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**Assignmen**t: classify the antimalarial agents and state the mechanism of action of each class of drug listed.

1. CHLOROQUINE

**Mechanism of action:**

* 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. Haeme itself or its complex with chloroquine then damages the plasmodial membranes. Clumping of pigment and changes in parasite membranes follow: death.

1. AMODIAQUINE

**Mechanism of action:**

* It is thought to inhibit heme polymerase activity. This result in accumulati0on of free heme, which is toxic to the parasite. The drug binds the free heme preventing the parasite from converting it to a form less toxic. This drug heme complex is toxic and disrupts membrane function.

1. MEFLOQUINE

**Mechanism of action**

* Mefloquine 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 erythrocytic stages of Plasmodium species. However, the drug has no effect against the exoerythrocytic (hepatic) stages of the parasite. Mefloquine is effective against malaria parasites resistant to chloroquine

1. QUINE

**Mechanism of action:**

* Same as chloroquine
* It is a weak base: gets concentrated in the acidic food vacuoles of sensitive plasmodia
* inhibits polymerization of haeme to hemozoin free haeme increases(toxic) or haeme-quinine 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. PYRIMETHAMINE

**Mechanism of action:**

* It is a directly acting inhibitor of plasmodial DHFRase.
* It gradually reduces the schizogony of malaria parasite in the blood.
* It is slowly acting erythrocytic schizontozide.

1. PROGUANIL

**Mechanism of action:**

* It is cyclized in the body to cycloguanil which inhibits plasmodial DHFRase in preference to the mammalian enzyme.

1. TETRACYCLINE

**Mechanism of action:**

* Tetracycline inhibits protein synthesis by blocking the binding of aminoacyl-tRNA charged to site A on the ribosome. This binds to the 30S subunit of the microbial ribosomes. Therefore, it prevents the introduction of new amino acids to the nascent peptide chain.
* The action is usually inhibitory and reversible when withdrawing the drug. Mammalian cells are less vulnerable to the effect of tetracyclines, despite the fact that tetracycline binds to the small ribosomal subunit of prokaryotes and eukaryotes (30S and 40S, respectively).
* This is because bacteria actively pump tetracycline in their cytoplasm, even against a concentration gradient, while mammalian cells do not. This explains the relatively small effect outside the tetracycline site on human cells.

1. ARTEMESININ

**Mechanism of action:**

* These compound have presence of endoperoxide bridge.
* Endoperoxide bridge interacts with heme in parasite
* Heme iron cleaves this endoperoxide bridge.
* There is generation of highly reactive free radicals which damage parasite membrane bycovalently binding to membrane proteins.

1. SULFONAMIDES

**Mechanism of action:**

* Bacteria synthesize their own folic acid of which p-aminobenzoic acid (PABA) is a constitutent, and is taken up from the medium.
* Sulfonamides are structural analogues of PABA, inhibit bacterial folate synthase and formation of folate get inhibited.
* Sulfonamides competitively inhibit the PABA with pteridine residue to form dihydropteroic acid which conjugates with glutamic acid to produce dihydrofolic acid
* Sulfonamide altered folate and which is metabolically injurious.

1. ATOVAQUONE

**Mechanism of action:**

* Atovaquone selectively inhibits the malarial cytochrome bc1 complex in the parasitic electron transport chain, collapsing the mitochondrial membrane potential. The malarial electron transport chain does not contribute significantly to ATP synthesis; thus it is believed that parasite death is due to the indirect inhibition of dihydroorotate dehydrogenase, which requires transport chain function and is essential to pyrimidine biosynthesis.

1. CLINDAMYCIN

**Mechanism of action:**

* Clindamycin works primarily by binding to the 50s ribosomal subunit of bacteria. This agent disrupts protein synthesis by interfering with the transpeptidation reaction, which thereby inhibits early chain elongation.
* Climdamycin may potentiate the opsonization and phagocytosis of bacteria even at subinhibitory concentrations. By disrupting bacterial protein synthesis, clindamycin causes changes In the cell wall surface, which decreases adherence of bacteria to host cells and increases intracellular killing of organisms. The drug also exerts an extended postantibiotic effect against some strains of bacteria, which may be attributed to persistence of the drug at the ribosomal binding site.

1. DOXYCYCLINE

**Mechanism of action:**

* Acts to inhibit the process of protein synthesis by binding to the 30S ribosomal subunit thus preventing the 50s and 30s unit from bonding. Doxycycline has bacteriostatic activity against a broad range of Gram-positive and Gram-negative bacteria.