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Pytomedicines used in a treatment of maleria .

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B.PHARMACY 4th YEAR

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The antimalerial medicinal plants used for the treatment of malaria in India

Abstract :

Malaria is known to cause around 1 million deaths per annum. It is getting very difficult to treat patients suffering from this disease.different vaccine has yet been developed for malaria because of the metabolic pathways during it's life cycle but nature still offer's us a secondary metabolites which have yet to be explored.

Plant based medicine have been used traditionally to treat malaria therefore one can hope that plant derived drugs can prove to be the source of Nobel lead compound to control malaria.six plant species namely Alstonia scholaris,coptis teeta, crotolaria occulta, ocimum sanctum, polygala persicarioefolia, vitex peduncularia.have been different parts of India.

The most frequently used plant parts were leaves (33%) roots (31%) and bark and whole plant (12%) which would help further workers to find out the suitable antimalerial plants by trough study.

Key words :

Malaria, medicinal plants, mosquito repellent, Alkaloids, traditional knowledge of medicine, plasmodium falciparum.

Introduction :

In the WHO south-east Asia region. Three countries accounted for 98% of the total reported cases in the region the main contributor being India (58%) followed by Indonesia (30%) and Myanmar (10%) according to the WMR 2019 India represents 3% of the global malaria burden.

► In India high risk of malaria the districts of balaghat, dindori, mandla and seoni in the state of Madhya Pradesh the district of amini in Arunachal Pradesh North- estern states of Meghalaya Mangalore.

India has sustained API less than one since year 2012 India has also contributed to the largest drop in case region wide from approximately 20million to about 6 million the percentage drop in the malaria cases was 71.8% and deaths was 73.9% between 2000 to 2019

The government of odisha has launched the malaria action coalition in collaboration with “malaria no more”india which is a non-profit organisation working to support India’s 2030 malaria elimination goal.

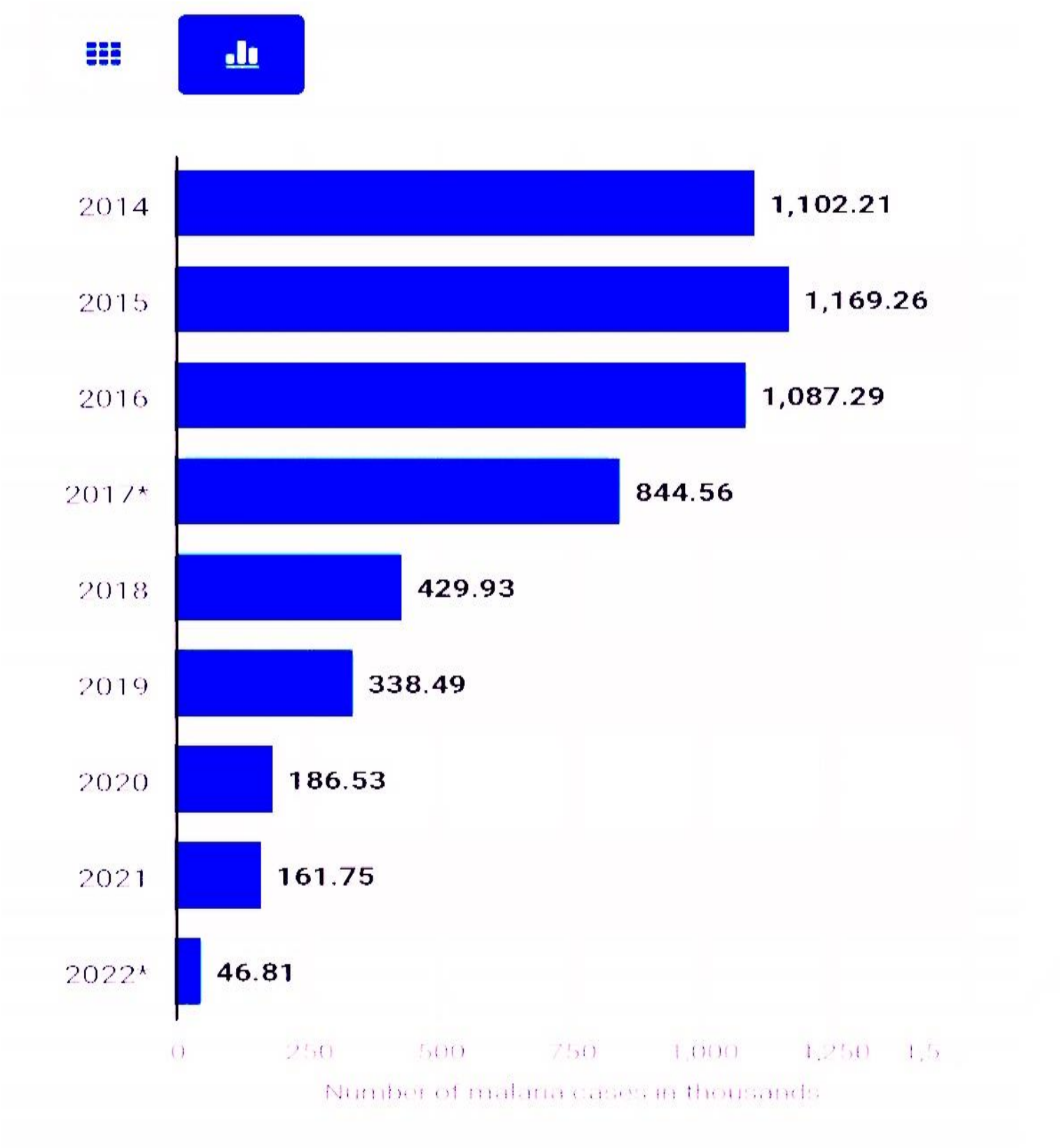
During June to September, the country experiences the manson, characterized by heavy rains across different states maximum transmission of malaria is due to collection of rainwater that promotes mosquito breeding.

According to the latest world malaria report there were 247 million cases of malaria in 2021 campared to 245 million cases in 2020 the estimated number of malaria death stood at 619000 in 2021 campared to 625000 in 2020.

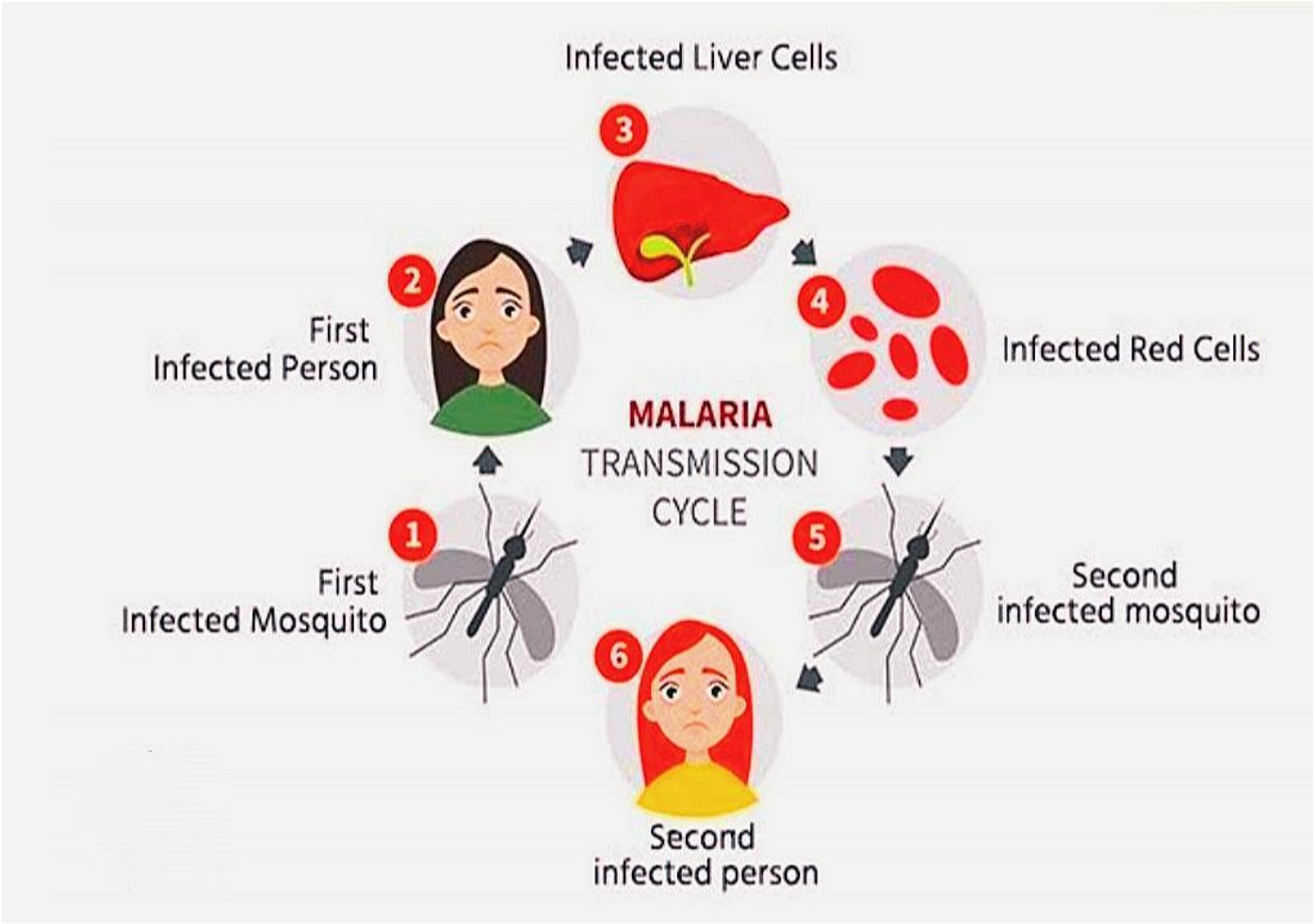
Graphical representation : In India a large number of plant species have been identified as anti-malarial medicinal plant pure products have been isolated from some of these plants.

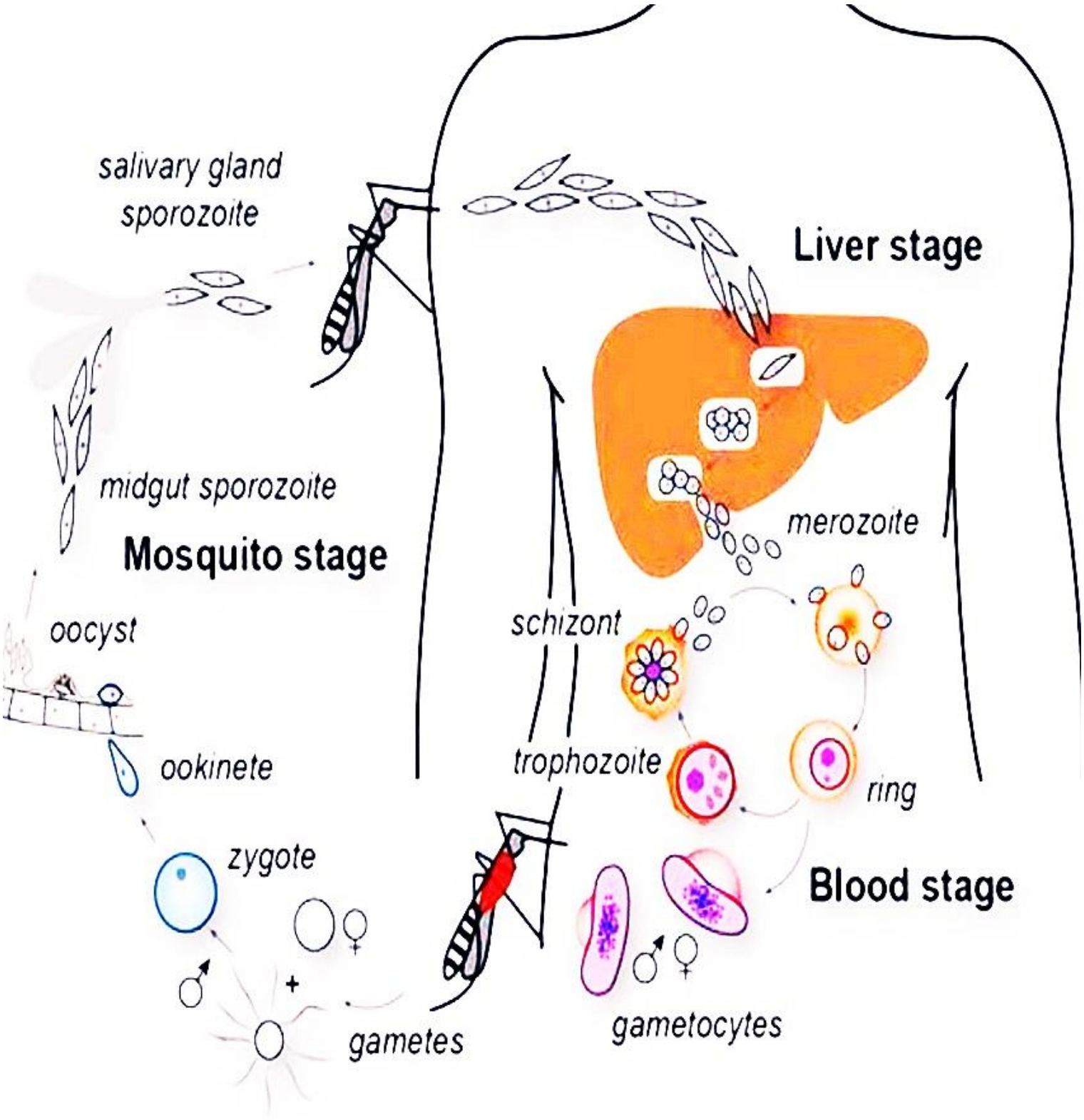
Pathology :

Malaria is a protozoal disease caused by any one or combination of four species of plasmodia: plasmodium vivax, plasmodium falciparum, plasmodium ovale And plasmodium malariae. While plasmodium falciparum



causes malignant malaria, the other three species produce benign form of illness. These parasites are transmitted by bite of female Anapheles mosquito. The disease is endemic in several parts of the world, especially in tropical Africa, parts of South and Central America, India and South-East Asia


Infected Liver Cells
3
2
First
Infected Person
4
Infected Red Cells
MALARIA
TRANSMISSION
CYCLE
1
First
Infected Mosquito
5
Second
infected mosquito
6
Second
infected person


salivary gland
sporozoite
Liver stage
midgut sporozoite
Mosquito stage
merozoite
oocyst
schizont
ookinete
trophozoite
ring
zygote
Blood stage
gametes
gametocytes

The life cycle of plasmodia is complex and is diagrammatically depicted in following fig.

P. falciparum differs from other forms of plasmodia species in 4 respects:

► It does not have exo-erythrocytic stage.

Erythrocytes of any age are parasitised while other plasmodia parasite juvenile red cells.

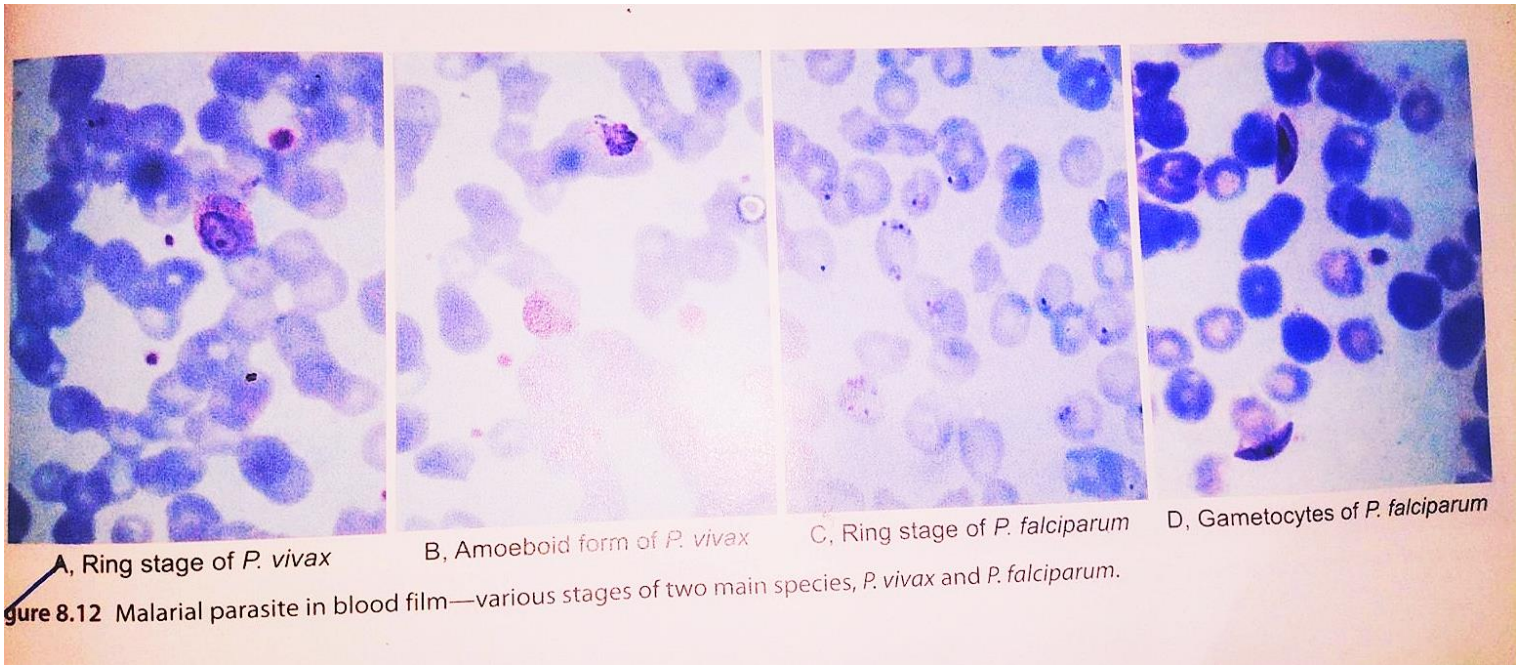
One red cell may contain more than one parasite.

The parasitised red cells are sticky causing obstruction of small blood vessels by thrombi, a feature which is responsible for extraordinary virulence of p.falciparam.

The main clinical features of malaria are cyclic peaks of high fever accompanied by chills, anaemia and splenomegaly.

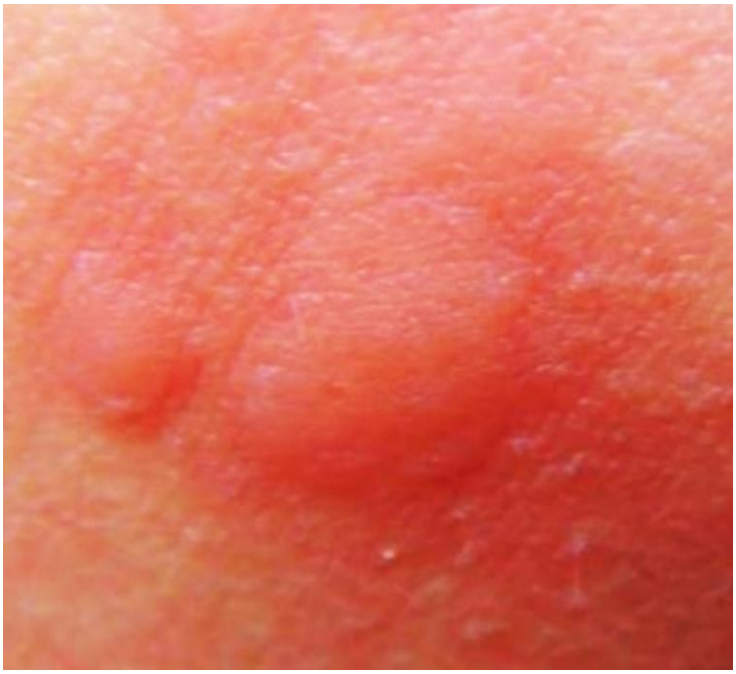
►Major complications occures in several falciparum malaria which may have manifestation of cerebral malaria (coma), hypoglycemia, renal impairment, severe anaemia, haemoglobinuria, jaundice.

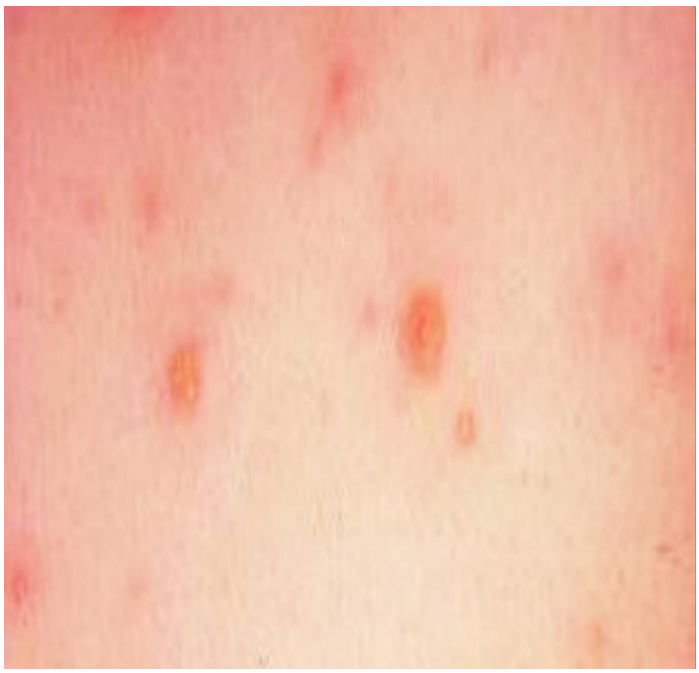
The diagnosis of malaria is made by demonstration of malarial parasite in thin or thick blood flims or sometimes in histologic section.



gure 8.12 Malarial parasite in blood film—various stages of two main species, *P. vivax* and *P. falciparum*.

Signs and symtoms :





How does a plant make an antimalerial medicine.

Introduction.

Malaria is a global health issue. Despite world wide efforts about half a million people die from malaria every year. To develop more effective treatments, biochemists have been studying the antimalerial propertys of artemisinin and how it's made. Malaria is deadly because of the dangerous parasite it creates in the body.

We know that the unusual convert another molecule (DHAA) into Aartimisinin.but no one understood how ! Here, we solved this biology problem using chemistry.

We tagged DHAA to Artemisinin. We found this conversation happens spontaneously, without enzymes.also, it occurs faster in the presence of light.our understanding of Artemisinin formation can help us develop better malaria medicines in laboratories.

Methods:

We created DHAA using previously known chemical reactions and prepared a sooutions.we devided this solution evenly into clear and Amber -colored glass containers(40 each) .we placed the clear glass container by an open window and we placed the Amber glass containers in a black box inside a cabinet.

Using the method of nuclear magnetic resonance (NMR) spectroscopy, we watched how the Artemisinin formed in the different cantainers.this helped us identify the chemical structures of the molecule (DHAA and Artemisinin) in the cantainer.but it didn’t give us accurate information on how quickly the Artemisinin formed, so we reviced our method

we developed a process in the lab that replace two hydrogen atoms in DHAA with deuterium atoms.atoms are made up protons, neutrons and electrons.deuterium has one extra neutron campair to hydrogen and is heavier than hydrogen.deuterium is called as isotope of hydrogen.

we used the same experimental setup as before (cantainers by the window vs in the cabinet) and this time we analysed Artemisinin formation through liquid chromatography – mass spectrometry (NCMS). Using the DHAA with two deuterium atoms formed over time.

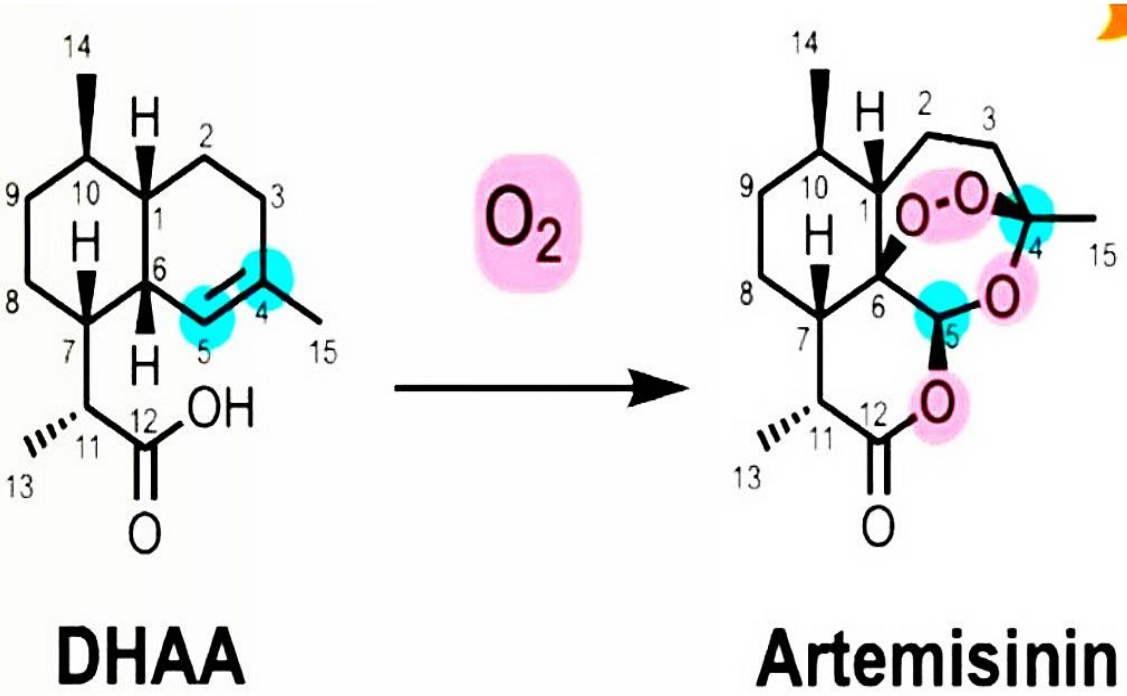


Figure 1:
During the conversion of DHAA to artemisinin, oxygen molecules merge into the molecule to form an endoperoxide bond.

Result :

We found that the conversion of DHAA into Artemisinin is a spontaneous reaction .it does not involve enzymes.the addition of oxygen from the air to the DHAA molecule formed the endoperoxide bridge

Artimisinin formed in all cantainers.how ever, the reaction to form Artemisinin with two deuteriums happed fourty times faster in the clear cantainers by the window than in the Amber cantainers in the dark cabinet.

Surprisingly, when the DHAA with two deuterium atoms converted to Artemisinin,some deuterium atoms were lost.

Recently published plant extracts with antiplasmodial activity :

Family	Species
Amaranthaceae	Amaranthus spinosus.
Annonaceaceae	Uvariopsis congolana
	Polyalthia oliveri
	Enantia cholrantha
Apiaceae	Aphloia theiforms
Apiaceae	Ferula oopoda
	Astrodaucus orientalis
Apocynaceae	Picralima nitida
Asclepiadaceae	Caralluma tuberculata
Asteraceae	Vernonia amygdalina
	Psiadia arguta

Family	Species
Asteraceae	Centaurea bruguieriana
	Centaurea golestanica
Boraginaceae	Heliotropim zeylanicum
Buxaceae	Buxus hyrcana
caesalpiniaceae	Cassia occidentalis
Capparaceae	Boscia angustifolia
Caryophyllaceae	Minuartia lineata
Cucurbitaceae	Momordica foetida
Dilleniaceae	Tefracera pogge
Fabaceae	Glycyrrhiza glabra
	Erythrina fusca
	Stylosanthes erecta
	Tetrapleura tetrapte
Geraniaceae	Erodium oxyrrhnchum

Some important phytomedicine used in treatment of malaria in India :

Chinchona Alkaloids

Qunine quinidine

Alkaloid

Qunine.

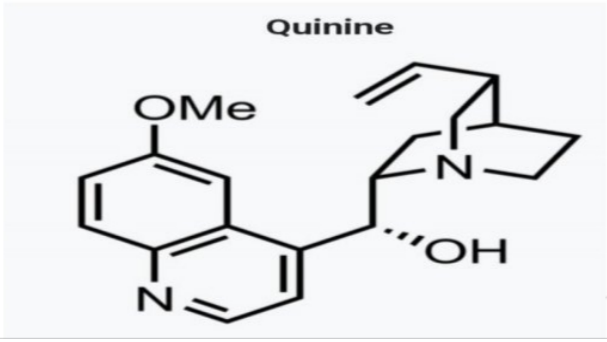
Isolation and extraction

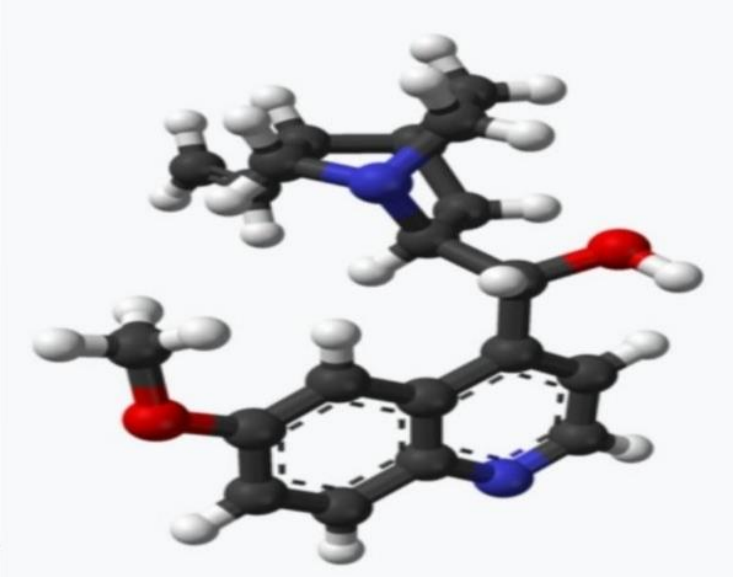
Qunine, as a component. The bark of the chinchona (quina-quina) tree.

The invention related to a process for the extraction of Qunine from ground chinchona bark by extraction with supercritical CO2 at a pressure of 100 to 500 bar and a temperature of 80 to 120°c. the extracted Qunine is precipitated as Qunine sulphate in a separation vessel which is partially filled with sulphuric acid.

Some basic information about Qunine :

Trade name.	=.	Qualaquin, Quinbisul and other
Routes of administration.	=.	By mouth, intramuscular, intravenous, rectal.
Legal stetus.	=.	Prescription only.
Protein binding.	=.	70-95%
Metabolism.	=.	Liver
Elimination half life.	=.	8-14 hr (adults) 6-12hours(child)
Excretion.	=.	Kidney (20%)
Chemical formula.	=.	C20H24N2O2.
Molecular masss.	=.	324.424gmol-1
Melting point.	=.	177°c.
Stuctural formula.	=.	





Uses :

Treat Lupus and arthritis, treatment for leg cramps at night but this has become less common due to a worning from the us FDA.

Adverse effects

Low platelet count and hemolytic uremic syndrome blackwater fever leukopenia and neutropenia, kidney failure.

List of some year of introduction and first report of resistance of antimalerial.

Quinine. =. **1632**

Chloroquine. =. **1945**

Proguanil =. **1948**

Mefloquine =. **1977**

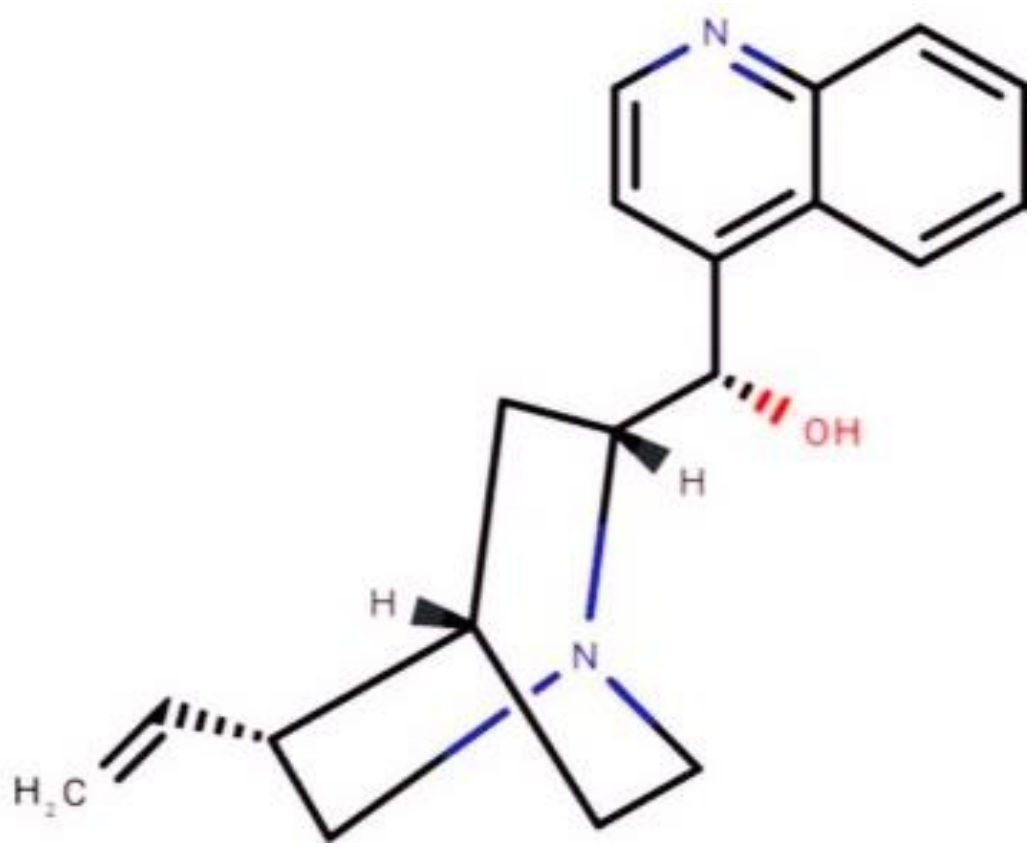
Artemisinin. =. **1971**.

Quinidine :

Qunidine is a medication used to restore normal sinus rhythm treat artrial fibrillation and flutter and treat ventricular aarhythamias.

Isolation and extraction

The powdered bark of chinchona is mixed with calcium hydroxide (or) calcium oxide and enough quality of sodium hydroxide (5%) solution then the pastly material is allowed to stand for a few hours.the moistened material is packed in the soxhlet apparatus and extracted with benzene



Some basic information about Quinidine :

Brand name = Nuedexta

Generic name = Qunidine

Type = Small molecule

Group = Approved, investigation

Weight = 324.4168

Chemical formula. = C20H24N202

Volume of distribution =. 2-3L/kg (adults) 0.5L/kg(patients with congestive heart failure and 3-5L/kg in patients with liver cirrhosis.

Protein binding. =. Bind with glycoprotein and albumin

Metabolism = Liver

Elemination =.Kidney

Half life =. 6-8hrs (adults) 3-4 hrs in pediatric patients

Sesquiterpine Lactones :

The Artemisinin series are the newest of the antimalerial drugs and are structurally unique when compared with the compounds previously and currently used.

The parent compund, Artemisinin, is a natural product extracted from the dry leaves of artemisia annua (sweet warm wood)

All of the compounds given in figure are active against the plasmodium genera that causes malaria.


PLANT- ARTEMISIA ANNUA

The key structure charecetstics appears to be a “ trioxane”

Consisting of the endoperoxide and dioxephine oxygens.

Note that the sterio chemistry at position 12 is not critical.

These are the artimisinin derivatives used in malaria

Artesunate

Artemether

Arteether

Arterolone

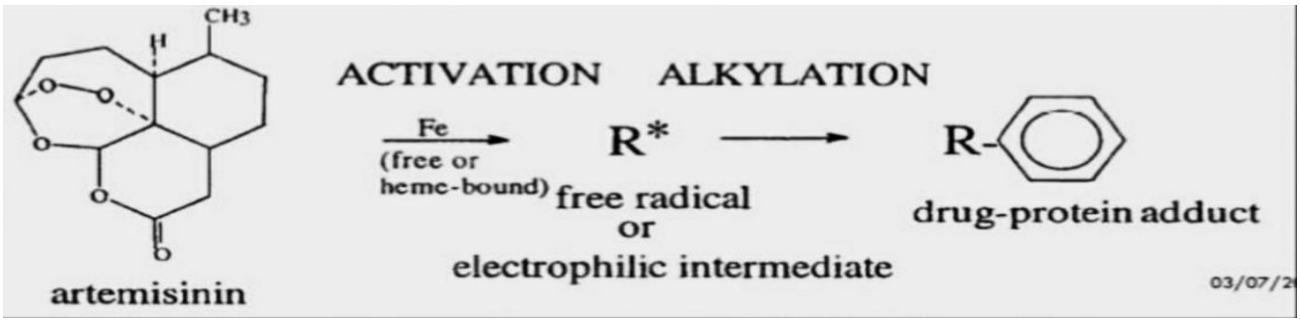
Mechanism of action

These compounds cantains endoperoxide bridge.

Endoperoxide bridge interacts with heme in parasite.

Heme ion clave this endoperoxide bridge.

There is generation of highly reactive free radicals which damage parasite membrane by covalently bonding to membrane proteins.



Conclusion :

There is ongoing research amining at the identification of effective plant extracts to treat malaria.

There is an urgent need for the development of Novel drug to treat malaria.

Biological investigation into plants used traditionally for primary health care are on obvious way in which searching for new leading compounds should concentrate.

Malaria still continues to be a burden to mankind and now it is high time to control and eradicate this distrous disease.

The only hope for finding a lead compound is plants .there are many plants species which have been left unexplored with its ability to treat malaria.

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