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**MATRIC NUMBER: 17/MHS02/055**

**NURSING SCIENCE DEPARTMENT**

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

**ASSIGNMENT TITLE: CHEMOTHERAPY OF MALARIAL PARASITES**

**COURSE CODE: PHA324**

**QUESTION**

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

**Classification**

1. 4-Aminoquinolines: chloroquine, Amodiquine
2. Quinolone Methanol: Mefloquine
3. Cinochona alkaloid:Quinine, Quinidine
4. Biguanides: proguanil (chologuanide)
5. Diaminopyrimidines: pyrimethamine
6. 8-Aminoquinoline: primaquine
7. Sulfonamides & sulfone: Sulfadoxine, sulfamethopyrazine, dapsone
8. Antibiotics: Tetracyclins, doxycycline
9. Sesquiterpinelactories: artesunate, artemether, arteether
10. Amino alcohols: halofantrine , lumefantrine
11. Nephthyridine: atovaquine.

**4-Aminoquinolines**

1. **Chloroquine**

**Mechanism of action**

* It is actively concentrated by sensitive intra-erythrocytic by accumulating in the acidic vesicles of the parasite and weakly basic where it raises the vesicular Ph. and thereby interferes with degradation of hemoglobin by parasitic lysosomes.
* Polymerization of toxic haeme to non-toxic parasite pigment hemozoin is inhibited by formation of chloroquine –heme complex
* Haeme itself or it’s complex with chloroquine then damages the plasmodial membranes clumping of pigment and changes in parasite membranes follow:death.
1. **Amodiaquine.**

**Mechanism of action**

* Like other quindine derivatives, it is thought to inherit heme polymerase activity. This results in accumulation of free heme which is toxic to the parasites.

**Quinoline methanol**

1. **Mefloquine**

**Mechanism of action**

Meflouine is an antimalarial agent which acts as a blood schizonticide. Its exact mechanism of action is not known. Activity in vitro and in vivo. Mefloquine is active against the erthrocytic stages of plasmodium species.

**Cinchona alkaloid**

1. **Quinine**

**Mechanism of action**

Same as chloroquine

* It is weak base: gets concentrated in the acidic food vacuoles of sensitive plasmodia
* Inhibits polymerization of haeme to hemozoin
* Free haeme increase( toxic) or haeme- quinie complex damages parasite membranes and kills it
* After oral administration, quinine is rapidly absorbed, reaches peak plasma levels in 1-3 hours, and is widely distributed in body tissues.
* The use of a loading dose in severe malaria allows the achievement of peak levels within a few hours.
1. **Quinidine**

**Mechanism of action**

Like all other class antiarrhythmic agents, quinidine primarily works by blocking the fast inward sodium current (INa) quinidine’s effect on INa is known as use dependent block: this means at higher heart rates, the block increases, while at lower heart rates, the block decreases.

**Biguanides**

1. **Proguanil (chloroguanide)**

**Mechanism of action**

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

**Diaminopyrimidines**

1. **Pyrimethamine**

**Mechanism of action**

Pyrimethamine interefers with the regeneration of tetrahydrofolic acid from dihydrofolate by competitively inhibiting the enzyme dihydrofolate reductase. Terahydrofolic acid is essential for DNA and RNA synthesis in many species, including protozoa.

**8-Aminoquinoline**

1. **Primaquine**

**Mechanism of action**

Primaquine’s mechanism of action is not well understood. It may be acting by generating reactive spices or by interfering with the electron transport in the parasite. Also, although its mechanism of action is unclear, primaquine may bind to and alter the properties of protozoal DNA.

**Sulfonamides & sulfone**

1. **Sulfadoxine**

**Mechanism of action**

Sulfadoxine, the constituent of fansidar, it is folic acid antagonist; sulfadoxine inhibits the activity of dihydropeteroate synthase whereas pyrimethamine inhibits dihydrfolate reductase.

1. **Sulfamethoxypyrazine**

**Mechanism of action**

Sulfamethxypyrazine is a competitive inhibitor of the bacterial enzyme dihydroptenate synthetase para-aminobenzoic acid (PABA),a substrate of the enzyme is prevented from binding. The inhibited reaction is necessary in these organisms for the synthesis of folic acid.

1. **Dapsone**

**Mechanism of action**

Dapsone inhibits bacterial synthesis of dihydrofolic acid, via competition with para-aminobenzonate for the active site of dihydroterate synthase, thereby inhibiting nucleic acid synthesis

**Antibiotics**

1. **Tertacycline**

Tetracycline antibiotic are protein synthesis inhibitors. They inhibit the initiation of translation in veriety of ways of 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

1. **Doxycycline**

Doxycycline inhibits bacterial protein synthesis by binding to the 30s ribosomal subunit, doxycycline has bacteriostatic activity abroad range of Gram-positive and Gram-negative bacteria.

**Sesquiterpine Lactones**

1. **Artesunate**

**Mechanism of action**

 Mechanism of artesunate is thought to involve cleavage of the endoperoxide bond through reaction with haeme^3. This produces free radicals with alkylate parasitic proteins. It has been shown to inhibit an essential parasite calcium adenosine triphosphatase enzyme.

1. **Artemether**

**Mechanism of action**

The drug works against the erythrocytic stages of inhibiting nucleic acid and protein synthesis artemether is administered in combination with lumefantrine for improved efficacy. Arthemther has a rapid onset of action and is rapidly cleared from the body.

1. **Arteether**

**Mechanism of action**

Several proposed including the production of free radicals, other reactive metabolites, and altered membrane transport properties of membranes which inhibit nutrient flow of the parasite.

**Amino alcohols**

1. **Halofantrine**

**Mechanism of action**

Falciparum malaria, the mechanism of action of halofantrine may be similar to that of the choloquine, quinine, mefloquine ; by forming toxic complexes with farriloprophylin IX that damages the membrane of the parasite.

1. **Lumefantrine**

**Mechanism of action**

The exact mechanism by which lumefantrine exerts its antimalarial effect is unknown. However, available data suggest that lumefantrine inhibits the formation of B-hematin by forming a complex with henin and inhibits nucleic acid and protein synthesis

**Nephthyridine**

1. **Pyronaridine**

**Mechanism of action**

Pyronaridine acts as antimalarial with a mechanism of action similar to that of the well-known 4-aminoquinoline choloroquine namely it inhibits B-hematin formation in vitro (a process which closely parallels hemozoin formation with the parasite food vacuole) .

**Nephthoquinone**

1. **Atovaquone**

Selectively inhibits the malarial cytochrome bcq complex in the parasitic electron transport chain, altapsing the mitochondrial membrane potential.