

Chapter 13

Anti-Malarial Drug Resistance: Need for Novel Natural Products

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ABSTRACT

Malaria is a life-threatening infectious disease caused by a protozoan parasite of the genus Plasmodium. It is transmitted through the bites of infected female Anopheles mosquitoes. The global burden is estimated to be around 219 million cases in 87 countries. Natural compounds have been used primarily in the traditional medicine for thousands of years. For the treatment of malaria, natural products were used until the development of synthetic drugs, and most of the currently available anti-malarial drugs have been derived based on the compounds from these traditional medicinal plants. The current chapter tries to briefly indicate the emerging resistance against anti-malarial drugs and to discuss the recent research on natural products that have been evaluated for anti-malarial activity. Rigorous evaluation of the efficacy and safety of traditional medicines is required along with identification of active constituents in order to develop new drugs with novel mechanisms of action.

INTRODUCTION

Traditional medicinal systems include various medicinal approaches and practices found at a particular region of the world and were the only system used for treating different types of diseases. These systems can be classified into various categories like Ayurveda, Siddha, Unani, Korean medicine, African medicine system, Irani system and traditional Chinese medicine (Lemonnier *et al.*, 2017). All these systems widely use medicinal plants in different combinations or formulations. In India, traditional systems are still being followed in many regions for treating different ailments. It is eminent that natural products

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have remained a high productive source for drug discovery and development process. Due to lack of modern medicines and medical facilities there is strong belief in the use of traditional medicinal system that relies upon the experience gained over thousands of years in diverse regions of the world (Deepak, 2008). Today, researchers have started to bank upon this vast array of knowledge for the development of modern drugs and have isolated various bioactive compounds including alkaloids, flavonoids, tannins, phenolics, amines, terpenoids, proteins, etc. that have been reported and used for curing various diseases.

Tropical and subtropical neglected infectious diseases such as leishmaniasis, dengue, leprosy, trachoma, lymphatic filariasis, malaria and tuberculosis affect almost one-sixth part of the world's population that resides mainly in non-developed countries. Malaria is one of the infectious diseases, prevalent in countries with low income groups leading to millions of deaths annually. The patients affected with malaria and the public health systems cannot afford the financial return required by most pharmaceutical companies. This leads to minimal interest of pharmaceutical companies for investing in research and development for novel drug development against neglected diseases. Currently, most research is being undertaken primarily by government research and academic institutions.

The main objectives of the proposed chapter is to review the current status of the traditional medicinal system, the development of plant-based anti-malarial drugs, the structure and activity relationships of the pure compounds with antimalarial potential, current status of the active molecules and future prospects of the natural products in antimalarial drug discovery programs.

HERBAL MEDICINE

Natural products are a large assemblage of diverse secondary metabolites with widespread biological activities and are usually obtained from plants, marine animals and microorganisms. These compounds are widely used as medicines, flavoring agents, or recreational drugs. Naturally these secondary metabolites are produced for self-defense, protection, competition, and species interactions (Demain, 2014).

Since prehistoric times, mankind is using medicinal plants for basic preventive and therapeutic health care. This form of knowledge known as “the traditional system of medicine” contains information about a large reservoir of herbal formulations and medicinal plants. Principles developed over the life time in different cultures are used in prophylactic, diagnostic or therapeutic purposes (Sen & Chakroborty, 2015). As per World Health Organization (WHO), around 80% of the global population depends on traditional medicine or drugs obtained from the natural world (WHO, 2002). Adverse effects can be observed if traditional medicines or practices are followed improperly as minor changes in the concentration of metabolites can lead to altered activities (Sen & Chakroborty, 2015). Modern healthcare system finds its roots in the plant based medicines. In countries like United States, one of the four allopathic prescriptions are either purified from plants or synthesized based on plant molecules (Mazid *et al.*, 2012). With the increasing population, allopathic medicines are out of reach from a large section of the communities living in rural and remote areas of the country due to high prices and their side effects. These parameters have led to the increase in popularity of alternative medicines especially among rural, tribal and remote populations.

Malaria is the second most common infectious disease across the world caused by protozoan parasite *Plasmodium* sp., and spread by infected female *Anopheles* mosquitoes. Five different species of *Plasmodium* parasites i.e. *Plasmodium falciparum*, *P. malariae*, *P. vivax*, *P. ovale* and *P. knowlesi* are known to infect humans amongst them *P. falciparum* and *P. vivax* are the most common species that

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