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Potential Use of Medicinal plants for Dengue: A Systematic Mini review of Scientific Evidence

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Abstract

Mosquito-borne diseases caused illness in approximately 700 million people per year globally. Dengue (DENV) is a one of them mosquito-borne emerging viral disease endemic prominently in many urban areas of tropical countries. Nature has provided us with various resources to fight and recover from such infectious diseases. This review focuses on the understanding of dengue, potential anti dengue activity and insecticidal activity of various medicinal plants. Further laboratory investigations and more research are needed to establish the product which having potential to control dengue disease. Thus, the development of a traditional medicinal plant-based antiviral product assures a more possible choice in combating dengue infection which may be replacement of inadequate drug with side effective.

Keywords: Anti-dengue activity, Dengue, Insecticidal activity, Medicinal plants

1. Introduction

Dengue fever also known as the hemorrhagic fever has nowadays emerged as one of the greatest health problem to Asian countries. It account for more than 70% of the prevailing diseases. The virus which is responsible for dengue fever belongs to the family *Flaviridae* and it is transmitted by *Aedes Aegypti* mosquito which has peculiar feature as white marking in its leg. The viral genome is a single-stranded and positive-sense RNA of about 10kb which encodes three structural and seven non-structural (NSP) proteins. This virus has four antigically different serotypes DENV 1, DENV-2 DENV-3 and DENV-4.These serotype shows 66% similarity in their genome distribution. DENV infection include two types one is mild fever known as dengue fever (DF), which constitutes about 95 % of cases, and a more serious type known as dengue hemorrhagic fever and/or dengue shock syndrome (DHF/DSS, 5 % of cases) (Sanchez I et al 2000). A symptom of dengue infection is seen three to fourteen days after infection. A severe dengue hemorrhagic fever result in bleeding, decrease in blood platelets and decrease in blood pressure. Dengue fever is a flu-like infection that affects all age group of people viz. newborns, children and adults, but most dangerous to pregnant women and weak immune person. Thus it becomes important to learn more and more about this dengue fever. So people can be aware of this disease and mortality could be prevented.

Dengue is endemic in India. In India first reported incidence of dengue was from Chennai in the year 1946. Normally in a year transmission of dengue virus start from April to November in northern part of the country while in southern part transmission is all the year round. In past few years severity of dengue virus fever has been increased. The number of dengue cases in 2017 was highest in any decade in India upto 2017 (Figure 1) according to a report Directorate of National Borne Diseases Control Programme.

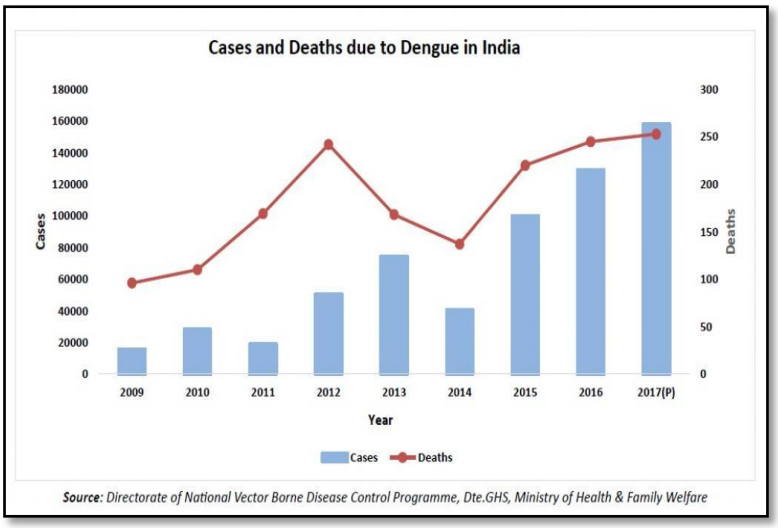

Figure1: Cases and death due to dengue reported from India upto 2017 (Sources: Directorate of National Vector Borne Disease Control programme)

Government of India is running various awareness campaign and vector control programme to combat the disease. At present day there is no vaccine for dengue fever (Guzman A, Isturiz RE 2010). Early diagnosis of the disease and immediate hospitalization is often required to save the life of patients with DHF. Among different strategies to combat dengue virus include the use of plants which have bioactive substances with insecticidal properties (Grzybowski A et al 2011).

Around the world many researchers are working on medicinal properties of traditional plants for their anti-dengue properties. Anti-dengue activities were identified in nineteen medicinal plant extracts that are used in traditional medicine in Malaysia (Rothan, H.A et al 2014). The highest inhibitory action against the dengue NS2B-NS3 pro was found in ethanolic leaves extract of *S. angustifolia*, methanolic leaves extract of *V. cinerea* and ethanol stems extract of *T. procumbens* plants.

The leaf extracts of four plants (*Elaeagnus indica, Blepharis maderaspatensis, Maesa indica, Memecylon edule and Phyllanthus wightianus*) in dfferennt organic solvents such as acetone, chloroform, ethyl acetate, hexane, and methanol were used for their larvicidal property against dengue vector *Aedes Aegypti* (M.S. Shivumar et al 2013). All the experimental extracts confirmed moderate to high larvicidal activities. However, the maximum larval mortality was detected in acetone extract of *E. indica* followed by *M. indica* acetone extract.

The larvicidal efficiency of five indigenous weeds against *Aedes Aegypti* was investigated by Aarti Sharma et al 2016. The stem and leaves of five plants medicinal plants (*Achyranthes aspera, Cassia occidentalis, Catharanthus roseus, Lantana camara, and Xanthium strumarium*) were selected for their larvicidal activity against dengue vector. They found *Achyranthes aspera* as an most potent larvicidal agent for controlling dengue vector *Aedes Aegypti*. The hexane extract of the stated plant have more efficiency than ethanol extracts. Chowdhury et al 2008 worked on *Solanum villosum* a common weed as a biocontrol agent against *S. Aegypt*. Their research shows significantly larvicidal effects of *S villosum* on dengue vector. The isolated extract can be used for control of mosquito in stagnant water. In 2006 investigation was done to test the larval toxicity and some repellant potential of *Albizzia amara* and *ocimum basilicum* against different in star larvae of *Aedes Aegypti* by Murgan et al 2007 (Table 1). The smoke toxicity of *A. amara* was found to be more effective against *Aedes Aegypti*.

Table 1: List of medicinal plants, its parts and extracts having anti-vector activities:

S. No.	Family	Species	Part Used	Extraction used	References
1	Malvaceae	*S. angustifolia*	Leaves	Methanol	Rothan H.A et al., 2014
2	Vitaceae	*V. Cinerea*	Leaves	Ethanol	Rothan H.A et al.,

					2014
3	Asteraceae	*T. procumbens*	Stems	Ethanol	Rothan H.A et al., 2014
4	Poaceae	*E. indica*	Leaves	Acetone	Govindarajan and Shivkumar .,2014
5	Anacardiaceae	*M. indica*	Leaves	Acetone	Govindarajan and Shivkumar .,2014
6	Liliaceae	*A. racemous*	Roots and Leaves	Hexane, Benzene Chloroform Ethyl acetate Methanol	Govindarajan and Shivkumar .,2014
7	Rutacia	*B. albiflroa*	Leaves	Petroleum ether	MF Alam et al.,2011
8	Amaranthaceae	*Achyranthes aspera*	Leaves and stems	Hexane	Aarti Sharma et al., 2016
9	Solanaceae	*Solanum villosum*	Berries (fruit)	Chloroform and Methanol	Chowdhury et al., 2005
10	Fabaceae	*Albizzia amara*	Leaves	Acetone	Murgan et al.,
11	Euphorbiaceae	*Cladogynos orientalis*	Leaves, stems	ethanol	Rahuman et al., 2008

Medicinal plants used for inhibitory effects on Dengue virus:

According to Dec 2008 technical report of world health organization (WHO) on dengue, 80% of the population in Asia and Africa depends on traditional medicine for treating primary health care. Also traditional medicinal plants have been believed to have anti viral activity (Betancur-Galvis LA et al 1999). The use of herbal based medicine is growing worldwide because of its very less side effects. Six medicinal plants (*Andrographis paniculata, Citrus limon, Cymbopogon citratus, Momordica charantia, Ocimum sanctum and Pelargonium citrosum)* was tested for the maximum non-toxic dose (MNTD) on dengue virus serotype 1 (DENV-1). The MNTD was determined by testing the methanolic extracts of the medicinal plants against Vero E6 cells (DENV1-infected) in vitro (Tang et al. 2012)**.** The invitro studies shows *A. paniculata* has the potent antiviral inhibitory results followed by *M. charantia* against DENV-1 by anti-viral assay based on cytophatic effects. Jiang WL et al 2005 examine the effects of *Alternanthera philoxeroides Griseb* extracts against dengue virus in vitro (Table 2). Four plant extracts were used and extracts from petroleum ether showed the strongest inhibitory effects on dengue virus. Some of the important traditional medicinal plants used to treatment in dengue fever are following-

Carica papaya

C. papaya is fruit plant belongs to the genus Carica of the family Caricaceae. In traditional medicinal system, their leaves have been used as a treatment for various diseases such as malaria (Titanji et al., 2008), as an abortifacient agents, a Laxatives, or smoked to relieve asthma and dengue (Deep et al., 2018). Its leaves extract significant associated with the raising blood platelets counts, white blood cells and neutrophils in blood samples of dengue patient, most significantly stop the conversion of Dengue fever into Dengue haemprrhagic fever, decrease in fever duration and hospital stay. According to WHO guideline, Platelet count is believed as warning indication not as criteria for severe dengue infection (Charan et al., 2016). It is suggested by many workers that *C. papaya* leaves extract to be given patient from the beginning days of dengue confirmation after the diagnosis with NS1 antigen.

Cymbopogon citrates

It is commonly known as lemongrass belongs to family Poaceae widely distributed in southeast Asia. Its little concentration of methanol extract showed effective anti-dengue activity against the DENV-1 serotype of dengue.

Andrographis paniculata-

Andrographis plant tradionally known as 'kalmegh' belongs to family Acanthaceae widely distributed in Southern and Southeastern countries, native to India and Sri Lanka. Andrographolide is the substance which having potant antiviral activity (Jarukamjorn et al., 2008; Leardkamolkarn et al., 2012). Its leave extract showed the anti-dengue activity against the DENV-1 serotype of dengue (Tang et al., 2012). It increases the blood counts and give strengthens to the immune system.

Azadirachta indica

Azadirachta tree commonly known as neem or Indian lilac belong to family Meliaceae distributed mainly in Indian subcontinent region throughout tropical and subtropical countries. Its leave extract showed in vitro and in vivo inhibitory capacity or anti-dengue activity against DENV-2 serotype replication (Parida et al., 2012; Deep et al., 2018).

Curcuma longa

Its commonly name is turmeric (Haldi) belongs to Zingiberaceae family. It reduce viremia period of viral infection and antiviral effect against DENV-2 in vitro as well as in vivo with low cytotoxicity, having no specific abnormalities in liver and kidney (Ichsyani et al., 2017).

Momordica charantia

Its commonly name is bitter gourd (karela) belongs to member of family Cucurbitaceae widely distributed plant is found in tropical and subtropical regions. It showed ability to approximately 50% inhibition anti-dengue activity against DENV-1(Tang et al., 2012).

Tinospora cordifolia

It is deciduous climbing shrub, common known as Giloy or Guduchi belongs to the family Menispermaceae. This plant is of great interest to researchers because of its various medicinal properties like Immunostimulant, anti-malarial, anti-diabetic, anti-spasmodic, anti-oxidant, anti-inflammatory, anti-arthritic, anti-stress, anti-allergic, anti-leprotic, immunomodulatory and anti-neoplastic activities (Saha & Ghosh, 2012). It gives the strength to the animal immune system and protects against various type of infections. It is a sure shot remedy against fevers of all etiologies including early recovery in dengue fever. Its uses as immunomodulatory action to manage the dengue fever by maintaining the platelets count and by antioxidant activities.

Ocimum sanctum

It is commonly name as holy basil (tulsi) belongs to the family Labiatae widely distributed in Asia and the Americas. It was suggested that methanol extract of *Ocimum sanctum* leaves used as traditional medicine for dengue (Tang et al., 2012).

Table 2: List of some medicinal plants, its parts and extracts having anti-dengue activities.

Sr. No.	Family	Species	Parts used	Extraction Used	References
1.	Caricaceae	Carica papaya	Leaves	aqueous extract	Ahmad et al., 2012
2.	Acanthaceae	*A. paniculata*	Whole Plant	Methanol	Tang Li et al.,2012
3.	Cucurbitacea	*M. charantia*	Roots and fruits	Methanol	Tang Li et al., 2012
4.	Amaranthaceae	*Alternanthera philoxeroides Griseb*	Whole Plant	Petroleum ether	Jiang WL et al., 2005
5.	Flagellariaceae	*Flagellaria indica*	Leaves and other parts	Ethanol	Rothwell et al., 2009

6.	Piperaceae	*Piper retrofractum*	Leaves	ethanol and dichloromethane	Rothwell et al., 2009
7.	Myrtaceae	*Psidium guajava*	Leaves	-	Roses et al., 2011
8.	Rhizophoraceae	*Rhizophora apiculata*	Leaves	ethanol	Rothwell et al., 2009., Kaushik et al., 2018
9.	Zingiberaceae	*Kaempferia parviflora*	leaves and stem	aqueous	Phurimsak et al., 2005
10.	Rutaceae	*Uncaria tomentosa*	root and bark	hydro-alcoholic	Reis et al., 2008; Kaushik et al., 2018
11.	Elaeagnaceae	*Hippophae rhamnoides*	Leaves	Aqous	Jain et al., 2008

Conclusion

Epidemic dengue is a very big challenge to us from more than two centuries. At the present date, there are no particular globally acknowledged treatments or vaccine for dengue infection in any system of medicine. In this review paper an attempt was made to gather information about the medicinal plants and its parts that could be used for its anti dengue activities. Many researchers have screened variety of flora for their inhibitory effect on dengue vector. We covered traditional medicinal plants for their efficacy in control dengue mosquito. Different plant parts have been used to research with different solvents. Each solvent extract have different insecticidal activity (Table 1). The use of natural extract as compared to conventional chemical insecticide for control of dengue vector has many benefits. This includes reduction of environmental hazard caused due to chemical insecticide. Thus more research is needed on dengue epidemiology and also the mode of action of these plants extracts in vitro so proper strategies and more powerful insecticide could be developed so the morbidity rate could be decreased due to dengue vector.

Conflict of interest:

Authors declare that they have no conflict of interest.

References:

1. Ahmad, N., Fazal, H., Ayaz, M., Abbasi, B.H., Mohammad, I. and Fazal, L. (2011). Dengue fever treatment with Carica papaya leaves extracts. Asian Pac J Trop Biomed; 2011(1):330-333.
2. Alam, M.F., Mohammed M. Safhi., Chopra, A.K. and Dua, V.K. (2011). Toxicological properties of several medicinal plants from the Himalayas (India) against vectors of malaria, filariasis and dengue Tropical Biomedicine; 28(2): 343–350.
3. Betancur-Galvis, L.A., Saez, J., Granados, H., Slazar, A. and Ossa, J.E. (1999). Antitumor and antiviral activity of Colombian medicinal plant extracts. Mem Inst Oswaldo Cruz; 94(4):531–535.
4. Charan, J., Saxena, D., Goyal, J.P. and Yasobant, S. (2016). Efficacy and safety of Carica papaya leaf extract in the dengue: A systematic review and meta-analysis. Int J Appl Basic Med Res; 6(4):249–254. doi:10.4103/2229-516X.192596.
5. Deep P., Srivastava V. and Verma, S. (2018). Current Perspectives of Medicinal Plants Having Anti Dengue Potential. Int. J. Pharm. Sci. Rev. Res., 49(2): 91-96
6. Govindarajan, M. and Sivakumar, R. (2014). Laboratory evaluation of Indian medicinal plants as repellents against malaria, dengue, and filariasis vector mosquitoes Parasitol Research DOI 10.1007/s00436-014-4222-0
7. Grzybowski, A., Tiboni, M., da Silva MAN., Chitolina, R.F., Passos, M., Fontana, J.D. (2011). The combined action of phytolarvacides for the control of dengue fever vector, Aedes aegypti. Braz J Pharmacogn; 22:549–557.

8. Guzman, A. and Isturiz, R.E. (2010). Update on the global spread of dengue. Int J Antimicrob Agents; 36:40–42.
9. Ichsyani, M., Ridhanya, A., Risanti, M., Desti, H., Ceria, R., Putri, D.H., Sudiro, T.M. and Dewi, B.E. (2017). Antiviral effects of Curcuma longa L. against dengue virus in vitro and in vivo. IOP Conf. Series: Earth and Environmental Science; 101(2017). 012005 doi:10.1088/1755-1315/101/1/012005.
10. Jain, M., Ganju, L., Katiyal, A., Padwad, Y., Mishra, K.P. and Chanda, S. (2008). Effect of *Hippophae rhamnoides* leaf extract against dengue virus infection in human blood-derived macrophages. Phytomedicine; 15:793-799.
11. Jarukamjorn, K. and Nemoto, N. (2008). Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent andrographolide. J Health Sci; 54: 370.
12. Jiang, W.L., Luo, X.L. and Kuang S.J. (2005). Effects of Alternanthera philoxeroides Griseb against dengue virus in vitro J First Mil Med Univ; 25(4):454–456.
13. Kamaraj., Rahuman, C., Bagavan, A.A., Elango, A., Zahir, G. and Santhoshkumar., T. (2011). Larvicidal and repellent activity of medicinal plant extracts from Eastern Ghats of South India against malaria and filariasis vectors Asian Pacific Journal of Tropical Medicine; 2011: 698-705.
14. Kaushik, S., Kaushik, S., Sharma V. and Yadav J.P. (2018). Antiviral and therapeutic uses of medicinal plants and their derivatives against dengue viruses. Pharmacognosy Reviews 12: 24177-185.
15. Leardkamolkarn, V., Sirigulpanit, W., Phurimsak, C., Kumkate, S., Himakoun, L. and Sripanidkulchai, B. (2012). The inhibitory actions of *Houttuynia cordata* aqueous extract on dengue virus and dengue-infected cells. J Food Biochem; 36: 86-92.
16. Murugan, K., Murugan, P. and Noortheen, A. (2007). Larvicidal and repellent potential of Albizzia amara Boivin and Ocimum basilicum Linn against dengue vector, Aedes aegypti (Insecta:Diptera:Culicidae) Bioresource Tech; 98 (1): 198-201.
17. Chowdhury, N., Ghosh, A. and Chandra, G. (2008) Mosquito larvicidal activities of Solanum villosum berry extract against the dengue vector *Stegomyia Aegypti* BMC Complementary and Alternative Medicine doi:10.1186/1472-6882-8-10.
18. Parida, M.M., Upadhyay, C., Pandya, G. and Jana, A.M. (2002). Inhibitory potential of neem (Azidarachta indica Juss) leaves on Dengue virus type-2 replication. J Ethnopharmacol, 79:273-278.
19. Phurimsak, C. and Leardkamolkarn, V. (2005). Screening for Antiviral Effect of Thai Herbs; *Kaempferia parviflora*, *Ellipeiopsis cherrevensis* and *Stemona tuberosa* Against Dengue Virus Type-2. In: 31st Congress on Science and Technology of Thailand at Suranaree University of Technology.
20. Rahuman, A.A., Gopalakrishnan, G., Venkatesan, P. and Geetha, K. (2008). Larvicidal activity of some Euphorbiaceae plant extracts against *Aedes aegypti* and *Culex quinquefasciatus* (Diptera: Culicidae). Parasitol Res; 102:867-873.
21. Reis, S.R., Valente, L.M., Sampaio, A.L., Siani, A.C., Gandini, M., Azeredo EL, LA D Avila., Mazzei, J.L. Henriques, M.d. and Kubelka, C.F. (2008). Immunomodulating and antiviral activities of *Uncaria tomentosa* on human monocytes infected with dengue virus-2. Int Immunopharmacol; 8:468-476.
22. Roses P. Guava Leaf Extract Potential Cure Dengue Fever; (2011). Available from: http://www.pinkroses.info/guava-leaf-extract-potential-cure-denguefever.
23. Rothan, H.A., Zulqarnain, M., Ammar, Y.A, Tan, E.C., Rahman, N.A. and Yusof, R. (2014). Screening of antiviral activities in medicinal plants extracts against dengue virus using dengue NS2B-NS3protease assay Tropical Biomedicine; 31(2): 286–296
24. Rothwell, C., Lebreton, A., Young Ng C., Lim, J.Y., Liu, W., Vasudevan S, M Labow., Gu, F. and Gaither, L.A. (2009). Cholesterol biosynthesis modulation regulates dengue viral replication. Virology; 389:8-19.
25. Saha S. and Ghosh, S. (2012). Tinospora cordifolia: One plant, many roles. Anc Sci Life; 31(4): 151–159. doi: 10.4103/0257-7941.107344.
26. Sanchez, I., Garibay, F.G., Taboada, J. and Ruiz, B.H. (2000). Antiviral effect of flavonoids on the Dengue virus. Phytother Res; 14:89–92.
27. Sharma A., Kumar S. and Tripathi P. (2016). Evaluation of the Larvicidal Efficacy of Five Indigenous Weeds against an Indian Strain of Dengue Vector, Aedes aegypti L. (Diptera: Culicidae) Journal of Parasitology Research; http://dx.doi.org/10.1155/2016/2857089
28. Shivakumar, M. S., srinivasan, R. and Natarajan, D. (2013). Larvicidal potential of some indian medicinal plant extracts against *aedes Aegypti*. Asian j Pharma and clinical res; 6 (3).
29. Swathi, S., Murugananthan, G., Ghosh, S.K. and Pradeep, A.S. (2012). Larvicidal and repellent activities of ethanolic extract of *Datura stramonium* leaves against mosquitoes. Int J Pharma Phyto Res; 4(1):25–27.
30. Tang, L., Ling, A.P., Koh, R.Y., Chye, S.M. and Voon, K.G. (2012). Screening of anti-dengue activity in methanolic extracts of medicinal plants. BMC Complement Altern Med;12:3.

31. Titanji, V.P., Zofou, D. and Ngemenya, M.N. (2008). The Antimalarial Potential of Medicinal Plants Used for the Treatment of Malaria in Cameroonian Folk Medicin. African Journal of Traditional, Complementary and Alternative Medicines; 5 (3): 302–321. PMC 2816552. PMID 20161952.
32. World Health Organization (2008). Traditional medicine. Fact Sheet. http://www.who.int/mediacentre/factsheets/fs134/en/