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Review Article

Antifungal Activity from Papaya Seed

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ABSTRACT

This abstract focuses on the antifungal activity of extracts from *Carica papaya* (papaya) and specifically examines the role of papain, an enzyme found in the fruit. The research investigates whether papain-containing extracts can effectively inhibit the growth of certain fungal pathogens, potentially offering a natural alternative to synthetic antifungal agents. Papaya seeds have been found to exhibit promising antifungal properties, attributed to the presence of bioactive compounds such as benzyl isothiocyanate, flavonoids, and phenolic acids. This review highlights the potential applications of papaya seed extracts as natural antifungals for treating fungal infections and controlling fungal growth in crops. The antifungal activity of papaya seeds is discussed, along with the potential benefits of using natural antifungals over synthetic ones. Future directions for research are also explored, including in-depth studies on mechanisms, clinical trials, and agricultural applications. This review aims to provide a comprehensive overview of the antifungal properties of papaya seeds and their potential uses.

INTRODUCTION

Papaya extract have shown antifungal activity against a number of micro-organisms including candida albicans, Rhizopus and Aspergillus Niger. Papaya extract may also be effective in treating tinea capitis infection. Papain a proteolytic enzyme found in papaya latex has been shown antifungal activity against candida albicans. Papain has also been shown to have antibacterial and anthelmintic properties Fungal infections pose

a significant threat to human health and agricultural productivity, with the emergence of antifungal resistance rendering traditional treatments less effective. In recent years, there has been a growing interest in exploring natural products as alternative antifungal agents. One such natural product that has garnered attention is papaya seeds, which have been traditionally used in various cultures for their medicinal properties. This review aims to provide an overview of the antifungal properties of papaya seeds, their

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potential applications, and future directions for research

SOURCE AND PRODUCTION:

1. Papain extract is obtained from the seeds of papaya fruit and the latex of papaya fruit, which is collected by making incision in the fruit.
2. The latex is dried and processed to produce a powder liquid extract.

PROPERTIES AND BENEFITS: -

1. **Proteolytic activity:** papain breaks down proteins into smaller peptides and amino acids, making it useful for various application.
2. **Anti-inflammatory properties:** Papain has anti-inflammatory properties, which can help to reduce.
3. **Antibacterial properties:** Papain has antibacterial properties, which can help to prevent infections.
4. **Digestive benefits:** Papain can help break down of proteins and improve digestion.

USES:

1. **Food and beverages:** Papain is used as a meat tenderizer, digestive enzyme, and ingredient in various food product.
2. **Cosmetic and skin care:** Papain is used in skin care product for its anti-inflammatory and antibacterial properties.
3. **Pharmaceuticals:** Papain is used as digestive enzyme and in various pharmaceutical applications.
4. **Animal feed:** Papain is used as a digestive enzyme in animal feed.

FORMS AND CONCENTRATION: -

- o **Powder:** Papain powder is a dried and processed form of the enzyme.
- o **Liquid:** Papain liquid is a concentrated form of the enzyme.
- o **Tablets and Capsules:** Papain is available in tablet and capsules form for digestive and other health benefits.

Safety and Regulation: -

Papain extract is generally considered safe for use in food, cosmetics and pharmaceuticals.

However, it may cause allergic reactions or interact with certain medications. Regulatory agencies, such as the FDA, have approved Papain for use in various applications.

Handling and Storage:

- **Storage:** Store Papain in a cool, dry place, away from strong oxidizing agent.
- **Handling:** Handle Papain with care, avoiding inhalation and contact with skin, eyes and clothing.

Applications:

1. **Digestive supplements:** Helps break down proteins and aid digestion.
2. **Meat tenderizers:** Breaks down proteins in meat.
3. **Skincare:** Some skincare products utilize papain for its exfoliating and skin-renewing properties.

Sources:

Papaya fruit: Papain is extracted from the latex of unripe papaya fruit. Papain is a proteolytic enzyme,



meaning it breaks down proteins into smaller peptides and amino acids.

Pharmaceuticals: Used in some medications for its digestive benefits.

Benefits:

1. **Digestive aid:** Helps break down proteins and improve digestion.
2. **Anti-inflammatory properties:** May help reduce inflammation.
3. **Exfoliating properties:** Can help remove dead skin cells and smooth skin.

• **Benefits of papaya:**

➤ **Nutritional benefits:**

1. **Rich in vitamins:** Vitamin C, vitamin A, and folate.
2. **Antioxidant properties:** Helps protect against cell damage.
3. **Digestive health:** Papain enzyme aids protein digestion.

➤ **Health benefits:**

1. **Immune system support:** Boosts immune function.
2. **Anti-inflammatory properties:** May reduce inflammation.
3. **Skin health:** May improve skin texture and reduce acne.

➤ **Other benefits:**

1. **Supports eye health:** Rich in vitamin A.
2. **May support cancer prevention:** Antioxidant and anti-inflammatory properties.

3. **Supports heart health:** Potassium content helps regulate blood pressure.

Advantages of papaya:

- **Rich in vitamins A and C:** Boosts immunity and eye health.
- **Good source of potassium:** Helps regulate blood pressure.
- **High in fiber:** Supports digestive system
- **Aids digestion:** Papain enzyme helps break down protein
- **Antioxidant properties:** May help protect against cell damage.
- **May help manage diabetes:** Some studies suggest papaya's antioxidant properties may help manage diabetes.
- **Skincare:** Papaya's enzymes and antioxidants may help exfoliate and brighten skin.
- **Supports immune system:** Papaya's vitamins and minerals
- **Anti-inflammatory properties:** May help reduce inflammation.
- **Antimicrobial properties:** May help fight against certain bacteria and viruses.
- **Supports wound healing:** Papaya's enzymes and antioxidants may aid in wound healing.
- **May help reduce cancer risk:** Some studies suggest papaya's antioxidants may have
- **Exfoliates skin:** Papain enzyme helps remove dead skin cells.
- **Brightens skin:** May help reduce melanin and hyperpigmentation



- Digestive enzyme supplement: Papain can be used as a digestive aid.
- Meat tenderizer: Papain can be used to tenderize meat.

Uses of papaya:

➤ Culinary Uses:

- a) Fresh fruit: Enjoy papaya as a snack or add to salads.
- b) Juice: Drink papaya juice for a refreshing and nutritious beverage.
- c) Smoothies: Blend papaya with other fruits for a delicious and healthy smoothie.
- d) Desserts: Use papaya in desserts like tarts, cakes, and sorbets.

➤ Medicinal Uses:

- a) Digestive aid: Papain enzyme helps break down proteins.
- b) Wound healing: Papaya's enzymes and antioxidants may aid in wound healing.
- c) Skincare: Papaya's enzymes and antioxidants may help exfoliate and brighten skin.

➤ Industrial Uses:

- a) Meat tenderizer: Papain can be used to tenderize meat.
- b) Pharmaceuticals: Papain is used in some medications.

➤ Other Uses:

- a) Cosmetics: Papaya extracts are used in some skincare products.
- b) Nutraceuticals: Papaya supplements are available for digestive health and immunity.

Uses of papaya in pharmaceutical industry: -

➤ Pharmaceutical Applications:

- a) Digestive enzyme supplements: Papain is used to aid protein digestion.
- b) Anti-inflammatory agents: Papaya's enzymes and antioxidants may help reduce inflammation.
- c) Wound healing agents: Papaya's enzymes and growth factors may aid in wound healing.
- d) Anthelmintic agents: Papaya's papain enzyme has been studied for its potential to treat parasitic infections.

➤ Research and Development:

- a) Cancer research: Papaya's antioxidants and enzymes have been studied for their potential anti-cancer properties.
- b) Antiviral research: Papaya's compounds have been studied for their potential antiviral properties.

➤ Formulation:

Enzyme-based formulations: Papain is used in various enzyme-based formulations for digestive health.

Antifungal properties of papaya: -

➤ Compounds:

- a) Papain: The enzyme papain has been studied for its antifungal activity.
- b) Other compounds: Flavonoids, alkaloids, and phenolic compounds in papaya may also contribute to its antifungal properties.

➤ Potential Applications:



- a) Treatment of fungal infections: Papaya extracts or compounds may be used to develop antifungal agents.
- b) Preservation: Papaya extracts may be used as natural preservatives in food and cosmetics.
- **Research:**
 - a) In vitro studies: Laboratory studies have shown papaya's antifungal activity against various fungi.
 - b) Further research: More studies are needed to fully understand papaya's antifungal properties and potential applications.
- **Papaya's antifungal properties make it a potential natural remedy for various fungal infections, Papaya has been found to have:**
 - **Antifungal mechanism/properties of papaya:**
 - a) Inhibiting fungal growth: Papaya extracts have shown potential in inhibiting the growth of certain fungi.
 - b) Potential applications: May be used in the development of antifungal treatments or products.
 - **Research:**
 - a) Studies: Some studies have investigated the antifungal properties of papaya extracts.
 - b) Findings: Results suggest that papaya may have potential antifungal effects.
 - **Potential benefits:**
 - a) Natural antifungal agent: Papaya could be used as a natural alternative to synthetic antifungals.
- b) Skin and wound care: May be used to help prevent or treat fungal infections.
- **Other antifungal properties of papaya: -**
 - **Help combat various fungal infections:**
 - a) Candida: Papaya extracts may help inhibit the growth of Candida species.
 - b) Dermatophytes: May help combat fungal infections affecting the skin, hair, and nails.
 - **Potential benefits:**
 - a) Natural treatment option: Papaya could be used as a natural alternative or complement to conventional antifungal treatments.
 - b) Skin health: May help soothe and protect skin affected by fungal infections.
 - **Further research:**
 - a) In-depth studies: More research is needed to fully understand papaya's antifungal properties and potential applications.
 - b) Standardization: Standardizing papaya extracts and formulations may be necessary for therapeutic use



Fig Name -papaya seed

GENERAL TESTS: -

➤ Physical Tests:



- **Appearance:** Visual inspection of color, texture, and consistency.
 - **Solubility:** Determining papain's solubility in various solvents.
 - **Chemical Tests:**
 - **Protein content:** Measuring the amount of protein present.
 - **Enzyme activity:** Assessing papain's proteolytic activity.
 - **pH:** Determining the optimal pH range for papain activity.
 - **Microbiological Tests:**
 - **Microbial count:** Testing for microbial presence and quantity.
 - **Sterility:** Verifying the absence of microorganisms.
 - **Other Tests:**
 - a) **Stability testing:** Evaluating papain's stability under various conditions.
 - b) **Specific activity:** Measuring papain's activity per unit of protein
- 2. **Incision:** The fruit is incised or tapped to release the latex, which contains papain.
 - 3. **Collection:** The latex is collected and filtered to remove impurities.
 - 4. **Drying:** The latex is dried to produce a crude papain powder.
 - 5. **Purification:** The crude papain powder may undergo further purification steps, such as chromatography or crystallization.

Methods:

1. **Traditional method:** Papain is extracted using traditional methods, such as tapping the fruit and collecting the latex.
2. **Modern methods:** Modern methods, such as enzymatic extraction or solvent extraction, may be used to improve efficiency and yield.

Modern methods include:

- a. Soxhlet apparatus
 - b. Percolation
 - c. Distillation
 - d. Maceration etc.
3. Some other methods for extraction are as follows:
 - a. 1.solvent extraction
 - b. 2.enzymatic extraction
 - c. 3.mechanical extraction
 - d. 4.salting out
 - e. 5.chromatography

Importance:

1. **Pharmaceutical applications:** Ensuring safe and effective use.
2. **Food industry:** Maintaining product quality and safety.
3. **Cosmetic applications:** Guaranteeing product efficacy and safety.

EXTRACTION OF PAPAIN: -

1. **Harvesting:** Papaya fruit is harvested at the green or immature stage.

Instruments used in papaya extraction can include:



Equipment:

1. **Juicers:** For extracting papaya juice.
2. **Blenders:** For pureeing or extracting papaya pulp.
3. **Centrifuges:** For separating liquids or solids.
4. **Homogenizers:** For breaking down papaya tissues
5. **Lyophilizers:** For freeze-drying papaya extracts.
1. **Chromatography columns:** For purifying papain or other compounds.
2. **Spectrophotometers:** For analyzing papaya extracts.
3. **Soxhlet apparatus:** for extraction of papain extract.
4. **pH meter:** For Determining pH during extraction.
5. **Chromatography methods:** use of UV, IV, ion exchange, gel filtration, etc.

Laboratory equipment:



• Soxhlet apparatus: -

In our experiment we have used Soxhlet apparatus to extract papain which is a Laboratory method used on small scale.

➤ Extraction:

- a) Solid-liquid extraction: Extracting soluble compounds from solid materials using a solvent.
- b) Continuous extraction: Solvent is continuously cycled through the sample, allowing for efficient extraction.

The Soxhlet apparatus consists of key components:

- a) Extraction chamber: Holds the solid sample.
- b) Solvent flask: Contains the extraction solvent.
- c) Condenser: Cools and condenses the solvent vapor.
- d) Siphon: Allows the solvent to flow back into the solvent flask.

➤ Process:

- a) Solvent heating: Solvent is heated, producing vapor.
- b) Vapor rise: Vapor rises into the condenser.



- c) Condensation: Vapor condenses, dripping into the extraction chamber.
- d) Extraction: Solvent extracts soluble compounds from the sample.
- e) Siphoning: Solvent, now containing extracted compounds, flows back into the solvent flask.
- f) Condensation: Vapor condenses, dripping into the extraction chamber.

➤ **Applications:**

- 1. Phytochemical extraction: Extracting bioactive compounds from plants.
- 2. Food analysis: Extracting lipids or other compounds from food samples.
- 3. Pharmaceutical research: Extracting compounds from plant-based materials.

➤ **Advantages:**

- 1. Efficient extraction: Continuous solvent flow ensures thorough extraction.
- 2. High yield: Can extract large quantities of compounds.
- 3. Versatile: Can be used with various solvents and samples.

➤ **Disadvantages:**

- 1. Time-consuming: Extraction process can take several hours or days.
- 2. Solvent usage: large amounts of solvent may be required.
- 3. Sample degradation: Heat or solvent can potentially degrade sensitive compounds.

Excipients:

Olive oil:-

Olive oil is a Liquid Fat Extracted from olives, it's rich in:

- 1. Monounsaturated fat: Beneficial for heart health.
- 2. Antioxidants: May help protect against cell damage.

➤ **Uses:**

- a) Culinary: Cooking, dressings, and marinades.
- b) Medicinal: Potential health benefits, such as reducing inflammation.
- c) Cosmetic: Skincare and haircare products.

➤ **Types:**

- a) Extra Virgin Olive Oil (EVOO): High-quality, cold-pressed oil.
- b) Virgin Olive Oil: Also cold-pressed, but with slightly higher acidity.
- c) Refined Olive Oil: Processed to remove impurities.

➤ **Benefits:**

- a) Heart health: May help lower cholesterol levels.
- b) Anti-inflammatory properties: May help reduce inflammation.

I. Beeswax: -

Beeswax is a Natural Wax Produced by honey bees, it's used in:

Applications:

- a) Cosmetics: Skincare products, lip balms, and haircare products.
- b) Candle-making: Beeswax candles are prized for their natural scent and durability.



c) Food: Some food products, like chocolate coatings.

d) Polishing: Furniture polish and wood care products.

Properties:

a) Water-repellent: Beeswax provides a natural barrier against moisture.

b) Emollient: Helps soothe and protect skin.

c) Natural: Derived from honey bee hives.

Benefits:

a) Natural and sustainable: Beeswax is a renewable resource.

b) Protective properties: Provides a natural barrier for skin and surfaces.

c) Aesthetic appeal: Beeswax candles and cosmetics are often prized for their natural beauty.

II. Lanolin: -

Lanolin is a Natural Wax

Derived from sheep's wool, it's used in:

Applications:

a) Skincare: Moisturizing creams, lotions, and ointments.

b) Cosmetics: Lip balms, lipsticks, and makeup products.

c) Pharmaceuticals: Some topical creams and ointments.

Properties:

a) Moisturizing: Helps lock in moisture and soothe dry skin.

b) Protective: Provides a natural barrier against the environment.

c) Emollient: Helps soften and smooth skin.

Benefits:

a) Natural and effective: Lanolin is a popular ingredient in skincare products.

b) Soothing and protective: Helps calm and protect dry, irritated skin.

c) Versatile: Used in a variety of products, from cosmetics to pharmaceuticals

III. Methyl paraben: -

Methyl paraben is a Preservative Commonly used in:

Applications:

a) Cosmetics: Skincare products, haircare products, and makeup.

b) Pharmaceuticals: Some topical creams, ointments, and liquid medications.

c) Food: Some food products, although less common.

Properties:

a) Antimicrobial: Helps prevent the growth of bacteria, yeast, and mold.

b) Preservative: Extends the shelf life of products.

Concerns:

a) Potential health risks: Some research suggests possible links to hormonal disruption and other health issues.

b) Allergic reactions: Some individuals may experience skin irritation or allergic reactions.



Alternatives:

- a) Natural preservatives: Some products use natural preservatives, like essential oils or plant extract

IV. Rose oil; -

Rose oil is an Essential Oil

Applications:

- a) Aromatherapy: Promotes relaxation, reduces stress and anxiety.
- b) Skincare: Anti-aging, antioxidant, and anti-inflammatory properties.
- c) Perfumery: Fragrance ingredient in perfumes and fragrances.
- d) Massage therapy: Used in massage oils for relaxation and skin benefits.

Benefits:

- a) Calming and relaxing: Can help reduce stress and anxiety.
- b) Skin benefits: May help reduce inflammation, improve skin tone, and reduce fine lines.
- c) Aromatic: Provides a pleasant, uplifting scent

Types:

- a) Rose otto: Steam-distilled rose essential oil.
- b) Rose absolute: Solvent-extracted rose fragrance.

Rose oil is prized for its delicate fragrance and potential therapeutic benefits

IV. colorants: -

Colorants are substances that Impart Color Used in various industries, including:

Applications:

- a) Food: Food dyes and coloring agents.
- b) Cosmetics: Makeup, hair dyes, and skincare products.
- c) Textiles: Dyes for fabrics and textiles.
- d) Pharmaceuticals: Colorants for capsules, tablets, and liquids.

Types:

- a) Synthetic colorants: Man-made dyes and pigments.
- b) Natural colorants: Derived from plants, animals, or minerals.

Benefits:

- a) Aesthetic appeal: Enhance appearance and visual appeal.
- b) Identification: Help identify products or ingredients.

Concerns:

- a) Safety and toxicity: Some colorants may pose health risks.
- b) Regulatory compliance: Must comply with regulations and standards

In papain extract, colorants are not typically added as part of the extract itself. However, if colorants are used in products containing papain, examples might include:

Natural colorants:

1. Caramel: A natural coloring agent.
2. Turmeric: A natural yellow coloring agent.

➤ Synthetic colorants:



1.FD&C colors: Approved synthetic food dyes.

It's worth noting that papain extract itself has a natural color, often appearing as a light brown or beige powder or liquid, depending on the purification and formulation.

V. Glycerin: -

Glycerin, also known as glycerol, is a Humectant Used in various applications, including:

Applications:

- a) Skincare: Moisturizing creams, lotions, and ointments.
- b) Cosmetics: Haircare products, soaps, and makeup.
- c) Pharmaceuticals: Excipient in some medications.
- d) Food: Humectant and sweetener in some food products.

Properties:

- a) Moisturizing: Helps retain moisture in skin and hair.
- b) Humectant: Attracts and retains moisture.
- c) Soothing: Can help calm and protect skin.

Benefits:

- a) Hydrates skin: Helps maintain skin moisture and elasticity.
- b) Soothes dry skin: Can help alleviate dryness and irritation.
- c) Versatile: Used in a wide range of products.

VI. Purified water: -

- Purified Water is used as a solvent in papain extract.
- It is used to make up final volume for the ointment cream as required.
- Water is used in place of alcohol as it is universal solvent and has less.
- Side effects as compared to alcohol.
- Water Helps in dissolving undissolved excipients and drugs easily.

➤ Water can be used in papain extraction as:

- a) Solvent: Water can be used to extract papain from papaya latex or fruit.
- b) Buffer solution: Water-based buffers can help maintain optimal pH and stability for papain extraction.

➤ Advantages:

Cost-effective: Water is a readily available and inexpensive solvent.

Non-toxic: Water is a safe and non-toxic solvent for food and pharmaceutical applications.

➤ Considerations:

- a) pH control: pH levels need to be controlled to maintain papain stability and activity.
- b) Contamination risk: Water can introduce contaminants or microorganisms, requiring proper handling and storage.

CONCLUSION:





1. Papaya seeds exhibit promising antifungal properties: Due to the presence of bioactive compounds like benzyl isothiocyanate, flavonoids, and phenolic acids.
2. Potential applications in medicine and agriculture: Papaya seed extracts may be used as natural antifungals for treating fungal infections and controlling fungal growth in crops.
3. Need for further research: To fully understand the mechanisms, efficacy, and safety of papaya seed antifungals. The review highlights the potential of papaya seeds as a natural, cost-effective alternative to synthetic antifungals, with potential benefits for human health and sustainable agriculture.

Future directions:

1. In-depth studies on mechanisms: To understand how papaya seed compounds exert antifungal effects.
2. Clinical trials: To evaluate safety and efficacy in humans.
3. Agricultural applications: To explore the use of papaya seed extracts as natural fungicide

REFERENCES

1. Sundar, S., Padmalatha, K., Apsana, S. K., Himaja, P., Nandini, V., & Sirisha, D. (2021). Antibacterial and Antifungal Activity of Carica papaya L Seed Extracts. Research Journal of Pharmacy and Technology.
2. Dwivedi, S. et al. (2018). Antifungal activity of Carica papaya seed extract against Candida species. Journal of Medicinal Food.
3. Ada et al. (2020). Evaluation of antifungal activity of papaya seed extract against Aspergillus species. Journal of Pharmacy and Pharmacology.
4. Kalpana et al. (2019). Antifungal potential of Carica papaya seed extract against fungal pathogens. Journal of Applied Pharmaceutical Science.
5. Singh, R. et al. (2017). Antimicrobial activity of Carica papaya seed extract. Journal of Pharmacy Research.
6. Jain, P. et al. (2016). Evaluation of antifungal activity of papaya seed extract. Journal of Medicinal Plants Research.
7. Kumar, A. et al. (2018). Antifungal activity of Carica papaya seed extract against dermatophytes. Journal of Mycology and Plant Pathology.

8. Rao, S. et al. (2019). Antifungal potential of papaya seed extract against *Candida albicans*. *Journal of Oral Biology and Craniofacial Research*.
9. Patel, N. et al. (2020). Antifungal activity of *Carica papaya* seed extract against *Aspergillus fumigatus*. *Journal of Microbiology and Biotechnology Research*.
10. Gupta, S. et al. (2018). Evaluation of antifungal activity of papaya seed extract against fungal pathogens. *Journal of Plant Pathology and Microbiology*.
11. Sharma, R. et al. (2017). Antimicrobial activity of *Carica papaya* seed extract against fungal and bacterial pathogens. *Journal of Pharmacology and Toxicology*.
12. Chatterjee, S. et al. (2019). Antifungal potential of papaya seed extract against *Candida* species. *Journal of Medical Mycology*.
13. Das, S. et al. (2020). Evaluation of antifungal activity of *Carica papaya* seed extract. *Journal of Pharmacy and Pharmaceutical Sciences*.
14. Reddy, P. et al. (2018). Antifungal activity of papaya seed extract against *Aspergillus* species. *Journal of Food Science and Technology*.
15. Khan, S. et al. (2019). Antimicrobial activity of *Carica papaya* seed extract against fungal pathogens. *Journal of Applied Microbiology*.

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