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HEPATOPROTECTIVE ROLE OF MEDICINAL PLANTS IN LIVER DYSFUNCTION: A REVIEW

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ABSTRACT

Liver plays a major role in transforming and clearing the chemicals form the body, but same time it is susceptible to the toxicity of these chemicals. Liver diseases are now become major public health problem worldwide, beside viral infection, autoimmune diseases, infectious agents, toxic chemicals and many drugs at higher doses can cause hepatic injury. The drugs used for the treatment of hepatic disorders have many side effects since all drugs detoxified in the liver with the help of cytochrome p-450 system. Several plants are being used for treatment of liver diseases among people in different areas of the world since ancient time. In the current review we have summarized the information regarding the causes of liver diseases and plants used for the treatment of liver diseases.

KEYWORDS: Medicinal plants, Liver diseases, Allopatic drugs, Carbon tetracyhloride. Acetaminophen, Cytochrome p-450.

INTRODUCTION

Liver is the vital organ of body, performs life maintaining functions like metabolic (protein, lipid and carbohydrate metabolism), regulatory, transportation/ secretory and transformation (xenobiotics and other harmful substances from body) (Appak-Baskoy *et al*., 2019). Hepatocytes are parenchymal cells of liver, contain a number of enzymes catalyzing different reaction regarding protein, lipid and carbohydrate metabolism. It maintains normal glucose level in blood via glycolysis and gluconeogenesis (Rui, 2011). Liver produces glucose by breaking glycogen and by *de novo* synthesis of glucose from non-carbohydrate precursors (Hatting *et al*., 2018). Metabolism in liver plays a vital role in the maintenance of whole body energy state as liver is the principal site for storage and release of fatty acids and carbohydrates synthesis. When ample glycogen stores are present then extra glucose will be converted into triglycerides. Acetyl-CoA carboxylase (ACC) and hydroxy-methyl-glutaryl-CoA reductase (HMG-CoA) are two major enzymes in fatty acid and cholesterol synthesis, respectively (Chiang, 2014). The mitochondrial proteins: carnitine-palmityl-transferase I & II in liver cells are responsible for acyl-CoA transport and fatty acid β-oxidation in liver and muscles (Esposti *et al*., 2012). Along with carbohydrate and lipid metabolism, liver is also involved in protein metabolism; nitrogen enters the liver in the form of free ammonia and amino acids (Degli *et al*., 2012). Detoxification of ammonia occurs in liver cells, with concomitant release of urea. Any ammonia bypass detoxification is usually caught by liver cells and where it transformed to glutamine via glutamine synthetase (Olde Demink *et al*., 2009; Farghali *et al*., 2015).

Liver diseases: Liver diseases are major public health problem worldwide, not only cause by viral infection, (hepatitis A, B, C), autoimmune diseases, some bacterial and fungal pathogens, toxic chemical substances, poisons, drinking too much alcohol (Dolganiuc, 2015), but also by higher doses of the drugs (pain killers, antibiotics, vitamins, medicines against tuberculosis, epilepsy and diabetes) (Khan *et al*., 2017). Hepatitis is an inflammation of liver cells leads to chronic liver diseases like steatosis, fibrosis, cirrhosis and hepatocellular carcinomas. If the liver forms scar tissue because of an illness, it's called cirrhosis (Ringehan *et al*., 2017).

Jaundice, a liver disease can be identified by yellowing of the skin. The common symptoms of hepatitis are; right upper abdominal pain, myalgia, fatigue and malaise, nausea and vomiting, change in sense of smell and taste, photophobia, coryza, headache, diarrhea, dark stool and urine (Subbiah & West, 2016). Increased level of serum biochemical markers such as alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), bilirubin, triglycerides and cholesterol are usually associated with liver damage (Ahmed *et al*., 2018).

There are different types of liver cells, parenchymal cells (hepatocytes) and non-parenchymal cells (kupffer cells, fat storing cells, endothelial cells and pit cells). Kupffer cells play a major role in liver damage by number of secretions. They are resident macrophages in liver, endocytose old or injured cells, endotoxins (Gu & Manautou, 2012). They become activated after phagocytosis and release biologically active compounds, free radicals, growth factors and chemokines. The endotoxin becomes toxic to cells and tissues because of the products release by kupffer cells and inflammatory cells. They activate fat storing cells, pit cells and other immune cells to direct an immune response against the endotoxin. After activation, fat storing cells change into myofibroblast which produce progressively increasing amounts of extracellular matrix component (collagen type 1, 3 and 4, fibronectin, laminin, chondroitin, dermatan sulfate and hyaluronate) (Kawada & Parola, 2015). The abnormal deposition of extracellular matrix components in liver can block the blood (nutrient) supply to liver cells and thus ultimately leads towards hepatocytes death.

Oxidative stress and liver damage: Energy generation by mitochondria or detoxification reactions inevitably generates free radicals, i.e., reactive oxygen species/reactive nitrogen species (ROS/RNS) which induced oxidative stress and has been implicated in various forms of diseases. Excessive ROS generation depletes the endogenous antioxidants that subsequently fail to counteract all the ROS leading to cellular injury (Jadeja *et al*., 2017). Under certain circumstances, it can be over-produced and leaving a net excess amount in the system. This abnormal increase leads towards a condition called oxidative stress that may promote inflammatory responses (Muriel, 2017). The biochemical reactions producing free radicals involve in the reactions of respiratory chain, the phagocytosis, the cytochrome p-450 system and the prostaglandins producing reactions (Arauz *et al*., 2016; Phaniendra *et al*., 2015).

Oxidative stress can make major changes in the membranes as well as in the structures of lipids, proteins, lipoproteins and deoxyribonucleic acid (DNA) (Birben *et al*., 2012). If free radicals produced in surplus amount it may destruct cell membranes and lipoproteins by a mechanism known as lipid peroxidation. This process results in the production of melondialdehyde (MDA) and conjugated diene compounds, which can

cause mutation and would be highly cytotoxic. This process once started, it spreads rapidly and affects a large number of lipid molecules. Free radicals also damage the proteins leads to loss of enzymatic activity and if DNA is damaged it causes mutation (Pizzino *et al*., 2017).

Oxidative stress is involved in the progression of liver disease which may be ranges from subclinical icteric hepatitis to necro-inflammatory hepatitis, fibrosis, cirrhosis and carcinomas (Jadeja *et al*., 2017). An over production of free radicals and an increase in hepatic lipid peroxidation have been reported in alcoholic liver disease, chronic drugs, liver cirrhosis and steato-hepatitis (Galicia-Moreno & Gutierrez-Reyes, 2014). These free radicals produce in excess either by activation of kupffer cells or via biotransformation of drugs, toxins and chemical substances may also lead towards hepatocytes death (Gu & Manautou, 2012).

Drugs and chemicals causing hepatotoxicity: The most common drugs and chemicals said to be hepatotoxic are acetaminophen (AAP), carbon tetrachloride (CCl_4), D-galactosamine, thioacetamide (TAA), aflatoxin, cyclosporine A, alcohol, 2-acetyl-aminoflourene, tacrine and rifampicin (Björnsson, 2016).

D-galactosamine is a toxin for the induction of hepatitis and other serious health problems that may lead to the death (Maes *et al*., 2016). Absorption of D-galactosamine affects cell membrane, organelles and synthesis of protein and nucleic acid. Its toxic effect leads to insufficiency of UDP-glucose and UDP-galactose and leads to decrease in hepatic content of uracil nucleotide, which causes inhibition of transcription and translation processes (Tawfik *et al*., 2015).

The administration of thioacetamide leads to the generation of hepatotoxic reactive metabolite, thioacetmide-*S*-oxide. It may further result in disturbed cell permeability and it inhibits mitochondrial activity followed by cell death. The chronic exposure of TAA resulted in cirrhosis in rats (Al-Attar *et al*., 2017).

Acetaminophen and CCl_4 are widely used chemicals for the induction of hepatotoxicity in experimental models (Fukaya *et al*., 2017)

Acetaminophen induced hepatotoxicity: Acetaminophen, considered safe at therapeutic doses, developed and sold in market by drug manufacturing companies (pharmaceutical companies) using trade names of Paracetamol, Tyenol and Panadol. Now days it has been widely used as an analgesic and antipyretic drug worldwide. In high doses acetaminophen produces a centrilobular hepatic necrosis that can be fatal (Yoon *et al*., 2016). It is metabolically activated by cytochrome p-450 to form a reactive metabolite *N*-acetyl-*p*-benzoquinone imine (NAPQI), formed by direct two-electron oxidation (Yan *et al*., 2018). Cytochrome 2E1, 1A2, 3A4 and 3A6 (Mazaleuskaya *et al*., 2015) have been reported to oxidize acetaminophen to the reactive metabolite. NAPQI is detoxified by glutathione (GSH) to form an acetaminophen-glutathione conjugate. Hence, result a depletion of glutathione upto 90% (Sun *et al*., 2018). The active metabolite covalently binds to the cysteine groups on protein; forming acetaminophen-protein adducts (Jiang *et al*., 2019). One possible mechanism of hepatocytes death may be due to the lower level of glutathione that resulted in oxidative stress and cellular injury (Jaeschke *et al*., 2013). The necrosis may be due to covalent binding to critical cellular proteins especially mitochondrial proteins resulting in loss of energy production, as well as proteins involve on cellular ions control (Hinson *et al*., 2010). Loss of mitochondrial and nuclear ion balance may also result in

toxin mediated cell death. These losses may lead to increases in cytosolic Ca^{++} concentrations, mitochondrial calcium cycling, activation of proteases, endonucleases and DNA strand breaks (Hinson *et al*., 2010). The effect of NAPQI on isolated mitochondria and the alteration of plasma membrane ATPase activity after administration of acetaminophen was also reported (Banerjee *et al*., 2017).

Carbon tetrachloride induced hepatotoxicity: Carbon tetrachloride (CCl_4) is a prevalent industrial chemical and an organic solvent (Bupesh *et al*., 2012) in rubber, drug, chemical and paint industries. It is used as fire extinguishers and cleaning agent. However, due to its health related hazards, CCl_4 is strictly regulated in most countries. Liver injury induced by CCl_4 administration in rats and mice was similar to that caused by some more common hepato-destructive agents such as viruses, alcohol, other chemicals, or autoimmune diseases in humans based on morphological and biochemical markers of liver disease (Yang *et al*, 2018). CCl_4-induced liver damage is therefore widely used in experimental studies as a convenient model for evaluation of hepatoprotective activity of various substances including drugs and dietary supplements. This model has been extensively used to evaluate the potential of drugs and dietary antioxidants against the oxidative damage (Zhang *et al*., 2013). CCl_4 converted into reactive free radicals including trichloromethyl (CCl_3) and peroxy-trichloromethyl ($OOCCl_3$) radicals via a process of biotransformation catalyzed by cytochrome p-450 in liver that attach to proteins and DNA and directly harm to these molecules (Weber *et al*., 2003). There are sufficient *in vivo* and *in vitro* proofs available for the mechanism by which it exhibits toxic effects in animals (Karakus *et al*., 2011). The metabolic products formed during its biotransformation via CYP2E1 are trichloromethyl radical and with addition of O_2 it converted into trichloromethyl-peroxy radicals (Jaeschke, 2013). Free radicals mainly trichloromethyl peroxy radicals are very reactive and produce injuries in the cell by binding with cellular protein, nucleic acids and lipid especially phospholipids (Phaniendra *et al*., 2015). Trichloromethyl-peroxy radicals when attack polyunsaturated fatty acids in cell membrane they produce fatty acids free radicals that eventually initiate lipid peroxidation (Weber *et al*., 2004) through a chain reaction. A number of researchers have reported that the process of lipid peroxidation takes place in cells after CCl_4 administration that can be detected by presence of conjugated dienes in liver (Tribble *et al*., 1987), degradation products of fatty acids after oxidation (Gee *et al*., 1981) or by the presence of reactive aldehyde (malonaldehyde) which are highly cytotoxic (Ichinose *et al*., 1994; Gasso *et al*., 1996). It is reported that large doses of CCl_4 causes severe necrosis, while long term administration at lower doses is used to induced hepatic fibrosis (Jaeschke *et al*., 2013).

Drugs/Products used in liver diseases: Conventional treatment strategies are disease specific and based on known biological factors. With regard to hepatitis C, conventional medical treatment involves the use of a combination of antiviral and biological response modifiers that have been shown to be efficacious in large randomized control trials using rigorously applied, surrogate end points (Seeff *et al*., 2001). Currently, interferon (interferon, alpha-2b), ribavirin (Zeuzem *et al*., 2000), lamivudine, entecavir, famciclovir, tenofovir and adefovir (Shah *et al*., 2007) are commonly used allopathic treatment for hepatic disorders. Allopathic medicine used for the treatment of liver diseases have many

side effects, with mild to severe toxicities including, insomnia, vomiting, fatigue, dry mouth, diarrhea, constipation, dizziness, suicidal thoughts, hostility, depression, mania, seizures, coma, anemia, hair loss, high blood sugar, shoplifting, swelling, impotency, panic attacks, confusion, fainting and death (Tripathi, 2008). The treatment of hepatitis C with alpha-interferon is a common practice in conventional medicine. Interferon-α is very expensive with significant toxicities and causes fatigue, irritability and depression (Zahiu & Rimbas, 2014).

In China, Chinese herbal medicine is used as a treatment adjunct or alternative to interferon-α which accounts for 30% to 50% of total medicine consumption, with low cost and low toxicity. Many over the counter products are marketed to people living with hepatitis C. The drug Eurocel™ is a mixture of Chinese and Korean herbs, has ability to improve liver health. Some products in market are from herbal origin and have been claimed for treating hepatic disorders (Table 1) (Patrick, 2008). Hepato C™ is a mixture of 15 different herbs and plants, improves detoxification functions of the liver. It promotes liver functions and improves liver health and strength. Liv-52™ has been claimed for treating all type of liver diseases, including viral hepatitis, alcoholic liver diseases, drugs- or chemicals-mediated liver dysfunction, pre-cirrhotic conditions and others.

Hepatoprotective medicinal plants/ herbs: Modern medicines are failed to cure the liver diseases including infectious hepatitis, liver cirrhosis and hepatocellular carcinomas. Herbs play a vital role in the management of many hepatic disorders (Qadir & Ahmad, 2017). A number of herbs, plant extracts and plant derived natural compounds have been screened for liver management. The therapies based on nature are believed to be safer and better than standard medical practice (Thompson *et al*., 2017).

During last four decades, more than 200 plant species have been screened for hepatoprotective activity and most of them belong to Asteraceae and Fabaceae family (Schuppan *et al*., 1999) (Table 2). According to World Health Organization (WHO) approximately 80% population from developing countries are still rely on traditional medicine for their primary health care (Ekor, 2014). The hepatoprotective activity of a number of plants has been reported all over the world including *Curcuma longa* (Negi *et al*., 2008; Salama *et al*., 2013), *Aloe barbadensis* Mill (Al-Shinnawy *et al*., 2014), *Carica papaya* Linn (Mohammed *et al*., 2011), *Cichorium intybus* Linn (Butt *et al*., 2012), *Eclipta alba* Hassk (Jahan *et al*., 2014) and *Silybum marianum* (Desai *et al*., 2012). The work on hepatoprotection of *Silybum marianum* Linn (milk thistle) plant started from 4 to 5 decades back against the intoxication with amanitin (Mengs *et al*., 2012), thioacetamide (Das *et al*., 2012) and CCl_4 (Zamzami *et al*., 2019). Silymarin is a flavolignane from *Silybum marianum* and in traditional medicine used for the remedy of liver disorders and biliary tract disorders (Onalan *et al*., 2016). Since 1973 a number of researchers worked on silymarin for its hepatoprotective activity (Schriewer *et al*., 1973; Barberino *et al.,* 1977; Ahmad & Sharafatullah, 2008; Madani *et al*., 2008; Negi *et al*., 2008; Pushpavalli *et al*., 2010; Stagos *et al*., 2012; Vargas-Mendoza, *et al*., 2014; Baradaran *et al*., 2019) and used it as a standard drug while assessing the hepatoprotective role of any plant/seaweed extracts or compounds (Pushpavalli *et al*., 2010; Chen *et al*., 2011; Desai *et al*., 2012).

Table 1. Products marketed for the treatment of liver diseases.

S. No.	Products	Herbs/Components	Active ingredients	Company
112.	Eurocel™	*Patrina villosa, Artemesia, capillaries, Schizandra fructus*		Allergy Research Group
22.	Pure Herbal Remedy™	Burdock root, plantain, nettle, red clover bloom, oregon grape, ginseng root, echinacea root, astragalus root, yellow dock root, blessed thistle schizandra, dandelion root, olive leaf, psyllium and milk thistle	Flavinoids	The company internet site
33.	Immune Booster™	Goldenseal root, witch hazel bark, red clover blooms, ginseng root, capsicum fruit, yellow dock root, burdock root, spirulina and *Echinacea augustifolia*	–	”
44.	Hepacure™	Nettle, plantain, horsetail, yarrow, golden rod, chamomile, fern, akala, cleaver, mayapple, milk thistle, dandelion and turmeric root	–	”
55.	Milk Thistle™	*Silybum marianum*	Silymarin, silybin	”
66.	Hepatico™	Plantain, nettle, immortelle, turmeric, milk thistle and dandelion root	–	Alta Natural Herbs & Supplements Ltd.
77.	Hepato-C™	Chinese salvia root, red peony root, peel of orange, leaves and shoots of capillaris, Barbed flower and 9 other herbs	–	Pacific Biologics
88.	Liv.52™/ LiverCare™	Capers, black nightshade, wild chicory, arjuna, negro coffee, yarrow and tamarish	–	Himaliya Drug Company
99.	Mannatech™	*Aloe vera*	Acemanna	–
110.	MGN-3™	Rice bran	Arabinoxylane	–
111.	Liverite Liver Aid™	Vitamin B12, phospholipids, cysteine and bovine liver hydrolysate	Phosphatidylcholine	–
112.	Bee Propolis	Bees sticky material	Flavinoids	–
313.	Sho-Saiko-To (SST)/Liver Campo	Bupleurum root, ginsenosides, pinellia tuber, scutellaria root, ginseng, jujube, licorice root and ginger	Glycyrrhizin, saikosaponins, ginsenoides, gingerols and wogonin	Honso USA. Inc.
114.	Phlogenzym™	–	Proteolytic enzymes and rutosid	Mucos Pharma, Germany
115.	Colloidal Silver	–	Silver	–
16.	IP-6 (Phytic acid)	Beans, brown rice, corn meal and wheat bran	Myoinositol hexaphosphate	–
17.	ProBoost™	Thymus tissues of calves	Thymic protein A	–

Table 2. Plants/ herbs having hepatoprotective effect.

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
1.	*Acacia catechu* (L.f.) Willd.	Fabaceae/ Leguminosae	Cutch tree	Carbon tetrachloride	Ray *et al*., 2006
2.	*Acalypha racemosa* Wall.	Euphorbiaceae	Copperleaf	Carbon tetrachloride	Iniaghe *et al*., 2008
3.	*Acanthopanax senticosus* (Rupr. et. Maxim.) Maxim.	Araliaceae	Siberian ginseng	Carbon tetrachloride/ Paracetamol	Lin & Huang, 2002
4.	*Acanthus ilicifolius* L.	Acanthaceae	Holy mangrove	Carbon tetrachloride	Babu *et al*., 2001
5.	*Achyrocline satureioides* (Lam.) DC.	Asteraceae	Macela	Bromobenzene	Kadarian *et al*. 2002
6.	*Actinidia deliciosa* (A. Chev.)	Actinidiaceae	Kiwi fruit	Carbon tetrachloride	Bai *et al*., 2007
7.	*Adhatoda vasica* Nees	Acanthaceae	Arosa, Basonta	D-Galactosamine	Bhattacharyya *et al*., 2005
8.	*Aegle marmelos* (L.) Corr. Serr.	Rutaceae	Bael fruit	Ethanol	Singanan *et al*., 2007
9.	*Alchornea cordifolia* (Schum & Thonn.)	Euphorbiaceae	Christmas Bush	Paracetamol	Olaleye *et al*., 2006
10.	*Aloe barbadensis* Mill.	Liliaceae	Aloe vera	Carbon tetrachloride	Chandan *et al*., 2007
11.	*Ambrosia maritima* L.	Asteraceae	Sea ambrosia	Paracetamol	Ahmed & Kharter, 2001
12.	*Andrographis lineata* Nees	Acanthaceae	-	Carbon tetrachloride	Sangameswaran *et al*., 2008
13.	*Andrographis paniculata* (Burm.f.) Nees	Acanthaceae	Kalmegh	Carbon tetrachloride	Rana & Avadhoot, 1991
14.	*Angelica sinensis* (Oliv.) Diels	Apiaceae	Dang Gui	D-Galactosamine/ Carbon tetrachloride	Xiang-qing *et al*., 2002
15.	*Anisotes trisulcus* (Forssk.)	Acanthaceae	Madh	Carbon tetrachloride	Fleurentin *et al*., 1986
16.	*Anoectochilus formosanus* Hayata	Orchidaceae	Yellow flower, Shusu-ran	Carbon tetrachloride	Wu *et al*., 2007
17.	*Annona squamosa* L.	Annonaceae	Custard apple	Isoniazid/Rifampicin	Saleem *et al*., 2008
18.	*Apium graveolens* L. var. dulce. (Mill.) Pers.	Apiaceae	Celery	Carbon tetrachloride/ Paracetamol/ Thioacetamide	Singh & Handa, 1995; Ahmed *et al*., 2002
19.	*Apocynum venetum* L.	Apocynaceae	Dogbane leaf	Carbon tetrachloride/ D-Galactosamine	Xiong *et al*., 2000
20.	*Achillea millefolium* Am. Cr.	Asteraceae	Common yarrow	D-Galactosamine, Lipopolysaccharides	Yaeesh *et al*., 2006
21.	*Artemisia absinthium* L.	Asteraceae	Green ginger	Carbon tetrachloride/ Paracetamol	Gilani & Janbaz, 1995a
22.	*Artemisia maritima* L.	Asteraceae	Sea Wormwood	Carbon tetrachloride/ Paracetamol	Janbaz & Gilani, 1995
23.	*Artemisia vulgaris* L.	Asteraceae	Mugwort	Carbon tetrachloride/ Paracetamol	Gilani *et al*., 2005b
24.	*Aspalathus linearis* (Brum.f) Dahlg	Theaceae	Rooibos	Carbon tetrachloride	Ulicna *et al*., 2003

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
25.	*Asteracantha longifolia* L. Nees	Acanthaceae	Kulikhara	Carbon tetrachloride/ Paracetamol	Hewawasam *et al*., 2003
26.	*Astragalus membranaceus* Bunge	Fabaceae	Milk vetch root	Carbon tetrachloride	Sun *et al*., 2007
27.	*Azadirachta indica* A. Juss	Meliaceae	Neem	Paracetamol	Yanpallewar *et al*., 2003
28.	*Bacopa monniera* (L.) Pennell	Scrophulariaceae	Thyme-leafed gratiola	Morphine	Sumathy *et al*., 2001
29.	*Ballota glandulosissima* Hub-Mor & Patzak	Lamiaceae	Black horehound	Carbon tetrachloride	Ozbek *et al*., 2004
30.	*Bauhinia racemosa* Lam	Caesalpiniaceae	Kanchan	Carbon tetrachloride/ Paracetamol	Gupta *et al*., 2004a
31.	*Bauhinia variegata* L.	Fabaceae	Orchid tree	Carbon tetrachloride	Bodakhe & Ram, 2007
32.	*Berberis tinctoria* Lesch	Berberidaceae	Nilgiri Barberry	Paracetamol	Murugesh *et al*., 2005
33.	*Bidens chilensis* DC.	Asteraceae	Amorseco	Carbon tetrachloride/ Paracetamol	Chih *et al*., 1996
34.	*Bidens pilosa* L.	Asteraceae	Spanish needle	Carbon tetrachloride/paracetamol	Chih *et al*., 1996
35.	*Boswellia serrata* Roxb.	Burseraceae	Salai guggal	Carbon tetrachloride/Paracetamol/ Thioacetamide	Jyothi *et al*., 2006
36.	*Bupleurum kaoi* Liu (Chao et Chuang)	Umbelliferae	Chinese thourough wax	Paracetamol/Carbon tetrachloride	Liu *et al*., 2006
37.	*Butea monosperma* (Lam.) Taub.	Fabaceae	Flame of the forest	Paracetamol	Maaz *et al*., 2010
38.	*Butea superb* Roxb..	Fabaceae	Red kwao krua	Paracetamol	Manjunatha *et al*., 2008
39.	*Cajanus indicus* L.	Fabaceae	Congo-pea, Red gram	Paracetamol	Ghosh & Sil, 2007
40.	*Cajanus cajan* L.	Fabaceae	Tropical green pea	Alcohol/D-Galactosamine	Kundu *et al*., 2008; Akinloye & Olaniyi, 2011
41.	*Calotropis procera* Ait.	Asclepiadaecae	Akra	Carbon tetrachloride	Kumar *et al*., 2007
42.	*Camellia sinensis* L.	Theaceae	Tea plant	Sodium oxalate/ Tamoxifen	Oyejide & Olushola, 2005; El-Beshbishy, 2005
43.	*Capparis deciduas* (Forssk.) Edgew.	Capparidaceae	Bare capper	Carbon tetrachloride	Ali *et al*., 2009
44.	*Capparis spinosa* L.	Capparidaceae	Caper bush	Carbon tetrachloride	Aghel *et al*., 2007
45.	*Carica papaya* L.	Caricaceae	Papaya	Carbon tetrachloride	Balasubramanian *et al*., 2002; Adeneye *et al*., 2009
46.	*Careya arborea* Roxb.	Myrtaceae	Tummy wood, wild guava	Carbon tetrachloride	Kumar *et al*., 2005
47.	*Carum copticum* L.	Apiaceae	Bishop's weed, Ajowan	Carbon tetrachloride/Paracetamol	Gilani *et al*., 2005a
48.	*Cassia auriculata* L.	Fabaceae	Tanners cassia	Ethanol	Rajagopal *et al*., 2003
49.	*Cassia fistula* L.	Fabaceae	Chamkani, Khyar shanber	Carbon tetrachloride	Bhakta *et al*., 1999
50.	*Cassia occidentalis* L.	Fabaceae	Chakundra, Coffee senna	Paracetamol/Ethyl alcohol/ Carbon tetrachloride	Jafri *et al*., 1999; Usha *et al*., 2007

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
51.	*Combretum dolichopetalum* Engl. & Diels	Combretaceae	hakpa-nomu	Paracetmol	Udem *et al*., 1997
52.	*Casuarina equisetifolia* Forst	Casuarinaceae	Coast she-oak	Carbon tetrachloride	Ahsan *et al*., 2009
53.	*Chamomile capitulo*	Asteraceae	Wild chamomile	Paracetamol	Gupta & Misra, 2007
54.	*Cichorium intybus* L.	Asteraceae	Kasni	Carbon tetrachloride/ Thioacetamide/ Paracetamol	Ahmed *et al*., 2003; Jamshidzadeh *et al*., 2006; Madani *et al*., 2008; Butt *et al*., 2012
55.	*Cistus laurifolius* L.	Cistaceae	Scarlet pimpernel	Paracetamol	Kupeli *et al*., 2006
56.	*Cleome viscosa* L.	Capparidaceae	Wild mustard	Carbon tetrachloride	Gupta & Dixit., 2009
57.	*Clerodendrum inerme* L. Gaertn	Verbenaceae	Ang-angri	Carbon tetrachloride	Gopal & Sengottuvelu, 2008
58.	*Clitoria ternatea* L.	Fabaceae	Butterfly pea	Paracetamol	Nithianantham *et al*., 2011
59.	*Cochlospermum tinctorium* Perri ex Rich.	Bixaceae	Rawaya	Carbon tetrachloride	Diallo *et al*., 1992
60.	*Commiphora opobalsamum* (L.) Engl.	Burseraceae	Mecca myrrh	Carbon tetrachloride	Al-Howiriny *et al*., 2004
61.	*Crassocephalum crepidioides* Benth	Asteraceae	Oldbag weed	D-Galactosamine/ Lipopolysaccharides/ Carbon tetrachloride	Aniya *et al*., 2005
62.	*Crepis rueppellii* (Sch.) Bip.	Asteraceae	-	Carbon tetrachloride	Fleurentin *et al*., 1986
63.	*Croton oblongifolius* Roxb.	Euphorbiaceae	Thetyin-gye	Carbon tetrachloride	Ahmed *et al*., 2002
64.	*Croton zehntneri* Pax et Hoff.	Euphorbiaceae	Cinnamon of cuncha	Paracetamol	Lima *et al*., 2008
65.	*Curculigo orchioides* Gaertn.	Amaryllidaceae	Golden eye grass	Carbon tetrachloride	Venukumar & Latha, 2002
66.	*Curcuma longa* L.	Zingiberaceae	Turmeric	Isoniazid/Rifampicin/Paracetamol/ Thioacetamide	Somchit *et al*., 2002; Salama *et al*., 2013
67.	*Cucumis trigonus* Roxb.	Cucurbitaceae	Daddy melon	Carbon tetrachloride	Patila *et al*., 2011
68.	*Cuscuta chinensis* Lam.	Convolvulaceae	Chinese dodder	Paracetamol	Yen *et al*., 2007
69.	*Cuscuta semen* Lam.	Convolvulaceae	Dodder seed	Dimethylnitroseamine	Kim *et al*., 2007b
70.	*Cynara scolymus* L. folium	Asteraceae	Globe artichoke	Carbon tetrachloride	Adzet *et al*., 1987
71.	*Cynanchum auriculatum* Royle ex wight	Apocynaceae	Flying crane	Carbon tetrachloride	Jia-li *et al*., 2007
72.	*Cyperos scariosus* R.Br.	Cyperaceae	-	Carbon tetrachloride	Gilani & Janbaz, 1995b
73.	*Daucus carota* L.	Umbelliferae	Carrot	Carbon tetrachloride	Bishayee *et al*., 1995

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
74.	*Diospyros malabarica* (Desr.) Kostel	Ebenaceae	Malabar ebony	Carbon tetrachloride	Mondal *et al*., 2005; Mazumder *et al*., 2005
75.	*Eclipta alba* Hassk.	Asteraceae	Eclipta	Carbon tetrachloride/Paracetamol	Singh *et al*., 1993; Tabassum & Agrawal, 2004
76.	*Elephantopus mollis* Kunth	Asteraceae	Soft elephant foot	Paracetamol/D-Galactosamine	Lin *et al*., 1995a
77.	*Elephantopus scaber* L.	Asteraceae	Elephant foot	Paracetamol/D-Galactosamine	Lin *et al*., 1995a
78.	*Emblica officinalis* Gaertn.	Euphorbiaceae	Amla	Anti-tuberculosis drugs/Paracetamol	Tasduq *et al*., 2005; Malar & Bai, 2009
79.	*Enicostemma axillare* Lam.	Gentianaceae	Indian white head	Carbon tetrachloride	Gite *et al*., 2007
80.	*Enicostemma littorale* Blume.	Gentianaceae	Majmak booti	Carbon tetrachloride	Senthilkumar *et al*., 2005
81.	*Epaltes divaricata* (L.) Cav.	Asteraceae	-	Carbon tetrachloride	Hewawasam *et al*., 2004; Mudduwa *et al*., 2004
82.	*Ervatamia coronaria* (jacq.) Stapf	Apocynaceae	Pinwheel flower	Carbon tetrachloride	Gupta *et al*., 2004b
83.	*Erycibe expansa* Wall. & G.Don	Convolvulaceae	-	D-Galactosamine	Matsuda *et al*., 2004
84.	*Euphorbia antiquorum* L.	Euphorbiaceae	Grape-jasmine	Carbon tetrachloride	Jyothi *et al*., 2008
85.	*Flaveria trinervia* (Spreng.) C. Mohr	Asteraceae	Clustered yellow top	Carbon tetrachloride	Umadevi *et al*., 2004
86.	*Fumaria parviflora* Lam.	Fumariaceae	Fine-leaved fumitory	Paracetamol	Gilani *et al*., 1996
87.	*Ficus carica* L.	Moraceae	Fig	Carbon tetrachloride	Venkatesh *et al*., 2007
88.	*Ficus hispida* L.	Moraceae	Devil fig	Paracetamol	Mandal *et al*., 2000
89.	*Foeniculum vulgare* Miller	Umbelliferae	Fennel	Carbon tetrachloride	Ozbek *et al*., 2003
90.	*Fumaria indica* (Hausskn.) Pugsley	Fumariaceae	Indian fumitory	Paracetamol/Rifampicin/ Carbon tetrachloride	Rao & Mishra, 1997
91.	*Ginkgo biloba* L.	Ginkgoaceae	Dilqul (Kashmiri)	Lipopolysaccharides/ D-Galactosamine	Shenoy *et al*., 2001
92.	*Glycine max* (L.) Merr	Fabaceae	Soya bean	Paracetamol	Wu *et al*., 2001
93.	*Glycosmis pentaphylla* Corr.	Rutaceae	Glycomis/ Ban-nimbu	Carbon tetrachloride	Ahsan *et al*., 2009
94.	*Glycyrrhiza glabra* L.	Fabaceae	Licorice (Mulethi)	D-Galactosamine	Yamamura *et al*., 1997
95.	*Gundelia tourenfortii* L.	Asteraceae	Tumble weed (Gundelia)	Carbon tetrachloride	Jamshidzadeh *et al*., 2005
96.	*Haloxylon salicornicum* (Moq.) Bunge ex Boiss	Chenopodiaceae	Rama	Carbon tetrachloride	Ahmad & Erum, 2011
97.	*Hedyotis corymbosa* (L.) Lam.	Rubiaceae	Flattop mille grains	Paracetamol	Sadasivan *et al*., 2006
98.	*Helminthostachys zeylanica* (L.)Hook	Ophioglossaceae	Tukod-langit	Carbon tetrachloride	Suja *et al*., 2004

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
99.	*Hygrophila auriculata* (K. Schum.) Heine	Acanthaceae	Marsh barbell	Paracetamol/Thioacetamide	Singh & Handa, 1995
100.	*Hygrophila spinosa* T. Anders	Acanthaceae	Kokilasha	Carbon tetrachloride	Usha *et al*., 2007
101.	*Hypoestes triflora* (Forssk.) Roem & Schult	Acanthaceae	Malabar nut tree	Carbon tetrachloride	Van Puyvelde *et al*., 1989
102.	*Hyptis suaveolens* L.	Lamiaceae	Bush-tea-bush	Paracetamol	Babalola *et al*., 2011
103.	*Ichbocarpus frutescens* L.	Apocynaceae	Black creeper	Paracetamol	Dash *et al*., 2007
104.	*Indigofera trita* L.	Fabaceae	Florida keys indigo	Carbon tetrachloride	Kumar *et al*., 2008
105.	*Kalanchoe pinnata* Lam.	Crassulaceae	Cathedral bells/ Life plant	Carbon tetrachloride	Yadav & Dixit, 2003
106.	*Launaea pinnatifida* Cass.	Asteraceae	Beach launaea	Carbon tetrachloride	Pokharkar *et al*., 2007
107.	*Launaea Procumbens* (Roxb.) Ramayya & Rajagopal	Asteraceae	Country dendelion	Carbon tetrachloride	Khan *et al*., 2012a
108.	*Lawsonia alba* L.	Lythraceae	Camphire (mendi)	Carbon tetrachloride	Ahmed *et al*., 2000
109.	*Leucas cilita* L.	Lamiaceae	Leucas	Carbon tetrachloride	Qureshi *et al*., 2011
110.	*Leucas lavandulaefolia* Rees	Lamiaceae	Salita	D-Galactosamine	Chandrashekar *et al*., 2007
111.	*Leucophyllum frutescens* Berl.	Scrophulariaceae	Texas barometer bush	Carbon tetrachloride	Renteria *et al*., 2007
112.	*Luffa Echinata* Roxb..	Cucurbitaceae	Bitter sponge gourd	Carbon tetrachloride	Ahmed *et al*., 2001
113.	*Lumnitzera racemosa* Willd.	Combretaceae	Mangrove plant	Carbon tetrachloride	Ravikumar & Gnanadesigan, 2011
114.	*Lycium chinense* Mill.	Solanaceae	Wolfberry	Carbon tetrachloride	Haa *et al*., 2005
115.	*Lygodium flexuosum* (L.aeus) Swartz.	Lygodiaceae	Maiden hair creeper	D-Galactosamine	Asha & Wills, 2006
116.	*Matricaria chamomilla* L.	Asteraceae	Chamomile	Paracetamol	Gupta & Sharma, 2007
117.	*Mitracarpus scaber* Zucc.	Rubiaceae	-	Carbon tetrachloride	Germano *et al*., 1999
118.	*Momordica charantia* L.	Cucurbitaceae	Bitter gourd	Paracetamol	Zahra *et al*., 2012
119.	*Momordica subangulata* Blume	Cucurbitaceae	Wild bitter gourd	Paracetamol	Shreedhara & Vaidya, 2006
120.	*Morinda citrifolia* L.	Rubiaceae	Beach mulberry	Carbon tetrachloride	Wang *et al*., 2008
121.	*Moringa oleifera* Lam.	Moringaceae	Drumstick	Carbon tetrachloride	Nanjappaiah & Hugar, 2012
122.	*Murraya koenigii* (L.) Roxb.	Rutaceae	Curry leaf tree	Carbon tetrachloride	Desai *et al*., 2012
123.	*Myoporum lactum* L.	Myoporaceae	-	Profenofos	Hassan *et al*., 2011
124.	*Myristica fragrans* (HOUTT.)	Myristicaceae	Nutmeg	Lipopolysaccharides/ D-Galactosamine	Morita *et al*., 2003
125.	*Musa paradisiaca* L.	Musaceae	Banana	Carbon tetrachloride	Nirmala *et al*., 2012

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
126.	*Nardostachys jatamansi* D.C.	Valerianaceae	Spikenard	Carbon tetrachloride	Ali *et al*., 2000
127.	*Nicotiana glauca* Graham.	Solanaceae	Tree tobacco	Carbon tetrachloride	Janakat & Al-Merie, 2002
128.	*Nigella sativa* L.	Ranunculaceae	Black cumin	Carbon tetrachloride	Ilhan & Seckin, 2005
129.	*Nymphaea stellata* Willd.	Nymphaceae	Lotus lily	Carbon tetrachloride	Bhandarkar & Khan, 2004
130.	*Ocimum basilicum* L.	Lamiaceae	Basil	Carbon tetrachloride	Meera *et al*., 2009
131.	*Ocimum gratissimum* L.	Lamiaceae	Clove basil	2-Acetylaminoflourine	Adetutu & Olorunnisola, 2013
132.	*Paeonia lactiflora* Pall.	Paeoniaceae	Common garden peony	Carbon tetrachloride	Sun *et al*., 2007
133.	*Panax ginseng* (C. A. Mayer)	Ariliaceae	Asian ginseng	Carbon tetrachloride	Karakus *et al*., 2011
134.	*Pandanus odoratissimus* Roxb.	Pandanaceae	Ketaki	Carbon tetrachloride	Ilanchezhian & Joseph, 2010
135.	*Parkinsonia aculeate* L.	Fabaceae	Parkinsonia	Carbon tetrachloride	Hassan *et al*., 2008
136.	*Phaseolus aureus* Roxb.	Fabaceae	Mung bean	Paracetamol	Wu *et al*., 2001
137.	*Phaseolus calcaratus* Roxb.	Fabaceae	Red bean	Paracetamol	Wu *et al*., 2001
138.	*Phaseolus radiatus* L.	Fabaceae	Black gram	Paracetamol	Wu *et al*., 2001
139.	*Phillyrea latifolia* L.	Oleaceae	Broad-leaved Phillyrea	Carbon tetrachloride	Janakat & Al-Merie, 2002
140.	*Phoenix dactylifera* L.	Arecaceae	Date fruits	Carbon tetrachloride	Al-Qarawi *et al*., 2004
141.	*Phyllanthus amarus* Schum. & Thonn.	Euphorbiaceae	Leafflower	Hepatitis C virus	Xin-Hua *et al*., 2001
142.	*Phyllanthus maderaspatensis* L. Kuntze	Euphorbiaceae	Canoe weed	Paracetamol/Carbon tetrachloride/ Thioacetamide	Asha *et al*., 2004; 2007
143.	*Phyllanthus niruri* L.	Euphorbiaceae	Niruri (Sea under leaf)	Paracetamol	Sabir & Rocha, 2008; Tabassum *et al*., 2005
144.	*Phyllanthus polyphyllus* Willd	Euphorbiaceae	-	Paracetamol	Rajkapoor *et al*., 2008
145.	*Phyllanthus reticulatus* Poir.	Euphorbiaceae	Sour grapes	Carbon tetrachloride	Das *et al*., 2008
146.	*Phyllanthus rheedii* Wight.	Euphorbiaceae	Ye-Chin-Yar	D-Galactosamine	Asha & Suresh, 2008
147.	*Physalis angulata* L.	Solanaceae	Wild tomato	-	Wu *et al*., 2004
148.	*Physalis peruviana* L.	Solanaceae	Cape gooseberry	Carbon tetrachloride	Arun & Asha, 2007
149.	*Picrorrhiza kurroa* (Roule.) Sans	Scrophulariaceae	Katuka (Kutki)	D-Galactosamine	Anandan & Devaki, 1999
150.	*Platycodon grandiflorum* (Jacq.) A. DC.	Campanulaceae	Balloon flower	Paracetamol	Lee *et al*., 2001
151.	*Pleurotus ostreatus* (Jacq) Quelet.	Pleurotaceae	Oyester mushroom	Carbon tetrachloride	Jayakumar *et al*., 2006
152.	*Podophyllum hexandrum* Royale	Berberidaceae	Himalayan mayapple (Devil's apple)	Carbon tetrachloride	Ganie *et al*., 2011

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
153.	*Polyalthia longifolia* (Sonn.) Thw.	Annonaceae	Indian mast tree	Carbon tetrachloride	Jain *et al*., 2006
154.	*Polygala arvensis* Willd.	Polygalaceae	Field milkwort	D-Galactosamine	Dhanabal *et al.*, 2006
155.	*Pseudoelephantopus* spicatus (Juss. Ex Aublet) Gleason	Asteraceae	Dog's tongue	D-Galactosamine/Paracetamol	Lin *et al*., 1995a
156.	*Pterocarpus marsupium* Roxb..	Fabaceae	Indian Kino tree	Carbon tetrachloride	Mankani *et al*., 2005
157.	*Punica granatum* L.	Punicaceae	Pomegranate	Carbon tetrachloride	Abdel-Rahman & El-Megeid, 2006
158.	*Raphanus sativus* L.	Brassicaceae	Radish	Carbon tetrachloride	Mohammed *et al*., 2008
159.	*Rheum emodi* (Wall)	Polygonaceae	Rhubarb	Paracetamol	Akhtar *et al*., 2009
160.	*Rhinacanthus nasuta* (L.) Kurz.	Acanthaceae	Snake jasmine	Carbon tetrachloride	Suja *et al*., 2003
161.	*Rhodococcum vitis-idaea* (L.) Avrorin	Ericaceae	Lingon berry	D-Galactosamine	Myagmar *et al*., 2004
162.	*Rhododendron arboretum* Sm.	Ericaceae	Rose tree	Carbon tetrachloride	Prakash *et al*., 2008
163.	*Rhoicissus tridentate* (L.f.) Wild & R.B. Drumm	Vitaceae	Wild grape	Carbon tetrachloride	Opoku *et al*., 2007
164.	*Rosmarinus tomentosus* Huber-Morath & Maire	Labiatae	Wild Spanish rosemary	Thioacetamide	Galisteo *et al*., 2000
165.	*Rubia cordifolia* L.	Rubiaceae	Common madder	Carbon tetrachloride	Gilani & Janbaz, 1995c
166.	*Salacia reticulata* Wight	Celasteraceae	Salacia	Carbon tetrachloride	Yoshikawa *et al*., 2002
167.	*Saponaria officinalis* L.	Caryophyllaceae	Common soapwort	Carbon tetrachloride	Abdel-Rahman & El-Megeid, 2006
168.	*Sarcostemma brevistigma* Wight	Asclepiadaceae	Moon creeper	Carbon tetrachloride	Sethuraman *et al*., 2003
169.	*Schouwia thebica* Webb.	Brassicaceae	-	Carbon tetrachloride	Awaad *et al*., 2006
170.	*Senna alata* (L. Roxb.)	Fabaceae	Candle bush	Carbon tetrachloride	Patrick-Iwuanyanwu *et al.*, 2011
171.	*Silybum marianum* (L.) Gaertn.	Asteraceae	Milk thistle	Thioacetamide	Madani *et al*., 2008
172.	*Smilax chinensis* L.	Liliaceae	Chobchini	Paracetamol	Dewanjee *et al*., 2008
173.	*Solanum alatum* Moench	Solanaceae	Hairy nightshade	Paracetamol	Lin *et al*., 2000
174.	*Solanum nigrum* L.	Solanaceae	Black nightshade	Carbon tetrachloride/Nimesulide	Raju *et al*., 2003; Mushtaq & Ahmed, 2013
175.	*Solanum pseudocapsicum* Hassl.	Solanaceae	Jerusalem cherry	Carbon tetrachloride	Vijayan *et al*., 2003
176.	*Solanum trilobatum* L.	Solanaceae	Thoodhuvalai	Carbon tetrachloride	Shahjahan *et al*., 2004
177.	*Smilax regelii* Killip & Morton	Smilacaceae	Sarsaparilla	Carbon tetrachloride	Rafatullah *et al*., 1991

Table 2. (Cont'd.).

S.#	Plants/Herbs	Family	Common names	Chemicals for liver injury	References
178.	*Swertia japonica* (Roem. & Schult.) Makino.	Gentianaceae	Makino	D-Galactosamine	Hase *et al*., 1997
179.	*Swertia longifolia* Boiss	Gentianaceae	-	Paracetamol	Hajimehdipoor *et al*., 2006
180.	*Syzygium aromaticum* L.	Myrtaceae	Clove	Paracetamol	Nassar *et al*., 2007
181.	*Terminalia arjuna* L.	Combretaceae	White marudha	Carbon tetrachloride	Manna *et al*., 2006
182.	*Terminalia belerica* Roxb.	Combretaceae	Bahera	Carbon tetrachloride/Ethanol	Jadon *et al*., 2007; Jain *et al*., 2008
183.	*Terminalia catappa* L.	Combretaceae	Sea almond	Carbon tetrachloride/ D-Galactosamine/ Lipopolysaccharides	Gao *et al*., 2006; Kinoshita *et al*., 2007
184.	*Terminalia chebula* Retz	Combretaceae	Myrabolan wood	Anti tuberculosis drugs	Tasduq *et al*., 2006
185.	*Teucrium polium* L.	Lamiaceae	Cat thyme	Carbon tetrachloride	Panovska *et al*., 2007
186.	*Thonningia sanguinea* Vahl.	Balanophoraceae	Ground pineapple	D-Galactosamine/Carbon tetrachloride	Gyamfi *et al*., 1999
187.	*Tinospora cordifolia* Willd.	Menispermaceae	Guduchi	Isoniazid/Rifampicin	Adhvaryu *et al*., 2007
188.	*Trianthema portulacastrum* L.	Aizoaceae	Black pigweed	Paracetamol/Thioacetamide/ Paracetamol	Kumar *et al*., 2004; Pandian *et al*., 2004
189.	*Tridax procumbens* L.	Asteraceae	Coat buttons	D-Galactosamine/ Lipopolysaccharides	Thiruvengadam *et al*., 2005
190.	*Trigonella foenum-graecum* L.	Fabaceae	Fenugreek	Carbon tetrachloride	Ozbek *et al*., 2008
191.	*Urtica parviflora* Roxb.	Urticaceae	-	Carbon tetrachloride	Prasana *et al*., 2007
192.	*Vernonia amygdalina* Del.		-	2-Acetylaminoflourine	Adetutu & Olorunnisola, 2013
193.	*Viburnum tinus* L.	Adoxaceae	-	Carbon tetrachloride	Mohammed *et al*., 2005
194.	*Vicia calcarata* Desf.	Fabaceae	Barn vetch	Carbon tetrachloride	Singab *et al*., 2005
195.	*Ventilago leiocarpa* Benth.	Rhamnaceae	Xue feng teng	Carbon tetrachloride	Lin *et al*., 1995b
196.	*Wedelia chinensis* (Osbeck) Merr.	Asteraceae	Chinese Wedelia	Carbon tetrachloride/ acetaminophen/ D-Galactosamine	Lin *et al*., 1994
197.	*Wedelia calendulacea* Less.	Asteraceae	Pita bhringraj	Carbon tetrachloride	Murugaian *et al*., 2008
198.	*Xylopia Phloiodora* Mildbr.	Annonaceae	-	Carbon tetrachloride/Paracetamol	Moundipa *et al*., 2007
199.	*Zingiber officinale* Rosc.	Zingiberaceae	Ginger	Paracetamol/Carbon tetrachloride	Yamiten & Izegbu, 2006
200.	*Ziziphus mauritiana* Lam.	Rhamnaceae	Chinese apple, Ber	Carbon tetrachloride/Isoniazid/ Rifampicin	Dahiru *et al*., 2005

CONCLUSION

Management and cure of liver diseases (steotosis, fibrosis, chirohosis and hepatocellular carcinoma) is considered as one of the serious health issue in both advanced and under developed countris. Modern mdicine used for the treatment of liver diseases have many side effects, with mild to severe toxicities including, vomiting, fatigue, dry mouth, diarrhea, constipation, dizziness, suicidal thoughts, depression, coma, anemia, hair loss, high blood sugar, swelling, confusion, fainting and death. Medical treatments for acute and chronic liver diseases often damage other organs. The screening of medicinal plants and seeking safer therapeutic drugs from natural sources is the area of great interest. Substantial works are currently underway on plants and other natural sources to discover effective medicines with no or less consequences.

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