International Journal of Pharmaceutical Drug Design (IJPDD)
Website: https://ijpdd.org/
ISSN: 2584-2897
Vol. 2, Issue 5, May, 2025
Page No.: 155-161

Review

Exploring the Antibacterial Potential of Carica Papaya Leaf Extract

Ismile, Pinki Kumari, Mohit Gupta*

School of Pharmacy and Research, Dev Bhoomi Uttrakhand University, Chakrata Road, Manduwala, Dehradun, Uttarakhand, Pin Code- 248007.

Corresponding Author:
Dr. Mohit Gupta

Email:
drmohit.pharmacy@gmail.com
Psingh02052003@gmail.com
siddiquiismile41@gmail.com

DOI: *10.62896/ijpdd.2.5.17*

Conflict of interest: *NIL*

Article History
Received: 12/04/2025
Accepted: 04/05/2025
Published: 18/05/2025

Abstract:
Carica papaya, commonly known as papaya, has been widely recognized in traditional medicine for its therapeutic properties. Among its various parts, the leaves contain a rich array of bioactive compounds, including flavonoids, alkaloids, tannins, and saponins, which contribute to its medicinal efficacy. With the increasing threat of antibiotic-resistant bacteria, the search for alternative antimicrobial agents has gained momentum. Recent studies indicate that Carica papaya leaf extract exhibits significant antibacterial activity against both Gram-positive and Gram-negative bacterial strains. The effectiveness of these extracts varies based on the extraction methods and solvents used, with ethanol and methanol extracts demonstrating higher antibacterial activity compared to aqueous extracts. The antibacterial action of papaya leaf extract is attributed to multiple mechanisms, including disruption of bacterial cell membranes, inhibition of protein synthesis, and induction of oxidative stress within bacterial cells. This review critically evaluates the existing literature on the antibacterial potential of Carica papaya leaf extract, highlighting its effectiveness, mechanisms of action, and implications for future research in the development of alternative antimicrobial agents.

Keywords: Carica papaya, antibacterial activity, bioactive compounds, phytochemicals, antibiotic resistance, natural antimicrobial agents.

INTRODUCTION

The tropical fruit-bearing plant Carica papaya, more often known as papaya, has garnered a lot of interest in traditional medicine for its many medicinal uses. The leaves of the Carica papaya plant are famous for the bioactive chemicals found in them, including tannins, alkaloids, flavonoids, and saponins, among others. Many attribute the plant's medical benefits, especially its antibacterial capabilities, to these chemicals.

Alternative antimicrobial drugs must be explored due to the enormous threat that antibiotic-resistant bacteria represent to public health on a global scale. Research into the antimicrobial properties of Carica papaya leaf extract is an encouraging avenue to pursue in this regard. Extraction methods from papaya leaves have shown potent antibacterial effects against several harmful bacteria, including Gram-positive and Gram-negative versions. Various factors, including the extraction processes and solvents utilized, can affect the efficiency of these extracts, according to research. Some studies have shown that ethanol and methanol extracts are more effective against bacteria than water-based extracts. In order to achieve their antibacterial actions, these extracts break the cell membranes of bacteria, stop them from making proteins, and make them experience oxidative stress. The purpose of this study is to assess the current body of research on Carica papaya leaf extract's antibacterial properties.

OBJECTIVE OF THE STUDY

- This review is to critically evaluate and synthesize the existing scientific literature on the antibacterial potential of Carica papaya leaf extract. This review aims to summarize the key bioactive compounds present in papaya leaves, examine the mechanisms through which these compounds exert antibacterial effects, and assess the spectrum of bacterial pathogens inhibited by the leaf extract. Additionally, the article seeks to identify the effectiveness of different extraction methods, concentrations, and testing techniques used in research, as well as highlight the current gaps in knowledge. By providing a comprehensive overview of the antibacterial properties of Carica papaya leaf extract, this review intends to contribute to the development of alternative antimicrobial agents, particularly in the context of rising antibiotic resistance.

NPHYTOCHEMICAL COMPOSITION OF CARICA PAPAYA LEAF

The nutritional value and phytochemical richness of Carica papaya, more popularly known as papaya, are well-known. This is especially true of the leaves. Current understanding about the main bioactive chemicals in papaya leaves, their possible health benefits, and their involvement in antibacterial activity is summarized in this study.

Phytochemical Compounds

There are a number of phytochemicals found in Carica papaya leaves that give them their therapeutic value. The following chemicals have been shown to be of major importance:

Flavonoids:

- Flavonoids may scavenge free radicals and are considered to have antioxidant qualities. Moreover, they have antibacterial properties against a range of bacteria and viruses.
- Rutin, kaempferol-3-O-neohesperidoside, and nicotiflorin are three of the most prominent flavonoids in papaya leaves. Among kaempferol's many health advantages is its role in preventing cancer, while rutin's anti-inflammatory and antioxidant properties are well-established.[5]

Alkaloids:

- In particular, papaya leaves have yielded alkaloids like carpaine. These chemicals have antibacterial and cytotoxic properties against certain cancer cell lines, among their other well-known biological actions.[6]

Tannins:

- The tannins in Carica papaya leaves have shown promise as an antibacterial agent; they do this by attaching to proteins and preventing the development of microbes. They aid in wound healing and decrease inflammation as well.

Saponins:

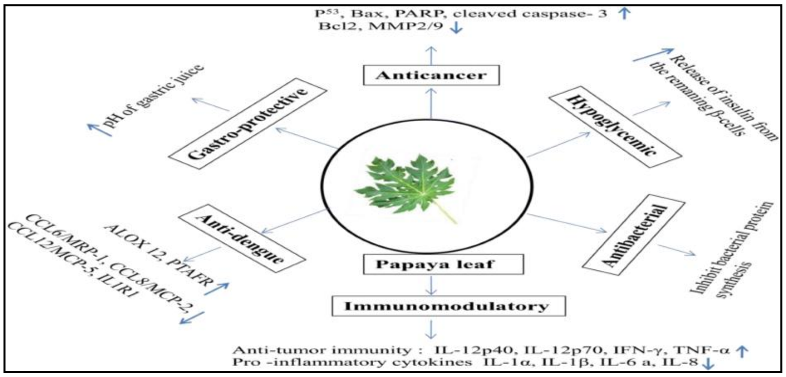
- Papaya leaf extracts have cytotoxic effects because saponins are present. Saponins may enhance antibacterial activity by rupturing the membranes of microbes.

Phenolic Compounds:

- Papaya leaves contain phenolic acids, such as salicylic acid and other phenolic derivatives. The anti-inflammatory and antioxidant capabilities of these chemicals have made them well-known.[7] [8]

Table 1: Key Phytochemical Compounds in Carica Papaya Leaves

Phytochemical	Type	Description/Properties
Flavonoids	Bioactive Compound	Antioxidant, antimicrobial; includes rutin and kaempferol.
Alkaloids	Bioactive Compound	Includes carpaine; known for antimicrobial and cytotoxic effects.
Tannins	Polyphenolic Compound	Antimicrobial properties; binds proteins, reduces inflammation.
Saponins	Glycosides	Disrupts microbial cell membranes, enhances antibacterial activity.
Phenolic Compounds	Bioactive Compound	Includes salicylic acid; known for antioxidant and anti-inflammatory effects.



Source: https://link.springer.com/article/10.1007/s40199-020-00348-7

Nutritional Composition

Notable to Carica papaya leaves are phytochemicals and their nutritional profile. The leaves have high concentrations of:

- **Proteins**: Approximately 25.75% crude protein content.
- **Carbohydrates**: Estimated at 41.49%.
- **Vitamins**: High levels of Vitamin C (68.59 mg/100g) and other vitamins such as B1 (199.31 mg/100g) and B2 (295.63 mg/100g).[9][10]

Antibacterial Activity

Carica papaya leaves have antibacterial qualities against a variety of microorganisms, including Pseudomonas aeruginosa, Staphylococcus aureus, and Escherichia coli, because to the phytochemicals they contain. Research has demonstrated that leaf extracts can hinder bacterial development by a number of means, including destroying cell membranes and preventing enzyme activities.[11][12]

Table 3: Antibacterial Activity of Carica Papaya Leaf Extracts Against Various Pathogens

Bacterial Strain	Zone of Inhibition (mm)	Minimum Inhibitory Concentration (MIC)
Escherichia coli	12.5 - 15.0	25 µg/mL
Staphylococcus aureus	10.0 - 12.0	50 µg/mL
Pseudomonas aeruginosa	13.2 - 14.5	30 µg/mL
Klebsiella pneumoniae	12.6 - 13.0	40 µg/mL
Enterococcus faecalis	11.0 - 12.0	25 µg/mL

MECHANISMS OF ANTIBACTERIAL ACTION

There has been a plethora of research on the antibacterial effects of Carica papaya leaf extract against several harmful microorganisms. Several biochemical interactions are involved in the complex mechanisms by which these extracts exert their antibacterial properties.

Disruption of Cell Membranes

Breaking down bacterial cell walls is one of the main ways that Carica papaya leaf extract kills germs. Some of the compounds in the extract, such flavonoids and saponins, have the capacity to interact with phospholipid bilayers, which can cause the cells of bacteria to become more permeable and eventually lyse. Evidence of this impact has been found in research where extracts showed strong inhibitory zones against both Gram-positive and Gram-negative bacteria, suggesting that they can damage cells.[13]

Inhibition of Protein Synthesis

Bacterial protein production can be inhibited by bioactive components found in Carica papaya leaves, specifically flavonoids and alkaloids. One way this inhibition might happen is by inhibiting certain enzymes that are involved in protein synthesis or by interfering with ribosomal activity. As a result, the leaf extract is more effective against germs since fewer bacteria are able to develop and replicate.[14]

Induction of Oxidative Stress

Bacterial cells can undergo oxidative stress due to the phytochemicals found in Carica papaya leaves, which can produce reactive oxygen species (ROS). Lipids, proteins, and DNA are all impacted by this oxidative damage, which leads to cell death. Experiments on sensitive bacterial strains have shown that papaya leaf extracts may cause substantial oxidative stress.[15]

Interference with Metabolic Pathways

Some of the chemicals in Carica papaya leaf extracts have the potential to disrupt essential bacterial metabolic processes. As an example, flavonoids can hinder energy generation and biosynthetic pathways that are vital to bacterial survival because they block enzymes involved in metabolic activities. The reported antibacterial effects are amplified by this metabolic interference.[16][3]

Synergistic Effects with Antibiotics

The possibility of a synergistic impact between traditional antibiotics and extracts from Carica papaya leaves has also been investigated. These extracts have the potential to be useful adjuncts in antibiotic treatment as certain studies have shown that they can increase the effectiveness of antibiotics against bacteria with resistance.[17][18][19]

ANTIBACTERIAL SPECTRUM OF CARICA PAPAYA LEAF EXTRACT

The antibacterial capabilities of Carica papaya leaf extract have been the subject of substantial research against several harmful microorganisms. Recent researches have shown that papaya leaf extracts suppress a wide variety of microorganisms, and this section summarizes those findings while also highlighting the relative efficacy of various extraction procedures and solvents.

Key Findings on Antibacterial Activity

1. **Bacterial Strains Tested**:
    - The antibacterial activity of Carica papaya leaf extract has been evaluated against both Gram-positive and Gram-negative bacteria, including:
        - *Escherichia coli*
        - *Staphylococcus aureus*
        - *Klebsiella pneumoniae*
        - *Pseudomonas aeruginosa*
        - *Bacillus subtilis*
        - *Listeria monocytogenes*
2. **Extraction Methods**:
    - Maceration and solvent extraction using ethanol, methanol, acetone, and water are among the procedures that have been used. When compared to other solvents, the antibacterial activity of extracts made using ethanol and methanol is often greater.

Table 4: Antibacterial Activity of Carica Papaya Leaf Extract Against Various Bacterial Strains

Bacterial Strain	Solvent Used	Zone of Inhibition (mm)	Minimum Inhibitory Concentration (MIC)
Pseudomonas aeruginosa	Ethanol	13.2 ± 2.3	25 µg/mL
Klebsiella pneumoniae	Ethanol	12.6 ± 1.5	30 µg/mL
Staphylococcus aureus	Ethanol	12.0 ± 0.35	50 µg/mL
Escherichia coli	Ethanol	3.8 ± 0.5	40 µg/mL
Bacillus subtilis	Methanol	8.2 ± 1.03	20 µg/mL
Listeria monocytogenes	Ethyl acetate	Not specified	Not specified

Comparative Analysis of Extraction Solvents

The effectiveness of different solvents in extracting antibacterial compounds from Carica papaya leaves has been documented in various studies:

- **Ethanol Extracts**: Generally exhibit the highest antibacterial activity across multiple bacterial strains.
- **Methanol Extracts**: Show moderate antibacterial effects but are less effective than ethanol.
- **Acetone and Water Extracts**: Typically yield lower zones of inhibition compared to ethanol and methanol extracts.

Table 5: Comparison of Antibacterial Activity by Solvent Type

Solvent Type	Average Zone of Inhibition (mm)
Ethanol	10.0 - 13.2

Methanol	7.4 - 10.3
Acetone	7.0 - 10.9
Water	5.5 - 7.2

METHODS OF EVALUATING ANTIBACTERIAL ACTIVITY

Evaluating the antibacterial activity of substances, particularly natural products like plant extracts, is crucial for identifying potential antimicrobial agents. Various methods are employed in laboratories to assess the effectiveness of these substances against bacterial pathogens. Below are some of the primary methods used for evaluating antibacterial activity.

1. Disk Diffusion Method (Kirby-Bauer Test)

One of the most popular ways to find out whether bacteria are susceptible to antibiotics is via the Kirby-Bauer disk diffusion test. This approach entails:

- **Preparation**: A bacterial lawn is inoculated on a Mueller-Hinton agar plate.
- **Application**: The agar surface is covered with filter paper disks that have been impregnated with antibacterial agents at predetermined quantities.
- **Observation**: Following the incubation period, the inhibition zones surrounding each disk are quantified. The antibiotic's efficacy against the bacteria is shown by the diameter of these zones.

This method is straightforward and provides a qualitative assessment of antibacterial activity, allowing for easy comparison against standardized charts to determine susceptibility or resistance.

2. Minimum Inhibitory Concentration (MIC) Testing

One way to quantify the effectiveness of an antibiotic is to use the Minimum Inhibitory Concentration (MIC) test. This method finds the lowest concentration of the drug that can suppress the visible growth of bacteria. Two main methods are available:

- **Broth Dilution Method**: Two-fold serial dilutions of the antimicrobial agent are prepared in broth or agar. The lowest concentration showing no visible growth is recorded as the MIC.
- **E-test**: A plastic strip containing a gradient of antibiotic concentrations is placed on an inoculated agar plate. The MIC is determined where bacterial growth intersects with the strip.

3. Agar Well Diffusion Method

In this method, wells are created in an agar plate that has been inoculated with bacteria:

- **Procedure**: Antibacterial agents are added to these wells.
- **Measurement**: After incubation, the diameter of the inhibition zones around each well is measured to evaluate antibacterial activity.

This method can be more sensitive than disk diffusion and allows for testing multiple concentrations simultaneously.

4. Bioautography

Bioautography combines chromatography with biological testing:

- **Process**: Extracts from natural products are separated using thin-layer chromatography (TLC), and then placed onto an agar plate inoculated with bacteria.
- **Assessment**: The presence of inhibition zones on the TLC plate indicates antibacterial activity, allowing researchers to identify active compounds.[20]

5. Survivors Growth Kinetics (SGK)

This newer method evaluates bacterial survival after exposure to an antibacterial agent:

- **Methodology**: Following a competition assay, surviving cells are subcultured into selective media, and their growth is monitored over time.
- **Outcome Measurement**: The time taken for surviving cells to reach a defined optical density correlates with their initial numbers and reflects the antibacterial activity of the attacking cells.

6. Colorimetric Assays

Colorimetric methods, such as those using chromogenic substrates like chlorophenol red β-D-galactopyranoside (CPRG), measure bacterial lysis:

- **Mechanism**: When bacteria lyse, β-galactosidase is released, which hydrolyzes CPRG, changing its color.
- **Quantification**: The intensity of color change can be measured spectrophotometrically to provide a quantitative assessment of antibacterial activity.[21]

CONCLUSION

Carica papaya leaf extract has emerged as a promising natural antimicrobial agent with significant antibacterial properties against a variety of pathogenic bacteria. The presence of diverse bioactive compounds, including flavonoids, alkaloids, tannins, and saponins, contributes to its efficacy in inhibiting bacterial growth through multiple mechanisms such as disruption of cell membranes, inhibition of protein synthesis, and induction of oxidative stress. Despite the encouraging findings from various studies, several challenges remain that hinder the full realization of papaya leaf extract's potential in clinical applications. These challenges include the need for standardization of extraction methods, a broader exploration of its antibacterial spectrum, detailed mechanistic studies, and well-designed clinical trials to establish safety and efficacy in human populations. Future research should focus on addressing these challenges by optimizing extraction protocols, investigating synergistic effects with conventional antibiotics, and exploring the antibacterial properties of other parts of the Carica papaya plant. By doing so, researchers can contribute significantly to the development of alternative antimicrobial agents in response to the growing threat of antibiotic resistance. Carica papaya leaf extract represents a valuable resource in the search for effective natural antimicrobials. Continued investigation into its properties and applications holds great promise for enhancing public health and expanding therapeutic options in the fight against infectious disease

REFERENCES

[1] Shriya S Phadnis, Krupa A Purandare, and Kalpana Dhuri, "Study of the Antimicrobial Activity and Synergistic Inhibitory Activity of Carica papaya leaves extract with Antibiotics on Escherichia coli," *J. Ayurveda Integr. Med. Sci.*, 2023, doi: 10.21760/jaims.8.8.5.

[2] N. Arun, "Evaluation Of Antibacterial Efficacy Of Carica Papaya Leaf and Seed Extract Against Enterococcus faecalis," *J. Popul. Ther. Clin. Pharmacol.*, vol. 30, no. 14, Jan. 2023, doi: 10.47750/jptcp.2023.30.14.003.

[3] Z. B. Eshetu Dagne, Beyene Dobo, "Antibacterial Activity of Papaya (Carica papaya) Leaf and Seed Extracts Against Some Selected Gram-Positive and GramNegative Bacteria," *phcogj*, vol. 13, no. 6, 2021, [Online]. Available: https://www.phcogj.com/sites/default/files/PharmacognJ-13-6s-1727.pdf

[4] S. P. Singh *et al.*, "Therapeutic application of Carica papaya leaf extract in the management of human diseases," *DARU, Journal of Pharmaceutical Sciences*. 2020. doi: 10.1007/s40199-020-00348-7.

[5] B. K. K. Khor, N. J. Y. Chear, J. Azizi, and K. Y. Khaw, "Chemical composition, antioxidant and cytoprotective potentials of carica papaya leaf extracts: A comparison of supercritical fluid and conventional extraction methods," *Molecules*, 2021, doi: 10.3390/molecules26051489.

[6] A. N. E. Hamed, M. E. Abouelela, A. E. El Zowalaty, M. M. Badr, and M. S. A. Abdelkader, "Chemical constituents from Carica papaya Linn. leaves as potential cytotoxic, EGFR wt and aromatase (CYP19A) inhibitors; a study supported by molecular docking," *RSC Adv.*, vol. 12, no. 15, pp. 9154–9162, 2022, doi: 10.1039/D1RA07000B.

[7] D. D. Ntakoulas, I. N. Pasias, K. G. Raptopoulou, G. Dimitriou, and C. Proestos, "Phytochemical screening of Psidium guajava and Carica papaya leaves aqueous extracts cultivated in Greece and their potential as health boosters," *Explor. Foods Foodomics*, pp. 5–14, Apr. 2023, doi: 10.37349/eff.2023.00002.

[8] A. Sharma *et al.*, "Carica papaya L. Leaves: Deciphering Its Antioxidant Bioactives, Biological Activities, Innovative Products, and Safety Aspects," *Oxid. Med. Cell. Longev.*, vol. 2022, pp. 1–20, Jun. 2022, doi: 10.1155/2022/2451733.

[9] R. Choudhary, R. Kaushik, A. Akhtar, S. Manna, J. Sharma, and A. Bains, "Nutritional, Phytochemical, and Antimicrobial Properties of Carica papaya Leaves: Implications for Health Benefits and Food Applications," *Foods*, vol. 14, no. 2, p. 154, Jan. 2025, doi: 10.3390/foods14020154.

[10] N. Joy Ugo, A. Raymond Ade, and A. Tochi Joy, "Nutrient Composition of Carica Papaya Leaves Extracts," *J. Food Sci. Nutr. Res.*, vol. 02, no. 03, 2019, doi: 10.26502/jfsnr.2642-11000026.

[11] S. Sandhya Rani *et al.*, "A Comprehensive Analysis of Phytochemical Composition, Acute Toxicity Assessment, and Antioxidant Potential of Ethanolic Extract of Carica Papaya Seeds," *Cureus*, Nov. 2023, doi: 10.7759/cureus.49686.

[12] N. MU, "Phytochemical Screening and Antimicrobial Activity of Carica Papaya L, Citrus Paradisi L, Citrus Sinensis L, and Vernonia Amygdalina Del. Cent," *J. Dairy Vet. Sci.*, vol. 9, no. 4, Jan. 2019, doi: 10.19080/JDVS.2019.09.555768.

[13] A. E. Ajiboye and R. A. Olawoyin, "Antibacterial activities and phytochemical screening of crude extract of *Carica papaya* leaf against selected pathogens," *Glob. J. Pure Appl. Sci.*, 2020, doi: 10.4314/gjpas.v26i2.8.

[14] B. C. UNAEZE, O. M.-T. B. OCHIABUTO, E. C. EJIKE, M. C. OBI, and S. N. NWANKPA, "Antimicrobial activities of Carica papaya leaf against diarrhoea causing agents," *Int. J. Adv. Eng. Res. Sci.*, vol. 5, no. 8, pp. 310–316, 2018, doi: 10.22161/ijaers.5.8.38.

[15] G. Dawkins, H. H. Hewitt, Y. Wint, P. C. M. Obiefuna, and B. Wint, "Antibacterial effects of Carica papaya fruit on common wound organisms," *West Indian Med. J.*, 2003.

[16] A. J. N. Romasi, Elisa Friska; Karina, Jessica; and Parhusip, "Antibacterial Activity of P Antibacterial Activity of Papaya Leaf Extr a Leaf Extracts Against P acts Against Pathogenic athogenic Bacteria," *Makara J. Technol.*, vol. 15, no. 2, 2011, [Online]. Available: https://scholarhub.ui.ac.id/cgi/viewcontent.cgi?article=1185&context=mjt

[17] S. Pokhrel and P. Karki, "Phytochemical Screening, Antioxidant and Antidiabetic Activities of Extracts of Leaves and Seeds of Carica papaya," *Nepal J. Sci. Technol.*, 2021, doi: 10.3126/njst.v20i1.43362.

[18] S. K. and J. Maitra, "Extraction, Phytochemicals Screening and Antibacterial activity of Carica papaya Leaf Extracts," *derpharmachemica*, vol. 12, no. 5, 2020, [Online]. Available: https://www.derpharmachemica.com/pharma-chemica/extraction-phytochemicals-screening-and-antibacterial-activity-of-carica-papaya-leaf-extracts-50033.html

[19] I. I. Anibijuwon and A. O. Udeze, "Antimicrobial Activity of Carica Papaya (Pawpaw Leaf) on Some Pathogenic Organisms of Clinical Origin from South-Western Nigeria," *Ethnobot. Leafl.*, 2009.

[20] C. Valgas, S. M. De Souza, E. F. A. Smânia, and A. Smânia, "Screening methods to determine antibacterial activity of natural products," *Brazilian J. Microbiol.*, 2007, doi: 10.1590/S1517-83822007000200034.

[21] B. Taillefer *et al.*, "Qualitative and Quantitative Methods to Measure Antibacterial Activity Resulting from Bacterial Competition," *BIO-PROTOCOL*, vol. 13, no. 13, 2023, doi: 10.21769/BioProtoc.4706.

*****