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Narrative Review

Potential Role of *Carica papaya* (Papaya) in Managing Inflammation and Hypertension

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Abstract

Background: *Carica papaya* is a tropical herb used traditionally for multiple medicinal uses. Its phytochemical compounds, like flavonoids and alkaloids, are antioxidant and anti-inflammatory in nature. The existing evidence indicates its possible involvement in cardiovascular health, especially in the control of hypertension. The objective of the current commentary is to highlight the dual therapeutic significance of *C. papaya* in the prevention and management of inflammation and hypertension.

Methods: This narrative review summarizes preclinical and clinical research on *C. papaya*. A targeted literature search (2000–2024) identified seven relevant studies on *C. papaya* in relation to hypertension and inflammation, which were included to support this commentary. Information was gathered from PubMed, Scopus, and Google Scholar, highlighting its antihypertensive and anti-inflammatory activity. Underlying mechanisms, such as antioxidant modulation and Angiotensin-converting enzyme (ACE) inhibition, were examined critically.

Results: Research indicates that *C. papaya* extracts decrease inflammatory markers and enhance vascular function. Animal models exhibit marked decreases in blood pressure and oxidative stress levels. The reported beneficial effects demonstrated that papaya may exert these effects through multiple mechanisms, such as the modulation of inflammatory pathways, augmentation of antioxidant defence, and direct vasodilation. Limited clinical trials have indicated favorable results, which justify further research.

Conclusion: *C. papaya* is a promising natural adjunct to inflammation and hypertension management. Its phytochemical complexity underlies its therapeutic effects through several mechanisms. Human studies are required to establish its efficacy and standardized dosing.

Keywords: *Carica papaya*, medicinal plants, inflammation, hypertension

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1. Introduction

Medicinal plants are widely used to treat various disorders due to their efficacy, affordability, and fewer side effects. Because of the close relationship between inflammation and hypertension, researchers have turned their attention to natural anti-inflammatory compounds as drug targets. *Carica papaya,* or papaya, has been used globally because of its nutritional value and healing properties. The fruit is used in processed foods or consumed raw globally. As it is an edible plant, it is not associated with any toxicity if taken in moderation. However, high doses of leaf or seed extracts may pose risks such as liver toxicity or antifertility effects. Unripe fruit and latex should be avoided during pregnancy due to potential uterine stimulation [1]. Tropical Mexico, Central America, and northern South America are the papaya's native habitat, and the botanical classification is provided in Table **1** [1, 2].

Table 1: Botanical classification of *Carica papaya*.

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Class	Magnoliopsida
Order	Brassicales
Family	Caricaceae
Genus	Carica
Botanical name	*Carica papaya* Linn.

Different parts of the plant are being utilized in traditional medicine to treat a variety of disorders, including inflammation, wounds, urinary tract infections, piles, diabetes, dysentery, arthritis, gout, ulcers, dermatitis, infections, cough, and to improve platelet count [3–5]. It contains numerous beneficial phytochemicals, such as flavonoids, polyphenols, and glycosaponins. The papaya fruit is an enriched reservoir of minerals, vitamins, and carotenoids. Papaya peel, often discarded as waste, also contains numerous phytochemicals. These valuable phytochemicals are responsible for the plant's therapeutic effects, including anti-inflammatory, antioxidant, antihypertensive, and antidiabetic effects. The earlier studies confirmed that these substances can modulate inflammatory processes, reduce oxidative stress, and improve endothelial function, making papaya suitable for managing inflammation and hypertension [3, 6].

2. Methods

2.1. Data search

To validate the pharmacological efficacy of *C. papaya* in treating inflammation and hypertension, a targeted literature search on the PubMed, Scopus, and Google Scholar databases was conducted using different combinations of the following keywords: "*Carica papaya,*" "papaya," "inflammation," "anti-inflammatory," "hypertension," "antihypertensive," "oxidative stress," "endothelial dysfunction," and "clinical trial." For this study, articles published in English between 2000 and 2024 were considered.

2.2. Inclusion criteria

For this commentary, English-language articles from 2000 to 2024 that examined the anti-inflammatory or antihypertensive effects of *C.*

papaya were included. Only full-text articles that were accessible and directly related to the research question were considered. Both preclinical and clinical studies were included in this analysis.

2.3. Exclusion criteria

This study excluded articles that were not available in full text or in English. Articles unrelated to inflammation or hypertension were also removed to maintain the study's focus. During screening, duplicate entries and poor-quality sources were filtered out.

2.4. Identification and screening of the studies

The preliminary search yielded 231 records in total. After removing 61 duplicates, 170 titles and abstracts were screened for relevance, leading to the retrieval of 18 full-text articles. Of these, seven studies were deemed directly relevant to the scope of this commentary and have been cited to support our discussion (see Supplementary Table S1 for details).

3. Results

Hypertension is a major public health issue, affecting millions of people worldwide and placing people at risk of life-threatening illnesses such as stroke, heart attack, and kidney disease. The pathogenesis of hypertension is multifactorial, with genetic, environmental, and lifestyle determinants. Different studies have shown that chronic inflammation could play a significant role in developing high blood pressure due to the generation of reactive oxygen species (ROS) and changes in the vascular endothelium [7]. Patients suffering from chronic inflammatory disorders, such as rheumatoid arthritis and systemic lupus erythematosus, have a higher prevalence of hypertension, lending support to the theory that systemic inflammation will lead to vascular changes that cause persistent hypertension. Several epidemiological studies have indicated a considerable association between hypertension and inflammatory markers. The key inflammatory events, such as vascular stiffness, endothelial dysfunction, and activation of the renin-angiotensin system (RAS), are significant parameters that can lead to the development of hypertension; thus, inflammation has been implicated both as a cause and a consequence of high blood pressure [8, 9].

Oxidative stress is a disparity between ROS and antioxidants induced by the chronic inflammatory mechanisms that may play a role in hypertension. ROS induces endothelial dysfunction by reducing the availability of Nitric oxide (NO), a key vasodilator and vascular homeostasis molecule. Oxidative stress triggers vascular remodelling, which increases arterial stiffness and resistance, both of which could contribute to chronic hypertension [5, 10].

Inflammatory mediators, such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α), are also said to be elevated in patients suffering from hypertension. IL-6 is an immunoregulatory cytokine and a vasoactive peptide that leads to vasodilatation by causing vascular dysfunction and stimulating angiotensin II [9, 11]. Additionally, TNF-α plays a fundamental role in promoting endothelial dysfunction and oxidative stress, thus enhancing the disease of hypertension [7, 10]. Moreover, inflammatory cytokines stimulate immune cells like macrophages and T cells, which invade the blood vessels and accelerate vascular inflammation. The combined effect of all these factors results in a vicious circle where inflammation and hypertension fuel and support each other and are, therefore, hard to cut off.

Since inflammation and hypertension are interconnected, researchers have set their sights on natural anti-inflammatory agents as drug targets [12, 13].

Research has indicated that *C. papaya* efficiently modulates inflammation by reducing the production of pro-inflammatory cytokines like IL-6, TNF-α, and interferon-gamma (IFN-γ). In addition, papaya inhibits vascular inflammation, maintains blood vessel function, and reduces the risk of high blood pressure by inhibiting nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activity. Papaya's antioxidant activity also suppresses oxidative stress by trapping free radicals and increasing the efficacy of natural antioxidant enzymes. This dual action of suppressing oxidative stress and inflammation makes papaya a natural option for preventing and managing high blood pressure [14, 15]. Besides its antioxidant and anti-inflammatory action, papaya has also been shown to exhibit a vasodilatory effect by restoration of NO levels, which preserves vascular tone and prevents excessive vasoconstriction, thus lowering blood pressure [16–18].

4. Discussion

Various preclinical studies have explored the anti-inflammatory activity of *C. papaya* in different parts, such as leaves and seeds. The research used widely accepted models of inflammation, such as carrageenan-induced paw edema, formalin-induced edema, and cotton pellet-induced granuloma in rats. Extracts given orally or intraperitoneally at various doses uniformly showed considerable inhibition of inflammatory reactions, and effects were found to be dose- and time-dependent in certain studies. Both aqueous and ethanolic extracts demonstrated significant activity, indicating the presence of active phytoconstituents that account for the observed effect. A summary of major preclinical studies, reporting extract type, models employed, sample size, and findings, is shown in Table **2** [19–22].

Additionally, animal studies have shown that *C. papaya* fruit and leaf extracts possess potent antihypertensive activities. Mechanistically, the fruit extract does so through adrenergic mechanisms, whereas the methanolic leaf extract inhibits the angiotensin-converting enzyme (ACE) and enhances baroreflex function. The findings together establish *C. papaya* as a potentially valuable natural antihypertensive agent and merit further translational investigations as presented in Table **2** [23, 24].

So far, few clinical trials have assessed the therapeutic value of *C. papaya* in humans, with sparse randomized controlled trials (RCTs). One double-blind RCT by Lorenzetti *et al.* compared fermented papaya preparation (FPP®) in aged subjects and found that it significantly improved endothelial function and quality of life and decreased inducible nitric oxide synthase (iNOS) and asymmetric dimethylarginine (ADMA) levels, indices associated with vascular inflammation [25]. Although encouraging, this study did not measure classical inflammatory markers like CRP, IL-6, or TNF-α directly. In the same vein, a controlled intervention trial by Pratiwi *et al.* showed that the chlorophyll content of papaya leaf jelly significantly reduces systolic and diastolic blood pressure in prediabetic women within 20 days, indicating a cardiovascular benefit. Yet, to this day, no RCT has been devoted to the specific assessment of *C. papaya*'s anti-inflammatory effects in humans, highlighting a lack of clinical evidence

of its anti-inflammatory value. The findings on clinical studies are summarized in Table **2** [25, 26].

The pharmacokinetic profile of *C. papaya* remains under-characterized and demands further elaboration, especially considering the phytochemical complexity of the plant. The active constituents—such as alkaloids, flavonoids, polyphenols, and glycosides—demonstrate substantial variability depending on factors like plant part used (leaves, seeds, fruit), extraction method, and growing conditions. This variability can influence the absorption, metabolism, and distribution of bioactive compounds. The bioavailability of these phytochemicals, particularly polyphenols and flavonoids, is often limited due to poor water solubility and first-pass metabolism, which can hinder their systemic therapeutic effects. Additionally, while many studies highlight beneficial effects at the preclinical level, comprehensive toxicity assessments are scarce. Some reports suggest possible hepatotoxicity or reproductive toxicity at high doses, underscoring the importance of safety profiling. Given these uncertainties and the lack of robust dose-response data, there is a strong rationale for conducting RCTs. RCTs are essential not only to validate the anti-inflammatory and antihypertensive potential of *C. papaya* in human subjects but also to determine appropriate dosing regimens, monitor adverse effects, and ensure consistent pharmacokinetic behavior across populations [19–26].

The reported beneficial effects in earlier studies indicate that papaya may exert effects through multiple mechanisms, such as the modulation of inflammatory pathways, augmentation of antioxidant defence, and direct vasodilation. Although the results are encouraging, additional clinical trials involving human subjects must be conducted to confirm the efficacy of papaya peel as a natural antihypertensive agent. Apart from its direct effect on inflammation and hypertension, papaya may have other properties that can indirectly contribute to heart health. Being rich in fibre, it maintains healthy guts and triggers the release of short-chain fatty acids that have been discovered to exert antihypertensive effects because of gut microbiota modulation. In addition, the bioactive compounds in papaya may imply potential renin-inhibiting activity, a mode of action shared by ACE inhibitors, which are clinical antihypertensive drugs. If subsequent studies confirmed this property, papaya would become a member of a natural alternative or adjunct to conventional antihypertensive treatment [17, 27, 28].

Table 2: Preclinical (Animal) vs clinical (human) studies evaluating anti-inflammatory and antihypertensive effects of *Carica papaya*.

Study (year)	Model	Extract/plant part used	Study design	Sample size & dose	Key findings	Reference
Anti-inflammatory activity						
Owoyele *et al.* (2008)	Animal	Ethanol extract of leaves	Carrageenan-induced paw edema, cotton pellet, and formaldehyde arthritis in rats	5 rats/group; oral 25–200 mg/kg	↓ Inflammation significantly in all models ($P < 0.05$)	[19]
Adeolu & Vivian (2013)	Animal	Aqueous extract of leaves	Carrageenan- and histamine-induced paw edema in rats	5 rats/group; oral 100–200 mg/kg	Dose- and time-dependent ↓ in edema ($P < 0.05$)	[20]

Table 2: Continued.

Study (year)	Model	Extract/plant part used	Study design	Sample size & dose	Key findings	Reference
Amazu *et al.* (2010)	Animal	Methanolic extract of seeds	Carrageenan- and histamine-induced inflammation in rats	5 rats/group; i.p. 50–200 mg/kg	Inhibition of inflammation by 57.1–64.2%	[21]
Ahmed *et al.* (2015)	Animal	Aqueous extract of seeds	Cotton pellet-induced granuloma and formalin-induced edema in rats	Not specified; dose per model	↓ Edema: 83.5% (carrageenan) & 79.06% (formalin) ($P < 0.01$)	[22]
Lorenzetti *et al.* (2023)	Human	Fermented papaya preparation (FPP®)	Double-blind RCT in elderly	78 subjects; oral 4.5 g twice daily (12-month interim)	↓ iNOS and ADMA ($P < 0.05$); ↑ physical, mental & general health scores ($P < 0.01$)	[25]
Antihypertensive activity						
Eno *et al.* (2000)	Animal	Ethanol extract of unripe fruit	*In vivo* (Wistar rats); *in vitro* on rabbit arterial strips	15 rats/group; 20 mg/kg i.v.	↓ MAP in all groups ($P < 0.01$); 28% > hydralazine; effect blocked by propranolol; vasorelaxation blocked by phentolamine	[23]
Brasil *et al.* (2014)	Animal	Standardized methanolic extract of leaves	SHR and Wistar rats; baroreflex, ACE inhibition, cardiac hypertrophy	100 mg/kg orally, twice daily for 30 days	↓ BP (similar to enalapril); ↓ ACE activity & cardiac hypertrophy; ↑ baroreflex sensitivity	[24]
Pratiwi *et al.* (2017)	Human	Papaya leaf jelly (chlorophyll-rich)	Pre–post control group study in prediabetic women	27 subjects; 24.6 g/day for 20 days	↓ SBP from 130.14 to 124.29 ($P = 0.008$); ↓ DBP from 89.00 to 84.43 ($P = 0.02$)	[26]

i.p., intraperitoneal; i.v., intravenous; MAP, mean arterial pressure; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACE, angiotensin-converting enzyme; SHR, spontaneously hypertensive rats; RCT, randomized controlled trial; iNOS, inducible nitric oxide synthase; ADMA, asymmetric dimethylarginine

5. Conclusion

Although recent studies point to the promising anti-inflammatory and antihypertensive activity of *C. papaya*, there are still massive gaps, most importantly, in human studies. The main limitation is variability in phytochemical content arising from variations in plant part, geographic origin, extraction technique, and ripeness stage. Such inconsistencies pose difficulties in reproducibility and impede clinical translation. In addition, issues concerning bioavailability, metabolism, and possible toxicity of active constituents are seldom touched upon in current research. There is an obvious requirement for rigorously designed RCTs with standardized extraction protocols, dosed quantities, and validated outcome measures to determine both safety and efficacy in human populations. Overcoming these obstacles is necessary to transition from traditional application and preclinical potential to evidence-based clinical use.

Declarations

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Ethical Considerations

Not applicable.

Competing Interests

None declared.

Availability of Data and Materials

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

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Abbreviations and Symbols

ROS: Reactive oxygen species

RAS: Renin-angiotensin system

IL-6: Interleukin-6

CRP: C-reactive protein

TNF-α: Tumor necrosis factor-alpha

ACE: Angiotensin-converting enzyme

iNOS: Inducible nitric oxide synthase

ADMA: Asymmetric dimethylarginine

AI Use Disclosure

The authors declare that no generative artificial intelligence (AI) tools were used in the writing, data analysis, figure generation, or editing of this manuscript.

Author Contributions

Concept or design of the work: KA, NS; Acquisition, analysis, or interpretation of data: KA, NS, MTK, KH; Drafting the work or reviewing it critically: KA, NS, MTK, KH; Final approval: KA, NS, MTK, KH; Accountability for all aspects of the work: KA, NS, MTK, KH.

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