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Review

Recent advances in use of silver nanoparticles as antimalarial agents

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ABSTRACT

Malaria is one of the most common infectious diseases, which has become a great public health problem all over the world. Ineffectiveness of available antimalarial treatment is the main reason behind its menace. The failure of current treatment strategies is due to emergence of drug resistance in *Plasmodium falciparum* and drug toxicity in human beings. Therefore, the development of novel and effective antimalarial drugs is the need of the hour. Considering the huge biomedical applications of nanotechnology, it can be potentially used for the malarial treatment. Silver nanoparticles (AgNPs) have demonstrated significant activity against malarial parasite (*P. falciparum*) and vector (female *Anopheles* mosquito). It is believed that AgNPs will be a solution for the control of malaria. This review emphasizes the pros- and cons of existing antimalarial treatments and in depth discussion on application of AgNPs for treatment of malaria. The role of nanoparticles for site specific drug delivery and toxicological issues have also been discussed.

Contents

1. Introduction

In the year 2000, estimated malaria incidence was approximately 262 million cases worldwide, of which approximately 839,000 resulted in death. However, in 2015, these figures

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declined, with approximately 214 million cases worldwide and 438,000 deaths (WHO, 2015). Although, the number of cases of the diseases was reduced, malaria is still a highly prevalent disease in tropical and sub-tropical countries. It is caused by protozoan parasites belonging to the *Plasmodium* genus. Among hundreds of species, four are of great importance for disease manifestation in humans *viz. Plasmodium malariae*, *P. ovale*, *P. vivax* and *P. falciparum* – all transmitted through female *Anopheles* mosquito bite (Aditya et al., 2013). A single mosquito bite introduces various *Plasmodium* species into the host; and of these different species, *P. falciparum* is the most dangerous and prevalent in Africa and India, accounting for the majority of malaria-related deaths. *P. vivax* has a wider geographical distribution than *P. falciparum* because this species can grow in *Anopheles* mosquito at lower temperatures and can survive at higher altitudes (WHO, 2015).

Malaria is among the world's neglected diseases, which do not only persist in conditions of poverty but also contribute to the maintenance of socio-economical inequality. The affected population has little financial support; therefore, the medical and pharmaceutical industry has no interest in the development of new drugs and treatments, which would result in a limited monetary return. Disease control measures are yet challenging and include: (i) vector control by insecticide utilization; (ii) chemoprevention by compounds that prevent the blood stage infection, and (iii) diagnosis and treatment (WHO, 2015). Treatment regimens often include $\geq$2 associated drugs that cause side effects and have poor patient adherence. The absence of an effective vaccine and mechanisms of resistance to traditionally used drugs and insecticides render it even more critical to control the disease and execute measures for its elimination (Santos-Magalhaes and Mosqueira, 2010).

Due to unavailability of effective treatment strategies, transmission vector elimination is an important tool to control the vector borne diseases. Use of insecticides in malaria endemic areas is essential for protection against the disease because the vector transmission rate is extremely high (Murugan et al., 2015). However, the toxicity of insecticides to humans and the environment has generated pressing need to search for novel antimalarial compounds. In this context, nanotechnology-based products (nanomaterials) would be helpful in the management of malaria. The nanomaterials have a wide range of applications particularly in medicine, which contributes to major advances in the development of materials for increasing drug efficacy, drug delivery, reducing toxicity of compounds and enabling scheduled and sustained release of nanomaterials.

2. Malaria – a major threat

The incidence of pathogens associated with vectors, such as mosquitoes and other insects, are common issues in tropical and sub-tropical countries (Veerakumar and Govindarajan, 2014). Because of typical climatic conditions, such as rising temperature in the most affected areas, and social causes (uncontrolled and disorganized occupation of locations close to forests and mosquitoes breeding sites), malaria is yet a serious health issue. Parasite life cycle is substantially the same in the four *Plasmodium* species that commonly infect humans, including an exogenous sexual phase within *Anopheles* female mosquito and an endogenous asexual phase within the human host.

3. Life cycle of malaria

As previously mentioned, malaria is caused by the transmission of a parasite (*Plasmodium*) by female *Anopheles* mosquito. The malarial infection begins with injection of *Plasmodium* sp. into human body by mosquitoes at the time of blood meal. After infection, the parasite is carried by the circulatory system to the liver and erythrocytes (red blood cells), where it undergoes asexual replication and forms gametocytes. The life cycle of malaria requires two hosts for its completion (Fig. 1). The events occurring in the life cycle are as follows:

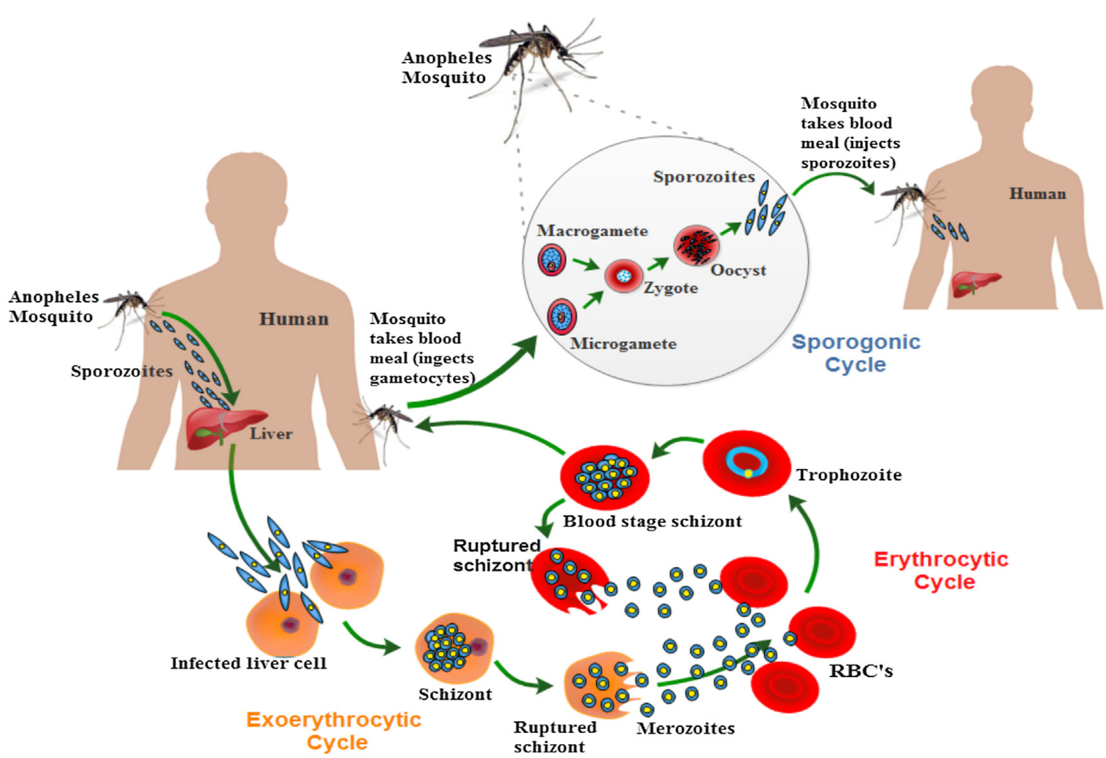

Fig. 1. Different stages of life cycle of malaria parasite.