Nauclea latifolia (Rubiaceae)
(syn. Sarcocephalus latifolius)

English: Pin cushion tree, African peach, Guinea peach, Sierra Leone peach
French: Scille maritime, oignon marine, medicinal squill
African vernacular names:
Hausa: Tafashiya, tashiyaigia (medicinally useful bark) Igbo: Ubuluinu
Trade name: Opepe

The plant
Nauclea latifolia is an evergreen multi-stemmed shrub or a tree; it grows up to an altitude of 200 m. It is widespread in the humid tropical rainforest zone or in savannah woodlands of West and Central Africa. Three other related species Nauclea. pobeguini, N. diderichii, and N vanderguchtii are forest trees. N. diderichii is planted in Omo forest reserve, Nigeria. In the folk medicine the species N. diderichii and N. orientalis are used in the same way as N. latifolia.
Nauclea latifolia has an open canopy and terminal spherical head lined cymes of white flowers. The flowers are joined with their calyces. The fruit is syncarp.
The tree is flowering from April to June. The fruits are ripening from July to September. Baboons eat them and disperse the seeds. Livestock eat shoots and leaves. The fruits are edible, too.
The wood of N. latifolia (Opepe wood) is termite resistant and is used as live stakes in farms.

Plant parts used
The leaves, the stem, the stem bark, the root

Constituents
Alkaloids:
All plant parts of the Nauclea species are a rich source of monoterpene indol alkaloids. There is a lot of works. In the abundance of these works not all publications can be cited, only such ones about the indole alkaloids from the **bark** of N. orientalis (19), and about the naucleamides A - E in the **bark** and **wood** of N. latifolia (15).
The indole alkaloid strictosamine has been found in the **root, the leaves** and **stem bark** (15).
In the water soluble extract of N. latifolia **stems** seven indole alkaloid glycosides were isolated, among them swerosid and loganin.
From the **bark** and from the **wood** the alkaloids naucleactonine A and B, naucleficine and nauclefidine were isolated (18).
For quantitative determination of such extracts the following HPLC method is recommended:
Water/acetonitrile 5%, 10%, 50%, flow rate 0.7 ml/min, detection wavelength 245 nm, total elution time 70 min) (10)

In the **leaves** of N. orientalis strictoseamide, vincoseamid and their glycosides 10-hydroxy-strictosamide and 6`-O-acetylstrictosamide could be found (6).

Saponins

The basic compound of the most saponines is quinovic acid, a five-cyclic triterpene. The structural difference between the single saponines consists in glycosidation; it means the interglycosidic linkage with sugars in a different steric conformations.

In a methanolic extract from N. diderichii **bark** eleven single saponines could be found. The quantitative determination is 4.62 % of the **extract** and 0.18 % of the **bark.**

Two of such saponines are: (1) quinovic acid-3-O-alpha-L-rhamnosy l(28→1) beta-D-glucopyranosyl ester and (2) quinovic acid-3-O-(beta-D-glucopyranosyl (1→2) beta-D-glucopyranosid) (11).

Further compounds

In the **leave extracts** from plants in Kinshasa; DR Congo, active polyphenols were found (16).

Traditional uses

In West and South Africa infusions and decoctions of the bark and leaves are used for the treatment of stomach pains, fever, diarrhoea, and against parasites, like nematodes in men and animals, and tropical diseases like malaria.

In Kano (Nigeria) N. latifolia is used as a chewing stick and as a remedy against stomach ache and tuberculosis (3). In Ivory Coast infusions and decoctions from stems and roots of N. latifolia are used against malaria by traditional healers (2).

In West and Central Africa N. diderichii is used for its insecticidal and antiparasitic properties. In Gabon, Congo and Nigeria infusions of leaves and bark are employed against fevers (4). In Kinshasa, DR Congo extracts and preparations together with other plants are applied against diarrhoea (16).

Results of experimental studies

Antibacterial activity

The root bark of N. latifolia collected from Falgore Forest in Kano, Nigeria was extracted by aqueous ethanol and divided in five fractions. Fractions containing alkaloids were very active on eleven bacterial and two fungal strains. The bioassay was done with two standard bacterial susceptibility assays ADM and MDM (3).

No test strains of bacteria, neither Gram positives nor Gram negatives, were susceptible to the hot water extract of N. latifolia (13).

Antimalarial activity in vitro

Aqueous extracts -infusions and decoctions- from stems and roots of N. latifolia were tested in vitro in two Plasmodium falciparum strains, FcB1-Colombia (chloroquine resistant) and a Nigerian strain (chloroquine-resistant) according to the methods used by traditional healers. The in vitro activity was assessed visually and by a radioactive method. The IC50 values ranged from 0.6-7.5 µg/ml of the initial dry weight of the plant. Here harvesting time influenced the antiparasitical activity of the plants, because activity of batch 1 -harvested in September- was half that from batch 2 -harvested four months later.

Irrespectively of the extract origin, stem or root, the IC50 values were similar for infusions or decoctions. In all batches root-decocted extracts brought the best results. N. latifolia extracts inhibited essentially the final developmental stages of the parasites (2).

Two novel tetrahydro-ß-carboline monoterpene alkaloid glycosides, naucleaorine and epimethoxy-naucleaorine, isolated by chloroform from the dried stem of N. latifolia, strictosidine lactam, and oleanolic acid showed moderate in vitro activities against Plasmodium falciparum (8).
In the Democratic Republic of Kongo crude extracts of the stem bark of N. pobeguini were tested for antimalarial activity in vitro against Plasmodium falciparum and in mice infected with P.berghei. Dichloromethane extracts from the stem bark of N. pobeguini were found to be very active with an IC50 value 1< µg/ml. The IC50 of the water extract was 5.3 µg/ml. The aqueous extract produced a lower but significant inhibition of parasitaemia (60-80 %) (12).
Out of thirty three plants, commonly used in West tropical Africa by traditional healers for the treatment of malaria N. latifolia showed a good antiplasmodial activity and a weak toxicity. The ethanolic extract, obtained by decoction was evaluated in vitro against the chloroquine-resistant FcB1 strain of Plasmodium falciparum. Cytotoxicity was evaluated on the human MRC-5 and the rat line L-6 cell lines (20).

Further antiparasitic activity
In Africa leishmaniosis is a disease with high incidence. Because of the lack of medicines people rely on traditional treatment with N. diderichii. Four quinovic acid glycosides and cadambine acid isolated from the bark of N. diderichii collected in the vicinity of Libreville, Gabon revealed a strong antileishmanial activity with IC50 =1 µM. The toxicity against human cells (IC5 100µM) seemed to be weak (4) in order to ensure adequate drug release (5). In Kinshasa, polyphenols from leaves inhibited Entamoeba histolytica growth with MAC <10 µg/ml (16).

Anthelmintic activity
In Bauchi, Bauchi State the anthelmintic efficacy of water extract from N. latifolia stem bark was studied in 30 sheep with natural parasitic gastroenteritis caused by mixed nematode species. Infected sheep were treated with stem bark extract (400, 800, 1600 mg/kg) for five consecutive days. A control group was treated with a single dose of 5 mg/albendazol per os once at the day 0, the standard anthelminthic. The faecal samples, collected daily in the morning were evaluated for the presence of worm eggs by salt flotation technique. After five days of the treatment with 400, 800, 1600 mg/kg the extract reduced the counted nematode eggs with 69.8, 82.4 and 93.8 %, respectively. The highest tested dose, 600 mg/kg for five days was comparable to the single dose of albendazol 5mg/kg on day 0. In the infected sheep the HB concentrations after five days treatment increased between 20 or 30 %, the leucocytes decreased significantly in the extract and albendazol treated groups when compared to pre-treatment values. These in vivo results follow the results of an in vitro study where egg hatching of Strongyloides nematodes was prevented significantly. The authors conclude that the extract inhibits the protein synthesis in the parasite eggs. These results could be the pharmacological basis for the folkloric medicinal application of this plant (14).
In Nigeria extracts (10ppm) of N. latifolia kill 50 % of brine shrimp nauplia. Against ascaris IC50 values are brought by doses of 2, 5, 10 µg/L. Nematode glutathione-S-transferases are potential drug targets (7).

Neuropharmacological and biochemical effects
The aqueous extract of N. latifolia root bark significantly decreased the spontaneous motor activity in mice and prolonged pentobarbital sleeping time in

rats dose-dependently. The extract also remarkably attenuated the intensity of apomorphine-induced stereotypy dose-dependently in mice, but had no effect on motor coordination in the rotarod. The authors conclude that psychoactive substances are present in the aqueous extract (1). In Kinshasa, DR Congo polyphenolic extracts from leaves of N. latifolia inhibited 70 % acetylcholine and/or KCl solution-induced contractions on isolated guinea-pig ileum (16).

Molluscicidal activity
Methanol and water extracts of 25 Nigerian plants used for different medicinal and domestic purposes were tested for molluscicidal activity. Between them N. latifolia was found active and LC50 was determined with upper and lower fiducial limits, but without any singular values in the summary cited. The authors recommend that the toxic effects of these extracts should be known in order to use such plants in right concentrations in fish ponds (9).

Results of clinical studies
No results were available

Antimalarial tablets
There is a first, preliminary information about the development of a suitable tablet dosage form for a medicament against malaria. Studies were done with the water extract of N. latifolia. It was oven dried and the mechanical properties were determined. The tablets produced had good mechanical properties, like hardness increasing with compression pressure. But the friability decreased and the disintegration was poor. A disintegrating material should be needed to be included in the formulation of the tablets (5).

Toxicity
The alkaloid rich extracts from N. latifolia were evaluated in vitro and in vivo systems for toxicity and genotoxicity. They can interact in vitro with DNA of bacteria and mammalian cells, leading to G2-M cell cycle arrest and heritable DNA-damage. In liver, kidney and blood cells they induce single-strand breaks (17).
No significant toxic effect was observed for the dried water extract of N. pobeguini, the LD50 was >5g/kg. Neither this extract affected the serum concentrations of GPT or the blood concentrations of creatinine and urea, but it increases the serum concentrations of GOT (12).

Evaluation
The main compounds of Nauclea plants are the toxic indole alkaloids and saponines. These are big molecules which only can be solved by organic solvents. Water extract do this only in very little amounts and solve mostly the non-toxic common components of the plant. Therefore alcoholic extracts must be viewed as very toxic. The water extract contains mainly polyphenols and saponines. It is less dangerous. But here no recommendation can be given for use with men or in animals, nor for water or for alcoholic extracts.

Because of its toxicity all uses of Nauclea latifolia with men and animals must be advised against.

Nauclea latifolia and related species

for uses with men and animals	**- - -**
against parasites in vitro	******
against parasites in animals	**(*)**

References Nauclea

1. Amos S, Abbah J, Chindo B et al.(2005) Neuropharmacological effects of the aqueous extract of Nauclea latifolia root bark in rats and mice J Ethnopharmacol 97,1: 53-7
2. Benoit-Vical F,Valentin A,Cournac V et al. (1998) In vitro antiplasmodial activity of stem and root extracts of Nauclea latifolia S.M. (Rubiaceae) J Ethnopharmacol 61: 173-8
3. Deeni YY, Hussain HSN (1991) Screening for antimicrobial activity and for alkaloids of Nauclea latifolia J Ethnopharmacol 35: 91-6
4. DiGeorgio C, Lamidi M, Delmas F et al. (2006) Antileishmanial activity of quinovic acid glycosides and cadambine acid isolated from Nauclea diderrichii Planta Med 72: 1396-1402
5. Emeje MO, Isimi CY, Oqua DA, Kunle OO (2005) Some compaction characteristics of the hot water leaf extract of Nauclea latifolia : A potential malaria agent J Herb Pharmacother 5,4: 23-30 PubMed 1663 5965
6. Erdelmeier CAJ, Wright AD, Orjala J et al. (1991) New indole alkaloid glycosides from Nauclea orientalis Planta Med 57: 149-52
7. Fakae BB, Campbell AM, Barrett J et al. (2000) Inhibition of glutathione-S-transferases (GSTs) from parasitic nematodes by extracts from traditional Nigerian medicinal plants Phytother Res 14,8: 630-4 PubMed 1111 4001
8. He ZD, Ma CY, Zhang HJ et al. (2005) Antimalarial constituents from Nauclea orientalis (L.) Chem Biodevers 2,10: 1378-86 PubMed 17191939
9. Kela SL, Ogunsusi RA, Ogbogu VC, Nwude N (1989) Screening of some Nigerian plants for molluscicidal activity Rev Elev Med Vet Pays Trop 42,2 :195-202 PubMed 2626572
10. Li T, Wang WJ, Hu X (2005) Study on fingerprint of unfinished product of Nauclea injection Zhongguo Zhong Yao Za Zhi 30,15: 1156-8 PubMed 1620 1688
11. Lamidi M, Ollivier E, Faure R et al. (1995) Quinovic acid glycosides from Nauclea diderrichii Phytochem 38,1: 209-12
12. Mesia GK, Tona GL, Penge O et al (2005) Antimalarial activities and toxicities of three plants used as traditional remedies for malaria in the Democratic Republic of Congo: Croton mubango, Nauclea pobeguinii and Pyracantha staudtii Ann Trop Med Parasitol 99,4: 345-57 PubMed 1594 9182
13. Okoli AS, Iroegbu CU (2004) Evaluation and extracts of Anthocleista djalonensis, Nauclea latifolia and Uvaria afzalii for activity against bacterial isolates from cases of non-gonococcal urethritis J Ethnopharmacol 92,1: 135-44
14. Onyeyili PA, Nwosu CO, Amin JD, Jibike JI (2001) Anthelmintic activity of crude aqueous extract of Nauclea latifolia stem bark against ovine nematodes Fitoter 72: 12-21
15. Shigemori H, Kagata T, Ishiyama H et al. (2003) New monoterpene alkaloids from Nauclea latifolia Chem Pharm Bull 51,1: 58-61
16. Tona L,Kambu K,Ngimbi N et al. (2000) Antiamoebic and spasmolytic activities of extracts from some antidiarrhoeal traditional preparations used in Kinshasa, Congo Phytomedicine 7,1: 31-8 PubMed 10782488
17. Traore F, Gasquet M, Laget M et al. (2000) Toxicity and genotoxicity of antimalarial alkaloid rich extracts derived from Mitragyna inermis O. Kuntze and Nauclea latifolia Phytoter Res 14,8: 608-11 PubMed 1111 3997
18. Xuan WD, Chen HS, Du IL et al. (2006) Two new indole alkaloids from Nauclea officinalis J Asian Nat Product Res 8,8: 719-22 PubMed 17145660

19. Zhang Z, ElSohly HN, Jacob MR et al. (2001) New indole alkaloids from the bark of Nauclea orientalis J Nat Prod 64,8: 1-5
20. Zirihi GN, Mambu L, Guede-Guinea F et al. (2005) In vitro antiplasmodial activity and cytotoxicity of 33 West African plants used for treatment of malaria J Ethnopharmacol 98,3: 281-5