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A REVIEW OF FORMULATION OF QUININE FROM EXTRACT OF CHINCHONA BARK

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ABSTRACT

Quinine remains an important anti-malarial drug almost 400 years after its effectiveness was first documented. However, its continued use is challenged by its poor tolerability, poor compliance with complex dosing regimens, and the availability of more efficacious anti-malarial drugs. This article reviews the historical role of quinine, considers its current usage and provides insight into its appropriate future use in the treatment of malaria. In light of recent research findings intravenous artesunate should be the first-line drug for severe malaria, with quinine as an alternative. The role of rectal quinine as pre-referral treatment for severe malaria has not been fully explored, but it remains a promising intervention In pregnancy, quinine continues to play a critical role in the management of malaria, especially in the first trimester, and it will remain a mainstay of treatment until safer alternatives become available. For uncomplicated malaria, artemisinin-based combination therapy (ACT) offers a better option than quinine though the difficulty of maintaining a steady supply of ACT in resource-limited settings renders the rapid withdrawal of quinine for uncomplicated malaria cases risky. The best approach would be to identify solutions to ACT stock-outs, maintain quinine in case of ACT stock-outs, and evaluate strategies for improving quinine treatment outcomes by combining it with antibiotics. In HIV and TB infected populations, concerns about potential interactions between quinine and antiretroviral and anti-tuberculosis drugs exist, and these will need further research and pharmacovigilance.

Keyword*: Quinine, honey, Cardamom.*

1. INTRODUCTION

Malaria:

Antimalarial are drugs used to prevent and treat malaria. Almost all of these agents are effective against the asexual erythrocytes stages of the malarial parasites, which cause attacks of malaria. Malaria remains an important cause of illness and death in children and adults in countries in which it is endemic. Malaria control requires an integrated approach, including prevention (primarily vector control) and prompt treatment with effective antimalarial agents. Since publication of the first edition of the Guidelines for the treatment of malaria in 2006 and the second edition in 2010, all countries in which P. falciparum malaria is endemic have progressively updated their treatment policy from use of monotherapy with drugs such as chloroquine.amodiaquine. and sulfadoxine –pyrimethamine (SP) to the currently recommended artisanal-based combination therapies.

Cinchona Use in malaria:

- It was used for the treatment of malaria.
- Cinchona, as a component of the bark of the cinchona (quina-quina) tree, was used to treat malaria from as early as the 1600s.
- Malaria caused by Plasmodium falciparum. Plasmodium falciparum is a parasite that gets into the red blood cells in the body and causes malaria. Cinchona works by killing the parasite or preventing it from growing.

Treatment of Malaria from cinchona bark:

Quinine is a cinchona alkaloid that belongs to the aryl amino alcohol group of drugs. It is an extremely basic compound and is, therefore, always presented as a salt Various preparations exist, including the hydrochloride, hydrochloride, sulphate, bisulphate, and gluconate salts; of these the 9 is the most widely used. Quinine has rapid schizonticidal action against intra-erythrocyte malaria parasites. It is also gametocytocidal for Plasmodium vivax and Plasmodium malaria but not for Plasmodium falciparum Quinine also has analgesic, but not antipyretic properties. The anti-malarial mechanism of action of quinine is unknown. Quinine is rapidly absorbed both orally and parenterally, reaching peak concentrations within 1-3 hours. It is distributed throughout the body fluids and is highly protein bound, mainly to alpha-1 acid glycoprotein. The binding capacity in plasma is concentration dependent, but also depends on the levels of alpha-1 acid glycoprotein, which therefore makes comparisons between different studies difficult. Quinine readily crosses the placental barrier and is also found in cerebral spinal fluid. Excretion is rapid - 80% of the administered drug is eliminated by hepatic biotransformation and the remaining 20% is excreted unchanged by the kidney.

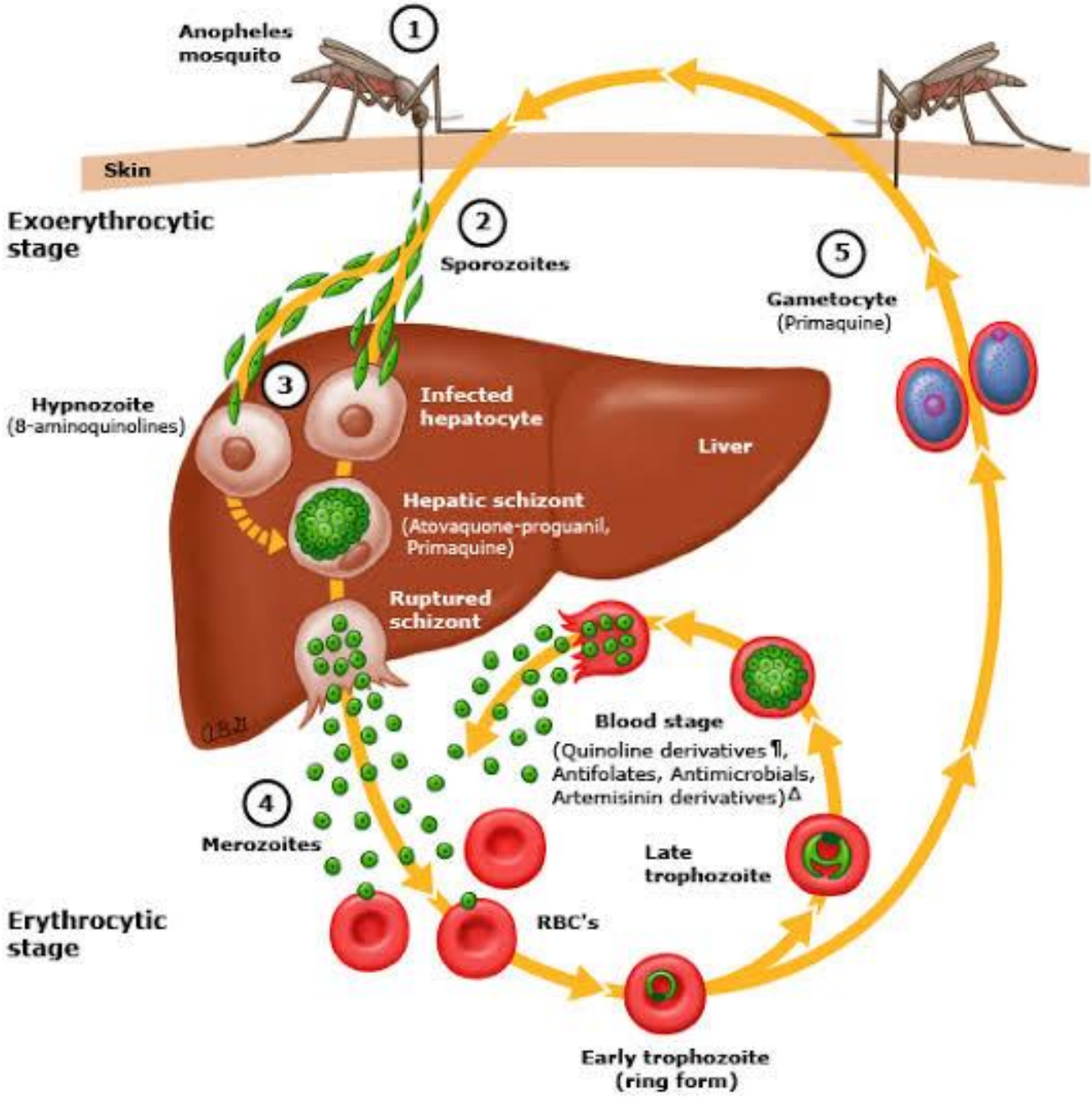

Fig. Life cycle of malaria

CINCHONA:

Fig. CHINCHONA BARK

Synonyms: Cortex Cinchonae, Countess, Peruvian or Jesuit's bark, Cinchona

Family: Rubiaceae.

Biological Source: Cinchona is the dried bark of the stem or of the root of *Cinchona calisaya* Wedd., *Cinchona ledgeriana* Moens., *Cinchona officinalis* Linn., and *Cinchona succirubra* Pavon., or hybrids of any of the first two species with any of the last two species, belonging to family Rubiaceae.

Geographical source: Tropical valleys of the Andes. Bolivia and Southern Peru. Cinchona is a native of South America, occurring wild there. At present, it is mainly cultivated in Indonesia (Java), Zaire, India, Guatemala, Bolivia, Ceylon etc.

Chemical constitution: The chiefly identified alkaloids are quinidine, quinine, cinchonine and cinchonidine. These constituents are the stereoisomers of each other like quinine is stereoisomer of quinidine and cinchonine is stereoisomer of cinchonidine.

Machanisam of Action: Chinchona Bark is used to treat malaria caused by Plasmodium falciparum. Plasmodium falciparum is a parasite that gets into the red blood cells in the body and causes malaria. Chinchona Bark works by killing the parasite or preventing it from growing.

Causes of Malaria: Malaria is an acute febrile illness caused by Plasmodium parasites, which are spread to people through the bites of infected female Anopheles mosquitoes. There are 5 parasite species that cause malaria in humans, and 2 of these species – P. falciparum and P. vivax – pose the greatest threat.

Sign and Symptoms:

1. Signs and symptoms of malaria may include:
2. Fevers
3. Chills
4. General feeling of discomfort
5. Headache

6. Nausea and vomiting
7. Diarrhea
8. Abdominal pain
9. Muscle or joint pain
10. Fatigue
11. Rapid breathing
12. Rapid heart rate
13. Cough

2. METHODOLOGY

Preparation cinchona extract:

An aqueous extract of cinchona Bark was prepared by grinding 20 g of cinchona Bark with double distilled water of 50 ml. After that heated that paste in water bath upto 70-80°C for 1 hrs.Then left alone for 20 min for extract get cool and then filtered it by whatmann filter paper.After that collected that cinchona Bark extract in a beaker.In that extract the concentration of Quinine is about 60-100 mg from 20 gm cinchona bark.

Material:

INGREDIENT	Quantity
Quinine	22 ml
Honey	6 ml
Cardamom	2 ml

3. RESULT AND DISCUSSION

Physical Examination (Colour, Odour, Taste, Smoothness, Relative Density) Formulated solution was evaluated for its colour. The visually colour was checked. Odour was found by smelling the product. Taste was checked manually by tasting the formulation. The Smoothness was tested by rubbing the Formulated solution between the fingers. Relative density was determine by weight in gram taken in 10 ml formulation and 10 ml distilled water using RD bottle in 10 ml formulation.

Transparency Approximately 5 ml of formulated solution was taken in the 10 ml test tube and its transparency was checked visual.

pH of the formulated solution was determined by using pH meter. In this method, 1 ml solution was dispersed in 100 ml purified water. The electrode was washed with double distilled water, dried by tissue paper and calibrated before use with standard buffer solution at 4.0, 7.0 and 9.0. The pH measurements were done in triplicate and average values were calculated. The average pH values was found to be 6.33.

Stability Study The stability study was performed as per ICH guidelines. The formulated solution was filled in collapsible tubes and stored at different temperature and humidity conditions, 25ºC±2ºC / 60% ± 5% RH, 30ºC±2ºC / 65% ± 5% RH, 40ºC±2ºC / 75%±5% RH for the period of three month and studied for appearance, pH and spread ability

Anti-microbial Activity The in-vitro anti-microbial study of formulated solution was performed by disc diffusion method in triplicate manner by using Muller Hinton Agar medium against a pathogenic bacterial strain Staphylococcus aureus (S. aureus, MTCC 3160). S. aureus was initially cultured in nutrient broth and incubated at 37ºC for 24 Hrs. and then cultured cells were tend to multiply in the Muller Hinton agar plates. Then the formulated tooth gel containing discs were placed over the bacterial plates and incubated at 37ºC for the 24 Hrs, comparing ciprofloxacin as the positive control. The diameter of zone of inhibition (ZOI) was measured in millimetres (mm). The minimum inhibitory concentration (MIC) is the smallest concentration in which the compound displays no visible microbial growth. It was determined by agar streak dilution method in triplicate manner. The protocol involve formation of microbial suspension (~105 CFU/mL), application to the petridish with serial dilution and incubation of petridish at 37±1ºC. The MIC value was determined and the average was taken.

Test name	Result
Colour	Brown
Odour	Spicy
Test	Sweet
PH	7
Stability	Stable up to 35°C.

4. CONCLUSION

Cinchona bark contains quinine, which is a medicine used to treat malaria. It also contains quinidine which is a medicine used to treat heart palpitations.

Quinine is used to treat malaria caused by Plasmodium falciparum. Plasmodium falciparum is a parasite that gets into the red blood cells in the body and causes malaria. Quinine works by killing the parasite or preventing it from growing.

The crude extracts of Cinchona bark were as effective as quinine in the treatment of both vivax and falciparum malaria and might be even more effective in dealing with quinine resistant Plasmodium falciparum. A limitation of these and later controlled studies was that the treatment benefit was assessed only by parasite clearance in the short term.