European Journal of Medicinal Plants

31(12): 29-51, 2020; Article no.EJMP.58966
ISSN: 2231-0894, NLM ID: 101583475

Nigerian Medicinal Plants for the Management of Liver Diseases: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author ACN designed the study. All authors wrote the first draft of the manuscript. Authors ACN and VOO proofread the final work. Authors OE and INEO analyzed the search results. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/EJMP/2020/v31i1230302
Editor(s):
(1) Dr. Daniela Rigano, University of Naples Federico II, Italy.
(2) Marcello Iriti, University of Milan, Italy.
Reviewers:
(1) P. Vinoth Kumar, J. J. College of Arts and Science, India.
(2) Kamurthy Hemalatha, Malla Reddy College of Pharmacy, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/58966

Review Article

Received 03 May 2020
Accepted 09 July 2020
Published 22 August 2020

ABSTRACT

The liver, despite its crucial role in metabolism is prone to several metabolic injuries and insults manifesting as liver damage. Thus, liver diseases arise from multiple aetiologies. In Nigeria, chronic liver diseases are rampant and constitute a significant cause of morbidity. Globally, medicinal plants play crucial roles in healthcare. Several Nigerian medicinal plants are used in the management of various liver disorders. This review focuses on medicinal plants that are used in the management of liver diseases in Nigeria. The search for novel active principles from plants must be sustained due to increasing prevalence of various liver ailments, challenges associated with liver transplantation and poor healthcare funding. The identification, isolation and characterization of active compounds from Nigerian medicinal plants could lead to the potential development of affordable and effective drugs for the management of liver diseases.

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Keywords: Liver disease; Medicinal plants; Nigeria; Ethnomedicine; Hepatoprotective.

1. INTRODUCTION

The liver is a vital organ that plays major roles in diverse metabolic pathways, detoxification process, breakdown of red blood cells and in the synthesis of proteins and hormones [1]. Despite its diverse metabolic functions, the liver (like the average Nigerian worker) is prone to suffer a lot of injuries (from infections) and metabolic insults (from toxic xenobiotics). These injuries and insults manifest as liver damage. Liver disease and hepatic failure have been studied by several authors [2,3,4].

Some of the risk factors that may increase the likelihood of hepatic diseases include heavy alcohol consumption, obesity, family history, exposure to toxins and chemicals [5,6,7]. Correspondingly, liver disease arise from multiple aetiologies such as viral, metabolic disorder (autoimmune deficiency) and hereditary factors as seen in cases of hepatitis B virus, hemochromatosis and type 2 diabetes respectively [8,9,10]. Generally, liver infections are classified into acute and chronic infections. The acute infections include hepatitis, hepatosis, liver cirrhosis, liver injury, acute hepatitis and chronic active hepatitis B. The chronic infections include primary sclerosis cholangitis (PSC), primary biliary cirrhosis (PBC), alcoholic fibrosis and alcoholic hepatitis [9,10]. A liver damage progresses to liver failure and possibly death if not properly treated and managed [11].

The long and uninterrupted history of herbal therapy usage in the developing countries of the world [12] is amply justified by the fact that nature provides the greatest source of remedy for many health challenges that affect man [13]. The World Health Organization (WHO) estimates that 80% of the world's population rely on herbal medicine for their health needs with an even higher rate of dependence amongst rural dwellers in African countries [14,15]. It has been suggested that phytotherapy is cheaper, more efficient and better than modern medicine [16]. In the face of a lack of prioritization of healthcare and poor healthcare systems, medicinal plants have continued to play significant roles in the healthcare systems of most of the world's population.

Nigerian local pharmacopoeia has an abundance of indigenous plants. While some of these plants serve food or medicinal purposes, there is a general assumption that phytochemicals, vitamins and minerals present in these plants are responsible for their medicinal potentials [16]. These active constituents occur in varying amounts in the different parts of the plant and among different species [15]. There is reported use of Nigerian medicinal plants in herbal preparations for the prevention and management of various liver disorders [16]. Moreover, the use of several traditional plant-based therapies among certain ethnic groups and indigenous people in the management of diseases including liver disease has been amply reported worldwide [17,18,19,20,21].

A complete reversal of cirrhosis can be achieved via liver transplantation but the supply of liver allografts is far lesser than the number of potential recipients [22]. The increasing risk factors for non-alcoholic fatty liver disease and hepatocellular carcinoma (probably due to approximately 2 billion obese or overweight adults and over 400 million adults having diabetes), a high prevalence of viral hepatitis, increasing cases of drug-induced acute hepatitis and an inability to meet global liver transplantation needs clearly depict a global public health dilemma [23]. In Nigeria, the challenge of liver disease management is further compounded by costly and commonly unavailable antiviral therapy as well as the dearth of endoscopic services which pose a challenge to the treatment of end-stage liver disease [24]. This, in addition to poor healthcare funding suggests that the search for novel active principles from locally available plants that could be hepatoprotective and ameliorative against liver damage must be sustained.

Therefore, it is within the purview of this study to carry out a review of Nigerian medicinal plants that are used ethnomedicinally as well as those that have been scientifically validated for the management of liver diseases.

2. THE BURDEN OF LIVER DISEASES

Liver disease may remain asymptomatic, thus posing significant challenges in gathering accurate population-wide data on its incidence and prevalence [25]. Chronic liver disease is very

rampant in Nigeria and it is an important cause of morbidity. In addition to hepatitis B virus (HBV) infection which is the most common cause of chronic liver disease, a high prevalence of hepatitis C virus (HCV) usually occurring with HIV infection as well as alcohol consumption and smoking has been recognized as significant causes of chronic liver disease. Liver cirrhosis and primary liver cancer are suggested to be the most prevalent forms of chronic liver disease [24,25,26]. Thus, there is a high global prevalence of liver cirrhosis, hepatitis B and hepatitis C infections [24,27,10]. Hepatocellular carcinoma is the fourth most common form of cancer in Africa and accounts for 5% of all cancers in the world. It has a high mortality rate with the number of new cases rising to 841,080 in 2018 [28]. Hepatic encephalopathy, a major neuropsychiatric complication of liver disease with a high mortality rate is linked to factors such as previous blood transfusions, hepatitis B and C infections and severe liver dysfunction [29].

The recurring and significant involvement of hepatitis B virus infection is not surprising as it is an aetiological factor for hepatocellular carcinoma, hepatitis and liver cirrhosis. A high prevalence of hepatitis B surface antigen (HBsAg), a specific marker of hepatitis B virus infection has been previously reported amongst Nigerian patients [30]. Consequently, a HBV infection prevalence rate of 12% has been reported in Nigeria [31]. Additionally, a recent Nigerian study has reported a 21% prevalence rate of liver fibrosis among HIV-patients with factors such as increasing age, elevated liver function parameters, tumor necrosis factor-alpha (TNF-α) and lower CD4 counts identified as predictors [32].

Globally, approximately two million deaths result from liver disease on an annual basis with mortality resulting mainly from complications of cirrhosis, viral hepatitis and hepatocellular carcinoma. Cirrhosis and liver cancer combine to account for 3.5% of all deaths worldwide. Also, over 75 million adults are at risk of alcohol-related liver disease [23].

Non-alcoholic fatty liver disease (NAFLD) is perhaps the most common chronic liver disease, affecting nearly a quarter of the world's population and a major reason for liver transplants, especially in Western populations [33,34]. The burden of the disease which is compounded by the growing wave of obesity and type 2 diabetes mellitus is linked to increased liver-related morbidity and mortality as well as extra-hepatic conditions like cardiovascular disease, colorectal cancers, chronic kidney disease and type 2 diabetes mellitus [33]. Sadly, there is paucity of data on the burden and scope of non-alcoholic fatty liver disease (NAFLD) in Africa [35]. This data unavailability is deceitful and should not be misconstrued to mean that NAFLD is not a major health challenge as it rather represents a failure to clearly highlight the grave danger that the disease portends.

3. THE QUEST FOR HERBAL REMEDY

Herbal medicines have remained popular for historical and cultural reasons, in addition to their cheaper costs. Globally, there has been a steady increase in the use of herbal medicines and the search for new phytochemicals that could be developed as potentially useful drugs [36]. The search for new phytochemicals with hepatoprotective activities has led to a renewed interest in indigenous medicine worldwide. This is also partly due to the realization that orthodox medicine is not widespread [37].

Ethnomedicine is a global practice that is recognized and encouraged by the World Health Organization (WHO) in the management of various diseases, including liver disorders [38]. The medicinal plants that are peculiar to ethnic groups are referred to as ethnomedicinal plants [39]. The study of ethnomedicinal plants has been recognized as the most viable method of identifying new medicinal plants or subsequent evaluation of those previously reported for bioactive constituents and this has led to the development of new drugs [40]. There is growing interest in ethnomedicinal plants because bioactive components could be extracted and prepared from either the leaves, seeds, fruits, stems, roots or the entire plant [41,42]. The herbal preparations may vary in taste (bitter, sour or sweet), their mode of administration varies (oral application, cold bathing, inhalation, and steam covering) and the dosage of administration varies from daily dosage, twice or trice daily while others may be freely administered [43].

Table 1. Ethnomedicinal plants used in the management of liver diseases in Nigeria

Medicinal plant	Family	Local name(s)	Common name(s)	Part(s) used	Zone (s) found	Source	Method of preparation	References
Acacia nilotica	Fabaceae	Bagaruwa (H), Baani (Y)	Black piquant	Bark, seed	North, West	Wild	Decoction	[51]
Acanthospernum hispidum	Asteracaae	Yawo (H)	Bristle star bur	Entire plant	North	Wild	Decoction	[52]
Acanthus montanus	Acanthaceae	Ahon ekun (Y)	Bear's breeches	Entire plant	East, South, West	Cultivated		[53]
Adansonia digitata	Malvaceae	Kuka (H), Ose (Y)	African baobab	Leaf, bark	North, West	Wild	Decoction	[54]
Aframomum melegueta	Zingeberaceae	Atare (Y)	Alligator pepper	Fruit	West	Wild	Decoction	[55]
Allium cepa	Liliaceae	Alubosa onisu (Y)	Onion	Bulb	North, West	Cultivated, wild	Decoction	[56]
Allium sativum	Amaryllidaceae	Tafarnuwa (H), Ayu (Y)	Garlic	Rhizome	North	Cultivated	Decoction	[57]
Aloe barbadensis	Asphodelaceae	Eti erin (Y)	Aloe vera	Root	East, North, South, West	Cultivated	Decoction	[58]
Amaranthus spinosus	Amaranthaceae	Alayyahu (H)	Spiny pigweed	Entire plant	North	Wild	Decoction	[59]
Annona senegalensis	Annonaceae	Gwandar daji (H)	African custard	Leaf, seed	North	Cultivated, wild	Decoction	[60]
Anogeissus leiocarpus	Combretaceae	Marke (H), Kojoli (F), Atara (I), Ayin (Y)	African birch	Bark, leaf	North	Wild	Decoction	[61]
Anthocleista djanlonensis	Gentianaceae	Kandare (H)		Bark, leaf	North	Wild	Decoction	[62]
Artemisia annua	Asteraceae	Tazargade (H)	Sweet annie	Leaf	North	Cultivated	Decoction	[63]
Azadirachta indica	Meliaceae	Bedi (H), Dongoyaro (Y)	Neem tree	Leaf	East, North, South, West	Cultivated, wild	Decoction	[64]
Balanites aegyptiaca	Zygophyllaceae	Aduwa (H), Enyi-ndi-mmuo (I), Tanni (F)	Desert date	Bark	East, North, South, West	Wild	Decoction	[65, 57]
Bauhinia reticulate	Fabaceae	Kalgo (H)	Mountain ebony		North	Wild	Decoction	[66]
Bauhinia rufescens	Fabaceae	Tsattsagi (H)	Silver butterfly	Bark, leaf	North	Wild	Decoction	[57]
Bidens pilosa	Asteraceae	Abere oloko, Omo langanran, Agomonyan,	Black-jack	Leaf	West	Cultivated, wild	Decoction	[43,54]

Medicinal plant	Family	Local name(s)	Common name(s)	Part(s) used	Zone (s) found	Source	Method of preparation	References
		Ewe abere (Y)						
Boscia salicifolia	Capparidaceae	Zure (H)	Willow-leaved	Leaf	North	Wild	Powder	[66]
Boswellia dalzielii	Connaraceae	Hano (H)	Frankincense tree	Leaf	North	Wild	Decoction	[67]
Byrsocarpus coccineus	Connaraceae	Tsamiyar kasa (H), Amuje wewe (Y)	Tamarind of the valley	Entire plant	East, North, West	Wild	Decoction	[68,62]
Calotropis procera	Apocynaceae	Tumfafiya (H), Bomubomu (Y)	Sodom apple	Leaf	North, West	Wild	Decoction	[51]
Carica papaya	Caricaceae	Ibepe (Y), Poopo (I), Gwanda (H)	Pawpaw	Leaf	East, North, South, West	Cultivated, wild	Decoction	[69]
Cassia arereh	Fabaceae	Malga (H)		Rhizome	North	Wild	Decoction	[57]
Cassia mimosoides	Fabaceae	Bagaruwar kasa (H)	Fishbone cassa	Entire plant	North	Wild	Decoction	[60,57]
Cassia nigricans	Fabaceae	Gewaya tsamiya (H)	Chamaecrista nigricans	Leaf	North	Wild	Maceration	[57]
Celosia trigyna	Amaranthaceae	Sepososun, Ajefowo, Ajemawofo (Y) Edafo (B)	Wool flower	Leaf, stem	West	Wild	Decoction	[70,54]
Chasmanthera dependens	Menispermaceae	Ato (Y)	Chasmanthera	Leaf, root, bark	West		Decoction	[71]
Citrus aurentifolia	Rutaceae	Lemun tsami (H), Lannea acida (I), Osan wewe (Y)	Lime	Leaf	East, North, South, West	Cultivated	Decoction	[72]
Cochlospermum tinctorium	Bixaceae	Belge/Kukur/ Rawaya (H), Yarudi (F),		Rhizome	North	Wild	Powder	[73,74]
Crateva adansonii	Capparaceae	Ungududu (H)	Three-leaved Caper		North	Wild	Decoction	[57]
Crotalaria spp.	Leguminosae	Bi-rana (H), Korupo (Y), Akedimwo (I), Biriji-bei (F)	Rattlepods	Entire plant	East, North, South, West	Wild	Decoction	[75]
Curcuma longa	Zingiberaceae	Ata-ile pupa (Y)	Tumeric	Entire plant	South, West	Wild	Decoction	[76]
Dichrostachys cinerea	Fabaceae	Dundu (H), Ami-ogwu (I)	Kalahari	Leaf	East, North	Wild	Powder	[77]
Enantia chlorantha	Annonaceae	Awopa (Y), Dokita igbo (I)	African yellow wood	Bark	East, South, West	Wild	Decoction	[78]

Medicinal plant	Family	Local name(s)	Common name(s)	Part(s) used	Zone (s) found	Source	Method of preparation	References
Eucalyptus camaldulensis	Myrtaceae	Turare (H)	River red gum	Leaf	North	Wild	Decoction	[79]
Euphorbia balsamifera	Euphorbiaceae	Aliyara (H)	Balsam spurge	Leaf, stem	North	Wild	Decoction	[59]
Euphorbia convolvuloides	Euphorbiaceae	Nonon kurciya (H)	Asthma herb	Whole plant	North	Wild	Decoction	[80]
Euphorbia hirta	Euphorbiaceae	Emile (Y)	Asthma herb	Whole plant	West	Wild	Decoction	[81]
Evolvulus alsinoides	Convolvulaceae	Kafi malam (H)	Dwarf morning glory	Entire plant	North	Wild	Decoction	[82]
Ficus congensis	Moraceae	Baure (H)	Fig	Bark	North	Wild	Decoction	[62]
Ficus platyphylla	Moraceae	Gamji (H)	Guttapercha tree	Bark, leaf	North	Wild	Powder	[62]
Ficus polita	Moraceae	Durumi (H)	Heart-leaved fig	Bark, leaf	North	Wild	Powder	[62]
Ficus thonningii	Moraceae	Cediya (H)	Strangler fig	Leaf	North	Wild	Decoction	[62]
Garcinia kola	Guttiferaceae	Orogbo (Y)	Bitter kola	Fruit, bark	East, North, South, West	Wild, cultivated	Consumption of seed	[83]
Gongronema latifolium	Asclepiadaceae	Madunmaro (Y), Utazi (I)	Amaranth globe	Root	East, South, West		Decoction	[84]
Hibiscus sabdariffa	Malvaceae	Soborodo (H)	Roselle	Flower, leaf	North	Wild	Decoction	[66]
Indigofera astragalina	Fabaceae	Kaikai koma (H)	Silky indigo	Entire plant	North	Wild	Decoction	[85]
Jatropha curcas	Euphorbiaceae	Cin da zugu (H), Lapalapa (Y)	Barbados nut	Leaf	North, South, West	Cultivated, Wild	Decoction	[51]
Khaya senegalensis	Meliaceae	Madaci (H), Oganwo (Y)	African mahogany	Bark	North, South, West	Wild	Decoction	[72]
Kohautia grandiflora	Rubiaceae	Rimin samari (H)	Oldenlandia	Leaf	East, North, South, West	Wild	Decoction	[86]
Lannea acida	Anacardiaceae	Faru (H)	Grape	Bark	East, North, South, West	Wild	Decoction	[51]
Leptadenia hastata	Asclepladaceae	Yadiya (H)		Entire plant	North	Wild	Decoction	[87]
Mangifera indica	Anacardiaceae	Mangwaro (H), Mangoro (Y)	Mango	Leaf, bark	North, West	Cultivated, wild	Decoction	[88]
Mitragyna inermis	Rubiaceae	Giyayya (H)	False abura	Bark	North	Wild	Decoction	[89]

Medicinal plant	Family	Local name(s)	Common name(s)	Part(s) used	Zone (s) found	Source	Method of preparation	References
Momordica balsamina	Cucurbitaceae	Garahun (H)	Balsam apple	Bark	North	Wild	Decoction	[90]
Momordica charantia	Cucurbitaceae	Daddagu (H), Ejinrin (Y), Alaban adene (I), Dagdaye (K)	Bitter melon	Leaf	East, North, South, West	Wild	Decoction	[90]
Moringa oleifera	Moringaceae	Gbogbonise/Ewe ile (Y), Zogalla (H), Okochi egbu (I)	Drumstick Tree	Bark, leaf, root, stem	East, North, South, West	Cultivated, wild	Decoction	[91]
Ocimum basilicum	Lamiaceae	Doddoya (H)	Sweet basil	Entire plant	North	Wild	Decoction	[92]
Olax subscorpioidea	Olacaceae	Ukpakon (B), Ifon/Mitin (Y)		Root, leaf, stem, bark, twig	East, North, South, West	Wild	Decoction	[93]
Parkia biglobosa	Fabaceae	Dorowa, Dawadawa (H), Ogiri (I), Iru, Igba (Y)	African locust bean	Bark	North, West	Wild	Decoction	[51]
Peristrophe bicalyculata	Acanthaceae	Tubanin dawaki (H)	Horse flower	Entire plant	North	Wild	Decoction	[94]
Phyllanthus amarus	Euphorbiaceae	Oyomokeisoamankedem (Ef), Iyin olobe (Y), Ebebenizo (B)	Sleeping plant	Entire plant	East, North, South, West	Wild	Decoction	[95,96]
Pleurotus tuberregium	Pleurotaceae	Osun (Y), Ero (I), Naman kaza (H)	Mushroom	Root, leaf	North, South, West	Wild	Decoction	[70]
Prosopis africana	Fabaceae	Kirya (H)	African mesquite	Bark	North	Wild	Decoction	[97]
Psidium guajava	Myrtaceae	Gwaba (H)	Guava	Leaf	North	Wild	Decoction	[98]
Rauvolfia vomitoria	Apocynaceae	Asofeyeje (Y)	Swizzle stick	Root, bark, leaf, sap	East, South, West	Wild	Decoction	[99]
Sclerocarya birrea	Anacardiaceae	Danya (H)	Marula	Bark	North	Wild	Maceration	[100]
Senna obtusifolia	Fabaceae	Tafasa (H)	Sickle pod	Leaf, root	North	Wild	Powder	[101]
Senna occidentalis	Fabaceae	Tafasar masar (H)	Coffee senna	Entire plant	North	Wild	Decoction	[102]
Striga hermonthica	Scrophulariaceae	Gaugai (H)	Purple witchweed	Entire plant	East, North, South, West	Wild	Decoction	[103]
Talinum	Talinaceae	Gbure (Y), Ebe-dondon	Water Leaf	Whole plant	East, South,	Cultivated,	Decoction	[104]

Medicinal plant	Family	Local name(s)	Common name(s)	Part(s) used	Zone (s) found	Source	Method of preparation	References
fruticosum		(Es)			West	wild		
Tamarindus indica	Fabaceae	Tsamiya (H), Ajagbon (Y)	Indian date	Bark, leaf		Wild	Decoction	[51]
Thaumatococcus daniellii	Marantaceae	Ewe-eran/Adundunmitan (Y), Akwukwo elele (I)	Miracle fruit	Leaf, seed	East, West, South	Cultivated, wild	Decoction	[54]
Vernonia amygdalina	Asteraceae	Onugbu (I), Shuwaka (H), Ewuro (Y)	Bitter leaf	Leaf	East, South, West	Wild	Powder	[69]
Vitellaria paradoxa	Sapotaceae	Kadanya (H)	Shea butter tree	Bark	North	Wild	Powder	[64]
Ximenia americana	Olacaceae	Tsada (H)	Tallow wood	Bark	North	Wild	Powder	[60]
Zaleya pentandra	Aizoaceae	Gadon maciji (H)		Entire plant	North	Wild	Decoction	[57]
Zingiber officinale	Zingiberaceae	Citta (H), Ataile (Y)	Ginger	Rhizome	North, West	Cultivated	Decoction	[105]
Ziziphus mauritiana	Rhamnaceae	Magarya (H)	Indian jujube	Leaf	North	Wild	Powder	[106]

B = Bini, Ef = Efik, Es = Esan, F = Fulani, H = Hausa, I = Igbo, K = Kanuri, Y = Yoruba

Table 2. Scientifically validated Nigerian medicinal plants for the management of liver diseases

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
Acalypha racemosa	Euphorbiaceae	Leaf	Water	Oral	60	CCl_4	Decreased serum total protein, AST and ALT activities. Decreased hepatic MDA and serum conjugated and total bilirubin	[107]
Acalypha wilkesiana	Euphorbiaceae	Leaf	Water	Oral	100/200/300	CCl_4	Decreased total bilirubin concentration, ALT, AST and ALP activities. As dose increased, histopathology revealed normal cells.	[108]
Aframomum melegueta	Zingiberaceae	Seed	Water	Oral	100/200	Ethanol	Increased hepatic GSH level and SOD activity. Decreased hepatic MDA level and serum ALT activity.	[109]

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
							The histology revealed that the extracts were able to reduce ethanol induced changes in the hepatocytes.	
Alchornea laxiflora	Euphorbiaceae	Root	95% n-Hexane	Oral	0.1/0.5/1/10/50/100	$NaASO_2$	Decreased ALT, AST, ALP 4-nitroanisole demethylase, glutathione-S-transferase activities and Cyt b5 levels. Reduced total protein, albumin and globulin.	[110]
Allium cepa	Liliaceae	Bulb	80% methanol	Oral	200/300/450	APAP	Decreased ALT, AST, ALP, LDH and total bilirubin	[56]
Alstonia boonei	Apocynaceae	Stem bark	Ethanol	Oral	200/400	DDVP	Decreased serum and hepatic MDA levels. Decreased serum ALT and AST acitivities. Increased hepatic GSH, GPx, CAT and SOD activities.	[111]
Anacardium occidentale	Anacardiaceae	Leaf	70% methanol	Oral	500/1000	CCl_4	Decreased AST, ALT and ALP activities. Preserved histoarchitecture of the liver.	[112]
Andrographis paniculata	Acanthaceae	Leaf	Water	Oral	100/200/300	CCl_4	Decreased bilirubin, MDA level, ALT, ALP and AST activities. Increased GSH, total protein and albumin levels.	[113]
Anogeissus leiocarpus	Combretaceae	Bark	Methanol	Intraperitoneal	2.5	CCl_4	Decreased ALT and AST activities	[61]
Balanites aegyptiaca	Zygophyllaceae	Stem bark	Water	Oral	100	APAP	Decreased ALT, AST and ALP activities.	[114]
Cajanus cajan	Fabaceae	Leaf	80% ethanol	Oral	200/400/800	NDEA	Decreased ALT and AST activities.	[115]
Carica papaya	Caricaceae	Leaf and unripe fruit	Aqueous	Oral	100/300	CCl_4 and APAP	Decreased bilirubin level, AST and ALP activities. Reversed histological	[116]

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
							changes induced by CCl_4 and Acetaminophen induced liver dysfunction.	
Cassia italica	Fabaceae	Leaf	Water/ 70% ethanol	Oral	200/200	CCl_4	Decreased serum total bilirubin, ALT, AST, ALP, GGT and CAT activities. Decreased serum lipid peroxidation.	[117]
Cassia singueana	Fabaceae	Root	Methanol	Oral	2.5/5	CCl_4	Decreased serum ALT, AST, total bilirubin and direct bilirubin. Increased hepatic CAT, SOD and reduced MDA levels.	[118]
Chrysophyllum albidum	Sapotaceae	Leaf	95% ethanol	Oral	500/1000/1500	CCl_4	Decreased ALT, AST and ALP activities. Increased total protein and albumin.	[119]
Cnidoscolus aconitifolius	Euphorbiaceae	Leaf	Methanol	Oral	100/200	Ethanol	Decreased ALP, GGT, ALT and AST activities. Increased SOD and CAT activities.	[120]
Corchorus olitorius	Tiliaceae	Leaf	80% ethanol	Oral	500/750/1000	CCl_4	Decreased albumin level, ALT, AST and ALP activities. Increased total protein and bilirubin levels.	[121]
Curcuma longa	Zingiberaceae	Rhizome	Ethanol	Oral	250/500	TAA	Induced apoptosis and inhibited hepatocytes proliferation.	[122]
Garcinia kola	Guttiferae	Seed	Absolute methanol	Oral	100	AZA	Increased hepatic GSH and CAT activity. Decreased hepatic MDA, AST and ALT activities and prevented changes in the cytoarchitecture of liver cells.	[123]
Gymnema	Apocynaceae	Leaf	60%	Oral	200/400	APAP	Decreased AST, ALT and	[124]

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
sylvestre			methanol				ALP activities. Fractions from the extract also showed same activity. Histology showed well defined nuclei of hepatocytes.	
Harungana madagascariensis	Hypericaceae	Root	Water	Oral	100/200/500	APAP	Decreased ALT, AST and ALP activities. Increased total protein and albumin levels. Reduced histopathological changes in the hepatocytes.	[125]
Hibiscus sabdariffa	Malvaceae	Flower	Methanol	Oral	50/100	CCl_4	Decreased serum LDH, ALT, AST and ALP activities. Increased hepatic GSH level, SOD and CAT activities. Decreased MDA levels.	[126]
Jatropha tanjorensis	Euphorbiaceae	Leaf	Methanol	Oral	100/200/400	CCl_4	Decreased serum albumin, ALP, AST and ALT activities.	[127]
Justicia carnea	Acanthaceae	Leaf	Methanol	Oral	200/500/1000	CCl_4	Decreased serum AST, ALT and ALP activities. Increased total protein and albumin concentrations. Reduced hepatic dysfunction induced by CCl_4.	[128]
Khaya senegalensis (Desr.)	Meliaceae	Stem bark	Water	Oral	100	APAP	Decreased ALT, AST and ALP activities.	[114]
Leptadenia hastate	Asclepiadaceae	Leaf	Methanol	Oral	250/500	Ethanol	Decreased ALT, AST, ALP activities and reduced bilirubin concentration.	[129]
Lophira lanceolata	Ochnaceae	Leaf	70% methanol	Oral	100/200/400	CCl_4	Decreased serum ALT and ALP activities.	[130]
Mangifera	Anacardiaceae	Stem	Water/	Oral	200	APAP	Decreased ALT, AST, ALP	[131]

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
indica		bark	ethanol				activities. Increased total protein and albumin concentrations. Increased hepatic GSH activity and reduced MDA level.	
Morinda lucida	Rubiaceae	Leaf	Propanol/ water	Oral	240/240	APAP	Increased hepatic GSH, CAT, GPx and SOD activities. Decreased nitric oxide and lipid peroxidation.	[132]
Musa paradisiaca	Musaceae	Fruit pulp	Methanol	Oral	500/1000/1500	CCl_4	Decreased AST, ALT and ALP activities. Histoarchitecture showed the preservation of liver parenchyma against CCl_4-induced liver damage.	[133]
Ocimum gratissimum	Lammiaceae	Leaf	n-Hexane/ ethylacetate/ ethanol/ water	Oral	400	APAP	Decreased bilirubin concentration, AST, ALT and ALP activities. Extracts minimized congestion, mononuclear infiltration and cytoplasmic vacuolation of the hepatocytes induced by paracetamol.	[134]
Picralima nitida (Stapf) T. Durand & H. Durand	Apocynaceae	Dried seed	Methanol	Oral	10/100/1000	CCl_4	Histology revealed decreased fat degeneration of liver cells. Increased hepatic GSH level and no significant changes in bilirubin, AST, ALT, ALP total protein, catalase in test groups when compared to CCl_4 toxicant group.	[135]
Prosopis africana	Fabaceae	Stem bark	Water	Oral	100	APAP	Decreased ALT, AST and ALP activities.	[114]
Sarcocephalu	Rubiaceae	Root bark	Water	Oral	100/200/300	CCl_4	Decreased serum AST, ALT	[136]

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
s latifolius (Smith) Bruce							activities and total bilirubin, conjugated bilirubin levels.	
Sida acuta	Malvaceae	Leaf	n-Hexane/ ethylacetate	Oral	150/300	TAA	Decreased ALT and ALP activities. Increased AST activity and albumin level.	[137]
Solanum melongena	Solanaceae	Fruit	Methanol	Oral	500/1500	CCl_4	Decreased ALT, AST, ALP activities. Increased SOD, CAT activities and reduced lipid peroxidation.	[138]
Sphenostylis stenocarpa	Fabaceae	Seed	Methanol	Oral	400/800	CCl_4	No significant change in ALT, AST and ALP activities of rats treated with extract relative to the CCl_4 induced toxicity group. Increased GSH concentration, CAT and SOD activities.	[139]
Spondias mombin L.	Anacardiaceae	Leaf and stem bark	50% methanol	Oral	500/1000	CCl_4	Decreased ALT, AST, ALP, conjugated bilirubin and total bilirubin levels. Increased hepatic GSH, CAT, SOD activities and reduced MDA levels.	[140]
Swietenia mahogany	Maliaceae	Leaf	Aqueous	Oral	250/500	Ethanol	Decreased bilirubin level, ALT and AST activities. Significant improvement on the histological changes in the extract treated animals.	[141]
Talfairia occidentialis	Cucurbitaceae	Leaf	Ethanol	Oral	500	APAP	Decreased AST, ALP activities and prevented histological alteration in the liver.	[142]
Tapinanthus bangwensis	Loranthaceae	Leaf	80% Methanol (ethylacetate and butanol fraction)	Oral	400	CCl_4	Decreased bilirubin level, AST and ALT activities. Increased total protein and albumin levels. Decreased	[143]

Plants	Family	Part(s) used	Solvents	Route of administration	Dose of extract (mg/kg)	Toxicant	Pharmacological activity	References
							lipid peroxidation.	
Telfairia occidentalis	Cucurbitaceae	Leaf	Water	Oral	200/400	$CdCl_2$	Increased SOD, CAT and GST activities. Reduced MDA and GSH levels. Decreased ALT and AST activities.	[144]
Tetracarpidium conophorum	Euphorbiaceae	Nut oil	n-Hexane	Oral	5/10 (mL/kg)	DiNa	Decreased ALT, ALP, AST and total bilirubin. Histology revealed that the oil prevented diclofenac sodium induced hepatic injury.	[145]
Uvaria afzelii	Annonaceae	Root	Methanol	Oral	125/250/500	CCl_4	Decreased bilirubin level, ALT, ALP, AST activities. Increased albumin and total protein levels.	[146]
Vernonia amygdalina	Asteraceae	Leaf	Methanol	Oral	200/400	APAP	Reduced hepatic lipid peroxidation. Maintained antioxidant enzymes within normal levels. Increased levels of reduced glutathione.	[147]
Vitellaria paradoxa	Sapotaceae	Stem bark	Water	Oral	100	APAP	Decreased ALT, AST and ALP activities.	[114]
Zea mays	Poaceae	Husk	50% ethanol	Oral	187/347/748	CCl_4	Decreased ALT, AST, ALP, liver weight, direct and total bilirubin. Increased total protein. Histology revealed that the extract protected the liver against CCl_4 induced damage.	[148]

APAP = Acetaminophen, AZA = Azathioprine, CCl_4 = Carbon tetrachloride, $CdCl_2$ = Cadmium chloride, DDVP = 2,2-dichlorovinyl dimethyl phosphate or Dichlorvos, DiNa = Diclofenac sodium, $NaASO_2$ = Sodium arsenate, NDEA = N-Nitrosodiethylamine, TAA= Thioacetamide, ALT = Alanine transaminase, ALP = Alkaline phosphatase, AST = Aspartate transaminase, CAT = Catalase, GGT = γ-glutamyl transferase, GPx = Glutathione peroxidase, GSH = Reduced glutathione, GST = Glutathione S-transferase, LDH = Lactate dehydrogenase, MDA = Malondialdehyde, SOD = Superoxide dismutase

The bioactive constituents such as alkaloids, curcuminoids, cyanogenetic glycosides, flavonoids, furyl compounds, terpenoids, polyphenolics, lignans, coumarins, proteins and other groups of substances present in ethnomedicinal plants are responsible for the potency and efficacy of these plant remedies [44]. The pharmacodynamic and pharmacokinetic study of phytochemicals present in ethnomedicinal plants [45,46] revealed that these phytochemicals are active against the formation of viral DNA or RNA, enhances DNA repair and stimulates immune function. In particular, isoquinoline alkaloids demonstrate effective antiviral activity against HBV [46]. Most studies suggest that some of these plants may exert their antifibrotic properties by interfering with leukotriene formation in Kupffer cells [47] and may thereby inhibit hepatic stellate cell (HSC) activation, which is a crucial event in fibrogenesis [48]. Medicinal plants used against viral infections such as hepatitis B virus infection may possibly act through interference with polymerase activity, mRNA transcription and replication [49,50].

4. METHOD OF DATA SEARCH

A keyword search was done in May-June 2020 using the following words: Nigerian, medicinal plants, ethnomedicinal plants, liver diseases, management of liver diseases, hepatoprotective, liver function, antioxidants, natural products, carbon tetrachloride, acetaminophen, ethanol and paracetamol. The search was done using the following scientific databases: Scopus (http://www.scopus.com), Science Direct (http://www.sciencedirect.com), PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Google Scholar (https://scholar.google.com), Wiley (http://www.onlinelibrary.wiley.com) and Science Domain (http://www.sciencedomain.org). The results of the search were sorted and considered on the basis of contextual relevance to the study. All authors debated in order to resolve differences in opinion wherever they existed and only the search results that were of critical relevance to the study were eventually selected.

5. NIGERIAN ETHNOMEDICINAL PLANTS USED FOR MANAGING LIVER DISEASES

There is need to fill the knowledge gap on the use of local herbal therapy in the management of liver diseases across Nigeria since most of the previous ethnomedicinal reviews were limited in scope to specific regions of the country. There appears to be a preponderance of oral administration for most herbal remedies. It is noteworthy that all the ethnomedicinal plants reported in this study are orally administered. Several ethnomedicinal plants used across Nigeria for the management of liver diseases are presented in Table 1.

6. SCIENTIFIC VALIDATION OF PLANTS WITH POTENTIALS FOR LIVER DISEASE MANAGEMENT

Several plants such as *Curcuma longa* (turmeric) and *Garcinia kola* (bitter kola) are employed by several Nigerian tribes in the management of liver diseases. The major active metabolite of turmeric is tetrahydrocurcumin (THC) which has been shown to prevent erythromycin estolate induced liver disease [88]. The seed extract of bitter kola has been shown to demonstrate a protective effect against carbon tetrachloride induced liver injury [97]. At the molecular level, various plant extracts act through different mechanisms of action against the different liver infections. Antioxidation has been recognized as one of such common mechanisms [59].

The information obtained from the sourced research articles in this review include; scientific names (genus and species name), family name, part of the plant used, the solvent used for extraction, route of administration, dosage of extracts used in the study, toxicant used, pharmacological activity on hepatocytes. Following the search, the entire findings are summarized in Table 2.

7. CONCLUSION

This study has attempted to review the various Nigerian medicinal plants that are used ethnomedicinally as well as those that have been scientifically validated for the management of liver diseases. The identification, isolation and characterization of active compounds from these Nigerian medicinal plants could lead to the potential development of affordable and effective drugs for the management of liver diseases. Thus, the identification of these medicinal plants which hold the possibility of serving as potential drugs for the management of various liver disorders that are becoming increasingly prevalent holds enormous potentials for the health sector. It is hoped that this review will be useful to the growing Nigerian population in stemming the tide of liver diseases.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

While we acknowledge all the authors whose works we have consulted in preparing this review, we concede that the seminal works of some authors might have been omitted. This unintentional omission is highly regretted.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
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