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Molecular Approaches in Plant Medicine for Tropical Mosquito-Borne Diseases

Arshad H. Rizvi, Mohd. Zahid Rizvi* & Murtaza Abid

Department of Botany, Shia P.G. College, Sitapur Road Lucknow, U.P., India

***Corresponding Author Email:** zahid682001@gmail.com

ABSTRACT

Mosquito is a common insect found in any tropical countries. Several diseases are transmitted by mosquito. The mosquito borne infection becomes important public health problem globally. To control and manage the mosquito borne infectious disease is still the present challenge. For treatment and prevention of mosquito borne infectious disease, the use of medicinal plant is an interesting trend. There are some reports on medical plants for management of mosquito borne infectious disease. Some specific interesting studies are on molecular pathobiology. In this specific chapter, the author specifically summarizes and discuss on the molecular plant medicine for tropical mosquito borne disease.

Keywords: Mosquito, Molecular, infectious disease and Plant.

INTRODUCTION

The insect is the common kind of animal. Many insects are considered medically important. Mosquito is an important insect that can lead several diseases to human beings. The disease that is transmitted by mosquito is considered a vector borne disease. Mosquito is an important vector of several important diseases such as malaria. At present, the mosquito borne infectious disease is still an important public health globally. Naturally, mosquitoes are abundant in tropical zones. Several tropical countries still have mosquito borne infectious diseases as the local public health problems (Benelli et al., 2023).

The diseases caused by mosquito are considered medially important. It is still hard to control the mosquito. In medicine, mosquito can transmit several kinds of pathogens including to parasite and virus. For the virus, the good examples of mosquito borne infections are dengue fever, Chikungunya virus infection, yellow fever, West Nile virus infection and Zika virus infection. For the parasite, the good examples of mosquito borne infections are malaria, filariasis and dirofilariasis. Those important mosquito borne infectious diseases are

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considered high prevalent in several countries in the present day. The tropical countries are well-known as endemic areas of those infectious diseases.

Also, due to the global warming and globalization, there are reports on new emerging tropical mosquito borne infections in non – tropical countries. Several diseases, are considered increased in prevalence and newly emerge in new settings due to the impact of climate change (Rossati et al., 2014). The existence of the new emerging mosquito borne infectious diseases in the new setting can show the expansion of the endemic area of disease and the emerging disease usually becomes the important problem for the new setting to be managed.

The mosquito borne infection has several clinical features. Some cases of mosquito borne infections are serious and might result in death. To early diagnose and manage of the patient is required. For treatment and prevention of mosquito borne infectious disease, the use of medicinal plant is an interesting trend. There are some reports on medicinal plants for management of mosquito borne infectious disease. The usefulness of medicinal plant might be for prevention of the mosquito or treatment of the illness. Research and development for medicinal plant against mosquito borne infectious disease has been continuously done for several years. Some specific interesting studies are on molecular pathobiology. In this specific chapter, the author specifically summarizes and discusses on the molecular plant medicine for tropical mosquito borne disease.

Table 1. Important Mosquito Borne Infection.

Disease	Pathogen	Clinical features
Dengue	Virus	Acute febrile illness with hemorrhagic complications as well as shock in a very severe case
Malaria	Parasite	Acute febrile illness with several possible clinical complications including to neurological problem
Filariasis	Parasite	Lymphatic vessel obstruction and disability, especially at lower limb
Chikungunya	Virus	Acute febrile illness with joint complaint
Yellow fever	Virus	Acute febrile illness with hemorrhagic complications
Zika virus disease	Virus	Dengue like illness with possible neurological complications and teratogenic effect

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How can medicinal plant be useful for management of tropical mosquito borne infection

Similar to other medical problems, there are many reports on the possible advantage of medicinal plants be useful for management of tropical mosquito borne infections. In fact, many medicinal plants has been used by local people as herbal regimens for management of the mosquito borne infection. The local herbal regimen is considered a hidden gem. The local wisdom on using medicinal plant for management of diseases including mosquito borne infection disease can be seen in several tropical countries. If there is a good systematic study by modern technology, the new effective drug for management of mosquito borne infectious disease can be derived. For example, Qinghaosu (*Artemisia annua L.),* a Chinese herb, is the most well-known medicinal plant that has been widely studied for many years (Klayman, 1985). Indeed, Qinghauzu has a very long history in traditional medicine for more than four thousand years. (Hsu, 2006) The antimalarial drug, artemesin is the result from the research and development on this medicinal plant (Li et al, 2003).

In addition to the usage of medicinal plant for pharmaceutical process for development of new drug for treatment of mosquito bone infectious disease, the advantage of the plant is also for prevention of mosquito. In fact, the most effective way for management of mosquito borne infectious disease is the primary prevention by prevention of mosquito bite. There are several means for prevention of mosquito bite such as using bed net, insecticide, etc. The use of medicinal plant for chasing mosquito is considered the interesting trend. The natural product derived from medicinal plant is considered safe and environmental friendly comparing to the hazardous synthesized chemical. The development of new medicinal plant based agent for control of the mosquito is the interesting area for green technology research (Tisgratog et al., 2016).

Molecular plant medicine for malaria

Malaria is considered medically important disease that is still the global public health threaten. In each year, there are still many deaths due to malaria worldwide. This protozoa infection can cause severe febrile illness. The pathogen is the plasmodium parasite transmitted by Anopheles mosquito. After getting bite by mosquito vector, the pathogen will enter into blood stream and directly affect erythrocyte and further cause the clinical illness.

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The diagnosis of malaria usually requires blood test for identifying intracellular parasite within red blood cell (Chandel et al., 2023).

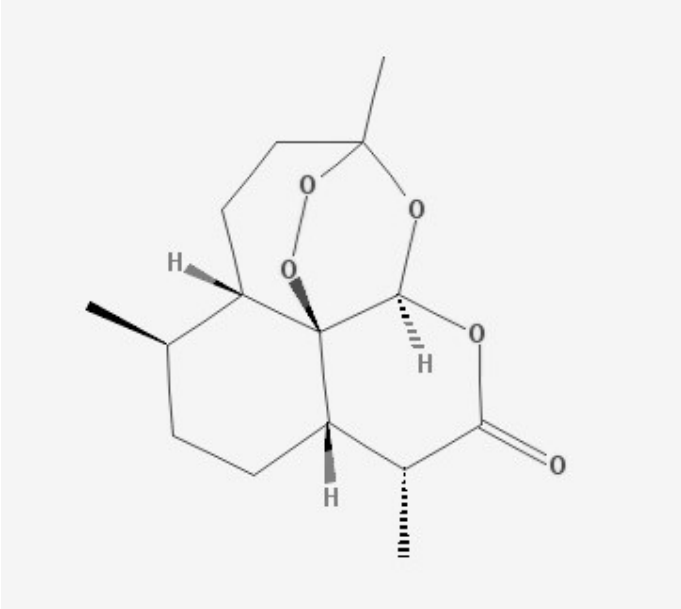


Figure 1. Artimisinin.

As already mentioned, the Qinghaosu is the well-known Chinese herb that was successfully developed into new antiamalarial drugs, artemesin and artemisinin. The molecular structure of the artemesin is well clarified and some derivative are already developed (Lin et al, 1997).In general artemisinin has molecular weight equal to 282.332 gram/mole and has chemical formula as C15H22O.

Regarding the molecular mechanism, Wiwanitkit (2006) performed a quantum chemical analysis and showed that the pharmco-molecular mechanism of artemisinin is composed of two important steps: (a) active ation and (b) alkylation. Focusing on the iron activation possible, two possible pathways (a) 1.5 H-shift and (b) C-C cleavage are mentioned for inducing C-4 free radical production that can be further affect the parasite (Wiwanitkit 2006). Presently, there are still ongoing researches for further improvement of the drug effectiveness. The attempts to extend the application of artemesin for management of other diseases such as leishmaniasis (Want et al, 2017) and cancer (Wong et al, 2017) are also the present trend of molecular research on Qinghaosu.

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Molecular plant medicine for dengue

Dengue is another important tropical mosquito borne infection. This arbovirus infection is highly endemic in several areas of the world including to Southeast Asia and South Asia. The patient usually has high fever and complicated by hemorrhagic episode. To manage the dengue patient, there is still no effective antiviral drug and the fluid replacement therapy is the standard management (Wiwanitkit, 2010). The use of medicinal plant for management of dengue is an interesting issue and there are some phytomedicine researches on dengue. Of several plants, papaya is an interesting plant that is widely mentioned for its usefulness in dengue management (Wiwanitkit, 2013). The papaya extract is reported for its usefulness in management of thrombocytopenia in dengue hemorrhagic fever.In in vitro study, the reduction on platelet aggregation in dengue sera is observable (Chinnappan et al, 2016). The molecular mechanism of papaya against dengue is very interesting and there are some specific reports on this issue. (Aziz et al. 2015) found that papaya extract could induce thrombopoietic cytokines synthesis in cells of hematopoietic and mesenchymal origin which is the explanation for usefulness of papaya leaf for dengue management. (Senthilvel et al. 2013) also found that flavonoid from papaya could inhibitdengue NS2B-NS3 protease and further interfere viral assembly process (da Silva et al., 2024).

Molecular plant medicine for filariasis

Filiariasis is a tropical mosquito borne infection. The main affected organ is the lymphatic system. The infection might be chronic and can result in elephantiasis, which is a permanent disability. There are several species of mosquito vectors that can transmit pathogenic parasite. The early diagnosis and prompt treatment for identified filiariasis patients is important in disease management and control. Since there is an effective antifilarial drug, there are only a few studies on the medicinal plant against filiariasis. An interesting study is by Dutta and Sukul (1982). Dutta and Sukul (1982) found that a wild herb, *Andrographispaniculata*filaricidal properties. However, there is no further study on the molecular pharmacomenism of *A.paniculata*against filarial parasite.

Molecular plant medicine for Chikungunya infection

Chikungunya virus infection is a dengue like tropical mosquito borne infection. The patient might present with acute febrile illness with specific complaint on arthralgia. The specific

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antiviral drug against Chikungunya virus is still not available. The use of herbal regimen against Chikungunya virus is very interesting.

The *A. paniculata* is also reported for usefulness in management of Chikunguna virus infection (Hussain et al., 2024), similar to filariasis. (Wintachai et al. 2015) found that andrographolide from *A. paniculata* could inhibit replication of the virus and mentioned that the andrographolide could be further developed into new antiviral drug against Chikungunya virus infection.

Molecular plant medicine for yellow fever

Yellow fever is a preventable arbovirus infection. The yellow fever vaccination is proven effective primary prevention of the disease. In case that a patient gets an infection, the disease might be severe and the management is usually difficult. There are some herbal regimens that are claimed for usefulness against yellow fever (Ajaiyeoba et al., 2003). However, there is still no systematic evaluation of those regimens.

Molecular plant medicine for Zika virus infection

Zika virus infection is a new emerging infection that becomes the global public health issue at present. The great concern is on the report of abnormal infants with microcephaly born to Zika virus infected mothers. Until present, there is still no *effective* specific treatment for Zika virus infection. The development of new antiviral drug against Zika virus becomes the important issue. On the other hand, the ethnopharmacology research on medicinal plant against Zika virus is very interesting. For example, Clain et al. (2018) reported the possible usefulness of Aphloiatheiformis, a tropical plant seen in tropical African island, extract against Zika virus.

CONCLUSION

The use of medical plant against mosquito becomes infectious disease become the interesting hope in clinical medicine. Many medicinal plants are proven effective for management of the diseases. The molecular mechanism of those medicinal plants is an interesting issue for further researches. With good knowledge on the molecular mechanism of the medicinal plant,

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the development of the new effect drug against tropical mosquito borne infectious disease is expected.

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