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A Comprehensive Review on Fruit-Based Interventions in Dengue Treatment

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ABSTRACT:

This review paper delves into the impact of dengue on platelets and the intervention of fruits and medicinal plants to increase platelet count in treatment of dengue. Dengue infection causes thrombocytopenia, hypokalemia which leads to produce acute neuromuscular weakness which can be prevented and managed by diet therapy. Fruits are excellent reservoirs of essential vitamins like A, C, D, K, B-9, and B-12, as well as minerals like iron, and antioxidants which play a pivotal role in bolstering platelet counts. Dragon fruit, papaya, kiwi, giloy, tulsi, beetroot, and bitter gourd are recognized for their therapeutic potential to combat DENV and are highly recommended due to their accessibility, cost-effectiveness, and zero adverse effects. Their efficacy and safety make them an indispensable facet of the treatment regimen.The purpose of this review paper is to explore, learn, and study brief information about dengue infection and its effect on platelet count, thrombocytopenia, the role of different fruits and medicinal plants in platelet formation and treatment of dengue, also an overview of statistical data which can be ebneficial for faster recovery of dengue.

KEYWORDS: Dengue virus, *Aedes* mosquitoes, thrombocytopenia, dragon fruit, papaya, kiwi, giloy, beetroot, tulsi, bitter gourd.

1.INTRODUCTION:

Dengue virus is the most significant human arbovirus, transmitted by mosquito bites and first emerged as "water poison" associated with flying insects in a Chinese medical encyclopedia from the Jin Dynasty between 265-420 AD. (1)(2) In 1779, the first dengue epidemic was reported in Jakarta, Indonesia. (3) The global incidence of infected cases is estimated around 100 to 400 million per year (WHO, 2021). (4)

Dengue has four antigenically distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4). A novel DENV-5 serotype was discovered in Sarawak, Malaysia, in 2013. This serotype has distinct phylogenetics from the other four present serotypes. (4) DENV was predominantly observed in monkeys between 100 and 800 years ago, and it eventually propagated to humans. On a geographic level, DENV remained restricted till the 1950s, but during World War II, it transmitted quickly within the globe. (5) Dengue's expansion is presumed to be caused by a combination of factors: including escalating urbanization, rise in population, and international travel, as well as the challenges in effective vector management. Environmental alterations may contribute to dengue's worldwide emergence.(6)

Fruits are a natural source of antioxidants and antimicrobial agents that may be featured in a diet to help avoid illnesses triggered by pathogenic organisms. To carry out such reactions and ensure the proper functioning of the body, we need ample amounts of nutrients, which can be obtained from fruits and herbs such as dragon fruit, kiwi, papaya, giloy, pomegranate, beetroot, tulsi, bitter gourd, etc.(7) Fruits contain significant quantities of water, which keeps the body hydrated, which is essential for dengue fever therapy. Some fruits are great sources of vitamins including vitamin A, C, D, K, B-9, and B-12, minerals like iron, and antioxidants that aid in increasing platelets.(8) Dragon fruit strengthens bones, and dengue which is referred to as "bone-breaking fever." Citrus fruits are rich in vitamin C, which is necessary for improving an individual's immune system and protecting against infectious diseases.(9)

The World Health Organisation (WHO) and Ayurveda suggests the use of medical plant extracts and their derivatives are beneficial in combating dengue infection, and believe that extracts obtained from medicinal plants are predominantly more reliable, non-toxic, comparatively less hazardous, and more affordable than synthetic drugs.(10) Many medicinal plants have been investigated, especially those with antiviral characteristics. Researchers will develop advanced and novel therapies for infectious diseases worldwide.(11)

2.DENGUE:

2.1. Lifecycle:

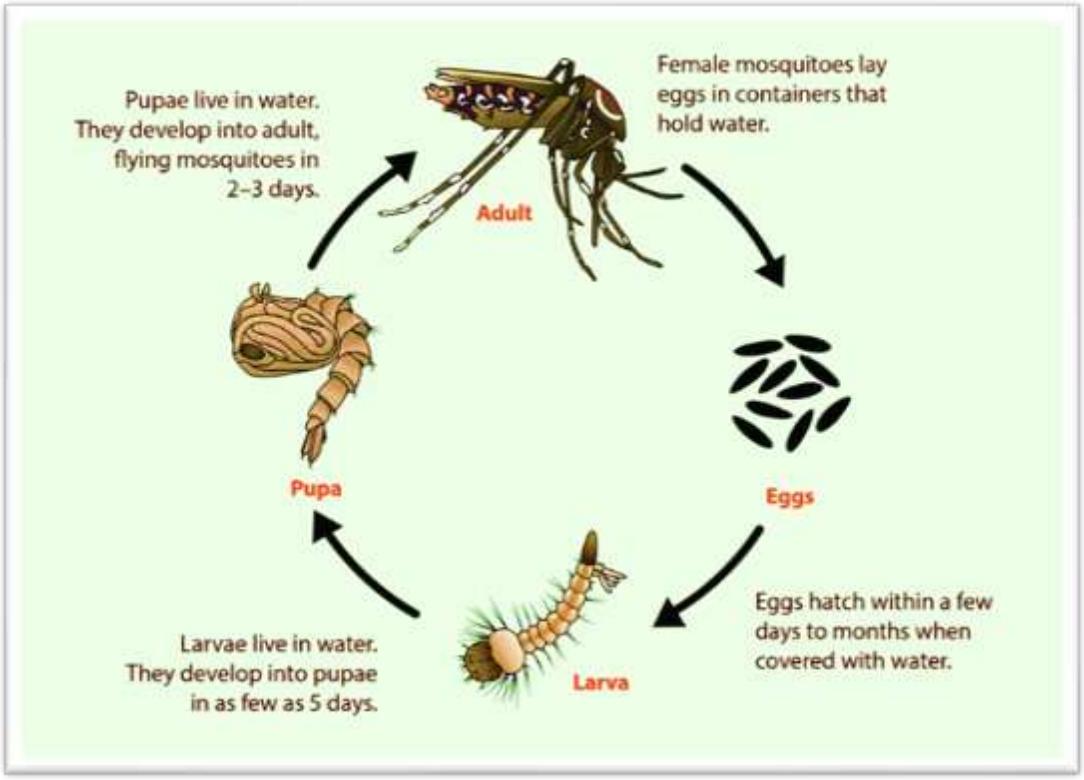


Fig.1- Life stages of Aedes mosquitoes (*Ae. aegypti* and *Ae. albopictus)*

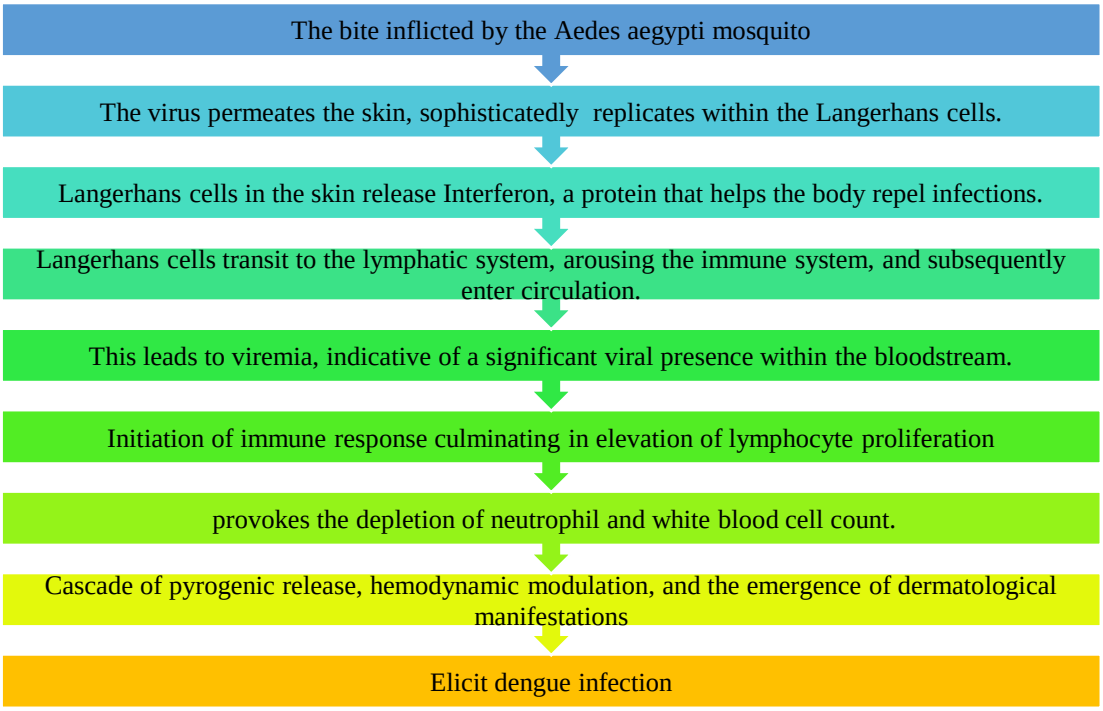
There are four life stages for Aedes mosquitoes: egg, larva, pupa, and adult. It takes approximately 8

10 days for them to complete their entire life cycle.

Mosquitoes have the potential to survive and reproduce inside and outside of the house.

- Eggs: Mature female mosquitoes deposit their eggs over the waterline and inside the moist walls of water carrying containers. They generally produce 100 eggs at a time. The eggs are abrasion-resistant and adhere to the walls of a container like glue. A female mosquito can be enticed with only a small quantity of water.
- Larva: Larvae develop from eggs only after the water level escalates sufficiently to submerge the eggs. Larvae consume aquatic microbes and after three molts, the larva develops into a pupa.
- Pupa: Pupae grow until the body of fully grown winged mosquito burst off from pupal skin and escapes the water.
- Adult Mosquito: After the emergence of adult mosquitoes, male mosquitoes consume nectar from flowers, but female mosquitoes consume blood from humans and animals to form eggs. After feeding, female mosquitoes explore watery areas to lay their new eggs. During its entire existence Aedes aegypti fly only a handful of blocks. Aedes aegypti mosquitoes are known for their tendency to bite humans as compared to other mosquito species.(12)(13)

2.2 Pathogenesis:



(14)

2.3 Vaccines:

As stated below, there are certain vaccines that can be used against dengue:

1. CYD-TDV - Brand name: - Dengvaxia

2. TDV (Inviragen/takeda) in phase 2 trial

3. TDEN in phase 2 trial

4. V180 (merck/ NIAID) in phase 1 trial

The current vaccine approach is based on six different vaccine approaches being tested in human clinical trials, and a single candidate has now completed phase 3rd clinical testing.

1) Live attenuated virus (traditional)

2) Live attenuated virus (molecular)

3) Yellow fever chimera.

4) Dengue chimera

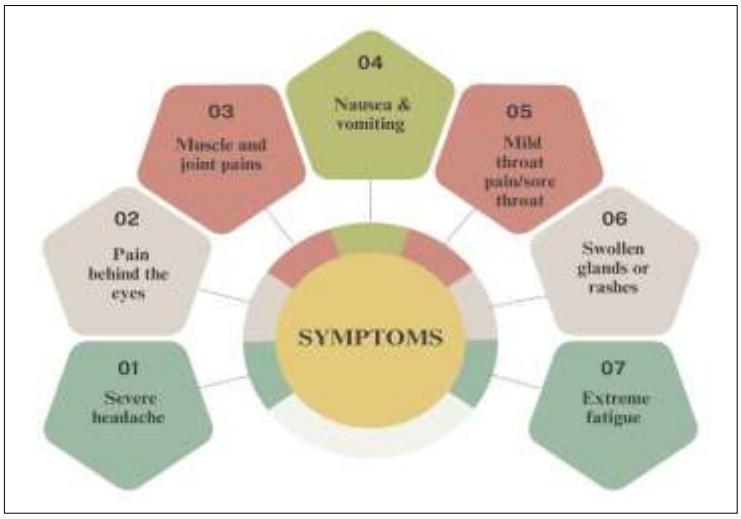
5) Purified inactivated

6) Recombinant subunit

7) DNA: pEII*EIII/NS1

2.4 Symptoms:

Dengue fever affects individuals of all age groups, Dengue Fever typically lowers platelet count and sometimes blood pressure. A high fever (40°C/104°F) would indicate the threat of dengue. Which is accompanied with following symptoms:



(7)

2.5 Thrombocytopenia:

Thrombocytopenia is defined as the condition when the platelet count drops down below the normal lower limit i.e.,150000/microliter (for adults) suggested by the third US National Health and Nutrition Examination Survey (NHANES III). Blood cells called platelets aid in blood coagulation and wound healing.(15)(16) Platelets are essential in order to maintain the integrity of the vessel walls. Clinically considerable spontaneous bleeding usually does not take place until the platelet count is below $10\text{-}20\times10^9$/L.(16)

DENV infects the circulating platelets and their progenitor megakaryocytes in the bone marrow and interacts with them through the cell surface receptor FcγRII. The mechanism of platelet depletion consists of various processes like lysis, aggregation, clot formation, and phagocytosis of platelets.

There are two significant events responsible for the emergence of thrombocytopenia in dengue patients:

- Decreased generation of platelets in the bone marrow
- Increased demolition and clearance of platelets from peripheral blood.(17)

Symptoms of Thrombocytopenia:

1] Abdominal pain: = Haemolysis, elevated liver enzymes, and low platelet count(HELLP) syndrome/preeclampsia, Hemolytic uremic syndrome(HUS), platelet sequestration.

2] Recent fever: viral infections- Cytomegalovirus(CMV), Epstein-Barr virus(EBV), Human immunodeficiency virus(HIV), influenza A [H1N1], parvovirus B19), Thrombotic thrombocytopenic purpura(TTP).

3] Weight loss or night sweats: Human immunodeficiency virus, malignancies (acute leukaemia, myelodysplastic syndrome)(18)

Physical Examination:

The physical assessment involves examining the bleeding risk, location, and severity of symptoms, as well as any other abnormalities that can aid in the diagnosis of thrombocytopenia. The presence of organomegaly or skeletal abnormalities, joint or extensive soft tissue bleeding caused due to coagulation abnormalities. Mucocutaneous bleeding is typically experienced in patients with thrombocytopenia.(16)

Table 1- Location or process for examination and associated conditions.

Examination of specific location or process	Conditions
1)Eyes	Central nervous system bleeding
2)Skin	Petechiae, Purpura, Bruising
3)Abdomen	Splenomegaly, Hepatomegaly
4)Bleeding	Epistaxis, Mucosal, Gastrointestinal, Genitourinary

Evaluation:

1)Patients with isolated thrombocytopenia are examined for the following tests:-

- Complete blood count test(CBC)

- Peripheral blood smear
- Human immunodeficiency virus (HIV)
- Hepatitis C virus (HCV) tests.

2) A bone marrow biopsy is advised, when a hematologic disorder is identified and the cause of thrombocytopenia is undetermined. Patients with asymptomatic and mild thrombocytopenia are advised to perform routine follow-ups and repeat the CBC test.

3)Immediate action is required in the conditions of thrombocytopenic emergencies like:

Noticed Heparin induced thrombocytopenia (HIT), Thrombotic thrombocytopenic purpura (TTP), Hemolytic uremic syndrome (HUS), Drug-induced immune thrombocytopenic purpura (DI-ITP), severe thrombocytopenia in pregnancy, leukopenia, and aplastic anaemia.(15)

Treatment/Management:

The Management of thrombocytopenia involves the diagnosis of the underlying cause and treating it, platelet transfusion is used for the treatment of patients with bleeding and severe thrombocytopenia.

1)Primary immune thrombocytopenia:

The treatment involves the following agents:

First-line treatment- Glucocorticoids, intravenous immune globulins(these agents inhibit platelet degradation and autoantibody production)

Second-line treatment- Rituximab, immunosuppressive drugs, splenectomy

Third-line treatment- Thrombopoietin receptor agonists (these agents stimulate platelet generation)

2)Drug-induced thrombocytopenia:

Discontinuation of causative drugs generally results in the increase of platelet counts in the instance of drug-induced thrombocytopenia. The key purpose of HIT treatment is to withdraw the heparin products and initiate the anti-thrombin and anti-Xa activity to measure anticoagulant therapy. Normal platelet count can be achieved by the use of dicoumarol agents. H. pylori associated thrombocytopenia can be cured by eradication of H. pylori and thus raises the platelet count. Immunosuppressive agents are utilized in the treatment of systemic lupus erythematosus (SLE).(15)

3. ROLE OF FOOD PRODUCTS OR FRUITS IN DENGUE TREATMENT:

Papaya :

Papaya (Carica papaya L) is known as the "powerhouse of nutrients" and was titled as "The fruit of angels." by Christopher Columbus. Since 20th century papaya has contributed incredibly to beneficial results in a broad spectrum of diseases and disorders.(19) Carica papaya Linn. a member of the Caricaceae family. It has an average life span of five to ten years and grow as a single, unbranched trunk. Its fruits weigh approximately between 1-3 Kg and are produced throughout the year.(20) Carica papaya L. Leaf is gaining recognition as an effective therapeutic option for both dengue- and non-dengue-associated thrombocytopenia. According to research, C. Papaya leaf consumption in humans is normally safe for short-term use; although cautioned for pregnant women and persons with hepatic impairment. The most often reported side effects were gastrointestinal disturbances and rashes.(21)

Table 2 - Taxonomical classification of Carica papaya L:

Kingdom :	Plantae
Genus :	Carica L.
Subkingdom :	Tracheobionta
Division :	Magnoliophyta
Class :	Magnoliopsida
Order :	Violales
Family :	Caricaceae
Species :	papaya L.

Carica papaya leaf has been used conventionally to treat Dengue. The leaves has been analysed for its anti-dengue capabilities. Papaya leaf extract is a potent IL-6 stimulator, and SCF may assist to ameliorate thrombocytopenic conditions in patients. Papaya leaf includes anti-oxidant vitamins and minerals that may help boost haemoglobin, haematocrit, red blood cells, thrombocytes, and total protein levels. Magnesium ions in papaya leaves have been proven to increase erythrocyte hydration. Sodium ions aid in maintaining electrolyte balance and avoid hyponatremia during dengue infection. Vitamin B12

helps to maintain a normal thrombocyte count and combat thrombocytopenia. Carica papaya inhibits NS2B-NS3 protease, which inhibits DEN-2 Virus assembly.(19)

Table 3 – Phytoconstituents of Carica papaya:

Part	Constituent
Fruit	Protein, fat, fibre, carbohydrates, minerals(calcium, phosphorous, iron), Vitamin (vitamin C, thiamine, riboflavin, niacin, and carotene), amino acids, citric and malic acids (green fruits), volatile compounds (linalool, benzyl iso-thiocyanate, cis and trans 2, 6-dimethyl-3,6 epoxy-7-octen-2-ol), Alkaloid (carpaine, benzyl- β -D glucoside, 2-phenylethyl -β-D-glucoside, 4-hydroxy- phenyl-2 ethyl-β-D-glucoside and four isomeric malonated benzyl-β-D-glucosides).
Juice	N-butyric, n-hexanoic, and n-octanoic acids, lipids; myristic, palmitic, stearic, linoleic, linolenic and cis-vaccenic, and oleic acids.
Bark	B-Sitosterol, glucose, fructose, sucrose, galactose and xylitol
Seed	Fatty acids, crude protein, crude fibres, papaya oil, alkaloid Carpaine, some volatile compounds benzyl iso-thiocyanate, benzyl glucosinolate, glucotropacolin, benzyl thiourea, hentriacontane, β-sitosterol, caricin and myrosin
Root	Carposide and an enzyme myrosin
Leaf	Alkaloids carpain, pseudocarpain and dehydrocarpaine I and II, choline, carposide, vitamin C and E
Latex	Proteolytic enzymes, papain and chemopapain, glutamine cyclo transferase, chymopapain A, B, and C, peptidase A and B

(19)

Research suggests that carica papaya leaf extract may have antiviral and hematological effects, potentially contributing to its implementation as a dengue therapy.(22) The strong antioxidant and free radical-scavenging properties allow it to protect the membrane of red blood cells. Consequently, it has preventive action against hemolysis in conditions involving extreme stress(23) Since the leaf of CP exhibits an LD50 of greater than 15g per kg of body weight, it is considered as nontoxic. Additionally, it was discovered that the extract from Carica papaya leaves exhibited antimicrobial, anti-inflammatory, antitumor, and immunomodulator properties.(24)

Dragon Fruit:

Dragon fruit is an exotic fruit grown all over the world. This long-day plant boasts a breathtaking night-blooming flower that is affectionately called as "Noble Woman" or "Queen of the Night". It is a member of the Cactaceae family. Dragon fruit has different names including pitaya, strawberry pear (Hylocereus spp. and Selenicereus spp.) and Kamalam, red pitahaya, night blooming cereus, and strawberry.

It originates from Central and South America and is successfully grown in Thailand, Malaysia, Vietnam, Sri Lanka and Bangladesh for commercial purpose.(25)

Table 4 - Taxonomical classification of Dragon fruit:

Domain:	**Eukaryota**
Kingdom:	Plantae
Subkingdom:	Tracheobionta
Superdivision:	Spermatophyta (Seed plants)
Division:	Magnoliophyta (Flowering plants)
Class:	Magnoliopsida (Dicotyledons)
Subclass:	Caryophyllidae
Order:	Caryophyllales
Family:	Cactaceae (Cactus family)
Subfamily:	Cereoideae
Tribe:	Hylocereae
Genus:	Hylocereus

(26)

Dragon fruit can be classified into four types based on their color:

1. Hylocereus undatus has red colour fruit with white colour flesh.

2. Hylocereus polyrhizus bears red colour fruit with red colour flesh.

3. Hylocereus megalanthus yields yellow colour fruit with white colour flesh.

4. Hylocereus costaricensis has pink colour fruit with violet red colour flesh.

Dragon fruit is a rich source of vitamin C and various minerals such as calcium and phosphorus. This fruit owes deep red or pink color due to the presence of betalains. It has a fluffy pulp with edible black seeds that are rich in nutrients. The plant is a perennial semi-epiphytic climbing cactus vine. Red dragon fruit juice has a significant effect on improving platelet count in dengue patients due to its antioxidant properties.(25) Dragon fruit has an exceptionally low cholesterol level, which ultimately decreases the chances of heart attack and other diseases caused by accumulating cholesterol. The high fiber content aids in cleansing the digestive system and can assist with poor digestion and constipation.(27)

Table 5 -Nutritional value of dragon fruit flesh per 100g:

Nutrient	Value
Water	87 g
Protein	1.1 g
Fat	0.4 g
Carbohydrates	11.0 g
Fiber	3 g
Vitamin B1 (Thiamine)	0.04 mg
Vitamin B2 (Riboflavin)	0.05 mg
Vitamin B3 (Niacin)	0.16 mg
Vitamin C (Ascorbic acid)	20.5 mg
Calcium (Ca)	8.5 mg
Iron (Fe)	1.9 mg
Phosphorus (P)	22.5 mg

(27)

Betacyanin, a red-violet pigment, is a member of the betalain class. Betacyanin extracts from several different plants exhibit a wide range of biological actions, involving antioxidant, anticancer, antilipidemic, and antibacterial actions.(28) Dragon fruit assists with bone strength restoration.(29) It is an excellent natural source of antioxidants, which help guard against the risks posed by free radicals, that can lead to cancer and other problems to health. Many dietary supplements are unable to compete with the abundance, diversity, and amount of antioxidants found in dragon fruit.(27)

Giloy:

Tinospora cordifola is often referred as Guduchi or Giloy. The herb is a potent rasayana that has been documented in Indian Ayurvedic literature. Hindu mythology states that it is the 'nectar of immortality' and the 'heavenly elixir' that protect the body from a wide range of ailments. It is acknowledged as an excellent immunomodulator and bitter tonic. It is also known as Amrita/Guduchi or Giloy, is the plant known by several names, including Amritvali, Amara, Vatsadani, Chinmarrhuha, and Chinnodebha. The genus Tinosopra has 34 species. Giloy can be consumed as juice, kadha (a decoction), or even in the form of powder.(30)(31)

Table 6 - Taxonomical Classification of Giloy:

Kingdom	**Plantae**
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales

Family	Menispermaceae
Genus	Tinospora
Species	T.cordifolia

(32)

The antispasmodic effects of the bitter ingredients in the medications aid to prevent infectious diseases like dengue, swine flu, malaria, etc. This amazing Ayurvedic herb has anti-inflammatory, anti-rheumatic, and anti-allergic properties. It also helps to increase the potency of protective WBC (white blood cells) and strengthen the immune system. Dengue patients experience a decline in platelet counts and weak body strength. Tinospora cordifolia plays a significant role in boosting strength. Tinospora has the ability to promote liver regeneration. Dengue can sometimes be associated with liver degeneration problems. This herb combats degeneration by enhancing the effectiveness of white blood cells in the body.(33)

Giloy possess following medicinal properties like anti-pyretic, anti-spasmodic, anti-inflammatory, anti-arthritic, anti-oxidant, anti-diabetic, anti-periodic, immuno-modulator, anti-neoplastic, anti-allergic, anti-stress, anti-leprotic, anti-malarial and hepatoprotective(34)

Table 7 - Active constituents of Giloy with pharmacological actions:

Sr no	source	Class of active Component	Compounds	Pharmacological Response
1	Stem Root	Alkaloids	Berberine, Choline, Palmatine Tembetarine, Magnoflorine, Tinosporin, Isocolumbin	Anticancer, Antiviral infections, Neurological Disorder and Anti-diabetic
2	Stem	Glycosides	Tinocordiside, Cordioside	Treat Neurological Disorder like Parkinsons
3	Whole plant	Diterpenoid	Furanolactone	Vasorelaxants, Anti-infammatory, Antimicrobial Antihypertensive, Antiviral
4	Stem aerial parts	Steroids	Beta-Sitosterol	Induce Osteoporosis in early inflammatory arthritis
5	Whole plant	Aliphatic compound	Octacosanol	Anti-nociceptive and anti-inflammatory
6	Root	Others	Giloin, Tinosporic acid	Used to treat anxiety, Protease inhibitors for HIV

(34)

T. cordifolia possesses potent and inhibiting antiviral activity against DENV-2 and has the potential to stop DENV-2 from infecting the host cell. (35)

Tinosponone, which is found in Tinospora cordifolia, has been reported to demonstrate highest binding affinity (−2.8 kcal/mol), minimal docking score (−5.5 kcal/mol), and free energy (−4.5 kcal/mol), making it a strong inhibitor of the NS2B-NS3 receptor in Dengue virus. (36)

Report of case study: A case study indicates that after giving 40 millilitres of giloy juice BID to a female dengue patient for 15 days, the patient's platelet counts significantly improved and her fever and rash reduced. • In another trial, 200 individuals with low platelet counts received a 5 ml combination of papaya and giloy leaf extracts for 5 days; no obvious negative effects were seen. Every patient showed a notable increase in their platelet counts. Thus, it is legitimate to state that giloy or Tinospora gas potential for initial dengue therapy.

Dosage: It is safe to consume up to 5 ml of giloy stem or leaf juice and 1-2 g of giloy stem or leaf powder without being concerned significantly about any adverse effects. However, a patient's age, health, and other considerations determine the appropriate dose for a given plant.(32)

Kiwi:

Kiwi fruit belongs to the Actindia genus and is renowned all over the world, particularly for its exquisite taste and health-promoting properties.(37) Kiwifruit is also known as the "king of fruits" due to its thick flesh, dominant flavor, high pulp fluid content, and ample nutrients, which enhance its commercial and economic significance.

Table 8 - Taxonomical Classification of Kiwi fruit:

Family:	**Actinidiaceae**
Kingdom:	**Plantae**

Division:	**Magnoliophyta**
Class:	**Magnoliopsida**
Order:	**Ericales**
Super order :	**Asteranae**
Genus:	**Actinidia**
Species:	**A. deliciosa**

Kiwi contains an extensive list of phytochemicals, comprising triterpenoids, saponins, phenolic compounds (anthraquinones, polyphenols, flavonoids, and coumarins), vitamins, and minerals. The abundance of vitamins found within fruits assists in strengthening the immune system against inflammation and ailments. Kiwifruit is rich in antioxidant vitamins A, C, and E, as well as B complex vitamins. Generally prevalent in both commercial species. kiwifruit has more than three times the amount of vitamin C than other fruits. The main function of vitamin C is to assist in maintaining the proper operation of metabolic processes. The enzymes needed to produce carnitine, collagen, catecholamines, l-peptide, and neurotransmitters are regulated by vitamin C. Vitamin C is also believed fortifying immunity.(38)

kiwi possess inherent pharmacological properties, which include anti-oxidant, anti-diabetic, anti-inflammatory, and anti-hypertensive properties, as well as anti-thrombin, anti-asthmatic, hepatoprotective, anti-platelet, anti-nociceptive, anti-microbial, anti-constipation, anti-carcinogenic, anti-fungal, antiviral, and anti-tumor properties, have been linked to broad range of bioactive substances present in A.deliciosia.(39)

Kiwi and other fruit juices high in vitamin C are essential for dengue patients. It aids in creation of lymphocytes and fosters the immunity system of body. Due to the popular belief among patients that eating kiwi fruit will elevate their blood platelet count, it is currently accessible in almost every vegetable shop.(40)

Beetroot:

Beetroot is obtained from the fresh root of the Beta vulgaris plant species. This root vegetable is known for its deep red colour, earthy flavour, and high nutritional content.

Table 9 - Taxonomical classification of beetroot:

Family:	**Chenopodiaceae**
Kingdom:	Plantae
Subkingdom:	Tracheobionta
Order:	Caryophyllates
Genus:	Beta
Species:	B. vulgaris

(41)

Table 10 - Constituents of raw red beetroot flesh per 100 g:

Compounds	**Value**	
	Tubers	**Leaves**
Water (g)	91.3 ± 4.29	91.00 ± 4.00
Protein (g)	1.89 ± 0.3	2.20 ± 0.5
Carbohydrate, by difference (g)	7.23 ± 2.33	4.33 ± 1.5
Fiber, total dietary g	3.25 ± 0.55	3.7
Sugars, total (g)	6.76 ± 1.23	0.50
Total lipid (fat) (g)	0.15 ± 0.05	0.13

Ash (g)	1.08 ± 0.72	2.33
α-Carotene (µg)	22.0 ± 2.0	3.5 ± 0.5
β-Carotene (µg)	0	11.64
Lycopene (µg)	30 ± 0.3	0
Lutein + zeaxanthin (µg)	0	1.503
Betaine (µg)	128.7 ± 22.0	0
Folate (µg)	109	15
Niacin (mg)	0.334	0.400
Vitamin A, IU	0	6.326
Vitamin B6	0.067	0.106
Vitamin C (mg)	7.2 ± 2.5	30
Sodium, Na (mg)	78.0 ± 5.0	226
Potassium, K (mg)	325 ± 4.5	762
Phosphorus, P (mg)	40.00	41
Magnesium, Mg (mg)	23.0 ± 2.0	70
Calcium, Ca (mg)	16 ± 3.5	117
Manganese, Mn (mg)	0.359 ± 0.04	0.391
Zinc, Zn (mg)	0.365 ± 0.015	0.38
Copper, Cu (mg)	0.075	0.191
Iron, Fe (mg)	0.80	2.57

Red beet roots are the most well-known and widely consumed sources of betalains. Betalains are a class of nitrogen-containing pigments found in plants of the order Caryophyllales**.** The two major betalain pigments found in red beetroot are red betanin and yellow vulgaxanthin I.(42) Extensive research has conclusively demonstrated the antiviral activity of betalains against dengue virus serotype-2.(43)

Beetroot juice is a powerful antioxidant that can help combat diseases and proven to elevate platelet count in just 3-4 days, by mixing 2-3 tablespoons of beetroot juice with a glass of carrot juice and drinking it 2-3 times a day.(44)(45)

Tulsi:

Tulsi (Ocimum sanctum L.), also known as Tulasi (in Sanskrit)or holy basil (in English), is a fragrant herb from the Lamiaceae family that is native to the Indian subcontinent and has been used in Ayurvedic medicine for over 3,000 years.(46) Ocimum sanctum has been shown in numerous scientific research to possess hepatoprotective, antioxidant, and anti-stress properties,Immune-suppressive, anti-inflammatory, antiviral, antibacterial, antifungal, antipyretic, antidiuretic, antidiabetic, antimalarial, and hypolipidemic qualities with a large safety margin.(47)

Table 11 - Taxonomical classification of Tulsi (Ocimum sanctum):

Family:	**Labiatae**
Kingdom:	Plantae
Division:	Magnoliophyta
Class:	Magnoliopsida
Order:	lamiales
Genus:	Ocimum

Species:	sanctum

Table 12 - Phytoconstituents of Tulsi (Ocimum sanctum L.):

1	Seeds	Fixed oil	Linoleic acid, Linolenic acid, Oleic acid, Palmitric acid, Stearic acid.
2	Leaves	Essential oil	Aromadendrene oxide, Benzaldehyde, Borneol, Bornyl acetate, Camphor, Caryophyllene oxide, cis-αTerpineol, Cubenol, Cardinene, D-Limonene, Eicosane, Eucalyptol, Eugenol, Farnesene, Farnesol, Furaldehyde, Germacrene, Heptanol, Humulene, Limonene, n-butylbenzoate, Ocimene, Oleic acid, Sabinene, Selinene, Phytol, Veridifloro, α-Camphene, αMyrcene, α-Pinene, β-Pinene, α-Thujene, β-Guaiene, β-Gurjunene, methyl chavicol and linalool.
3	Whole plant	Mineral content	Vitamin C, Vitamin A, Calcium, Phosphours, Chromium, Copper, Zink, Iron.
4	Areal parts/ Leaves	Alcoholic Extract	Aesculectin, Aesculin, Apgenin, Caffeic acid, Chlorgenic Acid, Circineol, Gallic Acid, Galuteolin, Isorientin, Isovitexin, Luteolin, Molludistin, Orientin, Procatechuic acid, Stigmsterol, Urosolic acid, Vallinin, Viceni, Vitexin, Vllinin acid.

(48)

Other constituents:

Leaves contain 0.7% volatile oil, composed of eugenol (71%), with methyl eugenol (20%). Additionally, the oil has sesquiterpine hydrocarbon caryophyllene and carvacrol. Certain phenolic chemicals (antioxidants), including rosameric acid, apigenin, isothymusin, cirsilineol, and circimaritin, were extracted from fresh leaves and the stem.From the aqueous leaf extract, two flavonoids have been identified i.e orientin and and vicenin.(49)

Dengue can also be cured using tea preparation from O. sanctum leaves. O. sanctum extract has an Maximum Non-toxic Dose(MNTD) value of 0.10 mg mL−1 and cytotoxic values of 1.5 mg mL−1.On the other hand, the MNTD value reported in Vero E6 cells was significantly higher than that of HepG2 cells, which was 0.023 mg mL−1. The extracts are more cytotoxic to HepG2 cells, as evidenced by this As opposed to Vero cells. The cytopathic effect of O. sanctum methanolic extract on DENV-1 was shown to be slightly inhibitive. (10)(50)

Bitter gourd:

Momordica charantia L. Also known as bitter gourd, bitter melon(in English), karela (in hindi) or peria (Malaysia), member of family Cucurbitaceae. Due to its high nutritional value and therapeutic qualities, it is considered a significant vegetable. The main growing regions of bitter gourds encompass the Caribbean, South America, Middle East, East Africa, and South, Southeast, and East Asia. The bitter gourd plant is a perennial that grows up to 5 meters in length on a climbing and blooming vine. The fruits are long and have ridges on their surface.(51)

Table 13 - Taxonomical classification of Bitter Gourd (Momordica charantia L.):

Kingdom:	**Plantae**
Family:	Cucurbitaceae
Subfamily:	Cucurbitoideae
Phylum:	Magnoliophyta
Class:	Magnoliopsida
Order:	Cucurbitales
Genus:	Momordica
Species:	charantia

(52)

It is gaining popularity due to its wealth of hydrophilic and lipophilic substances, such as proteins, steroids, alkaloids, glucosides, saponins, fixed oils, triterpenes, and polyphenolics that are linked to antioxidants, anti-diabetes, antimicrobial, anti-cancer, hypertensive properties and antiviral, and antiulcer.(53) The greater levels of protein, ascorbic acid, calcium, iron, and phosphorus in bitter gourds make them extremely nutrient-dense, Vitamin A, Vitamin C, and vitamins B1, B2, B3, and B12 are all abundant.(51) It is bitter in taste because of following constituents: phenols, isoflavones, anthraquinones, flavonoids, terpenes, quinines, and curcumin. It serves as an antimalarial, laxative, and purgative therapeutic drug. Additionally used in treatment of gout, jaundice, kidney stones, and eczema.(54)

Table 14 - Phytoconstituents of Momordica charantia L:

Sr. No	Source	Phytochemicals
1.	Plant body	Momorcharins, momordenol, momordicilin, momordicins, momordicinin, momordin, momordolol, charantin, chlorine, cryptoxanthin, cucurbits, cucurbitacins, cucurbitanes, cycloartenols,diosgenin, eleostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, multiflorenol. Glycosides, saponins, alkaloids, fixed oils, cucurbitane-type triterpenes, proteins and steroids. Momordicine, charantin, polypeptide- p insulin, ascorbigen.
2.	Fruits	Amino acids – aspartic acid, serine, glutamic acid, threonine, glutamic acid, threonine, alanine, g-aminobutyricacid and pipecolic acid, luteolin. Fatty acids – Lauric, myristic, palmitic, palmitoleic, stearic, oleic, linoleic, linolenic acid. Enzyme-Urease
3.	Seeds	Amino acids – valine, threonine, methionine, isoleucine, leucine, phenylalanine and glutamic acid

(53)

Researchers evaluated M. charantia's larvicidal activity by macerating the fruits and flowers in methanol, hexane, and methyl acetate. According to the results, hexane was not particularly damaging, and methanol extract showed considerable anti-DENV 1 effect.(54) A study was conducted in vitro to examine the MNTD of Momordica charantia's methanolic extract against Vero E6 cells.I.e. Maximum dose of 0.20 mg mL-1 that did not cause cellular toxicity was recorded by M. charantia. According to cytopathic effects in an antiviral experiment, the methanolic extract of M. charantia inhibited DENV-1.(50)

4. Statistical Data:

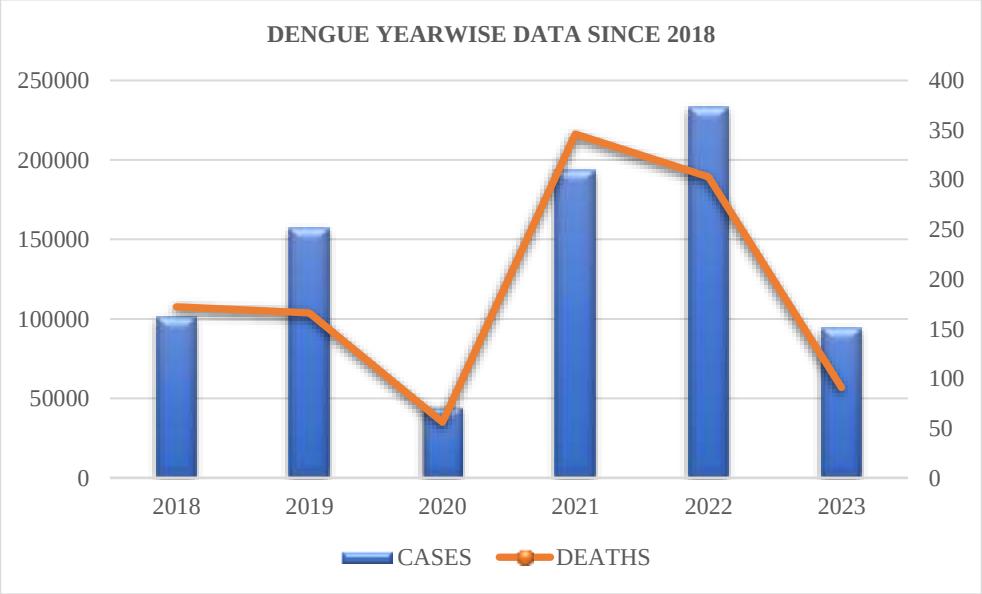
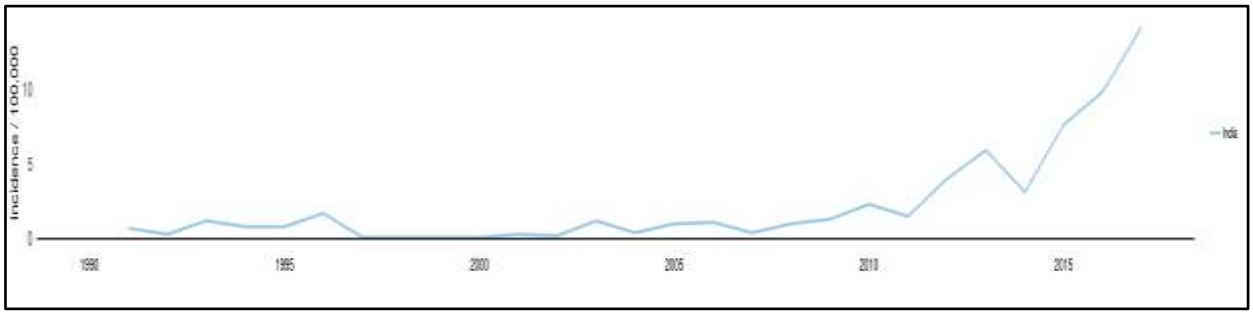
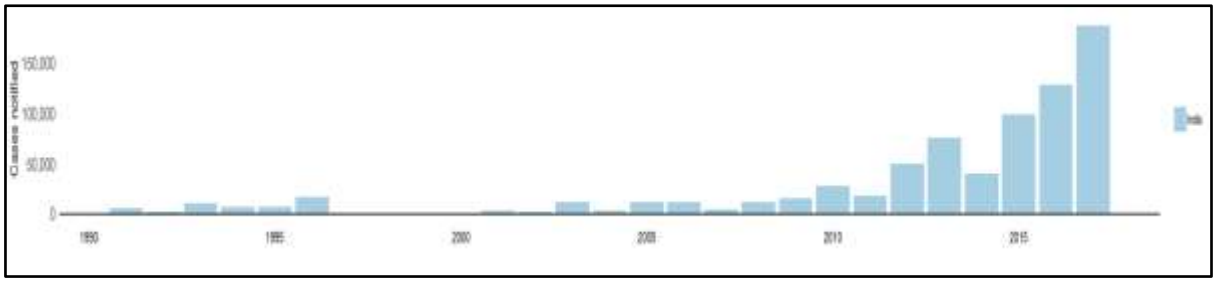


Fig.2 – Statistical data of dengue cases (2018-2023) (55)

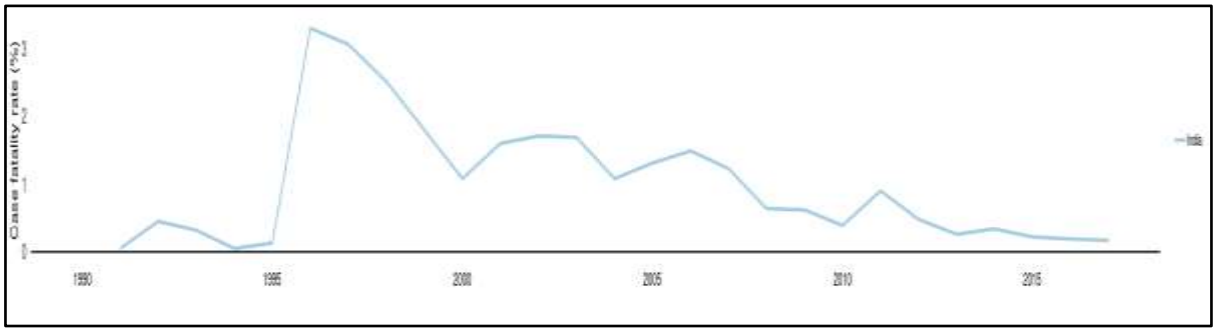
Graph 1: Incidence of dengue cases from 1990-2015



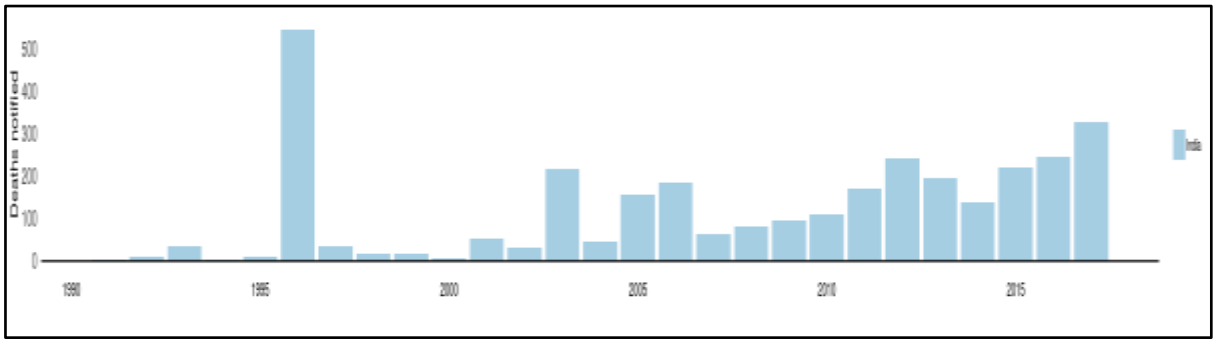
Graph 2: Cases notified between 1990-2015



Graph 3: Case fatality rate between 1990-2015



Graph 4: Death notified from 1990-2015(56)



https://ntdhq.shinyapps.io/dengue5/

The analysis of the incidence of dengue cases from 1990 to 2015 reveals a concerning trend in the escalating burden of this disease over the years. The data on cases notified between 1990 and 2015 underscore the growing impact of dengue on public health systems and communities worldwide. Furthermore, the examination of case fatality rates between 1990 and 2015 highlights the severity of the disease and its potential to cause fatal outcomes. The recorded deaths notified from 1990 to 2015 serve as a stark reminder of the human toll inflicted by dengue infection.

In conclusion, the findings from this analysis emphasize the urgent need for enhanced preventive measures, public health interventions, and research efforts to combat the rising incidence of dengue and mitigate its associated morbidity and mortality

5. Conclusion:

Dengue fever presents a significant global health challenge, prompting exploration of additional therapeutic avenues. This review examines the emerging roles of various fruits and medicinal plants, such as papaya, dragon fruit, kiwi, giloy, bitter gourd, and tulsi, in dengue management. These natural remedies, rich in essential nutrients like vitamins A, C, D, K, B-9, B-12, iron, and potassium, have demonstrated efficacy in boosting platelet counts—an essential aspect of dengue recovery. Furthermore, novel innovative formulations leveraging these ingredients show promising treatment efficacy. Importantly, this dietary approach is not limited to conventional medical practices but applicable to across allopathic, homeopathic, and ayurvedic treatment modalities. Additionally, these interventions offer potential benefits for pediatric patients, serving as safe adjuncts to standard therapies and contributing to overall immunity. This review highlights the multifaceted therapeutic potential of integrating nutrient-rich fruits and medicinal plants into dengue treatment protocols, calling for further research and clinical exploration.

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