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Review Article

OLAX SUBSCORPIOIDEA OLIV. (OLACACEAE): AN ETHNOMEDICINAL AND PHARMACOLOGICAL REVIEW

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Abstract

Background: *Olax subscorpioidea* Oliv. (Olacaceae) is a woody shrub that is widely distributed in Africa. It has trado-medicinal importance and is used in the treatment of asthma, cancer, convulsion, diabetes, intestinal worm infections, jaundice, mental illnesses, neurodegenerative disorders, sexually transmitted infections, swellings and rheumatism, and yellow fever.

Aims: To review available literature on the phytochemistry, ethnobotany, pharmacology and toxicity of *Olax subscorpioidea* Oliv.

Method: Published findings were searched in online databases such as Web of Science, Scopus, Pubmed, Google Scholar and other relevant sources, and the data were sorted by relevance. Combinations of keywords used in the search include *Olax subscorpioidea*, Olacaceae, Olax, Ewe Ifon, and African medicinal plants.

Results: The presence of alkaloids, anthraquinones, cardiac glycosides, flavonoids, phenolic compounds, proanthocyanidins, saponins, tannins and triterpenes has been reported from *O. subscorpioidea*. Several secondary metabolites have been identified, importantly the cytotoxic santalbic acid from the seeds. Bioactivity studies on this plant demonstrated its medicinal potential mainly as an analgesic, anthelmintic, anti-arthritic, antidepressant, antihyperglycaemic, anti-inflammatory, antioxidant, antimalarial and antimicrobial agent. Oral acute toxicity of the leaf extracts in rats appears to be negligible.

Conclusion: Published literature available to date on *O. subscorpioidea* Oliv. provides some preliminary scientific basis for the ethnomedicinal uses of this plant. However, some ethnomedicinal uses have not been scientifically validated yet, and similarly, only a limited amount of information is available on properly isolated and identified phytochemicals from this plant that link to its bioactivities.

INTRODUCTION

Olax subscorpioidea is a shrub or tree which belongs to the family Olacaceae. The family Olacaceae comprises about 30 genera and about 200 species (Rogers, 2006). The genus *Olax* has more than 50 species of evergreen trees or shrubs. The name *Olax* has its origin in a Latin word which means odorous or malodorous due to the unpleasant smell of some parts of *Olax* plants, including the roots and stem barks of *O. subscorpioidea*. It can grow to a height of about 10 metres. The branches are slender, long and often hang downwards. The fruit is green while unripe but the ripe one is yellow. The roots and cut stem bark have garlic smell.

It is commonly called by several names by the local people, but the common name in English is Stink Ant forest (West African Herbal Pharmacopoiea, 2020). In Nigeria, the Yoruba people of Southwestern Nigeria call it "Ewe Ifon," it is known as "Aziza" in Nsukka, "Ukpakon" among Esan people in Edo (Victoria et al., 2010), "Gwaanon kurmii" in Hausa, "Osaja or Igbulu" in Igboland and "Ocheja" among the Igalas (Odoma et al., 2015). The Fon or Dahomey people of Benin Republic know it as "Amitin"; Dioula people of Burkina Faso call it "Kouassoumbara"; it is known as "Samanua" (Akan), "hacbéchémon zaku" (Akye) and "akanji baka" (Ando) in Côte d'Ivoire; "Ahoohenedua" (Twi) in Ghana; "Gwano kurmi" (Gwandara) in Nigeria/Niger (West African Herbal Pharmacopoiea, 2020).

GEOGRAPHICAL DISTRIBUTION

O. subscorpioidea grows in most of the West and Central African countries (Figure 1). It can be found in Senegal, Nigeria (Ayandele & Adebiyi, 2007), Cameroon, Côte d'Ivoire, and the Democratic Republic of the Congo (Kazeem et al., 2015).

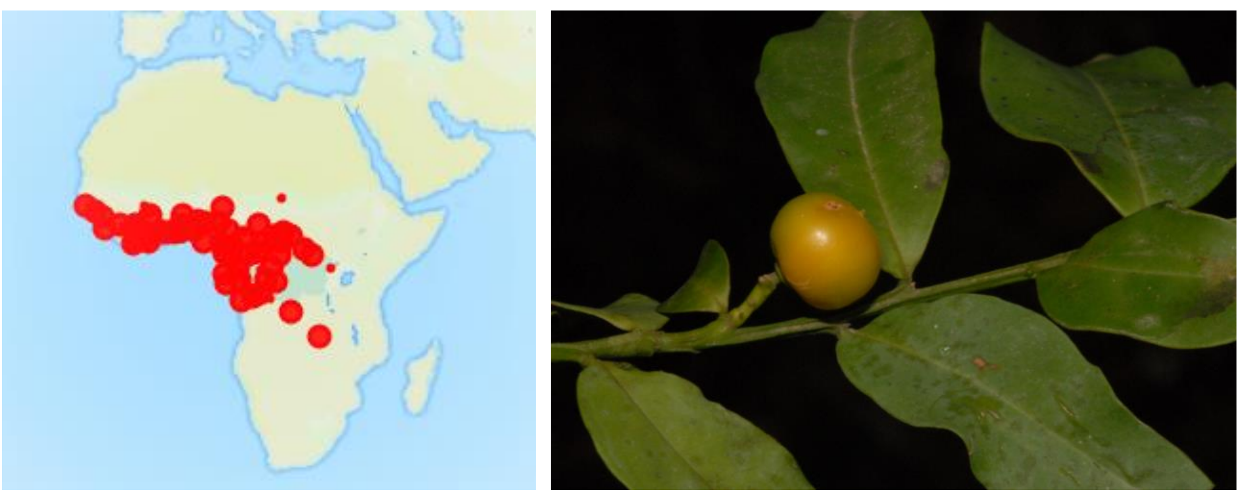


Figure 1. Geographical distribution (African Plant Database, 2022) and appearance of *O. subscorpioidea* Oliv. (Brunken et al., 2008)

SCIENTIFIC CLASSIFICATION

The scientific classification of *Olax subscorpioidea* Oliv. is shown below (The Plant List, 2013).

Kingdom:	Plantae
Clade:	Angioperms
Order:	Santalales
Family:	Olacaceae
Genus:	*Olax*
Species:	*Olax subscorpioidea* Oliv.
Synonyms:	*Olax chariensis* A. Chev, *Olax durandii* Engl., *Olax laurentii* (De Wild.) Engl., *Olax schlechteri* Engl., and *Ptychopetalum laurentii* De Wild.

ETHNOMEDICINAL USES

O. subscorpioidea maintains a rich medicinal usefulness among the Yoruba people in South-western Nigeria (Ajao et al., 2022) (Table 1). Historically, *O. subscorpioidea* (whole plant) is a part of medicinal recipes used for healing in most West and Central African countries (Table 1). This plant has also found its usefulness in foods (Kuete et al., 2011; Dzoyem et al., 2014). The oral decoction of the leaves of *O. subscorpioidea* has been traditionally used in the treatment of convulsion and mental illnesses (Nazifi et al., 2015), constipation, diabetes mellitus (Olabanji et al., 2014), Guinea worm, jaundice and venereal diseases such as infections of *Neisseria gonorrhea* (Okoli et al., 2007; Chukwuma et al., 2015), oedema, pains and swellings (Okoli et al., 2007; Chukwuma et al., 2015; Odoma et al., 2015). The root is used for the treatment of asthma (Sonibare & Gbile, 2008; Fatokun et al., 2016;), cancer (Soladoye et al., 2010), constipation and reduction of fat in pregnancy (Okoli et al., 2007), diabetes mellitus (Soladoye et al., 2012), rheumatoid arthritis (Ogunmefu & Gbile, 2012) and typhoid fever (Fadimu et al., 2014). The decoction of the roots with other plants such as *Alafia barteri* leaf, *Calliandra portoricensis* root, *Clausena anisata* stem bark; *Triclisia subcordata* leaf*, Xylopia aethiopica, Tephrosia vogelii* stem bark, *Anthocleista djalonensis* root, *Macaranga barteri* stem bark and potash is used in the management of breast cancer among Abeokuta people in Ogun State, Nigeria (Gbadamosi & Erinoso, 2016). The stem bark is used in treating infectious diseases (Ayandele & Adebiyi, 2007). The root is also used in Côte d'Ivoire to treat intestinal worm and malaria (Koné et al., 2012; Kipre et al., 2015). Stem and root barks have been reported to be used in treating jaundice, malaria and sexually transmitted infection in Ekiti State, Nigeria (Kayode, 2015).

The Gwandara tribe (Nigeria) use the whole plant to treat mental illnesses (Ibrahim et al., 2007). The root, leaf and stem bark are traded in Lagos (Nigeria) as a remedy for guinea worms, jaundice, mental disorder, toothache, venereal diseases, and yellow fever (Olowokudejo et al., 2008). In Ibadan (Nigeria), the seeds of *O. subscorpioidea* mixed with other plants such as *Xylopia aethiopica* and *Tetrapleura tetraptera* then with traditional black soap are used in the treatment of scalp infections in children. Aqueous decoction of the roots together with other recipes is used in treating abscess (Aworinde & Erinoso, 2015). A survey of the indigenous recipe used in the management of haemorrhoids in six southwestern states in Nigeria included *O. subscorpioidea* (Soladoye et al., 2010). The root decoction is used in Ferkessedougou and Tiassale (Cote d'Ivoire) for the management of anaemia (Koné et al., 2012). An ethnobotanical survey revealed that *O. subscorpioidea* root is used in Bauchi Local Government, Bauchi State (Nigeria) as an aphrodisiac (Sabo et al., 2018).

Table 1. Traditional uses of *Olax subscorpioidea* Oliv. Among different people groups in Africa.

Region/Tribe	Local Name	Plant Part	Traditional Uses	Sources
Yoruba and Esan, Nigeria	Ifon, Ukpakon	Leaf	Yellow fever, pains, oedema	(Okoli et al., 2007; Ajao et al., 2022)
Ekiti, Nigeria	Ifon	Leaf Root stem	*Neisseria gonorrhoea* infections, jaundice, constipation, worm infections	(Okoli et al., 2007, Kayode, 2015)
South-western Nigeria	Ifon	Leaf, root	Diabetes mellitus	(Soladoye et al., 2012; Olabanji et al., 2014)
Yoruba, Nigeria	Ewe Ifon	Leaf	Convulsion in children	(Oyedapo et al., 1997)
Ogun, Nigeria	Ifon	Root	Cancer, breast cancer	(Soladoye et al., 2010; Gbadamosi & Erinoso, 2016; Popoola et al., 2016)
Gwandara, Nigeria	Gwano kurmi	Whole plant	Mental illness	(Ibrahim et al., 2007)
Lagos, Nigeria	Ifon	The root, leaf, stem bark	Jaundice, yellow fever, toothache, mental disorder, guinea worms, venereal diseases	(Olowokudejo et al., 2008)
Ferkessedougou and Tiassale, Cote d'Ivoire	–	Root decoction	Anaemia	(Koné et al., 2012)
Ibadan, Nigeria	Ifon	Root	Abscess in children	(Aworinde & Erinoso, 2015)
South-western Nigeria	Ifon	Root	Haemorrhoids	(Soladoye et al., 2010)
Igala, North Central Nigeria	Ocheja	Leaf	Swellings and pains	(Odoma et al., 2015)
Esanland, Nigeria	Ukpakon	Root	Reduction of fat in pregnancy, constipation	(Okoli et al., 2007)
Akan, Akye & Ando, Cote d'Ivoire	Samanua, hacbéchémon zaku, and akanji baka	–	Intestinal worm and malaria	(Koné et al., 2012)
South-western Nigeria	Ifon	Root	Asthma	(Sonibare & Gbile, 2008; Fatokun et al., 2016)
Bauchi, Nigeria	Gwaanon kurmii	Root	Aphrodisiac	(Sabo et al., 2018)
South-western Nigeria	Ifon tutu	Stem bark	Rheumatism	(Ogunmefu & Gbile, 2012)
Ibadan, Nigeria	Igi Ifon	Stem bark	Neurodegenerative diseases	(Sonibare & Ayoola, 2015)

PHYTOCHEMISTRY

Most of the phytochemical studies carried out on this plant to date is qualitative preliminary phytochemical screening without isolation and identification of individual phytochemicals. The methanol extract of *O. subscorpioidea* roots was found to contain alkaloids, anthraquinones, flavonoids, glycosides, proanthocyanidins, saponins, steroids, tannins and terpenes (Victoria et al., 2010; Gbadamosi et al., 2017) (Table 2). A similar preliminary phytochemical screening of the stem bark revealed the presence of alkaloids, flavonoids and steroids in both aqueous and ethanol extracts. The aqueous extract also contained saponins and tannins (Ayandele & Adebiyi, 2007). Nazifi et al. (2015) reported the presence of alkaloids, carbohydrate, cardiac glycosides, flavonoids, saponins and tannins in the methanol leaf extract of *O. subscorpioidea* while Odoma et al. (2015) reported their presence in the aqueous, *n*-butanol, ethyl acetate and *n*-hexane fractions obtained from methanol extract. A methanol seed extract was reported to contain alkaloids, anthraquinones, flavonoids, phenols, tannins and triterpenes (Fankam et al., 2011).

Some compounds reported from the leaf and seed of *O. subscorpioidea* are shown in Figure 3. The first compound reported from this plant is santalbic acid (*trans*-II -octadecen-9-ynoic acid). Santalbic acid (also known as ximenynic acid) was isolated from the seed of *O. subscorpioidea* and it was evaluated against *Artemia salina* for general toxicity (Cantrell et al., 2003). Santalbic acid was previously isolated and characterized from the kernels of *Santalum acuminatum* which showed antimicrobial activity (Jones et al., 1995). Other compounds revealed by HPLC analysis of the *n*-butanol leaf extract of *O. subscorpioidea* include caffeic acid, quercetin, morin and rutin (Adeoluwa et al., 2019). The GC-MS analysis of the *n*-hexane leaf extract indicated the presence of *n*-hexadecanoic acid (palmitic acid), 7,10,13-hexadecatrienoic acid and methyl ester, hentriacontane, 9,17-octadecadienal (Z)-, 9,12-octadecadienoic acid (*Z,Z*)-, squalene, nonacosane, octadecanoic acid (Oladipupo et al., 2018). No compounds have been isolated from the root and stem bark of this plant (Agbabiaka & Adebayo, 2021).

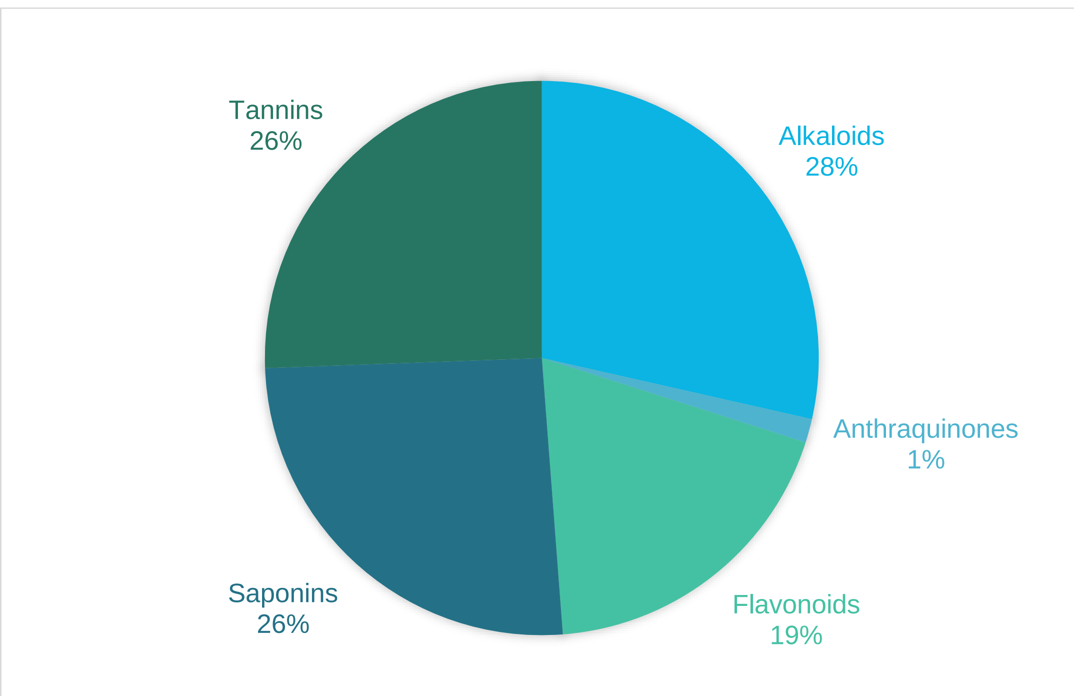
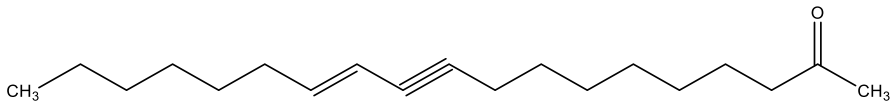


Figure 2. Phytochemical constituents of *O. subscorpioidea* Oliv. (Gbadamosi et al., 2017).

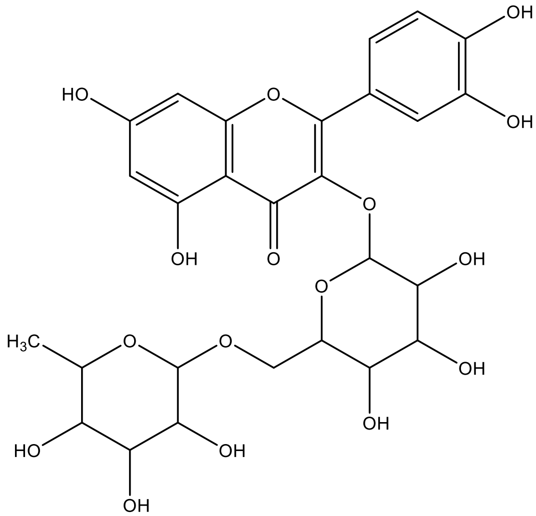
Table 2. Compounds identified from *O. subscorpioidea* Oliv.

Compounds	Method of Identification	Plant Parts	Solvents of Extraction	Biological Activities	Source
Santalbic acid	Flash Chromatography, prep-HPLC	Seed	Methanol	Brine shrimp toxicity	(Cantrell et al., 2003)
Quercetin	HPLC analysis	Leaf	*n*-Butanol	nd	(Adeoluwa et al., 2019)
Morin	HPLC analysis	Leaf	*n*-Butanol	nd	(Adeoluwa et al., 2019)
Rutin	HPLC analysis	Leaf	*n*-Butanol	nd	(Adeoluwa et al., 2019)
Caffeic acid	HPLC analysis	Leaf	*n*-Butanol	nd	(Adeoluwa et al., 2019)
n-Hexadecanoic acid (palmitic acid)	GC-MS analysis	Leaf	*n*-Hexane	nd	(Oladipupo et al., 2018)
7,10,13-Hexadecatrienoic acid and methyl ester	GC-MS analysis	Leaf	*n*-Hexane	nd	(Oladipupo et al., 2018)
Hentriacontane	GC-MS analysis	Leaf	*n*-Hexane	nd	(Oladipupo et al., 2018)
9,17 Octadecadienal (Z)-, 9,12 Octadecadienoic acid (Z,Z)-	GC-MS analysis	Leaf	*n*-Hexane	Nd	(Oladipupo et al., 2018)
Squalene	GC-MS analysis	Leaf	*n*-Hexane	nd	(Oladipupo et al., 2018)
Nonacosane	GC-MS analysis	Leaf	*n*-Hexane	nd	(Oladipupo et al., 2018)
Octadecanoic acid	GC-MS analysis	Leaf	*n*-Hexane	nd	(Oladipupo et al., 2018)

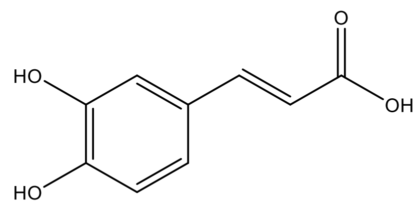
nd: activity not determined



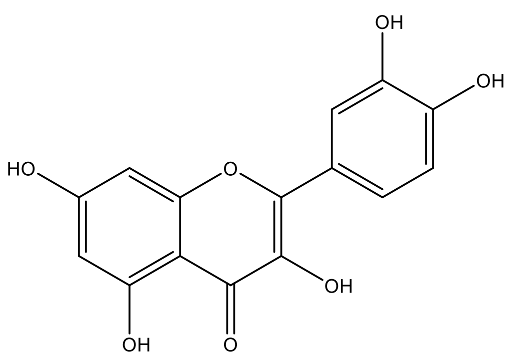
Santalbic acid*



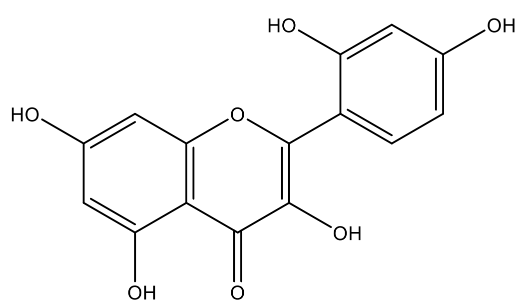
Rutin‡



Caffeic acid‡



Quercetin‡



Morin‡

Figure 3. Compounds identified from *O. subscorpioidea* Oliv. *(: from seed; ‡: from leaf).**

BIOACTIVITIES LINKING ETHNOPHARMACOLOGICAL PROPERTIES

Many scientific studies have provided preliminary evidence for some of the ethnobotanical information on *O. subscorpioidea* and suggested that this plant could be a good source of new drug candidates (Table 3). Some of the pharmacological activities that have been established in the literature include anti-arthritics, anticonvulsive, antidepressant, antidiabetic, anti-inflammatory, antimicrobial, antinociceptive, antioxidant, antiproliferative, anti-ulcer, cytotoxic, and hepatoprotective effects, among others (Agbabiaka & Adebayo, 2021; Ahmad et al., 2021).

Anticancer activity

The root, seed and leaf extracts of *O. subscorpioidea* have been investigated for their anticancer potentials. Popoola et al. (2020) demonstrated chemotherapeutic potential of *O. subscorpioidea* root through its DNA-damaging effect and ability to ameliorate cisplatin-induced oxidative stress in an animal model. Using indices such as free-radical-scavenging, protection against oxidative stress, and lipid peroxidation, antimitotic effect and DNA damage, the study demonstrated possible chemopreventive and antiproliferative potentials of the extracts. A methanol extract of *O. subscorpioidea* root demonstrated potent Nrf-2-inducing, antioxidant and anti-inflammatory effects in cell-based models as a way to further establish its mechanisms of anticancer activity (Popoola et al., 2021). The leaf extracts were shown to induce intrinsic apoptosis via mitochondrial membrane permeability transition (Adegbite et al., 2015), while a seed extract displayed significant activity against multidrug resistance in CEM/ADR5000 cells (IC_{50}: 10.65 μg/mL) (Kuete et al., 2011).

Cytotoxicity and Genotoxicity

Brine shrimp lethality assay (BSLA) and *Allium cepa* root were used to assess the general toxicity and genotoxicity of the leaf and stem extracts of *O. subscorpioidea*. The leaf extract had IC_{50} of 10.7 μg/mL against brine shrimp (*Artemia salina*) nauplii, and 47.03 and 60.16 μg/mL against *Allium cepa* root after 24 and 48 h of exposure, respectively. The stem extract had IC_{50} of 45.2 μg/mL against brine shrimp *(Artemia salina)* nauplii, and 71.87 and 81.93 μg/mL against *Allium cepa* root after 24 and 48 h of exposure (Oladipupo et al., 2019).

Anticonvulsant activity

Pentylenetetrazole-induced and strychnine-induced seizure models in rats as well as maximal electroshock test in chicks were used to evaluate the anticonvulsant effect of the methanol leaf extract of *O. subscorpioidea* at different concentrations. At a dose of 200 mg/kg, 70% protection against maximal electroshock-induced seizure in chicks and 50% protection against strychnine-induced seizure in rats were observed (Nazifi et al., 2015). The leaf extract showed mild sedative property and it ameliorated symptoms of seizures using the pentylenetetrazole-, picrotoxin- and strychnine-induced convulsion models (Adeoluwa et al., 2016).

Antinociceptive activity

An ethanol extract of the leaf exhibited significant analgesic effect in both chemical (acetic acid-induced abdominal writhing and formalin paw-licking tests) and thermal (hot plate kept at 55±0.5°C) nociception models in mice in a dose-dependent manner (Adeoluwa et al., 2014). Ishola et al. (2015) estimated that the antinociceptive effect of the aqueous leave extract of O. *subscorpioidea* is mediated via serotonin ($5\text{-}HT_2$) and dopaminergic (D_2) pathways and sensitive potassium ATP channels. The root extract also displayed significant analgesic effect by inhibiting formalin-induced pain and anti-inflammatory effect by inhibiting xylene-induced ear oedema (Popoola et al., 2016). The analgesic activity of the leaf extract was established using acetic acid writhing induction, hot plate tests and formalin pain induction models in mice. The results showed that leaf extracts reduced induced pains significantly (Odoma et al., 2015). The study by Odoma et al. (2017) suggested that the mechanisms of analgesic activity might involve serotonin, opioid and nitric oxide-l-arginine pathways.

Anti-arthritic activity

In order to provide scientific basis for the popular use of this plant as an anti-arthritic remedy, the root extract of *O. subscorpioidea* was evaluated in an induced arthritis rat model using the chicken type II-complete Freund's adjuvant (CFA) (Ezeani et al., 2019). The aqueous and ethanol extracts of the roots showed significant anti-arthritic potential when compared to the positive reference drug indomethacin.

Table 3. Biological activities of *O. subscorpioidea* Oliv.

Activity	Plant part	Solvent of Extraction	Type of Experiment	Results	Sources
Anticancer	Seed, root	Methanol	*In vitro*	Seed: IC_{50}: 10.65 μg/mL against CEM/ADR5000 cells	(Kuete et al., 2011; Popoola et al., 2020)
Cytotoxicity	Seed, leaf, stem bark	Methanol	*In vitro* Brine shrimp lethality assay (BSLA)	Leaf IC_{50}: 10.7 µg/mL; Stem IC_{50}: 45.2 µg/mL; Seed IC_{50}: 44.8 µg/mL	(Cantrell et al., 2003; Oladipupo et al., 2019)
Antidepressant	Leaf	Ethanol	*In vivo*	Active	(Adeoluwa et al., 2016)
Antiulcer	Root	Methanol	*In vivo*	Active	(Victoria et al., 2010)
Anti-arthritis	Root	Aqueous, ethanol	*In vivo*	Active	(Ezeani et al., 2019)
Analgesic	Leaf, root	Ethanol	*In vivo*	Active	(Adeoluwa et al., 2014; Ishola et al., 2015; Odoma et al., 2015, 2017)
Antimicrobial	Root, seed	Ethanol, methanol	*In vitro*	MIC: 5–40 mg/mL (bacteria) MIC: 0.048–0.097 mg/mL (*Candida* sp)	(Ayandele & Adebiyi, 2007; Fankam et al., 2011; Dzoyem et al., 2014)
Antioxidant & anti-inflammatory	Leaf	Hydro-ethanolic, methanol, butanol, aqueous	*In vivo*	Active	(Konan et al., 2015; Odoma et al., 2015; Odoma et al., 2020)
Anthelmintic	Root	90% ethanol	*In vitro*	Active	(Koné et al., 2012)
Anticonvulsant	Leaf	Methanol	*In vivo*	Active	(Nazifi et al., 2015)
Hepatoprotective	Leaf	Hydro-ethanolic, ethanol	*In vivo*	Active	(Konan et al., 2015; Okoro et al., 2021)
Anti-hyperglycaemic	Leaf	n-hexane, ethyl acetate, acetone	*In vitro &* *In vivo*	n-hexane IC_{50}: 0.72 mg/mL (α-amylase); 0.10 mg/mL (α-glucosidase)	(Kazeem et al., 2015)
Hypolipidemic	Root	Ethanol	*In vivo*	Active	(Gbadamosi et al., 2017)

Antioxidant and anti-inflammatory activities

Konan et al. (2015) reported the *in vivo* antioxidant properties of the hydro-ethanolic leaf extract in experimental animals. Rats were injected intraperitoneally with hydro-ethanolic leaf extract *of O. subscorpioidea* at 25 mg/kg and 100 mg/kg body weight for 7 days and CCl_4 on the 7th day. The animals were sacrificed on the 8th day. Serum sample was collected and then analysed for antioxidant activity using DPPH free radical scavenging assay. Pretreatment of animals with hydro-ethanolic extracts of *O. subscorpioidea* was observed to significantly enhance serum antioxidant potential compared with CCl_4 treated group (Konan et al., 2015). Odoma et al. (2015) also reported anti-inflammatory potential of the methanol leaf extract using the carrageenan-induced hind paw oedema model in rats. In a 2020 study, using *n*-butanol and aqueous leaf fractions of *O. subscorpioidea,* a significant reduction in the concentrations of pro-inflammatory cytokines IL-1, VEGF & EGF, and a significant increase in the concentrations of anti-inflammatory cytokines IL-5, IL-6 & IFN-γ in the carrageenan-induced hind paws exudates in rats were observed. This study suggested that the plant's extracts inhibit pro-inflammatory cytokines IL-1, VEGF & EGF; and/or enhance the production of anti-inflammatory cytokines IL-5, IL-6 & IFN-γ (Odoma et al., 2020). Aqueous leaf extract was reported to have inhibited carrageenan-induced oedema by more than 70% (Ishola et al., 2015)

Antimicrobial activity

O. subscorpioidea root (ethanol extract) showed activities against Gram-negative bacteria, Gram-positive bacteria and some fungal species, with zones of inhibition ranging from 7.2 to 21.5 mm, and MICs ranging from 5 to 40 mg/mL (Ayandele & Adebiyi, 2007). Fankam et al. (2011) also reported antibacterial effect of the methanol seed extract against some strains of gram-negative bacteria, including MDR strains. *O. subscorpioidea* fruit extract also exhibited significant inhibitory activity against *Candida albicans* and *Candida tropicalis* (MIC, 0.097 mg/mL & 0.048 mg/mL, respectively). Oral pre-treatment of experimental rats with *O. subscorpioidea* fruit extract also displayed promising antifungal activity by reducing *Candida albicans* cell loads (cfu/mL) in rat blood (Dzoyem et al., 2014). An *in vitro* antimicrobial study against clinical oral isolates which include fungal (*Aspergillus fumigatus* and *Candida albicans*) and bacterial (*Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus species* and *Lactobacillus acidophilus*) strains was conducted using methanol stem bark extract of *O. subscorpioidea.* A more significant growth inhibition was observed for *Aspergillus fumigatus* (MIC: 51.2 mg/mL; zone of inhibition: 20–26.5 mm) (Orabueze, Amudalat, 2016).

Anthelmintic activity

A single oral dose of 400 mg/mL of *O. subscorpioidea* root extract was able to achieve total worm burden reduction of 60.2% and female worm burden reduction of 84.5% in *Schistosoma mansoni* infected mice (Koné et al., 2012).

Anti-ulcer activity

A methanol extract of *O. subscorpioidea* root produced dose-dependent anti-ulcer effect in indomethacin- and ethanol-induced ulcer models in experimental animals. A more significant reduction of the ulcers was observed in the ethanol model than the indomethacin model (Victoria et al., 2010).

Antidepressant activity

The antidepressant potential of *O. subscorpioidea* ethanol leaf extract was evaluated using the forced swimming, tail suspension, yohimbine-induced lethality and reserpine-induced depression models. The extract exhibited dose-dependent decrease in the immobility time in forced swimming test and in tail suspension test, and reduced diarrhoea in the reserpine-induced depression test (Adeoluwa et al., 2015). Adeoluwa et al. (2019) reported the involvement of monoaminergic pathways in the depression inhibitory effect of the butanol leaf extract of *O. subscorpioidea* in rats.

Antisickling activity

O. subscorpioidea together with other 27 plants formed a recipe for the management of sickle cell anaemia among indigenous people in Ibadan, Nigeria. An *in vitro* antisickling effect of this recipe was investigated using the method which involves inhibiting sodium metabisulphite-induced sickling of red blood cells collected from patients without symptoms of sickle cell disease. The result showed 63.4% inhibition of sickling of HbSS red blood cells (Egunyomi et al., 2009).

Hepatoprotective activity

A study by Konan et al. (2015) induced hepatotoxicity in rats using carbon tetrachloride (CCl_4), manifested with increase in the concentration of serum total bilirubin, GOT, GGT and ALP, as well as reduction in the serum activities of albumin, α_1-globulin and total protein. Pre-treatment with the hydro-ethanolic leaf extract of *O. subscorpioidea* was reported to decrease enzyme activities and total bilirubin levels. Histopathological examinations of the liver cells also revealed no significant cellular damage, as evidence of hepatoprotective properties. Similar results were reported for the ethanol extracts of *O. subscorpioidea* leaf and stem bark in CCl_4-induced hepatic injury in rats (Okoro et al., 2021).

Antihyperglycaemic activity

The *in vitro* effect of the *n*-hexane, ethyl acetate and acetone extracts of the leaf of *O. subscorpioidea* on diabetic-related α-amylase and α-glucosidase activities was examined. With *n*-hexane extract displaying highest inhibition on the enzymes (IC_{50}: 0.72 mg/mL for α-amylase; and 0.10 mg/mL for α-glucosidase), it was further studied in an *in vivo* model by administering it orally to starch-loaded rats. The rats' blood glucose level was monitored for 2 h. A significant reduction in the sugar levels of the rats was noted (Kazeem et al., 2015).

Hypolipidaemic activity

The lipid lowering potential (hypolipidaemic) of the ethanol root extract of *O. subscorpioidea* was studied in rats in order to provide scientific support for its use in the management of obesity in traditional medicine. A significant decrease was noted in total cholesterols (TC), triglycerides (TG) and low density lipoprotein (LDL) of extract-treated animal groups (Gbadamosi et al., 2017).

Antimalarial activity

The effect of *O. subscorpioidea* on the improvement of chloroquine efficacy was investigated by Kipre et al. (2015). When examined alone, the ethyl acetate leaf extract had IC_{50} of 32.47±0.31µg/mL and 28.16±0.5µg/mL against chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum,* respectively. However, addition of *O. subscorpioidea* at a concentration of 12 µg/mL to chloroquine against *Plasmodium falciparum* resistant strain FCB1 significantly reduced its IC_{50} to 43.5±1.5 nM from 105.05±2.87 nM (Kipre et al., 2015).

TOXICITY

An oral median lethal dose (LD_{50}) of >5,000 mg/kg was obtained for aqueous and butanol leaf fractions of O. *subscorpioidea* in mice and rats. However, a decreased value (2,154 mg/kg) was obtained for hexane fraction in mice and 3,808 mg/kg in rats (Odoma et al., 2015). The result also showed that the leaf extract induced some alterations on liver and kidney functions biomarkers (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, urea and creatinine, total bilirubin, total albumin) and haematopoietic parameters (white blood cells, % lymphocyte, % neutrophils, haemoglobin levels), but had no deleterious anatomical alterations on rats' liver and kidney tissues (Abiodun et al., 2014).

ETHNOMEDICINAL USES YET TO BE CONFIRMED BY SCIENTIFIC REPORT

Although the folklore claims of *O. subscorpioidea* have been largely established in the literature by both *in vivo* and *in vitro* experiments, evidence has not been provided for some of the traditional uses. In an ethnobotanical survey by Sabo et al. (2018), traditional users mentioned *O. subscorpioidea* root as a recipe in the management of sexual problems. It has also been reported that the plant is used in the management of asthma (Sonibare & Gbile, 2008) and haemorrhoids (Soladoye et al., 2010). There is scanty information in the literature linking *O. subscorpioidea* directly to aphrodisiac effect, asthma, constipation, haemorrhoids, hyperbilirubinaemia (jaundice) and viral infections (yellow fever) (Table 1).

CONCLUSIONS

O. subscorpioidea Oliv. is a key ingredient in Western-African traditional medicinal practices, with many ethnomedicinal uses, including as an aphrodisiac and in the management of asthma, cancer, constipation, convulsions, diabetes, haemorrhoids, jaundice, neurodegenerative disorders, rheumatism, sexually transmitted diseases (STDs), swelling and pains, worm infections in children, and yellow fever. Several of these popular uses have been confirmed by the scientific literature. However, its roles as an aphrodisiac and in the management of a few other conditions which include asthma, haemorrhoids and viral infection are yet to be reported. Similarly, even though several studies confirmed anticancer potentials of the root extracts of *O. subscorpioidea,* with other studies suggesting the mechanisms of its chemopreventive and chemotherapeutic actions, its anticancer bioactive molecules have not been characterised. There is also a need for thorough phytochemical investigation of various extracts of several plant parts, especially the bioactive compounds responsible for the bioactivities of this plant.

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AUTHORS CONTRIBUTION

(Y.A.A.) (B.B.S.) (A.A.F.) (L.N.) (S.D.S.) Conceptualization, Methodology, Formal analysis, Investigation, Writing, Review & Editing.

Conflict of Interests

Authors declare no conflicts of interests.

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REFERENCES

Abiodun, H. A., Oluwatobi, S. A., Joseph, A. O. O., Oyetomiwa, O. F., & Kenechukwu, B. O. (2014). Toxicological evaluation of extract of *Olax subsorpioidea* on albino Wistar rats. *African Journal of Pharmacy and Pharmacology*, *8*(21), 570–578.

Adegbite, O. S., Akinsanya, Y. I., Kukoyi, A. J., Iyanda-Joel, W. O., Daniel, O. O., & Adebayo, A. H. (2015). Induction of rat hepatic mitochondrial membrane permeability transition pore opening by leaf extract of *Olax subscorpioidea*. *Pharmacognosy Research*, *7*, S63–S68.

Adeoluwa, A. O., Aderibigbe, O. A., Agboola, I. O., Olonode, T. E., & Ben-Azu, B. (2019). Butanol Fraction of *Olax Subscorpioidea* Produces Antidepressant Effect: Evidence for the Involvement of Monoaminergic Neurotransmission. *Drug Research*, *69*(1), 53–60.

Adeoluwa, O. A., Aderibigbe, A. O., & Agu, G. O. (2016). Pharmacological Evaluation of Central Nervous System Effects of Ethanol Leaf Extract of *Olax Subscorpioidea* in Experimental Animals. *Drug Research*, *66*(4), 203–210.

Adeoluwa, O.A., Aderibigbe, A.O., & Bare, A.G. (2015). Evaluation of Antidepressant-like Effect of *Olax Subscorpioidea* Oliv. (Olacaceae) Extract in Mice. *Drug Research*, 65(6), 306–311.

Adeoluwa, O. A., Aderibigbe, A. O., & Olonode, E. T. (2014). Antinociceptive property of *Olax subscorpioidea* Oliv (Olacaceae) extract in mice. *Journal of Ethnopharmacology*, *156*, 353–357.

African Plant Database (version 4.0.0). Conservatoire et Jardin botaniques de la Ville de Genève and South African National Biodiversity Institute, Pretoria. Retrieved July 2022, URL: http://africanplantdatabase.ch

Agbabiaka, T. O., & Adebayo, I. A. (2021). The medicinal properties of *Olax subscorpioidea*. In *Phytomedicine*, 555–580. Elsevier.

Ahmad, M. H., Jatau, A. I., Alshargi, O. Y., Julde, S. M., Mohammed, M., Muhammad, S., Mustapha, S., Bala, A. A., Wada, A. S., Aminu, M., & Usman, A. M. (2021). Ethnopharmacological uses, phytochemistry, pharmacology, and toxicology of *Olax subscorpioidea* Oliv (Olacaceae): a review. *Future Journal of Pharmaceutical Sciences*, *7*(115).

Ajao, A. A. nun, Mukaila, Y. O., & Sabiu, S. (2022). Wandering through southwestern Nigeria: An inventory of Yoruba useful angiosperm plants. *Heliyon*, *8*(1), e08668. https://doi.org/10.1016/j.heliyon.2021.e08668

Aworinde, D. O., & Erinoso, S. M. (2015). Ethnobotanical investigation of indigenous plants used in the management of some infant illnesses in ibadan, south-western nigeria. *African Journal of Traditional,* *Complementary and Alternative Medicines*, *12*(1), 9–16.

Ayandele, A. A., & Adebiyi. (2007). The phytochemical analysis and antimicrobial screening of extracts of *Olax subscorpioidea*. *African Journal of Biotechnology*, *6*(7), 868–870.

Brunken, U., Schmidt, M., Dressler, S., Janssen, T., Thiombiano, A. & Zizka, G. 2008. West African plants - A Photo Guide. www.westafricanplants.senckenberg.de Forschungsinstitut Senckenberg, Frankfurt/Main, Germany.

Cantrell, C.L., Berhow, M. A. Phillips, B. S., Duval, S. M., Weisleder, D., & Vaughn, S. F. (2003). *Phytomedicine,* 10, 325–333

Chukwuma, EC., Soladoye, MO., Feyisola, R. (2015). Traditional medicine and the future of medicinal Plants in Nigeria. *Journal of Medicinal Plant Studies*, *3*(4), 23–29.

Dzoyem, J. P., Tchuenguem, R. T., Kuiate, J. R., Teke, G. N., Kechia, F. A., & Kuete, V. (2014). In Vitro and In Vivo antifungal activities of selected Cameroonian dietary spices. *BMC Complementary and Alternative Medicine*, *14*.

Egunyomi, A., Moody, J. O., & Eletu, O. M. (2009). Antisickling activities of two ethnomedicinal plant recipes used for the management of sickle cell anaemia in Ibadan, Nigeria. *African Journal of Biotechnology*, *8*(1), 020–025.

Ezeani, N. N., Ibiam, U. A., Orji, O. U., Igwenyi, I. O., Aloke, C., Alum, E., Aja, P. M., & Ugwu, O. P. C. (2019). Effects of aqueous and ethanol root extracts of *Olax subscopioidea* on inflammatory parameters in complete freund's adjuvant-collagen type II induced arthritic albino rats. *Pharmacognosy Journal*, *11*(1), 16–25.

Fadimu, O.Y., Iliya, M. & Sani, R.Z. (2014). Ethnomedicinal Survey of Anti-Typhoid Plants in Ijebu Ode Local Government Area of Ogun State, Nigeria. *International Journal of Science and Nature*, 5(2), 332-336.

Fankam, A. G., Kuete, V., Voukeng, I. K., Kuiate, J. R., & Pages, J. M. (2011). Antibacterial activities of selected Cameroonian spices and their synergistic effects with antibiotics against multidrug-resistant phenotypes. *BMC Complementary and Alternative Medicine*, *11*.

Fatokun, O. T., Wojuola, T. E., Esievo, K. B., & Kunle, O. F. (2016). Medicinal plants used in the management of asthma : a Review. *European Journal of Pharmaceutical and Medical Research*, *3*(7), 82–92.

Gbadamosi, I. T., & Erinoso, S. M. (2016). A review of twenty ethnobotanicals used in the management of breast cancer in Abeokuta, Ogun State, Nigeria. *African Journal of Pharmacy and Pharmacology*, *10*(27), 546–564.

Gbadamosi, I. T., Raji, L. A., Oyagbemi, A. A., & Omobowale, T. O. (2017). Hypolipidemic effects of *Olax subscorpioidea* oliv. root extract in experimental rat model. *African Journal of Biomedical Research*, *20*(3), 293–299.

Ibrahim, J. A., Muazzam, I., Jegede, I. A., Kunle, O. F., & Okogun, J. I. (2007). Ethno-medicinal plants and methods used by Gwandara tribe of Sabo Wuse in Niger State, Nigeria, to treat mental illness. *African Journal of Traditional, Complementary and Alternative Medicines*, *4*(2), 211–218.

Ishola I. O, Akinyede A, Lawal S. M, Popoola T. D, L. A. M. (2015). Antinociceptive and anti-inflammatory effects of Olax subscorpioidea Oliv. (Olacaceae) leaf extract in rodents: possible mechanisms of antinociceptive action Ismail. *West African Journal of Pharmacy*, *26*(1), 99–112.

Jones, G. P., Raol, K. S., Tucker, D. J., Richardson, B., Barnes, A., & Rivet, D. E. (1995). Antimicrobial activity of santalbic acid from the oil of *Santalum acuminatum* (Quandong). *International Journal of Pharmacognosy,* 33(2), 120-123

Kayode, J. (2015). Stem Barks and Roots Extravitism in Ekiti State Nigeria: Need for Conservation as a Sustainable Innovation in Healthcare Management in Rural Areas. *American Journal of BioScience*, *3*(2), 28.

Kazeem, M. I., Ayeleso, A. O., & Mukwevho, E. (2015). *Olax subscorpioidea* Oliv. leaf alleviates postprandial hyperglycaemia by inhibition of α-amylase and α-glucosidase. *International Journal of Pharmacology*, *11*(5), 484–489.

Kipre, G. R., Akakpo-Akué, M., Brice Bla, K., & Djaman, A. J. (2015). Assessment of the combined action of chloroquine and *Olax subscorpioidea* on plasmodium falciparum strains resistant in vitro culture. *International Journal of Innovation and Applied Studies*, *11*(4), 947–952.

Konan, K., Justin, N. K., Lydie, B., Souleymane, M., Francis, Y. A., & David, N. J. (2015). Hepatoprotective and in vivo antioxidant activity of *Olax subscorpioidea* Oliv. (Olacaceae) and Distemonathus benthamianus Baill. (Caesalpiniaceae). *Pharmacognosy Magazine*, *11*(41), 111–116.

Koné, W. M., Koffi, A. G., Bomisso, E. L., & Tra Bi, F. H. (2012). Ethnomedical study and iron content of some medicinal herbs used in traditional medicine in Cote d'Ivoire for the treatment of anaemia. *African Journal of Traditional, Complementary and Alternative Medicines*, *9*(1).

Koné, W. M., Vargas, M., & Keiser, J. (2012). Anthelmintic activity of medicinal plants used in Côte d'Ivoire for treating parasitic diseases. *Parasitology Research*, *110*(6), 2351–2362.

Kuete, V., Krusche, B., Youns, M., Voukeng, I., Fankam, A. G., Tankeo, S., Lacmata, S., & Efferth, T. (2011). Cytotoxicity of some Cameroonian spices and selected medicinal plant extracts. *Journal of Ethnopharmacology*, *134*(3), 803–812.

Nazifi, A. B., Saidi, O., & Ismail, H. F. (2015). Evaluation of anticonvulsant effects of methanolic extract of *Olax subscorpioidea* Oliv. leaves in chicks and mice. *Journal of Pharmacy & Bioresources*, *12*(2), 165.

Odoma, S., Umar Zezi, A., Mohammed Danjuma, N., Ahmed, A., & Garba Magaji, M. (2017). Elucidation of the possible mechanism of analgesic actions of butanol leaf fraction of *Olax subscorpioidea* Oliv. *Journal of Ethnopharmacology*, *199*, 323–327.

Odoma, S., Zezi, A. U., Danjuma, M. N., Abubakar, A., & Magaji, G. M. (2020). Effects of aqueous and butanol leaf fractions of olax subscorpioidea oliv. On inflammatory cytokines in wistar rats. *Tropical Journal of Natural Product Research*, *4*(9), 606–611.

Odoma, S., Zezi, A. U., Danjuma, N. M., & Ahmed, A. (2015). Analgesic and anti-inflammatory activities guided- fractionation of olax suscorpioidea leaf extract in mice and rats. *Nigerian Journal of Pharmaceutical Sciences*, *14*(1), 30–43.

Ogunmefun, O.T., & Gbile, Z. O. (2012). An Ethnobotanical Study of Anti-Rheumatic Plants in South-Western States of Nigeria. *Science and Technology Research Article, 4(11), 063-066*

Okoli, R. I., Aigbe, O., Ohaju-Obodo, J. O., & Mensah, J. K. (2007). Medicinal Herbs Used for Managing Some Common Ailments among Esan People of Edo State, Nigeria. *Pakistan Journal of Nutrition*, *6*(5), 490–496.

Okoro, C. O., Aloke, C., Ibiam, U. A., Obasi, N. A., Orji, O. U., Ogbonnia, E. C., Ogbu, P. N., Emelike, C. U., Ufebe, G. O., & Ezeani, N. N. (2021). Studies on ethanol extracts of *Olax subscorpioidea* against carbon tetrachloride-induced hepatotoxicity in rats. *Pakistan Journal of Biological Sciences*, *24*(6), 724–732.

Olabanji, S. O., Adebajo, A. C., Omobuwajo, O. R., Ceccato, D., Buoso, M. C., & Moschini, G. (2014). PIXE analysis of some Nigerian anti-diabetic medicinal plants (II). *Nuclear Instruments and Methods in Physics Research, Section B: Beam Interactions with Materials and Atoms*, *318*(Part A), 187–190.

Oladipupo, A. R., Alaribe, C. S., Ariyo, I. A., Coker, H. A. B., & Ogunlaja, A. S. (2019). Cytotoxic, anti-mitotic and cytogenetic effects of the leaves and stems of *Olax subscorpioidea* Oliv. (Olacaceae) against Artemia salina nauplii and Allium cepa meristematic cells. *Macedonian Pharmaceutical Bulletin*, *65*(01), 3–10.

Oladipupo, A. R., Alaribe, C. S., Balogun, O. T., Akere, H. T., Ayanda, F. A., Toye, E. T., & Coker, H. A. B. (2018). Investigation of chemical, genotoxic and haematological properties of secondary metabolites from n-Hexane extract of *Olax subscorpioidea* oliv. (Olacaceae) leaves. *Tropical Journal of Natural Product Research*, *2*(12), 506–511.

Olowokudejo, J., Kadiri, A., & Travih, V. (2008). An ethnobotanical survey of herbal markets and medicinal plants in Lagos state of Nigeria. *Ethnobotanical Leaflets*, 12, 851-865

Orabueze IC, Amudalat AA, U. A. (2016). Antimicrobial value of Olax subscorpioidea and Bridelia ferruginea on micro-organism isolates of dental infection. *Journal of Pharmacognosy and Phytochemistry*, *5*(5), 398–406.

Oyedapo, O. O., Akindele, V. R., & Okunfolami, O. K. (1997). Effects of extracts of Olax subscorpioides and Aspilia africana on bovine red blood cells. *Phytotherapy Research*, *11*(4), 305–306.

Popoola, T. D., Awodele, O., Babawale, F., Oguns, O., Onabanjo, O., Ibanga, I., Godwin, H., Oyeniyi, T., Fatokun, A. A., & Akinloye, O. (2020). Antioxidative, antimitotic, and DNA-damaging activities of Garcinia kola stem bark, Uvaria chamae root, and Olax subscorpioidea root used in the ethnotherapy of cancers. *Journal of Basic and Clinical Physiology and Pharmacology*, *31*(3), 1–11.

Popoola, T. D., Awodele, O., Omisanya, A., Obi, N., Umezinwa, C., & Fatokun, A. A. (2016). Three indigenous plants used in anti-cancer remedies*, Garcinia kola Heckel* (stem bark), *Uvaria chamae* P. Beauv. (root) and *Olax subscorpioidea* Oliv. (root) show analgesic and anti-inflammatory activities in animal models. *Journal of Ethnopharmacology*, *194*, 440–449.

Popoola, T. D., Guetchueng, S. T., Ritchie, K. J., Awodele, O., Dempster, N. M., Akinloye, O., Sarker, S. D., & Fatokun, A. A. (2021). Potent Nrf2-inducing, antioxidant, and anti-inflammatory effects and identification of constituents validate the anti-cancer use of *Uvaria chamae* and *Olax subscorpioidea. BMC Complementary Medicine and Therapies*, *21*(1).

Rogers, Z. S. (2006). A synoptic revision of *Olax* L . (Olacaceae) in Madagascar and the Comoro Islands. *Adansonia, sér*. 3, 28(1), 71-100

Sabo, S., Otimenyin, S., Uguru, M., & Bukar, B. (2018). Ethnobotanical Survey of Medicinal Plants Used as Aphrodisiacs in Bauchi Local Government Area. *Journal of Complementary and Alternative Medical Research*, *4*(4), 1–13.

Soladoye, M. O., Adetayo, M. O., Chukwuma, E. C., & Adetunji, A. N. (2010). Ethnobotanical Survey of Plants Used in the Treatment of Haemorrhoids in South-Western Nigeria. *Annals of Biological Research*, *1*(4), 1–15.

Soladoye, M.O., Amusa, N.A., Raji-Esan, S.O., Chukwuma, E.C. and Taiwo, A.A. (2010). Ethnobotanical Survey of Anti-Cancer Plants in Ogun State, Nigeria. *Annals of Biological Research*, 1(4), 261-273.

Soladoye, M. O., Chukwuma, E. C., & Owa, F. P. (2012). An ' Avalanche ' of Plant Species for the Traditional Cure of Diabetes mellitus in South-Western Nigeria. *Journal of Natural Product and Plant Resources*, *2*(1), 60–72.

Sonibare, M. A., & Ayoola, I.O. (2015). Medicinal plants used in the treatment of neurodegenerative disorders in some parts of Southwest Nigeria. *African Journal of Pharmacy and Pharmacology*, *9*(38), 956–965.

Sonibare, M. A., & Gbile, Z. O. (2008). Ethnobotanical survey of anti-asthmatic plants in South western Nigeria*. African Journal of Traditional, Complementary and Alternative Medicines*, 5(4), 340-345.

The Plant List (2013). Version 1.1. URL: http://www.theplantlist.org/ (accessed 07/07/2022).

Victoria, U. C., Michael, U. C., & Johnny, M. U. (2010). Evaluation of the antiulcer activity of Olax subscorpioidea Oliv. roots in rats. *Asian Pacific Journal of Tropical Medicine*, *3*(1), 13–16.

West African Herbal Pharmacopoeia (2013). *West African Health Organisation (WAHO),* Burkina Faso. Pp 186-196.