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Phytochemistry and Pharmacology of *Anogeissus leiocarpus* (DC.) Guill. & Perr. - A Review

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Abstract: The relevance of medicinal plants as a primary source of therapeutic agents in the modern world cannot be overemphasized. *Anogeissus leiocarpus (A. leiocarpus)*, of the family *Combretaceae*, is a renowned medicinal plant used in folkloric medicine for the management of various illnesses, particularly in developing countries. In African traditional medicine, the edible stem bark used as a chewing stick reportedly possesses numerous biological activities. Stem bark extract from *A. leiocarpus* exhibits anti-parasitic, anti-hypertensive, and anti-tubercular effects. Additionally, *A. leiocarpus* bark extract is used in traditional medicine in Sudan to alleviate cough and in Ivory Coast to treat parasitic diseases. The plant reportedly possesses other medicinal properties, including anti-diabetic, anti-inflammatory, anti-malarial, and anti-cancer activities due to the presence of important phytochemicals, such as phenols, flavonoids, saponins, and alkaloids. Compounds including, serinic acid, arjungenin, isoquercetin, vitexin, kaempferol and some others have been identified as bioactives from various parts of the plant.

Key Words: *Anogeissus leiocarpus*, secondary metabolites, anti-malarial, antioxidant, anti-cancer

1. Introduction

Indigenous plants are a primary source of secondary metabolites, which play an intriguing role in traditional medicine [1]. The presence of several bioactive chemicals with chemo-preventive, antioxidant, antifungal, anti-inflammatory, antibacterial, analgesic, and other activities is what gives these plants their medical relevance [2].

Africa and other developing nations still rely heavily on medicinal plants as a therapeutic option for the management of variety of illnesses and diseases [3]. Recently, more attention has been directed at finding new drugs from a plant origin. Hence, there is a compelling need to find new bioactive compounds and new "leads" with vital pharmacological activities from herbal plants, such as the *Anogeissus leiocarpus*, a tropical indigenous medicinal plant in Africa. *A. leiocarpus* is the most abundant tree species in the woodland [4], which can be used in the production of charcoal [5]. *A. leiocarpus* is consumed as herbal tea and used for therapeutic purposes in the treatment of many ailments [6]. The leaf of *A. leiocarpus* has been found to be effective in treating sickle cell anemia [7]. The stem bark and leaf of *A. leiocarpus* offers potential alternatives and conveniently accessible sources of antibacterial compounds for the treatment of numerous bacterially induced illnesses [8-10]. The stem bark extract of *A. leiocarpus* has been utilised for a long time in conventional tanneries as a native agent for softening hide and skin [11].

2. Methodology

Data were gathered from various online databases such as ScienceDirect, PubMed, Scopus, Google Scholar and Web of Science by selecting the most comprehensive, recent and relevant articles on *Anogeissus leiocarpus* from the year 2014 to 2023.

3. Plant Profile

Occurrence and Distribution

A. leiocarpus, a deciduous tree (Figure 1) native to Asia and Africa belonging to the *Combretaceae* family, flourishes in a variety of environments, including forests, savannas, bushlands, semiarid grasslands, and drylands [12-14]. *A. leiocarpus*, also called African birch or axle wood, is called Ayin in the South-West region of Nigeria.

Figure 1. Pictures of *A. leiocarpus*

The *A. leiocarpus* are endemic in the forests and savanna zones of the Sudanese region. Its extensive biological activities extend from the edge of the Sahara to the uppermost layer of wet tropical forests. Senegal to Cameroon in West Africa, as well as Ethiopia and East Africa, are other places where it can be found or grown. in they thrive well at both dry forests and at the riverbank of wet regions [15].

Botanical Description

A. leiocarpus is a deciduous tree that typically reaches heights of 15 to 18 m and has light green foliage. In form, leaves range from elliptic to ovate-lanceolate, alternating to subopposite, and are 2 to 8 cm long by 1.5 to 3.5 cm wide [16]. The bark is fibrous with tiny scales, grey to beige in colour, and becomes blackish with age. The stems are coarsely pubescent. There are around 40 seeds of 10 g each that are spread by wind in an *A. leiocarpus* [16]. The leaves are attenuated at the base, pointed at the apex, and hairy below. The flowers lack petals and are bisexual; two-centimetre-wide, yellow inflorescence globose heads. The fruits are globose cone-like heads that are extensively winged, dark grey, and 3 cm in diameter. It reproduces both vegetatively and by seeds [12].

Ethnobotanical Uses

A. leiocarpus has a long history of being used as an infusion to treat a number of diseases. Extracts from the roots, leaves, stem bark, and twigs are used to treat illnesses, such as gonorrhoea, wounds, acute respiratory tract infections, stomach infections, TB, dysentery, and malaria. The stem bark, which is typically consumed as chewing sticks or used as home beverages, is known to contain wound-healing, anti-pneumonia, anti-arthritis, antibacterial, anti-malaria and antitrypanosomal effects [2,12,17-19]. Crude extract from this plant has been investigated to be effective in termite control [20]. Stem bark extracts have also been demonstrated to have the ability to protect liver function [21] and act as anti-parasitic, anti-hypertensive and anti-tuberculosis agents [22-25]. The aqueous extract of *A. leiocarpus* could be utilised as an alternate treatment and control method for coccidiosis [26].

Traditional Sudanese medicine uses a decoction of the bark to treat coughs [27]. The herb is used by traditional healers in the Ivory Coast to cure parasitic illnesses such malaria, trypanosomiasis, helminthiasis, and diarrhoea [28]. In traditional Togolese medicine, the decoction of the leaves is used to cure stomach problems and fungi infections including dermatitis and mycosis [29]. The plant extracts are effective in treating diabetes, ulcers, generalised body aches, blood clots, asthma, coughing, and tuberculosis [30].

4. Phytochemical Profile

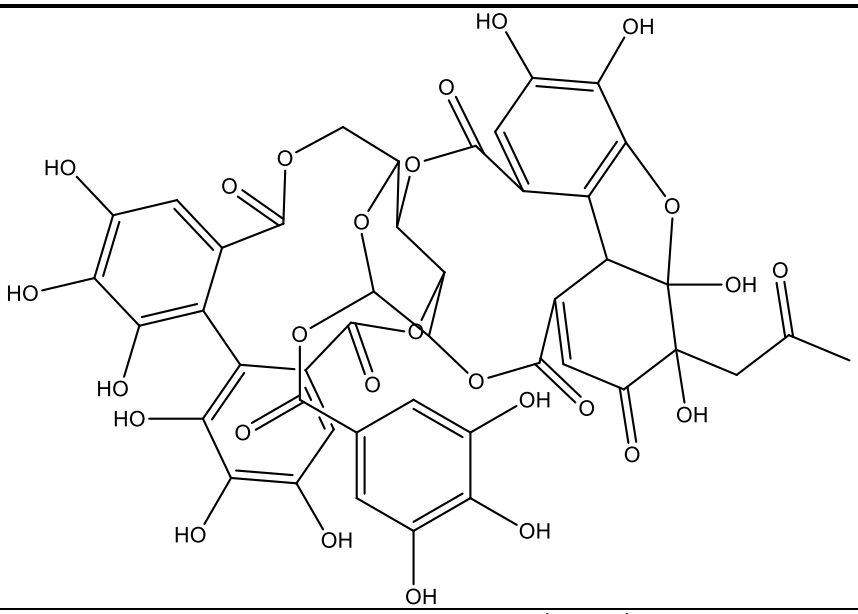
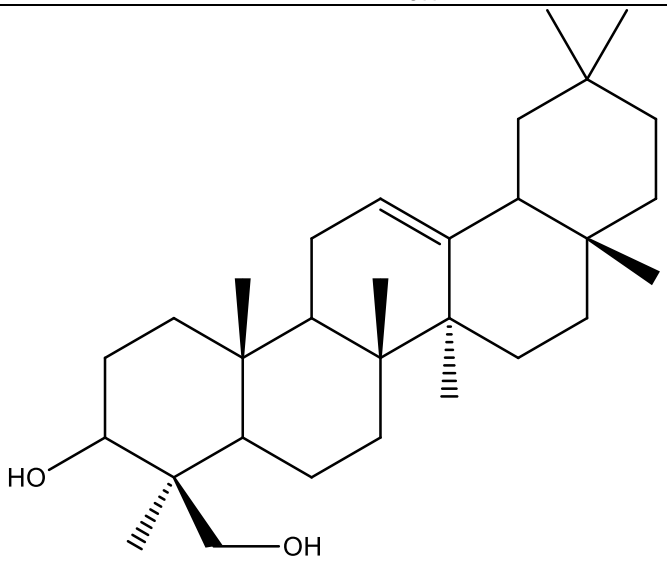
Many potent phytochemical components found in *A. leiocarpus* have been demonstrated to be responsible for the therapeutic properties of the plant [31-34]. Secondary metabolites found in *A. leiocarpus* stems include alkaloids, tannins, flavonoids, cardiac glycosides, and saponins [35, 36]. Preliminary phytochemical screening of the *Anogeissus leiocarpus* stem bark for the major secondary constituents revealed that the plant, which was obtained from a local farm in Jigawa, Nigeria, was abundant in tannins and contained significant amounts of flavonoids, terpenes, and saponins, but was devoid of anthraquinones [12]. According to Hussaini *et al.* [37], the stem bark extract contained saponins, tannins, phenols, phytosterols but was devoid of flavonoids.

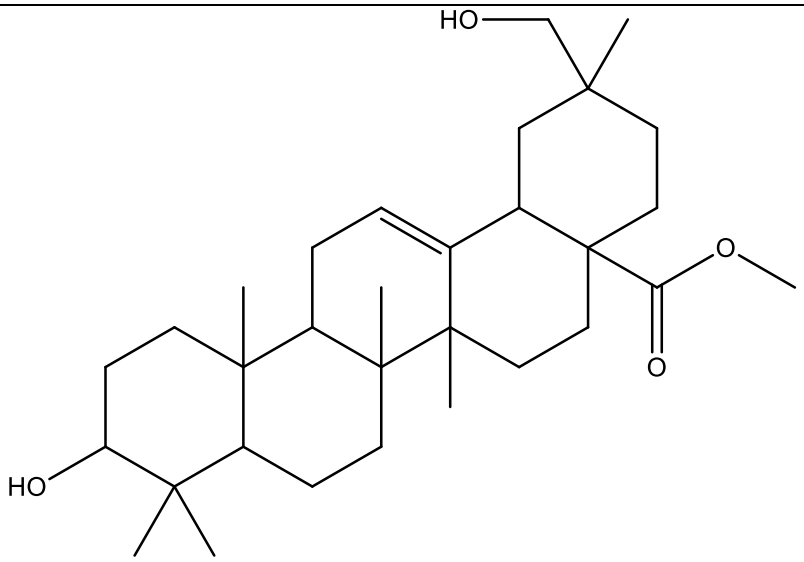
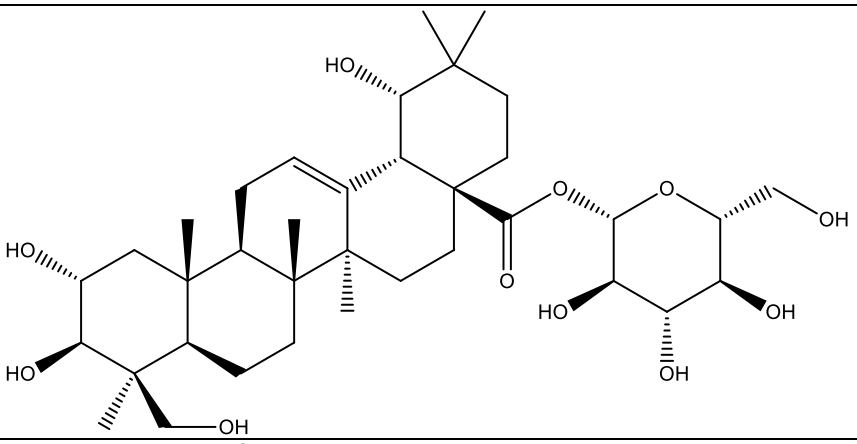
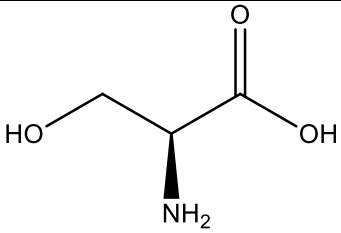
Despite its widespread use, only a few studies have established the phytochemical profile of *A. leiocarpus* stem bark to date [23,38]. In a qualitative chemical assessment of *A. leiocarpus* leaf and stem bark extracts by HPLC-ESI-MSn analysis, a significant number of phenolic components, including ellagitannins **1**, and some flavonoids were identified [38].

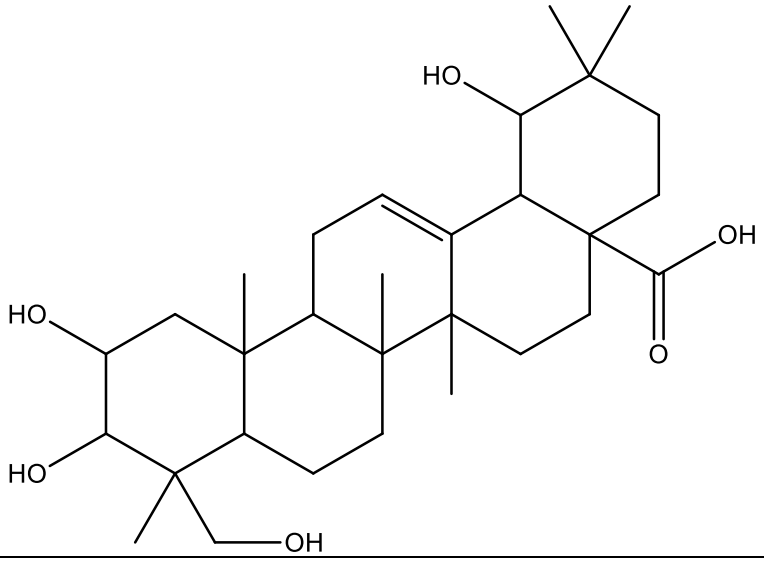
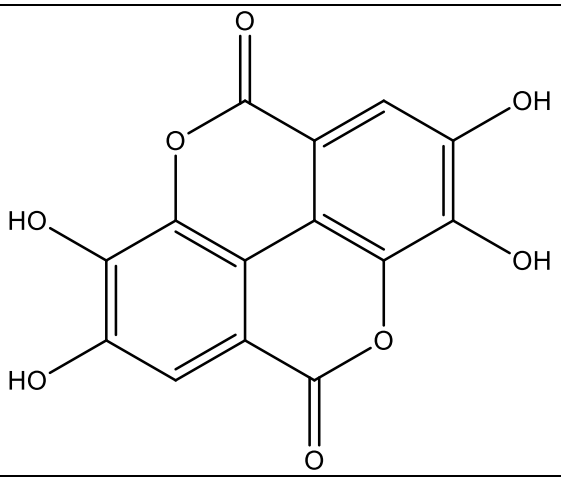
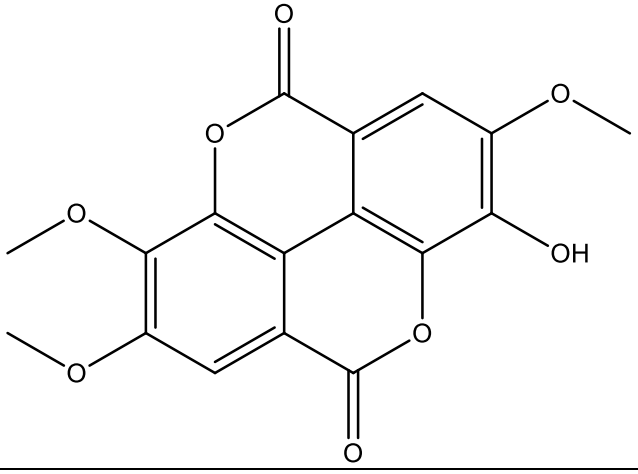
The stem bark of *A. leiocarpus* contains two oleanane-type compounds (4S, 6aR, 6bS, 8aR,14bR)-4-(hydroxymethyl)-4, 6a, 6b, 8a, 11,11,14b-heptamethyl-1, 2, 3, 4, 4a, 5, 6, 6a, 6b, 7, 8, 8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-3-ol **2** and methyl 10-hydroxy-2-(hydroxymethyl)-2, 6a, 6b, 9, 9, 12a - hexamethyl-1, 2, 3, 4, 4a, 5, 6, 6a, 6b, 7, 8, 8a, 9, 10,11,12,12a,12b,13,14b-icosahydropicene-4a-carboxylate **3**, as well as other triter penoids, including sericoside **4**, serinic acid **5** and arjungenin **6** [39,40]. Several ellagic acid compounds, including 2,3,7,8-tetrahydroxychromeno[5,4,3-cde] chromene-5,10-dione **7**, were identified [23].

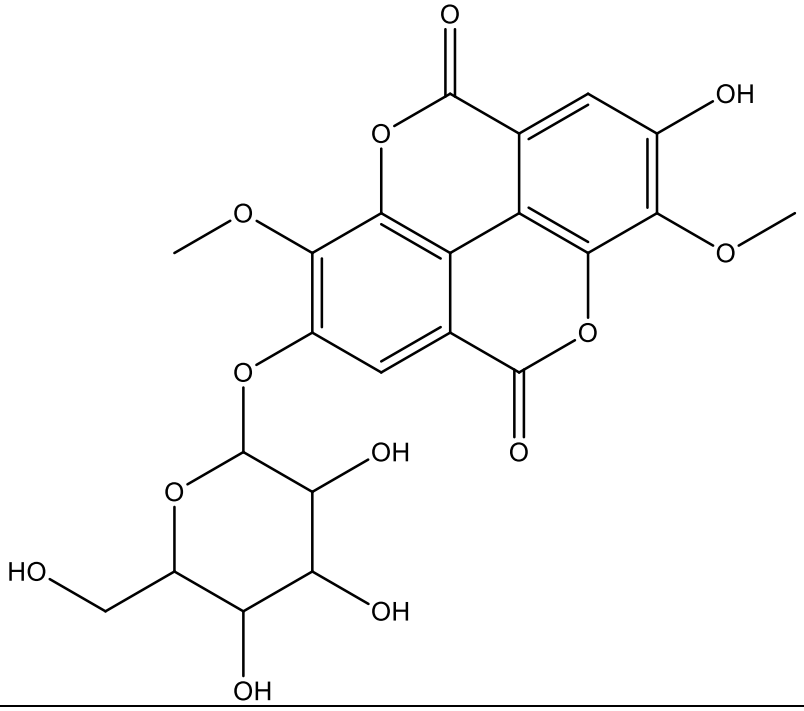
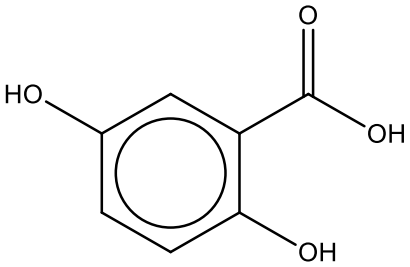
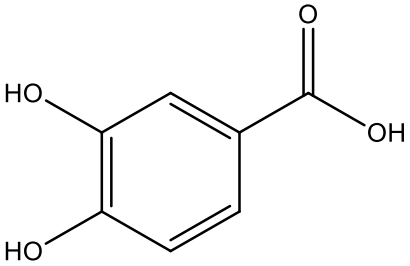
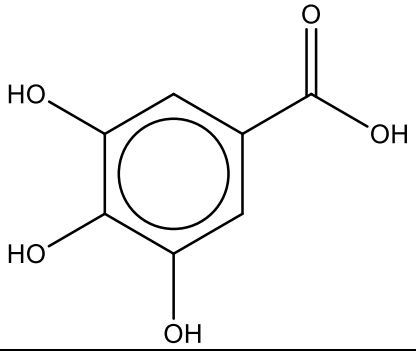
Polyphenolic substances found in the stem bark included 3, 3, 4-tri-o-methylellagic acid **8**, 3, 3, 4 - tri-o-methylellagic acid – 4 - d-glucoside **9**, gentisic **10**, protocatechuic acid **11**, gallic acid **12**, chebulagic acid **13** and chebulinic acid **14**. The stem bark also contained flavogallonic acid **15**, bislactone **16**, castalagin **17**, and ellagic acid **7**, [12]. 4H-1-Benzopyran-4-one **18**, and (S)-7-((2-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2,3-dihydro-5-hydroxy-2-(4-methoxy-3(phenylmethoxy)phenyl) -4H – 1 - benzo-pyran-4-one **19**. The leaf contained -5-hydroxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-7-olate **20**, catechin **21**, quercetin **22**, isoquercetin **23**, rutin **24**, vitexin **25**, kaempferol **26**, and procyanidin B2 **27** [12]. Analysed essential oils with the aid of GC-MS obtained by hydro-distillation using a Clevenger-type apparatus from the leaf, stem bark and root of *A. leiocarpus* revealed the prominence of z-9-octadecenoic acid **28**, n-hexadecanoic acid **29**, n-octadecanoic acid **30** and methylhexadecanoate **31** [13].

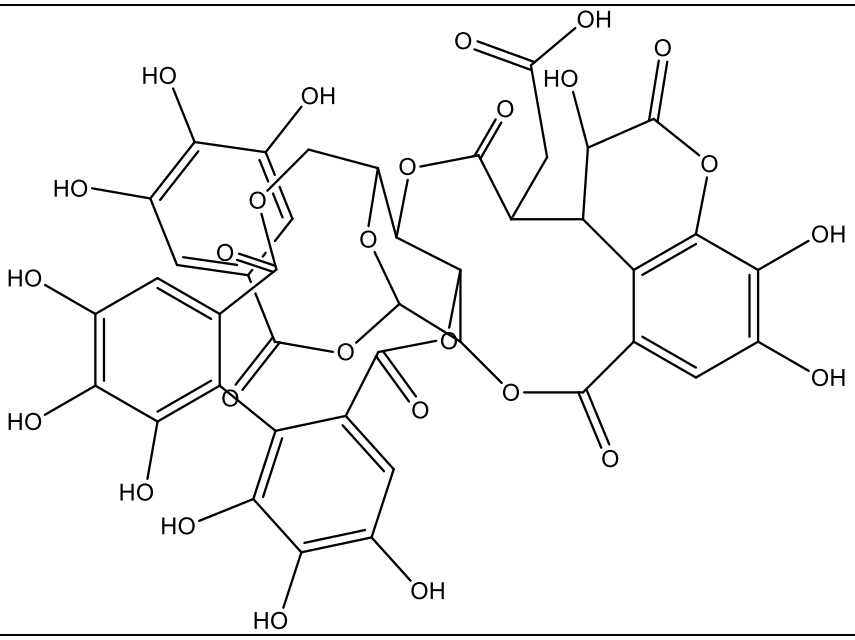
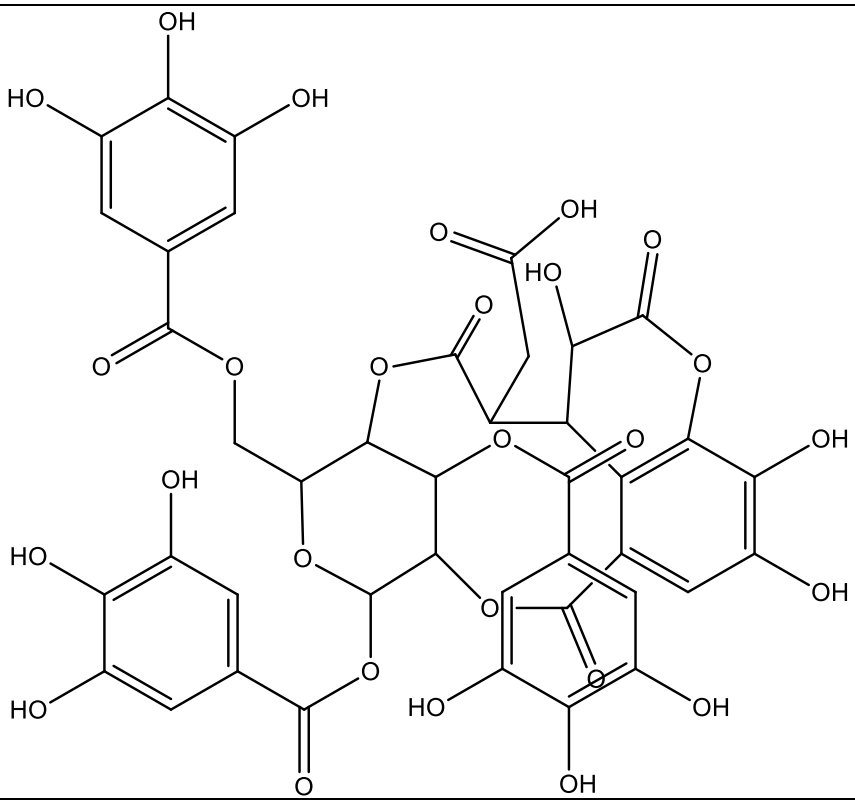
Table 1. Some Phytochemical Compounds in *A. leiocarpus*

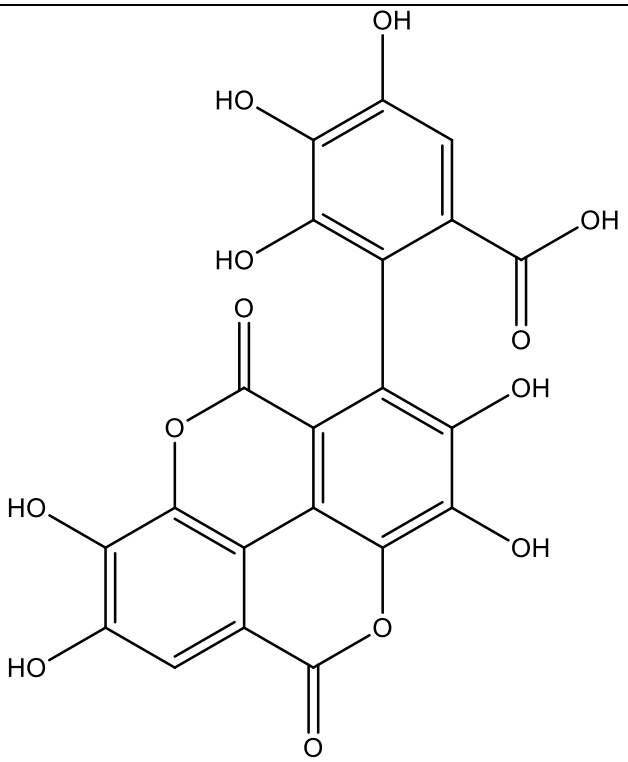
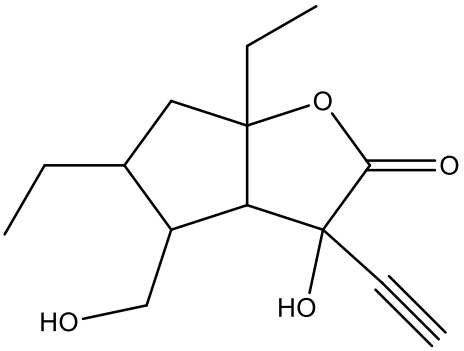
Compound ID	Structure	Name	Plant part
1		Ellagitannin	Leaf and Stem bark
2		(4S,6aR,6bS,8aR,14bR)-4-(hydroxymethyl)-4,6a,6b,8a,11,11,14b-heptamethyl-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-3-ol	Stem bark

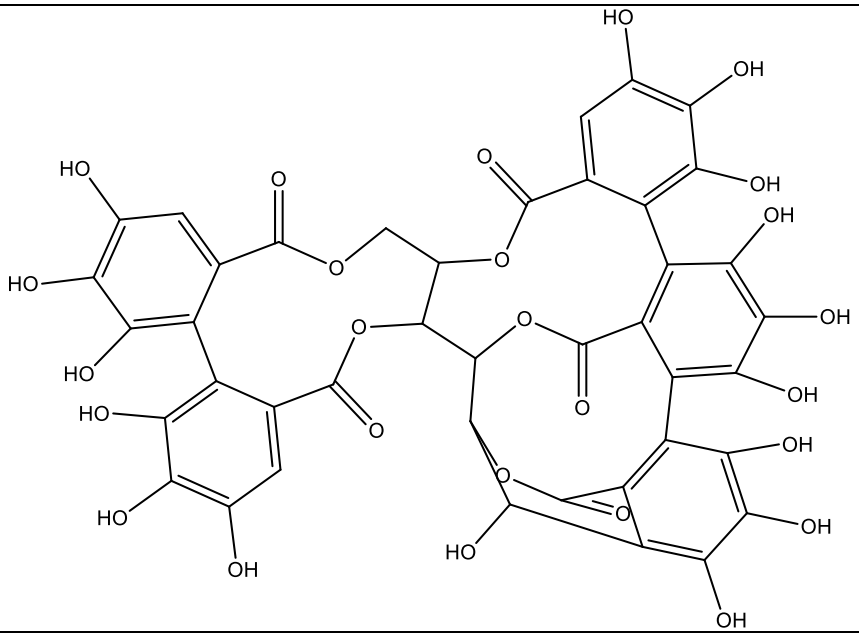
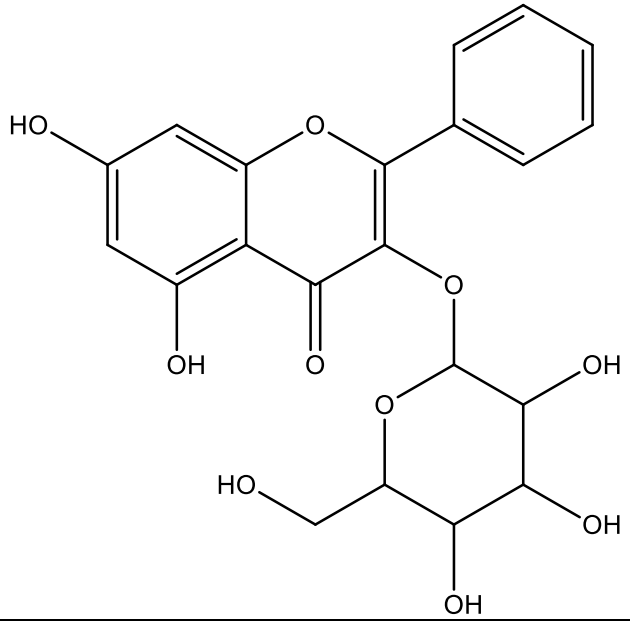
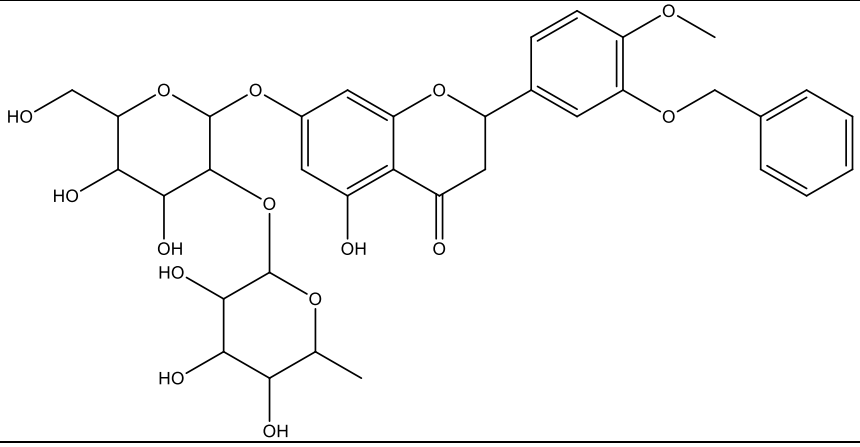
3		methyl 10-hydroxy-2-(hydroxymethyl)-2,6a,6b,9,9,12a-hexamethyl-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-icosahydropicene-4a-carboxylate	Stem bark
4		Sericoside	Stem bark
5		Serinic acid	Stem bark

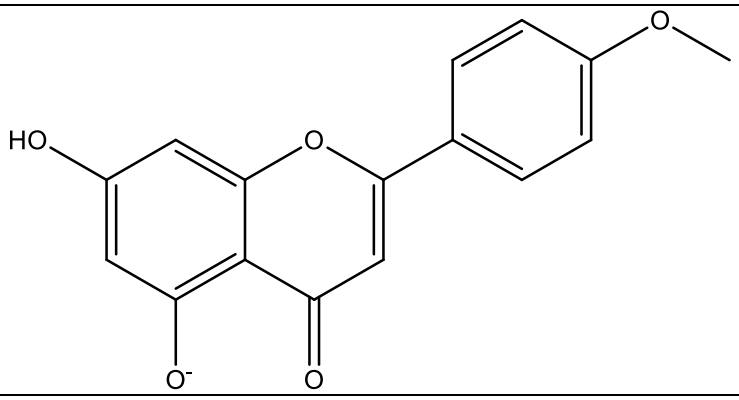
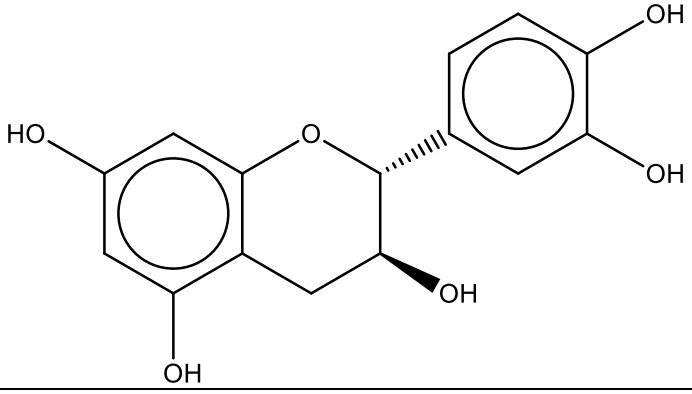
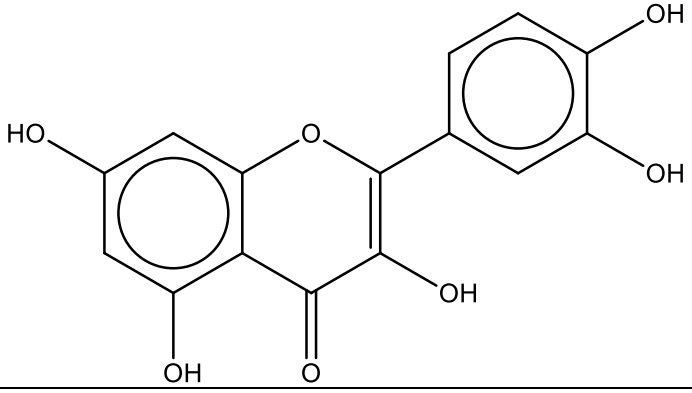
6		Arjungenin	Stem bark
7		2,3,7,8-tetrahydroxychromeno [5,4,3-cde] chromene-5,10-dione	Stem bark
8		3,3,4-tri-o-methylellagic acid	Stem bark

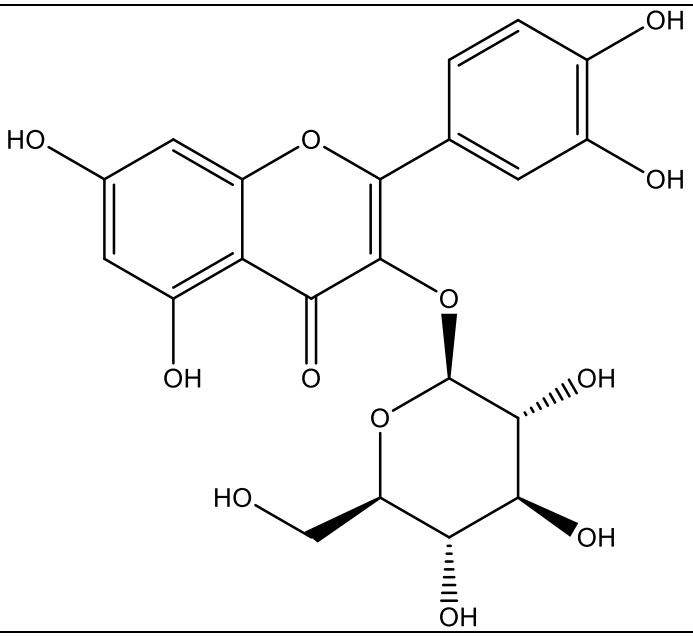
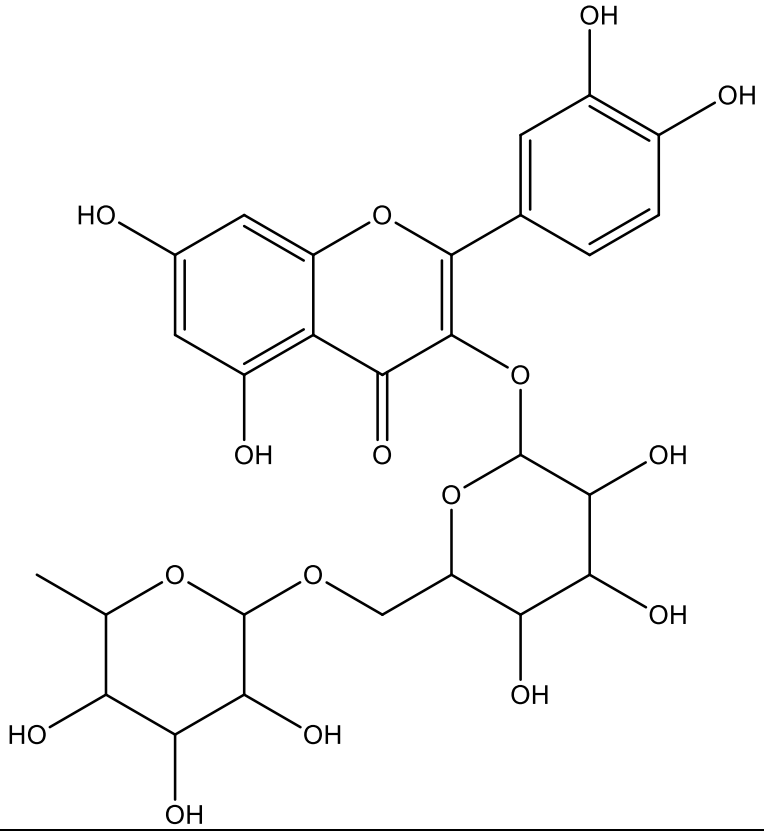
9		3,3,4-tri-o-methylellagic acid-4-d-glucoside	Stem bark
10		Gentisic	Stem bark
11		Protocatechuic acid	Stem bark
12		Gallic acid	Stem bark

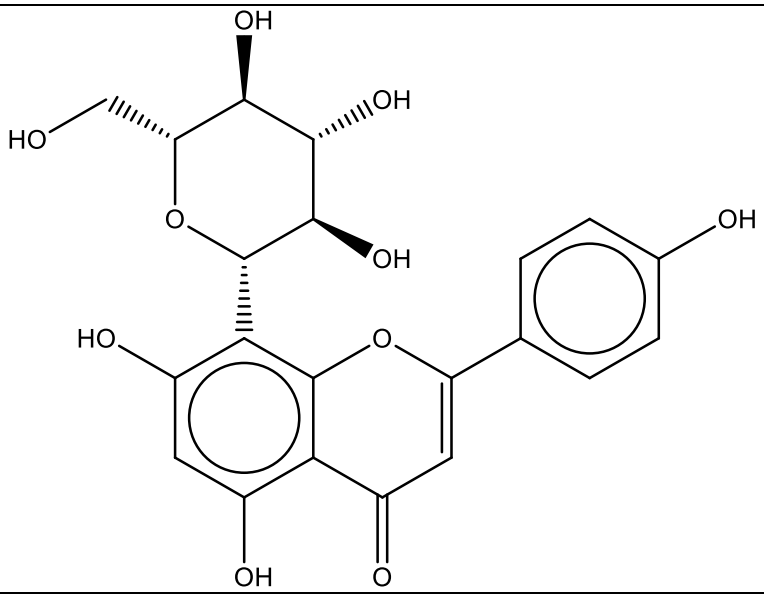
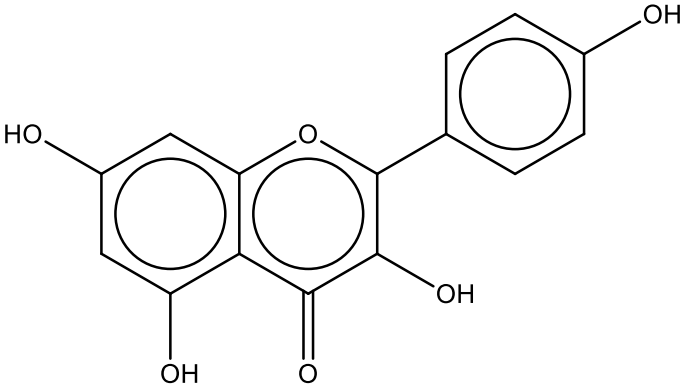
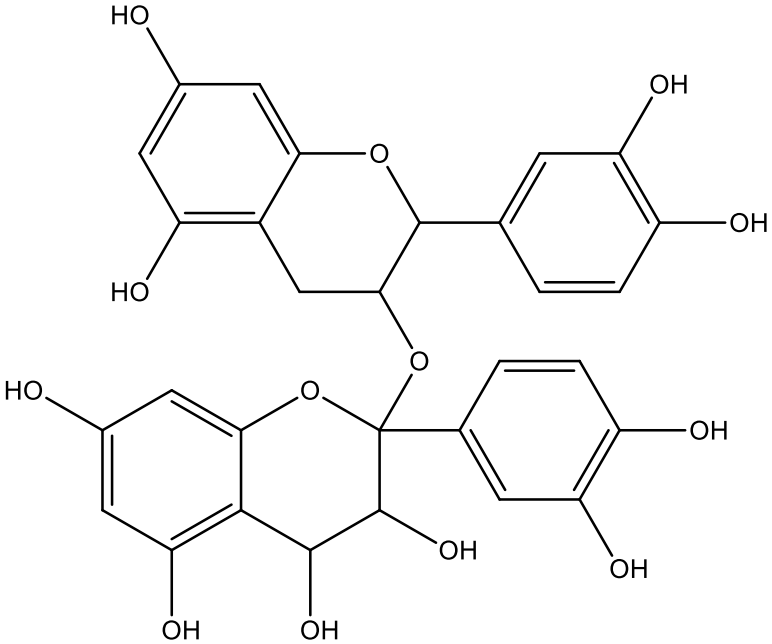
13		Chebulagic acid	Stem bark
14			

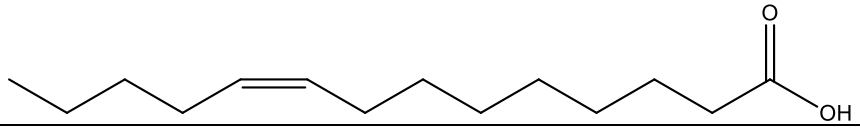
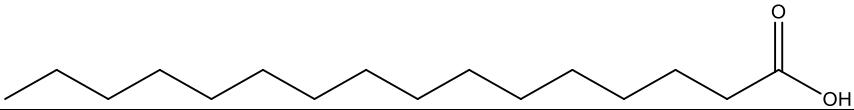
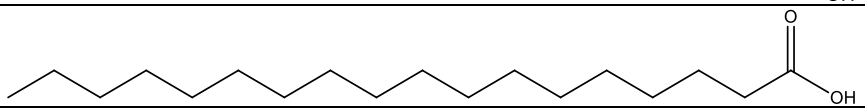
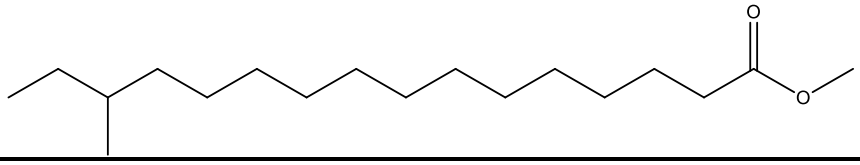
15		Flavogallonic acid	Stem bark
16		Bislactone	Stem bark

17		Castalagin	Stem bark
18		4H-1-Benzopyran-4-one	Stem bark
19		(S)-7-((2-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2,3-dihydro-5-hydroxy-2-(4-methoxy-3(phenylmethoxy)phenyl) -4H-1-benzopyran-4-one	Stem bark

20		-5-hydroxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-7-olate	Leaf
21		Catechin	Leaf
22		Quercetin	Leaf

23		Isoquercetin	Leaf
24		Rutin	Leaf

25		Vitexin	Leaf
26		Kaempferol	Leaf
27		Procyanidin B2	Leaf

28		z-9-octadecenoic acid	Leaf, Stem bark and Root
29		n-hexadecanoic acid	Leaf, Stem bark and Root
30		n-octadecanoic acid	Leaf, Stem bark and Root
31		Methylhexadecanoate	Leaf, Stem bark and Root

5. Nutritional Values

The proximate analysis of the leaf of *A. leiocarpus* revealed a high content of crude protein (17.31%). The mineral analysis showed high levels of calcium and potassium, moderate levels of magnesium, iron and zinc, and low levels of copper and manganese [41]. Sawdust from *A. leiocarpus* (Hardwood) is more beneficial for growing mushrooms with a good nutritional composition that can promote good health in man [42].

6. Pharmacological Activities

A. leiocarpus has been subjected to a variety of *in vivo* and *in vitro* biological evaluations. This plant is equally known as a source of antimicrobial agents and for treatments of a variety of infection-related ailments [43]. Some of the pharmacological evaluations of the plant are as highlighted.

Antioxidant and Anti-hyperlipidaemic Characteristics

The aerial plant extract and supernatant of *A. leiocarpus* root bark significantly reduced serum and hepatic triglyceride levels, the amount of VLDL (Very Low-Density Lipoprotein) cholesterol and hyperlipidemic levels in mice. The crude extract and constituent fractions showed significant overall antioxidant activity [44]. It was discovered that *A. leiocarpus* crude extract and fractions possessed strong antioxidant [45] and anti-hyperlipidemic properties. The polyphenolic-rich extract of the plant may be useful in treatment of *Diabetes mellitus* [46]. *A. leiocarpus* leaves and stem bark extracts were similarly found to inhibit glucosidase activity [47]. The extract and the supernatant fraction of the roots of *A. leiocarpus* demonstrated a strong antidiabetic potential by hyperglycemia reduction, hyperlipidemia and glucose intolerance in rats induced with

diabetes [48,49]. In cases when insulin is unaffordable, *A. leiocarpus* can be used as an unconventional treatment for diabetes-related oxidative stress [50,51]. In diabetic patients, a crude ethanol extract of *A. leiocarpus* stem bark lowers blood glucose levels [52,53].

Antimicrobial Potentials

The antimicrobial properties of *A. leiocarpus* support the beliefs of traditional healers that the plant's roots and stem bark can treat a variety of diseases [54,55]. Various antimicrobial activities which include antibacterial and antifungal activities of the plant have been established as highlighted.

Antibacterial effects

The root of the plant reportedly possesses huge antibacterial potential against pathogenic organisms which include *Escherichia coli*. The root material is sold in Nigeria as chewing sticks for the prevention of oral infections and mouth odour. The study suggested that plants with huge antibacterial potential against oral germs could also possess extended activities against throat infections, gum disease, and tooth decay [56,57]. In another evaluation, the tested isolates exhibited resistance to the crude leaf extract of *A. leiocarpus* [58,59]. The *in vitro* susceptibility of five bacteria, including *Staphylococcus aureus, Escherichia coli, Klebsiella aerogens, Pseudomonas aeruginosa,* and *Salmonella typhi* to the leaf, bark, and root extracts of *A. leiocarpus* revealed the strong antibacterial properties of the extracts [60,61].

Anti-fungal effects

A plant source of antifungal activity is *A. leiocarpus* [62-64]. The *in vitro* antifungal activity of root extracts from *Anogeissus leiocarpus* against *Aspergillus niger*, *Aspergillus fumigatus*, *Penicillium species*, *Microsporum audouinii*, and *Trichophyton rubrum* was investigated using the radial growth technique. The extracts inhibited the growth of all the test organisms significantly. The minimum inhibitory concentrations (MIC) and minimum fungicidal concentrations (MFC) of the extracts ranged from 0.03 to 0.07 g/mL and 0.04 to 0.08 g/mL, respectively. *A. leiocarpus* appears to be effective as an antifungal drug [65]. The *in vitro* susceptibility of two fungi, *Candida albicans* and *Aspergillus niger*, to the leaf, bark, and root extracts of *A. leiocarpus* revealed the strong antifungal properties of the extracts [60].

Anti-plasmodial Activities

A. leiocarpus stem bark fractions and crude methanol extracts were found to be highly effective against a field isolate of *Plasmodium falciparum*. The study therefore validated the traditional use of this herb as an effective malaria treatment option [66]. The methanolic extract of *A. leiocarpus* has been considered locally to have the same antimalarial activities as artemisinin derivatives in malaria-infected organisms [67,68].

Antidiarrheal Effects

The aqueous extract of *A. leiocarpus* leaves exhibited antidiarrheal properties by delaying intestinal peristalsis and decreasing gastrointestinal output of fluids and electrolytes. This explains why this plant is used to treat diarrhoea in conventional medicine [69,70].

Anticancer and Anti-ulcerogenic Effects

A possible source of anticancer through the angiogenesis pathway is *A. leiocarpus* [71]. According to Olugbami *et al*. [72], extracts from the leaves and roots of *A. leiocarpus* can inhibit the rapid replication of cancer cells. Ehrlich ascites carcinoma cell lines were prevented from proliferating by the root extract of *A. leiocarpus*, whilst liver cancer HepG2 cell proliferation was equally inhibited by the ethanolic leaf extract [73]. Bioactive compounds which include elagic acid, castalagin, and flavogallonic acid from *A. leiocarpus*, have been demonstrated to inhibit the proliferation of cancer cells *in vitro* [74]. Methanol extract of *A. leiocarpus* leaves inhibited cholinesterase activity while the tyrosinase activity was suppressed by a methanol extract of the stem bark [38].

The effects of acetic acid-induced ulcerative colitis in rats were studied in relation to *A. leiocarpus* leaf aqueous extract. The aqueous extract of *A. leiocarpus* leaves exhibited anti-colitis actions by increasing superoxide dismutase (SOD) and catalase (CAT) levels, decreasing glutathione (GSH) levels, and elevating superoxide dismutase (GSH) levels while lowering MDA (Malonidialdehyde) and NO (Nitric oxide) levels. The extract preserved normal haematological parameters and treated inflammation brought on by acetic acid at doses of 100 and 200 mg/kg [75,76].

Antinociceptive and Anti-pyretic Activities

In a recent study involving acid-induced writhing in Wistar rats' model, the anti-nociceptive and antipyretic properties of *A. leiocarpus* aqueous leaf extract were examined. The extract was also assessed for safety using the median lethal dose (LD_{50}). The extract significantly ($p < 0.05$) reduced/eliminated the induced pain and pyrexia at doses of 200 and 400 mg/kg in a way that was equivalent to the positive controls. *A. leiocarpus* aqueous leaf extract reportedly possesses antinociceptive and antipyretic properties [77].

Effects on Reproductive System

A. leiocarpus stem bark extract significantly modifies the activities of phosphodiesterase-5, arginase, and acetylcholinesterase in male rats receiving paroxetine treatment thereby altering sexual behaviour and boosting anti-oxidant status, as well as biomolecules such as total thiol, malondialdehyde, nonprotein thiol and nitric oxide levels. These actions indicate some potential mechanisms that may under-line their application in the treatment of erec-tile dysfunction induced by anti-depressants [78,79,80]. *A. leiocarpus* extract

has a pro-fertility effect. As a result, it serves as a good alternative for treating male infertility [80].

7. Conclusion

A. leiocarpus, a ubiquitous plant in the tropical woodlands and savannas is a multi-medicinal plant. Its folkloric applications which include the management of cough, wounds, stomach infections, tuberculosis, diarrhoea, and malaria make it highly desirable. Its other applications in the management of erectile dysfunction, antimicrobial, antibacterial, anticancer, antifungal, antioxidant, antinociceptive and antipyretic, anti-plasmodial activities among others makes it a target plant for more extensive investigations. Alkaloids, tannins, terpenoids, flavonoids, cardiac glycosides, and saponins are the secondary metabolites that have been found in *A. leiocarpus*. While the compounds identified in the plant include gentisic, gallic acids, chebulagic acid, bislactone, castalagin, catechin, quercetin and some others, many more chemical compounds are yet to be identified and characterized particularly from the root, wood, fruit and flower which have been grossly underexplored. The increasing demand for more potent antimicrobial agents makes the investigation of important underexplored folkloric medicinal plant such as *A. leiocarpus* more imperative particularly for the discovery of a drug lead. Future work should focus on the establishment of the possible mechanism of action of the identified compounds, discovery of potential drug leads and establishment of the toxicity of the extracts and constituent compounds. Apparently, more robust *in vivo* and holistic clinical studies are necessary to fully validate the traditional claims on the plant.

8. Conflict of Interest

The authors declare that there is no conflict of interest.

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