

Review Article

CANNABIS SATIVA: DENGUE VIRAL DISEASE- VECTOR CONTROL MEASURES

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ABSTRACT

This review paper highlights medicinal applications of Cannabis sativa particularly used in the form of Cannabis oil as a dengue mosquito repellent. Various tropical and subtropical countries are home to Aedes aegypti (Ae. aegypti), a vector of dengue fever. Dengue is a mosquito borne disease caused by any of the 4 known serotypes of the dengue virus (DENV1-4). Dengue and the more severe dengue hemorrhagic fever (DHF) have been a very critical public health problem globally. Millions of people especially in the tropical areas get infected with dengue. Dengue fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) represented a spectrum of disease resulting from infection with the dengue virus, which is transmitted primarily by the female mosquito, Aedes aegypti. The spectrum of clinical illness varied from mild symptoms such as fever to death. Cannabis sativa also finds mentions in Ayurveda text as Desi 'Vijaya' and has been recommended for its medicinal properties. Traditional healers with rich knowledge of medicinal plants have been exploited for the purpose of treatment of many patients in the rural parts of India. Essential oils are considered to be potent against a diverse range of viral, fungal and bacterial pathogens. However, clinical trials supporting dengue mosquito repellent activity of Cannabis oil is lacking. Therefore, further research should focus on exploring the molecular mechanisms of essential oils and their individual chemical compounds.

Keywords: Aedes aegypti, antiviral, Cannabis sativa, dengue, Essential oil, India.

INTRODUCTION

Dengue is a mosquito-born viral infection which is one of the serious threats to human population and economic burden in tropical and sub-tropical region particularly in Asia (1-15). The severity of dengue fever is further amplified by the lack of treatment. Dengue is a mosquito-borne viral infection caused by four distinct but closely related virus serotypes (DENV-1, DENV- 2, DENV-3 and DENV-4) which are classified under the genus Flavivirus, family Flaviviridae (1-15). The viral infection causes flu-like symptoms and can develop into a potentially fatal form of the disease – dengue haemorrhagic fever (DHF) which eventually leads to dengue shock syndrome (DSS) (1-15). All dengue virus serotypes are pathogenic affecting particularly children and young adults but virulence of the dengue serotypes can differ (1-15). Dengue viral infection occurs by an infected female of Aedes genus especially Aedes aegypti or Aedes albopictus mosquito to the human host (1-15). Dengue mosquito's breed in water and vector control programs are not yet successful in preventing uncontrolled spread of the virus vector. Female Aedes aegypti mosquito is also a major responsible vector for other viral infectious diseases like chikungunya, Zika virus, and Ebola virus diseases too(1-15). Epidemic dengue is one of the leading arthropod-borne viral disease causes an acute febrile illness known as dengue fever (DF) followed by dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). Dengue induced thrombocytopenia is life threatening and a major health disorder resulted in the lower platelet count in patients with dengue fever (DF) (1-15).

Dengue virus disease is endemic in more than 100 countries including India leading to the death of 390 million people with children in dengue endemic region (1-15). The common dengue virus diseases symptoms are sudden onset of high fever accompanied by abdominal pain, nausea, cold, headache, pain in the neck, eyes, myalgia and arthralgia, flushing of the face, anorexia (1-15). Laboratory abnormalities may include leukopenia and thrombocytopenia (1-15). Warning signs of severe dengue include abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy or restlessness, liver enlargement of >2 cm, or an increase in haematocrit concurrent with a rapid decrease in platelet count (1-15). Criteria for severe dengue include any sign of severe plasma leakage leading to shock or fluid accumulation with respiratory distress, severe bleeding, or severe organ impairment (1-15). There are numerous dengue vaccine candidates in pipeline throughout world including India but none of them not yet promoted vaccination. The serotype characterization of dengue has made a very difficult task for the development of a dengue vaccine (1-15). Till today there is no treatment or medicine for controlling the dengue fever and except Dengvaxia which is not enough for the protection from infection of all the four serotypes of dengue (1-15). Dengvaxia (CYD-TDV) confirmed unbalanced protection against the different dengue serotypes and increased risk for haemorrhagic disease particularly among children (1-15). In the following section the herbal medicine treatment of dengue has been updated and discussed.

DENGUE: HERBAL MEDICINE TREATMENT

Medicinal plants plays an important role in primary health care and therefore, becomes an integral part of human life to combat

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many diseases (16-19). India and Brazil (Amazon Forest) has a rich diversity of herbal medicine which is used in traditional ethno medicine. Indian rural population still depends upon herbal medicine for the treatment of various viral fevers including dengue virus disease because of its cost effectiveness and easily availability (16-19). Therefore, Indian traditional/folk medicine system known as **Ayurveda** plays an important role in controlling many viral infections including dengue disease (1-37). Hence new antiviral medicines of botanical origin could be easily accepted, being non-toxic and inexpensive. Herbal medicines of antiviral activity are of great interest and have been widely explored (16-19). Plant based antiviral compounds can block or inhibit dengue virus replication cycle by interfering with virus attachment to cells, interfering with viral enzymes or suspending dengue viral genome replication. In India, traditional use of herbal medicines known as *Ayurveda* is being passed from one generation to generation due to many reasons such as availability, acceptability, compatibility, and affordability (16-19). *Ayurveda* is the most ancient Indian science of life having a holistic health approach. *Ayurvedic* system of medicines is one of the world's oldest use of herbal medicines which was originated and practised in India more than 5000 years ago and remained one of the best solution for many human health ailments (16-19). Therefore, *Ayurvedic* science is dynamic and progressive (16-19). Traditional healers with rich knowledge of medicinal plants have been exploited for the purpose of treatment of many patients in the rural parts of India. It is one of the age-old tradition of using plant-based-medicines for preventive and curative healthcare in India. In India dengue fever is currently being managed by clinicians through various adjuvant and alternative therapeutic options (16-19).

Carica papaya is not only consumed as a nutritious and delicious fruit but also used as a chief and the best herbal medicine for many health disorders (12). On the basis of experimental studies, clinical data and pilot studies, the **Carica papaya** leaf extract could help to increase platelet levels in patients suffering from dengue (12). All these studies strongly confirmed antiviral properties of *Carica papaya* and supported a strong scientific evidence for the treatment of dengue (1-19). Therefore, the use of *Carica papaya* leaf extract (**Caripill**) in the management of thrombocytopenia associated with dengue is significant and considered as an alternative herbal medicine for dengue (12).

CANNABIS OIL: DENGUE MOSQUITO REPELLENT

Cannabis sativa belongs to *Cannabiaceae* as a medicine was used before the Christian era in Asia, mainly in **India**, China, Bhutan, Nepal, Afghanistan, Pakistan and Iran, and Persians (20-36). Cannabis has been used for thousands of years for recreational, medicinal, or religious purposes (20-36). Cannabis is also a wild noxious weed with notorious psychoactive principle (THC) found growing in all the parts of India. Cannabis has a long history in India, recorded in legends and religion. It was found in various habitats ranging from sea level to the temperate and alpine foothills of the **Indian Himalaya Region** from where it was probably spread over the last 10,000 years (20-36). Many historians believed that **Indian Himalayan Region** was the centre of origin of *Cannabis sativa* and *Cannabis indica* (20-36). Tribal people in the Himalayan region used Cannabis as a homemade herbal medicine for many diseases. During, Covid-19, the infusion of Cannabis flower with a morning cup of tea has saved the life of many people. Cannabis has been used for centuries as a medicine in the treatment of a variety of inflammatory disorders including rheumatic arthritis (RA), gastrointestinal (GI) diseases such as Crohn's disease (CD) and inflammatory bowel disease (IBD), and other GI problems such as anorexia, emesis, abdominal pain, diarrhea, and diabetic gastroparesis (20-36). The

large number of compounds found in Cannabis spans many chemical classes including phytocannabinoids, nitrogenous compounds, amino acids, proteins, enzymes, glycoproteins, hydrocarbons, simple alcohols, aldehydes, ketones and acids, fatty acids, simple esters and lactones, steroids, terpenes, non-cannabinoid phenols, flavonoids, vitamins, and pigments (20-37).

According to **Ayurveda** in India, the medicinal value of the Cannabis plants was well documented more than 5,000 years ago (20-36). This was the first Indian evidence to support the medicinal value of Cannabis plants which was well documented in **Ayurveda** in India (1-300). **This was the first hand information** about the medicinal value of Cannabis (20-36). The earliest written reference to Cannabis in India may occur in the *Atharvaveda*, dating to about 3000 BCE (20-36). Cannabis also finds mentions in *Ayurveda* text as **Desi 'Vijaya'** and has been recommended for its medicinal properties. In the traditional pharmacopeia of human history, both recreational and medicinal uses of the Indian *Cannabis sativa* L. have been described for several centuries (20-36). Introduced into Western medicine by William O'Shaughnessy in 1838 to treat a variety of conditions, including rheumatic pain and epilepsy, the use of Cannabinoids (CBs) in clinical practice entered a period of latency and oblivion due to political barriers and problems in establishing quality control (20-36, 37).

Local traditional healers in the rural part of India used Cannabis oil as the dengue mosquito, **Aedes aegypti** repellent. Cannabis oil was used as dengue mosquito repellent for controlling **dengue viral fever**, bacterial infections and fungal diseases (20-36). However, clinical reports and experimental studies have been lacking for supporting Cannabis oil as the best dengue mosquito repellent and further studies are warranted. Herbal plants are a natural source of many important phytochemicals and widely used in the pharmaceutical, food and cosmetic industries (16). Cannabidiol (CBD) and Cannabinol (CBN) can alter the functional activities of the immune system (20-36). Many inflammatory conditions are associated with dysfunction of the immune system (20-37).

According to one of the study reported, four essential oils, Lemon, Lavender, Peppermint, and Neem, were tested for larvicidal efficacy against the dengue fever vector *Aedes aegypti* larvae under laboratory conditions using dipping bioassay techniques (38). Among the essential oils tested, lemon, peppermint, and lavender oils showed high larvicidal activity against larvae of *Aedes aegypti*. Lemon oil showed the highest effects (LC₅₀ 10.676 ppm), while Peppermint, Lavender and Neem oil showed the lowest effects (LC₅₀ 21.380, 29.818 and 38.058 ppm, respectively) (38). As a result, the mixture of lemon oil (LC₅₀) with Peppermint oil (LC₂₅) showed the highest co-toxicity factor, whereas the mixture of Lemon oil (LC₅₀) with Diesel oil (LC₂₅) showed the lowest co-toxicity factor (38). Based on the results of this study, it appears that essential oils may be useful as larvicides against *Aedes aegypti* larvae (38). By using these insecticides, there is an effective control measures of the pest but their frequent use has become a danger to the biological ecosystems and thus the widespread development of resistance (38).

Hemp has historically been attractive for its top-quality fiber and edible oil. Hemp fibers are used in paper, carpeting, home furnishing, construction materials, insulation materials, hempcrete, auto parts and composites. The female inflorescence is the main product of Medical Cannabis sativa (marijuana or drug type). Cannabis sativa has developed full of glandular type of trichomes (20-37). Phytocannabinoids are produced and stored in glandular trichomes, located all over the aerial part of the plant. Phytocannabinoids possess therapeutic, antibacterial, and

antimicrobial properties (20-37). The nutritional value of hemp is attracting special attention since hemp seed protein and oil is used in treatment of several human diseases (20-37).

Plant essential oils are valuable natural products, and used as a raw materials in aromatherapy, phytotherapy, perfumery, cosmetics, spices and nutrition (16). Essential oils are odorous and volatile compounds found in plants and are stored in special fragile secretory structures, such as glands, secretory hairs, secretory ducts, secretory cavities or resin ducts (16). Aromatic plants produced a diversity of chemical constituents with the potential to inhibit viral replication (16). Essential oils of plants are hydrophobic, soluble in alcohol, non-polar or weakly polar solvents but only slightly soluble in water (16). Essential oils have the ability to hamper the growth of a diverse range of pathogens because of the presence of natural compounds produced by the organs of plants. Importantly, the unique aroma and other bioactive properties of an essential oil depends on its chemical constituents (16). Essential oils have several biological properties such as antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, wound-healing and anti-cancer effects in *in vitro* and *in vivo* (16). Therefore, essential oils have been analyzed and described as good antiviral agents against respiratory tract viral infections, hence are excellent prospective candidate against dengue virus (16). Thus, essential oils and their constituents can hopefully be considered in near future for more clinical assessment and possible applications in controlling the dengue pandemic (16). Essential oils are among the plant-derived antiviral molecules that are being employed in phytomedicine, and are considered as prospective drug candidate against (16). Therefore, essential oils should be created as potential natural pesticides for *Aedes aegypti* larvae integrated pest control, although oil mixes must be further assessed for human safety and activity.

CONCLUSION

Cannabis, or marijuana, has potential therapeutic and medicinal properties related to multiple compounds, particularly Δ -9-tetrahydrocannabinol and Cannabidiol (CBD). Cannabis oil has been used as a dengue mosquito repellent by the local traditional healers as a **vector control measures** in India. Plant based essential oils are comprised of a complex mixture of volatile phytochemicals from diverse classes including monoterpenes, sesquiterpenes, and phenylpropanoids. Medicinal plants continue to be the main source of new lead bio-active molecules. Virucidal activity of essential oils, which are lipophilic by nature, is probably due to the disruption of the viral membrane or interference with viral envelope proteins involved in the host cell attachment. The reactivity of essential oils depends upon the nature of their functional groups and orientation. Essential oils are considered to be potent against a diverse range of pathogens. Therefore, further research should focus on exploring the molecular mechanisms of essential oils and their individual chemical compounds. Hence there is a ray of hope in near future for the application of essential oils of botanicals could be used to protect from dengue viral pandemic outbreak. In addition, preclinical and clinical trial evaluations of these essential oils particularly Cannabis oil as agents against dengue have not specifically been conducted, so further investigations related to this are warranted.

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