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# Development Of Technology and Study of Solubility Of «Fatifiltrum» Capsules

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**ABSTRACT**

The article presents the results of experimental studies on the development of the optimal composition of **«**Fatifiltrum**»** capsules, formulated based on purified and activated natural glauconite. By analyzing the physical and mechanical properties of purified glauconite and applying experimental design methods—multifactorial plans based on 3×3 Latin squares—the optimal composition of the capsule mass was selected. Additionally, the solubility of **«**Fatifiltrum**»** capsules was studied.

***Keywords:*** *adsorption, enterosorbent, glauconite, physical and mechanical properties, mathematical planning of the experiment, optimization of the composition, technology, «Fatifiltrum» capsules, solubility.*.

## 1. INTRODUCTION

Recently, due to its wide range of molecular-sorption and ion-exchange properties, thermal stability, and radiation resistance, as well as its ability to enrich the body with micro- and macroelements essential for vital functions, the mineral glauconite has been attracting increasing interest from pharmacists. It is used both externally and internally for the treatment of allergic dermatoses and other inflammatory skin diseases, osteochondrosis, gout, and more [1, 2, 3]. Therefore, studying the physicomechanical and qualitative characteristics of purified and activated glauconite is relevant for the development of a new biologically active supplement in capsule form, tentatively named «Fatifiltrum» recommended for oral use as an encapsulated enterosorbent.

**Researchobjectives**. Development of the technology and study of the solubility of **«**Fatifiltrum**»** capsules.

**Materials and research methods**. For the development of the composition of "Fatifiltrum" capsules, glauconite mined from the Changi quarry in the Parkent district of the Tashkent region was used as the primary raw material in the study.

Intermediate research objects included samples of stepwise purified and activated glauconite, processed at the "Scientific Laboratory of Innovative Pharmaceutical Compounds" established at the Tashkent Pharmaceutical Institute (under the supervision of Doctor of Pharmaceutical Sciences, Professor A.T. Sharipov). Additionally, model samples of the encapsulated enterosorbent mass «Fatifiltrum» were obtained using various binding materials [4].

The excipients used in the development of «Fatifiltrum» capsules are well-studied and widely applied in the pharmaceutical industry, particularly in the industrial production of encapsulated medicinal products. The excipients used in the production of «Fatifiltrum» capsules meet the quality requirements of regulatory documentation (RD) [5].

For the development of «Fatifiltrum» capsules, the technological characteristics of the purified and activated glauconite substance, hereafter referred to as «Glauconite-Neo» were studied using methods described in the literature: appearance, fractional composition, relative and bulk densities, flowability, angle of repose, compaction degree, compressibility, and residual moisture content [6].

The creation of new oral medications with high enterosorbent efficacy requires conducting a large number of experiments and studying many factors. At the first stage of the research, when the composition of the components is still unknown, the focus is on studying qualitative factors. Based on this, multi-factorial plans, based on 3x3 Latin squares, were used to optimize the composition and technology of "Fatifiltrum" capsules. Such plans are economical in terms of the number of experiments, which is crucial when conducting practical tests [7].

**Results and Discussion.** The results of the studies on the physical and mechanical characteristics of the «Glauconite-Neo» substance are presented in Table 1.

**Table 1.Comparative Study of Physical and Mechanical Characteristics of Initial Glauconite and «Glauconite-Neo» Substance**

| № | Studied indicators | Unit of measurement | Results obtained | |
|---|---|---|---|---|
| | | | Natural glauconite | Purified and activated substance «Glauconite-Neo» |
| 1. | Appearance | | Polydisperse powder of isodiametric shape, in the form of spherical grains, yellowish-green colour, odorless and tasteless, insoluble in water | |
| 2. | Fractional composition:<br>+1000<br>- 1000 +800<br>- 800 +500<br>- 500 +200<br>- 200 +150<br>- 150 +100<br>- 100 | µm, % | <br>1,1<br>3,2<br>4,2<br>38,9<br>46,5<br>3,6<br>2,5 | <br>0,1<br>3,9<br>56,9<br>18,5<br>16,5<br>3,0<br>1,1 |
| 3. | Relative density | g/cm³ | 1,29 | 1,26 |
| 4. | Bulk Density | kg/m3 | 652±4,2 | 413,2±2,2 |
| 5. | Flowability | 10-3 kg/s | 8,43±0,5 | 4,19±1,2 |
| 6. | Angle of natural repose | degree | 25,2±0,5 | 23,2±1,2 |
| 7. | Degree of compaction | | 1,25 | 1,22 |
| 8. | Compressibility | N | 25±1,7 | 26±1,5 |
| 9. | Residual moisture | %, (100 $^0$C) | 8,1±2,4 | 2,02±1,4 |

The external characteristics of glauconite before and after purification changed relatively little: it remained a polydisperse powder with an isodiametric shape in the form of spherical grains of yellowish-green colour, odourless and tasteless, insoluble in water.

The fractional composition of natural glauconite consists of particles ranging from 100 to 800 µm, with the average mass size represented by particles ranging from 200 to 500 µm (85.4±1.7%). The main fraction of the purified and activated glauconite substance consists of particles from 150 to 800 µm (91.9%). The relative density before purification is 1.29 g/cm³, and after purification, it is 1.26 g/cm³. The bulk density before purification is 652±4.2 kg/m³, and after purification, it is 413.2±2.2 kg/m³. Flowability is 8.43±0.5×10⁻³ kg/s and 4.19±1.2×10⁻³ kg/s; the angle of repose is 25.2±0.5° and 32.2±1.2°; compressibility is 25±1.7 N and 26±1.5 N; residual moisture content (% at 100°C) is 8.1±1.24 and 2.02±1.4 before and after purification, respectively.

As the results of the studies showed, after purification and activation, the glauconite substance—a polydisperse powder consisting of particles with an isodiametric shape in the form of spherical and globular grains—demonstrates good bulk density indicators. It is classified as a medium-heavy powder. In terms of shape-forming ability (adhesion properties), the substance exhibits a relatively low degree of compaction (1.25) and a small compressibility value (26±1.5 N). The unsatisfactory strength (1-4 kg/cm²) of the glauconite during compression at 0.5 g per mold with 11 mm hole diameter on a manual hydraulic press at a pressure of 120 MPa was observed. The small angle of repose—23.2±1.2°—characterizes the heterogeneity of particle size, as well as their tight packing. At the same time, the residual moisture content improved twofold. This can likely be explained by the removal of silica impurities during purification and the positive effect of the activation process through additional

calcination of the substance at temperatures of +400°C and above.

Model capsules were prepared by filling the encapsulating mass into capsules made from various materials, using a manual method and with the help of a hand-operated device in a WK-187 capsule machine (China). When developing the biologically active supplement in capsule form, «Fatifiltrum» it was taken into account that the dose of the active ingredient is 300 mg.

Manual filling allowed for uniformity in the dosing of the mass in the capsules. When filling with the automatic machine, it was found that the dosing error averaged more than 12% (the standard for masses of 0.3 g and above is 7.5%) [8]. Although characteristics such as flowability and bulk density of the «Glauconite-Neo» substance are satisfactory, due to the polydispersity of the powder, capsule filling was uneven, which affected dosing accuracy and led to deviations from the average mass, complicating production. Therefore, to ensure dosing accuracy, additional grinding and wet granulation were proposed. Although the particles of the «Glauconite-Neo» substance have an isodiametric spherical shape, the powder is polydisperse, medium-heavy, and poorly compressible, which necessitates the use of wet granulation with highly binding agents (Table 2.) when creating oral dosage forms.

**Table 2. Compositions of Model Samples of the Encapsulating Mass for «Fatifiltrum» Capsules**

| № | Components | Composition, mg | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Active pharmaceutical ingredient | | | | | | |
| 1. | “Glauconite-Neo” | 300 | 300 | 300 | 300 | 300 |
| Excipients | | | | | | |
| 1. | Magnesium stearate | 2,0 | | | | |
| 2. | Calcium stearate | | 2,0 | | | |
| 3. | Aerosil 380 and calcium stearate mixture (1:1) | | | 2,0 | 2,0 | 2,0 |
| 4. | 5% potato starch gel | q.s.* | | | | |
| 5. | 2% gelatin gel | | q.s. | | | |
| 6. | 2% PVP gel | | | q.s. | | |
| 7. | 2% MC gel | | | | q.s. | |
| 8. | 2% Na CMC gel | | | | | q.s. |
| Weight of contents of one capsule, g | | 305 | 305 | 305 | 305 | 305 |

*q.s. – the required amount to obtain an optimally moist mass.

The influence of excipients on the technological properties of the encapsulating mass for «Fatifiltrum» capsules after wet granulation was studied based on the following criteria: equivalent granule diameter[1] (mm), ensuring dosing accuracy (g), with an allowable deviation of 6 mg for size «0» capsules; flowability (g/s); angle of repose (degrees); bulk density, without compaction (g/cm³); residual moisture content at 100°C (%), as shown in Table 3.

[1]To characterize a polydisperse particle layer, the concept of equivalent diameter $d_Э$, is used, which refers to the diameter of spherical particles in a monodisperse layer that have the same average characteristics as the polydisperse layer. The equivalent diameter is most often calculated as the mass average diameter:

$$d_Э = \sum x_i \cdot d_i$$

Where: $d_Э$ – is the equivalent diameter, mm; $x_i$ — is the mass fraction of particles of a given size; $d_i$ — is the diameter of the corresponding fraction of the bulk material, mm.

**Table 3.Technological Characteristics of Model Samples of Mass for Encapsulation**

| Composition number | Dose deviation, no more than ±6 mg | Flowability, g/s | Angle of natural slope, degrees | Bulk density, g/cm3 | Residual moisture, % |
|---|---|---|---|---|---|
| 1 | 8,9 | 4,6±1,4 | 26,5±0,3 | 433,5±2,0 | 4,50±1,4 |
| 2 | 8,5 | 5,5±0,3 | 27,4±0,1 | 450,2±1,5 | 6,25±1,7 |
| 3 | 5,5 | 7,5±0,25 | 35,2±0,5 | 705,5±1,8 | 2,25±1,5 |
| 4 | 6,8 | 7,2±0,52 | 32,7±0,2 | 664,7±1,4 | 5,50±1,4 |
| 5 | 7,2 | 6,5±0,18 | 30,8±0,3 | 545,2±2,7 | 4,25±1,5 |

As shown by the results in Table 3 of the study on the technological properties of the encapsulating mass for «Fatifiltrum» capsules, the use of highly binding agents demonstrated the following priority sequence for moistening the granulating mass: PVP 2% gel > MC 2% gel > Na CMC 2% gel > Gelatin 2% gel > 5% starch paste. However, as a result of the studies, the solutions of gelatin and 5% starch paste were excluded due to the high fragility of the final granules.

When using Aerosil A-380 as a disintegrant and calcium and magnesium stearates as lubricants, no visible changes were observed.

To develop the wet granulation technology in the subsequent stage of the study, it was necessary to select the most optimal moisturizing component, specifically determining its concentration. During preliminary wet granulation, widely used binding agents with strong binding capabilities were chosen: methylcellulose (MC) gels, sodium carboxymethylcellulose (Na-CMC) gels, and polyvinylpyrrolidone (PVP).

To select the binding agent, the «Glauconite-Neo» powder was moistened with gels made from the above-mentioned substances at various concentrations until an optimally moist mass was obtained. The moistened mass was then passed through a perforated surface—a sieve with 2000 µm hole diameter—and dried in a drying chamber for 1.5–2 hours at 75°C. After drying, the granulate was sieved through a sieve with 1000 µm hole size. To prevent particle agglomeration, the granulate was dusted with up to 1% of the granule mass using a mixture of Aerosil A-380 and calcium stearate (in a 1:1 ratio), where the mixture of the disintegrant and lubricant was sieved through a sieve with a 100 µm hole diameter. The results of the technological characteristics of the granules are presented in Table 4.

**Table 4. Technological Properties of the «Fatifiltrum» Encapsulating Mass Prepared with Various Moisturizers**

| Studied indicator, unit of measurement | 2% solution MC | 2% solution of Na CMC | 2% PVP solution | 3% solution MC | 3% solution Na CMC | 3% PVP solution |
|---|---|---|---|---|---|---|
| Flowability, g/s | 7,2±0,52 | 6,5±0,18 | 7,5±0,25 | 8,2±0,45 | 7,5±0,32 | 7,5±0,54 |
| Strength, %* | ++ | + | +++ | +++ | ++ | +++ |
| Bulk density free, g/cm3 | 664,7±1,4 | 545,2±2,7 | 705,5±1,8 | 689,4±1,2 | 634,7±1,1 | 732,5±1,9 |
| Bulk density compacted, g/cm3 | 675,3±1,8 | 575,0±1,5 | 678,5±1,5 | 695,2±1,3 | 665,8±1,9 | 750,7±1,0 |
| Disintegration, min. | 7,5±1,1 | 7,0±1,7 | 6,5±1,2 | 7,9±0,2 | 7,6±1,0 | 7,2±1,5 |
| Residual moisture, 100 $^0$C, % | 5,50±1,4 | 4,25±1,5 | 2,25±1,5 | 6,50±1,4 | 5,25±1,5 | 3,25±1,5 |

Note: * - «+» - abrasion resistance of granules – 90-95%;

- «++» - abrasion resistance of granules – 95-97%;

- «+++» - abrasion resistance of granules – more than 97% [8].

However, the use of PVP in the form of 2-3% solutions contributed to the enlargement of particles and a slight decrease in their specific surface area and adsorption capacity. Additionally, 2-3% PVP solutions exhibit detoxification properties, which involve their ability to form complexes. [9].

During the granulation of activated glauconite, the most optimal binding agent, based on the quality characteristics of the final granules, was found to be a 2% PVP solution of grade K-17 [10].

To develop and further optimize the composition and technology of «Fatifiltrum» capsules, the method of mathematical experiment design was used – a three-factor Latin square 3x3, where each factor under study was investigated at three levels of change, without repeated observations.

In performing analysis of variance without repeated observations, each cell contains only one measured value. The mathematical model is represented as linear:

$Y_{ijk} = \mu + A_i + B_j + C_k + E_{ijk}$ (1),

Where $Y_{ijk}$ – experimental result; μ - overall effect; $A_i$ – factor effect A; $B_j$ – factor effect B; $C_k$ – factor effect C; $E_{ijk}$ - experimental error.

Since the substance of purified and activated glauconite, «Glauconite-Neo» exhibits highly elastic properties, wet granulation was performed using moisturizing agents with strong binding properties (gelatin, 2% Na-CMC gel, 2% PVP gel, and 5% potato starch gel) [9].

The process of developing the optimal composition and rational technology for capsules requires consideration of a number of variable factors, such as: the type of binding agent (factor A), the type of antifriction substance (factor B), and the material from which the empty capsule is made (factor C). Each of these factors influences, to varying degrees, the quality indicators that determine the technological properties and sorption activity of the enterosorbent preparation (Table 5).

**Table 5.Characteristics of variable factors affecting the quality indicators of «Fatifiltrum» capsules**

| Levels | Factors | | |
|---|---|---|---|
| | Type of binder (A) | Type of antifriction substance (B) | Capsule material (C) |
| 1 | 2% PVP gel | Magnesium stearate | Hard gelatin capsules with cap |
| 2 | 2% Na CMC gel | Calcium stearate | Hard capsules based on HPMC<br>with cap |
| 3 | 5% potato starch gel | Mixture of Aerosil 300 and calcium stearate (1:1) | Hard capsules based on starch and polyvinyl alcohol (PVA) with a cap |

To test the significance of the specified factors, 9 experiments were conducted according to the experimental plan, under the conditions provided by the planning matrix.

The following factors served as optimization criteria: humidity, % (Y1); disintegration, s (Y2); sorption activity of «Fatifiltrum» capsules, % (Y3). The planning matrix and the results of studies on optimization of the composition and technology of «Fatifiltrum» capsules are presented in Table 6, where all three factors vary at three levels.

Based on technological feasibility, based on a comparison of average values, an assessment was made of the influence of the type of binding agents, the type of antifriction agent and the type of capsule material on the quality characteristics (residual moisture (%), capsule disintegration (sec), the sorption capacity of «Fatifiltrum»

capsules relative to the sorption capacity of the encapsulated mass (%).

**Table 6.Experimental planning matrix and technological characteristics of mixtures of model compositions of «Fatifiltrum» capsules**

| Experience number | Factors | | | Optimization criteria | | | D |
|---|---|---|---|---|---|---|---|
| | A | B | C | Residual moisture content of the encapsulated mass, %, $Y_1$ | Capsule disintegration (sec.), Y2 | Sorption activity of capsules, %, Y3 | |
| 1 | $a_1$ | $b_1$ | $c_1$ | 4,81±1,50 | 1075,5±0,92 | 83,5±1,2 | 0,422 |
| 2 | $a_1$ | $b_2$ | $c_2$ | 5,02±1,34 | 1100,6±0,45 | 85,5±1,1 | 0,623 |
| 3 | $a_1$ | $b_3$ | $c_3$ | 3,73±1,02 | 965,0±0,75 | 98,5±1,2 | 0,955 |
| 4 | $a_2$ | $b_1$ | $c_2$ | 5,32±1,09 | 1200,0±0,38 | 80,5±1,6 | 0,450 |
| 5 | $a_2$ | $b_2$ | $c_1$ | 4,52±1,05 | 1056,0±0,65 | 84,5±1,8 | 0,460 |
| 6 | $a_2$ | $b_3$ | $c_3$ | 4,32±1,12 | 1003,5±0,60 | 86,5±0,8 | 0,742 |
| 7 | $a_3$ | $b_1$ | $c_1$ | 4,03±1,22 | 1030,1±0,74 | 90,5±1,7 | 0,536 |
| 8 | $a_3$ | $b_2$ | $c_2$ | 3,92±1,29 | 1025,1±0,86 | 95,5±1,3 | 0,702 |
| 9 | $a_3$ | $b_3$ | $c_3$ | 3,75±1,02 | 1000,3±0,80 | 94,2±1,9 | 0,835 |

The results of the experiments conducted according to the experimental design matrix were subjected to analysis of variance. As a result, if, for certain values of the $F_{эксп}$-criterion for interaction, the results were greater than the tabulated value, testing the significance of the main effects would have been impossible. However, as seen from the results of the analysis of variance, the obtained value of the FexpF_{\text{exp}}Fexp-criterion for all studied factors and the triple interaction is less than the tabulated value of the Fisher criterion. Therefore, the linear model described by Equation 1 is suitable for analysis, and the significance of the main effects can be tested.

The physical meaning of the significance of interaction is that when the value of the level of one factor changes, the value of the level of the other factor changes.

In order to optimize the composition and technology of the Fatifiltrum capsules, criteria with different measurement values were studied. In order to identify the degree of influence of all responses on the process of preparing the «Fatifiltrum» capsules, it was necessary to generalize these measurement values into one common indicator - a generalized desirability function (D), defined as the geometric mean of the desirability of individual properties:

$$D = \sqrt[3]{d_1 \cdot d_2 \cdot d_3} \quad (2)$$

To convert natural quantities with different measurement units into partial quantities, the Harrington's desirability function scale was used. The desirability scale was constructed using the method of quantitative assessments with a desirability range from zero to one. Intermediate desirability values correspond to points reflecting specific quality levels of the «Fatifiltrum» capsules (Table 7).

**Table 7 Standard Desirability Scale Ratings**

| Empirical system of preferences (desirability) | Numerical system of preferences (system of psychological parameters) |
|---|---|
| Very good | 1,00-0,80 |
| Good | 0,80-0,63 |
| Satisfactory | 0,63-0,37 |

| | |
|---|---|
| Bad | 0,37-0,20 |
| Very bad | 0,20-0,00 |

The numerical preference system presented in Table 7 is a dimensionless desirability scale developed by Harrington. The values of this scale range from 0 to 1 and are denoted by d (from desirable in French, meaning desirable). The value of the i optimization parameter, converted into the dimensionless desirability scale, denoted by $d_i$ , is called the partial desirability, where i=1,2,3,…, n-1, 2, 3, is the current parameter number, n - is the total number of parameters. A value of $d_i$=0 corresponds to an absolutely unacceptable level for the I optimization parameter, while $d_i$=1 corresponds to the best value for the i parameter. The desirability function corresponding to Harrington's desirability scale has the following form (for a one-sided constraint):

$d = \exp(-\exp(-y'))$ (3)

When constructing the desirability scale, which establishes the relationship between the response values $y_1$, $y_2$, $y_3$ and the corresponding partial desirability criteria $d_1$, $d_2$, $d_3$, it was assumed that the worst quality (d = 0) corresponds to the following values: the moisture content of the encapsulating mass at 5.32 ± 1.09%, disintegration time at 1200.0 ± 0.32 seconds, and sorption activity at 80.5 ± 1.6%. The best quality is represented by the following response values: $Y_1$=3,75±1,02%, $Y_2$=965,0±0,75 seconds, $Y_3$=98,5±1,2% effect with intermediate response values chosen accordingly. A graphical representation of the desirability function is shown in Figure 1.

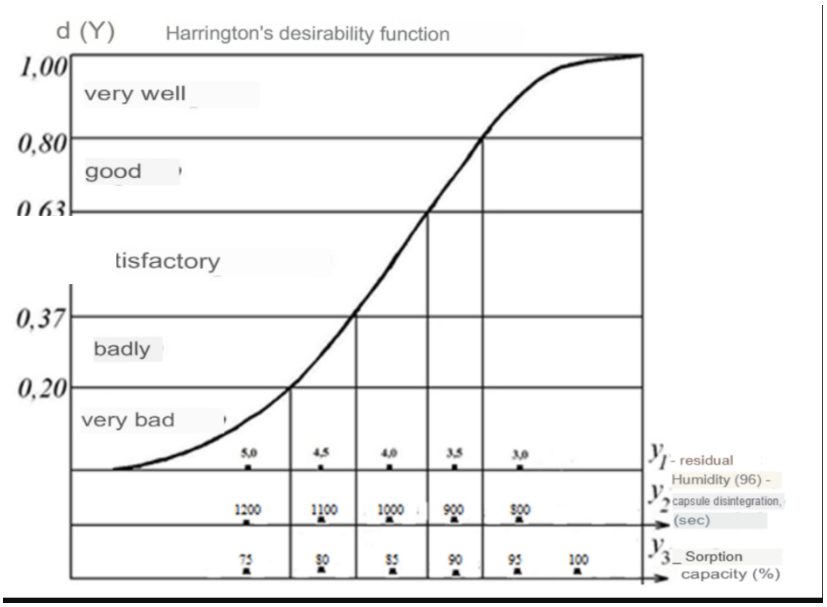



**Figure 1. Desirability function scale**

According to the experimental planning matrix, 9 experiments were conducted and, according to optimization criteria, the significance of the selected auxiliary substances was determined, arranged in the following order: type of humidifier – a1≥a2≥a3 (PVP ≥ Na-CMC ≥ potato starch); type of antifreeze – b3≥ b2 ≥ b1 (aerosil 300 + calcium stearate (11) ≥calcium stearate≥magnesium stearate); capsule material – c3≥c2≥c1 (hard capsules based on starch and polyvinyl alcohol (PVA) with lid ≥ hard capsules based on HPMC with lid ≥ hard gelatin capsules with lid). In this case, the property of the desirability function d(x) varies from 0 to 1 and the exponents di≈0.

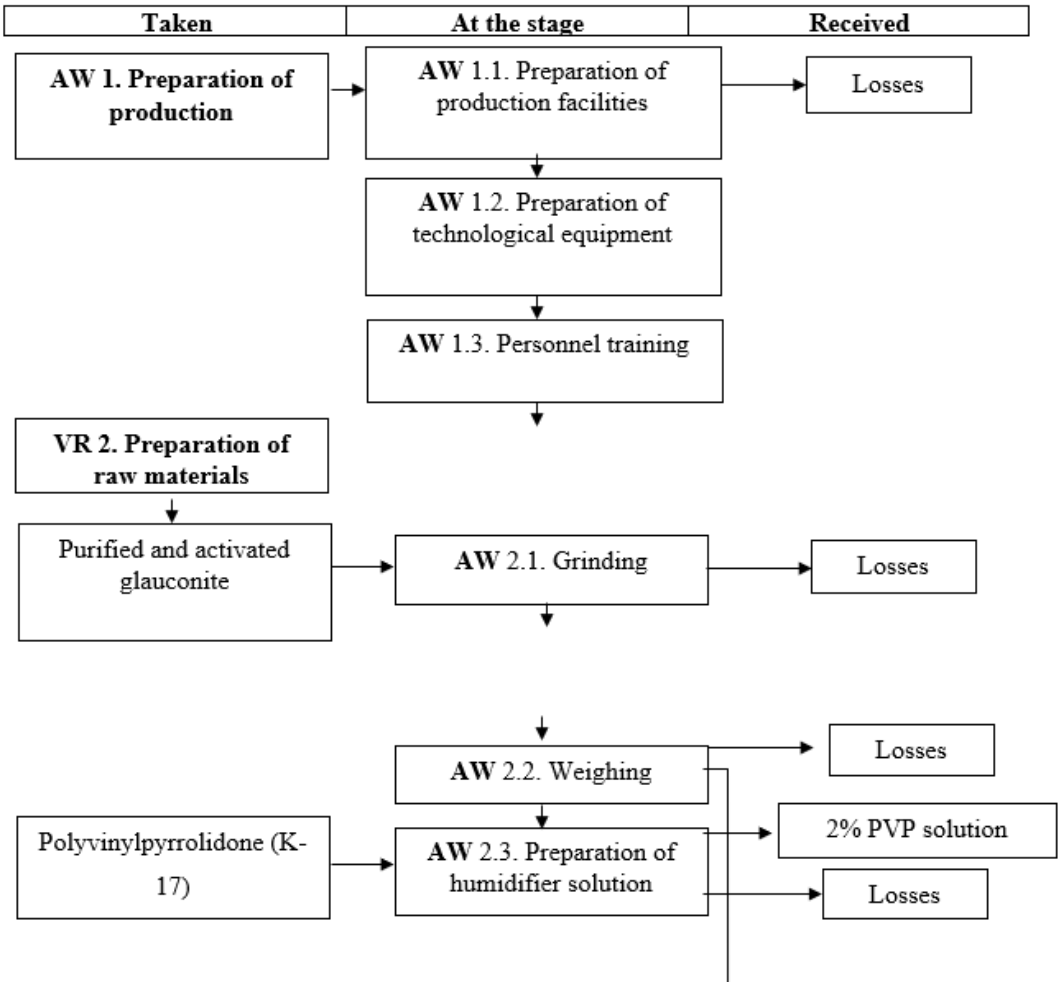
As a result of the conducted research, composition No. 3 (a1, b3, c3) was selected to ensure a satisfactory technological process for the preparation of «Fatifiltrum» capsules [9].

Based on the results of the research, the following composition of «Fatifiltrum» capsules (composition per 1 capsule) was developed by the method of mathematical planning of the experiment:

**Composition of «Fatifiltrum» capsules (composition per 1 capsule):**

| Name of substance | Amount, mg | Qualification characteristics |
|---|---|---|
| Active ingredient: | | |
| «Glauconite-Neo» | 300 | Active substance |
| Excipients: | | |
| Polyvinyl pyrrolidone 2% gel | 1,0 | Humidifier |
| Calcium stearate | 2,0 | Lubricant |
| Aerosil | 2,0 | Disintegrant |
| Weight of capsule contents: | 305,0 mg | |

**Technology supplement capsules «Fatifiltrum»:** The purified and activated glauconite was further ground and sieved through a sieve with hole diameters of 150 µm. After weighing, the glauconite mass was moistened with a 2% solution of polyvinylpyrrolidone (PVP K-17). The optimally moistened mass was granulated by passing it through a sieve with hole diameters of 2000 µm. The wet granules were dried at a temperature of 75±5°C in a drying oven until the residual moisture reached 3% (for 1.5-2 hours). The dried granules were passed through a sieve with hole diameters of 1000 µm. Then, the mass was dusted with a mixture of Aerosil and calcium stearate (1:1), previously sieved through a sieve with hole diameters of 100 µm (Figure 2).



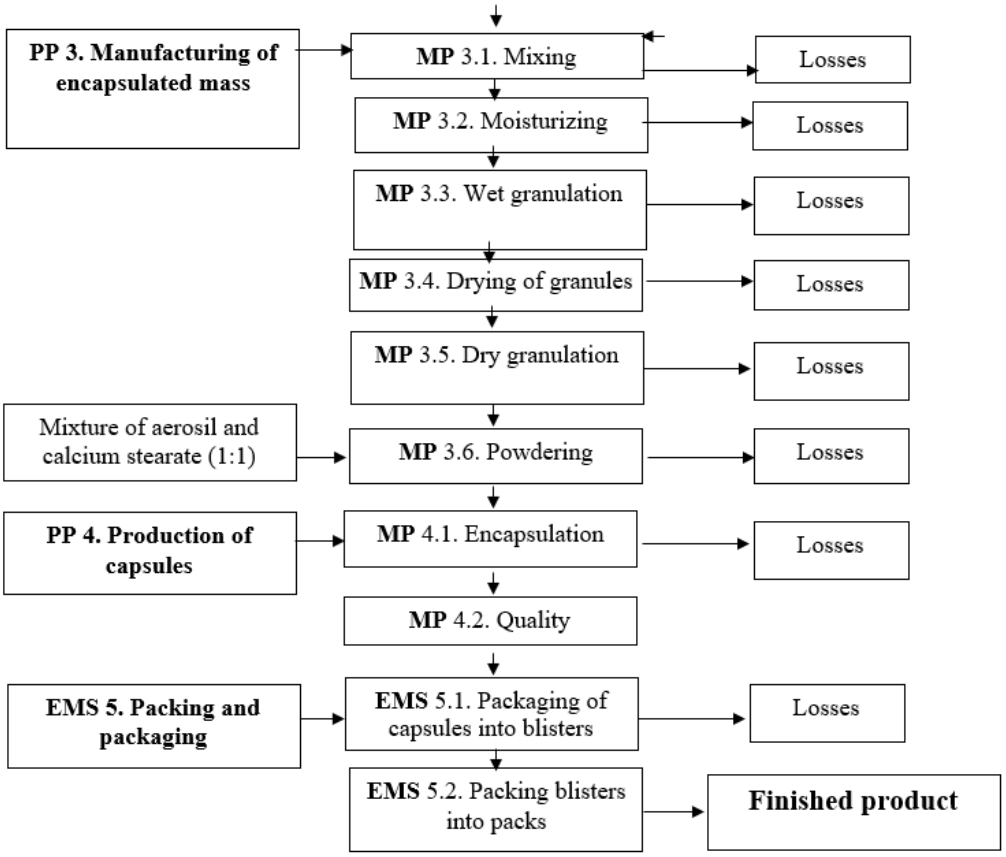



**Figure 2. Scheme of the technological process for obtaining «Fatifiltrum» capsules**

Next, a study of the solubility of the capsules was conducted. «Fatifiltrum».

The study of the physical and mechanical properties of the substance «Glauconite-Neo» and the encapsulated mass of the capsules «Fatifiltrum» was studied using the methods described in the literature (Table 8) [10].

Studies were also conducted to pre-select the size of hard gelatin capsules using an encapsulation weight of 0.305 g per capsule.

**Table 8.Choosing the Optimal Size of Fatifiltrum Hard Gelatin Capsules**

| Capsule number | Average capsule capacity, ml | Volume occupied by 0.305 g of granulate, %* | Free volume of capsule, % |
|---|---|---|---|
| 000 | 1,37 | 47 | 53 |
| 00 | 0,95 | 68 | 32 |
| 0 | 0,68 | 95 | 5 |
| 1 | 0,5 | 129 | - |
| 2 | 0,37 | - | - |
| 3 | 0,3 | - | - |
| 4 | 0,21 | - | - |
| 5 | 0,13 | - | - |

Notes: *- with seal.

The volume of the selected mixture was within ≤0.600 ml (85.0%), with the free volume of the capsule accounting

for 15%. In practice, this corresponded to the size «0» of hard gelatin capsules with a cap (empty gelatin capsules, 100% beef gelatin, ACG "Europe", Croatia).

The size of vegetarian capsules matches that of gelatin capsules: the volume of the contents in a size "0" capsule is the same as in gelatin capsules, approximately from 400 to 800 mg. The selection of the optimal size for hard capsules based on HPMC with a cap ("Veg-Caps", Sainty International Group (SaintyCo), China) and hard capsules based on starch and polyvinyl alcohol (PVA) ("Nutraonly", Ningbo Jiangnan Capsule Co., Ltd., China) with a cap was carried out according to the formula for calculating the capsule volume:

$V = \pi r^2(4/3*r+h)$ (4)

Where: r – capsule base radius, см; h – capsule height, см.

An example of calculation for hard capsules based on HPMC with a cap: length - 21 mm, diameter - 7 mm, capacity - 0.68 ml, which corresponds to the size «0». After evaluating the technological indicators of the encapsulated mass, hard gelatin capsules with a cap of size «0» were used to fill the capsules.

To select the appropriate capsule size, the encapsulating mass was filled by tamping into capsules made of different materials (hard gelatin capsules with a cap; hard capsules based on HPMC with a cap; hard capsules based on starch and polyvinyl alcohol (PVA) with a cap) using both a manual method and a capsule filler model WK-187 (China).

The size of empty gelatin capsules for filling with the encapsulated mass depends on the capacity, as well as on the type of medicinal substance and its density.

When selecting capsule size according to the Standard system, eight commonly accepted sizes are identified in the category of hard capsules. Additionally, capsules of the Supro type are imported from abroad, which include five standard sizes. The standards for gelatin capsule sizes are determined by the State Pharmacopeias of various countries, ensuring dosing accuracy [5, 8].

The mass of the capsule contents is 0.305 g. The optimal capsule number was selected according to the bulk density of the mass – 0.679±1.5 g/cm3.

The filled «Fatifiltrum» capsules were packaged in blister contour-cell packs made of polyvinyl chloride film, grade EP-73 (according to state standard 25250-88), and lacquered aluminium foil (according to TS 48-21-270-78).

The correctness of the selected composition of the encapsulating mass, as well as the material from which the capsules are made, is largely determined by biopharmaceutical studies [11].

The sorption activity of «Fatifiltrum« capsules, encapsulated in hard gelatin capsules with a cap, hard capsules based on HPMC with a cap, and hard capsules based on starch and polyvinyl alcohol (PVA) with a cap, was conducted using the «Rotating Basket» device model TDT-06L («Electrolab», India), according to the method outlined in the Pharmacopeia of Uzbekistan (SPH RUz), Volume I, Part 1, p. 435, "2.9.3. Tests for «Dissolution of Solid Dosage Forms» [11].

The following standard experimental conditions were observed: for determining the dissolution profile of «Fatifiltrum» capsules, purified water in a volume of 900 ml was used as the dissolution medium, with methylene blue (analytical grade) dissolved in it as a marker (C0(MS) = 2·10^-5 mol/L; solution volume 900 mL). The temperature of the thermostatted dissolution medium was maintained at 37±0.5°C. For determining capsule dissolution, a basket with holes of 0.25 mm in diameter was used. The optimal rotational speed, experimentally determined, was 100 min^-1. The amountof methylene blue adsorbed from the solution was determined spectrophotometrically using the UV-1900i instrument (Japan) at a wavelength of 665 ± 2 nm [12].

**Table 9.Results of determination of sorption properties of glauconite by methylene blue**

| Type of capsule material | Capsule disintegration (sec.) | Concentration of methylene blue, mol/l | | Sorption activity of capsules (%) after | |
|---|---|---|---|---|---|
| | | $Cx_{org.}$ | $C_{rem.after}$ 60 minutes | 45 minutes | 60 minutes |
| Starch and PVA | 1075,5±0,92 | $2,0 \cdot 10^{-5}$ | $0,19 \cdot 10^{-5}$ | 82,5±0,12 | 90,5±1,2 |
| HPMC | 1200,0±0,38 | $2,0 \cdot 10^{-5}$ | $0,27 \cdot 10^{-5}$ | 80,5±0,17 | 86,5±0,8 |
| Gelatin | 965,0±0,75 | $2,0 \cdot 10^{-5}$ | $0,31 \cdot 10^{-5}$ | 78,3±1,1 | 84,5±1,8 |

The study of the sorption properties of «Fatifiltrum» capsules in vitro experiments showed the following priority of hard capsules with a cap based on: starch and (PVA) > HPMC > gelatin capsules. Despite the fact that the results of capsule solubility were inversely proportional to the established priority.

## 2. CONCLUSION.

Based on the study of the physicochemical properties of purified glauconite, as well as using methods of experimental design — multifactorial plans based on 3x3 Latin squares, the optimal composition of the encapsulating mass was selected. The following binders with strong binding properties were used as the moistening agents: 2% PVP gel > 2% Na-CMC gel > 2% gelatin gel > 5% starch paste; as anti-friction agents: a mixture of Aerosil 300 and calcium stearate (1:1) > calcium stearate > magnesium stearate.

When selecting the material used for the production of hard capsules with a cap, it was established that all capsules could be used for filling the enterosorbent preparation. However, the preference was given to vegetarian capsules: hard capsules based on starch and polyvinyl alcohol (PVA) with a cap > hard capsules based on HPMC with a cap > hard gelatin capsules with a cap.

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