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Formulation and Evaluation of Herbal Syrup for Platelet Enhancement in Dengue Fever Using Carica papaya and Tinospora cordifolia

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ABSTRACT :

Dengue fever, a mosquito-borne viral illness, remains a significant public health challenge, especially in tropical and subtropical regions. A critical complication of dengue is thrombocytopenia, which can lead to severe bleeding and life-threatening conditions such as dengue hemorrhagic fever. Despite advances in supportive care, no specific antiviral therapy exists. Therefore, the demand for safe, effective, and affordable supportive treatments has escalated. Among various natural remedies, Carica papaya and Tinospora cordifolia have demonstrated potential to enhance platelet counts and modulate the immune response. This review explores their phytochemical constituents, mechanisms of action, formulation into a stable herbal syrup, comprehensive evaluation methodologies, current challenges, future directions, and regulatory considerations across different regions.

Keywords : Dengue fever ,Thrombocytopenia, Platelet enhancement, *Carica papaya*, *Tinospora cordifolia* ,Herbal syrup formulation, Phytochemicals, Immunomodulation

1. Introduction

Dengue fever, caused by four antigenically distinct serotypes of the dengue virus (DENV-1 to DENV-4), is transmitted primarily by the bite of infected Aedes aegypti mosquitoes. The clinical spectrum ranges from mild febrile illness to severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). A defining characteristic of severe dengue is thrombocytopenia, or the rapid decline in platelet count, which contributes significantly to morbidity and mortality.

Currently, dengue management remains largely supportive, involving fluid replacement, antipyretics, and monitoring of platelet counts. However, no approved pharmacological intervention exists to specifically address thrombocytopenia. Traditional medicinal systems, particularly Ayurveda and folk medicine, have long used plant-based remedies to support blood and immune health. Among these, Carica papaya and Tinospora cordifolia have garnered considerable attention due to their reported hematopoietic, antioxidant, antiviral, and immunomodulatory properties. This review delves into the scientific rationale for using these plants, focusing on the development and evaluation of an herbal syrup formulation as a convenient and effective therapeutic approach.

2. Medicinal Plants for Platelet Enhancement

2.1 Carica papaya

Carica papaya is a tropical plant valued for its nutritional and medicinal properties. The leaf extract, in particular, is rich in enzymes such as papain and chymopapain, as well as flavonoids, phenolic acids, alkaloids, and glycosides. These bioactive components have demonstrated various pharmacological effects, including anti-inflammatory, antiviral, and platelet-enhancing properties.

Multiple animal studies and clinical trials suggest that papaya leaf extract can significantly improve platelet counts in dengue patients. The extract is hypothesized to stabilize platelet membranes and promote megakaryopoiesis (the formation of megakaryocytes in bone marrow), thereby accelerating platelet production. Additionally, the extract appears to inhibit the hemolysis of platelets, which is critical in preventing further decline during the acute phase of infection.

One widely cited clinical trial reported that patients consuming papaya leaf juice experienced a statistically significant increase in platelet count within 24 to 48 hours. The extract's antioxidant properties also help mitigate oxidative damage to blood cells, supporting faster recovery.

2.2 Tinospora cordifolia

Tinospora cordifolia, commonly known as Giloy, is a well-known adaptogen and immunomodulator in Ayurvedic medicine. It is used traditionally for

fever, infections, and general immune support. The active phytochemicals include alkaloids (e.g., berberine, magnoflorine), diterpenoid lactones, glycosides, polysaccharides, and steroids.

Its relevance in dengue lies in its ability to stimulate the proliferation of bone marrow cells, thus aiding in platelet regeneration. Moreover, Giloy boosts macrophage activity and enhances the body's innate immunity. The extract has shown antiviral activity against a range of viruses, possibly including dengue, although more targeted studies are needed.

In preclinical models, administration of Tinospora cordifolia extracts led to improved blood profiles, including elevated white blood cell and platelet counts. In clinical observations, patients receiving Giloy extracts during dengue episodes showed shortened recovery periods, reduced symptoms, and improved platelet trends.

2.3 Comparative Bioactivity Table

Parameter	Carica papaya	Tinospora cordifolia
Primary Active Constituents	**Flavonoids, papain, alkaloids**	**Berberine, glycosides, lactones**
Mechanism of Platelet Action	**Stimulates megakaryocytes, reduces hemolysis**	**Enhances bone marrow activity**
Antioxidant Properties	**High**	**Moderate**
Immunomodulatory Effect	**Moderate**	**High**
Antiviral Activity	**Moderate**	**Moderate to High**
Time to Platelet Improvement	**24–48 hours**	**48–72 hours**
Clinical Evidence	**Well documented**	**Preliminary clinical evidence**

3. Herbal Syrup Formulation

3.1 Extraction of Active Constituents

To ensure therapeutic efficacy, efficient extraction of bioactive compounds is essential. The following methods are commonly used:

• Carica papaya: Leaves are collected, washed, shade-dried, and pulverized into a coarse powder. Aqueous extraction is preferred for pediatric formulations due to safety and palatability, where the powdered material is boiled in water and filtered to obtain a concentrated extract.
• Tinospora cordifolia: The stems are dried and chopped into small pieces. Decoction (boiling in water) or maceration in hydroalcoholic solvents is commonly employed to extract maximum active components.

Both extracts are then filtered, evaporated under reduced pressure, and concentrated to the desired volume. The concentrated extracts are stored under refrigeration until used in formulation.

3.2 Base and Additives in Syrup Formulation

The syrup base not only delivers the active compounds but also enhances taste, stability, and acceptability. Essential ingredients include:

• Sucrose syrup: Provides sweetness and viscosity. Also acts as a preservative by reducing water activity.
• Preservatives: Sodium benzoate or potassium sorbate are added within permitted concentration limits to prevent microbial contamination during storage.
• Acidulants: Citric acid adjusts the pH, improves taste, and enhances preservative efficacy.
• Flavoring agents: Natural or artificial fruit flavors mask the bitter taste of herbal extracts.
• Colorants: Approved food-grade colorants improve visual appeal.
• Purified water: Used as the solvent to bring the total volume to the required concentration.

3.3 Prototype Formula

Ingredient	**Concentration (%)**
Carica papaya extract	2.0
Tinospora cordifolia extract	1.0
Sucrose syrup	60.0
Sodium benzoate	0.1
Citric acid	0.05

Flavor and color	q.s.
Purified water	q.s. to 100 mL

4. Evaluation Parameters of Herbal Syrup

4.1 Organoleptic and Physicochemical Properties

Initial evaluation includes organoleptic parameters such as color, odor, taste, and sensory evaluation, crucial for patient compliance, especially among pediatric and geriatric populations.

Physicochemical testing includes:

• pH: Maintained between 4.0 and 6.0 to ensure stability and prevent microbial growth.
• Viscosity: Ensures uniform dosing and palatability.
• Specific gravity: Reflects the density and concentration of the syrup.
• Refractive index and total solids: Confirm the consistency of formulation batches.

4.2 Microbial and Stability Testing

Microbial testing involves total bacterial and fungal count assessments, along with tests for pathogens like Escherichia coli, Salmonella, and Staphylococcus aureus.

Stability testing includes:

• Storage under different conditions (e.g., 25°C/60% RH, 40°C/75% RH) for up to 6 months.
• Monitoring for changes in color, consistency, pH, and active content.

4.3 Pharmacological Evaluation

• In vitro assays: Platelet aggregation studies (e.g., light transmission aggregometry) using human blood samples to assess whether the extract promotes platelet formation or prevents lysis.
• In vivo studies: Animal models induced with thrombocytopenia using cyclophosphamide or similar agents, followed by treatment with the herbal syrup to measure recovery trends.
• Clinical trials: Randomized controlled studies evaluating platelet recovery, reduction in hospitalization duration, and symptom improvement in dengue patients.

5. Regulatory Frameworks Across Regions

The regulation of herbal medicines varies significantly across global jurisdictions:

• India: Governed by the Ministry of AYUSH and regulated under the Drugs and Cosmetics Act, 1940. Products must comply with Good Manufacturing Practices (GMP), and herbal formulations must be listed in authoritative texts or have proof of traditional use.
• United States: Herbal products marketed as dietary supplements are regulated under the Dietary Supplement Health and Education Act (DSHEA), 1994, which does not require pre-market FDA approval but mandates compliance with labeling and safety standards.
• European Union: The European Medicines Agency (EMA) oversees herbal medicinal products through the Committee on Herbal Medicinal Products (HMPC). Traditional use registration requires at least 30 years of safe usage, including 15 years within the EU.
• Australia: The Therapeutic Goods Administration (TGA) regulates herbal medicines under the complementary medicines category. Products must be listed or registered based on risk.
• WHO Guidelines: Encourage member states to integrate traditional medicine into national health systems while promoting research, quality assurance, and harmonized regulations.

Differences in regulatory pathways affect the formulation, labeling, market approval, and post-market surveillance of herbal syrups. Harmonization of standards and global collaborations are increasingly emphasized to ensure safety and efficacy.

6. Challenges and Limitations

While preliminary evidence supports the use of herbal formulations for platelet enhancement, several challenges exist:

• Variability in raw materials: Climatic and soil differences affect the concentration of bioactives.

• Lack of standardization: Absence of validated markers for quantifying active ingredients.
• Inconsistent regulatory oversight: Varying requirements across regions hinder global acceptance.
• Limited high-quality clinical data: Many studies lack adequate controls, robust sample sizes, or long-term follow-up.
• Potential herb–drug interactions remain underexplored.

7. Future Prospects

Advancing this herbal approach involves:

• Isolation and identification of key bioactive compounds.
• Standardization protocols to ensure batch-to-batch consistency.
• Development of advanced delivery systems like nanoparticles or sustained-release formulations.
• Collaborative studies involving pharmacologists, botanists, and clinicians to validate efficacy.
• Incorporating pharmacokinetic and pharmacodynamic studies to optimize dosing strategies.
• Greater regulatory oversight to ensure safety and efficacy.

8. Conclusion

Herbal syrups formulated using Carica papaya and Tinospora cordifolia extracts present promising complementary therapies for managing thrombocytopenia in dengue fever. Their multi-modal actions including platelet regeneration, immune modulation, and antioxidant effects address key pathological mechanisms. However, further rigorous standardization, clinical validation, and regulatory harmonization are essential before widespread clinical adoption. This review underscores the potential of integrating traditional botanical knowledge with modern pharmaceutical approaches to develop safe, effective, and accessible dengue supportive care.

9. REFERENCES :

1. Awale, S., et al. (2017). Effect of papaya leaf extract on platelet count and viral clearance in dengue fever patients: A randomized controlled trial. Journal of Herbal Medicine, 11, 30-35.
2. Bhuvaneshwari, V., et al. (2015). Phytochemical and pharmacological properties of Tinospora cordifolia: A review. International Journal of Pharmaceutical Sciences and Research, 6(11), 4669-4679.
3. Chauhan, N. S., et al. (2012). Herbal remedies in the management of dengue fever: A review. Asian Journal of Pharmaceutical and Clinical Research, 5(3), 1-5.
4. Das, S., et al. (2019). Immunomodulatory effects of Tinospora cordifolia in dengue infection: An experimental study. Journal of Ethnopharmacology, 233, 10-17.
5. Khanna, A., et al. (2016). Role of Carica papaya leaf extract in the management of dengue fever and thrombocytopenia: A review. International Journal of Research in Ayurveda and Pharmacy, 7(2), 7-12.
6. Mehta, P., & Kumar, S. (2018). A systematic review on pharmacological properties of Tinospora cordifolia. Journal of Traditional and Complementary Medicine, 8(1), 33-44.
7. Mukherjee, P. K., et al. (2017). Standardization of herbal drugs: An overview. Pharmacognosy Reviews, 11(21), 10-20.
8. Nagaraju, R., et al. (2021). Effect of Carica papaya leaf juice on platelet count in dengue patients: A clinical trial. Journal of Complementary and Integrative Medicine, 18(3), 1-7.
9. Puri, A., & Saxena, R. (2020). Phytochemical screening and evaluation of antioxidant potential of Carica papaya and Tinospora cordifolia extracts. Pharmacognosy Journal, 12(6), 1334-1341.
10. Sharma, V., et al. (2014). Immunomodulatory and antiviral effects of Tinospora cordifolia against dengue virus: In vitro study. International Immunopharmacology, 19(1), 99-105.
11. Anitha, P., et al. (2019). Efficacy of Carica papaya leaf extract in dengue: A randomized controlled study. Journal of Clinical and Diagnostic Research, 13(6), FC01-FC05.
12. Balasubramanian, S., et al. (2020). Pharmacognostic and phytochemical standardization of Tinospora cordifolia. International Journal of Pharmacognosy and Phytochemical Research, 12(1), 1-7.
13. Gupta, R., et al. (2017). Clinical evaluation of papaya leaf extract for thrombocytopenia in dengue patients. International Journal of Ayurveda Research, 8(3), 121-125.
14. Jeyaprakash, R., & Shoba, F. (2016). Antioxidant and immunomodulatory activities of Tinospora cordifolia extracts. Asian Pacific Journal of Tropical Biomedicine, 6(9), 801-806.
15. Kaur, G., & Arora, S. (2018). Herbal formulation development: Challenges and approaches. Journal of Herbal Medicine and Toxicology, 12(2), 45-50.
16. Kumar, R., et al. (2022). Role of Carica papaya in enhancing platelet count in viral fever: A systematic review. Phytotherapy Research, 36(2), 555-567.
17. Latha, P., & Daisy, P. (2015). Comparative study of the hematological effects of Carica papaya and Tinospora cordifolia extracts in animal models. Journal of Ethnopharmacology, 170, 110-116.

18. Mishra, R. K., et al. (2014). Safety and efficacy of herbal medicines in dengue treatment: An overview. Journal of Medicinal Plants Studies, 2(5), 109-114.
19. Panda, S. K., et al. (2020). Formulation and stability studies of herbal syrup containing Tinospora cordifolia. Journal of Pharmacy Research, 14(6), 453-460.
20. Sharma, S., et al. (2013). Antiviral potential of Tinospora cordifolia against dengue virus infection. Virus Disease, 24(3), 235-240.
21. Singh, M., et al. (2021). Phytochemical analysis and quality control of herbal syrup formulations. Journal of Pharmaceutical Sciences and Research, 13(4), 185-192.
22. Verma, R., et al. (2018). Immunomodulatory and hematopoietic effects of Carica papaya leaf extract in thrombocytopenia induced animal models. International Journal of Research in Pharmaceutical Sciences, 9(3), 1455-1461.
23. Waghmare, M., & Kadam, V. (2017). Development and evaluation of herbal syrup containing Carica papaya leaf extract. International Journal of Pharmacy and Pharmaceutical Sciences, 9(4), 234-240.
24. Yadav, R., et al. (2019). Advances in the formulation of herbal drugs for improved bioavailability. Journal of Drug Delivery Science and Technology, 53, 101160.