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The phytochemistry and pharmacological potentials of *Flabellaria paniculata* cav. (malpighiaceae): A review of an unexplored medicinal plant

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Abstract
Flabellaria paniculata is a traditional herb used to treat dysentery, diarrhea, wounds and sores, snake immunization, skin infections, and cancer in West Africa. The plant is known to have some pharmacological and phytochemical activities. However, existing publication indicated that the plant's full potential is unexplored or has yet to be investigated. As a result, the focus of this review will be on critical information reported about *Flabellaria paniculata* ethnomedicinal uses, pharmacological and phytochemical activities, and potential toxicity, in order to highlight its therapeutic prospects in traditional use, as well as research opportunities for more investigations aimed at developing promising pharmacologically active compounds. Phytochemical studies revealed that the plant contains various types of bioactive compounds and a number of compounds from its essential oils. *Flabellaria paniculata* has antioxidant, anti-inflammatory, anticancer, antiulcer, antifungal, anthelmintic, and wound healing properties according to its pharmacology studies. The review on *Flabellaria paniculata* showed its ethnopharmacological use. Other folkloric claims, on the other hand, have received little scientific studies. Furthermore, due to the plant's unexplored nature, pure serendipity, rather than scientific research on its folkloric claim is encouraged. Thus, the plant's potency could be tested on disease conditions such as hypertension (high blood pressure), high cholesterol, Arthritis, heat diseases, diabetes, chronic kidney disease, depression, Alzheimer's disease and dementia. These are major causes of death among humans and *Flabellaria paniculata* might be the breakthrough research for these disease conditions.

Keywords: Ethnomedicinal**,** *Flabellaria paniculata*, medicinal plant, phytochemistry, pharmacology

1. Introduction
The uncovering of bioactive molecules from plant origin offers an attractive approach to the control of infectious or non-infectious diseases. Our inability to develop successful medications against a large number of diseases using the in silico docking approach coupled with chemical combinatorial synthesis has led to a revival of great interest in plants as polypharmacies. Medicinal plants, either through serendipity or by standardized screening programs – have a paramount position in drug discovery and many modern drugs have their origin in traditional medicine of different cultures [1-3]. These medicinal plants have received attention in traditional medicine and continue to be the primary source of naturally occurring drugs used by many groups around the world [4]. According to the World Health Organization (WHO), about 80% of the people worldwide rely on medicinal plants for primary health care intervention [5]. Hence, traditional knowledge of naturally occurring products derived from plants plays an important role in pharmaceutical drug research and also a source of nutraceuticals [6].
Flabellaria paniculata Cav. (Malpighiaceae) is a climbing shrub that grows to a height of 3-15 m. The leaves are silvery on the underside, and the flowers range from white to pale pink. It is a tropical African herb native to West Africa (Figure 1). The plant is found in wooded savannah riverine desert or forest subjected to flooding throughout the territory, from Senegal to West Cameroon and beyond the Congo Basin to Uganda and Tangayika. In Yoruba land, Nigeria, it is known as "Lagbolagbo" or "Ajidere."

It is known as'manding maninka Conombo' in Senegal, 'Lokohebe' in Sierra Leone, 'baule' in Ivory Coast, and 'adangma' in Ghana [7-9]. The leaf laminae are broadly elliptic, ovate, or rarely lanceolate, and the petioles are 1 - 2.5 cm long. The lainous stem is used as ties in some Ghana hut buildings [10].

To the best of our knowledge, there is no detailed information on *Flabellaria paniculata* (*F. paniculata*) ethnomedicinal uses, phytochemistry, and pharmacological properties. As a result, this review summarized *F. paniculata* ethnomedicinal uses, pharmacological properties, phytochemical components, and toxicological studies. Hence, we hope that this review will provide insight into the untapped potentials of this plant, and identify research potentials that could be explored immediately

1.1 Botanical classification of *Flabellaria paniculata*

Kindom: Plantae; Phylum: Magnoliophyta; Class: Magnoliopsida; Order: Malpighiales; Family: Malpighiaceae; Genus: Flabellaria; Species: Paniculata

2. Method

The available information on the plant was acquired from an internet database (Scifinder and Google Scholar), using the search terms *Flabellaria paniculata* Cav. Malpighiaceae, traditional uses, ethnomedical uses, pharmacology, phytochemistry, toxicity, and safety.

3. Results

3.1 Ethnopharmacological uses of *Flabellaria paniculata*

F. paniculata leaves and roots are used as a traditional herb in West Africa, particularly in Nigeria, Ghana, Senegal, Cameroon, Sierra Leone, and Ivory Coast, to treat ulcers and wounds, diarrhea, dysentery, snake vaccination, and cancer [11]. In Nigerian traditional medicine, the plant is used to treat skin infections, wound dressing, cancer, amenorrhoea, ancebolic, ulcer therapy, and disorders connected with pain and swelling [8, 12-17]. Locally, *F. paniculata* has been suggested to have antibacterial, antifungal, and anti-infective effects [8, 18]. The investigation on the roots of *F. paniculata* established the inhibitory concentrations of the crude extract and fractions utilized by traditional healers in Nigeria for the treatment or prevention of breast cancer [19]. The pharmacological impacts of ethanol extracts of *F. paniculata* leaves and roots on gastric ulcers in rats, as well as the gastroprotective effects of the ethyl acetate fraction of the methanol leaf extract, have also been described [20, 21]. The essential oil extracted from the leaves of *F. paniculata* possesses anti-inflammatory properties, making reference to the plant's usage in traditional medicine [22]. The plant's chloroform extract has been shown to be a potential anti-infective and wound healing agent, having *in-vitro* antibacterial and *in-vivo* healing actions that are consistent with the plant's traditional usage for skin disorders and wounds [9, 23]. *Flabellaria paniculata* has also been discovered to have anti-candidal properties on candida species [24]. The plant was known to have anthelmintic effect in Cote d'Ivoire; therefore it was used to treat parasitic infections [25]. Sofodiya and Familoni (2012) determined the antioxidant properties of various solvent extracts of *F. paniculata* root and leaves [26]. Table 1 summarizes the documented ethnopharmacological applications of various components of *Flabellaria paniculata*.

Table 1: Ethnomedicinal uses of *Flabellaria paniculata* and research activities

Ethnomedicinal uses	Plant part	References	Research activities
Diarrhoea	Leaves and roots	[11]	Not confirmed
Dysentery	Leaves and roots	[11]	Not confirmed
Sore	Leaves and roots	[11]	Not confirmed
Wound healing	Leaves and roots	[11, 17]	Confirmed [23]
Snake immunization	Leaves and roots	[11]	Not confirmed
Breast cancer	Leaves and roots	[11]	Confirmed [19]
Skin infection	Leaves	[8]	Not confirmed
Ulcer	Leaves	[8]	Confirmed [20, 21]
Pain	Leaves	[8]	Not confirmed
Amenorrhoea	Whole plant	[15, 16]	Not confirmed
Ancebolic	Whole plant	[15, 16]	Not confirmed
Bacteria	Leaves	[13, 18]	Confirmed [9]
Fungi	Whole plant	[13, 18]	Confirmed [24]
Inflammation	Leaves and roots	[22]	Confirmed [22]
Anthelmintic	Leaves	[25]	Confirmed [25]
Antioxidant	Leaves and roots	[26]	Confirmed [26]
Cancer	Leaves	[14]	Not confirmed

3.2 Phytochemical content of *Flabellaria paniculata*

Phytochemical screening of *F. paniculata* extracts revealed saponins, alkaloids, anthraquinones, flavonoids, and tannins, but no phenols [24]. Abo and Olugbuyiro's (2004) findings also revealed the presence of saponins, cardenolides, alkaloids, and tannins in the leaf of *F. paniculata*, but no anthraquinones, cyanogenic glycosides, or flavonoids [9]. Preliminary investigations into the chemical contents of *F. paniculata* leaf and root extracts indicated the presence of terpenoids, tannins, and saponins, with anthraquinone found in the root but not the leaf [26].

3.3 Quantitative phytochemical content of *Flabellaria paniculata*

The quantitative phytochemical content of *Flabellaria paniculata* is shown in table 2.

Table 2: Quantitative phytochemical content of *Flabellaria paniculata*

Plant part	Solvent	Phytochemical	References
Root	Ethanol	TPCC (216.42), TPC (59.96), TFC (33.08)	[26]
Root	Aqueous	TPCC 12.99, TPC (18.68), TFC (13.21)	[26]
Root	Chloroform	TPCC (24.47), TPC (101.75), TFC (25.42)	[26]
Leaf	Ethanol	TPCC (47.89), TPC (91.23), TFC (97.46)	[26]
Leaf	Aqueous	TPCC (12.72), TPC (33.23), TFC (4.64)	[26]
Leaf	Chloroform	TPCC (44.36), TPC (54.78), TFC (90.48)	[26]

TPCC: Total proanthocyanidins (mg catechin/g extract), TPC: Total phenolics (mg garlic acid/g extract), TFC: Total flavonoids (mg quercetin/g extract).

3.4 Chemical compounds isolated from *Flabellaria paniculata*

Campesterol glucoside and Sitosterol were discovered from the roots of *F. paniculata* [19]. The ethyl acetate fraction contained two triterpenoids (friedelin and friedelinol), two steroids (sitosterol and sitosterol-d-glucoside), and a flavonoid glycoside (kaemp-ferol-3-O-l-rhamnopyranosyl-(16)-d-glucopyranoside) [21]. Chemical compounds identified by Oladosun *et al*. (2012) in the essential oils of the leaves and roots of the plant are listed in table 3. The chemical structures of the major isolated compounds from *Flabelaria paniculata* are presented in figure 2.

Table 3: Chemical compounds isolated and identified from *Flabellaria paniculata*

Compound	Plant part	Solvent	Activity	References
Friedelin	Leaves	Ethyl acetate	NP	[21]
Friedelinol	Leaves	Ethyl acetate	NP	[21]
Sitosterol	Leaves,	Ethyl acetate,	NP	[21]
	Root	Hexane	Breast cancer	[19]
Sitosterol-β-d-glucoside	Leaves	Ethyl acetate	NP	[21]
Kaemp-ferol-3-O-α-l-rhamnopyranosyl-(1→6)-β-d-glucopyranoside	Leaves	Ethyl acetate	NP	[21]
Campesterol glucoside	Root	Hexane	Breast cancer	[19]
alpha-pinene	Root, leaves	Aqueous	NP	[22]
alpha-sabinene	Leaves	Aqueous	NP	
1,8 cineol	Leaves	Aqueous	NP	
alpha-ocimene	Leaves	Aqueous	NP	
2-methylisobomeol	Leaves	Aqueous	NP	
alpha-patcholene	Leaves, Roots	Aqueous	NP	
beta-elemene	Leaves	Aqueous	NP	
alpha-cedrene	Leaves, Roots	Aqueous	NP	
alpha-cryophyllene	Leaves, Roots	Aqueous	NP	
alpha-bergamotene	Leaves	Aqueous	NP	
beta-farnesene	Leaves, Roots	Aqueous	np	
trans-sci-ionone	Leave	Aqueous	NP	
Muurolene	Leaves. Roots	Aqueous	NP	
alpha-farnesene	Leaves	Aqueous	NP	
gamma-trans-nerolidol	Leaves, Roots	Aqueous	NP	
Spathulenol	Leave	Aqueous	NP	
alpha-cadinol	Leaves	Aqueous	NP	
beta-Santalol	Leaves	Aqueous	NP	
Hexanoic acid	Roots	Aqueous	NP	
Manool	Roots	Aqueous	NP	
9-Octadecanoic acid	Leaves, Roots	Aqueous	NP	
Thymol	Leaves	Aqueous	NP	
Octadecanoic acid	Leaves, Roots	Aqueous	NP	
Phytol acetate	Leaves	Aqueous	NP	
Tricosane	Leaves	Aqueous	NP	
Farnesol	Leaves, Roots	Aqueous	NP	
Geranyl linalool	Roots	Aqueous	NP	
Unknown Retinol derivatives	Roots	Aqueous	NP	

NP: no pharmacological screening reported

3.5 Pharmacological activities of *Flabellaria paniculata*

Flabellaria paniculata extracts and fractions were investigated for antioxidant, antifungal, anti-inflammatory, antiulcer, anticancer, antibacterial, wound healing capabilities, and antihelmintic activity. Table 4 summarizes the reported pharmacological activity of several extracts and fractions derived from various parts of *F. paniculata.*

Table 4: Reported pharmacological activities of *Flabellaria paniculata*

Activity	Solvent	Plant part	Assay	Reference
Wound healing	Chloroform	Leaves	*In vitro, In vivo*	[23]
Anthelmintic	Ethanol	Leaves	*In vitro*	[25]
Antibacterial	Petroleum ether, choloform, methanol, aqueous	Leaves	*In vitro*	[19]
Antiulcer	Ethanol	Leaves, root	*In vivo*	[20]
	Methanol, fractions (ethyl acetate, dichloromethane, hexane, aqueous)	Leaves	*In vivo*	[21]
Anti-inflammatory	Aqueous	Leave, root	*In vitro*	[22]
Anticancer (Breast cancer)	Methanol, fractions (ethyl acetate, butanol, hexane, aqueous)	Roots	*In vitro*	[12]
Antioxidant	Ethanol, aqueous, chloroform	Leaves, roots	*In vitro*	[26]
Antifungal	Ethanol	whole plant	*In vitro*	[14]

3.5.1 Anticancer activity
MTT (3-(4, 5-Dimethylthiazol-2-yl)-2, 5-Diphenyltetrazolium Bromide) test was used to evaluate anticancer activities in MCF-7 breast cancer cells. Campesterol glucoside and sitosterol were isolated from the roots of *F. paniculata*. Campestrol glucoside, with an IC_{50} of 1.18 mg/mL, exceeded sitosterol (1.79 mg/mL). When compared to a common anticancer medication, Paclitaxel (IC_{50} 0.07 mg/mL), the activities were lower. The two compounds exceeded a known flavonoid, quercetrin, in terms of activity (IC_{50} 2.05). Among the fractions studied (ethyl acetate, butanol, and aqueous), the hexane fraction was the most active [19].

3.5.2 Antifungal activity
The minimum inhibitor concentration (MIC) of *F. paniculata* whole plant on Candida species was found to be 5-8 mg/mL. Thus, the MIC for *Candida albicans* and *Candida glabrata* was 5 mg/mL, for *C. stellatoidea* and *C. torulopsis* was 8 mg/mL, and for *C. krusei* was 7 mg/mL [24].

3.5.3 Antioxidant activity
The antioxidant properties of several solvent (ethanol, aqueous, and chloroform) extracts of *Flabellaria paniculata* leaves and roots were tested using various assay techniques. The extracts from the leaves and roots significantly inhibited lipid peroxidation and scavenged hydroxyl radicals. The extracts also demonstrated mild chelating properties, indicating their antioxidant capacity. However, in 2, 2-diphenyl-1-picryl hydrazyl (DPPH) radical scavenging and reducing power experiments, the ethanol extract of the root extract exhibited stronger activity than all other extracts, and the activity is equivalent to that of conventional drugs, quercetin, and tocopherol at higher doses (80 to 100 g/ml) of the extract [26].

3.5.4 Anti-inflammatory activity
The anti-inflammatory effects of extracted essential oils from leaves and roots were assessed by inhibiting tetradecanoylphorobol-13 acetate-induced ear edema in mice. By 4 and 24 hours following treatment, all tetradecanoylphorobol-13 acetate-treated animals had developed ear edema. The oils at 5.0 and 2.5 mg dosage levels had a stronger effect on edema reduction than indomethacin (0.25 mg) [22]

3.5.5 Antiulcer activity
When ethanol leaf extract was administered at 400 mg/kg in a pylorus ligation model, it significantly reduced ulcer index when compared to the control group. At 100 mg/kg, *F. paniculata* leaf significantly decreased stomach lesions by 82.22% and 67.32% in ethanol and indomethacin generated ulcer models, respectively, but *F. paniculata* root (100, 200, and 400 mg/kg) had no impact in either model [20].Using indomethacin and pylorus ligation-induced ulcer models, the ethylacetate fraction significantly protected the stomach mucosa from indomethacin-induced injury when compared to the control. The ethylacetate fraction inhibited ulcers in a dose-dependent manner. At a dosage of 100 mg/kg, the fraction demonstrated a 65.9% ulcer prevention efficacy, as well as a considerable decrease in stomach acid level. When compared to the control, there was no significant difference in stomach pH or amount of gastric juice. Cimetidine (100 mg/kg) provided a considerable inhibition of lesion development (72.7%), as well as a significant increase in gastrointestinal pH and reduction in gastric acid level [21].

3.5.6 Antibacterial
Staphylococcus aureus, Pseudomonas aerugniosa, Escherichia coli, and *Klabellia pneumoniae* were used to test antibacterial activity. Aqueous extract at 50 mg/mL exhibited a zone of inhibition of 2 mm (*P. aerugniosa*) and 3 mm (*S. aureus*), but was inert against *E. coli* and *K. pneumonia*. At 10 mg/mL, chloroform extract inhibited *P. aerugniosa* by 2 mm, *S. aureus* by 3 mm, *K. pneumoniae* by 3 mm, and *E. coli* by 2 mm (*E. coli*). *P. aerugniosa* and *S. aureus* had MICs of 1.75 and 2mg/mL, respectively. The petroleum ether extract has no antimicrobial activity against the bacteria tested [9].

3.5.7 Anthelmintic activity
S. mansoni NTS was eliminated by extracts *of Flabellaria paniculata* leaves at 20 g/mL, whereas *E. caproni* and *T. muris* at 2000 µg/mL and *H. bakeri* at 200 µg/mL [25].

3.5.8 Wound healing properties
The contraction and duration of epithelization of the rat abdomen were used to determine the pace of wound healing. The excision model was used to inflict wounds on Wistar rats. 108 cells/ml inoculums of *Staphylococcus aureus* and *Pseudomonas aeruginosa* were used to infect rat abdominal wounds. When given in rat abdominal excision, the chloroform fraction of the methanol extract of *Flabellaria paniculata* leaf revealed considerable wound healing activity, as well as good potency on wounds injected with pathogenic organisms [23].

3.6 Toxicological studies on *Flabellaria paniculata*
The oral route median lethal dosage (LD_{50}) of *F. paniculata* leaf was 4570 mg/kg, whereas the LD_{50} of *F. paniculata* root was 2754 mg/kg. The LD_{50} in intraperitoneal injection was determined to be 1202.26 mg/kg for *F. paniculata* leaf and 1380.38 mg/kg for *F. paniculata* root, respectively [20].

Fig 1: A whole *Flabellaria Paniculata* plant in natural habitation

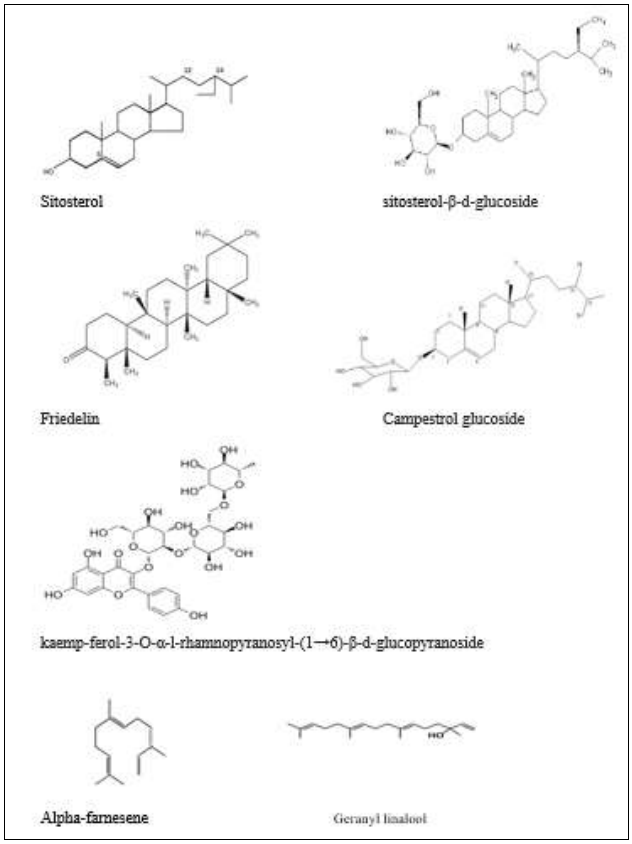

Fig 2: Chemical structures of isolated compounds from Flabellaria paniculata

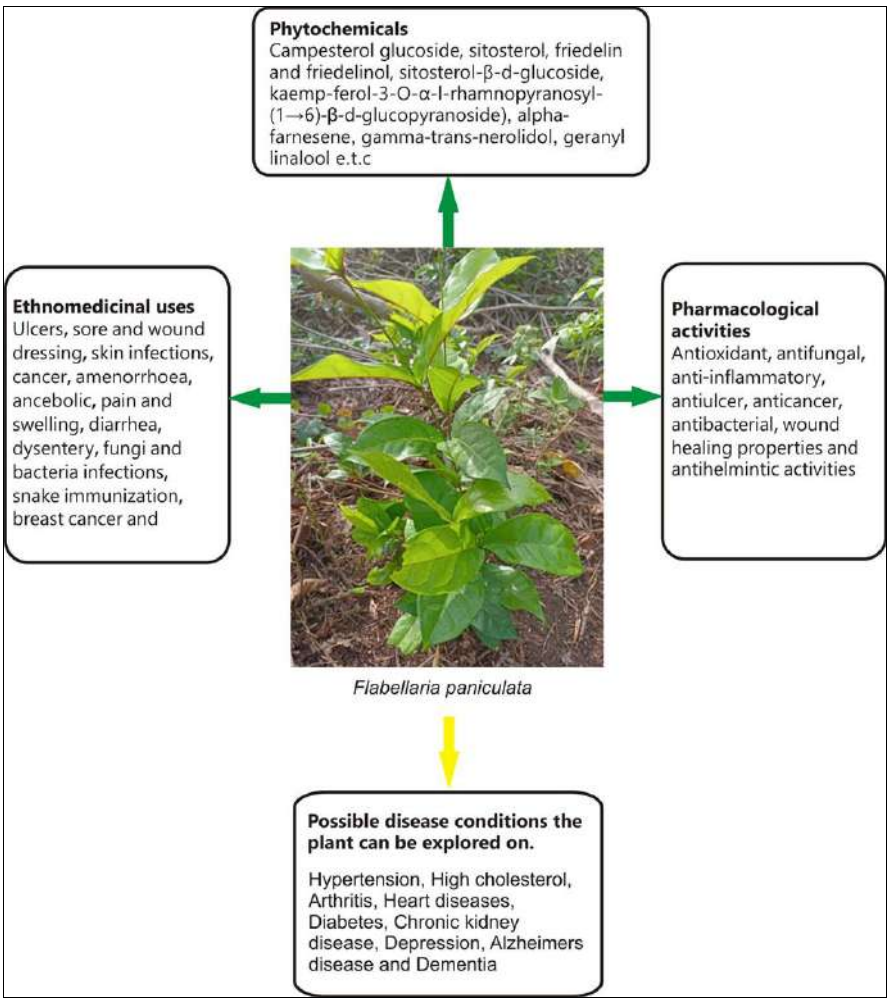

Fig 3: Pictorial summary of review

4. Conclusion

The review has shown that *Flabellaria paniculata* has ethnopharmacological uses as well as medicinal potential against different ailments (Fig. 3). It also revealed the research gaps in its pharmacological activities, which might help to substantiate various folklore claims. Hence, to maximize the therapeutic potential of this untapped medicinal plant, and elucidate its mechanism of action, detailed phytochemical isolation, and characterization, as well as additional preclinical efficacy and safety analysis, may be required. Also, due to the untapped nature of this plant, pure serendipity, rather than scientific research on its folkloric claim is encouraged. This may turned out to be the breakthrough research on the plant.

5. Acknowledgements: Not applicable

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