IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ON ANTI-MALARIAL

Nadar Gokul Selvakumar[1] Nushrat Khan[2]

M.S. College of Pharmacy, Devghar, Taluka Wada, District Palghar.

ABSTRACT

The main mechanism of action of antimalarial medications is to eradicate the erythrocytic stages of malaria parasites, which cause disease in humans. P. falciparum and P. vivax, the two most common malaria parasites, require different drug regimens for therapy. Artemisinin-based combination therapy (ACT) is currently advised for the treatment of uncomplicated falciparum malaria in almost all regions due to the drug's common resistance to earlier versions.7. In most areas, the first-line treatment for vivax malaria is still chloroquine + primaquine. ACT is made up of a strong artemisinin component that quickly eradicates the majority of parasites and a partner medication that acts more slowly to kill any leftover parasites and prevent the development of artemisinin resistance.7. Artemether/lumefantrine, artesunate/amodiaquine, artesunate/mefloquine, dihydroartemisinin/piperaquine, artesunate/pyronaridine, and artesunate/sulfadoxine–pyrimethamine are the ACTs that the World Health Organization (WHO) recommends.

KEYWORDS

Drug Resistance, Novel Targets, Antimalarial agents, Mode of action.

INTRODUCTION

A medication that targets malaria. Quinine, which got its name from the Peruvian Indian term "kina," which means "bark of the tree," was the first anti-malarial agent. The most significant alkaloid in Cinchona bark is quinine, a big, complicated compound. Antimalarial medications are used to treat and prevent infections with malaria. The majority of anti-malarial medications focus on the infection's erythrocytic stage, which is when symptoms of the disease first appear. Most antimalarial medications' level of pre-erythrocytic (hepatic stage) action is poorly defined. Antimalarial drugs, also known as antimalarials, are a class of chemical agents that are antiparasitic and are frequently obtained from natural sources. They can be used to cure malaria or, in the case of the latter, to prevent it. In the case of prevention, the two most common target populations are small children and pregnant women. As of 2018, parenteral (injectable) medications quinine and artesunate served as the foundation for several contemporary pharmacological classes, with treatments, particularly those for severe malaria, still relying on these medicines. In particular, three groups of people can be treated for malaria with antimalarial medications:

1. Those whose infection is suspected or proven.
2. Individuals traveling to areas where malaria is endemic but lacking immunity can use malaria prophylaxis to avoid infection.

3. In bigger groups of persons, in routine but intermittent prophylactic treatment in places where malaria is endemic using intermittent preventive medication.

Primaquine phosphate, atovaquone-proguanil (Malarone), quinine sulfate (Qualaquin) plus doxycycline (Oracea, Vibramycin, etc.).

MEDICATION

It makes sense to classify antimalarials according to their chemical structures because these are linked to crucial characteristics of each medication, like their mode of action.

QUININE AND RELATED DRUGS

Quinine has a long history that dates back to Peru, when the cinchona tree was discovered and its bark was found to have medicinal properties. It is still widely used today, along with a number of its derivatives, to treat and prevent malaria. An alkaloid called quinine functions as a blood. The complexity of quinine treatment depends mostly on the parasite's resistance level and the purpose of pharmacological therapy (i.e., prophylactic or acute treatment). When used in conjunction with doxycycline, tetracycline, or clindamycin, quinine is recommended by the World Health Organization at doses of 20 mg/kg for the first time and 10 mg/kg every eight hours for five days in cases where parasites are susceptible to it. It is possible to administer doses orally, intravenously, or intramuscularly. (i.e. sterilized needles for IV or IM injections).

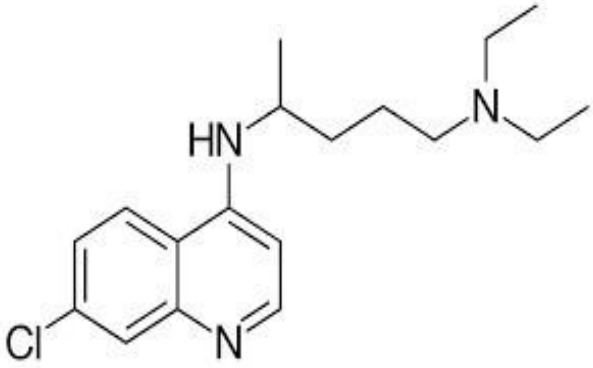
QUINOLINE SIDE EFFECT

Cinchoninium is an often-reported condition associated with quinine use. The most typical symptoms include vertigo, rashes, nausea, vomiting, and stomach discomfort in addition to tinnitus, a hearing impairment. The drug's neurotoxic qualities can occasionally result in neurological consequences. Quinine interacts with other substances to reduce the excitability of motor neuron end plates, which mediates these activities. This frequently leads to functional damage of the eighth cranial nerve, which can cause delirium, unconsciousness, and confusion.

The two quinine-related alkaloids that are most frequently used in the treatment or prevention of malaria are quiname and quinidine. Four alkaloids make up quiname: quinine, quinidine, cinchonine, and cinchonine. Numerous investigations have demonstrated that this combination is more effective than quinine, perhaps because the four cinchona derivatives work in concert. One direct derivative of quinine is quinidine. Since it is a Di stereoisomer, its anti-malarial qualities are comparable to those of the parent molecule. Quinidine should only be used to treat extremely severe instances of malaria.

CHLOROQUINE

Until recently, the most used anti-malarial medication was chloroquine. It was the initial model from which the majority of therapeutic approaches are adapted. It is also the least costly, most thoroughly studied, and securest medication on the market.

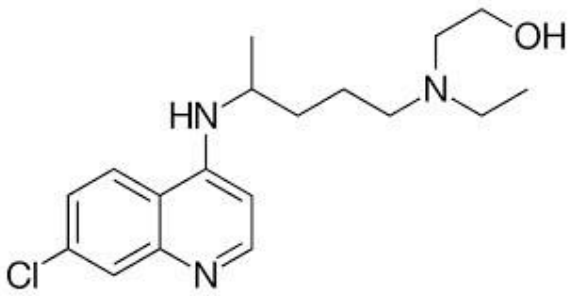


Its efficiency is quickly diminishing due to the advent of parasite strains that are resistant to drugs. The 4-aminoquinolone chemical chloroquine has a convoluted and yet-to-be-explained mode of action. It is thought to accumulate to high quantities in the parasite's vacuoles, where its alkaline properties cause the internal pH to rise.

Chloroquine (25 mg/kg) should be administered over three days to both adults and children. The WHO recommends a pharmacokinetically better regimen that starts with a dose of 10 mg/kg and increases to 5 mg/kg after 6–8 hours, then 5 mg/kg for the next two days. It is recommended to administer 5 mg/kg/week as a single dosage or 10 mg/kg/week split into six daily doses for chemoprophylaxis. It is only advised to use chloroquine as a preventative medication in areas where sensitive P. falciparum strains and P. vivax are present. Since chloroquine has been used for many years to treat malaria, there have been no documented teratogenic or abortifacient effects during this time, making it regarded as extremely safe to use during pregnancy.

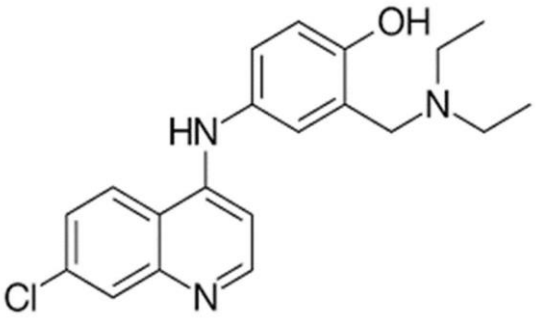
HYDROXYCHLOROQUINE

Hydroxychloroquine is an antirheumatic medication and a member of the antimalarial medicine class. It functions by eradicating the malaria-causing germs. By lowering immune system activity, hydroxychloroquine may be used to treat rheumatoid arthritis and systemic lupus erythematosus.



AMODIAQUINE

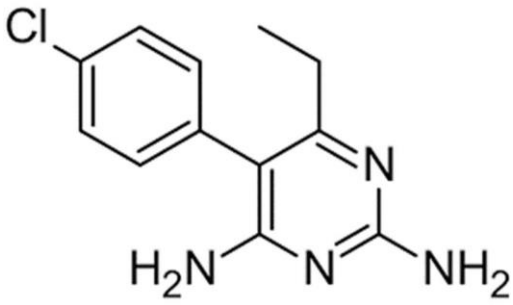
Amodiaquine, a 4-aminoquinolone antimalarial medication, functions similarly to chloroquine in terms of both structure and mode of action. Although amodiaquine tends to produce less itching than chloroquine, some patients prefer it because it has been used in places where chloroquine resistance has developed.



The World Health Organization recommends artemisinin-combination therapy, and amodiaquine is one of them. It is currently available in a combined formulation with artesunate (ASAQ). It is not advised to combine pyrimethamine and sulfadoxine.

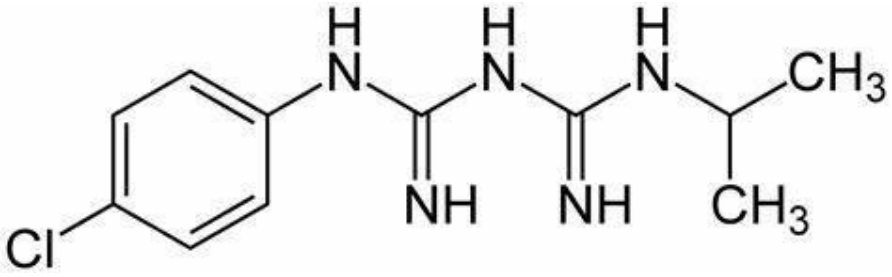
PYRIMETHAMINE

The U.S. Food and Drug Administration (FDA) has authorized the prescription drug pyrimethamine, an antiparasitic, to treat toxoplasma gondii infection (toxoplasmosis). To treat toxoplasmosis, pyrimethamine is typically taken in conjunction with a sulfonamide (sulfa) medication. Pyrimethamine is a drug used in conjunction with leucovorin to treat parasite disorders such toxoplasmosis and cystoisosporiasis. It is marketed under various brand names, including Daraprim. In HIV/AIDS patients, it is also used as a second-line treatment to prevent Pneumocystis jiroveci pneumonia.



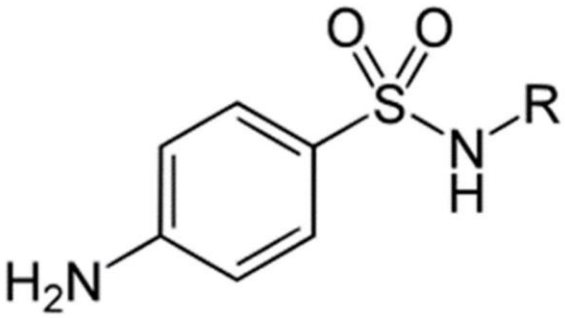
PROGUANIL

A drug called proguanil is prescribed to treat and prevent Plasmodium falciparum malaria. Proguanil is a preventive antimalarial medication that functions by preventing Plasmodium falciparum and Plasmodium vivax, the malaria parasites, from proliferating once they have entered red blood cells.



SULFONAMIDES

Antibacterial substances called sulfonamides helped make antibiotics widely used. Sulfonamides, sometimes known as "sulfa drugs," are used to treat burns, inflammatory bowel disease, malaria, UTIs, and infections of the skin, vagina, and eyes, among other ailments.



Several drug groups known as sulphonamides, sulfa medicines, or sulpha medications are based on the functional group sulfonamide. Synthetic antimicrobial compounds containing the sulfonamide group are the initial antibacterial sulfonamides

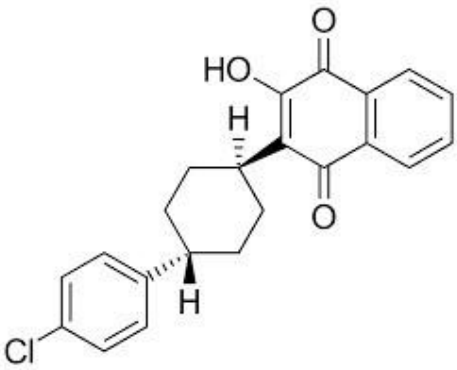
MEFLOQUINE

Mefloquine prescriptions are available for both malaria treatment and prevention. This fact sheet offers details on how it can be used to stop travel-related malaria infections. Mefloquine can be taken by whom? All age groups of adults and children can be prescribed mefloquine.

Mefloquine is a drug used to treat or prevent malaria. It is marketed under several trade names, including Lariam. It is usually started prior to possible exposure and continued for several weeks following potential exposure when used as a preventative measure.

ATOVAQUONE

Mepron, a brand name for atovaquone, is an antibacterial drug used to treat and prevent Pneumocystis jirovecii pneumonia. The chemical compound atovaquone is a member of the naphthoquinones class. A hydroxy-1,4-naphthoquinone, atovaquone is a homolog of lawsone and ubiquinone.

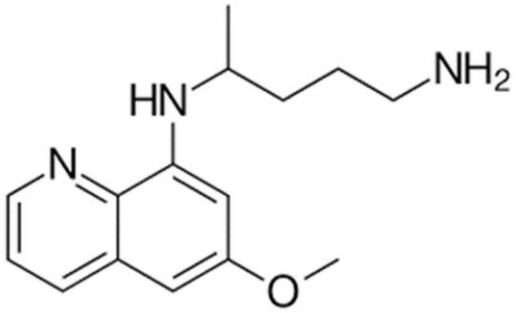


Mepron, a brand name for atovaquone, is an antibacterial drug used to treat and prevent Pneumocystis jirovecii pneumonia. The chemical compound atovaquone is a member of the

naphthoquinones class. A hydroxy-1,4-naphthoquinone, atovaquone is a homolog of lawsone and ubiquinone.

PRIMAQUINE

After other drugs, such chloroquine, have eliminated the malaria parasites residing inside red blood cells, primaquine is administered. Once within other bodily tissues, the malaria parasites are eliminated by primaquine. This stops the illness from spreading again. For a full recovery, both medications are required.



Primaquine is a drug used to treat Pneumocystis pneumonia and to prevent and treat malaria. In particular, it is used in conjunction with other medications to treat malaria caused by Plasmodium vivax and Plasmodium ovale, as well as to prevent the disease in the case that other treatments are not possible.

RESISTANCE

The majority of malaria infections have simple symptoms, such as fever, chills, malaise, frequent stomach ache, and mild anemia. If efficient medications are easily accessible, the death rate linked to this presentation in falciparum malaria is roughly 0.1%. Untrammeled parasite growth causes substantial parasite burdens in a tiny percentage of P. falciparum infections. These parasite burdens impair crucial organ function, causing acidosis, more severe anemia, and impaired consciousness. In contrast to adults, who are more likely to experience jaundice, pulmonary edema, and abrupt renal failure, children are more likely to experience seizures, hypoglycemia, and severe anemia as symptoms of severe malaria. Despite treatment, the mortality increases to 15%–20%. Preventing the current generation of P. falciparum malaria parasites—that is, the parasites present when the patient seeks medical attention—from maturing from the less pathogenic circulating ring stages (0–16 hours) to the more pathogenic sequestered stages is crucial because the majority of patients who die from severe malaria do so within 48 hours of presentation, or one asexual cycle of the blood-stage infection. The assessment of medication action's stage specificity is crucial. However, suppression of parasite

multiplication is more significant in cases of simple malaria since it stops the disease from getting worse and relieves symptoms such as fever. A first-order process called inhibition of parasite multiplication causes a log-linear decline in parasite population over time. The parasite multiplication rate (PMR) of uninhibited blood-stage multiplication at 100% efficiency is equal to the median number of viable merozoites released by rupturing schizonts. In patients who are not immunological compromised, in vivo efficiency can reach 50% or more, with roughly 10 PMRs produced for each asexual cycle. This positive value is changed to a negative value by antimalarial medications, resulting in PMRs that vary from 10–1 to 10–4 per cycle. Parasite killing rates or parasite reduction ratios are other names for these negative PMRs. After therapy with medications like tetracyclines, which have relatively modest antimalarial activity, the higher values (i.e., lower killing rates) are obtained; artemisinin derivatives yield the greatest values. A change in the concentration-effect (dose-response) relationship to the right is indicative of drug resistance to an anti-infective agent. This relates to stopping

the parasite from multiplying in cases of simple malaria; hence, when resistance builds, less inhibition of parasite multiplication occurs at any given free plasma concentration of the antimalarial medication.

FACTORS AFFECTING:

GENETIC FACTORS

The uncommon and spontaneous genetic processes that give resistance to antimalarial drugs (while maintaining parasite survival) are believed to occur independently of the medicine being administered. These are alterations in the copy number of genes that encode or relate to the drug's target parasite or to influx/efflux pumps that influence the drug's intraparasitic concentrations. It might just take one genetic event, or it might take several unrelated events (epistasis). This is a much uncommon occurrence since the likelihood of multigenic resistance developing is the product of the probabilities of its constituent parts. It has been demonstrated that Southeast Asian P. falciparum parasites are more likely to become resistant to medications.

PREGNANCY

Pregnancy affects how well malaria infections are controlled. P. falciparum infections are more severe in low-transmission environments, while babies born to women with malaria (both P. falciparum and P. vivax infections) had a lower birth weight at all transmission levels. The negative consequences of P. falciparum are more severe in primigravidae. The placenta appears to be a "privileged" site for parasite proliferation and a site of P. falciparum sequestration, while it is unclear exactly how this local immune paresis to malaria parasites works. This has not yet been assessed ramifications for the increased establishment and dissemination of resistance. Pregnant women always respond worse to antimalarial drug treatment regimens in low transmission environments than do age-matched nonpregnant women from the same locale.

Resistance develops because of treatment failures. The likelihood of selection is raised by the possibility that the placenta has a high concentration of parasites. These parasites often exhibit a single surface-antigen phenotype, binding to hyaluronic acid and chondroitin sulphate A, indicating the expression of a single conserved var gene. The infecting parasites are not seemingly selected by the immune response to surface-expressed antigens after the infection is established in a pregnant woman who has never had malaria in pregnancy before. As a result, if a drug-resistant mutation arises, it does not appear to need to arise in a variant subpopulation to ensure its survival. The rise and dissemination of resistance are also aided by other causes. Antimalarial drugs typically have different pharmacokinetics, which lead to lower drug levels at any given dose. Examples of these drugs include quinine, mefloquine, atovaquone, and proguanil, which frequently have an increased apparent volume of distribution. Pregnant people may even attract mosquitoes more, according to certain statistics. Pregnant women are generally advised to receive antimalarial prophylaxis; however, the only medications deemed safe are proguanil, which has decreased biotransformation to the active antifol metabolite cycloguanil, and chloroquine, which is almost universally ineffective against P. falciparum. Although SP is becoming less effective, intermittent presumptive therapy (IPT) with SP, which involves administering a treatment dose twice or three times throughout pregnancy, has replaced prophylaxis for expectant mothers. Since the antimalarial medication is typically given to healthy women in IPT, the biomass of parasites the medication confronts is smaller than that of symptomatic infections, albeit it is unclear by how much. When considered collectively, these findings imply that pregnant patients may play a significant role in the development of antimalarial medication resistance.

HIV INFECTION

The data supporting the link between HIV infection and falciparum malaria is growing. While HIV has greater rates of mortality in both children and adults, malaria is primarily a pediatric illness in areas with significant transmission of the disease. However, when antiretroviral medications become more widely available, HIV-positive individuals will live longer, increasing the likelihood that the two illnesses will coexist. A higher birth weight loss is linked to HIV coinfection during pregnancy than it is to malaria infection alone. To achieve the same benefits in birth weight as 8–12 weekly treatments in HIV-negative pregnant women, IPT with SP must be administered on a monthly basis. HIV-positive nonimmune patients experience more severe malaria than HIV-negative nonimmune patients, and HIV-infected individuals

with highly impaired immune systems in high-transmission environments have greater parasite densities. This implies that HIV-related immunosuppression may have an impact on malaria parasite population management, which could jeopardize the effectiveness of antimalarial immunity in limiting the emergence and spread of antimalarial drug resistance. Patients with HIV/AIDS are frequently prescribed trimethoprim-sulfamethoxazole as a preventative measure against opportunistic infections. Also antimalarial is this combination of sulfonamide and antifol. It is unknown if this encourages the development of antifol resistance or if it slows it down (by decreasing malaria infections). The available information on these progressively significant issues is inadequate.

PREVENTION AND RESISTANCE BY ANTI-MALARIAL COMBINATION THERAPY

The well recognized idea that underpins the combination medicine therapy of HIV infection, leprosy, and tuberculosis is also widely acknowledged in the context of malaria (5, 8, 55–58). The per-parasite likelihood of developing resistance to both medications is the product of their individual per-parasite probabilities if two drugs are used with separate modes of action and, consequently, different resistance mechanisms. Because there are very few malaria parasites in the world—roughly 1017—this is especially effective against malaria. For instance, every 1 in 1024 parasites will spontaneously produce a concurrently resistant mutant if the per-parasite probabilities of gaining resistance to drugs A and B are both 1 in 1012. Since there are less than 1020 malaria parasites in the world at any given time, a parasite with simultaneous resistance would emerge naturally about once per 10,000 years, assuming that the medications always target the parasites simultaneously. Therefore, the longer it takes for resistance to emerge, the lower the de novo per-parasite probability of resistance developing.

Since stable, therapeutically meaningful resistance to the artemisinin derivatives has not yet been found and cannot be produced in the lab, it is possible that this is an extremely uncommon occurrence. However, it would be naive to assume that it won't happen, and if it did, it would be catastrophic for the entire world. The only way to prevent drug resistance in these medications is to take them in combination with other antimalarials.

HERBS

Malaria symptoms can be alleviated by using herbs such as Tulsi, Neem, Ginger, Cinnamon, Turmeric, Guduchi, and Krishna musali. It is not recommended, however, to utilize these herbs in place of conventional medical care. Use these herbs only after speaking with your physician.

You can utilize some herbs and cures to help alleviate the symptoms of malaria and speed up your recovery. But never substitute using these herbs for conventional medical care. Rather, consult your healthcare physician before using any malaria home treatment.

1. **Ginger**

Symptoms of malaria in patients may include nausea and vomiting. Numerous scientific investigations indicate that ginger may be useful in reducing these symptoms.3. One well-known recipe that works well in many situations is ginger tea. Boil

some freshly crushed ginger in a glass of water to make ginger tea. A tablespoon of honey or some lemon juice pair nicely with ginger tea.

2. **TURMERIC**

Based on animal studies, the primary component of turmeric, curcumin, has demonstrated antimalarial action against bacteria that cause malaria. Turmeric may therefore aid in the quick recovery of malaria patients.4 Turmeric can be used in numerous ways. To reap the advantages, mix some turmeric into a glass of warm milk. Turmeric can also be added to meals and foods.

3. **CINNAMON**

A typical cooking spice with numerous health benefits is cinnamon. For instance, cinnamon has demonstrated inhibitory activity against microorganisms that cause malaria in a number of lab and animal investigations.5. You can flavor your herbal teas with cinnamon powder. The cinnamon powder can also be consumed with a warm water glass. To improve the flavor, you can also add a dash of powdered black pepper and honey.

4. **TULSI**

One well-known plant utilized in the ayurveda medical system is Tulsi. There are several proven health benefits of Tulsi. Numerous scientific investigations have shown ample evidence of Tulsi's antimalarial action. Moreover, Tulsi may strengthen the immune system's defenses against infectious agents. Six Boiling fresh Tulsi leaves in water yields Tulsi tea. Your Tulsi tea is ready when you strain this mixture into a cup. For more flavor, you can add a drop of honey or lemon juice.

5. **NEEM**

For millennia, neem has been used as a malaria preventive. Neem contains compounds that have been demonstrated to be beneficial against malarial parasites. Malaria risk may also be lowered by using neem leaves or consuming neem tea. To expedite healing, neem may also help reduce fever and strengthen the immune system.7. To benefit from neem's antimalarial properties, you can chew fresh neem leaves or drink neem tea. Boil a glass of water to prepare neem tea. Pour some neem leaves into the water that's boiling. Give it some time to steep. Pour the mixture through a strainer into a cup. Your tea is ready to serve when you add some honey to taste it.

VACCINE

Vaccines against malaria are designed to prevent the disease, which is spread by mosquitoes and affects an estimated 247 million people globally each year, killing 619,000 people.[2] RTS, S, also marketed as Mosquirix, is the first malaria vaccine to be authorized. As of April 2023, 1.5 million children residing in regions with moderate-to-high malaria transmission had received the vaccination.[3] By the age of two, infants need to receive at least three doses, and a fourth dose prolongs the protection for an additional one to two years.[4][5] About 30% fewer hospital admissions due to severe malaria are caused by the vaccination. Mosquirix, also known as RTS, S/AS01, is the first malaria vaccine that has been authorized for general use [1]. When given to infants by the age of two, it takes at least three doses; a fourth dose prolongs the protection for an additional one to two years.[4] About 30% fewer hospital admissions due to severe malaria are caused by the vaccination.[4] With funding from the Bill and Melinda Gates Foundation, PATH Malaria Vaccine Initiative (MVI) and GlaxoSmithKline (GSK) created RTS, S. Plasmodium falciparum circumsporozoite protein (CSP) from the pre-erythrocytic stage makes up the recombinant vaccine. The CSP antigen triggers a cellular response that permits the elimination of infected hepatocytes and produces antibodies that can stop hepatocyte invasion. Due to its low immunogenicity, the CSP vaccination caused issues during the experimental phase. By combining the protein with a hepatitis B virus surface antigen, RTS, S made an effort to prevent these and produce a more effective and immunogenic vaccine. In experiments, the vaccine, administered as an oil-in-water emulsion with additional adjuvants of monophosphorylate A and QS21 (SBAS2), provided protective protection against P. falciparum in 7 out of 8 volunteers.[11] RTS, S was created by combining a component of the hepatitis B virus, genes from the outer protein of the P. falciparum malaria parasite, and a chemical adjuvant to enhance the immune response. By raising antibody titers, the parasite is prevented from infecting the liver and causing infection.[12] A Phase III experiment conducted in November 2012 on young newborns revealed that RTS, S offered a moderate level of protection against both clinical and severe malaria.[13]

CONCLUSION

Malaria is a prevalent yet dangerous illness that requires prompt medical attention in order to prevent life-threatening consequences such as brain damage and death. You can employ a number of herbal treatments at home to assist manage the symptoms and hasten the healing process. A few common culinary herbs and spices, such as ginger, Tulsi, neem, turmeric, and cinnamon, may work well as treatments for malaria. It is recommended that you consult your healthcare provider and not rely solely on home cures. Do not treat malaria with any natural cures without first talking to your physician. By 2050, malaria can and should be completely eradicated, making it one of the deadliest and most ancient diseases known to man. We cannot eradicate malaria in a "business as usual" setting. To guarantee that eradication is accomplished, specific and crucial activities are needed at the national, regional, and international levels. An international commitment to eradicating malaria as a specific, time-bound goal will support these initiatives. Eliminating malaria has significant social and economic benefits and is a wise investment. The advantages of elimination will far outweigh the disadvantages. Eradicating malaria will benefit human welfare and the economies of many African, Asian, and American countries; it will also contribute to UHC, global health security, and the accomplishment of the SDGs. Ultimately, it will save countless lives. The cost of eradicating malaria might be covered by a combination of reasonably accessible domestic and international resources. The eradication of malaria is affordable. The key to success will be a mixed strategy that emphasizes management and efficiency on the ground while boosting total spend.

ACKNOWLEGDEMENTS

My sincere gratitude goes out to my friends who have played a vital role in our growth both at the institutions and throughout my graduate and undergraduate education. Along with meeting many outstanding instructors from many fields and other well-known pharmacy professionals, my professions have also allowed me to network and receive advice from many remarkable people in the field of pharmacy. They have all taught me a great deal, therefore I'm grateful that they have shared their expertise and experiences with us.

Appreciation should also be extended to the entire faculty and staff of the M.S. College of Pharmacy at Mumbai University.

Permission granted to express gratitude to the writers of every one of our chapters for their diligent efforts. The writers' commitment to these subjects was taken into consideration in addition to their credentials in pharmacy and pharmacy education when selecting them for their works. Without their help, I would not have been able to finish writing this post.

REFERENCE

1. Marsh, K. Malaria disaster in Africa. Lancet. 1998. 352:924-925. View this article via: PubMed CrossRef Google Scholar
2. Korenromp, EL, Williams, BG, Gouws, E, Dye, C, Snow, RW. Measurement of trends in childhood malaria mortality in Africa: an assessment of progress toward targets based on verbal autopsy. Lancet Infect. Dis. 2003. 3:349-358. View this article via: PubMed CrossRef Google Scholar
3. Nosten, F, et al. Effects of artesunate-mefloquine combination on incidence of Plasmodium falciparum malaria and mefloquine resistance in western Thailand: a prospective study. Lancet. 2000. 356:297-302. View this article via: PubMed CrossRef Google Scholar
4. Trape, JF, et al. Impact of chloroquine resistance on malaria mortality. C. R. Acad. Sci. III. 1998. 321:689-697.

View this article via: PubMed Google Scholar

5. White, NJ. Antimalarial drug resistance and combination chemotherapy. Philos. Trans. R. Soc. Lond. B Biol. Sci. 1999. 354:739-749.

   View this article via: PubMed CrossRef Google Scholar

6. Hastings, IM, D'Alessandro, U. Modelling a predictable disaster: the rise and spread of drugresistant malaria. Parasitol. Today. 2000. 16:340-347.

   View this article via: PubMed CrossRef Google Scholar

7. WHO. 2001. Antimalarial drug combination therapy. Report of a technical consultation. WHO. Geneva, Switzerland. WHO/CDS/RBM 2001.35.

8. Better Health Channel. Malaria [Internet]. [cited 2022 Jul 14]. Available from: https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/malaria

9. Ali BH, Blunden G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): a review of recent research.

   Food Chem Toxicol [Internet]. 2008 [cited 2022 Jul 10];46(2):409–20. Available from: https://pubmed.ncbi.nlm.nih.gov/17950516/

10. Nandakumar DN, Nagaraj VA, Vathsala PG, Rangarajan P, Padmanaban G. CurcuminArtemisinin Combination Therapy for Malaria. Antimicrobial Agents and Chemotherapy [Internet]. 2006 May [cited 2022 Jul 15];50(5):1859. Available from: https://pubmed.ncbi.nlm.nih.gov/16641461/

11. Parvazi S, Sadeghi S, Azadi M, Mohammadi M, Arjmand M, Vahabi F, et al. The Effect of Aqueous Extract of Cinnamon on the Metabolome of Plasmodium falciparum Using 1HNMR Spectroscopy. Journal of Tropical Medicine [Internet]. 2016 [cited 2022 Jul 15];2016. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4745969/

12. Cohen MM. Tulsi – Ocimum sanctum: A herb for all reasons. Journal of Ayurveda and Integrative Medicine [Internet]. 2014 Oct 1 [cited 2022 Jul 15];5(4):251. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4296439/

13. The neem tree, a wonder tool against Malaria [Internet]. [cited 2022 Jul 15]. Available from: https://www.fawco.org/global-issues/environment/environment-articles/289-the-neemtree-a-wonder-tool-against-malaria

14. "Mosquirix: Opinion on medicine for use outside EU". European Medicines Agency (EMA). Archived from the original on 23 November 2019. Retrieved 22 November 2019.
15. ^ World Malaria Report 2022 - World Health Organization. Switzerland: World Health Organization. 8 December 2022. ISBN 978-92-4-006489-8.
16. ^ Jump up to:[a] [b] [c] "Q&A on RTS,S malaria vaccine - WHO". World Health Organization. 19 April 2023. Retrieved 29 April 2023.
17. ^ Jump up to:[a] [b] [c] [d] "First malaria vaccine hits 1 million dose milestone — although it has its shortcomings". NPR. 13 May 2022. Archived from the original on 13 November 2022. Retrieved 2 January 2023.
18. ^ World Health Organization (2022). "Malaria vaccine: WHO position paper – March 2022". Weekly Epidemiological Record. 97 (9): 60–78. hdl:10665/352337.
19. ^ Jump up to:[a] [b] Roxby P (23 April 2021). "Malaria vaccine hailed as potential breakthrough". BBC News. Archived from the original on 24 April 2021. Retrieved 24 April 2021.
20. ^ Jump up to:[a] [b] "Malaria vaccine becomes first to achieve WHO-specified 75% efficacy goal". EurekAlert!. 23 April 2021. Archived from the original on 27 July 2021. Retrieved 24 April 2021.
21. ^ "WHO recommends R21/Matrix-M vaccine for malaria prevention in updated advice on immunization". 2 October 2023. Retrieved 4 October 2023.
22. ^ Jump up to:[a] [b] [c] Gallagher J (12 April 2023). "Ghana first to approve 'world-changer' malaria vaccine". BBC News. Archived from the original on 13 April 2023. Retrieved 13 April 2023.

23. ^ Jump up to:[a] [b] "The country with the highest rate of malaria deaths in the world has approved Oxford's vaccine". Quartz. 18 April 2023. Retrieved 19 April 2023.
24. ^ "RTS,S malaria candidate vaccine reduces malaria by approximately one-third in African infants". malariavaccine.org. Malaria Vaccine Initiative Path. Archived from the original on 23 March 2013. Retrieved 19 March 2013.
25. ^ Foquet L, Hermsen CC, van Gemert GJ, Van Braeckel E, Weening KE, Sauerwein R, et al. (January 2014). "Vaccine-induced monoclonal antibodies targeting circumsporozoite protein prevent Plasmodium falciparum infection". The Journal of Clinical Investigation. 124 (1): 140–4. doi:10.1172/JCI70349. PMC 3871238.
26. van Vugt M, Ezzet F, Nosten F, Gathmann I, Wilairatana P, Looareesuwan S, White NJ. 1999. No evidence of cardiotoxicity during antimalarial treatment with artemetherlumefantrine. American Journal of Tropical Medicine and Hygiene 61(6):964-967. [PubMed]
27. van Vugt M, Angus BJ, Price RN, Mann C, Simpson JA, Poletto C, Htoo SE, Looareesuwan S, White NJ, Nosten F. 2000. A case-control auditory evaluation of patients treated with artemisinin derivatives for multidrug-resistant Plasmodium falciparum malaria. American Journal of Tropical Medicine and Hygiene 62(1):65-69. [PubMed]
28. van Vugt M, Leonardi E, Phaipun L, Slight T, Thway KL, McGready R, Brockman A, Villegas L, Looareesuwan S, White NJ, Nosten F. 2002. Treatment of uncomplicated multidrugresistant falciparum malaria with artesunate-atovaquone-proguanil. Clinical Infectious Diseases 35:1498-1504. [PubMed]
29. Von Seidlen L, Milligan P, Pinder M, Bojang K, Anyalebeschi C, Gosling R, Coleman R, Ude JL, Sadiq A, Duraisingh M, Warhurst D, Alloueche A, Targett G, McAdam K, Greenwood B, Walraven G, Olliaro P, Doherty T. 2000. Efficacy of artesunate plus pyrimethaminesulphadoxine for uncomplicated malaria in Gambian children: A double-blind, randomized controlled trial. Lancet 355(9220):352-357. [PubMed]
30. White N. 1999. Antimalarial drug resistance and mortality in falciparum malaria. Tropical Medicine and International Health 4:469-470. [PubMed]
31. WHO. 2003. Assessment and monitoring of antimalarial drug efficacy for the treatment of uncomplicated falciparum malaria Geneva: World Health Organization. WHO/HTM/ RBM/2003.50.
32. Wongsrichanalai C, Webster HK, Wimonwattrawatee T, Sookto P, Chuanak N, Thimasarn K, Wernsdorfer WH. 1992. Emergence of multidrug-resistant Plasmodium falciparum in Thailand: In vitro tracking. American Journal of Tropical Medicine and Hygiene 47(1):112116. [PubMed]