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Harnessing *Anisotes* Species for Sustainable Development: Traditional Medicine, Phytochemistry, and Bioactivities

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Abstract

Integrating medicinal plants into healthcare supports the Sustainable Development Goals (SDGs) and facilitates the development of new drugs. *Anisotes*is a genus of medicinal plants traditionally used to treat various diseases, including diabetes, hepatitis, jaundice, gallstones, and other hepatic disorders. The genus comprises 19 species that are widely distributed in tropical eastern and southern Africa, Madagascar, and the Arabian Peninsula. Among them, *Anisotestrisulcus* and *A. sessiliflorus* are the most extensively studied species. Phytochemical investigations reveal that pyrroloquinazoline alkaloids, such as vasicine, vasicinone, anisotine, and trisulcusine derivatives, are dominant constituents, with several exhibiting potent biological activities. The purpose of this review is to provide information on the traditional uses, chemical constituents, spectral data of isolated alkaloids, and biological activities of *Anisotes*species. The reported biological properties include antioxidant, anti-hypercholesterolemic, antismoking, anorexigenic, hepato-protective, acetyl cholinesterase (AChE) inhibitory, anti-inflammatory, cytotoxic, and antihyperglycemic activities, largely attributed to their alkaloidal content. By documenting the traditional uses and biological activities of *Anisotes*species, we aimed to support new research on these plants, especially on those species whose biological potential has not yet been studied.

***Keywords*:**Acanthaceae; *Anisotes;* traditional uses, chemical constituents; life on land; no poverty; good health and well-being; biological activities

1. Introduction

The importance of natural product drug discovery as a substantial tool for future health care has been widely recognized [1]. At least 130 nations have official programs, promoting traditional therapies at the national level and most populations depend on traditional medicine for their healthcare needs [2,3]. This dependence has prompted scientific research into natural remedies, particularly folk remedies by various ethnic or cultural groups has significantly aided in the development of contemporary treatments [4]. Despite developments in modern medicine, there are no effective pharmacological therapies for the main fatal illnesses. In addition, there is a rise in medication resistance to current chemotherapy regimens for AIDS, cancer, malaria, and fungal diseases, representing a raised challenge. This situation emphasizes the critical need for innovative, low-cost remedies in line with SDG 3 (Good Health and Well-Being), which encourages all to have access to essential medicines and healthcare.

In response to these problems, decision-makers, governments, international organizations, and the pharmaceutical industry have been encouraged to continue investing in the sustainable development of natural products as medicinal agents, especially in countries with limited resources, due to the challenges facing health care to achieve SDGs by providing access to safe and affordable medicines for all [5].

Since ancient times, plants and natural products have been known to humans in every culture throughout the world as an effective source of modern and traditional medicines [6,7]. Currently, an interest in traditional medicines has increased, thus leading to rapid development and studies of many remedies employed by various cultures of the world [8]. These natural medicines are preferred due to their effectiveness, low costs, and minimal side effects [9]. Considering the need to recognize medicinal plants as a component of primary healthcare, effective herbal medicine integration and promotion could result in an increase in utilization of medicinal plants and the growth of the herbal medicine supply chain. This directly contributes to achieving SDGs 15 (life on land) by placing a strong emphasis on preserving and making effective use of biodiversity-rich resources, as well as goal 1 (no poverty) through minimizing the healthcare expenses [10,11].

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Their interesting properties are due to the presence of various secondary metabolites with different chemical structures, such as alkaloids, phenols, steroids, flavonoids, and terpenoids, which also act as a defense system for the plants against environmental stresses and pathogenic attacks[12].

Acanthaceae is a tropical dicotyledonous family comprising about 2500 species and 250 genera worldwide [13,14]. Most of them are shrubs, tropical herbs or twining vines. Its common genera include *Justicia*, *Anisotes*, *Reullia*, *Stopbilanthes*, *Barleria*, *Acanthus,Aphelandra*, *Andrographis, Staurogyne*, *Dicliptera*, *Blepharis*, *Lepidagathis*, *Hygrophila*, *Thunbergia*, *Adhatoda,Avicennia*, and *Dyschoriste* [15]. The members of this family are cultivated as ornamentals and have horticultural importance [16,17]. They are mainly distributed in Indonesia, Malaysia, Brazil, Africa, the Mediterranean, Australia, and Central America [18]. Many Acanthaceae plants have been used in traditional medicine to treat several diseases, such as antidiabetic, bronchodilator, hypotensive, and local anesthetic [19].

The genus *Anisotes* comprises 19 species, 3 subspecies, and 1 variety, which are represented by shrubs, herbs, or sometimes climbers (Table 1) [20-22].*Anisotes*species are widely distributed in tropical eastern and southern Africa, Madagascar, and the Arabian Peninsula [23,24]. This genus is known to be rich in pyrroloquinazoline alkaloids, which are the major constituents in this genus [25-30]. These alkaloids exhibited various pharmacological activities: antimicrobial, anti-inflammatory, and bronchodilation [31,32]. Unfortunately, limited research has been conducted on this genus to study its chemical constituents and biological properties. Recently, phytochemical research has been conducted only on two species: *A. trisulcus*and *A. sessiliflorus*, however, no profound research on other species has been found. This review will primarily compile the traditional uses, phytochemicals, and biological activities of the *Anisotes*genus, aiming to encourage new research on the other species.

The current state of knowledge regarding the chemistry and pharmacology of the genus Anisotes suggests its potential for developing antihyperglycemic, anti-smoking, and hepatoprotective agents; however, few studies with species of this genus have been reported. Due to the importance of the genus *Anisotes*, as a source of new medicinal agents, a review is worthwhile. In this review, traditional uses, chemical constituents, and biological activities of the genus *Anisotes* are reviewed. Also, the spectral and physical data of the isolated alkaloids from this genus have been listed. These data may assist future multidisciplinary research involving phytochemical studies of the genus species.

Table 1: List of the genus *Anisotes* different species.

Species name	Species name	Species name	Ref.
A. bracteatus Milne-Redhead	*A. macrophyllus* (Lindau) Heine	*A. subcoriaceus* T. F. Daniel, Letsara& Martín-Bravo	
Anisotescomorensis (Lindau) T. F. Daniel	*A. mayottensis*T. F. Daniel	*A. tangensis* Baden	
A. divaricatus T. F. Daniel, Mbola, Almeda & Phillipson	*A. madagascariensis* Benoist	*A. trisulcus* (Forssk.) Nees	
A. diversifolius Balf. f.	*A. nyassae* Baden	*A. tanensis* Baden	[20, 22,23]
A. dumosus Milne-Redhead	*A. parvifolius* Oliv.	*A. ukambensis* Lindau	
A. formosissimus (Klotzsch) Milne-Redhead	*A. perplexus* T. F. Daniel, Letsara& Martín-Bravo	*A. umbrosus* Milne-Redhead	
A. guineensis Lindau	*A. pubinervis* (T. Anderson) Heine	*A. zenkeri* (Lindau) C.B.Clarke	
A. hygroscopicus T. F. Daniel, Letsara& Martín-Bravo	*A. rogersii* S. Moore	*A. velutinus* Lindau	
A. involucratus Fiori	*A. sessiliflorus* (T. Anderson) C.B. Clarke	*A. venosus* T. F. Daniel, Letsara& Martín-Bravo	

2. Search methodology

The literature reviewed for this work was obtained through a computer search of data on ScienceDirect, Web of Knowledge, SCOPUS, PubMed, JACS, and Google Scholar journal papers published from 1959 to 2025. Data was also obtained from book chapters, reviews, and theses indexed in the databases.

3. Traditional uses of some *Anisotes*species

Anisotestrisulcus (Forssk.) Nees is known as Madid, Mudhadh, Almodh, Madh, Moze,Mudhidh, Modaidمض, مضيض in Saudi Arabia and Yemen (**Figure 1)**. In the Arabian Peninsula, folk medicine treats diabetes, urine retention, kidney stones, eye infection, fever, malaria, foot inflammation, edema, epilepsy, hepatitis, jaundice, gallstones, and other hepatic disorders. Locally, it is also used in several pharmaceutical forms to suppress appetite and to limit tobacco consumption [19,29,33-38]. In Kenya, *A. ukambensis* (Mugituri) is utilized for bleeding control in pregnant women [39]. *A. formosissimus*is used as a purgative in Mozambique [40]. Moreover, *Anisotes*sp. (JRST 423) Basajabakilana is used for treating worms in Uganda [41].

However, in Southern Yemen, the stems are used for making house ceilings, while the flowers are an important nutritional source for honeybees, and the dead wood is used as a good fuel for firewood [42].

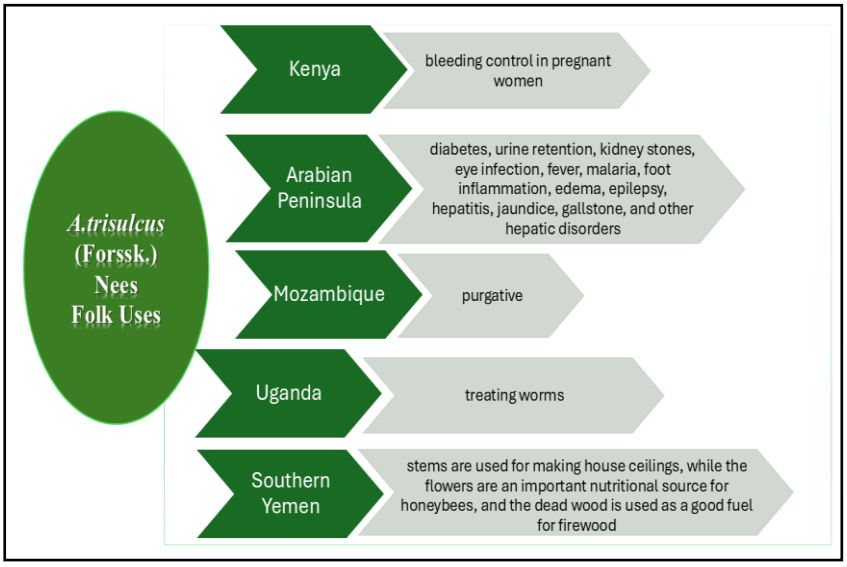

Figure 1. Summary of the Folk Uses of *Anisotestrisulcus* in different regions.

4. Phytochemistry

Anisotes species are a rich source of pyrroloquinazoline alkaloids, in addition to, flavonoids, quaternary ammonium compounds, triterpenes, sterols, and ceramide (Table S1-S3, Figures 2 and 3). Moreover, GC and MS analysis by Khurgain et al. of *Anisotestrisulcus*revealed the existence of flurandrenolide, cyclotrisiloxanehexaphenyl-, cholestano[7,8-a]cyclobutane, and 3-methoxy-6-oxo-2-methyl [19].

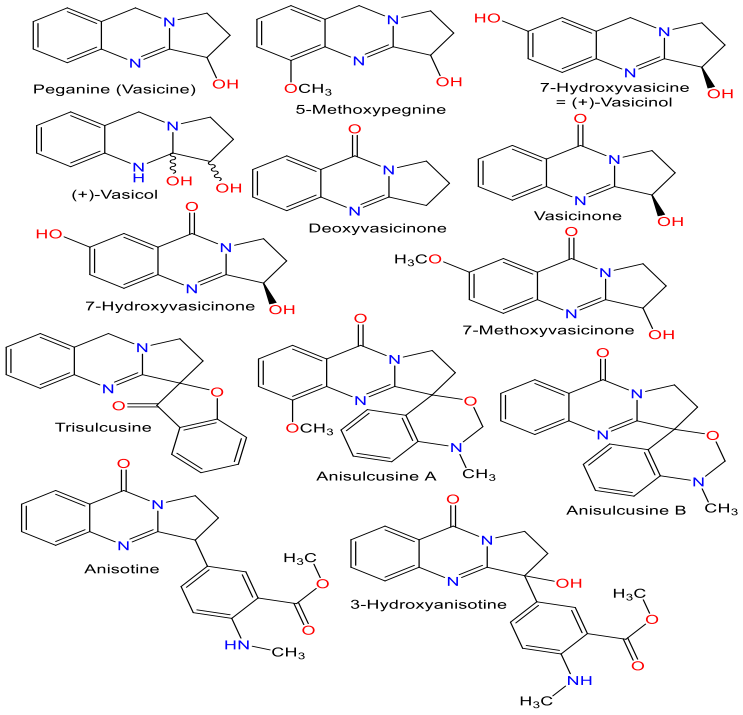

Figure 2. List of alkaloids isolated from *Anisotestrisulcus*.

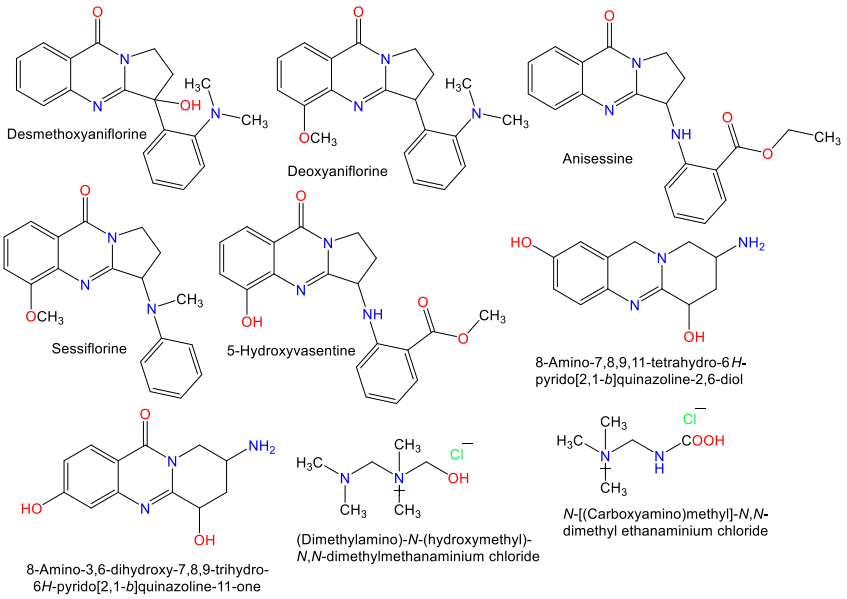

Figure 3. List of alkaloids isolated from *Anisotestrisulcus*.

5. Biological activities

The chemical components and extracts that have been separated from the many species of genus *Anisotes* have a broad range of biological effects. These species are rich mainly in pyrroloquinazoline alkaloids and related compounds exhibit diverse biological activities, making them attractive targets for drug discovery. These compounds demonstrate antibacterial, antiviral, antimalarial, anticancer, antidiabetic, and anticoagulant properties [43]. Several activities of Anisotestrisulcus are summarized in Figure 4.

5.1. Antimicrobial and antimalarial activities

The EtOH and EtOAc extracts of A. trisulcus showed moderate activity towards *S. aureus* ATCC 29213 and *S. aureus* ATCC 25923, with inhibition zone diameter (IZD) 5 and 7 mm, and 3 and 2 mm, respectively, in comparison to ampicillin IZD 22 and 25 mm, respectively. Meanwhile, they had weak activity towards *Enterococcus faecalis*with IZD 3 and 4 mm, respectively (ampicillin IZD 26 mm) [35]. The MeOH, n-hexane, and $CHCl_3$ extracts *of A. trisulcus* had mild antimalarial activity against the tested *P. falciparum* (D6 clone) relative to chloroquine [44]. Vasicine exhibited antibacterial activity at a MIC of 20 µg/mL against E. coli, compared to tetracycline (MIC 2.70 µg/mL) and gentamicin (MIC 4.55 µg/mL). Additionally, it demonstrated antifungal activity against *C. albicans* at a MIC greater than 55 µg/mL [31].

Figure 4. Biological Effects of Anisotestrisulcus (Forssk.)Nees

5.2. Cytotoxicactivity

Anisulcusines A and B, 3-*hydroxyanisotine*, (+)-vasicinol, and 7-hydroxy (±)-vasicinone isolated from *A. trisulcus*were tested for their anti-proliferative capacity towards HuH-7 (human hepatoma) cells. Anisulcusine Bexerted moderate anti-proliferative activity with CC_{50} 32.5 µg/mL, whereas the other compounds showed mild activity (1.12-1.22-fold) at 50 µg/mL [25]. The total MeOH extract and $CHCl_3$ fraction of *A. trisulcus*exhibited potent effects towards *Artemia salina* with % mortality of 60 and 61, respectively, while the *n*-hexane, EtOAc, and aqueous fractions had mild activity using the brine shrimp bioassay [27].

5.3. Anti-hyperglycemicactivity

The leaves' MeOH extract of *A. trisulcus* showed the highest antidiabetic effect than the extracts of its other parts through *in vitro α*- glucosidase inhibitory effect assessment with IC_{50} 118.10 ± 2.81 µg/mL [45,46]. It significantly decreased fasting and postprandial blood glucose, increased serum insulin, and decreased homeostasis model of insulin resistance (HOMA-IR) values in HFD/STZ diabetic rats [47]. Moreover, Okla et al. mentioned that the aqueous extract of *A. trisulcus* lowered sugar level from 267.3 to 141.39 mg/dL in diabetic mice and returned the numbers of white blood cells and platelets, hemoglobin concentration, and granulocytes percentage to the normal level [48]. A significant hypoglycemic effect was observed after 1h with MeOH, *n*-hexane, and EtOAC extracts of *A. trisulcus* at doses of 400 mg/kg BW, when they were concurrently given to mice with the glucose load, while the $CHCl_3$ extract showed the least hypoglycemic effect [26,28].

5.4. Anti-hypercholesterolemic activity

Al-Joufi stated that A. trisulcus leaves MeOH extract (400 mg/kg) decreased total cholesterol, serum triglycerides, vLDL-cholesterol, and LDL-cholesterol and increased HDL-cholesterol in HFD/STZ diabetic rats [47]. Also, it significantly reduced serum triglycerides, cholesterol, LDL-cholesterol, and vLDL-cholesterol in HCD-fed rats and decreased the cardiovascular risk values and increased the antiatherogenic index (AAI). Moreover, it increased LDLR and decreased FAS gene expression [49].

5.5. Antioxidantactivity

Al-Joufi reported that A. trisulcus leaves MeOH extract increased SOD and GSH and decreased thiobarbituric acid reactive species (TBARS) in HFD/STZ diabetic rats [47]. *Okla et al. evaluated the antioxidant effect of different A. trisulcusextracts and reported that the stem extract has the biggest free radical inhibition effect, followed by leaves and roots extracts* [48]. In addition, *A. trisulcus* extract decreased TBARS and enhanced GSH, SOD and catalase in the liver of HCD-fed rats [49]. The total MeOH extract and EtOAc fraction of *A. trisulcus* showed high antioxidant activity 75% and 68%, respectively in comparison to quercetin (100%) using the DPPH assay [26,28].

5.6. Anti-inflammatory activity

A. trisulcus leaves MeOH extract decreased lipid peroxidation and the gene expression levels of phosphoenolpyruvatecarboxykinase and increased hepatic hexokinase, glutathione, glycogen, and superoxide dismutase in HFD/STZ diabetic rats [47]. The serum IL-6, TNF-*α*, IL-1*β*, AST, ALT, and ALP levels were decreased by treating HCD-fed rats by *A. trisulcus* extract [49]. Moreover, the *n*-hexane and $CHCl_3$fractions at a dose of 400 mg/kg had potent anti-inflammatory activity compared with indomethacin using the carrageenan-induced paw edema method [26,28]. Singh and Sharma reported that vasicine (dose 20.0 mg/kg) showed potent anti-inflammatory effects (59.51%) at 6h after carrageenan injection, while vasicinone (dose 10.0mg/kg) exhibited maximum inhibition rate of 63.94% at 4 days after complete Freund's adjuvant (CFA) injection [31].

5.7. Hepato-protective activity

A 50:50 mixture of*Crepisrueppelli*iand *A. trisulcus*extractsat 200 mg/kg showed hepato-protective potential against ethanol and $CC1_4$ hepatotoxic agents. They reduced lethality in mice after injection of 6.4 g/kg of ethanol and prevented an increase of plasma GPT activity in rats given CCl_4 [38].

5.8. Antismoking and anorexigenic

The EtOH extract of *A. trisulcus* and peganine were evaluated for their capacities to suppress tobacco intake and appetite. The EtOH extract (600 mg/100 mL in H_2O) decreased food intake by 84.9% and oral nicotine intake by 87.7% in Wistar rats. However, peganine (1.4 mg/mL in H_2O) decreased food intake and nicotine consumption by 77.8%, and 79%, respectively. The EtOH extract enhanced nicotine effects by >70% and mimicked nicotine in inducing intestinal stimulation in the isolated guinea-pig ileum [50].

5.9. Acetyl cholinesterase (AChE) inhibitor

Vasicine reversibly and competitively inhibited AChE with *ki* (Dissociation constant for the enzyme/inhibitor complex) value of 11.24 µM, while vasicinone, vasicole, and anisotine possessed no/or weak inhibitory effect on AChE. Vasicine showed binding similarity to both tacrine and galantamine in the catalytic site [51].

Conclusion and Future Direction

Limited studies have been performed to evaluate the traditional uses of *Anisotes* species, and all of the research supported their traditional claims. Among the 19 reported species, *A. trisulcus*and *A. sessiliflorus* are the most studied species. These species yield diverse secondary metabolites, including pyrroloquinazoline alkaloids, flavonoids, quaternary ammonium compounds, triterpenes, sterols, and ceramides with promising bioactivities. Hence, further research is needed to exploit the chemical constituents and bioactivities of the lesser-investigated *Anisotes* species that could assist in the development of effective herbal remedies, supporting SDG 3. Additionally, the sustainable use and exploration of *Anisotes* and related plant resources align with SDG 15 by supporting the safeguarding of biodiversity and the responsible utilization of terrestrial ecosystems.

Future research on *Anisotes* should focus on linking traditional knowledge with scientific methodologies. Comprehensive metabolomic profiling and biosynthetic pathway investigation are needed to fully explore the phytochemicals and their mechanisms of action. Computational approaches such as molecular docking, molecular dynamics simulations, and *in-silico* ADMET analyses can enhance the identification of promising bioactive compounds. Preclinical investigations should be expanded to include mechanistic and toxicological assessments, followed by clinical trials to validate safety and therapeutic efficacy. Such integrative research not only supports the development of standardized, safe, and effective herbal remedies but also aligns with the Sustainable Development Goals by advancing affordable healthcare solutions and promoting responsible utilization of natural resources.

Conflict of interest

The authors declare no conflict of interest.

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