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**MATRIC NO: 17/MHS02/086**

**COURSE TITLE: SYSTEMIC PHARMACOLOGY IN NURSING PRACTICE**

**COURSE CODE: PHA 324**

**ASSIGNMENT TITLE: CHEMOTHERAPY OF MALARIAL PARASITES**

**QUESTION: CLASSIFY THE ANTI MALARIA AGENTS AND STATE THE MECHANISM OF ACTION EACH CLASS OF THE DRUG LISTED.**

**ANSWER**

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| CLASSIFICATION | EXAMPLES |
| 1. Cinchona alkaloid | 1. Quinine 2. Quinidine |
| 1. 4-aminoquinolines | 1. Chloroquine 2. Amodiaquine 3. Piperaquine |
| 1. 8-aminoquinolines | 1. Primaquine 2. Bulaquine 3. Tafenoquine |
| 1. Diaminopyrimidines | 1. Pyrimethamine |
| 1. Sulfonamides & sulfone | 1. Sulfadoxine 2. Sulfamethopyrazine 3. Dapsone |
| 1. Quinoline- methanol | 1. Mefloquine |
| 1. Biguanides | 1. Proguanil 2. Chlorproguanil |
| 1. Antibiotics | 1. Tetracyclines 2. Doxycycline |
| 1. Amino alcohols | 1. Halofantrine 2. Lumfantrine |
| 1. Sesquiterpine lactones | 1. Artesunate 2. Artemether 3. Arteether |
| 1. Naphthoquinone | 1. Atovaquone |
| 1. Naphthyridine | 1. pyronaridine |

**MACHANISM OF ACTION OF EACH CLASS**

1. **4-AMINOQUINOLINES**

4-**aminoquinolines** **e.g** **chloroquine:** Chloroquine and other similar quinolones e.g hydroxychloroquine become concentrated in parasite food vacuoles, preventing the polymerization of the hemoglobin 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 on amino acid obtained from the breakdown of host hemoglobin molecules in the digestive vacuoles. 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 unreactive malarial pigment called hemozoin. When polymerization of ferriprotoporphyrin IX is inhibited, its increased concentration in the parasite food vacuoles will cause oxidation damage to membrane and death of the parasite.

1. **CINCHONA ALKALOID**

**Cinchona alkaloid e.g quinine:** In *Plasmodium falciparum* quinine has been found to inhibit nucleic acid synthesis, protein synthesis and glycolysis, it bind with hemezoin 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-erythrocytic tissue forms.

1. **Quinoline-methanol**

**Quinoline**-**methanol** **e.g mefloquine:** unknown, chemically related to quinidine. Has blood schizonticidal activity against *P. falciparum and P. vivax* but not against hepatic stages or gametocytes.

1. **8-AMINOQUINOLINES**

**8-aminoquinolines e.g primaquine:** Active against the hepatic stages of all human malarial parasites. Some gametocytes are destroyed while others can not undergo maturation division in the gut of the mosquito. Evidence suggests that one or more highly reactive metabolites of primaquine inflict extensive oxidative damage that interferes with mitochondrial electron transport in parasites.

1. **SESQUITERPINE LACTONES**

**Sesquiterpine lactones e.g artesunate:** 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, but no activity against the hepatic stages of the malarial parasite.

1. **DIAMINOPYRIMIDINES & SULFONAMIDES AND SULFONE**

**Diaminopyrimidines & sulfonamides and sulfone e.g pyrimethamine+sulfadoxine:** The rationale for their 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. The activity is highly selective against plasmodia and Toxoplasma gondii. Pyrimethamine is chemically related to trimethoprim. It acts slowly against erythrocytics forms of susceptible strains of all four human malaria species. It is not adequately gametocidal or effective against liver stages.

1. **AMINO ALCOHOLS**

**Amino alcohols e.g lumefantrine:** Lumefantrine inhibit nucleic acid and formation of beta-hematin by **forming** a complex with hemin. It is a blood schizontocides.

1. **BIGUANIDES**

**Biguanides e.g proguanil:** Proguanil inhibits dihydrofolate-reductase-thymidylate synthase.

1. **NAPHTHOQUINONE**

**Naphthoquinone e.g atovaquone:** Atovaquone inhibits mitochondrial electron transport in the cytochrome bc 1 complex.

1. **ANTIBIOTICS**

**Antibiotics e.g tetracyclines:** Tetracyclines are effective antimalarials but their mechanism of action is unclear. Since these agent block prokaryotic protein synthesis, it has been proposed that they disrupt the mitochondrion or the apicoplast, both of which include prokaryotic ribosomal subunits in their genomes.