# ANTIMALARIAL DRUGS

These are drugs used for prophylaxis, treatment and prevention of relapses of malaria. Malaria, caused by 4 species of the protozoal parasite Plasmodium, is endemic in most parts ofIndia and other tropical countries.

CLASSIFICATION

**4-Aminoquino/ines** Chloroquine, Amodiaquine, Piperaquine.

**Quinoline-**methanol Mefloquine.

**Cinchona alkaloid** Quinine, Quinidine

**Biguanides** Proguanil, (Chloroguanide), Chlorproguanil

**Diaminopyrimidines** Pyrimethamine

**8-Aminoquino/ine** Primaquine, Bulaquine

**Sulfonamides** Sulfadoxine and sulfone Sulfamethopyrazine, Dapsone

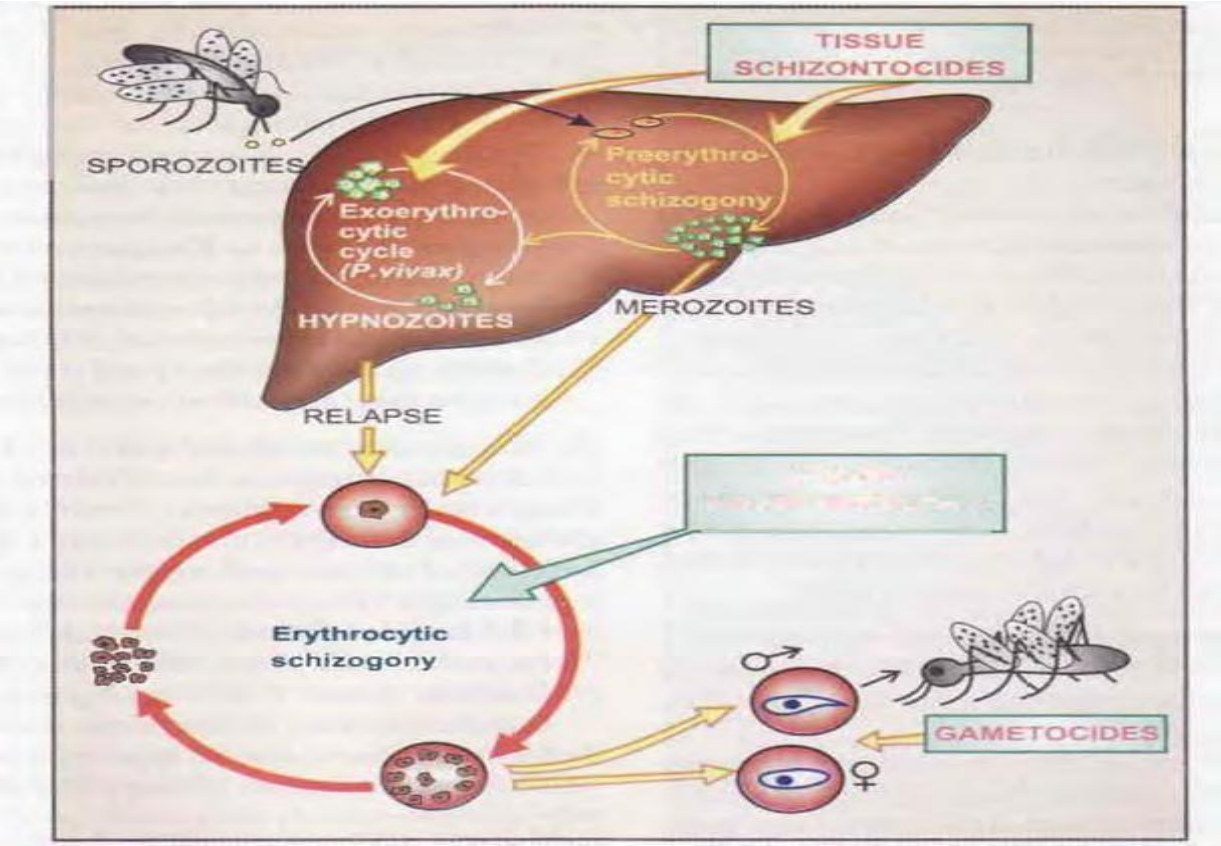
**Tetracyclines** Tetracycline, Doxycycline

**Sesquiterpine lactones** Artesunate, Artemether, Arteether

**Amino alcohols** Halofantrine, Lumefantrine

**Mannich base** Pyronaridine

**Naphthoquinone** Atovaquone




**CHLOROQUINE**

It is a rapidly acting erythrocytic schizontocide against all species of plasmodia; controls most clinical attacks in 1-2 days with disappearance of parasites from peripheral blood in 1-3 days. Therapeutic plasma concentrations are in the range of 15-30 ng/ml.

The mechanism of action of chloroquine is not completely known. It is actively concentrated sensitive intraerythrocytic plasmodia: higher concentration is found in infected RBCs. *By accumulating in the acidic vesicles of the parasite and because of its weakly basic nature, it raises the vesicular pH and thereby interferes with degradation of haemoglobin by parasitic lysosomes.* Polymerization of toxic haeme to nontoxic parasite pigment hemozoin is inhibited by formation of chloroquine-heme complex. Heme itself or its complex with chloroquine then damages the plasmodial membranes

***Blood schizonticide: Mefloquine***

***Mefloquine*** [MEF-lo-kween] appears to be promising as an effective single agent for suppressing and curing infections caused by multidrug-resistant forms of P. falciparum. Its exact mechanism of action remains to be determined, but like *quinine*, it can apparently damage the parasite's membrane.

***Mefloquine*** is absorbed well after oral administration and concentrates in the liver and lung. It has a long half-life (17 days) because of its concentration in various tissues and its continuous circulation through the enterohepatic and enterogastric systems. The drug undergoes extensive metabolism. Its major excretory route is the feces.

**Adverse reactions** at high doses range from nausea, vomiting, and dizziness to disorientation, hallucinations, and depression. Electrocardiographic abnormalities and cardiac arrest are possible if *mefloquine* is taken concurrently with *quinine* or *quinidine*.

***Blood schizonticides: Quinine and quinidine***

*Quinine* and its stereoisomer, quinidine interfere with heme polymerization, resulting in death ofthe erythrocytic form of the plasmodial parasite. These drugs are reserved for severe infestations and for malarial strains that are resistant to other agents, such as *chloroquine*. Taken orally,*quinine* is well distributed throughout the body and can reach the fetus. Alkalinization of the urine decreases its excretion.

The major **adverse effect** of *quinine* is cinchonisma syndrome causing nausea, vomiting, tinnitus, and vertigo. These effects are reversible and are not considered to be reasons for suspending therapy. However, *quinine* treatment should be suspended if a positive Coombs' test forhemolytic anemia occurs.

**Drug interactions** include potentiation of neuromuscular-blocking agents and elevation of *digoxin* levels if taken concurrently with *quinine*. *Quinine* absorption is retarded when the drug is taken with aluminum-containing antacids. *Quinine* is fetotoxic.

***Blood schizonticide: Artemisinin Artemisinin*** is derived from the qinghaosu plant, which has been used in Chinese medicine for more than two millennia in the treatment of fevers and malaria. *Artemisinin* (or one of its derivatives) is available for the treatment of

severe, multidrug-resistant P. falciparum malaria. Its *antimalarial action involves the production offree radicals within the plasmodium food vacuole, following cleavage of the drug's endoperoxide bridge by heme iron in parasitized erythrocytes*. It is also believed to covalently bind to and damage specific malarial proteins. Oral, rectal, and intravenous preparations are available, but the short half-lives precludetheir use in chemoprophylaxis. They are metabolized in the liver and are excreted primarily in the bile. Adverse effects include nausea, vomiting, and diarrhea, but overall, *artemisinin* is remarkably safe. Extremely high doses may cause neurotoxicity and prolongation of the QT interval.