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Anti-dengue Medicinal Plants: A Mini Review.

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Review Article

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ABSTRACT

Dengue is a mosquito-borne infection found in tropical and sub-tropical regions around the world. In recent years, transmission has increased predominantly in urban and semi-urban areas and which has been of major concern to governments and the World Health Organization (WHO). Dengue fever regardless of its serotypes has been the most prevalent arthropod-borne viral diseases among the world population. The development of a dengue vaccine is complicated by the antibody-dependent enhancement effect. Thus, the development of a plant-based antiviral preparation promises a more potential alternative in combating dengue disease. The demand for plant-based medicines is growing as they are generally considered to be safer, non-toxic and less harmful than synthetic drugs. Current studies show that natural products represent a rich potential source of new anti-dengue compounds. Further laboratory investigations are needed established the potential of identified species in contributing to dengue control. This is short review to notice some phytochemical structure from plant sources for dengue fever.

INTRODUCTION

Cause of Dengue Fever and role of virus

During the past five decades 50–100 million new infections are estimated to occur annually in more than 100 endemic countries, with a documented further spread to previously unaffected areas; every year hundreds of thousands of severe cases arise, including 20 000 deaths. The World Health Organization (WHO) estimates that 50–100 million dengue infections occur each year and that almost half the world's population lives in countries where dengue is endemic, currently close to 75% of the global population exposed to dengue are in the Asia-Pacific region [1].

Dengue is fast emerging pandemic-prone viral disease in many parts of the world. Dengue fever virus (DENV) is an RNA virus of the family *Flaviviridae* and genus *Flavivirus* [2]. The dengue virus genetic material contains about 11,000 nucleotide bases and that code for the three different types of protein molecules (C, pr M and E) that form the virus particle and seven other types of protein molecules (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5) that are only found in infected host cells and are required for replication of the virus [3, 4].There are four strains of the virus, which are called serotypes and to date, four antigenically related but distinct virus serotypes (DENV-1, 2, 3 and 4) have been identified as belonging to the genus *Flavivirus* in the *Flaviviridae* family [5,6,7]. Dengue disease regardless of its serotypes is transmitted from person to person by *Aedes aegypti* and *Aedes albopictus* mosquitoes in the domestic environment [8, 9].

When antibody from the first infection is neutralized, secondary infections by other serotypes can cause more serious infection [10], DENV-2 is known to be more lethal than other serotypes [11] and some studies have revealed that primary infection with DENV-1 or DENV-3 always results in more dangerous disease than infection with DENV-2 or DENV-4 [12]. The full life cycle of dengue fever virus involves the role of mosquito as a transmitter (or vector) and humans as the main victim and source of infection.

In recent past, the current dengue epidemic has become a focus of international public health awareness. Unlike malaria, which is more prevalent in remote areas, cases of dengue are distributed mostly in urban and sub-urban areas [13, 14]. This has made the epidemic more lethal as an outbreak is difficult to control due to highly populated areas in cities, for example Odisha people suffered more in last year and nearly thousands of people were dead by dengue infection.

Overview of studies on plant species used as anti-dengue

Medicinal plants have been traditionally used for different kinds of ailments including infectious diseases. There is an increasing need for substances with antiviral activity since the treatment of viral infections with the available antiviral drugs often leads to the problem of viral resistance and development of a dengue vaccine is complicated by the antibody-dependent enhancement effect. So demand for plant-based medicines is growing as they are generally considered to be safer, cheaper, non-toxic and less harmful than synthetic drugs. A number of natural compounds reported in traditional medicinal plants to have anti-dengue properties were studied and were also screened for anti-dengue compounds structure.

Cladosiphon okamuranus (F; Chordariaceae)
Cladosiphon okamuranus belongs to family Chordariaceae. It is brown seaweed found naturally in Okinawa. A sulfated polysaccharide named fucoidan from Cladosiphon okamuranus was found to potentially inhibit DENV-2 infection [15].The active compound is Fucoidan against dengue.

Leucaena leucocephala (F; Fabaceae)
Leucaena leucocephala belongs to family Fabaceae. Galactomannans extracted from seeds of Leucaena leucocephala have demonstrated activity against yellow fever virus (YFV) and DENV-1 in vitro and in vivo and L. leucocephala show protection against death in 96.5 % of YFV-infected mice [16].

Mimosa scabrella (F; Fabaceae)
Mimosa scabrella belongs to family Fabaceae and Galactomannans extracted from seeds of Mimosa scabrella have demonstrated activity against YFV and DENV-1 in vitro and in vivo [16].

Tephrosia madrensis (F; Fabaceae)
Tephrosia madrensis also belongs to family Fabaceae and Glabranine is the main active compound for dengue fever treatment [17]. The flavonoids isolated from T. madrensis, glabranine and 7-O-methyl-glabranine exert strong inhibitory effects on dengue virus replication.

Cryptonemia crenulata (F; Halymeniaceae)
Cryptonemia crenulata belongs to family Halymeniaceae. It is a marine species found throughout the Indian Ocean Islands, Southeast Asia and Pacific Islands. The sulfated polysaccharides from Cryptonemia crenulata, i.e., galactan were selective inhibitors of DENV-2 multiplication [18].

Gymnogongrus torulosus (F; Phyllophoraceae)
Gymnogongrus torulosus belongs to family Phyllophoraceae. It is red seaweed found in Australia and New Zealand. Gymnogongrus torulosus was investigated for its in vitro antiviral properties against DENV-2[19].

Houttuynia cordata (F; Saururaceae)
Houttuynia cordata belongs to family Saururaceae. It is herbaceous perennial flowering plants growing between 20 and 80 cm, and is native to Japan and Southeast Asia. The hyperoside was the predominant bioactive compound,and was likely to play a role in this inhibition action against DENV-2[20].

Meristiella gelidium (F; Solieriaceae)
Meristiella gelidium belongs to family Solieriaceae. It is a marine species found in Atlantic Islands. The antiviral activity of kappa carragenan in Meristiella gelidium was evaluated against DENV-2[21].

Boesenbergia rotunda (F; Zingiberaceae)
Boesenbergia rotunda belongs to family Zingiberaceae. It is a medicinal and culinary herb known as Chinese ginger.The activity of some compounds extracted from B. rotunda for the inhibition of dengue virus protease has been tested on DENV-2[22].

Zostera marina (F; Zosteraceae)
Zostera marina belongs to family Zosteraceae. It is an aquatic plant known as eelgrass and is native to North America and Eurasia. A compound from the temperate marine eelgrasss Zostera marina has been identified as possessing antidengue virus activity [23].

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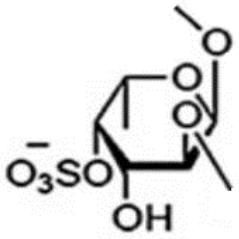
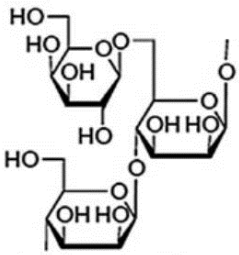
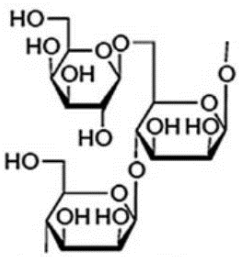
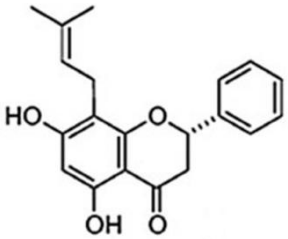
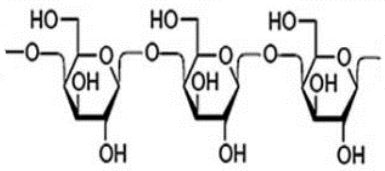
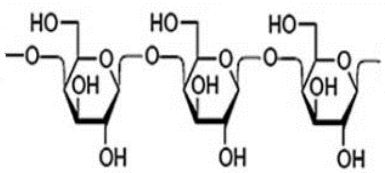
Myrtopsis corymbosa (F; Rutaceae)
Myrtopsis corymbosa belongs to family Rutaceae. Compound ramosin, myrsellinol and myrsellin are the main active compound of M. corymbosa from its bark. The bark extract is the strongest and even inhibits 87% of DENV polymerase [24]. Alkaloids content of leaves were also investigated compounds identified as skimmianine, γ-fagarin and haplopin but isolated alkaloids were only slightly active against the DENV-NS5.

Plants compounds structure and their anti-dengue activity

Plants from which extracts have been prepared and tested to detect inhibition activity against DENV are listed in Table 1. The active compounds showed a wide range of activity against DENV. The isolated products belong to various chemical classes such as sulfated polysaccharides, flavonoids, quercetin and natural chalcone compounds. The chemical structures of these different phytochemicals isolated from different plants.

Table 1

Family	Species	Compound isolated	Compound structure
Chordariaceae	*Cladosiphon okamuranus*	Fucoidan	
Fabaceae	*Leucaena leucocephala*	Galactomanan	
Fabaceae	*Mimosa scabrella*	Galactomanan	
Fabaceae	*Tephrosia madrensis*	Glabranine	
Halymeniaceae	*Cryptonemia crenulata*	Galactan	
Phyllophoraceae	*Gymnogongrus torulosus*	Galactan	

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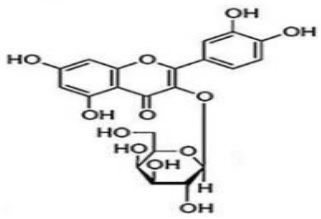
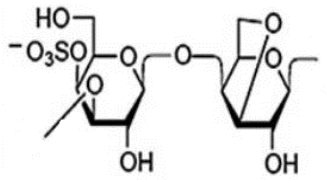
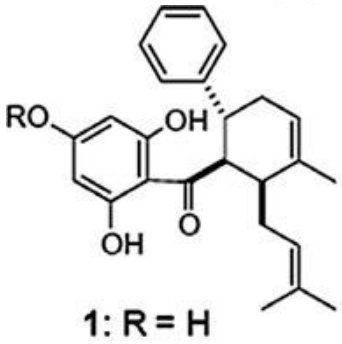
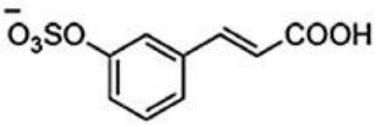
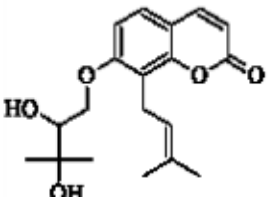
Saururaceae	*Houttuynia cordata*	Hyperoside	
Solieriaceae	*Meristiella gelidium*	Kappa carrageenan	
Zingiberaceae	*Boesenbergia rotunda*	4-hydroxypandurat in A	
Zosteraceae	*Zostera marina*	Zosteric acid	
Rutaceae	*Myrtopsis corymbosa*	myrsellinol	

CONCLUSION

This review has covered only 11 species and their potential active compounds that could be used in the treatment of dengue. The available research highlights the information available for various parts and extracts types of medicinal plants for the treatment of dengue. The present review is about all the prominent pharmacological activity of plant compounds against dengue. Moreover, such discoveries review may lead to the development of highly efficient and safe anti-dengue treatments and great impact on future viral research along with interesting for isolation of more and more natural compounds for medical treatment.

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