

Article

Development of Composition and Technology of «Fatufiltrum» Granules

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Abstract: This study focuses on the development of "Fatufiltrum" granules, a comprehensive enterosorbent drug based on purified and activated glauconite. Enterosorbents are essential for detoxification in medical treatments, yet improved formulations are needed to enhance efficacy. The research addresses this gap by creating a scientifically substantiated composition containing activated glauconite, dry extract of common chicory, L-carnitine, and chromium picolinate. The granules were developed using a novel technology, and their qualitative indicators and sorption capacity were thoroughly investigated. Results demonstrate that "Fatufiltrum" has promising potential as an effective enterosorbent, with implications for advancing detoxification treatments.

Keywords: Enterosorbent, Granules, Technology, Glauconite, Quality indicators, Sorption capacity

1. Introduction

Enterosorbent preparations of natural origin are widely used in medical practice. These are primarily agents that facilitate the removal of toxic substances (both exogenous and endogenous) from the body, and they are also used in diet therapy due to their selective binding of amino acids, bile acids, and active enzymes. For example, silicon dioxide is used as a thickener in producing ointments, suspensions, gels, etc. [1, 2].

An analytical review of official sources of information on pharmaceuticals and biologically active supplements registered in the Republic of Uzbekistan with enterosorbing properties and detoxifying action was conducted. The aim was to study measures to expand the range of enterosorbent drugs using raw materials with promising sorption properties, using glauconite mined in Uzbekistan as an example [3, 4].

Based on the analytical review of official sources of information on pharmaceuticals and biologically active supplements registered in Uzbekistan, it was found that to date, one pharmaceutical substance with sorption properties and 20 names of drugs and supplements have been registered in the republic [5, 6]. These enterosorbent preparations are based on the following substances: activated charcoal (4 preparations), colloidal silicon dioxide (2 preparations), polymethylsiloxane polyhydrate (1 preparation), dioctahedral smectite (5 preparations), hydrolytic lignin (2 preparations), and 6 supplements containing various groups of sorbent substances. Enterosorbent preparations are produced in the form of powder (suspensions), granules, tablets, capsules, paste, and gel [6, 7].

In the development of enterosorbent drugs, it is necessary to study the raw materials for safety (absence of local irritative and damaging effects, absence of toxicity, maintenance of intestinal microflora, good elimination from the intestinal tract) and a convenient dosage

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form. Additionally, one of the important factors is the availability and low cost of raw materials with high enterosorbing potential [8].

The study and development of drugs based on mineral raw materials, possessing a wide range of sorption properties and the ability to release several micro- and macro elements necessary for the body's vital functions, is an urgent task for pharmacy [9].

Recently, specialists have shown increased interest in the natural mineral glauconite, which has a wide range of sorption properties. Glauconite (from the Greek "glaucos" - bluish-green) is a mineral of the hydromica group in the class of layer silicates, widely distributed in sedimentary rocks. It is a hydrated aluminosilicate of potassium, magnesium, and iron. It occurs as small rounded green grains measuring 0.1-0.9 mm in phosphorite ores, sands, and clays, which are called glauconitic when they contain a high amount of glauconite. Its content in ore can reach 70-80%.

Glauconite has a very variable chemical composition, usually containing potassium oxide (K₂O) 4.4-9.4%, sodium oxide (Na₂O) 0-3.5%, aluminium oxide (Al₂O₃) 5.5-22.6%, iron oxide (Fe₂O₃) 6.1-27.9%, ferrous oxide (FeO) 0.8-8.6%, magnesium oxide (MgO) 2.4-4.5%, silicon dioxide (SiO₂) 47.6-52.9%, water (H₂O) 4.9-13.5%. Glauconite has the ability to absorb moisture and exchange cations, improve soil structure, reduce water hardness, and contain biologically active microelements due to the presence of potassium and magnesium [8, 10].

Dermatologists in Uzbekistan have studied the effectiveness of purified and activated glauconite minerals in experiments on allergodermatoses both topically and internally [11, 12]. It was found that the use of activated glauconite ("Fatufiltrum") in complex therapy in patients with atopic dermatitis contributes to a more significant reduction in the degree of endogenous intoxication of the body and the SCORAD index by 4.04 times compared to standard therapy. The obtained data indicate the detoxifying ability of activated glauconite "Fatufiltrum", which can be recommended for widespread implementation in dermatological practice [13, 14].

2. Materials and Methods

To determine the scientifically substantiated composition and technology for the "Fatufiltrum" granules as an enterosorbent, natural glauconite mineral of variable composition (chemical formula – (K,Na)(Fe³⁺,Al,Mg)₂(Si,Al)₄O₁₀(OH)₂) was used. Glauconite mineral samples were mined by open-pit method in the Parkent district of Tashkent region (Changi quarry), Republic of Uzbekistan, and provided by LLC "Fati-Derm". These samples were then sequentially purified and activated at the "Scientific Laboratory of Innovative Pharmaceutical Compounds" (under the guidance of D.Sc., Professor A.T. Sharipov), and recommended for oral use as an enterosorbent, conditionally named "Fatufiltrum".

In addition, corresponding pharmaceutical and auxiliary substances approved for medical use in the Republic of Uzbekistan were used in the study. Besides the purified and activated enterosorbent glauconite "Fatufiltrum," the following was also used: chicory extract (GOST R 55512-2013), recommended as a source of inulin (4-25%) – a prebiotic that improves intestinal microflora and peristalsis; levocarnitine (GF RUz.Vol. 2, part 2, 12/2021:1339, pp. 3875-3876) – recommended for stimulating muscle energy and fat burning; chromium picolinate (CAS 14639-25-9), recommended for stimulating muscle energy, improving energy metabolism, reducing cravings for sweets, and promoting weight loss. In accordance with the physicochemical and mechanical properties, the corresponding auxiliary substances recommended for medical use were also used to improve the qualitative characteristics of the "Fatufiltrum" granules: lyophilized serum (milk) from oats (ST RK 2672-2015), which helps normalize stool and relieve flatulence. Oat milk stimulates gastrointestinal tract activity, and gently coats the mucous

membranes, protecting them from harmful microorganisms. Additionally, granules suspended in purified water before ingestion help recover faster from food poisoning and prevent the development of gastritis or stomach ulcers. Erythritol (CAS 149-32-6. GOST R 53904-2010) – a sweetener, used to eliminate the unpleasant taste and bitterness of medicines. Vanillin (CAS 121-33-5; GOST 16599-71) or chocolate flavouring (GOST 31721-2012). All raw materials (main and auxiliary) and packaging materials were subjected to incoming inspection in accordance with current documentation.

To develop the composition and technology of the "Fatifiltrum" granules, methods described in the literature were used to study the physicochemical and mechanical properties (fractional composition, bulk density, flowability, compressibility, residual moisture) of the activated glauconite "Fatifiltrum" powder and dry extract of common chicory roots, as well as the finished granules [15].

3. Results and Discussion

The results of the study of the physicochemical properties of the "Fatifiltrum" substance showed that the particles of the activated glauconite powder are isodiametric, in the form of spherical grains of various sizes, yellow-green in colour, odourless and tasteless, and insoluble in water. The fractional composition of natural glauconite is represented by the main fraction from -100 to +1000 μm (100%), the "Fatifiltrum" substance is represented by the main fraction from +200 to +500 μm ($85.4 \pm 1.7\%$), and the "Fatifiltrum" granules are represented by the main fraction from +200 to +500 μm ($90.3 \pm 1.02\%$).

The glauconite powder before and after purification has a satisfactory bulk density ($650 \pm 2.5 \text{ kg/m}^3$ and $413.2 \pm 2.2 \text{ kg/m}^3$, respectively) and belongs to the category of medium-heavy powders. The flowability of the powder is good: before purification, it was $8.5 \pm 2.2 \text{ kg/s} \times 10^{-3}$, and after purification, it decreased by half to $4.19 \pm 1.2 \text{ kg/s} \times 10^{-3}$. Residual moisture content was $8.1 \pm 1.2\%$ before purification and $5.04 \pm 2.4\%$ after purification. The glauconite substance has unsatisfactory compressibility, with the fracture strength of model tablets being $25 \pm 2.7 \text{ N}$. Therefore, solutions of highly effective binding agents were used for moistening [16, 17].

Activated glauconite, based on its physicochemical properties, cannot be granulated without a binding agent, and the wet granulation method produces poorly granulated, over-wet granules of various sizes that do not maintain stability during storage, and most importantly, their adsorptive capacity decreases. To improve the technological characteristics and enhance the quality of the resulting product, strongly binding auxiliary substances were added to the granulating liquid.

Next, the effect of the type and concentration of the moistening agent used for wet granulation on the qualitative and adsorptive characteristics of the granulated mass was comparatively studied. The granulating liquid must meet several requirements: it should not dissolve the active substance, nor should it bind at the expense of the sorptive properties. In preliminary studies, binding agents with various degrees of binding activity were used as moistening agents: 1-5% gelatin solution, 1-3% solutions of MC and Na CMC, and widely used in the pharmaceutical industry to improve the plasticity of the granulating mass, 3-5% PVP (Kollidon 30 F) solutions. When studying the adsorptive properties of the obtained granules [5], the adsorptive properties relative to a $1 \times 10^{-5} \text{ mol/g}$ methylene blue solution at a wavelength of 245 nm (where maximum adsorption of $3.61 \cdot 10^{-7} \text{ mol/g}$ was observed) indicated the following priority of binding agents: $\text{PVP} > \text{MC} > \text{Na CMC} > \text{gelatin}$.

Table 1. Study of the technological properties of the substance "Fatifiltrum"

№	Studied indicators	Unit of measurement	Results obtained		
			Natural glauconite	Substance "Fatifiltrum"	Granules "Fatifiltrum"
1.	Appearance		Polydisperse powder of activated glauconite of isodiametric form - in the form of spherical grains of various sizes, yellowish-olive-green color, odorless and tasteless, insoluble in water		Granules of various shapes, yellow-olive-green, odorless and tasteless, insoluble in water
2.	Fractional composition: +1000 -1000+ 500 - 500+ 200 - 200+150 - 150+100 - 100	mcm, %	0,7 6,1 8,3 22,8 46,5 15,6	0,1 3,9 56,9 28,5 6,5 4,1	- 38,3 28,5 27,5 5,2 0,5
3.	Relative density	g/cm ³	1,9	1,26	2,04
4.	Bulk Density	kg/m ³	652±4,2	413,2±2,2	367±2,2
5.	Flowability	10 ⁻³ kg/s	8,443±0,5	4,19±1,2	5,6±1,15
6.	Compaction degree		1,25	1,22	1,18
7.	Compressibility	N	25±1,7	26±1,5	32±1,4
8.	Residual moisture	%, (100 °C)	8,1±2,4	5,04±2,4	2±1,04

In the course of the research, the composition and technology for producing "Fatifiltrum" granules were developed. The composition for one sachet is as follows: activated glauconite "Fatifiltrum" 2.0 g; chicory extract 0.5 g; L-carnitine 0.5 g; chromium picolinate 0.2 g. Excipients include lyophilized oat powder 3.0 g; erythritol 8.0 g; vanillin (or chocolate flavour) 0.02 g. As a humidifier, a 5% solution of low molecular weight povidone was used in the necessary amount to form an optimally moist mass.

The production of "Fatifiltrum" granules from model compositions was carried out considering the nature and physicochemical properties of the main and auxiliary substances. A comparative analysis of the qualitative and quantitative composition of the moistening agent on the sorption properties of the granules was optimized using the method of mathematical experiment planning, specifically through one-factor analysis of variance with an equal number of trials for comparative evaluation of binding agents [17, 18, 19].

The granules were obtained by the wet granulation method. During the wet granulation of the activated glauconite substance, particle agglomeration was observed, resulting in a decrease in its specific surface area. When using a 5% PVP solution as a humidifier, a slight increase in adsorption capacity was noted [20].

As a result of studies of model mixtures with various humidifiers, the following composition was selected:

"Fatifiltrum" granules composition per 1 sachet package (grams):

- Activated glauconite "Fatifiltrum" 2.0 (up to 10 g are accepted)
- Extract of ordinary chicory 0.5
- L-carnitine 0.5
- Chromium picolinate 0.2
- Auxiliary substances:
- Freeze-dried whey (milk) from oats 3.0
- Erythritol 8.0
- Vanillin (or chocolate flavouring) 0.02
- Low molecular weight povidone (polyvinylpyrrolidone) 5% solution the required amount before is the formation of granules.
- Weight per dose is 14.22 grams (2 teaspoons of granules).

Application: 14.0 grams (2 teaspoons of granules are dissolved in 150-200 ml of boiled water, stirred until smooth, and drink after cooling to room temperature).

Technology of granules "Fatifiltrum". Activated glauconite "Fatifiltrum" 2.0, pre-sieved through a sieve with a hole diameter of 150 microns, then sifted chicory extract 0.5, L-carnitine 0.5, chromium picolinate 0.2, lyophilized oat powder 3.0, erythritol 8.0, vanillin (or chocolate flavour) 0.02. The mixture is thoroughly mixed and moistened with a 5% solution of low molecular weight polyvinylpyrrolidone to an optimally moist mass. The wet mass is passed through a sieve with a hole diameter of 2000 microns. The mass is dried in a drying cabinet at a temperature of 45-500 C to a residual moisture of 3-4%. Next, they are sieved through a sieve with a hole diameter of 1000 microns. The finished granules are packed in sachet bags of 14.0 grams or plastic jars of 100 or 200 grams. The flow diagram of the technological process is shown in Figure 1.

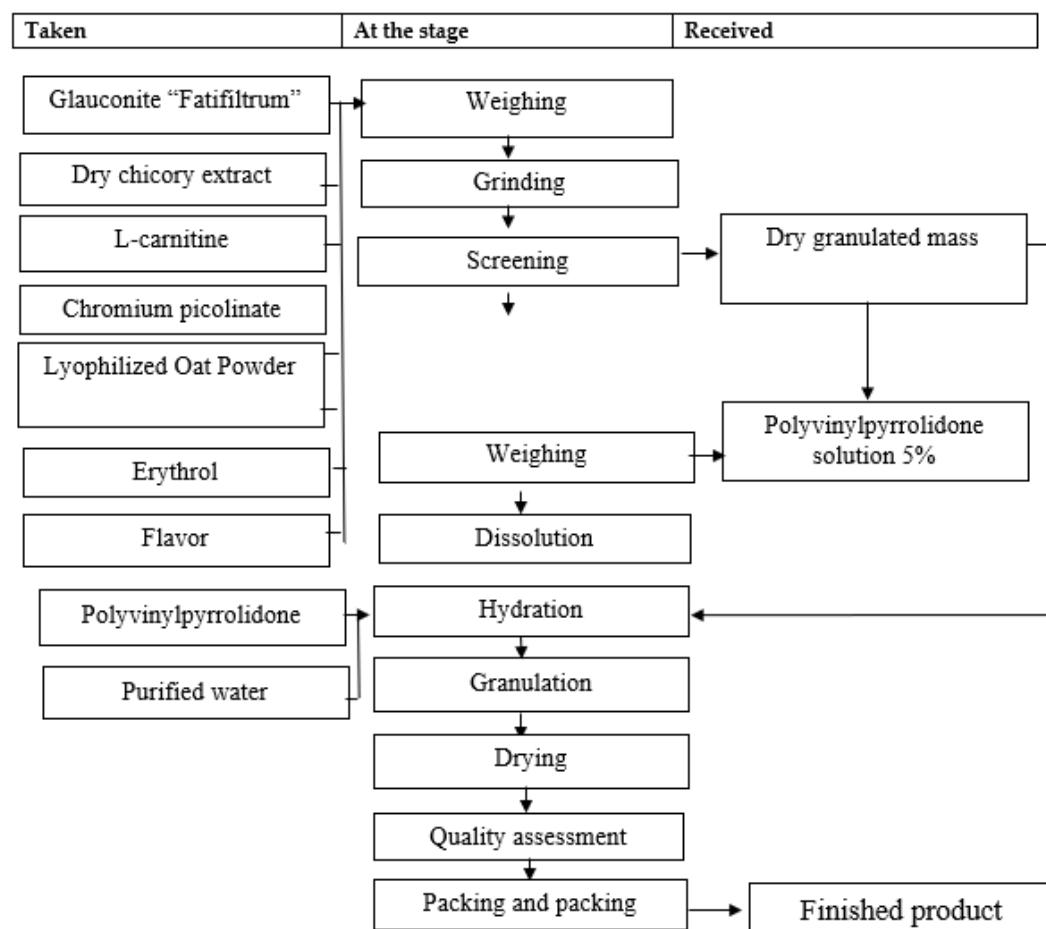


Figure 1. Scheme of the technological process of "Fatifiltrum" granules

4. Conclusion

The studies examined the physico-mechanical properties of natural glauconite, extracted by open-pit mining in the Parkent district of the Tashkent region (Changi quarry), Republic of Uzbekistan, and presented by Fati-Derm LLC. Additionally, the technological properties of the sequentially purified and activated enterosorbent substance "Fatifiltrum" were evaluated. The results of the studies indicated that, despite the highly favourable technological properties: glauconite particles of isodiametric shape in the form of spherical grains of various sizes exhibited good flowability (before purification - 8.5 ± 2.2 kg/s. 10^{-3} and 4.19 ± 1.2 kg/s. 10^{-3} , after purification it decreased by half), satisfactory bulk density (650 ± 2.5 kg/cm³ and 413.2 ± 2.2 kg/cm³, respectively) and are classified as medium-heavy powders; the powder has relatively low residual moisture content - before purification $8.1 \pm 1.2\%$ and $5.04 \pm 2.4\%$ after purification. However, the "Fatifiltrum" substance demonstrated unsatisfactory compressibility (fracture strength less than 25 ± 2.7 N) and is an elastic powder, therefore, solutions of highly effective binding agents were used for moistening. The selection of a granulation moistener was conducted, taking into account the qualitative and adsorption characteristics of the granulated mass about a methylene blue solution at a concentration of 1×10^{-5} mol/g, measuring optical density at a wavelength of 245 nm (where maximum adsorption of $3.61 \cdot 10^{-7}$ mol/g was observed), establishing the following priority of binding agents: PVP>MCC>Na CMC>gelatin.

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