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## Phytochemistry, ethnomedicinal uses and pharmacological activity of *Diodia scandens*; a review of current scientific literature

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### ABSTRACT

Plants are natural sources of readily available phytochemicals which possesses interesting biological activities. The plant *Diodia scandens* is a creeping and straggling perennial herb commonly dispersed in tropical Africa, tropical Asia and some parts of Cameroon, Congo and Nigeria. It is used traditionally in the treatment of several disease conditions such as snake bites, rheumatic inflammatory disorders, earache, venereal diseases, hypertension and epilepsy. It is also used as an aphrodisiac and in the treatment of uterine inertia and post-partum hemorrhage. Despite its vast traditional uses, a comprehensive information on the plant is still lacking. In this review, we aimed to provide concise information on reported ethnomedicinal uses, phytochemistry, and pharmacological activities of *Diodia scandens* to support its traditional usage in exploring its therapeutic potentials. Available information about the plant was retrieved from online databases including PubMed and Google Scholar using the search terms '*Diodia scandens*', 'ethnomedicinal uses and *Diodia scandens*', 'phytochemistry and *Diodia scandens*' and 'pharmacological activity and *Diodia scandens*'. The available literatures supported several ethnobotanical claims on the use of *D. scandens* in traditional medicine. Other claims not yet scientifically verified should be explored to ascertain the veracity of such claims on its therapeutic potentials.

### ARTICLE HISTORY

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## Introduction

Plants as natural products are readily available sources of wide range of phytochemical constituents. They possess beneficial biological activities more of which are yet to be scientifically elucidated to provide relevant information needed to support their ethnobotanical claims and also in advancing medical knowledge as to cheaper alternatives [1]. The use of herbal products in complementary and alternative medicine (CAM) is growing rapidly worldwide [2,3], approximately 80% of people living in developing countries rely

on traditional medicines for their health needs [4]. The need for diverse, natural, affordable and easily accessible substitutes with relatively low side effects may warrant increasing popularity of traditional medicine [2,5].

Despite such popularity, many of the medicinal plants have not been scientifically evaluated for their safety as well as efficacy. Scientific validation of the safety and efficacy of herbal medicines should be essential for their incorporation into healthcare systems globally. In this review, a comprehensive

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**Table 1.** Table showing the ethnobotanical claim, reported pharmacological activity and plant part reported to possess activity.

S/N	Traditional Uses	Traditional method of use	Reported method of used	Reported Activity	References
1	Antidote against snake bite and other venomous stings	Aerial parts (water-soluble fraction)	Whole plant [Soxhlet extraction with 95% ethanol]	Prolonged survival upon pretreatment against <i>E. carinatus</i> specie	28 15 13 38 41
2	Hemorrhoids, fibroid	Dried leaf chewed and swallowed with water	Not reported	Not reported	Not reported
3	Edema, rheumatism & inflammation, fever, generalized pain antioxiants, and dropsy.	Aqueous leaf extract (orally and/or topical application to the inflamed part; plant is chewed alone and swallowed with water or pounded together with pepper for rheumatism)	Aqueous decoction of the leaf; petroleum ether leaf extract	The result of the studies revealed that the plant is endowed with anti-inflammatory activity.	6 25 31 44
4	Veneral diseases	Dried leaves or root pounded and extracted with water, then taken daily for various veneral diseases	Not reported	Not reported	Not reported
5	Wounds, earache, eczema, urticaria, flu, ring worm, cowpea disease and other Parasitic infection	Sap of the plant instilled into ear for earache Sap of the plant	Whole plant [Soxhlet extraction with absolute ethanol] Leaves [Aqueous maceration]	Antibacterial property against <i>S. aureus</i> Antifungal activity by inhibiting the mycelial growth and sporulation of <i>C. destructivum</i>	8 37 34 20
6	Ulcer	Sap of the plant	Aqueous and methanol leaf extracts	Definite anti-plasmodial activity against clinical isolate of Congolese <i>P. falciparum</i> strain	23 40 39 35 36 42,
7	Hypertension	The plant is boiled in pig's blood or combined with pork and applied to legs for urticaria Dried leaves chewed and often apply to the ulcers to promote healing Aqueous leaf extract	Not reported Not reported	Not reported Not reported	Not reported Not reported
8	Postpartum hemorrhage, Uterine disorder and other gynecological problems	Plant extract [Aqueous] taken orally to stimulate fetus who show sign of no activity;	Leaf extract [taking orally as aqueous Mist Diodia herbal-based therapy] Not reported	Decline in both systolic and diastolic blood pressure Increases in the force and tone of contraction of Guinea-pig uterus	16 23 43
9	Stimulate lactation	Root decoction taken along with leaf sap to promote the flow of milk	Not reported	Not reported	Not reported

(Continued)

**Table 1. (Continued).**

S/N	Traditional Uses	Traditional method of use	Reported method of used	Reported Activity	References
10	Dysentery	Plant is chewed and swallowed with water to stop dysentery. Pepper and salt are often added to pounded dried leaves	Not reported	Not reported	Not reported
11	Paralysis, nervous debility, spasm	Sap of the plant	Not reported	Not reported	Not reported
12	Epilepsy	Plant sap applied topically to children's chest for convulsions	Not reported	Not reported	Not reported
13	Kidney and Genito-urinary tract	Decoction of the whole plant	Not reported	Not reported	Not reported
14	Cough, Asthma	Plant sap taken orally as expectorant or also rubbed to chest for persistent cough	Not reported	Not reported	Not reported
15	Aphrodisiac	Plant extract (Aqueous) taken orally	Not reported	Not reported	Not reported
16	Jaundice	Plant extract (Aqueous) taken orally	Not reported	Not reported	Not reported
17	Constipation	Dried leave extract macerated with water	Not reported	Not reported	Not reported
18	Diabetes	Plant decoction taken orally	n- hexane leaf extract	reduction in blood glucose	45

information on the ethnobotanical uses, therapeutic benefits, pharmacological activities and phytochemical relevance of *Diodia scandens* is discussed, which is aimed at supporting its traditional usage in exploring its therapeutic potentials.

Several pharmacological (Table 1) and phytochemical studies have been conducted on the plant, and phytochemical constituents reported to be present in *D. scandens* including saponins, tannins, alkaloids, flavonoids, phenolic compounds, steroidal and cardiac glycoside could be responsible for the observed pharmacological activities. The reports supported its analgesic, antioxidant and anti-inflammatory activity, anti-plasmodial and other antimicrobial activities, antivenom, antihypertensive and antidiabetic activities as well as uterotonnic, laxative and sexual enhancement activities as shown below.

### Taxonomy and vernacular names

*Diodia scandens* belong to the kingdom (Plantae), Phylum (Tracheophyta), Class (Magnoliopsida), Order (Gentianales), family (Rubiaceae) and Genus (Hexasepalum Bartl. ex DC). It is commonly known as Itching grass (English), *Lukaya kua lota* (Doondo), *Tâdza* (Ndassa), *Loukaya loualota* (Soundi) in Congo; *Yendeyendo*, (Kono) *Fasa-Yamba*, (Limba), *Bukbonbo*, (Loko), *Ndantawu*, *Diroi*, (Mende) *Ndatawulu*, (Temne); in Sierra Leone; *Abure*, *Naosi*, *Naosifa*, *Naouassinfa* in Ivory Coast; *Ewé Idatcha*, *Ehin aribo* or *Irawo ile* (Yoruba), *Agukwu*, *Onaedi* (Igbo), *Fasa-Yamba* (Hausa) in Nigeria.

### Ecology

*Diodia scandens* Sw is dispersed in tropical Africa, tropical Asia and America. It grows wildly in southern parts of Nigeria with a remarkable survival ability in the dry season [6–8].

### Botanical description

*Diodia scandens* is a creeping, and straggling perennial herb with luxuriant dark-green, ovate to lanceolate, alternate scabrid leaves and slender angular stem of 1–3 m. The flowers are white, aggregated in large numbers at the nodes and end of branches. The plant grows luxuriantly during the rainy season but may slightly wither in the dry season. It is tasteless, odorless and has solitary inflorescence [7,9–12,13].

### Ethnobotanical uses

*Diodia scandens* is traditionally employed in the treatment of several diseases (Table 1); it is used as an antidote against snake bite and other venomous stings. It is also employed in rheumatic inflammatory disorders, earache (in Nigeria) and venereal diseases in Congo and Ghana [14,15]. It is commonly used as a pain killer in Congo and used in the treatments of bruises, wounds and minor cuts in Nigeria. It is also used in ulcer treatment, hypertension and afterbirth treatment as hemostatic in Congo and Gambia. It is also useful in cutaneous and subcutaneous parasitic infection, dysentery, dropsy, edema and as a lactation stimulant in Tanganyika. The plant is used in management of paralysis, epilepsy, spasm, eczema and ring worm in Congo (Brazzaville) and Nigeria (Northern and Southern part). It is also used as an aphrodisiac (in Nigeria), used in the treatment of jaundice, constipation, diabetes, flu (in Tanganyika and Ghana), kidney ailments and as an oxytocic agent in the treatment of uterine inertia and postpartum hemorrhage, genito-urinary tract infections (in Niger Delta part of Nigeria), hemorrhoids, fibroid and other uterine disorder [7,8,11,16–23]. The plant is also utilized as poultry feeds in small ruminant feeding in Anambra state Nigeria [7,24].

## Phytochemical components

A quantitative analysis of phytochemicals in *D. scandens* revealed the presence of saponin (6.58%), tannin (2.27 mg/100 g), alkaloids (10.53%) and phytin phosphorus (1.80 mg/g) [8]. Other phytochemicals also present in qualitative test of the phytochemicals include flavonoids, essential oils, phenols, polyphenol, phytate, phytin phosphorus and oxalate, steroidal and cardiac glycoside [7,10,25–27]. Spectroscopic analysis of the column fractions using n-hexane-ethyl acetate fraction, CHDS11 identifies *cis,cis*-9,12-octadecadienoic acid and CHDS12 identified as 1,2,3-propanetriyl tris (*cis,cis*-9,12-octadecadienoate). These compounds may be responsible for the anti-inflammatory activities observed with the plant [10,15,28].

Simple chemical screening tests are usually performed to ascertain the phytochemicals present using appropriate chemical reagents. Tannins which are found to be present and having astringent and detergent properties could be responsible for its activity when used for diarrhea and dysentery [29,30]. Saponins have been reported to poses anti-inflammatory, antifungal, anti-parasitic, anti-tumor and anti-viral activities were as such could be responsible for its observed usefulness in traditional medicine. Naturally occurring cardiac glycosides have proven useful in the treatment of various heart diseases [30].

## Pharmacological activity

### Analgesic and anti-inflammatory activity

The aqueous leaf extract of *D. scandens* exhibited anti-inflammatory activity in acute model of inflammation. It significantly ( $P < 0.01$ ) inhibits paw edema in linear circumference of the injected paw. 1% carrageenan [marine colloids] in 0.9% saline solution and fresh egg-white were used as the phlogistic agent injected into the sub plantar surface of the rat right hind paw. The linear circumference of the injected paw was measured immediately and

3 h after administration of the phlogistic agent. Consequently, it may also have blocked certain mediators of inflammation as reported by [28]. The petroleum ether extract of *Diodia scandens* also significantly protected rats against aspirin, indomethacin and reserpine-induced ulcers in a dose-dependent manner and increased the threshold of pain stimulus in mice [6,31,32].

### Antimicrobial activities

Ethanol extract of *D. scandens* showed great potentials as an antibacterial agent. The rate of growth inhibition of *staphylococcus aureus* sourced from 200 patient's wounds and burns was noteworthy at a minimum inhibitory concentration (MIC) of 200  $\mu\text{g}/\text{mL}$ , the continuous average logarithm reduction in viable cell count at 6-hour time interval had also been reported [8,33].

The aqueous leaf extract of *D. scandens* significantly ( $P < 0.05$ ) inhibits the in vitro sporulation and mycelial growth of *Colletotrichum destructivum*, as against a standard fungicide, benomyl [34]. *Colletotrichum destructivum* is the causative agent of anthracnose disease of cowpea (an ancient crop known to man rich in quality protein and energy), which lowers their production and yield potentials. Farmers do rely on the addition of fungicide chemicals to control these phytopathogens; however, such chemicals pose potential threats to human health and the environment. Current advances in knowledge encourages the use of botanicals as a better alternative [34–36].

It also inhibited the growth of *Microspodium gypseum*, *Trichophyton mentagrophytes* and *Trichophyton rubrum* at a minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) values of 6.25/12.5 mg/ml, 3.13/6.25 mg/ml and 3.13/6.25 mg/ml, respectively [20]. In vivo antibacterial activity of the ethyl acetate and n-hexane extracts of *Diodia scandens* revealed appreciable activity against *Staphylococcus epidermidis* with a resultant increase in lymphocytes as described by [37].

### **Anti-Snake venom activities**

As previously reported, the antivenom property of the plant by [15,28]. A preliminary study by [13], showed a statistically significant ( $P < 0.05$ ) reduction (50%) in mortality due to *Echis Carinatus* venom in mice and cats [38]. The water-soluble fraction of the plant prolonged the survival of the tested animals in addition to protection against venom-induced clonic convulsions observed just before death due to envenomation [38]. This study is in conformity with previous studies by [28], which reported its use as an antidote against the venom. *Echis Carinatus* is a saw-scaled viper very common in the grass land areas of Nigeria.

### **Anti-malarial activities**

A study to investigate the in vitro anti-plasmodial activity of aqueous and methanol leaf extracts of *Diodia scandens* against a Congolese *P. falciparum* strain (isolated clinically) showed definite anti-plasmodial activity at  $IC_{50} < 5 \mu\text{g/ml}$ . Both the extracts and various fractions showed appreciable anti-plasmodial activity against plasmodial parasite strain at  $IC_{50} < 10 \mu\text{g/ml}$  [23,39,40].

### **Uterotonic, laxative and sexual activities**

A study on ethanol extract of *D. scandens* revealed that it increases the force of contraction and tone of the pregnant Guinea-pig uterus in a concentration dependent manner [23,43]. The extract at subliminal concentrations potentiated Acetyl choline (ACh) and adrenaline-induced contractions in Guinea-pig vas deferens. It also induced a dose-related vasodilatation in the rat hind quarters and depressed the blood pressure in an anaesthetized cat [23].

### **Antihypertensive properties**

A retrospective study involving hypertensive patients with persistent elevated blood pressure of over 140/80 mmHg with at least two (2)

cardinal signs and symptoms was carried out in the center for plant medicine research (CPMR) clinic in Ghana. The study included patients not previously on any antihypertensive product for at least a month prior to their first visit. The patients were prescribed Mist Diodia, herbal remedy made out of the leaves of *D. scandens* alternatively used in the management of hypertension by the CPMR. The result showed a significant decline in participant's blood pressure over 3 weeks observational period. This resultant effect could be attributed to the diuretic properties *D. scandens* [16].

### **Antioxidant properties**

The antioxidant properties of the aqueous and ethanol extract of *Diodia scandens* was assessed via the DPPH assay, thiobarbituric acid assay and total antioxidant capacity assay. The DPPH assay revealed significant antioxidant activity of the extract, the  $IC_{50}$  (inhibitory concentration at 50%) value of aqueous and ethanol extracts of *D. scandens* were 10.121 and 10.994  $\mu\text{g/mL}$ , respectively, as compared (lower) to ascorbic acid (17.916  $\mu\text{g/mL}$ ). The aqueous extract showed a significantly higher percentage inhibition compared to the ethanol extract in the thiobarbituric acid assay. Furthermore, total antioxidant capacity assay showed that the aqueous extract had higher ascorbic acid equivalent values compared to the ethanol extract [44].

### **Antidiabetic activities**

The *n*-hexane leaf extract of *Diodia scandens* produced a significant ( $P < 0.05$ ) reduction in blood glucose at day 7 when compared to the untreated diabetic rats. The result demonstrated potential antidiabetic properties of the extract on alloxan-induced diabetic Wistar rats [45].

## Toxicity profile

### Acute toxicity

Acute toxicity of aqueous extract of *Mist Dioda*; (a poly-herbal preparation for the management of hypertension in Ghana) on adult Sprague–Dawley rats was carried out according to OECD guidelines with some modifications. The test animals were observed for mortality and physical signs of toxicity including lack of alertness, presence of staggering gait and pilo-erection on a daily basis for 14 days. The median lethal dose was found to be above 5000 mg/kg [26]. The extract also at doses of 40, 400 and 800 mg/kg administered daily over a period of 6 months with periodic observation according to OECD guidelines showed no physical signs of toxicity or mortality. There was no effect on hematological parameters such as Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), total and direct bilirubin, serum concentrations of creatinine and urea. There was also no effect on the hemopoietic system morphology of the lungs, kidney, liver and heart [26].

## Conclusion

Medicinal plants still remain integral part of the health practices especially among population in developing countries, scientific validation of their safety and efficacy should be essential in ascertaining such traditional claims as well as for possible incorporation into healthcare systems globally. Available literatures have supported several ethnobotanical claims on the use of *D. scandens* in traditional medicine. Other claims not yet scientifically verified should be explored to ascertain the veracity of such claims on its therapeutic potentials. It is also recommended that more studies be conducted to isolate and characterize bioactive compounds responsible for the pharmacological activities in the extracts and fractions of *Diodia scandens* as well as detailed toxicity and safety evaluation.

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## Author contributions

Abubakar S. Wada conceptualized the original idea and co-wrote the manuscript. Sa'adatu M. Julde, Safiya B. Borodo, and Mubarak H. Ahmad performed the literature review and co-wrote the manuscript. Abubakar S. Wada and Sani Malami edited the final draft and Abdullahi H. Yaro critically reviewed the manuscript for intellectual content. All authors reviewed and approved the final version of the manuscript.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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