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STUDY OF TECHNOLOGICAL ASPECTS OF MANUFACTURE OF POLYMER COMPOSITE MATERIAL BY CENTRIFUGAL FIBER FORMING METHOD

The object of the study is the technological aspects of manufacturing the hesperidin polymer composite material by the method of centrifugal fiber formation. This method is considered the basis of a relatively new and cost-effective way of producing solid dispersion systems. Using the centrifugal molding method, it is possible to obtain highly soluble forms of active pharmaceutical ingredients in the form of fibers of various sizes using a wide range of polymeric materials with high speed and low cost due to simple equipment. Due to the innovative design of the centrifugal fiber formation method, it was chosen for the development of solid dispersion systems of the bioflavonoid hesperidin, which has a wide range of different pharmacological properties, but low bioavailability.

Solid dispersed systems of hesperidin by the method of centrifugal fiber formation were produced on the basis of a pharmaceutically acceptable polymeric carrier of polyvinylpyrrolidone and mannitol. For the obtained solid dispersed systems, such basic pharmaco-technological characteristics as loss in mass during drying, bulk volume, bulk volume after shrinkage, bulk density, bulk density after shrinkage, compressibility index, Gaussner coefficient were determined.

Comprehensive tests of the stability of the studied samples of the solid dispersion system of hesperidin were carried out under the conditions of accelerated tests for 6 months. According to the obtained results, it was established that the developed polymer composite material is stable in the studied conditions, and its conditional shelf life is 2 years.

A technological scheme for the production of the hesperidin polymer composite material in the form of solid dispersed systems by the method of centrifugal fiber formation has been developed. In particular, the technological process is described step by step and the critical indicators of quality control of the obtained composite material are determined. The proposed technology can be implemented in modern chemical and pharmaceutical industries. This will contribute to the expansion of the market of highly effective socially oriented medicines.

Keywords: *hesperidin, solid dispersion system, polymer, centrifugal formation of fibers, polymer composite material.*

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1. Introduction

Polymeric compounds are widely used in various fields, in particular, in biomedicine and the pharmaceutical industry, where they have long been the subject of active research. Today, it is difficult to imagine a modern dosage form that could be completely prepared without the use of polymers. Currently, high-molecular polymeric substances are most often used in the process of developing pharmaceutical dosage forms, for example, to improve the pharmaco-technological properties of drugs, increase stability, controlled release, and improve the bioavailability of active pharmaceutical ingredients (APIs) [1, 2]. It is known that polymers play a key role in the development of solid dispersion systems (SDS) – composite materials in which a poorly soluble API is dispersed in a polymer matrix, which, in turn, leads to improved solubility and faster release from pharmaceutical compositions [3]. This technology is one of the most effective for increasing the bioavailability of various compounds, and currently solid dispersed systems are manufactured using a wide range of pharmaceutically acceptable polymers using various methods and already have commercial applications [4, 5].

The analysis of literary sources shows that in recent years, spray drying, hot melt extrusion, and electroforming of fibers are considered to be the most common methods of forming polymer composite materials in the SDS form [4]. At the same time, it is reported that there is currently a growing research interest in the method of centrifugal fiber formation, which is a simpler, more cost-effective and highly productive alternative to electroforming [6]. The theoretical basis of the centrifugal forming process is that due to the high-speed rotation of the head with holes, the viscous solution or melt contained in it is subject to the influence

of centrifugal force, which, in turn, squeezes the material outward in the form of fibers [7]. This method allows obtaining fibers of different sizes from a wide range of materials with high speed and low cost due to simple equipment and the absence of the need to use high voltage. In addition, in the process of centrifugal formation of fibers, the materials are exposed to high temperatures for a short time, which accordingly reduces the risk of their destruction [7].

It is worth noting that the method, which is based on the process of formation of fibrous structures under the action of centrifugal force, is not completely new to the chemical industry, because it has been widely used in the production of glass fibers (also known as glass fiber or glass wool) for more than half a century [8]. However, the use of this method as the basis for the production of fibrous solid dispersion systems was proposed not so long ago, and therefore it is currently considered innovative.

One of the first examples of the use of the technology of centrifugal formation of fibers for the production of solid dispersions is considered to be the production of microfiber SDS containing olanzapine and piroxicam based on sucrose using a modified machine for the production of cotton candy [9]. The solubility of both active pharmaceutical ingredients in solid dispersion systems in the form of fibers was much higher compared to pure compounds and to physical mixtures with sucrose. From scientific and literary sources it is also known about the successfully obtained fibrous solid dispersions of oxcarbazepine [10], ibuprofen [11], itraconazole [12] and miconazole [13] obtained by this method.

Considering the effectiveness and innovative design of the method of centrifugal fiber formation, it is possible to choose it for the development of solid dispersion systems containing the bioflavonoid hesperidin. For pharmaceuticals, hesperidin is considered an extremely interesting compound because it has a high safety profile, is non-accumulating, and exhibits antioxidant, neuroprotective, anti-inflammatory, antibacterial, photoprotective, antidiabetic, and anticarcinogenic effects [14]. However, low permeability through cell membranes and low solubility in water (class IV according to the biopharmaceutical classification system (BCS)) lead to reduced bioavailability, which limits its wide application [15].

The aim of the paper is to develop a technological scheme for the production of a solid dispersed system of hesperidin by the method of centrifugal fiber formation, to study the pharmaco-technological indicators of the obtained composite material and to study its stability. This will make it possible to speed up the development and scaling of new highly economical technologies of SDS of poorly soluble substances for the chemical and pharmaceutical production of APIs.

2. Materials and Methods

Crystalline hesperidin was purchased from Chengdu Okay Pharmaceutical Co., LTD (China), polyvinylpyrrolidone (PVP) K-17 (average molecular weight 10,000 Da) was purchased from JRS PHARMA GmbH&Co. KG (Germany), and mannitol, which was used as an excipient for the formation of hesperidin SDS, was obtained from Merck (Germany).

2.1. Preparation of solid dispersed systems of hesperidin in the form of fibers. For the manufacture of solid dispersed systems of hesperidin by the method of centrifugal fiber formation, a commercial cotton candy maker (China) was used. It consists of housing, heating elements, a stainless steel collector bowl and a rotating head with holes through which the fibers are formed. The control panel has sensors for setting temperature and rotation speed.

2.2. Determination of pharmaco-technological indicators of solid dispersion systems of hesperidin

2.2.1. Loss in mass during drying. Loss in mass during drying (moisture) of the formed solid dispersed system of hesperidin was studied using a RADWAG MA 50.R moisture meter (RADWAG, Republic of Poland). 1 g of polymer composite material was placed in a moisture meter and dried at a temperature of 105 °C until a constant mass was reached. Measurements were made 3 times and the average was calculated.

2.2.2. Bulk density and density after shrinkage of powders. The bulk density was measured in a graduated cylinder according to method 1 of the European Pharmacopoeia 9.0. 100 g (m) of the tested sample of the hesperidin polymer composite material was poured into a dry graduated cylinder with a capacity of 250 ml (with a division price of 2 ml). Bulk volume before shrinkage (V_0) was recorded. Bulk density ($\rho_{(bulk)}$) is calculated by the formula m/V_0 in grams per milliliter. Measurements were performed 3 times and the average value was calculated [16].

The bulk density after shrinkage was obtained by mechanical shaking of a graduated measuring cylinder containing 100 g (m) of a sample of hesperidin polymer composite material. On one sample of hesperidin SDS, 10, 500, 1250 cylinder jumps were performed and the volumes V_{10}, V_{500}, V_{1250} were recorded. The bulk density after shrinkage ($\rho_{(tapped)}$) was calculated using the formula m/V_f (where V_f is the final volume after shrinkage) [16].

2.2.3. Compressibility index and Gaussner coefficient. The compressibility index and the closely related Gaussner coefficient are simple, fast and popular methods of predicting the flow characteristics of a powder and can be calculated using the measured values of the bulk density and the density after shrinkage according to the formulas:

$$\text{compressibility index} = 100 \cdot \frac{\rho_{(tapped)} - \rho_{(bulk)}}{\rho_{(tapped)}}; \quad (1)$$

$$\text{Gaussner coefficient} = \frac{\rho_{(tapped)}}{\rho_{(balk)}}. \quad (2)$$

2.3. Study of the stability of solid dispersed systems of hesperidin. In this work, accelerated tests of the SDS stability of hesperidin under storage conditions were carried out in accordance with Guideline 42-3.3:2004 «Medicinal products. Stability test» [17]. The study of the stability of solid dispersed systems of hesperidin was carried out on three experimental laboratory series under stress testing conditions at a temperature of 40±2 °C and a relative humidity of 75±5 % for 6 months in closed vials in a climate chamber HPP 750 (Memmert GmbH+Co.KG, Germany).

During accelerated stability tests before the start of the test and at control points after 3 and 6 months, FTIR spectra of the tested samples and indicators of the quantitative content of hesperidin in solid dispersion systems were recorded.

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2.3.1. Fourier transform infrared spectroscopy (FTIR) method. FTIR spectra of solid dispersed systems of hesperidin were obtained using a Nicolet IS50 FTIR spectrometer with a diamond crystal ATR (Thermo Fisher Scientific, USA), which were recorded in the range of wave numbers from 4,000 to 400 cm^{-1} with 32 scans with a resolution of 4 cm^{-1}.

2.3.2. Quantitative determination of hesperidin in solid dispersion systems. Hesperidin concentration was determined spectrophotometrically on an OPTIZEN POP UV spectrophotometer (Mesasys, South Korea) according to a validated method. It is based on the qualitative reaction of hesperidin with ferrum (III) chloride, resulting in the formation of a green compound, the maximum optical absorption of which is observed at a wavelength of 602 nm [18].

3. Results and Discussions

3.1. Pharmaco-technological indicators of solid dispersion systems of hesperidin. For the preparation of solid dispersed systems of hesperidin by the method of centrifugal fiber formation, a pharmaceutically acceptable polymer carrier was chosen – polyvinylpyrrolidone K-17, because it is non-toxic, non-ionic, inert, heat-resistant, pH-stable, biocompatible and shows complex affinity to both hydrophilic and hydrophobic APIs [19]. Also, this polymer is characterized by good fiber-forming properties. To increase the number of formed fibers of the composite material and improve their technological indicators, mannitol was added to the composition of the composite.

In general, first a physical mixture was prepared in the mass ratio of PVP K-17, hesperidin and mannitol 80:10:10, from which solid dispersed systems in the form of light brown fibers with grayish shade. The formed fibers were crushed to a powdery state and the main pharmaco-technological indicators of the obtained material were determined.

The main pharmaco-technological characteristics of powdered medicinal substances include: loss in mass during drying, bulk volume, bulk volume after shrinkage, bulk density, bulk density after shrinkage, compressibility index, Gaussner coefficient, fluidity. The results of studies of the pharmaco-technological indicators of the polymeric solid dispersion system of hesperidin are shown in the Table 1.

Thus, the polymeric hesperidin SDS, which was obtained using the method of centrifugal formation of fibers, can be considered acceptable for introduction into automated production according to the indicators presented in Table 1. According to the defined pharmaco-technological indicators, the control of finished products of the hesperidin polymer composite material, obtained by the method of centrifugal fiber formation, will be carried out.

Table 1

Pharmaco-technological indicators of hesperidin SDS

Indicators	Units of measurement	Indicators of hesperidin SDS
Loss in mass during drying (moisture)	%	2.18±0.09
Bulk volume, V_0	ml	230±2
Bulk volume after shrinkage, V_{10}	ml	220±2
Bulk volume after shrinkage, V_{500}	ml	197±3
Bulk volume after shrinkage, V_{1250}	ml	196±2
Bulk density, $\rho_{(bulk)}$	g/ml	0.435±0.004
Bulk density after shrinkage, $\rho_{(tapped)}$ (V_{1250})	g/ml	0.510±0.005
Compressibility index	%	15±1
Gaussner coefficient	–	1.17±0.01
Fluidity	–	Good [16]

3.2. Results of stability studies of solid dispersed systems of hesperidin. Before the beginning of the tests and at control points after 3 and 6 months, FTIR spectra of the centrifugally formed solid dispersed system of hesperidin were recorded. And then it was possible to evaluate the changes in the characteristic absorption bands taking into account the frequency values of the absorption maxima, the shape and intensity of the bands and compared them with the corresponding structural elements of the studied samples (Fig. 1).

According to the graphical data presented in Fig. 1, it can be stated that no changes are observed in the FTIR spectrum of the solid dispersion system of hesperidin after 3 months. However, after 6 months of the test, the absorption band in the range of 3500–3000 cm^{-1} has a slightly smaller area compared to the data obtained before the start of the test and after 3 months, however, the absorption maximum does not change. This may indicate a slight destruction of hydrogen bonds. Other characteristic bands have no differences. The maxima of the characteristic absorption bands of the solid dispersed system of hesperidin before the start of the test and at the control points after 3 and 6 months are presented in Table 2.

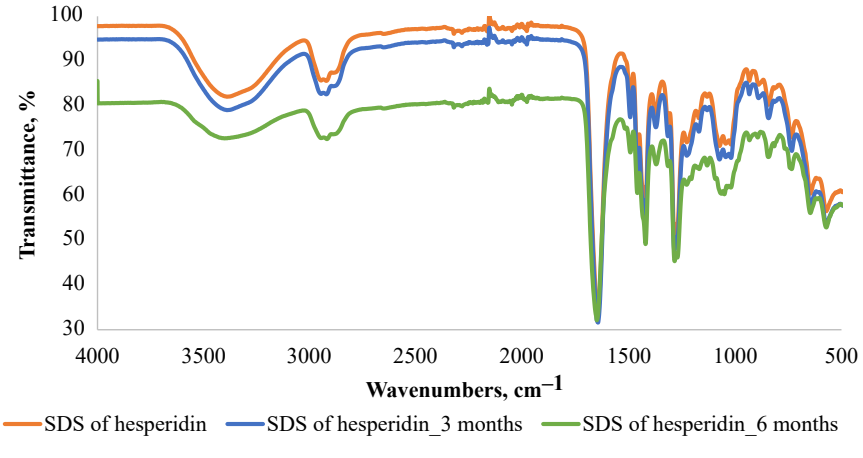

Fig. 1. FTIR spectra of the solid dispersed system of hesperidin before the start of the test and at control points after 3 and 6 months

Table 2

The maxima of the characteristic absorption bands of the solid dispersion system of hesperidin before the beginning of the tests and at the control points after 3 and 6 months

Group name	Maximum frequency, cm^{-1}		
	Before the test	In 3 months	In 6 months
–O–H	3390	3389	3386
Valent –C–H	2923	2922	2922
–C=O	1651	1651	1651
Deformation –C–H	1461, 1421	1461, 1421	1461, 1421
–C–N	1286	1285	1285
–C–O	1073	1074	1074
Out-of-plane –O–H	733, 645, 572	733, 646, 572	733, 646, 572

Therefore, according to the obtained data and their comparative analysis, it was established that there were no significant differences in the absorption bands of the studied samples during the entire test period. Therefore, it can be concluded that the solid dispersed system of hesperidin produced by the centrifugal molding method and all its components are chemically compatible and stable under the investigated conditions.

To determine the shelf life of the solid dispersed system of hesperidin, an analysis of the results of determining the quantitative content of API in the conditions of an accelerated study was performed for three experimental laboratory series, the results of which are shown in Table 3.

To confirm the possibility of establishing the shelf life of hesperidin SDS, statistical data processing and extrapolation beyond the period of accelerated tests were carried out [20]. Fig. 2 shows the extrapolation of experimental data for the determination of hesperidin content in SDS under conditions of accelerated tests.

Extrapolation data from stability studies for a period of 6 months indicate that at the time of storage of 24 months (2 years) the quantitative content of hesperidin API in SDS will be within the limits of the acceptance criterion [20].

Table 3

Results of API quantification in SDS before the start of tests and at control points in 3 and 6 months

Period	Quantitative content of hesperidin API in 100 g of SDS, g
	Acceptability criterion (from 9.90 g to 10.10 g)
0 point	9.99±0.02
3 months	10.00±0.03
6 months	9.98±0.03

Based on the results of complex studies of tests on the stability of hesperidin SDS under conditions of accelerated tests for 6 months at a temperature of 40±2 °C and a relative humidity of 75±5 %, it can be stated that the conditional shelf life of the developed polymer composite material of hesperidin is 2 years.

3.3. Technological scheme of the production of the hesperidin polymer composite material by the method of centrifugal formation of fibers. A technological scheme for obtaining the hesperidin polymeric composite material in the form of solid dispersed systems by the method of centrifugal fiber formation has been developed. To visualize the technological process in Fig. 3 shows the scheme of obtaining hesperidin SDS by the method of centrifugal fiber formation.

The process diagram shows:

– the sequence of stages with the designation of the stages that are critical (in gray);

– parameters that are monitored at each of the stages;

– raw materials and packaging materials.

According to the developed technological scheme, the proposed technological process consists of five stages, each of which is described in detail below.

Stage 1. Preparation of raw materials.

The active pharmaceutical ingredient hesperidin, which meets the quality indicators, is weighed on electronic scales.

Auxiliary raw materials that meet the quality indicators are weighed on electronic scales.

The components are weighed according to the amount calculated for one series. After each weighing of raw materials, electronic scales are cleaned.

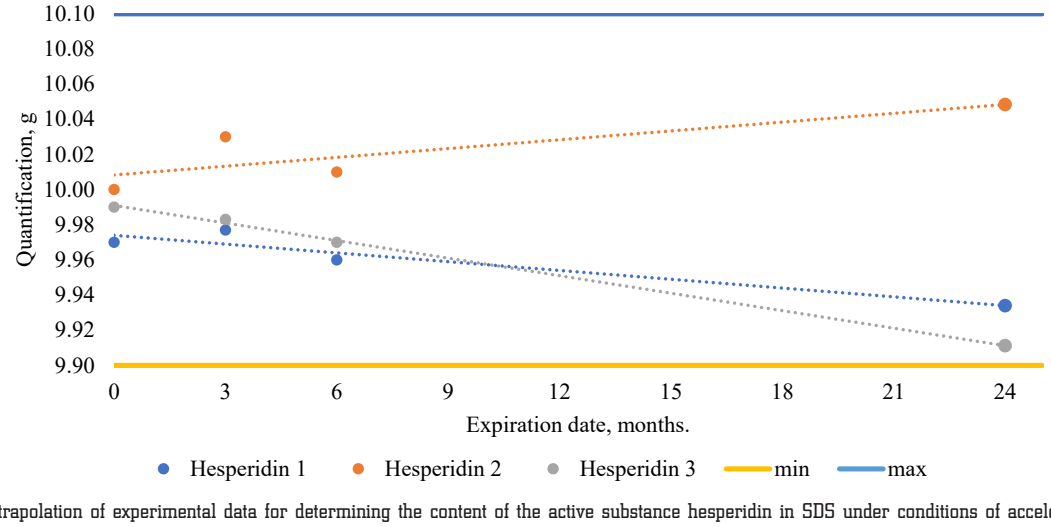

Fig. 2. Extrapolation of experimental data for determining the content of the active substance hesperidin in SDS under conditions of accelerated tests: • experimental data on the content of the active substance; – the lower and upper limits of the acceptance criterion

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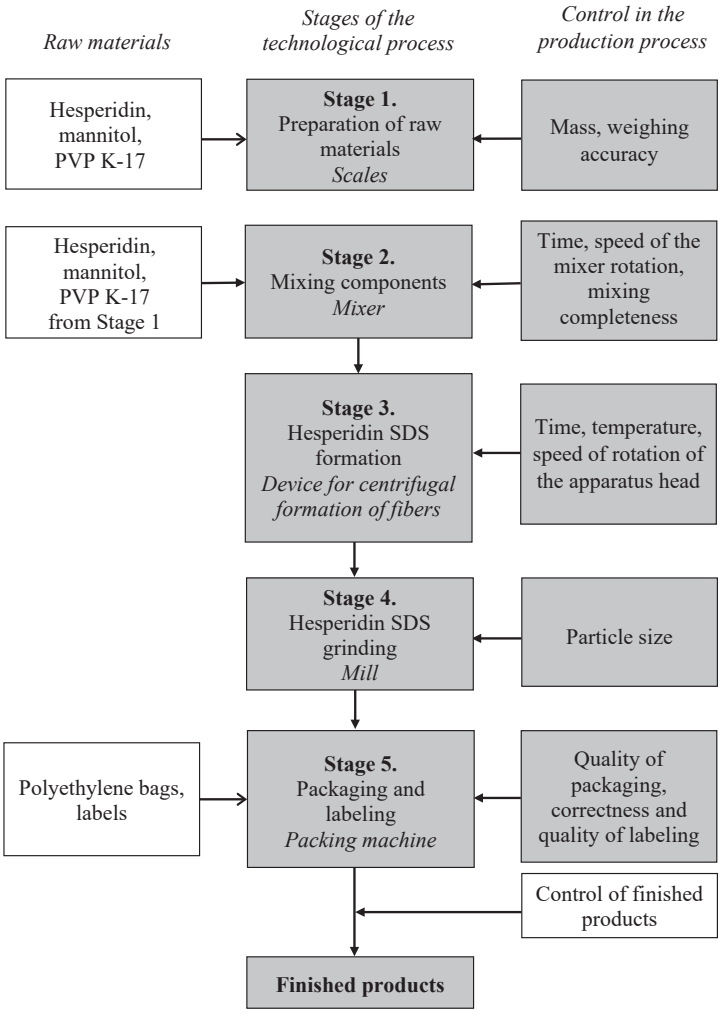

Fig. 3. Technological scheme of obtaining hesperidin SDS by the method of centrifugal fiber formation

Stage 2. Mixing the components.

At this stage of the technological process, it is necessary to obtain a homogeneous mass by mixing all components. The main parameter is the homogeneity of the mixture, namely the same ratio of all components in any part of the mixture. PVP K-17, mannitol and hesperidin are loaded into the mixer in portions. The component with the largest mass in the mixture, i. e. PVP K-17, is loaded first. The mixture is mixed for 20 minutes at room temperature.

Stage 3. Production of hesperidin SDS.

For the SDS production by the method of centrifugal fiber formation, a cotton candy production plant is used. The heating element is set to a temperature of 175±5 °C. The mixture of components from stage 2 is loaded into the preheated rotating head of the unit, which rotates at a fixed speed of 2400 rpm. The molten mass passes through 0.8 mm diameter dies with the help of centrifugal force and immediately cools to room temperature. After ejection of the molten mixture, stretching and immediate cooling in the air, thin fibers are formed, which are collected in a receiving collector bowl with a diameter of 50 cm. During production, the temperature of the heating device and the speed of rotation of the apparatus head are controlled.

Stage 4. Grinding of polymeric hesperidin SDS.

The resulting SDS fibers are crushed by a mill to obtain a homogeneous mixture with the same particle size.

Stage 5. Packaging and labeling.

Crushed SDS of hesperidin is packaged in primary packaging, namely polyethylene bags with labels indicating the name, concentration, batch and date. The parameters that are controlled are the quality of the packaging and the correctness of the labeling.

Critical stages for the quality of hesperidin SDS are all stages of the technological process.

Control of finished products.

At the final stage, the finished products must be controlled according to the following quality indicators: description, weight loss during drying, quantitative content of hesperidin, bulk volume. The criterion of acceptability of these indicators for hesperidin SDS is given in Table 4.

So, the basics of the technology of the hesperidin polymer composite material in the form of solid dispersed systems by the method of centrifugal fiber formation, which can be implemented in modern chemical and pharmaceutical industries, have been developed. The developed technology of the highly soluble form of hesperidin will allow to expand the domestic market of effective socially oriented medicines.

During the transfer of the technology for obtaining solid dispersed systems of hesperidin by the method of centrifugal fiber formation to industrial production, certain difficulties may arise. Because in order to use the plant for the production of cotton candy at chemical and pharmaceutical enterprises, it is necessary to ensure its compliance with the specific requirements of this sector of the industry. As for pharmaceutical production, it is necessary to develop and implement equipment qualification procedures and validation of all stages of the manufacturing process of polymer composite materials of hesperidin in accordance with Good Manufacturing Practice (GMP) standards.

Also, at chemical and pharmaceutical enterprises, it is necessary to install automated systems for constant monitoring of process parameters and the quality of fibrous solid dispersion systems and to implement effective systems for sterilization of all parts of the installation that come into contact with the product. The application of these measures will ensure the effective use of cotton candy production units in chemical and pharmaceutical production for the purpose of obtaining fibrous solid dispersed systems of hesperidin and will guarantee the quality of the manufactured composites.

Table 4

Critical indicators of the hesperidin SDS quality

Parameter name	Parameter acceptability criterion
Description	The powder is light brown with a grayish tint
Loss in mass during drying	2.00±0.30 %
Homogeneity of the content of the active substance hesperidin	9.90–10.10 g per 100 g of SDS
Bulk density	from 0.42 g/ml to 0.45 g/ml
Bulk density after shrinkage	from 0.50 g/ml to 0.52 g/ml
Compressibility index	15±3 %
Gaussner coefficient	from 1.15 to 1.20

During the implementation of this work, there were some delays in the timing of experimental research due to

power outages caused by massive missile attacks during the war in Ukraine.

Prospects for further research consist in the development and study of pharmaco-technological characteristics of dosage forms based on highly soluble dispersed systems of hesperidin, obtained using the method of centrifugal fiber formation.

4. Conclusions

This work presents the technological aspects of the production of the polymer composite material hesperidin by the method of centrifugal fiber formation, in particular, the technological process is described step by step, the technological scheme is given, and the critical indicators of the quality of the obtained composite material are determined. The main pharmaco-technological characteristics of the powdery solid dispersed system of hesperidin were established, such as loss in mass during drying, bulk volume, bulk volume after shrinkage, bulk density, bulk density after shrinkage, compressibility index, Gaussner coefficient. Comprehensive tests of the stability of the investigated samples of hesperidin SDS under conditions of accelerated tests were carried out for 6 months. It has been established that the developed polymer composite material is stable under the studied conditions, and its expected shelf life is 2 years.

Conflict of interest

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

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Data availability

The manuscript has no associated data.

Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the presented work.

References

1. Li, J., Yu, F., Chen, Y., Oupický, D. (2015). Polymeric drugs: Advances in the development of pharmacologically active polymers. *Journal of Controlled Release, 219*, 369–382. https://doi.org/10.1016/j.jconrel.2015.09.043
2. Adams, J. S., Sutar, Y., Dhoble, S., Maiti, C., Hanjankar, S. N., Das, R. et al. (2024). Pharmaceutical and biomedical polymers: Basics, modifications, and applications. *Polymers for Pharmaceutical and Biomedical Applications*, 1–86. https://doi.org/10.1016/b978-0-323-95496-9.00001-6
3. Nair, A. R., Lakshman, Y. D., Anand, V. S. K., Sree, K. S. N., Bhat, K., Dengale, S. J. (2020). Overview of Extensively Employed Polymeric Carriers in Solid Dispersion Technology. *AAPS PharmSciTech, 21 (8)*. https://doi.org/10.1208/s12249-020-01849-z
4. Malkawi, R., Malkawi, W. I., Al-Mahmoud, Y., Tawalbeh, J. (2022). Current Trends on Solid Dispersions: Past, Present, and Future. *Advances in Pharmacological and Pharmaceutical Sciences, 2022*, 1–17. https://doi.org/10.1155/2022/5916013
5. Tran, P., Pyo, Y.-C., Kim, D.-H., Lee, S.-E., Kim, J.-K., Park, J.-S. (2019). Overview of the Manufacturing Methods of Solid Dispersion Technology for Improving the Solubility of Poorly Water-Soluble Drugs and Application to Anticancer Drugs. *Pharmaceutics, 11 (3)*, 132. https://doi.org/10.3390/pharmaceutics11030132
6. Satish, S., Priya, R. (2022). A mini review on centrifugal spinning technique for production of nanofibers and its applications in drug delivery. *Journal of Medical Pharmaceutical and Allied Sciences, 11 (1)*, 4349–4352. https://doi.org/10.55522/jmpas.v11i1.2176
7. Zhang, X., Lu, Y. (2014). Centrifugal Spinning: An Alternative Approach to Fabricate Nanofibers at High Speed and Low Cost. *Polymer Reviews, 54 (4)*, 677–701. https://doi.org/10.1080/15583724.2014.935858
8. Farhaj, S., Conway, B. R., Ghori, M. U. (2023). Nanofibres in Drug Delivery Applications. *Fibers, 11 (2)*, 21. https://doi.org/10.3390/fib11020021
9. Marano, S., Barker, S. A., Raimi-Abraham, B. T., Missaghi, S., Rajabi-Siahboomi, A., Craig, D. Q. M. (2016). Development of micro-fibrous solid dispersions of poorly water-soluble drugs in sucrose using temperature-controlled centrifugal spinning. *European Journal of Pharmaceutics and Biopharmaceutics, 103*, 84–94. https://doi.org/10.1016/j.ejpb.2016.03.021
10. Nasir, S., Hussain, A., Abbas, N., Bukhari, N. I., Hussain, F., Arshad, M. S. (2021). Improved bioavailability of oxcarbazepine, a BCS class II drug by centrifugal melt spinning: In-vitro and in-vivo implications. *International Journal of Pharmaceutics, 604*, 120775. https://doi.org/10.1016/j.ijpharm.2021.120775
11. Hussain, A., Hussain, F., Arshad, M. S., Abbas, N., Nasir, S., Mudassir, J. et al. (2021). Ibuprofen-loaded centrifugally spun microfibers for quick relief of inflammation in rats. *Drug Development and Industrial Pharmacy, 47 (11)*, 1786–1793. https://doi.org/10.1080/03639045.2022.2059500
12. Priya, R., Satish, S. (2023). Centrifugal Melt Spun Microfi brous Solid Dispersion of Diclofenac Sodium with Enhanced Solubility. *International journal of pharmaceutical quality assurance, 14 (1)*, 165–170. https://doi.org/10.25258/ijpqa.14.1.28
13. Alfassam, H. A., Booq, R. Y., Almousained, M. M., Alajmi, A. M., Elfaky, M. A., Shaik, R. A. et al. (2024). Fabrication and evaluation of centrifugal spun Miconazole-loaded sugar-based fibers. *Journal of Drug Delivery Science and Technology, 98*, 105872. https://doi.org/10.1016/j.jddst.2024.105872
14. Choi, S.-S., Lee, S.-H., Lee, K.-A. (2022). A Comparative Study of Hesperetin, Hesperidin and Hesperidin Glucoside: Antioxidant, Anti-Inflammatory, and Antibacterial Activities In Vitro. *Antioxidants, 11 (8)*, 1618. https://doi.org/10.3390/antiox11081618
15. Donia, T., Dabbour, N. M., Loutfy, S. A.; Xiao, J. (Ed.) (2023). Hesperidin: Advances on Resources, Biosynthesis Pathway, Bioavailability, Bioactivity, and Pharmacology. *Handbook of Dietary Flavonoids*. Cham: Springer, 1–55. https://doi.org/10.1007/978-3-030-94753-8_28-1
16. *European Pharmacopoeia 9.0 Volume* 1. (2018). Strasbourg: Council of Europe.
17. Heorhiievskyi, V., Liapunov, M., Bezuhla, O. et al. (2004). *Nastanova z yakosti. Likarski zasoby. Vyprobuvannia stabilnosti.* Nastanova 42-3.3.2004. Ministerstvo okhorony zdorovia Ukrainy. Kyiv: Morion, 60.
18. Lisovyi, V., Bessarabov, V., Goy, A., Kostiuk, V. (2024). Spectrophotometric method for determining the assay of hesperidin in the composition of polymer composite material obtained by centrifugal fiber formation. *Herald of Khmelnytskyi National University. Technical Sciences, 335 (3 (1))*, 135–141. https://doi.org/10.31891/2307-5732-2024-335-3-19
19. Kurakula, M., Rao, G. S. N. K. (2020). Pharmaceutical assessment of polyvinylpyrrolidone (PVP): As excipient from conventional to controlled delivery systems with a spotlight on COVID-19 inhibition. *Journal of Drug Delivery Science and Technology, 60, 1*02046. https://doi.org/10.1016/j.jddst.2020.102046
20. Hureieva, S. M., Kondratova, Yu. A. (2016). Vyvchennia stabilnosti likarskoho zasobu Antral, tabletky, vkryti obolonkoiu. *Farmatsevtychnyi zhurnal, 2,* 70–76.

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