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Research Article

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Study of Technological Parameters of Antioxim Compound Medicine

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Abstract
This work is the first scientific study on the development of the composition and technology of a new antioxidant agent based on a combination of extracts of tree medicinal plants and the study of the technological parameters of a dry extract. Further draw up technological regulations for their production and their introduction into production. This study aims to the antioxidant activity of dry extract "Antioxim" was determined. In order to create this herbal collection of plant, first of all, to study the technological parameters of raw materials, such as mass size, porosity, dispersibility, free volume of layers of raw materials, water absorption coefficient of extractives, and technological process efficiency to study the effect of parameters, developed at the Department of "Industrial Technology of Medicines" of the Tashkent Pharmaceutical Institute.

Keywords: Dry Extract, Antioxidant, Collection of Plant, Phyto Preparation, Antioxidant Compound Medicine, Technological Parameters.

1. Introduction

The flora of the Republic of Uzbekistan has a large and rich resource of medicinal plant raw materials. One of the main priorities for the development of the pharmaceutical industry in Uzbekistan is the creation of Phyto preparations based on the raw materials of local medicinal plants, the development of high-efficiency technologies for their production and their implementation in industry. Herbal preparations containing a complex of biologically active substances (BAS) have a pharmaco- therapeutic effect on the metabolic processes in the body, the functions of the cardiovascular system, the central nervous system, gastrointestinal tract and other organs. Medicinal plants growing in Uzbekistan are of practical interest, because of the large plant flora of the country.

Among plant containing antioxidants, the use of combined preparations should be noted. The combination of several active substances in one drug allows to achieve greater effectiveness of therapy due to the multidirectional action of the components, as well as to increase its safety due to the possibility of using lower doses in combined drugs due to the synergism of their effects. "Antioxim" is a complex Phyto preparation with plants in the composition of the three-component complex, developed at the Department of "Industrial Technology of Medicines" of the Tashkent Pharmaceutical Institute: Melissa, Saffron and Hypericum perforatum.

Hypericum perforatum - perennial herbaceous plant of Hypericum perforatum family, 30-100 cm tall, with dihedral branched stem. Grass Hypericum, perforated contains dyes: up to 0.4% hypericin, pseudo hypericin, protopseudohypyricin. In addition, essential oil, esters of isovaleric acid. Hypericum perforatum consists of the following components: opioid kappa receptors (antagonists) of amino flavone, as well as the benzodiazepine segment of gamma-aminobutyric acid (GAMK)-receptors, which has a certain antidepressant and anti-depressant effect and is used in the treatment of depression. Hy-perforin is an inhibitor of monoamines, including serotonin and dopamine, which eases depression. Hypericin - selectively inhibits the enzyme dopamine-beta-hydroxylase, as a result of which it increases the amount of dopamine [1-37].

Crocus sativus L. from the Iridaceae family is commonly known as saffron, which is the name of the spice obtained from the dried stigma of C. sativus. Saffron is used medicinally in Chinese, Ayurvedic, Persian and Unani traditional medicine. The therapeutic properties of saffron used for healing purposes could be found in the book Materia Medica written by a Greek physician (Padania's Iosco rides) in the first century AD. Modern pharmacological studies have shown that saffron extract or its bioactive components, such as apocarotenoids, monoterpenoids, flavonoids, phenolic acids and phytosterols, have a wide range of therapeutic effects. The main carotenoids in saffron extract (SE) include crocin, crocetin, picrocrocin and safranin. Crocin, a digentiobiosyl ester of crocetin, is one of the few water-soluble carotenoids found in nature. These compounds have been shown to have a broad spectrum of biological activities, including several antioxidant and anti-inflammatory properties. Saffron (Crocus sativus) is rich in chemical compounds. They are picrocrocin in the form of glucoside, essential oils (0.6-0.9%), fats (up to 13%), lycopene, flavonoids, group B vitamins, nitrogenous substances, calcium, potassium, phosphorus. The active ingredients are crocin, crocetin, picrocrocin and safranin. Due to the high content of crocin, a carotenoid derivative, saffron provides antioxidant properties [10, 14, 20, 30, 31].

Antioxidants are a group of substances, a group of substances that neutralize the oxidizing effect of free radicals by changing the superoxide and peroxide valences of iron and copper ions in the human body. It is known that damage to vessel walls, cell membranes, cardiovascular, oncological diseases, diabetes and many other diseases can occur as a result of exposure to radicals. It protects cells (or their membranes) from the harmful effects of free radicals [5, 12].

Melissa officinalis (Melicca officinalic L.), which is grown as an essential oil crop, is one of the valuable aromatic plants of the Lamiaceae family. Melissa officinalis contains biologically active substances that can be used to enrich food products. From the fresh leaves of lemon balm, an essential oil is obtained, which contains valuable substances citronellal, Citra geraniol, linalool. Melissa officinalis has sedative, spasmolytic, antidepressant, sedative, anxiolytic, ant depressive, spasmolytic, anxiolytic and immunomodulating properties. Medicinal preparations containing Melissa have a wide therapeutic effect and contain various biologically active additives, for example: citronella has a sedative effect, geraniol and citronella have an antispasmodic effect. This plant is used as an immunomodulator, antihistamine, antimicrobial and antioxidant biologically active supplement (BAS) [32, 33].

Within the scientific research which conducted at the "Industrial Technology of Medicines" department of the Tashkent Pharmaceutical Institute, the antioxidant activity of the three-component compound "Antioxim" was determined. In order to create this herbal medicinal plant, first of all, it is necessary to choose the most optimal method of extracting biologically active substances (BAS), to study the technological parameters of raw materials, such as mass size, porosity, dispersibility, free volume of layers of raw materials, water absorption coefficient of extractives, and technological process efficiency, to study the effect of parameters.

According to the requirements of General pharmacopeia monograph (GPM) 1.4.1.0018.15, separate morphological groups of medicinal plant raw materials are pre-crushed when obtaining an aqueous extract. Usually, flowers are not more than 5 mm, and roots and stems are not more than 3 mm. It is necessary to study the effect of particle size of the components of medicinal plant raw materials. It is planned to produce "Antioxim" compound in 1 g filter packs [1, 2, 6, 8].

2. The Purpose of the Study

Determining the technological parameters of the antioxidant compound"Antioxim", developing the optimal technology for the production of the drug.

3. Materials and Methods

The object of research is the Melissa officinalis, Saffron (Crocus sativus) and Hypericum perforatum, the antioxidant complex "Antioxim" obtained on their basis, which met the requirements of the regulatory document. Within our research, the following technolo-gical indicators were studied: study of the influence of technological parameters such as specific gravity, volume of mass, porosity, dispersibility, free volume of layers of raw materials, water absorption coefficient of extractives and efficiency of the technological process.

Determination of the Specific Gravity of the "Antioxim" Package: Relative weight (d_γ) is the ratio of the mass of completely crushed raw materials (aggregate) to the volume of plant raw materials. Raw materials weighing 5.0 g (net weight) are mixed occasionally, filled with 100/2 volume of purified water and kept in a boiling water bath for 1.5-2 hours, placed in a 2 ml flask. The flask is cooled to 20℃, filled to the mark with purified water. The flask is drawn with raw materials and water. The weight of the flask with water filled to the mark was pre-measured. Relative weight is determined by the following formula:

$$d_\gamma = \frac{\mathrm{P\,d}}{\mathrm{P+G-F}} \qquad (1)$$

where:
P- is the weight of the suspension of dry raw materials, g;
G- is the mass of the flask with purified water, g;
F- is the mass of the flask with purified water and raw materials, g;
d- - density of water, g / cm (d= 0.9982);

Determination of Volume Mass of Raw Materials: Volumetric mass (d^o) is the ratio of the mass of the raw material at a given moisture content to the occupied volume, which includes air-filled pores, cracks and capillaries. Pour 50 ml of purified water into a 100 ml measuring cylinder. 10.0 g of the test kit (weighed accurately) is quickly placed in a measuring cylinder with purified water and the volume of the obtained result is measured. The volume occupied by the raw material was determined by the volume difference in the measuring cylinder before and after placing the raw material.
Volumetric mass was determined by the following formula:

$$d^\circ = \frac{P^\circ}{V^\circ} \qquad (2)$$

P^0- is the mass of uncrushed raw material at a certain humidity, g;
V^o - volume, the volume occupied by raw materials (volume difference), cm^3;

Determination of the Scattering Density of Raw Materials: The bulk density (dH) is defined as the ratio of the aggregate mass crushed in natural moisture to the volume occupied by this raw

material, which includes the parts and spaces between them. The crushed raw material was put into a measuring cylinder, slightly shaken to level the raw material, and the total volume occupied by it was determined. After that, its mass is measured.
Spreading density was determined by the following formula:

$$dH = \frac{PH}{VH} \quad (3)$$

where:
PH - is the specific moisture content of the ground raw material, g;
VH- volume, occupied raw material, cm;

Determination of Porosity of Raw Materials: Porosity (Ps) characterizes the amount of voids inside the raw particles and is defined as the ratio of the difference between the specific gravity (absolute) and the specific mass for the volume mass.
The porosity of the raw material was calculated by the following formula:

$$\mathbf{Ps} = \frac{d_\gamma - d^o}{d_\gamma} \quad (4)$$

where:
$\mathbf{d_\gamma}$ - specific mass of raw material, g/cm³;
$\mathbf{d^0}$ - volumetric mass of raw material, g/cm³;

Determination of Free Volume of Layers of Raw Materials: The free volume of the layers (V) refers to the relative volume of the voids per unit of the raw material layer (spaces inside and between the particles) and is defined as the ratio of the specific gravity and volume mass to the specific mass. The free volume of the floor was calculated by the following formula:

$$V = \frac{d_\gamma \; dH}{d_\gamma} \quad (5)$$

where:
$\mathbf{d_\gamma}$ - is the specific gravity of the raw material, g/cm³
dN - is the scattering mass of the raw material, g/cm³

Determination of the Composition of Extractive Substances: The determination was made according to the methodology described in the general pharmacopoeia article and medicinal plant raw materials in medicinal plant preparations. General pharmacopeial monograph (GPM).1.5.3.0006.15 GP (Governmental pharmacopeia) XII.

Study of the Degree of Grinding of Extractives in "Antioxim" Compound: Medicinal plant raw materials included in the antioxidant composition were crushed in separate sizes: 1-2, 3-5 and 5-7 mm. All components were mixed until homogeneous. About 1 g (accurately measured) was passed through a sieve with a size of 0.2 mm. "Antioxim" ground aggregate was placed in a conical flask with a capacity of 200-250 ml, 50 ml of purified water was added, the flask was closed with a stopper, weighed (with an error of 0.01 g) and left for 1 hour. Then the flasks are connected to a reflux condenser, heated, and boiled over low heat for 2 hours. After cooling, the mouth was tightly closed again with the same extract in it. The contents of the flask were shaken well and filtered through a dry paper filter into a dry 150-200 ml flask. 25 ml of the obtained filtrate is transferred to a constant mass previously dried from 100 to 105°C using a pipette, cooled in a desiccator with anhydrous calcium chloride under it for 30 minutes, and immedia-tely weighed. The content of extractive substances in a collection of completely dry medicinal plants is calculated in percent (X) using the formula:

$$X = \frac{m \cdot 100 \cdot 100 \cdot V}{a \cdot (100 - W) \cdot 25} \quad (6)$$

Where:
m- dry residual mass,g;
a- weight of medicinal plant raw materials, g;
V- the amount of extract used in the processing of medicinal plant raw materials, ml;
W- moisture content of medicinal plant raw materials, drug,%;

4. Results

Definitions of the technological parameters of the antioxidant aggregate: specific gravity, volume mass, specific density, porosity, dispersibility, free volume of the raw material layer are given in Table 1.

Technological parameters	Medicinal plant raw materials, 1-2 mm			Antioxidant collection		
	Melissa herb	Grass Hypericum	Saffron stigmas	Melissa herb	Grass Hypericum	Saffron stigmas
Specific gravity, g/cm³	2,52± 0,11	0,53 ±0,04	0,43 ±0,03	1,48 ±0,09	1,35 ±0,08	1,23 ±0,06
Volume mass, g/cm³	0,63 ±0,06	0,53 ±0,03	0,41 ±0,02	0,58 ±0,05	0,46 ±0,03	0,53 ±0,02
Scattering density, g/cm³	0,37 ±0,02	0,28 ±0,03	0,21 ±0,03	0,38 ±0,05	0,31 ±0,03	0,26 ±0,02
Porosity, g/cm³	0,57 ±0,03	0,53 ±0,02	0,33 ±0,03	0,40 ±0,02	0,45 ±0,02	0,49 ±0,03
Free volume of layers of raw materials, g/cm³	0,88 ±0,05	0,68 ±0,03	0,61 ±0,05	0,78 ±0,03	0,83 ±0,04	0,81 ±0,02

Table 1: Results of Determination of Technological Parameters of "Antioxim" Antioxidant Collection

It is known that the larger the phase contact surface, the faster the extraction proceeds. However, as practice has shown, very fine vegetable powders for extraction cannot be used due to a number of reasons:

• fine powders contain a lot of destroyed cells, from which a large amount of ballast substances, insoluble particles and colloids will pass into the hood, resulting in a cloudy liquid, which will subsequently be difficult to clean.

Usually, depending on the type, plant material is recommended to be crushed to the following sizes:

• grass, leaves, flowers up to particles 3-5 mm in size;

• stems, roots and bark to particles 1-3 mm in size;

• fruits and seeds, since the shell of their cells is covered with hydrophobic substances, up to a particle size of 0.3-0.5 mm. The obtained results show that the optimal technological parameters of the "Antioxim" package for packaging in filter bags were observed with a grinding level of 1-2 mm.

In addition, the influence of the degree of grinding of medicinal plant raw materials concentrated in the Antioxim antioxidant complex on the effectiveness of extractive substances was investigated. The results are presented in Table 2.

	GRINDING METHOD	EXTRACTIVE SUBSTANCES, IN %	THE COMPOSITION OF ACTIVE SUBSTANCES, %	
			AMOUNT OF FLAVONOIDS, %	AMOUNT OF EXTRACTIVES, %
COMPLEX, CRUSHED TO 1-2 MM				
1.	INFUSUM	13,68±0,56	1,63±0,23	15,31
2.	DECOCTUM	15,41±0,89	1,74±0,33	17,43
COMPLEX, CRUSHED TO 3-5 MM				
1.	INFUSUM	14,17±0,41	1,54±0,51	18,34
2.	DECOCTUM	16,10±0,26	1,61±0,32	21,52
COMPLEX, CRUSHED TO 5-7 MM				
1.	INFUSUM	11,87±0,41	1,33±0,11	20,59
2.	DECOCTUM	12,25±0,26	1,41±0,09	22,55

Table 2. Antioxim Antioxidant Complex on the Effectiveness of Extractive Substances

As can be seen from table 2, the amount of flavonoids obtained by extraction of extractive substances from the aggregate, preparation of decoctions is slightly higher than that of extractive substances in the preparation of tincture. Grinding level of medicinal plant raw materials included in the three-component set affects the level of release of extractive and active substances, the optimal grinding level for the production of "Antioxim" antioxidant composite filter bags was 1-2 mm particles. As it can be seen from the data, it was found that the maximum efficiency of extractive and active substances was observed at the level of crushing of medicinal plant raw materials in 1-2 mm.

5. Discussion

The results of the data obtained from the technological parameters of the three-component assembly recommended as antioxidant raw materials show that their technological parameters depend on the degree of grinding: specific gravity, volume mass, porosity, scattering density, free volume of the raw material layer, water absorption coefficient, as well as the sum of the extract and effect of active substances. Finer grinding of plant material is impractical, since the process of extraction of medicinal substances slows down. An important factor in the process of extraction is the temperature of the extractant, since under the influence of temperature the process of diffusion and dialysis intensifies, the material swells faster, microflora dies, enzymes are inactivated, and when fresh plant material is extracted, plasma is destroyed, proteins coagulate, i.e. the process is greatly accelerated. The obtained experimental results made it possible to determine the optimal grinding level of raw materials (1-2 mm).

6. Conclusions

On the basis of a combination of local medicinal plants: Melissa herb, Grass Hypericum and Saffron stigmas. Determination of technological parameters of the antioxidant compound "Antioxim", developed the optimal technology of the drug. Given the fact that the population's demand for this drug remains high, this area today remains relevant for further research Thus, the optimal technology of "Antioxim" aggregate was created in 1.5 g filter packs with a raw material grinding level of 1-2 mm. This indicates that in the future it is necessary to develop the technology for the production other types of drugs produced by domestic manufacturers.

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