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Review of the Ethno-medical, Phytochemical, Pharmacological and Toxicological Studies on *Dissotis rotundifolia* (Sm.) Triana

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Authors' contributions

This work was carried out in collaboration between both authors. Authors OKY and NO designed the study, wrote the protocol and wrote the first draft of the manuscript. Author OKY managed the literature searches and author NO proof read the manuscript. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Ethnopharmacological Relevance: *Dissotis rotundifolia* (Sm.) Triana, commonly called 'pink lady', is employed in West and Eastern African folkloric medicine for managing a number of infections including dysentery, cough and sexually transmitted infections. The review aims at highlighting the traditional benefits, ethno-medical, phytochemical, pharmacological and toxicological importance of the plant.
Materials and Methods: Excerpta Medica database, Google Scholar, Springer and PubMed Central, were the electronic databases used to search for and filter primary studies on *Dissotis rotundifolia*.
Results: This summary of relevant pharmacological, phytochemical and toxicological data from primary studies on *D. rotundifolia* gives a telling indication of its potential therapeutic benefits as a chemotherapeutic agent and possibly as a source of compounds with contraceptive potential.

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Conclusion: This concise review on *D. rotundifolia* will be relevant in identification of areas of further research with the focus of identifying biologically active compounds which hold prospect in therapy.

Keywords: Dissotis rotundifolia; ethno-medicine; phytochemistry; pharmacology; toxicology.

1. INTRODUCTION

The creeping herb *Dissotis rotundifolia* (Sm.) Triana, commonly called 'pink lady', is an important part of the folkloric medicine in most parts of West and East Africa. It is used in the treatment of various ailments such as diarrhea, dysentery, conjunctivitis, sexually transmitted infections, cough, relieving symptoms of stomach ache [1], dysentery, hookworm infestation [2,3], fibromyalgia, infertility [4] and Trypanosomiasis [5]. In tropical Africa, the whole plant is used in the treatment of rheumatism and yaws [3,6]. A number of studies have led to the establishment of the anti-inflammatory [4], antioxidant [7], anti-infective [3] and anti-ovulatory effects [4] of the herb. These studies have also led to the characterization of certain secondary metabolites that may serve as probable source of lead compounds for future drug development. However, to the best of the knowledge of the authors, no review exists on the reporting of the phytochemical composition, biological and pharmacological activities of this perennial herb which has called for the need to compile all available data on *D. rotundifolia*. This review therefore seeks to highlight the folkloric significance, phytochemical composition, biological and pharmacological activities of *D. rotundifolia*. This review will also aid future studies aimed at isolation, purification and characterization of the various bioactive compounds responsible for the reported biological and pharmacological activities of the plant.

2. HISTORICAL PERSPECIVE

Dissotis rotundifolia has been used in its native range for a wide range of medicinal purposes as indicated in Table 1 and has been documented in a handful of research articles. Aside its medicinal value, the bright pink flowers, ovate, fleshy leaves and prickly fruits of the herb makes it useful in landscape. The slender, creepy nature of the herb makes it an excellent ground-cover though it will be an annual in non-tropical or non-subtropical zones [8].

3. TAXONOMY AND LOCAL NAMES

3.1 Classification

Dissotis rotundifolia belongs to the Kingdom Plantae, the subkingdom Tracheobionta and the super division of Spermatophyta. It is in the division Magnoliophyta and belongs to the class Magnoliopsida. It is classified under the subclass Rosidae and the order Myrtales. It belongs to the family melastomataceae, the genus *Dissotis* and the species is *rotundifolia* (Fig. 1).

Fig. 1. The leaves and flowers of *Dissotis rotundifolia* (Adapted from plant breeding in the 21st century – University of Georgia)

Table 1. Ethnopharmacological use of *Dissotis rotundifolia*

Part	Value	References
Leaves	Dysentery	[9,10]
Leaves	Stomachache, diarrhoea, cough, stop abortion, conjunctivitis, circulatory problems and veneral diseases	[10]
Leaves	Bilharzias	[2]
Fresh aerial parts	Malaria	[11]
Leaves	Tuberculosis	[12]
Roots and leaves	Wound, Asthma, Boil, Abscess, Gonorrhea	[13]
Leaves	Diarrhoea	[10,13]
Leaves	Sinusitis and bronchitis	[14]

Table 2. Vernacular names of *Dissotis rotundifolia*

No.	People	Vernacular name	References
1	English	Pink Lady	[15,16,17]
2	English	Spanish Shawl	[18]
3	Benin	Ebafo	[10,19]
4	Yuroba	Awede	[19,20]
5	Igbo	Nkpisi-nku	[19,20]
6	Kimboza	Kinzasu	[13]
7	Liberia	Rockrose	[21,22]
8	Diola	é soso	[21,22,23]
9	Mankanya	ba poti	[21,22]
10	Biafada	mandafnade	[21,22]
11	Kissi	yσngч̃	[21,22]
12	Koranko	legbe	[21,22]
13	Loko	ɛbowa	[21,22]
14	Mende	febungi	[21,22]
15	English	Trailing dissotis	[24]
16	Cook Islands	Creeping Melastoma	[25]

This plant is known across tropical West and East Africa and other parts of the world by several names some of which have been noted in this review (Table 2 above).

4. ECOLOGY AND BIOGEOGRAPHY

Dissotis rotundifolia is native to tropical West Africa though it can be found in other parts of the world (Australia's Virtual Herbarium). It is very common in Nigeria and Western Papua New Guinea where they thrive in brown clay soil especially along river banks. According to Porembski et al. [26] the herb can also be found on rock outcrops, in the bottom of sandy depressions, and may also grow as weed alongside roads and in waste spaces in its native range.

5. PHARMACOGNOSTIC DATA

Dissotis rotundifolia is a versatile perennial slender creeping herb with ascending stems up to 40 cm high. It roots at the nodes and is produced from seeds and stolon. The leaves are ovate to ovate-lanceolate or suborbicular, 1.5-7.0 cm long, 0.8-4.0 cm wide, 3-nerved, both surfaces sparsely to densely pilose, margins ciliate and more than a little but not too crenuate, apex acute, base truncate to short-attenuate and petioles are 0.5-2.5 cm long. Like other species in the family Melastomataceae, *D. rotundifolia* has poricidal anthers and pollen dehisces from the anthers (Botanical description of *D. rotundifolia*). *D. rotundifolia* also has two kinds of anthers: feeding anthers and pollinating anthers [27]. As with other plants of the Melastomataceae family, the flowers of *D. rotundifolia* are herkogamous with the style often longer than the stamen [28]. The herkogamous nature of the flowers and the poricidal nature of the anthers promotes outcrossing. Before anthesis, the anthers are folded up with their ends protected from the stigma making self-pollination rarely likely. However, self-pollination may occur if the anther unfolds and the ends touch the stigma causing the pollen to dehisce. This implies that *D. rotundifolia* is self-compatible [8] though it can also set seed by agamospermy [28].

6. CHEMICAL COMPOSITION

Plants are useful components in ethno-medicine and proper screening of phytochemical compositions can yield useful products of pharmaceutical significance [1,3]. Quantitative phytochemical analysis of the root and leaves by Aja et al. revealed the presence of flavonoids, phenols, polyphenols, alkaloids, tannins, cyanogenic glycosides, anthocyanin, saponins, sapoginin and anthraquinone [20]. Abere et al. had also previously reported on the presence of alkaloids, cardiac glycosides and saponins [3]. In the study by Aja et al. it was also identified that, the root sample contained high levels of these phytochemical constituents than the leaves with the exception of anthocyanin and saponins [20].

D. rotundifolia has been shown to contain appreciable amount of ascorbic acid [7,14]. Off or detected an ascorbic acid amount of 0.31 ± 0.02 (mg/100 g) [7], an amount significantly lower than the amount detected by Okeri and Alonge, 90.40 ± 0.38 (mg/100 g) for fresh leaves and 41.00 ± 0.35 (mg/100 g) for dried leaves [14]. The study by Offor further revealed the presence of high levels of retinol, tocopherol, cholecalciferol, thiamine and low levels of pyridoxine, niacin, riboflavin, cobalamin and phylloquinone [7].

7. PHARMACOGNOSTIC EVALUATION

Establishment of the pharmaognostic profile of plants assists in standardization which can guarantee purity, quality and identification of samples. Microscopic evaluation of the leaves by Abere et al. revealed that the stomata was anomocytic, the epidermal cells were straight and polygonal with uniseriate and multiseriate covering trichomes [10]. It has a dorsiventral leaf arrangement with the mid-rib bundle surrounded by a zone of collenchyma on both surfaces and the phloem vessels embedding the proto- and meta-xylem vessels. Chemomicroscopic characters identified in the study included lignin, starch, mucilage and calcium oxalate crystals [10].

8. ANALYTICAL TECHNIQUES

Chemical and chromatographic tests have been employed in the preliminary phytochemical analysis of secondary metabolites contained in *D. rotundifolia*. However, not much further studies has been conducted into finding the various bioactive compounds contained in the plant. Abere et al. employed the methods of Brain and Turner [29], Ciulei [30] and Harborne [31] in the screening of secondary metabolites [3].

In their preliminary phytochemical investigations, tannins were tested using the phenazone, iron complex, formaldehyde and modified iron complex tests. Mayer's, Dragendorff's, Wagner's and the 1% picric acid reagents were used to test for alkaloids while cardiac glycosides were tested for using the Keller Killiani, Lieberman, Legal and Kedde tests. The team also tested for anthracene derivatives using the Borntrager's test for combined and free anthraquinones while the sodium picrate paper test was used to test for cyanogenetic glycosides. Thin layer chromatography of aqueous ethanol extract of the plant containing 10% H_2SO_4, shaken with chloroform and free alkaloids, precipitated by by the addition of excess ammonia and extracted with chloroform, on silica gel-G, activated by heating at 110℃ for 30 minutes was developed with the solvent system methanol: chloroform (3:7). The developed plates were viewed under UV light, sprayed with Dragendorff's spray and the R_f values were calculated. Using the ascending method, Whatman No. 3 mm and the solvent system n-butanol: water: acetic acid (4:1:5), Paper chromatography was developed and examined in both daylight and under UV light at 25 nm, sprayed with ferric chloride until colours developed and the R_f values were calculated. In the determination of alkaloids, tannins, cyanogenetic glycosides and anthracene derivatives, Aja et al. employed similar methods as used by Abere et al. [20,3]. Aja et al. used the method of Harborne [21] in the assessment of the presence of flavonoids and saponins [20,31]. In the determination of phenols and polyphenols, the authors employed the method of Malick and Singh, and that of Katzung respectively [32,33].

Rath et al. used high performance liquid chromatography with UV diode-array detection linked by a thermospray interface with a triple stage quadrupole mass spectrometer to characterize the C-glycosylflavones of *D. rotundifolia* [34]. The four C-glycosylflavones, i.e. isoorientin **(1)**, orientin **(2)**, vitexin **(3)** and isovitexin **(4)** were detected in the methanol and hydroalcohol extract of the plant (Fig. 2). Although the UV data and TSP mass spectra allowed for rapid characterization of all C-glycosylflavones, the authors were not able to achieve the exact attribution of the peaks to their structures as neither the UV spectra nor the TSP mass spectra allowed for differentiation of one position isomer from the other. However, a successful attempt was made to distinguish the 6-C from the 8-C-glycosylflavones by thermospray tandem mass spectrometry. The collision induced dissociation spectra of the particular ion gave fragments which permitted differentiation of position isomers [34]. Soyinka et al. detected the presence of 8-β-D-glucopyranosyl apigenin (vitexin) by subjecting the n-butanol fraction of *D. rotundifolia* to reversed column chromatography and eluted with MeOH:H_2O (50:50), increasing the MeOH gradient to 100% afterwards [35]. Fractions collected were bulked by normal phase TLC and further purified on Sephadex LH-20 column chromatography using 100% of both methanol and acetone. By subjecting the ethylacetate fraction of DRE to repeated column

chromatography using 100% n-hexane followed by increasing the both ethylacetate and methanol gradients in n-hexane to 100%, the group detected the presence of 8-β-D-glucopyranosyl luteolin (orientin) after purifying the bulk fractions on Sephadex LH-20 column chromatography equilibrated with 10% ethanol in toluene and eluted with the same system. This was then followed by increasing the ethanol gradient to 60% in toluene (Fig. 3).

Okeri and Alonge determined the ascorbic acid content by using iodimetry and indophenol methods as according to USP, 1980 and Association of Official Analytical Chemists [14,36]. In determination of the ascorbic acid content of *D. rotundifolia*, Offor used in addition to the method of the Association of Official Analytical Chemists, the method of Antonelli which involves a microcalorimetric method which uses the oxidation of ascorbic acid catalyzed by the enzyme ascorbate oxidase, which gets the specificity of the reaction [7,36,37].

9. PHARMACOLOGICAL ACTIVITY

9.1 Antiplasmodial Activity

Plants serve as important sources of antiprotozoal compounds for development into drug molecules for the treatment of protozoan infections, including malaria [38]. A study conducted by Nondo et al. aimed at providing evidence to support the traditional use of certain plants in the treatment of malaria, *D. rotundifolia* inclusive [11]. *In vitro* antiplasmodial activity was assessed using the parasite lactate dehydrogenase assay where non-synchronized 1% parasitized red blood cells at 2% haematocrit in 96 well cell culture plates were incubated in triplicates with 100 µg/ml crude extracts or 1.25 µg/ml artemether. This study showed a percentage inhibition of *Plasmodium falciparum* Dd2 strain by *D. rotundifolia* by 33.64 ± 0.44. This signifies the possible presence of antiplasmodial constituents in the plant.

9.2 Antitrypanosomal Activity

Trypanosome, the causative organism of Trypanomiasis is most prevalent in Africa and it is thought to be responsible to an extent for the low socio-economic status of most parts of the continent [39,40]. Treatment of the condition has been a challenge owing to the development of resistance and toxicity [41,42]. It is therefore imperative that safer and cost-effective agents be developed to aid in the combat of the disease in the region. The potential activity of *D. rotundifolia* against *Trypanosoma brucei brucei* was investigated in adult Wistar rats infected with the parasite. The animals were treated orally or intraperitoneally with doses 200, 600 and 800 mg/kg body weight. Parasitaemia was reduced by 66.7% and 78.4% after 800 mg/kg oral and intraperitoneal administration of extract respectively. *In vitro* exposure of blood films to a higher concentration of 800 mg/kg resulted in complete paralysis or death within 45 seconds of exposure [5]. This may indicate the possible presence antitrypanosomal constituents in *D. rotundifolia*.

9.3 Antibacterial Activity

The antibacterial activity of the crude and fractionated extracts were investigated against clinical strains of *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Salmonella typhi*. The aqueous methanol extract of *D. rotundifolia* showed activity against all strains of tested bacteria. A dose of 100 mg/ml showed a zone of inhibition of 8, 11, 8 and 9 mm for *E. coli*, *P. aeruginosa*, *S. aureus* and *S. typhi* respectively; gentamicin gave zones of inhibition of 13, 15, 14 and 14 respectively against the tested organisms. All three fractions of the extract showed activity against *S. aureus* strains while the butanol fraction showed activity against all tested strains with zones of inhibition of 5, 7, 5 and 4 mm respectively. The chloroform fraction failed to show activity against *E. coli* and *P. aeruginosa* while the ethylacetate fraction showed activity against all but the *P. aeruginosa* strain [3]. Soyinka et al. also identified that the ethylacetate and butanol fractions were moderately effective in inhibiting bacteria growth as shown in Table 3. The most susceptible strains were *S. aureus* (NCTC 6571) and *B. subtilis* (NCTC 8236) while little or no activity against *E. coli* (NCTC 10418) and *P. aeruginosa* (ATCC 10145) was observed. From the study, *C. pseudotropicalis* (NCYC 6) was totally resistant [35].

9.4 Antidiarrhoeal Effects

Abere et al. [3], investigated the antidiarrhoeal effects of *D. rotundifolia* in Swiss albino mice and male Wistar rats using the charcoal plug method and castor oil-induced diarrhoea respectively. Administration of 100, 200, 300 and 400 mg/kg of the ethanol extract of *D. rotundifolia* produced a percentage movement of 14.35 ± 1.10, 5.45 ±

2.99, 2.64 ± 0.35 and 1.90 ± 0.20% of the charcoal plug respectively compared to the 25.30 ± 3.5 and 68.49 ± 10.34% achieved upon the administration of 2.5 mg/kg of Atropine and 0.5 mg/kg of Carbachol. This implies a dose-dependent decrease in gastric motility by *D. rotundifolia*. In the castor oil induced diarrhoea, the concentrations of 100, 200, 300 and 400 mg/kg of the ethanol extract used as well as 0.03 mg/kg of Loperamide, the reference standard, did not produce wet feaces. This work signifies the antidiarrhoeal effects of *D. rotundifolia*.

9.5 Ovarian and Hormonal Effects

A study done by Olufemi et al. showed a decrease in follicle production and an increase in atretic ovarian follicles with endometrial and glandular cell loss in the uterus of adult female Wistar rats upon administration of the methanol extract of *D. rotundifolia* [4]. Treatment with methanol extracts at doses of 25 and 100 mg/kg resulted in a significant (p<0.05) reduction in the serum levels of luteinizing hormone (LH) (5.5 ± 2.17, 3.9 ± 0.31) and follicle stimulating hormone (FSH) (4.4 ± 0.17, 4.6 ± 0.50) compared to 17.5 ± 2.50 of the normal saline treated group. Despite significant reduction, decrease in serum levels of FSH was not dose dependent. Hormonal levels returned to baseline 7 days post treatment except for LH in the high dose treated group. There was a prolonged dioestrus phase with a decreased oestrus phase and an almost unchanged proestrus phase upon administration of the extract. Dose of the extract however appeared not to affect recovery of normal oestrus cycle. From this study, it is has been identified that *D. rotundifolia* promotes follicular cell degeneration, endometrial lining destruction and reduction in FSH and LH resulting in unfavourable conditons for ovulation and pregnancy. The extract therefore has anti-fertility potential and may be useful traditionally for contraception considering recovery post treatment. *D. rotundilfolia* may further serve as a possible source of active compounds for development into agents for medical abortions.

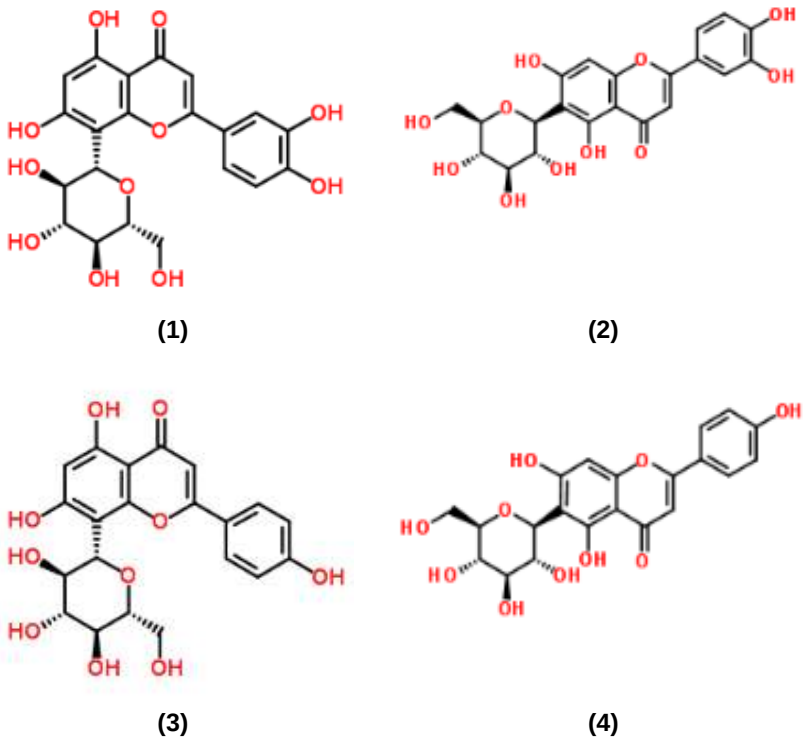

Fig. 2. Structures of characterized C-glycosylflavones. Scheme – (1) orientin (8-β-D-glucopyranosyl luteolin, lutexin); (2) isoorientin (6-β-D-glucopyranosyl luteolin, homoorientin, lutonaretin); (3) vitexin (8-β-D-glucopyranosyl apigenin, orientoside); (4) isovitexin (6-β-D-glucopyranosyl apigenin, homovitexin)

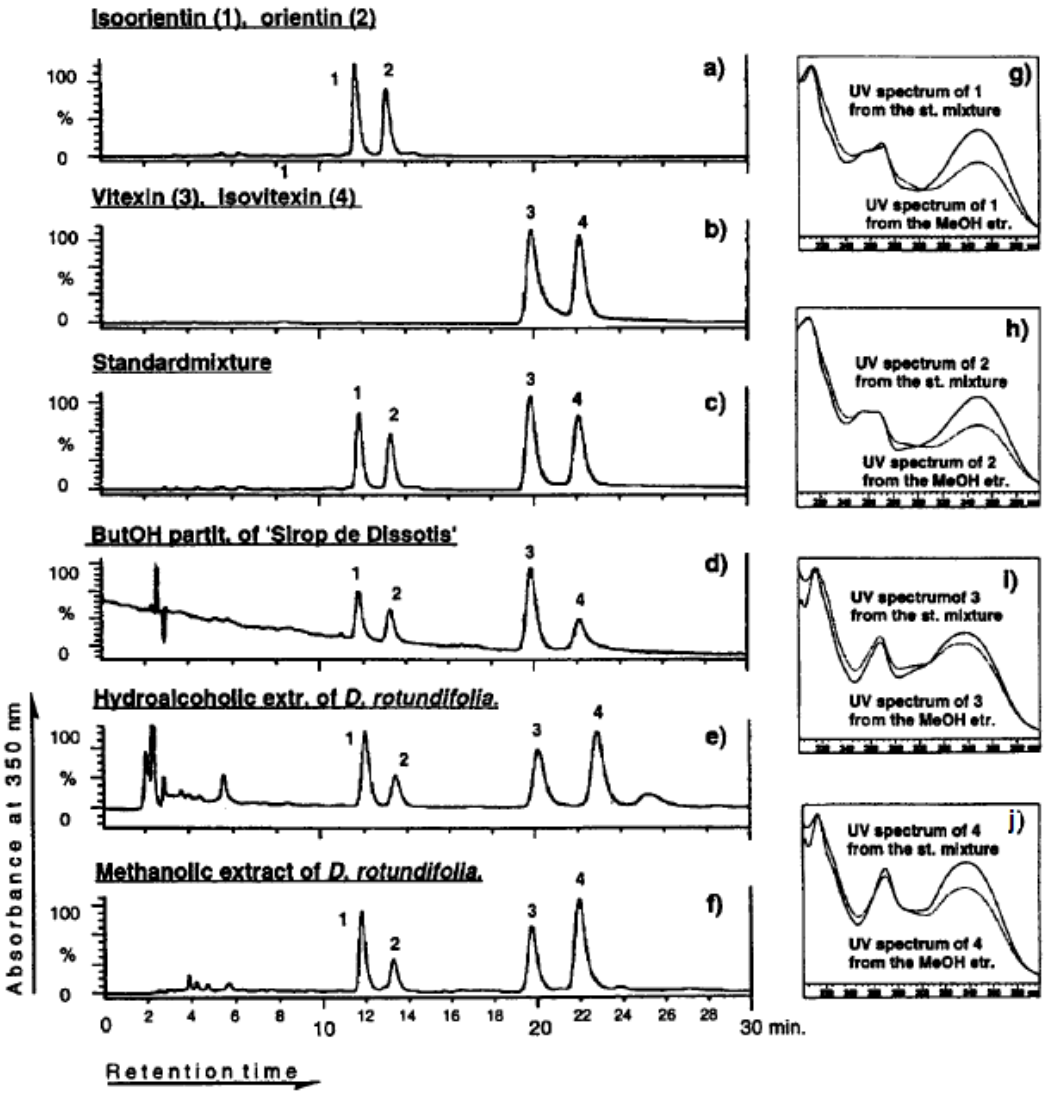

Fig. 3. Comparison of several samples by HPLC-UV, at 350 nm: a) isoorientin (1) an orientin (2); b) vitexin (3) and isovitexin (4); c) mixture of a) and b); d) 2-butanol extract of 'Sirop de Dissotis'; e) ethanol-water (50:50, v:v) extract of *Dissotis rotundifolia*; f) methanol extract of *D. rotundifolia*; g)-j) Comparison of UV spectra recorded from standard mixture with those from methanol extract of *D. rotundifolia*. (Adapted from Rath et al. [34])

Table 3. Antimicrobial activity of ethanol extract and partition fractions of *D. rotundifolia* as reported by Soyinka et al. [35]

Extract (mg/ml)	Average diameters of zones of inhibition (mm)				
	E. coli	***S. aureus***	***P. aeruginosa***	***B. subtilis***	***C. pseudotropicalis***
EtOH extract (20 mg/ml	9	12	9	13	9
EtOAc extract (20 mg/ml)	11	17	10	15	9
BuOH extract (20 mg/ml)	9	14.5	11	16.3	9
H_2O extract (20 mg/ml)	9	11.8	9	12.5	9
Streptomycin (1 mg/ml)	17	24	11.5	23	9
Acriflavine (6.3 mg/ml)	ND	ND	ND	ND	17.8

EtOH: ethanol; EtOAc: ethylacetate; BuOH: n-butanol; H_2O: Aqueous; ND: Not determined

9.6 Antioxidant Effect

Disturbance in the balance between the production of reactive oxygen species and antioxidant defense systems has been implicated in a number of chronic conditions with serious disease burdens [43,44,45,46]. This has necessitated the search into identifying potent antioxidants to aid in mitigating the harmful effects of free radicals. Soyinka et al. [35] showed that the ethylacetate and n-butanol fractions of *D. rotundilfolia* extract had strong antioxidant activities. Phenols and polyphenols are strong antioxidants which prevent oxidative damage to essential biomolecules such as lipids, proteins and DNA. Oxidation of these biomolecules have been implicated in various chronic diseases such as cardiovascular diseases and cancer [47]. Gill reported that, the high levels of phenols and polyphenols in *D. rotundifolia* might be the reason for their traditional use in treatment of rheumatism, painful swelling and circulatory problems [1]. *D. rotundifolia* also contain flavonoids which has also been shown to be antioxidant [20,48]. The high amounts of ascorbic acid in *D. rotundifolia* indicates the plant's potential antioxidant activity.

9.7 Anti-ulcer Activity

Traditionally, *D. rotundifolia* is employed in several illness which include gastrointestinal disorders such as peptic ulcer disease [49]. Study by Adinortey evaluated the gastroprotective activity and gastrohealing effects of *D. rotundifolia*. Administration of *D. rotundifolia* to rats, prophylactically, before ulcer induction with cold, acetylsalicylic acid and ethanol, resulted in mild disruption of the surface epithelium with only mild oedema and leucocyte infiltration into the submucosal layer. This shows the anti-ulcer potential of *D. rotundifolia* against cold, acetylsalicylic acid and ethanol. In the anticholinergic studies, *D. rotundifolia* decreased the propulsive movement of charcoal meal through the gastrointestinal tract [50].

Anti-*Helicobacter pylori* activity showed that *D. rotundifolia* and the standard antibacterial agents (amoxicillin and clarithromycin) were active against clinical isolates of *H. pylori* with the extract showing maximal activity at 400 mg/ml. Coupled with that was an observed decreased activity of H^+/K^+-ATPase with *D. rotundifolia* administration in all rat models when compared with negative control rats [50].

The results of the *in vivo* antioxidant studies in the ethanol-induced ulcer model showed an increased catalase and superoxide dismutase activities as well as an increased levels of reduced glutathione. There was also a marked decreased levels of malondialdehyde showing decreased rate of lipid peroxidation with *D. rotundifolia* administration. These give scientific credence to the folkloric use of *D. rotundifolia* in the management of peptic ulcer disease [50].

10. TOXICITY

Rhesus Monkey Kidney Epithelial Cells (LLC-MK2 cells) are normal mammalian cells hence toxicity against these cells most likely is a predictor of lack of selectivity and thus toxicity of an agent. Nondo et al. identified the crude extract of *D. rotundifolia* to be relatively safer with a cytotoxic concentration 50% against LLC-MLK2 cells of 125.90 ± 1.86 *μ*g/ml [11]. Abere et al. in an acute toxicity study could not determine the lethal dose (LD_{50}) because doses up to 5 g/kg administered to mice *per os* were not lethal [3]. However, in a subacute study, histopathological analysis of the liver of rats administered 250 and 500 mg/kg ethanol extracts daily showed increased cytoplasmic eosinophilia and densely stained nuclei compared to control. These together with increased vascular congestion are evidence of hepatocyte damage. Renal tubular necrosis and degeneration were also observed. Other vital organs such as the heart, however showed normal architectures with no signs of morphological disruptions [3].

In an acute toxicity studies by Ansah et al., no mortality was recorded at all doses (10-5000 mg/kg) of the whole-plant extract used over a 24-h period [51]. Compared to the control group, treatment groups at all dose levels did not show signs of aggressiveness, respiratory distress, sedation, salivation, vomiting and diarrhoea. Post-treatment evaluation for 14 days did not reveal the presence of any latent *D. rotundifolia* extract-related toxicity. Histopathological examination of the liver, kidneys, spleen and the stomach showed no significant changes in these organs confirming no cellular damage in treatment groups [51]. Though studies by Nondo et al. [11], Abere et al. [3] and Ansah et al. [51] provides evidence of the relative safety of *D. rotundifolia* extract, it may be toxic in pregnancy due to its anti-ovulatory and LH-FSH reducing ability as reported by Olufemi et al. [4]. The reversibility of the anti-fertility effects of

phytoconstituents makes them potentially clinically relevant in contraception [52]. As such the reproductive toxicity of *D. rotundifolia* extract can be exploited in the development of contraceptives.

Studies by Makanjuola et al. [53] investigated the effect of the methanol extract of *D. rotundifolia* on the histology, sperm parameters and tissue antioxidant parameters in cadmium-damaged testis and also its potential pro-fertility effect. From the study, it was realized that the administration of *D. rotundifolia* to cadmium-induced testicular damaged Wistar rats showed ameliorative effect through an improved histology of the testis and sperm parameters. Upon the administration of *D. rotundifolia* to healthy Wistar rats, there were signs of pro-fertility effect coupled with improvement of the histology of the testis, increased expression of antioxidant enzymes and improved sperm parameters when 50 mg/kg of the extract was administered [53].

11. CONCLUSION

Dissotis rotundifolia has been widely used in folklore medicine and has been documented in but a handful of publications. With yet a whole lot to probe, it is essential that future research consider a number of studies, some of which have been listed below.

To the best of the knowledge of the authors, claims of the anti-inflammatory effects of *D. rotundifolia* are just speculations by various authors based on certain phytochemical constituents and effects of *D. rotundifolia* and that no actual work on the anti-inflammatory effects of the plant extract had been done as at the time this document was written. Future studies should utilize appropriate models of inflammation to establish if any, the anti-inflammatory property of the plant after which pathway-specific *in vitro* and *in vivo* protocols could be employed to elucidate the exact mechanism of the anti-inflammatory action.

Data from acute and sub-acute toxicity studies establishes the relative safety of the plant extract however, studies on ovarian and hormonal effects may suggest the possibility of reproductive toxicity. Further robust studies, which may be single or multigenerational, are needed to clearly understand the effect the extract on reproductive performance, developmental toxicity and post-natal developments. The exact biomolecules responsible for these effects must also be characterized possibly for further development into contraceptives.

In vitro assays have shown promising results on the antioxidant effect of *D. rotundifolia*, however, future studies must consider *in vivo* assays since they offer a more reliable data on antioxidant effects than do *in vitro* assays.

Future research may also focus on identifying bioactive compounds responsible for the antimicrobial activity of the plant extract. Further work is also needed in establishing the time-kill kinetics. Characterization of these compounds may produce potential candidates for further development into drug molecules.

To the best of the knowledge of the authors, no published study is available on the effect of *D. rotundifolia* on neoplasms. Given the global need for more effective but less toxic anti-cancer agents, future studies on *D. rotundifolia* can screen for possible antiproliferative effects of the extract.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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