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Review Article

Ameliorative Effects of Indigenous Medicinal Plants against Hepatic Diseases in Southern Region of India- A Review

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ABSTRACT

Purpose: Liver is an important part in human beings and plays a major role in metabolism and excretion of xenobiotics from the body.

Selection of Data: Further, hepatotoxicity is caused by different types of toxic chemicals, such as antibiotics, and chemotherapeutic agents like paracetamol ($C_8H_9NO_2$), thioacetamide (C_2H_5NS), carbon tetrachloride (CCl_4), silymarin ($C_{25}H_{22}O_{10}$), ethanol (C_2H_5OH), and excessive alcohol in taking and microbes are well researched. The markedly available synthetic drugs to treat liver sickness in this condition also cause further damage to the liver. Hence herbal medicines have being become popularize and their utilized is wide-spread. In plant derived drugs have been utilized in the treatment of liver diseases for a long time and to protect a healthy liver. Liver injury induced by toxins is more common now-a-days. Herbal remedies are focused in the pharmaceutical industry to evolve a safe route for liver disorders and which is very low prize and also no side effects compared with synthetic drugs.

Conclusion: Hence an attempt has been made to reviewed and compiled the available data on photochemical from medicinal plants that have tested in hepatoprotective models using modern scientific system. For the present investigation the selected plants are *Avicennia alba, Anisochilus carnosus Baliospermum montanum, Centella asiatica, Clitoria ternatea, Eclipta alba, Justicia adhatada, Phyllanthus emblica, Pisonia Grandis* and *Syzgium cumini* .

Keywords: Liver diseases, Hepatotoxicity, Hepatoprotective, Medicinal plants.

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INTRODUCTION

Liver diseases are strong position as one of the chief health troubles in the global with it cirrhosis was drug stimulated liver injury accordingly 9th place of death in developed and developing countries [1]. The infectious agents or ingestion of toxic substances from food, chemicals, and over dose of drugs that cause liver damage are called hepato toxins [2,3]. It may be possible side effect of chronic medications or can be caused by chemicals such as microcystins, as well as artificial chemicals, like antibiotics of tetrachloride, chemotherapeutic agents, dimethyl nitrosamine, aflatoxin, CCl_4, pyrrolizidine alkaloids, allyl alcohol, C_2H_5NS, biomobenzene[4,5]. Susceptibility of the liver to chemical attacks, which comes in close contact with many harmful substances, environmental pollutants, xenobiotics, and chemotherapeutic agents could represents. However, maintaining a healthy liver is a challenge for overall health and well human being, and the treatment of such diseases are taken away standard using artificial pharmaceuticals, or secondary, by using separated main compounds or

importance parts of indigenous medicinal plants utilized in popular medicine [6, 7]. In spite of, there are nevertheless few drugs utilized to treat liver diseases, with possible effects on human [8, 9].

Thus, important medicinal plants with hapatoprotective or curative process utilized for the therapy of hepatic disorders become important mostly important subjects of studies to explain their mechanism of action and characterize compounds that can be utilized for the increased of new hepatoprotective drugs [10,11]. Some experimental models are **CCl_4**

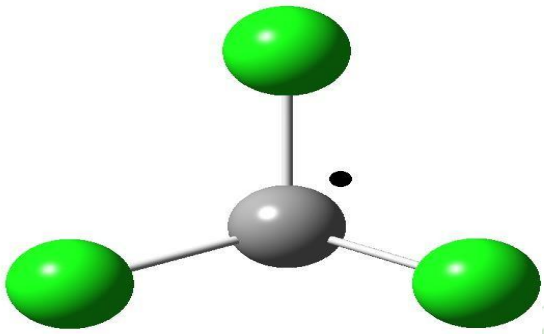

Fig. 1a. *3D* structure of CCI4

Liver injury caused due to CCl_4 (fig. 1a) in rats was first reported in 1936 and broadly and successfully utilized by continuous so many researchers[14,15]. CCl_4 toxicity depends on dosage and the duration of exposure. In low dose, effects like loss of Ca_2^+ homeostasis, lipid peroxidation, and release of cytokines are produced, and apoptotic events may be generated, followed by cellular regeneration. Further, in high doses or if there is a longer exposure, the effects are more severe and the damage occurs during a longer period of time, the patient may develop fibrosis, cirrhosis, or even cancer [16], is metabolized by the cytochrome P450 dependent of monooxygenases, mainly through the CYP_2E1 isoform in the endoplasmic reticulum and mitochondria [17]. Hepatotoxicity is produced by the formation of the trichloromethyl radical (CCl_3) (fig. 1b), which is highly reactive.

These radicals may saturate the organism's antioxidant defence system, react with proteins, attack unsaturated fatty acids, generating lipid peroxidation, reduce the amount of cytochrome P450, which leads to a functional failure with the consequent lowering of protein and accumulation of triglycerides (fatty liver), and alter water and electrolyte equilibrium with an increase of hepatic enzymes in plasma [18]. Lipid per oxidation leads to a cascade of reactions, such as the destruction of membrane lipids, the generation of endogenous toxic substances, which originate more hepatic complications and functional anomalies. For this reason, lipid peroxidation is considered a critical factor in the pathogenesis of liver injuries induced by CCl_4 [19]. The utilized to show the hepatoprotective action of certain medicinal plants, especially against C_2H_5NS stimulated liver damage[12,13].

Hepatotoxicity agents

Several chemicals have been known to induce hepatotoxicity, and CCl_4, C_2H_5NS, C8H9NO2, C_2H_5OH, and $C_{25}H_{22}O_{10}$ are used to induce experimental hepatotoxicity in laboratory animals.

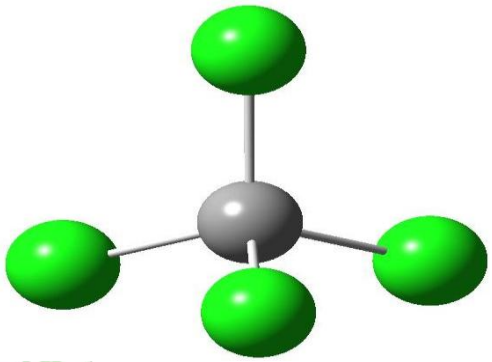

Fig. 1b. *3D* structure of CCI3

inhibition of the radical CCl_3 generation is a key point in the protection against the damage generated. Because of this, model is widely utilized for the evaluation of pharmaceuticals and natural products with hepatoprotective and antioxidant activity [20,21].

C_2H_5NS

C_2H_5NS was particularly utilized as a fungicide to maintain agricultural citrus materials later it was denied that it was a strong, potent hepatotoxin and carcinogen due to organ-sulfur-containing compound enriched with liver damaging and carcinogenic activities [22,9]. Currently, it is focused as a carcinogen, and very speedily metabolized into freebie radical derivatives such as C_2H_5NS sulfoxide, TAA-S-S-dioxide, even though it leads to lipid peroxidation, thus eventually culminates in centrilobular damages and liver injuries [13]. Earlier studies have also demonstrated that, rodents intoxicated with C_2H_5NS (fig. 2) was caused such as fibrosis, liver injury, cirrhosis, and steatosis in test animals of this disease with etiology, and pathology comparable equal to the one seen in humans [23,24,25]. However, C_2H_5NS was recognized as an exemplary of liver fibrosis in rats. Though currently, the broadly utilized treatment of liver fibrosis and cirrhosis is inadequate; thus there is no effectively broadly utilized therapy that can prevent the improvement of hepatic diseases. Despite, newly improved drugs have been utilized to heal liver diseases; presently these drugs have abundant side effects. There is an urgent need for alternative deputing remedies or drugs, to the treatment of chronic liver disorders to change

current drugs of uncertain safety and non-effectiveness [26]. The liver markers are found of AST, Transaminases, APT, γ- glutamyltransferase, ALT, lipids, Bilirubin, cholesterol, and proteins are discharged into the blood. As a result of cell leakage, and the measurement of the particularly serum markers of the liver could be utilized for diagnosis of injuries [27]. Many products available commercially are of herbal origin, and herbal elements and dietary supplements have power as possible choice medicines for the therapy of chronic liver diseases and associated metabolic derailments [28,29].

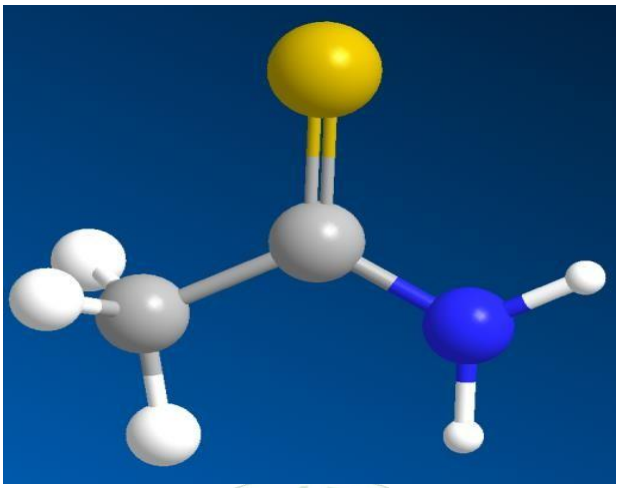

Fig. 2. *3D* structure of C_2H_5NS

$C_8H_9NO_2$

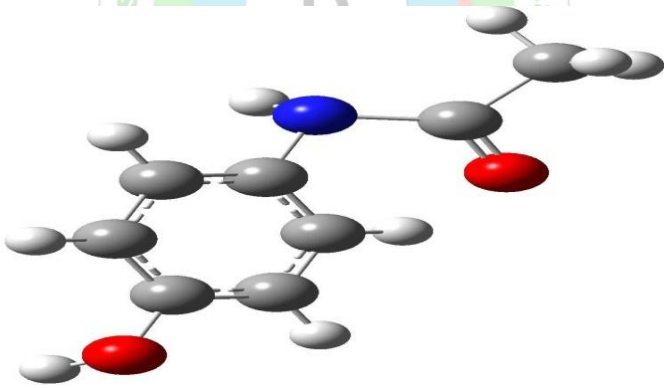

Fig. 3. *3D* structure of $C_8H_9NO_2$

C8H9NO2, (fig. 3) is a widely used analgesic, antipyretic drug, and hepatocellular injury through three mechanisms, independently or in association. It produces acute liver damage in high doses [5], and is a widely used experimental model of clinical importance as an example of drug-induced liver damage [18]. At therapeutic doses, it is mainly metabolized to glucuronic or sulfated and excreted derivatives, the rest metabolizes to intermediate reactive, which are eliminated by conjugation with glutathione. The Ist and most common mechanisms is ingestion of doses higher than 10 g by adults and up to 150 mg/kg by children, popularly known as "overdose" and 2nd, is the cytochrome P450 (CYP) at N-acetyl-p-benzoquinone (NAPQI), which quickly attaches to glutathione, resulting from the use of enzyme inducing drugs and chronic alcohol abuse, 3rd occurs with glucagon depletion in hepatocytes through alcohol intake or malnutrition [30]. Under excessive conditions of NAPQI and glutathione depletion, a covalent bond of metabolite to proteins, adduct formation, mitochondrial dysfunction and oxidative stress occurs. The result is necrosis or hepatocellular death [31].

C_2H_5OH

The Liver is the most susceptible organ to the toxic effects of C_2H_5OH (fig. 4). Damage mechanism is due to the metabolism of ethanol by the CYP_2E1 isoform of the cytochrome P450 producing oxidative stress with the generation of reactive species of oxygen and the increase of lipid peroxidation, leading to the alteration of the compositions of the phospholipids of the cellular

membrane [32]. Membrane lipid peroxidation results in the loss of its structure and integrity, elevating serum levels of glutamyl-transpeptidase, a membrane bonding enzyme. C_2H_5OH inhibits glutathione peroxidase; it reduces the activity of catalase and dismutase superoxide [18]. The decrease in the activity of antioxidant enzymes, dis-mutase superoxide and peroxidase glutathione is believed to come as a result of the harmful effects of free radicals produced after exposure to C_2H_5OH, or alternatively, they could be a direct effect of acetaldehyde, a product of C_2H_5OH oxidation[33].

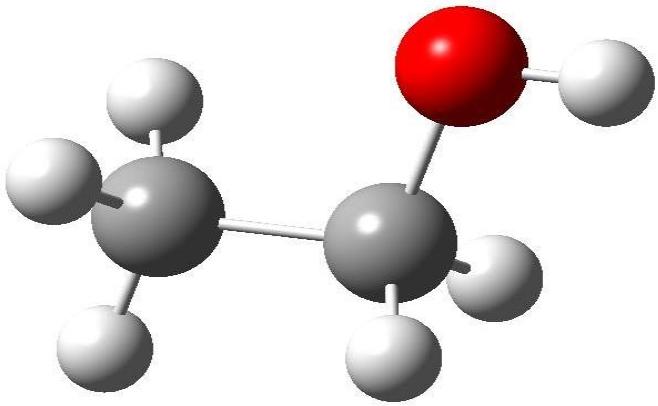

Fig. 4. *3D* structure of $C_2H_5OH_2$

$C_{25}H_{22}O_{10}$

$C_{25}H_{22}O_{10}$ (fig. 5) is an important component of Silybum marianum. Thus, it has been evidenced to be mostly hepatoprotective, and has been utilized for the therapy of abundant liver disorders such as cirrhosis, fatty acid infiltration due to alcohol and toxic chemicals, and hepatitis, its specifically characterized by functional impairment or deterioration of necrosis [34]. However, it's mechanisms of the process are not entirely understood, it appears that it acts in various ways, including anti-inflammatory activities and antioxidant, membrane stabilizer, cell permeability regulator, inhibiting the deposition of collagen fibers and stimulating liver regeneration, which may be lead to cirrhosis [35].

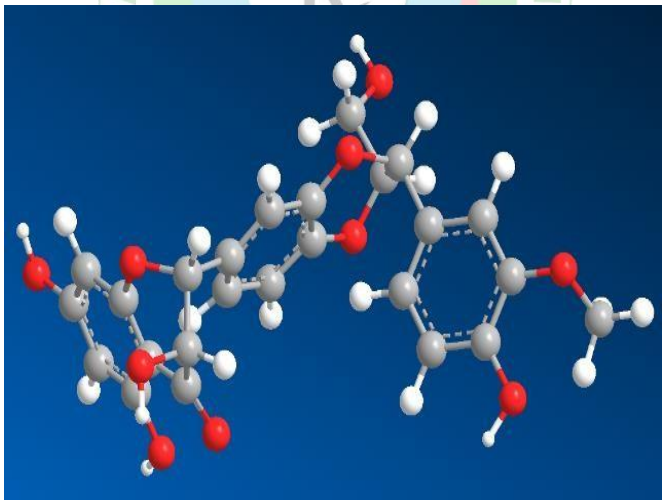

Fig. 5. *3D* structure of $C_{25}H_{22}O_{10}$

Liver function markers

Functions performed by the liver, there is a wide range of markers through which we are able to determine the functionality or damage generated by this organ or its cells [36]. Although there is no biochemical marker specific to liver damage, the combination of several of these, and knowing the correlation they have with the liver, will help to better interpret the results of the hepatoprotective models. Markers can be divided into tests related to the liver's excretory function (bilirubin), tests related to synthetic function (albumin and prothrombin time) and tests related to the integrity of hepatocytes (transaminases, alkaline phosphatase, GGT).

Hepatoprotective Plants

The medicinal plant plays a key role in the human health care. About 80% of the world population relies on the use of traditional medicine, which is predominantly based on plant materials [37]. Traditional medicine refers to a wide range of ancient natural health care practices, including

folk/tribal practices as well as Ayurveda, Siddha, Amchi and Unani. These medicinal plant practices originated from time immemorial and developed gradually, to a large extent, by relying or based on practical experiences without significant references to modern scientific principles. This estimated that about 7,500 plants are used in local health traditional in, mostly, rural and tribal villages of India. Out of these, the real medicinal plant value of over 4,000 plants is either little known or hitherto unknown to the mainstream populations. This is a classical system of medicine such as Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants [38,39]. Plants based therapeutics for liver diseases has been in uses in India for a long time and have been popularized world over by leading pharmaceuticals. The despite their important popularity several plant medicines in general and for liver diseases in particular, they are still unacceptable treatment modalities for the liver diseases. Medicinal plant remedies are focused on the pharmaceutical industry to evolve a safe route for liver disease (Table 1). Hence, in this review we are focused some medicinal plants such as A. alba, A. carnosus, B. montanum, C. asiatica, C. ternatea, E. alba, J. adhatada, P. emblica, P. Grandis, S. cumini.

Table: 1. Hepatoprotective Plants with Chemical Constituents and Hepatotoxic Agents

S. No.	Plant/Tamil name	Family/Part Used	Part used	Constituents	Hepatotoxicity inducing agents
1	*Anisochilus carnosus* wall	Lamiaceae	Leaves	phytosterols, triterpenoids, saponins, tannins, carvacrol, α-cis-bergamotene, caryophyllene, β-selinene, camphor	CCl4
2	*Avicennia alba*	Avicenniaceae	Leaves	**Alkaloids, Flavonoids, tannins, terpenoids, proteins, and steroids** , glycosides and terpenoids	$C_9H_{10}O_2$
3	*Centella asiatica*	Apiaceae	Whole parts	Thujene, α-pinene, Camphen, γ -2-carene, α-Terpene, P-Cymene, Limonene, P-Menth, 3,8-diene, C-Terpinens, Linalool, Allo-Ocimene, 3-Non-2-one, Menthone, Mthyl cavacrol, Trans myrtenol, Bornyl acetate, Myrtenyl acetate, α-Elemene, Bicyoloelemens, Nonanal, E-Caryophyllene, Guaiene, B-caryophyllene	C8H9NO2
4	*Clitoria ternatea*	Fabaceae	Whole plant	tannins, phlobatannin, carbohydrates, saponins, triterpenoids, phenols, flavanoids, flavonol glycosides, proteins, alkaloids, antharaquinone, anthocyanins, cardiac glycosides, Stigmast- 4-ene-3,6-dione, volatile oils and steroids.	C8H9NO2
5	*Syzygium cumini* L.	Myrtaceae	Leaves	Friedelin, Kaempferol, Tannins, Quercetin, Bita- Sitosterol, Betullinic acid. Anthocyanin acid,Eugin, Ellagic acid, Oxalic acid, Citric acid, Glycolic acid, Glucose, Fructose, Gallic acid, Glycine, Alanin, Leucin, Tyrosin	CCI4
6	*Baliospermum montanum* (Tamil name – Nakatanti)	Euphorbiaceae	Root	Alkaloids, Phenols, Carbohydrates, Tannins, Steroids, Saponins, Flavonoids, Cardiac Glycosides, Proteins, Terpenoids, Resins, and Glycosides	C8H9NO2
7	*Eclipta alba*	Asteraceae	Leaves	Demethylwedelol actone, desmethyl-wedelolactone-7glucoside , ecliptal, Я-amyrin, luteolin-7-O-glucoside,	CCI4

				hentriacontanol, heptacosanol, stigmasterol.	
8	*Justicia adhatada*	Acanthaceae	Leaves	alkaloids, tannins, saponins, phenolics and flavonoids. he most important is vasicine, a quinazoline alkaloid.	CCI4
9	*Phyllanthus emblica (Perunelli) perunelliIpp*	Euphorbiaceae	Whole plant	Protein, Fats, Fibres,Carbohyderates, Vitamin-C, Nicotinic acid, Tannins, Gallic acid,Ellagic acid, Flavin and Glucose, Linolenic acid, Oleic acid.	$C_8H_9NO_2$
10	*Pisonia Grandis*	Nyctaginaceae	Stem bark	Protein, Carbohydrate, Sterols, Alkaloids, Flavanoids, Quinone, Fatty acid, Tannin, Terpenoids Phenol, Saponins, Glycosides, Coumarin, Xanthoproteic acid	CCl_4

***Avicennia alba* (Blume)**

A. alba, (Family: Avicenniaceae), is used in Indian system of medicine for the treatment of several types of conditions such as scabies, rheumatism, paralysis, asthma and snakebites, skin disease and ulcer[40]. The plant is rich source of steroids, triterpenes, saponins, flavonoids, alkaloids and tannins[41]. Recently, find the three naphthoquinones and their analogues, named avicequinone-A, avicequinone-B, avicequinone-C and avicenol-A, avicenol-B, avicenol-C respectively[42]. These are compounds isolated from the stem bark and isolated a new flavonoid, 2-[3'-(3''-(hydroxymethyl) oxiran-2''-yl)-2'-methoxy-4'- (methoxymethyl) phenyl]-4Hchromen-4-one from the aerial parts. Hepatotoxicity was induced by paracetamol, and this experiment was assessment by biochemical parameters such as AST, ALP, ALT, and total bilirubin (serum bilirubin). The in-vivo antioxidant such as SOD, CAT, GSH, vitamin C and E, and thiobarbituric acid reactive substances, and histopathological changes in liver were studied along with silymarin as standard hepatoprotective agent[43]. The results of this study showed a preliminary phytochemical analysis of the ethanolic extract the presence of alkaloids, flavonoids, tannins, terpenoids, proteins, and steroids. Treatment with plant extract to paracetamol administered rats caused a significant reduction in the values of AST, ALP, ALT, and total bilirubin almost comparable to standard drug silymarin. Hepatoprotective activity was confirmed by histopathological assessment of the liver tissue of control and treated animals. In this research, it can be concluded that ethanolic extract of leaves possesses hepatoprotective effect[44].

***Anisochilus carnosus* (L) Wall.**

A carnosus Family Lamiaceae) "Karppura-Valli" is an annual herb and has been traditionally used for the treatment of gastrointestinal disorders respiratory disorders cough, cold, fever [45]. Its popular herbal preparation together with *Ocimum basilicum (O.basilicum), Mentha piperia (M. piperita) and Alpinia galangal (A. galanga)* is used against the symptoms of influenza, dermatitis and the slight illness that derives from the bites of bugs [46]. Essential oils have been extracted by hydro distillation from the leaves and leaves have been reported to be antimicrobial in nature [47]. A pharmacological activity of this plant is show anti-inflammatory activity[48], antiulcer activity[49], antifungal property[50] and anticancer property[51]. Previously, reported that, this plant shows phytochemicals active compounds such as saponins, tannins, flavonoids (apigenin and luteolin), phytosterols, triterpenoids, and essential oil components (carvacrol, β-selinene, camphor, α-cis-bergamotene, and caryophyllene) *etc.*,[52]. Its analysis of leaf and leaf callus extracts was done by qualitative analysis, and was used for hepatotoxicity induced by Alcohol. This research results revealed that the ethanolic leaf extract pretreated Hep G2 cells show 94% cell viability compared to the standard silymarin pretreated Hep G2 cells which showed 81% cell viability. This plant Leaf callus extracts also showed significant hepatoprotective activity where ethanolic callus extract pretreated Hep G2 cells showed 86% viability after intoxication with alcohol. Results revealed that Hep G2 cell viability percentage is dose dependent. Phytochemical studies revealed the presence of different secondary metabolites in leaf and leaf callus extracts that shows hepetoprotective activities[53].

***Baliospermum montanum* (Willd) Muell.- Arg**

B. montanum (Family - Euphorbiaceae) "pey-amanakku" is one of the very must plant of Ayurveda being used for millennia as a purgative along with its wide-ranging health benefits and useful against many more disorders Danti has been explained in various classics as a major as well as a minor ingredient of various formulations used in different diseases. Single handed information on the external application of usage of Danti is not available [54].

Ethanolic leaf extract GC-MS spectrum showed various phyto-constituents like Olean-12- ene, 3 methoxy, -(3β) α-

Amyrin, Lanosterol, Lup-20 (29) - en-3-ol, acetate, Betulin etc.,[55]. On the other hand hepatoprotective activity of methanol extract from the roots of *B. montanum* and its methanol fraction were carried out using C_2H_5NS induced liver damage in albino rats. This study assessed by glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, total bilirubin, total cholesterol, total protein and albumin in serum. At the same time analyzed of histopathology of liver sections confirmed that, pre-treatment with methanol extract and methanol fraction prevented hepatic damage induced by C_2H_5NS. It is suggested that, the presence of flavonoids in methanol extract and its methanol fraction may be responsible for hepatoprotective properties. HPTLC profile of flavonoids of bio-active extracts was developed using quercetin-3-O-galactosyl-7-O-rhamnoside as a marker. Methanolic extract of *B. montanum* has shows strong hepatoprotective activity[56].

Centella asiatica L.

C asiatica (Family: Apiaceae), which is a slender, prostrate, glabrous, perennial creeping herb rooting at the nodes, with simple petiolate, palmately lobed leaves, and it has various pharmacological activities like memory enhancing, anti-inflammatory, antioxidant, wound healing, and immune-stimulant, anti-anxiety (anti-hypertensive), anti-stress and anti-epilepsy. Various health benefits of *C. asiatica* have lead to the amplified usage of this plant in food and beverages[57]. It has been extensively used for the treatment of ailments like inflammation, syphilis, mental illness, skin diseases, rheumatism, epilepsy, hysteria, diarrhea, wounds, dehydration, and ulcers[58]. Aqueous extract of the plant aerial parts extracted from essential oil. Around 64 volatile compounds were identified from the essential oil P-Cymene (35%) is the predominant compound in the leaf essential oil, such as α-Thujene, α-pinene, Camphen, γ -2-carene, α-Terpene, P-Cymene, Limonene, P-Menth, 3,8-diene, C-Terpinens, Linalool, Allo-Ocimene, 3-Non-2-one, Menthone, Mthyl cavacrol, Trans myrtenol, Bornyl acetate, Myrtenyl acetate, α-Elemene, Bicyoloelemens, Nonanal, E-Caryophyllene, Guaiene, B-caryophyllene etc.,[59]. The protective effect of *C. asiatica* is against paracetamol liver injury which may be attributed to its hepatoprotective activity[60].

***Clitoria ternatea* L. (CT)**

C. ternatea (Family: Fabaceae) "Kannikkodi" is a medicinal plant native to tropical equatorial Asia is commonly used in folk medicine to treat various diseases [61]. The leaves and roots are used in the treatment of a number of ailments, including body aches, infections, urinogenital disorders, and as an anthelmintic and an antidote to animal stings. The young shoots, leaves, flowers and tender pods are eaten as a vegetable in Kerala (India) and in the Philippines. In Malaysia, the leaves are employed to impart a green color to food and the flowers to impart a bright blue color to rice cakes. It's commonly used in Ayurvedic medicine to treat various types of ailments including as memory enhancer, no tropic, anti stress, anxiolytic, antidepressant, anticonvulsant, tranquilizing and sedative agent. Various secondary metabolites such as polyphenolic flavonoids, anthocyanin glycosides, pentacyclic triterpenoids and phytosterols have been reported from this plant. Flavonoils *i.e.,* kaempherols, quercetin and myricetin and their glycosides were also isolated from this plant[62].

Mass spectral analysis of leaf methanolic extract compounds, such as Butyl-2- methylpropylphthalate, Pentadecanoic acid ME, Decyloctylphthalate, 3-methylhexane, Cyclotetradecane, 2-methylpentane, Decyloctylphthalate, 3-methylhexane, Butyl-2-ethylhexylphthalate, Isopropylbenzene etc.,[63]. Rats treated with CT leaf extracts showed positive results in protecting themselves against damage caused by paracetamol. Interestingly, the treated group with CT extracts was observed to possess a reduced level of enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin compared to a raised level in AST, ALT, and bilirubin in paracetamol-treated group[64].

***Eclipta alba* (Linn)**

The plant *E. alba* (Family: Asteraceae) having an important role in the traditional Ayurvedic, "Karisilanganni" Unani systems of holistic health and herbal medicine of the east, it has reported to possess hepatoprotective, antimicrobial, anti-inflammatory, analgesic, immunomodulatory, antiviral and promoter for blackening and growth of hair. An important source of chemicals is wedelolactone, demethylwedelolactone exhibit antihepatotoxic activities. The traditional knowledge with its holistic and systematic approach supported through experimental base can serve as an innovative and powerful discovery of natural 5α-reductase inhibitor[65]. *E. alba* having important role in the traditional Ayurvedic and Unani systems of holistic health and herbal medicine of the east. The principal constituents of *Eclipta alba* are coumestan derivatives like wedololactone (1.6%), demethylwedelolactone, desmethyl-wedelolactone-7 glucoside and other constituents are ecliptal, ß-amyrin, luteolin- 7-O-glucoside, hentriacontanol, heptacosanol, stigmasterol. All the parts of *Eclipta alba* and chemical constituents are used as anticancer, antileprotic, analgesic, antioxidant, antimyotoxic, antihaemorrhagic, antihepatotoxic, antiviral, antibacterial, spasmogenic, hypotensive, hepatoprotective ovicidal, promoter for blackening and growth of hair[66]. Therefore this plant plays a momentous role in medicinal field and it has promising cosmetic as well as therapeutic application & hence its extraction is essential. Root parts have analyzed mass spectra, and exhibit various Phyto-constituents such as, 2-Thiophenecarbaldehyde, 5- [5- (thien-2-yl)thien-2-yl]-, Benzyl .beta.-d-glucoside, Octadeca-9,12-dienoic acid methyl ester, 2-Propenoic acid, 3-(4-hydroxy-3-methoxyphenyl)-, methyl ester, Hexadecanoic acid, 2-hydroxy-1- (hydroxymethyl)ethyl ester, Dodecanoic acid, Benzenepropanoic acid, 2,5-, 4- ((1E)-3-Hydroxy-1-

propenyl)-2-methoxyphenol, Retinol[67]. It's significantly counteracted CCl4-induced inhibition of the hepatic microsomal drug metabolizing enzymes. Further, the loss of hepatic is lysosomal acid, phosphatase, and alkaline, phosphatase by CCl4. The study shows that hepatoprotective activity[68].

***Justicia adhatada* (L) Willd**

J. adhatoda (Family: Acanthaceae) with the common name ''Adathodai" is a perennial shrub, and mainly consist of pyrroquanazoline alkaloids like visicine, vasicinone, vasicol, preganine along with other minor constituents like adhatonine vasicinol and vasicinolone[69]. Extracts have been used for the treatment of various diseases and disorders in Ayurved and tuberculosis[70]. *Vasaka* leaf extract is a known antioxidant and has also been reported to possess hepatoprotective activity[71]. The present study has been undertaken to we explore the hepatoprotective action of isolated vasicinone from the leaves in mice. Preliminary phytochemical analysis shows Alkaloids, carbohydrates, glycosides, cardiac glycosides, saponins, hydroxyanthraquinones, phlobatannins, proteins, xanthoprotein, amino acids, steroids, terpenoids, phenols, volatile oil, fatty acid, emodins[50]. Leaf showed significant hepatoprotective effect at doses of 50 to 100 mg/kg on liver damage induced by D- galactosamine in rats[72].

***Phyllanthus emblica* (Linn.)**

P. emblica (Family: Euphorbiaceae) all parts of the plant are used for medicinal purposes, the fruits especially are found having tremendous pharmacological applications. They are used both as a medicine and as a tonic to build up lost vitality and vigor, and highly nutritious, then important dietary source of vitamin C, amino acids, and minerals. In traditional medicine, the fruits are used for the treatment of diarrhea, jaundice, and inflammation. Further, they also showed antidiabetic, hypolipidemic, antibacterial, antioxidant, antiulcerogenic, hepatoprotective, gastroprotective, and chemopreventive properties[73]. Phenolic components were find out from *Emblic* leaf flower fruit by column chromatography and associated with NMR spectrum. It is acknowledged that gallotannins and are the major phenolic constituents of Emblic leaf flower fruit. The NMR data with the literature led to identification of compound 2 as mucic acid 1,4-lactone 5-O-gallate, 2-keto-glucono-lactone, 6-methyl ester[74]. The study also confirms the hepatoprotective and antioxidant activities of leaves of *P. emblica* and *P. polyphyllus*[75].

***Pisonia grandis* R.Br**

P. grandis (Family: Nyctaginaceae) is leaves, stems and roots of this species are extensively used by the tribals in the preparation of several folk medicines, and is traditionally used as anti-rheumatic and antifungal. It is also pharmacologically studied for its anti-fungal, anti- oxidant, anti-microbial, anti-inflammatory, anti-diabetic, diuretic, analgesic and wound healing properties[76], then phytoconstituents such as Protein, Carbohydrate, Sterols, Alkaloids, Flavanoids, Quinone, Fatty acid, Tannin, Terpenoids Phenol, Saponins, Glycosides, Coumarin, Xanthoproteic acid *etc.*,[77] from the ethanol extract. The ethanolic and aqueous extracts of leaves are screened for its hepatoprotective potential against liver injury induced by CCl4, paracetamol or C_2H_5NS and chronic liver damage induced by CCl_4 in rats. Pretreatment of animals with the extract reduced inflammation and degenerative changes. Histological examination of liver tissues supported the hapatoprotection by both the extracts and thus the ethanolic and aqueous extracts showed significant hepatoprotective activity in CCl_4 induced acute and chronic liver damage[73].

***Syzygium cumini* (L.) Naval**

S. cumini (Family: Myrtaceae), gives authority of due to the presence of the various phytochemical constituents such as alkaloids, fatty acids, steroids and tannins. Biochemical analysis and histopathology were achieved by collecting the blood samples and liver tissues. The methanol extracts of plant seed was significantly increase the serum protein and decrease the enzyme level in control and treated groups as compared to that of the CCl_4 treated group.

The hepatic tissues protected by the extract of seeds in both the doses and silymarin from CCl_4 induced stress which indicates by histological examination of liver tissues. It was concluded that extract of seed has hepatoprotective activity[50].

Some studies were carried out antidiabetic, hepatoprotective activity, antiinflammatory, antioxidant, antiulcers, antidiarrhea and antimicrobial. It's containing anthocyanins, glucoside, ellagic acid, isoquercetin, kaemferol and myrecetin[14]. Phytochemical analysis of this plant identified gallic acid, cyanidin glycoside, glycoside jamboline, triterpenoids, tannins, gallitanins, essential oils, myricetine, β-sitosterol, myricyl alcohol etc.,[78]. Leaves and seeds from aqueous extracts (LASc, SASc, respectively) as well as their effect in a 2,2 azobis-2-amidinopropane dihydrochloride (AAPH) induced model of oxidative damage in human lymphocytes, in vitro[77].

CONCLUSION

This research results exhibit S. Cumini has protective and immune-modulatory effects on AAPH-induced damage in lymphocytes, by assessed in vitro. The protective effect of these indigenous medicinal plant extracts against CC14, Paracetamol, and C2H5NS may be related to polyphenolic compounds, terpenoids, alkaloids, coumarines, phytosterols. Polyphenolic compounds such as flavonoids can protect the cells against emptying reduced glutathione via increasing the capability of antioxidant enzymes, and is activity because antioxidant, free radical scavenging and anti-lipoperoxidant agent as helpful for hepatoprotection.

Furthermore, these phytocompounds with antioxidant properties can counteract free radicals in the environment and therefore avoid their destructive effects. Terpenoids such a carotenoids with anti-hepatotoxic activity are also known as antioxidants. Ursolic acid is a triterpene, with potential hepatoprotective effects. Therefore, herbal medications should be recommended within the setting of more finely-conducted clinical trials, In spite of, better training of both patients and physicians about herbal preparations seems necessary.

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