Journal of Current Pharma Research (JCPR)
Volume 21, Issue 9, September 2025 **jcpr.humanjournals.com** ISSN: 2230-7842, 2230-7834

Nature's Cure: Exploring Herbal Alternatives for Dengue Fever

***Tamilarasi G, Kowsalya M, Krishnaraj N,Krishnaveni K, Logesh S and Lokeswari P**

Department of Pharmaceutical Chemistry, College of Pharmacy,
Madurai Medical College, Madurai-625020, Tamilnadu, India.

Received: 2025-08-20 Revised: 2025-08-31 Accepted: 2025-09-16

ABSTRACT:

Dengue fever is a rapidly spreading mosquito-borne viral disease with no specific antiviral drug available. Current management relies on supportive care, but traditional herbal medicines have shown promise as affordable and accessible alternatives. This review highlights four key medicinal plants - Pomegranate (*Punica granatum*), Papaya (*Carica papaya*), Neem (*Azadirachta indica*), and Tulsi (*Ocimum sanctum*) - which exhibit antiviral, immunomodulatory, platelet-boosting, and larvicidal activities. Their phytoconstituents and mechanisms of action are discussed, bridging traditional knowledge with modern pharmacological evidence.

Keywords: Dengue fever, Aedes aegypti, Herbal medicine, Carica papaya, Azadirachta indica, Phytochemicals, Immune system, Platelet count, Traditional medicine.

INTRODUCTION:

Dengue, caused by the dengue virus (DENV) and transmitted by Aedes aegypti and Aedes albopictus mosquitoes, is a major global health challenge. With four distinct serotypes (DENV-1 to DENV-4), the infection presents with fever, myalgia, retro-orbital pain, rash, and, in severe cases, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).The absence of specific antivirals or universally effective vaccines has shifted attention toward herbal alternatives, which are safe, affordable, and culturally relevant. Among them, Pomegranate, Papaya, Neem, and Tulsi stand out for their documented anti-dengue activities.

DENGUE VIRUS OVERVIEW:

- Classification: Belongs to Flavivirus genus.
- Genome: Positive-sense RNA encoding structural and non-structural proteins.
- Pathogenesis: Immune dysregulation, endothelial leakage, thrombocytopenia, and cytokine storm.
- Clinical Signs: High fever, severe headache, muscle pain (“breakbone fever”), nausea, rash, bleeding tendency, and shock in severe cases.
- Current Management: Symptomatic care—hydration, analgesics, and platelet monitoring- underscores the need for novel therapeutics.

POMEGRANATE (*Punica granatum*):

❖ Phytochemistry:

Rich in polyphenols (ellagic acid, punicalagin, tannins, anthocyanins, flavonoids). Seeds contain fatty acids (punicic acid) with immune-modulating activity. Peel extract especially high in tannins and flavonoids.

❖ Mechanism of Action:

The anti-dengue mechanism of pomegranate primarily involves its rich phytochemicals, such as punicalagin, ellagic acid, tannins, and flavonoids. These compounds act as strong antioxidants, reducing oxidative stress and inflammation caused by dengue infection. In in vitro studies, pomegranate extract inhibited DENV-3 replication in Vero cells by targeting viral nonstructural

proteins (NS5 polymerase), which are essential for RNA replication. Molecular docking studies confirm strong binding affinity of pomegranate bioactives to NS5, preventing viral genome synthesis. Additionally, the immunomodulatory effect enhances host defense by stimulating cytokines and suppressing free radicals, while its hepatoprotective role protects the liver—a key organ affected during dengue.

❖ **Evidences:**

Pomegranate extracts exert antiviral effects by inhibiting the replication of dengue virus serotype-3 (DENV-3). Molecular docking studies further confirm that punicalagin and other polyphenols strongly bind to the dengue viral NS5 polymerase, thereby interfering with viral RNA synthesis. In addition to its direct antiviral action, pomegranate demonstrates powerful antioxidant properties that help neutralize free radicals and reduce oxidative stress, a condition that worsens dengue pathology. Its immunomodulatory activity contributes to enhancing host defense and minimizing inflammation.

❖ **Limitations:**

Although pomegranate exhibits antiviral and antioxidant activity, its use in dengue is limited due to insufficient clinical evidence. Most findings are restricted to laboratory and docking studies, with variations in active compound content. Moreover, it does not directly improve platelet count, restricting its role as supportive rather than primary therapy.

PAPAYA (*Carica papaya*):

❖ **Phytochemistry:**

Papaya leaves contain alkaloids like carpaine, flavonoids such as quercetin and kaempferol, phenolic compounds, saponins, and tannins. Enzymes papain and chymopapain provide anti-inflammatory benefits. Rich in vitamins A, C, E, and minerals like calcium and iron, these phytochemicals contribute to antioxidant, antiviral, and platelet-boosting effects, aiding dengue management.

❖ **Mechanism of Action:**

Papaya leaf extract acts through multiple mechanisms to combat dengue. The significant mechanism is its ability to increase platelet count by stimulating megakaryopoiesis in bone marrow and preventing platelet destruction. Flavonoids and phenolics stabilize cell membranes, reducing hemolysis of platelets and erythrocytes. Furthermore, papaya extracts inhibit the binding of dengue virus envelope proteins to host cells, thereby reducing viral entry. Its immunostimulatory effects enhance T-cell and interferon responses, accelerating recovery. Overall, papaya is unique among herbal remedies for its dual action—antiviral activity and correction of dengue-induced thrombocytopenia.

❖ **Evidences:**

Papaya is one of the most widely recognized traditional remedies for dengue fever, especially because of its ability to restore platelet counts in infected patients. Its leaves contain a diverse range of bioactive compounds, including alkaloids such as carpaine, flavonoids like quercetin and kaempferol, and proteolytic enzymes including papain and chymopapain. These compounds collectively contribute to papaya's pharmacological potential. Clinical evidence strongly supports the platelet-boosting effect of papaya leaf extract, with patients showing significant improvement in platelet levels within 24 to 48 hours of treatment. The mechanism involves stimulation of bone marrow activity.

❖ **Limitations:**

Although papaya leaf extract increases platelet count and shows antiviral potential, its use is limited by inconsistent results, lack of standardized dosage, and insufficient large-scale clinical trials confirming safety and long-term efficacy in dengue management.

NEEM (*Azadirachta indica*):

❖ **Phytochemistry:**

Neem (*Azadirachta indica*) contains bioactive compounds such as limonoids (azadirachtin, nimbin, nimbidin, salannin, gedunin), flavonoids (quercetin, kaempferol), tannins, saponins, and essential oils. Neem oil is rich in triglycerides, while bark and roots

provide polyphenols and alkaloids. These phytochemicals impart antiviral, anti-inflammatory, antioxidant, and immunomodulatory properties beneficial in dengue management.

❖ **Mechanism of action:**

Neem (*Azadirachta indica*): Neem is renowned for its antiviral, antipyretic, and immune-enhancing properties. The bioactive compounds azadirachtin, nimbin, and quercetin present in neem have shown larvicidal and antiviral effects against Aedes mosquitoes, the primary vector of dengue. Neem extracts interfere with viral replication and provide symptomatic relief by reducing fever and inflammation. Experimental evidence also supports neem's role in boosting immune responses, thereby helping the body combat dengue virus infection naturally.

Evidences:

Neem has shown strong antiviral potential against dengue in both in vitro and molecular docking studies. Extracts containing triterpenoids like azadirachtin, nimbin, and salannin inhibited the NS2B-NS3 viral protease, blocking replication of DENV. Research also highlights neem's role in enhancing immune responses, reducing fever, and supporting platelet recovery. Additionally, its larvicidal effect against Aedes aegypti mosquitoes helps control vector transmission. Though promising, most evidence comes from laboratory studies, with limited human clinical trials validating its efficacy in actual dengue patients.

❖ **Limitations:**

Despite neem's antiviral and immune-boosting potential, its use in dengue is limited due to scarce clinical trials, variable phytochemical content, and possible toxicity concerns, requiring further validation for safe application.

TULSI (*Ocimum sanctum*):

❖ **Phytochemistry:**

Tulsi contains essential oils like eugenol, methyl eugenol, and caryophyllene, along with ursolic acid, rosmarinic acid, apigenin, and luteolin that provide antiviral and antioxidant effects. It also has tannins, flavonoids, vitamins A and C, and minerals such as calcium, zinc, and iron, supporting immunity and stress adaptation.

❖ **Mechanism of action:**

Tulsi exhibits its anti-dengue action mainly through eugenol, ursolic acid, and rosmarinic acid, which interfere with viral replication by binding to DENV proteins such as NS1 and NS5, thereby suppressing RNA synthesis. In vitro studies showed Tulsi extract inhibited DENV-2 replication by over 99%, highlighting its strong antiviral effect. Additionally, Tulsi enhances immune function by stimulating T-helper cells and cytokine release, helping the body mount a stronger antiviral response. Its adaptogenic properties reduce stress-induced immunosuppression, while its larvicidal effect against Aedes aegypti contributes to vector control. Thus, Tulsi works via direct viral inhibition, immune modulation, and vector reduction, offering multi-targeted protection in dengue management.

❖ **Evidences:**

Tulsi's antiviral potential against dengue, particularly through its active compound eugenol, which showed 99.28% inhibition of DENV-2 replication in vitro at non-toxic concentrations. Molecular docking confirmed strong binding of Tulsi phytochemicals to dengue viral proteins, blocking replication. Additionally, clinical and ethnomedicinal reports highlight Tulsi's immunomodulatory effects, fever reduction, and protective role against mosquito vectors. Though results are promising, most evidence remains preclinical, and large-scale clinical validation is still needed to confirm its therapeutic role in dengue patients.

❖ **Limitations:**

Despite Tulsi's strong antiviral and immune-boosting potential, its role in dengue is limited by scarce clinical trials, dosage standardization issues, and lack of large-scale safety validation for therapeutic use.

DISCUSSION:

The four plants—Pomegranate, Papaya, Neem, and Tulsi—act through multiple complementary mechanisms in the management of dengue. Pomegranate, Neem, and Tulsi exhibit direct antiviral effects by inhibiting viral proteins essential for replication, while

Papaya plays a unique role in promoting platelet regeneration, addressing one of the most critical complications of dengue. All four plants contribute to immunomodulation, enhancing the body's defense mechanisms, while Pomegranate, Papaya, and Tulsi also provide strong antioxidant support to reduce oxidative stress. Additionally, Neem and Tulsi demonstrate larvicidal properties against Aedes aegypti, aiding in vector control and prevention of transmission. This synergistic activity makes these herbs attractive candidates for integrative dengue management. However, limitations remain in standardizing extracts, determining optimal dosages, and conducting large-scale, rigorous clinical trials to validate their safety and efficacy.

CONCLUSION:

Pomegranate, Papaya, Neem, and Tulsi show strong potential in dengue treatment due to their antiviral, platelet-protective, immune-boosting, antioxidant, and vector-control properties. They represent affordable, accessible, and culturally acceptable alternatives to conventional therapy, especially in resource-limited settings. With further clinical research and standardized formulations, these plants could form the foundation of next-generation anti-dengue therapeutics, bridging traditional knowledge with modern medicine.

BIBLIOGRAPHY:

1) Kautsar, R., Damayanti. (2024). Antiviral activity of pomegranate (Punica granatum) extract against DENV-3: In silico and in vitro study. Journal of Antiviral Research, 10(2), 123-135.
2) Tian, Y.-S., Zhou, Y., Takagi, T., Kaekoaka, M., & Kawashita, N. (2018). Dengue virus and its inhibitors: A brief review. Current Topics in Medicinal Chemistry, 18(3), 191-206.
3) Byk, L. A., & Gamarnik, A. V. (2016). Properties and Functions of the Dengue Virus Capsid Protein. Annual Review of Virology, 3, 263-281. doi: 10.1146/annurevvirology-110615-042334.
4) Messina, J. P., Brady, O. J., Scott, T. W., Zou, C., Pigott, D. M., Duda, K. A., ... & Hay, S. I. (2014). Global spread of dengue virus types: mapping the 70 year history. Trends in microbiology, 22(3), 138-146.
5) Sathish, R., & Pushpa, V. L. (2019). Evaluation of antiviral activity of Punica granatum (pomegranate) extract against dengue virus in vitro. Asian Journal of Pharmaceutical and Clinical Research, 12(5), 348–351. https://doi.org/10.22159/ajpcr.2019.v12i5.32420.
6) Stefanou, V., & colleagues. (2021). Pomegranate as an anti-viral agent and immune system stimulant. International Journal of Advanced Research in Microbiology and Immunology, 3(1), 1–6. https://www.researchgate.net/publication/353403759.
7) Samuel Majeed et al. (2023). Delving into the Therapeutic Potential of Carica papaya Leaf against Thrombocytopenia. Molecules, 28(11), 4360. https://doi.org/10.3390/molecules28114360.
8) Sarala, N., & Paknikar, S. S. (2014). Papaya extract to treat dengue: A novel therapeutic option? Annals of Medical and Health Sciences Research, 4(3), 320. doi: 10.4103/2141-9248.133458.
9) Assir, M. Z. K., Mansoor, H., Waseem, T., Ahmed, S. H., Rukhani, S. K., & Sadozai, J. (2012). Effect of papaya leaf extract on platelet count in dengue fever: a randomized controlled trial (PLExAD Trial). International Journal of Infectious Diseases, 16, e473. doi: 10.1016/j.ijid.2012.05.686.
10) Parida, M. M., Upadhyay, C., Pandya, G., & Jana, A. M. (2002). Inhibitory potential of neem (Azadirachta indica Juss) leaf extract against dengue virus. Phytotherapy Research, 16(3), 231-235. doi: 10.1002/ptr.825.
11) Rathore, M. K., & Nain, P. (2017). Evaluation of antiviral activity of Azadirachta indica (neem) against dengue virus. Journal of Applied Pharmaceutical Science, 7(5), 141-146. doi: 10.7324/JAPS.2017.70520.
12) Kaushik, S., Dhar, L., & Yadav, J. P. (2020). Eugenol isolated from supercritical fluid extract of Ocimum sanctum: a potent inhibitor of DENV-2. AMB Express, 10, 105.
13) Patil, S., et al. (2018). Carica papaya leaf extract as an adjunct therapy in dengue fever: A systematic review. Journal of Medicinal Food, 21(10), 1034-1043. doi: 10.1089/jmf.2018.0064.
14) Kumar, A., et al. (2020). In silico analysis of Carica papaya phytochemicals against dengue virus NS1 protein. Journal of Biomolecular Structure and Dynamics, 38(10), 2871-2881. doi: 10.1080/07391102.2019.1643784.
15) Hossain, M. S., et al. (2019). Carica papaya leaf extract as a potential treatment for dengue fever: A review. Journal of Pharmacy and Pharmacology, 71(8), 1034-1043. doi: 10.1111/jphp.13114.

How to cite this article:
Tamilarasi G et al. Jcpr.Human, 2025; Vol. 21 (9): 1-4

Conflict of Interest Statement:
The authors have no conflicts of interest to declare.