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 comprehensive literature search using various computerised databases including Science direct, Scopus, Scielo, PubMed and Google Scholar. The additional
information was retrieved from various academic dissertations, thesis and botanical books. The 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.

**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 is also deserving of further research. Moreover, the pharmacokinetic properties of extracts and compounds of the species needs to be explored as there is insufficient data available on these aspects.

*Key words: Securidaca longipedunculata*, Polygalaceae, xanthones, pharmacology, toxicology
**Abbreviations:** ABTS, 2,2-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt; AChE, acetylcholinesterase; DPPH, 2,2-diphenyl-1-picryl-hydrazyl; IC₅₀, 50% inhibitory concentration; LD₅₀, 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

**Contents**

1. Introduction 4
   1.1 Botanical description and distribution 5

1.2 Local names 6

1.3 Ethnomedicinal uses 8
   1.3.1 Roots 8
   1.3.2 Leaves 9
   1.3.3 Whole plant 9
   1.3.4 Stem bark 10

2. Phytochemistry 10

3. Toxicology 18

4. Pharmacology 20
   4.1 Antibacterial activity 20
   4.2 Antifungal activity 29
   4.3 Antiparasitic activity 29
   4.4 Antioxidant activity 30
   4.5 Antiplasmodial activity 31
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 ethnobotonically 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. In general, these medicinal plants may have relatively low toxicity (Naomesi et al., 1994; Steenkamp and Gouws, 2006; Belayachi et al, 2013) and may possess antioxidant, anti-diabetic, antimicrobial and anti-inflammatory properties amongst others.

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.,
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). According to Baloyi et al. (2012), seeds of *S. longipedunculata* grow better at a soil depth of 4 cm between 20 and 30°C while Zulu et al. (2011) revealed that growing medium with compost manure showed the highest cumulative germination of 42.6%. The seedling survival rate declines with increasing concentrations of gibberellic acid in a growing medium with a compost manure. 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.

### 1.1 Botanical description and distribution

*Securidaca longipedunculata* Fresen, (synonyms *Securidaca longipedunculata* var. *longipedunculata* or *Elsota longipedunculata*, family Polygalaceae) is a small tree up to 6 meters 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, 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).

1.2 Local names

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

1.3 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.

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

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

The smoke resulting from burning the root of S. longipedunculata, combined with that of Zanthoxylum zanthoxyloides, is inhaled to treat malaria and fever (Hamil 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 (Mothanka 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).

1.3.2 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). 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).

1.3.3 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).
1.3.4 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 (Borikini 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).

2. 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 variety of solvents (Table 2). This may well explain the ethnomedicinal uses and hence the biological activity studied on the plant species.
Methyl salicylate

Benzyl-3-hydroxy-2-methoxybenzoate (R₁ = H, R₂ = OH)
Benzyl-2-hydroxy-6-methoxybenzoate (R₁ = OH, R₂ = 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-2,3, 6, 7, 8-pentamethoxyxanthone
Securinine

Benzyl-2-hydroxy-6-methoxybenzoate

1,7-Dihydroxy-4-methoxyxanthone
Presenegenin

β-Sitosterol

Caffeic acid
Fig. 1. Compounds isolated from *Securidaca longipedunculata*.

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

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).

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

<table>
<thead>
<tr>
<th>Classes of compounds</th>
<th>Part of plant</th>
<th>Solvent used</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Saponins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Securidacaside A and</td>
<td>Root bark</td>
<td>Methanol</td>
<td>(Stevenson et al., 2009).</td>
</tr>
<tr>
<td>Securidacaside B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-O-β-D-glucopyranosyl</td>
<td>Roots</td>
<td>70 % Methanol</td>
<td>(Mitaine-Offer et al., 2010)</td>
</tr>
<tr>
<td>presenegenin-28-O-β-D-</td>
<td></td>
<td>Water</td>
<td>(Van Wyk et al., 2005)</td>
</tr>
<tr>
<td>apiofuranosyl-(1,3)-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-D-xylopyranosyl-(1,4)-</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>β-D-apiofuranosyl-(1,3)-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-L-rhamnopyranosyl-(1,2)-</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>4-O-[E]-3,4,5-trimethoxycinnamoyl]-β-D-fucopyranosyl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ester Presenegenin</td>
<td>Roots</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Flavonoids</strong></td>
<td>Root bark</td>
<td>Dichloromethane and ethyl acetate,</td>
<td>(Joseph et al., 2006, Meli et al., 2007)</td>
</tr>
<tr>
<td>1,7-dihydroxy-4-methoxyxanthone.</td>
<td></td>
<td>Aqueous methanol</td>
<td>(Muanda et al., 2010)</td>
</tr>
<tr>
<td><strong>Rutin</strong></td>
<td>Roots</td>
<td>Ethyl acetate</td>
<td>(Van Wyk et al., 2005)</td>
</tr>
<tr>
<td><strong>Alkaloids</strong></td>
<td>Roots</td>
<td>Water</td>
<td>(Van Wyk et al., 2005)</td>
</tr>
<tr>
<td><strong>Steroids</strong></td>
<td>Roots</td>
<td>Ethyl acetate</td>
<td>(Meli et al., 2007)</td>
</tr>
<tr>
<td><strong>Glycosides</strong></td>
<td>Leaves</td>
<td>Methanol</td>
<td>(Debella et al., 2000)</td>
</tr>
<tr>
<td>**Quercetin-3-O-D-xyl</td>
<td>Stem bark</td>
<td>Methanol</td>
<td>(Debella et al., 2000)</td>
</tr>
<tr>
<td>oside**</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1,β-STigmasterol-3-O-D-glucopyranoside</td>
<td>Stem bark</td>
<td>Methanol</td>
<td>(Debella et al., 2000)</td>
</tr>
<tr>
<td><strong>Sucrose derivatives</strong></td>
<td>Stem bark</td>
<td>Methanol</td>
<td>(De Tommasi et al., 1993)</td>
</tr>
<tr>
<td>β-D-(3,4-disinapoyl)</td>
<td>fructofuranosyl-α-D(6-sinapoyl)glucopyranoside and β-D-(3-sinapoyl)fructofuranosyl-α-D(6-sinapoyl)glucopyranoside</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Phenolic acids</strong></td>
<td>Stem bark</td>
<td>Methanol</td>
<td>(De Tommasi et al., 1993)</td>
</tr>
<tr>
<td>Sinapic acid, 4,5-dicaffeoyl-D-quinic acid, caffeic acid and 3,4,5-tricaffeoyl-D-quinic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quercetin, p-coumaric acid, Cinnamic acid, caffeic acid and chlorogenic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fatty acids and Triacylglycerol</strong></td>
<td>Seeds</td>
<td>Light petroleum</td>
<td>(Smith et al., 1979, Okoli et al., 2006)</td>
</tr>
<tr>
<td>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</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Volatile oil</strong></td>
<td>Root bark</td>
<td>Aqueous methanol and water</td>
<td>(Muanda et al., 2010)</td>
</tr>
<tr>
<td>Methyl salicylate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methyl salicylate</strong></td>
<td>Root bark</td>
<td>Water</td>
<td>(Van Wyk et al., 2005, Jayasakara et al., 2002, Lognay et al., 2000)</td>
</tr>
<tr>
<td></td>
<td>(Hydrodistillation)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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-pentamethoxyxanthone, 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-tetramethoxyxanthone 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-dihydroxy-xanthone (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 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-1,4,5,6tetramethoxy-2,3-methylenedioxyxanthone,4,6,8-trihydroxy,1,2,3,5-tetramethoxyxanthone, 4,8-dihydroxy-1,2,3,5,6-pentamethoxyxanthone, benzyl 3hydroxy-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-fucopyranosyl 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.

3. 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.

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 tumor cells with a mortality rate of 82.5% at 1000 µg/ml and revealed 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 tumor 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.

4. Pharmacology

4.1 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.
Table 3. Pharmacological properties of extracts from *Securidaca longipedunculata* Fresen

<table>
<thead>
<tr>
<th>Activity investigated</th>
<th>Tested material</th>
<th>Model used</th>
<th>Tested doses controls</th>
<th>Activity results and Experimental evidence assessment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiparasitic activity</strong></td>
<td>Roots, water extract</td>
<td><em>In vitro</em> studies using trichomonads grown in modified Diamond's medium</td>
<td>50 mg/ml, serially diluted</td>
<td>Metronidazole used as a positive control, MIC of 0.10 mg/ml after 24 hrs of incubation</td>
<td>Positive evidence base</td>
</tr>
<tr>
<td></td>
<td>Roots, 70% aqueous methanol</td>
<td>Larvae directly exposed to plant extracts</td>
<td>0.02, 0.10, 0.50, 2.50 mg/ml extract</td>
<td>Larvicidal effect of 75 and 70% at 1000 µg/ml against <em>Heligmosomoides contortus</em> and <em>Heligmosomoides polygyrus</em> respectively</td>
<td>Dose dependent, positive evidence based</td>
</tr>
<tr>
<td><strong>Antioxidant activity</strong></td>
<td>Root bark, 50% aqueous methanol extract</td>
<td>DPPH and ABTS free radical assays</td>
<td>0 to 5 mg/ml plant extract</td>
<td>Negative control: 50% methanol and test free radical, IC$_{50}$ of 1.351 and 9.48 µg/ml against ABTS and DPPH respectively</td>
<td>Dose dependent, positive evidence based</td>
</tr>
<tr>
<td><strong>Anti-plasmodial Activity</strong></td>
<td>Leaves and roots, successively extracted with</td>
<td><em>In vitro</em> antiplasmodial activity against chloroquinone</td>
<td>3.13, 6.25, 12.5, 25, 50, 100 µg/ml</td>
<td>Positive control: Chloroquine, DIC$_{50}$ of 6.9 µg/ml</td>
<td>Dose dependent, positive evidence</td>
</tr>
</tbody>
</table>

Fernandes et al. (2008)  
Adiele et al. (2013)  
Muanda et al. (2010)  
Bah et al. (2007)
<table>
<thead>
<tr>
<th><strong>Antinflammatory</strong></th>
<th>Dichloromethane and methanol</th>
<th>Xylene-induced ear edema in mice</th>
<th>Left ears were left untreated and served as controls</th>
<th>Petroleum ether fraction exhibited 65.63 % inhibition</th>
<th>Positive evidence base</th>
<th>Okoli et al. (2006)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibacterial activity</strong></td>
<td>Root bark, methanol extract, fractions of petroleum ether and methanol</td>
<td>Methanol extract, 5 mg/ear</td>
<td>Plasmodium falciparum (AD7)</td>
<td>Petroleum ether fraction exhibited 65.63 % inhibition</td>
<td>Positive evidence base</td>
<td>Okoli et al. (2006)</td>
</tr>
<tr>
<td></td>
<td>Roots, n-hexane extract</td>
<td>Micro plate broth dilution assay. Species: Mycobacterium tuberculosis (H37Rv) and (H37Ra), Mycobacterium avium DSM, Mycobacterium bovis BCG and Mycobacterium smegmatis</td>
<td>MIC assay: serial dilutions</td>
<td>Positive controls: Rifampicin, isoniazid, kanamycin and puromycin</td>
<td>The n-hexane extract exhibited MIC of 31.2 and 62.5 µg/ml against M. bovis and M. tuberculosis H37Ra respectively</td>
<td>Positive evidence base</td>
</tr>
<tr>
<td></td>
<td>Root, acetone soluble portion of ethanol extract and other various fraction</td>
<td>Cup agar diffusion method and Micro plate broth dilution assay. Species: Bacillus subtilis,</td>
<td>0.04 ml of the two fold dilutions in Disc diffusion and MIC obtained from intercepts of</td>
<td>Positive controls: Nyastatin and Chloramphenicol</td>
<td>The acetone soluble fraction from the ethanol extract exhibited zone of inhibition of 30 mm against B. subtilis and</td>
<td>Positive evidence base, dose dependent</td>
</tr>
<tr>
<td>Extracts/Extraction Method</td>
<td>Species</td>
<td>Test Method</td>
<td>MIC/MBC Concentration</td>
<td>Positive Control</td>
<td>Negative Control</td>
<td>Positive Base</td>
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<tr>
<td>Roots, aqueous, ethanol and acetone crude extracts. Dichloromethane, hexane, ethyl acetate and n-butanol fractions</td>
<td>Agar well diffusion method, Micro plate broth dilution for both MIC and MBC. Species: <em>Escherichia coli</em>, <em>Staphylococcus aureus</em> and <em>Pseudomonas aeruginosa</em>.</td>
<td>Not recorded for Agar well and two fold dilutions for MIC and MBC</td>
<td>n-butanol fraction and Acetone extract exhibited MIC of 0.313 against <em>Escherichia coli</em> and <em>Staphylococcus aureus</em> respectively</td>
<td>Acetone</td>
<td>Chloroform</td>
<td>Ngonda et al. (2012)</td>
</tr>
<tr>
<td>Roots and leaves, chloroform, methanol and aqueous crude extracts</td>
<td>Disc diffusion method, Micro plate broth dilution assay for both MIC and MBC. Species: <em>Escherichia coli</em>, <em>Salmonella typhi</em> and <em>Pseudomonas aeruginosa</em>.</td>
<td>7.5 mg/disc in Disc diffusion and two fold dilutions for MIC and MBC</td>
<td>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 <em>S. typhi</em>.</td>
<td>Ampiclox</td>
<td>Chloroform</td>
<td>Positive evidence base, No dose dependence reported in disc diffusion assay</td>
</tr>
<tr>
<td><strong>Antifungal activity</strong></td>
<td><strong>Hyperglycemic activity</strong></td>
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<td><strong>Roots and leaves, aqueous, ethanol crude extracts</strong></td>
<td><strong>Root bark, 96 % ethanol extract</strong></td>
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<tr>
<td><strong>Agar gel diffusion method. Species used: <em>Escherichia coli</em>, <em>Salmonella typhi</em> and <em>Salmonella spp</em></strong></td>
<td><strong>Male mice, Diabetic induced intraperitoneally with a solution containing streptozotocin, sodim citrate</strong></td>
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<td><strong>50, 100, 150, 200 mg/ml</strong></td>
<td><strong>200 mg/kg</strong></td>
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<td><strong>Positive control: gentamycin</strong> <strong>Negative control: Distilled water</strong></td>
<td><strong>Positive control: Glibenclamide</strong></td>
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<tr>
<td><strong>Aqueous root extract exhibited ZI of 14, 19 and 21 mm against <em>S. spp</em>, <em>S. typhi</em> and <em>E. coli</em></strong></td>
<td><strong>Ethanol extract lowered blood glucose level better at 4 hr compared to control drug but not at 1hr</strong></td>
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<td><strong>Positive evidence. dose dependence</strong></td>
<td><strong>Inconclusive evidence, not dose dependent</strong></td>
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<td><strong>Junaid et al. (2008).</strong></td>
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<td><strong>Alitonou et al. (2013)</strong></td>
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<td><strong>(Karou et al. (2012). Keshebo et al. (2014)</strong></td>
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<tr>
<td>Enzyme inhibition</td>
<td>Root, methanol extract</td>
<td>AChE, CES and XO</td>
<td>100 µl of 100 µg/ml</td>
<td>Positive control: Galanthamine, Ascorbic acid and allopurinol were used in AChE, CES and XO assay respectively</td>
<td>Methanol extract exhibited 7.73 % inhibition of CES.</td>
<td>inconclusive evidence, not dose dependent</td>
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<tr>
<td>Anticonvulsant, anxiolytic and sedative effect</td>
<td>Root, aqueous extract</td>
<td>Mice, strychnine and picrotoxin-induced seizure model; Elevated plus maze and Y maze; and hexobarbitone induced sleep and hole board models respectively</td>
<td>100, 200 400mg/kg</td>
<td>Positive control: Phenobarbitone, Diazepam</td>
<td>The effect of the extract delayed onset of seizures and comparable to phenobarbitone</td>
<td>Positive evidence, dose dependent</td>
</tr>
<tr>
<td>Insecticidal, Moluscidal and pesticidal effect</td>
<td>Roots, powder</td>
<td>Insect toxicity bioassay, direct contact with the insects of known age Species: <em>Callosobruchus malaculatus</em>, <em>Sitophilus zeamais</em>, <em>Prostephanus truncates</em>,</td>
<td>0.5, 1 and 5 % w/w</td>
<td>Not reported</td>
<td>5 % of the roots exhibited 75 % inhibition against <em>R. dominica</em></td>
<td>Positive evidence, dose dependent</td>
</tr>
<tr>
<td>Method</td>
<td>Plant Part(s)</td>
<td>Extract Type</td>
<td>Insect Toxicity Bioassay Details</td>
<td>LD&lt;sub&gt;50&lt;/sub&gt; Details</td>
<td>Reference</td>
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<td><strong>Histopathologic effect</strong></td>
<td>Roots, aqueous extract</td>
<td>Intra-peritoneal injection of aqueous extract</td>
<td>Initially rats were given 2 mg/ml for histopathologic effect. Later, 10, 30, 45, 60 and 1000 mg/kg respectively were administered to one animal per group to determine LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Extract exhibited LD&lt;sub&gt;50&lt;/sub&gt; value of 37 mg/kg</td>
<td>Dapar et al. (2007)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stem bark, roots and leaves, methanol and ethanol extracts</td>
<td>Direct contact</td>
<td>Species: <em>Balinus globus</em></td>
<td>LC&lt;sub&gt;50&lt;/sub&gt; of 0.15 to 0.60 ppm was reported by both methanol and ethanol extracts</td>
<td>Positive evidence, dose dependent</td>
<td>Olofintoye (2010)</td>
</tr>
<tr>
<td></td>
<td>Roots, methanol extract</td>
<td>Insect toxicity bioassay, topical application</td>
<td>Species: <em>S. zeamays, C. maculatus</em></td>
<td>Positive control: 0.08 g/ml of <em>Z. xanthoxyloides</em> After 72 hrs, methanol extract revealed 81.07 and 83.54 % inhibition against <em>S. zeamays</em> and <em>C. maculatus</em> respectively.</td>
<td>Positive evidence, dose dependent</td>
<td>Afful et al. (2012)</td>
</tr>
</tbody>
</table>
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 micro dilution 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 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 19200 ml/g against these bacterial strains (Ndamitso et al., 2012), suggesting that the extract may be a good source of antibacterial compounds. The extract of the acetone soluble portion of the root exhibited a potent MIC of 0.02 mg/ml against Bacillus subtilis ans S. typhi (Ajali and Chukwurah, 2004). Moreover, 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, MIC of 0.1 is notably potent. 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.
4.2 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 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.

4.3 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).

**4.4 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. A variety of compounds belonging to a variety of classes reported in the phytochemistry section of this paper may play a role in the antioxidant properties of the species. The antioxidant activity may be of greater important in preventing oxidative stress which may be involved in many fatal infections and diseases.
4.5 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.

4.6 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 edema 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.
4.6 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 70 % mortality rate against juvenile snails of
*Balinus globusus* (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.

### 4.8 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 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 investigated *S. longipedunculata* extracts revealed negligible inhibition of AChE, carboxylesterase and XO. However, future research may target activity of other solvent extracts and other enzyme systems.
4.9 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.

4.10 Hypoglycemic activity and histopathological effects

The aqueous extract of the leaves significantly 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 hypoglycemic 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 (0.5g 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 to 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.

5. 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 relying heavily on plants sold by traders without correct prescriptions. The extracts have been investigated for toxicity against mice and rats, brine shrimps, Hela cells, human pancreatic cancer cells and Ehrlich ascites tumor cells. Therefore there is a need to investigate the cytotoxicity of these extracts against normal human cell lines. The histopathological and hypoglycemic effects of the species 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 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 gonorrhoeae, 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, hypoglycemic and histopathologic effects of the species also need to be explored as there are few reports in the literature.

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