***NAME***

***FELIX-AREMO OLUWATOMISIN.I***

***MATRIC NUMBER***

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***ASSIGNMENT***

***CHEMOTHERAPY OF MALARIA PARASITES.***

***COURSE TITLE***

***SYSTEMIC PHARMACOLOGY IN NURSING PRACTICE.***

***COURSE CODE***

***PHA 324***

***QUESTION.***

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

***SOLUTION***

***CLASSIFICATION OF ANTIMALARIA AGENTS.***

* ***ARYL aminoalcohol compounds: quinine,quinidine,chloroquine,amodiaquine,mefloquine,halofantrine,lumefantrine,piperaquine,tafenoqine.***
* ***Antifolate compounds(“antifols”): pyrimethamine,proguanil,chlorproguanil,trimethoprim***
* ***Artemisinin compounds(artemisinin,dihydroartemisinin,artemether,artesunate.***

***MECHANISM OF ACTION OF ANTIMALARIA AGENTS.***

***ARYL amino alcohol compounds:***

***CHLOROQUINE MODE OF ACTION***

* *Chloroquine and other quinolones(hydrochloroquine, quinine) become concentrated in the parasite food vacuoles, preventing the polymerization of the hemeoglobin products,heme,into hemozoin and thus eliciting parasite toxicity due to the build up of heme.*
* *It is not active against liver stage parasites(and primanquine must be added for the radical cure of these species)*
* *Malaria parasites have limited ability to synthesize amino acids and rely upon amino acids obtained by the breakdown of host haemoglobin molecules in digestive vacuoles. Degradation of haemoglobin releases boh amino acis as well as a toxic heme metabolites ferriprotoporphyrin IX, which is normally detoxified by a PH-dependent polymerization to an unreactive malarial pigment named hemozoin . when polymerization of ferriprotoporphyrin IX is inhibited, its increased concentration in the parasites food vacuole will cause oxidative damage to membranes and death of the parasite.*

***QUININE(&QUINIDINE)MECHANISM OF ACTION***

* *Its precise mechanism as an antimalarial is poorly understood.*
* *In plasmodium falciparum quinine has been found to inhibit nucleic acid systhesis, protein systhesis, and glycolysis; it also binds with hemazoin in parasitized erythrocytes.*
* *Quinine is effective as a malarial suppressants and in control of overt clinical attacks. Its primary action is schizontocidal, no lethal effects is exerted on sporozoties or pre-erythrocitic tissues forms.*
* *Quinine blocks cardiac K&Na channels similar to quinidine.*

***PRIMAQUINE MECHANIAM OF ACTION***

* *Active against the hepatic stages of all human malarial parisites. Some gametocytes are destroyed while others cannot undergo maturation division in the gut of the mosquito.*
* *Primaquine’s cellular mechanism of action is still poorly understood*
* *Fourteen primaquine metabolites have been detected, and few have been fully assessed for their biological activity.*
* *Evidence suggest that one or more highly reactive metabolites of primaquine inflict extensive oxidative damage that interferes with mitochondrial electron transport in parasites. (NOTE: primaquine is also known to increase the oxidative stress on human red blood cells, an effect that contributes to its haemolytic side effects).*

***MEFLOQUINE MECHANISM OF ACTION***

* *Unknown , chemically related to quinidine. Has strong blood schizonticidal activity against P.falciparum and P.vivax, but not against hepatic stages or gametocytes.*

***PYRIMETHAMINE+SULFADOXINE MECHANISM OF ACTION.***

* *Folic acid antagonists.the rationale for there combination is a synergisitic effect to inhibit folic acid synthesis, and a differential requirement between host and parasites for nucleic acid precusors involved in growth.*
* *This activity is highly selective against plasmodia and Toxoplasma gondii.*
* *Pyrimethamine is chemically related to trimethoprim . it acts slowly against erythrocytic forms of susceptible strains of all four human malaria species. It is not adequately gametocidal or effective against liver stages.*

***ARTESUNATE & ARTEMETHER (ARTEMISININ******ANALOGS) MECHANISM OF ACTION.***

* *Produce a free radical when it undergoes an iron-catalyzed cleavage of an endoperoxide bond in the parasite food vacuole.*
* *It is rapid acting blood schizonticide, with some activity against gametocytes, but no activity against the hepatic stages of the malarial parasites.*