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Breaking Barriers in Malaria Treatment: How Encapsulation Technology is Revolutionizing Antimalarial Drugs

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Abstract

Malaria remains a major global health challenge, affecting millions of people annually. Despite significant efforts to combat this infectious disease, the emergence of drug-resistant strains and logistical challenges in drug delivery continue to hinder effective treatment. Encapsulation technology includes the encapsulation of active pharmaceutical ingredients in various carriers such as liposomes, nanoparticles, or polymer microspheres. This technique offers several advantages, including increased drug stability, prolonged release kinetics, and targeted delivery to specific cellular compartments. In the field of malaria treatment, encapsulation technology overcomes key challenges such as poor drug solubility, limited bioavailability, and the need for frequent dosing. This article reviews recent advances in encapsulation technology used in antimalarial drugs, highlighting studies that demonstrate drug efficacy, reduced side effects, and increased patient acceptance. In conclusion, encapsulation technology is a promising way to break the barriers in malaria treatment. This innovative approach has the potential to revolutionize the antimalarial treatment landscape by addressing drug resistance, improving drug bioavailability, and increasing access to treatment. Continued research and development in this area is key to advancing the fight against malaria and improving health care outcomes globally.

Keywords: Malaria, Encapsulation, Antimalarial drugs, Plasmodium.

Introduction

Malaria, an infectious mosquito-borne disease caused by Plasmodium parasites, remains a global health challenge, particularly in sub-Saharan Africa and resource-limited regions (Gelband et al., 2020). This life-threatening parasitic disease is widely spread by the female Anopheles mosquito and its transmission is high during hot and humid seasons. These mosquitoes transmit Plasmodium protozoa to the

human bloodstream. There are over a hundred species of the genus Plasmodium, however, only five of them have been shown to infect humans. P. vivax, P. ovale, P. knowlesi, P. malariae, and the most common, P. falciparum (Singh et al., 2013). Despite significant progress in malaria prevention and control efforts, the emergence of drug-resistant strains and barriers to drug delivery have hindered effective treatment. In this context, the integration of advanced technologies becomes necessary to overcome these obstacles and increase the efficacy of antimalarial drugs (Hyde., 2007). One such innovative technology that promises to revolutionize malaria treatment is encapsulation technology. Traditional approaches to antimalarial drug delivery face limitations related to drug solubility, bioavailability, and resistance development. Encapsulation technology by encapsulating active pharmaceutical ingredients in carriers provides a new strategy, which provides a means to address these challenges and revolutionize the malaria treatment landscape (McBride., 2010; Moles et al., 2015). This article reviews the current state of malaria treatment and highlights ongoing challenges and the need for innovative solutions. It then introduces encapsulation technology as an advanced approach with the potential to redefine how antimalarial drugs are delivered and administered. By encapsulating drugs in various carriers such as liposomes, nanoparticles, or polymeric microspheres, this technology offers unique advantages in terms of drug stability, controlled release, and targeted delivery. The purpose of this introduction is to set the stage for further exploration of recent advances in encapsulation technology used in antimalarial drugs. By understanding the current shortcomings in malaria treatment and recognizing the potential of encapsulation to address these issues, researchers and healthcare professionals can appreciate the importance of this innovative approach. Ultimately, the integration of encapsulation technology into the development of antimalarial drugs has the potential to break down existing barriers and provide more effective, accessible, and sustainable solutions for malaria treatment.

Antimalarial drugs

Antimalarial drugs work by killing the parasite in the affected red blood cells. Antimalarial drugs are used to treat and prevent malaria. 1. Artemether/ lume-fantrine: Inhibits nucleic acid and protein synthesis of the parasite via endoperoxide or possibly by inhibition of beta-hematin formation. 2. Artesunate: contains endoperoxide bridge activated by heme iron and leads to oxidative stress. It inhibits protein and nucleic acid synthesis and ultrastructural changes and reduces parasite growth and survival. 3. Atovaquone: inhibits the electron transport chain in the cytochrome bc1 complex and collapses the mitochondrial membrane of the parasite

in Plasmodium. 4. Atovaquone/proguanil: disrupts electron transport and collapses mitochondria, while proguanil inhibits the dihydrofolate reductase enzyme essential for parasite reproduction. 5. Chloroquine: works against erythrocytic forms of Plasmodium. However, the exact mechanism of action is unknown. 6. Hydroxychloroquine sulfate: The exact effect against Plasmodium is unknown. Since it is a weak base, it may affect the acidic vesicles of the parasite and prevent heme polymerization. It may also inhibit other essential enzymes. 7. Mefloquine: a structural analogue of quinine. Although its exact mechanism is unknown, it kills schizonts in the blood. This may increase intravesicular pH in parasites. 8. Primaquine: disrupts the mitochondria of Plasmodium and leads to the death of the parasite. 9. Pyrimethamine: folic acid antagonist, selectively inhibits the plasmodial form of dihydrofolate reductase enzyme and reduces the production of folic acid required for nucleic acid synthesis in the parasite. 10. Quinidine: It is created in the food vacuole of the parasite and forms a complex together and kills Plasmodium from starvation. 11. Quinine: Although the mechanism of action of this drug is unknown. Quinine may disrupt Plasmodium DNA transcription/replication and interfere with hemoglobin digestion. This leads to starvation and death of the parasite. 12. Tafenoquine: Tafenoquine metabolite is active against pre-erythrocytic form in liver and erythrocytic form in blood and gametocytes of Plasmodium and prevents its development and thus prevents malaria recurrence (Marealle et al., 2018; Nahhas et al., 2019).

Reasons for resistance to antimalarial drugs

Several regions around the world have reported an increase in the incidence of Plasmodium drug resistance. Increasing drug resistance of Plasmodium sp is one of the main causes of malaria treatment failure (Rai et al., 2017; L-QuraishAy et al., 2020). In addition, the use of drugs from the same chemical family or with a similar mode of action may exacerbate cross-resistance to antimalarial drugs (Capela et al., 2019; Tse et al., 2019). Studies have shown that molecular mechanisms of resistance to antimalarial drugs occur in several species of parasites and involve polymorphisms in proteins that alter the physiological regulation of the parasite (Menard and Dondorp, 2017; Wicht et al., 2020). The incidence of polymorphisms indicates that resistance to antimalarial drugs is related to the genetic factors of the parasites. Single, double or quadruple mutations in different genes cause the parasite to become resistant to antimalarial drugs. For example, mutations in Pfmdr1, Pfcrt, Pfmrp, and Pfnhe1 genes cause drug resistance (Cubides et al., 2018). Drug resistance can occur through various pathways, such as processes that reduce drug toxicity, some catalytic processes that cause changes in enzymatic reactions, or amplification of the gene encoding the target enzyme or transporter that pumps the drug out of the parasite (Ross et al., 2018). With the progress of molecular biology,

metabolomics and proteomics details of this parasite support the development of new medicinal agents such as nanomedicines (Deda et al., 2020).

What is encapsulation technology?

Encapsulation technology is a process that involves enclosing or enclosing a substance in a protective barrier. In the field of malaria treatment, encapsulation technology is used to improve the delivery of antimalarial drugs. Encapsulation of antimalarial drugs involves the use of specialized carriers or vehicles, such as liposomes or nanoparticles (Figure 1), to protect the drug molecules and enhance their delivery to the target site in the body. These carriers can be designed to release the drug in a controlled and sustained manner and ensure the optimal concentration of the drug at the site of infection (Haas et al., 2009).

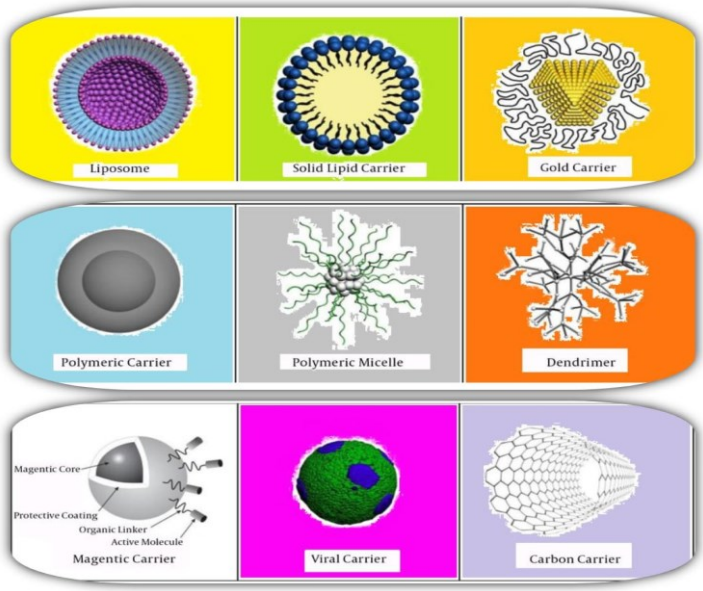

Figure 1. Different Types of Nanocarriers Have Used for Drug Delivery

The role of encapsulation technology in antimalarial drug delivery

Encapsulation technology plays an important role in improving the delivery of antimalarial drugs. By encapsulating drugs, their stability and bioavailability can be increased and the possibility of drug distribution and targeting can be improved. This can lead to increased effectiveness and reduced toxicity of drugs. In addition, encapsulation technology can overcome some of the challenges associated with

traditional drug delivery methods. For example, some antimalarial drugs have poor solubility or are rapidly metabolized in the body. By encapsulating these drugs, their solubility can be improved and their degradation reduced, leading to increased drug concentration and long-lasting therapeutic effects. In addition, encapsulation technology allows the controlled release of antimalarial drugs (Witika et al., 2020). This is especially important for drugs that have a narrow therapeutic window or must be administered in a specific dosing regimen. By controlling the drug release from the encapsulation system, it is possible to maintain the drug concentration in the body in the desired range and ensure the desired therapeutic effects. Encapsulation technology also offers the potential for combination therapy in the treatment of malaria. Multiple antimalarial drugs can be encapsulated in a single carrier, allowing simultaneous delivery of different drugs with complementary mechanisms of action. This can help overcome drug resistance and improve treatment outcomes (Lima et al., 2018).

Advances in encapsulation technology for antimalarial drugs

In recent years, significant advances have been made in the field of antimalarial drug encapsulation technology. Researchers have developed new carriers and delivery systems that offer improved drug delivery and targeting capabilities. One of these advances is the development of liposomal formulations for antimalarial drugs (Pinheiro et al., 2018). Liposomes are lipid-based vesicles that can encapsulate hydrophilic and hydrophobic drugs. They can improve the solubility and stability of drugs as well as increase their targeting to infected cells. Liposomal formulations have shown promising results in preclinical and clinical studies, indicating increased drug efficacy and reduced toxicity. Another development is the use of nanoparticles as carriers of antimalarial drugs. Nanoparticles can be engineered to have specific properties such as size, shape, and surface charge that can influence their interaction with biological systems. By modifying these properties, nanoparticles can be designed to effectively deliver antimalarial drugs to the target site and improve their therapeutic effects (Memvanga et al., 2021).

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Case Studies: Success Stories of Encapsulation Technology in Malaria Treatment

In recent years, significant advances have been made in the field of antimalarial drug encapsulation technology. Researchers have developed new carriers and delivery systems that offer improved drug delivery and targeting capabilities. One

of these advances is the development of liposomal formulations for antimalarial drugs. Liposomes are lipid-based vesicles that can encapsulate hydrophilic and hydrophobic drugs. They can improve the solubility and stability of drugs as well as increase their targeting to infected cells. Liposomal formulations have shown promising results in preclinical and clinical studies, indicating increased drug efficacy and reduced toxicity. Various antiparasitic drugs have been loaded in nanocapsules to reduce drug toxicity such as halofantrine or increase the therapeutic potential of drugs such as primaquine, atovaquone and halofantrine. Of these reports, only halofantrine-loaded nanocapsules were evaluated in vivo for the treatment of malaria. Poly (d,l-lactide) (PLA) nanocapsules with halofantrine showed activity similar to or better than that observed for the drug solution when administered as single intravenous doses in P. berghei-infected mice (Mosqueira et al., 2004; Leite et al., 2007). In a study, liposomes were used as artesunate carriers. Although the effect of artesunate liposomes was less than that of free artesunate liposomes after 24 hours, the effect of artesunate liposomes remained the same 72 hours after the effect of free artesunate had diminished. It suggests that liposomes sustain the release of artesunate at the target site (Jin et al., 2013). In another study, liposomes encapsulating chloroquine were injected intramuscularly, intraperitoneally, and subcutaneously into mice. After intraperitoneal injection of liposome-encapsulated chloroquine, the concentration of chloroquine in the spleen and liver was higher than that of free chloroquine after 2-8 hours, indicating that the encapsulated chloroquine reached the blood compartments and was gradually released. Further comparisons were made between free subcutaneous and intramuscular chloroquine and liposome-encapsulated chloroquine. The latter was found to contain a higher concentration of chloroquine, indicating sustained release by the liposome (Titulaer et al., 2011). Musabayane et al. avoided the bitter taste of orally administered chloroquine to increase patient adherence by using a hydrogel chloroquine-pectin patch to be applied on the skin. The chloride-hydrochloric acid was used as a solution to test drug release. It was concluded that this patch might have potential applications for the transdermal delivery of antimalarials (Musabayane et al., 2003). Chitosan, a biodegradable polymer, was also used to coat the magnetic nanoparticles encapsulating artemisinin. The loading capacity of artemisinin in chitosan magnetic nanoparticles increased with increasing chitosan concentration. This demonstrated how nanoparticles may be modified to fit the intended application of a formulation. These magnetic chitosan nanoparticles were delivered to the desired site, which had a higher drug concentration (Natesan et al., 2017).

Challenges and limitations of encapsulation technology in malaria treatment

While encapsulation technology is promising in the treatment of malaria, there are still several challenges and limitations that need to be addressed. A challenge is the scalability of the manufacturing process. Encapsulation technology often requires specialized equipment and complex manufacturing processes, which can limit its widespread implementation in resource-constrained settings (Santos-Magalhães et al., 2010). Another challenge is the potential for immune responses to carriers. Some carriers, such as liposomes or nanoparticles, can trigger immune responses in the body that lead to side effects or reduced drug effectiveness. This suggests the need for careful design and characterization of carriers to minimize immunogenicity. In addition, the long-term stability and safety of encapsulated drugs should be fully evaluated. The encapsulation process can affect the stability and release kinetics of drugs, which may affect their therapeutic effects. In addition, the safety profile of carriers and their potential to accumulate in the body must be carefully evaluated to ensure patient safety (Aditya et al., 2013).

Conclusion

Encapsulation technology promises a revolution in malaria treatment. By improving the delivery of antimalarial drugs, encapsulation technology can overcome challenges associated with drug resistance, poor solubility, and rapid metabolism. It offers several advantages including increased drug bioavailability, controlled release and targeted delivery. With continued advances in carrier design, manufacturing processes, and clinical evaluation, encapsulation technology has the potential to break barriers and significantly improve outcomes for millions of people with malaria. One area of future research is the development of targeted delivery systems for antimalarial drugs. By combining encapsulation technology with targeting ligands or antibodies, drugs can be selectively delivered to infected cells or tissues, improving efficacy and reducing off-target effects.

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