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**DEPTMENT: NURSING SCIENCE**

**COURSE: PHARMACOLOGY**

 **ASSIGNMENT**

Classify the antimalarial agents and state the mechanism of action of each of the drug listed

 **ANSWER**

1**.CHLOROQUINE**

**Drug Class:** Antimalarial & Antirheumatoid

**Classification:** Blood schizonticide

**Antimalarial Mechanism of Action:** Chloroquine and other similar quinolones (e.g. hydroxychloroquine, quinine) become concentrated in parasite food vacuoles, preventing the polymerization of the hemeoglobin product, heme, into hemozoin and thus eliciting parasite toxicity due to the build up of heme.

It is not active against liver stage parasites (and primaquine must be added for the radical cure of these species).

Malarial parasites have a limited ability to synthesize amino acids, and rely upon amino acids obtained by the breakdown of host hemoglobin molecules in digestive vacuoles (Figure 1). Degradation of hemoglobin releases both amino acids as well as a toxic heme metabolite ferriprotoporphyrin IX, which is normally detoxified by a pH-dependent polymerization to an unreactive malarial pigment named hemozoin (Figure 6). When polymerization of ferriprotoporphyrin IX is inhibited, its increased concentration in the parasites food vacuole will cause oxidative damage to membranes and death of the parasite.

2.**QUINNINE (& QUINIDINE) FOR MALARIA**

**Drug Class:** Antimalarial (P. falciparum)

**Classification:** haemozoin biocrystallization

**Mechanism of Action:** 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. Quinine 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. Quinine blocks cardiac K & Na channels similar to quinidine.

3.**PRIMAQUINE**

**Drug Class:** Antimalarial (P. vivax & P. ovale)

**Classification:** hypnozoiticidal and gametocytocidal

**Mechanism of Action:** Active against the hepatic stages of all human malarial parasites. Some gametocytes are destroyed while others cannot undergo maturation division in the gut of the mosquito. Primaquine’s cellular mechanism of action is still poorly understood. Fourteen primaquine metabolites have been detected, and few have been fully assessed for their biological activity. Evidence suggests that one or more highly reactive metabolites of primaquine inflict extensive oxidative damage that interferes with mitochondrial electron transport in parasites (NOTE: primaquine is also known to increase the oxidative stress on human red blood cells, an effect that contributes to its haemolytic side effects) (Butterworth et al, 2013).

 4.**MEFLOQUINE**

**Drug Class:** Antimalarial

**Classification:** Blood schizonticidal

**Mechanism of Action:** Unknown, chemically related to quinidine. Has strong blood schizonticidal activity against P. falciparum and P. vivax, but not against hepatic stages or gametocytes.

5.**PYRIMETHAMINE + SULFADOXINE**

**Drug Class:** Antimalarial

**Mechanism of Action:** 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.

6.**ARTESUNATE & ARTEMETHER** (Artemisinin analogues)

**Drug Class:** Blood schizonticide (synthetic analogues of a natural product isolated from Chinese shrub)

**Mechanism of Action:** It produces a free radical when it undergoes an iron-catalysed 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.