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EVALUATION OF SIX HERBAL PLANTS USED IN THE TREATMENT OF MALARIA IN SOUTH-EASTERN NIGERIA: A REVIEW.

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Abstract

The work was aimed at reviewing six herbal plants used in treating malaria in South-Eastern, Nigeria. Malaria caused by parasite of the genus *Plasmodium*, is one of the leading infectious diseases in many tropical regions, including Nigeria where transmission occurs all year round. The high cost of malaria treatment has left poor masses of Nigeria heavily reliant on traditional practitioners and medicinal plants as remedies against fever and other symptoms of malaria. The use of some herbs in South-Eastern, Nigeria was x-rayed in this review work and the methods of their formulations were extensively discussed. It was ascertained from other works carried out that in some cases the herbal remedies were more potent than orthodox medicines when administered for malaria treatment.

INTRODUCTION

Medical treatment has shifted to being less invasive and more prophylactic and alternative sources for new therapeutic molecules are being investigated (Yoko and Hideki, 2004). Clinical studies of herbal medicine as complementary and alternative medicine (CAM) have been re-evaluated and demonstrate supportive evidence for their empirical efficacy (Pitter and Ernst, 2000; Akase et al, 2003; Xu et al, 2003). The herbal drug preparation in its entirety is regarded as the active substance and the constituents are either of known therapeutic activity or are chemically defined substances or group of substances generally accepted to contribute substantially to the therapeutic activity of the drug (Wickramasinghe, 2006). Malaria has continued to cause deaths and ill health on a large scale, especially among the highly vulnerable groups, young children and pregnant women in tropical countries. In Africa, it causes more than one million deaths every year, and in Nigeria, the infection rate has been described as holoendemic, with more than 75 per cent of children aged between five and nine years infected (Sade, 2010) and there is need for alternative therapy in order to combat the scourge. This need has further been highlighted by the current recommendation of artemisinin (a plant product) based combination therapies. Artemisinin, obtained from *Artemisia annua*, and quinine, obtained from Cinchona species, are proven instances of compounds derived from plants with anti-malarial potential. Plant preparations have a very special characteristic that distinguishes them from chemical drugs: a single plant may contain a great number of bioactive phytocompounds and a combination of plants even more. This complexity is one of the most important challenges to phytoscientists attempting to identify a single bioactive phytocompound or chemical group in the enormous universe that comprise single crude extract (Ricardo, 2006). Many plant genera were found to be used either as alone or in combination with each other for the treatment of malaria. Malaria is an infectious disease caused by a parasite transmitted to humans by mosquitoes. *Plasmodium falciparum* causes malaria with immense public health and economic problems in most developing countries and for many years these problems have been

intensified by the emergence and spread of resistance to the currently available antimalarial drugs. Herbs for malaria work in diverse ways. Some contain chemicals that interact with your immune system to kill the *Plasmodium* parasite. Malaria was ranked the 8th highest contributor to the disability adjusted life years (DALY) leading to almost 3 % of DALY globally (WHO, 2002). This pandemic affects poorest of population residing in 107 countries (Hay et al, 2004). Clinical manifestations can include fever, chills, prostration and anaemia. Severe disease can include delirium, metabolic acidosis, cerebral malaria and multi-organ system failure, coma and death may ensue. Blood-stage infection also generates sexual-stage parasites (gametocytes) that are infectious for mosquitoes, leading to fertilization and genetic recombination in the mosquito midgut. This is followed by production of haploid sporozoite forms that invade the salivary glands and are subsequently transmitted back to humans (David et al, 2004). The torment due to morbidity, debility and loss of productive man hours is colossal. Vicious cycle of malaria and poverty continues in its most severe form in the developing economies where poorest of poor do not have access to unaffordable costly treatment (Amit et al, 2009).Ideally, new drugs for uncomplicated *P. falciparum* malaria should be efficacious against drug-resistant strains, provide cure within a reasonable time (ideally three days or less) to ensure good compliance, be safe, be suitable for small children and pregnant women, have appropriate formulations for oral use and above all, be affordable (Ridley, 2002; Nwaka and Ridley, 2003). However, Nigerian researchers have also developed herbal cures for malaria that can take care of resistant strains. They have produced potent anti-malaria cocktails from local plants. This may possibly explain the reported use of both leaves together with other plant parts by herbalists for malaria treatment in Nigeria. According to (Uhegbu et al, 2009) on Comparative Anti-malarial effects of Sulphadoxine/Pyrimethamine (SP) and aqueous leaf extracts of *Carica Papaya, Magnifera Indica* in Mice there were consistency with reported anti-malarial activity of these plants.. According to (Oparaocha and Okorie, 2009) aqueous extracts of the stem bark, fruit pericarp, seeds and leaves of *Pentaclethra*

macrophylla Benth.; the leaves of *Phyllanthus niruri* L and the leaves of *Euphorbia hirta* L. were tested for anti-plasmodial activity using albino mice. These studies inferred that extracts of these herbs can be used by local communities of South Eastern Nigeria to treat malaria. Modern Herbalists have several ways of preparing their herbal therapies before dispensing them to patients.

These methods are: (a) Decoction (in this approach parts of medicinal plants (leaves, barks, roots, flowers, seeds etc) are boiled together in water for some minutes and allowed to steep for sometimes before filtering). The mixture is administered orally or for bathing a patient especially in febrile conditions. (b) Infusion (the aerial parts of medicinal plants – flowers, stem, barks etc are normally extracted through infusion with water), here the herbs are not boiled but a boiled water is poured into these herbs and covered for some minutes in form of tea and is taken orally. (c) Tinctures (it is a system whereby alcoholic solution like hot gin is used to extract the active ingredient or properties or properties of medicinal herbs). (d) Fermentation (herbs prepared by infusion or decoction is soaked or dipped with a cloth and wringed out and thereafter applied to the affected part(s) of the body externally especially in swollen and inflammatory conditions). (e) Powders (barks of woody trees, roots, berries, leaves, seeds of plant are ground to fine powders or triturate which in turn are dissolved into hot or cold water, cream, corn-pap, hot gin, soup, lime juice, honey, grape juice and shea-butter). The powders are also licked whole and can be placed on open sores to enhance healing. This system has a wide range of uses in natural medical therapeutics).

Resistance to anti-malarial drugs is caused by the ability of the parasite to survive or multiply in the presence of the anti-malarial drug concentrations that normally destroy the parasite or control their multiplication (WHO, 2005). The resistance to older and affordable anti-malarial drugs has been implicated as the key factor leading to the increasing rate of morbidity and mortality from malaria (WHO, 2003a). Quality control of herbal drugs has traditionally been based on appearance and today microscopic evaluation is indispensable in the initial identification of herbs as well as in identifying small fragments of crude or

powdered herbs and detection of foreign matters and adulterants. A primary visual evaluation, which seldom needs more than a simple magnifying lens, can be used to ensure that the plant is of the required species and that the right part of the plant is being used. At other times, microscopic analysis is needed to determine the correct species and/or that the correct part of the species is present. Animal matters such as insects and invisible microbial contaminants which can produce toxins are also among the potential contaminants of herbal medicines ((WHO, 2003b); WHO, 2004; EMEA, 2002)]. Macroscopic examination can easily be employed to determine the presence of foreign matter, although microscopy is indispensable in certain special cases (for example, starch deliberately added to "dilute" the plant material). Furthermore, when foreign matter consists, for example, of a chemical residue, Thin Layer Chromotography is often needed to detect the contaminants (WHO, 1998; WHO, 1999; AOAC, 2005).

Many plants have been used to treat or prevent diseases and screening of extracts of these plants for activity is relatively uncomplicated. Agar or broth dilution methods are able to yield quantitative results by determining growth inhibition indices, minimal inhibitory concentrations, or minimal lethal concentrations (Kalemba and Kunicka, 2003). Antiprotozoal screening has been carried out using methods analogous to those used for antibacterial assessment. Typically, *Plasmodium falciparun berghi*, *Entamoeba histolytica* or *Giardia lamblia* trophozoites are inoculated into test-tubes containing medicinal plant extracts. After incubation, samples of the tubes are taken and tested for cell viability using trypan blue dye exclusion or tetrazolium salt metabolism assay methods (Meckes et al, 1999).

Herbs are still marketed without sufficient research but evidence must always be shown to consumers to support claims of products (Moundipa et al, 2005; Ziesel, 1999; Petrovick et al, 1999). More clinical studies are needed and doctors, along with other health professionals, should work towards untangling this herbal maze. Standards should be developed for each natural health product and the same regulatory standards that apply to manufactured pharmaceuticals should apply equally to herbal products as well.

Unlike conventional drugs, herbal products are not regulated for purity and potency and this could cause adverse effects and drug interactions (Jowel, 1999). Herbal manufacturing processes should be refined in order to improve the purity, safety and quality of products and the herbal industry needs to follow strict guidelines as herbal products are now classified as medicines. Manufacturers and producers tend to resist these laws because such laws will increase cost, which will have to be passed on to consumers and thus the appeal or herbal drugs might then be lost.

Just as retinopathy and hyperpigmentation of the retina are caused by chloroquine administration which is an orthodox medicine, herbal traditional medicines have a lot of criticisms. The problems associated with standardization are: secrecy of the ingredients (in most cases, the ingredients of traditional medicine are not known as they are kept secret by their practitioner, who is often uncooperative and guards his recipe very closely); absence of legal control over production of herbal products (in the past there is no legal control over the production of drugs); the complex nature of the preparation (the preparations are multi-component and involved a number of complex procedural methods in their preparation including some unhygienic processes and cultural or religious rituals); vagueness in therapeutic claims (in their eagerness to impress the users and the general public, the traditional practitioner often make sweeping claims about the effectiveness of their preparations). Also there is the problem of instability in the preparations; most of the preparations are prepared on requirement and are intended to be used within a short time, thus no preservatives are normally used to improve keeping quality which makes their standardization meaningless.

Toxicity in herbal medicine may be due to (1) accidents due to a mistake in botanical identification, (2) accidental ingestion of cardiotonic plants, (3) inappropriate combinations, including the use of potentially toxic plants, (4) or plants that interfere with conventional pharmacological therapy, such as plants containing coumarinic derivatives, a high content of tyramine, estrogenic compounds, plants causing irritation and allergic problems, plant containing photosensitive compounds etc (Rates,

2001; Thomson, 2000; Stewart and Steenkamp, 2000; Wojcikowski et al, 2004; Goldman, 2001). Recent scientific research has demonstrated that many traditionally used herbal medicines are potentially toxic and some are even mutagenic and carcinogenic (Shimmer et al, 1988; Schimmer et al, 1994; De SaFerrira and Vargas, 1999).

ANTI-MALARIA PLANTS IN USE

Azadirachta indica

Botanical description

The name is derived from the Persian word "azaddhirakt" which means "noble tree".

Kingdom: plantae

Division: magnoliophyta

Class: magniliopsida

Order: sapindales

Family: meliaceae

Genus: azadirachta

Species: azadirachta indica

Scientific/Botanical Name: *Azadirachta indica*

Common names: Neem, margrose (E)

Nigerian names

Igbo: Oguru akam, obisikeosiso

Hausa: Dogo'nyaro

Yoruba: Aforo oyinbo

Geographical distribution

It is found in every part of South-Eastern, Nigeria. It exists in colonies and originated from India.

Description of plant

It is a shady tree of about 25 m in height and can reach up to 100 m high as shown in Fig. 1. Neem tree is found in abundance in tropical and semi-tropical regions. It has striped and dark brown fissured bark with a strong odour and characteristic bitter taste. The leaves are pinnate or alternate in arrangement with ovoid fruit containing one seed and yellow when ripe. The morphological parts used are the leaves, fruit, bark, root and seed. The season of collection is usually wet and the plant is collected from cultivated or wild plant. The condition of collection of the plant parts for use is usually fresh (leaves, barks) at any time of the day.

Method of extraction and preparation of Neem

The tender parts of the branches are cut and the leaves with other parts are washed thoroughly and put inside a pot (metal or clay) after the size must have been reduced with knife. About 4 L of water are then added and the content boiled for about 30 min. It is then allowed to cool for some time and filtration is done with a muslin cloth. The filtrate which is the drug product is administered orally with a glass cup once three times daily, more water is added to continue extraction if the extracts reduces. The drug extract can sometimes be used as anti-inflammatory, anti-spasmodic and as insecticidal agents. Other medical situations in which Neem can be used are liver ailments, gastric ulcers, constipation, urinary tract conditions, fever, skin problems etc.

Neem products have been shown to exhibit a wide range of effects that are potentially useful for malaria control and include antifeedancy (Tanaka et al, 1986), ovicidal activity, insect growth regulation [WHO, 2003b; WHO, 2004) and repellency (Lucantoni et al, 2006). These effects are frequently attributed to the azadirachtin contents of the products (Su and Mulla, 1998; WHO, 2003b). Neem-based products are relatively safe towards non-target biota, with only minimal risk of direct adverse effects on aquatic macro invertebrates resulting from contamination of water bodies with neem-based insecticides (Kreutzweiser, 1997; Stark, 2001; Goektepe et al, 2004). In addition, the products are less likely to induce resistance due to their multiple modes of action on insects (Mulla and Su, 1999). Research on neem products for the control of arthropods of medical and veterinary importance has been ongoing for some time and various studies have focused on the culicine species *Culex tarsalis* and *Culex quinquefaciatus* (Mulla and Su, 1999; Segar and Sehgal, 1996), besides *Aedes aegypti* (Monzon et al, 1994; Boschitz and Grunewald, 1994; el-Shazly and el-Sharnoubi, 2000). There have also been studies that assessed the larvicidal potential of neem products on anophelines, notably *Anopheles culicifacies*, *An. arabiensis*, *An. gambiae* and *Anopheles stephensi* (Ziba, 1995; Nathan et al, 2005).

Alstonia boonei

Botanical description

Kingdom: plantae

Unranked: angiosperms

Unranked: eudicots

Unranked: asterids

Order: gentianales

Family: apocynaceae

Genus: alstonia

Species: boonei

Scientific/botanical name: *Alstonia boonei*

Common names: emien

Nigeria names

Igbo: Egbu

Geographical distribution

The tree is widely distributed in every part of South-Eastern, Nigeria.

Description of plant

The tree is of about 30 m tall. Fig. 2 showed that it has broad leaves and the plant normally sheds the leaves during the dry season. The morphological parts used are always the bark and leaves. The plant part can either be collected in dry or wet season from the wild plant. The collection of the plant part (the fresh leaves) is usually done either in the morning or evening.

Method of extraction and preparation of Alstonia boonei

The fresh barks and leaves are cut with knife, washed thoroughly and put inside a pot containing about 2 L of water. The pot content is allowed to boil for 30 minutes and left to cool for 10 min after which the content of the pot is filtered using a muslin cloth. The drug filtrate is taken two glassfuls three times daily in feverish conditions to treat malaria. *Alstonia boonei* also finds usage in the following ailments hypertension, fever, rheumatism, lactation stimulant, parasites, snakebite, arrow poison etc.

Terminalia catappa

Botanical description

Kingdom: plantae

Subkingdom: tracheobionta

Superdivision: spermatophyta

Division: magnoliophyta

Class: magnoliopsida

Subclass: rosidae

Order: myrtales

Family: combretaceae

Genus: terminalia L

Species: *Terminalia catappa* L.

Common name: Indian almond

Nigeria names

Igbo: edo

Geographical distribution

The tree is popularly cultivated as a shady plant in some homes in South-Eastern, Nigeria.

Description of plant

Terminalia catappa is tall a deciduous and erect tree reaching 15-25 m high, the trunk is 1.0 -1.5 m in diameter, often buttressed at the base as shown in Fig. 3. Whorls of nearly horizontal, slightly ascending branches spaced 1-2 m apart in tiers or storey up the trunk. The pagoda-like habit becomes less noticeable as the branches elongate and droop at the tips. Bark grey-brown, rough with age. The leaves alternate with short petioles, spirally clustered at the branch tips, 15-36 cm long, 8-24 cm wide, dark green above, paler beneath, leathery and glossy. *T. catappa* is a conspicuous, semi-deciduous tree of coastal areas throughout the warm tropics that grows best in moist tropical climates. The tree is well adapted to sandy and rocky coasts and flourishes on oolitic limestone. The species loses its leaves twice a year in most areas, with a brilliant red-and-yellow display of leaf colour before doing so. The wig are young foliage velvety with hairy glabrous. The fruit are fleshy and un-winged, having the usual type of inflorescence. The morphological parts used are fruits, hard edible nut and leaves. The plant parts are usually collected during wet season from the cultivated plant. The condition of collection of the leaves is fresh mostly in the night or morning. Apart from its use as anti-malaria herbs, most homes use it as shady tree.

Method of extraction and preparation Terminalia catappa

The leaves of *T. catappa* contain many hydrolysable tannins, such as punicalagin, punicalin, terflavins, A and B tergallagin, tercatain, chebulagic acid, geraniin, granatin B, and corilagin, but no caffeine (Oparaocha and Okorie, 2009). The leaves are combined with other components of the plants and boiled. The contents are allowed inside the

pot and glass cups are used to scoop the extract and administered orally once two times daily for malaria therapy. The leaves have many medicinal uses including diaphoretic, anti-indigestion and anti-dysentery. An infusion of the young leaves or scraped bark is occasionally taken as a portion for treating mouth infections in Tonga and Samoa and is used in the Cook Islands to bathe fractures. Young leaves are used in the Philippines to cure headache and colic. The bark is used as an astringent in dysentery and thrush.

Carica papaya

Botanical description

Kingdom: plantae

Division: magnoliophyta

Class: magniliopsida

Order: brassicales

Family: caricaceae

Genus: carica

Species: papaya

Scientific/botanical name: *Carica papaya*

Family name: Caricaceae or Papayaceae

Common names: Pawpaw (E), Papayer (F)

Nigeria names

Igbo: mabimabi, okworo-beke

Urhobo: eto

Geographical distribution

The tree is found everywhere in South-Eastern, Nigeria. It originated from Central America.

Description of plant

Papaya, *Carica papaya* L., is one of the major fruit crops cultivated in tropical and sub-tropical zones. Worldwide over 6.8 million tonnes (Mt) of fruit were produced in 2004 on about 389,990 Ha, of this volume, 47 % was produced in Central and South America (mainly in Brazil), 30 % in Asia and 20 % in Africa. Fig. 4 showed that it is a shrub of about 4-5 m high with swollen straight trunk and branches out without explicit design. Papaya is a fast-growing, semi-woody tropical herb. The stem is single, straight and hollow and contains prominent leaf scars. Papaya exhibits strong apical dominance rarely branching unless the apical meristem is removed or damaged. Palmately-lobed leaves, usually large are arranged spirally.

Carica papaya has remarkable foliar scars; the leaves for the most part are petiolated with extremely divided lamina. It is deocious with female feet having sessile on the trunk and male stock with flowers borne by large loose panicles. The fruits vary in size and colour, green when unripe but pulp yellow or red when ripe with a faintly aromatic odor and sweet taste. The plant contains copious white latex. Fruit is berry, oblong ovate in shape, dark green becoming yellowish on ripening with numerous seeds on parietal placenta. The epicarp is leathery and the mesocarp is unidentified. The fruit is about 15-22 cm long and 7-11 m broad. The morphological parts used are fruits and leaves which are collected in rainy/wet season from the wild or cultivated plant. The collection of the fresh or dry leaves can be done at any time of the day.

Method of extraction and preparation of Carica papaya

The leaves are mixed with guava leaves, lime leaves and lemon grass. They are then put inside a pot and the mixture is boiled though the leaves do not have to soften so much. On noticing the coffee colour of the mixture it is assumed that the extraction is complete and boiling is stop instantly. From the content in the pot two glass cups are taken orally twice daily without filtration of the content to treat malaria. *Carica papaya* can still be used in the following sickness hypertension, digestive problems, stomach pain, diuretic, malaria, parasites etc.

The inhibition of â-lactamase activity by *Carica papaya* (papain) has been demonstrated (Zhao et al, 2002; Cole, 1979; Yam et al, 1998).

The extracted product apart from being used in malaria therapy is used to treat amoebicide, antihelmintics and as a carminative in our local villages and towns. Papayas are susceptible to the papaya ringspot virus, which causes premature molting and malformation of the leaves (Ridley, 2002). Genetically altered plants that have some of the virus's DNA incorporated into the DNA of the plant are resistant to the virus (Ridley, 2002). The papaya is also susceptible to the fruit fly, a small wasp-like insect that lays its eggs in young fruit.

Picralima nitida

Botanical description

Kingdom: plantae

Division: not found

Class: not found

Order: not found

Family: apocynaceae

Genus: picralima

Species: nitida

Common name(s):

Nigeria names

Igbo: Osu-igwe

Yoruba: Erin

Geographical distribution

It is mostly found in Abakiliki and Calabar axis of the South-Eastern, Nigeria.

Description of plant

It is a small bushy tree about 40 ft high with large glossy leatherly leaves, conspicuous white flowers and large orange colored fruits as depicted in Fig. 5. The wood is yellowish and hard, the seed being embedded in pulp. The parts used for treatment are the leaves, seed, fruits and barks which can be collected at every season of the year from the cultivated plant. The freshly parts are collected at any time of the day for treatment of malaria and sometimes used as antihypertensive medicine.

Method of extraction and preparation of Picralima nitida

The exudates of stems are collected and the fruit content is scooped out and the empty shell filled with palm wine. The wine will soak the shell and absorbed the bitter principle inside the shell. The mixture formed after absorption is taken three times daily with a glassful of it to treat malaria. Apart from malaria, it can also be used for hypertension, stomach pain, liver problems, pneumonia, sleeping sickness, yellow fever etc.

A new indole alkaloid, picranitine, has been isolated from the seeds of *Picralima nitida*, along with five known indole alkaloids picratidine, akuammine, pseudoakuammine, akuammicine and akuammidine previously identified from the same source. A method of preparing substantially purified alkaloids from seeds, stems, uit-rind and bark of a plant selected from Picralima nitida, for use in the

treatment of protozoal diseases (Xiamen, 2012).

Newbouldia laeves

Botanical description

Kingdom: plantae

Division: not found

Class: not found

Order: not found

Family: bignoniaceae

Genus: newbouldia

Species: laevis

Scientific/botanical name: *Newbouldia laeves*

Common name: not found

Nigeria names

Igbo: ogirisi/ari

Tiv: konkor

Efik: obat

Geographical distribution

It is found almost everywhere in secondary forest of South-Eastern, Nigeria.

Description of plant

It is found around grooves and slurries. It is readily recognized by its twisted trunk, short branches and gnarled twigs. It usually has toothed leaflets, purple and white flowers as seen in Fig. 6. The tree is about 30 ft high of a full mature one. Morphological parts for malaria treatment are seeds and leaves which are collected in dry season usually January-February period. It is most often collected in the morning from cultivated and wild plants. Condition of collection before use is seed (dry) and leaves (fresh).

Method of extraction and preparation

For stomach-ache and malaria; the leaves are washed and given to the patient to chew. The patient is later given a glassful of water to drink to wash down the leaves.

For snakebite or scorpion bite; the leaves are plucked and squeezed to extract the fluid content. The leaves are then used to scrub on the bite site (snake or scorpion) to relieve the pain.

The study of the chemical constituents of the roots of *Newbouldia laevis* (Bignoniaceae) has resulted in the isolation and characterization of a naphthoquinone–anthraquinone coupled pigment named

newbouldiaquinone A whose antimalarial activity against *P. falciparum in vitro* shows moderate chemo suppression of parasitic growth and 14 other known compounds (apigenin, chrysoeriol, newbouldiaquinone, lapachol, 2-methylanthraquinone, 2-acetylfuro-1,4-naphthoquinone, 2,3-dimethoxy-1,4-benzoquinone, oleanolic acid, canthic acid, 2-(4-hydroxyphenyl)ethyl triacontanoate, newbouldiamide, 5,7-dihydroxydehydroiso-α-lapachone, β-sitosterol, and β-sitosterol glucopyranosid) (Kenneth et al, 2006).

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Fig. 1. Diagram of Neem tree

Fig. 2. Diagram of *Alstonia boonei* plant

Fig. 3. Diagram of *Terminalia catappa* tree

Fig . 4. Diagram of *Carica papaya* tree

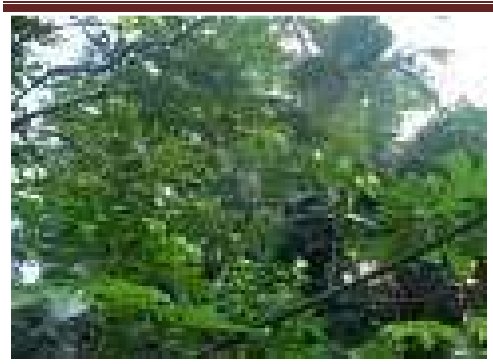

Fig. 5. Diagram of P*icralima nitida*

Fig. 6. Diagram of *Newbouldia laevis*

REFERENCES

1. AOAC. Official Methods of Analysis of AOAC International, 18th edn. AOAC International, Gaithersburg, MD, (2005).

2. Akase T, Akase T, Onodera S, Jobo T, Matsushita R, Kaneto M and Tashiro S: A comparative study of the usefulness of toki-shakuyaku-san and an oral iron preparation in the treatment of hypochromotic anaemia in cases of uterine myoma. Yakugaku zasshi. 2003; 123:817-824.

3. Amit Kumar Banerjee, Neelima Arora & U.S.N. Murty. Structural model of the *Plasmodium falciparum* Thioredoxin reductase: a novel target for antimalarial drugs. J Vector Borne Dis.2009; 46: 171–183

4. Boschitz C, Grunewald J. The effect of Neem Azal on *Aedes aegypti* (Diptera: Culicidae). Appl Parasitol. 1994; 35: 251-256.

5. Cole, M. Inhibition of beta lactamases. (1979). In Beta Lacatamases, Hamilton-Miller, J.M.T., Smith, J.T. (2nd ed). pp. 205–290. Academic Press, London.

6. David A. Fidock, Philip J. Rosenthal, Simon L. Croft, Reto Brun and Solomon Nwaka.. antimalarial drug discovery: efficacy models for compound screening. Drug discovery. 2004; 3: 509-520.

7. De SaFerrira ICF, V.M. Ferrago Vargas: Mutagenicity of medicinal plant extracts in. Salmonella/microsome assay. Phytotherapy Res. 1999; 13: 397–400.

8. El-Shazly MM, el-Sharnoubi ED: Toxicity of a neem (*Azadirachta indica*) insecticide to certain aquatic organisms. J Egypt Soc Parasitol. 2000; 30: 221-231.

9. EMEA. Points to Consider on Good Agricultural and Collection Practice for Starting Materials of Herbal Origin. EMEA/HMPWP/31/99 Review. European Agency for the Evaluation of Medicinal Products (EMEA), London, *(*2002).

10. Evangeline T. Oparaocha and C. Okorie. *In vivo* evaluation of anti-malarial activity of three medicinal Plants used in South Eastern Nigeria. Journal of herbs, mpices & Medicinal Plants. 2009; 15(1): 121-128.

11. FO Uhegbu, CU Igwe, AO Ojiako, GO Oze. Comparative Anti-malarial Effects of Sulphadoxine/Pyrimethamine and aqueous leaf extracts of Carica papaya, Magnifera indica in Mice. Nigerian Journal of Biochemistry and Molecular Biology: unpublished (2009).

12. Goektepe I, Portier R, Ahmedna M. Ecological risk assessment of neem based pesticides.

13. J Env Sci Hlth B. 2004; 39(2)**:**311-320.

14. Goldman P. Herbal medicines today and the roots of modern pharmacology. Ann Intern Med. 2001; 135: 594–600.

15. Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW: The global distribution and population at risk of malaria: past, present and future. Lancet Infect Dis. 2004; 4(6): 327–36. (Hay et al, 2004)

16. Jowell T*:* Herbal medicines. House of Commons official report *(*Hansard). March .1999; 26: 426-427.

17. Kalemba, D. and Kunicka A: Antibacterial and antifungal properties of essential oils. Curr. Med. Chem*.,* 2003; 10*:* 813-829.

18. Kenneth Oben Eyong, Gabriel Ngosong Folefoc, Victor Kuete, Veronique Penlap Beng, Karsten Krohn′ Hidayat Hussain, Augustin Ephram Nkengfack, Michael Saeftel, Salem Ramadan Sarite, Achim Hoerauf. Newbouldiaquinone A: A naphthoquinone–anthraquinone ether coupled pigment, as a potential antimicrobial and antimalarial agent from *Newbouldia laevis.* Phytochemistry. 2006; 67(6): 605-609.

19. Kreutzweiser DP: Non-target effects of neem based insecticides on aquatic invertabrates.

20. Ecotoxicol Env Safety.1997; 36**:** 109-117

21. Lucantoni L, Giusti F, Cristofaro M, Pasqualini L, Esposito F, Lupetti P, Habluetzel A: Effects of neem extract on blood feeding, oviposition and oocyte ultrastructure in *Anopheles stephensi* Liston (Diptera: Culicidae). Tissue Cell.2006; 38**:**361-371.

22. Meckes M*,* Calzada F*,* Tapia-Contreras A, Cedillo-Rivera R: Antiprotozoal properties of Helianthemum glomeratum. Phytother Res. 1999; 13*:*102–105.

23. Monzon RB, Alvior JP, Luczon LL, Morales AS, Mutuc FE: Larvicidal potential of five Philippine plants against *Aedes aegypti* (Linnaeus) and *Culex quinquefasciatus* **(**Say). Southeast Asian J Trop Med Public Health. 19994; 25:755-759

24. Moundipa PF*,* Flore KGM*,* Bilong Bilong*,* CF*,* Bruchhaus *I.* Afr. J. Trad. Complement. Alternat. Med. 2005; *2:* 113–121.

25. Mulla MS, Su T. Activity and biological effects of neem products against arthropods of medical and veterinary importance. J Am Mosq Control Assoc. 1999; *15*(2)**:**133-152.

26. Nathan SS, Kalaivani K, Murugan K: Effects of neem limonoids on the malaria vector, *Anopheles stephensi* Liston (Diptera: Culicidae). Acta Trop. 2005; 96: 47-55.

27. Nwaka S, Ridley RG: Virtual drug discovery and development for neglected diseases through public–private partnerships. Nature Rev. Drug Discov. 2003*;* 2: 919–928.

28. Petrovick PR*,* Marques LC*, De* Paula IC: New rules for phytopharmaceutical drug registration in Brazil. J Ethnopharmacol. 1999; 66*:* 51-55.

29. Pitter MH and Ernst E: Ginkgo biloba extract for the treatment of intermittent claudication: a meta-analysis of randomized clinical trials. Am. J. Med.2000; 108: 276-281.

30. Rates SMK. Plants as source of drugs. Toxicon. 2001; 39*:* 603-613.

31. Ricardo Ramos Mendonça-Filho. (2006). Modern Phytomedicine (Eds Iqbal Ahmad, Farukkh Aqil, Mohammad Owais) In*:* Bioactive Phytocompounds: New Approaches in the Phytosciences. pp.1-24.

32. Ridley RG. Medical need, scientific opportunity and the drive for antimalarial drugs. Nature.2002*;* 415: 686–693.

33. Sade Oguntola. Tribune Newspaper. Mango, pawpaw leaves have similar potency to malaria drug; pp.22-23 (02 Dec. 2010).

34. Sagar SK, Sehgal SS. Effects of aqueous extract of deoiled neem (*Azadirachta Indica* A. juss) seed kernel and karanja (Pongamia Glabra vent) seed kernel against *Culex quinquefasciatus*. J Commun Dis. 1996; 28: 260-269.

35. Shimmer O. Haefele, F., Kruger, A. Mutat: Res. (1988). In: Modern Phytomedicine: Turning Medicinal Plants into Drugs by Iqbal Ahmad, Farrukh Aqil, Mohammad Owais **(**2nd Ed.) pp. 201–208.

36. Schimmer O*.,* Krüger A., Paulini H*.,* Haefele F*:* An evaluation *of* 55 commercial plant extracts in the. Ames mutagenicity test. Pharmazie. 1994; 49: 448-451.

37. Stark JD. Population level effects of neem insecticide, Neemix on Daphnia pulex. J Env Sci Hlth B.2001*;* 36: 457-465.

38. Stewart*,* M.J. *&* V. Steenkamp*.* Toxicology of African herbal remedies. South African Ethnobotany.2000; 1:32-33.

39. Su T, Mulla MS: Antifeedancy of neem products containingAzadirachtin against *Culex tarsalis* and *Culex quinquefasciatus* **(**Diptera: Culicidae**).** J Vector Ecol.1998; 23**:** 114-122.

40. Tanaka T, Nonaka GI, Nishioka I: Tannins and related compounds. XLII. Isolation and characterization of four new hydrolysable tannins, terflavins A and B, ergallagin and tercatain from leaves of Terminalia catappa L. Chemical and Pharmaceutical Bulletin. 1986; 34: 1039–1049.

41. The world health report. (2002). Reducing risks, promoting healthy life. Geneva: World Health Organization.

42. Thomson SA: South African Government Genoside and Ethnopiracy. The Gaia Research Institute, South Africa, 2000**.**

43. WHO. Quality Control Methods for Medicinal Plant Materials, World Health Organization, Geneva, (1998).

44. WHO. Quality Control Methods for Medicinal Plant Materials. World Health Organization, Geneva, (1999).

45. WHO. Malaria Control in Complex Emergency. Inter-agency Field Handbook, p. xxii (2005).

46. WHO. The African Malaria Report. WHO, CDS, MAL, /2003.1093, Geneva (2003).

47. WHO Guidelines on Good Agricultural and Collection Practices (GACP). World Health Organization, Geneva, 2003.

48. WHO. Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants. World Health Organization, Geneva, 2004.

49. Wickramasinghe M: Bandaranayake. Modern Phytomedicine (eds Iqbal Ahmad, Farukkh Aqil, Mohammad Owais*)* In*:* Quality control, screening, toxicity, and regulation of herbal drugs. 2006: 25-57.

50. Wojcikowski K*,* Johnson DW*,* Gobe G*:* Medical herbal extracts—renal friend or foe? Part one: The toxicities of medicinal herbs. Nephrology 2004*;* 9*:* 313–318

51. Xiamen JieJing Biology Technology Co., Ltd,2009.Service@NaturalHerbalExtracts.com. Feb (2012).

52. Xu AH, Chen HS, Sun BC, Xiang XR, Chu YF, Zhai F, Jia LC: Therapeutic mechanism of gingko biloba exocarp polysaccharides on gastric cancer. World J. Gastroenterol. 2003; 9: 2424-2427.

53. Yam TS, Hamilton-Miller JM, Shah SJ: Antimicrob. Chemother. 1998; 42: 211–216.

54. Yoko Shoji and Hideki Nakashima: Nutraceutics and delivery systems. Journal of drug targeting. 2004; 12(6): 385-391.

55. Zeisel SH: Regulation of "nutraceuticals". Science. 1999; 285: 1853-1855.

56. Zhao WH, Hu ZQ, Hara Y, Shimamura T: Antimicrob. Agents Chemother. 2002; 46: 2266–2268.

57. Ziba MM**:** Preliminary laboratory trial of Neem on *Anopheles* and culex larvae in Zambia. Cent Afr J Med. 1995; 41: 137-138.