Antimalarial plants

Antimalarial plants are a major reason for Africa having any humans living in the continent at all. Malaria is a deadly disease and I have read that until Europeans had access to quinine, they pretty much stayed out of Africa because malaria killed them rapidly.

I searched PubMed for "antimalarial plants" and "malaria and plants".

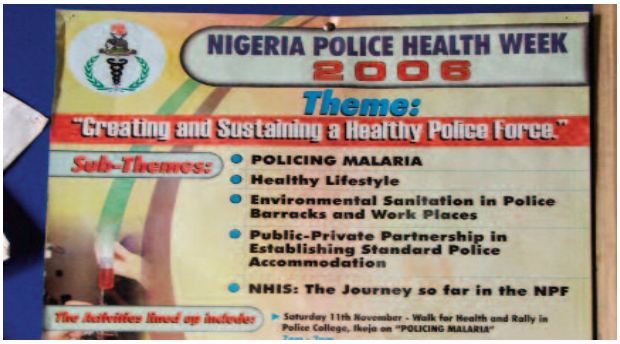
These plants are all effective when they are ingested: however, the continent of Africa is filled with plants that are effective antimalarials because they kill mosquitoes, or repel mosquitoes just by sitting and growing (pyrethrum) or when they are burned (orange peels).

My interest in plants repelling mosquitoes came from my association with the Faculty of Pharmacy and the brilliant Nigerian scientist Professor HAB Coker, who cheerfully nurtures medicinal plants that are known to heal or cure or prevent any disease. He has a lovely farm in land at the University of Lagos main campus that gently slopes down into the bay. He has planted around his house plants that repel mosquitoes, snakes, and probably a whole lot of other living creatures that make life uncomfortable or deadly for humans living in Africa. Professor Coker is Nigerian, was trained in Pharmacy at Nigeria's first school of Pharmacy at the University of Lagos, and has a PhD in pharmaceutics from the University of Strathclyde in Scotland. He was a young full professor, a young Chairman of Pharmacy and a young Deputy Vice Provost of the University of Lagos. Amongst his achievements was setting up a Quality Control laboratory for the state of Lagos; all drugs administered in a state-run hospital or clinic throughout Lagos are tested in his laboratory.

During the 2008 summer in New Jersey, Kenyan Macharia Waruingi, who lived in my house for 7 months, liked to work on his computer in my back garden: citronella candles were not as effective repelling mosquitoes as the incense sticks my daughter lit for him. More than 30 years of burning incense and I never knew they repelled mosquitoes. What else do I not know about repelling mosquitoes, eliminating malaria?

Trager W, Polonsky J. Antimalarial activity of quassinoids against chloroquine-resistant Plasmodium falciparum in vitro. Am J Trop Med Hyg. 1981;30(3):531-7.

The growth of *Plasmodium falciparum* in vitro was inhibited by quassinoids (the bitter principles from plants of the family *Simaroubaceae*). The most active compound, simalikalactone D, completely inhibited at 0.005 microg/mL. Glaucarubinone and soularubinone inhibited at 0.006 microg/mL. Chaparrinone and simarolide were not inhibitory at 0.01 microg/mL. These inhibitions parallel their antineoplastic effects.



Malaria is endemic in Nigeria and Kenya, where the above photographs were taken.

Obih PO, Makinde M, Laoye OJ. Investigations of various extracts of Morinda lucida for antimalarial actions on Plasmodium berghei berghei in mice. Afr J Med Med Sci. 1985;14(1-2):45-9.

Morinda lucida extracts, the stem bark, the root bark and the leaves were screened for antimalarial activity in a "4-day schizontocidal test' against a chloroquine-sensitive strain of *P berghei berghei* in mice. Each extract was administered as a single daily dose on days 0, 1, 2 and 3 to mice that had received an intraperitoneal inoculum of 1 X 10^7 infected erythrocytes. Each extract suppressed parasitaemia. Chromatographic fractions of the stem bark extracts at the highest dose suppressed parasitaemia 96.4%.

O'Neill MJ, Bray DH, Boardman P, Chan KL, Phillipson JD, Warhurst DC, Peters W. Plants as sources of antimalarial drugs, Part 4: Activity of Brucea javanica fruits against chloroquine-resistant Plasmodium falciparum in vitro and against Plasmodium

BERGHEI IN VIVO. J NAT PROD. 1987;50:41-8.

Extracts of *Brucea javanica* fruit were tested. Its antimalarial activity results from its quassinoid constituents. Nine of the quassinoids had in vitro IC50 between 0.046-0.0008 microg/mL against the chloroquine resistant *Plasmodium falciparum* strain (Kl) tested. The 2 quassinoid glycosides tested were considerably less active in vitro than the aglycones. Four quassinoids had activity in vivo against *Plasmodium berghei* infections in mice after oral dosing. All 5 quassinoids tested in vivo had toxicity.

MORETTI C, DEHARO E, SAUVAIN M, JARDEL C, DAVID PT, GASQUET M. ANTIMALARIAL ACTIVITY OF CEDRONIN. J ETHNOPHARMACOL. 1994;43(1):57-61.

Cedronin was isolated from *Simaba cedron Planchon* (Simaroubaceae), a species popularly believed in South America to have antimalarial properties. Cedronin was active against chloroquine-sensitive and resistant strain, with an IC50 of 0.25 microg/mL. It was also found to be active in vivo against *Plasmodium vinkei* with an IC50 of 1.8 mg/kg in the classic 4-day test. Cedronin is in a subgroup of quassinoids with a C19 basic skeleton and has low cytotoxicity against KB cells (IC50 = 4microg/mL) compared with C20 biologically active quassinoids; however its toxic/therapeutic ratio (10/1.8) is lower than chloroquine (10/0.5).

ANG HH, CHAN KL, MAK JW. IN VITRO ANTIMALARIAL ACTIVITY OF QUASSINOIDS FROM EURYCOMA LONGIFOLIA AGAINST MALAYSIAN CHLOROQUINE-RESISTANT PLASMODIUM FALCIPARUM ISOLATES. PLANTA MED. 1995;61(2):177-8.

Three quassinoids from the roots of *Eurycoma longifolia Jack* were evaluated for antimalarial activity against 9 *Plasmodium falciparum* isolates from patients who had chloroquine-resistant malaria. Eurycomanol, eurycomanol 2-O-beta-D-glucopyranoside, and 13 beta, 18-dihydroeurycomanol had IC50 values of 1.2 to 4.9 microM, 0.4-3.5 microM, and 0.5-2.3 microM, respectively, compared with 0.3-0.8 microM for chloroquine.

FRANÇOIS G, DIAKANAMWA C, TIMPERMAN G, BRINGMANN G, STEENACKERS T, ATASSI G, VAN LOOVEREN M, HOLENZ J, TASSIN JP, ASSI LA, VANHAELEN-FASTRE R, VANHAELEN M. ANTIMALARIAL AND CYTOTOXIC POTENTIAL OF FOUR QUASSINOIDS FROM HANNOA CHLORANTHA AND HANNOA KLAINEANA, AND THEIR STRUCTURE-ACTIVITY RELATIONSHIPS. INT J PARASITOL. 1998;28(4):635-40.

Hannoa chlorantha and *Hannoa klaineana* (Simaroubaceae) are used in traditional medicine of Central African countries for fevers and malaria. Four stem bark extracts from *H klaineana* and 4 quassinoids from *H chlorantha* were examined in vitro against *Plasmodium falciparum* NF 54. The quassinoids IC50: chaparrinone was 0.04 and 15-desacetylundulatone was 0.05 microg/mL. Chaparrinone is 5 times more active than 14-hydroxychaparrinone against *P falciparum*. Compared with chaparrinone, 14-hydroxychaparrinone has a 7-times higher cytotoxic activity against P-388 cells. 15-Desacetylundulatone was the most active compound, almost totally suppressing the parasitaemias of OF1 mice for 7 days. Both chaparrinone and 14-hydroxychaparrinone were active for 4 days. Quassinoids have ED50 values under 50 mg/kg-body weight day and none had side effects. The keto function at C-2 in 15-desacetylundulatone is apparently of crucial importance for its high activity. 6-alpha-Tigloyloxyglaucarubol was not active.

MUÑOZ V, SAUVAIN M, BOURDY G, CALLAPA J, ROJAS I, VARGAS L, TAE A, DEHARO E. THE SEARCH FOR NATURAL BIOACTIVE COMPOUNDS THROUGH A MULTIDISCIPLINARY APPROACH IN BOLIVIA. PART II. ANTIMALARIAL ACTIVITY OF SOME PLANTS USED BY MOSETENE INDIANS. J ETHNOPHARMACOL. 2000;69(2):139-55.

Forty-six species collected in the Mosetene ethnia, dwelling in the Andean Piedmont of Bolivia, were screened as antimalarials. Thirty-three extracts were screened in vitro on *Plasmodium falciparum* chloroquine resistant strain (Indo), and 47 extracts were evaluated in vivo on the rodent malaria *P vinckei petteri 279BY*. Only 2 plants are specifically used in combination by the Mosetene against malaria attack (*Hymenachne donacifolia* and *Tesseria integrifolia*); they had no activity in vivo at 1,000 mg/kg. The in vivo most active extracts were *Swietenia macrophylla bark*, *Trema micrantha* bark and *Triplaris americana* bark, not all of them were used for antimalarial purposes by the Mosetene. The following extracts were moderately active: *Jacaratia digitata* inner bark and *Momordica charantia* aerial part (both traditionally used as febrifuge), *Kalanchoe pinnate* aerial part (used in inflammatory processes), *Lunania parviflora* twigs and leaves, *Phyllanthus acuminatus* (used as piscicide), *Tynanthus schumannianus* fruit (used against diarrhoea), *Triumfetta semitrilobata* (used as febrifuge, to alleviate kidney and gynecological pain) and finally *Solanum mammosum* fruit (used against scabies).

CHAN KL, CHOO CY, ABDULLAH NR, ISMAIL Z. ANTIPLASMODIAL STUDIES OF EURYCOMA LONGIFOLIA JACK USING THE LACTATE DEHYDROGENASE ASSAY OF PLASMODIUM FALCIPARUM. J

Ethnopharmacol. 2004;92(2-3):223-7.

The roots of *Eurycoma longifolia Jack* have been used as traditional medicine to treat malaria. A systematic bioactivity-guided fractionation of this plant was conducted involving the determination of the effect of its various extracts and their chemical constituents on the lactate dehydrogenase activity of in vitro chloroquine-resistant Gombak A isolate and chloroquine-sensitive D10 strain of *Plasmodium falciparum* parasites. Their antiplasmodial activity was also compared with their known in vitro cytotoxicity against KB cells. Four quassinoids, eurycomanone (1), 13,21-dihydroeurycomanone (3), 13 alpha(21)-epoxyeurycomanone (4), eurycomalactone (6) and an alkaloid, 9-methoxycanthin-6-one (7), displayed higher antiplasmodial activity against Gombak A isolate but were less active against the D10 strain when compared with chloroquine. Compounds 1 and 3 had higher selectivity indices for the cytotoxicity to antiplasmodial activity ratio than 14,15 beta-dihydroxyklaineanone (2), eurycomanol (5), 6 and 7.

Coombes PH, Naidoo D, Mulholland DA, Randrianarivelojosia M. Quassinoids from the leaves of the Madagascan Simaroubaceae Samadera madagascariensis. Phytochemistry 2005;66(23):2734-9.

The leaves of the Madagascan *Simaroubaceae Samadera madagascariensis* have 3 C18 quassinoids: 5beta,6-dihydrosamaderine A, 2-chloro samaderine A, and samaderolactone A; a C19 quassinoid: 3,4beta-dihydrosamaderine C, and the known quassinoids samaderine A, samaderine B, and cedronin. The compounds isolated had little or no anti-tumour activity.

Cheplogoi PK, Mulholland DA, Coombes PH, Randrianarivelojosia M. An azole, an amide and a limonoid from Vepris uguenensis (Rutaceae). Phytochemistry. 2008;69(6): 1384-8.

The limonoid derivative, methyl uguenenoate, the azole, uguenenazole, and the amide, uguenenonamide, together with the known furoquinoline alkaloids flindersiamine and maculosidine, and syringaldehyde have been isolated from the root of the East African *Rutaceae Vepris uguenensis*. While methyl uguenenoate and the furoquinoline alkaloids displayed mild antimalarial activity, the azole and amide were completely inactive.

Ramanandraibe V, Grellier P, Martin MT, Deville A, Joyeau R, Ramanitrahasimbola D,

Antiplasmodial phenolic compounds from Piptadenia pervillei. Planta Med. 2008;74(4):417-21.

Piptadenia pervillei Vatke (Fabaceae) was selected from a screening programme devoted to the search of naturally-occuring antimalarial compounds from plants of Madagascar. Bioassay-guided fractionation of the ethyl acetate extract of the leaves led to the isolation of four phenolic compounds, (+)-catechin (1), (+)-catechin 5-gallate (2), (+)-catechin 3-gallate (3) and ethyl gallate (4). Structures were determined by NMR and mass spectroscopy. Compounds 2 and 3 displayed the highest in vitro activity against the chloroquine-resistant strain FcB1 of *Plasmodium falciparum* (IC50: 1.2 microM and 1.0 microM, respectively) and were not significantly cytotoxicagainst the human embryonic lung cells MRC-5 (IC50>75 microM). Five analogues (5 to 9) of (+)-catechin 5-gallate (2) were synthesized and evaluated for their antiplasmodial activity.

Dapper DV, Aziagba BN, Ebong OO. Antiplasmodial effects of the aqueous extract of Phyllantus amarus Schumach and Thonn against Plasmodium berghei in Swiss albino mice. Niger J Physiol Sci. 2007;22(1-2):19-25.

Phyllantus amarus Schumach and Thonn is a medicinal plant used to treat malaria in southeastern Nigeria. We report antiplasmodial effects of aqueous extracts of the leaves and stems against *Plasmodium berghei* infection in Swiss albino mice. The blood schizonticidal activity of the aqueous extract in early infection and in established *Plasmodium berghei* infection was assessed and compared to the activities of chloroquine and sulfadoxine/pyrimethamine. The repository activity of the extract was also assessed and compared to the activity of pyrimethamine. The LD50 of the aqueous extract of *Phyllantus amarus Schumach and Thonn* was 650 mg/kg in albino Wistar rats. In early infection, the extract at doses of 108.33 mg/kg, 165 mg/kg and 325 mg/kg significantly and dose-dependently suppressed of *P berghei* parasites [P<0.05] sulfadoxine/pyrimethamine caused a similar significant suppression of *P berghei* parasites [P<0.05] while chloroquine at a dose of 5 mg/kg did not cause a significant effect on *P berghei* parasites. The extract at all doses suppressed *P berghei* parasites via a repository action, P<0.05. This effect was comparable to the effects of pyrimethamine a standard repository agent. In established infection, the extract at all doses administered, significantly suppressed *P berghei* parasites after 24 and 72 hours, P<0.05. Sulfadoxine/pyrimethamine caused a similar suppression of the parasites of *P berghei* but the effects were more sustained over 72 hours.

Udeinya JI, Shu EN, Quakyi I, Ajayi FO. An antimalarial neem leaf extract has both sch-

IZONTICIDAL AND GAMETOCYTOCIDAL ACTIVITIES. AM J THER. 2008;15(2):108-10.

A crude acetone/water (50/50) extract of neem leaves (IRAB) was evaluated for activity against the asexual (trophozoites/schizonts) and the sexual (gametocytes) forms of the malarial parasite, *Plasmodium falciparum* in vitro. In separate 72-hour cultures of both asexual parasites and mature gametocytes treated with IRAB (0.5 microg/mL), parasite numbers were less than 50% of the numbers in control cultures, which had 8.0% and 8.5% parasitemia, respectively. In cultures containing 2.5 microg/mL, asexual parasites and mature and immature gametocytes were reduced to 0.1%, 0.2%, and 0% parasitemia, respectively. No parasites remained in the cultures with 5.0 microg/mL.

BAPNA S, ADSULE S, SHIRSHAT MAHENDRA S, JADHAV S, PATIL LS, DESHMUKH RA. ANTIMALARIAL ACTIVITY OF *ECLIPTA ALBA* AGAINST *PLASMODIUM BERGHEI* INFECTION IN MICE. J COMMUN DIS. 2007;39(2):91-4.

The antimalarial activity of *Eclipta alba* leaves extract was evaluated against *Plasmodium berghei* ANKA strain in mice. A standard inoculum of 1 x 10^6 infected erythrocytes was used. The methanolic leaf extract (250 to 750 mg/kg) produced a dose-dependant chemosupression or schizontocidal effect during early and established infection and high mean survival times particularly in the group administered 750 mg/kg/day of extract. The plant extract also had repository activity.

SITI NAJILA MJ, NOOR RAIN A, MOHAMAD KAMEL AG, SYED ZAHIR SI, KHOZIRAH S, LOKMAN HAKIM S, ZAKIAH I, AZIZOL AK. THE SCREENING OF EXTRACTS FROM GONIOTHALAMUS SCORTECHINII, ARALIDIUM PINNATIFIDUM AND ANDROGRAPHIS PANICULATA FOR ANTI-MALARIAL ACTIVITY USING THE LACTATE DEHYDROGENASE ASSAY. J ETHNOPHARMACOL. 2002;82(2-3):239-42.

Goniothalamus scortechinii, *Andrographis paniculata* and *Aralidium pinnatifidum* are plants used as anti-malarials screened for antimalarial activity towards *Plasmodium falciparum* in vitro using the lactate dehydrogenase assay. *G scortechinii* extracts had the most potent schizonticidal activity compared to the other extracts. It is effective against both the chloroquine resistant isolate, Gombak A and the sensitive strain, D10 of *Plasmodium falciparum*. A better IC50 value was obtained against the resistant strain, 40 microg/mL. When the crude extract was fractionated into 3, the chloroform fraction yielded the best activity, exhibiting equipotency against both strains of parasite used; IC50 of 23.53 microg/mLagainst Gombak A and 21.06 microg/mL against D10.

KAOU AM, MAHIOU-LEDDET V, HUTTER S, AÏNOUDDINE S, HASSANI S, YAHAYA I, AZAS N, OLLIVIER E. ANTIMALARIAL ACTIVITY OF CRUDE EXTRACTS FROM NINE AFRICAN MEDICINAL PLANTS. J ETHNOPHARMACOL. 2008;116(1):74-83.

In Comores (Ngazidja), antimalarial activity of 76 vegetal extracts obtained from 17 species traditionally used to treat malaria symptoms, was evaluated in vitro using Plasmodium falciparum chloroquine-resistant strain (W2). Antiproliferative activity was evaluated on human monocytic THP1 cells and the selectivity index of the plant extracts was calculated. The results showed that 10 plant extracts had a moderate activity (5 < IC50 < or = 10 microg/ml), and 6 a good in vitro activity with IC50 value < or =5 microg/ml. The highest antiplasmodial activity was found for the MeOH/H(2)O leaves extract of *Flueggea virosa* (Roxb. Ex Willd.) *Voigt subsp. virosa* (Euphorbiaceae) (IC50=2 microg/ml), for roots decoction of *Flueggea virosa* (IC50=3 microg/ml) and for chloromethylenic roots extract of *Vernonia colorata* (Willd.) Drake subsp. grandis (DC.) C. Jeffrey (Asteraceae) (IC50=3 microg/ml). Extracts with moderate antiplasmodial activity IC50 < 5 microg/ml): *Vernonia colorata* (aerial part), Piper capense L.f. (Piperaceae), and *Leptadenia madagascariensis Decne* (Asclepiadaceae) chloromethylenic extracts (IC50=6 microg/mL; 7 microg/mL and 9microg/mL, respectively). All the plants tested displayed a low cytotoxicity on THP1 cells.

MORITA H, OSHIMI S, HIRASAWA Y, KOYAMA K, HONDA T, EKASARI W, INDRAYANTO G, ZAINI NC. CASSIARINS A AND B, NOVEL ANTIPLASMODIAL ALKALOIDS FROM CASSIA SIAMEA. ORG LETT. 2007;9(18):3691-3.

Two novel alkaloids with an unprecedented tricyclic skeleton, cassiarins A (1) and B (2), have been isolated from the leaves of *Cassia siamea*, and the structures were elucidated on the basis of spectroscopic data. Cassiarin A (1) showed a potent antiplasmodial activity.

MUTHAURA CN, RUKUNGA GM, CHHABRA SC, OMAR SA, GUANTAI AN, GATHIRWA JW, TOLO FM, MWITARI PG, KETER LK, KIRIRA PG, KIMANI CW, MUNGAI GM, NJAGI EN. ANTIMALARIAL ACTIVITY OF SOME PLANTS TRADITIONALLY USED IN TREATMENT OF MALARIA IN KWALE DISTRICT OF KENYA. J ETHNOPHARMACOL. 2007;112(3):545-51.

Methanolic and water extracts of 5 medicinal plant species used to malaria in traditional health systems

of Kwale people in Kenya were tested for antimalarial activity against *Plasmodium falciparum* and *Plasmodium berghei*, respectively and for their cytotoxic effects. The most active extracts (IC50<10microg/mL) screened against chloroquine (CQ) sensitive (D6) and resistant (W2) P falciparum clones, were the water and methanol extracts of *Maytenus undata* (Thunb.) *Blakelock* (Celasteraceae), methanol extracts of *Flueggea virosa* (Willd.) *Voigt* (Euphorbiaceae), *Maytenus putterlickioides* (Loes.) *Excell and Mendoca* (Celastraceae), and *Warburgia stuhlmannii Engl.* (Canellaceae). These extracts showed various cytotoxic levels on Vero E6 cells with the water extract of *M undata* exhibiting least cytotoxicity. At least 1 plant species extract exhibited a high chemo suppression of parasitaemia >70% in a murine model of *P berghei* infected mice. These results indicate that potential for isolation of a lead compound from the extracts of the 5 plants.

Clarke SE, Jukes MCH, Njagi JK, Khasakhala L, Cundill B, Otido J, Crudder C, Estambale BBA, Brooker S. The Lancet 2008; 372:127-38. Effect of intermittent preventive treatment of malaria on health and education in schoolchildren: a cluster-randomised, double-blind, placebo-controlled trial.

We examined the effect of intermittent preventive treatment in reducing anemia and improving classroom attention and educational achievement in semi-immune schoolchildren in an area of high perennial transmission.

A stratified, cluster-randomised, double-blind, placebo-controlled trial in 30 primary schools in western Kenya. Schools were randomly assigned to sulfadoxine-pyrimethamine plus amodiaquine or dual placebo. Children from 5 to 18 were treated 3 times at 4-month intervals (IPT n=3,535, placebo n=3,223). The primary endpoint was anaemia, defined as a hemoglobin concentration below 110g/L. Anemia was assessed through surveys 12 months after treatment.

2604 children given preventive treatment and 2302 given placebo were included in intention-to-treat analysis of the primary outcome. Prevalence of anaemia at 12 months averaged 6.3% in the preventive treatment group and 12.6% in the placebo group (adjusted risk ratio 0.52, 95% CI 0.29–0.93; p=0.028). Significant improvements were also seen in 2 class-based tests of sustained attention, with a mean increase in code transmission test score of 6.05 (95% CI 2.83–9.27; p=0.0007) and counting sounds test score of 1.80 (0.19–3.41; p=0.03), compared with controls. No effect was shown for inattentive or hyperactive-compulsive behaviours or on educational achievement. The per-protocol analysis yielded similar results. 23 serious adverse events were reported within 28 days of any treatment (preventive treatment: 19; placebo: 4); the main side-effects were problems of balance, dizziness, feeling faint, nausea, or vomiting shortly after treatment.

De Wet H, Van Heerden FR, Van Wyk BE, Van Zyl RL. Antiplasmodial activity and cytotoxicity of Albertisia delagoensis. Fitoterapia. 2007;78(6):420-2.

Leaves and rhizome methanol extracts of *Albertisia delagoensis* tested positive against *Plasmodium falciparum*, with low cytotoxic activity in leaves against the Graham cell line.

Dikasso D, Makonnen E, Debella A, Abebe D, Urga K, Makonnen W, Melaku D, Kassa M, Guta M. Anti-malarial activity of withania somnifera L. Dunal extracts in mice. Ethiop Med J. 2006;44(3):279-85.

Investigation of in vivo antiplasmodial activity of a traditionally used medicinal plant, *Withania somnifera*, L. Dunal, (Solanaceae).

Rodent malaria parasite *Plasmodium berghei*, 0.2 ml of x $l0^7$ parasites, was inoculated into Swiss albino mice intraperitoneally. Extracts were administered by intragastric tube daily for 4 days starting from the day of parasite inoculation. Negative controls received the same amount of solvent used to suspend the extracts and the positive controls were given chloroquine by the same route. Parasitemia inhibition of *W somnifera* roots and root barks were 50.43% and 29.13% respectively, with 600 mg/kg dose. Inhibition was statistically significant at all doses ($p < 0.05$), and maximum inhibition was at 600 mg/kg. Extracts of eaves and root barks of *W somnifera* suppressed parasites and protected against packed cell volume drop (at higher doses), both were dose-related.

Pillay P, Vleggaar R, Maharaj VJ, Smith PJ, Lategan CA, Chouteau F, Chibale K. Antiplasmodial hirsutinolides from Vernonia staehelinoides and their utilization towards a simplified pharmacophore. Phytochemistry. 2007;68(8):1200-5.

The dichloromethane extract of the leaves of *Vernonia staehelinoides Harv. (Asteraceae)* showed in vitro activity (IC50 approximately 3microg/mL) against the chloroquine-sensitive (D10) and the chloroquine-resistant (K1) strains of *Plasmodium falciparum*. Through conventional chromatographic techniques and bioassay-guided fractionation 2 structurally-related hirsutinolides displaying in vitro

antiplasmodial activity (IC50 approximately 0.2 microg/mL against D10) were isolated and identified by spectroscopic data. Compounds 1, 8 alpha-(2-methylacryloyloxy)-3-oxo-1-desoxy-1,2-dehydrohirsutinolide-13-O-acetate, and 2, 8 alpha-(5'-acetoxysenecioyloxy)-3-oxo-1-desoxy-1,2-dehydrohirsutinolide-13-O-acetate were found to be cytotoxic to mammalian Chinese Hamster Ovarian (CHO) cells at similar concentrations but were attractive scaffolds for structure-activity relationship studies. Two main privileged substructures, a 2(5H)-furanone unit and a dihydrofuran-4-one unit, were identified as potential pharmacophores which may be responsible for the observed biological activity.

Mucochloric and mucobromic acids were selected as appropriate 2(5H)-furanone substructures. They had comparable activity against the D10 and superior activity against the K1 strains relative to the hirsutinolide natural product. Mucochloric and mucobromic acids have selective cytotoxicity to malaria parasites. These data suggests that the 2(5H)-furanone substructure is key.

Plants that prevent, modify and cure diseases have long been a part of the daily foods in malaria-endemic regions. Nigeria's mega-city Lagos now has daily bread-baking and other prepared flour-foods such as noodles, are agressively marketed on bill-boards and on television. Diabetes is increasing, as are cardiovascular diseases including hypertension.

Portet B, Fabre N, Roumy V, Gornitzka H, Bourdy G, Chevalley S, Sauvain M, Valentin A, Moulis C. Activity-guided isolation of antiplasmodial dihydrochalcones flavanones from Piper hostmannianum var. berbicense. Phytochemistry. 2007;68(9): 1312-20.

The leaves of *Piper hostmannianum var. berbicense* were extracted with n-hexane: isolated were 4 monoterpene or prenyl-substituted dihydrochalcones (1a, 1b, 2, 3) as well as the known compounds 2',6'-dihydroxy-4'-methoxydihydrochalcone (4), linderatone (5), strobopinin (6), adunctin E (7) and (-)-methyllinderatin (8). Their structures were established on the basis of NMR and X-ray analysis. (-)-Methyllinderatin, linderatone and 2',6'-dihydroxy-4'-methoxydihydrochalcone exhibited the most potent antiplasmodial activity with IC50 values of 5.64, 10.33 and 12.69 microM, respectively against both chloroquine-sensitive and resistant strains of *Plasmodium falciparum* (F32,FcB1). The activity of (-)-methyllinderatin was confirmed in vivo against *Plasmodium vinckei petteri* in mice (80% of reduction of parasitemia) at a dose of 20 mg/kg/day.

By SJ Dodgson BSc(Hons), PhD