

**RECENT ADVANCES IN THE MANAGEMENT OF DENGUE USING
HERBAL REMEDIES-A COMPREHENSIVE REVIEW****Prekshita Dhapke¹, Khushi Shahare², Ganesh Derkar^{*3}**^{1,2,3}School of Pharmacy, G H Raison University, Saikheda, Madhya Pradesh, India.

Article Received on 05 April 2026,
Article Revised on 25 April 2026,
Article Published on 01 May 2026,

<https://doi.org/10.5281/zenodo.20021483>

Corresponding Author*Ganesh Derkar**

School of Pharmacy, G H Raison
University, Saikheda, Madhya
Pradesh, India.



How to cite this Article: Prekshita Dhapke¹,
Khushi Shahare², Ganesh Derkar^{*3} (2026).
Recent Advances In The Management Of
Dengue Using Herbal Remedies-A
Comprehensive Review. World Journal of
Pharmacy and Pharmaceutical Sciences, 15(5),
1214-1233

This work is licensed under Creative Commons
Attribution 4.0 International license.

ABSTRACT

Dengue represents a major mosquito-borne viral infection affecting millions worldwide, with management currently limited to supportive care due to the absence of a specific antiviral drug. In recent years, herbal remedies have gained attention as potential adjuncts owing to their antiviral, immunomodulatory, and hematopoietic properties. Carica papaya leaf extract has garnered the most significant clinical evidence, especially in improving platelet recovery and accelerating symptomatic relief. Other botanicals like Momordica charantia, Azadirachta indica, Tinospora cordifolia, Andrographis paniculata, and Glycyrrhiza glabra have also shown promising effects against dengue virus infection in preclinical models, targeting viral replication, immune regulation, and organ protection. However, outside of papaya leaf extract, clinical studies remain scanty and are often fraught

with limitations such as small sample sizes, inconsistent formulations, and flimsy safety data. This review provides a fresh look at herbal interventions in the management of dengue, emphasizing their therapeutic potential, limitations, and future scope. Standardized formulations and well-designed clinical trials are crucial to establish herbal remedies as safe and effective adjuncts in the treatment of dengue virus infection.

KEYWORDS: Dengue; Mosquito-borne viral infection; Supportive care; Antiviral drug; Herbal remedies; Adjunct therapy; Antiviral properties; Immunomodulatory properties; Hematopoietic properties.

INTRODUCTION

Dengue is a vector-borne disease transmitted by the dengue virus, belonging to the family Flaviviridae. Overall, it spreads among humans through the bites of female *Aedes aegypti* mosquitoes, less rarely via the *Aedes albopictus* and some other mosquito species. There are four different serotypes of this virus: DENV-1, DENV-2, DENV-3, and DENV-4. The nature of the transmission dictates that once a person has an infection with one serotype, lifelong immunity against that specific serotype is obtained.¹ (Tayal et al., 2023).

According to the WHO, there are about 390 million people infected with dengue fever every year, placing almost half of the world's population in danger. The symptoms of dengue can be as mild as those of the flu or as serious as DSS and DHF, which are life-threatening conditions. There are no specific antiviral drugs for the treatment of dengue. Thus, the main care consists of maintaining hydration and alleviating symptoms of the patients. Due to the rising cases of dengue and the non-availability of any special medicines, many people have started looking at alternative treatments, including traditional herbal medicine. This need for effective and easily available treatments has inspired further studies on the usage of herbs in fighting dengue.² (Ansari et al., 2023)

The symptoms that most commonly occurred in Dengue virus infection were high-grade fever, vomiting, backache, discomfort behind the eyes, and skin rash. Severe cases manifested with abdominal pain, bleeding, and shock, which may be life-threatening. According to most of the literature, during a dengue infection, platelet counts usually fell significantly.. Dengue fever is a severe health problem for the whole world, leading to high rates of illness and death worldwide.³(Tewari et al., 2024)

A vaccine, Dengvaxia, has been approved in some countries to prevent dengue, but it does not protect against all types of dengue virus and its effectiveness is not uniformly distributed across all age groups. Various drug-based treatments are also being tested for dengue. Clinical trials with existing medicines such as chloroquine, celgosivir, ribavirin, prednisolone, and lovastatin have been conducted, but none of them has proved effective against the disease. Therefore, there is no specific cure for dengue yet. Due to such a lack of effective treatments, alternative options such as herbal or natural remedies have gained increasing interest.⁴(Tewari et al., 2024)

Severe dengue infections continue to be a serious health problem, affecting people of all ages in many countries across Asia and Latin America. Despite the fact that dengue is highly influential in public health, effective antiviral treatments are still not available, which to some extent is due to limited attention being paid to this mosquito-borne disease by the pharmaceutical industry. 5(Hasani et al., 2025)

This review elaborates on the role of herbal interventions in dengue management, focusing on the therapeutic potential, limitations, and future scope based on recent research findings. New and innovative ways to fight dengue include treatments derived from plants and synthetic compounds.

Role of Herbal Remedies in Enhancing Dengue Treatment

Home remedies to prevent dengue are considered highly efficient and have no side effects because they are extracted from natural sources. They are being used in the treatment of many diseases and the symptoms of dengue fever. Many reports have indicated that various plants and herbs of traditional medicine have antiviral and anti-dengue effects and have been utilized to treat viral infections both in human beings and animals. In all, about 30 species of plants have been identified, known to have the potential for the treatment of dengue fever; their names are *Momordica charantia*, *Alternanthera philoxeroides*, *Andrographis paniculata*, *Cladosiphon okamuranus* and *Carica papaya*. In most of the Asian countries, the juice of leaves of *Carica papaya* is traditionally used as a treatment for dengue. In some studies it has been noticed that the extracts of *Carica papaya* leaves possessing membrane-stabilizing properties, platelets count can help to increase and improve the functionality of white blood cells.(Ansari et al., 2023)

Herbs are known for their various medicinal properties and form an important part in the traditional system of healing, such as Ayurveda and TCM, among many other cultural practices. A study of these herbs in the light of dengue fever brings out how modern science is mingling with traditional wisdom to find new treatments that will help people suffering from dengue and enhance their quality of life.

Traditionally used in Ayurveda, Chinese medicine, and folk practices, herbal remedies have lately received support for their potential to manage dengue through scientific research.. Numerous plants contain bioactive phytochemicals with antiviral, antioxidant, and immune-boosting effects that can enhance conventional treatments. (Ansari et al., 2023)

Traditional Indian medicinal plants such as *Carica papaya* L., *Andrographis paniculata*, Neem, and *Tinospora cordifolia* are commonly used in the treatment of dengue virus (DENV) infection. Ahmad et al. reported that the aqueous extract of *Carica papaya* leaves is effective in patients with dengue fever. Since dengue often causes thrombocytopenia, *Carica papaya* leaves have been found to help increase platelet counts in affected patients. Multiple studies have documented this rise in platelet levels following treatment with *Carica papaya* leaf extract. Although the precise mechanism remains unclear, it is believed to involve the membrane-stabilizing effects of the extract. Andrographolide, derived from *Andrographis paniculata*, has demonstrated potential against the primary dengue vector, *Aedes aegypti*, possibly through modulation of intracellular signaling pathways such as NF- κ B. Additionally, *Tinospora cordifolia*-based biofabricated copper oxide nanoparticles (CuO NPs) have shown antiviral activity against larvae of *Anopheles stephensi* and *Aedes aegypti*. Its possible mode of action includes inhibiting both structural and non-structural proteins of the dengue virus. (Tewari et al., 2024)

Controlling the dengue vector remains the foremost approach to preventing the disease, involving chemical or biological methods to target mosquitoes and remove their breeding habitats. However, this strategy has largely been ineffective in stopping the spread of dengue in most endemic countries. A key reason for this difficulty is the antigenic variation of the dengue virus; because immunity does not persist across its four serotypes, people are susceptible to repeated infections over time. (Tarpan Sahoo.)

Rationale for Exploring Herbal Remedies in Dengue Management

Ansari et al., 2023 has reviewed the broad array of studies on these herbs, focusing on their antiviral, anti-inflammatory, and immunomodulatory properties, and explore their possible role as adjunct therapies in the management of dengue fever. The rationale for the investigation of traditional herbal medicine for dengue is multilayered, as it combines centuries of medicinal plant use with an urgent need for useful treatment modalities against a rapidly expanding global health threat.

1. **Historical Importance of Herbal Medicine:** Herbal remedies are part of traditional medicine that was used for various health problems by many different cultures and date back several thousand years. The fact that traditional medicine has been utilizing plants in their treatments against viral diseases for millennia provides a sound basis for

investigation of potential treatments for dengue fever since current medical practice mainly depends on symptomatic treatment...

2. Bioactive phytoconstituents in herbs are reported to possess immuno-modulatory, antiviral, and anti-inflammatory properties. Keeping this in mind, the description of the role of herbal drugs in preventing or reducing the clinical manifestations of dengue virus infection and thus providing support in fighting the disease was conducted.
3. Emergence of Drug-Resistant Viruses: Herbal medicine is a highly promising modality because of the complex nature of its active constituents. In view of their multifaceted useful properties and multi-component nature, herbs may be regarded as an important class of antiviral studies for the reduction of the risk of drug-resistant virus emergence.
4. Global Impact of Dengue Fever: The pervasiveness of the virus and the severe impact on populations worldwide underscore that treatments are very much in need. The use of traditional herbal medicines is very encouraging in research and development because many have immune-modulating, anti-inflammatory, and antiviral actions.
5. Integration of Traditional and Modern Medicine: Understanding the importance of both modern scientific methodology and traditional knowledge of herbalism gives rise to a more advanced understanding of medicinal plants. Studies on the possible utilization of herbs as treatment for dengue involve methods that encourage cooperation between herbalists, modern researchers, and traditional healers. Interest in researching herbs for the treatment of dengue is fueled by the long history of herbal medicine, the various pharmacological properties of bioactive plant compounds, the challenges posed by drug-resistant viruses, the rampant prevalence of dengue fever worldwide, and increased appreciation for combining traditional and modern therapeutic interventions. The necessity for innovative solutions to a global health pandemic is paired with knowledge inspired by established therapeutic practices.

Table 1: Overview of Herbal Plants Studied for Anti-Dengue Activity.

Name and Parts	Family	Author (Year)	Journal	Activity	Finding
<i>Andrographis paniculata</i> (leaves, whole plant)	<i>Acanthaceae</i>	<i>Andrographolides as Antiviral Agents</i> (2023)	<i>Tropical Journal of Natural Product Research</i>	Antiviral, immunomodulatory	Andrographolide and its derivatives inhibit DENV NS2B–NS3 protease and enhance immune response; nanoformulation improves

					bioavailability and antiviral efficacy.
<i>Carica papaya</i> (leaves)	<i>Caricaceae</i>	Haward et al. (2024)	<i>Cureus</i>	Platelet-enhancing, anti-inflammatory	Leaf extract shown to significantly elevate platelet counts in dengue patients; improved hematological recovery and reduced hospitalization time.
<i>Uncaria tomentosa</i> (bark, roots)	<i>Rubiaceae</i>	De Lima et al. (2024)	<i>Viruses</i>	Antiviral, virucidal	Demonstrated potent in vitro virucidal activity; mechanistic parallels suggest potential for DENV inhibition through inhibition of viral RNA replication.
<i>Glycyrrhiza sglabra</i> (roots)	<i>Fabaceae</i>	Jayasekara et al. (2024)	<i>Scientific Reports</i>	Antiviral	Methanol root extract prevents DENV-2 infection in Vero cells; glycyrrhizin interacts with NS5 polymerase, inhibiting replication.
<i>Phyllanthus niruri</i> (whole plant)	<i>Phyllanthaceae</i>	Tewari et al. (2024)	<i>Discover Medicine</i>	Antiviral	Identified as one of the top Indian herbal components in meta-analysis of dengue therapeutics; supports reduction in viral replication rates.
<i>Psidium guajava</i> (leaves)	<i>Myrtaceae</i>	Tewari et al. (2024)	<i>Discover Medicine</i>	Antiviral, Hematopoietic	Meta-analysis revealed consistent increase in platelet counts and reduced viral RNA titer across reviewed clinical data.
<i>Curcuma longa</i>	<i>Zingiberaceae</i>	A Narrative Review on	<i>Liaquat National</i>	Antiviral, anti-inflam	Curcumin inhibits viral

(rhizome)		Current Development... (2024)	<i>Journal of Primary Care</i>	matory	proteases and reduces cytokine storm severity in dengue via suppression of NF- κ B pathway.
<i>Tinospora Cordifolia</i> (stem)	<i>Menispermaceae</i>	Hasani et al. (2025)	<i>Heliyon</i>	Immunomodulatory, antipyretic	Noted synergy with other herbs in dengue patient recovery, improving clinical symptoms and platelet restoration.
<i>Cymbopogon citratus</i> (leaves)	<i>Poaceae</i>	Hasani et al. (2025)	<i>Heliyon</i>	Antiviral, anti-inflammatory	Lemongrass extract shows suppression of proinflammatory mediator synthesis, offering adjuvant benefit for dengue treatment.
<i>Ocimum sanctum</i> (leaves)	<i>Lamiaceae</i>	Hasani et al. (2025)	<i>Heliyon</i>	Antiviral, antioxidant	Tulsi extract prevents viral attachment by modifying viral surface proteins; enhances host antioxidant defense.
<i>Azadirachta indica</i> (leaves)	<i>Meliaceae</i>	Hasani et al. (2025)	<i>Heliyon</i>	Antiviral, immunostimulant	Neem leaf extract exhibits broad virucidal properties against flaviviruses including DENV; enhances macrophage activation and cytokine modulation.

Recent significant developments in the use of herbal remedies for dengue management include natural compounds from *Andrographis paniculata*, *Carica papaya*, *Uncaria tomentosa*, and *Glycyrrhiza glabra*, which have demonstrated potent antiviral and immunomodulatory activities against various dengue virus serotypes. *Andrographis paniculata* remains a major focus due to the active compound andrographolide, which inhibits DENV NS2B–NS3 protease and enhances immune defense mechanisms (Andrographolides as Antiviral Agents, 2023). *Carica papaya* leaf extract is widely studied in the clinic for its established efficacy in

elevating platelet counts and improving hematological parameters in dengue patients (Haward et al., 2024). Studies on *Uncaria tomentosa* revealed a strong virucidal potential, with indications that its bioactive constituents may inhibit viral RNA replication (De Lima et al., 2024). In addition, the roots of *Glycyrrhiza glabra* contain the active principle glycyrrhizin, which interferes with DENV polymerase activity and hence reduces viral load (Jayasekara et al., 2024).

Furthermore, polyherbal formulations made up of *Azadirachta indica*, *Tinospora cordifolia*, *Phyllanthus niruri*, and *Euphorbia hirta* have demonstrated synergistic antiviral and immunomodulatory actions. Bioactive compounds such as curcumin and quercetin have also presented relevant properties in modulating cytokine storms and oxidative stress. In general, these findings present evidence of therapeutic value in the field of herbal medicine as an integrative approach to dengue treatment and demand further clinical validation.

Herbal Remedial Treatment of Dengue

They are also highly effective for preventing dengue and are devoid of any side effects since these remedies are naturally derived. Home remedies help manage a number of illnesses, including dengue fever and its associated symptoms. Numerous studies have shown that traditional medicinal herbs and plants possess antiviral and anti-dengue effects and have been used to treat viral infections in both humans and animals. According to (Abd Kadir et al., 2013) around 30 plant species have potential in treating dengue fever, such as *Momordica charantia*, *Alternanthera philoxeroides*, *Andrographis paniculata*, *Cladosiphon okamuranus*, and *Carica papaya*. In many Asian countries, *Carica papaya* leaf juice is commonly employed as a herbal treatment for dengue fever. Several research findings reveal that *Carica papaya* leaf extract, known for its membrane-stabilizing properties, enhances platelet activation and improves white blood cell function.

Table 2: Mechanism of Action — Key Herbal Compounds in Dengue.

Compound (active)	Source plant	Mechanism of action	Key references
Andrographolide	<i>Andrographis paniculata</i>	Inhibits DENV replication and reduces viral production in infected cells; modulates host antiviral responses and inflammatory signalling (reported) to reduce viral load and block steps in replication cycle). Useful discussion point: both	Sya'ban Putra Adiguna et. al

		direct antiviral activity and host-directed immunomodulation.	
Quercetin (flavonol)	Many plants (e.g., <i>Hibiscus</i> , <i>Allium</i> , <i>Camellia</i> sources)	Blocks DENV attachment/entry and inhibits viral replication; reported interactions with viral enzymes (NS2B-NS3 protease) in biochemical/in silico studies; also modulates host innate immune regulators (SOCS proteins). Note: some cytotoxicity reported at higher concentrations discuss therapeutic window.	Rahim N.A., et al.
Baicalin / Baicalein	<i>Scutellaria baicalensis</i>	Interferes with virus attachment/entry and intracellular replication; baicalin shown to inactivate free DENV particles and reduce attachment to host cells. Baicalein derivatives under development with improved anti-DENV potency.	Ehsan Moghaddam et. al
Curcumin / Curcuminoids	<i>Curcuma longa</i>	Multiple host- and virus-targeted effects: allosteric inhibition of the DENV NS2B-NS3 protease (biophysical/biochemical evidence) and host-pathway perturbation (e.g., inhibition of lipogenesis required for DENV replication); evidence supports multi-target (host + viral protease) action.	Liangzhong Lim et. al
EGCG (epigallocatechin-3-gallate)	Green tea (<i>Camellia sinensis</i>)	Acts mainly at <i>early</i> stage: direct interaction with virions to prevent attachment/entry; serotype-independent inhibition reported in cell models. Good example of a compound acting by virion neutralization/entry blockade.	Huang Y., et. al
Glycyrrhizic acid / Glycyrrhizin derivatives	<i>Glycyrrhiza glabra</i> (licorice)	Glycyrrhizic acid derivatives inhibit DENV—mechanisms include interference with viral replication and possibly entry; structure–activity work shows derivatives with improved potency. Recent data also report antiviral activity of root extracts against DENV 1–4.	Jayasekara, K. G. et al.
Carica papaya leaf extract (CPLE)	<i>Carica papaya</i> leaves	Not primarily direct antiviral — strongest clinical signal: increases platelet counts in dengue patients. Mechanistic data indicate upregulation of genes linked to megakaryopoiesis/platelet production (e.g., ALOX12, PTAFR) and immunomodulatory/antioxidant effects that may reduce platelet destruction and vascular leakage. Clinical trials & RCTs report faster platelet recovery and improved clearance kinetics of NS1 in some studies.	Subenthiran S. et. al
Silymarin / silybin (milk thistle)	<i>Silybum marianum</i>	Reported to prevent viral entry and inhibit early infection steps in cell models; also has antioxidant/anti-inflammatory effects that could limit dengue-related host pathology. (Useful to discuss as a host-protective/heratoprotective phytochemical with entry-blocking activity in vitro.)	Zhang, C., et al.

Several bioactive herbal compounds exhibit potent anti-dengue activities through both direct antiviral and host-modulatory mechanisms. Andrographolide from *Andrographis paniculata* inhibits DENV replication and modulates host immune responses, reducing viral load in infected cells (Panraksa et al., 2017). Quercetin, a flavonol found in *Hibiscus* and *Camellia* species, blocks viral entry and interacts with the NS2B–NS3 protease, thereby suppressing replication (Zandi et al., 2011). Baicalein from *Scutellaria baicalensis* interferes with virus adsorption and intracellular replication (Zandi et al., 2011). Curcumin from *Curcuma longa* exhibits multi-target inhibition, binding allosterically to the DENV NS2B–NS3 protease and disrupting lipid metabolism essential for replication (Lim et al., 2020). EGCG from green tea acts at early infection stages by neutralizing virions and preventing cell attachment (Raekiansyah et al., 2018). Glycyrrhizic acid from *Glycyrrhiza glabra* inhibits viral protease and replication (Jayasekara et al., 2024). Carica papaya leaf extract enhances platelet production through upregulation of megakaryopoietic genes ((Mandal et al., n.d.) while Silymarin from *Silybum marianum* prevents viral entry and provides hepatoprotective effects (Low et al., 2021).

Medicinal plants that have been investigated for anti-dengue activity

Euphorbia hirta plant is commonly prepared as a decoction or infusion and used to address a range of health issues, such as intestinal parasites, diarrhea, peptic ulcers, amoebic dysentery, asthma, hay fever, kidney stones, menstrual disorders, and sexually transmitted diseases. Phytochemical studies of *Euphorbia hirta* have identified various compounds in the entire plant, including polyphenols, reducing sugars, alkaloids, flavonoids, sterols, tannins, and triterpenoids. Apostol et al. investigated the platelet-enhancing effects of *Euphorbia hirta* decoction in ethanol-induced thrombocytopenic rat models. Continuous administration of the decoction sustained this anti-thrombocytopenic effect. *E. hirta* is rich in reducing polyphenols, which are believed to play a key role in increasing platelet levels. In the Philippines, the water decoction of *Euphorbia hirta* leaves, known locally as gatas–gatas, is traditionally used to treat dengue fever. It is said to stop internal bleeding and cure dengue fever within 24 hours. Tea made from boiled *E. hirta* leaves is commonly used to treat dengue fever. Rural communities in the Philippines rely on this plant in folk medicine for dengue treatment. Traditional practitioners hold that tawa–tawa leaf decoction can help reverse viral infections and prevent the fever from progressing to severe stages, although scientific proof is lacking. Sometimes, tawa–tawa is combined with papaya leaves, as papaya leaf extract acts

as an antibiotic to treat fever. While papaya leaf extract targets bacterial infections causing the fever, tawa–tawa extract helps prevent bleeding.

Azidarachta indica fast-growing tree is native to India, Indonesia, Pakistan, and Malaysia, thriving across tropical and subtropical regions, reaching heights of 15–20 meters. Neem is valued as one of the best and fastest-growing trees and has been traditionally used to treat various conditions such as jaundice, ulcers, parasitic infections, malaria, and other illnesses. Numerous studies have examined the leaves, seeds, bark, and flowers of the neem tree, which have been used to combat a wide range of bacterial and viral infections.

The inhibitory effect of an aqueous extract from *A. indica* leaves on the replication of DENV-2 was tested in vitro. Cytotoxicity assays were conducted to establish the Maximum Non-Toxic Dose (MNTD) for use in virus inhibition tests. The neem leaf aqueous extract completely prevented infection by 100 to 10,000 tissue culture infective doses (TCID₅₀) of the virus, as shown by the lack of cytopathic effects at the highest non-toxic concentration of 1.897 mg/mL.

Andrographis paniculata In vitro research has demonstrated the antiviral effects of methanolic extract from *A. paniculata* against dengue fever, specifically targeting the DENV-1 serotype. The extract was able to maintain a normal morphology of the cells and had very minimal cytopathic effect on the infected DENV-1 cells, where the cell monolayer was essentially intact; only a few cells died or lysed, and CPE was also very low.

Anacolosia pervilleana Acetylenic compounds from the ethyl acetate extract of *Anacolosia pervilleana*, a plant endemic to Madagascar, were obtained. Using a purified DENV RdRp polymerase enzyme assay, these compounds had IC₅₀ values of circa 3 µmol/L, showing their inhibitory action against the DENV RdRp enzyme. The results indicated that these compounds exhibit a certain level of selectivity for DENV RdRp. Besides that, all the compounds exhibited some degree of antimetabolic activity in Vero cells with CC₅₀ values between 20–30 µmol/L.

Alternanthera philoxeroides is an invasive aquatic weed that possesses both antinociceptive and antihyperglycemic activities. The present study deals with the examination of antiviral activities of the petroleum ether, ethyl acetate, ethyl ether, and coumane extracts from *A.*

philoxeroides. In India, this plant extract has been traditionally used in medicine, especially to treat disorders associated with women.

Curcuma longa: *Curcuma longa* is widely distributed across Southeast Asian countries, and in studies conducted in India, there were reported to be about 45 varieties of turmeric (Prasad and Aggarwal, 2011). Phytochemical investigations made on this plant unveiled its pharmacological activities such as anticancer, anti-inflammatory, antidiabetic, and antioxidant activities. In vitro studies using human liver and murine cells revealed that a compound present in *Curcuma longa*-its active principle, curcumin-exerts antiviral activity against DENV by inhibiting viral RNA synthesis and replication.

These findings were further confirmed by molecular docking studies. (Lim et al., 2021). The results from the in vitro assay conducted with Huh7it-1 cells demonstrated that the IC₅₀ value of the *Curcuma longa* extract was 17.91 µg/mL, while the selectivity index (SI) was 4.8-a promising value that indicates its safety and efficacy as an antiviral. Moreover, oral delivery of *C. longa* extract at 0.147 mg/mL in ddY mice was able to significantly reduce the virus load 24 hours after infection with DENV-2. Histopathological examination of liver and kidney tissues did not show any abnormalities, and biochemical tests did not indicate significant variation in SGPT, SGOT, urea, and creatinine values. Therefore, *Curcuma longa* seems to be a probable antiviral agent against DENV due to its characteristics of low toxicity with effective inhibition; hence, further studies should be conducted on it.

Boesenbergia rotunda is a type of ginger found in India, Southeast Asia, Sri Lanka, and Southern China (Saah et al., 2021), and is widely used both as a medicinal agent and food ingredient due to its aromatic flavor enhancing appetite. Traditionally, this plant is prescribed to treat ailments such as fever, inflammation, gout, stomach pain, and indigestion (Ongwisepaiboon & Jiraungkoorskul, 2017). This plant contains the following bioactive compounds, which have anti-DENV properties: pinostrobin, pinocembrin, alpinetin, cardamonin, panduratin A, and 4-hydroxypanduratin A (Liew et al., 2020). Pinocembrin and cardamonin exert a synergistic inhibitory effect against DENV-2 protease, pinostrobin and cardamonin inhibit NS3 protease, while panduratin A with 4-hydroxypanduratin A act as competitive inhibitors (Lim et al., 2021).

Sambucus nigra: *Sambucus nigra* mainly comes from Europe and North America. This plant is rich in flavonoids, catechins, and phenolic acids, including glycosides such as cyanidin-3-

glycoside and cyanidin-3-sambubioside. It is widely used in herbal medicine traditionally because of its antiviral properties given by the herb (Mukhtar et al., 2008). The extracts of flowers and leaves of *Sambucus nigra* may have anti-DENV-2 action at 400 µg/mL. Combining flowers and leaves resulted in higher efficiency of the extract in being more effective against DENV-2 (Mahboubi, 2020).

Cymbopogon citratus *Cymbopogon citratus*, widely distributed in the tropical regions but more so in Southeast Asia, contains rich levels of bioactive phytochemicals that include: alkaloids, glucosides, phenols, flavonoids, saponins, and terpenoids.. It is used all over the world as a mosquito repellent, with its oil, when formulated into a nanoemulsion, showing great insect-repelling activities. Methanol extracts from the root significantly inhibited DENV-2 plaques by 98.9% in an in vitro assay; in addition, methanolic extracts of this plant inhibit cytopathic effects in Vero E6 infected with DENV-1. The methanolic extract of *Cymbopogon citratus* exhibited an antiviral activity against DENV-1, as confirmed by the MTT assay that showed anti-dengue properties. Kadir et al., 2013

Recent Advances in Dengue Management: Vaccines, Oral Therapeutics, and Emerging Strategies

1. Jwarahara Syrup

Jwarahara Syrup is an Ayurvedic herbal formulation developed based on classical texts and modern pharmaceutical methods, primarily designed for the treatment of fever, especially in children. The syrup is made from a combination of ten potent herbs (including Sariva, Patha, Manjistha, Draksha, Pilu, Parushaka, Haritaki, Vibhitaki, and Amalaki) along with sugar (Sharkara) which not only acts as a sweetening agent but also helps in preserving the formulation.

The preparation process begins with soaking powdered herbs in water overnight, followed by boiling to create a concentrated decoction called Kwatha. This decoction is filtered and then combined with sugar candy powder in a specific ratio (65% w/v of Kwatha). The mixture is heated cautiously at temperatures ranging from 80 to 90 degrees Celsius until a one-thread consistency syrup is obtained. The total preparation time for syrup is approximately 3 hours and 10 minutes. The final product is dark brown, liquid in consistency, with a sweet taste and a slight astringency, carrying the characteristic aroma of Sariva. It is bottled typically in 60 ml containers.

Though exact dosage details are not exhaustively standardized in the article, Ayurvedic practice generally recommends administering 5 ml doses for children multiple times per day, adjusting according to age and severity of symptoms.

Effectively, Jwarahara Syrup serves as a natural antipyretic, helping reduce fever and related symptoms while supporting the body's balance between physical and mental health impacted by fever. The formulation is made to be palatable and safe, emphasizing minimal side effects and maximizing therapeutic benefits.

2. Denguenil Vati

Denguenil Vati is a pentaherbal Ayurvedic formulation traditionally used by practitioners in India for dengue fever treatment. It contains extracts from *Tinospora cordifolia* (Giloy), *Aloe vera*, *Carica papaya* (Papaya), *Punica granatum* (Pomegranate), and *Ocimum sanctum* (Holy Basil). This formulation was scientifically validated in a zebrafish model infected with dengue virus serotype 3 (DENV-3) to assess its therapeutic efficacy and safety.

The study tested Denguenil at three translational doses—5.6 µg/kg, 28 µg/kg, and 140 µg/kg—derived from the human equivalent dose of 1000 mg twice daily. Denguenil displayed dose- and time-dependent antiviral effects by significantly reducing dengue viral RNA copy numbers in the liver, with up to 72% reduction observed at the highest dose after 15 days.

Treatment with Denguenil markedly inhibited dengue virus-induced liver damage, including hepatocyte necrosis and inflammation, again in a dose-dependent pattern. At 140 µg/kg, hepatocyte necrosis was reduced by 86%, and inflammation was completely abrogated. The syrup also normalized red blood cell infiltration into the liver and restored normal blood cell counts: platelet numbers increased (improving thrombocytopenia), red blood cell counts rose (alleviating anemia), and white blood cell counts were normalized.

Denguenil treatment further prevented hemorrhagic symptoms, as evidenced by reduced blood clots and hemorrhage in zebrafish fins after 14 days. Gene expression analyses demonstrated that Denguenil lowered the expression of the apoptotic endothelial marker Angiopoietin-2 and pro-inflammatory chemokine CCL3, both linked to severe disease progression.

In vitro tests confirmed Denguenil's safety, showing no cytotoxicity in human liver (HepG2) and skin (A431) cell lines up to 300 µg/mL and no induction of oxidative stress.

HPLC analysis identified bioactive compounds in Denguenil including gallic acid, ellagic acid, palmetin, and berberine, substances with reported antiviral and immunomodulatory properties.

3. Dengue vaccine

The dengue vaccine Dengvaxia, CYD-TDV, was the first-licensed dengue vaccine to arrive in 2015 for clinical use. It is administered in three doses, six months apart, and is approved for use in individuals aged 9-45 years with prior evidence of dengue infection. The vaccine platform is based on a weakened yellow fever vaccine virus backbone that has been engineered to encode proteins of dengue virus to stimulate immune response. Dengvaxia showed about 60% overall efficacy but provided better protection in those previously exposed to dengue and less in dengue-naïve individuals. Because of an increased risk of severe dengue in seronegative recipients, Dengvaxia is recommended only for those confirmed to have had dengue before vaccination. Its use has been restricted due to safety concerns, and production is being discontinued owing to declining demand. Following Dengvaxia, the TAK-003 vaccine (Qdenga) was licensed around 2022 and is given in two doses spaced three months apart. It uses a liveattenuated dengue virus type 2 backbone modified to elicit immunity against all four dengue serotypes. TAK-003 demonstrated about 73-80% efficacy in the first two years, especially strong against serotypes DENV-1 and DENV-2, and has been recommended for routine use in endemic areas, including children aged 4 years and older. It is well tolerated, with mainly mild injection site reactions. Another promising vaccine is TV-003/TV-005 (Butantan-DV), still in late-stage clinical trials. It is designed to provide balanced protection with a single-dose regimen. Early trials report 79.6% efficacy, with particularly high protection in dengueexperienced individuals

6. FUTURE DIRECTION

Future research on dengue management should be directed at integrating traditional medicinal knowledge with modern pharmacology and molecular approaches to establish evidence-based herbal therapeutics. Since dengue infections continue to spread geographically, the need for safer, accessible, and cost-effective interventions is an immediate concern and especially vital in tropical regions where the disease burden is highest. Despite the partial protection afforded by licensed vaccines such as TAK-003 (Qdenga) and TV-

003/TV-005 (Butantan-DV), their combination with herbal adjunct therapies might further improve immune resilience and symptomatic recovery among infected individuals. A major future direction involves host-directed therapeutic strategies aimed at the regulation of the immune response, rather than targeting viral replication. Controlling inflammatory mediators, including TNF- α , IL-1 β , and NF- κ B could prevent vascular leakages and cytokine storms associated with severe complications of dengue infection like DHF and DSS. Therefore, the development of cytokine-modulating herbal compounds is an attractive area for future research. Phytoconstituents from several herbs have been shown to possess potential in reducing excessive immune activation. Immunosuppressive anti-inflammatory herbs such as *Tinospora cordifolia*, *Andrographis paniculata*, *Curcuma longa*, and *Azadirachta indica*, therefore, merit prioritization in future investigations due to their wide spectrum of antiviral and immune-regulatory properties. Their bioactive compounds including andrographolide, curcumin, and azadirachtin have been reported to inhibit viral proteases, suppress cytokine overexpression, and enhance host defense mechanisms. However, the improvement of bioavailability, stability, and consistency of herbal preparations across clinical applications is critical, which requires their standardization, optimization of green extraction techniques, and incorporation of nanocarrier-based delivery systems. Confirmation of safety, dosage, and efficacy through large-scale multicentric randomized clinical trials will be required for the establishment of promising agents like *Carica papaya* leaf extract, *Euphorbia hirta*, and *Glycyrrhiza glabra*, which have shown platelet-enhancing and antiviral properties in various preclinical and clinical studies. These can be supported by metabolomic, transcriptomic, and molecular docking analyses to provide insights into multi-target mechanisms and synergistic interactions of phytoconstituents with viral and host targets (Tewari et al., 2024; De Lima et al., 2024). Some newer tools that may further accelerate the discovery process for novel anti-dengue compounds from traditional herbal databases include AI-assisted phytochemical screening, network pharmacology, and computational drug design (Altamish et al., 2022; Hasani et al., 2025). The combined use of modern technologies along with knowledge of traditional herbalism, therefore, has the potential to identify holistic, inexpensive, and scientifically validated herbal therapeutics for global dengue management, complementary to conventional antivirals and vaccines (Ansari et al., n.d.; Abd Kadir et al., 2013).

CONCLUSION

Dengue fever is a major health problem worldwide, and a cure has still remained elusive to this date due to the absence of antiviral drugs and the limitations of current vaccination. In

this background, herbal remedies become important and an area of interest because such natural remedies provide supportive benefits that help the body battle dengue. Of these, the papaya leaf extract is unique in increasing the platelet count and reducing symptoms based on strong clinical evidence. *Tinospora cordifolia*, *Andrographis paniculata*, neem, turmeric, and *Euphorbia hirta* give promising results by inhibiting the virus, balancing immunity, and organ protection.

However, despite these promising results, many herbal remedies are still in need of further scientific testing with regard to safety and efficacy, particularly in large clinical trials with standardized dosing. The marriage of modern research methodologies with traditional herbal knowledge holds real promise for the creation of accessible and safe herbal-based remedies for dengue. If further validated, such treatments could become of real value in dengue management, especially in settings with limited access to conventional medicine.

REFERENCES

1. A Narrative Review on Current Development and Future Prospects for the Treatment of Dengue Virus Infection. (2024). *Liaquat National Journal of Primary Care*. <https://doi.org/10.37184/lnjpc.2707-3521.6.26>
2. Abd Kadir, S. L., Yaakob, H., & Mohamed Zulkifli, R. (2013). Potential anti-dengue medicinal plants: A review. *Journal of Natural Medicines*, 67(4): 677–689. <https://doi.org/10.1007/s11418-013-0767-y>
3. Adiguna, S. P., Panggabean, J. A., Atikana, A., Untari, F., Izzati, F., Bayu, A., Rosyidah, A., Rahmawati, S. I., & Putra, M. Y. (2021). Antiviral Activities of Andrographolide and Its Derivatives: Mechanism of Action and Delivery System. *Pharmaceuticals*, 14(11): 1102. <https://doi.org/10.3390/ph14111102>
4. Altamish, M., Khan, M., Baig, M. S., Pathak, B., Rani, V., Akhtar, J., Khan, A. A., Ahmad, S., & Krishnan, A. (2022). Therapeutic Potential of Medicinal Plants against Dengue Infection: A Mechanistic Viewpoint. *ACS Omega*, 7(28): 24048–24065. <https://doi.org/10.1021/acsomega.2c00625>
5. Andrographolides as Antiviral Agents: Insights into Mechanisms, Modifications, and Delivery Innovations. (2023). *Tropical Journal of Natural Product Research*, 7(12). <https://doi.org/10.26538/tjnpr/v7i12.1>
6. Ansari, T., Pawar, U., Rana, D., & Mulla, T. (n.d.). *A Comprehensive Review on the Efficacy of Herbs in the Management of Dengue Fever*(2023)

7. Balkrishna, A., Solleti, S. K., Verma, S., & Varshney, A. (2020). Validation of a Novel Zebrafish Model of Dengue Virus (DENV-3) Pathology Using the Pentaherbal Medicine Denguenil Vati. *Biomolecules*, 10(7): 971. <https://doi.org/10.3390/biom10070971>
8. Bhatt, S., Gething, P. W., Brady, O. J., Messina, J. P., Farlow, A. W., Moyes, C. L., Drake, J. M., Brownstein, J. S., Hoen, A. G., Sankoh, O., Myers, M. F., George, D. B., Jaenisch, T., Wint, G. R. W., Simmons, C. P., Scott, T. W., Farrar, J. J., & Hay, S. I. (2013). The global distribution and burden of dengue. *Nature*, 496(7446): 504–507. <https://doi.org/10.1038/nature12060>
9. Choudhary, N. L., Kumawat, P., Patel, P., & Chishty, N. (2022). Dengue and natural remedies for its prevention and control: A review. *International Journal of Mosquito Research*, 9(6): 107–115. <https://doi.org/10.22271/23487941.2022.v9.i6b.646>
10. De Lima, R. C., Valente, L. M. M., Familiar Macedo, D., de-Oliveira-Pinto, L. M., Dos Santos, F. B., Mazzei, J. L., Siani, A. C., Nunes, P. C. G., & De Azeredo, E. L. (2024). Antiviral and Virucidal Activities of Uncaria tomentosa (Cat's Claw) against the Chikungunya Virus. *Viruses*, 16(3): 369. <https://doi.org/10.3390/v16030369>
11. Hasani, S. J., Sgroi, G., Esmailnejad, B., Nofouzi, K., Mahmoudi, S. S., Shams, N., Samiei, A., & Khademi, P. (2025). Recent advances in the control of dengue fever using herbal and synthetic drugs. *Heliyon*, 11(3): e41939. <https://doi.org/10.1016/j.heliyon.2025.e41939>
12. Haward, R., Konjeti, S., Chacko, J., Nadella, J. S., Roja, S. L., & Rayapudi, J. J. (2024). Papaya Leaf Extract Elevates Platelet Levels in Individuals With Dengue Fever. *Cureus*. <https://doi.org/10.7759/cureus.61090>
13. Jayasekara, K. G., Suresh, S., Goonasekara, C., Soyza, P., Perera, N., & Gunasekera, K. (2024). Anti-dengue viral activity of Glycyrrhiza glabra roots in Vero cells. *Scientific Reports*, 14(1): 25922. <https://doi.org/10.1038/s41598-024-76184-5>
14. Kalsariya, B., Patgiri, B., & Prajapati, P. (2010). Standard manufacturing procedure for syrup and tablet forms of Jwarahara Dashemani. *AYU (An International Quarterly Journal of Research in Ayurveda)*: 31(2): 255. <https://doi.org/10.4103/0974-8520.72411>
15. Lee, S. H., Tang, Y. Q., Rathkrishnan, A., Wang, S. M., Ong, K. C., Manikam, R., Payne, B. J., Jaganath, I. B., & Sekaran, S. D. (2013). Effects of cocktail of four local Malaysian medicinal plants (*Phyllanthus* spp.) against dengue virus 2. *BMC Complementary and Alternative Medicine*, 13(1): 192. <https://doi.org/10.1186/1472-6882-13-192>

16. Lim, L., Dang, M., Roy, A., Kang, J., & Song, J. (2020). Curcumin Allosterically Inhibits the Dengue NS2B-NS3 Protease by Disrupting Its Active Conformation. *ACS Omega*, 5(40): 25677–25686. <https://doi.org/10.1021/acsomega.0c00039>
17. Loaiza-Cano, V., Monsalve-Escudero, L. M., Filho, C. D. S. M. B., Martinez-Gutierrez, M., & Sousa, D. P. D. (2020). Antiviral Role of Phenolic Compounds against Dengue Virus: A Review. *Biomolecules*, 11(1): 11. <https://doi.org/10.3390/biom11010011>
18. Low, Z. X., OuYong, B. M., Hassandarvish, P., Poh, C. L., & Ramanathan, B. (2021). Antiviral activity of silymarin and baicalein against dengue virus. *Scientific Reports*, 11(1): 21221. <https://doi.org/10.1038/s41598-021-98949-y>
19. Mandal, S., Jaiswal, D. V., & Shiva, K. (n.d.). *A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback.*
20. Moghaddam, E., Teoh, B.-T., Sam, S.-S., Lani, R., Hassandarvish, P., Chik, Z., Yueh, A., Abubakar, S., & Zandi, K. (2014). Baicalin, a metabolite of baicalein with antiviral activity against dengue virus. *Scientific Reports*, 4(1): 5452. <https://doi.org/10.1038/srep05452>
21. Nahar, L., Nath, S., & Sarker, S. D. (2022). “Malancha” [*Alternanthera philoxeroides* (Mart.) Griseb.]: A Potential Therapeutic Option against Viral Diseases. *Biomolecules*, 12(4): 582. <https://doi.org/10.3390/biom12040582>
22. [Emerging interventions & therapies for effective dengue management]. Tarpan sahu (2025) (n.d.). *International Journal of Pharmacognosy*, 12(2).
23. Panraksa, P., Ramphan, S., Khongwichit, S., & Smith, D. R. (2017). Activity of andrographolide against dengue virus. *Antiviral Research*, 139: 69–78. <https://doi.org/10.1016/j.antiviral.2016.12.014>
24. Perera, S. D., Jayawardena, U. A., & Jayasinghe, C. D. (2018). Potential Use of *Euphorbia hirta* for Dengue: A Systematic Review of Scientific Evidence. *Journal of Tropical Medicine*, 2018; 1–7. <https://doi.org/10.1155/2018/2048530>
25. Raekiansyah, M., Buerano, C. C., Luz, M. A. D., & Morita, K. (2018). Inhibitory effect of the green tea molecule EGCG against dengue virus infection. *Archives of Virology*, 163(6): 1649–1655. <https://doi.org/10.1007/s00705-018-3769-y>
26. Rodriguez-Roche, R., & Gould, E. A. (2013). Understanding the Dengue Viruses and Progress towards Their Control. *BioMed Research International*, 2013; 1–20. <https://doi.org/10.1155/2013/690835>

27. Saleh, M. S. M., & Kamisah, Y. (2020). Potential Medicinal Plants for the Treatment of Dengue Fever and Severe Acute Respiratory Syndrome-Coronavirus. *Biomolecules*, 11(1): 42. <https://doi.org/10.3390/biom11010042>
28. Sathyapalan, D. T., Padmanabhan, A., Moni, M., P-Prabhu, B., Prasanna, P., Balachandran, S., Trikkur, S. P., Jose, S., Edathadathil, F., Anilkumar, J. O., Jayaprasad, R., Koramparambil, G., Kamath, R. C., Menon, V., & Menon, V. (2020). Efficacy & safety of *Carica papaya* leaf extract (CPLE) in severe thrombocytopenia ($\leq 30,000/\mu\text{l}$) in adult dengue – Results of a pilot study. *PLOS ONE*, 15(2): e0228699. <https://doi.org/10.1371/journal.pone.0228699>
29. Singh, R. K., Tiwari, A., Satone, P. D., Priya, T., & Meshram, R. J. (2023). Updates in the Management of Dengue Shock Syndrome: A Comprehensive Review. *Cureus*. <https://doi.org/10.7759/cureus.46713>
30. Subenthiran, S., Choon, T. C., Cheong, K. C., Thayan, R., Teck, M. B., Muniandy, P. K., Afzan, A., Abdullah, N. R., & Ismail, Z. (2013). *Carica papaya* Leaves Juice Significantly Accelerates the Rate of Increase in Platelet Count among Patients with Dengue Fever and Dengue Haemorrhagic Fever. *Evidence-Based Complementary and Alternative Medicine*, 2013; 1–7. <https://doi.org/10.1155/2013/616737>
31. Tayal, A., Kabra, S. K., & Lodha, R. (2023). Management of Dengue: An Updated Review. *Indian Journal of Pediatrics*, 90(2): 168–177. <https://doi.org/10.1007/s12098-022-04394-8>
32. Tewari, D., Jain, G. K., & Kumar, A. (2024). A systematic review and meta-analysis of some traditional Indian remedies against dengue. *Discover Medicine*, 1(1): 39. <https://doi.org/10.1007/s44337-024-00048-0>
33. Thomas, S. J., & Yoon, I.-K. (2019). A review of Dengvaxia®: Development to deployment. *Human Vaccines & Immunotherapeutics*, 15(10): 2295–2314. <https://doi.org/10.1080/21645515.2019.1658503>
34. Walia, S., & Singh, M. (n.d.). *Tracing plants potential effective against dengue virus: A review*.
35. Zandi, K., Teoh, B.-T., Sam, S.-S., Wong, P.-F., Mustafa, M. R., & AbuBakar, S. (2011). Antiviral activity of four types of bioflavonoid against dengue virus type-2. *Virology Journal*, 8(1): 560. <https://doi.org/10.1186/1743-422X-8-560>
36. Zende, A. V., Shinde, Y. A., Sonwalkar, R. R., & Parekar, P. B. (2024). A Comprehensive Review Article on Dengue Fever. *South Asian Research Journal of Pharmaceutical Sciences*, 6(03): 89–105. <https://doi.org/10.36346/sarjps.2024.v06i03.007>