A Synthesis and Review of Medicinal Uses, Phytochemistry and Pharmacological Properties of *Cissampelos mucronata* A. Rich. (Menispermaceae)

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Abstract: *Cissampelos mucronata* A. Rich. is a perennial climber widely used as traditional medicine in tropical Africa. This study is aimed at providing a critical review of medicinal uses, phytochemical and pharmacological properties of *C. mucronata*. Documented information on medicinal uses, phytochemical and pharmacological properties of *C. mucronata* was collected from several online sources such as Scopus, Google Scholar, PubMed and Science Direct, and pre-electronic sources such as book chapters, books, journal articles and scientific publications obtained from the University library. The articles published between 1962 and 2020 were used in this study. This study revealed that leaves, rhizome, roots and stems, and whole plant parts of *C. mucronata* are mainly used as traditional medicines for sexually transmitted infections, fever, swellings, headache, respiratory problems, snakebite, malaria, pregnancy problems and gastro-intestinal problems. Phytochemical compounds identified from the species include alkaloids, anthraquinones, flavonoids, glycerine, glycosides, phenolics, reducing sugars, resin, saponins, steroids, tannins and triterpenes. Pharmacological research revealed that *C. mucronata* extracts and alkaloids isolated from the species have antibacterial, anti-mycobacterial, antifungal, antiplasmodial, antitrypanosomal, anti-ulcer, anti-androgenic, anti-steroidogenic, enzyme tyrosine kinase p56 inhibitory, hypoglycemic, larvicidal, molluscicidal, sedative, tocolytic, uterine relaxant and cytotoxicity activities. There is need for extensive toxicological evaluations of crude extracts and compounds isolated from the species since *C. mucronata* contains potentially toxic compounds

Keywords: *Cissampelos mucronata*, indigenous knowledge, Menispermaceae, traditional medicine.

INTRODUCTION

Cissampelos mucronata A. Rich. is a shrubby climber with a woody rootstock belonging to the Menispermaceae family which is commonly referred to as monkey vine or curare family. The generic name "*Cissampelos*" is derived from two Greek words "*kissos*" and "*ampelos*" which mean "climber" and "vine", respectively [1]. The specific name "*mucronata*" is a Latin word which means "each leaf has a single short hair or bristle at its tip" [1]. The English common name are "hairy heartleaf" and "heart-leaved vine". Synonyms associated with *C. mucronata* include *C. apiculata* Hochst., *C. aristolochiifolia* Fenzi, *C. comata* Miers, *C. macrostachya* Klotzsch, *C. pareira* L. var. *mucronata* (A. Rich.) Engl., *C. senensis* Klotzsch, *C. vogelii* Miers and *C. zairensis* Miers [2]. *Cissampelos mucronata* has twining shoots growing up to 4 metres in height [1]. The leaves are oval in shape with a cordate base, velvety and dark green in colour with a bristle at the tip. Female and male flowers are axillary or in false racemes and borne on the same plant. Fruits are green, turning bright red when ripe and held in pubescent leaf-like bracts. *Cissampelos mucronata* is common and widespread in tropical Africa, distributed from Senegal east to Ethiopia and south to South Africa [3]. *Cissampelos mucronata* has been recorded in open habitats, deciduous bushland, grassland, burnt veld, often on termite mounts and rock outcrops, in riverine forests and swamps at altitude ranging from 15 m to 1850 m above sea level [2].

The *Cissampelos* L. species are widely used as sources of traditional medicines in tropical Africa [3-5]. The leaves and roots of *C. mucronata* are sold as traditional medicines in informal herbal medicine markets in Benin, Malawi and Mozambique [6-8]. *Cissampelos mucronata* is also commonly planted in home gardens as a medicinal plant in some countries in the tropical Africa [3]. The rhizomes of *C. mucronata* are traditionally used in the preparation of arrow poison [3] and fish poison while the leaves of the species are cooked as leafy vegetables in Botswana [1]. *Cissampelos mucronata* is also included in two monographs focusing on poisonous plants, "mind-altering and poisonous plants of the world" and "poisonous plants of South Africa" [10,11]. In these two monographs, Van Wyk *et al*. [10] and Wink and Van Wyk [11] provide basic information about the poisonous ingredients, the pharmacological effects and associated symptoms of human and animal poisoning as a result of ingesting documented plant species. It is, therefore, within this context that this review was undertaken, aimed at reviewing the ethnomedicinal

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Table 1: Medicinal uses of *Cissampelos mucronata*

Disease	Plant part	Country	Reference
Abdominal pain	Roots	Ethiopia, Tanzania and Zimbabwe	[12-16]
Anaemia	Leaves	Ethiopia	[17]
Arthritis	Leaves, stems and roots	Nigeria	[18]
Backache	Leaves and roots	South Africa, Uganda and Zimbabwe	[12,19-21]
Bilharzia	Roots	Benin, South Africa and Zimbabwe	[12,19,21-23]
Bleeding gums	Leaves and roots	Zambia	[24]
Blood pressure	Roots	Angola	[25]
Cancer	Roots	Ghana and Nigeria	[26,27]
Epistaxis	Leaves	Angola	[28]
Erectile dysfunction	Leaves	Angola	[28]
Fever	Rhizome and roots	Eswatini, Nigeria, South Africa and Tanzania	[13,18,19,21,29]
Gastro-intestinal problems (diarrhoea, digestive problems, dysentery, indigestion and stomachache)	Leaves and roots	Benin, Ethiopia, Gambia, Guinea-Bissau, Malawi, Mozambique, Nigeria, South Africa, Tanzania, Uganda, Zambia and Zimbabwe	[12-14,18-21,23,30-42]
Haemorrhoids	Leaves and roots	Angola and Benin	[8,25]
Headache	Roots	Angola, Nigeria, South Africa, Tanzania and Uganda	[13,19,21,28,43,44]
Hernia	Roots	Tanzania	[13]
Heart problems	Roots	Ethiopia	[45]
Jaundice	Leaves	Ethiopia and Nigeria	[17,18]
Kidney problems	Roots	Ethiopia	[45]
Liver diseases	Whole plant	Rwanda	[46]
Malaria	Leaves, roots and whole plants	Benin, Democratic Republic of Congo (DRC), Kenya, Nigeria, Senegal, Tanzania, Uganda and Zimbabwe	[23,47-56]
Menstrual problems	Roots	Ethiopia, South Africa and Zimbabwe	[12,19,21,57,58]
Nausea	Roots	Tanzania	[13]
Obesity	Leaves, stems and roots	Nigeria	[18]
Pain (head, neck and muscle)	Roots	Namibia and South Africa	[19,21,32,59]
Pregnancy problems (abortifacient, expel placenta, induce labour, infertility, postpartum bleeding, prevention of miscarriage, sexual stimulation and uterine pain)	Leaves and roots	Angola, Ethiopia, Guinea-Bissau, Nigeria, Senegal, South Africa, Tanzania, Uganda, Zambia and Zimbabwe	[12,13,19,21,24,28,32,36,37,39,57-63]
Respiratory problems (asthma, cough, lung problems and sore throat)	Leaves, rhizome, roots and stems	Angola, Nigeria, South Africa, Togo and Zimbabwe	[3,12,18,19,28,36]
Sexually transmitted infections (chancroid, syphilis and venereal diseases)	Leaves and whole plant	Malawi, Nigeria, Zambia and Zimbabwe	[12,64-66]
Skin diseases (chicken pox and measles	Leaves	Nigeria	[44]

(Table 1). Continued.

Disease	Plant part	Country	Reference
Snakebite	Roots	Ethiopia, Nigeria, South Africa, Tanzania and Uganda	[13,14,18,19,20,32,67]
Sore eyes	Leaves	Zimbabwe	[12,19]
Swellings	Leaves and roots	DRC, Ethiopia, Tanzania, Uganda and Zimbabwe	[12,13,20,68,69]
Tonic	Roots	South Africa	[70]
Ulcers	Leaves	Nigeria	[34,61]
Yellow fever	Leaves and roots	Uganda	[71]
Worms	Leaves and roots	Tanzania and Uganda	[13,43]
Wounds	Roots	Benin and South Africa	[19,23,36]
Ethnoveterinary medicine (amoebiasis, expel placenta, heartwater, helminthosis and rabies)	Leaves and roots	Ethiopia and Tanzania	[67,72-75]

uses, phytochemical and pharmacological properties of *C. mucronata* so as to provide baseline data required in evaluating the therapeutic potential of the species.

Medicinal Uses

The leaves, rhizome, roots and stems and whole plant parts of *C. mucronata* are mainly used as traditional medicines for sexually transmitted infections, fever, swellings, headache, respiratory problems, snakebite, malaria, pregnancy problems and gastro-intestinal problems (Table **1**, Figure **1**). Other medicinal applications reported in two countries and supported by at least two literature reports include the use of leaves, rhizome, roots and stems and whole plant parts of *C. mucronata* against abdominal pain, backache, bilharzia, cancer, haemorrhoids, jaundice, menstrual problems, pain, worms, wounds and as ethnoveterinary medicine (Table **1**).

Phytochemistry

Ferreira *et al.* [76] identified a bisbenzylisoquinoline alkaloid, l-isochondodendrine from the roots of *C. mucronata*. De Wet [77] identified the alkaloids cycleanine, dicentrine, salutaridine, reticuline and pronuciferine from the leaves and rhizomes of *C. mucronata*. Other phytochemical compounds identified from the aerial parts, leaves and roots of *C. mucronata* include anthraquinones, carbohydrates, flavonoids, glycerine, glycosides, phenolics, reducing sugars, resin, saponins, sterols, steroids, tannins and

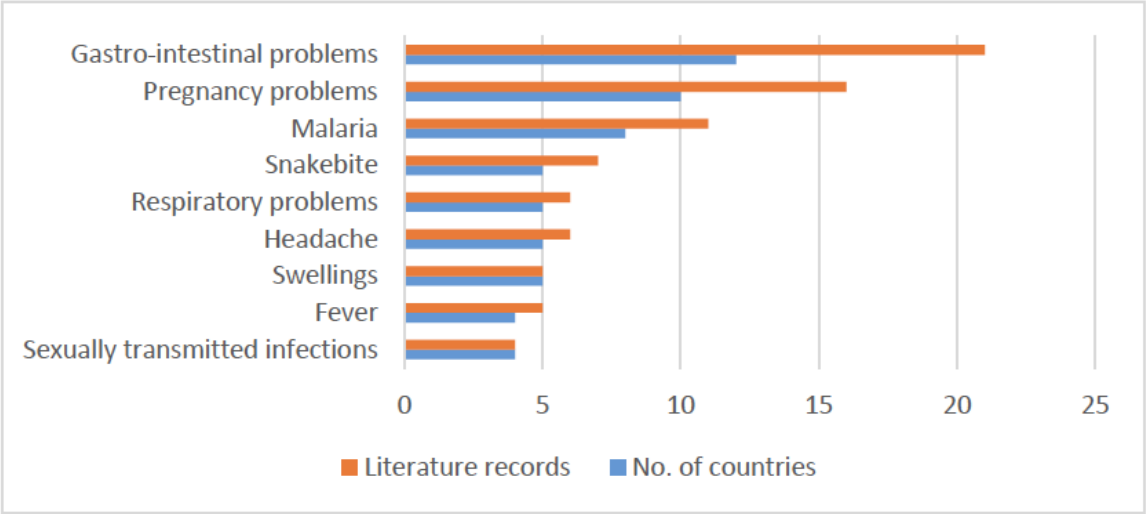

Figure 1: Medicinal applications of *Cissampelos mucronata* derived from literature records.

triterpenes [62,78-86]. Some of the identified phytochemical compounds may be responsible for the biological activities associated with the species.

Pharmacological Properties

The following pharmacological activities have been documented from the aerial parts, leaves, rhizome, roots and root bark extracts of *C. mucronata* and alkaloids isolated from the species: antibacterial [23,34,81,87,88], anti-mycobacterial [86], antifungal [88], antiplasmodial [47,58,82,89-92], antitrypanosomal [90], anti-ulcer [34,80,93] anti-androgenic and anti-steroidogenic [62], enzyme tyrosine kinase p56 inhibitory [90], hypoglycemic [83], larvicidal 88], molluscicidal [94], sedative [78], tocolytic [95-98], uterine relaxant [79], cytotoxicity [23,89,99] and toxicity [34,88,93,98] activities.

Antibacterial Activities

Taniguchi *et al.* [87] evaluated the antibacterial activities of the crude extracts of *C. mucronata* leaves at a concentration of 100.0 µg/ml against *Bacillus subtilis* and *Escherichia coli*. The extract caused complete growth inhibition of *Bacillus subtilis* but no activities against *Escherichia coli* were observed [87]. Akah and Nwafor [34] evaluated the antibacterial activities of methanolic extracts of *C. mucronata* leaves against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia* and *Pseudomonas aerguinosa* using the agar disc diffusion method. The extract exhibited activities against tested pathogens with the zone of inhibition ranging from 3.2 mm to 9.5 mm [34]. Tor-anyiin *et al.* [81] evaluated the antibacterial activities of water and methanol : dichloromethane (1:1) extracts of the leaves of *C. mucronata* against *Streptococcus pyogenes, Staphylococcus aureus, Salmonella typhi* and *Escherichia coli* using the agar dilution method. The extracts exhibited moderate activities against tested pathogens [81]. Nondo *et al.* [88] evaluated the antibacterial activities of dichloromethane and ethanol extracts of the roots and aerial parts of *C. mucronata* against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Vibrio cholera, Bacillus anthracis* and *Streptococcus faecalis* using microdilution method with gentamicin as a positive control. The extracts exhibited activities against tested pathogens with minimum inhibitory concentration (MIC) values ranging from 0.2 mg/mL to >25.0 mg/mL [88]. Catteau *et al.* [23] evaluated the antibacterial activities of hexane, dichloromethane, ethyl acetate and methanol extracts of the aerial parts of *C. mucronata* against *Staphylococcus aureus* using the checkerboard method with ampicillin and oxacillin as positive controls. All the extracts exhibited moderate activities against the tested pathogen with the MIC value of >500 mg/L [23].

Anti-Mycobacterial Activities

Aska *et al.* [86] evaluated the anti-mycobacterial activities of methanol extracts of *C. mucronata* roots against *Mycobacterium bovis* using broth micro-dilution method with rifampicin as a positive control. The extract exhibited activities with the MIC value of 5.0 mg/ml [86].

Antifungal Activities

Nondo *et al.* [88] evaluated the antifungal activities of dichloromethane and ethanol extracts of the roots and aerial parts of *C. mucronata* against *Candida albicans* and *Cryptococcus neoformans* using the microdilution method. The extracts exhibited activities against the tested pathogens with the MIC values ranging from 0.2 mg/mL to >25.0 mg/mL [88].

Antiplasmodial Activities

Gessler *et al.* [47] evaluated the antimalarial activities of ethanol, petroleum ether, ethyl acetate and water fractions of *C. mucronata* roots using the G-^{3}H-hypoxanthine incorporation assay against multidrug resistant *Plasmodium falciparum* strain K1 and the chloroquine sensitive strain NF54. The ethyl acetate fraction exhibited the best activity against *Plasmodium falciparum* strain K1 with the half maximal inhibitory concentration (IC_{50}) value of 0.4 µg/ml whilst other fractions exhibited IC_{50} values ranging from 1.2 µg/ml to 8.0 µg/ml [47]. Tshibangu *et al.* [90] evaluated antiplasmodial activities of the dichloromethane and methanol extracts of *C. mucronata* roots against chloroquine sensitive (D6) and chloroquine resistant (W2) *Plasmodium falciparum* strains using the ^{3}H-hypoxanthine incorporation assay with artemisinin as a positive control. The extract exhibited activities with the IC_{50} values ranging from 1.1 µg/ml to 2.9 µg/ml [90]. Van Zyl *et al*. [91] evaluated the antimalarial activities of methanol extracts of *C. mucronata* rhizome against a chloroquine-resistant *Plasmodium falciparum* strain using the ^{3}H-hypoxanthine incorporation assay. The extract exhibited activities at a concentration less than 5 µg/ml [91]. Muthaura *et al.* [92] evaluated the antiplasmodial activities of methanol extract of the leaf and root bark of *C. mucronata* against the chloroquine sensitive (D6) and resistant (W2) *Plasmodium*

falciparum using the semi-automated micro-dilution technique that measures the ability of the extracts to inhibit the incorporation of G-^{3}H-hypoxanthine into the malaria parasite. The leaf and root bark extracts exhibited activities with IC_{50} values of 4.4 µg/ml and 8.8 µg/ml, respectively, against D6, and the root bark extract exhibited IC_{50} value of 9.2 µg/ml against W2 [92].

Gessler *et al.* [89] evaluated the antimalarial activities of ethyl acetate extracts of *C. mucronata* roots using a four day suppressive test in *Plasmodium berghei*-infected mice. The extract administered orally to the mice at 500 mg/kg body weight/day produced 58.5% suppression of parasitaemia [89]. Assefa *et al.* [58] evaluated *in vivo* antimalarial activities of aqueous and methanol extracts of *C. mucronata* leaves in a four-day suppressive assay against *Plasmodium berghei* Anka strain in mice. An oral dose of 400 mg/kg/day, the aqueous extract of the roots exhibited the best activities and reduced parasitemia by 47.5% [58]. Katsayal and Obamiro [82] evaluated the antiplasmodial activities of the ethanol extract of the leaves of *C. mucronata* using suppressive, curative and prophylactic procedures in Swiss albino mice. The extract at a dose of 200.0 mg/kg/day, intraperitoneally administered in mice, inhibited the growth of *Plasmodium berghei* at a range from 60.0% to 73.7% when compared with the standard chloroquine at a dose of 5.0 mg/kg/day, which inhibited the growth of the parasites within the range from 89.5% to 100% [82].

Antitrypanosomal Activities

Tshibangu *et al.* [90] evaluated antitrypanosomal activities of the dichloromethane and methanol extracts of *C. mucronata* roots against *Trypanosoma brucei rhodesiense* and *Trypanosoma cruzi* using the Alamar Blue and an enzyme-linked immunosorbent assays with benznidazole as a positive control. The extracts exhibited activities against tested pathogens with the MIC values ranging from 11.0 µg/ml to >100.0 µg/ml [90].

Anti-Ulcer Activities

Akah and Nwafor [34] evaluated the anti-ulcer activities of methanol extracts of *C. mucronata* leaves in experimental animals. On isolated guinea pig ileum, the extract inhibited contractions caused by acetylcholine, histamine and serotonin. The extract decreased the propulsive movement of gastro-intestinal content and protected the rats from indomethacin, histamine and stress-induced ulcers [34]. Nwafor and Akah [80] evaluated the anti-ulcer activities of methanol extracts of *C. mucronata* leaves against indomethacin-induced ulcers in rats. At the dose of 450.0 mg/kg, the extract showed varying degrees of activities against ulcers induced by indomethacin [80]. Nwafor and Okoye [93] evaluated the anti-ulcer activities of ethanol extracts of *C. mucronata* roots using three models of experimental ulcer induction in rats. The extract exhibited dose-dependent activities in indomethacin, histamine and stress-induced ulcers [93].

Anti-Androgenic and Anti-Steroidogenic Activities

Olaolu *et al.* [62] evaluated the anti-androgenic and anti-steroidogenic activities of aqueous extracts of *C. mucronata* leaves in male albino rats. The rats administered with 1200 mg/kg body weight of extract resulted in reduced concentrations of acid phosphatase, alkaline phosphatase and total testicular protein indicating anti-androgenic and anti-steroidogenic activities [62].

Enzyme Tyrosine Kinase p56^{lck} (TK) Inhibitory Activities

Tshibangu *et al.* [90] evaluated the enzyme tyrosine kinase p56^{lck} (TK) inhibitory activities of the dichloromethane and methanol extracts of *C. mucronata* roots using the inhibition assay against T cell TK p56^{lck}. The extract exhibited activities with TK % inhibition of 71.0% to 92.0% at a concentration of 200 µg/ml [90].

Hypoglycemic Activities

Tanko *et al.* [83] evaluated the hypoglycemic activities of ethanol extract of the leaves of *C. mucronata* using the streptozocin-induced diabetic rats by intraperitoneally administering the extract at doses of 200, 400 and 800 mg/kg. The extract resulted in reduced blood glucose levels in all the doses administered, with a dose of 200 mg/kg showing the highest glycemic change of 67.0% after 24 hours of extract administration [83].

Larvicidal Activities

Nondo *et al.* [88] evaluated the larvicidal activities of dichloromethane and ethanol extracts of the roots and aerial parts of *C. mucronata* using the *Culex quinquefasciatus* mosquito larvae. The dichloromethane and ethanol root extracts exhibited activities with the median lethal concentration (LC_{50}) values of 126.1 µg/mL and 220.0 µg/mL, respectively [88].

Molluscicidal Activity

Kela *et al.* [94] evaluated the molluscicidal activities of aqueous and methanol extracts of *C. mucronata* roots against *Lymnaea natalensis* with copper sulphate as a positive control. The extracts exhibited weak activities at higher concentrations of the extract [94].

Sedative Activities

Akah *et al.* [78] evaluated the sedative activities of the ethanol root extract of *C. mucronata* in mice. The extract showed changes in behavioural patterns of mice, which were indicative of central nervous system depression. The extract also reduced ephedrine-induced spontaneous motor activities in rats and prolonged pentobarbitone-sleeping time in the animals. The pre-treatment of rats with the extract protected 40.0% of the rats against pentylenetetrazole-induced convulsions [78].

Tocolytic Activities

Ndu *et al.* [96] evaluated the tocolytic activities of ethanol leaf extract of *C. mucronata* on the length of gestation period in pregnant albino rats with salbutamol (0.2 mg/kg/day) and 3% Tween 85 (5 ml/kg/day) as controls. The extract extended the mean gestation period relative to control values suggesting tocolytic activities [96]. Ndu *et al.* [97] evaluated the tocolytic activities of ethanol leaf and root extracts of *C. mucronata* on the onset of parturition in pregnant albino rats with salbutamol (0.2 mg/kg/day) and 3% Tween 85 (5 ml/kg/day) as controls. Both extracts delayed the onset of parturition relative to the controls suggesting tocolytic activities [97]. Similarly, Garba *et al.* [98] reported embryofetal activities of the methanol root extracts of *C. mucronata* which showed increase in resorption sites in the uterus of rats that had received 100.0 mg/kg to 300.0 mg/kg dose levels of the extract. Lampiao *et al.* [95] assessed the relationship between intake of aqueous extract of *C. mucronata* leaves and the outcome of delivery using a rat model. The administration of the extract during pregnancy resulted in early induction of labour [95].

Uterine Relaxant Activities

Nwafor *et al.* [79] evaluated the uterine relaxant activities of the ethanol extract of *C. mucronata* roots on non-gravid and gravid rat uterus. The extract exhibited activities by relaxing the non-gravid rat uterus in a concentration and time-dependent manner [79].

Cytotoxicity Activities

Gessler *et al.* [89] evaluated the cytotoxicity activities of ethyl acetate extracts of *C. mucronata* roots by determining the MIC by comparing microscopically the cells of the extract with the cells of the control and also by using the colorimetric cytotoxicity assay using the human cell lines KB and HT 29. The MIC values were 12.6 µg/mL and 37.0 µg/mL for H29 and KB, respectively, while the MIC value for the control chloroquine was 111 µg/mL for KB. The IC_{50} values for HT29 and KB were 8.5 µg/mL and 19.0 µg/mL, respectively, while the IC_{50} value for the control chloroquine was 58.0 µg/mL for KB [89]. De Wet *et al.* [99] evaluated cytotoxicity activities of crude alkaloidal extracts isolated from the rhizomes of *C. mucronata* using MCF7 (breast), UACC62 (melanoma) and TK10 (renal) cancer cell lines with adriamycin and 5-fluorouracil as positive controls. The extracts exhibited weak activities with total growth inhibition (TGI) values ranging from 15.0 µg/ml to 24.0 µg/ml. The GI_{50} (concentration required for 50% inhibition of cell growth) values ranged from <6.3 µg/ml to 9.0 µg/ml [99]. Catteau *et al.* [23] evaluated cytotoxicity activities of hexane, dichloromethane, ethyl acetate and methanol extracts of aerial parts of *C. mucronata* against J774 and WI38 cells using tetrazolium salt MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphényltetrazolium bromide] colorimetric assay with camptothecin as a positive control. The extracts exhibited activities against the tested cells with the IC_{50} values ranging from 18.3 mg/L to 99.6 mg/L [23].

Toxicity Activities

Akah and Nwafor [34] evaluated the acute toxicity activities of methanolic extracts of *C. mucronata* leaves in Swiss albino mice. The extract exhibited an oral median lethal dose (LD_{50}) value of 8.5 g/kg [34]. Nwafor and Okoye [93] evaluated the acute toxicity activities of ethanol extracts of *C. mucronata* roots in mice. The extract exhibited a LD_{50} value of 288.5 mg/kg [93]. Nondo *et al.* [88] evaluated the toxicity activities of dichloromethane and ethanol extracts of the roots and aerial parts of *C. mucronata* using the brine shrimp lethality test. The extracts exhibited activities with LC_{50} values ranging from 59.6 µg/ml to 143.0 µg/ml [88]. Garba *et al.* [98] evaluated the toxicological activities of the methanol extracts of *C. mucronata* roots on liver and kidney tissues of mice. Administration of 100, 200 and 300 mg/kg of the extract caused a decrease in body weight, and increase in the serum levels of alanine aminotransferase, alkaline

phosphatase, total protein and albumin. The liver and kidney tissues showed moderate lymphocytic infiltration and thrombus formation in central veins in the liver and epithelial sloughing of the proximal convolated tubules in renal tissues. The extract showed the LD_{50} value of >2000 mg/kg [98].

CONCLUSION

Cissampelos mucronata is a known component of the traditional arrow and fish poison [3,9-11], and there is need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. Although *C. mucronata* is a well-known poisonous plant [10,11], there is no information on human poisoning. Therefore, the widespread use of *C. mucronata* in tropical Africa as traditional medicine suggests that the species is not taken at toxic dosages. But the use of *C. mucronata* for the treatment of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies of the leaves, rhizomes, roots, stems and compounds isolated from the species are necessary.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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