

Technologies for Producing Capsules “Yuyuzin”

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Abstract

Hypertension is a disease whose main symptom is an increase in blood pressure due to neuro-functional disorders of vascular tone. Hypertension affects men and women equally. The disease usually begins after the age of 40. This is a very common pathology. It is called the disease of the fall of life, although in recent decades hypertension has become much younger.

Capsule, substance, extract, calcium Hypertension is one of the causes of disability and mortality in patients with disorders of the cardiovascular system.

One of the causes of hypertension is prolonged and frequent neuropsychological stress, prolonged stress. Hypertension very often occurs in people whose work is associated with constant emotional stress. People who have suffered a concussion often suffer from it.

The paper presents the results of the development of the optimal composition and hard gelatin capsules based on the dry extract of Jujube fruit - *Ziziphus jujuba* (jujube, jilanjiya). The formulation and technology of the single - source pharmaceutical product in the form of capsules “Yuyuzin” with antihypotensive activity was developed. As excipients used MCC, Aerosil, calcium stearate.

Keywords: *Technology, excipients, substance, capsule, antihypotensive activity.*

Introduction

More than 1 billion people on earth suffer from arterial hypertension (AH). AH remains the most common disease of the cardiovascular system in many countries. It has been diagnosed in 30% of adult population in developed countries, and it has reached 44% among men of working age, and it has reached 55-60% among people over 60 years of age. AH is the most common reason for medical appointment and administration of medications^[1].

AH is also a leading cause of cardiovascular morbidity and mortality. It has been established that the risk of Myocardial Infarction increases with an increase in blood pressure (BP). Acute cerebrovascular accident

In 95% of cases, 94% of Myocardial Infarction in women and 75% in men occur against the background of hypertension. Studies show that about 75% of elderly patients with heart failure have a background of AH. It is also the most common cause of atrial fibrillation, which occurs among other permanent forms of arrhythmias. In general, the incidence of hypertension in patients with cardiovascular pathology is 96%, and only 4% of patients do not have this background disease^[2].

One of the most important tasks of modern pharmaceutical technology is the development of dosage forms boosting to enhance the bioavailability of drugs and reduce side effects. This is achieved in various ways, among which the usage of special excipients

and technological method can be distinguished. Of the greatest interest from oral dosage forms are capsules, due to a number of advantages and positive characteristics: accuracy and uniformity of dosage, corrective ability, high bioavailability, stability, aesthetics.

Currently, much attention is paid to the search for new antihypotensive medications based on local drug raw materials. One of such unique plants growing in Uzbekistan is Jujube - *Ziziphinsjube* (jujube, jilanjija). Jujube fruits have been used as a hypotensive agent in traditional medicine [3]. The technology for obtaining a dry extract of Jujube fruits, based on Jujube fruits with a hypotensive effect, was developed at UzKFITI[4].

Objective: Formulation development and technology of the single - source pharmaceutical product in the form of capsules “Yuyuzin”

As you know, the technology of solid dosage forms of herbal preparations has its own characteristics, associated with the physicochemical properties of the starting substances, which must be taken into account when choosing excipients when establishing the regime of production operations.

The initial stage in the development of the technology for producing solid dosage forms of drugs is the study of the structural, mechanical and technological properties of active substances, depending on which the pressed material can behave differently. According to the indicators of the technological properties of the substance, it is possible to predict the types and quantities of necessary auxiliary substances, as well as the progress of the process [5].

The Jujube fruits substance we have been studying is a product of plant origin, which has a variety of physical and mechanical properties and absorbability. Absorbability plays an important role in the technology of solid dosage forms (TDLF) containing plant extract It affects the technological properties of the substance, such as fluidity, bulk, compressibility, elasticity, viscosity, ductility, which determine a number of technological parameters, such as the rate of granules formation, pressure, speed of pressing.

Our studies showed that the substance has non-positive technological parameters (Table 1).

In order to scientifically substantiate the type and amount of excipients introduced into the capsule composition and the optimal encapsulation method, the

physicochemical and technological properties of the dry extract of Jujube fruits have been studied according to the method described in the literature. The results of the experiments are presented in table 1.

Table 1: The results of the study of the technological properties of dry extract of Jujube fruits

| № | Test characteristic | UM | Results | |
|---|----------------------------|--------|---------|------|
| 1 | Grain particle size | µm,% | | |
| | +500 | | | 0.4 |
| | -500 +300 | | | 5.8 |
| | -300 +200 | | | 37.4 |
| | -200 +150 | | | 49.3 |
| | -150 +100 | | | 6.3 |
| | -100 | | | 0.8 |
| 2 | Friability | µm,% | no | |
| 3 | Angle of repose | degree | 42 | |
| 4 | Bulk volume | g / ml | 0.66 | |
| 5 | Residual humidity | % | 5 | |

As can be seen from table 1, the examined dry extract as a whole does not have satisfactory technological characteristics for the production of encapsulated dosage forms, which requires the introduction of excipients into the capsule composition.

It is necessary to choose an optimal particle size distribution for the development of a dosage form of the drug in the form of capsules.

Analysis of the dry extract showed that it contains about 5% moisture, i.e. dry Jujube fruit extract is a hygroscopic substance.

Preliminary pharmacological studies to determine the specific hypotensive activity of the dry extract of Jujube fruits showed that the optimal single dose is 0.35 g.

As a result of studying the properties of the dry extract, it was found that it is a brown powder with sweet astringent taste and distinct smell.

The following are the results of the development of the technology for producing an encapsulated dosage form of the dry extract of Jujube fruits. In addition to pharmacologically active substance, auxiliary ingredients that must be biologically indifferent are introduced into the composition of the mass for filling capsules in order to give it necessary technological characteristics, as well as to set, if necessary, biopharmaceutical properties[6].

Considering the above factors, various excipients has been used to obtain the capsules of the Yuyuzin preparation. Fillers or diluents are most often used. They give the mixture for filling capsules the necessary optimal volume. For these purposes, in the manufacture of medicine in the form of hard capsules, milk sugar, microcrystalline cellulose (MCC), dibasic calcium phosphate, crospovidone and other substances are used that allow to adjust bulk density and give the filler necessary flowability, and MCC, in addition, allows to slow down the absorption process, which is important for the prolonged action of the drug. Tamped powders break up 2 times longer than freely filled ones, but the difference becomes insignificant with the introduction of disintegrants. Aerosil, talc, calcium carbonate are used in this quality. Calcium or magnesium stearate, etc. are commonly used to impart friability. MCC, aerosil-200,

potato starch, lactose anhydride, crospovidone, calcium stearate in various proportions were tested as auxiliary substances.

Subsequently, each batch was individually moistened with 96% ethanol, 2%, 5%, starch paste, MC gel, Na-CMC, MCC, Aerosil, starch, lactose, crospovidone, calcium stearate to form the optimal wet substance. The data are shown in table 2.^[7]

As can be seen from table 2, we tested MCC, aerosil, lactose anhydride, crospovidone, calcium stearate in various ratios as auxiliary substances. Based on the results, the capsule mass had been prepared in 8 different formulations and the influence of excipients on the technological properties of the substance was determined (table 3).

Table 2: The composition of the components of the capsules Yuyuzin

| Composition, g | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---------------------------|-------|------|-------|-------|-------|------|------|------|
| Dry Peony Extract Evasion | 0.35 | 0.35 | 0.35 | 0.35 | 0.35 | 0.35 | 0.35 | 0.35 |
| MCC | 0.095 | 0.08 | 0.092 | 0.095 | 0.085 | 0.07 | - | 0.02 |
| Aerosil | - | 0.01 | - | 0.002 | 0.01 | - | - | - |
| Lactose | - | 0.01 | - | - | - | - | 0.01 | 0.01 |
| Crospovidone | - | - | - | - | - | 0.03 | 0.09 | 0.03 |
| Calcium Stearate | 0.005 | - | 0.008 | 0.003 | 0.005 | - | - | - |
| Total weight (g) | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 |

Table 3: The results of studies to determine the technological properties of the substance and masses obtained on the basis of the composition selected for encapsulation Yuyuzin

| Studied properties | Compositions | | | | | | | |
|---|---------------------|------|------|------|------|------|------|------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| Form | Brown powder | | | | | | | |
| Fractional composition, μm | | | | | | | | |
| + 500 | 42 | 50 | 45 | 40.7 | 50.4 | 48.4 | 44.4 | 50.2 |
| - 500 + 300 | 35.8 | 35.8 | 35 | 25.8 | 39.2 | 36.8 | 38.8 | 36.8 |
| - 300 + 200 | 7 | 7.4 | 6.8 | 6.4 | 7.3 | 7.0 | 6.4 | 7.4 |
| - 200 + 150 | 1.5 | 1.9 | 1.3 | 3.3 | 1.9 | 2.3 | 2.0 | 2.3 |
| - 150 + 100 | 1.1 | 1.3 | 1 | 2.3 | 1.2 | 1.3 | 1.2 | 1 |
| - 100 | 0.2 | 0.0 | 0.8 | 1.5 | 0.0 | 0.0 | 0.8 | 0.0 |
| Friability $\mu\text{m},\%$ | no | 22.1 | no | 19.8 | 24.9 | 20.2 | no | 19 |
| Angle of repose degree | 47 | 31 | 48 | 43 | 30 | 44 | 41 | 44 |
| Bulk volume (g / ml) | 0.26 | 0.39 | 0.32 | 0.28 | 0.43 | 0.40 | 0.24 | 0.28 |
| Residual humidity % | 5 | 3.5 | 4.8 | 5.5 | 3.1 | 4.5 | 5 | 4.1 |

The analysis of the physicochemical properties of the capsules was carried out in accordance with the requirements of National Pharmacopeia, vol. XI. The results of the analysis showed that of the 8 investigated compounds, the most satisfactory results were obtained for compounds 2 and 5. However, taking into account the presence of the production of excipients in the Republic of Uzbekistan, composition 5 has been selected as the most suitable in the future for organizing the production of Yuyuzin capsules.

To obtain Yuyuzin capsules of 0.35 g each, to 37.2 g of the crushed dry extract of Jujube fruit, 9.0 g of MCC, 0.53 g of calcium stearate, 1.06 g of Aerosil are added and the mixture passes through a sieve with a hole size of 0.25 mm. Then the resulting mass in the amount of 47.7 g is moistened with 10 ml of 96% ethyl alcohol and repassed through a sieve with a hole size of 0.63 mm. The obtained granules are dried at a temperature of 45 + 5 ° C for 30-45 min to the optimal residual humidity.

The dried mass in the amount of 45.1 g is sieved through a sieve and the finished granules are transferred to the stage of filling capsules. 0.45 g "0" gelatin capsules are filled on a capsule filling machine from Pharma-ChemIndustris (India). 100 pcs capsules received.

The resulting Yuyuzin capsules of 0.45 g are packed in 30 or 60 pcs in bottle.

Ethical Clearance: No ethical approval is needed.

Source of Funding: Self

Conflict of Interest: Nil

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