Prospects for the use of fruits and leaves of papaya (Carica papaya L.) in medicine

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SUMMARY

This paper provides an analytical review of the literature data and the results of our own phytochemical studies of fruits and leaves of papaya growing in India and introduced in the territory of the Republic of Bashkortostan.

Key words: papaya, papaya fruit, papaya leaves, chemical composition, application in medicine.

RESUME

This work provides an analytical review of the literature data and the results of our own phytochemical studies of fruits and leaves of papaya growing in India and introduced in the territory of the Republic of Bashkortostan.

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INTRODUCTION

Nowadays, natural herbal remedies are increasingly used in modern medical practice. One of the promising and developing areas of modern medicine and pharmacy is the appeal to edible plants as a source of biologically active compounds. Plant biologically active substances are well absorbed by the body, being involved in many life processes, have a wide pharmacological activity, low toxicity, and are softer than synthetic drugs. Papaya (Carica papaya L.).

The purpose of this work is to systematize data on the chemical compositionand the medicinal use of the fruit and leaves of the caricum papaya (Carica papaya L.).

Melon tree, or carica papaya (Carica papaya L.) is a perennial low tropical palm-like plant of the papaya family (Caricaceae) with a thin cylindrical, herbaceous trunk with scars of dead leaves without branches. The plant is rapidly growing, can reach 4–6 meters by the age of five. The maximum tree height reaches 10 meters. There is a rosette at the top of the plant.

large, finger-dissected leaves with long petioles, in the axils of which flowers are formed, and subsequently fruits. FlowersCarica papaya L. Light yellow in color with a spinal corolla and a barely distinguishable spinal calyx, five-membered, actinomorphic, with a fragrant aroma that attracts insects. The fruits have a juicy endocarp, polyspermous, in size and shape resemble a melon. Fruit weight reaches 6-7 kg, in cultivars 1-3 kg. The homeland of the melon tree is the south of Mexico, Central America and the north of South America. The plant is grown now in all tropical countries, in Russia it is cultivated indoors [1, 11, 17].

Various researchers have found that the fruits and leaves of papaya contain a variety of biologically active compounds. Papaya fruits contain: carotenoids - β-carotene, lycopene, lutein, violaxanthin, zeaxanthin, cryptoxanthin; terpenes - α-terpinene, γ-terpinene; monoterpenoids - linalool, 4-terpinol, α-pellandrene, cis-trans-linalool oxide; phytoalexin - danielon; glycosides - benzyl-β-D-glucoside, 2-phenyl-ethyl-β-D-glucoside, 4-hydroxy-phenyl-2-ethyl-β-D-glucoside and four isomeric malonated benzyl-β-D-glucosides; isothiocyanate - benzyl isothiocyanate; minerals - calcium, phosphorus, iron, sodium, potassium; vitamins - vitamin C, thiamine, riboflavin, niacin; proteins, carbohydrates, fats, amino acids, citric acid, malic acid, and other compounds: α-linolenic acid, butanoic acid, methylbutanoate [11, 12, 13–15, 17]. Found in papaya leaves: flavonoids - myricetin, kaempferol, quercetin; phenylpropanoids - caffeic acid, p-coumaric acid, chlorogenic acid; carotenoids - β-carotene, lycopene, lutein, cryptoxanthin, violaxanthin and zeaxanthin; glycosides - cyanogenic glucoside, benzyl glucosinolate; vitamins - thiamine, riboflavin, niacin, ascorbic acid, α-tocopherol; minerals - calcium, phosphorus, potassium, magnesium, zinc, manganese, iron; amino acids - tryptophan, methionine, lysine; other compounds - saponins, tannins, anthraquinolones, reducing sugars [10, 13, 16, 18]. The fruits, leaves and stems of papaya contain milky juice - latex. It includes a complex of proteolytic enzymes: papain, chymopapain, proteinase IV, carikain, proteinase w, which are of great medical importance [6, 8]. quercetin; phenylpropanoids - caffeic acid, p-coumaric acid, chlorogenic acid; carotenoids - β-carotene, lycopene, lutein, cryptoxanthin, violaxanthin and zeaxanthin; glycosides - cyanogenic glucoside, benzyl glucosinolate; vitamins - thiamine, riboflavin, niacin, ascorbic acid, α-tocopherol; minerals - calcium, phosphorus, potassium, magnesium, zinc, manganese, iron; amino acids - tryptophan, methionine, lysine; other compounds - saponins, tannins, anthraquinolones, reducing sugars [10, 13, 16, 18]. The fruits, leaves and stems of papaya contain milky juice - latex. It includes a complex of proteolytic enzymes: papain, chymopapain, proteinase IV, carikain, proteinase w, which are of great medical importance [6, 8]. quercetin; phenylpropanoids - caffeic acid, p-coumaric acid, chlorogenic acid; carotenoids - β-carotene, lycopene, lutein, cryptoxanthin, violaxanthin and zeaxanthin; glycosides - cyanogenic glucoside, benzyl glucosinolate; vitamins - thiamine, riboflavin, niacin, ascorbic acid, α-tocopherol; minerals - calcium, phosphorus, potassium, magnesium, zinc, manganese, iron; amino acids - tryptophan, methionine, lysine; other compounds - saponins, tannins, anthraquinolones, reducing sugars [10, 13, 16, 18]. The fruits, leaves and stems of papaya contain milky juice - latex. It includes a complex of proteolytic enzymes: papain, chymopapain, proteinase IV, carikain, proteinase w, which are of great medical importance [6, 8]. lutein, cryptoxanthin, violaxanthin, and zeaxanthin; glycosides - cyanogenic glucoside, benzyl glucosinolate; vitamins - thiamine, riboflavin, niacin, ascorbic acid, α-tocopherol; minerals - calcium, phosphorus, potassium, magnesium, zinc, manganese, iron; amino acids - tryptophan, methionine, lysine; other compounds - saponins, tannins, anthraquinolones, reducing sugars [10, 13, 16, 18]. The fruits, leaves and stems of papaya contain milky juice - latex. It includes a complex of proteolytic enzymes: papain, chymopapain, proteinase IV, carikain, proteinase w, which are of great medical importance [6, 8]. lutein, cryptoxanthin, violaxanthin, and zeaxanthin; glycosides - cyanogenic glucoside, benzyl glucosinolate; vitamins - thiamine, riboflavin, niacin, ascorbic acid, α-tocopherol; minerals - calcium, phosphorus, potassium, magnesium, zinc, manganese, iron; amino acids - tryptophan, methionine, lysine; other compounds - saponins, tannins, anthraquinolones, reducing sugars [10, 13, 16, 18]. The fruits, leaves and stems of papaya contain milky juice - latex. It includes a complex of proteolytic enzymes: papain, chymopapain, proteinase IV, carikain, proteinase w, which are of great medical importance [6, 8]. iron; amino acids - tryptophan, methionine, lysine; o

Papain - monothiolcysteine endoprotease. The nature enzymatic action it is called "plant pepsin". Unlike pepsin, papain is active not only in acidic, but also in neutral and alkaline media (pH range - 3–12, optimum pH - 5). The catalytic center of papain contains a dithioacyl group. The enzyme binds to the substrate at the sites of localization of disulfide bonds, giving preference to the aromatic amino acid residue in the next position. The papain gene has been cloned and sequenced. It was found that it is produced by the plant in the form of propapain, which, after cleavage of the peptide fragment, is converted into an active enzyme, papain. Propapain gene derived from papaya fruit cloned in yeast Saccharomyces cerevisiae [6].

Chymopapain is a monothiol cysteine proteinase. Thanks to the substratethe specificity is similar to papain, but differs from it in electrophoretic mobility, persistence and solubility. It is a polypeptide consisting of 218

amino acid residues, exhibits significant structural similarities to papain and papaya proteinase, including a conserved catalytic site and disulfide bonds. Several isozyme fractions of chymopapain are isolated from latex during chromatography: chymopapain A, B, and M. Nevertheless, immunological studies indicate their homogeneity. It was found that chymopapain M is identical

the previously described papaya cysteine proteinases, peptidase B and proteinase IV. In terms of the specificity of the enzymatic action, it resembles papain, since it binds to the substrate at the sites of localization of disulfide bonds, but, unlike papain, the cleavage of the substrate occurs only if leucine, valine, threonine, or proline are in the next position [6].

Proteinase IV - cysteine proteinase, the main proteinase of latex,makes up about 30% of the protein present in it. Shows a high degree of homology with proteinase III of papaya (81%), chymopapain (70%) and papain (67%). It is very close to chymopapain in molecular weight and molecular charge [6].

Caricain is the most alkaline of the papaya latex cysteine proteinases.Like papain, caricaine is first produced in the form of the inactive zymogen procaricaine containing an inhibitory pro-region of 106 N-terminal amino acids. Enzyme activation consists in the cleavage of the pro-region of the molecule without its subsequent conformational changes. The structure of papaya proteinases has been studied using X-ray structural analysis [6].

Proteinase w (endopeptidase A, peptidase A) - monothiol cysteineproteinase. It is a polypeptide containing 216 amino acid residues and 3 disulfide bonds. For the manifestation of its enzymatic activity, the presence of a free cysteine residue in the active center is important. Shows a high degree of homology with papain (68.5%). In terms of the specificity of the enzymatic action, it resembles papain, since it binds to the substrate in the areas of localization of disulfide bonds. Cleavage occurs when leucine, valine or threonine are in the next position [6].

The latex of unripe papaya fruit also contains inhibitors of proteolytic enzymes: cystatin (a proteinase inhibitor) and a protein with the properties of an inhibitor of cysteine proteinases. The latter has the ability to block the activity of cattle trypsin and α-chymotrypsin by screening the binding sites of these enzymes on their substrates [6, 8].

The biological properties of papaya became known to Europeans in the 16th century. In 1519, Fernando Cortez, the Spanish conqueror, while in Mexico, was cured of poisoning with a drink made from papaya pulp. Then the Spaniards settled papaya in other tropical and subtropical countries [19].

Papaya has a number of pharmacological properties. Papaya-based preparations have anti-inflammatory, proteolytic, decongestant, regenerative, anthelmintic, antioxidant, antiviral effects [5].

Enzymes of papaya latex in their action are close to chymotrypsin and trypsin and are characterized by selective proteolytic activity - they hydrolyze proteins of necrotic tissues to polypeptides, but they are

inactive in relation to healthy tissues due to the presence of protease inhibitors in them. As a result of many years of scientific research, it was found that the complex of proteolytic enzymes of papaya latex has a positive effect on the cartilaginous tissues of the body, stimulates the regeneration of intervertebral discs and acts on hernias, reducing their size. Enzymes, penetrating into tissues and creating a depot in the area of the affected intervertebral discs, have a local effect on connective tissue, including the tissue of the intervertebral disc and hernial protrusion. They promote collagen production, which leads to mild scarring of the fibrous lining of the disc. Preservation of the biosynthesis of chondroitin sulfates by part of the disc cells increases the trophic role of the nucleus pulposus and restores disc turgor, making it more elastic. In addition to proteolytic activity, enzymes also have a pronounced anti-edematous and anti-inflammatory effect, improve blood circulation, stimulate phagocytosis, suppress hyaluronidase activity and enhance tissue regeneration. In case of IIIA burns, proteolytic enzymes of papaya latex help accelerate the rejection of scabs and cleanse granulating wounds from the remnants of purulent-necrotic tissues [5, 6].

Thanks to the action of its enzymes, papaya ensures the normal breakdown of proteins, fats and carbohydrates, even if the body lacks its own digestive enzymes. Therefore, regular intake of fresh papaya fruit pulp prevents constipation, flatulence, belching, nausea and feeling of heaviness after eating. Papaya enzymes break down proteins even in a neutral environment, therefore papaya is recommended to use to improve food digestion, especially with low stomach acidity and enzymatic pancreatic insufficiency. Papaya stimulates the synthesis of bile acids, preventing the formation of calculi and stagnation in the biliary system of the liver [8, 12]. There is a papain-based drug on the pharmaceutical market, which is used in the complex therapy of conditions, accompanied by a violation of the exocrine function of the pancreas, with flatulence, nausea, a feeling of fullness in the stomach - "Unienzyme with MPS", produced by UNICHEM LABORATORIES, Ltd. (India).

Papaya leaf extract is used in weight loss programs. It enhances the breakdown of fats and their excretion from the body, including cholesterol. Studies have shown that papaya reduces the need for insulin, which makes it possible to use it in the complex treatment of diabetes mellitus [6, 8].

Papaya is now widely cultivated in Southeast Asia, and modern Ayurveda uses its juice and seeds to treat amoebiasis, dysbiosis and helminthic infestations. Papaya suppresses the vital activity of ascaris, lamblia, nematodes and a number of other parasites [12, 14, 15].

In South Africa, papaya leaves and fruits are used for poorly healing wounds and festering ulcers. In the United States, papaya fruits are used to produce drugs that are used to treat herpes. Due to the high content of antioxidants, the fruits can be used in preventive

courses of treatment of diabetes mellitus, atherosclerosis and other heart diseases [7, 9, 10, 14, 15].

In some countries (Pakistan, Malaysia, Sri Lanka, etc.), papaya leaf extract is effectively used for thrombocytopenia [16, 17].

Papaya fruit is an ideal dietary food rich in nutrients, vitamins, minerals, dietary fiber [14].

Papaya enzymes are widely used in cosmetology, they help smooth the skin surface, freeing it from dead cells, eliminating collagen crosslinks and normalizing skin turgor. Papaya is effective when applied topically to eliminate acne, freckles, fungi and warts [6, 8, 9].

In the pharmaceutical industry of foreign countries, more than 100 papaya-based drugs are produced, which are widely used in various fields of medicine. However, in our country, it remains poorly studied.

Today, our country produces two preparations based on proteolytic enzymes of papaya latex: Karipazim (in the form of a lyophilisate for preparing a solution for external use) and Karipain (in the form of external forms - cream, gel, dry balm and in the form of capsules for oral administration). These drugs are successfully used in the therapy of the musculoskeletal system.

We carried out a comparative phytochemical study of papaya leaves (Carica papaya L.), native to India, and papaya leaves (Carica papaya L.) introduced on the territory of the Republic of Bashkortostan. In the course of the analysis, a comparative was established for some groups of biologically active substances: the quantitative content of ascorbic acid, tannins, flavonoids, polysaccharides.

The content of ascorbic acid in papaya leaves (India) was 1.4 ± 0.02%, in papaya leaves (Bashkortostan) - 2.1 ± 0.03%; the content of tannins was 2.9 ± 0.06% and 1.7 ± 0.02%, respectively. The quantitative content of the sum of flavonoids in the leaves in terms of rutin was 0.7 ± 0.02% for papaya (India) and 0.38 ± 0.02% for papaya (Bashkortostan), the content of polysaccharides was 11.8 ± 0.03% and 8.5 ± 0.02%, respectively [2.4].

CONCLUSIONS

Analyzing received results carried out phytochemical research, several conclusions can be drawn:

1) Based on the above literature review, papaya is promising plant for further pharmacological research.

2) The chemical composition of papaya has been studied only mainly by enzymatic composition.

3) Comparative phytochemical study of some groups biologically active substances showed that the introduced species of papaya are practically not inferior in content to wild-growing species.

Thus, samples of wild and introduced plants are comparable with each other in terms of the content of biologically active substances and introduced species of papaya in the conditions of the Republic of Bashkortostan can be

used for a qualitative replacement of wild-growing papaya and are a promising source for further deep phytochemical and pharmacological studies.

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