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Research Article

Production Technology of Phytogranules for The Treatment of Diabetes and Evaluation of Their Quality Criteria

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Abstract

Objectives: The aim of the research work is to prepare phytogranules using inulin and pectin obtained from the tubers of Jerusalem artichoke (Bird pear or *Jerusalem artichoke - Heliantus Tuberosus*) from aqueous extract concentrate of cinnamon bark (*Cortex Cinnamomi*) and ginger roots (*Rhizoma Zingiber*), is to study its technological and physico-chemical properties.

Materials and Methods: An aqueous extract-concentrate was obtained from cinnamon bark and ginger roots with the presence of 30% ethyl alcohol by ultrasonic extraction method. An AKAY brand machine was used to crush Jerusalem artichoke tubers, calcium oxide to alkalinize the juice, 5% oxalic acid to neutralize, 95% ethyl alcohol as a precipitating agent, and acetone as a cleaning agent. On the basis of inulin, plant extracts and pectin, granules used as biological additives to food were prepared in a model YK-60 granulator with a frequency of 50 Hz using wet granulation method for the treatment of diabetes.

Results: Inulin with a whitish-gray color, well soluble in water and a yield of 28.7% was obtained from Jerusalem artichoke. A 1:2 aqueous extract concentrate was obtained from cinnamon bark and ginger roots with the presence of ultrasound in a Stegler DG 360 model device (extraction time 5 minutes, temperature 35°C, frequency 50 Hz, power 360 W). Physico-chemical properties of aqueous extract-concentrates were studied: organoleptic properties of cinnamon extract (smell-specific cinnamon smell, cherry red color), pH-5.7±0.2; density: 0.9030±0.001g/cm^3, dry residue: 2.1±0.4; organoleptic properties of ginger extract (smell-specific ginger smell, yellow color), pH-6.2±0.2; density: 0.8804±0.001g/cm^3, dry residue: 1.4±0.3. Some quality criteria of prepared phytogranules have been determined. Thus, phytogranules decompose in an acidic environment: 8±0.4 min, scattering mass: 3.57±0.01 g/cm^3, fluidity - 6.25 0.13g/sec, 0.2 mm in size when analyzing the fractional composition granule particles were 50.43%.

Conclusion: In the 3 variants developed as a result of research, the 2nd component of the phytogranules differed from the other two components due to a number of biopharmaceutical properties and had superior properties. Thus, the use of pectin, a natural polymer, as a complementary substance caused its swelling and the rapid release of biologically active substances from phytogranules and showed a high pharmacotherapeutic effect. This is due to the synergistic effect of pectin, inulin and phytoextracts.

Keywords: Type 2 Diabetes, Artichoke, Cinnamon and Ginger Aqueous Extract-Concentrate, Phytogranules, Inulin, Pectin, Quality Criteria

Introduction

Currently, conducting research in the direction of developing biologically active substances for food used in diabetes is considered one of the priority issues of pharmacy. The practical significance of the work is the development of the technology for obtaining phytogranules as a biologically active food supplement for the treatment of type II diabetes for the first time from inulin obtained from the tubers, as well as from cinnamon and ginger extracts and pectin. The prevalence of diabetes in the world population is increasing. Diabetes already affects one in ten of the world's adults - more than 537 million people, these numbers have tripled since 2000 and are estimated to reach 643 million by 2030.

According to the information of the International Diabetes Federation as of January 1, 2018, the number of diabetes patients aged 20-79 in the world exceeded 425 million, including type 2 diabetes and gestational diabetes. However, these data do not accurately es timate the actual number of patients, as they only take into account identified and reported cases of the disease. Thus, the results of a large-scale epidemiological study confirm that only 54% of type 2 diabetes is diagnosed in routine clinical practice, and in 46% of patients, diabetes is detected only through active screening. Impaired insulin secretion and insulin resistance are considered the main pathogenetic mechanisms, but the number of new defects that cause chronic hyperglycemia in type 2 diabetes is constantly increasing. The FDA has studied the prevalence of diabetes between the ages of 20 and 79 in the world and has come to the following conclusion. It is a pandemic with an exponential increase in incidence: in 2021, the number of people with diabetes was 537 million (International Diabetes Federation, Diabetes Atlas, 10th edition), and by 2045 this figure is estimated to reach 783 million. https://servier.ru/stati/saharnyiy-diabet-2-tipa-boleznobraza-zhizni/ (Figure 1).

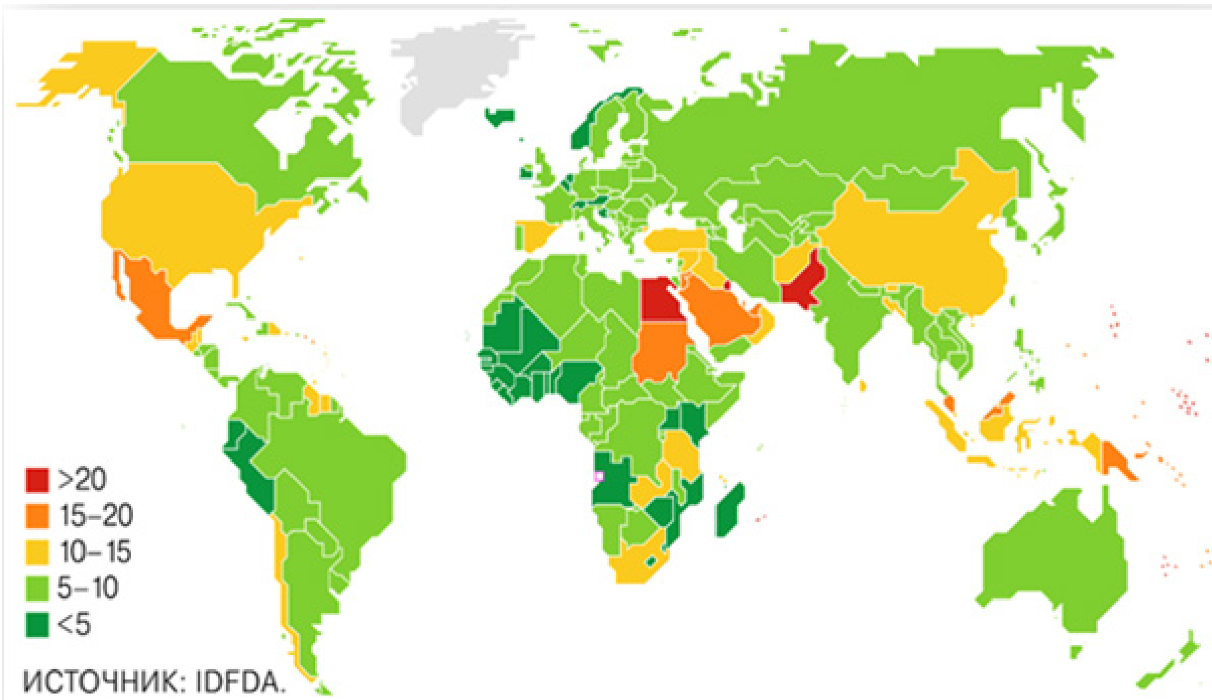

Figure 1:

Causes of Type 2 Diabetes

The key mechanism of the development of the disease is insulin resistance - the insensitivity of body tissue cells to the action of insulin, the reduction of their biological response to one or several effects of insulin at its normal concentration in the blood. Insulin resistance leads to the inability of muscle and fat tissues to absorb glucose and to the violation of glycogen synthesis (one of the main forms of "reserve" energy in the human body) in the liver. Mild hyperglycaemia with elevated fasting or postprandial blood glucose at a level below threshold for diabetes is frequently found among people with obesity, hypertension, fatty liver and elevated lipids. The International Diabetes Federation labels that risk category prediabetes. Prediabetes increases the risk of developing type 2 diabetes and even worse the risk of cardiovascular disease and fatty liver. The excessive quantity of sugar requires insulin to be moved out of the blood, more insulin is needed in type 2 diabetes with insulin resistance and when progressing, more insulin than the pancreas can produce. Chronic hyperglycaemia constantly stimulating the production of insulin poses a threat to the β-cells of the pancreas, has harmful effects on insulin producing cells, and thus, causes deficits in insulin secretion. Then starts a vicious cycle because, with impaired insulin secretion, blood sugar levels spiral out of control, hyperglycaemia worsens and exerts harmful effects on β-cells, which impairs insulin secretion even more. In addition to deficits in insulin secretion, hyperglycaemia can worsen the development of insulin resistance [1-7] (Figure 2).

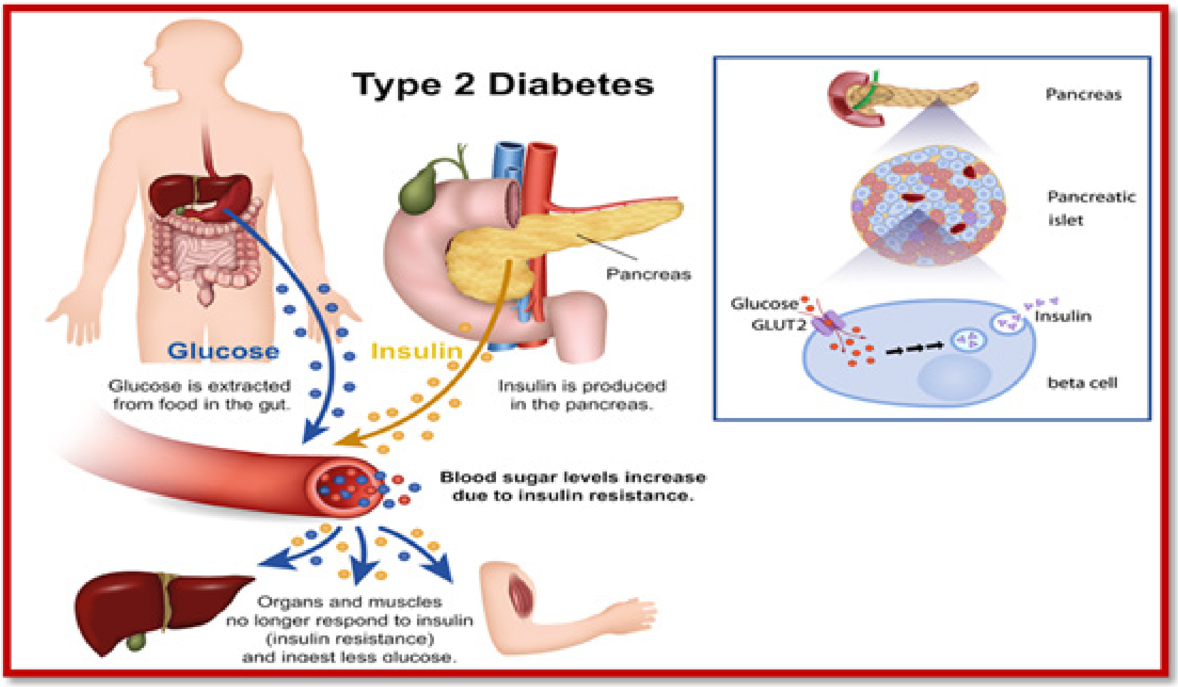

Figure 2:

In a healthy person, the insulin molecule binds to a special receptor located on the cell membrane and ensures the passage of glucose (the main source of energy) into the cell. In a patient with type II diabetes, the ability of insulin to transmit a signal for the entry of glucose into the cell is lost, as a result of which the cell cannot absorb glucose [4,6,7]. The International Classification of Diseases of the 10th revision offers the following classification of type II diabetes:

a) E11.2 - Type 2 diabetes with kidney damage,

b) E11.3 - SD type 2 with eye lesions,

c) E11.4 - type 2 diabetes with neurological complications,

d) E11.5 - Type 2 diabetes with peripheral blood supply disorders,

e) E11.6 - type 2 diabetes with other specified complications,

f) E11.7 - type 2 diabetes with multiple complications,

g) E11.8 - type 2 diabetes with unspecified complications,

h) E11.9 - SD type 2 without complications [3,6].

Despite the rapid development of the production of synthetic drugs, the demand for the production of herbal drugs for the prevention and treatment of diseases is still relevant. Biologically active compounds and herbal medicines continue to occupy an important place in modern pharmacy. Herbal medicines fully meet all modern medical and biological requirements. Their effectiveness is not inferior to drugs of synthetic origin, at the same time, they have very high bioavailability and tolerance in therapeutic doses, are characterized by a wide range of medicinal properties and have fewer side effects. This allows them to be used as symptomatic, long-term and preventive treatment in all age groups [7]. The wide spread of type 2 diabetes makes the preparation of biologically active food additives - preparations containing inulin, along with drugs for the treatment and prevention of the disease, even more urgent. According to the current definitions, "Biological food additives are natural (same as natural) biologically active substances intended for consumption at the same time as food or for inclusion in food products. Biological food supplements are more and more required tools in the nutrition of different groups of the population. To consider food supplements, they are conventionally divided into three main groups: nutraceuticals, parapharmaceuticals and probiotics [8].

Inulin is a polymer consisting of several fructose units (from 10 to 36) in the form of furanose. This polysaccharide is the second most common carbohydrate in plants after starch and is more characteristic of members of the *Asteraceae* and *Campanulaceae* families. The highest amount of inulin was found in *Arctium sp*. in the roots of plants of the Asteraceae family (burdock), *Cichorium sp*. (Candina), *Taraxacum sp*. (Dandelion), *Smallanthus sp*. (Yacon), *Inula sp*. (*Elecampane*) etc. happens. Industrially, inulin is obtained from Jerusalem artichoke and agave. Inulin synthesis in plants is regulated by several fructosyltransferase enzymes, the most important of which are genes such as sucrose: sucrose-1-fructosyltransferase (1-SST) and Fructan: Fructan-1-Fructosyltransferase (1-FFT).

Inulin, a natural polymer with a wide range of pharmacological and therapeutic effects, is also widely used in the preparation of a number of drug delivery systems. These include microcapsules, nanocapsules, microgels, etc. can be mentioned. Inulin is widely used as a food additive as a prebiotic. Consumption of inulin with food ensures the creation of optimal conditions for the development of normal intestinal microflora; causes an increase in the resistance of the digestive system to bacterial and viral infections. There is also a great demand for inulin in the country, but this diet is not produced on an industrial scale in our country. From this point of view, it is very promising for our country to start operation of inulin production plants from plant raw materials [9-12].

In the last decade, interest in the application of twin-screw granulation as a continuous wet granulation method for pharmaceuticals has increased in the pharmaceutical industry. The main advantage of twin-screw granulation is flexibility in design and output power, which allows for retrofits and production on the same machine. Therefore, in this research work, we have referred to obtaining granules by wet granulation method by performing the mixing and distribution of granulation liquid during continuous twin-screw granulation using the composition mentioned above. First, the residence time of the material in the reservoir as a function of screw speed and moisture was studied, then the granulation fluid distribution was visualized as a function of various formulation and process parameters (fluid delivery rate, fluid input method, screw configuration, humidity, and barrel filling rate). At the same time, the relationship between unit moisture content and granule size distribution was also investigated. After optimizing the screw configuration, a two-level full factorial experimental design was conducted to evaluate the effects of moisture content, screw speed, and powder feed rate on the mixing efficiency of the powder and liquid phase. Thus, it was concluded that increasing the humidity significantly improves the distribution of granulation fluid [13]. Based on the conducted scientific research, a number of pharmaceutical plants around the world are producing pre- and probiotics, which are biologically active additives to a wide variety of foods, based on pectin and inulin for the treatment of type 2 diabetes [14]. Taking into account the indicated relevance, it was considered important to conduct research in this direction.

The Purpose of The Study

One of the urgent problems facing medical and pharmaceutical science is the development of a new drug based on phytoextract, inulin and pectin for use in the treatment of type 2 diabetes.

Objects of Research

Jerusalem artichoke roots, ginger rhizomes, cinnamon sticks, pectin were used as research objects. *Jerusalem artichoke (Bird pear or Jerusalem artichoke) - Heliantus Tuberosus* - is the plant that attracts the most attention among plants that store inulin. The tubers of the plant are very rich in biologically active substances. They contain 15-35% inulin, 2.5-3.5% fructose, up to 2% protein, pectin substances, hemicellulose and fats. Tubers are also rich in minerals, including phosphorus (3.7 mg %), potassium (47.7 mg %), iron (3.7 mg %), silicon (10 mg %), calcium (3.3 mg %) and also with vitamins - carotene (12-24 mg/kg), vitamin C (42-318 mg/kg), B1 (7.6 mg/kg), B2 (0.8-3 mg/kg), PP (10.7-27.2 mg/kg), very rich in choline (1936-3100 mg/kg). The tubers of the plant have soothing, immunostimulating, general strengthening, tonic, antisclerotic and membrane stabilizing effects. It should be noted that the blood-sugar-lowering effect of tubers, which is used both in traditional and non-traditional medicine, in the prevention and prevention of diabetes, especially type 2 diabetes, is primarily related to the inulin contained in them. Therefore, the preparation of more effective food supplements based on inulin obtained from the tubers of yarrow, which can be used in the treatment of type 2 diabetes, is one of the most urgent problems of the modern era [15,16].

Cinnamon tree - Cinnamomum is one of the most recognizable spices on our planet. Its characteristic smell and taste are concentrated in its fatty part, namely cinnamon aldehyde. Calories of cinnamon vary between 247-303 kcal/100g. There are two main types of cinnamon - Ceylon (true) and cassia. The latter is more common due to its lower market price, but it also has a higher concentration of coumarin. Cinnamon thins the blood, it is included in medicines to prevent the formation of thrombus. Some experts believe that it is enough to take 2-4 g (0.5-1 tsp) of cinnamon powder per day to get the beneficial effect. However, some studies increase this dose to 6 g. The components and other antioxidants in the composition have antibiotic and immune stimulating properties. They reduce the risk of heart disease, blood sugar levels and markers of inflammation. Antioxidants (polyphenols) contained in cinnamon limit the activity of free radicals and prevent or reduce their harmful effects. In this way, cinnamon reduces the risk of many deadly diseases and has an anti-aging effect. Research has shown that cinnamon has superior properties to other food additives, even oregano and garlic, and these properties allow it to be used as a natural preservative. Cinnamon extract has been showing a prebiotic effect in the treatment of gastrointestinal diseases for a long time, it is used to eliminate symptoms such as flatulence, indigestion, it ensures the growth of beneficial bacteria in the intestine, and it prevents the development of pathogenic bacteria. As a preventive measure, cinnamon extract reduces the growth of cancer cells and the formation of blood vessels in tumor cells. The mechanism of action of cinnamon in this field has not been fully studied, but scientists have clarified that the plant is toxic to cancer cells and destroys diseased tissues without affecting healthy tissues. Studies have already confirmed the effectiveness of cinnamon extract in the fight against colorectal cancer and leukemia. Fights infections, fungi, viruses - the nutritional supplement contains useful cinnamon aldehyde. The antimicrobial effect of substances contained in cinnamon prevents the development of respiratory tract infections and salmonella from food bacteria, eliminates bad breath, caries, and most importantly, research conducted in the fight against the HIV-1 virus strain revealed that cinnamon has a more effective effect in the fight against the virus. Diseases of the central nervous system - Parkinson's disease, Alzheimer's disease, etc. - associated with death of nerve cells, atrophy of brain and spinal cord cells.

Cinnamon stops the activity of the protein that causes these pathologies, protects neurons and nerve connections. Animal studies have confirmed that cinnamon significantly improves neurodegenerative diseases. Just 120 mg of the spice per day is enough to prevent the development of most heart problems. A small portion reduces blood pressure, "bad" LDL cholesterol, triglycerides and stabilizes "good" HDL cholesterol levels. Another important feature of cinnamon is that it lowers blood sugar and has a positive effect on type 2 diabetes. Cinnamon powder slows down the breakdown of carbohydrates by affecting certain enzymes of the pancreas. It also prevents metabolic syndrome, insulin resistance and mimics the effects of the hormone. Several studies have confirmed that after taking 1-6 g of spices, blood glucose concentration decreases by 10-29% [17].

Medicinal ginger (*Zingiber officinale Roscoe, Zingiberaceae L.*) is a plant widely used in folk medicine in Southeast Asia. Ginger is grown in all tropical regions of the world and is more common in Southeast Asia, especially in Malaysia. The main producer of ginger is Jamaica. Ginger was first scientifically studied by the English botanist William Roscoe in 1807. The sour aroma of ginger is due to the presence of essential oils in its composition (from 0.5% to 3%), its sharp burning taste is due to the presence of the phenolic compound gingerol. Since ancient times, ginger has been valued for its ability to relieve headaches, heart and rheumatic pains, fatigue and apathy; in subsequent studies, the use of medicinal ginger as an antioxidant and in the treatment of cancer was investigated.

The value of medicinal ginger as a raw material is determined by the presence of flavonoids of various nature. In addition, ginger also contains beta-carotene, capsaicin, caffeic acid, and curcumin. Medicinal ginger contains a number of essential amino acids (tryptophan, threonine, leucine, methionine, phenylalanine, valine), magnesium salts, calcium and phosphorus, and a complex of vitamins. Ginger flavonoids are used in medicine as choleretic, hepatoprotective, anti-ulcer and capillary wall strengthening agents. The combination of low toxicity and high pharmacological activity makes them extremely promising for the prevention and treatment of a number of serious diseases. The component composition of non-volatile phenolic substances of ginger roots consists of the following compounds: the dominant substance 6-gingerol (about 48.2%), 8-gingerol and 10-gingerol gallic acid (21.5%) are present in smaller amounts, chlorogenic acid (14, 2%), caffeic acid (14.2%). Of the different chain length gingerols in the plant, 6-gingerol is the most important.

As a result of research, it was determined that it inhibits cyclooxygenase, lipoxygenase, prostaglandin synthesis; blocks TRPV1-receptors; stops the synthesis of substances that inhibit the intracellular synthesis of proteins, as well as collagen synthesis in the extracellular matrix; inhibits angiogenesis; blocks serotonin receptors; increases oxygen consumption by cells; has a cardiotonic effect; reduces colonic peristalsis. The total content of phenol compounds in ginger rhizomes is equal to 157 mg/100 g in fresh rhizomes. From the terpinoids in ginger rhizomes: terpenes (α-phellandrene, camphene), terpene alcohol (linalool), terpene aldehydes (citral, nonanal), sesquiterpenoids (α-, β-, γ-bisabolin), sesquiterpene alcohol (farnesol), 4-amino oil acid. Among the organic acids, ginger rhizomes contain oxalic and succinic acids. Other components of the chemical composition: amino acids, proteins, proteolytic enzymes, lipids (6-8%), sterols, fibers, vitamins (*ascorbic acid*, *niacin*, *thiamin*, *riboflavin*, etc.), starch (up to 50%, mucus, there are monosaccharides, inorganic substances. In addition, ginger rhizomes contain the following compounds: kaempferol, rutin, naringenin, catechin, epicatechin, saponins and alkaloids. Biologically, the quantity and quality of active substances in ginger rhizomes vary depending on cultivation conditions, harvesting period, storage conditions and technology. Scientists I.A. While analyzing the composition of biologically active substances in ginger rhizomes, Kharchilava discovered the following groups of compounds during chemical analysis: gingerols - 2.3%; tannins (gallic, chlorogenic and coffee acids) -1.96%; flavonoids (luteolin-7-glycoside, ferulic acid and hyperoside); organic acids (oxalic, succinic, malic) 0.75%; polysaccharides (maltose, lactose, glucose and xylose) 17.68% in terms of glucose; terpene compounds (geraniol, bornyl acetate, α-pinene, β-pinene, citral and cineole). Ginger rhizomes contain significant amounts of gingerol, shogaol and dehydrogingerdiones. Chogols and dehydrogingerdiones make up a smaller proportion because they are biogenetically only by-products of gingerols.

During drying and storage of ginger rhizomes, gingerols are partially dehydrated to the corresponding shogaols, which can then be converted to paradols, gingerdiones, gingerdiols, and gingerdiol acetates. During the drying process, 6-gingerol is converted to shogaols. In accordance with the requirements of the European Pharmacopoeia (EPh) 8.0 and USP 38 ginger root according to the standards gingerdiols and gingerols at least 0.8%, the content of shogaols (not more than 0.18%), essential oil (1.8 ml per 100 g not less than), starch (at least 42%), alcohol-soluble extractives (not less than 4.5%) and water-soluble extractives (not less than 10%) it is necessary to ensure the standard composition of active components [18,19]. Pectin is a gum found in many plants, but mainly found in citrus fruits (oranges, lemons, grapefruit) and apples. During ripening, pectin becomes a more water-soluble component than an insoluble substance. Pectin is a linear polysaccharide containing about 300-1000 monosaccharide units, mainly d-galacturonic acid and some polysaccharides. d-galacturonic acid molecules are linked by α-(1→4)-glycosidic bonds. Galacturonic acid residues in pectin can be esterified with methyl groups. There are different types of pectins. A pectin in which more than 50% of the galacturonic acid residues are esterified is called high methoxy or HM pectin. Pectin in which less than 50% of the galacturonic acid residues are esterified is called low methoxy or LM pectin. Pectin is widely used in the food industry as a gelling agent to create a gelled texture in foods, and it also has hypocholesterolemic properties. Scientific studies on rats have shown that pectin reduces blood glucose and triglyceride levels. Pectin also reduced the volume of edema and the release of myeloperoxidase (0.1-100 μg/mL). It also significantly reduced neutrophil infiltration and partially reduced immunostaining for tumor necrosis factor-α and inducible nitric oxide synthase. The anti-inflammatory properties of pectin further prove that it has anti-diabetic activity [14, 20,21].

Research Methods

Aqueous extract-concentrate was obtained from ginger roots and cinnamon sticks by ultrasonic high-speed extraction method. The extraction was carried out in an ultrasonic High-Speed Disperser, a modified method of the maceration method. Wet granulation method was applied during the preparation of granules. The quality criteria of phytoextracts and developed phytogranules were fulfilled according to the methods specified in the relevant pharmacopoeia articles. Fractional composition was performed by sieve analysis method. Developing the technology of obtaining the finished form of the drug, pharmacists pay special attention to the study of the fractional composition of the substances of powders, auxiliary substances, dyes, fillers, because they are the main components of many medicines. In this process, every detail is important and can affect the final result. Therefore, all devices, sampling methods, as well as their grinding and analysis must meet the standards.

Study of fractional composition. Fractional (granulometric) composition is an important pharmaco-technological property of powdery pharmaceutical substances. Indicators that are affected by the fractional composition: Fluidity, bulk density, dosage accuracy, level of granulation and pressing, qualitative characteristics of the preparation (appearance, dissolution, homogeneity by mass, content of the active substance, etc.), production safety parameters - dust formation, and finally, bioavailability and pharmacological efficiency of ready-made medicinal forms [22-26].

Results and Their Discussion

The Course of The Technological Process

Technology of extracting inulin from roots and rhizomes. In November, the freshly collected roots and rhizomes are washed clean with water and dried after cleaning them from other impurities. After some round crushing, it was crushed in the AKAY brand shredder. The crushed mass was filtered through 4 layers of filtration into a clean container and the juice was separated. It is then alkalized with calcium oxide. The processed sediment is removed by filtering. The filtrate is treated with 5% oxalic acid until a neutral reaction is obtained. The neutralized solution is treated with 95% ethyl alcohol, the separated precipitate is filtered, and the residue remaining on the filter is washed several times with alcohol. The precipitate is placed in another clean container and dissolved in a small amount of purified water, then treated with acetone. At this time, inulin is separated in the form of a precipitate. Purified inulin (28.7%) is obtained by repeated precipitation with acetone. Inulin is a whitish-gray powder that is very soluble in water (Figure 3).

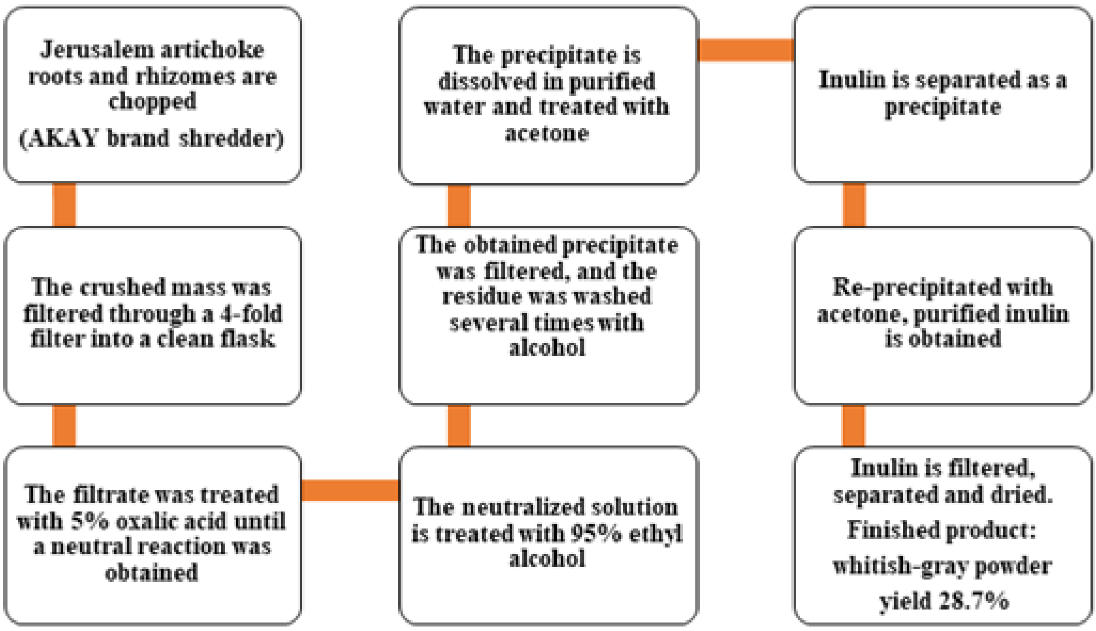

Figure 3: Technology of obtaining purified inulin.

Preparation of Aqueous Extract-Concentrate from Ginger Roots

A 1:2 aqueous extract-concentrate was prepared from ginger roots.

Production technology of extract-concentrates

It is known that concentrated extracts are the starting material or preparations for making infusions and decoctions. They can be liquid or dry. Low-concentration (20-40%) water-alcohol solutions are used in the composition of the substances extracted for their preparation to bring them closer to aqueous extracts. Liquid extract concentrates are water-alcohol extracts, which are obtained in a 1:2 ratio of raw materials. Dry extract-concentrates are prepared in a ratio of 1:1.

For this purpose, 50 g of plant raw materials were weighed on an electronic scale and transferred to a chemical beaker with a volume of 1000 ml. 175 ml of 30% ethyl alcohol was added to it. The volume of the solvent was calculated according to the formula V=V1+PK. V= V1+PK= 100+ 50 x1.5=175 ml. The extraction process was carried out for 7 minutes in the Stegler DG 360 model device in the High Speed Disperser with the presence of ultrasound (extraction time 5 minutes, temperature 35°C, frequency 50 Hz, power 360 W). The obtained extract was filtered, the plant residue was compressed. The compressed plant residue was placed in a clean chemical beaker, 100 ml of 30% ethyl alcohol was added to it, and the extraction process was carried out in the previous order. Extracts were combined. It was stored at 8°C for 3 days, filtered through a paper filter into a clean flask, evaporated until an aqueous extract was obtained in a vacuum-evaporator, and its physicochemical properties were determined (Table 1).

Table 1: Some physico-chemical properties of the aqueous extract-concentrate obtained from the roots and rhizomes of ginger.

Organoleptic Properties	pH	Density, g/cm³	Dry Residue, in %
Yellowish-brown color, delicate ginger smell, bitter taste	6,2±0,2 Min-max 6,2-6,4	0,8804±0,001 Min-max 0,8804-0,8809	1,4±0,3 Min-max 1,4-1,7

Preparation of Aqueous Extract-Concentrate from Cinnamon Tree Barks

Aqueous extract-concentrate of cinnamon barks is prepared in a ratio of 1:2. For this purpose, 50 g of cinnamon sticks were weighed on an electronic scale, crushed in a mortar and transferred to a chemical beaker with a volume of 1000 ml. 175 ml of 30% ethyl alcohol was added to it. The extraction process was carried out as described above. The volume of the extractant was calculated as follows. V=V1+PK= 100+ 50 x1.5=175 ml. Further operations were continued as in ginger extract. Some physicochemical properties of the aqueous extract-concentrate obtained from cinnamon sticks are given in (Table 2).

Table 2: Some physico-chemical properties of aqueous extract-concentrate obtained from cinnamon sticks.

Organoleptic Properties	pH	Density,g/cm³	Dry Residue, in %
Cherry-brown color, specific cinnamon smell, burning taste	5,7±0,2 Min-max 5,7-5,9	0,903±0,001 Min-max 0,9030-0,9033	2,1±0,4 Min-max 2,1-2,5

Phytogranules Production Technology

Preparation of biologically active food supplement - granules based on purified inulin was carried out by wet granulation method. For this purpose, 40 g of inulin is mixed with 53.5 g of pectin in the mortar. The mixture is moistened with the aqueous extract-concentrate of cinnamon barks and ginger rhizomes, which we prepared in advance in a ratio of 1:2 (taking 3.75 ml of each). That mass is granulated by passing through the granulation machine. The received granules are dried at a temperature of 45-50°C. Some technological properties of phytogranules have been comparatively studied. The obtained results are shown in (Table 3).

Table 3: Composition of phytogranules and some technological indicators.

Contents	I	II	III
Aqueous extract-concentrate of cinnamon	3,0	3,75	3,2
Aqueous extract-concentrate of ginger	2,5	3,75	3,5
İnulin	40	40	40
Sorbitol	-	-	Quantity required
Lactose	Quantity required	-	-
Pectin	-	Quantity required	-
Description	Brown color, specific smell	Light-brown color with specific smell	White color, specific smell
Moisture absorption,%	2,23±0,01	2,58±0,04	2,95±0,02
Decomposition in acidic environment, min	12±0,6	8±0,5	10±0,5
bulk mass, g/cm³	3,44	3,57	3,89
Fluidity, g/sec	6,16±0,14	6,25±0,13	6,46±0,12
Particle size, mm	0,2-0,3	0,3-0,5	0,6-1,0

As can be seen from the table, the optimal phytogranules are considered the 2nd ingredient. During the comparative studies, it became clear that the decomposition of 1-component granules in an acidic environment was 12.0±0.6 min; 2nd ingredient 8.0±0.5 min; Granules with the 3rd follow-up occur within 10±0.5 minutes. It should be noted that one of the positive aspects of the preparation of granules using pectin is that it lowers the concentration of sugar in the blood. This is explained by the increase of synergistic effect together with inulin and phytoextracts.

Study of Biopharmaceutical Properties of Phytogranules In *In Vitro* Experiments

The study of biological absorption of drugs is one of the important stages of research, which allows to substantiate the pharmacotherapeutic effect of the selected composition. The study of biological assimilation of phytogranules was carried out *in vitro* experiments ("Rotating basket") according to the "Dissolution test" method. Here, the pH of the environment, the speed of rotation of the basket, etc. affect the separation of the medicinal substance from the granule. such factors influence. We comparatively studied the release rate of the medicinal substance from the granule in the 3 ingredients we prepared. Studies have been continued in the direction of developing the optimal conditions of the "dissolving" test. For this purpose, water, artificial gastric medium (pH-1.2: water-1000 ml, hydrochloric acid-3 ml, pepsin-1.5 g) was used. The research work was carried out in a "rotating basket" device with 5 g of phytogranules, 200 volume/min rotation speed, and 1000 ml of solvent volume. 5, 10, 15, 20, 25 minutes after the device was started, samples (25 ml) were taken from the solutions passing biologically active substances and fresh solutions were added to the dialysate. Thus, according to this procedure, a sample of the dialysate was taken and the amount of biologically active substances released from the granules and transferred to the dialysate was determined. The determinations were repeated 5 times. Each of the samples taken for this is concentrated in a porcelain bowl until a dry residue is obtained and its weight is determined. Experiments were performed separately for each composition. The obtained results are given in (Table 4).

Table 4: The rate of separation of active substances in different compositions from phytogranules.

Release time of Active Substances, Min	Amount of Active Substances, in %		
	I Composition	II Composition	III Composition
5	22,48	28,56	21,33
10	57,34	70,37	54,71
15	73,53	100	69,93
20	100	-	95,18
25	-	-	100

As can be seen from Table 4, 100% of active substances are separated from component I in 20 minutes, 100% from component II in 15 minutes, and 100% from component III in 25 minutes. The different rate of separation of medicinal substances from the 3 investigated ingredients occurs depending on the amount of excipients in the composition. This also affects the completeness and intensity of separation of the active substance. Thus, complete separation of active substances occurs in component II, which causes it to show a high therapeutic effect. It became clear from the researches that complete disintegration of granules in a liquid environment takes place within 10-15 minutes. This, in turn, plays an important role in the emergence of the blood sugar effect of the phytogranules used in a very short period of time.

After that, the study of storage conditions and suitability of phytogranules with optimal composition was carried out. Phytogranules prepared for this purpose were placed in orange glass vials (2 g each), technological properties were checked on the first day and recorded in the table. Then, every 4 months, the changes in the technological properties of the phytogranules were studied. The obtained results are given in (Table 5).

Table 5: Studying the stability of phytogranules (n=6).

Technological Indicators	For Months						
	4	8	12	16	20	24	25
Inulin quantity, in %	5,0 ±0,03	5,0 ±0,03	5,0 ±0,03	5,0 ±0,03	5,0 ±0,02	5,0 ±0,02	4,81±0,02
Moisture absorption,%	2,58±0,04	2,58±0,04	2,58±0,04	2,58±0,04	2,58±0,04	2,58±0,04	2,75±0,03
Decomposition in acidic environment, min	8±0,5	8±0,5	8±0,5	8±0,5	8±0,5	8±0,5	9±0,5
Spreading mass, g/cm^3	3,57±0,01	3,57±0,01	3,57±0,01	3,57±0,01	3,57±0,01	3,57±0,01	3,42±0,01
Fluidity, g/sec	6,25±0,13	6,25±0,13	6,25±0,13	6,25±0,13	6,25±0,13	6,25±0,13	6,14±0,13
Particle size, mm	0,2	0,2	0,2	0,2	0,2	0,2	0,2

As can be seen from the table, prepared phytogranules remained stable for 2 years and did not undergo any physico-chemical changes. However, in the following month, some changes were observed in the phytogranules (in the amount of active substance, moisture absorption, scattering mass, etc.).

Conclusion

As a result of the conducted research, the technology for the preparation of phytogranules for the treatment of type 2 diabetes was developed. First, Jerusalem artichoke tubers were studied. White inulin, which is well soluble in water, with a yield of 28.7% was obtained from Jerusalem artichoke tubers using an efficient technological method. In the subsequent operations, aqueous extract-concentrate was obtained from cinnamon bark and ginger roots with the presence of ultrasound. Some criteria have been studied in these extracts. Thus, the organoleptic properties of cinnamon extract (smell-specific cinnamon smell, cherry red color), pH-5.7±0.2; density: 0.9030±0.001g/cm3, dry residue: 2.1±0.4; organoleptic properties of ginger extract (smell-specific ginger smell, yellow color), pH-6.2±0.2; density: 0.8804±0.001g/cm3, dry residue: 1.4±0.3. Finally, phytogranules, an effective drug for the treatment of type 2 diabetes, have been developed. Wet granulation method was applied in the process. Phytogranules were prepared in 3 variants. During the technological process, 3 types of phytogranules were prepared using sorbitol, lactose and pectin as complementary substances. It became clear from the comparative experiment that the release of biologically active substances from phytogranules made with pectin in an acidic environment occurs faster (100% in 15 minutes). At the same time, phytogranules with this content were decomposed in an acidic environment for 8 minutes. When the fractional composition of phytogranules with optimal composition was studied according to the known methodology, it was found that phytogranules passing through a sieve with a hole diameter of 20 microns make up 50.43%. Also, flowability of phytogranules was determined as -6.25 ± 0.13g/sec and scattering mass - 3.57±0.01 g/cm3. The stability of phytogranules with optimal composition intended to be used for the treatment of diabetes was studied according to individual parameters and it was found that these granules can remain stable for 2 years. The production technology of granules with high biopharmaceutical properties is considered convenient for patients of all ages in terms of easy and convenient administration. It can be hoped that the production of phytogranules proposed as a biologically active food additive in the local pharmaceutical industry will contribute to the elimination of the current problem.

Acknowledgements

None.

Conflict of Interest

None.

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