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Chemotherapy of malaria parasites

Antimalarials currently fall into three broad categories according to their chemical structure and mode of action:

1.

Aryl aminoalcohol compounds: quinine, quinidine, chloroquine, amodiaquine, mefloquine, halofantrine, lumefantrine, piperaquine, tafenoquine

Mechanism of Action of Aryl aminoalcohol:

- Its precise mechanism as an antimalarial is poorly understood.
    - In *Plasmodium falciparum* quinine

has been found to inhibit nucleic acid synthesis, protein synthesis, and glycolysis; it also binds with hemazoin in parasitized erythrocytes.
    - It is effective as a malarial suppressant and in control of overt clinical attacks. Its primary action is schizontocidal, no lethal effect is exerted on sporozoites or pre-erythrocitic tissue forms.

2.

Antifolate compounds ("antifols"): pyrimethamine, proguanil,

chlorproguanil, trimethoprim

- Mechanism of Action of Antifolate compounds:
  - Folic acid antagonists**.** The rationale for there combination is a synergistic effect to inhibit folic acid synthesis, and a differential requirement between host and parasite for nucleic acid precursors involved in growth.
  - This activity is highly selective against plasmodia and Toxoplasma gondii.
  - Pyrimethamine is chemically related

to trimethoprim. It acts slowly against erythrocytic forms of susceptible strains of all four human malaria species. It is not adequately gametocidal or effective against liver stages.

3.

Artemisinin compounds (artemisinin, dihydroartemisinin, artemether, artesunate

Mechanism of action of Artemisinin compounds:

- Produces a free radical when it undergoes an iron-catalyzed cleavage of an endoperoxide bond in the parasite food vacuole.

- It is a rapidly acting blood schizonticide, with some activity against gametocytes, but no activity against the hepatic stages of the malarial parasite.