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A Review on Hepatoprotective Activity Leads

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ABSTRACT

Liver harm is most vital health issues or so a lot of than 900 medicines involved in case of liver injury. World health organization estimate that eightieth of total population used herbal drugs for some characteristic of primary health care while not any facet effects. Herbal medicine has emerged as a skilled approach with sensible values in handling various diseases, developing an affordable phytotherapy to treat severe liver diseases needs economical exploration of properties like antiviral action, antihepatotoxicity, stimulation of liver regeneration besides choleretic activity. The search used keywords such as herbal drugs, hepatoprotective effects, every crossed with the term drug elicited liver harm, with explicit stress on experimental models, effective dose and hepatoprotective effects of those herbal preparations. The scientific basis for the statement that plants and their active constituents play a crucial role within the bar malady is endlessly advancing. The search result unconcealed twelve of the major herbs active constituents having hepatoprotective properties that area unit organic compound, flavonoids, glycoside, lignan, organ sulphur compounds, phenylethanoid organic compound, phenolic resin acids, polyprenols, poly phenols, quinine, resins and triterpenoid. The current review is aimed toward collecting information on promising active phytoconstituents from medicinal plants that are tested in hepatotoxicity models exploitation fashionable scientific system.

Keywords: Antioxidant, Biotransformation, Hepatotoxic, Hepatoprotective, Leads, Medicinal plants, Phytoconstituents

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INTRODUCTION

The most necessary organ involved with the organic chemistry activities within the anatomy is liver. It detoxicates completely different unhealthful substances by employing a development known as biotransformation. In current days it's an enormous deal for researchers to spot a compound that may be helpful for defense of liver from injury caused by toxicants typically they referred as hepatotoxicants. Within the maintenance of metabolic functions and detoxification from varied exogenous and endogenous challenges, like xenobiotic, drugs, microorganism infections, microorganism infections and chronic & acute alcoholism liver act as paramount organ. The distinctive property of liver is metabolizing substances through two completely different pathways known as phase-I and phase-II. Many mechanisms could also be cited to be accountable for either causation various injury or worsening the injury method even if the precise mechanism of liver injury remains mostly mysterious, it seems to involve two pathways, first one is direct hepatotoxicity and an extra is adverse immune reactions. In most instances, various injuries is initiated by the bio-activation of medicine to chemically reactive metabolites, that have the capacity to act with cellular macromolecules such as proteins, lipids, DNA and RNA, resulting in protein dysfunction, lipid peroxidation, polymer injury and aerobic stress[1]. Moreover, these reactive metabolites might induce interruption of ionic gradients and intracellular calcium stores, leading to mitochondrial dysfunction and damage of energy production. Stimulation of CYP enzymes connected family additionally results in aerobic stress. Injury to hepatocyte and epithelial duct cells result in gathering of steroid within liver. This promotes further liver injury and impairment of cellular role will terminate in death and attainable liver failure[2]. As a result of activation of different cells known as natural killer (NK) cells, Kupffer cells (KC), and natural killer T (NKT) cells by stress and that they cause injury to liver. It's been incontestable that many inflammatory cytokines, like tumor necrosis factor (TNF)-α, interferon (IFN)-γ and interleukin (IL)-1β, formed throughout various grievances are tough in promoting tissue injury[3]. Hepatotoxicants are chemicals that cause liver injury, and over 900 medicines are concerned in inflicting liver injury and it is the important reason for a drug to be withdrawn from the market. Chemicals normally cause subclinical injury to liver; indirectly they will cause intensive manifestations in liver enzymes additionally. Some medicine whenever taken in overdoses and/or at intervals therapeutic ranges it's going to cause injury to the liver. Different chemical agents like those are utilized in industries and laboratories, natural chemicals (e.g. microcystins) and seasoning therapies can even encourage hepatotoxicity. Throughout this

development liver subjected to wear and tear mechanism with varied chemicals and medicines like paracetamol, tetra chloromethane, thioacetamide, alcohol and eventually it results in completely different diseases like infectious disease, cirrhosis, alcohol connected disorders and carcinoma[4]. Once liver injury was occurred it's related to cellular caspase-mediated cell death, increase tissue lipoid peroxidation and depletion within the tissue GSH levels in conjunction with this elevation in humour levels of assorted organic chemistry parameters like SGOT, SGPT, triglycerides, steroid alcohol, bilirubin, alkaline enzyme[5, 6]. For the prevention and treatment of ailments, seasoning plants extracts are extraordinarily a prosperous supply everywhere the planet as and eightieth of the planet population majorly within the developing countries for primary health care they're exploitation seasoning drugs solely. As a result of eco-friendly nature of seasoning drug merchandise from precedent days for a few age-related diseases particularly cognitive state, pathology, diabetic wounds, immune and liver disorders, they used seasoning drugs solely[7]. From many years, before the event fashionable drugs ancient drugs (including seasoning drugs) as therapeutic practices that are breathing and are still in use nowadays additionally. The pity nature has bestowed some seasoning plants that have helpful result on liver disorders with fewer facet effects. These hepatoprotective agents shield liver from injury or facilitate in regeneration of hepatic cells. Healthful herbs are important supply of hepatoprotective medicine. There's tremendous analysis goes on currently on a daily basis for management of liver disorders in a very precise manner on seasoning medicines that are claimed to possess hepatoprotective activity[8]. The incredible complexness of liver chemistry and its essential role in biotransformation of medicine is therefore discouraging to researchers that they visualize that maybe easy seasoning plants remedies can be helpful in treatment for hepatotoxicity. Up to now investigator according that some phytoconstituents isolated from different plants belongs to fifty five families do possess hepatoprotective activity[9]. Liver protecting seasoning medicine contain a selection of chemical constituents like alkaloid[10], flavonoids[11, 12], glycoside[13, 14], lignan[15], organ sulphur compounds[16], phenolic acids[17], phenyl ethanoid organic compound [18], polyphenols[19, 20, 21, 22], polyprenols[23], antimalarial[24], resins[25], triterpenoid[26]. The supported clinical analysis findings additionally it shown that seasoning drugs have real utility in the treatment of liver diseases. However as a result of lack of refined outfit's small portion of hepatoprotective plants solitary utilized in ancient drugs are pharmacologically evaluated for its effectiveness[27].

From ancient time, varied plants and plant derived compounds are utilized in the treatment of hepatotoxicity by reducing levels of assorted SGOT, SGPT, LDH, AST, ALT, and bilirubin.

There are many reviews on the hepatoprotective activity a lot of notably medical plants [28]. Asian nation features a made history of exploitation varied effective herbs and seasoning parts for treating hepatotoxicity. Several Indian medicinal plants are investigated for his or her helpful use in several styles of hepatotoxicity and according in various scientific journals. The current review, deals with some leads of selective Indian medicinal plants having pharmacologically established hepatoprotective potential. This text highlights on the chemo profiles from Indian region for treating liver diseases with major thrust on the indefinite quantity and attainable mode of action of the seasoning hepatoprotective up to now according. From Indian region, varied plant species having potent hepatoprotective activity are delineated within the following section.

HEPATOPROTECTIVE ACTIVE LEADS FROM DIFFERENT INDIAN MEDICINAL PLANTS:

Allium sativum (Alliaceae)

Garlic, *Allium sativum* L. is an associate of Alliaceae family, has been widely familiar as a valuable spice and a popular medication for various ailments and physiological complaints. Garlic has been used as both food and medicine in many cultures for thousands of years. The fresh bulb comprises of volatile oils, alliin and allicin. Characteristic pungent smell of garlic is due to presence of allicin only[29]. Alliin and ajoene are important constituents present in garlic which have fibrinolytic activity. It declines both total low-density lipoprotein and cholesterol in addition to reducing blood pressure[30]. In addition to that garlic comprises of wide variety of organosulphar compounds (thioethers, thioesters, thioacetals, sulfones and thiosulfinates, sulfimides, sulfoximides, sulfonediimines). These compounds have an optimistic role in prevention of valproicacid induced hepatotoxicity[16]. The other recommended uses of garlic include the hepatoprotective, anti-inflammatory, anti-helminthic, and antifungal, anti-oxidant and wound healing[31].

***Andrographis paniculata* (Acanthaceae)**

Kalmegh (*Andrographis paniculata* Nees, family Acanthaceae) is commonly known as king of bitters, Maha-tita, Bhui-neem as the plant, though much smaller in size, shows similar appearance and bitter taste similar to that of Neem (*Azadiractha indica*). It is, known on the Indian subcontinent as Chirayetah and Kalmegh in Urdu and Hindi languages, respectively, it is an annual plant, 1-3 ft high, that is one of the most commonly used plants in the traditional systems of Unani and Ayurvedic medicines. It is called Creat in English and is known as the "king of bitters." It grows in hedge rows throughout the plains of India and is also cultivated in gardens. It also grows in many other Asian countries and is used as a traditional herbal medicine

in China, Hong Kong, the Philippines, Malaysia, Indonesia, and "thailand. Traditionally, the plant was used as an infusion, decoction, or powder, either alone or in combination with other medicinal plants. Due to its "blood purifying" activity it is recommended for use in cases of leprosy, gonorrhoea, scabies, boils, skin eruptions, and chronic and seasonal fevers. 1Juice or an infusion of fresh leaves is given to infants to relieve griping, irregular bowel habits, and loss of appetite. The leaves and root are also used in general debility, during convalescence after fevers, for dyspepsia associated with gaseous distension, and in advanced stages of dysentery. In China, the herb derived from the leaves or aerial parts of *Andrographis paniculata* is known as Chuanxinlian, Yijianxi or Lanhelian. It is described as bitter and cold, is considered to be antipyretic, detoxicant, anti-inflammatory, and detumescent, and is thought to remove "pathogenic heat" from the blood. *A. paniculata* is used for the treatment of pharyngolaryngitis, diarrhoea, dysentery, and cough with thick sputum, carbuncle, sores, and snake bites. Various preparations and compound formulas of the herb have been used to treat infectious and non-infectious diseases, with significant effective rates reported for conditions such as epidemic encephalitis B, suppurative otitis media, neonatal subcutaneous annular ulcer, vaginitis, cervical erosion, pelvic inflammation, herpes zoster, chicken pox, mumps, neurodermatitis, eczema, and burns. Pharmacologically *Andrographis paniculata* has been reported as antibacterial, antifungal, antiviral, choleretic, hypoglycaemic, hypocholesterolemic, and adaptogenic effects. In the Unani system of medicine, it is considered aperient, anti-inflammatory, emollient, astringent, diuretic, emmenagogue, gastric and liver tonic, carminative, antihelmintic, and antipyretic. A part from this it also contains a large number of chemical constituents, mainly lactones, diterpenoids, diterpene glycosides, flavonoids, and flavonoid glycosides. Hepatoprotective[32] activity of *Andrographis paniculata* in ethanol induced hepatotoxicity in albino wistar rats was given below in Table 1 & Tabel 2.

***Atractylodes macrocephala* (Compositae)**

Atractylodes macrocephala is a plant of the chrysanthemum family and its rhizome is the one of the famous material of chinese traditional medication. The rhizome of *Atractylodes macrocephala* has been widely used in traditional Chinese medicine for invigorating the functions of the stomach and spleen, benefiting vital energy, and eliminating dampness. It has been reported that extracts of the rhizome of *Atractylodes macrocephala* possess various pharmacological properties including anti-obesity, anti-inflammatory, antioxidant, neuroprotective, immunostimulant, and anti-allergic effects. Atractylon, β-eudemol and hinesol

were active constituents isolated from *Atractylodes macrocephala* showed hepatoprotective[33] activity was mentioned below in Table 1 and Table 2.

***Bupleurum falcatum* (Apiaceae)**

Bupleurum falcatum is a perennial growing to 1 m (3ft 3in) by 0.6 m (2ft). It is hardy to zone 3. It is in flower from July to October. The flowers are hermaphrodite (have both male and female organs) and are pollinated by Insects. The plant is self-fertile. Traditionally this plant is used for at least 2,000 years in china. The root of this plant is used as alterative, analgesic, antibacterial, anti-inflammatory, antiperiodic, antipyretic, antiviral, carminative, diaphoretic, emmenagogue, haemolytic, hepatic, pectoral, and sedative. It is taken internally in the treatment of malaria, black water fever, uterine and rectal prolapse, haemorrhoids, sluggish liver, menstrual disorders, abdominal bloating. The root contains saikosides. These saponin-like substances have been shown to protect the liver [33] from toxicity (Table 1 & Table 2) whilst also strengthening its function, even in people with immune system disorders. These saikosides also stimulate the body's production of corticosteroids and increase their anti-inflammatory affect.

***Buddleia officinalis* (Loganiaceae)**

Genus *Buddleia* ("Mi-meng-hua") involves around 100 species inborn to humid lands of America, Asia, and Africa. In old-style medicine, the flower buds of *B. officinalis* are used for the treatment of conjunctival congestion and clustered nebulae and antiseptic[34]. In traditional Korean medicine it is frequently used to treat headache, stroke, and neurological disorders [35]. *Buddleia officinalis* has also been cultured and its flowers used as food colorant in festivals. It consists of numerous phytoconstituents like flavonoids, terpenoids, iridoids, and phenylethanoids. A part from this it shows many pharmacological actions such as antitumor, antioxidant, anti-inflammatory, antinephritic and antimetastatic. Acteoside a phenylethanoid glycoside is an important constituent play a role in carbon tetrachloride induced hepatotoxicity was revealed in Table 1& Table 2.

***Cistus laurifolius L.* (Cistaceae)**

Cistus laurifolius L. (Cistaceae) frequently named laurel-leaf *cistus* or laurel-leaved rock rose, is a species of greatly branched flowering evergreen shrub native to some areas around the Mediterranean. In traditional medicine it is widely used for rheumatism, fever, cold, urinary inflammations and also it is used as folk medicine in Turkey for the treatment of peptic ulcer[36]. Different parts of this plant have wide variety of active constituents majorly flavonoids, shows antinociceptive, anti-inflammatory principals and the hepatoprotective activity of this flavonoids given in Table 1& Table 2.

***Camellia sinensis* (Theaceae)**

Tea is the most commonly swallowed liquid on earth after water. Tea is a cultured evergreen plant, is native to China, later it is indigenous to India and Japan. Tea leaves consists of different active constituents like polyphenols (catechins and flavonoides), alkaloids (caffeine, theobromine, theophylline), amino acids, volatile oils, polysaccharides, lipids, vitamin C[37]. The polyphenols present in green tea (30% to 40%) are collectively called as green tea polyphenols (GTP) are primarily responsible for the beneficial properties like antioxidative, anti-inflammatory, antiallergic, antimutagenic and anticarcinogenic[38]. A part from this green tea polyphenols decreases inflammatory response by preventing the production of arachidonic acid metabolites such as pro-inflammatory prostaglandins and leukotriene's. Green tea comprises of catechin and its related compounds (epicatechin, gallocatechin, epigallocatechin, epigallocatechin gallate and epicatechin gallate) and flavonoids. The protective effect of green tea poly phenols against hepatotoxicity was explained further in Table 1 & Table 2.

***Curcuma longa* (Zingerberaceae)**

Turmeric is a rhizomatous herbaceous perennial plant fits to family called as, Zingiberaceae. It is refined widely in Asia and China. In traditional Chinese medicine and ayurveda systems of medicine, turmeric is used for anti-inflammatory, flatulence, jaundice, haematuria, menstrual difficulties, haemorrhage and colic. Turmeric can also be applied topically in poultices to relieve pain and inflammation. Various active constituents present in turmeric are curcumin (diferuloylmethane), volatile oils, tumerone, atlantone, zingiberone, sugars, proteins, and resins. Curcumin, which comprises 0.3-5.4% of raw turmeric, is the principal curcuminoid widely used in India for various pharmacological activities such as antiviral, antifungal, anti-inflammatory[39], antioxidant, hepatoprotective, anticarcinogenic, antimicrobial, cardiovascular disease and gastrointestinal ailments. Tetrahydro curcuminoid is metabolite obtained from the curcumin play a protective role in erythromycin estolate-induced hepatotoxicity (Table 1 & Table 2).

***Corydalis saxicola* (Fumariaceae)**

In ancient Chinese medication *Corydalis saxicola* genus is a very important constituent in numerous prescriptions within the treatment of liver diseases. *Corydalis saxicola* genus has completely different medical specialty activities like antibacterial, antiviral and malignant neoplasm activities[40]. It's been according to possess a possible helpful impact of protecting internal organ tissues from serum hepatitis virus and hepatitis A virus it can even be used for up fever, detoxification and as a medicament . This plant consists of alkaloids in higher proportion.

Dehydrocavidine is one among the organic compound plays a key role in hepatotoxicity/hepatoprotective (Table one & two).

***Egletes viscosa* (Asteraceae)**

Egletes viscosa was popularly known as "Macela da terra" and it is a small medicinal herb that grows profusely in the north east of Brazil. From flowers of this plant generally infusions are prepared and they are frequently useful in popular medicine for the treatment of intestinal colic, gastritis, liver complaints and as an emmenogogue[41]. Ternatin is an energetic ingredient obtained from this plant shows variety of pharmacological activities such as anti-inflammatory, antianaphylactic, antithrombotic and antihepatotoxic[12, 42].Table 1 & Table 2.

***Gardenia jasminoides* (Rubiaceae)**

Gardenia jasminoides is also called as common gardenia, Cape jasmine or cape jessamine. The genus *Gardenia* includes over 200 species out of which *Gardenia jasminiodes* is very well known. The key component of *Gardenia jasminoides* fruit is geniposide. Its folkloric use has been for the handling of inflammation, jaundice, fever, headache, edema, hypertension, and hepatic disorders for years[43]. The *Gardenia* nuts contain carbohydrates, minerals, fats, vitamins, picrocrocin and volatile oils. This is mainly used as colouring material and the products that are produced and process is likely to be well recognised by food and pharmaceutical industry[44]. In addition, crocins obtained may also be used for anti-carcinogenic activity[45]. Inhibitory effect of geniposide on the hepatotoxicity and hepatic DNA binding of aflatoxin B1 in rats was shown in Table 1 and Table 2.

***Gossypium herbaceum* (Malvaecae)**

Gossypium herbaceum also called levant cotton, is a species of cotton inborn to the semi-arid regions of sub-Saharan Africa and Arabia. It is a plant species that mainly useful in textile industry. In animal feed cotton seed oil is used as high-protein is obtained as a by-product from cotton. A poly phenolic yellow compound called gossypol is obtained from this plant only[46]. Seeds of *Gossypium herbaceum* are used as a demulcent, laxative, galactagogue, expectorant, aphrodisiac, abortion and nervine tonic. The root and the bark of this plant are used as emmenagogue and galactagogue. The juice obtained from leaves of *Gossypium* is used against scorpion sting and snakebite. Its effectiveness in conjugation with albumin in treating hepatotoxicity was well studied in Table 1 & Table 2.

***Ginkgo biloba* (Ginkgoaceae)**

Ginkgo biloba similarly known as the Maidenhair tree fits to family known as Ginkgoaceae. This plant has a wide diversity of traditional uses due to presence of polyprenols. Organization and

bioactivity of *Ginkgo biloba* polyphenols are equivalent with that of dolichols which commonly occurred in human and mammalian organs[23]. Different active constituents present in *Ginko biloba* such as flavonoids, glycosides, diterpenes, bioflavones, quercitin, isorhamnetine, kaempferol, proanthocyanidins, sitosterols, lactones, and anthocyanin. Ginkgolide the active component of *Ginkgo biloba* somehow inhibits a chemical found in the body called platelet activating factor (PAF) which plays a role in organ rejection. Laterally *Ginkgo biloba* poly phenols have antivirus, antitumor, antioxidant and hepatoprotective effects (Table 1 & Table 2), as well as treating Alzheimer, and enhancing immunity[47]. It may also beneficial for angina, congestive heart failure, multiple sclerosis, shock and burns.

***Hibiscus sabdariffa* (Malvaceae)**

Hibiscus sabdariffa is shrub going to family Malvaceae and it is native to Asia. It is a dynamic ingredient in local beverage and in herbal medicine of China it has long lasting effects in dealing hypertension, pyrexia and liver damage. Protocatechuic acid is a phenolic compound obtained from the roots of *Hibiscus sabdariffa*s how strong anti-oxidant and anti-tumour activities[48]. Protocatechilicacid is an important lead molecule shows protective effect in hepatotoxicity was illustrated in Table 1 & Table 2.

***Larrea tridentate* (Zygophyllaceae)**

Larrea tridentate Coville (creosotebush) is the leading shrub of the warm deserts of North America. This plant consists of wide variety of resins, monoterpenoids, aromatic sesquiterpenoids, glycosylated flavonoids, sapogenins, essential oils, halogenic alkaloids[49]. Even though it contains so many compounds, a resin called Nordihydroguaiaretic acid is present in excess amount (50%), shows promising effect against hepatotoxicity was explained further in (Table 1 & Table 2). A part from this it shows various pharmacological actions like antiseptic, as an emetic, expectorant, and diuretic to treat venereal disease, tuberculosis, bowel cramps and rheumatism. It may also use for menstrual cramps, stiff limbs, skin ailments, snakebites and chicken pox.

***Magnolia officinalis* (Magnoliaceae)**

It is a Chinese herb. Traditionally it is used in the treatment of anxiety, fever, abdominal fullness, head ache, constipation and thrombotic stroke. Magnolol (5, 5'-diallyl-2, 2' dihydroxybipheny) and Honokiol (5, 3'-diallyl-2, 4'-dihydroxybiphenyl) are two major active constituents obtained from stem bark of *Magnolia officinalis*. Magnolol is a *much* more potent antioxidant than alpha-tocopherol[50]. It has been reported that Magnolol has potential therapeutic beneficial activity on neurodegenerative diseases[51]. Chemical constituents present in this plant are isoquinolines,

lignans, neolignans, alkaloids, mono and sesquiterpenes. The anti-hepatotoxic activity of magnolol on N-acetyl-p-aminophenol/APAP-induced toxicity was illustrated in Table 1 & Table 2.

***Mangifera indica* (Anacardiaceae)**

Mangifera indica L. is a large perennial tree, long existing, 10-45 m high with a strong trunk and heavy crown native to tropical Asia. It belongs to family called Anacardiaceae and genus *Mangifera*. It consists of various vernacular names in India depending on region such as aam, alfonso mango, alipriya, kamayudha, am, amm, amva, asm, amra, bhramavapriya, kamavallabha, kokilavasa, kires, kamaphala, kokilananda, maamidi, mam-maram, mango, mango tree, mango fruit, oegkoti-tong, pitavallabha. *Mangifera indica* L. stem bark has been reported in cuba as antioxidant, anti-inflammatory and immunomodulatory possessions. Bark extract *Mangifera indica* is proposed as both nutritional supplement and analgesic and handling to avoid disease progress or increase the patient's quality of life in AIDS, dermatological disorders, gastric, cancer and asthma[52]. Different types of active constituents present *mango* bark are mangiferin, protocatechicacid, catechin, alanine, glycine, γ- kinic acid, shikimicacid, aminobutyricacid and the tetracyclic triterpenoids[53]. *Mango* peel and pulp contains carotenoids, polyphenols and omega-3 and -6 polyunsaturated fatty acids. A part from above chemicals mango consists of triterpinoid called lupeol[54]. Lupeol shows wide variety of medicinal properties in different pathological conditions[13]. Phytoconstituent of lupeol shown hepatoprotective effect (Table 1& Table 2).

***Nigella sativa* (Ranunculaceae)**

It is a yearly flowering plant, native southwest Asia. *Nigella sativa* seed is differently called as nutmeg flower, fennel flower and roman coriander. Seeds of these plants have various pharmacological actions; include immunomodulation[55], Anti-inflammatory[56] and antitumor activities of colon, ovarian, lung, osteosarcoma and myeloblastic leukaemia[57]. The seeds of *N. sativa* have different types of wide spectrum of events such as antibacterial[58], antitumor[59], CNS depressant and analgesic[60], hypoglycemic[61], smooth muscles relaxant[62] cytotoxic and immunostimulant[63]. Thymoquinone is a major active constituent of *Nigella sativa and* shows strong anti-oxidant properties[56]. Along with these alkaloids, steroids, phenolic compounds are also present in *Nigella sativa*. Protective effect of thymoquinone on sodium fluoride-induced hepatotoxicity and oxidative stress was mentioned in Table 1 & Table 2.

***Peumus boldus* (Monimiaceae)**

Peumus boldus Molina (Monimiaceae) is an evergreen shrub or small tree indigenous to Chile

and Peru. The dried leaves have been reported in medicinal usage since the 19th century in South America against diseases of the liver and gallstones. Pharmacognostical texts, pharmacopoeias and handbooks list the therapeutic uses as cholagogue, choleretic, digestive disturbances, diuretic, hepatic stimulant, stomachic, sedative and anthelmintic. Boldo leaf has also been reported as used for the treatment of headache, earache, toothache, rheumatism and urinary tract inflammation. Pharmacologically it has been widely used for choleretic activity, laxative effect, spasmolytic effect, antioxidant activity, anti-inflammatory, antipyretic. A part from this, the plant also contains active principles such as alkaloids, flavanoids, volatile oils, resins and tannins. The alcoholic extract of *Pemus boldus* contain important phytoconstituent called boldine is responsible for hepatoprotective [33, 79] activities was mentioned below in Table 1 and Table 2.

***Polygonum cuspidatum* (Polygonaceae)**

Polygonum cuspidatum often called as Japanese weed, is the component of the family polygonaceae. It also known under the names *Polygonum japonicum, Reynoutria japonica, Pleuropteris zucarinii*, and *Polygonum zucarinii*, as well as false bamboo. It is a medicine and food dual purpose plant, native to eastern Asia in Japan, China and Korea, whose young stems and shoots are edible as a spring vegetable, with a flavor much like mild rhubarb. The roots and rhizomes of *Polygonum cuspidatum* are safe and effective in the treatment of many diseases. Pharmacologically it was used for anti-diabetes, anti-hepatitis B virus, antibacterial, anti-inflammation, antioxidant. Apart from this the rhizome of *Polygonum cuspidatum* contains stilbens, aromatic hydro carbohydrates as a phytoconstituents. Pieced obtained from roots of *Polygonum cuspidatum* partly inhibited the deposition of lipid peroxides[64] in liver (Table 1 & Table 2).

***Picrorhiza kurroa* (Scrophulariceae)**

Picrorhiza kurroa is one of the oldest medicinal plants traded from the Karnali zone. It is grown-up in himalayan region. This plant shows wide variety of pharmacological actions they include liver disorders, fever, and asthma; jaundice[13]. It is also useful in gastrointestinal and urinary syndromes, leukoderma, scorpion sting, snake bite and inflammatory affections[65, 66]. Other activities such as anti-periodic, cholagogue, stomachic, laxative, cathartic, immunomodulation and anti-asthmatic have been reported for the plant[67]. Hepatoprotective effect of this plant is mainly due to presence of kutkin, it is a mixture of both picroside-I and picroside-II (Table 1 & Table 2).

***Phyllanthus amarus* (Euphorbiaceae)**

It is a slight, erect, yearly herb native to Amazon and other tropical regions throughout the India.

Phyllanthus is the largest genus in the flowering plant family Phyllanthaceae. This plant shows various pharmacological actions like hypotensive, analgesic, antiviral, and anti-bacterial, anti-hepatotoxic, diuretic, anti-mutagenic, and hypoglycaemic, anti-inflammatory, anti-lithic. It consists of number of dynamic constituents such as lignans, glycosides, flavonoids, alkaloids and phenylpropanoids. *Phyllanthus amarus* and its related Indian plants show excellent antiviral properties due to presence of phyllanthin, hypophyllanthin, and polyphenols. *Phyllanthus amarus* shows protective effect against CCl_4 induced hepatotoxicity (Table 1 & Table 2).

***Pinus maritima* (Pinaceae)**

It is a French maritime pine, native to the western and south-western Mediterranean area and it contains a standardized extract called pycnogenol. It is used extensively in multi-vitamins, dietary supplements, and health products because of its direct, strong antioxidant activity. Catechin, epicatechin, and taxifolin[68] and polyphenol are the active principles present in pycnogenol shows protective effects against hepatotoxicity (Table 1 & Table 2).

***Rubia cordifolia* (Rubiaceae)**

Rubia cordifolia, fitting to family Rubiaceae, regularly known as Indian Maddar and Manjistha in Sanskrit and it is native to himalayas and further hilly districts of India. Roots of *Rubia cordifolia* is also used as folk medicine for jaundice in West Bengal and Uttaranchal[69]. Roots have also been reported as anti-oxidant, anti-inflammatory, anti-cancer, immunomodulation and hepatoprotective and are extensively used against blood, urinary and skin diseases[70]. In the Chinese system of medicine, *Rubia cordifolia* is employed for the management of insomnia, rheumatism, vertigo, hematemesis, menstrual disorders, tuberculosis, and contusions. Rubaidin shows various pharmacological properties such as antioxidant[71], anti-inflammatory[72], immunomodulatory[73], anticonvulsant, anxiolytic[74] and antitumor activities[75]. It consists of energetic elements like phenolics, triterpenoids, anthraquinones and cyclopeptides. Defending effect of rubaidin on CCl_4 encouraged hepatotoxicity was indicated in Table 1& Table 2.

***Schisandra chinensis* (Magnoliaceae)**

According to the Chinese Materia Medica the standard species of *Schisandra* genus are *Schisandra chinensis* (Turcz) Baill. and *Schisandra sphenanthera* Rehd & Wils. of the Magnoliaceae family. Schisandra species grow in China, Japan, Eastern Russia, the Himalayas and Korea. The common names are Schisandra in English, Wu Wei Zi (*S. chinensis*) or Northern Schisandra and Hua Zhong Wu Wei Zi (*S. sphenanthera*) or Southern Schisandra in Mandarin, Gomishi in Japanese and Omija in Korean[2]. In TCM this plant is widely used for nocturnal emissions, vaginal discharge, spermatorrhea, irritability, insomnia, palpitations, dream-distur and

urinary frequency due to Kidney deficiency. In the species *S. chinensis* the principal pharmacologicalactive compounds are thought to be the dibenzo [a, c] cyclooctadiene lignans. Other primary lignans are Schisandrin A or deoxyschisandrin, Schisandrol B also known as Gomisin A. Schisandra also contains volatile oil constituents, glycosides and organic acids . Hepatoprotective[76] effects of *Schisandra chinensis* pollen extract on CCl_4-induced acute liver damage in mice was illustrated in Table 1 & Table 2.

***Sedum sarmentosum* (Crassulaceae)**

It is a perennial herb widely distributed on the mountain slopes in Oriental countries, has been traditionally used for the treatment of certain inflammatory diseases. It has been frequently used for the treatment of chronic inflammatory diseases. Recently, six new megastimane glycoside, sedumosides E1, E2, E3, F1, F2 and G, were purified from the whole plant. Activity of *S. sarmentosum* partly arises from its prevention from the release of inflammatory mediators at the first stage. Suppressive effect of this herb on the production of NO has been confirmed. With the assumption that the suppression of NO production by herb is being caused by a diminishment in the iNOS level, the herb concentration-dependently suppressed iNOS induction without changes in the levels of β-actin, an internal control, indicating the specific inhibition of iNOS expression. However, at the concentrations capable of reducing the NO production in the activated macrophages has been unable to modulate expression of COX-2. This fact suggests that the herb might exhibit its anti-inflammatory activity independent of COX-2. Hepatoprotective [77] Effects of *Sedum sarmentosum* on D-Galactosamine/ Lipopolysaccharide–Induced murine fulminant hepatic failure was mentioned below in Table 1 & Table 2.

***Silybum marianum* (Asteraceae)**

Silybum marianum (milk thistle) is an annual or biannual plant of the Asteraceae family has been used pharmaceutically in Europe since the first century. In Chinese medicine, milk thistle seeds are well known as “Shui Fei Ji”. Lots of synonyms are there for this particular plant listed as blessed milk thistle, marian thistle, mediterranean milk thistle, mary thistle, saint mary's thistle, scotch thistle and variegated thistle. Historically milk weed is employed to protect the liver, secretion of digestive juice and shelter against oxidative injuries like radiation. So far it is widely used as hepatoprotective agents (Table 1 & Table 2) because of its antioxidant property, easy availability and most importantly lack of toxicity and side effects even at high doses[15]. It consists of assorted phytoconstituents such as apigenin, betainehydrochloride, dehydrosilybin, deoxysilycristin, deoxysildianin, neosilyhermin, silymarin, silidianin, silychristin and siliandrin, silybinome, silyhermin, stearic acids.

***Sida cordifolia* (Malvaceae)**

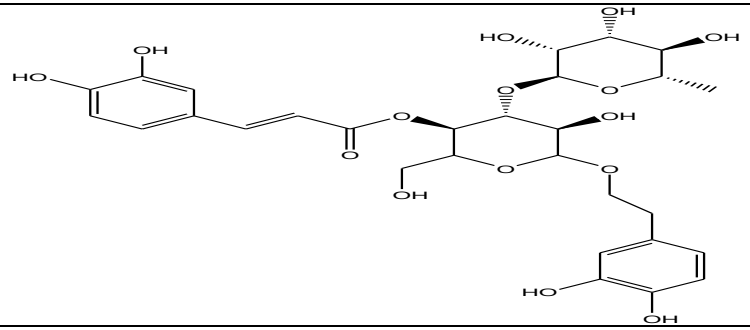
Sida cordifolia (linn) syn. Country Mallow of Malvaceae family is widely distributed along with other species are common throughout the tropical and sub tropical plains all over India and Srilanka up to an altitude of 1050m., growing wild along the roadside. It grows as wasteland weed. It is also known as the "Bala" in Hindi and Sanskrit. It has a long history of use by Ayurveda and rural area mainly for medicinal properties. It is in use as folk medicine in India since time immemorial. According to ayurveda, the plant is tonic, astringent, emollient, aphrodisiac and useful in treatment of respiratory system related troubles. Bark is considered as cooling. It is useful in blood, throat, urinary system related troubles, piles, phthisis, insanity etc . A part from this it shows many pharmacological actions such as CNS depressant , analgesic and anti-inflammatory, hypotensive, antiparkinsons, wound healing, anti microbial, adaptogenic activity, hepatoprotective and antioxidant activity. It consist of a range of phytoconstituents like ephedrine, pseudoephedrine, sterculic, malvalic and coronaric acid, fatty acids, saponine, betaphenethylamine, hypaphorine, ecdysterone, indole alkaloids, palmitic, stearic and β–sitosterol. Fumaric acid is one of the key active constituent isolated from *Sida cordifolia* was reported to be hepatoprotective[78] (Table 1, Table 2) after partial hepatectomy.

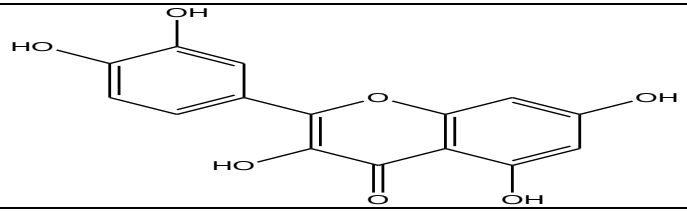
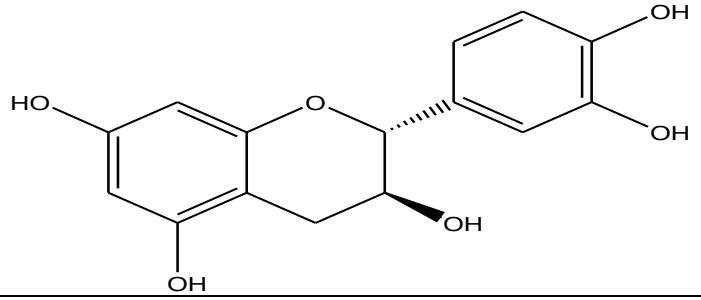
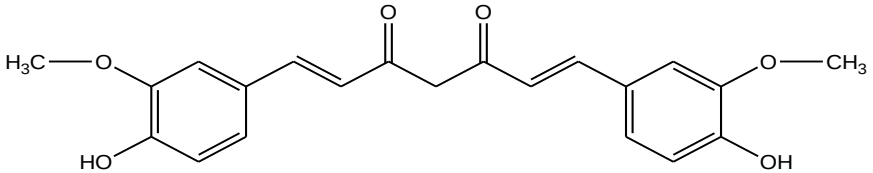
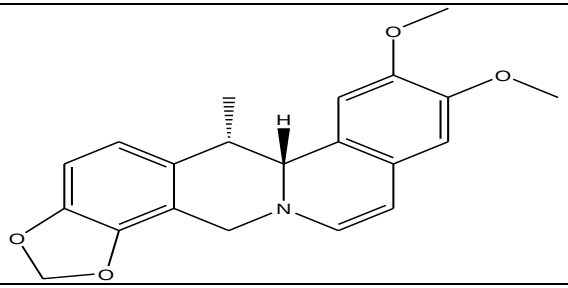
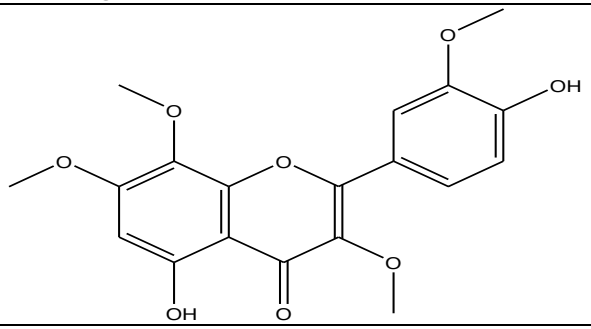
Table 1. Selected leads from Medicinal plants for Hepatoprotective activity.

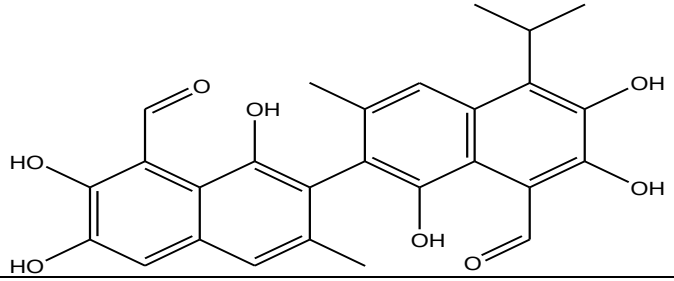
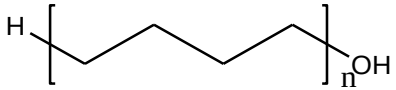
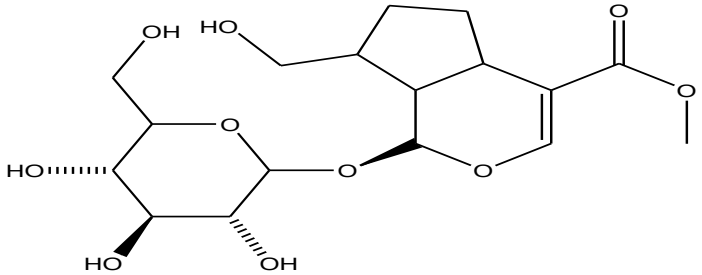
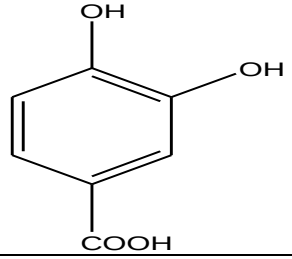
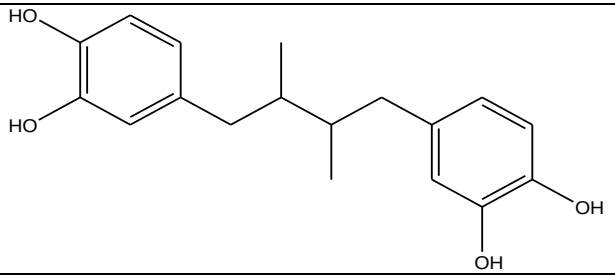
Name	Family	Type of active constituent	Name of active constituent	Mechanism	Ref.
Allium sativum	Lilliaceae	Organosulphar compounds	Organosulpharcompunds	Prevention of GSH depletion. Alteration of GSH dependent enzymes	[16]
Andrographis paniculata	Acanthaceae	diterpinoid	Andrographolide	Reduction in fatty degeneration and centrizonal necrosis	[32]
Atractylodes macrocephala	Compositae	sesquiterpinoid	Atractylon, β-eudemol and hinesol	antioxidant	[33]
Buddleia officinalis	Loganiaceae	Phenyl ethanoid glycoside	Acteoside	Decreased levels of AST,ALP	[18]
Bupleurum falcatum	Apiaceae	saikosides	Saikosaponins	Potent antioxidant	[33]
Camellia sinensis	Theaceae	Polyphenols	Catechin	Inhibited hepatocellular apoptosis and up-regulated Bcl-2 protein expression.	[20]
Cistus laurifolius L.	Cistaceae	Flavonoid	Quercetin	MDA, AST, GSH levels decreased.	[11]
Corydalis saxicola	Fumariaceae	Alkaloid	Dehydrocavidine	Decreased levels MDA, SOD, GPx	10]
Curcuma longa	Zingerberaceae	Diferuloyl methane	Curcumin	Decreased levels SGOT, SGPT, ALP	[39]
Egletes viscosa L.	Asteraceae	Flavonoid	Ternatin	Decrease lipid peroxidation	[12, 42]
Gardenia jasminoides	Rubiaceae	Iridoid Glycoside	Geniposide	Antioxidant	[43]
Ginkgo biloba L	Ginkgoaceae	Poly prenols	Polyprenols	ALT, AST, ALP, ALB, TP, HA, LN, TG, and CHO levels decreased	[23]
Gossypium herbaceum	Malvaecae	Poly phenol	Gossypol	Antioxidant	[46]
Hibiscus sabdariffa L.	Malvaceae	Polyphenols	Protocatechuic acid	LDH, AST, ALP, MDA levels Decreased	[48]
Larrea tridentate	Zygophyllaceae	Resin	Nor DihydroGuaiaretic Acid	Antioxidant	[25]
Magnolia officinalis	Magnoliaceae	Polyphenols	Magnolol	Antioxidant	[51]

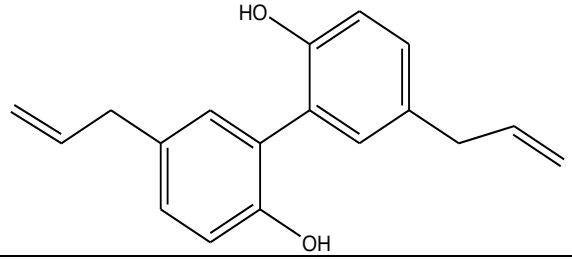
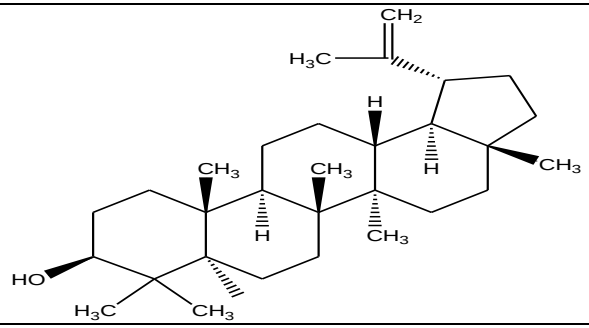
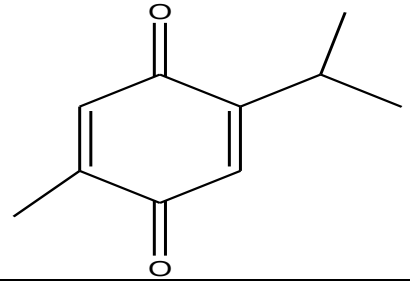
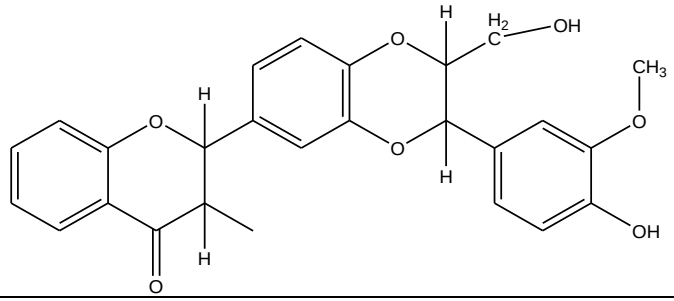
Mangifera indica	Anacardiaceae	Triterpene	Lupeol	Decreased levels SGOT, SGPT, ALP, Bilurubin	[26]
Nigella sativa	Ranunculaceae	Quinone	Thymoquinone (TQ)	scavenger of superoxide, hydroxyl radical and singlet molecular oxygen	[24]
Ocimum basilicum	Lamiaceae	Phenolic Acids	Rosmarinic acid (RA),	AST, ALP, SGOT levels decreased	[17]
Peumus boldus	Monimiaceae	Alkaloid	Boldine	Lipid peroxidation	[33, 79]
Phyllanthus amarus	Euphorbiaceae	Polyphenols	Phyllanthin	SGOT, SGPT, ALKP, SBLN & total protein levels decreased.	[21]
Picrorhiza kurroa	Scrophulariaceae	Glycoside	PicrosideI&II(Kutkin)	Antioxidant	[13]
Pinus maritama	Pinaceae	Polyphenols	Pycnogenol	SOD, GSH-Px, GSH-reductase, and TBARS levels decreased	[22]
Polygonum cuspidatum	Polygonaceae	Glycoside	Pieced	Lipid peroxidation	[64]
Rubia cordifolia	Rubiaceae	Glycoside	Rubiadin	Decreased levels SGOT, SGPT, SALP and gamma-GT	[14]
Schisandra chinensis	Magnoliaceae	Lignan	Wuweizisu	Antioxidant	[76]
Sedum sarmentosum	Crassulaceae	Glycoside	Sarmentosins	Decreased levels of AST, ALP	[77]
Sida cordifolia	Malvaceae	Organic compound	Fumaric acid	Antioxidant	[78]
Silybum marianum	Asteraceae	Lignan	Silymarin	Antioxidant	[15]

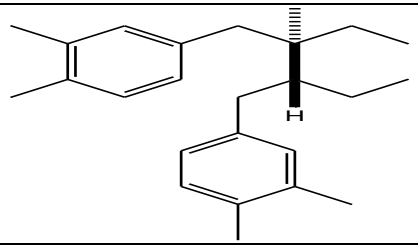
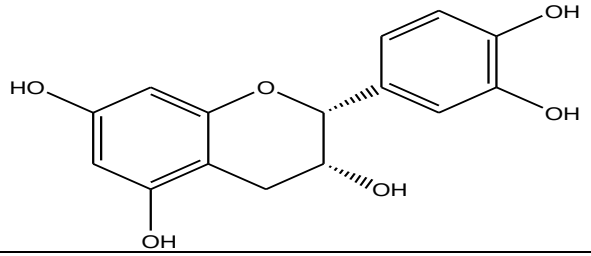
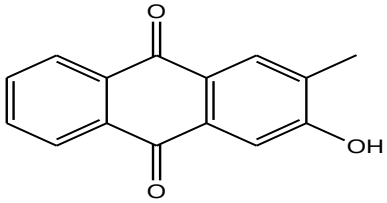
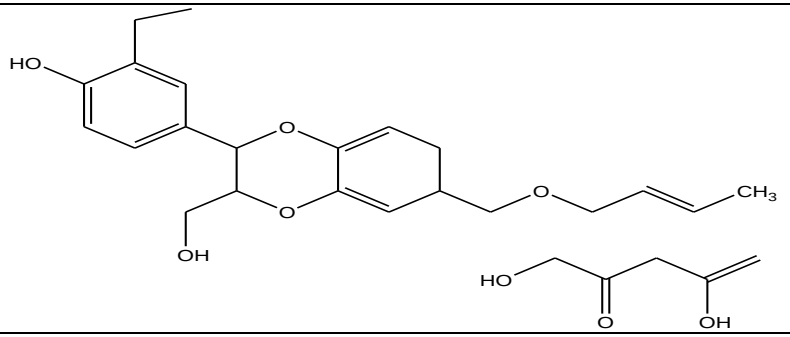
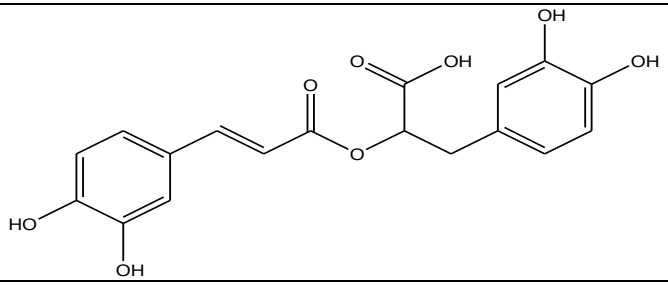
Table 2. Leads with IUPAC name and structure.

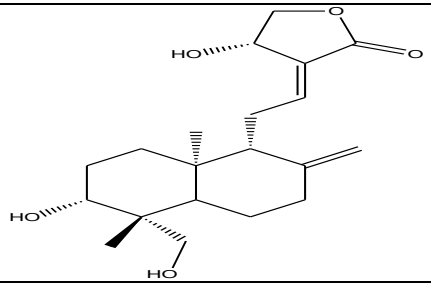
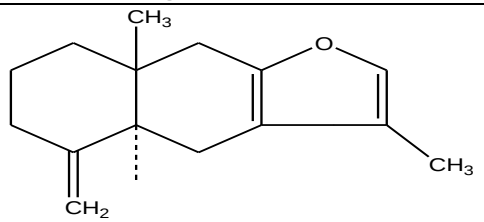
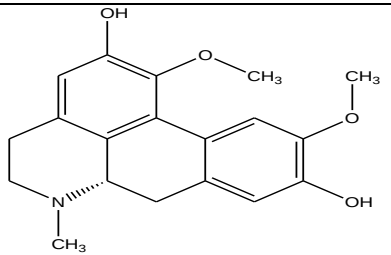
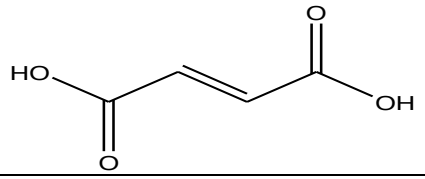
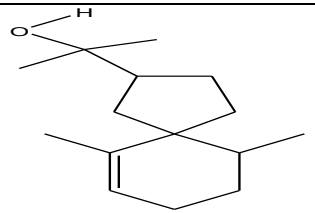
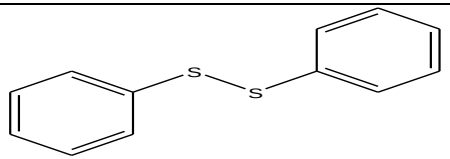
Acteoside	[(2R,3R,4R,5R,6R)-6-[2-(3,4-dihydroxyphenyl)ethoxy]-5-hydroxy-2-(hydroxymethyl)-4-[(2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxyoxan-3-yl](E)-3-(3,4-dihydroxyphenyl)prop-2-enoate	

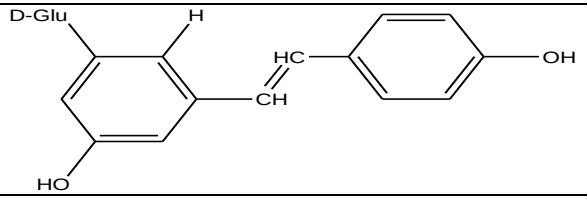
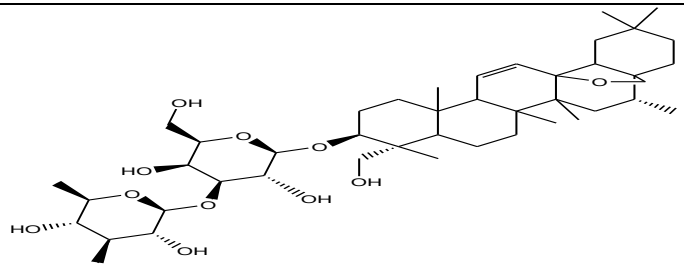
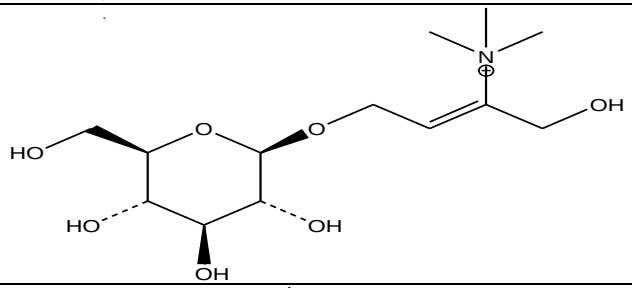
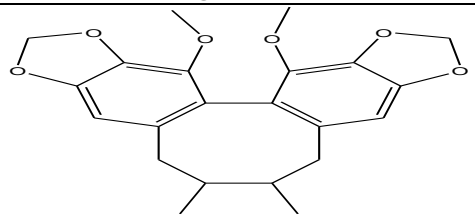
Quercetin	3,5,7-trihydroxy-2-(3,4-dihydroxyphenyl)-4H-chromen-4-one	
Catechin	(2R,3S)-3,4-dihydro-2-(3,4-dihydroxyphenyl)-2H-chromene-3,5,7-triol	
Curcumin	(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione	
Dehydrocavidine	8,9-Dimethoxy-6-methyl[1,3]dioxolo[4,5-h]isoquino[2,1-b]isoquinolin-13-ium	
Ternatin	4',5-dihydroxy-3,3',7,8-tetramethoxyflavone	

Gossypol	2,2′-bis-(Formyl-1,6,7-trihydroxy-5-isopropyl-3-methylnaphthalene)	
Poly prenols	butan-1-ol	
Geniposide	(1R)-methyl 1-((3R,4S,5S)-tetrahydro-3,4,5-trihydroxy-6-(hydroxymethyl)-2H-pyran-2-yloxy)-1,4a,5,6,7,7a-hexahydro-7-(hydroxymethyl)cyclopenta[c]pyran-4-carboxylate	
Proto catechulic acid	3, 4-dihydroxyBenzoic acid	
Nor dihydroguaiaretic acid	4-(4-(3,4dihydroxyphenyl)-2,3-dimethylbutyal)benzene-1,2-diol.	

Magnolol	4-Allyl-2-(5-allyl-2-hydroxy-phenyl)phenol	
Lupeol	(1R,3aR,5aR,5bR,7aR,9S,11aR,11bS,13aR,13bR)-icosahydro-3a,5a,5b,7a,8,8,11a-heptamethyl-1-(prop-1-en-2-yl)-1H-cyclopenta[a]chrysen-9-ol	
Thymoquinone	2-Isopropyl-5methylcyclohexa-2,5-diene-1,4-di one	
Kutkin	2,3-dihydro-2-(2,3-dihydro-2-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)benzo[b][1,4]dioxin-7-yl)-3-methylchromen-4-one	

Phyllanthin	(2R,3R)-2,3-diethyl-2-methyl-1,4-bis(3,4-dimethylphenyl)butane	
Pycnogenol	(2R,3R)-3,4-dihydro-2-(3,4-dihydroxyphenyl)-2H-chromene-3,5,7-triol	
Rubaidin	2-hydroxy- 3-methylanthracene-9,10-dione	
Silymarin	2-(2,3-Dihydro-2-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-1,4-benzodioxin-6-yl)-2,3-dihydro-3,5,7-trihydroxy-4H-1-benzopyran-4-one	
Rosamarinic acid	2-((E)-3-(3,4-dihydroxyphenyl)acryloyloxy)-3-(3,4-dihydroxyphenyl)propanoic acid	

Andrographalide	(S,E)-dihydro-3-(2-((1R,2R,4aS,5R)-decahydro-2-hydroxy-1-(hydroxymethyl)-1,4a-dimethyl-6-methylenenaphthalen-5-yl)ethylidene)-4-hydroxyfuran-2(3H)-one	
atractylon	(5aS)-5,5a,6,7,8,9,9a,10-octahydro-3,5a,9a-trimethyl-6-methylene-4H-benzo[g]chromene	
Boldine	(8S)-1,13-dimetossi-7-metil-5,6,6a,7-tetraidro-4H-dibenzo[de,g]chinolin-2,12-diolo	
Fumaric acid	Butenedioic acid	
Hinesol	2-(6,10-dimethylspiro[4.5]dec-9-en-3-yl)propan-2-ol.	
Organo sulphur compound	1,2-diphenyldisulfane	

Pieced	3,5, 4'-trihydroxystilbene-4'-O-beta-D-glucopyranoside	
Saikosaponins	(3β,4α, 16β)-13,28-Epoxy-16, 23-dihydroxyolean-11-en-3-yl	
Sarmentosin	2-butenenitrile,4-(beta-D-glucopyranosyloxy)-2-(hydroxymethyl)-, (E)	
Wuweizisu-C	(6R,7S,13aS)-5,6,7,8-Tetrahydro-13,14-dimethoxy-6,7-dimethylcycloocta[1,2-f:3,4-f']bis[1,3]benzodioxole	

CONCLUSION

From this study, it is clear that the so numerous herbal plants constituents play an important role against hepatotoxicity caused by numerous agents (drugs, chemicals etc...). The hepatoprotective activity is in all probably due to the presence of assorted active constituents like polyphenols, polyprenols, phenolic acids, triterpenoid, resins, glycosides, alkaloids, flavonoids in all few herbal plants. The outcomes of this study indicate that extracts of leaves, stem bark, root and plants extracts of some healthful plant have sensible potentials to be used in liver poisoning, viral hepatitis and cirrhosis. The current review study offers important info that the active constituent and mechanism of action of healthful plants against experimentation elicited hepatotoxicity. Nevertheless many of herbal therapies that are used for liver ailments haven't undergone suspicious scientific observation and assessment. Some had the potential to cause adverse toxic effects. In order that during this state of affairs continued analysis is important to explain the phytochemical and pharmacological events of herbal preparations currently being employed to treat liver ailments.

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