**NAME: ONOJAKPOR PRINCESS EMUOBOMESA**

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**COURSE TITLE: CHEMOTHERAPY.**

**COURSE CODE: PHA 324.**

**LEVEL 300**

Classify Antimalarial agents and state the mechanism of action of each of the drug .

**CLASSIFICATION OF ANTIMALARIAL AGENTS.**

(1). 4-aminoquinoline:

.Chloroquine.

.Amodiaquine.

(2). Quinoline Methanol:

.Mefloquine.

(3). Cinchona alkaloid:

.Quinine

.Quinidine.

(4). Biguanides:

.Proguanil(chloroguanide).

(5). Diaminopyrimidine:

.Pyrimethamine.

(6). 8-aminoquinoline:

.Primaquine.

.Tafenoquine.

(7). Sulfonamide and sulfone:

.Sulfadoxine.

.Sulfamethopyrazine.

.Dapsone.

(8). Antibiotics:

.Tetracycline.

.Doxycycline.

(9). Sesquiterpine lactones:

.Artesunate.

.Artemether.

.Arteether.

(10). Amino alchohols:

.Halofantrine.

.Lumefantrine.

(11). Naphthyridine:

.Pyronaridine.

(12). Naphthoquinolone.

.Atovaquone.

**MECHANISM OF ACTION OF 4-AMINOQUINOLINE.**

It is actively concentrated by sensitive intra-erythrocytic plasmodia by accumulating in the acidic vesicles of the parasites and weakly basic in nature, it raises the PH of the vessel and thereby interfere with degradation of hemoglobin by parasite lysosome.

Polymerization of toxic haeme to nontoxic parasite pigment Hemozoin, is inhibited by formation of Chloroquine or Amodiaquine-Heme complex.

Haeme itself or its complex with Chloroquine or Amodiaquine then damages the plasmodial memebranes, clumping of pigment and changes in parasitic membrane and then folow death.

EXAMPLES OF 4-AMINOQUINOLINE ARE: CHLOROQUINE, AMODIAQUINE.

**MECHANISM OF ACTION OF QUINOLINE METHANOL.**

It is actively concentrated by sensitive intra-erythrocytic plasmodia by accumulating in the acidic vesicles of the parasites and weakly basic in nature, it raises the PH of the vessel and thereby interfere with degradation of hemoglobin by parasite lysosome.

Polymerization of toxic haeme to nontoxic parasite pigment Hemozoin, is inhibited by formation of Chloroquine or Amodiaquine-Heme complex.

Haeme itself or its complex with Mefloquine then damages the plasmodial memebranes, clumping of pigment and changes in parasitic membrane and then folow death.

EXAMPLE QUINOLINE METHANOL: MEFLOQUINE.

**MECHANISM OF ACTION OF CHINCHONA ALKALOIDS.**

It is actively concentrated by sensitive intra-erythrocytic plasmodia by accumulating in the acidic vesicles of the parasites and weakly basic in nature, it raises the PH of the vessel and thereby interfere with degradation of hemoglobin by parasite lysosome.

Polymerization of toxic heme to nontoxic parasite pigment Hemozoin, is inhibited by formation of Chloroquine or Amodiaquine-Heme complex.

Heme itself or its complex with Quinine or Quinidine then damages the plasmodial memebranes, clumping of pigment and changes in parasitic membrane and then folow death.

EXAMPLES OF CHINCHONA ALKALOIDS : QUININE, QUINIDINE.

**MECHANISM OF ACTION OF BIGUANIDES.**

Is a prophylactic antimalarial drug, which works by stopping the malaria parasite, plasmodium falciparum and plasmodium vivax from reproducing once it is in the red blood cells. It does this by inhibiting the enzymes, dihydrofolate reductase which is involved in the reproduction of the parasite.

**MECHANISM OF ACTION OF DIAMINOPYRIMIDINES.**

It inhibits plasmodial hydrofolate reductase, reducing the production of folic acid required for nuclei and synthesis in the malaria parasite. It is used to treat acute malaria but not for prophylaxis.

**MECHANISM OF ACTION OF 8-AMINOQUINOLINE.**

It eliminates tissue erythrocytic infection. Thereby, kit prevents the development of the erythrocytic forms of the parasite which is responsible for relapse in vivax and ovale malaria. Primaquine phosphate is also active against gametocyte to plasmodium falciparum.

**MECHANISM OF ACTION OF SULFONAMIDE AND SULFONE.**

They interfere with folic acid synthesis by preventing addition of para-aminobenzoic(PABA) into the folic acid molecule through competying for the enzyme, dihydropteroate synthase.

**MECHANISM OF ACTION OF ANTIBIOTICS.**

They inhibit the initiation of translation In variety of ways by binding to the 30S ribosomal subunit, which is made up of 16S-Rrna and 21 proteins. They inhibit the binding of aminoacyl-tRNA to the mRNA translation complex.

**MECHANISM OF ACTION OF SESQUITERPINE LACTONES.**

The mechanism of action for Artesunate is thought to involve the cleavage of the endoperoxide bond. Though reaction with haeme. This produces free radicals with alkylate parasitic proteins. It has been shown to inhibit an essential parasite calcium adenosine triphosphate enzyme.

**MECHANISM OF ACTION OF AMINO ALCOHOLS.**

**I**t is actively concentrated in the sensitive intra erythrocytic plasmodial by accumulating in the acidic vesicles of the parasite and the weakly basic nature. It raises the vascular PH and thereby interfering with the degradation of hemoglobin by parasite lysosomes. Polymerization of toxics haeme to nontoxic parasite pigment hemozoin is inhibited by formation of the Lumefantrine haeme complex. Haeme itself or in complex with Lumefantrine then damages the plasmodial membranes. Clumping of pigment and changes in parasite membranes follow death.

**MECHANISM OF ACTION OF NAPHTHYRIDINE.**

It is actively concentrated in the sensitive intra erythrocytic plasmodial by accumulating in the acidic vesicles of the parasite and the weakly basic nature. It raises the vesicular PH and thereby interfering with the degradation of hemoglobin by parasite lysosomes. Polymerization of toxics haeme to nontoxic parasite pigment hemozoin is inhibited by formation of the Pyronaridine-haeme complex. Haeme itself or in complex with Lumefantrine then damages the plasmodial membranes. Clumping of pigment and changes in parasite membranes follow death.

**MECHANISM OF ACTION OF** **NAPHTHOQUONE.**

It possesses a novel model of action against Plasmodium falciparum through inhibition of the electron transport system at the level of cytochrome bc1 complex. Avotaquone also causes the collapse of the parasite mitochondrial potential in Plasmodium falciparum.