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Medicinal Plant Species Used for Formulation of Herbal Products Against Liver Diseases in Ghana; A Field Survey and Review

Dongsogo Julius[1]*, Larbie Christopher[2], Idrissu Abdul Mumeen[1], Regina Appiah-Oppong[3], Benjamin Emikpe[4], Daniel A. Abera[5]

[1]Department of Biochemistry and Molecular Biology, University for Development Studies, Tamale, Ghana

[2]Department of Biochemistry and Biotechnology, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

[3]Department of Biochemistry and Biotechnology, University of Ghana, Legon, Ghana

[4]Department of Veterinary Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

[5]Department of Medical Laboratory Technology, Kumasi Technical University, Kumasi, Ghana

Research Article

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***For Correspondence:** Dongsogo Julius, Department of Biochemistry and Molecular Biology, Faculty of Biosciences, University for Development Studies, Tamale, Ghana; **E-mail: jdongsogo@uds.edu.gh**

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ABSTRACT

Hepatic disorders are conditions that affect the structure and function of the human liver. Causes include microbes and their toxins, ionizing radiations and abuse of drugs. Medicinal plant products have been an alternative for the management of these diseases due to the expensive, unavailability and harmful side effects of pharmaceutical drugs. The aim of this study was to determine whether plant species used in preparing herbal medicinal products for treatment of liver diseases have reported hepatoprotective activity. A field survey was conducted using information from television, radio, marketing vans to identify the medicines and purchased them from the herbal shops. The plant species and parts used in manufacturing were extracted from the product insert and the Traditional and Alternative Medicine Council log book. A search was conducted on Google Scholar, PubMed and Elsevier databases on hepatoprotection activity of the plant species. In all, 56 plants species were used by 20 manufacturing companies in producing 25 herbal medicinal products. *Khaya senegalenesis* was the most predominant plant species used (9/25, 36.0% products). In terms of parts, leaves (40/56, 71.4% of plant species) were the most prevalent part used. On databases, 41/56 (73.2%) plant species had hepatoprotective activity while 15 (26.8%) had no data for hepatoprotective activity. *Cratagus oxyacanthea* was the plant species with most parts reported parts (7 different parts). *Moringa oleifera* was most extracted (7 different solvents) and most tested against hepatotoxicity induced with 20 different toxicants. There is sufficient scientific data on hepatotoxicity activity of plant species used for herbal formulations against liver disorders. Practitioners and Researchers should focus on isolation and testing of the active phytochemicals.

Keywords: Hepatic; Herbal; Species; Hepatoprotection; Phytochemicals

INTRODUCTION

The liver performs various physiological functions that ensure systemic homeostasis for optimum metabolic activities, growth and repairs [1,2]. The liver is also involved in biosynthesis of amino acids, bile and clotting factors [3]. Detoxification of drugs, xenobiotics, heavy metals, food toxins, toxins from pesticides, plastics, weedicides and food additives are also undertaken by the liver [4,5]. The liver is further responsible for the storage of glycogen and fat-soluble vitamins.

Hepatic disorders are conditions that alter the structure and functions of the liver resulting in alteration in its physiological activities. They include hepatitis, cirrhosis, hepatocellular carcinoma, hepatoma, hepatosteatosis, jaundice, cholestatic injury, hepatobiliary obstruction, hepatovascular lesions and hepatozonal necrosis. Hepatic diseases are caused by pathogens, toxins, environmental contaminants such as pesticides, weedicides, plastics, heavy metals and factory waste [6]. Abuse of alcohol, pharmaceutical drugs and food additives as well as iron overload also cause hepatic disorders.

Globally, 10% of the world population are living with various complications of hepatic disorders, leading to a million deaths yearly. In Sub-Saharan Africa, 250 million persons are affected by various hepatic disorders whereas in Ghana, complications of hepatitis B and C alone account for 10,000 deaths yearly.

Serum markers of liver function and histopathological examination have been used to diagnose and characterize hepatic disorders [7]. Elevation in serum transaminases and bilirubin with low levels of proteins indicate parenchymal hepatic disease and hepatosteatosis [8]. Hepatobilliary and cholestatic conditions are characterized by high serum Alkaline Phosphatase (ALP) and Gamma Gutammyl Transferase (GGT) [9]. Histopathological indication of nuclear pkynosis, cytoplasmic pigmentation and DNA fragmentation are features of hepatic necrosis.

Pathophysiology of liver diseases are centered on oxidative stress and synthesis of abnormal physiological proteins [10,11]. Oxidative stress results from overproduction of reactive oxygen, nitrogen and sulphate species from heavy metals, aflatoxin B_1 and alcohol [12,13]. Consequently, these reactive species deplete glutathione stores and inhibit synthesis of free radicals scavenging enzymes such as catalase, glutathione peroxidase and superoxide dismutase. Oxidative stress also activates the transcription factor Nuclear Factor-Kappa Beta (NF-kβ). Activated Nuclear Factor-Kappa Beta (NF-kβ) translocate from cytosol to nucleus where it causes continuous overexpression of proinflammatory and fibrogenic cytokines including Tumor Nuclear Factor Alpha (TNF-α), Interleukin-6 (IL-6), Transforming Growth Factor-Beta (TGF-β) and Epidermal Growth Factor (EGF). These pro-inflammatory cytokines result in sustained differentiation and proliferation of hepatic stellate cells into myoblast cells with collagen and muscle actins resulting in cirrhosis of the liver. Cirrhosis obstructs blood flow to the liver resulting in hepatocyte hypoxia and necrosis. In oxidative stress, transcription factors, Sterol Regulatory Element Binding Protein-1c (SREPBP-1c), Peroxisome Proliferator Activated Receptor-alpha (PPAR-α) and Carnitine Palmitoyl Transferase-1 (CPT-1) are also overexpressed leading to hepatic lipogenesis, peroxidation and steatosis.

Pharmaceutical drugs have been the primary line of treatment for hepatic conditions in Ghana. However, due to unavailability, cost and deleterious side effects, herbal medicines prepared from parts of medicinal plants have been used as alternative. Majority of plant-based herbal practitioners in Ghana rely on folk knowledge and common daily experiences to select the choice of plants species and parts for preparation of medicines to treat hepatic diseases. The aim of this study was to determine whether plant species used in preparing herbal medicinal products for treatment of liver diseases have reported hepatoprotective activity.

MATERIALS AND METHODS

The study involved a field survey and a literature database search. In the field survey, information on the herbal products and diseases were obtained from radio stations and televisions advertisements. The products were purchased from Tamale central, Bolga Central Market, Wa Central Markets and herbal stores. The inclusion criteria include Food and Drugs Authority (FDA) registration number, company batch number, not expired, plant species and parts should be available and meant for liver disease. Exclusion criteria involve those not targeting any liver disease, expired, no batch or FDA number and plant species and part not indicated [14]. The plant species and parts used in manufacturing were extracted from the manufacturer's user instructions and the traditional and alternative medicine council log book at Tamale zonal office.

Database search was conducted using plants botanical names and parts and various hepatic diseases as keywords. Medline, PubMed, Google Scholar, Elsevier and science direct databases were searched. Primary and secondary articles published from 2005 to 2021 on the plant species or their parts about a real or induced hepatic disorder were included in the review [15,16]. Quality criteria for the articles include the availability of the plant species, part used, extraction solvent and inducing model or toxin.

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Statistical analysis

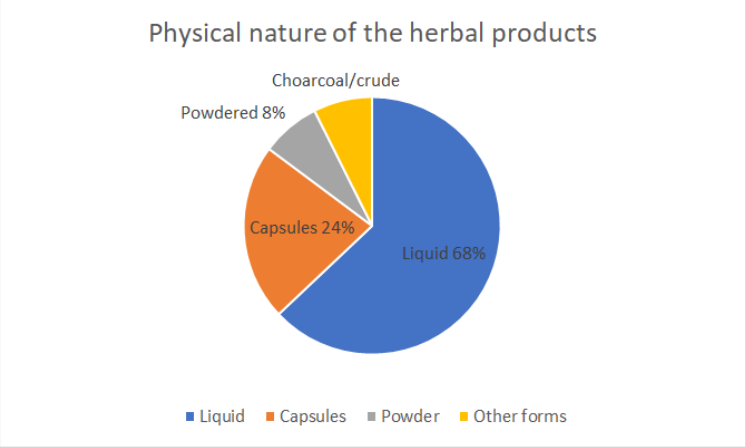
Discrete data were reported as percentages and presented as bar charts. All entries were done using Microsoft excel, 2016 version (Microsoft, Incorporated, New York). Analysis was done with Minitab version 17 (Lead Technologies Inc, New York). A p-value of 0.05 or less were deem statistically significant.

RESULTS

Physical nature of the herbal products purchased

From the information provided by the manufacturers and logbook of alternative medicinal council, 56 plant species were used by 20 companies to formulated 25 herbal medicinal products against liver diseases as well as other illnesses. Of these, 17 (68%) were in liquid form while 6 (24%) were capsules. Powdered form was 2 while other forms such as charcoal and crude extract were also 2 (8%) (Figure 1).

Figure 1. Distribution of the physical forms of the herbal drugs.



Frequency of each plant species among the herbal products

Khaya senegelensis was the most prevalent plant species used in formulating 9 different products followed by *Azadirachta indica* (7). *Vernonia amygdalina, Moringa oleifera* and *Syzgium aromaticum* were found in 6 products whereas *Curcuma longa, Taraxacum officinale, Zingibar officinale* were found in 5 herbal products. *Allium sativum, Bidens pilosa, Trema orientalis, Piper guineense, Sida acuta* were each found in 4 products whereas *Phyllantus carolinum* was used in manufacturing just 1 product. *Zingibar officinale*, *Vittellaria paradoxa, Trema orientalis, Acasia* spp., *Ageratum conyzoides, Allium cepa, Angosphora hispida, Cida acuta, Ferruginea gigantea, Kigelia africana, Tamarindus indica* were found in 2 products each while *Aloe barbadensis*, *Aloe vera*, *Altonia boonei, Bombax buonopozense, Centella asiatica*, *Citrus aurantifola, Citrus lemon, Clausea anisate, Cola gigantea, Crataegus oxycanthea, Cucumis sativus, Eucalyptus glotus, Ficus exasperate were* each found in 1 product separately.

Diseases that herbal products were targeted in addition to liver diseases

Apart from liver-related diseases, herbal drugs were made for other sicknesses. Fever was the most frequent targeted by 8 (32%) products followed by joint pain 6 (24%) products. Malaria, typhoid and hypertension were each targeted by 3 (12%) products. About 2 (8%) products are made against each of immune disorders, ulcer and piles while 1 (4%) product was made against kidney diseases (Figure 2).

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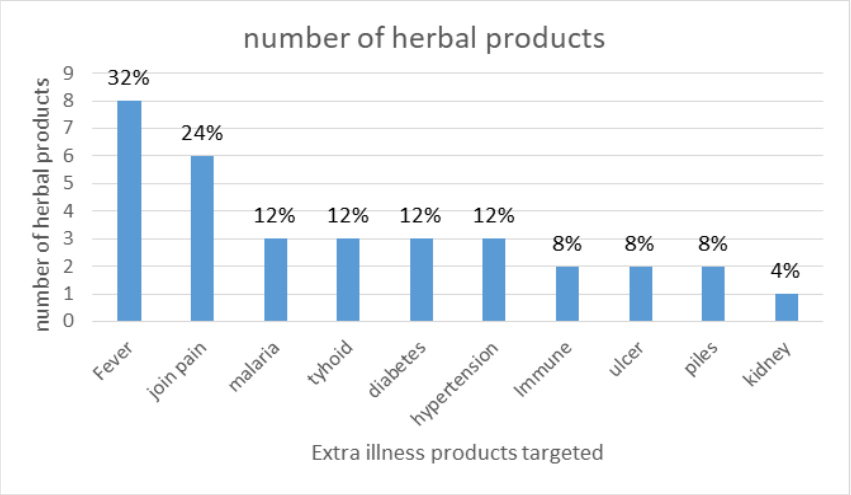
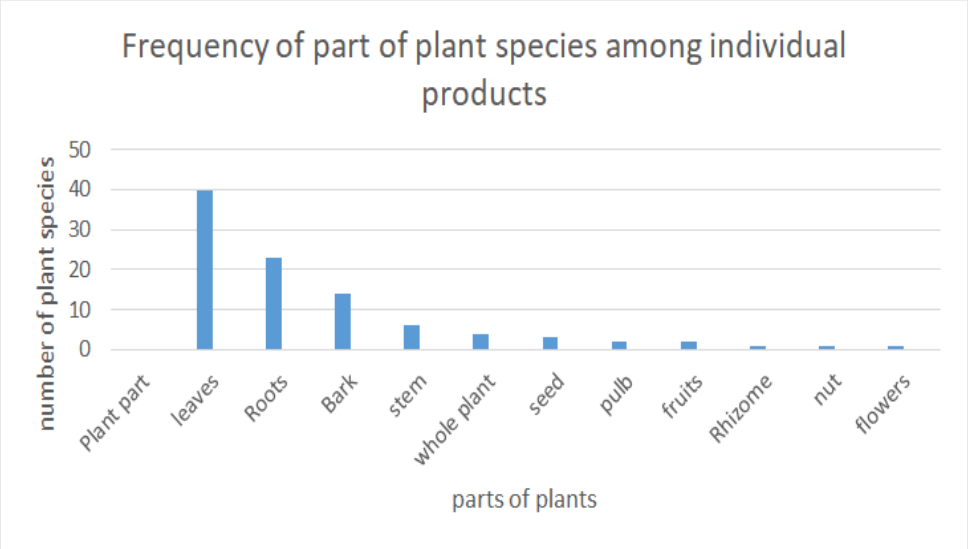
Figure 2. Frequency of conditions herbal products were targeted at.



Parts of the plants used to formulate the herbal products

Different parts of the same or different plant species were used in manufacturing a particular product. From Figure 3, majority of the plant species (40/56, 71.4%), leaves were used. This was followed by roots (23/56, 41.1%) plant species. Very few plants species (1/56, 1.8%) that their flowers, nut and rhizomes were used to produce a product (Figure 3).

Figure 3. Frequency of plant parts among the herbal medicinal products.



Categorization of the plants species, parts and diseases according to information from literature databases

On databases, 41/56 (73.2%) plant species had hepatoprotective activity while 15 (26.8%) had no data for hepatoprotective activity as indicated in Table 1.

Table 1. Plant species with data on hepatoprotective activity and those without data from the databases.

Category	Plant species
Had hepatoprotective activity	*Crataegus oxyacanthea, Tamarindus indica, Parkia biglobosa, Moringa oleifera, Sida acuta, Taraxacum officinale, Kigellia Africana, Syzgium aromaticum, Zanthoxylon zanthoxyloides, Pericopsis laxiflora, Spathodea campanulatha, Gentiana lutea, Citrus lemon, Azadirachta indica, Trema orientalis, Zangiber officinale, Piper guinease, Khaya Senegalensis, Momordica charantia, Magnifera indica, Magnifera indica, Picus religiosa, Citrus aurantifolia, Aloe barbadensis, Vitteleria paradoxa, Ficus exasperate, Pulinia pinnata, Solanum tarvum, Vernonia conferta, Allium cepa, Cucumis sativus, Aspillia Africana, Eucalyptus globulus, Hilleria latifolia, Occium gartissium, Vernonia amygdalina, Allium sativum, Bidens Pilosa, Curcuma longa, Acacia spp, Phyllanthus fraternus*
No hepatoprotective activity	*Nandea catifolien,Clausena aniseta, Cola giganthea, Bombax buonopozense, Securindacalongi pedunculata, Paulinia acuminate, Altnia boonei, Trichilla heudelotil, Panicum flavidum, Mondia whitei, Phyllanthus carolinum, Solanum erianthum, Angophora hispida, Ferruginea gigantea,Chrysophyllum africanum*

Frequency of parts of the plant species reported

From data search, several parts of 41 plant species including leaves, bark, wood, root, seed, pud, flowers, fruits, fig, sap, twist were extracted with various organic and inorganic solvents and test against hepatotoxicity induced by various toxins. Tables 2, indicates the number of parts of each plant species that was reported.

Table 2. Number of parts of each plant species reported.

Plant species	Number of parts studied
Crataegus oxyacanthea	7
Tamarindus indica	6
Parkia biglobosa, Moringa oleifera	5
Sida acuta, Taraxacum officinale, Kigellia Africana, Syzgium aromaticum, Zanthoxylon zanthoxyloides, Pericopsis laxiflora, Spathodea campanulatha, Gentiana lutea, Citrus lemon	3
Azadirachta indica, Trema orientalis, Zangiber officinale, Piper guinease, Khaya Senegalensis, Momordica charantia, Magnifera indica, Picus religiosa, Citrus aurantifolia, Aloe barbadensis, Vitteleria paradoxa, Ficus exasperate, Pulinia pinnata, Solanum tarvum, Vernonia conferta, Allium cepa	2
Cucumis sativus,Aspillia Africana, Eucalyptus globulus, Hilleria latifolia, Occium gartissium, Vernonia amygdalina, Allium sativum, Bidens Pilosa, Curcuma longa, Acacia spp*., Phyllanthus fraternus*	1

Types of extraction solvents used to extract plant parts

Various solvents including distilled water, ethanol, methanol, phenol, chlorofoam, petroleum ether and butanol were used to extract plant active components and indicated in Table 3.

Table 3. Number of different solvents used to extract parts of the plants.

Plant species	Types of extraction solvents
Moringa oleifera	7
Momordica charantia, Curcuma longa	5
Tamarindus indica, Parkia biglobosa, Sida acuta, Kigellia Africana, Syzgium aromaticum, Zanthoxylon zanthoxyloides, Gentiana lutea, Magnifera indica, Allium cepa, Occium gartissium, Vernonia amygdalina	4
Crataegus oxyacanthea, Spathodea campanulatha, Citrus lemon, Zangiber officinale, Picus religiosa, Ficus exasperate, Cucumis sativus, Allium sativum, Phyllanthus fraternus	3
Bidens Pilosa, Aspillia Africana, Eucalyptus globulus, Pulinia pinnata, Citrus aurantifolia, Magnifera indica, Solanum tarvum, Piper guinease, Trema orientalis, Pericopsis laxiflora	2

Acacia spp, *Hilleria latifolia, Vernonia conferta, Aloe barbadensis, Vitteleria paradoxa, Khaya Senegalensis, Taraxacum officinale*	1

Toxins used to induce liver diseases and tested against plant extracts

Various substances including carbon tetrachloride, paracetamol, tuberculosis drugs, etc were used to induce liver disease in experimental models and then challenged with plant extracts. Table 4, indicates the number of different toxins that were used to induce liver disease in an experimental models and test against each plant.

Table 4. Number of different toxins used to induce liver diseases and challenged against plant extracts.

Plant species	Number of inducing toxicants
Moringa oleifera	15
Curcuma longa	13
Zingiber officinale, Allium cepa	12
Azadirachta indica	10
Taraxacum officinale, Syzgium aromaticum	7
Occimum gartissium	6
Tamarindus indica, Parkia biglobosa, Cucumis sativus, Vernonia amygdalina, Allium sativum	5
Citrus lemon, Momordica charantia, Eucalyptus globulus	4
Acacia spp, *Solanum tarvum, Magnifera indica, Spathodea campanulatha, Kigellia Africana, Sida acuta, Crataegus oxyacanthea*	3
Gentiana lutea, Trema orientalis, Picus religiosa, Citrus aurantifolia, Aloe barbadensis, Vitteleria paradoxa, Ficus exasperate, Pulinia pinnata, Bidens Pilosa, Phyllanthus fraternus	2
Hilleria latifolia, Aspillia Africana, Vernonia conferta, Piper guinease, Khaya Senegalensis, Zanthoxylon zanthoxyloides, Pericopsis laxiflora	1

Comparison between frequency of plant usage and report on hepatoprotective activity

A comparism was made to determine if frequency of data on hepatoprotective activity of a plant species in terms of parts, extracting solvents and testing models determines its usage to formulate an herbal product and the vice versa. There was no significance of difference between the frequency of usage in an herbal product and that of number of parts as well as number of extraction solvents reported. There was however significance of difference between frequency usage in a product and number toxins used in inducing models ($p=0.017$) (Table 5).

Table 5. Comparism between frequency of plant species in herbal products and hepatoprotective activity in databases.

Plant species	Frequency in products	Number of parts	Number of solvents	Number of toxicants
Khaya senegalensis	9	2	1	1
Azidirachta indica	7	2	4	10
Vernonia amygdalina	6	1	4	5
Moringa oleifera	6	5	7	15
Syzgium aromaticum	6	3	4	7
Curcuma longa	5	1	5	13
Taraxacum officinale	5	3	1	7
Zingibar officinale	5	2	3	12
Allium sativum	4	1	3	5
Bidens pilosa	4	2	2	2

Trema orientalis	4	2	2	2
Piper guineense	4	2	2	1
Sida acuta	4	3	4	3
Crataegus oxyacanthea	1	7	3	3
Tamarindus indica	2	6	4	5
Parkia biglobosa	1	5	4	5
Momordica charantia	1	2	5	4
Allium cepa	2	2	4	12
Occium gartissium	1	1	4	6
Cucumis sativus	1	1	3	5

DISCUSSION

The aim of the study was to determine whether plant species used in preparing herbal products for liver diseases have scientific basis in term of the plant species, parts and diseases targeted. This is essential to determine whether scientific information forms the choice of plant, their parts and methods of preparing these herbal products. The search for ideal hepatoregenerative agent will be successful if practitioners select plants, parts and methods based on scientific information while researchers explore indigenous fore knowledge in addition to filling research gaps established with latest available scientific information.

Majority of the plant species (41/56, 73.2%) used in formulating the herbal products had data on the search engines in terms of parts, extracting solvents and inducing models. Whereas, the products and the companies were wholly from Ghana, most of the journals reviewed were not published by Ghanaian Authors [17]. This suggests that most of the plant species in Ghana have active components that can restore liver injury or companies and practitioners are relying on scientific information of the choice of plants for their medicines. This can also be attributed to the rapid upgrading of herbal medical practice in industry, academia and research.

A greater number of the herbal products (17/25, 68.0%) were in the liquid form. Liquid phase of a product provides appropriate surface areas which increase the rate of absorption into the blood when ingested or injected. It also provides a large surface area for reaction with enzyme and other components for effective pharmacokinetics [18]. Formulation of liquid of medicinal is also more cost-effective industrial process because it requires less effort, personnel and processes.

Khaya senegalensis (Mahogany) was the most predominant plant used in formulating the herbal products. *Khaya senegalensis* is abundant in all parts of Ghana where it used as banks on roads, folder for ruminants and for building purposes. Herbal medical practice apart from health benefits, it's also an economic and industrial activity which depends heavily on the availability of raw plant materials. *Khaya senegalensis* has also been long use in Ghanaian ancient medicine to treat illness including jaundice [19]. The abundance of *Khaya senegelensis* and its long use in folk medicine could account for its frequent use in the formulation of this product.

Leaves were also the most prevalent plat part used in the manufacturing of these herbal products. This could to attributed to the fact that leaves accumulate more synthetic plant nutrients, accumulate less plant toxins and are more conspicuous. While the roots of the plants hold the plant firmly to the ground and absorb water, minerals and chemicals from the underground. The roots are likely to accumulate minerals, heavy metals and other chemicals from fertilizers. The leaves are responsible for excretion, photosynthesis and respiration and could accumulate metabolites and excretory products. Mahboubi and Mahboubi, reported differences in inteolin and chrysoaerial levels in different parts of plants. While the flowers were rich in iteolin and chrysoaerial, the ariel parts were rich in hydroxycinnamic acid and flavonoid glycosides and leaves in phenolic actives. Din et al also demonstrated that, 200 mg/Kg of ethanoic flower and seed extracts of *Azadirachta indica* had higher free radical scavenging index than leaves, stem and bark.

On the databases, *Cratagus oxycanthea* was most reported in terms of parts while *Moringa oleifera* was the most reported in terms of extracting solvents and inducing models. *Crategus oxycanthea* comparatively more abundant and exist in more different and diverse parts than *Moringa oleifera* and others [20]. *Moringa oleifera* is one of the plants that has been used in ancient medines to treat several illnesses. *Moringa oleifera* used for various purposes such as ornamentals, drink, oil, vegetable, salat, etc.

Finally, there was significance of difference between the frequency usage in an herbal product and number of toxins used

to induce a model for study. Scientific investigation of hepato-efficacy of a plant extract involves modelling the liver diseases in an organism or tissue and challenged with the plant extract. Whereas few parts of plant and solvents exist, there are over 65 substances that can be used to induce liver disease. Further, the nature of the toxin determines the kind of liver disease either acute, chronic, glandular, steatosis, parenchymal, hepato-biliary or zonal that will be modelled. These toxins therefore influence the scientific investigation and reports which in turn influence the choice of the plant or part a practitioner or manufacturer chooses.

CONCLUSION

Majority of plant and parts used for manufacturing herbal medicines in Ghana has scientific data supporting usage. Researcher, Practitioners and Botanist should collaborate to ensure agricultural production of medicinally effective plant species and isolation of active phytochemicals to support herbal industries.

CONFLICT OF INTEREST

The authors declared no conflict of interest in any aspect of the work.

FUNDING

Authors were responsible for funding the project and no external source of funding was received.

AUTHORS CONTRIBUTION

Authors Dongsogo Julius, Larbie Christopher, Idrissu Abdul Mumeen were responsible for design, supervision and conceptualizing of the study. Authors Regina Appiah-Oppong, Benjamin Emikpe, Daniel A. Abera carried the experimentation, manuscript drafting. All Authors proof-read and accepted the final manuscript.

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