

Prospects for The Development of Enterosorbent Preparations Based on Local Glaucosite Mineral Raw Materials

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Abstract: Enterosorbents are widely used in gastroenterology, toxicology, infectious diseases, allergology, dermatology, surgery, oncology, hepatology, nephrology, and addiction medicine.

To expand the range of enterosorbent preparations using natural raw materials, the physicochemical and technological properties of the natural mineral glaucosite were studied as a promising source for the developing granulated, encapsulated, and tablet-form oral enterosorbent preparations.

Keywords: Enterosorbent, adsorption, absorption, endotoxins, exotoxins, technology, oral preparations, granules, and capsules.

Introduction: The development of enterosorbent preparations with adsorption and detoxification pharmacological effects is one of the promising areas in pharmaceutical practice.

Enterosorbents are medicinal substances of various structures and nature, whose mechanism of action is aimed at binding and eliminating exo- and endotoxins from the body through the gastrointestinal tract by adsorption, absorption, ion exchange, and complex formation. Depending on the mechanism of action, sorbents can be divided into: 1) adsorbents - substances with ion-exchange properties; 2) complexing agents - substances that, in a molecular or ionic state, form stable compounds with ligands that, in turn, bind and eliminate from the body toxins of biologically active substances (antigens, histamines, prostaglandins, bilirubin, xenobiotics, etc.), pathogenic bacteria, and their toxins.

In the cases mentioned above, the mechanism of sorption is related to both direct and indirect effects. The therapeutic-chemical classification of enterosorbents includes compounds such as activated charcoal, bismuth preparations, pectin, kaolin, croscarmellose, attapulgit, diosmectite, and their combined compositions [1, 2].

Currently, enterosorbent preparations are mainly imported into Uzbekistan from abroad and do not fully meet the needs of our country. Therefore, expanding the range of preparations with sorptive properties is an urgent task for modern pharmaceutical technology.

Based on the above, this study aims to analyze the market of enterosorbent pharmaceutical preparations and biologically active additives (BAA) registered in the Republic of Uzbekistan and to determine the potential for expanding the range of medicinal products and BAAs with enterosorbent properties using local natural

raw materials with sorptive properties, such as glauconite. The study will examine the physicochemical and adsorption properties, as well as the pharmacological properties of the natural mineral sorbent glauconite, to develop granulated and encapsulated enterosorbent forms in the future.

METHODS

The analysis of official sources of information on pharmaceutical preparations and biologically active additives (BAA) registered in the Republic of Uzbekistan [3, 4] was conducted. The object of the study was the natural highly dispersed glauconite powder extracted by open-pit mining from the sandstone of the "Changi" quarry (Parkent district, Tashkent region, Republic of Uzbekistan) and thermally processed to activate it in the laboratory production conditions of LLC "Fati-Derm." The thermal activation process was carried out in a laboratory drying oven "SHSU-M1" (Russia) at temperatures ranging from 100 to 300°C, as well as in a laboratory muffle furnace "MP-2UM" (Vilnius, Lithuania) at temperatures ranging from 400 to 800°C. Thermogravimetric studies of the sieved fraction of glauconite were conducted using a derivatograph from MOM company in the temperature range of 200-800°C with a heating rate of 10K/min.

The study of the physicochemical and technological properties of thermally activated glauconite, as well as the quality indicators of trial samples of granules and encapsulating mass of glauconite, was carried out according to the methods described in the literature [5].

RESULTS AND DISCUSSION

Currently, the State Register of Medicinal Products, Medical Devices, and Equipment permitted for use in medical practice in the Republic of Uzbekistan includes 1 pharmaceutical substance with sorptive properties and 20 pharmaceutical products and dietary supplements (BAA). These medicinal products contain enterosorbents derived from substances of 5 types: activated charcoal (4), colloidal silica (2), polymethylsiloxane polyhydrate (1), dioctahedral smectite (5), hydrolytic lignin (2), and 6 types of BAAs [3, 4]. The listed enterosorbent products are available in the form of powders (suspensions), granules, tablets, capsules, pastes, and gels [2, 3]. Among the registered enterosorbent products in Uzbekistan, the most popular are Smecta®, Polysorb MP, and Enterosgel®. For many years, enterosorbents based on wood charcoal, wood, limestone, and silica have been widely used worldwide. However, as experiments have shown, activated charcoal has the lowest sorptive activity—10 mg/g (D.A. Markelov, O.V. Nitsak, I.I. Gerashchenko, 2008). Therefore, the demand for these substances is

gradually decreasing. As a result, scientists from various countries are actively researching new promising sorptive materials with a wide range of sorptive activity [2, 5].

Given the above, a promising sorbent with a broad spectrum of action is the natural mineral glauconite.

Glauconite (Glauconite) is a potassium-containing aluminosilicate with a complex and variable composition (chemical formula - $(KNa)(Fe^{3+}AlMg)_2(SiAl)_4O_{10}(OH)_2$). Glauconite belongs to the group of hydrous micas, a subclass of layered silicates.

This relatively inexpensive natural mineral has a wide range of sorptive activity, high ion-exchange and buffering properties (depending on fractionation from 200 to 600 μm, the sorptive properties of glauconite range from 20 to 100 mg/g, and after activation using magnetic separation methods, its activity increases by an additional 45%). A large absorption area was also noted, with the specific sorption surface ranging from 0.10 to 0.16 mmol/g depending on the pH of the medium (pH 5.2-7.5). Additionally, the coating (encapsulating) properties of glauconite were studied.

The sample of glauconite mineral under study is a polydisperse powder of a dark olive-green colour, odorless and tasteless, and insoluble in water. Examination of the glauconite powder under a scanning electron microscope (SEM) showed that the particles of glauconite have an isodiametric globular form, in the shape of spheres, ovals, and kidney-like forms. A significant number of particles have an irregular shape with a bumpy, matte surface, and the surfaces of the particles are cracked. The density of the powder ranges from 2.2 to 2.9 g/cm³; the particle size after fractionation was less than 0.2 mm (84.6% = 2.2%).

Porosity plays a significant role in the sorption process, i.e., the presence of spaces between interconnected pores. Porosity is a property of solid bodies characterized by the presence of voids between granular particles, crystals, and layers. Particles of different enterosorbents differ from each other in structure and pore radius. The porosity of glauconite was determined according to GOST 30629-99, and it was found that the porosity of the glauconite fraction ranging from 200-500 μm is 22±1.8%.

Glauconites extracted from various regions of Uzbekistan have different chemical compositions (Table 1). The type of glauconite in which potassium predominates is called celadonite (for example, samples of glauconite extracted from the deposits in the Namangan region are rich in potassium ions).

Table 1
Chemical composition of glauconites mined in the republics of Uzbekistan and Karakalpakstan

| The place where the raw material is mined | Main Components, % | | | | | |
|--|--------------------|--------------------------------|------|------|--------------------------------|------------------|
| | SiO ₂ | Al ₂ O ₃ | CaO | MgO | Fe ₂ O ₃ | K ₂ O |
| Republic of Uzbekistan Parkent district Tashkent region, quarry "Changi" | 54.5 | 1.9 | 8.8 | 1.9 | 10.0 | 4.5 |
| Republic of Karakalpakstan, Krantau mine | 59.4 | 3.3 | 5.1 | 1.29 | 88.1 | 6.5 |
| Republic of Uzbekistan Namangan region | 52.0 | 3.1 | 1.3 | 1.3 | 12.0 | 8.5 |
| Russian Federation, Tambov region, Bandarsky district* | 66.7 | 6.6 | 5.14 | 1.62 | 0.28 | 2.43 |

*Glauconite is imported to the Republic of Uzbekistan.

The results in Table 1 show that the chemical composition of the main components of glauconites mined in different quarries differs significantly. The effect of temperature treatment on the quantitative

composition of the main components of glauconite was also studied (Table 2).

Table 2

Results of changes in the chemical composition of glauconite mined in the Parkent district of the Tashkent region of the Republic of Uzbekistan during the purification process

| Purification method | Main Components, % | | | | |
|---|--------------------|--------------------------------|-----|------|--------------------------------|
| | SiO ₂ | Al ₂ O ₃ | CaO | MgO | Fe ₂ O ₃ |
| Sample of purification | 54.5 | 1,9 | 8.8 | 1.,9 | 10.0 |
| After 20 minutes of heat treatment (at a temperature of 400 0C) | 54.2 | 2.0 | 6.1 | 1.6 | 10.0 |
| After 30 minutes of heat treatment (at a temperature of 400 0C) | 54.0 | 3.1 | 5.0 | 1.5 | 12.0 |

In order to study the possibility of producing oral granulated and encapsulated enterosorbent pharmaceutical preparations, the physicochemical properties of thermally activated glauconite samples were examined after heating for 30 minutes at 400°C. The results of the studies are presented in Table 3.

As shown by the results of the study of the physicochemical properties of the thermally activated glauconite substance: it is a polydisperse powder, the particles of which are isodiametric in shape (spherical grains of various sizes), olive-green in colour, odourless, tasteless, and insoluble in water. During fractionation, it was found that the majority of

the particles are less than 200 µm in size (69.84%). This indicates the need for further grinding of the substance and sieving through a sieve with a hole diameter of 150 µm.

The following properties of glauconite, such as relative density, bulk density, flowability, angle of repose, degree of compaction, and residual moisture, are within the normal range. However, the compressibility index is unsatisfactory; glauconite powder is classified as an elastic substance, and to obtain quality granules and encapsulating mass, a wet granulation process with the use of binders with high adhesive activity is required.

Table 3.

Comparative study of the physical and mechanical properties of activated glauconite and its granules and encapsulating mass

| № | Studied indicators | Unit of measurement | Results obtained | | |
|----|--|---------------------|--|---|---|
| | | | Purified and activated substance | Granules | Encapsulated mass |
| 1. | Appearance | | "Glauconite-Neo" | Granules in the form of irregularly shaped particles, various sizes, olive-green in color, odorless and tasteless, insoluble in water | Particles of various shapes and sizes, green in color, odorless and tasteless, insoluble in water |
| 2. | Fractional composition: +1000 - 1000 +800 - 800 +500 - 500 +200 - 200 +150 - 150 +100 - 100 | Mkm, % | 0,1 3,9 56,9 18,5 16,5 3,0 1,1 | 37.18 24.25 21.15 16.22 1.20 - - | 0,03 1,24 10,25 42,11 46,20 0,15 0,02 |
| 3. | Relative density | g/cm ³ | 1,26±0,6 | 1.5±0.1 | 1,4±0,1 |
| 4. | Bulk Density | kg/m ³ | 413,2±2,2 | 1232±2,2 | 678,5±1,5 |
| 5. | Flowability | 10-3 kg/s | 4,19±1,2 | 13,2±0,7 | 7,5±0,25 |
| 6. | Angle of natural repose | degree | 23,2±1,2 | 26.2±0.2 | 35,2±0,5 |
| 7. | Degree of compaction | | 1,22±0,10 | 1.07±0.03 | 2,57±0,03 |
| 8. | Compressibility | N | 26±1,5 | 37±1.7 | 36,6±1,2 |
| 9. | Residual moisture | %, (40 °C) | 2,02±1,4 | 2.04±1.8 | 2,25±1,5 |

When preparing model granules and encapsulating mass, highly effective binders were used: a 5% starch paste, 3-5% gelatin solution, 1-2% solutions of methylcellulose and sodium carboxymethylcellulose, as well as 1%, 3%, and 5% solutions of polyethylene oxide, polyvinyl alcohol, and low molecular weight polyvinylpyrrolidone. The studies determined the feasibility of using a 3% solution of low molecular weight polyvinylpyrrolidone, which ensures good binding of glauconite particles, and the resulting

granules retain their sorptive properties. For obtaining the encapsulating mass, the use of a 2% solution of low molecular weight polyvinylpyrrolidone was found to be appropriate.

CONCLUSION

As a result of the analysis of official sources of information on pharmaceutical drugs and dietary supplements, it was established that the range of enterosorbent drugs in the Republic of Uzbekistan is relatively broad: 1 pharmaceutical substance, 14

pharmaceutical drugs, and 6 named dietary supplements. These drugs are mainly available in the form of powders (42.9%), tablets (42.9%), and capsules (7.1%), as well as one original product in a sachet-paste form, "Enterosgel" (7.1%). The composition of the listed dietary supplements is diverse, and they are available in the form of powders, capsules, tablets, and syrup for drinking. Since most enterosorbent drugs are imported into the Republic of Uzbekistan, a promising direction is the study of the physicochemical properties of glauconite to develop the composition and technology for granulated and encapsulated enterosorbent oral drugs based on it.

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