Securidaca longipedunculata Fresen (Polygalaceae): A review of its ethnomedicinal uses, phytochemistry, pharmacological properties and toxicology

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Review

Securidaca longipedunculata Fresen (Polygalaceae): A review of its ethnomedicinal uses, phytochemistry, pharmacological properties and toxicology

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ABSTRACT

Ethnopharmacological relevance: Securidaca longipedunculata Fresen (Polygalaceae) is a multi-purpose plant with a long history of use in African traditional medicine to treat various sexually transmitted infections, hernias, coughs, fever, ascariasis, constipation, headaches, rheumatism, stomach ache, malaria, tuberculosis, pain, epilepsy, pneumonia, skin infections, and it is also used as an aphrodisiac for men. The current paper provides an overview of the present phytochemistry, toxicology, ethnomedicinal uses and pharmacological properties of *S. longipedunculata*.

Materials and methods: The information reported in this paper was collected from a literature search using various computerised databases including ScienceDirect, Scopus, Scielo, PubMed and Google Scholar. The extra information was sourced from various academic dissertations, theses and botanical books.

Results: Phytochemically, extracts from various parts of *S. longipedunculata*, especially the root bark, contain numerous valuable compounds including xanthones, some benzyl benzoates and triterpene saponins amongst others. Toxicity studies, both *in vivo* and *in vitro*, revealed that extracts are only toxic at relatively high concentrations. Furthermore, extracts have antimicrobial, antioxidant, antiparasitic, anti-diabetic, anti-inflammatory, antimalarial, insecticidal, pesticidal, and anticonvulsant properties.

Conclusions: S. longipedunculata is an important plant species with potential benefits in the treatment of transmissible and infectious diseases, including malaria, tuberculosis, and those caused by community acquired microorganisms. Although extracts from this species generally have little toxicity at low concentrations, further efforts are required to investigate the potential toxicity of *S. longipedunculata*. The antimicrobial properties of extracts and purified compounds against microorganisms causing sexually transmitted infections are also deserving of further research. Moreover, the pharmacokinetic properties of extracts and compounds of the species need to be explored as there is insufficient data available on these aspects.

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Abbreviations: ABTS, 2,2-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) diammonium salt; AChE, acetylcholinesterase; DPPH, 2,2-diphenyl-1-picryl-hydrazyl; IC_{50}, 50% inhibitory concentration; LD_{50}, 50% lethal dose concentration; LPS/IFN-gamma, lipopolysaccharide/interferon gamma; MIC, minimum inhibitory concentration; MBC, minimum bactericidal concentration; MFC, minimum fungicidal concentration; NO, nitric oxide; XO, xanthine oxidase; ZI, zone of inhibition

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1. Introduction

Medicinal plants serve as a source of medicines in a variety of communities for the treatment of numerous pathogenic infections, tonics for general wellbeing, as spices and condiments and for magical purposes. Some African medicinal plants have been ethnobotanically and scientifically implicated in the treatment of a variety of human infections (Van Wyk and Albrecht, 2008; Ojewole et al., 2010; Mongalo and Mafoko, 2013; Mongalo, 2013; Zongo et al., 2013). The pharmacology of these plants may be attributed to various classes of compounds occurring within these plants.

The genus *Securidaca* comprises about 80 species, characterised by papillionaceous purplish flowers and mostly scandent shrubs and lianas, which produce compounds known as securixanthones with antimicrobial and antioxidant properties (Wallnöfer, 1998; Yang et al., 2001, Yang et al., 2003, Da Costa et al., 2013). Although protected under provincial and national legislation, *S. longipedunculata* stem bark and roots are still found amongst the most traded medicinal plants in Africa (Moeng, 2010; Tabuti et al., 2012). The species is threatened by various anthropogenic and environmental conditions including seasonal fires, droughts, and debarking (Oni et al., 2014). The current paper is aimed at highlighting the phytochemical constituents, pharmacology, indigenous ethnobotanical uses, and toxicity of *S. longipedunculata* – an important multipurpose African medicinal plant.

2. Materials and methods

The information reported in this paper was collected from a literature search using various computerised databases including ScienceDirect, Scopus, Scielo, PubMed and Google Scholar. Additional information was retrieved from various academic dissertations, theses and botanical books. Key words such as *Securidaca longipedunculata*, ethnomedicinal uses, antimicrobial activity, pharmacological properties, cytotoxicity, phytochemistry, anti-inflammatory, antioxidant properties, anti-diabetic, antimalarial, pesticidal effect, antiparasitic, anthelmintic, anti-convulsant and insecticidal effect were used.

3. Description and ethnomedical uses

3.1. Botanical description and distribution

Securidaca longipedunculata Fresen (synonyms *Securidaca longipedunculata* var. *longipedunculata* or *Elsota longipedunculata*, family Polygalaceae) is a small tree up to 6 m high with a pale grey, smooth bark and oblong, more or less hairless alternate leaves that are variable in size and shape and crowded towards the stem tips (Van Wyk et al., 2009). Clustered flowers are small, pink to lilac or purple in colour, sweet scented and are produced in early summer (Van Wyk et al., 2005). Fruits are a round nut, heavily veined, occasionally smooth, oblong, purplish green when young and possess a membranous wing of about 4 cm long (Coates-Palgrave, 2005). The species is mostly distributed in various tropical African countries, including Angola, Benin, Botswana, Burundi, Cameroon, Chad, Cote d'Ivoire, Democratic Republic of Congo, Eritrea, Ethiopia, Gambia, Ghana, Guinea, Kenya,

Table 1
Ethnomedicinal uses of *S. longipedunculata* in different countries.

Country	Plant part	Uses	Reference
Zimbabwe	Roots	Venereal diseases, syphilis, pains, fever, epilepsy, pneumonia, tuberculosis.	Maroyi, 2013; Mustapha, 2013a; Viol, 2009
Nigeria	Leaves	Dislocated jaw, headaches, skin cancer, skin infections, contraceptive purposes	Mustapha, 2013a; Mustapha, 2013b
South Africa	Roots	Flu, blood purifier, aphrodisiac, psychoactive purposes	Semenya and Potgieter, 2013; Sobiecki, 2008; Moeng, 2010; Mabogo 1990
Kenya	Whole plant	Malaria, tick prevention in animals	Wanzala et al., 2012; Nguta et al., 2010a; Nguta et al., 2010b
Burkina Faso	Roots	Malaria	Nadembega et al., 2011
	Stem bark	Skin diseases	Nadembega et al., 2011
Uganda	Roots	Fever, malaria, ascariasis	Hamill et al., 2003
Nigeria	Roots	Abortion, constipation, coughs, fever, pneumonia, sexual boost, toothache, tuberculosis, rheumatism	Mustapha, 2013a; Ogunmefun and Gbile, 2012
Nigeria	Stem bark and roots	Treat infections related to nervous and circulatory system	Borokini et al., 2013
Nigeria	Stem bark	Dysentery, malaria, typhoid and frequent stomach ache	Mustapha, 2013a
Botswana	Roots	Coughs and as an aphrodisiac	Motlhanka and Nthoiwa, 2013

Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, South Africa, Sudan, Tanzania, Uganda, Zambia, Zimbabwe, Mozambique, as well as in the North West and Limpopo Provinces of South Africa (Baloyi and Tshisikhawe, 2009; Tshisikhawe et al., 2012).

3.2. Local names

In South African languages, the plant species is called violet tree, fibre tree, or Rhodesian violet (English), krinkhout (Afrikaans), umfufu (Ndebele), mupesu (TshiVenda) and mmaba in both Sotho and Tswana. In other African countries, various names in different cultural and ethnic groups have been used: es a manahi (Amharic); saggat, alali (Arabic); mwinda (Lozi); mutata (Lunda); mwinda, mpuluka (Nyanja); mupapi (Bemba); lilo (Luganda); uwar magunguna, sanya (Hausa); yodo, juto, jodo (Mandinka); mufufu (Shona); muteya, mzigi, Chipvufana, mufufu, munyapunyapu, munyazvirombo, mutangeni, umfufu (Swahili); shotora (Tigrigna); njefu, bwazi, mufufuma (Tongan); fouf (Wolof); ipeta (Yoruba) (Orwa et al., 2009).

3.3. Ethnomedicinal uses

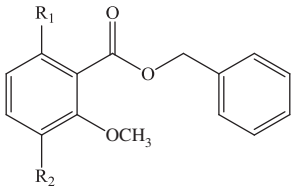
The major ethnomedicinal uses of *S. longipedunculata* in different countries are documented in Table 1. These suggest that the most commonly used plant part is the root and that the species is used in the treatment of a variety of ailments including coughs, fever, malaria, tuberculosis and sexually transmitted diseases in different geographical areas. This provides support for a pharmacological basis of the use of the plant species in the treatment of such ailments.

3.3.1. Roots

The smoke resulting from burning the root of *S. longipedunculata*, combined with that of *Zanthoxylum zanthoxyloides,* is inhaled to treat malaria and fever (Hamill et al., 2003). A root decoction may also be drunk to treat fever, malaria, hernias, gonorrhoea, palpitations, headaches, oedema, rheumatism, diabetes, sexual impotence, toothache, fungal infections and malaria (Maroyi, 2013; Ogunmefun and Gbile, 2012; Chhabra et al., 1991; Moshi et al., 2007).

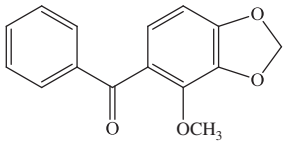
An infusion of the soaked root bark may be drunk as an aphrodisiac or mixed with other medicines and used as an emetic (Mabogo, 1990). Alternatively, a root decoction may be drunk in beer as an aphrodisiac (Motlhanka and Nthoiwa, 2013). The root bark is pulverised in water and the resulting mixture is inhaled or used to wash the head, treating excessive headache (Nordeng et al., 2013). A handful of roots are combined with the roots of *Sphedamnocarpus pruriens* subsp. *pruriens* for treating people believed to be possessed by evil spirits while the powdered root is mixed with porridge and eaten to treat epilepsy and convulsions (Sobiecki, 2008). The decoction from the root is drunk or applied topically to treat cancer (Ashidi et al., 2010).

Roots may also be ground into powder form, dissolved in water and taken orally for constipation, pneumonia, back ache, blood purification, sexually transmitted infections and as an aphrodisiac (Viol, 2009). Dried roots are soaked in water, along with *Citrus aurantifolia* and the resulting juice is taken orally for three days to treat constipation while the dried root is boiled in distilled water along with that of *Annona senegalensis* and used to treat pneumonia (Mustapha, 2013a). Moreover, the dried root is ground into powder, along with that of *Parkia biglobosa* and then taken with cow's milk as a sexual boost. The pounded root may be mixed with that of *Zanthoxylum humile* and taken with soft porridge to treat erectile dysfunction (Semenya and Potgieter, 2013).

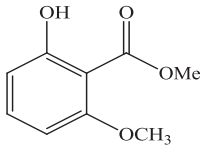


Benzyl-3-hydroxy-2-methoxybenzoate (R_1 = H, R_2 = OH)

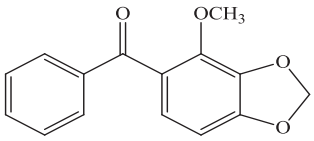
Benzyl-2-hydroxy-6-methoxybenzoate (R_1 = OH, R_2 = H)



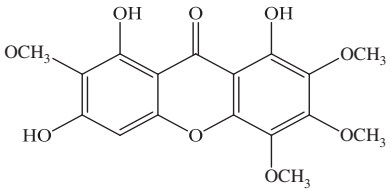
2-Methoxy-3,4-methylenedioxybenzophenone



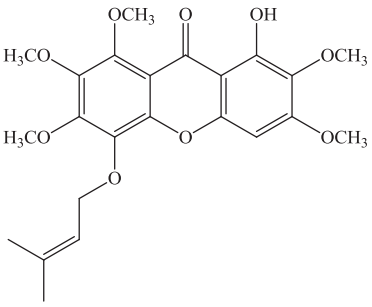
Methyl-2-hydroxy-6-methoxybenzoate



4-Methoxy-benzo [1, 3] dioxol-5-yl-phenylmethanone



1,6,8-Trihydroxy-2,3,4,7-tetramethoxyxanthone

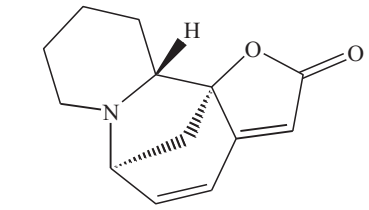


5-*O*-prenyl-1-hydroxy-3, 4, 6, 7, 8-pentamethoxyxanthone

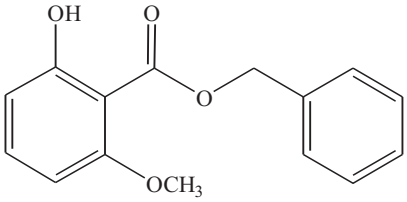
Fig. 1. Some compounds isolated from *Securidaca longipedunculata*.

3.3.2. Leaves

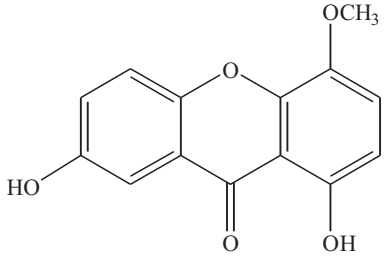
Fresh leaves are made into paste with little or no water along with the bark of *Gardenia erubescens* and applied externally twice a day for sixty-three days to treat skin cancer (Mustapha, 2013a).



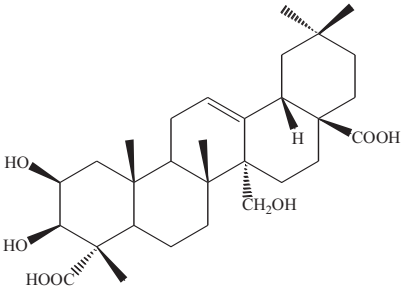
Securinine



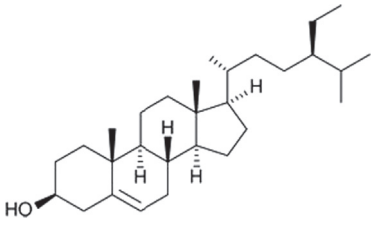
Benzyl-2-hydroxy-6-methoxybenzoate



1,7-Dihydroxy-4-methoxyxanthone



Presenegenin



β-Sitosterol

Fig. 1. (*continued*)

Moreover, fresh leaves are made into paste with little or no water along with leaves of *Jussiaea suffruticosa* and shea butter and the resulting mixture is applied externally, twice a day to treat a variety of skin infections. Dry leaves are also ground into powder and put into the fire and the resulting smoke is inhaled to treat headaches while the boiled leaves are taken orally for contraceptive purposes (Mustapha, 2013b). The leaves are either chewed fresh or both orally and nasally administered to treat epilepsy, headaches, stomach ache, infertility, snakebite, toothache and to expel the placenta (Augustino et al., 2011).

3.3.3. Whole plant

One cup from a whole plant decoction may be taken orally three times a day for three to four days to treat malaria (Nguta et al., 2010a; Nguta et al., 2010b). The decoction of the whole plant may either be drunk or used to wash the mouth and treat infections which include oral candidiasis, excessive coughing and other opportunistic infections associated with HIV/AIDS (Chinsembu and Hedimbi, 2010).

3.3.4. Stem bark

A spoonful of powdered stem bark is mixed with *Mondia whitei* (stem bark), *Uvaria afzelii* (root bark), *Allium ascalonicum* (bulb) and *Parkia biglobosa* (seeds) and then taken with hot porridge to treat a variety of viral infections (Borokini et al., 2013). The dried bark is ground into a powder and taken orally with cow's milk or porridge for fourteen days to treat dysentery (Mustapha, 2013a). A decoction from the stem bark may be taken orally to treat stomach ache, headaches, inflammation, chest complaints, abortion, jaundice, ritual suicide, constipation, snake bites, infertility problems, epilepsy and venereal diseases (Das, 2009; Bruschi et al., 2011; Oladunmoye and Kehinde, 2011; Kadiri et al., 2013). The powdered stem bark is also mixed with hot water and taken orally to treat syphilis and gonorrhoea (Hedimbi and Chinsembu, 2012).

4. Phytochemistry

Some of the compounds isolated from *S. longipedunculata* are shown in Fig. 1. The volatile oil of the roots contains large amounts of methyl salicylate (Van Wyk et al., 2005). The report agrees with those of Jayasakara et al. (2002) and Lognay et al. (2000), which revealed that the major component (over 90%) of the volatile material from the root bark is methyl-2-hydroxybenzoate (methyl salicylate). Furthermore, securinine, presenegenin, 2-hydroxybenzoate esters such as methyl 2-hydroxy-6-methoxybenzoate and its benzyl analogue were also reported. In general, most classes of compounds have been isolated from the roots, using a variety of solvents (Table 2). This may well explain the ethnomedicinal uses and hence the biological activity of the plant species.

The aqueous root and ethanol extracts yielded alkaloids, cardiac glycosides, flavonoids, saponins, tannins, volatile oils, terpenoids and some steroids (Junaid et al., 2008; Haruna et al., 2013a; Auwal et al., 2012; Gbadamosi, 2012) while chloroform and ethanol extracts indicated flavonoids, saponins, coumarins, tannins and alkaloids (Adebayo and Osman, 2012). The ethyl acetate fraction of the root contained compounds such as 1,5-dihydroxy-3,4,6,7,8-pentamethoxyxanthone, 1,7-dihydroxyxanthone, 5-O-prenyl-1-hydroxy-2,3,6,7,8-pentamethoxyxathanthone, 2-hydroxy-1, 7-dimethoxyxanthone, β-sitosterol, 1,7-dihydroxy-4-methoxyxanthone, quercetin-3-O-β-galacto-pyranoside and 3-hydroxy-6-methoxysalicylic acid (Meli et al., 2007). The compounds 1,3,6,8-tetrahydroxy-2,5-dimethoxyxanthone and 1,6,8-trihydroxy-2,3,4,7-tetra-methoxyxanthone were also isolated from the acetone extract of the fresh root bark (Meyer et al., 2008). Moreover, the hexane extract of the root indicated the presence of 1,5-dihydroxy-2,3,6,7,8-pentamethoxyxanthone, 2-hydroxy-l, 7-dimethoxyxanthone and 1,6-dihydroxyxanthone (Lannang et al., 2006).

The water and aqueous methanol extracts from the root yielded a variety of compounds in varying amounts, including gallic acid, chlorogenic acid, caffeic acid, epicatechic acid, rutin, p-coumaric

Table 2
Classes of compounds, plant parts investigated and isolated compounds from *S. longipedunculata*.

Classes of compounds	Part of plant	Solvent used	References
Saponins			
Securidacaside A and securidacaside B	Root bark	Methanol	Stevenson et al. (2009)
3-O-β-D-glucopyranosylpresenegenin-28-O-β-D-apiofuranosyl-(1,3)-β-D-xylopyranosyl-(1,4)-[β-D-apiofuranosyl-(1,3)]-α-L-rhamnopyranosyl-(1,2)-{4-O-[(E)-3,4,5-trimethoxycinnamoyl]}-β-D-fucopyranosyl ester	Roots	70% Methanol	Mitaine-Offer et al. (2010)
Presenegenin	Roots	Water	Van Wyk et al. (2005)
Flavonoids			
1,7-dihydroxy-4- methoxyxanthone	Root bark	Dichloromethane and ethyl acetate	Joseph et al. (2006), Meli et al. (2007)
Rutin	Roots	Aqueous methanol	Muanda et al. (2010)
Alkaloids			
Securinine	Roots	Water	Van Wyk et al. (2005)
Steroids			
β-Sitosterol	Roots	Ethyl acetate	Meli et al. (2007)
Glycosides			
Quercetin-3-O-D-xyloside	Leaves	Methanol	Debella et al. (2000)
Δ-Stigmasterol-3-O-D-glucopyranoside	Stem bark	Methanol	Debella et al. (2000)
Sucrose derivatives			
β-D-(3,4-disinapoyl)fructofuranosyl-α-D(6-sinapoyl)glucopyranoside and β-D-(3-sinapoyl) fructofuranosyl-α-D(6-sinapoyl)glucopyranoside	Stem bark	Methanol	De Tommasi et al. (1993)
Phenolic acids			
Sinapic acid, 4,5-dicaffeoyl-D-quinic acid, caffeic acid and 3,4,5-tricaffeoyl-D-quinic acid	Stem bark	Methanol	De Tommasi et al. (1993)
Quercetin, *p*-coumaric acid, cinnamic acid, caffeic acid and chlorogenic acid	Root	Aqueous methanol and water	Muanda et al. (2010)
Fatty acids and Triacylglycerol			
13-hydroxyoctadeca-cis-9-trans-11-dienoic acid, 11-hydroxyhexadeca-cis-7-trans-9-dienoic acid and 9-hydroxytetradeca-cis-5-trans-7-dienoic acid	Seeds	Light petroleum	Smith et al. (1979), Okoli et al. (2005)
Volatile oil			
Methyl salicylate	Root bark	Water (Hydrodistillation)	Van Wyk et al. (2005), Jayasakara et al. (2002), Lognay et al. (2000)

acid, cinnamic acid, apigenin, quercetin glucosyl and quercetin dihydrate (Muanda et al., 2010). Four highly oxygenated xanthones, muchimangins A–D, with a diphenylmethyl substituent have also been isolated from the root as minor constituents (Dibwe et al., 2012). The dichloromethane extract of the root bark yielded 4-methoxy-benzo[1,3]dioxol-5-yl-phenyl methanone and three other known compounds namely 1,7-dihydroxy-4-methoxyxanthone, benzyl-2-hydroxy-6-methoxybenzoate and methyl-2-hydroxy-6-methoxybenzoate (Joseph et al., 2006). The chloroform extract of the root contained compounds such as 2-methoxy-3,4-methylenedioxybenzophenone, benzyl 2-hydroxy-6-methoxybenzoate, 6-hydroxy-2-methoxy benzoic acid, 1,6,8-trihydroxy-2,3,4,5-tetramethoxyxanthone, 1,6-dihydroxy-2,3,4,5,8-pentamethoxyxanthone, 8-hydroxy-1,4,5,6-tetramethoxy-2,3-methylenedioxyxanthone-4,6,8-trihydroxy,1,2,3,5-tetramethoxyxanthone, 4,8-dihydroxy-1,2,3,5,6-pentamethoxyxanthone, benzyl 3-hydroxy-2-methoxybenzoate and some other xanthones (Dibwe et al., 2013).

Triterpene saponins such as 3-O-β-D-glucopyranosyl presenegenin 28-O-β-D-apiofuranosyl-(1→3)-β-D-xylopyranosyl-(1→4)-[β-D-apiofuranosyl-(1→3)]-α-L-rhamnopyranosyl-(1→2)-{4-O-[(E)-3,4,5-trimethoxycinnamoyl]}-β-D-fucopyrano ester and three other related esters have been isolated from the 70% aqueous methanol root extract (Mitaine-Offer et al., 2010).

Besides sinapoic acid, caffeic acid, 4,5-dicaffeoyl-D-quinic acid, 3,4,5-tricaffeoyl-D-quinic acid and a considerable number of monosaccharide and polysaccharide conjugates, the methanol extract of the stem bark revealed the two bitter principles β-D-(3,4-disinapoyl)(fructofuranosyl-α-D-(6-sinapoyl)glucopyranoside and β-D-(3-sinapoyl)(fructofuranosyl-α-D-(6-sinapoyl)glucopyranoside (De Tommasi et al., 1993). Although many compounds have been isolated from the root and root bark, there is a need to further explore the phytochemistry of the stem bark and leaves of the species.

5. Toxicology

The aqueous root bark extract was slightly toxic to albino rats with an LD_{50} of 0.771 g/kg (Auwal et al., 2012), while Agbaje and Adekoya (2012) reported an LD_{50} of 3.16 g/kg when administered orally to rats. Moreover, acute toxicity studies of the aqueous whole root extract on mice revealed LD_{50} values of 1.740 g/kg and 0.020 g/kg for the oral and intraperitoneal application routes respectively (Adeyemi et al., 2010), while Dapar et al. (2007) reported an LD_{50} of 0.037 g/kg when aqueous root extracts were administered orally to albino rats (Sprague Dawley strain). Elsewhere, the 80% ethanol extract of the root bark exhibited an LD_{50} of 0.547 g/kg against albino mice (Keshebo et al., 2014). These findings may well suggest that the root bark extract has greater acute toxicity than the whole root extract following oral administration. In a repeated dose toxicity study, there was no mortality observed when varying doses of 0.3, 0.9 and 2.7 g/kg of the aqueous root extract were administered orally on a daily basis for a period of 28 days to Swiss albino mice (Etuk et al., 2006). Besides the method of preparation of the extracts, the difference in LD_{50} may be due to differences in collection site, geographical area and the season of collection. However, there is no data in the literature on the administration of various isolated compounds from *S. longipedunculata* to mice or rats.

Table 3
Pharmacological properties of extracts from *Securidaca longipedunculata* Fresen.

Activity investigated	Tested material	Model used	Tested doses	Controls	Activity and results	Experimental evidence assessment	Reference
Antiparasitic activity	Roots, water extract	*In vitro* studies using trichomonads grown in modified Diamonds medium	50 mg/ml, serially diluted	Metronidazole used as a positive control	MIC of 0.10 mg/ml after 24 h of incubation	Positive evidence based	Fernandes et al. (2008)
	Roots, 70 % aqueous methanol	Larvae directly exposed to plant extracts	0.02, 0.10, 0.50, 2.50 mg/ml extract	Positive control:1 mg/ml of levamisole Negative control: distilled water	Larvicidal effect of 75% and 70% at 1000 μg/ml against *Heligmosomoides contortus* and *H. polygyrus* respectively	Dose dependent, positive evidence based	Adiele et al. (2013)
Antioxidant activity	Root bark, 50 % aqueous methanol extract	DPPH and ABTS free radical assays	0–5 mg/ml plant extract	Negative control: 50% methanol and test free radical	IC_{50} of 1.351 and 9.48 μg/ml against ABTS and DPPH respectively	Dose dependent, positive evidence based	Muanda et al. (2010)
Anti-plasmodial activity	Leaves and roots, successively extracted with dichloromethane and methanol	*In vitro* antiplasmodial activity against chloroquinone sensitive *Plasmodium falciparum* (AD7)	3.13 ,6.25, 12.5, 25, 50, 100 μg/ml	Positive control: chloroquine	Dichloromethane extract exhibited IC_{50} of 6.9 μg/ml	Dose dependent, positive evidence based	Bah et al. (2007)
Anti-inflammatory	Root bark, methanol extract, fractions of petroleum ether and methanol	Xylene-induced ear oedema in mice	5 mg/ear	Left ears were left untreated and served as controls	Petroleum ether fraction exhibited 65.63% inhibition	Positive evidence based	Okoli et al. (2005)
Antibacterial activity	Roots, *n*-hexane extract	Microplate broth dilution assay. Species: *Mycobacterium tuberculosis* (H37Rv) and (H37Ra) , *M. avium* DSM, *M. bovis* BCG and *M. smegmatis*	MIC assay: serial dilutions	Positive controls: rifampicin, isoniazid, kanamycin and puromycin	The n-hexane extract exhibited MIC of 31.2 and 62.5 μg/ml against *M. bovis* and *M. tuberculosis* H37Ra respectively	Positive evidence based	Luo et al. (2011)
	Root, acetone soluble portion of ethanol extract and other various fraction	Cup agar diffusion method and microdilution assay. Species: *Bacillus subtilis*, *Escherichia coli*, *Salmonella typhi* and *Pseudomonas aeruginosa*	0.04 ml of the two fold dilutions in disc diffusion; MIC obtained from intercepts of log concentration axis of graph of IZD^2 against log concentration.	Positive controls: nystatin and chloramphenicol	The acetone soluble fraction from the ethanol extract exhibited zone of inhibition of 30 mm against *B. subtilis* and MIC of 0.010 against both *Pseudomonas aeruginosa* and *Escherichia coli*	Positive evidence based, dose dependent	Ajali and Chukwurah (2004)
	Roots, aqueous, ethanol and acetone crude extracts. Dichloromethane, hexane, ethyl acetate and n-butanol fractions	Agar well diffusion method, microdilution for both MIC and MBC. Species: *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.	Not recorded for Agar well and two fold dilutions for MIC and MBC	Negative control: acetone. Positive control: chloramphenicol	*n*-butanol fraction and acetone extract exhibited MIC of 0.313 against *Escherichia coli* and *Staphylococcus aureus* respectively	Positive evidence based	Ngonda et al. (2012)
	Roots and leaves, chloroform, methanol and aqueous crude extracts	Disc diffusion method, microdilution assay for both MIC and MBC. Species: *Escherichia coli*, *Salmonella typhi* and *Pseudomonas aeruginosa*.	7.5 mg/disc in disc diffusion and two fold dilutions for MIC and MBC	Positive control: ampiclox	Chloroform and methanol extracts of the leaves exhibited ZI of 15 to 19 mm. Similar extract exhibited MIC of 0.591 mg/ml and MBC of 5.91 against *S. typhi*.	Positive evidence based, no dose dependence reported in disc diffusion assay	Ndamitso et al. (2013)
	Roots and leaves, aqueous, ethanol crude extracts	Agar gel diffusion method. Species used: *Escherichia coli*, *Salmonella typhi* and *Salmonella spp*	50, 100, 150, 200 mg/ml	Positive control: gentamicin Negative control: Distilled water	Aqueous root extract exhibited ZI of 14, 19 and 21 mm against *S spp.*., *S. typhi* and *E. coli*.	Positive evidence based, dose dependence	Junaid et al. (2008)
Antifungal activity	Roots, essential oil (sample containing variety of compounds)	Microdilution. Species used: *Candida albicans*	Two fold dilutions for MIC	Positive control not reported	Essential oil revealed MIC of 0.40 mg/ml	Positive evidence based	Alitonou et al. (2012)
	Leaves, 70% methanol extract	Microplate broth dilution. Species used: *Rhizopus nigricans*, *Fusarium oxysporum* and *Mucor rouxi*	Two fold dilutions for MIC	Positive control not reported	70% methanol extract exhibited MIC of 1.2 mg/ml against *M. rouxi*, *F. oxysporum* and *Rhizopus nigrigans*.	Positive evidence based	Karou et al. (2012)
Hypoglycaemia activity	Root bark, 96% ethanol extract	Male mice, diabetes induced intraperitoneally with a solution containing	200 mg/kg	Positive control: glibenclamide	Ethanol extract lowered blood glucose level better at 4 h compared to	Inconclusive evidence, not dose dependent	Keshebo et al. (2014)

Table 3 (*continued*)

Activity investigated	Tested material	Model used	Tested doses	Controls	Activity and results	Experimental evidence assessment	Reference
		streptozotocin, sodium citrate and dH_2O at pH 5.			control drug but not at 1hr		
Enzyme inhibition	Root, methanol extract	AChE, CES and XO	100 μl of 100 μg/ml	Positive control: galanthamine, ascorbic acid and allopurinol were used in AChE, CES and XO assay respectively	Methanol extract exhibited 7.73% inhibitionof CES.	Inconclusive evidence, not dose dependent	Bangou et al. (2011)
Anticonvulsant, anxiolytic and sedative effect	Root, aqueous extract	Mice, strychnine and picrotoxin-induced seizure model; elevated plus maze and Y maze; and hexobarbitone induced sleep and hole board models respectively	100, 200, 400 mg/kg	Positive control: phenobarbitone, diazepam	The effect of the extract delayed onset of seizures comparable to phenobarbitone	Positive evidence based, dose dependent	Adeyemi et al. (2010), Okomolo et al, (2011)
Insecticidal, molluscidal and pesticidal effect	Roots, powder	Insect toxicity bioassay, direct contact with the insects of known age Species: *Callosobruchus maculatus*, *Sitophilus zeamais*, *Prostephanus truncatus*, *Rhyzopertha dominica*	0.5%, 1% and 5% w/w	Not reported	5% of the roots exhibited 75% inhibition against *R. dominica*	Positive evidence based, dose dependent	Belmain et al. (2001)
	Roots, methanol extract	Insect toxicity bioassay, topical application Species: *S. zeamays*, *C. maculatus*	0.02; 0.04; 0.06; 0.08 and 0.1 g/ml	Positive control: 0.08 g/ml of *Z. xanthoxyloides*	After 72 h, methanol extract revealed 81.07% and 83.54% inhibition against *S.zeamays* and *C. maculatus* respectively.	Positive evidence based, dose dependent	Afful et al. (2012)
	Stem bark, roots and leaves, methanol and ethanol extracts	Direct contact. Species: *Balinus globosus*	0.1, 0.2, 0.5, 1.0, 2.0, 3.0, 5.0, 7.5 and 10.0 ppm	Not reported	LC_{50} of 0.15–0.60 ppm was reported by both methanol and ethanol extracts	Positive evidence based, dose dependent	Olofintoye (2010)
Histopathologic effect	Roots, aqueous extract	Intra-peritoneal injection of aqueous extract to rats daily for fourteen consecutive days	Initially rats were given 2 mg/ml for histopathologic effect. Later, 10, 30, 45, 60, 1000 mg/kg respectively administered to one animal per group to determine LD_{50}	Negative control: distilled water	Extract exhibited LD_{50} value of 37 mg/kg	Positive evidence based	Dapar et al. (2007)

In the brine shrimp bioassay, the 70% methanol extract of the root exhibited a 100% mortality rate at a concentration of 1000 μg/ml (Adiele et al., 2013), while the 80% methanol root extract exhibited an LC_{50} of 77.1 μg/ml (Moshi et al., 2007), suggesting that these extracts are relatively toxic. However, the brine shrimp assays have some problems as the counting of the viable larvae is performed while the live larvae are continually moving around the petri dish.

The aqueous root bark extract was toxic to Ehrlich ascites tumour cells with a mortality rate of 82.5% at 1000 μg/ml and an IC_{50} of 67 μg/ml (Lawal et al., 2012). Compounds such as 1,6,8-trihydroxy-2,3,4,5-tetramethoxyxanthone and 1,6-dihydroxy-2,3,4,5,8-pentamethoxyxanthone showed potent cytotoxicity with IC_{50} values of 22.8 and 17.4 μM respectively against human pancreatic cancer cells (Dibwe et al., 2013) while the 70% methanol extract of the root bark exhibited average inhibition of cell proliferation of 22.6% at a concentration of 1 μg/ml against HeLa cells (Runyoro et al., 2005). However, this is not a useful result, when compared to the IC_{50} which will explain the overall average concentration at which 50% of the cells will be inhibited by the test plant extract. In summary, *S. longipedunculata* extracts have been investigated for cytotoxicity against human pancreatic cell lines, brine shrimp larvae, Ehrlich ascites tumour cells, HeLa cells and both albino rats and mice. However, there is a need to investigate the cytotoxicity of various extracts and some compounds isolated from this species against normal human cell lines.

6. Pharmacology

The pharmacological properties of *S. longipedunculata* extracts are summarised briefly in Table 3.

6.1. Antibacterial activity

In a recent disc diffusion study, the aqueous leaf extract yielded zones of inhibition (ZI) of 15 mm against both *Escherichia coli* and *Salmonella typhi*, while the chloroform leaf extracts exhibited a ZI of 18 mm against *Pseudomonas aeruginosa* at a concentration of 7.5 mg/disc (Ndamitso et al., 2013). The methanol extracts and the chloroform fraction of the root bark exhibited ZI of 28 mm against methicillin resistant *Staphylococcus aureus*, while hexane and ethyl acetate fractions exhibited ZI ranging from 14 to 19 mm against *Streptococcus pyogenes*, *Pseudomonas fluorescens* and *Klebsiella pneumoniae* (Musa et al., 2013). Adebayo and Osman (2012) reported a ZI of 15.10 mm by the ethanol extracts of the root bark at a concentration of 100 mg/ml. The disc diffusion assay is not a good method in comparing the antibacterial activity of the plant

extracts as it is dependent upon a number of factors, including the concentration of the bacterial inoculum, the type of agar used and the diffusion rate of the plant extract. These factors may well affect the activity of the extracts. However, it may be used as a starting point in comparing the antibacterial activity of various plant extracts.

In the broth microdilution assay, the chloroform extracts of the leaf had a minimum inhibitory concentration (MIC) of 0.591 mg/ml against both *S. typhi* and *P. aeruginosa* while the aqueous extracts of the leaf revealed a MIC of 6.25 mg/ml and minimum bactericidal concentration (MBC) of 62.5 mg/ml against *S. typhi*. Besides exhibiting a MIC of 0.313 and MBC of 0.625 mg/ml against both *Staphylococcus aureus* and *Pseudomonas aeruginosa*, the acetone extract of the root had a total activity of 19 200 ml/g against these bacterial strains (Ndamitso et al., 2013), suggesting that the extract may be a good source of antibacterial compounds. The units of total activity are ml/g and indicate the degree to which the active compounds in one gram of plant material can be diluted and still inhibit the growth of the tested microorganism (Eloff, 2000). The extract of the acetone soluble portion of the root exhibited a potent MIC of 0.02 mg/ml against *Bacillus subtilis* and *S. typhi* (Ajali and Chukwurah, 2004). Moreover, a similar extract exhibited MIC of 0.10 mg/ml against both *E. coli* and *P. aeruginosa*.

In other reports, the essential oil from *S. longipedunculata* had MIC of 12.79 mg/ml against *E. coli* (Alitonou et al., 2012), while the 70% methanol extract of the leaves exhibited a MIC of 0.45 mg/ml and 0.23 mg/ml against *Serratia marcescens* and *Shigella flexneri* respectively (Karou et al., 2012).

The *n*-hexane extract of the root exhibited MIC values ranging from 0.0312 to >0.250 mg/ml against *Mycobacterium* species such as *M. smegmatis*, *M. tuberculosis*, *M. bovis* and *M. avium* (Luo et al., 2011; Ferreira et al., 2012). Moreover, an acetone extract of the leaf was reportedly less active against two *Mycobacterium tuberculosis* strains, with MIC of >0.1 mg/ml compared to the reference drug (isoniazid) which exhibited a MIC of 0.0001 and 0.005 mg/ml (Green et al., 2010). The result of >0.1 mg/ml is not useful information as it cannot be compared to information from other authors. In general, it is difficult to assess the biological activity of *S. longipedunculata* against *M. tuberculosis* as there is sparse information available. Moreover, there is a need to further investigate the biological activity of the various extracts of these species and some of the individual isolated compounds against *M. tuberculosis*. Elsewhere, water extracts of the root bark exhibited MIC of 1000 mg/ml against *S. aureus*, *E. coli* and *P. aeruginosa* using the cylinder plate technique (Lino and Deogracious, 2006). Although there are differences in methods, the antibacterial activity of the aqueous root extract is not comparable to those of the organic extracts as Ngonda et al. (2012) reported a MIC of 3.13 mg/ml of the aqueous extract against both *S. aureus* and *P. aeruginosa*. Some of the active compounds in the aqueous extract might have been destroyed by the freeze drying process. In general, crude extracts with MIC values of 0.1 mg/ml and below are held to be potent and worthy of further studies (Eloff, 1998). In the current work, various extracts from *S. longipedunculata* revealed potent antibacterial activity against *E. coli*, *P. aeruginosa*, *M. smegmatis*, *M. tuberculosis*, *M. bovis* and *M. avium*. These pathogens are important causative agents of various human infections.

6.2. Antifungal activity

Recently, it was reported that the 70% methanol extract of the leaf exhibited a MIC of 1.2 mg/ml against *Mucor rouxi*, *Fusarium oxysporum* and *Rhizopus nigricans* (Karou et al., 2012). Furthermore, both an acetone extract of the root and the *n*-butanol fraction exhibited a MIC and minimum fungicidal concentration (MFC) of 1.25 and 2.5 mg/ml respectively against *Candida albicans* (Ngonda et al., 2012), while the 80% methanol extract of the root bark exhibited a ZI of <4 mm against *C. albicans* (Runyoro et al., 2006). Moreover, the essential oils from the root bark revealed a MIC of 0.40 mg/ml against *C. albicans* (Alitonou et al., 2012). The acetone extracts of the root exhibited a MIC of 3.75 mg/ml against *Fusarium verticillioides* and *Fusarium oxysporum* while the hexane extract of the root exhibited a MFC of 3.75 mg/ml against *F. verticillioides, F. nygamai, F. proliferatum* and *F. graminearum* (Samie and Mashau, 2013). Although the extracts from *S. longipedunculata* revealed potent antibacterial and antifungal activity, the mode of action remains unknown.

6.3. Antiparasitic activity

According to Fernandes et al. (2008), the water extract from the root exhibited a potent MIC of 0.10 mg/ml against *Trichomonas vaginalis*, a causative agent of the urogenital infection known as vaginal trichomoniasis, suggesting that the plant may serve as an alternative source of treatment for sexually transmitted infections in humans.

The methanol extract from the root inhibited motility of *Trypanosoma brucei brucei* and *Trypanosoma congolense* in 50 and 30 min respectively at a concentration of 0.4 mg/ml (Atawodi et al., 2003), while the petroleum ether extract from the stem bark inhibited motility of *Trypanosoma brucei* in 55 min at a concentration of 2 mg/ml (Atawodi, 2005). The aqueous root extract caused a gradual decrease in parasitemia in rats infected with *T. brucei* for seven days at 100 and 200 mg/kg (Haruna et al., 2013a). Moreover, 5, 10 and 20% fractions from the ethyl acetate fraction of the root revealed a LD_{50} of 0.14, 0.28 and 0.56 mg/kg respectively against Wistar rats infected with *T. brucei* (Haruna et al., 2013b). Water and methanol extracts of the root bark exhibited antitrypanosomal activity yielding a MIC of 56 μg/ml against *Trypanosoma brucei rhodesiense* (Freiburghaus et al., 1996). The 70% aqueous methanol extracts of the root exhibited a larvicidal effect of 75% and 70% at 1000 μg/ml against *Heligmosomoides contortus* and *Heligmosomoides polygyrus* at the L3 stage (Adiele et al., 2013).

6.4. Antioxidant activity

A 70% methanol extract of the leaf exhibited an IC_{50} of 79.35 μg/ml against 2,2-diphenyl-1-picryl-hydrazyl (DPPH), a stable free radical (Karou et al., 2012), while the essential oil of the root bark exhibited an IC_{50} of 500 mg/l (Alitonou et al., 2012). The aqueous methanol extract (50%) of the root bark exhibited an IC_{50} of 1.351 and 9.48 μg/ml against ABTS and DPPH respectively (Muanda et al., 2010). Although the extraction methods of the leaf and root bark were slightly different, these results may well suggest that the root bark extract quenches DPPH much better than the leaf extract.

6.5. Antiplasmodial activity

The dichloromethane extract of the leaves showed antiplasmodial activity with an IC_{50} of 6.9 μg/ml against *Plasmodium falciparum* (Bah et al., 2007), while the methanol extract of the root suppressed *Plasmodium berghei* by 82% at a dose of 0.56 mg/kg (Haruna et al., 2013c). Furthermore, the methanol and chloroform extracts of the root exhibited an IC_{50} of >250 μg/ml against the chloroquinone resistant *P. falciparum* strain (Ancolio et al., 2002). Elsewhere, extracts from seeds of *S. longipedunculata* did not show any activity at 50 μg/ml against *P. falciparum* FCA-2 from Ethiopia (Kassa et al., 1998), suggesting that the antimalarial compounds may only be present in the leaves and roots.

6.6. Anti-inflammatory properties

The 50% aqueous methanol extract showed good anti-inflammatory activity in a dose dependent manner by exhibiting reduction of NO production in macrophages stimulated with LPS/IFN-gamma yielding 51.3% inhibition at a concentration of 150 μl (Muanda et al., 2010). The methanol extracts, petroleum ether and methanol fractions obtained from solvent extraction of the root bark were also investigated for anti-inflammatory properties using topical oedema of the mouse ear model (Okoli et al., 2005). The petroleum ether fraction, methanol fraction and methanol extract revealed 65.63%, 53.13% and 40.63% inhibition respectively. The extracts of these species exhibited good anti-inflammatory activity in different models. Interestingly, the water extracts, namely decoctions and infusions, are commonly applied in African indigenous medicine for treating various infections.

6.7. Insecticidal, molluscicidal and pesticidal properties

The methanol extracts of the root exhibited mean repellence of 60% and 80% against *Prostephanus truncatus* and *Tribolium casteneum* respectively at concentrations of 1 and 2 g/ml (Eziah et al., 2013). The methanol extract of the roots revealed mean % repellency of 70.1 and 60.3 at 0.10 g/ml against *Callosobruchus maculatus* and *Sitophilus zeamais* respectively (Afful et al., 2012). Moreover, the extract revealed mean adult emergence of 1.0 on pupae of both C. *maculatus* and *S. zeamais* at 0.10 g/ml. Furthermore, the extract exhibited mean adult emergence ranging from 1.0 to 2.0 against both the eggs and larvae of C. *maculatus* and *S. zeamais*. In both studies, the extract inhibited the selected insects in a dose dependent manner.

Leaf powders from *S. longipedunculata* collected from two different geographical areas, Atacora and Borgou in Benin (West Africa), exhibited percentage mortality rates of 18.9 and 77.2 respectively against *Callosobruchus maculatus* (Boeke et al., 2004). Besides considering the collection times, climatic conditions and the age of the leaves, these results may well suggest that the phytochemistry of the species in two localities is different. The methanol extract of the root exhibited contact toxicity of 95% and 100% against *Tribolium casteneum* and *Prostephanus truncatus* respectively (Eziah et al., 2013). The root powder of *S. longipedunculata* revealed a mean percentage mortality rate ranging from 25.1 to 75.4 against four storage insect pests, namely *Rhyzopertha dominica*, *Sitophilus zeamais*, *Callosobruchus maculatus* and *Prostephanus truncatus* (Belmain et al., 2001). The methanol extract of the leaf showed a 50% mortality rate at 1.0, 2.0 and 3 ppm, while the ethanol extracts of both the stem bark and leaf resulted in a 70% mortality rate against juvenile snails of *Balinus globosus* (Olofintoye, 2010). Moreover, the ethanol and methanol extracts of the root, leaf and stem bark exhibited high toxicity causing a 70–100% mortality rate at a concentration of 10.0 ppm against *B. globosus*. Generally, the species revealed high pesticidal effects against the eggs, pupae, larvae and adult species of C. *maculatus* and *S. zeamais*. The ethanol extracts showed good molluscidal activity compared to the methanol extracts.

6.8. Enzyme inhibition activity

The methanol extract of the root exhibited enzyme inhibition percentages of 6.95%, 7.73% and 5.93% against acetylcholinesterase (AChE), carboxylesterase (CES) and xanthine oxidase (XO) respectively (Bangou et al., 2011). Allopurinol exhibited 96.38% inhibition against XO while galanthamine and ascorbic acid exhibited 50.76% and 56.72% against AChE and CES respectively. According to Niño et al. (2006), AChE is an attractive target for the rational drug design and discovery of mechanism-based inhibitors because of its role in the hydrolysis of the neurotransmitter acetylcholine. Moreover, AChE inhibitors are most active in the treatment of a variety of diseases, including Alzheimer's disease, Parkinson's disease, ataxia and senile dementia. XO catalyses the oxidation of xanthine and hypoxanthine into uric acid, which may lead to a disease known as gout (Kong et al., 2000). Some drugs and plant-derived extracts which serve as XO inhibitors may block uric acid biosynthesis, lower the plasma uric acid concentration and are used to treat gout (Nguyen et al., 2004). The tested *S. longipedunculata* extracts revealed negligible inhibition of AChE, CES and XO. However, future research may target activity of other solvent extracts and other enzyme systems.

6.9. Anticonvulsant, sedative and anxiolytic properties

The aqueous extract of the root exhibited anticonvulsant, anxiolytic and sedative activities against mice in a dose dependent manner (Adeyemi et al., 2010; Okomolo et al., 2011), suggesting that the plant extract may be used in the management of convulsion and psychosis.

6.10. Hypoglycaemia activity and histopathological effects

The aqueous extract of the leaves lowered the blood glucose concentration from 96.3 to 71.6 mg/dl after 8 h in rats treated with 2100 mg/kg plant extract (Onyeche and Kolawole, 2005). This is a high concentration and the effect may not be useful in practice. The 96% ethanol extract of the root bark had no hypoglycaemic effect on mice when administered at 200 mg/kg (Keshebo et al., 2014). The 200 mg/kg concentration is also relatively high, limiting the extract's practicality. The buffer extract (0.5 g of the plant material dissolved in 2.5 ml buffer at room temperature for 20 min) from the root had some antidiabetic activity through exhibiting 20–45% inhibition of α-amylase (Funke and Melzig, 2006). This inhibition is relatively low so probably does not justify further research although other mechanisms of action may be applicable. No information was found on the bioavailability or pharmacokinetic parameters of the extract.

The aqueous root extracts reportedly affect the tissue morphology of rats, resulting in irreversible cellular injury affecting the epithelial parenchyma and endothelial cells when administered at 2 mg/kg using intra-peritoneal injection for 14 consecutive days (Dapar et al., 2007). The extract histopathologically resulted in acute tubular necrosis in the kidneys, diffused alveolar and alveolar capillary damage in the lungs and severe ballooning degeneration with early steatohepatitis in some foci of the liver. It is difficult to conclude the effect of *S. longipedunculata* on various tissues due to the lack of information reported.

7. Conclusions

It is evident that *S. longipedunculata* is a very important medicinal plant used extensively for various purposes within African traditional culture. Studies on the toxicology, both *in vivo* and *in vitro* revealed that various extracts, particularly the aqueous root bark, may be toxic especially at high concentrations. This finding is concerning as some people from poor communities rely heavily on plants sold by traders without accurate prescriptions or directions for use. The extracts have been investigated for toxicity against mice and rats, brine shrimps, HeLa cells, human pancreatic cancer cells and Ehrlich ascites tumour cells. There is a need to investigate the cytotoxicity of these extracts against normal human cell lines. The histopathological and hypoglycaemia effects of the species, as well as many other aspects, also need to be further explored.

Phytochemically, salicylic acid, a variety of xanthones and esters form an integral part of this plant. These phytochemicals may well explain the antimicrobial, anthelmintic, antimalarial and other biological activities of this plant as highlighted in the current paper. However, these phytochemicals were reported from the root extract and the removal of the roots may be detrimental to plant life. The conservation status of this plant is also of great concern because the roots are mostly used for medicinal purposes and are traded between communities and neighbouring countries.

Interestingly, the use of the plant species has been validated for treatment of malaria, erectile dysfunction, pain, sexually transmitted infections and other infections. Various extracts from the species exhibited anthelmintic, antioxidant, molluscicidal, pesticidal, various enzyme inhibitory and anti-inflammatory properties. Extracts from *S. longipedunculata* revealed potent antimicrobial activity against *Candida albicans* and *Trichomonas vaginalis*, validating to an extent the use of the plant species in the treatment of sexually transmitted infections. However there is a need to explore the biological activity of various extracts from the species against microorganisms such as *Neisseria gonorrhoeae*, *Klebsiella granulomatis, Mycoplasma hominis*, *Mobiluncus* spp. and *Mycoplasma genitalium* as the most common causative agents of gonorrhoea, bacterial vaginitis, donovanosis and other urogenital infections. There is also a need to investigate the biological activity of the other compounds occurring in the plant extracts. Moreover, the anti-diabetic, hypoglycaemia and histopathologic effects of the species also need to be explored as there are few reports in the literature regarding these aspects.

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