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POTENTIAL THERAPEUTIC EFFECT OF ANTI-DENGUE MEDICINAL PLANTS: A DETAILED REVIEW

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ABSTRACT

One of the viral infections spread by mosquitoes that is quickly infecting people is dengue fever. Particularly in tropical and subtropical areas of the world, it has high mortality and morbidity rates. The question of whether dengue infection is endemic in Guangdong has been brought up because dengue has been a continuous pandemic in Guangdong from its initial outbreak in Foshan, Guangdong province, China, in 1978. The study's entire foundation is made out of secondary data sources, including relevant publications, governmental bodies, and related papers. Due to the dramatic rise in cases, complications, and severity, there may be an epidemic danger. Aedes is the name of the species of mosquito that transmits dengue. Depending on how severe they are, medical symptoms can be anything from trivial to fatal. Only a few of the many variables that affect the dengue virus's ability to spread include topography, rainfall, temperature, rapid urbanization, and globalization. Due to its rapid global development, the lack of a specific treatment, an accessible technology for early infection diagnosis, and an effective vector control system, it is a problem of the utmost concern for public health. Dengue treated with numerous herbs some of these are explained in this manuscript.

Keywords: Aedes, Clinical Symptoms, Depression, Febrile Illness, and Treatment.

INTRODUCTION

The World Health Organization (WHO) ranks infectious diseases as the sixth most common global cause of mortality. Infectious diseases that are still emerging and reemerging continue to worry the entire population. Viral infections brought on by a variety of both old and novel viruses have, among other infectious diseases, presented a severe threat to human life. Viral illnesses continue to be one of the main killers on a global scale [1]. It's terrible that more people are receiving these diagnoses each year. The worst viral infections, according to Nicastri et al. (2019), are dengue fever, Ebola, AIDS, which claimed 1.1 million lives globally, and influenza, which kills between 300,000 and 500,000 people each year [2]. As a result, the primary objective of medical research is to create effective antiviral regimens that are affordable and may also contain additional medications derived from herbal sources [3]. The introduction of new virus strains, a growth in antiviral drug resistance, and the general non-specificity of the bulk of antiviral drugs now available on the market are the main causes of this [4]. There are already antiviral vaccinations available to protect against the human papilloma virus, varicella, measles, mumps, and rubella [5]. There are further viral diseases for which vaccines are still unavailable [6].

Dengue, which is spread by mosquitoes, is the most prevalent virus carried by an arthropod worldwide.

During the last two decades, dengue cases have skyrocketed. The disease is currently widespread throughout numerous continents. Acute capillary permeability and bleeding are observed in a small number of people who have already been exposed to one subspecies of the dengue virus. Dengue hemorrhagic fever is the name for this illness [7,8]. Tropical and subtropical regions have experienced severe economic hardship as a result of the viral disease dengue fever [9]. Over 300 million occurrences are reported annually, and as a result, about 22,000 people pass away [10]. Over 2.5 billion people are affected by dengue disease worldwide [11]. Out of the more than 100 nations where the endemic disease is present. Recently, dengue cases dramatically increased and are now regarded as pandemic [12]. Between 1960 and 2017, nearly 20 African countries were affected by an outbreak. Many epidemics, however, go unnoticed for a very long time [13]. Dengue virus seems to be the most deadly of the four diverse but antigenically comparable serotypes of flavivirus. The disease, which is spread by female Aedes aegypti mosquitoes, is common in urban and semi-urban regions. After the virus enters the human body, between 3 and 14 days, is marked by the onset of mild to severe symptoms. Early warning signs include headache, fever, and severe joint and muscular discomfort. It requires both standard care for general fever and extra symptomatic medicines to manage it. Dengvaxia, the first dengue vaccine, recently acquired clinical use approval. But research suggests that those who have never had DENV may be more at risk of getting severe dengue fever as a result of the vaccination, raising questions about its safety [14].

1.1 Pathophysiology

Dengue fever is caused by any of the four Flavivirus single-stranded RNA viruses, with a lifetime immunity to a specific serotype. Up to 75% of patients show no symptoms, while only 0.5-5% progress to severe stages [15]. Without proper treatment, the fatality rate might be more than 20%. The main victims of them are children. Usually lasting 4 to 7 days, the disease's incubation period can last anything from 3 to 10 days. Less frequently do signs of dengue fever occur more than two weeks after exposure [16]. What exactly transpires following a mosquito bite that infects the skin with the dengue virus is uncertain. First targets seem to be dendritic cells and skin macrophages. The diseased cells could then proceed via the lymphatic system to other organs after reaching the lymph nodes. Maybe viralemia existed for 24 to 48 hours before the symptoms started to show. Mild, normal, or severe infection relies on how this complex host-viral interplay plays out. The most likely reasons of severe dengue fever, which presents as shock syndrome and increased microvascular permeability, are a second infection with an other serotype of the virus and the patient's immune system.

Even when just one viral serotype is present, a serious dengue disease can still occur. Microvascular permeability often worsens as virus titers decrease as shown in figure 1 [17].

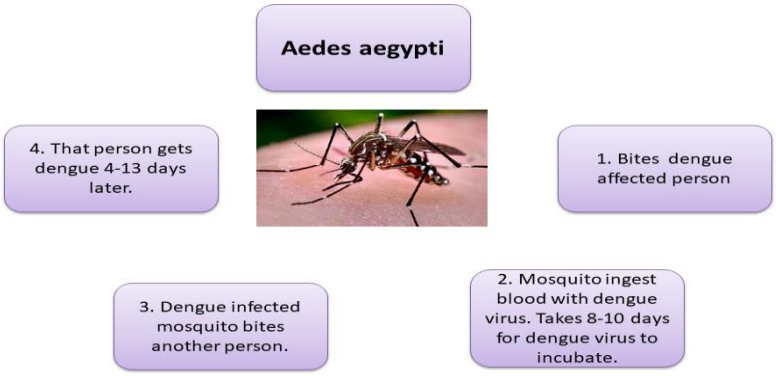

Figure 1 (pathophysiology) (I am the author of this figure)

1.2 Environmental factor for dengue fever

Low socioeconomic status, inadequate water supply, high population density, improper solid waste management, and climate change have all been identified as significant risk factors for dengue and severe dengue. Environmental factors that are important for the development of dengue include temperature, humidity, and precipitation [18].

The main dengue vector thrives in urban environments, congregating close to people and reproducing in tiny containers that catch rainwater and water storage tanks.

The natural ecology is instantly impacted by global temperature change, which also accelerates the spread of disease vectors. Dengue is the most prevalent of these illnesses.

We were able to show that temperature peaks corresponded to dengue epidemic peaks, despite statistical research not establishing a link between temperature and dengue cases. It would be fascinating to conduct further research on how environmental pollution affects the Aedes aegypti mosquito's growth at every stage of its life cycle and to improve monitoring methods like campaigns and surveillance [19].

1.3 Aedes

Over the past 50 years, Aedes Aedes-borne diseases like dengue, Zika, chikungunya, and yellow fever have either reemerged or spread abroad as depicted in figure 2.

Figure 2 (Aedes)

Around 390 million human illnesses are brought on by the dengue virus each year, which is also to blame for the early 2000s resurgence of yellow fever in Africa and the Americas, the global spread of chikungunya, zika, and other diseases [20]. International trade, haphazard urbanization, on the part of the local government, and the ineffective execution of vector control programs due to a lack of human, financial, and infrastructure resources are all factors that contribute to the spread of these diseases [21]. The Asian tiger mosquito (Aedes albopictus), which has temperate and tropical strains, and the tropical yellow fever mosquito (Aedes aegypti) are the main vectors of all the viruses that cause these disorders [22]. Dengue is projected to cause annual economic losses of at least $9 billion in the United States [23,24].

2. Symptoms of dengur fever (physical, clinical, etc)

Dengue has three stages: feverish, critical, and recovering.

The sudden, high-grade fever that defines the febrile phase usually lasts two to seven days. Six percent of cases have saddleback or biphasic fever, most often in those with severe dengue and DHF. Before the second and at least second-longer fever spike starts, the first one lasts for at least one day. Anorexia, flushing of the face, headaches, sore throats, conjunctival injections, myalgias, arthralgias, nausea, and vomiting are examples of concomitant symptoms. An alternative is that a subsequent maculopapular rash could appear within a day [25].

The crucial time is marked by defervescence, which occurs on days three through seven when the temperature is between 37.5 and 38 C or lower. Related to it is increased capillary permeability. Usually, this phase lasts one or two days. The critical phase has started when the platelet count quickly drops, the hematocrit rises, and warning symptoms appear. This could lead to shock, organ failure, widespread intravascular coagulation, or hemorrhage as fig. 3 illustrates.

Over the healing process, extravascular fluid gradually drains over two to three days. Bradycardia will now strike the sufferer [26].

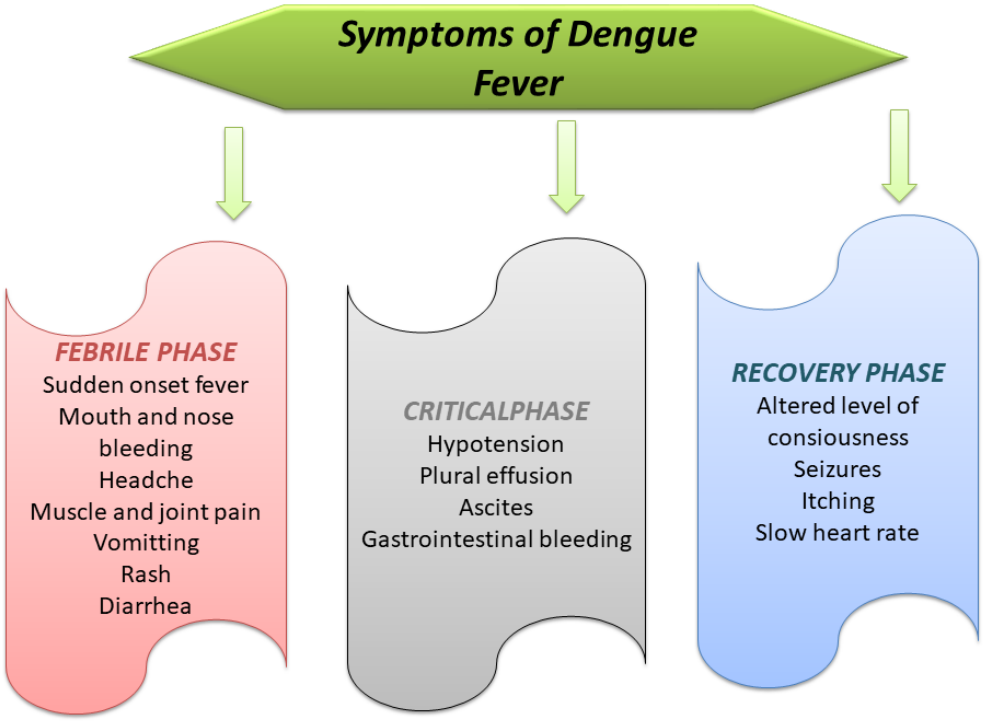

Figure 3 (symptoms) (I am the author of this figure)

Expanded dengue syndrome refers to the symptoms that patients may experience when the nervous system, liver, kidneys, or other isolated organs are impacted by dengue. It could result from a tremendous shock. Cerebral hemorrhage, encephalitis, aseptic meningitis, and febrile seizures in youngsters are only a few neurological signs. Signs of gastrointestinal involvement and other symptoms that it may exhibit [27].

3. Evaluation

Thrombocytopenia, leukopenia, and increased aspartate aminotransferase levels are frequent test results. The condition is categorized as severe dengue or dengue [28].

3.1 Criteria for Dengue Include

The patient lives in or is visiting a region where dengue fever is an endemic illness. Among the symptoms include a fever, myalgias, leukopenia, rash, arthralgias, and a positive tourniquet test.

• Consistent vomiting, pleural effusion, ascites, lethargy, mucosal bleeding, an enlarged liver measuring more than 2 cm, an increase in hematocrit, and thrombocytopenia are some of the symptoms of dengue.

• Severe Dengue: An highly serious case of dengue fever that is accompanied by bleeding, transaminitis (more than 1000 I.U./liter), impairment of consciousness, cardiac dysfunction, and pulmonary dysfunction [29]. Preeclamptic and dengue symptoms might be somewhat similar, thus it is important to assess pregnant dengue patients.

4. Treatment / Management

When treating dengue, the patient's disease stage is taken into consideration. For individuals who appear early and without any warning symptoms, treatment choices include acetaminophen and adequate oral fluids. These patients need to be informed of the warning indicators and instructed to see the hospital right away if they appear. When a patient displays warning signs, IV crystalloids can be started; the fluid dosage is then changed in accordance to the patient's response. Platelet transfusion is an alternative when there is a significant danger of bleeding. [30]. A major

illness's beginning cannot be predicted by a scientific test.

4.1 Treatment: plant vs dengue fever

Different tribes all over the world employ a variety of herbs from the Lamiaceae family to cure DENV infection. However, as shown in Table 1.

Table 1. Ethnomedicinal plants for the treatment of dengue fever.

Plants	**Parts used**	*Details of study*	*References*
Hippophae rhamnoides L. 	Leaves extract	In vitro test against type-2 dengue virus indicates that extract is highly anti-dengue.	*31*
Carica papaya L. 	Leaves extract	Increasing platelet count in dengue patients and disease control.	32
Solanum virginianum L. 	Leaves decoction along with pepper and ginger	Used by gilgit community.	33

Tinospora cordifolia L. 	Stem decoction	Used by Gujjar community .	34
	Stem decoction	Employed by locals and tribes.	
	Stem and leaves	Employed by locals and tribes.	
Ocimum sanctum L. 	Leaves	Apparently used as a leaf decoction.	35
	Leaves	Apparently used as a leaf decoction.	
Andrographis paniculata L. 	Whole plant	In many places, traditional healers use it.	36
Alternanthera sessilis L.	Whole plant	In many places, traditional	37

		healers use it.	
Achyranthus aspera L. 	Whole plant	In many places, traditional healers use it.	38
Calotropis procera L. 	Leaf and bark	In many places, traditional healers use it.	39

Solanum xanthocarpum L. 	Whole plant	In many places, traditional healers use it.	40
Plectranthus vettiveroides L. 	Whole plant	In many places, traditional healers use it.	41
Brassica juncea L. 	Whole plant	In many places, traditional healers use it.	42
Adhatoda vasica L.	Leaves extract	use in formulation	43

			
Euphorbia hirta L. 	Whole plant	Use in traditional healers	44
Cassia fistula L. 	Root	use as tonic	45
Swertia chirata L.	Whole plant	use as decoction	46

			
Datura metel L. 	Leaves	use as decoction	47
Coriandrum sativum L. 	Leaves	use as decoction.	48
Peganum harmala L.	Powdered seed	use as decoction	49

			
Abutilon indicum L. 	Whole plant	use as decoction or infusion	50
Cissampelos pareira L. 	Whole plant	Effective against all four serotypes.	51
Azadirachta indica L.	Leave extract	In vitro and in vivo study done against dengue virus	52

			type-2 showed positive effect in reduction of virus. Used by tribal and traditional healers.	

Conclusion

High rates of death and morbidity are associated with the viral infection dengue fever, which is carried by mosquitoes. Due to the sharp increase in cases, complications, and severity, it has been questioned if dengue infection is endemic in Guangdong. It is crucial to be aware about the various clinical presentations and laboratory investigations in order to create a differential diagnosis, start the right course of treatment, and avoid related issues. Several tilapia feeding programs take advantage of ignorance. A literature search turned up about twenty-two plants that were suggested for use as dengue fighters. Nevertheless, only two or three plants or extracts have undergone scientific testing and demonstrated efficacy. In order to fully utilise their anti-dengue potential, it is necessary to find more herbal formulations that are being used locally, accurately document them, and validate them scientifically to confirm efficacy, understand mechanistic action, and ensure safety. Low hanging fruit, or herbal formulations that have the potential to be used by communities and healers, may offer adjuvant or alternative medicine if the right procedures for product development, value addition, and validation are followed.

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