Australian Journal of Science and Technology

ISSN Number (2208-6404)
Volume 2; Issue 2; June 2018

Review Article

Review of toxic effects of medicinal plants found in Nigeria

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ABSTRACT

Majority of the world population use plants as a source of medicinal substances for their well-being. There has been a growing concern on the safety of some of these medicinal plants in current use. The present study seeks to bring an up-to-date review of literature that has reported toxicities associated with plants used for medicinal purposes in Nigeria. We searched literature using Google Scholar and PubMed. 50 plants belonging to 34 families met the criteria for selection. Many of these plants used for medicinal purposes are noted to have a potential toxic effect associated with their irrational consumption. Therefore, we recommend that caution should be observed when using them as medicinal sources.

Keywords: Medicinal plants, toxic effects, toxicity

Submitted: 27-03-2018, **Accepted:** 10-04-2018, **Published:** 29-06-2018

INTRODUCTION

From time immemorial, plants are known to be sources of medicinal substances used for prevention and treatment of various diseases around the globe.[1] About 80% of the world's population has accepted plants as an indispensable source of medicinal substances used for maintenance of well-being.[2]

Despite the above-mentioned medicinal benefits of plants, some of their chemical substances are toxic to man[3] when consumed at high, moderate or even at small concentrations, depending on the type of plant.[4] Some of these toxic substances can affect the entire organ system while some only affect specific organs in the system, for example, digitoxin, oleandrin, neriifolin, and thevetin A and B (cardiac glycosides) target the heart.[5] The presiding effect may lean on the wrong identity of the plant, state or condition of the plant, stage of development (growth), plant part used, species, amount consumed, and vulnerability of the victim.[3]

Nigeria, being in the tropical region is known to harbor numerous plants containing high levels of heterogeneous chemical substances (alkaloids, tannins, flavonoids, saponins, anthraquinones, glycosides, proteins, etc.) for protection against predators and adaptation to the harsh tropical environmental conditions.[6] The use of medicinal plants in Nigerian traditional medical practices is currently not properly checked resulting to increased risk of toxicity due to wrong administration especially of those plants that are toxic at low concentrations.[7] Another area of concern is the risk of genotoxicity associated with chronic exposure to most commonly used medicinal plants.[8]

Numerous research works have pointed out chemical constituents or phytochemical content of some poisonous plants. It is necessary to identify plants with toxicity potentials among the plants used for therapeutic purposes.[4] This will help in reducing the rate of plant-associated poisoning or toxicity. It will also help researchers in making decisions on the dose to use in evaluating the therapeutic effect of a toxic plant.

The aim of this review is to provide an index of Nigerian medicinal plants with potentials for toxicity.

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METHODOLOGY

Literature in different local and international peer-reviewed journals that featured on the toxicity of medicinal plants found in Nigeria and is used by the populace in any part of the country for medicinal importance was extensively searched. The scientific search engines used in the study were the Google scholar (https://scholar.google.com) and PubMed (www.ncbi.nlm.nih.gov/pubmed). The study database included research articles, books, these and other scientific write-ups, known for their academic rating, covering various aspects of the plant species (Botany, traditional use, pharmacology, or toxicology) dating from 1982 to 2016. The search strategy used, as employed by Félix-Silva *et al*.[9] contained one or a combination of the following terms "toxic Nigerian medicinal plants" or "toxic medicinal plants in Nigeria" or "Nigerian toxic plants" or "toxic medicinal plants" or "toxicity" "medicinal plants" "review" or "medicinal plants in Nigeria" "toxicity" or "toxic effect" "Nigerian plants" or "poisonous effect" "Nigerian plants" or "toxicity" or "toxic effect" or "poisonous part." Search results were screened for relevance in the study. Only literature published in English that reported toxicities or poisonous effects (including human, animal, and *in vitro* studies) of medicinal plants that can be found in Nigeria were included. Information on toxicities of the studied plants and summary of the work was extracted from the consulted literature [Table 1].

DISCUSSION

The results above show common medicinal plants found in Nigeria having potential toxic effects to either humans or animals at certain concentrations (where specified) according to various scholarly articles reviewed by the present research. 50 plants belonging to 34 families were recorded in this review article. Euphorbiaceae family had the highest number in this research (11.8%) followed by Apocynaceae and Fabaceae (9.8% each), Sapotaceae (5.9%), Cucurbitaceae, Malvaceae, and Rubiaceae (3.9% each), with the rest having 1.9% each.

The parts of the plants found to be toxic include leaves (25.5%), roots (23.5%), stem bark (9.8%), seeds (9.8%), fruits (2.0%), whole plant (2.0%), aerial part (2.0%), and latex (3.9%), with 21.6% accounting for parts not specified by the studies. The identified plant parts were extracted using either organic solvents (ethanol, methanol, hexane, acetone, and petroleum ether) or water (aqueous).

All the plants mentioned in this study are used medicinally in different parts of the country. This could be due to their therapeutic benefits at lower concentrations and toxic effects usually occur at higher concentrations or when an overdose is used. The plants identified in this study mainly caused

Table 1: Results of literature search

S. No	Family	Botanical name	Common name	Ethnomedicinal uses	Summary of the study	Toxic effects	Reference(S)
1	Agavaceae	*Sansevieria trifasciata*	Snake plant	Analgesic, antipyretic	Cases of intoxication of pets were investigated by personal visits to residences, including homes, yards, apartments, and common garden areas, in Rio Grande do Sul, Brazil, from 1998 to 2002	Intoxication of pets (i.e., companion animals)	[10]
2	Amaranthaceae	*Aerva lanata*	Mountain knotgrass	Anti-diabetic, anti-inflammatory, diuretic, control of kidney disorders	Ethanolic extract of the Aerial parts of the plant evaluated on Rat spermatozoa (*in vitro*) models at 200 mg/kg b/w. Pre-implantation loss of 20% and percentage pregnancy loss of 30% was observed.	Abortion, cytotoxicity	[11,12]
3	Amaryllidaceae	*Allium sativum*	Garlic	Common cold, cancer, cardiovascular health.	Garlic extract was found to be toxic to rats at >50 mg/kg (intraperitoneal administration more toxic than oral)	Respiratory arrest, hepatotoxicity, nephrotoxicity, cardiotoxicity, death	[13]

(Contd...)

Table 1: ***(Continued)***

S. No	Family	Botanical name	Common name	Ethnomedicinal uses	Summary of the study	Toxic effects	Reference(S)
4	Anacardiaceae	*Anacardium occidentale*	Cashew	Hypoglycemic and renoprotective effects	Leaf hexane extract, administered in mice. Toxicity was observed at doses ≥6 g/kg b/w. LD50 16 g/kg. Subacute toxicity was seen at doses of 6, 10, and 14 g/kg (oral) for 56 days.	Acute: Asthenia, anorexia, diarrhea, syncope. Subacute: Reduction in food intake, weight gain, behavioral effects and abnormal liver and kidney function tests.	[14]
5	Apocynaceae	*Calotropis procera*	Giant milkweed	Anti-tumor activity	Latex administered in goats at 1ml/kg b/w Orally, 0.005 ml/kg i.v and i.p caused death between 20 min and 4 days.	Nervous signs, frequent urination, frothing at the mouth, dyspnea, and death	[15]
6	Apocynaceae	*Rauwolfia vomitoria* Afzel	Serpentwood	Hypolipidemic effect	An aqueous root extract of R. vomitoria administered to Wistar rats at 200 mg/kg b/w daily. Sacrificed after receiving 1, 3, 5, 10, 20, and 30 oral doses.	Significant changes in the activity of ALP, ACP, and fluctuation in AST and ALT	[16]
7	Apocynaceae	*Nerium oleander*	Common oleander	Heart failure, leprosy, malaria, indigestion, ringworm	Single doses of 1 or 0.25 g/kg of dried leaves of the plant given to Najdi sheep caused toxicity 4–24 h after administration. Toxicity in chickens also reported	Restlessness, dyspnea, ruminal bloat, movement incoordination, limb paresis, recumbency and death	[5,17]
8	Apocynaceae	*Thevetia peruviana*	Yellow oleander	Heart failure, malaria, ringworm	A seed of the plant milled in saline solution and given to adult Taconic mice orally at doses of 78.13, 156.25, to 937.5 mg/kg. This led to tremors, restlessness, muscular relaxation, seizures 7–10 min after dosing and death within 24 h.	Nausea, vomiting, diarrhea, dysrhythmias, A-v block, abortifacient	[5,18]
9	Apocynaceae	*Calotropis procera*	Sodom apple	Fever, joint pain, muscular spasm,	A report of 29 eyes accidentally inoculated with a latex of the plant between January 2003 and December 2006. All patients had sudden painless dimness of vision, photophobia, conjunctival congestion and corneal edema	Ocular toxicity, hepatotoxicity, cardiotoxic	[19,20]
10	Asphodelaceae	*Aloe vera*	Aloe	Analgesic,	500 mg of *Aloe vera* tablet was toxic when taken by a woman for about 4 weeks	Acute hepatitis	[21-23]
11	Bignoniaceae	*Kigelia africana*	Sausage tree	Antimalarial, antimicrobial, malaria, diabetes	Toxic to human white blood cells at 250–500 µg/ml	Genotoxicity	[7]

(Contd...)

Table 1: ***(Continued)***

S. No	Family	Botanical name	Common name	Ethnomedicinal uses	Summary of the study	Toxic effects	Reference(S)
12	Cannabaceae	*Cannabis sativa*	Marijuana	Sedative, antiemetic, antiparasitic, antipyretic	Cannabidiol injected iv at 150–300 mg/kg was found to be toxic to rhesus monkeys within 30 min after administration	Respiratory arrest, cardiac failure, hepatotoxicity, nephrotoxicity, cardiotoxicity, and death.	[24]
13	Caricaceae	*Carica papaya*	Pawpaw	Anti-diabetic, antihypertensive, wound healing	0.03% of aqueous roots extract was found to be teratogenic to zebrafish embryo in 72 h and 3% caused death	Embryotoxic, abortion	[25]
14	Plumbaginaceae	*Plumbago zeylanica*	Ceylon lead worth	Antimicrobial, antioxidant	Acetone and methanolic extract, when given to rats at 200–400 mg/kg, was found toxic	Infertility, abortion	[26]
15	Clusiaceae	*Garcinia kola*	Bitter Kola	Treatment of a cough and fever, antiparasitic	Ethanolic root extract was toxic to brine shrimp at 9.42	Genotoxicity	[8]
16	Combretaceae	*Anogeissus leiocarpus*		Antiplasmodial activity	Acute toxicity evaluated using aqueous leaf extract of the plant administered in rats orally and i.p. oral showed depression and inappetence but no death up to 3200 mg/kg b/w. I.p route showed CNS toxicity and death with LD50 of 1400 mg/kg.	Inappetence, depression, unsteady gait, tremor, respiratory distress and death	[27]
17	Cucurbitaceae	*Momordica charantia*	Balsam pear		Aqueous extract at 300–600 mg for 7 days was found to be nephrotoxic to Wistar rats	Nephrotoxicity	[28]
18	Cucurbitaceae	*Luffa aegyptiaca*	Vegetable sponge	Antimalarial, antiviral, anti-inflammatory, antimycobacterial	Aqueous leaves extract of unspecified concentration causes abortion in women. When given at higher levels during labor can lead to death of child or ruptured uterus	Infertility, abortion	[29]
19	Dioscoreaceae	*Dioscorea bulbifera L*	Air potato	Anti-diarrhea, dysentery	Ethanol extract of rhizomes at 480 mg/kg once daily for 14 consecutive days was toxic to mice	Inflammation	[30]
20	Euphorbiaceae	*Jatropha gossypifolia L.*	Bellyache bush	Antihypertensive, antineoplastic, antimicrobial	Intake of fresh leaves in a single dose of 40 g/kg was lethal to sheeps	Cytotoxicity	[9]
21	Euphorbiaceae	*Croton penduliflorus* Hutch	Turk's carp	Hypertension	Acute toxicity study using the petroleum-ether extract of the seed of the plant was found to be toxic to mice and frog with LD50 of 543 mg/kg and 49 mg/kg, respectively.	Tachypnea, decreased motor activity, convulsion, and death	[31]
22	Euphorbiaceae	*Euphorbia hirta L.*	Asthma weed	Asthma, dysentery	Methanolic extract of leaves was found to be toxic to Brine shrimp at 660 µg/mL after 24 h	Death	[32]

(Contd...)

Table 1: ***(Continued)***

S. No	Family	Botanical name	Common name	Ethnomedicinal uses	Summary of the study	Toxic effects	Reference(S)
23	Euphorbiaceae	*Euphorbia kamerunica*	Spurge	Laxative, leprosy treatment	Phorbol and ester extract of bark at 0.5mg/5ml for 7 days was toxic to man	Dermatitis	[33]
24	Euphorbiaceae	*Euphorbia lateriflora* (Thinner)	Little cactus	Treatment of bronchitis, asthma-related problems, skin irritation, conjunctivitis	An aqueous root extract of the plant administered in rats at 100 and 250 mg/kg showed significant hepatotoxicity. LD50 was above 5000 mg/kg	Hepatotoxicity, death in rats	[34]
25	Euphorbiaceae	*Jatropha curcas*	Physic nut	Laxative, antimicrobial	1. Sodium Chloride solution extracts 2. 20 school and 2 preschool children were poisoned after consuming nuts of this plant in India and Nigeria, respectively	Nausea, vomiting, abdominal cramp, loose stools, restlessness, and dehydration	[35,36]
26	Fabaceae	*Erythrophleum suaveolens*	Sasswood	Anticancer activity	Saponin fractions (90:10, 80:20, and 70:30) from stem-bark of the plant in white albino rats.	Hemolysis, hepatic damage, renal impairment, metabolic derangement, elevation of plasma and liver AST ALT, total bilirubin, total protein, etc.	[37]
27	Fabaceae	*Tephrosia vogelii*	Fish-poison-bean	Treatment of TB, typhoid, and localized fungal infection	Aqueous extract of the plant used on *Tilapia zillii* at concentration of 4.00, 2.00, 1.00, 0.50, and 0.25 ml/L over 96 h	Respiratory distress, loss of balance, gulping of air, settling at bottom motionless, erratic swimming and death	[38]
28	Fabaceae	*Parkia biglobosa*	African locust bean	Antihypertensive, antimalarial, antibacterial	Aqueous pods extract was toxic to fish at 109.42 mg/L after 42 h of exposure.	Agitated behavior, respiratory distress, excessive mucus secretion, death	[39]
29	Fabaceae	*Tamarindus indica*	Tamarind tree	Anti-inflammatory, antimicrobial, gingivitis, conjunctivitis	Ethanolic extract of steam bark was toxic to brine shrimp at 200 µg/ml	Death	[40]
30	Gramineae	*Arundo donax*	Spanish reed	diuretic, pertussis, cystitis, analgesic	A lectin isolated from the plant induced toxicity in mice at 300–800 mg/kg. 100% death occurred after 30 h of i.p administration	Death	[41]

(Contd...)

Table 1: ***(Continued)***

S. No	Family	Botanical name	Common name	Ethnomedicinal uses	Summary of the study	Toxic effects	Reference(S)
31	Loganiaceae	*Strychnos nux-vomica L*	Strychnine tree	Anti-tumor effect, analgesic, anti-inflammatory	A root extract of the plant screened (*in vitro*) using human MM-cell line, RPMI 8226. It produced anti-proliferative activity in a dose-dependent fashion associated with apoptosis, cells accumulation at G0/G1 phase, mitochondrial membrane disruption, and mitochondrial cytochrome C leakage.	Anti-proliferative and cytotoxic activity	[42]
32	Lythraceae	*Lawsonia inermis*	Henna tree	Arthritic pains, headache	Aqueous root extract was toxic to rats at 800–1600 mg/kg after 48 h of administration	Dizziness, loss of appetite, partial paralysis, temporary amnesia and spontaneous abortion	[43]
33	Malvaceae	*Sida acuta*	Horn bean leaf	Fever, headache, antimicrobial	A fallow deer was poisoned after taking the leaves (duration not specified)	Muscular weakness, tremors, visual deficit, abnormal behavior, and posture	[44]
34	Malvaceae	*Hibiscus rosa sinensis L*	Red hibiscus	Stomach ache, pain, induce labor	Aqueous paste of root bark (about 100 g) and seeds of black pepper taken orally was found to cause abortion in women	Embryotoxic, infertility, abortion	[45]
35	Moraceae	*Ficus exasperata*	Sandpaper plant	Treatment of diabetes, wounds, anticancer, anti-inflammatory	Ethanolic extract of leaves was poisonous at 50–500 mg/kg when given to rats for 14 days	Hepatotoxicity and nephrotoxicity	[46]
36	Moringaceae	*Moringa oleifera*	Drumstick	Diabetes, antimicrobial, antipyretic	Methanolic extract of roots was found to be toxic in guinea pigs at 4.6–7.0 mg/kg i.p for 3 weeks	Nephrotoxicity, hepatotoxicity	[47]
37	Nymphaeaceae	*Nymphaea lotus*	Water-lily	Antimicrobial, antifungal, cancer treatment.	Methanolic extract of the whole plant was toxic to brine shrimp at 2.84×10^{-5}	Genotoxicity	[8]
38	Papaveraceae	*Argemone mexicana*	Mexican prickly poppy	Antimalarial	Seeds milled in saline solution was found to be toxic in mice at 447 mg/kg 7–10 min and death within 24 h	Death, itching	[48]
39	Phyllanthaceae	*Hymenocardia acida*	Large red heart	Antitrypanosomal, anti-sickling, antibacterial, antiamoebic, antiplasmodial	Ethanolic stem bark extract was toxic to brine shrimp at $>13.76\times10^{-5}$ mcg/mol	Chromosomal damage	[8]
40	Poaceae	*Bambusa vulgaris*	Common Bamboo	Emmenagogue, respiratory disease, gonorrhea	Aqueous Leaves extract given 3 times daily to pregnant rabbits was found to be toxic at 250–500 mg/kg on 18^{th}-20^{th} day of pregnancy	Abortion, Infertility	[49]

(Contd...)

Table 1: ***(Continued)***

S. No	Family	Botanical name	Common name	Ethnomedicinal uses	Summary of the study	Toxic effects	Reference(S)
41	Polyporaceae	*Ganoderma lucidum*	The king of herbs	Antidiabetic, antiviral, antibacterial	A capsule containing powdered plant 500 mg was taken by a woman daily for 1–2 months	Hepatitis	[50]
42	Rubiaceae	*Sarcocephalus latifolius*	African peach	Treatment of diabetes, hypertension, malaria	Aqueous leaf extract was found to be acutely toxic in rats at 500–2000 mg/kg for 24 h while subacute toxicity was noticed at 250–583 mg/kg for 28 days.	Weakness, dizziness, loss of appetite, restlessness, hepatotoxicity, nephrotoxicity	[51]
43	Rubiaceae	*Morinda lucida*	Brimstone tree	Anticancer	Ethanolic extract of root bark was toxic to brine shrimp at 4.3×10−5	Genotoxicity	[8]
44	Salicaceae	*Flacourtia indica*	Governor's plum	Antimalarial	Aqueous leaves and stem bark extracts were found to be toxic to brine shrimp with LC50 of <100 µg/ml	Cytotoxicity	[52]
45	Sapindaceae	*Blighia sapida*	Ackee tree	Cold, fever, edema, epilepsy	Ingestion of unripe fruit by humans was found to have an immediate toxic effect.	Profound hypoglycemia, intractable vomiting	[53]
46	Sapotaceae	*Butyrospermum paradoxum*	Share tree	Treatment of measles, diarrhea and skin diseases	Aqueous extract of stem bark was toxic when given to rats at LD50 250 mg/kg	CNS toxicity, hepatotoxicity and nephrotoxicity	[54]
47	Sapotaceae	*Chrysophyllum albidum G.*	Cherry	Anemia, malaria, asthma	Ethanolic extract of leaves at 1000 mg/kg for 16 days was toxic to albino rats	Anti-platelet, hypoglycemic effects and selective organ toxicity	[55]
48	Sapotaceae	*Capsicum annuum L.*	Chili pepper	Athletes foot, arthritis	Intravenous and left atrial administration of the plant extract in cat led to pulmonary vasoconstriction fall in BP and death of the animal	Pulmonary vasoconstriction, fall in BP and death in cat	[56]
49	Verbenaceae	*Lantana camara L.*	Spanish flag	Cancer, skin itches, leprosy.	Acute toxicity was tested with methanolic leaf extract of the plant in adult mice (in vivo) at a single dose of 2 g/kg. Showed elevated TBIL and ALT. Cytotoxicity test on Vero cell line (*in vitro*) inhibited cells growth at concentration up to 500µg/mL	Weight loss, loss of organ mass ESP kidney and heart	[57]
50	Asteraceae and Fabaceae	*Acanthospermum hispidum and cajanus cajan*	Goat's head and pigeon pea	Treatment of epilepsy, headache, anti-pyretic, antimicrobial, antidiabetic, laxative	Aqueous extract of the plants was found to be teratogenic to Wistar rats when administered together (1:1.3) at a concentration of 600 mg/kg b/w daily throughout pregnancy	Teratogenicity	[58]

TB: Tuberculosis, ALT: Alanine transaminase, BP: Blood pressure, CNS: Central nervous system, ALP: Assessment of the alkaline, ACP: Acid phosphatase, AST: Aspartate aminotransferase

Table 2: Organ systems affected by the plants

Organ system	Number of plants with reported organ toxicity (%)
Hepatotoxicity	13 (14.0)
Nephrotoxicity	10 (10.8)
Neurotoxicity	10 (10.8)
Reproductive toxicity	9 (9.7)
Respiratory toxicity	9 (9.7)
Cardiovascular toxicity	6 (6.5)
Genotoxicity	4 (4.3)
Cytotoxicity	5 (5.4)
Gastrointestinal toxicity	4 (4.3)
Endocrine toxicity	3 (3.2)
Hematotoxicity	3 (3.2)
Ocular toxicity	2 (2.2)
Skin toxicity	2 (2.2)
Deaths	13 (14.0)

intoxication through consumption. Organs systems most affected are shown in Table 2. Some of the plants were shown to demonstrate multi-organ toxicity.

CONCLUSION

According to this study, many indigenous plants around us that are used medicinally possess toxicity potentials at certain levels. They have the ability to cause either immediate (acute) toxic effect (*Argemone mexicana*, *Cannabis sativa*, *Nerium oleander*, *Jatropha gossypifolia*, *Blighia sapida*, *Thevetia peruviana*, *Luffa aegyptiaca,* etc.) or chronic toxicity when used for a long period of time (*Morinda lucida*, *Kigelia africana*, *Garcinia kola,* etc.). Therefore, caution should be exercised when using these plants for especially medicinal purposes.

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