Review of Medicinal uses, Phytochemistry and Biological Activities of *Antidesma laciniatum* and *A. membranaceum*

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Abstract: *Antidesma laciniatum* and *A. membranaceum* are small trees used as traditional medicines in tropical Africa. This extensive literature review synthesizes the information currently available on the medicinal uses, phytochemistry and biological activities of *A. laciniatum* and *A. membranaceum*. The university library and electronic search engines such as Google Scholar, Scopus, Web of Science, ScienceDirect, and PubMed were searched for pertinent information on the medicinal uses, phytochemistry, and biological activities of *A. laciniatum* and *A. membranaceum*. Traditionally, the species have been used as aphrodisiac, and traditional medicine for cough, kwashiorkor, mouth ulcers, pneumonia, prevent miscarriage, snakebites, stomachache and wounds. Various phytochemicals such as essential oils, isoflavonoid glycosides, phytosterols, benzopyranones, lignin glucosides, megastigmane, phenolics, steroids, squalene, terpenoids, triterpenoids, and tetrahydroisoquinoline alkaloids have been isolated from *A. laciniatum* and *A. membranaceum*. *In vitro* studies have confirmed the biological activities of *A. laciniatum* and *A. membranaceum* which, include antimicrobial, antioxidant, antiplasmodial, antitrypanosomal, leishmanicidal, molluscicidal and cytotoxicity activities. More pharmacological studies including phytochemical, toxicological, *in vitro* and *in vivo* experiments are needed to provide evidence for the clinical effectiveness of remedies prepared from the species.

Keywords: *Antidesma laciniatum, Antidesma membranaceum*, indigenous knowledge, Phyllanthaceae, traditional medicine, tropical Africa.

INTRODUCTION

The genus *Antidesma* L. is one of the most important sources of herbal medicines among the Phyllanthaceae family. Moreover, the Phyllanthaceae species have been used in folk medicine in several countries in the treatment of skin infections, kidney and urinary bladder problems, sexually transmitted infections, gastro-intestinal infections, respiratory infections, wounds, hypertension, and diabetes [1-4]. The Phyllanthaceae species are reported to have pharmacological activities such as anti-inflammatory, antitumour, analgesic, antimicrobial, antineoplastic, antiplasmodial, antihepatoxic, antioxidant, mutagenic, hepatoprotective, hypotensive and antiallergic [1-9]. Similarly, species belonging to the genus *Antidesma* are widely used in tropical Africa as food sources and traditional medicines [10-12]. Some *Antidesma* species, for example *A. madagascariense* Lam. are characterized by sterols, phenols, saponins, tannins, alkaloids, flavonoids, cyanogenetic heterosides, leucoanthocyanins, triterpenes and carpusin [12]. The crude extracts of *A. madagascariense* showed antibacterial, antifungal, antioxidant, antiglycation, anti-diabetic activities as well as its immunomodulatory properties [12]. *Antidesma laciniatum* Müll. Arg. and *A. membranaceum* Müll. Arg. are among the species widely used as herbal medicines in tropical Africa [13]. Antidesma laciniatum and *A. membranaceum* have been recorded in overlapping geographical areas in tropical Africa, extending from Guinea Bissau eastwards to Ethiopia and Kenya, through the Democratic Republic of Congo (DRC) southwards to central and southern Africa [13]. It is, therefore, within this context that the current review was undertaken aimed at providing a comparative analysis of the botanical, medicinal, chemical and biological activities of *A. laciniatum* and *A. membranaceum*.

Botanical Description

Antidesma laciniatum is a shrub or small dioecious tree with a spreading crown growing to a height of 15 metres [14]. The leaves of *A. laciniatum* are alternate, simple, entire, and linear to oblong in shape. *Antidesma laciniatum* has been recorded in the understorey of dense forests, rain forests, moist deciduous forests, including secondary forest and forest edges from sea level to 1200 metres above sea level [14-16]. *Antidesma membranaceum* is a shrub or a small dioecious tree of about 20 metres in height with a dense crown [17,18]. The bole of *A. membranaceum* is fluted and there are small buttresses on larger trees. The bark of *A. membranaceum* is rough and dark brown in colour in older specimens while young branchlets are characterized by brown, velvety hairs. The leaves are alternate, simple, entire, narrowly elliptic to oblong in shape, dark green and velvety

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above and yellowish below. *Antidesma membranaceum* has been recorded in mixed and moist woodland, evergreen forest, riverine vegetation, ravines, fringe forest, lakeshores, coastal forest, thicket and woodlands in the savanna biome from sea level to 1850 metres above sea level [19-29].

The bark, fruit, leaf, root, seed and stem decoction or infusion of *A. laciniatum* and *A. membranaceum* are mainly used as aphrodisiac, and as traditional medicine for cough, kwashiorkor, mouth ulcers, pneumonia, prevent miscarriage, snakebites, stomachache and wounds (Table **1**). Other medicinal applications of *A. membranaceum* that are supported by at least two literature reports include the use of the bark, leaf, root and seed infusion or decoction, as an anthelmintic [13,30], aphrodisiac [10,13], chest problems [10,13] and colic [10,13].

Phytochemistry

A variety of chemical compounds have been isolated and identified from the leaves and stem bark of *A. laciniatum*, including essential oils, isoflavonoid glycosides, phytosterols, squalene, terpenoids, and triterpenoids [33,47-50] (Table **2**). Similarly, compounds such as benzopyranones, lignin glucosides, megastigmane, phenolics, steroids, terpenoids and tetrahydroisoquinoline alkaloids have been isolated and identified from the bark, leaves, roots, root bark and stem bark of *A. membranaceum* [48,51-56]. Some of these phytochemical compounds

Table 1: Medicinal uses of *Antidesma laciniatum* and *A. membranaceum*

Medicinal uses	Part used	Country	Reference
A. laciniatum			
Aphrodisiac	Bark decoction taken orally	Cameroon and Guinea	[31-33]
Bleeding	Fruit decoction applied topically	Angola	[34]
Cough	Stem decoction taken orally	Cameroon	[35]
Fish poison	Leaves and roots	Central African Republic	[36]
Prevent miscarriage	Leaf decoction taken orally	Guinea	[32]
A. membranaceum			
Anthelmintic	Seed decoction taken orally	Tanzania	[13,30]
Aphrodisiac	Bark decoction taken orally	Côte d'Ivoire	[10,13]
Asthma	Bark and leaf decoction taken orally	DRC	[37]
Chest problems	Leaf and root infusion taken orally	Zimbabwe	[10,13]
Colic	Root infusion taken orally	DRC	[10,13]
Cosmetic	Milky juice applied topically	Liberia	[38]
Cough	Leaf and root infusion taken orally	DRC and Zimbabwe	[10,13,39,40]
Diabetes	Bark and leaf decoction taken orally	DRC	[37]
Diarrhoea	Bark and leaf decoction taken orally	DRC	[37]
Flu	Stem decoction taken orally	Tanzania	[41]
Hernia	Bark and leaf decoction taken orally	DRC	[37]
Kwashiorkor	Root decoction taken orally	Tanzania	[11,13,30,42,43]
Mouth ulcers	Root decoction taken orally	DRC and Tanzania	[11,13,30,40,43]
Pneumonia	Root decoction taken orally	Tanzania	[11,13,30,43]
Prevent miscarriage	Leaf decoction used as a bath	Liberia	[10,13,32,44-46]
Snakebites	Leaf and root infusion applied topically	DRC and Tanzania	[10,11,13]
Stomachache	Leaf and root infusion taken orally	DRC	[10,11,13,45,46]
Tonic	Root infusion taken orally	Tanzania	[11]
Wounds	Stem bark powder applied topically	DRC and Tanzania	[13,30,40]

Table 2: Phytochemical Compounds of *Antidesma laciniatum* and *A. membranaceum*

Compound	Value	Plant part	Reference
A. laciniatum			
2E,7ξ,11ξ)-phyt-2-en-1-ol	-	Leaves	[48]
30-hydroxybetulinic acid	-	Stem bark	[49]
30-oxobetulinic acid	-	Stem bark	[49]
(E)-Anethole (%)	0.5	Leaves	[33,47]
Benzyl acetate (%)	1.5	Leaves	[33,47]
Benzyl benzoate (%)	19.1	Leaves	[33,47]
Benzyl salicylate (%)	3.0	Leaves	[33,47]
Betulinic acid	-	Stem bark	[49,50]
β-Bourbonene (%)	0.5	Leaves	[33,47]
α-Cadinene (%)	0.3	Leaves	[33,47]
δ-Cadinene (%)	1.3	Leaves	[33,47]
γ-Cadinene (%)	0.3	Leaves	[33,47]
α-Cadinol (%)	3.0	Leaves	[33,47]
epi-α-Cadinol (%)	0.2	Leaves	[33,47]
β-Caryophyllene (%)	5.2	Leaves	[33,47]
Caryophyllene oxide (%)	8.5	Leaves	[33,47]
Chevalierinosides A - C	-	Stem bark	[49,50]
(E)-Cinnamyl acetate (%)	0.6	Leaves	[33,47]
α-Copaene (%)	2.2	Leaves	[33,47]
β-Copaene (%)	0.3	Leaves	[33,47]
(E,E)-α-Farnesene (%)	0.5	Leaves	[33,47]
(E,E)-Farnesol (%)	2.0	Leaves	[33,47]
(E,E)-Farnesyl acetate (%)	1.3	Leaves	[33,47]
Friedelin	-	Stem bark	[49,50]
Friedelan-3b-ol	-	Stem bark	[50]
Genistein 7-O-β-D-glucopyranoside	-	Stem bark	[49]
Geraniol (%)	0.5	Leaves	[33,47]
Geranyl acetate (%)	14.9	Leaves	[33,47]
Germacrene D (%)	8.5	Leaves	[33,47]
Germacrene D-4-ol (%)	0.4	Leaves	[33,47]
α-Humulene (%)	2.1	Leaves	[33,47]
Humulene oxide (%)	3.5	Leaves	[33,47]
Kaempferol 3-O-β-D-glucopyranoside	-	Stem bark	[49]
Linalool (%)	9.4	Leaves	[33,47]
Methyl benzoate (%)	0.5	Leaves	[33,47]
p-Methyl anisole (%)	2.1	Leaves	[33,47]
α-Muurolene (%)	1.5	Leaves	[33,47]
γ-Muurolene (%)	0.7	Leaves	[33,47]
α-Muurolol (%)	1.0	Leaves	[33,47]
epi-α-Muurolol (%)	2.5	Leaves	[33,47]
Squalene	-	Leaves	[48]
Sitosterol	-	Leaves	[48]
Spathulenol (%)	1.4	Leaves	[33,47]

(Table 2). Continued.

Compound	Value	Plant part	Reference
A. membranaceum			
2-Nonadecyl-2,5,7-trihydroxy-chromanone	-	Leaves, roots and stem bark	[51]
2-Eicosyl-2,5,7-trihydroxy-chromanone	-	Leaves, roots and stem bark	[51]
2-Heneicosyl-2,5,7-trihydroxy-chromanone	-	Leaves, roots and stem bark	[51]
3-oxo-α-ionyl β-D-glucopyranoside	-	Leaves	[55]
4′-*O*-methyllyoniresin-4-yl β-D-glucopyranoside	-	Leaves	[55]
(5S)-l,4-Dimethoxy-3-methyl-5-octyl-5,6,7,8-tetrahydroisoquinolin-8-one	-	Bark, leaves and roots	[52]
5,7-Dihydroxy-2-heneicosyl-chromone	-	Leaves, roots and stem bark	[51]
5,7-Dihydroxy-2-nonadecyl-chromone	-	Leaves, roots and stem bark	[51]
5,7-Dihydroxy-2-eicosyl-chromone	-	Leaves, roots and stem bark	[51]
8,8-bis(dihydroconiferyl)-diferuloylate	-	Leaves, roots and stem bark	[51]
(17*RS*)-17-(β-D-glucopyranosyloxy)antidesmone	-	Leaves	[55]
(17*RS*)-8-deoxo-17-(β-D-glucopyranosyloxy)antidesmone	-	Leaves	[55]
Amentoflavone	-	Leaves	[48]
Antidesmone	-	Bark, leaves and roots	[52-55]
Blumenyl A β-D-glucopyranoside	-	Leaves	[55]
Blumenyl B β-D-glucopyranoside	-	Leaves	[55]
Blumenyl C β-D-glucopyranoside	-	Leaves	[55]
Lyoniresin-4-yl β-D-glucopyranoside	-	Leaves	[55]
N-trans-feruloyl-octopamine	-	Leaves, roots and stem bark	[51]
N-cis-feruloyl-octopamine	-	Leaves, roots and stem bark	[51]
N-trans-feruloyl tyramine	-	Leaves, roots and stem bark	[51]
Secoisolariciresin-4-yl β-D-glucopyranoside	-	Leaves	[55]
(-)-Syringaresinol	-	Leaves, roots and stem bark	[51]

may be responsible for the pharmacological properties exhibited by the two species.

Biological Activities

Pharmacological research revealed that different extracts of *A. laciniatum* and *A. membranaceum*, and the compounds isolated from the species have various biological activities such as antimicrobial, antioxidant, antiplasmodial, antitrypanosomal, leishmanicidal, molluscicidal, and cytotoxicity activities.

Antimicrobial Activities

Preliminary antibacterial activity evaluations of aqueous and methanol leaf extracts of *A. membranaceum* carried out by Ogunlana and Ramstad [57] revealed activities against Bacillus subtilis. Magadula *et al.* [56] evaluated the antimycobacterial activities of ethanol extracts of *A. membranaceum* root bark against *Mycobacterium madagascariense* and *Mycobacterium indicus pranii* using the two-fold microdilution method with ciprofloxacin as a positive control. The extract exhibited activities against *Mycobacterium indicus pranii* and *Mycobacterium madagascariense* with the minimum inhibition concentration (MIC) values of 0.3 mg/ml and 1.3 mg/ml, respectively, in comparison to a MIC value of <0.05 mg/ml exhibited by the positive control [56]. The compound antidesmone isolated from the bark, leaves and roots of *A. membranaceum* exhibited antifungal activities to the amount of 1.25 nmol in a bioassay based on *Cladosporium cucumerinum* [52].

Antioxidant Activities

Boyom *et al.* [47] evaluated the antioxidant activities of the essential oils isolated from the leaves of *A. laciniatum* using 2,2-diphenyl-1-picrylhydrazyl (DPPH)

free radical scavenging assay with ascorbic acid (10.0 – 50.0 µM), butylated hydroxytoluene (BHT) (10.0 – 50.0 µM) and δ-tocopherol (10.0 – 50.0 µM) as positive controls. The essential oils exhibited weak activities with half maximal scavenging concentrations (SC_{50}) value of 25.0 g/l in comparison to the SC_{50} values of 6.2 mg/l to 15.3 mg/l exhibited by the positive controls [47].

Antiplasmodial Activities

Bringmann *et al.* [54] evaluated the antiplasmodial activities of the compound antidesmone isolated from the stem bark of *A. membranaceum* against NF54 strain of *Plasmodium falciparum,* which is sensitive to all known drugs and K1, a strain resistant to chloroquine and pyrimethamine using the [G-^{3} H]-hypoxanthine incorporation assay with chloroquine as a positive control. The compound exhibited weak activities against K1 and NF54 with the median inhibitory concentration (IC_{50}) values of 3.8 µg/ml and >5.0 µg/ml, respectively [54]. Boyom *et al.* [47] evaluated the antiplasmodial activities of the essential oils isolated from the leaves of *A. laciniatum* against the W2 strain of *Plasmodium falciparum* using the [G-^{3} H]-hypoxanthine incorporation assay with chloroquine phosphate as a positive control. The essential oils exhibited activities with an IC_{50} value of 29.4 µg/ml in comparison to an IC_{50} value of 30.4 nM exhibited by the positive control [47].

Antitrypanosomal Activities

Bringmann *et al.* [54] evaluated the antitrypanosomal activities of the compound antidesmone isolated from the stem bark of *A. membranaceum* against *Trypanosoma brucei rhodesiense* and *Trypanosoma cruzi* using the Alamar Blue assay, and rat skeletal myoblasts (L-6 cells) infected with trypomastigotes of *Trypanosoma cruzi*. The compound exhibited activities against *Trypanosoma cruzi*, rat skeletal myoblasts (L-6 cells) and *Trypanosoma brucei rhodesiense* with IC_{50} values of 0.02 µg/ml, 11.8 µg/ml and 20.1 µg/ml, respectively [54].

Leishmanicidal Activities

Bringmann *et al.* [54] evaluated the leishmanicidal activities of the compound antidesmone isolated from the stem bark of *A. membranaceum* against *Leishmania donovani* using mouse peritoneal macrophages. The compound exhibited weak activities with an IC_{50} value of 7.2 µg/ml [54].

Molluscicidal Activities

Adewunmi and Sofowora [58] evaluated the molluscicidal activities of methanol extracts of *A. laciniatum* roots against *Bulinus globosus*. The extract showed 100% mortality to the snails at a concentration of 100.0 ppm [58].

Cytotoxicity Activities

Magadula *et al.* [56] evaluated the cytotoxicity activities of ethanol extracts of *A. membranaceum* root bark using the brine shrimp toxicity assay with cyclophosphamide as a positive control. The extract exhibited activities with half maximal lethal concentration (LC_{50}) value of 36.1 µg/ml in comparison to LC_{50} value of 16.3 µg/ml exhibited by the positive control [56].

CONCLUSION

The present review summarizes the medicinal uses, phytochemistry and biological activities of *A. laciniatum* and *A. membranaceum*. Based on the presented information, these two species are closely related and deemed as potent traditional medicines for treating and managing cough, kwashiorkor, mouth ulcers, pneumonia, prevent miscarriage, snakebites, stomach ache, and wounds. *Antidesma laciniatum* and *A. membranaceum* should be subjected to detailed phytochemical, pharmacological, and toxicological evaluations aimed at correlating their medicinal uses with their phytochemistry and pharmacological properties.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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