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Ethnopharmacological Properties of *Ceasalpinia benthamiana* - A Mini Review

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Author's contribution

This study was carried out by AO, who carried out the literature review and wrote the manuscript single handedly. The final manuscript is hereby approved.

Mini-review Article

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ABSTRACT

Caesalpinia benthamiana (Baill.) Herend. and Zarucchi (synonym. *Mezoneuron benthamianum* Baill.) belongs to the family Fabaceae, it is a climbing or a straggling shrub and is well known in some West African countries for its medicinal properties where it is used to cure general malaise, wound, urethral discharge, ulcer, pile, skin infection and believed to have aphrodisiac property. Phytochemical studies have revealed the leaf to contain essential oils, Gallic acid derivatives, tannins, saponins, flavonoids, phenols, anthraquinones and reducing sugars while the aqueous fractions of the root contain Gallic acid, resveratrol and tannins. Pharmacological assays have established the plant to be anti-inflammatory, anti-diarrheal, anti-bacterial, anti-candida, and to have vasorelaxation and aphrodisiac properties. This review presents information on the morphology, ecology, ethnopharmacology, phytochemistry, biological activities and toxicological properties of *C. benthamiana* and aims at providing an up-to-date detail that should constitute baseline information for future research on the plant.

Keywords: Ethnopharmacology; phytochemical; anti-inflammatory; vasorelaxation; aphrodisiac; Caesalpinia benthamiana.

1. INTRODUCTION

Caesalpinia benthamiana (Baill.) Herend and Zarucchi (=*Mezoneuron benthamianum* Baill.) (Caesalpiniaceae) [1], belongs to the family Fabaceae and was first identified in 1866. There

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are over 236 genera in Fabaceae and 24 species in the genus *Caesalpinia* to which *C. benthamiana* is one of them. It is commonly call "tiger's claw" because of its prickly thorns. it is generally found in the tropical part of the world and situated mainly in West African countries (from Senegal to Garbon). It has been traditionally used in management of several diseases including erectile dysfunction, dysentery, urethral discharges, skin diseases and wounds [2]. Information on this plant are scanty as no mention of this plant was made in Ayurvedic system in India and hence no definitive botanical description of this plant exists. Aside the mere listing of this plant as being used for the treatment of diarrhea in South-South, South East and South West of Nigeria [3], no detailed documentation exist in literature on this plant.

Fig. 1. The image of *Caesalpinia Benthamiana*
(Source:http://herbaria.plants.ox.ac.uk/vfh/image/index.php?item=4101&taxonomy=1400&photo=4542)

2. TAXONOMY

Kingdom :	Plantae
Subkingdom:	Tracheobionta (Vascular plant)
Superdivision:	Spermatophyta (Seed plants)
Division:	Angiospermae
Class:	Magnoliopsida (Dicotyledoneae)
Subclass:	Rosidae
Order:	Fabales
Family:	Fabaceae
Subfamily:	Caesalpiniaceae (Leguminosae - Caesalpinioideae)
Tribe:	Caesalpinieae
Genus:	*Caesalpinia*
Species:	*Caesalpinia benthamiana* (Baill.) Herend. and Zarucchi
Synonyms:	*Mezoneuron benthamianum* Baill. (1866).

3. TRADITIONAL USES AND VERNACULAR NAMES

The plant, whose image is shown in Fig. 1, is called Tiger's claw because of its many recurred thorns. The plant is generally found in the West African countries. In Nigeria it is called "Jenifiran" in the western part of the country [4]. In Nigeria, Guinea and Senegal the

decoctions of the leaves, bark and roots are used to cure urethral discharge while in some part of Nigeria and Ghana, the stem and the roots are used for oral hygiene and are believed to have aphrodisiac properties. Also, the Senegalese use the infusion of the dried roots to bath and drink against general malaise. The leaf ash, the mashed-up of the leaf or macerate of the twigs are used for the treatment of skin infections, ulcers, wounds and piles in some west African countries such as Senegal, Cote d'Ivoire and Ghana [5,6]. In Ghana especially, Dickson et al. [7] stated that a paste of the root bark is made and mixed with vehicle such as shea butter or palm kernel oil to be applied topically to affected wound area. The plant also finds application in the treatment of venereal diseases and dysentery. In Cote d'Ivoire, the liquid collected from the stem is used for the treatment of eye inflammation and cataract and the mash-up of the leaf is used as paste to treat snakebites [8].

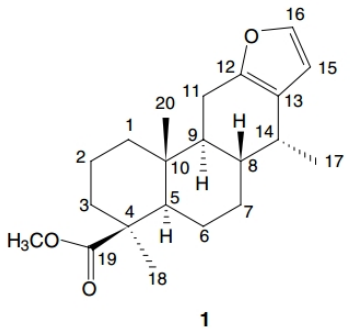
4. HABIT AND HABITAT

Caesalpinia benthamiana is a climbing or a straggling shrub. The body surface of the stem is filled with recurred spines and the stem can measure up to 20 m long and 8 cm in diameter. Its leaves are bi-pinnate showing alternate arrangement with 5- 6 pairs of pinnae. The stipules are small and inconspicuous. The leaf petiole is usually between 5 to 10 cm long with swollen base and has rachis that maybe 15 to 20 cm long bearing the recurred spines at the base of the pinnae. The leaflets are arranged alternately with 5 pairs per pinna, usually they are elliptical, ranging from 3 to 4 cm by 1.5 to 2.5 cm. The base and apex are rounded and glabrous. The inflorescence (terminal raceme) is usually hairy and densely flowered, may or may not form branches, and can be up to 20cm in length. The flowers are bisexual, zygomorphic and pentamerous [8].

5. CHEMICAL CONSTITUENTS OF THE LEAF, ROOT BARK AND ESSENTIAL OIL

The leaf of *M. benthamianum* is rich in saponins and tannins [9]. The aqueous extract of the whole plant has been analyzed to contain flavonoids, phenols, anthraquinones, reducing sugars, tannins and saponins [10]. The root bark is also rich in phenolic compounds (gallic acid, resveratrol and tannins) [11]. The chloroform ($CHCL_3$) and butanol (BuOH) extracts of *M.benthamianum* contain methyl gallate, gallic acid, shikimic acid-3-*O*-gallate, 1- *O* -methyl-D-chiro-inositol, (-)-epicatechin, (-)-epicatechin-3- *O* -gallate and Kaempferol-3-(6"-galloyl)glucoside [12].

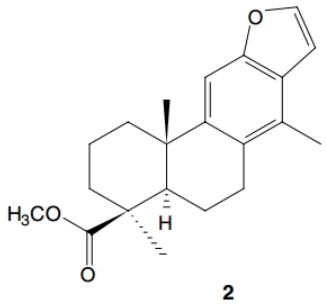
Three compounds have been isolated from the petroleum ether fraction of the root bark and these are the: deoxycaesaldekarin C (also known as methyl vouacapenate) [Fig. 2], Benthaminin 1 [Fig. 3] and Benthaminin 2 [Fig. 4]. The structures of these compounds were elucidated using a combination of 1D and 2D NMR spectroscopy, mass spectrometry (LREIMS, HREIMS and ESI).The structure formulae of these compounds were as follows:



1

Fig. 2. The Structure of compound 1 (deoxycaesaldekarin C) isolated from *C. benthamiana*

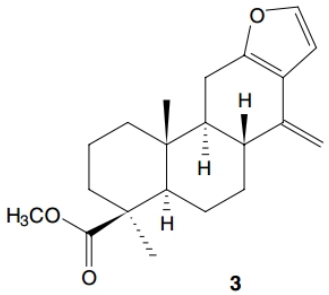
*(**Systematic name**: (4S) - 4, 7β, 11 bα - Trimethyl - 1, 2, 3, 4, 4aβ, 5, 6, 6aα, 7, 11, 11aβ,11b-dodecahydrophenanthro[3,2-b]furan-4α-carboxylic acid methyl ester)*



2

Fig. 3. The structure of compound 2 (Benthaminin 1)

*(**Systematic name**: 4,7,11b-trimethyl-1,2,3,4,4a,5,6,11b-octahydro-10-oxa-cyclopen[b]phenanthrene-4-carboxylic acid methyl ester)*



3

Fig. 4. The structure of compound 3 (Benthaminin 2)

*(**Systematic name**:4,11b-dimethyl-7-methylene-1,2,3,4,4a,5,6,6a,7,11,11a,11b-dodecahydro-10-oxa-cyclopental[b]phenanthrene-4-carboxylic acid methyl ester)*

The leaves of *C. benthamiana* contain essential oil which has its own characteristic strong pungent odour which has been attributed to its constituents. Fifteen compounds which constitute about 93.4% of the total constituents were identified from the essential oil and

these include monoterpenes (36.5%), sesquiterpenes (20.4%), sesquiterpenoids (19.6%) and and a non-ubiquitous apocarotenoid $C_{20}H_{30}O$ (16.7%) [13].

6. ANTI-INFLAMMATORY

The topical anti-inflammatory activity of the essential oil of the leaves of the *M. benthamianum* was evaluated as the inhibition of the 12-O-tetradecanoylphorobol-13 acetate (TPA) induced ear edema in mice. Results indicated that all the mice treated with the oil at 5.0 and 2.5 mg dose levels had reduction in the ear edema ranging from 92.3% and 76.9% respectively. The oil significantly performed better against Indomethacin a standard anti-inflammatory drug [13].

7. ANTI-DIARRHEAL

M. banthamianum showed strong anti-diarrheal effect when tested on Winstar rat and Swiss mice weighing between 170 to 200g and 25 to 30 g respectively. Castor-oil (0.2 ml/animal) induced diarrhea in mice orally fed with 400 – 1600 mg/kg of the aqueous extract 30 minutes before the administration of castor-oil, generated a dose dependent and significant ($p<0.05$) delay in the onset of diarrhea. Also, the frequency of stooling was reduced and a general decrease in weight of wet stools, hard, mild and copious diarrhea (Mbagwu and Adeyemi, 2007). Although not as effective as the standard anti-diarrheal drug, morphine (100 mg/kg, s.c.).

8. VASORELAXATION PROPERTY

The aqueous root bark extract of *C. benthamiana* has exhibited a vasorelaxing properties. In an experiment involving the aorta ring of rat strip, the application of the aqueous extract (1-20 mg/L) on the aorta ring whose contraction was induced with phenylephrine, resulted in an immediate relaxation of the aorta which continued to reach a plateau after 15 minutes. Furthermore, the QPCR analysis revealed that the extract triggered eNOS mRNA expression ($p< 0.001$) of 2.4 ± 0.5, 4.3 ± 0.7 and 5.7 ± 0.7 at 0.1, 1 and 10 mg/L concentrations of root bark extract respectively, these are of great interest considering the fact that, scale stimulation only occurs when relative quantity is superior to 1.5 in eNOS QPCR evaluation [11].

9. APHRODISIAC PROPERTY

In a test carried out to determine the aphrodisiac property of the aqueous extract of the root, two groups of five sexually matured rats were given 1mL of tap water (control group) and 50 mg/kg body weight of the aqueous extract of *C. benthamiana* (test group). Results indicate that the mounting frequency (MF) ($p< 0.001$) increased significantly while the mounting latency (ML) decreased after 30 minutes, 1.15hr and 3.15hrs of observations when compared to that of untreated rats [11].

10. RESISTANCE MODIFYING ACTIVITY

Dickson et al. [7] assayed for the Modulation properties of the root extracts of *C. benthamiana* using the standard antibiotics such as norfloxacin, tetracycline and erythromycin, in 96-well plates on multi-drug resistant strains of *Staphylococcus aureus*. It was reported that a 4-fold potentiation of the activity of norfloxacin was observed for

ethanolic and the chloroform extracts of *C. benthamiana* (=*M. benthamianum)* against the norfloxacin-resistant strain of *S. aureus* possessing the efflux pump NorA (the characterized drug pump in the pathogen) while the petroleum spirit extract resulted in a 2-fold potentiation for the same antibiotic. The observed property was compared at 10 µg/mL for the extracts and 20 µg/mL for reserpine which served as the standard MDR (Multidrug resistance) inhibitor and found to be promising. Results also showed that a 2-fold reduction was observed in the tetracycline concentration needed to inhibit growth strain of *S. aureus* with the TetK efflux mechanism

11. ANTIBACTERIAL AND ANTI-CANDIDAL ACTIVITIES

Petroleum spirit, chloroform and ethanol extracts of the root bark of *M. benthamianum* have shown recorded activity against gram-positive and gram-negative bacteria and some dermatophytes: *Micrococcus flavus* (NCTC 7743), *Bacillus subtillis*, (NCTC 10073), *Staphylococcus aureus* (NCTC4163).

Multidrug-resistant *S. aureus* SA-1199B (over-expressing the NorA MDR transporter), tetracycline-resistant S. aureus XU212 (TetK expresser), erythromycin-resistant *S. aureus* RN 4220 (expresser of the MsrA, macrolide pump), *Streptococcus faecalis* (NCTC 775), *Salmonella abony* (NCIMB6017), *Pseudomonas aeruginosa* (NCIMB 10421), *Escherichia coli* (NCTC 9002), *Klebsiella aerogenes* (NCTC 5055), *Candida albicans* (NCPF 3179), *Saccharomyces cerevisiae* (NCTC 080178).

Trichophyton interdigitale (NCPF 654) and *Microsporum gypseum* (NCPF261). The MIC values against these organisms ranged from 31.2 to 1000 µg/mL [7]. However, the gallic acid and its methyl ester isolated from the leaf of *C benthamiana* were found to be weak activity against *Staphylococcus aureus (*ATCC 29213*)*, *Bacillus subtilis (*ATCC 21394*) Escherichia coli (*ATCC 25922*)* and *Pseudomonas aeruginosa* (ATCC 27853) [12].

The three compounds (deoxycaesaldekarin C , Benthaminin 1 and Benthaminin 2) isolated from the petroleum ether fraction of the root bark of the plant possessed high antibacterial properties with Benthaminin 2 showing better performance than others, it recorded 47.0 uM against *S. aureus* and *M. flavus* [14].

Equally, *C.benthamiana* has been shown to have activity against *Candida* species. The leaf extracts recorded an MIC value of 8mg/ml against *C. albicans* and *C. stellatoidea*, 15 mg/ml against *C. krusei*, 6 mg/ml against *C. torulopsis* and 5 mg/ml against *C. glabrata* [9].

12. ANTIOXIDANT AND SCAVENGING PROPERTIES OF ROOT BARK OF *C. benthamiana*

C. benthamiana has shown a high level of antioxidant properties for example in a comparative study of three medicinal plants; *Mezoneuron benthamianum*, *Securinega virosa* and *Microglossa pyrifolia*; the petroleum spirit and chloroform extracts of *C.benthamiana* recorded higher antioxidant properties among the three medicinal plant with IC_{50} values of 15.55ug/mL and 19.72ug/mL for free radical scavenging activity and 23.15 and 30.36ug/mL respectively for inhibition of lipid peroxidation of bovine brain liposomes [7].

Of the three compounds (deoxycaesaldekarin C , Benthaminin 1 and Benthaminin 2) isolated from the petroleum ether fraction of the root bark of the plant, compound 1 and 3

showed high antioxidant properties [14]; with Compound 3 recording better results with IC_{50} values of 42.7 and 74.2 uM for DPPH (2,2-diphenyl-1-picrylhydrazyl) spectrophotometric and TBA (thiobarbituric acid) lipid peroxidation assays respectively. The performance of Compound 3 was attributed to the presence of an exocyclic methylene functional group in the compound.

13. TOXICITY

The aqueous extract of the whole plant has been found to be none toxic to Winstar rats and Swiss mice. The LD_{50} of the extract administered intraperitoneally was 1021.31 mg/kg. Oral administration up to 2 g/kg produced no deleterious effect 24 h after dosing and up to 7 days afterwards [10].

14. CONCLUSION

The few numbers of scientific researches available on this suggests that *C banthamiana* has a huge biological property that could prove to be of immense benefit clinically that might lead to developing novel compounds for the management of various disorders. Giving the traditional uses of this plant there is the need to justify some of these claims through more pharmacological studies to determine the antimalarial, anticancer, antiviral, anti-diabetic, etc of some the compounds isolated and others that are yet to be isolated from the extracts of this plant. Of particular significance in this case of the non-ubiquitous apocarotenoid $C_{20}H_{30}O$ isolated from the essential oil of the plant [13] which needs to be further studied and its pharmacological importance determined. The scanty information on the plant notwithstanding, there is the need for correlation between the revealed phytochemical properties and their mode of actions in order to establish their pharmacological actions for clinical use, particularly through the profiling of the molecular interaction of the bioactive phytochemicals and their molecular targets that may eventually lead to drug development.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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