

Medicinal Plants Used In Treatment and Management of Dengue: An Overview

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Abstract

Aim of study: Dengue virus (DENV) causes a clinical infection called dengue hemorrhagic fever (DHF). Millions of people are impacted by this condition. However, there is currently no specific medication available to stop it. Despite having recently received approval for use in preventing illness, a vaccination against some dengue virus (DENV) serotypes was proven to be ineffective. Some preventative methods utilizing plant extracts demonstrated some encouraging ovicidal action against *Aedes aegypti*.

Summary: Some antiviral medications are being tested in clinical settings to treat dengue fever, but the results have not yet been reported or validated. Numerous researches have revealed that the possibility of using compounds with plant origins could be excellent agents for the creation of secure and effective treatments for certain illnesses. This review provides scientifically validated knowledge on plants used in the treatment and management of dengue fever along with phytoconstituents responsible for the activity and type of solvent used to extract it.

Keywords: Dengue; Flavivirus; Plant extracts; Platelet count; Treatment; Management

Introduction

The mosquitoes *Aedes aegypti* and *Aedes albopictus* are the arthropods that transmit the flavivirus that causes dengue fever. Dengue virus (DENV) exists in different four serotype (DENV-1 to DENV-4) [1]. The large number of instances is unclear because many are asymptomatic or moderate and self-treated. Many cases are not appropriately diagnosed [2]. The prevalence of dengue fever has significantly increased recently. As of April 30, 2022, 8278 instances and one fatality had been documented, according to the media, which cited health authorities. Since March 21, 2022, there have been 7878 more cases and one death [3]. The management of the vector is still necessary for dengue prevention [4].

About The Review

Dengue and severe dengue are not specifically treated. Death rates from severe dengue are reduced to about 1% when disease progression is identified early and patients have access to quality medical care [5]. Medical plants have long been practiced a wide range of vector-borne illnesses, including chicken guniya and malaria [6]. There is a greater need now than ever for novel anti-dengue medicines derived from medicinal plants. Plant-based medications are in greater demand since they are usually regarded as being safer, non-toxic, and less hazardous than synthetic drugs. Research in recent years has focused on the scientific validation of ethanobotanical data as well as its effectiveness in treating dengue fever. Several of the preventive techniques included the use of plant extracts, which may have had ovicidal effects on *Aedes aegypti*. Plant (Table 1) extracts or molecules can act as virocidal and immunomodulators. Various mechanisms like elevation of the platelet count, larvicidal activity, virocidal activity against the dengue virus DENV-1, etc, by which plant extracts exhibit their therapeutic effect have been described. The current review article focuses on information about plants with anti-dengue effects and phytoconstituents with the same potential [7-9].

Conclusion

In various regions of India, several plants and their formulations have been traditionally utilised to treat dengue. The present review gives a detailed idea of the scientifically proven action of herbal extract. As per the stage of dengue, these herbal formulations can be used for treatment or management of the disease. Finding better, more potent and less harmful anti-dengue medications requires the formulation and development of novel anti-dengue medicines from bioactive chemicals. Therefore, the compilation of potent isolated active phytoconstituents with anti-dengue action and their toxicity in preclinical and clinical studies should be done. **The mechanisms like** ovicidal, larvicide against dengue vectors, antiviral activity, inhibitor of the multiplication of diverse strains of DENV-2, cytotoxic effect, and increase in the platelet count of different plant extracts prove that herbal formulations provide either potent or adjuvant therapy.

Acknowledgement

The authors would like to thank to Rajendra Gode Institute of Pharmacy, for contributing the knowledge.

Disclosure

In this paper, the authors disclose no conflict of interest.

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Received: 20-Jul-2022, Manuscript No: ijrpl-22-69782, **Editor assigned:** 22-Jul-2022, PreQC No: ijrpl-22-69782(PQ), **Reviewed:** 03-Aug-2022, QC No: ijrpl-22-69782, **Revised:** 05-Aug-2022, Manuscript No: ijrpl-22-69782(R) **Published:** 12-Aug-2022, DOI: 10.4172/2278-0238.1000134

Citation: Manekar SS, Bakal RL, Turankar AR (2022) Medicinal Plants Used In Treatment and Management of Dengue: An Overview. Int J Res Dev Pharm L Sci, 8: 134.

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Table 1: Total summary of the review.

Common name	Scientific name	Part Used	Extract	Chemical Composition	Result
Indian Abutilon, Monkey Bush	<i>Abutilon indicum</i> Family: Malvaceae	Whole plant, Leaves	Petroleum ether	Beta-sitosterol	Beta-sitosterol isolated, identified and evaluated against <i>Aedes aegypti</i> L. It shows potential new mosquito larvicidal compound with LC50 value of 11.49, 3.58 and 26.67 ppm.
Sweet-flag, Calamus	<i>Acorus calamus</i> Family: <i>I*</i> - 0Acoraceae	Root	Ethanol	Tatanan A	Among 12 isolated compounds Tatanan A showed best anti-DENV activity with an EC50 of 3.9 µM. The antiviral efficacy of tatanan A was further validated by an RNA replication assay. The Time-addition assay demonstrated that Tatanan A inhibited DENV2 mRNA and protein levels.
Neem, Margosa	<i>Azadirachta indica</i> Family: Meliaceae	Leaves	Lyophilized aqueous extract	---	Aqueous extract at 500µg/ml gives better antiviral activity for Dengue 2 and 4.
Bitterweed, King of Bitters, Creat, Green Chireta, Indian Echinachea, Hempedu Bumi	<i>Andrographis paniculata</i> Family: Acanthaceae	Leaves	Ethanol	Andrographalide	Increased phosphorylation of eIF2 in response to andrographolide is a main determinant of andrographolide's anti-DENV action. The andrographolide showed the 97.23% anti-dengue activity against the dengue-2 virus in C6/36 cell lines.
	<i>Andrographis paniculata</i> Family: Acanthaceae	--	--	Andrographalide (Marketed pure sample)	Showed significant anti DENV activity in both cell lines with EC50 for DENV 2 is 21.3 µM and 22.73 µM for HepG2 and HeLa respectively.
Adulsa, Malabar nut	<i>Adhatoda vasica</i> Family: Acanthaceae	Leaves	Methanolic fractions		The LC50 and LC90 values for fraction III of <i>Aedes aegypti</i> were 157.5 and 215.5 ppm, respectively, and 120 and 243.5 ppm for fraction V of <i>Aedes aegypti</i> .
Custard apple, Sugar apple or bullock's-heart	<i>Nhunnhhhhhhh</i> / Family: Annonaceae	Barks and bulb Leaves, bark, fruits and seeds	Ethyl acetate Acetone, chloroform and methanol		Ethyl acetate extract showed the highest mortality (100%) at 200 ppm against <i>Aedes aegypti</i> . Against the 4th instar larvae of <i>Aedes aegypti</i> at a lethal concentration (LC50: 72.5 ppm), all enzyme patterns showed differential expression on exposure to the ethyl acetate extract. Acetone, chloroform and methanol extracts of leaves, bark, fruits and seeds of <i>Annona reticulata</i> L. at different concentrations 500, 250, 125, 62.5, 31.25, 15.63 and 7 mg/l were evaluated against fourth instar larvae of <i>Aedes aegypti</i> . Among the plant parts studied, seed extracts showed maximum mortality rate. Methanolic seed extract was found to have higher rate of larvicidal rate against <i>A. aegypti</i> .
Alligator weed, Ponnanakanni	<i>Alternanthera philoxeroides</i> Family: Amaranthaceae	Whole plants	Petroleum ether		The antiviral activity of four extracts petroleum ether, ethyl acetate, ethyl ether and coumane was tested. The petroleum ether extract showed the strongest inhibitory effects on dengue virus (ED(50)=47.43).
Flossflower, bluemink, blueweed, pussy foot or Mexican paintbrush	<i>Ageratum houstonianum</i> Family: Asteraceae	leaves	methanol		The effect of 0.1 % methanol extract on oviposition of <i>Aedes</i> species indicated effective deterrence ranging from 79.0 to 100.0 % in indoor and 74.6 to 100.0 % in outdoor ovitraps.
Indian siris, Shar Sarad, , lebeck tree	<i>Albizia lebeck</i> Family: Fabaceae	Leaf	Methanolic methanol		The methanol extract showed the highest ovicidal activity. 100% mortality was observed at 250, 200, and 150 ppm for methanolic leaf extract.
Arrabidaea chica	<i>Arrabidaea pulchra</i> Family: Bignoniaceae	Leaves	Ethanol	Caffeoylcalleryanin, Verbascoside, ursolic acid	Inhibited DENV-2 (EC50 = 46.8 ± 1.6 µg mL ⁻¹). AP 2 was the most effective anti-DENV-2 constituent, with a Selectivity Indexes (SI) of 20.0.
Neem, Margosa, Margo	<i>Azadirachta indica</i> Family: Meliaceae.	Leaves	Aqueous	Azadirachtin Gedunin and Pongamol	An in vivo study on the inhibitory effects on virus of NL aqueous extract in day-old suckling mice was carried out by intracerebral inoculation. It was shown that the aqueous extract inhibited the virus at nontoxic doses in the range of 120–30 mg mL ⁻¹ as indicated by the absence of 511-bp dengue group specific amplicons upon RT-PCR. Isolated two molecules, Gedunin and Pongamol have strong interactions with important proteins of virus and its required human proteins. The human proteins responsible for attachment of virus to the host cell and viral proteins themselves are blocked by some of the Neem molecules.
Finger Root, Chinese Ginger	<i>Boesenbergia rotunda</i> Family: Zingiberaceae	Rhizome	Methanol	4-hydroxypanduratin A, panduratin A pinostrobin, pinocembrin, Cardamonin	<i>B. rotunda</i> showed good competitive inhibitory activities towards DENV-2 NS3 protease with Ki values of 21 µM and 25 µM, respectively. The small value of Ki shows the potential of 4- hydroxypanduratin A to inhibit DENV-2 NS3 protease in vitro.

Lemongrass	<i>Cymbopogon citratus</i> Family: Poaceae	Aerial parts Leaf	Methanol Water (gold nanoparticles prepared)		Inhibited DENV-2 replication (98.9% at a dose of 20 µg/mL) The predatory efficiency of the cyclopoid crustacean <i>Mesocyclops aspericornis</i> against <i>A. aegypti</i> was 56% (larva I) and 35.1% (larva II). Predation against late-instar larvae was minimal.
Papaya, papaw or pawpaw	<i>Carica papaya</i> Family: Caricaceae	Leaf	Aqueous juice		One study reported that crude papaya leaves at 15 mg/kg of body weight increases of thrombocyte count in mice while in another study they observed that 400 and 800 mg/kg of <i>C. papaya</i> leaf aqueous extract increases the platelet count.
		Capsule containing 70 % ethanol leaf extract of <i>C. papaya</i> .	Ethanol		An open-labelled randomized controlled trial was carried out on 80 patients with DF including both the control group (n=40) and test group (n= 40). The test group was treated with two capsules 3 times daily. They had found the significant increase (P< 0.01) of the platelet count while maintaining the hematocrit in the normal level
Velvet Leaf, False Pareira Brava, Abuta, Pereira Root	<i>Cissampelos pareira</i> Family: Menispermaceae	Aerial part	Alcoholic extract		Alcoholic extract inhibited the replication of dengue viruses in living cells in culture and protected mice against dengue infection. Extract tested in in vitro and in vivo conditions and found effective against all four serotypes.
Red seaweed	<i>Cryptonamia crenulata</i> Family: Halymeniaceae	Whole plants		Galactan (DL galactan hybrid C2S3)	It is a potent and selective inhibitor of the multiplication of diverse strains of DENV-2 in Vero cells with higher effectiveness.
Sabah Snake Grass, belalai gajah, ki tajam	<i>Clinacanthus nutans</i> Family: Acanthaceae	leaves	Chloroform	Phaeophorbide a	Phaeophorbide a Suppressed DV2 replication in A549 cell. It could also inhibit the DV2 replication in post incubation.
Adenogynum, Chloradenia	<i>Cladogynos orientalis</i> Family: Euphorbiaceae	Whole plant	Ethanol extract		At a conc. of 12.5 µg/ml ethanolic extract inhibited activity against DENV2 with 34.85% inhibition. The 50% cytotoxic concentration (CC50) of ethanol extract were 312 µg/ml.
Brown seaweed	<i>Cladosiphon okamuranus</i> Family: Chordariaceae	Whole plant	Water	Fucoidan	Elimination of the sulfated function group from fucoidan significantly attenuated the inhibitory activity on DEN2 infection with <1% fucoidan. DEN2 particles bound exclusively to fucoidan, indicating that fucoidan interacts directly with envelope glycoprotein (EGP) on DEN2.
Haldi, turmeric, Curcuma	<i>Curcuma longa</i> Family: Zingiberaceae	Rhizome	Alcohol (90%), Methanol (Fractions)	Curcuminoid	Antiviral activity (IC50) and toxicity (CC50) in vitro was examined on Huh7it-1 cells by focus assay and a MTT assay, respectively, the acquired value of IC50 was 17,91 µg/mL whereas the value of CC50 was 85,4 µg/mL. The value of SI of <i>C. longa</i> was 4.8. <i>C. longa</i> remarkable reduced of viral load after 24 hour
Apple of sodom, Calotrope, and Giant milkweed	<i>Calotropis procera</i> Family: Apocynaceae	Latax and Leaf	Methanol		Methanol extracted latex was found effective and feasible larvicide against dengue vectors in the field conditions. Methanol extracts of seed, leaf and flower are more effective as compared to aqueous extract against dengue vectors.
Amaltas, Golden Shower Tree, Indian laburnum, or pudding-pipe tree.	<i>Cassia fistula</i> Family: Fabaceae (Leguminosae)	Leaf	Methanol, benzene and acetone		The extract exhibited dose dependent activity and produced significant mortality. The 24 h LC50 concentration of the extract against <i>Aedes aegypti</i> were observed at 10.69, 18.27 and 23.95 mg/l respectively. Mean percent hatchability of the ovicidal activity was observed 120.00 h after treatment. The percent hatchability was inversely proportional to the concentration of extract and directly proportional to the eggs.
Cape periwinkle, graveyard plant, Madagascar periwinkle, Sadabahar.	<i>Catharanthus roseus</i> Family: Apocynaceae	Leaves	Methanol		Inhibited DENV-2 replication (60% at a dose of 0.078 mg/mL)
Nam Nam, Katak Puru, Puki Anjing.	<i>Cynometra cauliflora</i> Family: Fabaceae	Leaves	Methanol		Cytotoxicity screening against Vero cells using MTT assay showed that the CC50 values for the extract was 36 mg/ml and the 50% Effective Concentration, EC50, was 2.19 mg/ml. The selectivity index (SI = CC50 / EC50) for the extract was 16.

Amphilophium elongatum	<i>Distictella elongate</i> Family: Bignoniaceae	Leaves, stems and fruits Leaves	Ethanol	Pectolarin and Acacetin-7-O-rutinoside (Fruit)	Fruit ethanolic extract has presented anti-DENV-2 activity (EC ₅₀ 11.1±1.6 µg ml ⁻¹); SI > 45).
Tawa-Tawa, Asthma Weed, snake weed, spurge	<i>Euphorbia hirta</i> Family: Euphorbiaceae	Leaves	Ethyl acetate extract Water	Taraxerone, Lupeol.	Potent antiviral activity against DENV 1 and 2 by plaque reduction neutralization test. The EtOAc fraction significantly reduced (85 %) the plaque forming capacity of dengue virus serotype 1 from ~1400 to ~200 PFU & serotype 2 (~90 % reduction) . The percentage increase of mean platelet counts after reduction with anagrelide was <i>Euphorbia hirta</i> group (80.92%).
Tongkat Ali, Pasak bumi, or Longjack	<i>Eurycoma longifolia</i> Family: Simaroubaceae	Root	Water		<i>In vitro</i> -Inhibited DENV-1, DENV-2, DENV-3 and DENV-4 (IC ₅₀ = 33.84, 33.55, 58.35 and 119 g/mL, respectively) <i>In vivo</i> -30% lower viral load and 12% higher platelet count compared to the control group. The selectivity index (SI) values determined as the ratio of cytotoxic concentration (CC ₅₀) to inhibitory concentration (IC ₅₀) was the lowest for DENV-2 at 28.9.
Pak Kan Thong, Chameleon Plant	<i>Houttuynia cordata</i> Family: Saururaceae	Whole plant Aerial parts (fresh leaves)	Aqueous Ethanol extract and ethyl acetate fraction.	Hyperoside uercetin, Quercitrin and Rutin	The results showed that pre- and post-incubation of <i>H. cordata</i> extract (10–100 µg/mL) with HepG2 cells significantly reduced intracellular DEN-2 RNA production correlating with the decrease in dengue protein expression. In the direct blocking mode, the extract bound with DEN-2 and strongly inhibited the intracellular viral RNA replication with an effective dose (EC ₅₀) of 0.8 µg/mL. The 50% inhibitory concentrations (IC ₅₀) of the Ethyl Acetate fraction added before the viral adsorption stage were 0.98 mg/mL
Sea buckthorn	<i>Hippophae rhamnoides</i> Family: Elaeagnaceae	Leaf Leaf	Ethanol Ethanol	 Phenolic compounds	Ethanolic extract decreased the TNF-α and increased the IFN-γ production in Dengue-infected cells. SBTLAE proved its antidengue activity by indicating decreased plaque numbers after the treatment of infected cells. Ethanolic extract U937 cell line did not show any cytotoxicity at any concentration. Percent cell viability of infected and of extract treated cells showed highest cell viability of infected cells at concentration of 50 µg/mL.
Ramontchi, Governor's plum, Madagascar plum and Indian plum	<i>Flacourtia ramontchi</i> Family: Salicaceae	Stem barks	Ethyl acetate	phenolic glycosides, named flacourtosides A–F	In the DENV RNA polymerase assay, significant inhibition was observed with betulinic acid 3β-caffeate (IC ₅₀ = 0.85 ± 0.1 µM) and to a lesser extent for the flacourtosides A and E (1 and 5, respectively), and scolochinenoside D (IC ₅₀ values ~10 µM).
Common Flagellaria, Rotan Dini, False Rattan	<i>Flagellaria indica</i> Family: Flagellariaceae	Whole plant	Dichloromethane		Inhibited DENV-2 (45.52% at a dose of 12.5 g/mL)
<i>Faramea</i>	<i>Faramea bahinensis</i> Family: Rubiaceae	Leaves	Methanol	Flavanone glycoside: 5-hydroxy-4'-methoxy-flavanone-7-O-β-D-apiofuranosyl-(1 → 6)-β-D-glucopyranoside, the known 5,4'-dihydroxy-flavanone-7-O-β-D-apiofuranosyl-(1 → 6)-β-D-glucopyranoside and a diastereoisomeric epimer pair of the known 5,3',5'-trihydroxy-flavanone-7-O-β-D-glucopyranoside.	The treatment of DENV-2 infected HepG2 cells with the new flavanone was able to control viral replication promoting a reduction of the number of infected cells (12%), together with a decrease of infectious particles in the culture supernatant (97%) and of the number of RNA copies of DENV-2 in HepG2 cells (67%).

Sweet potato, Water Spinach	<i>Ipomea batata</i> Family: Convolvulaceae	Leaves	Water		<i>Ipomea batatas</i> violet variety (p=0.0070) and green variety (p=0.0000), have significant platelet augmentation (p<0.05) activity. The percentage increase of mean platelet counts after reduction with anagrelide was <i>Ipomea batatas</i> green variety group (107.88%), <i>Ipomea batatas</i> violet variety group (106.07%).
Malabar nut, Adhatoda, Vasa, Vasaka	<i>Justicia adhatoda</i> Family: Acanthaceae	Leaf	hexane, ethyl acetate and methanol		Methanolic extract of <i>J. adhatoda</i> (LC ₅₀ =75.30) showed highest mortality against the test larvae.
White Lead tree, Petai Belalang	<i>Leucaena leucocephala</i> Family: Fabaceae	Seed	Ethanol	Galactomanan	In vitro experiments with DEN-1 in C6/36 cell culture assays showed that concentrations that produced a 100-fold decrease in virus titer of DEN-1 were 347 and 37 mg/(-1).
White lippia, Bushy lippia	<i>Lippia alba</i> Family: Verbanaceae <i>Lippia citriodora</i> Family: Verbanaceae	Aerial parts	Essential oil	Linalool (Isolated)	The IC50 values for <i>L. alba</i> oil were between 0.4-32.6 microg/mL and between 1.9-33.7 microg/mL for <i>L. citriodora</i> oil. Inhibition was observed by treatment of virus before adsorption on cell IC50
Bitter-melon, bitter gourd or karela.	<i>Mormordica Charantia</i> Family: Cucurbitaceae	Root & Entire fruit Flowers & fruits	Methanol Methanol, ethyl acetate and hexane.		Shown 50 % inhibition of Vero cells that infected with DENV 1 based on cytopathic effect. In cytotoxicity study maximum non-toxic dose was 0.20 mg/mL. High toxicity to ethyl acetate extracts from flowers and fruits at concentrations of 200 µg/mL and 100 µg/mL, with 97% and 87% of larvae mortality (L3), respectively.
Myristica magnifica, Myristica nutmeg	<i>Myristica fatua</i> <i>Myristica fragrans</i> Family: Myristicaceae	Leaves	Methanol		<i>Myristica fatua</i> Shown antiviral effects against DENV 2 with highest percentage inhibition -122.7%.
Tulsi, Holy basil	<i>Ocimum sanctum</i> Family: Lamiaceae	Whole aerial parts	Methanol		Exhibit antiviral properties toward DENV 1 through inhibition of cytopathic formation and viral replication. The maximum non-toxic dose (MNTD) was 23.44 µg/mL. Upon treating the DENV-1 infected cells with <i>O. sanctum</i> , the percentage of cell viability recorded was 64.29% and 68.67%, respectively at MNTD and ½MNTD.
Cat's Whiskers, Java Tea, Kidneys Tea Plant, Misai Kuchin.	<i>Orthosiphon stamineus</i> Family: Lamiaceae	Leaves	Aqueous		Inhibited DENV-2 replication (88% at a dose of 0.31 mg/ mL). The EC50 value of the extracts tested against the DENV-2 was ~ 0.36 mg/ml
Guava, yellow guava, lemon guava, or apple guava	<i>Psidium guajava</i> Family: Myrtaceae	Bark Fruit	Ethanol Ethanol	Isolated compounds, Gallic acid, quercetin, catechin, naringin	All four compounds selectively inhibited DENV 2 replication with EC50 values bark (7.8 µg/mL), Gallic acid (28.8 µg/mL), quercetin(19.2 µg/mL), catechin (33.7 µg/mL), naringin (47.9 µg/mL) The stem cell factor mRNA expression significant increased (p<0.05) in group treated with guava extract leads to significantly enhanced platelet count in mice
Javanese long pepper, long pepper	<i>Piper retrofractum</i> Family: Piperaceae	whole plant	Dichloromethane, Ethanol		It exhibited an inactivated viral particle activity with 84.93% at a concentration of 100 µg/ml.
Indian gooseberry, gale of the wind	<i>Phyllanthus</i> sp Family: Phyllanthaceae (<i>Phyllanthus amarus</i> , <i>P. niruri</i> , <i>P. urinaria</i> , <i>P. watsonii</i>) Family: Phyllanthaceae	All Aerial part	Aqueous and methanol	Gallic acid, Geraniin (present in high amount), syringin, and corilagen	Inhibited DENV-2 replication (91.48% at a dose of 250 µg/ mL) MNTD for aqueous and methanolic extracts were 250 µg/ ml and 15.63 µg/ml, respectively. Phyllanthus showed the strongest antiviral activity against DENV2 during the simultaneous mode of treatment with more than 83 - 95% reduction of virus inhibition.
Gall oak, Dyer's oak	<i>Quercus lusitanica</i> Family: Fagaceae	Seed (galls)	Methanol extract	Methyl gallate	The crude methanol extracts at 180 µg/ ml was completely inhibit the dengue virus infection at TCID50 of 1-1000 by the absence of CPE. At 0.2 mg/ml of crude and fractionated methanolic extract show as more than 90% inhibition. Methyl gallate purified from fractionated crude extracts of <i>Q. lusitanica</i> at the MNTD of 100 µg/mL showed a 96% inhibition at TCID50 of 1000. DENV-2 virus protease inhibition assay of methyl gallate showed more than 98% inhibition at 0.3 mg/mL
Bakau Minyak, True mangroves	<i>Rhizophora apiculata</i> Family: Rhizophoraceae	Whole plant	Ethanol		Inhibited DENV-2 replication by 56.14 % at concentrations of 12.5.
Elderberry, European black elderberry, elder.	<i>Sambucus nigra</i> Family: Adoxaceae	Flowers and leaves	Methanol		Exhibit anti DENV 2 activity at 400 µg/ml. At this concentration, cell viability was between 60% and 80%.
Hog plum, Yellow mombin	<i>Spondias mombin</i> & <i>Spondias tuberosa</i> Family: Anacardiaceae	Leaves	Methanol:water (Hydroalcohol)	Rutin, quercetin and ellagic acid.	In vitro Inhibited DENV-2 replication (3.31% at a dose of 500 g/L) Inhibited DENV-2 replication (99% at a dose of 500 17.98 g/mL)

Chinese skullcap, huangqin, baikal, and scutellaria	<i>Scutellaria baicalensis</i> Family: Lamiaceae	Root	Water	Baicalein	The IC50 values for the <i>S. baicalensis</i> extract on Vero cells following DENV adsorption ranged from 86.59 to 95.19 µg/mL for the different DENV serotypes. The IC50 values decreased to 56.02 to 77.41 µg/mL when cells were treated with the extract.
Clove, Cengkih, Chengkeh	<i>Syzygium aromaticum</i> Family: Myrtaceae	Flower bud	Ethanol	Eugenin	Eugenin reported potent dengue protease inhibitory activity against DENV 2 and DENV 3 with IC50 94.7 nM and 7.5 µM.
Clove, Keriang Batu, Kelat Paya	<i>Syzygium grandulae</i> <i>Syzygium campanulatum</i> Family: Myrtaceae	Flower bud		Isolated compounds- Cyclododecane, nhexadecanoic acid and carrophyllene	The findings revealed that cyclododecane and n-hexadecanoic acid found in the leaf extracts of <i>S. grande</i> and caryophyllene in extracts of <i>S. campanulatum</i> were likely the lead-compound that imparted the observed inhibitory effect on the DENV2 NS2B-NS3 protease.
	<i>Tephrosia madrensis</i> <i>Tephrosia crassifolia</i> <i>Tephrosia viridiflora</i> Family:	Leaves and flowers		Glabranine , 7-O-methylglabranine	The flavonoids isolated from <i>T. madrensis</i> , glabranine and 7-O-methyl-glabranine exert strong inhibitory effects on dengue virus replication in LLC-MK2 cells. Methyl-hildgardtol A isolated from <i>T. crassifolia</i> exhibited a moderate to low inhibitory effect, while hildgargtol A from <i>T. crassifolia</i> and elongatine from <i>T. viridiflora</i> had no effect on viral growth.
Cat's claw,	<i>Uncaria tomentosa</i> Family: Rubiaceae	Stem barks	Water-alcohol	Alkaloid (oxindole alkaloids)	Reducing DENV-Ag+ cell rates
Marine eelgrass	<i>Zostera marina</i> Family: Zosteraceae	Whole plant	Water	Zosteric acid	The anti-adhesive compound zosteric acid (ZA), derived from <i>Z. marina</i> showed a modest IC50 of approximately 2.3 mM against DENV-2.

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