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## APPLICATION OF THE DIRECT ENCAPSULATION METHOD IN THE TECHNOLOGY OF MEDICINE WITH DRY RAUWOLPHIA EXTRACT (RAUVOLFIA SERPENTINA BENTH.)

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**The aim:** development of the composition and technology of a medicinal drug in the form of capsules with a dry extract of *Rauwolfia* for the treatment of hypertension.

**Materials and methods.** Experimental samples of masses for encapsulation contained 2.0 mg of dry *Rauwolfia* extract and various excipients used in the technology of solid dosage forms. The study of pharmaco-technological characteristics was carried out on the devices of the company “Pharma Test” (Germany). The time of decay was determined on the device of the company “Erweka” (Germany). A comparative analysis of the cost calculation of the production of tablets and capsules with dry *rauwolfia* extract was carried out by the “cost plus” method.

**Results.** The use of PROSOLV® SMCC HD 90 improved the flowability, homogeneity and homogeneity of the mass with *Rauwolfia* dry extract powder, considering the low dosage of the substance of 2 mg. It has been experimentally proven that PROSOLV® SMCC HD 90 shortens the disintegration time as a disintegrant, because due to silicate moisture easily penetrates into the MCCC, hydrophilic bridges are formed, wettability increases and mass swelling occurs. The multifunctionality of PROSOLV® SMCC HD 90 three-in-one excipient, which has the properties of a filler, a disintegrant and a glidant, makes it easy to apply direct encapsulation technology, replace and reduce the number of excipients and thus increase production efficiency.

**Conclusions.** When developing the composition of capsules with dry *rauwolfia* extract, the effect of various excipients on the pharmaco-technological properties of encapsulating masses and ready-made capsules was investigated. The combined excipient, namely PROSOLV® SMCC HD 90, having the properties of a filler, a disintegrant and a lubricant, in direct encapsulation technology is more effective in influencing the fluidity of the mass and disintegration of the capsules. The introduction of the direct encapsulation method will allow to expand the range of new medicines and improve existing technologies, in particular in the form of tablets, which are widely produced in industrial production. it is possible to attach specifically to *Rauwolfia*

**Keywords:** capsules, technology, direct encapsulation, *Rauwolfia* dry extract, hypertension

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### 1. Introduction

The competitive pharmaceutical market is rapidly developing and contributes to the production of effective, high-quality and affordable medicines in various forms, including capsules [1–3].

Today, the capsule is one of the most common forms, after tablets. Modernity and innovation are characteristic features of this dosage form. Several advantages provided them with wide opportunities in technology: high bioavailability, good appearance, easy to swallow, the shell protects the contents of the capsule from environmental factors [4–6].

The capsule, as a medicinal form, is constantly being improved and is convenient for the development of new and modernization of already existing medicines and their technologies [7–10].

The use of direct encapsulation technology allows to significantly reduce the time of the technological cy-

cle (1), especially due to the coating stage, to exclude the use of several equipment positions (2), to reduce production areas (3), to reduce energy and labour costs (4) and to have a positive effect on cost of the drug [7, 8].

Modern herbal preparations are widely used in the complex treatment of various diseases, in particular for cardiovascular diseases, which occupy a leading place among the morbidity in Ukraine [11, 12]. They differ in mild effectiveness, low toxicity and the possibility of long-term use without the risk of side effects [13–15]. The tropical plant *Rauwolfia serpentina* accumulates indole alkaloids, which are the most effective means for the treatment of hypertension with minimal side effects.

**The aim** of our work is to develop the composition and technology of a medicinal drug in the form of capsules with dry extract of *Rauwolfia serpentina* for the treatment of hypertension.

## 2. Research planning (methodology)

Considering the modern trends of industrial pharmacy, we have developed a methodology for the development of a medicinal preparation with a dry extract of *Rauwolfia serpentina* in the form of capsules.

The general methodology (Fig. 1) is based on the consistent conduct of information, marketing, economic, physico-chemical, pharmaco-technological, biopharmaceutical research, which will ensure the compliance of the medicinal product with modern GMP requirements.

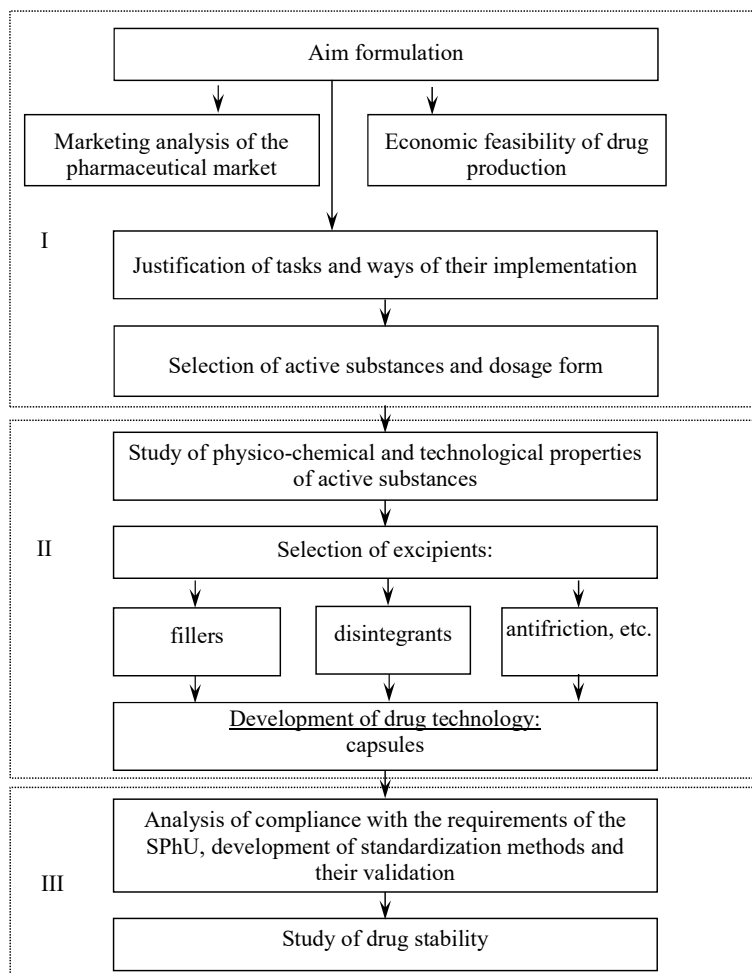


Fig. 1. General methodology for the development of a medicinal product in the form of capsules

## 3. Materials and methods

On the basis of the Department of Plant Technology of Medicines of the National Pharmaceutical University, Kharkiv (2021), capsules with a medicinal plant substance in the form of a dry extract of *Rauwolfia serpentina* produced by the company “Panthea Pharm Private Limited”, India were developed.

Experimental samples of masses for encapsulation contained 2.0 mg of dry extract of *Rauwolfia serpentina* and various excipients used in the technology of solid dosage forms. Five series of capsules No. 4 with a white body and a light green cap of the Snap-Fit type, produced by the company “Capsugel”, were produced. Mass samples of the powder mixture for each series were obtained by weighing and mixing the components. The total

weight of the filler for the capsules was 55 mg. Compositions of sample masses for capsules (Table 1).

The study of pharmaco-technological characteristics was carried out on the devices of the company “Pharma Test” (Germany). Flowability was assessed by the Carr Index powder compressibility index and the Hausner Index coefficient [1, 12, 16].

To determine disintegration, six capsules were taken from each batch and placed in the vessels of a disintegration tester from the company “Erweka” (Germany). Water at  $37\text{ °C} \pm 0.5\text{ °C}$  was used as a medium. The time of disintegration was recorded until the moment of opening the capsules and releasing the fillers [1, 12].

Table 1  
Compositions of sample masses for capsules containing dry extract of *Rauwolfia serpentina*

Substances	Compositions of samples of masses for encapsulation, mg				
	1	2	3	4	5
Dry extract of <i>Rauwolfia serpentina</i>	2.00	2.00	2.00	2.00	2.00
Lactose monohydrate 200/25 «Alpavit Kaserei Champignon Hofmeister», Germany	20.0	–	–	–	–
Manit PARTECKM 200 «Mersk», Germany	25.0	30.0	–	–	–
MCC 102 «Mingtai Chemical», Taiwan	–	18.0	15.0	–	–
Dicalcium phosphate 9214 «Budenheim», Germany	–	–	34.0	18.0	–
Croscarmellose sodium «Yung Zip Chemical Ind. Co., LTD», Taiwan	5.0	–	3.0	4.0	–
PROSOLV® SMCC HD 90«JRSPHARMA», USA	–	–	–	30.0	52.7
Calcium stearate SPE «Electrogazokhim», Ukraine	–	0.2	1.0	1.0	0.3
Aerosil SE «Orisil-Kalush», Ukraine	–	4.5	–	–	–
Talc «LUZENAS PHARMA», Italy	3.0	0.3	–	–	–

A comparative analysis of the calculation of the cost of production of tablets and capsules with dry extract of *Rauwolfia serpentina* was carried out using the “cost plus” method [17, 18].

Statistical processing of the obtained data was carried out according to generally accepted statistical methods using the Excel program (MS Office 2019) and the Statistica 8.0 program (StatSoftInc., USA). The obtained data were analyzed using methods of variational statistics. An acceptable level of significance is  $p < 0.05$ .

Quantitative parameters were calculated ( $M \pm SD$ ), where  $M$  is the mean and  $SD$  is the standard deviation of the mean. Values of  $p \leq 0.05$  were considered statistically significant.

#### 4. Research results

At the first stage of experimental research, the pharmaco-technological properties of the substance of the dry extract of *Rauvolfia snake* were studied (Table 2).

The results of studies of the pharmaco-technological properties of the substance of the powder of the dry extract of *Rauvolfia serpentina* showed that the powder has a very low fluidity value (Table 2). This indicator is confirmed by the high value of the angle of repose, as well as the fine dispersion and amorphous properties of the powder. The difference in the values of bulk density and density after shrinkage indicates the ability to clump. The values of Hausner index and Carr index confirm the poor value of turnover.

That is, for the application of direct encapsulation technology, it is necessary to use modern auxiliary substances to correct the pharmaco-technological indicators of the mass for encapsulation containing the dry extract of *Rauvolfia serpentina*.

As a result of the conducted research, it was established that when developing a new composition and technology of a drug with a powder substance of dry extract of *Rauvolfia serpentina* in capsules, it is advisable to use auxiliary substances in the technology from the group: fillers; disintegrants; antifriction agents.

At the first stage of the research, the influence of various excipients and their amount on the pharmaco-technological properties of samples of mass for capsules of *Rauvolfia serpentina* dry extract, obtained by the direct encapsulation method, was studied.

The results of the research of mass for encapsulation and ready-made capsules containing dry extract of *Rauvolfia serpentina* (Table 3).

The composition of the encapsulation mass sample No. 1 (disintegrant lactose monohydrate 200/25, filler mannitol PARTECKM 200 to improve fluidity, croscarmellose sodium as disintegrant, talc as lubricant) has mostly satisfactory pharmaco-technological values of the indicators, but they are close to the limit readings (Table 3).

The experimental sample of mass for encapsulation according to No. 2, which includes disintegrant MCC 102, PARTECKM 200 mannitol as filler to improve fluidity, aerosil with moisture absorption properties, calcium stearate as lubricant and glidant talc, has unsatisfactory powder fluidity and disintegration time.

To improve fluidity, dicalcium phosphate 9214 as filler, MCC 102 as disintegrant, croscarmellose sodium as disintegrant and calcium stearate were added to the composition of the next sample No. 3. According to the Table 3, the introduction of calcium phosphate 9214 into the composition improved the fluidity value to average readings and had a good effect on the disintegration time of the capsules. However, during the production of the studied mass, there was a slight delamination of the active substances, finely dispersed particles of the powder substance of the dry extract of *Rauvolfia serpentina* were located on the surface of the mass.

With such a ratio of components, the capsule mass requires an additional stage of mixing or shaking to ensure the uniformity and homogeneity of the mixture, as well as the ability to compactly form under pressure, so that the capsules meet the SPhU pharmacopoeial requirements for quality indicators.

For further experimental studies, it was decided to use multi-component excipients with improved functionality. In the pharmaceutical market of excipients, there is a tendency to use combined substances [19, 20]. One of the most common fillers is MCC of various brands as a universal filler, in particular PROSOLV® SMCC (multifunctional cellulose) of the third generation [21, 22]. It is a silicate MCC obtained by adding colloidal silicon dioxide to it before drying (98 % MCC+2 % colloidal silicon dioxide). Particles of colloidal silicon dioxide are contained on the surface and in the pores of PROSOLV® SMCC, thanks to which the surface area is increased by almost 5 times. Silication makes the powder looser and provides better fluidity compared to traditional MCC brands, homogeneity due to easy and good mixing, high disintegration rate.

The next encapsulation composition after No. 4 containing PROSOLV® SMCCHD 90 diluent, dicalcium phosphate 9214 bulking agent, croscarmellose sodium disintegrant and calcium stearate had better flow (18.10 s/100 g sample) and disintegration (15 minutes) values, according to the description, the mass is homogeneous, in comparison with composition No. 3.

Table 2  
Pharmaco-technological properties of the substance of *Rauvolfia serpentina* dry extract

Parameters/Units of measurement	Value
Bulk density, g/ml	0.37±0.01
Density after shrinkage, g/ml	0.56±0.02
Fluidity, s/100 g of sample	95.30±2.40
Angle of repose, degree	63±1.5
Carr index, %	34.0±1.0
Hausner Index	1.51±0.03

Note: n=5, P=95 %

Table 3  
Pharmaco-technological properties of masses for encapsulation and ready-made capsules

No.	Characteristics	Compositions of mass samples for encapsulation				
		1	2	3	4	5
1	Description	The mass is white, homogeneous	The mass is white, homogeneous	The mass is white, heterogeneous	The mass is white, homogeneous	The mass is white, homogeneous
2	Fluidity, s/100 g of sample	26.30±0.7	32±1.0	23±0.6	18±0.5	15.10±0.4
3	Angle of repose, degree	40±1.2	45±1.3	30±0.9	28±0.8	25±0.6
4	Carr index, %	22.0±0.6	30.0±0.9	18.0±0.5	14.0±0.4	5.0±0.1
5	Hausner index	1.30±0.04	1.42±0.04	1.23±0.04	1.15±0.03	1.05±0.03
6	Disintegration, min.	23±0.7	27±0.8	18±0.5	15±0.4	9±0.2

Note: n=5, P=95 %

The best fluidity (15.10 s/100g of sample) and disintegration time (9 minutes) was obtained from encapsulation mass sample No. 5, which contained 52.7 mg of PROSOLV® SMCCHD 90 diluent and 0.3 mg of calcium stearate. According to the description, the mass is homogeneous, easily mixed. The value of the Carr index coefficients is (5.0 %), the Hausner index reaches a value of (1.05), which indicates a very good fluidity of the powder.

On the pharmaceutical market of Ukraine there is a drug containing a dry extract of *Rauvolfia serpentina* (2.0 mg) and used for the treatment of hypertension and arrhythmia, ATC group C02A A04.

Thus, the basic technology of tablet production involves ten stages with a total duration of 48.5 hours, the new technology of capsules – four stages and, accordingly, 7 hours (Fig. 2). The weight of the tablet core is 65.1 mg, the shell is 80.0 mg. The total weight of the coated tablet is 145.1 mg.

The authors developed the composition and modern technology of a medicinal drug in the form of capsules with dry extract of *Rauvolfia serpentina* for the treatment of hypertension. The mass of the contents of the capsule is 55 mg.

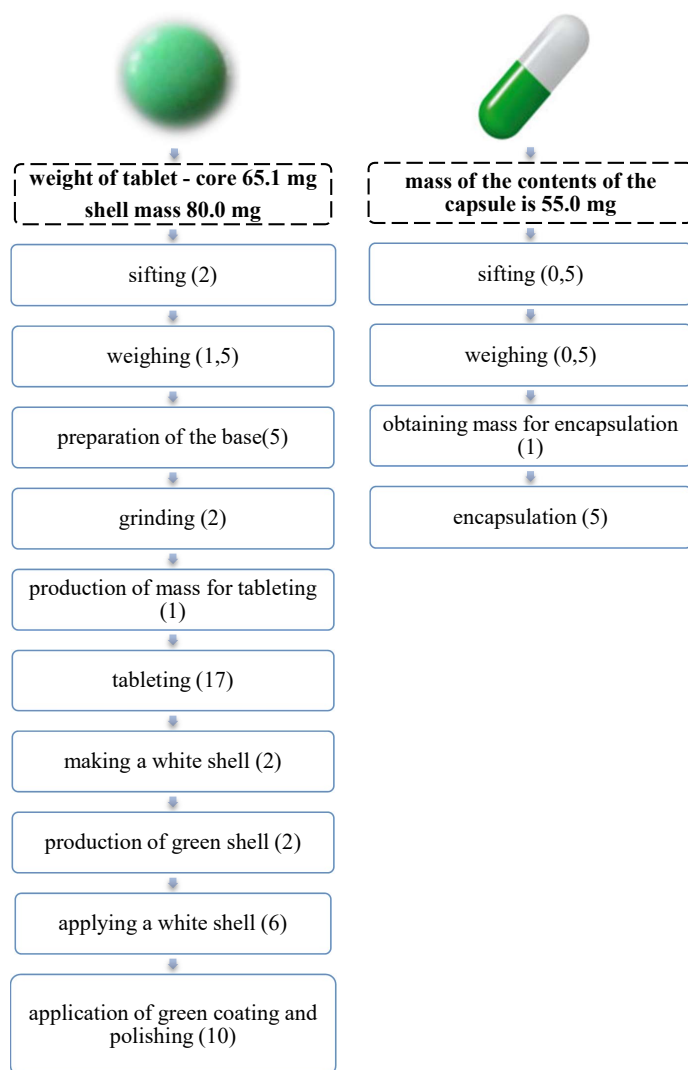


Fig. 2. Production stages with hours of tablets and capsules with dry extract of *Rauvolfia serpentina* (2.0 mg)

Comparative characteristics of the main technological and economic indicators in the production of tablets and capsules are shown in Fig. 3.

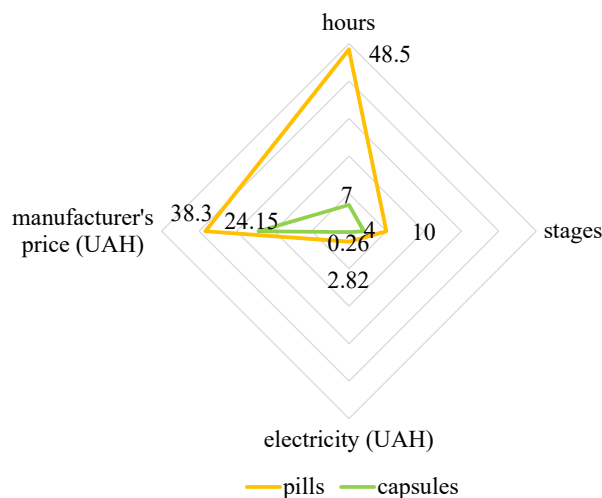


Fig. 3. Comparative characteristics of the main technological and economic indicators in the production of tablets and capsules

As a result of the study, it was established that when using the modern developed technology of the medicinal product based on the dry extract of *Rauvolfia serpentina* in capsules, hours are reduced by 86 %, the number of stages by 60 %, and electricity by 91 %, which allows to reduce the manufacturer's price by 37 %.

The introduction of the direct encapsulation method will allow not only to modernize Ukrainian industrial production, but also to obtain high-quality and affordable medicines for the population.

### 5. Discussion of research results

In [23], studies were conducted to study the influence of various excipients on the properties of capsules with metamizole sodium. The authors established that the composition containing VIVAPUR 102 microcrystalline cellulose has satisfactory pharmaco-technological properties of the powder and a fast release.

This is a standard brand of second-generation microcrystalline cellulose with medium-sized particles, combining good fluidity and high density. Such universal properties are suitable for most active substances in direct pressing or encapsulation technology.

The use of PROSOLV® SMCCHD 90 in our studies improved the flowability, homogeneity of the *Rauvolfia serpentina* dry extract powder mass, considering the low dosage of the substance of 2 mg. It has been experimentally proven that PROSOLV® SMCCHD 90 shortens the disintegration time as a disintegrant, because due to silicate moisture easily penetrates to the MCC, hydrophilic bridges are formed, wettability increases, and mass swelling occurs.

That is, the multi-functionality of PROSOLV® SMCCHD 90 “three-in-one” excipients, which has the properties of a filler, disintegrant and glidant, al-

allows you to easily apply direct encapsulation technology, replace and reduce the number of excipients and thus increase production efficiency.

**Practical value.** The application of the direct encapsulation method in the technology of a medicinal product based on the dry extract of *Rauvolfia serpentina* for the treatment of hypertension is a modern approach to modernization for industrial pharmacy because it will provide an opportunity to obtain a high-quality, convenient and affordable drug of domestic production.

**Study limitations.** In the experiment, the effect of various excipients on the pharmaco-technological properties of encapsulation masses and ready-made capsules was investigated, however, it is relevant to conduct research on modern industrial equipment in the enterprise conditions.

**Prospects for further research.** In the future, research is planned in the conditions of industrial production using modern equipment.

## 6. Conclusions

1. When developing the composition of capsules with dry extract of *Rauvolfia serpentina*, the influence of various excipients on the pharmaco-technological properties of encapsulation masses and ready-made capsules was investigated. Improvement of the main technological parameters was achieved when using the combined auxiliary substance PROSOLV® SMCCHD 90.

2. Experimental studies prove that the combined auxiliary substance, namely PROSOLV® SMCCHD 90, having the properties of a filler, a disintegrant and a sliding agent, is more effective in the direct encapsulation technology in terms of its effect on the fluidity of the mass and disintegration of the capsules.

3. Application of the direct encapsulation method proves technological and economic efficiency. The implementation of this method will allow to expand the range of new medicines and improve existing technologies, in particular in the form of tablets, which are widely produced in industrial production.

## Conflict of interests

The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this article.

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## Data availability

The manuscript has no associated data.

## References

1. Chuieshov, V. I., Hladukh, Ye. V., Saiko, I. V. et al. (2012). Tekhnolohiia likiv promyslovoho vyrobnytstva. Kharkiv: NFAU.
2. Augsburger, L. (2009). Hard- and Soft-Shell Capsules. Modern Pharmaceutics: Volume 1. Basic Principles and Systems, 499–564. doi: <https://doi.org/10.1201/9780824744694.ch11>
3. Schwedt, G. (2018). Chemieder Arzneimittel: Einfache Experimentemit Medikamentenaus der Apotheke. Mannheim: Wiley, 166.
4. Qiu, Y., Chen, Y., Zhang, G. G. Z., Yu, L., Mantri, R. V. (Eds.) (2017). Developing Solid Oral Dosage Forms: Pharmaceutical Theory & Practice. San Diego.
5. Augsburger, L. L., Hoag, S. W. (Eds.) (2017). Pharmaceutical Dosage Forms: Capsules. Boca Raton: CRC Press, 435. doi: <https://doi.org/10.1201/9781315111896>
6. Fares, R., Bobrytska, L., Germanyuk, T., Kryvoviaz, O., Ivko, T., Toziuk, O. et al. (2017). Diaplant: Manufacturing technology and rationalization of costs of acute in testin al infection pharmacotherapy. International Journal of Green Pharmacy, 11 (3), 584–589. doi: <https://doi.org/10.22377/ijgp.v11i03.1178>
7. Zlahoda, V. S., Bobrytska, L. O. (2022). Segmentation of modern dosage forms at the pharmaceutical market of Ukraine. News of Pharmacy, 104 (2), 45–48. doi: <https://doi.org/10.24959/nphj.22.94>
8. Tverdye kapsuly: istoriia postoiannykh izmenenii i usovershenstvovanii (2013). Farmatsevticheskaia otrasl, 2 (37). Available at: [http://archive.promoboz.com/n2\\_37/26-31.pdf](http://archive.promoboz.com/n2_37/26-31.pdf)
9. Sovremennye dostizheniia v oblasti proizvodstva tverdykh i miagkikh kapsul. (2015). Tverdye lekarstvennye formy: kapsuly. Farmatsevticheskaia otrasl, 3 (50).
10. Kinam, P. (2016). Solid dosage forms: capsule. Drug Delivery: Fundamentals and Applications. CRC Press.
11. Germanyuk, T., Bobrytska, L., Ivko, T., Fares, R. (2019). Diaplant: development of technology and pharmacoeconomic evidence of therapy. Lambert Academic Publishing of International Book Market Service Ltd., 60
12. Ivko, T., Aslanian, M., Bobrytska, L., Popova, N., Nazarova, O., Bereznyakova, N., Germanyuk, T. (2018). Development of the composition and manufacturing technology of the new combined drug Lavaflam. The Turkish Journal of Pharmaceutical Sciences, 15 (3), 263–270. doi: <https://doi.org/10.4274/tjps.79553>
13. Neokardyl (Neokardil). Dovidnyk likarskykh zasobiv No. 1 v Ukraini. Available at: <https://compendium.com.ua/info/173505/neokardil/>
14. Derzhavnyi reiestr likarskykh zasobiv Ukrainy. Available at: <http://www.drlz.com.ua/>
15. Kovalenko, V. M. (Ed.) (2019). Dovidnyk «Kompendium 2019 – likarski preparaty». Moryon. Available at: <https://compendium.com.ua/>
16. Derzhavna Farmakopeia Ukrainy. Vol. 1 (2015). Kharkiv: Derzhavne pidpriemstvo «Ukrainskyi naukovyi farmatsevtichnyi tsentr yakosti likarskykh zasobiv», 1128.

17. Nazarkina, V. M., Nemchenko, A. S., Kosiachenko, K. L., Babenko, M. M. (2022). Metodolohiia tsinoutvorennia na likarski zasoby v systemi okhorony zdorov'ia. Kyiv: Farmatsevt Praktyk, 288.
18. Nemchenko, A. S., Nazarkina, V. M. (2015). Obruntuvannia metodychnykh pidkhodiv do upravlinnia sobivartistiuvyrobnytstva LZ. Upravlinnia, ekonomika ta zabezpechennia yakosti v farmatsii, 3 (41), 38–43.
19. Demchuk, M. B., Hroshovi, T. A., Leskiv, O. M., Malanchuk, N. V. (2021). Comparative research of some brands of lactose as fillers for direct compression of tablets. *Pharmaceutical Review*, 2, 5–13. doi: <https://doi.org/10.11603/2312-0967.2021.2.12056>
20. Ruban, O. A., Pertsev, I. M., Kutsenko, S. A., Maslii, Yu. S. (2016). Dopomizhni rechovyny u vyrobnytstvi likiv. Kharkiv: Zoloti storinky, 720.
21. PROSOLV® SMCC (виробник «JRSPHARMA», USA). Available at: <https://www.jrs.cn/pharma-wAssets/docs/brochures/br-prosolv-smcc-1809.pdf>
22. Zlahoda, V. S., Bobrytska, L. O. (2023). Bahatofunktsionalnist prosolv® smcc v tekhnolohii priamoho kapsuliuвання. Aktualni pytannia medyko-biologichnykh i farmatsevychnykh nauk. Zhytomyr, 61–62.
23. Rogowska, M., Iwaniak, K., Polski, A., Slawinska, K., Sobotka-Polska, K., Modrzewska, J., Poleszak, E. (2016). Influence of different excipients on the properties of hard gelatin capsules with metamizole sodium. *Current Issues in Pharmacy and Medical Sciences*, 29 (3), 114–117. doi: <https://doi.org/10.1515/cipms-2016-0023>

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