MALARIA & NEEM

Overview

While questions still remain about the dosage required in human beings, neem clearly has great potential in preventing malaria, a parasite that kills more than a million people per year. Several in vitro studies indicate significant protection, including one that concluded it was more effective than chloroquine, a drug to which the parasite is becoming resistant. One interesting report indicates that it may increase the efficacy of chloroquine when the two are taken together.

Another important consideration is that malaria and AIDS both occur primarily in tropical countries, and treating AIDS patients who have malaria is a significant challenge. One report, funded partially through the US government, indicates that neem inhibits both malaria and the HIV virus in vitro, plus dramatically improved key parameters in human volunteers with AIDS, including major improvements in their CD4 counts.

(Reports on preventing malaria by using neem as an insect repellant or larvicide are included in the section on Neem & Mosquitoes).

Recent Research

AAm J Ther. 2008 March/April;15(2):108-110.n Antimalarial Neem Leaf Extract has Both
Schizonticidal and Gametocytocidal Activities.
Udeinya JI, **Shu EN**, **Quakyi I**, **Ajayi FO**.
1.Currently, the Rocitus Institute of Research, Enugu, Nigeria, formerly, Howard University College of Medicine, Washington, DC; 2.College of Medicine, University of Nigeria, Enugu Campus, Enugu, Nigeria; 3.Georgetown University, Washington, DC; and 4.Food and Drug Administration, Rockville, MD.
http://www.ncbi.nlm.nih.gov/pubmed/18356629?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

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 mug/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 mug/mL, asexual parasites and mature and immature gametocytes were reduced to 0.1%, 0.2%, and 0% parasitemia, respectively. There were no parasites in the cultures containing 5.0 mug/mL. This extract, if found safe, may provide materials for development of new antimalarial drugs that may be useful both in treatment of malaria as well as the control of its transmission through gametocytes.
PMID: 18356629 [PubMed - as supplied by publisher]

Malar J. 2007 May 22;6:63.
Larvicidal effects of a neem (Azadirachta indica) oil formulation on the malaria vector Anopheles gambiae.
Okumu FO, **Knols BG**, **Fillinger U**.
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http://www.ncbi.nlm.nih.gov/pubmed/17519000?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

BACKGROUND: Larviciding is a key strategy used in many vector control programmes around the world. Costs could be reduced if larvicides could be manufactured locally. The potential of natural products as larvicides against the main African malaria vector, Anopheles gambiae s.s was evaluated. METHODS: To assess the larvicidal efficacy of a neem (Azadirachta indica) oil formulation (azadirachtin content of 0.03% w/v) on An. gambiae s.s., larvae were exposed as third and fourth instars to a normal diet supplemented with the neem oil formulations in different concentrations. A control group of larvae was exposed to a corn oil formulation in similar concentrations. RESULTS: Neem oil had an LC50 value of 11 ppm after 8 days, which was nearly five times more toxic than the corn oil formulation. Adult emergence was inhibited by 50% at a concentration of 6 ppm. Significant reductions on growth indices and pupation, besides prolonged larval periods, were observed at neem oil concentrations above 8 ppm. The corn oil formulation, in contrast, produced no growth disruption within the tested range of concentrations. CONCLUSION: Neem oil has good larvicidal properties for An. gambiae s.s. and suppresses successful adult emergence at very low concentrations. Considering the wide distribution and availability of this tree and its products along the East African coast, this may prove a readily available and cheap alternative to conventional larvicides.
PMID: 17519000 [PubMed - indexed for MEDLINE]

Tissue Cell. 2006 Dec;38(6):361-71. Epub 2006 Nov 13.
Effects of a neem extract on blood feeding, oviposition and oocyte ultrastructure in Anopheles stephensi Liston (Diptera: Culicidae).
Lucantoni L, **Giusti F**, **Cristofaro M**, **Pasqualini L**, **Esposito F**, **Lupetti P**, **Habluetzel A**.
Department of Experimental Medicine and Public Health, University of Camerino, Camerino, Italy.
http://www.ncbi.nlm.nih.gov/pubmed/17097701?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

Secondary metabolites of the neem tree (Azadirachta indica A. Juss., Meliaceae) exhibit a wide range of biological activities in insects. However, few studies have addressed the effects of neem extracts or compounds in arthropods of medical importance. In this study, a laboratory strain of Anopheles stephensi was used to assess the effects of a commercial formulation (Neem Azal) (NA)), containing azadirachtin A at 34%, on blood feeding, oviposition and oocyte ultrastructure. Oral administration of Neem Azal) to A. stephensi females through artificial blood meals did impair blood intake and oviposition in a concentration dependent

manner. Similar results were obtained on females, which had consumed Neem Azal) in sucrose solution before taking a blood meal of plain blood. Neem treated females displayed a delay in oocyte development in both the phase of vitellogenesis and the phase of choriogenesis. The ultrastructural studies on ovaries from Neem Azal) treated females revealed distinct structural modifications indicative of: (i) a complete block of oogenesis, (ii) impairment of vitellogenesis and vitelline envelope formation, (iii) a severe degeneration of follicle cells. In agreement with results obtained in other insects, this study indicates that Neem Azal) impairs hormone control of oogenesis and exerts a cytotoxic effect on both follicular cells and oocytes of the Asian malaria vector A. stephensi.
PMID: 17097701 [PubMed - indexed for MEDLINE]

Afr Health Sci. 2006 Dec;6(4):240-6.
Community based vector control in Malindi, Kenya.
Kibe LW, **Mbogo CM**, **Keating J**, **Molyneux S**, **Githure JI**, **Beier JC**.
http://www.ncbi.nlm.nih.gov/pubmed/17604514?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

Background: Community involvement has become an important component of the National Malaria Control Strategy in Kenya, resulting in the organization of groups charged with addressing mosquito and malaria-related concerns within the community. Objectives: The purpose of this study was to identify community groups involved with intended malaria vector control activity in Malindi, Kenya. Methods: Information was obtained from key informant interviews, focus group discussions, and a stakeholder meeting. The objectives were to determine the roles of community groups, identify examples of past successes and obstacles to successful implementation of vector control, and assess the level of knowledge about malaria and mosquitoes among the groups. Results: Nineteen of 34 community groups (56%) registered at social services reported intended malaria vector control activities such as treating ditches, making and selling insecticide-treated mosquito nets, draining stagnant water, organizing clean-ups, making and selling neem soap, and the organization of campaigns such as the "Malaria Mosquito Day". Major challenges facing these groups include volunteerism, lack of technical expertise, supervision, and maintaining control activities in the absence of funds. Most groups reported limited knowledge about malaria vectors, and thus targeted all water bodies for control activities. Conclusions: We found that community groups are willing to participate in control operations, but lack government and technical support. We highlight the importance of strengthening organizational efforts and capacity building, as well as the need to clarify government policy on malaria vector control responsibilities within the communities.
PMID: 17604514 [PubMed - in process]

J Ethnopharmacol. 2006 Mar 10; [Epub ahead of print]
Anti-plasmodial activity and toxicity of extracts of plants used in traditional malaria therapy in Meru and Kilifi Districts of Kenya.
Kirira PG, **Rukunga GM**, **Wanyonyi AW**, **Muregi FM**, **Gathirwa JW**, **Muthaura CN**, **Omar SA**, **Tolo F**, **Mungai GM**, **Ndiege IO**.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16530996&query_hl=33&itool=pubmed_docsum

The methanol and aqueous extracts of 10 plant species (Acacia nilotica, Azadirachta indica, Carissa edulis, Fagaropsis angolensis, Harrissonia abyssinica, Myrica salicifolia, Neoboutonia macrocalyx, Strychnos heningsii, Withania somnifera and Zanthoxylum usambarensis) used to treat malaria in Meru and Kilifi Districts, Kenya, were tested for brine shrimp lethality and in vitro anti-plasmodial activity against chloroquine-sensitive and chloroquine-resistant strains of Plasmodium falciparum (NF54 and ENT30). Of the plants tested, 40% of the methanol extracts were toxic to the brine shrimp (LD(50)<100mug/ml), while 50% showed in vitro anti-plasmodial activity (IC(50)<100mug/ml). The methanol extract of the stem bark of N. macrocalyx had the highest toxicity to brine shrimp nauplii (LD(50) 21.04+/-1.8mug/ml). Methanol extracts of the rest of the plants exhibited mild or no brine shrimp toxicity (LD(50)>50mug/ml). The aqueous extracts of N. macrocalyx had mild brine shrimp toxicity (LD(50) 41.69+/-0.9mug/ml), while the rest were lower (LD(50)>100mug/ml). The methanol extracts of F. angolensis and Zanthoxylum usambarense had IC(50) values <6mug/ml while the aqueous ones had values between 6 and 15mug/ml, against both chloroquine-sensitive and resistant P. falciparum strains. The results support the use of traditional herbs for anti-malarial therapy and demonstrate their potential as sources of drugs.
PMID: 16530996 [PubMed - as supplied by publisher]

Ann Trop Med Parasitol. 2006 Jan;100(1):17-22.

Fractions of an antimalarial neem-leaf extract have activities superior to chloroquine, and are gametocytocidal.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16417709&query_hl=37&itool=pubmed_docsum

The antimalarial activities of two fractions (IRDN-A and IRDN-B) of an extract from the leaves of the neem tree (Azadirachta indica) were compared with those of chloroquine, in in-vitro assays against Plasmodium falciparum. The asexual stages of a chloroquine-sensitive clone (ITG2F6) and a chloroquine-resistant isolate (W2) and the gametocytes of the NF 54 (BD-7) isolate of P. falciparum were used as the drug targets. Activity against the asexual stages was generally evaluated as the concentrations inhibiting the parasitaemias recorded in the control cultures, after an incubation of 48-72 h, by 50% (IC50) or 100% (IC100). For the ITG2F6 strain, the IC50 and IC100 (in microg/ml) were, respectively, 10(-5) and 10(-4) for IRDN-A, 10(-3) and 10(-2) for IRDN-B, and 10(-2) and 1.0 for chloroquine. The corresponding values for the W2 strain were 10(-5) and 1.0 for IRDN-A, and 10.0 and >100 for chloroquine (even at 100 microg/ml, chloroquine only inhibited the parasitaemia by 85%).Each of the two neem-leaf fractions lysed 50% and 100% of developing gametocytes, at 10(-3) and 1.0 microg/ml, respectively; and 50% and 100% of mature gametocytes at 10(-3) and 10(2)

microg/ml, respectively. If they are found safe and effective in vivo, the neem-leaf fractions may form the basis of new antimalarial drugs that not only cure chloroquine-sensitive and chloroquine-resistant malaria but also markedly reduce transmission.
PMID: 16417709 [PubMed - indexed for MEDLINE]

Acta Trop. 2005 Oct;96(1):47-55.

Effects of neem limonoids on the malaria vector Anopheles stephensi Liston (Diptera: Culicidae).

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16112073&query_hl=37&itool=pubmed_docsum

The effects of the neem (Azadirachta indica A. Juss) limonoids azadirachtin, salannin, deacetylgedunin, gedunin, 17-hydroxyazadiradione and deacetylnimbin on Anopheles stephensi Liston (Diptera: Culicidae) were investigated. In exploring advantages of pure neem limonoids, we studied the larvicidal, pupicidal, adulticidal and antiovipositional activity of neem limonoids. Azadirachtin, salannin and deacetylgedunin showed high bioactivity at all doses, while the rest of the neem limonoids were less active, and were only biologically active at high doses. Azadirachtin was the most potent in all experiments and produced almost 100% larval mortality at 1 ppm concentration. In general, first to third larval instars were more susceptible to the neem limonoids. Neem products may have benefits in mosquito control programs.
PMID: 16112073 [PubMed - indexed for MEDLINE]

East Mediterr Health J. 2004 Jul-Sep;10(4-5):573-81.

Larvicidal activity of a neem tree extract (Neemarin) against mosquito larvae in the Islamic Republic of Iran.

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School of Public Health and Institute of Health Research, Tehran University of Medical Science, Tehran, Islamic Republic of Iran.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16335649&query_hl=37&itool=pubmed_docsum

An insecticide containing azadirachtin, a neem tree (Azadirachta indica) extract, was tested against mosquito larvae in the Islamic Republic of Iran under laboratory and field conditions. LC50 and LC90 values for Neemarin were 0.35 and 1.81 mg/L for Anopheles stephensi, the main local malaria vector, and 0.69 and 3.18 mg/L for Culex quinquefasciatus. The mortality in the pupal stage was significantly higher than the other stages. In field trials, using recommended dosages of 1 and 2 L/hectare, mortality of Anopheles spp. larvae was also higher than Culex spp. Prevention of adult emerged and pupal mortality was the main activity of this compounds. The maximum time of efficacy was 7 days at the highest concentration (2

L/hectare).
PMID: 16335649 [PubMed - indexed for MEDLINE]

Trans R Soc Trop Med Hyg. 2004 Jul;98(7):435-7.

An antimalarial extract from neem leaves is antiretroviral.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15138081&query_hl=37&itool=pubmed_docsum

An acetone-water neem leaf extract with antimalarial activity was evaluated in vitro at 5 microg/ml for inhibition of adhesion of malaria parasite-infected erythrocytes and cancer cells to endothelial cells, and at 10 microg/ml for protection of lymphocytes against invasion by HIV. The extract was also evaluated in 10 patients with HIV/AIDS at 1000 mg daily for 30 d. The mean binding of infected erythrocytes and cancer cells per endothelial cell was 15 and 11 respectively in the absence of the extract, and 0 and 2 respectively in with the extract. In the absence and presence of the extract, 0% and 75%, respectively, of lymphocytes were protected. In the treated patients, haemoglobin concentration, mean CD4+ cell count and erythrocyte sedimentation rate, which were initially 9.8 g/dl, 126 cells/microl and 90 mm/h respectively, improved to 12.1 g/dl, 241 cells/microl and 49 mm/h. Mean bodyweight and platelet count, initially 57 kg and 328 x 10(3)/mm3 respectively, increased to 60 kg and 359 x 10(3)/mm3. No adverse effects were observed during the study. The extract showed antiretroviral activity with a mechanism of action that may involve inhibition of cytoadhesion. The results may help in the development of novel antiretroviral and antimalarial drugs.
PMID: 15138081 [PubMed - indexed for MEDLINE]

Toxicology. 2004 May 20;198(1-3):83-90.

Pesticide exposure--Indian scene.

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Use of pesticides in India began in 1948 when DDT was imported for malaria control and BHC for locust control. India started pesticide production with manufacturing plant for DDT and benzene hexachloride (BHC) (HCH) in the year 1952. In 1958, India was producing over 5000 metric tonnes of pesticides. Currently, there are approximately 145 pesticides registered for use, and production has increased to approximately 85,000 metric tonnes. Rampant use of these chemicals has given rise to several short-term and long-term adverse effects of these chemicals. The first report of poisoning due to pesticides in India came from Kerala in 1958 where, over 100 people died after consuming wheat flour contaminated with parathion. Subsequently several cases of pesticide-poisoning including the Bhopal disaster have been

reported. Despite the fact that the consumption of pesticides in India is still very low, about 0.5 kg/ha of pesticides against 6.60 and 12.0 kg/ha in Korea and Japan, respectively, there has been a widespread contamination of food commodities with pesticide residues, basically due to non-judicious use of pesticides. In India, 51% of food commodities are contaminated with pesticide residues and out of these, 20% have pesticides residues above the maximum residue level values on a worldwide basis. It has been observed that their long-term, low-dose exposure are increasingly linked to human health effects such as immune-suppression, hormone disruption, diminished intelligence, reproductive abnormalities, and cancer. In this light, problems of pesticide safety, regulation of pesticide use, use of biotechnology, and biopesticides, and use of pesticides obtained from natural plant sources such as neem extracts are some of the future strategies for minimizing human exposure to pesticides.
PMID: 15138033 [PubMed - indexed for MEDLINE]

Acta Pharm. 2003 Dec;53(4):305-11.

Interaction between chloroquine sulphate and aqueous extract of Azadirachta indica A. Juss (Meliaceae) in rabbits.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14769237&query_hl=37&itool=pubmed_docsum

This study was carried out to investigate the effect of concurrent oral administration of aqueous leaf extract of Azadirachta indica (Meliaceae) on the pharmacokinetic properties of chloroquine sulphate in experimental rabbits. The results indicated that concurrent administration of both agents resulted in a significant decrease in serum concentration, slower absorption and elimination as well as longer half-life of chloroquine sulphate. The highest relative decrease of 78.0% was recorded 4 hours after concurrent administration, while the smallest decrease (64.6%) occurred 24 hours after concurrent administration. Significant reductions were also noted in some pharmacokinetic parameters of chloroquine and included the area under the curve (71.9%), maximum serum concentration (69.8%), absorption rate constant (37.3%), elimination rate constant (53.9%), clearance rate (76.5%) and volume of distribution (47.2%). However, there was a pronounced increase in the half-life of the drug (125.7%).
PMID: 14769237 [PubMed - indexed for MEDLINE]

Phytother Res. 2003 Aug;17(7):807-10.

Evaluation of the antimalarial properties and standardization of tablets of Azadirachta indica (Meliaceae) in mice.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12916083&query_hl=37&itool=pubmed_docsum

The antimalarial activities of the tablet suspension of the bark and leaf of Azadirachta indica were evaluated on Plasmodium yoelli nigeriensis infected mice. The tablet suspensions exhibited high prophylactic, mode-rate suppressive and a very minimal curative schizonticidal effect. No animal was cured of the infection in the curative test and there was not much increase in the survival time of the animals compared with the control. The tablet suspensions from the leaf and bark at a concentration of 800 mg/kg and chloroquine at a concentration of 62.5 mg/kg body weight produced average percentage (%) parasitaemia of 79.6%, 68.2% and 99.5% for leaf, bark and chloroquine, respectively, in chemosuppression. Also in the prophylactic treatment, the tablet suspensions at 800 mg/kg and pyrimethamine at a concentration of 0.35 mg/kg gave an average parasitaemia reduction of 75.3%, 65.6% and 98.3% for the leaf, bark and pyrimethamine, respectively. There was a clear indication that both tablet suspensions from the leaf and bark possess antimalarial activity and a suspension from the former is relatively more effective than the bark. Extrapolation of the results from the antimalarial activity of the tablet suspension of the crude plant parts showed that an adult human would need to ingest a minimum of 48 g of the powdered plant material per day, an amount that is impracticable. A survival index value of 0.33 was obtained with the 800 mg/kg dose level, indicating that the tablet suspension has some moderate beneficial effect.
PMID: 12916083 [PubMed - indexed for MEDLINE]

East Mediterr Health J. 2003 Jul;9(4):646-58.

Operational use of neem oil as an alternative anopheline larvicide. Part B: Environmental impact and toxicological potential.

Awad OM.
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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15748062&query_hl=37&itool=pubmed_docsum

This study was conducted to investigate the preliminary environmental and mammalian toxicology of neem oil, temephos and chlorpyriphos-methyl/fenitrothion. Culex pipiens, Daphnia magna and Gambusia affinis were used to study environmental impact. A high level of toxicity was observed, with slight differences between organisms. The emulsifiers individually also displayed toxicity towards the tested organisms. Up to 90 days daily oral crude neem oil treatment (5 g/kg body weight) of laboratory mice did not cause any significant changes in weekly body weight gain, nor in serum liver damage indicators, direct bilirubin or total bilirubin. Blood parameters of treated mice up to 90 days were not statistically different from those of control mice. Neem oil could be used as an environmentally friendly alternative to the traditional chemical anopheline larvicides.
PMID: 15748062 [PubMed - indexed for MEDLINE]

East Mediterr Health J. 2003 Jul;9(4):637-45.

Operational use of neem oil as an alternative anopheline larvicide. Part A:

Laboratory and field efficacy.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15748061&query_hl=37&itool=pubmed_docsum

We conducted a study to determine the laboratory and field efficacy of neem oil towards anopheline larvae. No difference in LC50 was observed between laboratory and field strains for temephos, chlorpyriphos-methyl/fenitrothion and neem oil. No difference in susceptibility was found after 3 months of application every 2 weeks. Water treated with a single application of traditional larvicides was free of larvae after 4 weeks; neem oil-treated water, however, was free after 2 weeks but not at 4 weeks. Application of chlorpyriphos-methyl/fenitrothion and neem oil every 2 weeks for 7 rounds resulted in dramatic reduction in larval density with no statistically significant differences. An adult survey after larviciding also showed no significant difference. The efficacy of crude neem oil appears to be below that of conventional larvicides.
Publication Types: Evaluation Studies
PMID: 15748061 [PubMed - indexed for MEDLINE]

Phytochemistry. 2003 Mar;62(5):747-51

Antiplasmodial and antifungal activities of iridal, a plant triterpenoid.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12620327&query_hl=37&itool=pubmed_docsum

Iridal, a triterpenoidic compound extracted from Iris germanica L., was previously shown to have an interesting activity on two cultured human tumor cell lines (A2780 and K562). In the present work, this same product was tested in vitro on Plasmodium falciparum chloroquine-resistant and -sensitive strains, in vivo on P. vinckei, and on some Candida albicans and C. parapsilosis strains too. The IC(50) obtained in vitro on human malaria strain ranged from 1.8 to 26.0 microg/ml and the ED(50) in vivo is about 85 mg/kg/day by intraperitoneal route. The minimal inhibitory concentrations were higher than to 50 microg/ml, whatever the strain of yeast tested. This product presents an antiplasmodial activity similar to that obtained with extracts from the plant Azadirachta indica classically taken as reference in malaria phytomedicine. Conversely iridal shows no important antifungal activity. The specific activity of iridal on human malaria parasite and on tumor cell lines is discussed.
PMID: 12620327 [PubMed - indexed for MEDLINE]

J Am Mosq Control Assoc. 2002 Jun;18(2):107-10.

Field evaluation of three plant-based insect repellents against malaria vectors in Vaca Diez Province, the Bolivian Amazon.

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London School of Hygiene and Tropical Medicine, United Kingdom.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12083351&query_hl=37&itool=pubmed_docsum

The efficacy of repellents against Anopheles darlingi, the main malaria vector in Bolivia, was evaluated. This mosquito has a peak in biting activity early in the evening. Three natural repellents (1 eucalyptus based, 1 neem based, and 1 containing several repellent essential oils) were tested in comparison with 15% deet in human landing catches in Bolivia. The eucalyptus-based repellent containing 30% p-menthane-diol applied at a dose similar to those used in practice gave 96.89% protection for 4 h. Deet gave 84.81% protection. The other 2 products did not provide significant protection from mosquito bites.
Publication Types: Evaluation Studies
PMID: 12083351 [PubMed - indexed for MEDLINE]

J Ethnopharmacol. 1998 May;61(1):31-9.
Inhibition of the growth and development of asexual and sexual stages of drug-sensitive and resistant strains of the human malaria parasite Plasmodium falciparum by Neem (Azadirachta indica) fractions.
Dhar R, **Zhang K**, **Talwar GP**, **Garg S**, **Kumar N**.
Department of Molecular Microbiology and Immunology, School of Hygiene and Public Health, Johns Hopkins University, Baltimore, MD 21205, USA.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9687079&query_hl=33&itool=pubmed_docsum

Neem (Azadirachta indica) has been shown to possess anti-malarial activity. In this study we systematically evaluated extracts of neem seeds and purified fractions further enriched in polar or non-polar constituents for their effect on in vitro growth and development of asexual and sexual stages of the human malaria parasite Plasmodium falciparum. Use of synchronized stages of parasites suggested trophozoites/schizonts as the susceptible target stages to various neem extracts. In addition, all the maturation stages of gametocytes were also killed by various neem fractions tested. The anti-plasmodial effect of neem components was also observed on parasites previously shown to be resistant to other anti-malarial drugs, i.e. chloroquine and pyrimethamine suggesting a different mode of action. Neem seed fractions are thus active not only against the parasite stages that cause the clinical infection but also against the stages responsible for continued malaria transmission.
PMID: 9687079 [PubMed - indexed for MEDLINE]

Indian J Malariol. 1996 Sep;33(3):139-43.
Preliminary evaluation of safety aspects of neem oil in kerosene lamp.
Valecha N, **Ansari MA**, **Prabhu S**, **Razdan RK**.
Malaria Research Centre (ICMR), Delhi, India.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9014397&query_hl=33&itool=pubmed_docsum

Kerosene lamps containing one per cent neem oil were used for mosquito repellent action in a village near Delhi. The safety aspects of this personal protection method developed by Malaria Research Centre were evaluated by animal studies and clinical examination of population before and after exposure. Single application of neem oil (1%) did not produce skin irritation in rabbits and adverse effect on guinea pigs after exposure to aerosol. Clinical examination of 156 adults and 110 children did not reveal any major adverse effects after one year of exposure to 1% neem oil.
PMID: 9014397 [PubMed - indexed for MEDLINE]

Indian J Malariol. 1996 Jun;33(2):81-7.

Operational feasibility of malaria control by burning neem oil in kerosene lamp in Beel Akbarpur village, District Ghaziabad, India.

Ansari MA, **Razdan RK**.
Malaria Research Centre, Delhi, India.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8952172&query_hl=33&itool=pubmed_docsum

A field trial in Beel Akbarpur village, Dadri PHC, District Ghaziabad (U.P.) was carried out to test the impact of burning neem oil in kerosene lamp from dusk-to-dawn in living rooms on vector populations and incidence of malaria. Results revealed that burning 1% neem oil in kerosene lamps resulted in the deviation of An. culicifacies from living rooms to cattlesheds. This was also reflected when malaria incidence was compared in experimental and control villages. Cases/000 and Pf/000 were 1.03 and 0.0 in experimental village as against 9.6 and 4.3 in control village. Discontinuation of burning 1% neem oil in kerosene lamp resulted in recurrence of An. culicifacies in living rooms and increase in malaria incidence in experimental village.
PMID: 8952172 [PubMed - indexed for MEDLINE]

Afr J Health Sci. 1995 May;2(2):309-311.

In vitro antimalarial activity of extracts of Albizia gummifera, Aspilia mossambicensis, Melia azedarach and Azadirachta indica against Plasmodium falciparum.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12160442&query_hl=33&itool=pubmed_docsum

Since chemotherapy is presently the primary strategy of malaria control in the world, and some malaria parasites are developing resistance to the commonly used antimalarial drugs, new antimalarial compounds are required. Therefore, it is important to test antimalarial activities of medicinal plant extracts which most herbalists claim to cure malaria. We evaluated the antimalarial activities of extracts of Albizia gummiffera, Aspilia mossambicensis, Melia azedar

and Azadirahchta indica against laboratory adapted isolates of Plasmodium falciparum using an in vitro radioisotopic uptake technique. Chloroquine was used as a reference antimalarial drug. Al. gummifera had the highest antimalarial activity (mean fifty percent inhibitory concentration {IC(50)S} in ug/ml of test culture =3.5 +1.6SD, n=3) followed by As. mossambicensis (mean IC(50)=29.3+11.8SD, n=4) and Me. Azedarach (mean IC(50) =299.7+202.0SD, n=4). And lastly Az. Indica (mean IC(50)=349.9+213.1 SD, n=4). The antimalarial activities of the reference drug, chloroquine, was far much higher (mean IC(50)=0.065+0.057SD, n=)4). These findings show that Al. gummifera and As. mossambicensis plant extracts have potent antimalarial compounds. Phytochemical analyses should be done on these two plants to isolate the compound(s) containing he active principles(s).
PMID: 12160442 [PubMed - as supplied by publisher]

Trans R Soc Trop Med Hyg. 1995 Mar-Apr;89(2):217-8.

Antimalarial activity in vitro of Cochlospermum tinctorium tubercle extracts.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7778154&query_hl=33&itool=pubmed_docsum

Resistance of Plasmodium falciparum to current antimalarial compounds has drastically increased during the last few years and is now a major public health problem. We have studied plants traditionally used in Africa against malaria. Extracts of the tubercles of Cochlospermum tinctorium A. Rich, commonly used in Burkina Faso, were tested in vitro on 2 strains of P. falciparum, one (FcB1-Colombia) chloroquine resistant and the other (F32-Tanzania) chloroquine sensitive. Extracts were obtained by infusion and decoction. The 50% inhibitory concentrations (IC50) were determined by measuring [3H]hypoxanthine incorporation and also by microscopical examination which permitted the determination of parasite stages. We obtained similar results with fresh extracts, frozen extracts, and lyophilized extracts of C. tinctorum. IC50 values were of the order of 1-2 micrograms/mL, about one-tenth of those reported for extracts of neem leaves (Azadirachta indica) and about half the values reported for Artemisia annua extracts.
PMID: 7778154 [PubMed - indexed for MEDLINE]

FEMS Microbiol Lett. 1994 Jul 15;120(3):267-73.

Sexual development of malaria parasites is inhibited in vitro by the neem extract azadirachtin, and its semi-synthetic analogues.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7980823&query_hl=33&itool=pubmed_docsum

We have shown that azadirachtin, a compound from the neem tree, Azadirachta indica, and

selected semi-synthetic derivatives, block the development of the motile male malarial gamete in vitro. Changes in the hemiacetal group at position C11 in the molecule result in a loss of activity in this assay. The motility of fully formed male gametes, and other selected flagellated cells, is unaffected by azadirachtin in vitro. These findings raise the possibility of developing azadirachtin-based compounds as antimalarials with transmission-blocking potential, as well as permitting the further study of structure-activity relationships in these compounds.
PMID: 7980823 [PubMed - indexed for MEDLINE]

World Health Forum. 1994;15(3):265-8.

Socioeconomic factors in malaria control.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7945758&query_hl=33&itool=pubmed_docsum

A knowledge of people's perceptions of malaria and of the socioeconomic implications of the disease is of considerable value when control programmes are being planned and implemented. Observations on these matters are reported from Ghana.
PIP: Some 9% of deaths in Ghana are attributed to malaria, which also accounts for 30% of outpatient visits and 9% of hospital admissions. A survey conducted in four areas of Ghana revealed that the factors perceived as causing malaria included malnutrition, mosquitos, excessive heat, excessive drinking, flies, fatigue, dirty surroundings, unsafe water, bad air, and poor personal hygiene. Most adolescents had no idea how the disease was spread from person to person. The symptoms most frequently considered to be linked to malaria were yellowing of the eyeballs, chills and shivering, headache, a bitter taste, body weakness, and yellowish urine. Malaria was considered to be the most important disease in the communities of Kojo Ashong, Barekese, Barekuma and Oyereko. There was a widespread understanding that malaria adversely impacted the ability of adults to work and of children to attend school. Herbal preparations for self-medication included liquids for drinking, liquids for use as enemas, and potions for hot fomentation. Most people used the leaves of the neem tree (Adzadi rachta indica) to make such preparations. Most interviewees were aware of chloroquine used in the treatment of malaria. A few people sprayed their rooms with insecticide before going to bed in order to kill mosquitos, while others used repellent coils. Bednets were rarely used. There was little knowledge of how the transmission cycle of the parasite could be broken. One social implication of the disease is that if the breadwinner dies, the children may have to cease attending school. For Africa as a whole the annual economic burden of malaria was $ 0.8 billion in 1987; by 1995 it is expected to be $ 1.7 billion. The first step in any control program should be to educate the people about the cause and treatment of the disease. District assemblies should enact bylaws on the cleanliness of households, which inspectors should enforce.
PMID: 7945758 [PubMed - indexed for MEDLINE]

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Mosquito repellent action of neem (Azadirachta indica) oil.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8245950&query_hl=33&itool=pubmed_docsum

Two percent neem oil mixed in coconut oil, when applied to the exposed body parts of human volunteers, provided complete protection for 12 h from the bites of all anopheline species. Application of neem oil is safe and can be used for protection from malaria in endemic countries.
PMID: 8245950 [PubMed - indexed for MEDLINE]

J R Soc Health. 1993 Aug;113(4):190-4.
Exploration of the frontiers of tradomedical practices: basis for development of alternative medical healthcare services in developing countries.
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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8410912&query_hl=33&itool=pubmed_DocSum

The study is a brief exploration of the functions and roles of the traditional healers in the total health care delivery system as a basis for tapping the salient features of this age old art: for the purpose of refining, and establishing it as an alternative medical health-care service. The investigation is considered relevant particularly in the developing countries where, in addition to the dearth of orthodox medical services, institutions and personnel, it is relatively cheaper, socio-culturally accessible and acceptable. Refining and developing some aspects of the traditional healers' services will serve the interest of the health consumers whose main concern is with service and not the source. Furthermore, it is hoped that the study will stimulate purposeful discussions on the need for an unbiased examination of the materials, methods and techniques of the traditional healers including, eventually, compiling a native pharmacopoeia. A more comprehensive account of the traditional healers contributions to the battle against diseases and maintenance of health and well being is envisaged.
PIP: In traditional healing, practitioners use barks, leaves, nuts, fruit juices and roots, and parts of domestic animals. They practice their craft mostly in Africa, Asia, and other Third World countries, and they are variously called juju priests, diviners, herbalists, and witch doctors. Cases of achievements in their contributions to preventive and curative health have been documented. In Nigeria, clients regularly patronize both orthodox and traditional medical practitioners. Their remedies include healing the bite of the very poisonous carpet viper, chronic bronchitis, peptic ulcer, and heart problems, as well as performing uvulectomy and tonsillectomy. Quinine, the cure for malaria, was originally the ritual medicine of the Incas of Peru. It was confirmed that Azadirachta Indica (Meliaceae), the neem tree, used against malaria in Nigeria, India, and Asia, had a potent antiplasmodial activity. The plant Streblus asper, Linn (Shakhotoha Siora) is well known in Indian Ayurvedic medicine to treat fever, filariasis, dysentery, and diarrhea. The alkaloids derived from the Madagascan periwinkle Catharanthus roseus (Apocynaceae), used in a West Indian remedy for diabetes mellitus, have antitumor activity. The drug Maytensine, obtained from Mytenus ovatus Loes (Celastraceae),

was found to be a powerful antitumor agent in animals. Tea made from the leaves of Osyris wightiana stimulated the flow of breast milk and also acted as a labor-inducing agent. Saponaria officinalis and Enterobbium cyclocarpum are both used in Egypt and Tanzania as spermicide contraceptives. A 1985 survey in Cross River State, Nigeria, demonstrated that 165 (61%) of respondents went to traditional healers for treatment. Part of their continued popularity is the person-centered approach that is virtually lacking in orthodox hospitals, although this humanistic approach to therapy is gradually gaining inroads into Western medical education. The services of both kinds of medicine could be harmonized by open-minded appraisal, identification of positive aspects, and acceptance of their complimentary nature.
PMID: 8410912 [PubMed - indexed for MEDLINE]

Trans R Soc Trop Med Hyg. 1993 Jul-Aug;87(4):471.

Anti-malaria activity of Nigerian neem leaves.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8249085&query_hl=33&itool=pubmed_DocSum

PMID: 8249085 [PubMed - indexed for MEDLINE]