FOOD PRODUCTION TECHNOLOGY

STUDY OF ORGANOLEPTIC, PHYSICAL-CHEMICAL AND TECHNOLOGICAL PROPERTIES OF THE PLANT ANALOGUES OF PHARMACEUTICAL GELATIN PRODUCTION FOR SOFT CAPSULES

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Abstract: Factors causing the urgency of developing technology of capsules based on non-traditional raw materials, which are mainly plant analogues are considered. Carboxymethylcellulose (CMC), starches, agar, hydroxypropyl methylcellulose (HPMC) are those of economic viability due to cheaper raw materials, consumer demand for the encapsulated drugs and biologically active additives (BAA). New different characteristics that satisfy a wide range of consumers, including those who do not use animal products for religious and / or behavioral (vegetarians) reasons are presented. In the course of studies complex characteristics of organoleptic, physical- chemical, optical, buffering, rheological and structural-mechanical properties, chemical reactivity indices of plant analogues of pharmaceutical gelatin, and combinations thereof to produce capsules were determined. The tested plant analogues of pharmaceutical gelatin for capsules exhibit the properties of weak electrolytes. Active amount of titratable groups in plant analogues of pharmaceutical gelatin from agar and HPMC is small, that makes the contribution of these compounds impossible when predicting the properties of the acid-base complex mixtures or solutions. Plant analogues of pharmaceutical gelatin from starches exhibit sufficiently strong buffering properties, the average number of active groups in a 1% starch solution being 1.9 mM, and the solution's pKa of plant analogues of pharmaceutical gelatin from pectins in the range from 4.3 to 4.9 pH units respectively. Solutions of plant analogues of pharmaceutical gelatin from carrageenans are chemically unstable in the presence of acid in the solution. Acidity tests showed, that among the studied samples of plant analogues of pharmaceutical gelatin from starch all the starch samples proved to have satisfactory characteristics. The complex properties of plant analogues of pharmaceutical gelatin were examined and the possibility of using plant analogues of pharmaceutical gelatin for soft capsules was proved.

Keywords: Capsules, plant analogues of pharmaceutical gelatin, physical- chemical properties of hydrocolloids, microbiological parameters

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INTRODUCTION

Market analysis of encapsulated drugs and biologically active food additives (BAA) suggests close attention of capsule manufacturing companies to seek alternatives to traditionally used gelatin. This trend is based on the laws of development of the global consumer market: economic viability due to cheaper raw materials, consumer demand for the encapsulated drugs and dietary supplements with new and diverse characteristics that meet a wide range of needs, including those who do not use animal products for religious and/or behavioral (vegetarians) motives. All these factors cause the urgency of developing technology of capsules based on non-traditional raw materials, which can act as the composition of the hydrocolloids of plant origin [1].

This project aims to develop technological operations for obtaining of plant analogue of pharmaceutical gelatin and capsules out of it. Selection of materials for the production of pharmacological capsules must be based on the safety requirements for such products, technological requirements for raw materials at the production stage and basic requirements for capsules themselves – effective delivery and release of the drug or biologically active substance in a given location of gastrointestinal tract (stomach, gut). Ideally, the properties of the capsule as a vehicle for medicinal substances should facilitate the minimization of side effects of drugs, and, if necessary, prolong the effect of the drug due to its gradual release. Plant hydrocolloids – carboxymethylcellulose, sodium alginate, hydroxy-propyl methyl cellulose are used as raw materials and components to produce capsules in this project. The complex characteristics of raw materials to be used is a necessary step for the technology development of capsules production out of these components, including:

– organoleptic characteristics, physical-chemical properties and safety performance;
– analysis of the stability of raw materials and components for different operating conditions (temperature, pH, and others);
– characterization of the rheological properties of aqueous solutions of components, as this parameter is crucial for the preparation of capsules with the walls of specified and uniform thickness;
– analysis of the conditions of gelation (pH, temperature, concentration of the gelling agent, and others);
– analysis of gel dry conditions, structure and properties of resulting polymer films.

Natural hydrocolloids are widely used in the pharmaceutical and food industries for stabilizing of cultures, reducing weight loss of the feedstock, improving consistency and for preventing "oedema" products. Currently, carboxymethylcellulose, sodium alginate, gelatin, collagen, and hydroxypropylmethylcellulose are widely used [2, 3].

The finished product, consisting of biopolymers and mixtures thereof (including capsule walls) in the first approximation can be considered as a gel-like culture with a complicated distribution of water molecules. According to one known definition of a gel, it is a structured culture "polymer-solvent" with a stable system of bonds, which does not flow under its own weight. Gels are complex multicomponent cultures containing high-molecular substance (s) and low molecular weight liquid (water). Solutions for capsules usually contain from 80% to 90% water, gelling agents are mostly proteins, polysaccharides or mixtures thereof. The elastic properties of gels are due to the formation of the spatial network of interacting macromolecules-gelling agents or their units [4].

The study of individual components in real multicomponent gel cultures is a great challenge nowadays. The functional properties of polymer suspensions depend on pH, temperature, particle size and the nature of their surface, as well as the content of salts, lipids and other components. Thus, the practical application of biopolymers in real multicomponent cultures requires an assessment of a wide range of physical-chemical and functional properties.

The conditions of liquid – gel transfer system have great importance for the use of plant pharmaceutical analogues of gelatin. These conditions should provide sufficiently rapid gelation process under control. Methods of thermotropic gel formation are mostly suitable for bulk products (three-dimensional network of the gel). Due to the relatively low rates of diffusion of metal ions in the solutions of biopolymers ionotropic gelation processes are most effective in obtaining single- and two-dimensional gels, fibers and films [5, 6].

The scientific and technological research was carried out according to the Treaty №1, dated 01.01.2013 on the implementation of research, technological works with the Supplement №1 dated 02.13.2013 under the Integrated Project "Development of technology and organization of high-tech industrial production of pharmaceutical gelatin and its analogues for medicinal capsules" by the decision of the Government of the Russian Federation № 218, Phase 3.

The aim of this study was to determine the organoleptic, physical-chemical, optical, rheological, structural and mechanical properties of plant analogues of pharmaceutical gelatin for soft capsules, their complex characteristics.

OBJECTS AND METHODS OF STUDY

The main objects of research in the process of plant analogues production of pharmaceutical gelatin were [7, 8]: carboxymethyl cellulose, hydroxypropylmethyl cellulose, starch, agar, pectin, carrageenan.

Commercial preparations for plant analogues of pharmaceutical gelatin are presented in Table 1.

Table 1. List of components used to produce plant analogues of gelatin

Designation	Name
Starch	
K1	Nutritional supplement acetylated distarch adipate «C'Tex 06201», Cargill BV (Czech Republic)
Pectin	
P1	Pectin APS 105 (China)
P2	Apple pectin (Russia)
Carrageenan	
Ca1	Iota-carrageenan, half-refined LLC "Nord Plus" (Russia)
Agar	
A1	Agar type QP, Panreac (Belgium)
A2	Agar, Helicon (Russia)
Carboxymethyl cellulose	
C1	CMC (Ukraine)
Hydroxypropylmethylcellulose	
H1	HPMC (Netherlands)
H2	HPMC (Germany)

This paper presents the results of studies of plant analogues of pharmaceutical gelatin.

The main and supplementary raw materials for obtaining of plant analogues of pharmaceutical gelatin and subsequent manufacture of medicinal capsules were packed in polyethylene PE2NT 76-17 and polyethylene PE2NT 22-12. To study the organoleptic and physical-chemical properties of raw materials for the production of plant analogues of pharmaceutical gelatin there were used: temperature sensor, the reference module, open top UV quartz cell 10 mm, calcium Ca, Uncoded HC Lamp.

The mass fraction of water was determined using a thermostat COP-65 and analytical balance ATL-220-d4-1 (Acculab, USA). The mass fraction of total ash was determined using a muffle furnace PL 10/2.5 (Russia) and analytical balance ATL-220-d4-1 (Acculab, USA). To determine the mass fraction of nitrogen analytical balance ATL-220-d4-1 (Acculab, USA), digester D8 (Foss Tecator, Sweden) and a semi-automatic nitrogen / protein analyzer Kjeltec 8200 (Foss Tecator, Sweden) were applied. In order to predict the properties of the capsules produced from the initial compounds it is necessary to investigate the stability of pharmaceutical gelatin in solutions against the influence of acids and

alkalis, as well as their buffering properties. As a result it will be possible to estimate the average number of reactive groups per gram of dry matter component. Buffering capacity of obtained solutions depends directly on this characteristic. Buffering capacity is the amount of strong acid or alkali, which must be added to the test solution to displace the pH by one unit. In this case, the buffering capacity is determined by the minimum of the two values obtained by titration: titration with acid or alkali.

Another no less important in the practical aspect, value determined in the course of research, was the stability of compounds with different values of pH units. In this case, during the test a certain amount of acid and then an equivalent amount of alkali were added to the solution of a substance. If the pH value of the final solution proved similar to that of the initial solution, then, it showed the reversibility of the reactions. In other words, the test substance was chemically inert in the studied range of pH units. If there were differences between the values of the initial and final pH solutions, it indicated that the chemical substance was changed during the experiment and therefore was not stable in the range of studied pH units. The use of such substances in the industrial process with the unstable environment presented a number of difficulties.

The following reagents were used in the study: deionized water MillyQ, hydrochloric acid (Sigma Tek, highly pure, Russia), and sodium hydroxide (Sigma Aldrich) [9].

Hydrochloric acid was used as a 0.1 M solution in deionized water, sodium hydroxide - in a 0.1 M or 0.4 M solutions in deionized water. Dependences of pH solutions of the components to obtain capsules on the concentration of added acid or alkali were determined for polymer solutions whose concentrations are given in Table 2.

Table 2. Test solutions of gelatin and its analogues

Name of plant analogues	Designation of plant analogues	Concentration of alkali	pH of the solutions of plant analogues
Carboxymethylcellulose (Ukraine)	C1	0.3	1.2
Hydroxypropylmethylcellulose (Netherlands)	H1	0.5	1.5
Hydroxypropylmethylcellulose (Germany)	H2	0.5	1.5
Carrageenan (Russia)	Ca1	0.5	1.5
Agar (Belgium)	A1	0.5	1.5
Agar (Russia)	A2	0.5	1.5

These plant analogues of gelatin were dissolved in deionized water, then heated with stirring to 60°C and their solution was stirred vigorously on a magnetic stirrer for 30 min. After that, the bottle with the solution was placed in a water bath for 30 min, the solution temperature being between 97 to 100°C. The solution was then stirred vigorously on a magnetic stirrer for 30 min more, while maintaining the solution temperature at 60°C.

The pH values of the solutions were recorded continuously using a pH-meter S20 (Mettler Toledo, Switzerland). During the measurement, the test solution was constantly stirred with a magnetic stirrer (Biosan, MMS-3000). Hydrochloric acid solution was added with an automatic pipette, 1 ml. The solution of alkali was added with a syringe Hamilton. The portion of added alkali solution ranged from 10 to 25 microliters.

The general scheme of the experiment was the same for all test solutions. 15 ml of the test solution was placed in a glass weighing bottle, the electrode was dipped in a solution and mixing began. Mixing intensity was to form a funnel in the solution. The pH value was fixed. A 0.1 M solution of hydrochloric acid was added and pH value was fixed again. After that, portions of sodium hydroxide solution were successively added, and pH value was then fixed. Alkaline solution titration was continued until the pH value of the resulting solution exceeded 10.5.

The pH values of HPMC and CMC solutions were measured at room temperature (22 to 26°C), those of agar solution - at the temperature from 45 to 60°C. At lower temperatures, these materials form gels, and this prevents pH value and buffering capacity determination of the respective components. The pH-meter was equipped with a sensor and a temperature compensator, which provided the correct definition of the pH value in a wide range of temperatures. The results were evaluated using the program Origin 7.5.

The pH value of the test substance solution depends both on the chemical nature of the substance and its concentration, and may vary greatly. This must be considered when creating blends for capsules.

Before titration hydrochloric acid was added to the experimental solution, thereby shifting the pH value in the acidic region. Thereafter, the resulting solution was titrated with sodium hydroxide.

In the present study, when dealing with the concentration of components in the solution, it is advisable to operate with the mass fraction of the component in the solution, w%. Using such a value is justified from the point of view of practical approach, since the studied components are not uniform at the molecular level.

Nevertheless, the mass fraction of substance in the solution directly reflects its buffering properties, determines the average number of active functional groups per unit weight of the component. Analysis of titration curves allows the concentration of active groups to be determined. Thus, the number of active groups should be directly proportional to the concentration of test component in the solution [10].

The spectrophotometer Cary 50 For was used for detection of transparency at a wavelength of 650 nm.

The work was conducted by testing plant analogues of pharmaceutical gelatin to obtain capsules in terms of chemical and microbiological safety. Raw materials and components for the production of plant analogues of pharmaceutical gelatin were tested for heavy metals and toxic elements, radionuclides, pesticide residues and microbiological parameters.

One of the main methods of physical-chemical analysis of aqueous solutions and dispersions of biopolymers is highly sensitive differential scanning calorimetry (DSC). This method makes possible to determine the temperature and enthalpy of conformational transitions in solutions and dispersions of biopolymers and accurately characterize the gel forming ability of gelatin and its plant counterparts. In this section thermodynamic properties of aqueous solutions of plant analogues for the manufacture of pharmaceutical gelatin capsules (carboxymethyl-cellulose, hydroxypropyl methylcellulose, agar, pectin, starch, carrageenan) were investigated by DSC.

Thermodynamic characteristics of the solutions of plant analogues of gelatin were determined using a differential scanning microcalorimeter DASM-4 (Puschino, Russia) in the temperature range from 10 to 120°C, at the heating rate of 2°C/min and overpressure 2.5 bar. Milli-Q water served as a comparison sample. The scale of the excess heat capacity for each experiment was calibrated using the Joule-Lenz effect.

The following concentrations of the solutions (dispersions): starch - 0.5%, CMC - 1%, carrageenan - 0.5%, agar - 0.5% were chosen for studies. Concentration of CMC solution increases due to the fact, that it shows sufficiently weak calorimetric effects at the solution concentration of 0.5%. Samples of plant analogues of gelatin were dissolved in Milli-Q water at the temperatures from 25 to 30°C, and kept under constant stirring for several hours prior to the experiments.

The average values of thermodynamic parameters were determined using three measurements. The enthalpy of transfer was calculated per gram of dry matter. The experimental error in determining the phase transition temperature T_m was ±0.1 K for the heat of phase transition ΔH_m and the heat capacity of phase transition ΔC_p, experimental error was ±5% of the determined value.

These systems were studied for the following physicochemical parameters:
(1) Toxic elements;
(2) Microbiological parameters;
(3) Organoleptic characteristics;
(4) Mass fraction of moisture, ash, protein impurities;
(5) Acidity.

Studies were performed using standard techniques.

RESULTS AND DISCUSSION

1. *The organoleptic and physical and chemical characteristics of the plant analogue of pharmaceutical gelatin from starch*

The results of appearance, color and odor of test samples of plant analogues of pharmaceutical gelatin from starch are shown in Table 3, and in accordance with Appendix A1. The results obtained after the complex characteristic of organoleptic properties of all the samples of plant analogues of pharmaceutical gelatin from starch are shown in Table 3.

Table 3. Analysis results of the organoleptic characteristics of plant analogues of pharmaceutical gelatin from starches

Rate	Sample*				Requirements GOST 51985-2002	Analysis technique
	Starch Sample 1	Starch Sample 2	Starch Sample 3	Starch Sample 4		
Appearance	homogeneous powder	homogeneous powder	homogeneous powder	homogeneous powder	homogeneous powder	GOST 23058-89
Odor	odor characteristic of starch	odor characteristic of starch	odor characteristic of starch	odor characteristic of starch	odor characteristic of starch	
Colour	white	white	white	white	white	

Note. * Some average starch samples K1 were taken.

According to the analysis of organoleptic properties (Table 3) it was found that all investigated samples of plant analogues of pharmaceutical gelatin from starch are homogeneous cream powders with the smell of starch.

Results of the analysis of physical and chemical parameters of plant analogues of pharmaceutical gelatin from starch are presented in Table 4.

As seen from the data presented (Table 4), all the investigated samples of plant analogues of pharmaceutical gelatin from starch have shown a satisfactory performance by the mass fraction of water (from 8.9% to 11.2%), mass fraction of protein in the dry matter (from 0.15% to 0.31%), the number of specks per 1 dm^2 of flat starch surface. The presence of sulfur dioxide (sulphureous gas) was not detected in any of the test samples of plant analogues of pharmaceutical gelatin from starch, because it is likely not to be used during their production processes. Studied samples microscopy of plant analogues of pharmaceutical gelatin from starch were characterized by high uniformity, size and shape of the starch granules being consistent with starch, indicating the absence of impurities in their composition.

Table 4. Results of the analysis of physical-chemical parameters of plant analogues of pharmaceutical gelatin from starch

Index	Sample*				Requirements GOST 51985-2002	Analysis technique
	Starch Sample 1	Starch Sample 2	Starch Sample 3	Starch Sample 4		
Number of specks on 1 dm^2 of flat surface when considering the naked eye	79	70	36	24	no more than 300	GOST 23058-89
Moisture content, %	no more than 14	no more than 14	no more than 13	no more than 13	no more than 14	
Mass fraction of total ash, based on dry matter, %	0.19	0.19	0.15	0.16	no more than 0.20	
Mass fraction of protein based on dry matter, %	0.5	0.6	0.8	0.8	no more than 0.8	
Acidity cm^3 of 0.1 mol / dm^3 of sodium hydroxide and 100 g of dry matter	20.5 ± 0.1	20.2 ± 0.5	15.6 ± 0.1	13.7 ± 0.4	no more than 20	
Sulfur dioxide content in mg/kg	not detected	not detected	not detected	not detected	no more than 50	
Impurities	absent	absent	absent	absent	not allowed	

Note. * Some average starch samples K1 were taken.

2. *The results of the pH value of solutions of plant analogues of pharmaceutical gelatin*

The pH values of all solutions of plant analogues of pharmaceutical gelatin from starch, CMC, HPMC, agar and carrageenan are shown in Table 5.

Aqueous solutions of plant analogues of pharmaceutical gelatin from starch, CMC and HPMC were characterized by close pH values in the range from 3 to 4 pH units. It should be noted that the pH values of starch solutions are higher if they do not undergo a boiling stage. In this case the pH value of solutions with the concentration from 1% to 10% are in the range of 5 to 6 units. The pH value of collagen solution ranges from 3.0 to 3.5. Agar solutions, unlike the rest of the test compounds are alkaline. PH value of these solutions are in the range from 8.5 to 9.0.

Table 5. The pH values of aqueous solutions of the investigated components to obtain capsules

Substance	Sample*							
	Starch Sample 1		Starch Sample 2		Starch Sample 3		Starch Sample 4	
Concentration, %	1.0	5.0	1.0	5.0	1.0	5.0	1.0	5.0
pH value	3.5	3.4	3.6	3.3	4.0	3.8	3.6	3.5
Substance	CMC sample 1		CMC sample 2		CMC sample 3		CMC sample 4	
Concentration, %	0.3	1.2	0.3	1.2	0.3	1.2	0.3	1.2
pH value	3.5	3.8	3.6	3.9	3.7	3.9	3.6	3.8
Substance	HPMC Sample 1		HPMC Sample 2		HPMC Sample 1		HPMC Sample 2	
Concentration, %	0.5	1.5	0.5	1.5	0.5	1.5	0.5	1.5
pH value	3.8	3.8	3.0	3.2	3.4	3.2	3.3	3.2
Substance	Agar Sample 1		Agar Sample 2		Agar Sample 3		Agar sample 4	
Concentration, %	0.3	1.2	0.3	1.2	0.5	1.5	0.5	1.5
pH value	8.5	8.9	8.8	8.9	8.6	8.6	9.0	9.0

Note. * Average samples of pharmaceutical gelatin analogues listed above were taken.

Increasing the concentration of substances in solution results in case of plant analogues of pharmaceutical gelatin from starch to lower pH values, and in the case of CMC, on the contrary - to its increase. This is not observed for plant analogues of pharmaceutical gelatin from agar, carrageenan, and HPMC.

When preparing mixtures, complex solutions and in the manufacture of the final product it is preferable to deal with chemically stable cultures. The use of substances in mixtures, which in certain conditions demonstrate the least predicted properties are not acceptable. In the present study several conditions in which test substances are not chemically stable were revealed.

Firstly, the same thing can be said about the solutions of plant analogues of pharmaceutical gelatin of carrageenan. After the standard procedure in the first hours in the solutions there continued colloidal processes that do not let to accurately predict the properties of the solutions. However, solutions were left at room temperature for eight hours. Their behavior was predictable.

Secondly, attention should be paid to the unique solutions of plant analogues of pharmaceutical gelatin

from agar. These solutions stand out from the line of solutions of all the studied components, because they have alkaline pH values, somewhat from 8 to 9 units. Furthermore, adding an acid to the solution of agar does not lead to the expected reduction of pH value. The pH value changes more differently than it would have happened to the solutions of substances chemically inert to acid. Gradual addition of the acid and an equivalent amount of alkali solution to the plant analogues of pharmaceutical gelatin from agar did not give initial pH value. The use of solutions of plant analogues of pharmaceutical gelatin from agar in the range of 3 pH units lower as compared with its own pH values of these solutions is not desirable.

3. *The results of the concentration determination of active groups in the solution of the test plant analogues of pharmaceutical gelatin*

Concentrations of active groups for all the studied solutions of plant analogues of pharmaceutical gelatin from starch were similar and ranged from 1.6 to 2.2 mM for 0.3% solutions and from 6.2 to 8.2 mM for 1.2% aqueous solutions (Table 6). Solutions of all the samples of plant analogues of pharmaceutical gelatin from starch trace the stoichiometric ratio between the percentage concentration of the solutions and the concentration of active groups.

The average concentration of active groups in a 1% solution of plant analogues pharmaceutical gelatin from starch was 1.9 mM. This value can be used for a rough prediction of buffering properties of solutions with various starch samples.

Solutions of plant analogues of pharmaceutical gelatin from agar show very weak buffering properties so that the concentration of active groups was not possible to determine.

During the titration of solutions of plant analogues of pharmaceutical gelatin from carrageenan there were obtained non-reproducible results. The gradual addition of the acid and an equivalent amount of alkali to the solution of plant analogues of pharmaceutical gelatin from carrageenan did not reveal the initial pH value. After the addition of acid to the solution of collagen, continuous growth was observed (several hours) in the direction of pH value increasing. The observed phenomena indicate the presence of irreversible reactions with acid in the solution of plant analogues of pharmaceutical gelatin from carrageenan.

For the aqueous solutions of substances the following relationship is true:

$$\mathrm{pKa} = 2 \cdot \mathrm{pH} \cdot \mathrm{units} - \lg(\mathrm{C}), \quad (1)$$

where pKa is the negative logarithm of the dissociation constant of the acid active group of substance; C – the concentration of active groups in the solution.

Given the previously established data for the number of active groups in the solutions of plant analogues of pharmaceutical gelatin from agar with various concentrations (Table 6) there were calculated pKa values (Table 7).

pKa values of the solutions of plant analogues of pharmaceutical gelatin from agar are in the range from 4.3 to 4.9. pKa value was defined for CMC C1as well and was 11.76.

Table 6. The concentration of active groups in the solutions of plant analogues of pharmaceutical gelatin from starch

Index	Sample rate *							
	Sample 1		Sample 2		Sample 3		Sample 4	
Mass fraction of gelatin in solution, % w / w	0.3	1.2	0.3	1.2	0.3	1.2	0.3	1.2
Concentration of active groups, mM	1.5	6.1	2.1	7.7	2.1	8.1	1.8	7.2

Note. *Some average starch samples K 1 were taken.

Table 7. pKa value of the solutions of plant analogues of pharmaceutical gelatin from agar

Index	Sample rate *							
	Sample 1		Sample 2		Sample 3		Sample 4	
Concentration of solutions of plant analogue of pharmaceutical gelatin, agar solution, % w / w	0.3	1.2	0.3	1.2	0.3	1.2	0.3	1.2
Concentration of active groups, mM	1.5	6.1	2.1	7.7	2.1	8.1	1.8	7.2
pKa	4.30	4.39	4.60	4.39	4.87	4.41	4.58	4.76

Note. * 1 and 2 were taken from the agar samples, A1and 3 and three samples from agar A2.

4. *The resuls of determination of the optical density of the solutions of plant analogues of pharmaceutical gelatin*

As a result of determination of the optical density D of the solutions of plant analogues of pharmaceutical gelatin there were obtained data shown in Table 8.

Of all the samples of plant analogues of pharmaceutical gelatin from CMC, 1 CMC sample had the highest degree of absorption. For the remaining samples absorption at the wavelength of 650 nm is approximately the same. After the heat treatment (even when heated to 40˚C) sample 3 from CMC shows reduced absorption. After cooling to room temperature, the optical density D of the sample solution from CMC 3 does not return to the original state, in contrast to other samples from CMC. That is, the sample of plant analogue of pharmaceutical gelatin from 3 CMC undergoes

irreversible changes in the solution under heating. Solutions of all the test gelatin samples were characterized by high values of optical density D compared with other substances (about 2), due to turbidity of resulting solutions.

The studied samples of plant analogues of pharmaceutical gelatin from agar are almost identical in transparency. Among all the studied hydrocolloids solutions and gels based on one sample from carrageenan were characterized as the most transparent. At the same time, the sample 2 from carrageenan is the most turbid among the investigated plant analogues of pharmaceutical gelatin from agar and carrageenan.

The study of optical properties of components' solutions to obtain capsules showed that all of the test groups of the compounds, solutions of starch are the most turbid. The optical density D of these solutions at the concentration of 1% is greater than 1.5 optical units. For the other groups of the compound optical density D is less than 0.5 optical units for all of these solutions.

Optical absorption of the solutions of studied components was practically independent of the conditions, such as pH value and temperature. The solutions of plant analogues of pharmaceutical gelatin particularly can be distinguished from sample 3 CMC, which after heat treatment exhibited lower optical density D than before. That may be indicative of irreversible changes at the molecular level.

Table 8. The optical density of aqueous solutions of plant analogues of pharmaceutical gelatin at the wavelength $\lambda = 650$ nm

CMC								
Concentration, %	Sample 1		Sample 2		Sample 3		Sample 4	
	Temperature, °C							
	25	100	25	100	25	100	25	100
0.5	0.1368	0.1193	0.0419	0.0405	0.0306	0.0134	0.0440	0.0279
1.0	0.1878	0.1701	0.0634	0.0780	0.0803	0.0561	0.0739	0.0614
1.5	0.2592	0.2722	0.1104	0.1120	0.1250	0.0290	0.1210	0.0962
Concentration, %								
1.5	0.5918	0.5460	0.2667	0.2503	0.1627	0.0858	0.2412	0.1308
Concentration, %								
1.5	0.5621	0.5192	0.2584	0.2494	0.1593	0.0868	0.2261	0.1782
1.5	0.5869	0.5450	0.2660	0.2620	0.1742	0.1229	0.2333	0.1733
Starch								
	Sample 1		Sample 2		Sample 3		Sample 4	
Concentration, %								
1.0	1.6897		1.5278		1.7421		-	
3.0	2.0876		2.0786		2.2906		2.2102	
5.0	2.2632		2.2240		2.6404		2.4020	
Concentration, %								
5.0	1.7023		2.1446		2.1446		2.0288	
Agars and Carrageenans								
	Agar				Carrageenan			
	Sample 1		Sample 2		Sample 1		Sample 2	
Concentration, %								
0.5	0.1785		0.1535		0.0460		0.5039	

CONCLUSION

In the course of studies the complex characteristic of organoleptic, physical-chemical, optical, buffering, rheological and structural-mechanical properties, chemical reactivity indices of plant analogues of pharmaceutical gelatin, and combinations thereof to produce capsules were determined. Samples of plant analogues of pharmaceutical gelatin from starch, carboxymethyl cellulose, agar, carrageenan and hydroxypropyl were characterized.

Summarizing the results of these studies, it should be noted:

– Investigated plant analogues of pharmaceutical gelatin to obtain capsules exhibit the properties of weak electrolytes;

– The number of titratable active groups in plant analogues of pharmaceutical gelatin from agar and HPMC is small and this allow us not to take into account the contribution of these compounds in the prediction of acid-alkali properties of mixtures or complex solutions;

– The plant analogues of pharmaceutical gelatin from starches exhibit very strong buffering properties. The average number of active groups in a 1% starch solution was 1.9 mM, and the pKa rate of the solutions of plant analogues of pharmaceutical gelatin from pectins lies in the range from 4.3 to 4.9 pH units;

– The solutions of plant analogues of pharmaceutical gelatin from carrageenan are chemically unstable in the presence of acid in solutions.

The acidity test results revealed that all the starch samples showed satisfactory characteristics among the test samples of plant analogues of pharmaceutical gelatin from starch. All the samples of plant analogues of pharmaceutical gelatin from starch, carboxymethylcellulose, hydroxypropylmethylcellulose, agar, and carrageenan did not exceed the rated values of the mass fraction of the total quantity of ash

based on the dry weight. Thus, sensory analysis of organoleptic and physical-chemical properties showed the possibility to use any representative sample of starch, carboxymethyl cellulose, hydroxypropyl methylcellulose, agar and carrageenan for the subsequent preparation of the mixture to produce plant analogues of pharmaceutical gelatin and capsules out of it.

The complex properties of plant analogues of pharmaceutical gelatin were finally examined and the possibility of using plant analogues of pharmaceutical gelatin for soft capsules was proved.

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