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Development of the Technology of Procurement of "Ginkrosmelan" Microcapsules from Natural Origin Materials and Assessment of Quality Criteria

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Abstract

In modern times, great prospects in the field of drug therapy are related to the effect of medicinal substances on organs, tissues or cells. In this regard, microencapsulated medicinal substances (microcapsules, microspheres, nanocapsules) have proven themselves to be due to intravenous injection into certain organs and tissues.

Taking into account the mentioned perspective, for the first time, for the treatment of atherosclerosis, an extract was obtained from a phyto composition developed in the ratio of 5:5:5:5 from ginkgo biloba, rose hips, lemon balm and fragrant dill plants. Based on this extract, the composition (phyto substance, aerosil, beeswax, hexane) and technology of miro capsules, which we conventionally call "Ginkrosmelan", were developed. Preparation of microcapsules was performed by physical method. Some technological properties of the developed microcapsules (size-5,20±0,1μm; moisture absorption 1,23±0,04%; fluidity-2,5±0,11g/sec; scattering mass-1,78±0,04g/cm3) and shelf life (5 years is stable) was studied. Quantification of flavonoids in microcapsules according to rutin was checked by spectrophotometric method and found to be 1.67%. During in vitro studies, the rate of release of biologically active substances from the microcapsules with the optimal composition was studied, and it was determined that the maximum release occurs within 7 hours and is 93.17±0.66%.

Keywords: Drug delivery systems; "Ginkrosmelan" microcapsules; Shelf life; In vitro; Routine; SEM analysis

Introduction

Currently, one of the priority issues of medicine and pharmaceutical science is to ensure targeted delivery of medicinal substances to organs and tissues, to achieve great prospects in the field of drug therapy. In these systems, microencapsulated drugs (microcapsules, microspheres, nano capsules) are prescribed for intravenous administration near the designated organs and tissues, as well as for transdermal and oral purposes.

The global microencapsulation market size was estimated at USD 13.05 billion in 2023 and is projected to grow at a CAGR of 10.4% from 2024 to 2030. The surge in interest around microencapsulation technology is anticipated to fuel market growth, particularly in safeguarding active drugs such as cisplatin, lidocaine, naltrexone, progesterone, insulin, proteins, peptides, and vaccines. This heightened interest is driven by the technology's ability to provide adequate protection to these sensitive compounds [1] (Figure 1).

It is known that therapeutic systems are divided into three groups according to the targeted delivery of medicinal substances:

i. Carriers of the first-generation medicinal substances (microcapsules, microspheres) are intended for intravenous injection close to a certain organ or tissue.

ii. Carriers of second-generation drugs (nanocapsules, liposomes) are less than 1 μm in size and are distributed mainly in cells rich in the reticuloendothelial system in the spleen and liver tissue. Nanocapsules with phenobarbital, diazepam, prednisolone,

insulin, prostaglandins; nanospheres with cytostatics and corticosteroids; A method of obtaining liposomes for the delivery of enzymes has been developed.

iii. Carriers of the third generation of medicinal substances (antibodies, glycoproteins) have a highly selective effect on the delivery of medicinal substances [2-6].

Microencapsulation is defined as the application of a thin polymeric coating to individual core materials (tiny particles or droplets of liquids and dispersions) that have an arbitrary particle size range from 5-5000 μm to give small capsules with many useful properties Capsule size greater than 1000 micrometer (1mm) are called microcapsule and which are smaller than 1 micrometer are called nanocapsule [2]. Microencapsulated drugs provide a long-term effect of hormones, antigens, peptides, enzymes and other medicinal substances, which improves the diffusion of microcapsules through the pores of the polymer layer (Figure 2), and also performs dissolution and fragmentation in parts [3,7,8].

Figure 1: US Microencapsulation Market.

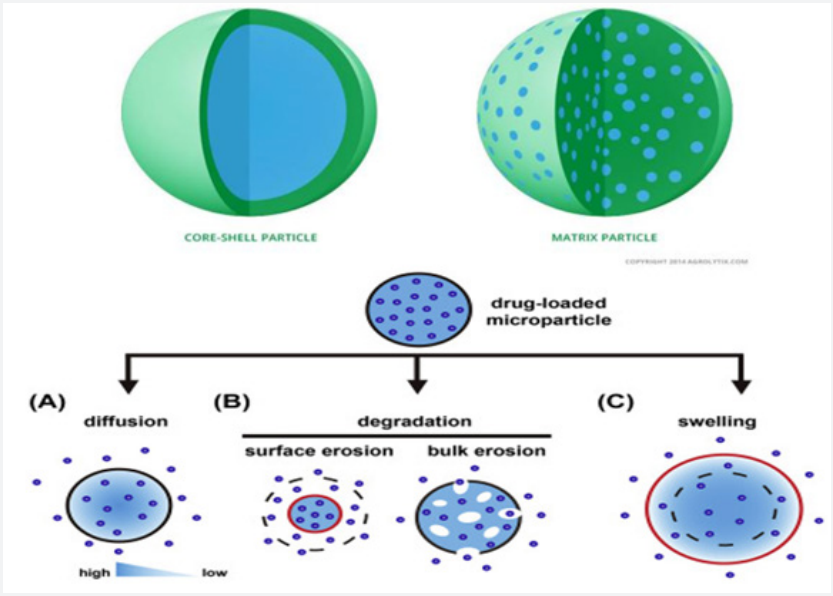

Figure 2: Mechanism of drug release from microcapsules.

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In addition to the above, encapsulation of extracts from medicinal plant raw materials remains a priority issue of pharmaceutical technology. It is considered important to coat phytoextracts with either hydrophobic or hydrophilic coating agents. It is also known that cerebral atherosclerosis is widespread among the population in our modern times.

Atherosclerosis is a chronic multifactorial disease characterized mainly by changes in the blood lipid profile and inflammation of the vessel wall. Cardiovascular diseases based on atherosclerosis are currently the main cause of death in developed countries. Therefore, timely prevention and treatment of atherosclerosis can reduce the risk of developing its clinical manifestations. The antiatherosclerotic activity of medicinal plants is mainly manifested in their numerous effects such as anti-inflammatory, antioxidant, antiatherogenic, hypotensive, lipid lowering, antithrombotic. In addition, most medicinal plants are characterized by pleiotropic anti-atherosclerotic effects. In addition, pharmacological substances and/or compounds obtained from medicinal plants are characterized by relative safety and less side effects, which allows to consider them as one of the potential anti-atherosclerosis effective means. The direct anti-atherosclerotic effect of some medicinal plants has been confirmed in clinical trials on the development of carotid intima-media thickness (IMT) during long-term drug administration with medicinal plants. It is known that atherosclerosis is a multifactorial process, and despite the great progress in understanding the mechanisms of development of atherosclerotic lesions in recent decades, the pathogenesis of atherosclerosis is the subject of research by a large circle of scientists all over the world. Nevertheless, the main points of the pathogenesis of atherosclerosis are known, and the possible pathogenetic mechanisms of the atherosclerotic effect of medicinal plants are being studied in cell cultures, animal models, and human studies [9].

Taking into account this relevance, the goal was to prepare microcapsules with long-term stability for the treatment of atherosclerosis based on raw materials of natural origin and to study their quality indicators.

Material and Methods

Extracts from ginkgo biloba leaves, rose hip fruits, lemon balm leaves, and fennel seeds, which we chose as research objects, were obtained (conditionally "Ginkrosmelan"), and their physical, chemical and technological properties were studied [10-13] (Figure 3). Microcapsules were purchased based on phytoextract, aerosil, and beeswax. The scheme of the technological process is shown in figure 4, and the structure of microcapsules is shown in figure 5.

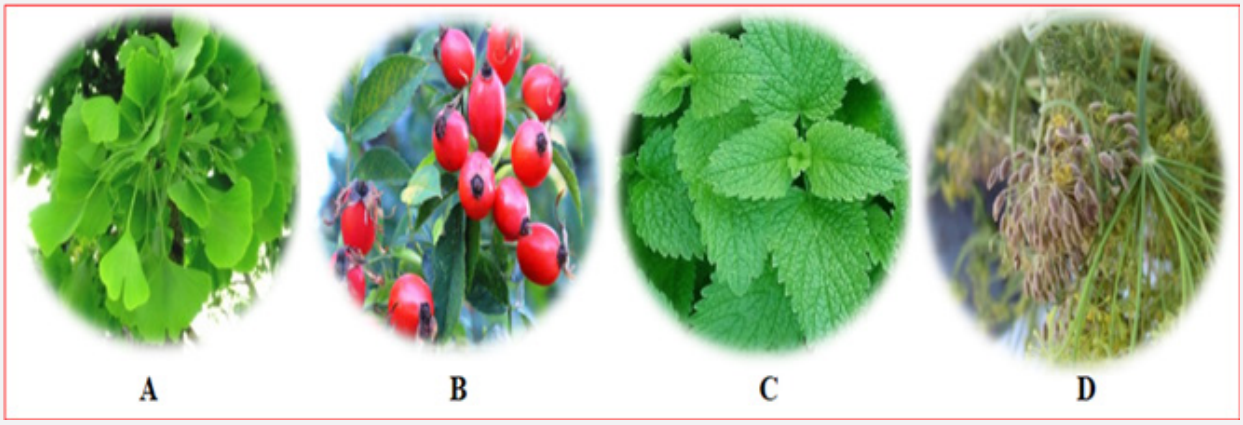

Figure 3: A-Ginkgo biloba leaf, B-hip fruits, C-melissa leaf, D-fennel seeds.

Shelf-life Study

For this purpose, 2 g microcapsules weighed on an electronic scale were placed in orange glass vials, tightly closed and stored in room conditions. Then, some technological properties of phytomicrocapsules prepared according to the optimal composition (organoleptic properties, moisture absorption, particle size, dispersion, fluidity), flavonoid quantity determination according to routine, release rate of biologically active substances were studied according to the methods specified in the relevant pharmacopoeias [14-18]. Organoleptic properties: dark brown, specific smell, tasteless. The studied microcapsules were observed under a microscope in a spherical and uneven shape.

Particle size

First, the image of microcapsules was observed with the help of a binocular microscope at x12, x42 magnification (Figure 6), then this image was analyzed in SEM. During the analysis, it was determined that the microcapsules were 5-9 μm at magnifications of X1000 and x2000 times. Microcapsules with a size of 5.2 μm made up 75% (Figures 7 & 8).

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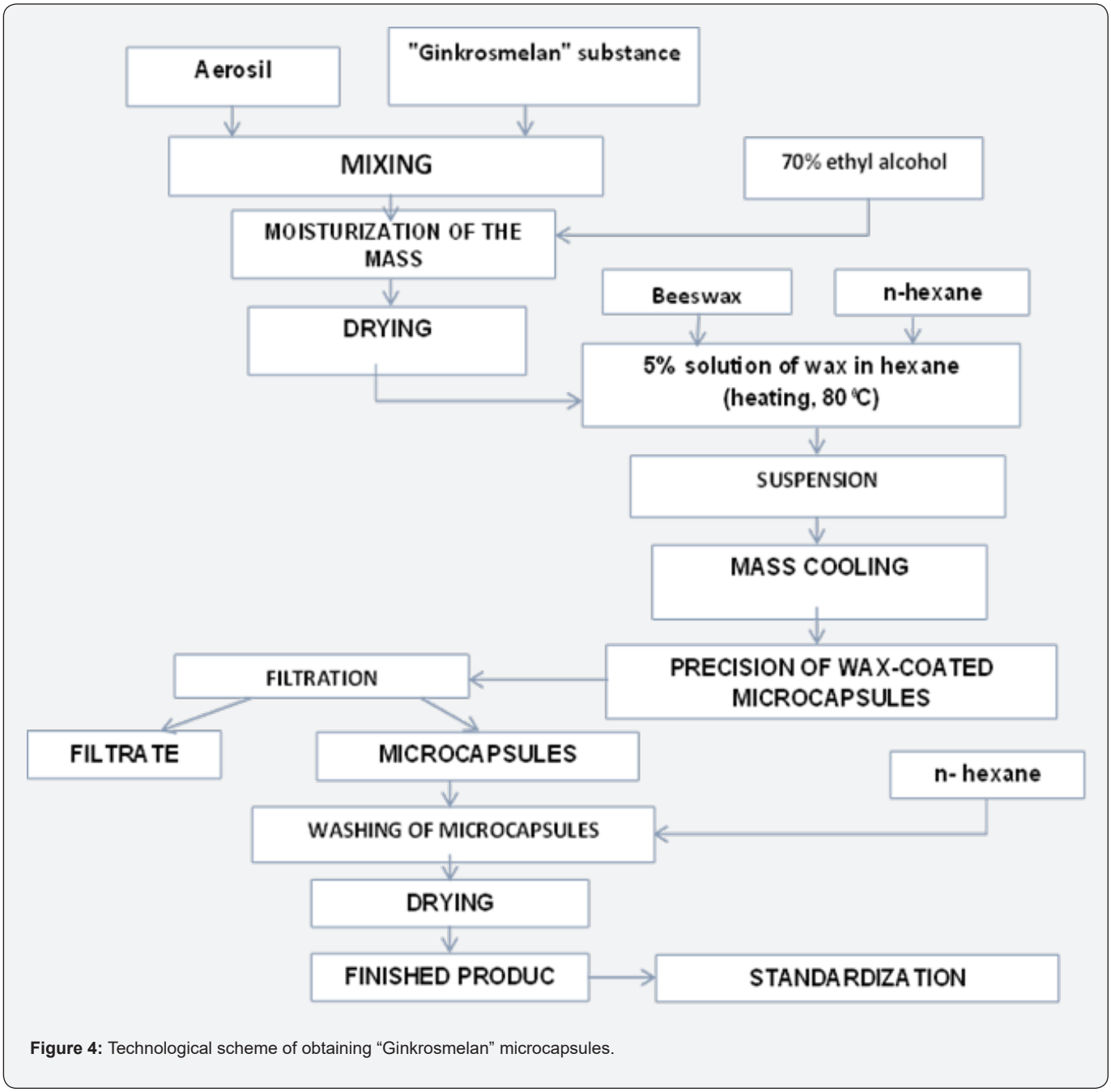

Figure 4: Technological scheme of obtaining "Ginkrosmelan" microcapsules.

Quantification of rutin in microcapsules

Initial solution. About 1 g (exact weight 0.1254 g) of microcapsules is weighed, dissolved in 30 ml of 70% ethyl alcohol, shaken on a magnetic shaker, heated to 500C for 5 minutes, filtered, placed in a volumetric flask with a volume of 50 ml. The solution is diluted with 70% ethyl alcohol and mixed. Compensation solution 1. Ethyl alcohol (70%). Check solution. 0.2336 g of the initial powder was taken into a 50 ml volumetric flask, 4.0 ml of 2% aluminum chloride and 1 drop of glacial acetic acid were added, the volume of the solution was made up to volume with ethyl alcohol (70%) and mixed. . After 40 minutes, the optical density indicator is measured in a Wavescan (Korea) spectrophotometer at a wavelength of 450 nm.

The number of flavonoids (according to routine) was calculated according to the following formula.

$$X = \frac{A_{samp.} \cdot m_{st.} \cdot V_{samp.} \cdot 100}{A_{st.} \cdot V_{st.} \cdot m_{samp..}}$$

$$X = \frac{0,252.50 \cdot 0,2626 \cdot 0,1254 \cdot 100}{1,064 \cdot 100 \cdot 0,2336} = 1,67\%$$

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here,

m st. - the exact weight of the standard powder, in grams.

m sample - the exact weight of the granulate, in grams.

V sample - sample solution volume, in ml.

Vst. -volume of standard solution in ml.

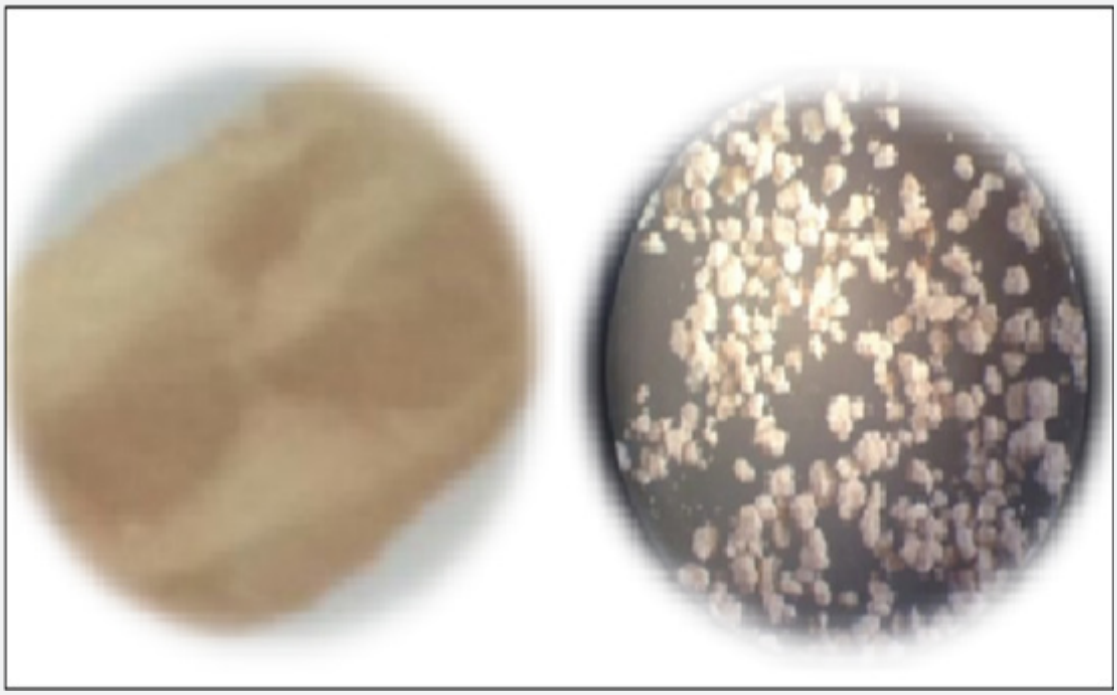

Figure 5: Visual and microscopic (by binocular) view of finished microcapsules.

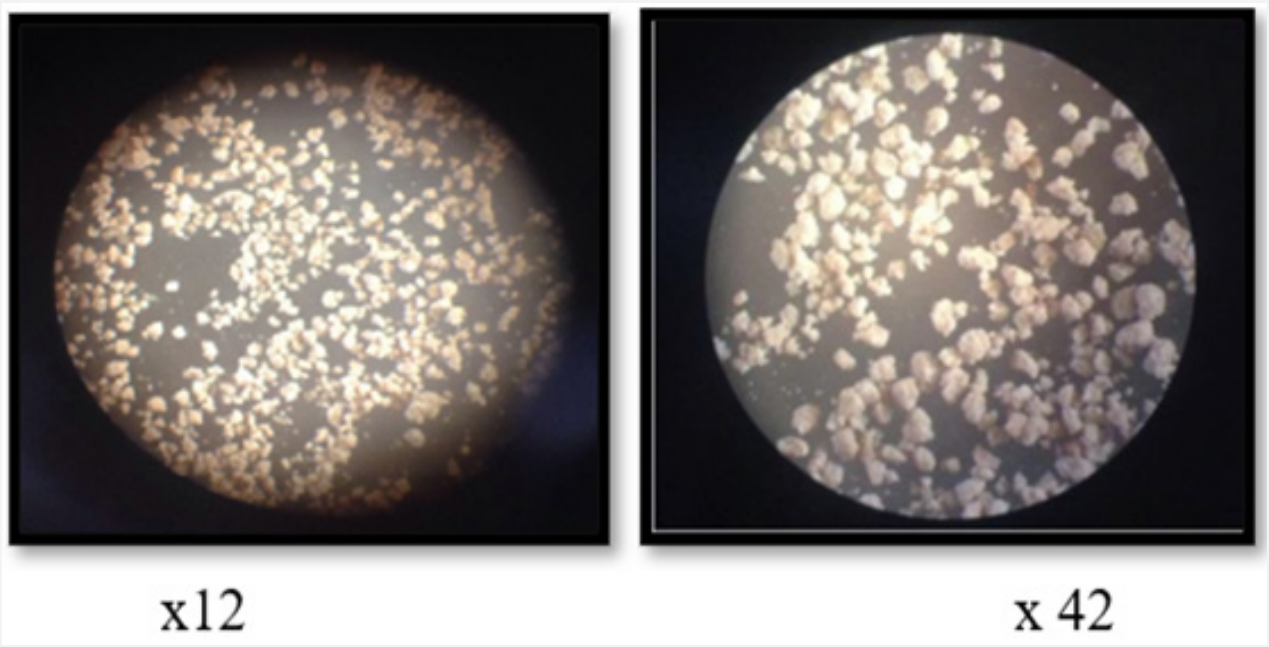

Figure 6: Visualization of microcapsules in transmitted light using a binocular microscope.

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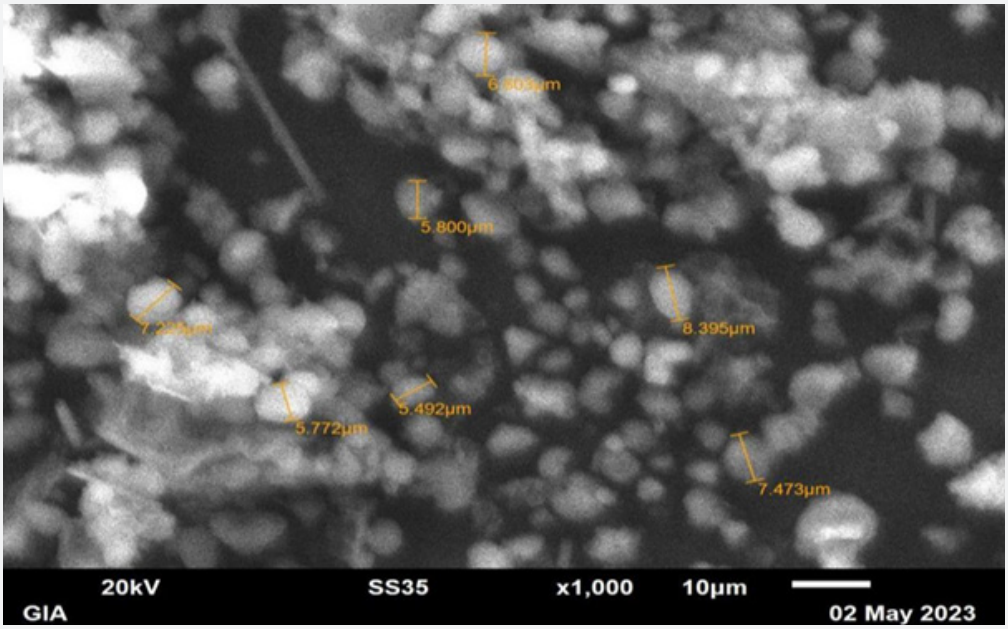

Figure 7: SEM image of "Ginkrosmelan" microcapsules (x1000).

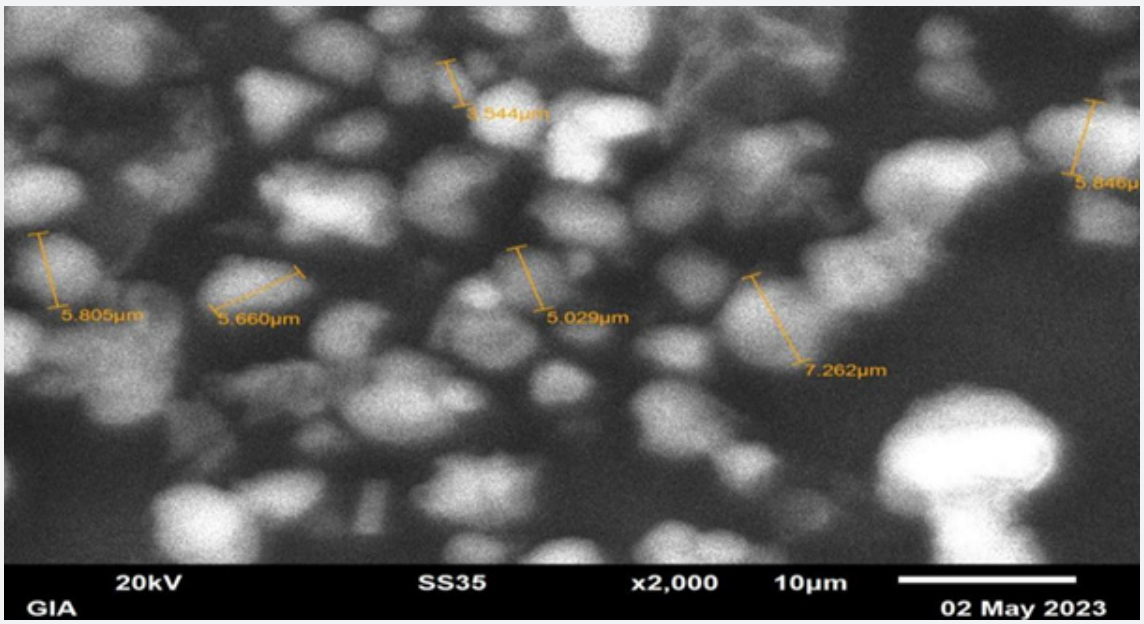

Figure 8: SEM image of "Ginkrosmelan" microcapsules (x2000).

Testing the release rate of biologically active substances from microcapsules

The separation rate of flavonoids from the prepared microcapsules was studied by the semipermeable membrane method. A cellophane film was used as a semiconducting membrane for the purpose of conducting the experiment. 2 g of the prepared microcapsules were added to the test bottle, 10 ml of artificial intestinal juice (pH=7.4) was added to it, it was dissolved well, and the mouth was closed with a cellophane membrane. A glass container containing Ringer's solution (dialysis medium 25 ml) was placed in the dialysis tube at a depth of no more than 2 mm. The passage of biologically active substances (flavonoids) through the cellophane membrane was carried out for 10 hours in a thermostat at a temperature of 37±0.5ºC. Dialysate sampling every 1, 2, 3, 4, etc. was carried out in hours. The rate of release of biologically active substances was calculated by the gravimetric

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method. In in vitro experiments (artificial intestinal environment), the amount of BFM transferred to the dialysate was 93.17±0.65% while studying pharmaceutical absorption of microcapsules for 7 hours using model systems. In the following 8-10 hours, no significant changes occurred in the system. During the 5 years of study of the shelf life of "Ginkrosmelan" microcapsules proposed for the treatment of atherosclerosis, no significant changes occurred in the organoleptic, technological, properties of these microcapsules. The amount of rutin contained in microcapsules remained stable (Table 1).

Table 1: Parameters of "Ginkrosmelan" microcapsules during storage (n=6).

Parameters	OVER THE YEARS						
	0	1	2	3	4	5	6
Amount of flavonoids, %	1,67±0,02	1,67±0,02	1,67±0,02	1,67±0,02	1,67±0,02	1,67±0,02	1,58±0,03
Moisture absorption,%	1,23±0,04	1,23±0,04	1,23±0,04	1,23±0,04	1,23±0,04	1,23±0,04	1,26±0,03
Scattering mass, q/sm3	1,78 ±0,04	1,78 ±0,04	1,78 ±0,04	1,78 ±0,04	1,78 ±0,04	1,78 ±0,04	1,75 ±0,04
Flowability, q/san	2,5±0,11	2,5±0,11	2,5±0,11	2,5±0,11	2,5±0,11	2,5±0,11	2,5±0,11
Organoleptic properties	light-brown color, specific smell, tasteless	light-brown color, specific smell, tasteless	light-brown color, specific smell, tasteless	light-brown color, specific smell, tasteless	light-brown color, specific smell, tasteless	light-brown color, specific smell, tasteless	light brown, tasteless
Kinetics of release of active substances (for 7 hours), %	93,17 ±0,66	93,17 ±0,66	93,17 ±0,66	93,17 ±0,66	93,17 ±0,66	93,17 ±0,66	92,23 ±0,54
Particle size, μm	5,2±0,1	5,2±0,1	5,2±0,1	5,2±0,1	5,2±0,1	5,2±0,1	5,2±0,1

Conclusion

From the evaluation of microcapsules prepared on the basis of phytoextracts from ginkgo biloba, common edelweiss, fennel, and watermelon fennel plants for the treatment of atherosclerosis, it was once again clear that the number of flavonoids in "Ginkrosmelan" microcapsules prepared by the physical method remains stable for 5 years. This is due to covering the surface of prepared microcapsules with beeswax, which is a hydrophobic substance, and using aerosil with drying properties.

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