A Review on the Potential Therapeutic Profile of Carica papaya Leaf Extract in the Management of Dengue Fever

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INTRODUCTION

- Acute viral infection
- Dengue viruses (DV): genus Flavivirus, family Flaviviridae
- Positive stranded encapsulated RNA virus
- 3 structural protein genes: C, M, E
- 7 NS protein genes
Aedes aegypti mosquito transmission

1997 WHO classification of Dengue infection

- Undifferentiated Fever
- Dengue Fever (DF) and
- Dengue Haemorrhagic Fever (DHF)

2009 WHO classification,

- Uncomplicated
- Severe
CLINICAL PRESENTATION

- Four main characteristic manifestations
  - Continuous high fever lasting 2-7 days;
  - Haemorrhagic tendency;
  - Thrombocytopenia (platelet count <100x10^9/L); and
  - Evidence of plasma leakage

- Incubation period: 3 to 14 days
After the incubation period, the illness begins abruptly.

Patients with moderate to severe disease, 3 phases:
- Febrile,
- Critical and
- Recovery

**Individual risk factors:** secondary infection, age (young children), ethnicity and possibly chronic diseases.

**Associated problems**
Diagnosis

- Typically made clinically
- A probable diagnosis is based on the findings of fever plus any 2 of the characteristic features
- The earliest change detectable on laboratory investigations
- Peripheral vascular collapse in children
- Warning signs are an important aspect for early detection
Laboratory tests

- Diagnosis confirmed by microbiological laboratory testing
  - Virus isolation in cell cultures
  - Nucleic acid detection by PCR
  - Viral antigen detection (such as for NS1) or
  - Specific antibodies (serology)

- All tests may be negative in the early stages of the disease

- PCR and viral antigen detection are more accurate in the first seven days
Problem Statement

- Risk population: Over 2.5 billion people – over 40% of the world’s population
- WHO estimation,
  - 50–100 million dengue infections and half a million DHF worldwide every year
  - Average case fatality rate ≈ 5%
- Endemic in over 125 countries
- The exact extent of the problem not known
Currently available treatment modalities

- Treatment depends on the symptoms & severity
- IV fluids- titrated
- Blood transfusion initiated early in patients presenting with unstable vital signs
- Packed red blood cells or whole blood recommended
- Thrombocytopenia not addressed till it gets lowered down to levels less than 20000 /μl
- Reduction of mortality due to DHF from 20% to less than 1%
- Corticosteroid
- TPO agonists and mimetics like **Eltrombopag and Romiplastim**
- Dengue vaccine – under trial
- Alternatively other options need to be explored
- Considerations for alternate therapies
- **Traditional medicine**
Carica papaya (CP)

- Genus *Carica* of the plant family Caricaceae
- Cosmopolitan in distribution
- Leaves of Papaw are rich in anthraquinone and alkaloids like carpaine, a glucoside named carposide, flavonols and vitamins C and E
- TJ O’Hare and DJ Williams - ‘Papaya As A Medicinal Plant’

anthelmintic activity, wound healing, antifertility properties, antifungal activity, antimalarial activity, antimicrobial activity, antiviral activity (dengue fever), anticancer and chemoprotection, anti-amoebic activity, diabetes and anti-hypertension
Literature search: consistent results

*NADEEM SHEIKH, NEELAM YOUNAS & TASLEEM AKHTAR on “Effect of Carica papaya leaf formulation on Haematology and Serology of normal rat” illustrated an exact mechanism of Thrombocyte formation

Consumption for longer period: hepatotoxicity and risk for cardiovascular disease

Probable action of Vitamin C

In a clinical trials, 1100 mg TID of Carica Papaya leaf extract tablet (Caripill) for 5 days – significant increase in platelet count
- Sathasivam et al. (2009) – mice
- NADEEM SHEIKH et al. “Effect of *Carica papaya* leaf formulation on Haematology and Serology of normal rat” - ↑ mean platelet count, MCH, MCV
- “Identification of Secondary Metabolites Present in *Carica Papaya* L. Leaf Extract Found in Northern India by HPTLC & Other Test Procedures, its Significance and Role in Curing Dengue/DHF Disease” by Dinesh Kumar et al. - physico-chemical and phytochemical evaluation
TLC fingerprinting profile of different extracts → Secondary metabolites → Bioactive components separated from the co extractives → Secondary metabolites

- Flavonoids like quercetin, alkaloids like piperine, glycosides, saponins, tannins, terpenoids like triterpenoids, phytosterols and phenolics

- None any single ingredient/constituent or factor found responsible
Significance

• Better & viable option in fever associated with thrombocytopenia
• Palatable and appropriately formulated
• Fewer side effects
• Decreases the cost of hospitalization
• Cost effective
• More affordable and accessible
• Averting the mortalities
➢ International Anti dengue day - June 15th

➢ Intention to meet the achievable goals
CONCLUSION

- Serious public health problem worldwide
- Validation of traditional claims
- Discrepancy regarding its safety profile
- Cost effective - positive influence on the national economy
- Need for further studies on a large scale
- Considerations for nutraceutical and its potential as pharmaceutical
References


Good Health Needs Good Care