Evaluation Of Medicinal Uses, Phytochemistry And Pharmacological Properties Of Strychnos Henningsii Gilg (Strychnaceae)

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Abstract: Strychnos henningsii is a small to medium-sized tree widely used as traditional medicine in tropical Africa. The current study critically reviewed the medicinal uses, phytochemistry and pharmacological properties of S. henningsii. A systematic review of the literature was carried out to document the medicinal uses, phytochemistry and pharmacological properties of S. henningsii. The results of the current study are based on literature survey conducted using various search engines such as Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis, and pre-electronic sources such as books, book chapters, scientific journals, theses and other grey literature obtained from the University library. This study revealed that S. henningsii is used as an anthelmintic, appetizer, blood cleanser, purgative, tonic and ethnoveterinary medicine, and traditional medicine for abdominal pain, bilharzia, colic, diabetes mellitus, gastro-intestinal problems, headache, malaria, menstrual problems, pain, respiratory diseases, rheumatism, snake bite and syphilis. Pharmacological research identified alkaloids, anthraquinones, cardiac glycosides, chalcones, flavonoids, phenolics, proanthocyanidins, saponins, steroids, tannins and triterpenes. The crude extracts of S. henningsii and phytochemical compounds exhibited analgesic, antibacterial, antidiabetic, anti-inflammatory, antioxidant, antiplasmodial, antiprotozoal, antispasmodic and cytotoxicity activities. Strychnos henningsii crude extracts and phytochemical compounds isolated from the species should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological properties.

Keywords: Ethnopharmacology, herbal medicine, indigenous pharmacopeia, Loganiaceae, Strychnos henningsii, Strychnaceae

1 INTRODUCTION

Strychnos henningsii Gilg is an evergreen to semi-deciduous small to medium-sized tree belonging to the Strychnaceae family but included in the family Loganiaceae in earlier literature. The genus name Strychnos L. is derived from the Greek word for deadly in reference to the alkaloid strychnine isolated from several Strychnos species which is known to be poisonous [1,2]. The species name henningsii is in honour of Prof Paul Christoph Hennings (1841-1908), a German botanist and mycologist who was based at the Royal Botanic Gardens at Berlin-Dahlem [3]. The synonyms of S. henningsii include S. albersii Gilg & Busse, S. barbata Chiov., S. elliottii Gilg & Busse, S. ligustroides Gossw. & Mendonca, S. myrcioides S. Moore, S. pauciflora Gilg, S. procera Gilg & Busse, S. reticulata Burtt Davy & Honoré, S. sennensis Baker and S. utilis Sim [4,5]. The English common names of S. henningsii include “Natal teak”, “coffee hard pear”, “Panda’s walking stick” and “red bitterberry” [2,3]. The crown of S. henningsii is wide-spreading, particularly dense, branch terminals pendent, stems long, upright, bare, fairly smooth, pale buff-grey but brown where the bark peels off in irregular sections. The leaves of S. henningsii are simple, borne in decussate pairs, elliptic to broadly ovate in shape, thinly leathery to brittle, slightly conduplicate upwards, glabrous, dark green, particularly glossy, marginally entire with three large veins originating in the leaf base. The flowers of S. henningsii are simple, yellow to orange in colour and borne in short cymes in the leaf axils in dense branched heads.

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The fruits of S. henningsii are small, slightly ovoid, glabrous, glossy, exocarp and fruit pulp firm. Strychnos henningsii has been recorded in Angola, Democratic Republic of Congo (DRC), Eswatini, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, South Africa, South Africa, South Sudan, Sudan, Tanzania, Uganda, Zambia and Zimbabwe [6-11]. Strychnos henningsii has been recorded in low-lying dry areas, riverine thickets, riverine fringes, scrub on termitaria, coastal evergreen forest, mist-belt evergreen forest and dry forests at altitudes ranging from sea level to 2300 m above sea level [7,12,13].

Strychnos henningsii is an important medicinal plant species in tropical Africa, listed in two monographs, “medicinal plants of South Africa” [14] and “plant resources of tropical Africa 11: medicinal plants 1” [15]. The bark, roots and root bark of S. henningsii are sold as sources of traditional medicine in informal herbal medicine markets in Kenya [16,17], Mozambique [18] and South Africa [19-21]. In Kenya, the bark, fruits, leaves, roots and stems of S. henningsii are added to soup as a flavouring agent [22,23]. Strychnos species contain strychnine and numerous other structurally related alkaloid compounds which are known to be poisonous and used as rodent, arrow and ordeal poisons [24-26]. Research by Wink and Van Wyk [27], showed that the alkaloid strychnine is extremely hazardous, as it is a cell and neurotoxin, mind altering, inhibiting glycine receptor (Cl^--channel), neurotransmitter, causing spasms, convulsions, salivation and death from respiratory arrest. It is therefore, within this context that the current study was conducted aimed at reviewing the medicinal uses, phytochemistry and pharmacological properties of S. henningsii.

2 MATERIALS AND METHODS

Several electronic databases were searched which included Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis. Additional

information was obtained from pre-electronic sources such as books, book chapters, scientific journals, theses and other grey literature obtained from the University library. The relevant term Strychnos henningsii was paired with keywords such as “medicinal uses of Strychnos henningsii”, “phytochemicals of Strychnos henningsii”, “biological activities of Strychnos henningsii”, “pharmacological properties of Strychnos henningsii”, “ethnobotany of Strychnos henningsii”, and various other synonyms and common names of the plant species. The ultimate goal of this search was to explore articles that investigated the medicinal uses, phytochemical and pharmacological properties of S. henningsii. A total of 114 articles published between 1960 and 2021 matched the inclusion criteria and were included in this review (Fig. 1).

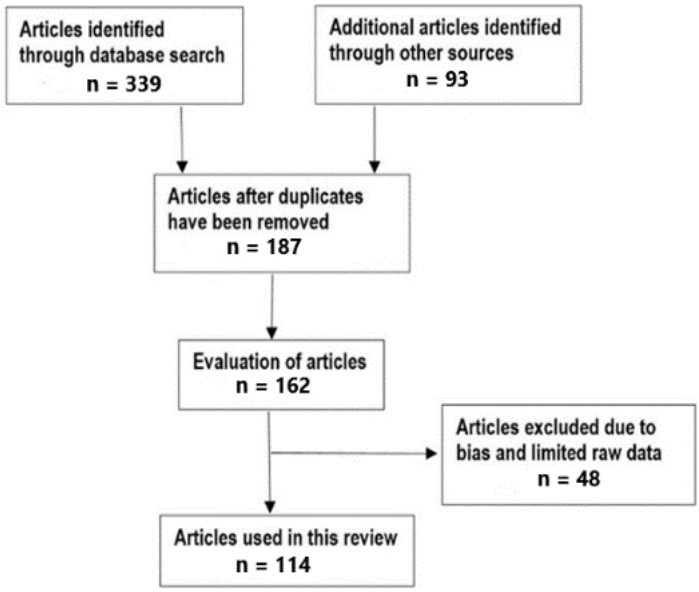

***Fig. 1**. Flow chart showing the number of research publications used in this study*

3 RESULTS AND DISCUSSION

3.1 Medicinal uses of Strychnos henningsii

The bark, leaves, roots, root bark, stems, stem bark and twigs of S. henningsii are mainly used as anthelmintic, appetizer, blood cleanser, purgative, tonic and ethnoveterinary medicine, and traditional medicine for abdominal pain, bilharzia, colic, diabetes mellitus, gastro-intestinal problems, headache, malaria, menstrual problems, pain, respiratory diseases, rheumatism, snake bite and syphilis (Table 1, Fig. 2). In Kenya, the leaves of S. henningsii are mixed with leaves of Boscia salicifolia Oliv. and root bark of Carissa spinarum L. as traditional medicine for joint pains [28]. Similarly, the leaves and stem bark of S. henningsii are mixed with leaves of Pavetta crassipes K. Schum., root bark of Carissa spinarum L. and leaves of Zanthoxylum chalybeum Engl. as traditional medicine for joint pains [28]. In South Africa, the bark of S. henningsii is mixed with roots of Turraea floribunda Hochst. as traditional medicine for rheumatic fever [29-31].

TABLE 1
MEDICINAL USES OF STRYCHNOS HENNINGSII

Medicinal use	Parts used	Country	Reference
Abdominal pain	Roots and root bark	Mozambique and South Africa	18,32-36
Anthelmintic	Bark and roots	Kenya, South Africa and Tanzania	3,16,37-44
Appetiser	Bark	Kenya and South Africa	16,30,40,45-48
Arthritis	Roots and root bark	Kenya	22,49-51
Aspergillosis	Bark	South Africa	52
Back pain	Root bark	Kenya	51,53
Bilharzia	Twigs	Madagascar and South Africa	30,54-56
Blood cleanser	Bark and roots	Kenya, South Africa	16,57
Boost immune system	Leaves	South Africa	58
Colic	Bark, leaves, stems and twigs	Madagascar and South Africa	2,14,38-40,42,45,48,50,56,59,60-63
Diabetes mellitus	Bark and leaves	Kenya and South Africa	32-36,42,52,64,65
Dizziness	Bark	South Africa	39,42
Fatigue	Root bark	Kenya	51
Gastric ulcers	Leaves, stems and twigs	Madagascar	56
Gastro-intestinal problems (constipation, diarrhoea, stomach ache and stomach complaints)	Bark, leaves, roots, root bark and stem bark	Kenya, Mozambique and South Africa	2,3,14,16,18,30,32-36,38,39,41-44,48-50,52,58,59,62,63,66-76
Gout	Root bark	Kenya	51
Headache	Bark and roots	Kenya and Madagascar	16,56
Internal injuries	Roots	Kenya	13,42,77,78
Joint pain	Leaves, roots and root bark	Kenya	22,23,28,38,50,51,62,63,79,80
Joint pains	Leaves mixed with Boscia salicifolia Oliv. leaves and Carissa spinarum L. root bark	Kenya	28,81
Joint pains	Leaves and stem bark mixed with Pavetta crassipes K. Schum. (leaves), Carissa spinarum L. (root bark) and Zanthoxylum chalybeum Engl. (leaves)	Kenya	28
Kidney pains	Bark, leaves and stem bark	Kenya	76,82
Malaria	Bark, leaves, roots, root bark, stems and stem bark	Kenya, Mozambique and South Africa	16,31-36,39,42,51,52,69,76,78,80,82-88
Menstrual problems	Bark and leaves	Kenya and South Africa	14,30,41,48,50,58,59,75
Nausea	Bark	South Africa	2,14,30,38,39,41,44,45,48,50,59,61-63
Pain	Root bark	Kenya and	22,23,38,44,

		South Africa	50,51,62,63,79
Poison antidote	Bark	South Africa	57
Postpartum pain	Stems	Kenya	53
Purgative	Bark	Kenya and South Africa	2,3,14,39,40,42,45,48,50,61-63,68,89
Respiratory diseases (chest pains, colds, influenza, pneumonia and tuberculosis)	Bark, leaves, roots, root bark and stem bark	Kenya and South Africa	13,16,28,39,51,75-77,80,82
Rheumatism	Bark, leaves and roots	Kenya and South Africa	2,14,28,30,32-36,38,39,41,42,50,52,59,61-63,66,68,73,75,86
Rheumatic fever	Bark mixed with roots of Turraea floribunda Hochst.	South Africa	30,31,48
Snake bite	Roots	Kenya, South Africa and Tanzania	13,14,30,32-36,38,39,42,44,50,62,63,68,73
Syphilis	Bark	Kenya and South Africa	3,34,36,50,59,61-63,68
Tonic	Bark	South Africa and Tanzania	14,39
Typhoid	Leaves and stem bark	Kenya	82
Ethnoveterinary medicine			
Anthelmintics in goats	Bark	South Africa	90
Babesiosis	Bark	South Africa	91
Diarrhoea in cattle	Bark	South Africa	39,92,93
East coast fever	Bark	East Africa	94
Heartwater in cattle	Bark	East Africa and South Africa	39,92-94
Paratyphoid	Bark	South Africa	95
Wounds in cattle and horses	Bark	Kenya and South Africa	3,34,36,50,63,79

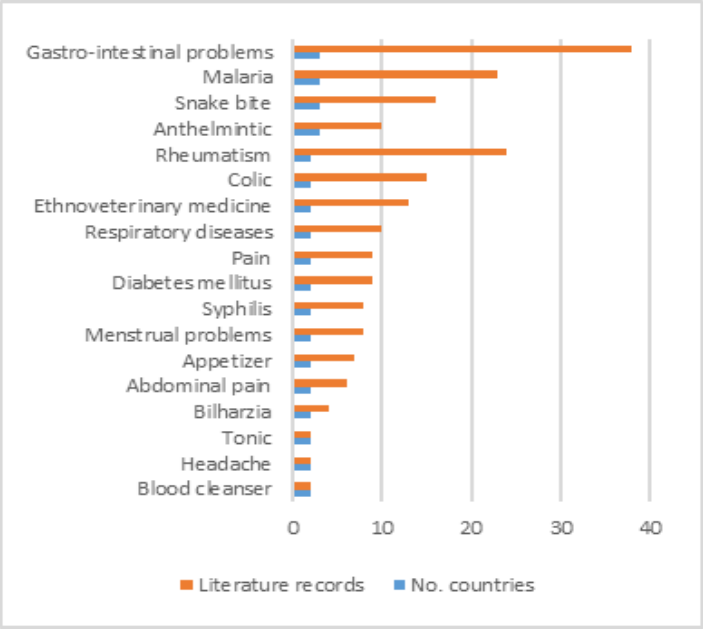

***Fig. 2**: Medicinal uses of Strychnos henningsii based on literature records*

3.2 Phytochemistry of Strychnos henningsii

Several phytochemical compounds including alkaloids, anthraquinones, cardiac glycosides, chalcones, flavones, flavonoids, flavonols, phenolics, proanthocyanidins, saponins, steroids, sterols, tannins and triterpenes (Table 2) have been identified from the bark, leaves, roots, root bark, stem bark and twigs of S. henningsii. Some of these phytochemical compounds may be responsible for the pharmacological properties exhibited by the species.

TABLE 2
PHYTOCHEMICAL COMPOUNDS IDENTIFIED FROM STRYCHNOS HENNINGSII

Compound	Plant part	Reference
3-hydroxyhenningsiine	Leaves	96
10-methoxy-tsilanine	Stems	97
11-methoxy-diaboline	Stem bark	98
11-methoxy-henningsamin	Stem bark	98
17,23-dihydroxyspermostrychnine	Leaves	96
18-hydroxy-isoretuline	Twigs	99
19-epi-23-hydroxyspermo-strychnine	Stem bark	96
23-hydroxyspermostrychnine	Roots and stem bark	96
23-hydroxyspermostrychnine-N(4)-oxide	Leaves	96
2,16-dehydrodiaboline	Stem bark	98
2,16-dehydro, 11-methoxy-diaboline	Stem bark	98
Anthraquinones	Bark, leaves and roots	35,62,100,101
Cardiac glycosides	Bark	32,33,35,101
Chalcones	Leaves	100
Condensamine	Stem bark	102,103
Cyclostrychnine	Leaves	96
Deshydroxyacetylhenningsamide	Leaves	96
Deshydroxyacetylhenningsiine	Leaves	96
Diaboline	Stem bark	98,104
Flavones	Leaves and roots	62,100
Flavonoids	Bark, leaves and roots	32,33,35,62,100,101
Flavonols	Leaves and roots	32,33,62,100
Henningsamide	Leaves	96
Henningsamine	Stem bark	104,105
Henningsiine	Leaves	96
Henningsiine-N(4)-oxide	Leaves	96
Henningsoline	Stem bark	104,105
Holstiine	Roots and stem bark	96,102,106,107
Holstiline	Stem bark	98,102,107
Na-acetyl-11-methoxystrychnosplendine	Root bark	108
Na-desacetyl-isoretuline	Twigs	99
Na-desacetyl-18-hydroxy-isoretuline	Twigs	99
Na-desacetyl,18-hydroxy,17-O-methyl-isoretuline	Twigs	99
O-acetyl-henningsamide	Leaves	96
O-acetyl-henningsiine	Leaves	96
O-acetyl-henningsoline	Stem bark	98
O-acetyl-retuline	Leaves	109
O-demethyl-tsilanine	Leaves and stem bark	97,107
O-demethyl,10-methoxy-tsilanine	Leaves	97
Phenolics	Bark	32,33,35
Proanthocyanidins	Bark	32,33,35
Retuline	Root bark and	96,102,10

	stem bark	3,110
Rindline	Stem bark	98,104,107
Saponins	Bark, leaves and roots	32,33,35,62,100,101
Spermostrychnine	Leaves	96
Splendoline	Roots and stem bark	96
Steroids	Bark	32,33,35,101
Sterols	Leaves and roots	62,100
Tannins	Bark, leaves and roots	32,33,35,62,100,101
Triterpenes	Bark	32,33,35,101
Tsilanimbine	Twigs	99
Tsilanine	Stems	97

3.3 Pharmacological properties of Strychnos henningsii

Pharmacological research revealed that different extracts of S. henningsii and phytochemical compounds isolated from the species have various biological activities such as analgesic [38], antibacterial [43,63,69,86], antidiabetic [34,35,42,100,111], anti-inflammatory [38], antioxidant [33,42], antiplasmodial [83,112,113], antiprotozoal [114], antispasmodic [38], cytotoxicity [42,111] and toxicity [32,47,62,83].

3.3.1 Analgesic activities

Tits et al. [38] evaluated the analgesic activities of the alkaloids retuline, brucine, holstiine, O-acetylisoretuline and isoretuline isolated from S. henningsii using an antinociceptive effect against chemical stimulus (phenylquinone writhing test). The alkaloid isoretuline exhibited activities [38].

3.3.2 Antibacterial activities

Kareru et al. [86] evaluated the antibacterial activities of aqueous extracts of S. henningsii leaves against Escherichia coli, Bacillus subtilis and Staphylococcus aureus using the agar disc diffusion assay with streptomycin (25.0 µg), tetracycline (100.0 µg), sulphamethoxazole (200.0 µg), gentamicin (10.0 µg) and cotrimoxazole (25.0 µg) as positive controls. The extract exhibited activities against the tested pathogens with zone of inhibition values ranging from 6.3 mm to 10.5 mm [86]. Njire et al. [69] evaluated the antibacterial activities of aqueous and methanol extracts of S. henningsii bark, leaf and roots against Escherichia coli using the agar disc diffusion method. The extracts exhibited activities against the tested pathogens with the inhibition zone ranging from 12.0 mm to 24.0 mm [69]. Khumalo [43] evaluated the antibacterial activities of dichloromethane and methanol extracts of S. henningsii bark against Enterococcus faecalis ATCC 29121, Bacillus cereus ATCC 11175, Escherichia coli ATCC 8739, Shigella sonnei ATCC 9290 and Salmonella typhimurium ATCC 14028 using the micro-titre plate technique with ciprofloxacin as a positive control. The extracts exhibited activities with minimum inhibitory concentration (MIC) values ranging from 1.0 mg/ml to >8.0 mg/ml in comparison to MIC values of 0.02 µg/ml to 0.07 µg/ml exhibited by the positive control [43]. Tirop et al. [63] evaluated the antibacterial activities of aqueous extract of S. henningsii leaves and roots against Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Salmonella typhi with tetracycline (30.0 µg), kanamycin (30.0 µg), gentamycin (10.0 µg), chloramphenicol (30.0 µg), cotrimoxazole (25.0 µg), augumentin (30.0 µg), cenfuroxime (30.0 µg) and ampicillin (10.0 µg) as positive controls. The extracts exhibited activities against the tested pathogens [63].

3.3.3 Antidiabetic activities

Ngugi et al. [100] evaluated the antidiabetic activities of the aqueous extract of S. henningsii leaves by intraperitoneally injecting varying doses of the extract into alloxanised mice. The extract exhibited activities [100]. Oyedemi et al. [34] and Oyedemi et al. [35] evaluated the antidiabetic activities of aqueous stem bark extract of S. henningsii by administering the extract at 125.0 mg/kg, 250.0 mg/kg and 500.0 mg/kg body weight in diabetic rats induced with streptozotocin-nicotinamide for 15 days. The extract decreased the blood glucose level [34,35]. Oyedemi et al. [111] and Oyedemi et al. [42] evaluated the antidiabetic activities of aqueous stem bark extract of S. henningsii by assessing the in vitro models known to target glucose homeostasis and their direct complications, including hepatocyte and adipocyte glucose utilization, intestinal carbohydrate digestion, oxidative stress and non-enzymatic protein glycation. The extract exhibited activities [42,111].

3.3.4 Anti-inflammatory activities

Tits et al. [38] evaluated the anti-inflammatory activities of the alkaloids retuline, brucine, holstiine, O-acetylisoretuline and isoretuline isolated from S. henningsii using the Carrageenan-induced paw oedema assay. The alkaloids retuline and isoretuline exhibited activities [38].

3.3.5 Antioxidant activities

Oyedemi et al. [33] evaluated the antioxidant activities of aqueous stem bark extract of S. henningsii by using the 2,2'-azinobis [3-ethylbenzothiazoline-6-sulfonic acid] diammonium salt (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH), ferric reducing antioxidant potential (FRAP), superoxide anions, hydrogen peroxide (H2O2) and nitric oxide (NO) with butylated hydroxytoluene (BHT), rutin, Vitamin C and Vitamin E. The extract exhibited concentration dependent activities against H2O2, ABTS, NO and DPPH with half maximal inhibitory concentration (IC50) values of 0.02 mg/ml, 0.09 mg/ml, 0.5 mg/ml and 0.7 mg/ml, respectively [33]. Oyedemi et al. [42] evaluated the antioxidant activities of aqueous stem bark extract of S. henningsii by using the ferric reducing antioxidant potential (FRAP) assay with BHT and quercetin as positive controls. The extract exhibited activities which were comparable to activities exhibited by the positive controls [42].

3.3.6 Antiplasmodial activities

Frederich et al. [112] evaluated the antiplasmodial activities of ethanol extract of S. henningsii leaves and the alkaloids holstiine, diaboline, strychnochromine and guianensine isolated from the root bark of the species against a chloroquine-sensitive strain FCA 20 Ghana of Plasmodium falciparum using an in vitro [3H]hypoxanthine incorporation assay with chloroquine and quinine as positive controls. The extracts exhibited weak activities against the tested pathogen with IC50 and IC90 values of 40.0 mg/ml and 200.0 mg/ml, respectively. The alkaloids holstiine, strychnochromine and guianensine exhibited activities against the tested pathogen with IC50 values ranging from 3.6 µM to 80.0 µM [112]. Philippe et al. [113] evaluated the antiplasmodial activities of ethyl acetate extracts of S. henningsii leaves and stems in vitro against a chloroquine-susceptible strain of Plasmodium

falciparum. The leaf extracts exhibited weak activities with IC50 and IC90 values of 15.9 µg/ml and 44.0 µg/ml, respectively [113]. Kirira et al. [83] evaluated the antiplasmodial activities of aqueous and methanol extracts of S. henningsii stem bark against chloroquine-sensitive and chloroquine-resistant strains of Plasmodium falciparum (NF54 and ENT30) using the [G-3H]hypoxanthine incorporation assay with chloroquine as a positive control. The extracts exhibited mild activities against the tested pathogens with IC50 values ranging from 67.2 µg/ml to 190.0 µg/ml [83].

3.3.7 Antiprotozoal activities

Wright et al. [114] evaluated the antiprotozoal activities of the alkaloids holstiline and holstiine isolated from S. henningsii against Entamoeba histolytica, Giardia intestinalis and Plasmodium falciparum using in vitro assays with chloroquine diphosphate, emetine dihydrochloride and metronidazole as positive controls. The alkaloids holstiline and holstiine exhibited activities against Plasmodium falciparum with IC50 values of 31.5 µM and 32.7 µM, respectively [114].

3.3.8 Antispasmodic activities

Tits et al. [38] evaluated the antispasmodic activities of the alkaloids retuline, brucine, holstiine, O-acetylisoretuline and isoretuline isolated from S. henningsii by assessing the myostimulating effect of histamine and bradykinin on guinea-pig ileum. The alkaloid isoretuline exhibited activities [38].

3.3.9 Cytotoxicity activities

Oyedemi et al. [111] and Oyedemi et al. [42] evaluated the cytotoxicity activities of aqueous stem bark extract of S. henningsii in Chang liver cells using the MTT toxicity assay. The extract exhibited activities with IC50 value of 130.0 µg/mL [42,111].

3.3.10 Toxicity activities

Ogeto et al. [47] evaluated the toxicity activities of the alkaloids isolated from S. henningsii bark on mice following intraperitoneal administration of extract on isolated innerverted skeletal muscles of the rat diaphragm as well as on local anatomic sites of guinea pig skin. The alkaloids induced convulsions and paralysis characteristic of strychnine poisoning [47]. Tits et al. [38] evaluated the toxicity activities of the alkaloids retuline, brucine, holstiine, O-acetylisoretuline and isoretuline isolated from S. henningsii by administering the alkaloids to groups of Swiss A mice in different doses and mortality rates observed after 24 hours and every day for 14 days. The alkaloid isoretuline administered intravenously exhibited half maximal lethal dose (LD50) value of 70.0 mg/kg in comparison to LD50 value of 0.5 mg/kg exhibited by strychnine [38]. Kirira et al. [83] evaluated the toxicity activities of aqueous and methanol extracts of S. henningsii stem bark against brine shrimp (Artemia salina) using the brine shrimp lethality test with emetine hydrochloride as positive control. The methanol extract exhibited mild activities with LD50 value of 101.2 µg/ml [83]. Oyedemi et al. [32] evaluated the in vivo acute and sub-acute toxicity of aqueous bark extract of S. henningsii leaf and root extracts in Wistar rats. The effect of the oral administration of the extract at 250.0 mg/kg, 500.0 mg/kg and 1000.0 mg/kg body weight was investigated on the hematological and biochemical parameters in Wistar rats for 28 days. The results of this study showed that sub-acute administration of the plant extracts were non-toxic to Wistar rats [32]. Tirop et al. [62] evaluated the in vivo acute and sub-acute toxicity of S. henningsii leaf and root extracts in Swiss mice. At dosages above 750.0 mg/kg body weight, the mice showed intestinal, hepatic and renal pathological alterations [62].

4 CONCLUSION

Van Wyk et al. [14] and Van Wyk et al. [25] argued that the fruits of S. henningsii could be poisonous and therefore, there is need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. Therefore, the widespread use of S. henningsii as source of traditional medicines throughout its distributional range suggest that the species is not taken at toxic dosages. But use of S. henningsii for the treatment of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies of the bark, fruits, leaves, roots and seeds, and compounds isolated from the species are necessary.

CONFLICTS OF INTEREST

No conflict of interest is associated with this work.

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