STM JOURNALS

Research & Reviews: A Journal of
Immunology

https://journals.stmjournals.com/rrjoi

ISSN: 2277-6206 (Online)
ISSN: 2349-1280 (Print)
Volume 15, Issue 1, 2025
January-April
DOI (Journal): 10.37591/RRJoI

Review RRJoI

Utilize Nature's Power: Nutraceuticals in the Fight Against Dengue

Mohd. Wasiullah[1], Piyush Yadav[2,*], Azhan Ahmad[3]

Abstract

*As dengue fever continues to surge across tropical and subtropical regions, the exploration of novel therapeutic approaches is crucial. Nutraceuticals, natural bioactive compounds derived from food sources, are emerging as promising adjuncts in the fight against this viral disease. Unlike conventional treatments that primarily target symptoms, nutraceuticals offer a complementary strategy by enhancing the body's immune defense and addressing key complications. This review highlights the diverse potential of nature's remedies, such as papaya leaf extract for boosting platelet count, quercetin for its antiviral effects, and curcumin for modulating the inflammatory response. Additionally, the role of coconut water and vitamin C in strengthening immune resilience is examined. These nutraceuticals not only provide symptomatic relief but may also play a pivotal role in reducing disease progression and severity. By leveraging the healing power of nature, nutraceuticals present a unique, holistic approach to dengue management–one that bridges the gap between natural wellness and clinical science, offering new avenues for future treatmen*t strategies.

Keywords: Curcumin, dengue treatment, dietary supplement, nutraceutical, platelets count, quercetin

INTRODUCTION

Dengue, a mosquito-borne viral illness, is one of the fastest-growing infectious diseases globally, primarily affecting tropical and subtropical regions. It is caused by the dengue virus (DENV), which is transmitted through the bite of female *Aedes mosquitoes*, especially Aedes aegypti and Aedes albopictus. With four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), dengue presents a unique challenge in that immunity to one serotype does not protect against the others, making reinfection with different serotypes possible and often more severe [1–4].

The disease's symptoms range from mild, flu-like conditions known as dengue fever to severe and life-threatening forms. These symptoms are:

- High fever.
- Joint pain.
- Muscle pain.
- Nausea and Vomiting.
- Skin rashes.
- Loss of appetite.
- Fatigue and restlessness, etc.

Also, some severe symptoms are seen, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). What sets dengue apart from many other viral diseases is the potential for a second infection to trigger these severe complications, making the disease particularly dangerous in areas of high transmission [5].

***Author for Correspondence**
Piyush Yadav
E-mail: piyush6118@gmail.com

[1]Principal, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India
[2]Academic Head, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India
[3]Scholar, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India

Received Date: December 14, 2024
Accepted Date: December 22, 2024
Published Date: February 07, 2025

Citation: Mohd. Wasiullah, Piyush Yadav, Azhan Ahmad. Utilize Nature's Power: Nutraceuticals in The Fight Against Dengue. Research & Reviews: A Journal of Immunology. 2025; 15(1): 19–27p.

In recent years, dengue has become more prevalent, driven by urbanization, globalization, and climate change, which have facilitated the spread of mosquito vectors. The disease now threatens nearly half the world's population, with more than 100 countries reporting cases. Despite progress in vaccine development and vector control, dengue remains a major global health challenge, particularly in densely populated urban centers where mosquitoes thrive (grow) [6–8].

The only way to treat dengue fever is to manage the symptoms of the dengue.

Life Cycle of Dengue Mosquito

- *Egg:* Female mosquitoes lay their eggs directly on the walls of their water containers, right just above the water line. Eggs are very tolerant and can survive for weeks or even months without immersion in water.
- *Larva:* After the eggs submerge in water, they hatch into larvae that last for about 4 to 5 days. Their larvae live in water to feed on organic matter before they molt four times growing.
- *Pupa:* After the larval stage, the mosquito will go to the pupal stage. This stage takes around 1–3 days. Pupae are active but do not feed. Instead, they develop into adult mosquitoes.
- *Adult:* Adult mosquitoes emerge from the pupa. It rests on the surface of the water until the body hardens. Female mosquitoes that need blood to develop eggs start biting humans and transmit dengue a few days after emergence.

Transmission of Dengue Virus

- An infected Aedes mosquito bites a human, injecting the dengue virus into the bloodstream. The virus targets immune cells, including monocytes, dendritic cells, and macrophages, attaching to cell receptors [7].
- The virus enters the cell through endocytosis. Within the cell, the acidic environment triggers fusion between the virus's envelope and the endosome membrane, releasing viral RNA into the cytoplasm [9].
- The viral RNA is translated to form a single polyprotein. Host and viral enzymes then cleave this polyprotein into structural and nonstructural proteins needed for virus replication and packaging. The RNA also serves as a template for creating new viral genomes [10].
- Newly formed viral particles are assembled in the endoplasmic reticulum. They then pass through the Golgi apparatus, where they mature into infectious virions.
- The mature virus particles are transported to the cell surface and released via exocytosis, allowing them to spread and infect additional cells.
- When another mosquito bites the infected individual, it takes up the virus with the blood meal. The mosquito can then transmit dengue to another person, continuing the infection cycle.

History

This is a viral disease caused by Aedes mosquitoes, which has an obscure history. It dates to some centuries ago. The first reports of this disease in China date back to the Jin Dynasty (265–420 AD). It was mentioned as "water poison." Arabic manuscripts referred to the disease as a painful "breakbone fever," signifying the severity of the illness [11, 12].

The saga of dengue really begins in the 18th century, marked by significant outbreaks across continents. In the years 1779 and 1780, a virulent wave swept through Asia, North America, and Africa, facilitated by burgeoning trade routes and maritime exchanges. This change made a once obscure illness, dengue, become something recognized worldwide. Its name comes from the Spanish word "dengue," meaning the cautious, fastidious movements of those afflicted by it, describing the severe joint pain they suffered from.

As the 20th century began, the secrets surrounding dengue transmission began to be unearthed. In 1906, researchers determined the main vector was the Aedes aegypti mosquito and untangled the

dynamics of this viral infection. The following year, they identified the dengue virus, marking it as one of the first viral entities recognized in medical science. Four later serotypes emerged (DENV-1, DENV-2, DENV-3, DENV-4), therefore clarifying the complexities regarding reinfection and immunity.

Emergence of Dengue Hemorrhagic Fever the 1950s were the beginning when the story took a grave turn with dengue hemorrhagic fever (DHF). Southeast Asian regions, mainly Thailand and the Philippines, became arenas for this serious form of dengue, displaying horrific symptoms including bleeding and plasma leakage leading to mortal dangers. This mysterious phenomenon, ADE (antibody-dependent enhancement), which came into notice, represented an evil kind of cooperation whereby prior infections enhanced future episodes [13–16].

Dengue fever became the late 20th century's global public health challenge. Urbanization, climatic changes, and an increase in international travel permitted the Aedes mosquito to spread to new territories. Millions were put at risk, and dengue became endemic in more than 100 countries. The World Health Organization estimated hundreds of millions of cases annually, bringing healthcare systems into alarm.

Dengue called forth a mass effort of its own, where various strategies came forward with the intent of eliminating this scourge. Among such efforts were public health projects: educating communities, above all towards mosquito control and prevention, became a dominant feature. With the existence of the Dengvaxia dengue vaccine-as a scientific marvel, massive deployment was still restrained to the safety concerns that are present with the non-exposure individual. Other newer solutions, such as introducing Wolbachia-infected mosquitoes for reduced levels of transmission, showed an inexorable attack on the refractory virus.

Today, the dengue fever saga continues, while scientists keep working hard at finding improved treatments, stronger vaccines, and better mechanisms of control. This thread of historical tapestry, which dengue fever attests testifies to man's fortitude and how resourceful he is towards infectious diseases [17–19].

Nutraceutical

Nutraceuticals is derived from two words "nutrition" and "pharmaceuticals". These are products derived from food sources that offer health benefits beyond basic nutrition. These include:

- Dietary supplements.
- Functional foods.
- Functional Drinks.
- Cookies and Dairy products, etc.

These products are designed to enhance well-being and prevent disease. Nutraceuticals are becoming increasingly popular due to their role in promoting health, managing chronic conditions, and improving overall quality of life. Common examples include – vitamins, minerals, probiotics, and herbal extracts, which are often used to support immunity, heart health, and cognitive function (Figure 1) [20–23].

The growing interest in nutraceuticals is driven by consumer demand for natural alternatives to traditional pharmaceuticals and an increasing focus on preventive health. As research continues to highlight the link between nutrition and disease prevention, nutraceuticals are playing an expanding role in modern healthcare. Their ability to provide therapeutic benefits without the side effects of conventional drugs has positioned them as a key component in personalized medicine and integrative health approaches. The global market for nutraceuticals is rapidly expanding, reflecting a broader shift toward proactive health management and wellness [24–26].

Role of Nutraceuticals in Dengue

Nutraceuticals are valuable in dengue care, supporting standard treatments by strengthening the body's natural defenses and aiding recovery. Though they do not cure the disease, these natural supplements offer helpful benefits, making them a worthwhile addition to the treatment process.

There are various nutraceutical supplement present in the nature which help in fight against dengue.

Figure 1. Nutraceuticals.

Papaya Leaves

One of the critical challenges in dengue is thrombocytopenia, i.e., the drop in platelet count, which can lead to complications, such as bleeding. Unlike conventional treatments, this natural remedy can offer a gentle, accessible way to address this dangerous symptom (Figure 2).

Figure 2. Papaya Leaf Extract.

How It Works

When a person intake/consume the carica papaya leaf extract, then it enhances the expression of gene.

- This increased gene expression will enhance the activation of ALOX 12 gene expression (arachidonic acid 12-lipoxygenase).
- This ALOX 12 gene expression will lead to production of megakaryocytes i.e.
- The cell which is responsible for the platelets production in bone marrow.
- So, more megakaryocytes will produce more platelets.
- This will help in treatment of thrombocytopenia in dengue fever.
- Also prevent excess bleeding in dengue patients.
- Papaya leaf extract will act as a good nutrient for patients recovering from dengue fever.

Quercetin

Another factor of dengue fever is viral infection and inflammatory symptoms like redness, itching, pain, temperature rise & fatigue, etc. (Figure 3) [27].

So, we use quercetin as a nutrient which acts as anti-inflammatory agent in dengue fever.

- Quercetin belongs to the flavonoid family found from many plants and vegetables. Mostly known for its antiviral activity.
- Quercetin has been investigated for its potential to treat dengue fever because of its antiviral, anti-inflammatory, and antioxidant effects. Studies suggest that quercetin may stop the dengue

virus from replicating and help regulate the immune response, which can lessen inflammation and oxidative stress during the infection.

- A different study emphasized quercetin's capacity to block the NS2B-NS3 protease of the dengue virus, an enzyme crucial for the virus's replication. By inhibiting this enzyme, quercetin presents a possible therapeutic approach for controlling dengue infections.

Figure 3. Nutraceuticals Quercetin.

How It Works

- Quercetin is administered to dengue patients as a nutraceutical.
- Then it interacts with dengue virus in the body by entering blood of the dengue infected patient and reaches the viral infected site.
- Now quercetin inhibits the NS2B-NS3 protease enzyme which is very necessary for the replication of viruses.
- Now this phenomenon will reduce the replication of dengue virus in dengue patient (host) body.
- So viral infection is slowly reduced.

Curcumin

Another nutraceutical is Curcumin, which is also known as golden nutraceutical but in case of dengue fever it is mostly used as anti-inflammatory agent (Figure 4) [28, 29].

Curcumin, the active compound in turmeric (Curcuma longa), has gained attention for its potential to modulate the inflammatory response in various diseases, including viral infections like dengue fever. In dengue, inflammation is a key factor contributing to disease severity, particularly in the more severe forms, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

- The inflammatory response in dengue fever is characterized by elevated levels of pro-inflammatory cytokines, which are signaling proteins that mediate inflammation. These cytokines include tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β). The excessive production of these cytokines can lead to severe inflammation, contributing to vascular permeability and the development of life-threatening conditions.

How It works

- Curcumin produces its anti-inflammatory effects primarily through the inhibition of NF-κB (nuclear factor-kappa B), a key transcription factor responsible to produce many pro-inflammatory cytokines.
- NF-κB is typically activated in response to viral infections, including dengue, and leads to the release of cytokines and chemokines that amplify the inflammatory response.
- Curcumin inhibits the phosphorylation and degradation of IκBα, an inhibitor of NF-κB.
- This stops NF-κB from relocating to the nucleus and triggering the expression of genes associated with inflammation.

- By blocking NF-κB signaling, curcumin reduces the expression of TNF-α, IL-6, IL- 1β, and other cytokines, thus modulating the overactive immune response in dengue patients.

Figure 4. Curcumin.

Coconut Water

If we are talking about the dengue virus treatment then, how can we forget the coconut water. It is the most important functional drink in the management of dengue fever (Figure 5) [30].

- It plays an important role in the management of dengue. Basically, coconut water does not directly treat dengue fever, it only act as a supportive role by producing their hydrating and electrolyte balancing property.
- Coconut water provides essential electrolytes that aid in quicker recovery and effective hydration, which is crucial for dengue patients who commonly suffer from dehydration. It serves as an excellent natural option to restore lost fluids.

Figure 5. Coconut Water.

Dragon Fruit

Dragon fruit is also a very helpful functional food in support of dengue fever. It is also known as "Pitaya". It can help to maintain the electrolyte balance of the body and can provide the necessary vitamins to the body, because dehydration is the major factor in the dengue (Figure 6) [31].

Dragon fruit is rich in antioxidants and various nutrients like vitamin c, magnesium and fiber and provide hydration to the body which can help in managing dengue fever.

How It Works

- When dengue fever occurs, then our body starts producing the Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) to fight against dengue virus.
- After some time, the ROS and RNS level increases in body against dengue, this may surpass the normal natural antioxidant defense of the body.
- This may lead to damage to the cells and tissue as well as harm the DNA.
- This may lead the inflammation.

- Now, we take the antioxidant rich food (dragon fruit).
- This antioxidant can help by neutralizing the ROS and RNS by donating their electrons.

Figure 6. Dragon Fruit.

Kiwi

Kiwi is an important nutraceutical in the treatment of dengue. Kiwis contain various factors which can help in dengue fever management (Figure 7) [32].

It is also rich in antioxidants which can help in removing the free radicals from the body and decreasing the oxidative stress.

Figure 7. Kiwi.

How It Works

- Kiwis contain a high amount of vitamin C, which is essential for enhancing the immune response by increasing the number of WBCs in body which can help in fight against dengue virus. Other vitamin c rich fruits are orange, guava and tomato.
- Kiwi also have some antioxidants property which may help in reducing or neutralizing the free radicals in the body due to viral disease.
- Kiwi fruit also has high water content which helps your body become hydrated throughout disease.
- All properties of the kiwi help in maintaining body blood health and platelets production.

CONCLUSIONS

Nutraceuticals offer promising adjunctive benefits in the management of dengue fever by enhancing the body's natural defenses and addressing complications, such as thrombocytopenia, inflammation, and dehydration.

Key nutraceuticals like papaya leaf extract, quercetin, curcumin, coconut water, and antioxidant-rich foods, such as dragon fruit and kiwi, demonstrate potential in alleviating symptoms and reducing disease severity.

While they do not cure dengue, these natural remedies may complement conventional treatments, providing a holistic approach to improving patient outcomes.

At last, as research continues in future, nutraceuticals could play a vital role in dengue management strategies.

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