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RESEARCH ARTICLE

Theoretical Justification of Structure and Development of Capsule Technology with Cerebroprotective Activity

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Abstract

Treatment of brain remains an urgent problem in the health system in Ukraine, due to the wide prevalence of the most common as a result of this disease causes cerebrovascular diseases, including atherosclerosis and hypertension, leading to a narrowing of the blood vessels of the brain and decreased cerebral blood flow. An alternative method of treatment of cerebrovascular diseases (CVD) it is expected pharmacological effect, which is achieved through use in medicines herbal drug that exhibits antyarytmichal, sedative, tranquilizing, antispasmodic, antiseptic hypotensive effects. According to literature data types such therapeutic activity black horehound grass, the grass dead-nettle herb wormwood and compatible whose presence leads to a potentiation of pharmacological action due to the fact that the components of the content biologically active substances (BAS) show a complex impact on different parts of body systems and increase reliability and predictable therapeutic effect. This complex of action reduces the possibility of side effects of display. The aim of this work is the theoretical basis structure and development of technology for rational drug cerebroprotective action in the form of hard gelatin capsules based on dry extracts medical plant material (MPM), namely black horehound grass, herb nettle deaf, sage herb. On the basis of experimental studies, we have proved the composition of masses for encapsulation of drug in the form of hard gelatin capsules number 0. Composition per capsule: a mixture of dry extracts MPM-400 mg; aerosol-50 mg; lactose monohydrate -50 mg. The weight of the contents of the capsule-500 mg.

Keywords: *Dry extracts, Development composition and technology, Gelatin capsules, Cerebroprotective activity.*

Introduction

Treatment of brain remains an urgent problem in the health system in Ukraine, due to the wide prevalence of the most common as a result of this disease causes cerebrovascular diseases, including atherosclerosis and hypertension, leading to a narrowing of the blood vessels of the brain and decreased cerebral blood flow [1-4]. Cerebrovascular accident is the second most common cause of adult deaths most countries in the group of diseases of the cardiovascular system after ischemic heart disease, which has positioned them as a problem with emergency medical and social value [1, 3]. However, despite the significant progress of basic sciences and clinical anhioneurology, pathoneurophysiology mechanisms involved in the implementation of the clinical picture, can influence the course, and out of cerebral ischemic stroke are insufficiently studied. An alternative method of treatment of cerebrovascular diseases (CVD) it is expected pharmacological effect, which is achieved through use in medicines herbal drug that

exhibits antyarytmichal, sedative, tranquilizing, antispasmodic, antiseptic hypotensive effects. According to literature data types such therapeutic activity black horehound grass, the grass dead-nettle herb wormwood and compatible whose presence leads to a potentiation of pharmacological action due to the fact that the components of the content biologically active substances (BAS) show a complex impact on different parts of body systems and increase reliability and predictable therapeutic effect. This complex of action reduces the possibility of side effects of display [5].

The Aim of the Study

In view of the above, the aim of this work is the theoretical basis structure and development of technology for rational drug cerebroprotective action in the form of hard gelatin capsules based on dry extracts medicinal plant material, namely black horehound grass, nettle deaf herb, sage herb.

Experimental

We have analyzed current data of scientific literature content BAS and type of pharmacological action of our chosen species MPM. The analysis showed that the most common in Ukraine plants of wormwood is bitter wormwood, common wormwood, mugwort, the Austrian wormwood, mugwort and wormwood officinalis [5-12] used as dried extracts and are often used in folk and official medicine as nootropic drugs.Pharmacology properties of plants of wormwood, primarily caused by the presence of various bar: terpenoids, sesquiterpene lactones, coumarins, phenolic compounds and others [5-7]. The department Pharmacognosy Pharmacy has been studied several species of the genus Artemisia: *A. vulgaris* L., *A. abrotanum* L., *A. annua* L., *A. austriaca* Jacq., *A. absinthium* L., *A. arenaria* DC.

In order to select items from these types of Sagebrush type as a component of capsules with MPM, we analyzed their biologically active substances belonging to terpenoids and organic acids, mono-and dicarboxylic aromatic acids, fatty acids, and hydroxycinnamic phenylcarboxylic acids.

In view of the above, and with reference to the literature [5], phytotherapy CVD in most advisable to use a mixture of herbal drugs in the form of dry extract in capsule form based black horehound grass, nettle deaf white herb, wormwood Austrian herb in equal proportions (1:1:1). Offered us healing, preventive action cerebroprotective capsule with dry extracts contain components such as: dry grass extract of black horehound, dead nettle herb and wormwood Austrian herb in equal proportions.

In modern conditions of production of medicines based on dry extracts of medicinal plants (MPM), an increasingly important current development of solid dosage forms, including tablets and capsules. According to literary sources herbal remedies (MPM) in the form of capsules have some definite advantages, as evidenced by their much larger range in relation to tablets [13-15] For example among dosage forms of industrial preparations in capsule form in third place after the tablet and injectable dosage forms (Fig. 1) [16-18].

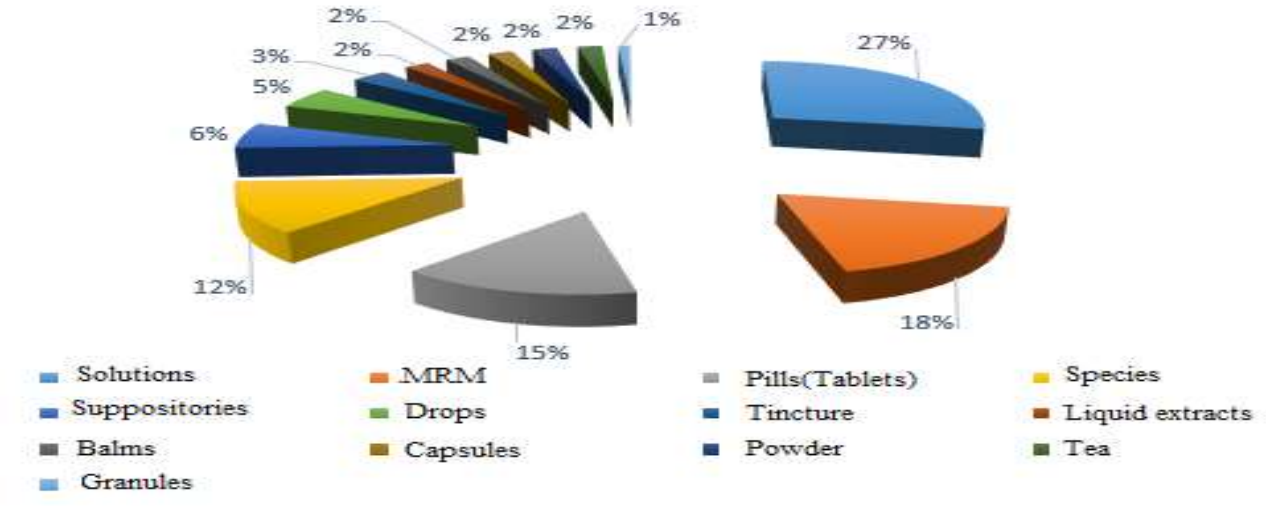

Fig. 1 Distribution of drugs A16A X19 group in the form of release

In order to justify the composition of solid dosage form in capsule form, the first stage of experimental research we studied the physicochemical and pharmaco-technological properties of dry extracts from the studied species MPM. The analysis showed that the powdery substance is polydisperse systems that have different shapes and sizes of particles [19]. Crystallographic studies have examined the shape and size of the particles studied medical plant material. This study is to predict the need for certain groups of excipients in the development of technology and solid dosage forms. Also, the shape and size of the particles causing substances such technological features as fluidity, ability for pressing, bulk weight, surface area, and others [19]. Crystallographic characteristics of powders determine the size and shape of powders, which in turn affects the volume and fluidity properties of substances. The study was conducted with a microscope "Bio lamp" with an increase of 100 times. Results crystallographic studies mixture of dry extracts studied species MPM (ratio 1:1:1) are shown in Fig. 2.

Fig. 2 Form the mixture of particles of dry extracts studied species MRM ratio of 1:1:1 (magnification 100 times)

The data in Fig. 2 indicate that the dry extract of herb mixture black horehound, dead nettle herb, herb wormwood-Austrian in the ratio 1:1:1 is a hygroscopic amorphous powder from light brown to brown color with a specific smell that is polydisperse crystal system of anisodiametric type particles.

The magnitude of the thickness and length of the powder particles present in the group include fine. The crystals have a smooth surface and jagged edges. Form factor ranging from 0.25 to 0.8, indicating a poor fluidity powder thereby possible to predict the introduction of auxiliary substances from the group of fillers and lubricants [19]. From the shape and size of powders depends on active substances and fractional composition. In this regard, the next stage of research was to study the fractional part of a mixture of dry extracts studied species MPM, which affects the technological properties and the accuracy of dosing drugs.

To assess the fractional composition of dry extracts used sieve analysis [19] the results are shown in Fig. 3. The studies, which are presented in Fig. 3 indicate that the number of the largest and the smallest particles of extract is low and mainly dominated by mass approximately the same size, which, given the lamellar structure of particles and their rough edges can cause poor technological properties of dry extracts.

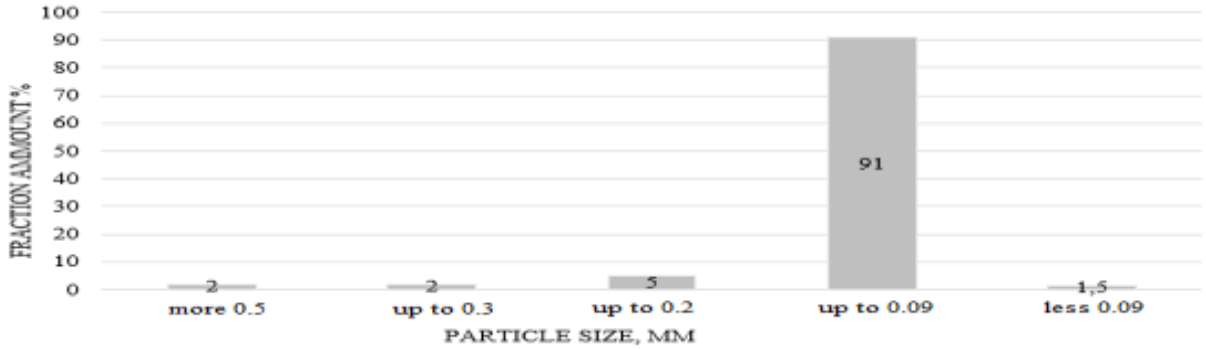

Fig. 3: Fractional the mixture of dried herbs extracts ballota nigra, nettle dead white herb, wormwood Austrian herb in 1: 1: 1

To achieve the positive properties of a mixture of dry extracts from herbal drugs, we need to study pharmaco-technological indicators mixture of dry extracts of black horehound grass, dead nettle herb, herb wormwood-Austrian usual to develop on the basis of solid dosage form in the form of capsules. Among the numbers studied pharmaco-technological parameters in the process of encapsulation most affected turnover, bulk density and moisture content of the studied substances [13-15, 19]. In accordance with the requirements of SPUs, we also studied these figures. The analysis given in the Table.1.

Table 1: Pharmaco-technological properties of dry grass black horehound extract, nettle deaf grass, herb wormwood-Austrian

Settings	Units of measurement	Results
Volume to shrink, Vo	ml	99,92 ± 0,02
Volume shrinkage after, V10	ml	85,01 ± 0,06
Volume shrinkage after, V500	ml	70,01 ± 0,05
Volume shrinkage after, V1250	ml	69,99 ± 0,04
The ability to shrink, V10 - V500	-	14,95 ± 0,06
Density to shrinkage, m / Vo	g / ml	0,49 ± 0,02
Density after shrinkage, m / V1250	g / ml	0,69 ± 0,06
Fluidity	s / 100 g	46,55 ± 0,04
Ability to pressing	N	95,01 ± 1,2
Moisture	%	1,90 ± 0,04

Table 1 shows that moisture content for the studied mixture of SPU meets that apply to dried extracts [19]. The flow rate and meet the requirements during the encapsulation (flow should not be less than 2.5-3.0 g / s and not more than 40-33 s / 100 g sample) [19]. As you know, dried extracts from medicinal plants can actively absorb moisture from the air. Therefore, we have conducted research hygroscopic mixture of extract.

According to preliminary data, the initial moisture content of the extract is about 2%. In the process of aging substance at 100% humidity, 2 hours after the experiment sample weight has doubled, and about 8 hours extract forms a thick viscous mass. The results of the experimental data definition mixture of dry extracts moisture absorption at a relative humidity 45% and 75% shown in Fig. 4.

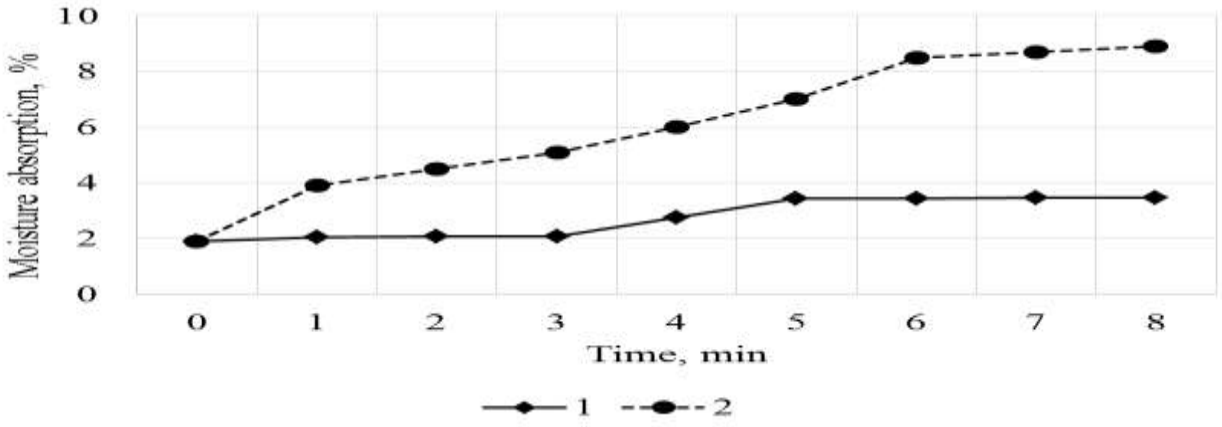

Fig. 4: Effect of relative humidity on the moisture absorption agent: 1- 45 %; 2 – 75 %

As seen from Fig. 4, at low humidity dry extract moisture content increases for 5 hours to about 3.5%, and then it does not change significantly. When the relative humidity of 75%, the moisture content of the substance increases to almost 9%, confirming the literature data on hygroscopic dry extracts [13-15, 19].The studies to predict the choice of excipients moisture regulating properties. In order to improve the technological properties of the mixture of dry extracts studied species MPM, and as a result, the choice of the optimal excipients,

we have studied the properties of extracts mixed with the following excipients: ICC (sample number 1), lactose (sample number 2) and lactose anhydrous (sample number 3). The choice of materials was due to the fact that these substances - some of the most common and widely used in the manufacture of solid dosage forms [13-15]. The compositions of the samples were injected in

a 1:1 of the studied fillers. To summarize data to determine the type of optimum filler, studies yield (for the accuracy of filling the capsule) ability to pressing (for predicting the disintegration of the finished dosage form) and density (to select the size of the capsule shell) mixtures of active ingredient with the same excipients used us in the above experiments Table 2.

Table 2: The results of the study technological characteristics mixtures for encapsulation

Indicator	Sample number 1	Sample number 2	Sample number 3
Closeness to shrinkage, m / Vo, g / ml	0,47 ± 0,03	0,56 ± 0,03	0,40 ± 0,05
Density after shrinkage, m / V1250, g / ml	0,67 ± 0,05	0,72 ± 0,06	0,66 ± 0,03
Ability to pressing, H	71 ± 1,2	64 ± 1,0	57 ± 1,3
Fluidity, s / 100g	84,0 ± 0,04	45 ± 0,03	69 ± 0,05

Note: n = 5, P = 95%

The data presented in Table 2, confirming that the study of dry mixes extracts with different adjuvants allow us to conclude that the optimal technological parameters for the filler is lactose (sample number 2), which exhibits satisfactory fluidity best ability to pressing and density

As found in previous studies, dry mixes extracts of herbal drugs are highly hygroscopic, which may adversely affect the stability of the product during storage. As we have chosen moisture regulating component-magnesium oxide, magnesium carbonate and Eros in the amount of 10% Table. 3.

Table 3: The mixture of moisture regulators

Sample number	Composition
1	Dry extract mixture MPM – 80 % Lactose monohydrate – 10 % Aerosil – 10%
2	Dry extract mixture MPM – 80 % Lactose monohydrate – 10% Magnesium oxide – 10 %
3	Dry extract mixture MPM – 80 % Lactose monohydrate – 10 % Magnesium carbonate – 10 %

The composition of the samples was added dry extracts of herbs black horehound, dead nettle herb, herb wormwood-Austrian, which was administered at a dose of 400 mg / kg (according to the results of preclinical pharmacological studies), representing 80% of the weight of the contents of the capsule.

Determination of water absorption mixtures were conducted in the following conditions: ambient temperature -15-25 °C, humidity -75 %. The study was conducted to determine the equilibrium moisture content. Results of water absorption depending on the content of capsules the mixture of different regulators humidity shown in Fig. 5.

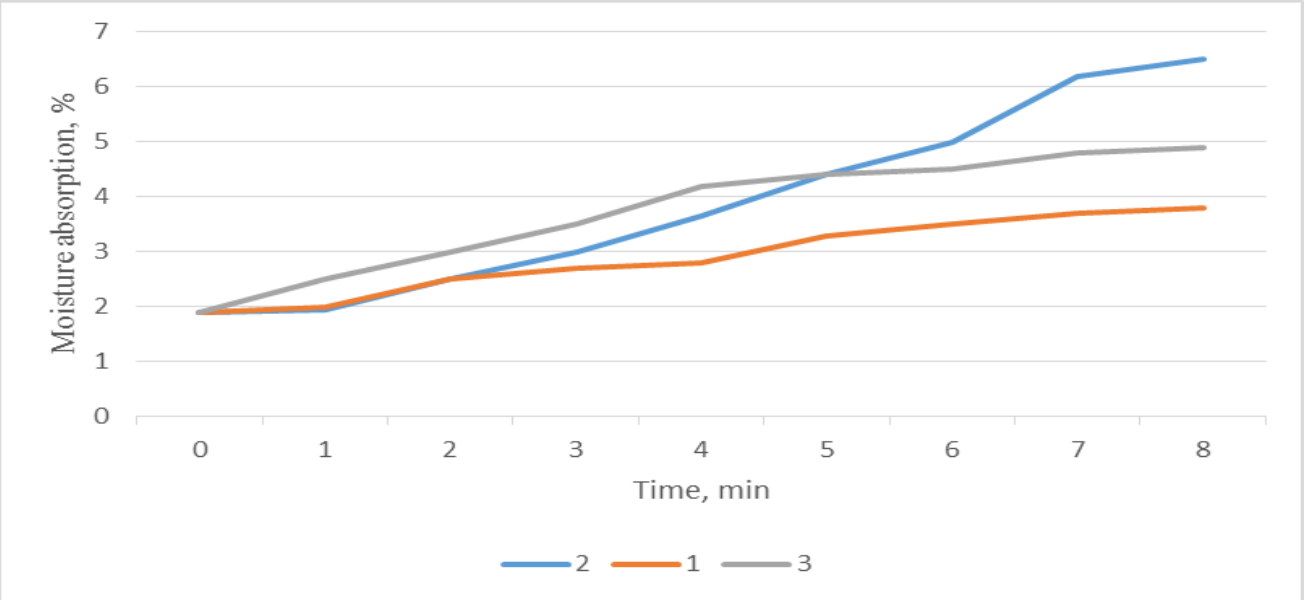

Fig. 5: Dependence of moisture absorption capsule mixture of different content moisture regulators 1 – sample number 1; 2 -sample number 2; 3 -sample number 3

As seen from Fig. 5 moisture regulator for optimal mix of species studied extracts from herbal drugs is aerosil, because this mixture at high humidity for moisture content does not exceed 4 %. This is probably due to the

fact that Eros has excellent absorption properties, absorbs 15 to 60 % of various liquids, depending on their nature, without changing the appearance and fluidity powder.

Thus, on the basis of experimental studies we have proved the composition of masses for encapsulation of drug in the form of hard gelatin capsules number 0. Composition per capsule: a mixture of dry extracts MPM-400 mg; aerosil -50 mg; lactose monohydrate -50 mg. The weight of the contents of the capsule-500 mg.

Conclusion

- The composition is theoretically substantiated and a rational technology of obtaining a drug of cerebroprotective action in the form of hard gelatin capsules based on dry extracts of medical plant material, namely black horehound grass, nettle deaf herb, sage herb has been experimentally developed.

- Crystallographic studies investigated the shape and size of particles of the investigated medical plant material, which allowed us to predict the need for the use of certain groups of excipients in the development of the composition and technology of solid dosage forms.

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