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Possibilities of Using Proteolytic Enzymes Carica Papaya L in Medical Practice

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ABSTRACT

The aim of this study is to investigate the proteolytic enzymes of the melon tree (Carica papaya L), grown in a solar greenhouse in Turkmenistan, to study the potential of these enzymes in medical practice.

Proteolytic enzymes of plant origin are contained in the milky juice of the melon tree (Carica papaya L.) These are papain, chymopapain A and B, peptidases A and B. Lekozyme , caripazim , lysozyme and many other drugs widely used in medical practice are produced from these proteolytic enzymes . We have experience in using proteolytic enzymes obtained from the milky juice of the melon tree in surgery (for purulent wounds, phlegmon and abscesses of the upper and lower extremities, purulent mastitis, trophic ulcers of the feet) and dentistry (for ulcerative gingivitis, periodontitis, etc.). Taking into account the encouraging results obtained, we plan to conduct research work on the treatment of urological diseases using various proteolytic enzymes obtained from the milky juice of the melon tree grown in local conditions of Turkmenistan.

The obtained solution from papaya allows to reduce the treatment time of purulent infections of soft tissues and oral cavity, which in turn is important for timely prevention of occurrence of abscesses and other complications. Agricultural technology of cultivation possibilities and technology of obtaining proteolytic enzymes from leaves and fruits of melon tree in conditions of Turkmenistan have been developed. Microclimate based on renewable energy sources has been created for cultivation.

Conclusion: The advantage of the claimed remedy compared to known ones is that the treatment uses the organic, natural composition of the plant's substances, which has effective properties in the treatment of inflammatory diseases and wounds.

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Introduction

Relevance of the problem. One of the main tasks of the State Program "Health" of the President of Turkmenistan is to provide the population with medicinal preparations of plant origin, to obtain valuable domestic preparations for use in medical practice and study of agricultural technology for the cultivation of medicinal plants in the conditions of Turkmenistan [1].

At present, much attention is paid to the use of proteolytic drugs of plant origin in medical practice.Modern medicine limits the use of antibiotics in medical practice, as they suppress the body's immune system and lead to various negative consequences. According to scientists, antibiotics can be replaced by super-antibodies that can freely penetrate cells and destroy pathogenic bacteria, viruses and toxins [1-6].

Proteolytic enzymes of plant origin are contained in the milky juice of the melon tree (Carica papaya L.), these are papain, chymopapain A and B, peptidases A and B. From these proteolytic enzymes, such drugs as lekozyme, caripazim, the mucolytic enzyme lysozyme and many others are produced, which are widely used in medical practice.

Biotechnological Features of Carica Papaya L

Botanical description. The melon tree, or papaya (Carica papaya L.), is a perennial tropical palm-like plant, up to 4-6 m high, of the papaya family (Caricaceae). The fruits hang on stalks under the crown, 10 to 30 см и1- long 4 кг, and resemble a melon in shape. Ripe fruits are yellow-orange, edible, and the inner cavity is filled with black seeds. The trunk is green, herbaceous, non-woody, has no branches, and at the top is a crown of large, palmately dissected, 5-7-lobed leaves with very long petioles. The leaves and fruits of the melon tree are used to improve the cooking of tough meat.

In the natural and climatic conditions of Turkmenistan, a microclimate has been created based on renewable energy sources, and agricultural technology for growing and obtaining domestic proteolytic enzymes from the milky juice of the melon tree in the conditions of Turkmenistan has been developed. The grown melon trees are shown in Figure 1 [2-6].

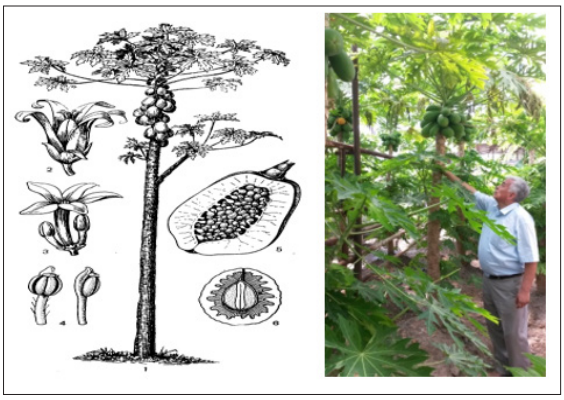

Figure: 1 Melon Tree (Carica Papaya L)

- General view of the plant
- Female flower of the branch
- Male flower
- Stamen
- Longitudinal section of the fruit
- Longitudinal section of the seed

Medicinal raw materials. Latex, seeds and dried milky juice (latex) were used as medicinal raw materials. The results of scientific research confirmed that papain is also found in smaller quantities in other parts of the plant, in particular in the leaves (Folia Caricae Papayae). The seeds of the melon tree contain fatty oils, which include oleic (75.50%), linoleic (2.13%), palmitic (11.38%), stearic ¬(5.25%) and arachidic (0.31%) acids. [2-6].

Biologically Active Substances of Latex. Seven Proteins were Identified in Carica Papaya l. Latex Using Electrophoresis in an Acidic Medium: Lipase, Chitinase, Lysozyme and a Complex of Proteolytic Enzymes

Papain (EC 3.4.22.2): Is a monothiol cysteine endoprotease. Due to the nature of its enzymatic action, it is called "plant pepsin". However, unlike pepsin, papain is active not only in acidic but also in neutral and alkaline environments (pH range 3-12, optimal pH 5) [2-9].

Chymopapain (EC 3.4.22.6): Is a monothiol cysteine proteinase. Due to its substrate specificity, it is similar to papain, but differs from it in electrophoretic mobility, stability and solubility [2-10].

Proteinase IV: Is a cysteine proteinase, the main proteinase of latex, making up about 30% of the protein present in it. It exhibits a high degree of homology with papaya proteinase III (81%), chymopapain (70%) and papain (67%). It is very close to chymopapain in molecular weight and charge of the molecule. Contamination of chymopapain with this enzyme is the reason for its heterogeneity during studies. M. P. Thomas et al. (1994) attribute this enzyme to the chymopapain M fraction [2-9].

Caricain (EC 3.4.22.30): Is The most alkaline of the cysteine proteases of papaya latex. Like papain, it is initially produced in the form of an inactive zymogen, procaricain, containing an inhibitory proregion of 106 N-terminal amino acids. Activation of the enzyme consists of cleavage of the proregion of the molecule without subsequent conformational changes. The structure of papaya proteases has been studied using X-ray structural analysis [2-9].

Proteinase w (Endopeptidase A, Peptidase A): Is a monothiol cysteine protease. It is a polypeptide containing 216 amino acid residues and 3 disulfide bonds. The presence of a free cysteine residue in the active center is important for its enzymatic activity. It exhibits a high degree of homology with papain (68.5%). In terms of specificity of enzymatic action, it resembles papain, since it binds to the substrate at sites of localization of disulfide bonds. Cleavage occurs when leucine, valine or threonine are in the next position.

Peptidase II : Alkaline monothiol cysteine proteinase. Contains a dithioacyl group in the catalytic center.

The latex of unripe papaya fruits also contains inhibitors of proteolytic enzymes: cystatin (a proteinase inhibitor with a molecular weight of 11,262 Da) and a protein with cysteine inhibitor properties proteinase, the molecule of which consists of 184 amino acid residues, contains 2 disulfide bonds and 2 carbohydrate residues in positions Asp84 and Asp90 [2-10].

Ripe fruits of the melon tree contain 8-12% sugar, a significant amount of vitamins A, B1, B2, C and D, and tonic substances.

Pharmacological properties. Proteolytic enzymes of the melon tree have anti-inflammatory, anticoagulant, dehydrating, analgesic, bactericidal, hemolytic properties. Given these properties of proteolytic enzymes of plant origin, they are widely used in medical practice: ophthalmology, surgery, neurosurgery, orthopedics, gastroenterology, etc. They help to destroy proteins of semi-peptides and amino acids, dissolve dead cells, without affecting normal ones.

In the pharmaceutical industry of ¬foreign countries, more than 100 medicinal products are produced using the milky juice of papaya (lekozyme, lekopain, caricaza, carcasme, caripain, wobenzym, super fat burner No. 1 and many others), widely ¬used in various fields of medicine [3-6].

Based on this, taking into account the biological characteristics of papaya and the natural and climatic conditions of Turkmenistan, we came to the conclusion that it is necessary to select a greenhouse design for its cultivation. At present, agricultural technology has been developed, a technology for obtaining proteolytic enzymes from the melon tree for use in clinical practice.

The Most Commonly Used Drugs and Proteolytic Enzymes

- Trypsin is an enzyme of animal origin, used in the form of a solution, prepared ex tempore
- Chymotrypsin – an enzyme of animal origin, used as trypsin
- Chymopsin is an enzyme of animal origin (a mixture of trypsin and chymotrypsin), a 0.1% solution of the drug is used
- Terrilitin – used in the form of a solution containing 40-50 proteolytic units (PU) per 1 ml
- Lysoamidase is a proteolytic enzyme that also has a bacteriolytic effect. It is used locally as a solution in 0.01 M sodium phosphate buffer (pH = 8.0) in concentrations of 5, 10, 25 PE in 1 ml
- Profezim is a proteolytic drug immobilized on aminocellulose, has a prolonged effect, has increased resistance to temperature factors, denaturing agents, changes in pH, and does not have a local irritant effect

The enzymes obtained in the work were used in surgery. The proteolytic and anti-inflammatory properties of papain allowed it to be used for the sanitation of various fistulas, cleansing wounds

of necrotic tissue, and preparing the surfaces of trophic ulcers for skin grafting [2-6].

In wet necrosis after a burn, papain allows for faster surface cleansing from necrotic tissue and its preparation for skin grafting. Enzymes were used in the hospital of military unit 2523 (Ashgabat) in the treatment of osteomyelitis, phlegmon, esophageal stenosis, and mastitis [2-6].

The use of domestic papain allows for the effective treatment of patients, while limiting the use of scarce, expensive imported drugs such as lekozyme, lekopain and others.

Results and Discussion

Having studied the biological and chemical properties of the milky juice of the melon tree, including testing for a negative reaction of the human body, we came to the conclusion that substances obtained from the leaves of the melon tree can be successfully used in the treatment of inflammatory purulent wounds of the skin surfaces (with purulent wounds, phlegmon and abscesses of the upper and lower extremities, purulent mastitis, trophic ulcers of the feet).

From the obtained biomass of melon tree latex, a 5%-20% solution is made in distilled water or saline solution.

The wound was covered with gauze ¬napkins soaked in 0.25-0.5% papain solution, and in cases of a large amount of necrotic tissue, the papain concentration was increased to 1%. It was noted that when applied locally, papain does not penetrate deeply into the tissue, but exerts its effect mainly on the wound surface, lysing non- ¬viable tissue. Therefore, in all cases, we infiltrated the papain solution into the necrotic ¬tissue, which contributed to rapid wound cleansing.

After the first papain applications, non-viable tissues were clearly ¬demarcated from healthy tissues, softened, especially the superficial layer, which resembled a mucoid mass. During dressings, ¬copious discharge from wounds with noticeable rejection of necrotic tissues was noted. Bright granulations appeared on the surface of wounds cleared of non-viable tissues, and a tendency toward epithelialization was noted along the edges.

The disappearance of the purulent-fibrous coating ¬was noted after 3-4 applications, epithelialization of wounds - after 6.

Good results were obtained in patients with phlegmon and abscesses of various locations in the upper and lower extremities: after opening the abscess and using papain applications, complete cleansing of the wound from non-viable ¬tissue and epithelialization of the wound were noted.

In patients with mastitis, after opening the abscess, ¬on the 4th day of using the applications, wound cleansing was noted, on the 7th day – good epigelization ¬, on the 11th day – complete wound healing by secondary ¬intention.

After 4 papain applications in patients with trophic ulcers in the foot area ¬, cleansing of the wound surface was observed, after 7 - good granulation, in connection with which on the 8th day the patients underwent surgery - free ¬skin grafting according to Tirsch. On the 12th day, wound healing was noted, the grafts were viable ¬, tissue granulation and skin scar were tender.

In addition to patients with surgical infections, we observed 23 more dental patients with purulent foci of the oral cavity, ulcerative gingivitis, periodontitis. They also used a remedy prepared from the biomass of latex of the melon tree. The method of conducting treatment procedures was the same as in the treatment of surgical infections. The result of treatment in pear patients using this remedy was reliably better than in patients who received standard treatment.

Moreover, in comparison with the known means and method, it is possible to reduce the treatment period for purulent infections by two to three days, which in turn is important for the timely prevention of the occurrence of abscesses and other side clinical effects.

The choice of the percentage ratio of the substance, made from the biomass of the leaves of the melon tree, and the frequency of treatment of areas of purulent infection in the oral cavity were determined experimentally, taking into account the course of the purulent process and the phase of the wound process itself.

With regard to the compliance of the declared method and means with the criteria of "novelty", "level of efficiency" and "industrial applicability", the following can be established: The conducted analytical search did not reveal any publications or patents that describe means and methods for treating purulent infections using a substance from the biomass of the melon tree latex. Thus, the method and method are not part of the previously known level of technology and meet the criterion of "scientific novelty".

A similar search did not reveal any data on the authors' findings. in percentage of the substance of the biomass of leaves for the purpose of treating humans, in particular in the treatment of purulent infections in surgical and dental practice. Thus, the essence of the method is not an obvious solution for a specialist in the field of medicine and meets the criterion of "inventive step".

Since the proposed means and method can be practically used in such a branch of human activity as medicine, the claimed method invention meets the criterion of "industrial applicability".

The conducted search did not reveal any publications or patents that describe means and methods of treating purulent infections using the substance of Papaya juice. Thus, the research is not part of the previously known level of technology and meets the criterion of "novelty".

A similar search did not reveal data on the percentage of the substance of the "Papaya" juice established for the purpose of effective treatment of humans. Since the proposed means and method can be practically used in such a field of human activity as medicine, the study meets the criterion of "industrial applicability" [2-6].

The use of enzymes in clinical surgery and dentistry allows for active and targeted ¬intervention in the course of suppurative processes, accelerating the cleansing of wounds from non-viable tissue. One of the advantages of using proteolytic enzymes is their necrolytic action in the absence ¬of a damaging effect on living tissue. According to a number of authors [1, 6], proteolytic enzymes of plant ¬origin, unlike animal ones (trypsin, chymotrypsin), are capable of acting on denatured proteins, which served as a theoretical justification for their use in purulent surgery to remove necrotic tissue, dissolve fibrin accumulations in body cavities and even blood vessels, liquefy wound discharge, and facilitate the penetration of medicinal substances through the intercellular subtraction.

Thus, the results of treatment of patients with purulent wounds of the skin surface and in the oral cavity indicate the effectiveness ¬of the use of proteolytic enzymes from the biomass of melon tree leaves.

Conclusion

The melon tree is a food product, but this plant has been found to contain biologically active substances such as lipase, chitinase, lysozyme and a complex of proteolytic enzymes, including cysteine inhibitors. proteinases.

In addition, the entire part of the melon tree contains proteolytic enzymes papain, chymopapain, proteinase, etc. These plant enzymes are widely used in medicine and various industries. For example, the proteolytic enzyme "Papain" is able to break down proteins into polypeptides and amino acids, and hydrolyzes any peptide bonds, with the exception of proline and glutamic acid bonds with a dissociated carboxyl group. It has a greater ability to break down proteins compared to most proteases of animal and bacterial origin. Although the activity of papain preparations varies depending on the method of preparation, it has the ability to break down lean meat in an amount 35 times greater than its own weight. High-quality papain digests egg albumin, the amount of which is 300 times greater than its own weight.

The separation of the milky juice of the melon tree was obtained by the method of ion-exchange chromatography: the protein released in the second peak has a proteolytic activity of 4000 ¬units / mg, the remaining proteins came together without separating. According to the electrophoregram, bands 1 and 5 are milky juice, 7 is the protein released in the second peak, electrophoretically pure, without any impurities. Papain from the company " Serva " (Germany) was used as a marker.

The enzymes obtained from the milky juice of papaya differ from known enzymes of animal origin in that, in certain concentrations, ¬they exhibit more pronounced chondro-, fibrino- and thrombolytic properties and more actively lyse and hydrolyze young connective ¬tissue and membrane formations [2].

A solution made from leaf biomass was used as a raw material for treatment. Since milk tubes contain milky juice in all parts of the melon tree, which contains proteolytic enzymes.

The use of enzymes in clinical surgery and dentistry allows for active and targeted ¬intervention in the course of suppurative processes, accelerating the cleansing of wounds from non-viable tissues. One of the advantages of using melon tree proteolytic enzymes is their necrolytic action in the absence ¬of damaging effects on living tissue. Unlike animal proteolytic enzymes (trypsin, chymotrypsin), plant-based proteolytic enzymes are capable of acting on denatured proteins, which served as a theoretical justification for their use in purulent surgery to remove necrotic tissue, dissolve fibrin accumulations in body cavities, liquefy wound discharge, and facilitate the penetration of medicinal ¬substances through intercellular subtraction.

The accumulated experience of papain treatment allows us to conclude that this enzyme ¬can be successfully used in the treatment of many diseases. Enzyme therapy in medicine deserves further study and implementation in the practice of medical institutions. The enzyme therapy method is simple, it can be used on an outpatient basis, does not cause serious complications and in many cases is economical and effective.

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