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**17/MHS02/069**

**NURSING SCIENCE**

**300LEVEL**

**PHARMACOLOGY ASSIGNMENT**

**CLASSIFICATION OF ANTIMALARIAL AGENTS.**

1. Cinchona alkaloid:-
2. Quinidine
3. Quinine
4. Quinoline methanol:-
5. Mefloquine
6. 4-Aminoquinolines:-
7. Chloroquine
8. Amodiaquine
9. Biguanides:-
10. Proguanil(Chloroguanide)
11. Diaminopyrimidines:-
12. Pyrimethamine
13. 8-Aminoquinoline:-
14. Primaquine
15. Tafenoquine
16. Sulfonamides & sulfone:-
17. Sulfadoxine
18. Sulfamethopyrazine
19. Dapsone
20. Antibiotics:-
21. Tetracycline
22. Doxycycline
23. Sesquiterpine lactones:-
24. Artesunate
25. Arteether
26. Artemeth
27. Amino alcohols:-
28. Halofantrine
29. Lumefantrine
30. Naphthyridine:-
31. Pyronaridine
32. Naphthoquinone:-
33. Atovaquone

**QUINIDINE**

The mechanism of action is interference with the parasite's ability to digest haemoglobin. Quinidine also inhibits the spontaneous formation of beta-haematin (haemozoin or malaria pigment) which is a toxic product of the digestion of haemoglobin by parasites.

**QUININE**

It is a weak base, gets concentrated in the

acidic food vacuoles of sensitive plasmodia. It inhibits polymerization of haeme to hemozoin. The haeme-quinine complex formed 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.

**MEFLOQUINE**

It is actively concentrated by sensitive intra-

erythrocytic plasmodia by accumulating in the acidic

vesicles of the parasite and 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.

**CHLOROQUINE**

It is actively concentrated by sensitive intra-

erythrocytic plasmodia by accumulating in the acidic

vesicles of the parasite and 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.

**AMODIAQUINE**

The mechanism of plasmodicidal action of amodiaquine is not completely certain. Like other quinoline derivatives, it is thought to inhibit heme polymerase activity. This results in accumulation of free heme, which is toxic to the parasites.

**PROGUANIL**

Proguanil 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 enzyme, dihydrofolate reductase, which is involved in the reproduction of the parasite.

**PYRIMETHAMINE**

Pyrimethamine selectively inhibits the plasmodial form of dihydrofolate reductase, reducing the production of folic acid required for nucleic acid synthesis in the malarial parasite. Pyrimethamine interferes with the regeneration of tetrahydrofolic acid from dihydrofolate by competitively inhibiting the enzyme dihydrofolate reductase.

**PRIMAQUINE**

Primaquine has gametocidal activity against all plasmodia, including P. falciparum. Primaquine's mechanism of action is not well understood. It may be acting by generating reactive oxygen species or by interfering with the electron transport in the parasite.

**TAFENOQUINE**

Tafenoquine is active against the liver stages including the hypnozoite (dormant stage) of P. vivax. In addition to its effect on the parasite, tafenoquine causes red blood cell shrinkage in vitro. The molecular target of tafenoquine is not known.

**SULFADOXINE**

Sulfadoxine is used in combination with pyrimethamine for the treatment or prevention of malaria. It is a folic acid antagonist. Sulfadoxine inhibits the activity of dihydropteroate synthase which is an enzyme necessary in the conversion of PABA to folic acid. As folic acid is vital to the synthesis, repair, and methylation of DNA which is vital to cell growth in Plasmodium falciparum.

**SULFAMETHOPYRAZINE**

Sulfametopyrazine is a competitive inhibitor of the bacterial enzyme dihydropteroate 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.

**DAPSONE**

dapsone inhibits bacterial synthesis of dihydrofolic acid, through competition with para-aminobenzoate for the active site of dihydropteroate synthase, thereby inhibiting nucleic acid synthesis.

**TETRACYCLINE**

It is a protein synthesis inhibitor. It inhibits 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. It inhibits the binding of aminoacyl-tRNA to the mRNA translation complex.

**DOXYCYCLINE**

Doxycycline inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit. Doxycycline has bacteriostatic activity against a broad range of Gram-positive and Gram-negative bacteria.

**ARTESUNATE**

Artesunate is an artemisinin drug capable of killing all erythrocytic stages of the malaria parasite including the ring stage, late schizonts, and the gametocytes responsible for transmission of malaria 3. It also increases splenic clearance of infected erythrocytes by reducing cytoadherence. The mechanism of artesunate is thought to involve cleavage of the endoperoxide bond through reaction with haeme 3. This produces free radicals which alkylate parasitic proteins. It has been shown to inhibit an essential parasite calcium adenosine triphosphatase enzyme. Artesunate inhibits malaria proteins EXP1, a glutathione S-transferase, responsible for breaking down cytotoxic hematin.

**ARTEMETHER**

The drug works against the erythrocytic stages of P. falciparum by inhibiting nucleic acid and protein synthesis. Artemether is administered in combination with lumefantrine for improved efficacy. Involves an interaction with ferriprotoporphyrin IX (“heme”), or ferrous ions, in the acidic parasite food vacuole, which results in the generation of cytotoxic radical species.

**HALOFANTRINE**

The mechanism of action of Halofantrine may be similar to that of chloroquine, quinine, and mefloquine. It works by forming toxic complexes with ferritoporphyrin IX that damage the membrane of the parasite.

**LUMEFANTRINE**

lumefantrine inhibits the formation of β-hematin by forming a complex with hemin and inhibits nucleic acid and protein synthesis.

**PYRONARIDINE**

It inhibits β-hematin formation in vitro (a process which closely parallels hemozoin formation within the parasite food vacuole).

**ATOVAQUONE**

Atovaquone selectively inhibits the malarial cytochrome bc1 complex in the parasitic electron transport chain, collapsing the mitochondrial membrane potential.