVATIVE DEVELOPMENT STRATEGIES IN PHARMACY

p. 17-20

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The aim *of the work is to analyze and systematize existing scientific approaches and mechanisms for the formation of innovation development strategies in pharmacy.*
Materials and methods. *Studies were conducted using a database on the Internet: Ukrainian patent office, SE "The State Expert Center" of the Ministry of Health of Ukraine, scientometric databases. Retrospective, systematic and analytical methods were been used.*
Results. *It has established that the most perspective directions of innovation development in pharmacy are: the search of priority therapeutic directions, where there is a low level of health care satisfaction, in effective and safe drugs; development of biosimilars; nanotechnology-based drugs; orphan drugs; antiretroviral drugs. Prospective strategies for patent protection prolongation of intellectual property objects in pharmacy have been analyzed and determined, which is an essential condition for the creation of effective mechanisms for their commercialization. It has proved actuality of the use state-private partnership mechanisms in Ukraine for modernization of health care system and pharmacy. This will increase the investment attractiveness of the pharmaceutical industry for foreign investors and international organizations, stimulating of innovation processes.*
Conclusions. *The rational choice of innovation strategy allows pharmaceutical companies to maintain and expand the quality and effectiveness of innovation, to bring new, original pharmaceutical drugs in different pharmaceutical forms available to the general population*
Keywords*: patent, drug, biosimilar, orphan drug, antiretroviral drug, state-private partnership*

References

1. Farmatsiia XX stolittia: tendentsii ta perspektyvy (2016). Kharkiv: NFaU, 1, 458.
2. Dmitrik, E. (2015). Struktura rynka lekarstvennykh sredstv v razreze rynochnogo statusa. Ezhenedel'nik Apteka, 1009 (38). Available at: http://www.apteka.ua/article/346577
3. Shelepko, S. (2015). Zaglyadyvaya v budushhee: blokbastery i perspektivnye R&D – novinki 2015 g. Ezhenedel'nik Apteka, 973 (2). Available at: http://www.apteka.ua/article/320463
4. Shelepko, S., Luk'yanchuk, E. (2016). Biosimilyary na evropeyskom farmrynke: kakovy uspekhi i perspektivy? Ezhenedel'nik Apteka, 976 (5). Available at: http://www.apteka.ua/article/322521
5. Piminov, A. F. (Ed.) (2014). Nanotekhnologii v farmatsii i meditsine. Kharkiv: Izd-vo Fakt, 672.
6. Shelepko, S. (2017). Rynok orfannykh preparatov: kakie faktory obuslovlivayut rost? Ezhenedel'nik Apteka, 1084 (13). Available at: http://www.apteka.ua/article/404764
7. Antunes, A., Fierro, I., Guerrante, R., Mendes, F., Alencar, M. (2013). Trends in Nanopharmaceutical Patents. International Journal of Molecular Sciences, 14 (4), 7016–7031. doi: 10.3390/ijms14047016
8. Giannuzzi, V., Conte, R., Landi, A., Ottomano, S. A., Bonifazi, D., Baiardi, P. et. al. (2017). Orphan medicinal products in Europe and United States to cover needs of patients with rare diseases: an increased common effort is to be foreseen. Orphanet Journal of Rare Diseases, 12 (1), 64–69. doi: 10.1186/s13023-017-0617-1
9. Clark, L., Beadle, D. (2012). Patent term extensions: issues, challenges and implications for pharmaceuticals. Pharmaceutical Patent Analyst, 1 (4), 427–435. doi: 10.4155/ppa.12.47
10. Cockburn, I., Long, G. (2015). The importance of patents to innovation: updated cross-industry comparisons with biopharmaceuticals. Expert Opinion on Therapeutic Patents, 25 (7), 739–742. doi: 10.1517/13543776.2015.1040762
11. Dmitrik, E. (2017). Gosudarstvenno-chastnoe partnerstvo v sfere zdravookhraneniya. Mezhdunarodnyy opyt. Ezhenedel'nik Apteka, 1104 (33). Available at: http://www.apteka.ua/article/423444

DOI: 10.15587/2519-4852.2017.118352

STUDY OF THE COMPOSITION OF CRYOPROTECTOR AND TECHNOLOGICAL REGIME IN LIOPHILIZATION OF LIPOSOMES WITH OXALIPLATINUM

p. 21-25

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Lyophilization is one of the most prospective and technologically logical methods for preserving the structure of nanobiotechnological products. Liposomes with oxaliplatin were obtained, and a screening experiment was performed to select a cryoprotectant.
Aim. *The aim of the research is to obtain liposomes with oxaliplatin, determine the type of cryoprotectant and its quantity, study the parameters of lyophilisation to obtain the product with maximum encapsulation of oxaliplatin, with the save of the size of liposomes in the nano-diapason, and the optimum residual moisture content.*
Methods. *Lyophilization was carried out in a Quarco lyophilizer (PRC). The liposomal form of oxaliplatin was obtained by the method of "passive" encapsulation in combination with the ion sorption method.*
Results. *Lactose, sucrose, maltose and trehalose dihydrate were studied as cryoprotectants. As the most perspective, was chosen - trehalose dihydrate. The optimal concentration of trehalose dihydrate in the liposomal form of oxaliplatin was researched at 8 % by weight. Also was optimized the program of freeze-drying. Primary drying with a duration of 1740 minutes was not sufficient. When the program was increased for 300 min, up to 2040 min, the values of*

the loss of encapsulation rate of 8 %, from 65 % before drying, to 57 % after drying were obtained. This is a good indicator, which shows an effectiveness of cryoprotectant and a rational program of freeze-drying. The size of the liposomes after drying was 112 nm, the residual moisture content, measured by K. Fischer's method, was 2.3 %, which is within the scope of the target range.

Conclusion. *A technology for obtaining liposomes with encapsulated oxaliplatin has been proposed and screening studies have been carried out to determine the optimal cryoprotectant. It is proposed to use as a cryoprotector trehalose dihydrate as the most perspective. The effect of different content of trehalose dihydrate on the degree of encapsulation of oxaliplatin in liposomes was studied. It was found that the optimal cryoprotectant concentration in the preparation is 8 % (by mass).*

Technological parameters of the lyophilization process of liposomes with oxaliplatin have been developed: drying time and freezing temperature. The decrease in the incorporation of oxaliplatin into liposomes during lyophilisation did not exceed 8.0 % with a residual water content of about 2.3 %. The size of liposomes after lyophilization in the nanoscale is 112 nm

Keywords*: Oxaliplatin, liposomes, high pressure extrusion, cryoprotectant, freeze drying*

References

1. Sharma, A., Sharma, U. S. (1997). Liposomes in drug delivery: Progress and limitations. International Journal of Pharmaceutics, 154 (2), 123–140. doi: 10.1016/s0378-5173(97)00135-x

2. Bajetta, E., Beretta, E., Bartolomeo, M. D., Cortinovis, D., Ferrario, E., Dognini, G., Toffolatti, L. et. al. (2004). Efficacy of treatment with irinotecan and oxaliplatin combination in FU-resistant metastatic colorectal cancer patients. Oncology, 66 (2), 132–137. doi: 10.1159/000077439

3. Shvets, V. I., Krasnopolskiy, Yu. M. (2008). Liposomyi v farmatsii. Produktyi nanobiotehnologii [Liposomes in pharmacy. Products of nanobiotechnology]. Provizor, 3, 18–24.

4. Torchilin, V. P., Weissig, V. (2003). Liposomes: A Practical Approach. New York: Oxford University Press, 384.

5. Chen, C., Han, D., Cai, C., Tang, X. (2010). An overview of liposome lyophilization and its future potential. Journal of Controlled Release, 142 (3), 299–311. doi: 10.1016/j.jconrel.2009.10.024

6. Wang, W., Mo, C., Guohua, C. (2012). Issues in freeze drying of aqueous solutions. Chinese Journal of Chemical Engineering, 20 (3), 551–559. doi: 10.1016/s1004-9541(11)60218-8

7. Franks, F., Auffret, T. (2007). Freeze-Drying of Pharmaceutical and Biopharmaceuticals. London: RSC Publishing, 206. doi: 10.1039/9781847557704

8. Chen, G., Wang, W. (2007). Role of freeze drying in nanotechnology. Drying Technology, 25 (1), 29–35. doi: 10.1080/07373930601161179

9. Stadnichenko, A. V., Krasnopolskiy, Yu. M., Shvets, V. I. (2015). Razrabotka i validatsiya metodiki opredeleniya stepeni inkapsulyatsii irinotekana gidrohlorida v liposomyi [Development and validation of the procedure for determining the degree of encapsulation of irinotecan hydrochloride in liposomes]. Biofarmatsevticheskiy zhurnal, 7 (1), 53–55.

10. Stadnichenko, O. V., Krasnopolskiy, Yu. M., Yarnih, T. G. (2016). Vivchennya vplivu zaryadu lipidnoyi membrani pri stvorenni liposom iz oksaliplatinom [Study of the influence of the lipid membrane in the treatment of liposomes with oxaliplatin]. Vistnik farmatsiyi, 4, 34–37.

DOI: 10.15587/2519-4852.2017.119490

STUDY OF SUPEROXIDE- AND NO-DEPENDENT PROTECTIVE MECHANISMS OF N-ACETYLCYSTEINE AND LOSARTAN IN RAT'S AORTA AND LIVER UNDER STREPTOZOTICIN-INDUCED TYPE 1 DIABETES MELLITUS

p. 25-31

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Aim. *The aim of the research was to investigate superoxide- (SR) and NO-dependent mechanisms of action of N-acetylcysteine (NAC) and losartan (LOS) in aorta and liver of rats with type 1 diabetes mellitus (DMI).*

Methods. *Diabetic rats were treated with NAC (1.5g/kg), LOS (20mg/kg) or combination (NAC+LOS) for 4 weeks.*

Results. *The rate of SR generation by mitochondria of aorta in untreated diabetic animals was significantly higher than in control, while the level of NO was decreased. Production of SR and NO in the liver of diabetic rats were dramatically increased. The marker of oxidatively damaged DNA, 8-oxoG, was raised in urine of diabetic rats. All of pharmacological schemes showed significant decrease the rate of SR generation by mitochondria of aorta and liver; NO level was lowered in the liver tissue compared to DMI. Only NAC significantly restored NO level in aorta of diabetic rats. Intervention with NAC / LOS or NAC+LOS increased the level of 8-oxoG in compare to DM1.*

Conclusion. *In conclusion, treatment with NAC and LOS or combination is associated with protection of aorta and liver cells in diabetic animals against toxic action of SR, preventing mitochondrial dysfunction and further DNA damage, which point out the cardioprotective effects and overall metabolic improvement*

Keywords: *streptozoticin, superoxide, aorta, liver, rats, N-acetylcysteine, losartan*

References

1. Global report on diabetes (2016). Geneva: World Health Organization. Available at: http://www.who.int/diabetes/global-report/en/

2. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants (2016). The Lancet, 387 (10027), 1513–1530. doi: 10.1016/s0140-6736(16)00618-8

3. Giacco, F., Brownlee, M. (2010). Oxidative Stress and Diabetic Complications. Circulation Research, 107 (9), 1058–1070. doi: 10.1161/circresaha.110.223545

4. Watanabe, K., Thandavarayan, R. A., Harima, M., Sari, F. R., Gurusamy, N., Veeraveedu, P. T. et. al. (2010). Role of Differential Signaling Pathways and Oxidative Stress in Diabetic Cardiomyopathy. Current Cardiology Reviews, 6 (4), 280–290. doi: 10.2174/157340310793566145

5. Ansley, D. M., Wang, B. (2012). Oxidative stress and myocardial injury in the diabetic heart. The Journal of Pathology, 229 (2), 232–241. doi: 10.1002/path.4113

6. Guo, R., Liu, B., Zhou, S., Zhang, B., Xu, Y. (2013). The Protective Effect of Fasudil on the Structure and Function of Cardiac Mitochondria from Rats with Type 2 Diabetes Induced by Streptozotocin with a High-Fat Diet Is Mediated by the Attenuation of Oxidative Stress. BioMed Research International, 2013, 1–9. doi: 10.1155/2013/430791

7. Fulbright, J. M., Egas-Bejar, D. E., Huh, W. W., Chandra, J. (2015). Analysis of redox and apoptotic effects of anthracyclines to delineate a cardioprotective strategy. Cancer Chemotherapy and Pharmacology, 76 (6), 1297–1307. doi: 10.1007/s00280-015-2879-4

8. Wang, J., Wang, H., Hao, P., Xue, L., Wei, S., Zhang, Y., Chen, Y. (2011). Inhibition of aldehyde dehydrogenase 2 by oxidative stress is associated with cardiac dysfunction in diabetic rats. Molecular Medicine, 17 (3-4), 172–179. doi: 10.2119/molmed.2010.00114

9. Dludla, P. V., Nkambule, B. B., Dias, S. C., Johnson, R. (2017). Cardioprotective potential of N-acetyl cysteine against hyperglycaemia-induced oxidative damage: a protocol for a systematic review. Systematic Reviews, 6 (1), 1–5. doi: 10.1186/s13643-017-0493-8

10. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD (2013). European Heart Journal, 34 (39), 3035–3087. doi: 10.1093/eurheartj/eht108

11. Axelsson, A., Iversen, K., Vejlstrup, N., Ho, C., Norsk, J., Langhoff, L. et. al. (2015). Efficacy and safety of the angiotensin II receptor blocker losartan for hypertrophic cardiomyopathy: the INHERIT randomised, double-blind, placebo-controlled trial. The Lancet Diabetes & Endocrinology, 3 (2), 123–131. doi: 10.1016/s2213-8587(14)70241-4

12. Ochiai, M., Brancalhao, E., Puig, R., Vieira, K., Cardoso, J., Oliveira-Jr, M., Barretto, A. (2014). Short-term add-on therapy with angiotensin receptor blocker for end-stage inotrope-dependent heart failure patients: B-type natriuretic peptide reduction in a randomized clinical trial. Clinics, 69 (5), 308–313. doi: 10.6061/clinics/2014(05)02

13. Council Directive 2010/63/EU of 22 September 2010 on the protection of animals used for scientific purposes (2010). Official Journal of the European Communities, 276, 33–79.

14. Brosius, F. (Ed.) (2003). Low-Dose Streptozotocin Induction Protocol (Mouse). The University of Michigan Medical Center, 3.

15. Burlaka, A. P., Sidorik, E. P. (2006). Radical forms of oxygen and nitric oxide in tumourogenesis. Kyiv Naukova Dumka, 227.

16. Burlaka, A. P., Ganusevich, I. I., Golotiuk, V. V., Vovk, A. V., Lukin, S. M. (2016). Superoxide- and NO-dependent mechanisms of antitumor and antimetastatic effect of L-arginine hydrochloride and coenzyme Q10. Experimental Oncology, 38 (1), 31–35.

17. Liu, Q., Wang, S., Cai, L. (2014). Diabetic cardiomyopathy and its mechanisms: Role of oxidative stress and damage. Journal of Diabetes Investigation, 5 (6), 623–634. doi: 10.1111/jdi.12250

18. Raza, H., Prabu, S. K., John, A., Avadhani, N. G. (2011). Impaired Mitochondrial Respiratory Functions and Oxidative Stress in Streptozotocin-Induced Diabetic Rats. International Journal of Molecular Sciences, 12 (12), 3133–3147. doi: 10.3390/ijms12053133

19. Wang, S., Wang, C., Yan, F., Wang, T., He, Y., Li, H. et. al. (2017). N-Acetylcysteine Attenuates Diabetic Myocardial Ischemia Reperfusion Injury through Inhibiting Excessive Autophagy. Mediators of Inflammation, 2017, 1–10. doi: 10.1155/2017/9257291

20. Sivitz, W. I., Yorek, M. A. (2010). Mitochondrial Dysfunction in Diabetes: From Molecular Mechanisms to Functional Significance and Therapeutic Opportunities. Antioxidants & Redox Signaling, 12 (4), 537–577. doi: 10.1089/ars.2009.2531

21. Liu, C., Lu, X.-Z., Shen, M.-Z., Xing, C.-Y., Ma, J., Duan, Y.-Y., Yuan, L.-J. (2015). N-Acetyl Cysteine improves the diabetic cardiac function: possible role of fibrosis inhibition. BMC Cardiovascular Disorders, 15 (1), 84. doi: 10.1186/s12872-015-0076-3

22. Su, W., Zhang, Y., Zhang, Q., Xu, J., Zhan, L., Zhu, Q. et. al. (2016). N-acetylcysteine attenuates myocardial dysfunction and postischemic injury by restoring caveolin-3/eNOS signaling in diabetic rats. Cardiovascular Diabetology, 15 (1), 1–46. doi: 10.1186/s12933-016-0460-z

23. Sleem, M., Taye, A., El-Moselhy, M. A., Mangoura, S. A. (2014). Combination therapy with losartan and l-carnitine protects against endothelial dysfunction of streptozotocin-induced diabetic rats. European Journal of Pharmacology, 744, 10–17. doi: 10.1016/j.ejphar.2014.09.032

24. Dianat, M., Hamzavi, G. R., Badavi, M., Samarbafzadeh, A. (2014). Effects of Losartan and Vanillic Acid Co-Administration on Ischemia-Reperfusion-Induced Oxidative Stress in Isolated Rat Heart. Iranian Red Crescent Medical Journal, 16 (7). doi: 10.5812/ircmj.16664

25. Kamper, M., Tsimpoukidi, O., Chatzigeorgiou, A., Lymberi, M., Kamper, E. F. (2010). The antioxidant effect of angiotensin II receptor blocker, losartan, in streptozotocin-induced diabetic rats. Translational Research, 156 (1), 26–36. doi: 10.1016/j.trsl.2010.05.004

26. Sytnyk, I. M., Khaitovych, M. V., Chernovol, P. A. (2016). Antioxidant activity of angiotensin II inhibitors and metabotropic cardioprotectors under the conditions in vitro and in silico. Pharmacology and Drug Toxicology, 48 (2), 80–85.

27. Wang, T., Qiao, S., Lei, S., Liu, Y., Ng, K. F. J., Xu, A. et. al. (2011). N-Acetylcysteine and Allopurinol Synergistically Enhance Cardiac Adiponectin Content and Reduce Myocardial Reperfusion Injury in Diabetic Rats. PLoS ONE, 6 (8), e23967. doi: 10.1371/journal.pone.0023967

28. Mao, X., Wang, T., Liu, Y., Irwin, M. G., Ou, J., Liao, X. et. al. (2013). N-Acetylcysteine and Allopurinol Confer Synergy in Attenuating Myocardial Ischemia Injury via Restoring HIF-1α/HO-1 Signaling in Diabetic Rats. PLoS ONE, 8 (7), e68949. doi: 10.1371/journal.pone.0068949

29. Kumar, S., Prasad, S., Sitasawad, S. L. (2013). Multiple Antioxidants Improve Cardiac Complications and Inhibit Cardiac Cell Death in Streptozotocin-Induced Diabetic Rats. PLoS ONE, 8 (7), e67009. doi: 10.1371/journal.pone.0067009

30. Falach-Malik, A., Rozenfeld, H., Chetboun, M. et. al. (2016). N-Acetyl-L-Cysteine inhibits the development of glucose intolerance and hepatic steatosis in diabetes-prone mice. American Journal of Translational Research, 9 (8), 3744–3756.

31. Chughlay, M. F., Kramer, N., Spearman, C. W., Werfalli, M., Cohen, K. (2016). N-acetylcysteine for non-paracetamol drug-induced liver injury: a systematic review. British Journal of Clinical Pharmacology, 81 (6), 1021–1029. doi: 10.1111/bcp.12880

32. Li, Y.-S., Song, M.-F., Kasai, H., Kawai, K. (2013). 8-Hydroxyguanine in Urine and Serum as an Oxidative Stress Marker: Effects of Diabetes and Aging. Journal of UOEH, 35 (2), 119–127. doi: 10.7888/juoeh.35.119

33. Kumar, P., Swain, M. M., Pal, A. (2016). Hyperglycemia-induced inflammation caused down-regulation of 8-oxoG-DNA glycosylase levels in murine macrophages is mediated by oxidative-nitrosative stress-dependent pathways. The International Journal of Biochemistry & Cell Biology, 73, 82–98. doi: 10.1016/j.biocel.2016.02.006

34. Simone, S., Gorin, Y., Velagapudi, C., Abboud, H. E., Habib, S. L. (2008). Mechanism of Oxidative DNA Damage in Diabetes. Diabetes, 57 (10), 2626–2636. doi: 10.2337/db07-1579

35. Kumar, P., Rao, G. N., Pal, B. B., Pal, A. (2014). Hyperglycemia-induced oxidative stress induces apoptosis by inhibiting PI3-kinase/Akt and ERK1/2 MAPK mediated signaling pathway causing downregulation of 8-oxoG-DNA glycosylase levels in glial cells. The International Journal of Biochemistry & Cell Biology, 53, 302–319. doi: 10.1016/j.biocel.2014.05.038

36. Lodovici, M., Bigagli, E., Tarantini, F., Di Serio, C., Raimondi, L. (2015). Losartan reduces oxidative damage to renal DNA and conserves plasma antioxidant capacity in diabetic rats. Experimental Biology and Medicine, 240 (11), 1500–1504. doi: 10.1177/1535370215570826

37. Cooke, M. S., Henderson, P. T., Evans, M. D. (2009). Oxidative Stress-Induced Carcinogenesis and Its Prevention Guest Editor: Shinya Toyokuni Sources of Extracellular, Oxidatively-Modified DNA Lesions: Implications for Their Measurement in Urine. Journal of Clinical Biochemistry and Nutrition, 45 (3), 255–270. doi: 10.3164/jcbn.sr09-41

DOI: 10.15587/2519-4852.2017.119622

STUDY OF CONSUMPTION OF DRUGS FOR THE TREATMENT OF SOLDIERS AS SURGICAL PATIENTS IN A MILITARY MOBILE HOSPITAL

p. 32-37

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The aim *is to analyze the consumption of medicines for the treatment of soldiers as surgical patients in a military mobile hospital (hereinafter MMH).*

Methods. *With the use of the quantity and cost method of ABC-analysis was investigated the structure of consumption of medicines by surgical patients of military mobile hospital. As the studied materials were reporting data indicators of the MMH medical work for 2014-2016, report application availability and medical needs property (p.8/med), statistical and analytical indicators of morbidity for the military (f.3/med), standards of medical care, clinical protocols of medical care on the urgent and most important diseases of soldiers in conditions of MMH.*

Results. *The analysis of the consumption of medicines for the treatment of military personnel in the military mobile hospitals determined a directly proportional relationship with the magnitude and structure of hospital morbidity. The received data testify to rationality of expenditure of money resources for drug maintenance of a researched contingent.*

Conclusions. *The obtained results allow us to forecast the need for medicines for the next year when planning medical supplies. The rationale for the presented fragment of the drug list is their inclusion in the clinical protocols of medical care for the treatment of surgical patients in a military mobile hospital. The data can be used in the future to develop cost standards for appropriate nosological forms.*

Keywords: *military mobile hospital, analysis of drug consumption, ABC-analysis, therapeutic category.*

References

1. Miroshnichenko, Yu. V., Goryachev, A. B., Golubenko, R. A. (2014). Organizatsionno-metodicheskie podhody k normirovaniyu meditsinskogo imushchestva dlya voyskovogo i korabel'nogo zven'ev meditsinskoy sluzhby Vooruzhennyh sil v sovremennyh usloviyah. Vestnik rossiyskoy voenno-meditsinskoy akademii, 4 (48), 185–192.

2. Rudenko, V. V. (2012). Retrospektivniy analiz razvitiya sistemy normirovannogo raspredeleniya meditsinskogo imushchestva v voenno-meditsinskoy sluzhbe. Voennaya meditsina, 2, 92–97.

3. Shmatenko, A. P., Pritula, R. L., Solomenniy, A. N. (2013). Medikamentoznoe obespechenie postradavshih s torakoabdominal'noy travmoy. Farmatsevticheskiy zhurnal, 4, 19–25.

4. Solomenniy, A. N. (2014). Obosnovanie normy medikamentoznogo obespecheniya postradavshih voennosluzhashchih s torakoabdominal'noy travmoy. Vestnik farmatsii, 3, 58–61.

5. Gul'pa, V. S., Hitriy, G. P., Kozeev, E. S. (2012). Normirovanie infuzionnyh sredstv i izgotovlenie ih v polevyh usloviyah dlya okazaniya kvalifitsirovannoy meditsinskoy pomoshchi v vooruzhennyh konfliktah. Voennaya meditsina Ukrainy, 12 (2), 77–82.

6. Zaporozhan, V. M., Maydanyuk, V. P., Iva, A. V. (2016). Vzaimodeystvie voennoy i grazhdanskoy meditsiny v ATO. Problemy voennogo zdravoohraneniya, 36, 304–306.

7. Andronatiy, V. B., Zhahovskiy, V. A., Bulah, A. Yu., Livinskiy, V. G. (2014). Sistema meditsinskogo obespecheniya Vooruzhennyh Sil Ukrainy: sovremennoe sostoyanie i napravleniya razvitiya s uchetom tendentsii izmeneniy v poryadke primeneniya voysk. Nauka i oborona, 3, 23–29.

8. Prikaz Ministra oborony Ukrainy ot 20.02.2008 No. 57 "Ob utverzhdenii Polozheniya o voennom mobil'nom gospitale (mnogoprofil'nyy na 100 koek)".

9. Frolov, M. Yu., Barkanova, O. N., Shatalova, O. V. (2012). Metodika provedeniya AVS/VEN-analiza. Lekarstvenniy vestnik, 46 (6), 3–6.

10. Matyuha, L. F., Avramenko, T. P., Lesnoy, I. I., Goyda, N. G. (2015). Raschet potrebnosti v lekarstvennyh sredstvah, soderzhashchih kontroliruemye veshchestva. Kyiv, 20.

11. Agripishin, S. V., Sereda, I. K. (2017). Analiz vhodyashchego potoka sanitarnyh poter' v 59 mobil'nyy voennyy gospital' vo vremya antiterroristicheskoy operatsii za 2014–2015 gg. Mater. konferentsii molodyh uchenyh Ukrainskoy voenno-meditsinskoy akademii. Kyiv: ChP «Chalchinskiy», 12–13.

DOI: 10.15587/2519-4852.2017.119744

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF COMBINATION DRUG WITH NEURALLY MEDIATED ACTION «MEMOFIT»

p. 38-44

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Aim. *The aim of this work is to develop composition of combination drug in the form of hard-gelatin capsules «Memofit», determine technological and microbiological parameters of intermediate products and ready medicinal product and develop of manufacturing process for capsules «Memofit».*

Methods of the research. *Investigations presented in the article were performed in accordance with the procedures described by the State Pharmacopoeia of Ukraine (SPh Ukraine).*

The results of the research. *Necessity of the development of dietary supplement to provide special dietary properties for the purpose of regulation of functions and systems of the organism within the physiologically normal states under the nervous system dysfunction was substantiated. Results of the study of pharmaco-technological and microbiological parameters of dry extracts that are included as a compound of hard-gelatin capsules «Memofit» were presented. Optimal technological parameters for manufacturing process of capsules «Memofit» were proposed. Results of mass balance for a batch of capsules «Memofit» proved rationality of selected manufacturing process were given. Technology of manufacturing process of capsules «Memofit» was introduced into the production on the TOV "DZ "GNCLS".*

Conclusions*. Possibility of the development of solid formulations in the form of capsules was established based on the obtained experimental findings of the determination of pharmaco-technological and microbiological parameters of dry extracts. It was shown that capsules «Memofit» are used in dietary food ration as additional source of biologically active substances for promoting normalization of brain function and sleep, improvement of attentiveness. This preparation has general tonic properties and improves mental and physical efficiency. Manufacturing process and process flow chart for this medication was substantiated*

Keywords: *technology, solid formulations, capsules, plant extracts, diseases of the nervous system*

References

1. Voznesenskaya, T. G. (2008). Emotional stress and prevention of its consequences. RMJ, 14 (9), 694–697.

2. Vorobyova, O. V. (2009). Stress and Adaptation Disorders. RMJ, 17 (11), 789–793.

3. Avdeyeva, T. I., Kinkulkina, M. A. (2008). Herbal preparations in the treatment of anxiety disorders. Doctor, 11, 49–52.

4. Grechany, I. A. (2015). Great illustrated guide to medicinal herbs and plants. 600 recipes and secrets of the hereditary herbalist. Kharkiv: Book Club "Family Leisure Club", 544.

5. Mosyakin, S. L., Fedoronchuk, M. M. (1999). Vascular plants of Ukraine: a nomenclatural checklist. Kyiv: National Academy of Sciences of Ukraine, M. G. Kholodny Institute of Botany, 345.

6. Borovikov, V. S. (2011). Useful species of the genus THALICTRUM L. (Meadowrue) Altai mountain country. Vestnik Altai State University, 1 (75), 32–34.

7. Vrchovska, V., Spilkova, J., Valentao, P., Sousa, C., Andrade, P. B., Seabra, R. M. (2007). Antioxidative properties and phytochemical composition of Ballota nigra infusion. Food Chemistry, 105 (4), 1396–1403. doi: 10.1016/j.foodchem.2007.05.016

8. Bylka, W., Studzinska-Sroka, E., Znajdek-Awizen, P. (2014). Stan badan nad zielem mierznicy czarnej (Ballotae nigrae herba). Postepy Fitoterapii, 3, 180–183.

9. Dezhi, F., Guanghua, Z. (2011). Thalictrum L Flora of China, 6, 282–302.

10. State Pharmacopoeia of Ukraine (2001). Kharkiv: REEREG, 556.

11. "Temporary hygienic norms of the content of chemical and biological contaminants Nature in Biologically Active Additives "GN 4.4.8.073-2001: Resolution Chief Sanitary Doctor of Ukraine dated April 20, 2001 (2001). Official bulletin Of Ukraine, 131, 316–332.

12. Chudeshov, V. I., Khokhlova, L. M., Lyapunov, O. O. et. al.; V. I. Chueshov (Ed.) (2003). Technology of medicines for industrial production. Kharkiv: Publishing NUPh "Golden pages", 720.

13. Shteyngardt, M. V., Kazarinov, N. A. (1996). Solid dosage forms. Technology and standardization of drugs. Kharkiv: LLC «Reereg», 539–605.

14. Savelieva, E. V., Vladymyrova, I. N., Tishakova, T. S. (2016). Determination of effect of Ballota nigra extract on the state of lipid peroxidation and rats' antioxidant system under chronic immobilization stress. Der Pharmacia Lettre, 8 (5), 227–230.

DOI: 10.15587/2519-4852.2017.119890

SUBSTANTIATION OF THE COMPOSITION OF SURFACE-ACTIVE SUBSTANCES IN DEVELOPMENT OF A CREAM WITH SILVER CITRATE

p. 44-51

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Pharmaceutical emulsions are now given increasing attention because they are widely used in medical practice. This became possible due to a qualitatively new level of scientific research and achievements in the field of emulsion systems creation, as well as expansion of assortment of auxiliary substances and use of new modern equipment. Emulsions are heterogeneous disperse systems that are potentially unstable. Therefore, the issue of stabilizing of emulsion systems is the main problem in area of emulsions technology.

Aim. *The aim of the experiment was to study structural and mechanical properties of concentrated emulsion systems, depending on the total concentration of surfactants, as well as investigation of colloidal and thermal stability of samples for substantiation of the composition of surfactants in the development of a cream with silver citrate.*

Methods. *Pharmaco-technological methods of research were conducted in accordance with the requirements of the State Pharmacopoeia of Ukraine.*

Research results. *Colloidal and thermal stability of the samples of emulsion cream with silver citrate was investigated. It has been established that the use of emulsifiers in concentrations of 4 % and 6 % does not provide physical stability. A dispersion analysis of the heterogeneous systems was carried out, which has shown that the samples obtained by using of the emulsifiers combination are homogeneous in size of particles of oil phase, which do not exceed 10 microns. The behavior of samples of the emulsion cream with silver citrate during and after mechanical destruction is investigated. The results guarantee stability of the system under the influence of mechanical processing during industrial production and use.*

Conclusion. *As a result of the experiment, the use of the combination of surface-active substances: emulsifier № 1 and cetostearyl alcohol of 8–10 % was used to stabilize the emulsion system with silver citrate*

Keywords*: emulsion system, surfactants, cream, silver citrate, stability*

References

1. Vasconcelos, T., Marques, S., Sarmento, B. (2017). Measuring the emulsification dynamics and stability of self-emulsifying drug delivery systems. European Journal of Pharmaceutics and Biopharmaceutics, 123, 1–8. doi: 10.1016/j.ejpb.2017.11.003

2. Zafeiri, I., Smith, P., Norton, I. T., Spyropoulos, F. (2017). Fabrication, characterisation and stability of oil-in-water emulsions stabilised by solid lipid particles: the role of particle characteristics and emulsion microstructure upon Pickering functionality. Food & Function, 8 (7), 2583–2591. doi: 10.1039/c7fo00559h

3. Chuieshov, V. I., Gladukh, I. V., Saiko, I. V. et. al. (2013). Technology of medicines for industrial production. Kharkiv: NFaU: Oryhinal, 638.

4. Kutts, G., Friss, S., Khenning, S. et. al. (2004). Cosmetic creams and emulsions: Composition. Receiving. Test methods. Moscow: Klavel, 272.

5. Sakamoto, K., Lochhead, R., Maibach, H., Yamashita, Y. (Eds.) (2017). Cosmetic science and technology: Theoretical principles and applications. Amsterdam: Elsevier, 854.

6. Pletnev, M. Yu. (2002). Surface-active substances and compositions. Moscow: «Firma Klavel», 768.

7. Walters, Y., Roberts, M. (Eds.) (2007). Dermatologic, cosmeceutic and cosmetic development. Boca Raton: CRC Press, 648. doi: 10.3109/9780849375903

8. Cheng, Q., Zhang, B., He, Y., Lu, Q., Kaplan, D. L. (2017). Silk nanofibers as robust and versatile emulsifiers. ACS Applied Materials & Interfaces, 9 (41), 35693–35700. doi: 10.1021/acsami.7b13460

9. Yang, Y., Fang, Z., Chen, X., Zhang, W., Xie, Y., Chen, Y. et. al. (2017). An Overview of Pickering Emulsions: Solid-Particle Materials, Classification, Morphology, and Applications. Frontiers in Pharmacology, 8. doi: 10.3389/fphar.2017.00287

10. Tadros, T. (2006). Principles of emulsion stabilization with special reference to polymeric surfactants. Journal of Cosmetic Science, 57, 153–169.

11. Aidarova, S., Sharipova, A., Kragel, J., Miller, R. (2014). Polyelectrolyte/surfactant mixtures in the bulk and at water/oil interfaces. Advances in Colloid and Interface Science, 205, 87–93. doi: 10.1016/j.cis.2013.10.007

12. Pertsev, I. M., Dmytriievskyi, D. I., Rybachuk, V. D. et. al.; Pertsev, I. M. (Ed.) (2010). Dopomizhni rechovyny v tekhnolohii likiv: vplyv na tekhnolohichni, spozhyvchi, ekonomichni kharakterystyky i terapevtychnu aktyvnist [Excipients in drugs technology: influence on technological, consumer, economic characteristics and therapeutic activity]. Kharkiv: Gold pages, 600.

13. Kukhtenko, H., Gladukh, I., Kukhtenko, O., Soldatov, D. (2017). Influence of excipients on the structural and mechanical properties of semisolid dosage forms. Asian Journal of Pharmaceutics, 11 (3), 575–578. doi: 10.22377/ajp.v11i03.1462

14. Polova, Zh. N. (2017). Justification of the composition of the cream of antimicrobial action on the basis of rheological studies. Republican scientific journal «VESTNIK» of the South Kazakhstan State Pharmaceutical Academy, 1 (78), 140–144.

15. Polova, Zh. N. (2017). Determination of the stability of veterinary cream containing silver citrate. ScienceRise: Pharmaceutical Science, 4 (8), 21–26. doi: 10.15587/2519-4852.2017.108947

16. Estanqueiro, M., Amaral, M. H., Sousa Lobo, J. M. (2016). Comparison between sensory and instrumental characterization of topical formulations: impact of thickening agents. International Journal of Cosmetic Science, 38 (4), 389–398. doi: 10.1111/ics.12302

17. Calixto, L. S., Maia Campos, P. M. B. G. (2017). Physical-Mechanical characterization of cosmetic formulations and correlation between instrumental measurements and sensorial properties. International Journal of Cosmetic Science, 39 (5), 527–534. doi: 10.1111/ics.12406

DOI: 10.15587/2519-4852.2017.119926

SCIENTIFIC SUBSTANTIATION OF THE PRODUCT RANGE RENEWAL MODEL FOR MANUFACTURING PHARMACEUTICAL ENTERPRISE

p. 52-55

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In modern conditions, aggravation of competition in the national pharmaceutical market, increase in cost of scientific developments and investments in pharmaceutical industry, raising of the level of requirements and needs of consumers of remedies, the use of the national drug manufacturers innovative approaches to the product range formation, which will ensure a stable market position of the company, economic stability and strategic development along

with the maintenance of available and affordable national drugs in Ukrainian market becomes particularly relevant.

Aim. *Development of the product range renewal model for manufacturing pharmaceutical enterprise and its study on example of the nonsteroidal anti-inflammatory drugs segment.*

Methods. *System, analytical and logical methods were used for analysis.*

Results. *On the basis of systematization of results of organizational and economic, marketing and pharmacoeconomic studies of the pharmaceutical market, the product range renewal model on the manufacturing PE was developed and substantiated; it consists of five successive stages. Each stage of the given model involves research of organizational and economic orientation and determination of performance indicators.*

Conclusion. *The developed product range renewal model on the manufacturing PE can be recommended as an effective support system for pharmaceutical organization grounded management decisions in marketing, which, we believe, will significantly reduce costs and increase the efficiency of business*

Keywords: *pharmaceutical enterprise, product range, pharmaceutical market, marketing research*

References

1. Moskalenko, V. F. (Ed.) (2007). Stan ta perspektyvy rozvytku farmatsevtychnoi promyslovosti v Ukraini: Statystychnyi dosvid. Kyiv: Karavella, 149.

2. Bratishko, Yu. S., Posylkina, O. V. (2015). Suchasni metodychni pidkhody do otsinky staloho sotsialno-ekonomichnoho rozvytku farmatsevtychnykh pidpryiemstv Ukrainy. Prostranstvennye aspekty razvitiya sotsial'no-ekonomicheskih sistem: ekonomika, obrazovanie i zdravoohranenie. Opole, 234–240.

3. Kubyshyna, N. S. (2010). Metodyka rozrobky stratehichnoho naboru tovariv na promyslovomu rynku. Ekonomichnyi visnyk NTTU «KPI», 7, 171–178.

4. Meshalkina, S. Yu., Gnatyuk, O. P. (2013). Otsenka effektivnosti sistemy upravleniya tovarnym assortimentom farmatsevticheskih organizatsiy Dal'nevostochnogo regiona. Vestnik Roszdravnadzora, 3, 40–44.

5. Pestun, I. V. (2009). Napriamky udoskonalennia Natsionalnoi likarskoi polityky v Ukraini za indykatoramy yii otsinky VOOZ. Zbirnyk naukovykh prats spivrobitnykiv KMAPO im. P. L. Shupyka. Kyiv, 717–723.

6. Pestun, I. V., Mnushko, Z. M. (2008). Stan ta perspektyvy vplyvu makrootochennia na diyalnist farmatsevtychnykh orhanizatsiy v Ukraini. Upravlinnia, ekonomika ta zabezpechennia yakosti v farmatsiy, 1 (1), 8–14.

7. Posylkina, O. V., Sydorenko, M. I. (2011). Naukovi pidkhody do upravlinnia yakistiu doslidzhen i rozrobok u farmatsevtychniy haluzi. Upravlinnia, ekonomika ta zabezpechennia yakosti v farmatsiy, 4 (18), 16–23.

8. Slobodianiuk, M. M., Zhadko, S. V., Samborskyi, O. S. (2010). Naukovo-metodychni pidkhody do optymizatsiy finansuvannia innovatsiynoho portfeliu farmatsevtychnoho pidpryiemstva. Ukr. zhurn. klin. ta lab. med., 2, 58–62.

9. Belyaevskiy, I. K. (2008). Marketingovoe issledovanie: informatsiya, analiz, prognoz. Moscow: Finansy i statistika, 319.

10. Mnushko, Z. M., Presniakova, V. V. (2007). Audyt rozdribnoi realizatsiy hormonalnykh likarskykh zasobiv. Visnyk farmatsiy, 2 (50), 54–57.

11. Baeva, E. E. (2007). Analiz faktorov, vliyayushchih na psihologiyu pokupatelya lekarstvennyh sredstv. Marketing v Rossii i zarubezhom, 1 (57), 20–23.

12. Zhadko, S. V., Slobodianiuk, M. M., Skrylova, N. M. (2009). Metody analizu ta otsinky asortymentu likarskykh preparativ v systemi upravlinnia tovarnym portfelem vyrobnychykh farmatsevtychnykh pidpryiemstv. Zbirnyk nauk. prats spivrobitnykiv NMAPO im. P. H. Shupyka, 18, 257–265.