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Monograph

Ethnopharmacological uses of *Antidesma madagascariense* Lam. (Euphorbiaceae)

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ABSTRACT

Antidesma madagascariense Lam. is an indigenous plant of the Mascarene Islands which has interestingly shined as a promising traditional medicinal plant. The ethnobotanical uses of this plant were geared toward the treatment and management of dysentery, albumin in the urine, jaundice, fever, diabetes, skin infections, rheumatic and body aches among others. Preliminary screening of this plant coupled with a plethora of *in vitro* and *in vivo* tests have furnished scientists with documented findings that have appraised its traditional use in the treatment and management of infectious diseases. The presence of antidesmin, a commonly characterized component of *Antidesma* species, might justify the medicinal virtues of this plant. The present monograph aims at providing the botanical description, traditional uses and latest findings documented on *A. madagascariense*. Nonetheless, continued research on this plant needs to be completed in order to rationalize the use of this promising plant as a potential source of beneficial constituents for the treatment and management of human diseases and hence set up promising optimism for drug development.

KEY WORDS: *Antidesma madagascariense,* antidesmin, ethnopharmacology, Mascarene Islands

INTRODUCTION

Antidesma madagascariense Lam., (Euphorbiaceae) is a tropical plant whose genus contains 170 species. It is indigenous to the Mascarene region in the Western Indian Ocean as well as to Madagascar [1,2]. The different species are adapted to survive in warm and tropical regions, for instance, Asia and Oceania, but also East Africa, which has a deep-rooted tradition to the use of these medicinal plants. Commonly known as "Bois bigaignon bâtard" and "Bois bigayon" in Mauritius, it is widely distributed in humid forests but can also be seen in Reunion Island in dense thickets of medium altitude (100-1600 m) [1,3,4]. Other familiar vernacular names include 'Bois de cabri', 'Bois de cabri blanc', 'Bois de gaulette blanc' and 'Bois d'oiseaux' in Reunion island [4]. The genus Antidesma is derived from the Greek words 'anti-against' and 'thema- band' and refers to a tree-like species which provides bast fibers for making rope. The epithet 'madagascariensis' demonstrates the origin of the species or to where it is widespread [1].

BOTANICAL DESCRIPTION

A. *madagascariense* is a genus of dioecious shrub or low tree, often little branching and stunted, with a slightly fissured brownish gray bark [Figure 1] reaching 5 m height [2,4,5]. The genus, formerly grouped in the *Phyllanthoideae* family now belong to the Euphorbiaceae family due to the elongated U-shaped connective of the anthers that is the most notable character of this family [2]. This plant is characterized by the ample variations in the size, texture and shape of the leaves, which can be coriaceous to papery, often oval to elliptic, 4-10 cm long and 3-5 cm wide, the margins entirely or slightly sinuous. The presence of domatia is very visible in the axils of primary nerves. This tree bears minute greenish or red flowers of different sexes [1,3]. Often abundant in clusters of small berries, the ovoid dark red fruits which turn into shiny purple-black when ripe, are more or less flattened and 6-7 mm long [1,4,5].

ETHNOPHARMACOLOGICAL USES

A. *madagascariense* is an indigenous and an endemic plant that has always been used in folkloric medicine among the local population of the Mascarene Islands for the treatment and management of various ailments. A decoction of the leaves of A. *madagascariense* has been traditionally used to treat dysentery [3,6]. The decoction obtained after boiling 10 leaves of A. *madagascariense* in 1 L of water can regularly be consumed for the treatment of albumin in the urine [3]. Furthermore, the leaves and barks have been reported to possess diuretic,

Figure 1: *Antidesma madagascariense*. (a) Whole plant, (b) bark/stems, (c) fruits and (d) leaves

astringent, as well as febrifuge properties, and also used diabetes management [3,6]. A bath in the leaf decoction has been reported to alleviate skin infections, rheumatic and body aches. The leaves of A. *madagascariense* mixed with those of *Aphloia theiformis* (Flacourtiaceae) and *Toddalia asiatica* (Rutaceae) are used to treat jaundice [1]. Interestingly, A. *madagascariense* can be used to treat edema in pregnancy and can also be employed in the case of stroke depending on the type of decoction which is prepared [Table 1] [3].

BIOLOGICAL ACTIVITIES OF SELECTED CONSTITUENTS

Preliminary phytochemical screening of the leaves of A. *madagascariense* indicates the presence of phenols, tannins, alkaloids, flavonoids, cyanogenetic heterosides as well as leucoanthocyanins, sterols and saponins [1,7,8]. Interestingly, A. *madagascariense* has also been found to contain triterpenes and hydrolysable tannins, carpusin, and a dimer - antidesmin [Figure 2], a common constituent also characterised in other *Antidesma* species [9,10]. The bacteriostatic and bactericidal properties of A. *madagascariense*, validated from the local folk medicine, can be attributed to the presence of tannins in the plant. Furthermore, the aqueous and methanol extracts of the leaves demonstrated their molluscicidal properties against species of *Biomphalaria* and *Bulinus* and antifungal properties against *Cladosporium cucumerinum* [1,3]. Different fractions of the leaves and stems (water, methanol, chloroform and hexane) of A. *madagascariense* were previously reported to have significant inhibitory effects on Gram-positive bacteria *Staphylococcus aureus*, Gram-negative bacteria *Pseudomonas aeruginosa* and the fungus *Aspergillus niger* showing their potent antimicrobial activities [6,11]. The ability of the methanol stem extracts of A. *madagascariense* to exhibit contractile properties on rat ileal smooth muscles coupled with the recent antioxidant and antimicrobial findings on A. *madagascariense*

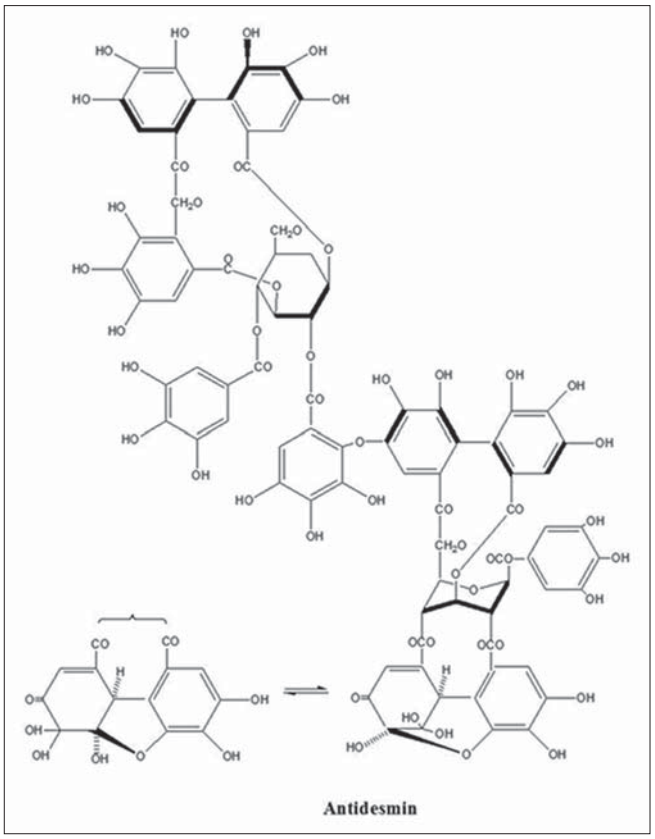

Figure 2: Antidesmin- a common constituent in all Antidesma species [10]

Table 1: Decoction preparation needed for the treatment of stroke and edema in pregnancy [3]

Decoction of 10 leaves of *A. madagascariense* with:
A small quantities of *Coix lacryma-jobi* roots
15 leaves of *A. theiformis*
15 cm bark of *E. laurifolium*
0.5 cm root of *R. mucronata*
3 entire plants of *B. pilosa*
10 leaves and vines of 'Betel sauvage' (*Piper* sp.)

A. madagascariense: Antidesma madagascariense, A. theiformis: Aphloia theiformis, E. laurifoliu: Erythroxylum laurifolium, R. mucronata: Rhizophora mucronata, B. pilosa: Bidens pilosa

validate its ethnobotanical use in the effective treatment of dysentery [1,6,7].

PHARMACOLOGICAL STUDIES

Antimicrobial Activities

The different crude extracts of A. *madagascariense* exhibited potent antimicrobial activity which was found to increase with increasing polarity. The methanol leaves extracts of A. *madagascariense* had potent inhibitory effects against *Enterococcus faecalis* (minimum inhibitory concentration [MIC] = 60 μg/ml), *S. aureus* (MIC = 500 μg/ml), Methicillin-resistant *S. aureus* (MRSA) (MIC = 250 μg/ml) and *Candida albicans* (MIC = 500 μg/ml) [7].

Antioxidant Activities

The antioxidant potential was validated in several *in vitro* assays carried out on different crude extracts and fractions of leaves of A. *madagascariense* with IC_{50} values ranging from 3.94-87.05 μg/ml, 3.18-13.26 μg/ml and 6.29-25.24 μg/ml for the 2,2-diphenyl-1-picrylhydrazine (DPPH), superoxide (SO) and nitric oxide (NO) radical scavenging assays respectively. While the *n*-butanol extracts of A. *madagascariense* had the most potent antioxidant activity for DPPH (% radical scavenging potential [RSP] = 93.68 ± 8.69%) and NO (% RSP = 65.56 ± 7.56%) assays, ethyl acetate extracts had a high percentage RSP (99.53 ± 7.53 %) in SO assay [12]. Similarly, a concentration of 0.5 mg/ml of methanol A. *madagascariense* leaves extracts were able to scavenge 70.6 ± 2.2% and 64.5 ± 1.8% of hydroxyl and hypochlorous acid radicals correspondingly, thus validating the antioxidant properties of A. *madagascariense* [7].

Antiglycation Activities

Antiglycation activities were confirmed in the ethylacetate (96.63 ± 10.36%), methanol (86.35 ± 5.65) and *n*-butanol (84.65 ± 6.35%) fractions of A. *madagascariense* and this was comparable to the anti-glycation drug aminoguanidine ($P < 0.05$). Nevertheless, A. *madagascariense* extracts were found to have no activity against mitochondrial respiration in a MTT cytotoxicity assay ($P > 0.05$) [12]. The efficacy of A. *madagascariense* extracts in managing diabetes was assessed through the inhibition of key carbohydrate hydrolyzing enzymes. All the extracts exhibited variable inhibitory effects on α-amylase activity ($P < 0.05$) with ethylacetate fraction having the best inhibitory effect (IC_{50} = 61.52 ± 11.09 μg/ml) which was lower than acarbose (IC_{50} = 75.86 ± 8.16 μg/ml). Moreover, active fractions of A. *madagascariense* were found to inhibit significantly ($P < 0.05$) amylase activity in mouse plasma from 7.80% to 49.37%. α-glucosidase activity was significantly inhibited by A. *madagascariense* extracts with IC_{50} values ranging from 19.70 ± 2.87 μg/ml to 44.92 ± 5.67 μg/ml, which was comparable to the drug 1-deoxynojirimycin.

The repressive capacity of A. *madagascariense* extracts to increase blood glucose concentration in mice was investigated by *in vivo* studies in glycogen-loaded mice. Ethyl acetate fraction was found to be more potent with glucose-lowering properties (−59.4%) comparable to acarbose (−55.1%) [8]. Moreover, *in vivo* studies of A. *madagascariense* on rat everted intestinal sacs indicated that aqueous extract A. *madagascariense* significantly ($P < 0.05$) enhanced the uptake of D-glucose and fluid transport. It was also noted that the concentration of above 0.375 mg/ml of the extract was needed to enhance mucosal disappearance, gut wall content and serosal appearance of fluid ($P < 0.05$). However, L-tyrosine and K^+ transport was not significantly enhanced to the contrary of Na^+. Therefore, the ability of A. *madagascariense* extracts to promote the transport of glucose, fluid and Na^+ across rat everted intestinal sacs might be attributed to the presence of bioactive phytochemicals, for instance, flavonoids, alkaloids, leucoanthocyanins, phenols and saponins, in A. *madagascariense* leaves, which have possibly interact with the Na^+/glucose co-transporter in the enterocytes [13].

IMMUNOMODULATORY PROPERTIES

The *in vitro* immunomodulatory property of A. *madagascariense* showed that extracts were able to modulate significantly ($P < 0.05$) the immune response of phagocytes and monocytes at different steps. At a concentration of 100 μg/ml, the inhibitory activity of crude methanol A. *madagascariense* extracts on whole blood phagocytes for reactive oxygen species (ROS) production was 94.2%. It was also suggested that A. *madagascariense* directly inhibited a final common biochemical target such as NADPH oxidase enzyme or scavenge ROS since it did not affect a specific transductional pathway [14].

Endophytic Fungi from *A. madagascariense*

Finally, due to its eminent and documented pharmacological activities, A. *madagascariense* was recently selected for the screening of endophytic fungi. The endophytic and saprobic fungi recovered from the living and dead leaves of A. *madagascariense* revealed that they were closely related to *Aspergillus*, *Guignardia*, *Fusarium*, *Penicillium*, *Pestalotiopsis* and *Trichoderma* genera. Phylogenetic analysis of the DNA extracts of these fungi successfully demonstrated that they belong to five different fungal lineages (Hypocreaceae, Trichocomaceae, Nectriaceae, Xylariaceae, and Botryosphaeriaceae) [15].

CONCLUSION

This monograph has attempted to throw into the limelight some of the ethnobotanical uses of the plant A. *madagascariense* which has been documented in the traditional Mauritian folklore as a promising plant possessing various biological activities. *In vitro* and *in vivo* studies conducted so far on A. *madagascariense* extracts revealed its potent antimicrobial, antioxidant, anti-diabetic as well as its immunomodulatory properties. However, continuing research needs to be performed in order to validate the potency of this plant as a good candidate for pharmacological action and thus appraise its traditional uses.

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