

**FORMULATION AND EVALUATION OF *CARICA PAPAYA* LEAF POWDER TABLETS FOR THE MANAGEMENT OF DENGUE FEVER****Sakibjiya Mujaffer Shaikh^{1*}, Prajkta Annasaheb Kate², Dr. Sampat D. Navale³**

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ABSTRACT

Dengue fever is a major mosquito-borne viral infection characterized by acute febrile illness and potentially severe thrombocytopenia, for which no specific antiviral therapy is currently available. Extracts and preparations of *Carica papaya* leaves have gained attention as adjunctive therapy to improve platelet counts and modulate the immune response in dengue patients. The extract exhibits multifactorial bioactivity, including anti-thrombocytopenic effects via ALOX12 and PTAFR gene upregulation, immunomodulatory modulation of cytokine profiles, antiviral enhancement of NS1 antigen clearance, and anti-inflammatory reduction of plasma leakage. This paper outlines the formulation and evaluation of 250 mg immediate-release tablets containing *Carica papaya* leaf powder prepared by wet granulation, designed as a supportive phytopharmaceutical dosage form for dengue-associated thrombocytopenia. The presence of bioactive phytoconstituents—carpaine, quercetin,

kaempferol derivatives, and phenolic compounds—underpins these pharmacological actions.

A concise review of clinical and preclinical evidence on papaya leaf extract in dengue is presented, followed by details of formulation design, manufacturing by wet granulation, and standard quality control tests such as weight variation, hardness, friability, disintegration and

in-vitro marker release, together with typical result ranges drawn from related herbal tablet studies.

KEYWORDS: *Carica papaya*, papaya leaf extract, dengue fever, thrombocytopenia, platelet count, immunomodulation.

1. INTRODUCTION

Dengue is an arboviral disease caused by dengue virus serotypes 1–4 and transmitted by *Aedes* mosquitoes, with hundreds of millions of infections estimated annually and a significant burden in tropical and subtropical regions.^[3,7] One key complication of dengue is thrombocytopenia, which increases the risk of bleeding and often prompts platelet transfusions, a costly intervention in resource-limited settings.^[1,3] Current management is largely supportive, and there is ongoing interest in safe, affordable adjuvant therapies that can improve platelet recovery and clinical outcomes.^[1,3,7]

Carica papaya (family Caricaceae) is widely used in traditional medicine in Asia and other regions, and its leaves contain multiple bioactive constituents, including flavonoids, alkaloids, glycosides, papain and other proteolytic enzymes, which may contribute to immunomodulatory, antioxidant and hematopoietic effects.^[2,7,8] Several clinical studies and meta-analyses report that papaya leaf extract, administered as juice, capsules, tablets or syrups, is associated with faster recovery of platelet counts and sometimes shorter hospital stay in dengue patients, though evidence quality and consistency vary.^[1,3,4]

Herbal solid dosage forms, such as tablets, offer advantages including accurate dosing, improved stability, ease of administration and better patient acceptability compared with traditional leaf juice preparations.^[5,9,16] Previous studies have formulated papaya leaf-containing tablets using direct compression, wet granulation or other techniques and evaluated their physical properties according to pharmacopoeial specifications.^[16,17,19] However, there is limited published work describing a detailed, reproducible formulation based on dried papaya leaf powder specifically targeting dengue-associated thrombocytopenia, with clear manufacturing and evaluation procedures.

This work aims to (i) summarize the scientific rationale for using *C. papaya* leaf preparations in the management of dengue and (ii) describe the formulation and evaluation of a 250 mg *C. papaya* leaf powder tablet prepared by wet granulation as an immediate-release dosage form.

The formulation strategy, processing parameters and evaluation methods are based on published herbal tablet and papaya leaf formulation literature^[5,9,19]



1.1. Phytochemical Composition

Advanced analytical techniques have revealed a complex matrix of bioactive compounds in *Carica papaya* leaves. The primary phytochemical classes and their specific pharmacological roles in dengue management are summarized in **Table 1**.

Table 1: Phytochemical Constituents and their Pharmacological Roles.

Phytochemical Class	Key Compounds Identified	Pharmacological Activity in Dengue
Alkaloids	Carpaine (approx. 60-65% of total), Pseudocarpaine, Dehydrocarpaine	Anti-thrombocytopenic; Stimulation of bone marrow megakaryopoiesis
Flavonoids	Quercetin, Kaempferol, Rutin, Kaempferol 3-(2G-rhamnosylrutinoside)	Antioxidant; Immunomodulation; Inhibition of viral replication
Phenolic Acids	Caffeic acid, Chlorogenic acid, Gallic acid, Ferulic acid	Free radical scavenging; Reduction of oxidative stress
Enzymes	Papain, Chymopapain	Anti-inflammatory; Reduction of inflammation markers

2. MATERIALS AND METHODS

2.1. MATERIALS

Common tablet excipients include Lactose as a diluent; starch as disintegrant and additional filler; starch paste (10% w/v) as binder; talc as glidant; and magnesium stearate as lubricant, selected in line with prior herbal tablet studies.^[16,19,21]

Purified water is used as the granulating fluid. All excipients should comply with relevant pharmacopeial specifications (IP, BP, USP), and the dried papaya leaf powder should be au-

thenticated botanically and tested for foreign matter, loss on drying, extractive values and microbial load according to herbal monograph practices.^[2,7]

2.2. Experimental design

A single-strength immediate-release tablet containing 250 mg of *C. papaya* leaf powder per unit is proposed. Assuming a target average tablet weight of approximately 440 mg to accommodate excipients, the remaining mass is apportioned among diluents, disintegrants, binder and lubricants. The formulation is prepared by wet granulation to improve flow and compressibility of the fine herbal powder, as recommended in multiple herbal tablet formulations.^[5,16,19]

Pre-formulation and preliminary trials can be used to optimize binder concentration, granulation end point and disintegrant level by monitoring granule flow properties and tablet quality attributes.^[16,19]

2.3. Formulation Development

2.3.1. Proposed Tablet Composition

A representative composition for *Carica papaya* leaf powder tablets containing 250 mg of papaya leaf powder per tablet with a total tablet weight of 440 mg is proposed below. The formulation is based on standard herbal tablet formulations and adjusted for high herbal drug loading.

Table 2: Formulation table of *Carica papaya* leaf tablet.

Sr. No.	Ingredient	Category	Qty/Tablet (mg)	Qty for 22 Tablets
1	<i>Carica papaya</i> leaf powder	Active ingredient	250 mg	5.5 g
2	Lactose	Diluent	120 mg	2.64 g
3	Starch	Disintegrant	60 mg	1.32 g
4	Starch paste (10% w/v)	Binder	q.s.	~2–3 mL
5	Talc	Glidant	5 mg	110 mg
6	Magnesium stearate	Lubricant	5 mg	110 mg

2.3.2. Wet granulation process

Wet granulation is chosen to improve the flowability and compressibility of papaya leaf powder and to achieve uniform distribution of the active ingredient with excipients. Herbal powders, including papaya leaf, often have poor flow and cohesive properties, making them challenging for direct compression and more amenable to wet granulation.^[16,19]

Step-by-step procedure

1. **Weighing**- Accurately weigh all ingredients.
2. **Sieving**- Pass papaya extract, lactose, starch through sieve no. 60.
3. **Dry Mixing**- Mix for 10 minutes:
 - extract = 5.5 g
 - Papaya Lactose = 2.64 g
 - Starch = 1.32 g
4. **Prepare Binder**- Make 10% starch paste:
 - Take 0.3 g starch
 - Add little cold water
 - Make slurry
 - Add hot water up to 3 mL
 - Heat till paste forms
5. **Granulation**- Add paste slowly to powder mix till damp mass forms.
6. **Screening**- Pass through sieve no. 10.



7. **Drying**- Dry at 55°C for 20–30 min.



8. Resieving- Pass dried granules through sieve no. 16.

9. Lubrication- Add

- Talc = 110 mg
- Magnesium stearate = 110 mg.
- Mix gently 3 min.

10. Compression- Compress tablets of 440 mg each.



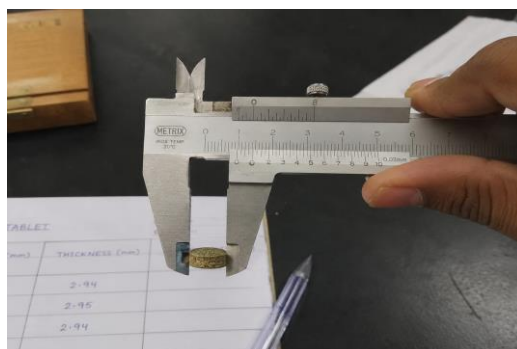
3. Evaluation of Tablets

Finished tablets are subjected to standard pharmacopoeial quality control tests used in herbal and conventional tablets.

1. General appearance: Tablets are visually inspected for color (light to dark greenish or brownish, depending on leaf powder), shape, presence of defects (chipping, cracking, capping) and surface characteristics.

2. Weight variation: Twenty tablets are individually weighed and the mean weight computed; individual tablet weights should generally be within $\pm 5\%$ of the average for tablets in the 250–500 mg range.

3. Thickness and diameter: Measured using a Vernier caliper or micrometer to ensure consistency and packaging compatibility.



4. Hardness (crushing strength): Measured using a tablet hardness tester; herbal tablets prepared by wet granulation commonly show hardness in the range of about 3–10 kg/cm², with several papaya-containing formulations reporting values around 3–6 kg/cm.

5. Friability: Evaluated using a Roche friabilator by rotating a sample of pre-weighed tablets at 25 rpm for 4 min, then re-weighing; friability below 1% is typically considered acceptable.



6. Disintegration time: Determined using a USP disintegration apparatus in distilled water at 37 ± 2 °C, with tablets considered compliant if they disintegrate within about 15–30 min for uncoated immediate-release tablets; many herbal formulations aim for faster disintegration, e.g. under 10 min.



4. RESULTS AND DISCUSSION

Post-compression evaluations in various herbal and papaya-containing tablets have demonstrated that weight variation remained within pharmacopoeial limits, hardness values in the approximate range of 3–6 kg/cm², friability below 1% and disintegration times generally under about 15 min for immediate-release or fast-disintegrating designs.^[16,17,19] For example, polyherbal tablets containing papaya and other botanicals achieved friability as low as 0.40% and acceptable hardness with wet granulation, indicating robust mechanical properties.^[19] It is important to note that while tablet quality parameters (mechanical strength, disintegration

and marker release) can be optimized using pharmaceutical principles, clinical efficacy in dengue depends on dose, bioavailability and patient factors, and should ideally be confirmed through controlled clinical trials using standardized preparations.^[22,23] Nonetheless, existing evidence that papaya leaf preparations (including capsules, tablets and juices) can improve platelet counts and possibly shorten hospital stay in dengue provides a justification for further development of robust tablet formulations as practical dosage forms.^[23,25]

5. CONCLUSION

Carica papaya leaf preparations have demonstrated potential as adjunctive therapy in dengue fever by enhancing platelet recovery and possibly modulating immune and viral markers, though more rigorous clinical trials are required to define optimal dosing and clinical benefit. The formulation of 250 mg papaya leaf powder tablets by wet granulation represents a pharmaceutically sound strategy to deliver standardized doses in an immediate-release solid form, leveraging established excipients and processing methods validated in related herbal tablet studies. Comprehensive pre-compression and post-compression evaluations, together with in-vitro release and marker assays, can ensure quality, while future work should focus on stability studies and controlled clinical evaluation of such formulations in dengue patients.

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