Chemical and Pharmaceutical Features of Obtaining Pectins from Apple Pomace and Prospects for Use in Medicine and Pharmacy

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Abstract. The COVID-19 pandemic has shown the need to increase the level of providing patients with medicines. The development of new drugs using natural biomaterials remains relevant. The chemical and pharmaceutical features of obtaining apple pectin have been studied. The influence of technological factors during the extraction of apple pulp from different varieties of apples on the yield of pectin substances was studied. A chemical analysis of pectin content and output was carried out. The fractional composition of pectin substances was analyzed. Prospects for the use of pectins in medicine and pharmacy are outlined. The effect of the technological conditions of extraction of pectin extract from apple pomace on the content and yield of pectin in apple pulp from different varieties of apples was investigated. The technology for obtaining pectins from apple pulp in the presence of various acidic agents is presented, and it is established that the conditions for obtaining apple pectins are optimal for obtaining the highest yield of pectin compounds when choosing the technological parameters of the first stage of hydrolysis for summer and autumn varieties of apples using citric acid with a concentration of 0.10-0.15%, at a temperature of 80-85°C, lasting 2 hours for autumn varieties of apples, and 2.5 hours for summer varieties of apples. Under the conditions of the proposed technology, highly esterified apple pectin (degree of esterification on average 75%) was obtained from apple pulp of autumn and summer varieties of apples, which can be used in medicine and pharmacy.
Keywords: pharmacy, organic chemistry, apple pectin, structure, technology, properties, application in medicine.

Introduction. The COVID-19 pandemic has shown the need to improve the organization of work in the field of medicine and pharmacy for the pharmaceutical supply of patients. Against the background of the spread of infections, covid, post-covid and long-covid disorders have intensified in accordance with ICD-11 [1-5].

Scientific studies of recent years confirm the effectiveness of using pectins in various sectors of the economy. Pectins are used in pharmacy in the creation of new drugs as gelling agents, adsorbents, emulsifiers, components of polymer therapeutic systems with controlled release of active substances, stabilizers, thickeners, water-retaining agents, brighteners, substances that facilitate filtration, means for encapsulation, production of nutrient media. In medicine, pectins are used as antioxidants, detoxifiers; to improve the metabolism of carbohydrates, nutrients; to increase the body's resistance to various painful pathologies, normalize lipid metabolism, function of the immune system; to improve digestion and the functional state of the gastrointestinal tract; in the treatment of heavy metal poisoning, diarrheal infections; with respiratory diseases, diabetes, polyarthritis, hemophilia; for healing wounds and burns; have the property of prolonging the effect of drugs [6-12].

Among pectins, attention is drawn to apple pectin by processing apple pomace. A third of the world volume of apple pectin is produced in the USA, China, Brazil, Great Britain, Denmark, Italy, Germany, Austria, Bulgaria, and Poland [13-15].

Ukraine's need for pectin only for carrying out annual periodic detoxification and prevention of the population affected by the Chernobyl disaster exceeds 300 tons/year, and it is met by only 1%.

That is, pectin is one of the most common polysaccharides, contained in sufficient quantities in many fruits, vegetables, roots, apple and citrus juices and other secondary resources, it is not cheap and available. Despite the availability of a raw material base, pectin is not produced in Ukraine, mainly due to the shortage of energy resources and the energy intensity of production. Therefore, further chemical-pharmaceutical research on the search for promising biomaterials of natural origin for the creation of new drugs is relevant.

The purpose of the study was to research the chemical and pharmaceutical features of apple pectin production based on the study of the influence of technological factors during the extraction of apple pulp from different varieties of apples on the yield of pectin substances; conducting a chemical analysis on the content and output of pectin; analysis of the fractional composition of pectin substances in comparison with other fruit and berry mixtures; prospects for use in pharmacy.

Materials and methods. Production of pectins from fruit and berry mixture is carried out using various technologies. The most traditional technology for obtaining pectins from a mixture of apple pulp is the extraction of pectin-containing fruit biomass, diluted with hot solutions of mineral acids (HCl, H2SO4, H3PO4, HNO3), at a hydromodule of 1:3, at a pH value of 1.5-3, t=45-80ºC, in the presence of complexing agents that bind divalent cations (ammonium oxalate, sodium hexametaphosphate, ethylenediaminetetraacetic acid), as well as in the presence of organic acids [16, 17]. During the extraction process, the resulting pectin is precipitated with alcohol followed by its reprecipitation with ethanol and regulation of the degree of esterification by methoxylation, followed by grinding and drying operations [18, 19].

Using the extraction process, pectins were obtained, but the hydrolysis conditions were chosen to be milder, resulting in higher yield pectins. Dried or freshly obtained apple pomace was used as raw material, which was washed three times with water (t=30-35°C) before the process of extracting pectin substances. When obtaining pectin with a low rate of coagulability, washing was carried out with water (t=55-60°C).

The technology consists of the following stages:

Stage 1. Extraction of pectin was carried out by the process of hydrolysis with an aqueous solution of mineral (nitric acid) or organic acid (citric acid) at a pH of 1.7-2.0 at a temperature of the hydrolysis mixture of 70–85°C, the ratio of raw materials and extractant: 1:10 within 3.0-3.5 hours. At the end of the process, 1-extract was separated on the presses.

Stage 2. Pressed apple pomace was again loaded into the extractor, poured with water (t=45-50°C) in the ratio: 1:12, and kept for 1.5-2 hours, 2-extract was obtained, which was separated by pressing the suspension. The moisture content of the pressed pomace was more than 80%, the residual pectin content was 0.8–1.0%.

Stage 3. 1-extract and 2-extract were mixed and stood for 2-4 hours to separate mechanical impurities. The average content of dry substances in the extract was 1.0-1.2%, including pectin substances 0.3-0.4%. The settled extract was separated and filtered.

Stage 4. Concentration of the extract was carried out in two-body vacuum evaporation units. The temperature of the product in the first housing was 70-75°C, in the second 45°C. The content of dry substances in the concentrate corresponded to 6-7%, the pH of the concentrate was 1.7-2.2, the concentration of alcohol-precipitated pectin substances was 2.5-3.5%. The resulting concentrate was cooled to 25°C.

Stage 5. Precipitation of pectin substances was carried out with ethyl alcohol with a strength of 90–95%. The volume amount of alcohol to the volume of pectin concentrate was: 3:1 part. Precipitation of pectin substances was carried out at pH=1.7-1.9.

Stage 6. First washing of the obtained pectin-alcohol suspension. The resulting pectin-alcohol suspension was sent for separation in a centrifuge, after which the pectin coagulates with a moisture content of 70-75% was sent to a washer with alcohol strength of 70% in a ratio of 1:8. The suspension of the 1st washing was sent for separation in a centrifuge.

Stage 7. Raw pectin was again poured into the washer, where the 2nd washing with 90-95% strength alcohol in a ratio of 1:8 took place. The suspension of the 2nd wash was also sent to a centrifuge to separate pectin.

Stage 8. Purified pectin was submitted for drying, which was carried out in a vacuum drying cabinet equipped with devices for removing condensed alcohol without stopping the process of capturing alcohol vapors and pectin dust at 55-60°C. Drying time is 2-3 hours.

Stage 9. Dry pectin was crushed and dried to a constant weight with a moisture content of no more than 10%.

At the end of the process, the obtained pectin was analyzed to determine the molecular weight, methoxyl number, acetyl number, content of carboxyl groups, water solubility, sol viscosity, draggle-forming ability, molecular weight, and yield of pectin according to NSTU (National Standards of Ukraine) 6088:2009 Pectin. Technical conditions and in accordance with standard methods [20-22].

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Results and discussion. Pectin is a powdered dry or pasty polysaccharide of plant origin, consisting mainly of partially etherified with methanol alkaline calcium and ammonium salts of polygalacturonic acid (Fig. 1). It is a mucilaginous, taste-tested, water-soluble product of different colors depending on the source of raw materials, production, and degree of purification [24].

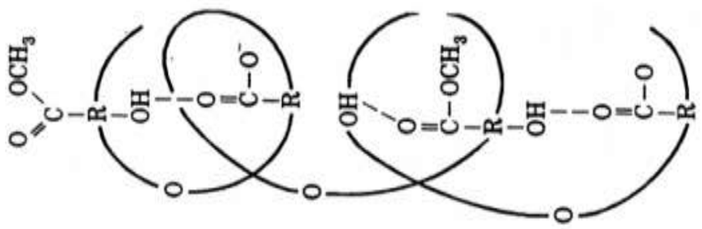


Fig. 1. Spatial structure of the pectin molecule.

Obtaining pectins from apple pomace and prospects for their use in the creation of new drugs is based on previous research by the authors of the article [25, 26]. In further studies, the technology of obtaining pectin was improved. Its properties were studied from vegetable crops – beet pulp.

Pectin substances are polysaccharides formed by the remains of partially methoxylated D-galacturonic acid, in which the hydrogen atom is replaced by a group – OCH3 (Fig. 2).

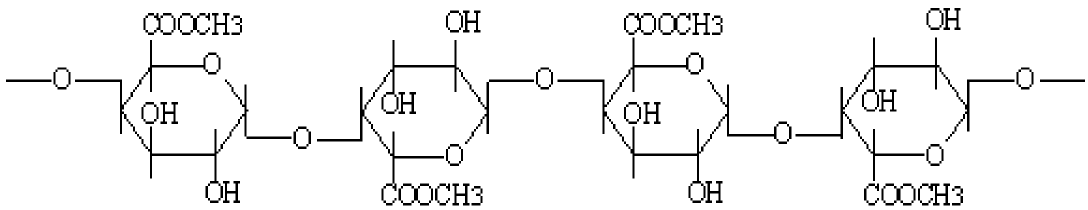


Fig. 2. Structure of pectin polysaccharides.

Polygalacturonic acid is an acid that is a linear polymer, the molecule of which consists of α-D-galacturonic acid residues and some L-rhamnose residues linked by 1,4-glycosidic bonds (Fig. 3, 4, 9) [17].

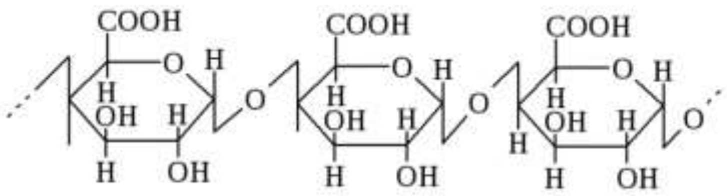


Fig. 3. Polygalacturonic acid.

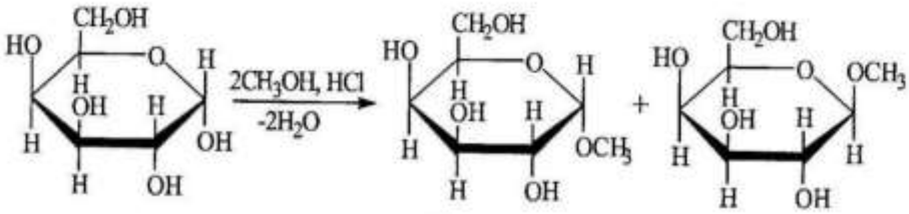


Fig. 4. The reaction of obtaining methyl-α-D-galactopyranoside and methyl-β-D-galactopyranoside.

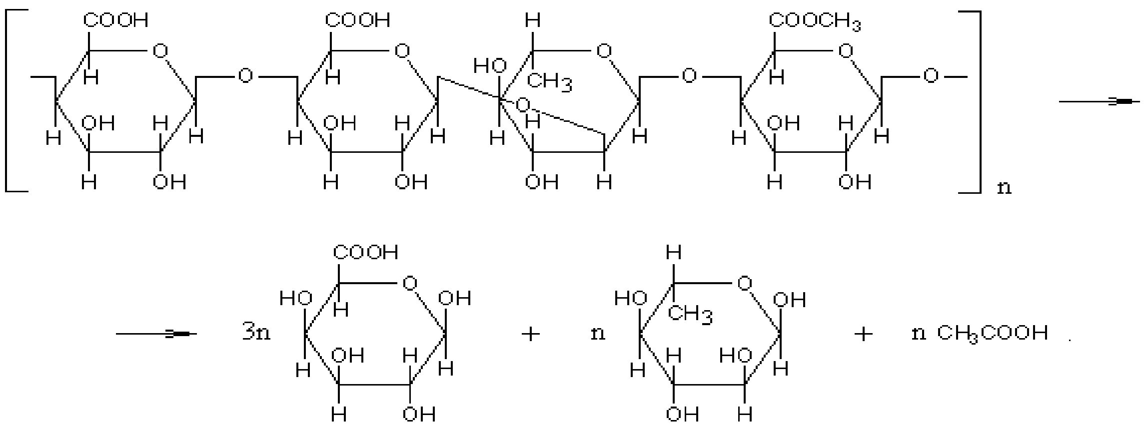
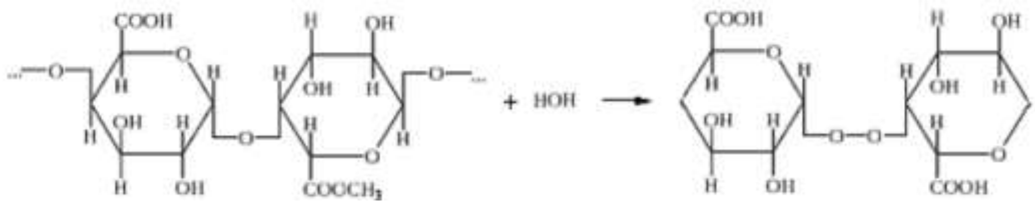


Fig. 5. Hydrolysis of polygalacturonic acid methyl ester.

Polygalacturonic acid methyl ester during hydrolysis forms pectic acid and methanol according to the reaction (Fig. 5, 6).



$+C_2H_5OH$

Polygalacturonic acid methyl ester Pectic acid Pectic acid Methanol

Fig. 6. Possible products of the hydrolysis reaction of the methyl ester of polygalacturonic acid.

Based on the results of the research, the authors selected the optimal conditions for obtaining pectins from apple pomace. Features of the technology and technological parameters were established:

- the first stage of hydrolysis should be carried out using concentrated citric acid of 0.1-0.15%;
- for summer and autumn varieties of apples at a temperature of 80-85°C;
- duration – 2 hours for autumn varieties of apples;

- duration – 2.5 hours for summer varieties of apples.

At the same time, the research results showed that the highest yield of pectin from apple biomass was obtained when citric acid was used at the extraction stage (Table 1).

Table 1. Yield of pectin substances from apple pulp.

Raw	Names of acids used for extraction	Pectin yield, % (to the mass of dry substances)
Apple squeezes (mixed varieties)	Nitric acid	3,2-5,6
	Citric acid	5,2-7,7
	Sulfate acid	2,4-2,8
	Hydrochloric acid	2,3-3,5
	Oxalic acid	2,7-3,6

However, the yield of pectin significantly depends not only on the chosen technology and extraction conditions, but also on the variety of apples from which the apple pulp was obtained (Table 2), as well as on many other factors.

The results of research using different varieties of apples, different mineral acids, and their influence on the yield of pectins at the extraction stage shown in the Table 2. Obtaining pectins from individual varieties of apples showed that the highest yield was obtained with the use of citric acid in the summer variety of Ranger apples (9.6%) and in the autumn variety of Hryv Ruzh apples (8.2%). However, a mixture of apple pulp is most often used to obtain pectins.

Table 2. Yield of pure pectin from apples of the studied varieties.

Studied varieties of apples	Pectin yield, % (to the weight of dry substances)	
	Nitric acid	Citric acid
Summer varieties		
Ranger	7,1	9,6
White pour	4,5	7,7
Autumn varieties		
Hryv Rouge	3,7	8,2
Gorden Grimes	6,5	10,3

The obtained apple pectin was sent for chemical analysis. The content of methoxyl, acetyl, carboxyl groups, yield of pectin and its molecular weight were studied (Table 3).

Table 3. The main average values of indicators of chemical analysis of apple pectin.

No.	Name of indicators	Value of indicators
1	Content of methoxyl groups, %	7,25-10,43
2	Content of acetyl groups, %	0,35-0,65
3	Esterified carboxyl groups in apple pectin (from dry pulp), %	10,4-11,8
4	Free carboxyl groups in the composition of pectin (from dry pulp), %	3,5-3,8
5	Degree of esterification, %	74,8-75,6

The chemical composition of pectin compounds determines their nutritional and medical and dietetic value, organoleptic properties, as well as suitability for further use. The content of dry substances in pectins is not a constant indicator. It depends on the quality and variety of fruit and berry pulp, weather and climate conditions and storage conditions of raw materials [7, 8, 9, 15, 27].

An important quality indicator of pectin is the degree of esterification. Depending on the value of the degree of esterification, pectins were divided into two groups – highly esterified (most often apple, citrus) and low esterified (for example, obtained from sugar beet) [28]. Depending on the raw material and the method of production, the degree of esterification of pectin can be 20-85% (Fig. 7).

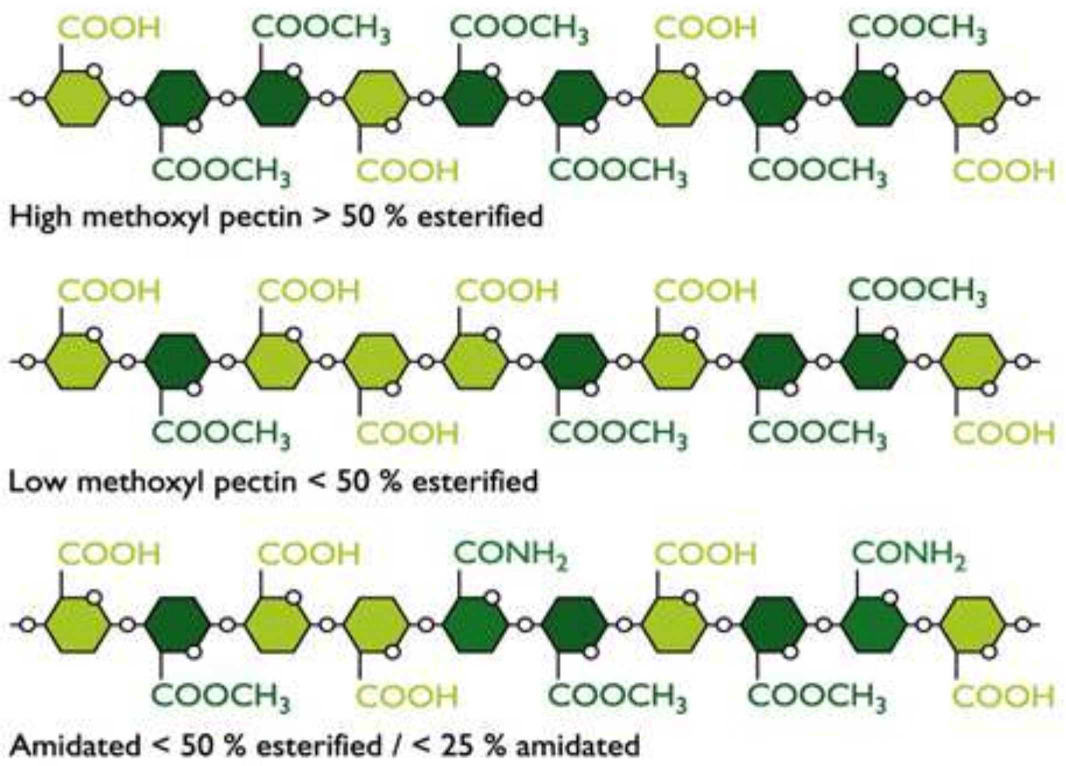


Fig. 7. The degree of esterification of pectin depends on the raw material and the method of production.

Pectins with a degree of esterification of more than 50% are classified as highly esterified (H-pectins), and less than 50% are classified as low-esterified (L-pectins). The structure of H-pectin is shown in Fig. 8. The chemical structure of the fragments of the D-galactoronic acid and L-rhamnose molecules is shown in Fig. 9.

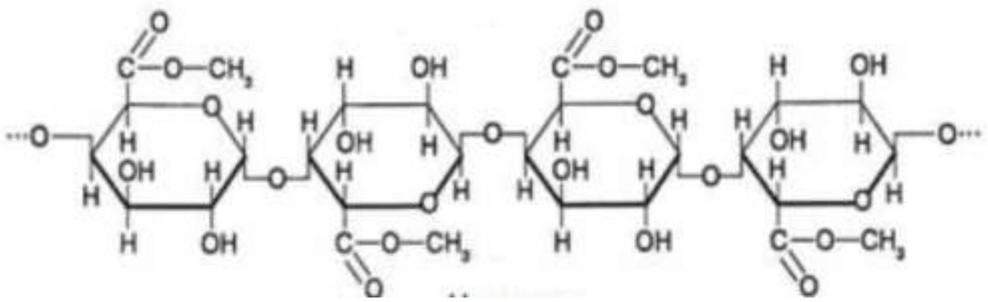


Fig. 8. Chemical structure of H-pectin.

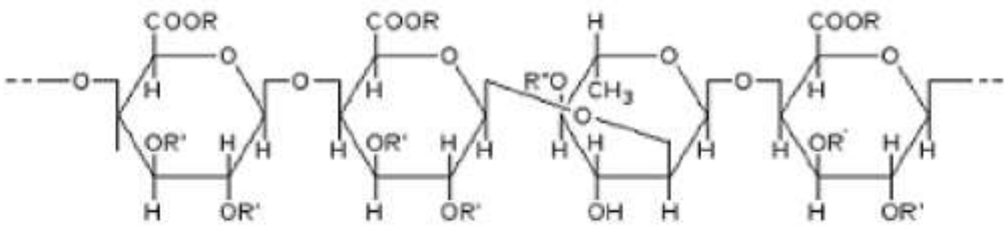


Fig. 9. Chemical structure of fragments of the D-galactoronic acid and L-rhamnose molecule.

Established that with an increase in the degree of esterification, the size of the molecule decreases [9].

Esterified carboxyl groups in apple pectin (from dry pulp) obtained by the proposed technology make up 10.4%, free carboxyl groups – 3.5% (Table 3). In the composition of the apple pectin obtained by the authors, the degree of esterification is 74.8%, which indicates the production of highly esterified pectins. A high degree of esterification indicates a high complex-forming ability (Fig. 10).

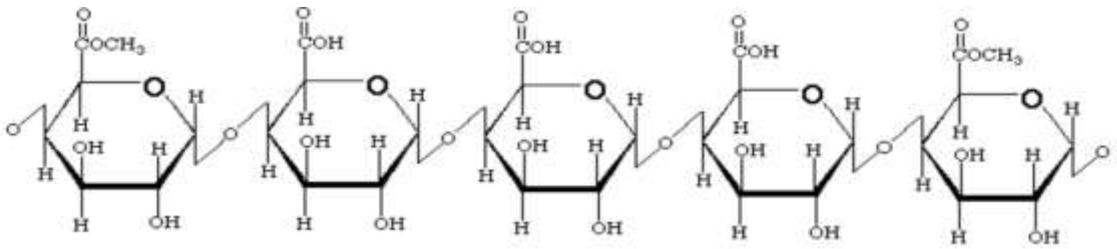


Fig. 10. Structural formula of highly esterified pectins.

The obtained technological and chemical indicators are the properties of the investigated pectins. Depending on the properties, the further use of pectins were determined.

High-esterified and low-esterified pectins have different mechanisms of jelly formation. For example, highly esterified pectins form gels in the presence of sugar and acid. At the same time, the content of dry substances in the medium should be at least 50%, and the pH should be 2.8-3.4. Under the same conditions and high temperatures, high-esterified pectins have a higher rate of gelatinization than low-esterified pectins.

The content of methoxyl groups also affects the time and temperature of gelatinization, which is an important criterion for the quality of highly esterified pectins. Therefore, the content of methoxyl groups should be at least 7%.

The content of acetyl groups should be no more than 1%. A higher content of acetyl groups has a negative effect on jelly formation.

The presence of free carboxyl groups in pectins is an important indicator. Due to the presence of carboxyl groups of galacturonic acid, pectins can bind heavy metal ions in the alimentary tract, followed by the removal of insoluble complexes from the body.

In the cosmetic industry, varieties of low-esterified, high-molecular-weight pectins are used as structure-builders in cosmetic lotions and shampoos, creams, pastes, ointments, and oils.

In dermatology, in the treatment of wounds, natural pectins are used in ointments. They show hemostatic and healing properties.

The molecular weight of all classes of pectins ranges from 25,000 to 300,000. The obtained pectins from apple pulp are a mixture of molecules with different molecular chain lengths. The molecular weight of the obtained pectins corresponds only to the average value, which ranges from 52,000 to 200,000, depending on the extraction conditions and biomass properties. Comparative indicators of chemical analysis of apple pectin, beet pectin from beet pulp [26] and citrus pectin obtained from citrus fruits [17] are given in Table. 4.

When metal salts are added to the pectin solution, insoluble, stable compounds are formed – metal pectinates, which are not absorbed in the intestines. Metal pectinates are easily formed from low-esterified pectin. For example, lead pectinates are formed.

Highly esterified (methoxylated) pectin envelops the intestinal wall. With the help of the gel filtration mechanism, it reduces the absorption of small molecules, such as heavy metals and radionuclides. Pectins can bind both heavy metals entering the alimentary canal from the outside, and prevent secondary resorption of metals when they enter the gastrointestinal tract with bile or as part of other digestive secretions, excreting them with feces.

Table 4. Comparative indicators of chemical analysis of pectin substances.

No.	Type of pectin	Molecular weight	Content of methoxyl groups, %	Content of acetyl groups, %
1	Apple pectin	52000-200000	7,25-10,43	0,35-0,65
2	Beet pectin	38000-62000	3,72-5,53	0,41-2,54
3	Citrus pectin (lime, lemon, orange, grapefruit)	23000-51000	6,90-9,60	0,24-0,50

Pectin substances with the formation of galacturonic acid and oligogalacturonic acid are able to partially hydrolyze intestinal microorganisms, which are reabsorbed in the intestine and enter the bloodstream. It was established that the maximum removal of lead with urine and feces and the reduction of lead content in bones is achieved at a degree of pectin esterification of 50-60%.

The complex-forming or chelating properties of pectins are also due to the presence of carboxyl and hydroxyl groups of galacturonic acid in the pectin polymer molecule. The activity and strength of the formation of chelates depends on the degree of esterification of pectins, that is, on the ratio between esterified and free carboxyl groups. The less esterified pectin, the freer carboxyl groups, the easier metal chelates are formed [9, 16]. Therefore, pectins belong to highly effective detoxifying agents.

In clinical conditions in Ukraine, the effectiveness of pectin prophylaxis for reducing organochlorine pesticides such as: hexachlorocyclohexane, dichlorodiphenyltrichloromethylmethane, organochlorine pesticides have been confirmed. The content of organochlorine pesticides decreases almost 4-4.5 times after taking pectin substances (Table 5) [16, 29].

Table 5. Preventive recommendations for the use of apple and beet pectins.

Pectin (powder)	Prophylactic dose, g	Course of administration, days	Therapeutic dose, g	Course of administration, days
1. Apple (highly esterified)	6 – 8	12 – 14	15 – 16	18 – 21
2. Apple (low esterified)	4 – 5	12 – 14	8 – 10	18 – 21
3. Beetroot (low-esterified)	4 – 5	12 – 14	8 – 10	18 – 21

In the literature, there are a limited number of reports on the use of pectin as the main gelling polymer in medical hydrogels. However, there is information about the antiseptic, hemostatic and detoxifying properties of pectin and its effective use as part of composite materials, ointments, and films for the treatment of wounds [11, 12, 14, 30].

Pectin is a source of natural fiber that contributes to:

- establishment of healthy food digestion;
- regulation of glucose content in the blood;
- reduction of cholesterol content in the body;
- increasing the body's resistance to allergic factors;
- stimulation of intestinal motility;
- stabilization of metabolism;
- reducing excess body weight;
- enveloping and protective effect due to the formation of a gel by pectin substances on the surface of the mucous membrane of the stomach and intestines.

The properties of pectin determine its use in medicine and pharmacy shown in the Table 6 [31, 32].

Table 6. Main functions of pectin and areas of its application.

Functional characteristics	Areas of application of pectins
Gel forming technology	Food production technology Technology of pharmaceutical production
Stabilizer	Food production technology Technology of pharmaceutical production
Complexing agent	Chemical technology
Properties of hemostasis and healing	Medicine. Pharmaceutical production
Blood plasma substitute	Medicine. Pharmaceutical production
Encapsulation of medicines	Technology of pharmaceutical production
Structure former	Technology of pharmaceutical production. Technology of cosmetic products
Thickener	Technology of pharmaceutical production. Technology of cosmetic products

In pharmaceutical cosmetics, pectin is used:
- ✓ as a stabilizer and emulsifier of pastes, ointments, creams, and oils with a vegetable base;
- ✓ in deodorants and toothpastes – to add a fresh aroma;
- ✓ in lotions and shampoos – as a tonic stabilizer and thickener.

In medicine, pectin is used [7, 17, 27]:
- ➢ during the treatment of acute intestinal infections;
- ➢ depending on the concentration of pectin and microbial load, the growth of microorganisms is inhibited for 2 hours or more;
- ➢ the most favorable biocenosis in terms of the composition of the microbial flora in the intestines is achieved when adding apple pectin of all pectins, which promotes better food absorption while simultaneously reducing appetite [16, 29, 31, 32].

Due to its complex-forming properties, pectin, as a natural biopolymer, is widely used as a preventive agent for the removal of toxic substances and heavy metals from the human body, and it is a natural "cleanser" of the body [10, 27]. Pectin acquires a gel-like structure in the small intestine and, moving along it and dehydrating it, absorbs and removes toxins, metals, anabolics, metabolic products, xenobiotics, bile acids and fats from the body. As a result, the product lowers the level of cholesterol in the blood and creates a favorable environment for the vital activity of useful microflora. In addition, polysaccharide slows down the movement of food mass through the large intestine, which improves its assimilation and prolongs the feeling of satiety. By cleaning the intestines, pectin prevents the absorption of harmful substances into the bloodstream, improving the general condition of the body and strengthening the immune system.

Enveloping the walls of the digestive tract, it prevents inflammatory processes and relieves pain in ulcerative lesions. By reducing the risk of cholesterol plaque formation and the development of atherosclerosis, pectin prevents cardiovascular diseases. All of the above effects lead to a significant improvement in the condition of the skin. With regular use of pectin, the skin is moisturized, its tone is evened out, small wrinkles are smoothed out, cells are restored and renewed faster [31, 32].

In pharmaceutical technology, when developing new drugs, pectins are used as [33-34]:
- ❖ auxiliaries in the preparation of many medicinal forms, serve as the basis for lozenges, suppositories, are raw materials for the preparation of hydrogels, tablets, soft gelatin and rectal capsules and suppositories;

❖ their prolonged action is used in tablets, mixtures together with various medicinal preparations;
❖ the use of pectin for encapsulation of medicines ensures a gentle mode of their absorption in the gastrointestinal tract;
❖ the introduction of pectin into the composition of medicines can enhance the therapeutic effect or reduce the side effects of medicines;
❖ pectins enhance the effect of anti-tuberculosis drugs;
❖ in the development of combined medicinal preparations, the combination of flavonoids with pectins contributes to the strengthening of their detoxification in liver diseases.

Conclusions. The chemical and pharmaceutical features of obtaining apple pectin have been studied. The influence of technological factors during the extraction of apple pulp from different varieties of apples on the yield of pectin substances was studied. A chemical analysis of pectin content and output was carried out. The fractional composition of pectin substances was analyzed. Prospects for the use of pectins in medicine and pharmacy are outlined. The technology of obtaining pectins from apple pulp in the presence of various acid agents was investigated. It has been established that for obtaining the highest yield of pectin compounds, the use of citric acid with a concentration of 0.10-0.15% at a temperature of 80-85°C and a duration of 2 hours is optimal for autumn varieties of apples, and 2.5 hours for summer varieties of apples. Under the conditions of the proposed technology, highly esterified apple pectin (degree of esterification on average 75%) was obtained from apple pulp of autumn and summer varieties of apples, which can be promising for use in medicine and pharmacy. Apple pectins are promising for use in the development of new combined, effective, high-quality, safe, and economically available medicines. Prospective use of pectins in the treatment of heavy metal poisoning, gastroenterological, pulmonological, endocrinological, dermatological and other diseases.

Conflict of interest. The authors confirm that they are the authors of this work and approve it for publication. The authors also certify that the obtained data and research were conducted in compliance with the requirements of moral and ethical principles based on medical and pharmaceutical law, respectively, and in the absence of any relationships that could be interpreted as conflict and/or potential conflict of interest.

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