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.

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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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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, hepatitis, 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 thrice daily while others may be freely administered [43].
| 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  | Asteraceae | Yawo (H)          | Bristle star bur        | Entire plant | North         | Wild         | Decoction              | [52]       |
| hispidum        |         |                     |                         |              |               |              |                        |            |
| Acanthus        | Acanthaceae | Ahon ekun (Y)     | Bear's breeches         | Entire plant | East, South,  | Cultivated   |                        |            |
| montanus        |         |                     |                         |              | West          |              |                        |            |
| Adansonia       | Malvaceae | Kuka (H), Ose (Y)  | African baobab          | Leaf, bark   | North, West   | Wild         | Decoction              | [54]       |
| digitata        |         |                     |                         |              |               |              |                        |            |
| Aframomum       | Zingeberaceae | Atare (Y)        | Alligator pepper        | Fruit        | West          | Wild         | Decoction              | [55]       |
| melegueta       |         |                     |                         |              |               |              |                        |            |
| Allium cepa     | Liliaceae | Alubosa onisu (Y)  | Onion                   | Bulb         | North, West   | Cultivated, wild| Decoction, Decoction | [56]       |
| Allium sativum  | Amaryllidaceae | Tafarnuwa (H), Ayu (Y) | Garlic                 | Rhizome      | North         | Cultivated,    | Decoction, Decoction | [57]       |
| Aloe barbadensis| Asphodelaceae | Eti erin (Y)     | Aloe vera               | Root         | North, East,  |              |                        |            |
|                 |         |                     |                         |              | North, South, |              |                        |            |
|                 |         |                     |                         |              | West          |              |                        |            |
| Amaranthus      | Amaranthaceae | Alayyahu (H)   | Spiny pigweed           | Entire plant | North         | Wild         | Decoction              | [59]       |
| spinosus        |         |                     |                         |              |               |              |                        |            |
| Annona          | Annonaceae | Gwandar daji (H)   | African custard         | Leaf, seed   | North         | Cultivated, wild| Decoction              | [60]       |
| senegalensis    |         |                     |                         |              |               |              |                        |            |
| Anthocleista    | Combretaceae | Marke (H), Kojoli (F), Atara (I), Ayin (Y) | African birch | Bark, leaf   | North         | Wild         | Decoction              | [61]       |
| djalononensis   |         |                     |                         |              |               |              |                        |            |
| Artemisia annua | Gentianaceae | Kandare (H)      | Bark, leaf              | North        | Wild         | Decoction, Decoction | [62]       |
| Azadirachta     | Asteaceae | Tazargade (H)     | Sweet annie             | Leaf         | North East,  | Cultivated, wild| Decoction              | [63]       |
| indica           | Meliaceae | Bedi (H), Dongoyaro (Y) | Neem tree            | Leaf         | East, South, |              |                        | [64]       |
| Balanites       | Zygophyllaceae | Aduwa (H), Enyi-ndi-| Desert date           | Bark         | East, South, | Wild         | Decoction              | [65, 57]  |
| aegyptiaca     |         | mmu (I), Tanni (F) |                         |              | West          |              |                        |            |
| Bauhinia        | Fabaceae | Kalgo (H)         | Mountain ebony          | North        | Wild         | Decoction, Decoction | [66]       |
| reticulate     |         |                     |                         |              |               |              |                        |            |
| Bauhinia        | Fabaceae | Tsattsagi (H)     | Silver butterfly        | Bark, leaf   | North         | Wild         | Decoction              | [57]       |
| rufescens       |         |                     |                         |              |               |              |                        |            |
| Bidens pilosa   | Asteraceae | Abere ooko, Omo langanran, Agomonyan, | Black-jack | Leaf         | West         | Cultivated, wild| Decoction              | [43,54]   |

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 |
|-----------------------------------------|-------------------|-------------------------------------------------|-------------------------|--------------|-------------------|----------|-----------------------|------------|
| **Bosnia salicifolia**                  | Capparidaceae     | Ewe abere (Y)                                   | Zure (H), Hano (H)      | Leaf, Leaf   | North, North     | Wild     | Powder                | [66]       |
| **Boswellia dalzielii**                 | Connaraceae       |                                                |                         |              |                   |          | Decoction             |            |
| **Byrsocarpus coccineus**               | Connaraceae       |                                                 | Tsamiyar kasa (H), Amuje wewe (Y) | Entire plant | East, North, West | Wild     | Decoction             | [68,62]    |
| **Calotropis procer**                   | 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, West | Wild     | Decoction             | [69]       |
| **Cassia arereh**                       | Fabaceae          |                                                 | Malga (H)               | Fishbone cassa | North, West       | Wild     | Decoction             | [57]       |
| **Cassia mimosoides**                   | Fabaceae          |                                                 | Bagaruwar kasa (H)      | Entire plant | North             | Wild     | Decoction             | [60,57]    |
| **Cassia nigricans**                    | Fabaceae          |                                                 | Gewaya tsamiya (H)      | 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    |                                                 | 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), Ungududu (H) | Rhizome                 | North        | Wild              | Powder               | [73,74]    |
| **Crataeva adansonii**                  | Capparidaceae     |                                                 | Three-leaved Caper      | North        | Wild              | Decoction             | [57]       |
| **Crotalaria spp.**                     | Leguminosae       | Bi-rana (H), Korup (Y), Akedimwo (I), Biriji-bei (F) | Entire plant            | East, North, South, West | Wild     | Decoction             | [75]       |
| **Curcuma longa**                       | Zingiberaceae     | Ata-ile pupa (Y)                                | Tumeric                 | Entire plant | East, North, South, West | Wild     | Decoction             | [76]       |
| **Dichrostachys cinerea**               | Fabaceae          | Dundu (H), Ami-ogwu (I)                         | Kalahari                | Leaf         | East, North     | Wild     | Powder                | [77]       |
| **Euphorbia 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 kuriya (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 congestis | 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 | Moraceae | Orogbo (Y) | Bitter kola | Fruit, bark | East, North, South, West | Wild, cultivated | Consumption of seed | [83] |
| Gongronema latifolium | Asclepiadaceae | Madunmaro (Y), Utazi (I) | Amarant globe | Root | North | Wild | 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 | Romin samari (H) | Oldenlandia | Leaf | South, West, East, North | Wild | Decoction | [86] |
| Lannea acida | Anacardiaceae | Faru (H) | Grape | Bark | South, West, East, North | Wild | Decoction | [51] |
| Leptadenia hastata | Asclepiadaceae | 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       | Cucurbitaceae | Garahun (H)                                       | Balsam apple             | Bark         | North         | Wild             | Decoction              | [90]       |
| balsamina       |             | Daddagu (H), Ejinrin (Y), Alaban adene (I),       | Bitter melon             | Leaf         | East, North,  | Wild             | Decoction              | [90]       |
| Momordica       |             | Dagdaye (K)                                       |                          |              | South, West   |                  |                        |            |
| charantia       |             | Gbogbonise/Ewe ile (Y), Zogalla (H), Okochi egbu  | Drumstick Tree           | Bark, leaf,  | East, North,  | Cultivated,      | Decoction              | [91]       |
|                 |             | (I)                                               |                          | root, stem   | South, West   | wild             |                        |            |
| Moringa         | Moringaceae  | Gbogbonise/Ewe ile (Y), Zogalla (H), Okochi egbu  | Drumstick Tree           | Bark, leaf,  | East, North,  | Cultivated,      | Decoction              | [91]       |
| oleifera        |             | (I)                                               |                          | root, stem   | South, West   | wild             |                        |            |
| Ocimum          | Lamiaceae   | Doddoya (H)                                       | Sweet basil              | Entire plant | North         | Wild             | Decoction              | [92]       |
| basilicum       |             |                                                  |                          |              |               |                  |                        |            |
| Olax            | Olacaceae   | Ukpakon (B), Ifon/Mitin (Y)                       | Root, leaf, stem, bark,  | Root, leaf,  | East, North,  | Wild             | Decoction              | [93]       |
| subscorpioidea  |             |                                                  | twig                     | leaf, root,  | South, West   |                  |                        |            |
| Parkia           | Fabaceae    | Dorowa, Dawadawa (H), Ogiri (I), Iru, Igba (Y)    | African locust bean      | Bark         | North, West   | Wild             | Decoction              | [51]       |
| biglobosa       |             | Tubanin dawaki (H)                                | Horse flower             | Entire plant |               |                  |                        |            |
| Peristrophe      | Acanthaceae | Oyomokeisoamankedem (Ef), Iyin olobe (Y), Ebebenn | Sleeping plant           | Entire plant | East, North,  | Wild             | Decoction              | [94]       |
| bicalyculata    |             | (B)                                               |                          |              | South, West   |                  |                        |            |
| Phyllanthus      | Euphorbiaceae | Oyomokeisoamankedem (Ef), Iyin olobe (Y), Ebebenn | Sleeping plant           | Entire plant | East, North,  | Wild             | Decoction              | [95,96]   |
| amarus           |             | (B)                                               |                          |              | South, West   |                  |                        |            |
| Pleurotus        | Pleurotaceae | Osun (Y), Ero (I), Naman kaza (H)                 | Mushroom                 | Root, leaf   | North, South, | Wild             | Decoction              | [70]       |
| tuberregium     |             | Kirya (H)                                         |                          |              | West          |                  |                        |            |
| Prospis         | Fabaceae    | Gwaba (H)                                         | African mesquite         | Bark         | North, South, | Wild             | Decoction              | [97]       |
| africana        |             | Asofeyeje (Y)                                     |                          |              | West          |                  |                        |            |
| Psidium         | Myrtaceae   | Guava                                             | Leaf                     | Root, bark,  | North, South, | Wild             | Decoction              | [98]       |
| guajava         |             | Asofeyeje (Y)                                     |                          | leaf, sap    | East, South,  |                  |                        |            |
| Rauwolfia       | Anacardiaceae | Danya (H)                                        | Marula                  | Bark         | North         | Wild             | Maceration             | [100]      |
| vomitoria       |             |                                                  |                          |              |               |                  |                        |            |
| Sclerocarya      | Fabaceae    | Tafasa (H)                                        | Sickle pod               | Leaf, root   | North         | Wild             | Powder                 | [101]      |
| birrea           |             | Tafasar masar (H)                                 | Coffee senna             | Entire plant | North         |                  | Decoction              | [102]      |
| Senna           | Fabaceae    | Gaugai (H)                                        | Purple witchweed         | Entire plant | East, North,  | Wild             | Decoction              | [103]      |
| obtusifolia     |             |                                                  |                          |              | South, West   |                  |                        |            |
| occidentalis    |             |                                                  |                          |              |               |                  |                        |            |
| Striga          | Scrophulariaceae | Tafasa (H)                                    | Purple witchweed         | Entire plant | East, North,  | Wild             | Decoction              | [103]      |
| hermonthica     |             |                                                  |                          |              | South, West   |                  |                        |            |
| Talinum         | Talinaceae  | Gbure (Y), Ebe-dondon                             | Water Leaf               | Whole plant  | East, South,  | Cultivated,      | Decoction              | [104]      |
|                 |             |                                                  |                          |              |               | wild             |                        |            |
| Medicinal plant         | Family       | Local name(s)       | Common name(s) | Part(s) used | Zone(s) found | Source      | Method of preparation | References |
|------------------------|--------------|---------------------|----------------|--------------|---------------|-------------|-----------------------|------------|
| fruticosum             | Fabaceae     | (Es)                | Tamarindus      | Bark, leaf   | West          | wild        | Decoction             | [51]       |
| Tamarindus indica      | Marantaceae  | Ewe-eran/Adundunmitan (Y) | Miracle fruit | Leaf, seed   | East, West, South, West | Cultivated, Wild | Decoction             | [54]       |
| Thaumatococcus danielli| Asteraceae   | Onugbu (I), Shuwaka (H), Ewuro (Y) | Bitter leaf | Leaf         | East, South, West | Wild        | Powder                | [69]       |
| Vernonia amygdalina    | Sapotaceae   | Kadanya (H)         | Shea butter tree | Bark         | North         | Wild        | Powder                | [64]       |
| Vitellaria paradoxa    | Olacaceae    | Tsada (H)           | Tallow wood     | Bark         | North         | Wild        | Powder                | [60]       |
| Ximenia americana      | Aizoaceae    | Gadon maciji (H)    | Entire plant    | North        | Wild          | Decoction   | Decoction             | [57]       |
| Thunbergia penduliflora| 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                      | CCl₄     | 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 CCl₄        |          | 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]      |
The histology revealed that the extracts were able to reduce ethanol induced changes in the hepatocytes. Decreased ALT, AST, ALP 4-nitroanisole demethylase, glutathione-S-transferase activities and Cyt b5 levels. Reduced total protein, albumin and globulin.

| Plants                  | Family          | Part(s) used | Solvents   | Route of administration | Dose of extract (mg/kg) | Toxicant | Pharmacological activity                                                                 | References |
|-------------------------|-----------------|--------------|------------|--------------------------|-------------------------|----------|----------------------------------------------------------------------------------------|------------|
| Alchornea laxiflora     | Euphorbiaceae   | Root         | 95% n-Hexane | Oral                     | 0.1/0.5/1/10/50/100    | NaASO₂   | The histology revealed that the extracts were able to reduce ethanol induced changes in the hepatocytes. 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 Decreased serum and hepatic MDA levels. Decreased serum ALT and AST activities. Increased hepatic GSH, GPx, CAT and SOD activities. | [56]       |
| Alstonia boonei         | Apocynaceae     | Stem bark    | Ethanol    | Oral                     | 200/400                 | DDVP     | Decreased serum and hepatic MDA levels. Decreased serum ALT and AST activities. Increased hepatic GSH, GPx, CAT and SOD activities. | [111]      |
| Anacardium occidentale  | Anacardiaceae   | Leaf         | 70% methanol | Oral                     | 500/1000                | CCl₄     | Decreased AST, ALT and ALP activities. Preserved histoarchitecture of the liver. Decreased bilirubin, MDA level, ALT, ALP and AST activities. Increased GSH, total protein and albumin levels. | [112]      |
| Andrographis paniculata | Acanthaceae     | Leaf         | Water      | Oral                     | 100/200/300             | CCl₄     | Decreased AST, ALT and ALP activities. Preserved histoarchitecture of the liver. 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                     | CCl₄     | Decreased ALT and AST activities Decreased ALT, AST and ALP activities. Decreased ALT and AST activities. Decreased ALT and AST activities. | [61]       |
| Balanites aegyptiaca    | Zygophyllaceae  | Stem bark    | Water      | Oral                     | 100                    | APAP     | Decreased ALT and AST activities Decreased ALT, AST and ALP activities. Decreased ALT and AST activities. Decreased ALT and AST activities. | [114]      |
| Cajanus cajan           | Fabaceae        | Leaf         | 80% ethanol | Oral                     | 200/400/800             | NDEA     | Decreased ALT and AST activities. Decreased ALT and AST activities. Decreased ALT and AST activities. Decreased ALT and AST activities. | [115]      |
| Carica papaya           | Caricaceae      | Leaf and unripe fruit | Aqueous | Oral                     | 100/300                | CCl₄ 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 |
|------------------------|----------|--------------|------------------------|-------------------------|-------------------------|----------|----------------------------------------------------------------------------------------|------------|
| Cassia italica         | Fabaceae | Leaf         | Water/ 70% ethanol     | Oral                    | 200/200                 | CCl₄     | 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                   | CCl₄     | 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           | CCl₄     | 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            | CCl₄     | 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. Decreased ALT, AST and ALP activities. Increased total protein and albumin levels. Reduced histopathological changes in the hepatocytes. | [125]      |
| *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                  | CCl4     | 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             | CCl4     | Decreased serum albumin, ALP, AST and ALT activities. | [127]      |
| *Justicia carnea*      | Acanthaceae             | Leaf         | Methanol | Oral                    | 200/500/1000            | CCl4     | Decreased serum AST, ALT and ALP activities. Increased total protein and albumin concentrations. Reduced hepatic dysfunction induced by CCl4. Decreased ALT, AST and ALP activities. | [128] [114] |
| *Khaya senegalensis*   | 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. Decreased serum ALT and ALP activities. | [129]      |
| *Lophira lanceolata*   | Ochnaceae               | Leaf         | 70% methanol | Oral              | 100/200/400             | CCl4     | Decreased serum ALT and ALP activities. | [130]      |
| *Mangifera*            | Anacardiaceae           | Stem         | Water    | Oral                    | 200                      | APAP     | Decreased ALT, AST, ALP activities. | [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. Increased hepatic GSH, CAT, GPx and SOD activities. Decreased nitric oxide and lipid peroxidation. Decreased AST, ALT and ALP activities. Histoarchitecture showed the preservation of liver parenchyma against CCl₄-induced liver damage. | [132]      |
| *Morinda lucida* | Rubiaceae    | Leaf         | Propanol/water | Oral                    | 240/240                 | APAP     |                                                                                           |            |
| *Musa paradisiaca* | Musaceae    | Fruit pulp   | Methanol     | Oral                    | 500/1000/1500           | CCl₄     | Decreased AST, ALT and ALP activities. Extracts minimized congestion, mononuclear infiltration and cytoplasmic vacuolation of the hepatocytes induced by paracetamol. | [133]      |
| *Ocimum gratissimum* | Lammmiaceae | 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             | CCl₄     | 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 CCl₄ 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             | CCl₄     | Decreased serum AST, ALT                                                                  | [136]      |
| Plants                       | Family     | Part(s) used          | Solvents                  | Route of administration | Dose of extract (mg/kg) | Toxicant | Pharmacological activity                                                                 | References |
|-----------------------------|------------|-----------------------|---------------------------|-------------------------|-------------------------|----------|-----------------------------------------------------------------------------------------|------------|
| *Sida latifolia* (Smith) Bruce | Malvaceae  | Leaf                  | n-Hexane/ethylacetate     | Oral                    | 150/300                 | TAA      | Decreased ALT and ALP activities and total bilirubin, conjugated bilirubin levels.       | [137]      |
| *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                | CCl₄     | Decreased ALT, AST, ALP activities. Increased SOD, CAT activities and reduced lipid peroxidation. | [138]      |
| *Sphenostylis stenocarpa*   | Fabaceae   | Seed                  | Methanol                  | Oral                    | 400/800                 | CCl₄     | No significant change in ALT, AST and ALP activities of rats treated with extract relative to the CCl₄ induced toxicity group. Increased GSH concentration, CAT and SOD activities. | [139]      |
| *Spondias mombin L.*        | Anacardiaceae | Leaf and bark         | 50% methanol              | Oral                    | 500/1000                | CCl₄     | Decreased ALT, AST, ALP, conjugated bilirubin and total bilirubin levels. Increased hepatic GSH, CAT, SOD activities and reduced MDA levels. | [140]      |
| *Swietenia mahogany*        | Malvaceae  | 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                     | CCl₄     | 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 |
|------------------------|--------------------|--------------|----------|-------------------------|-------------------------|----------|-----------------------------------------------------------------------------------------|------------|
| *Telfairia occidentalis* | Cucurbitaceae      | Leaf         | Water    | Oral                    | 200/400                 | CdCl₂    | 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             | CCl₄     | 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. Decreased ALT, AST, ALP, liver weight, direct and total bilirubin. Increased total protein. Histology revealed that the extract protected the liver against CCl₄ induced damage. | [114] [148]|
| *Zea mays*             | Poaceae            | Husk         | 50% ethanol | Oral                    | 187/347/748             | CCl₄     |                                                                                          |            |

**References**

[144] [145] [146] [147] [114] [148]

**Notes:**

- APAP = Acetaminophen
- AZA = Azathioprine
- CCl₄ = Carbon tetrachloride
- CdCl₂ = Cadmium chloride
- DDVP = 2,2-dichlorovinyl dimethyl phosphate or Dichlorvos
- DiNa = Diclofenac sodium
- NaASO₂ = 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, curcuminooids, cyanogenic glycosides, flavonoids, fufuryl 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 ethnomedical 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 ethnomedically 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.

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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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