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ROLE OF TERPENOIDS AS HEPATOPROTECTIVE

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ABSTRACT: The liver is the most vital organ in our body, involved in several vital functions such as metabolism, secretion, storage as well as detoxification of several drugs and xenobiotic. Liver cell injury caused by various toxic chemicals like certain antibiotics, chemotherapeutic agents, carbon tetrachloride, thioacetamide, excessive alcohol consumption microbes and so, on. Due to liver disease worldwide, approximately 2 million deaths, 1million due to complications of cirrhosis, and 1 million due to viral hepatitis and hepatocellular carcinoma have been found every year. Now a day number of synthetic medicine available in the market for the treatment of liver disorders, but they have lots of side effects. So, the developed countries recently give their interest in herbal drugs. Many Ayurveda herbs, such as Andrographis, Punarnava, kokum, and soon have a long history of traditional uses in revitalizing the liver and treating liver dysfunction from the various literature survey this can be concluded that the plant containing a high amount of terpenoids possess good hepatoprotective effect. There are some plants enriched with a high amount of terpenoids such as Andrographolide, *Podophyllum hexanderum*, *Origanum vulgare*, and soon are very potential for hepatic disorders. The aim of this review is to enlighten the number of plants containing terpenoids and terpenoids for their hepatoprotective activity.

INTRODUCTION: The liver is the largest organ in the body, situated in the right of Hypo-chondrium, approximate weight 1400-1600 gm of the males and 1200-1400 gm of the females. It is located mainly in the upper right portion of the abdomen, beneath the diaphragm and above the stomach. The liver performs multifold functions such as metabolism, excretion of bile, manufacture of plasma protein like albumin, fibrinogen, vitamins (A, D, and B12), iron, and detoxification of toxic substances such as alcohol and drugs [1, 2]. Recently large number of people affected in liver disorders, about 20,000 deaths are found every year due to liver disorders.

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Hepatocellular carcinoma is one of the ten most common tumors in the world 2, 50,000 new cases each year. The main causes of liver diseases are excessive drug therapy, environmental pollution, and alcoholic intoxication. The liver diseases include liver cirrhosis (cell destruction and increase in fibrous tissue), inflammatory diseases, and non-inflammatory diseases. There is some 200 million chronic carriers of the hepatitis B virus, of which 40% are accepted eventually to die of hepatocellular carcinoma and 15% of cirrhosis [3].

The Various Types of Liver Disease are given below:

- Alcoholic steatosis (Fatty liver)
- Cirrhosis
- Hepatocellular carcinoma (HCC)
- Viral hepatitis – Hepatitis A, B, C, D, E
- Jaundice
- Hepatic failure
- Cholangitis

- Hepatic tuberculosis
- Echinococcosis.
- Cholelithiasis (gallstones)
- Cholecystitis

1. Alcoholic Steatosis: Alcoholic steatosis is a fatty liver disease, and it is also known as hepatic steatosis. It is a condition of excess fat in the liver [4-5]. Hepatic steatosis is two types shown in **Fig. 1.**

- Non-alcoholic fatty liver disease (NAFLD)
- Alcoholic liver disease [6].

2. Cirrhosis: Cirrhosis is a condition of liver damage, and it is the last stage of scarring of the liver caused many diseases such as hepatitis, chronic alcoholism, hepatitis B, hepatitis C. Cirrhosis occur due to take alcohol more than 3 times (20-40%) per day and liver doesn't properly work. It is also known as hepatic or liver cirrhosis. The basic Symptoms for liver cirrhosis generally found are: weakness, nausea, vomiting, swelling in the lower legs and fluid buildup in the abdomen, unconsciousness, yellow skin and so on [7] the liver cirrhosis shown in the **Fig. 1.**

3. Jaundice: Jaundice is a basic very serious liver problem known as icterus. The normal range of bilirubin is 5-19 µ mole/liter, and in case of jaundice level of bilirubin becomes high. In the time of jaundice skin, sclera and mucous membranes of the skin become faded yellow color due to a raised plasma bilirubin. From the various literature surveys, it was found that the basic region of jaundice is imbalance production and clearance of bilirubin [8], and it is shown in **Fig. 2**.

Jaundice can be classified as:

1. Pre-hepatic (resulting from excessive hemo-lysis).
2. Hepatic (due to congenital or acquired liver disorders causing impaired intra-hepatic bilirubin metabolism).

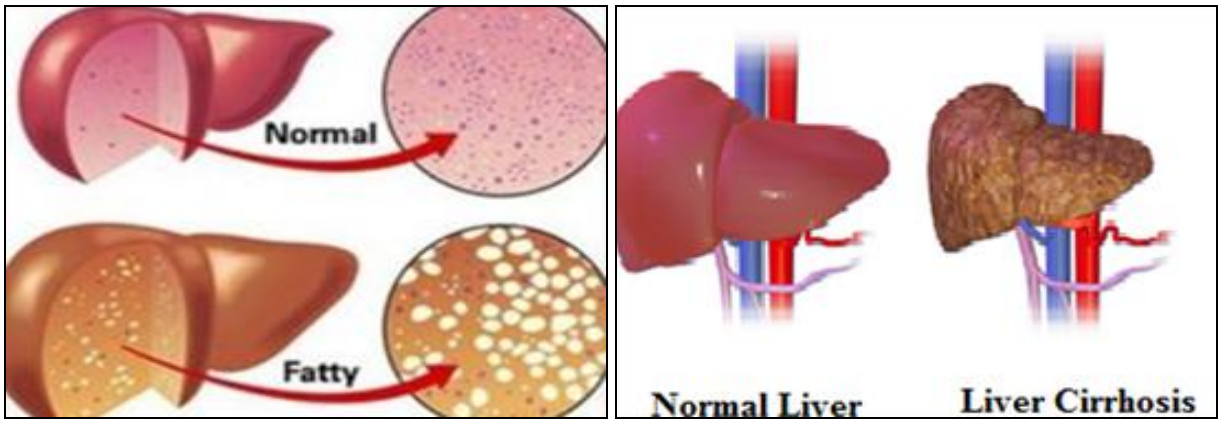

FIG. 1: LIVER DISORDER A. FATTY LIVER B. LIVER CIRRHOSIS

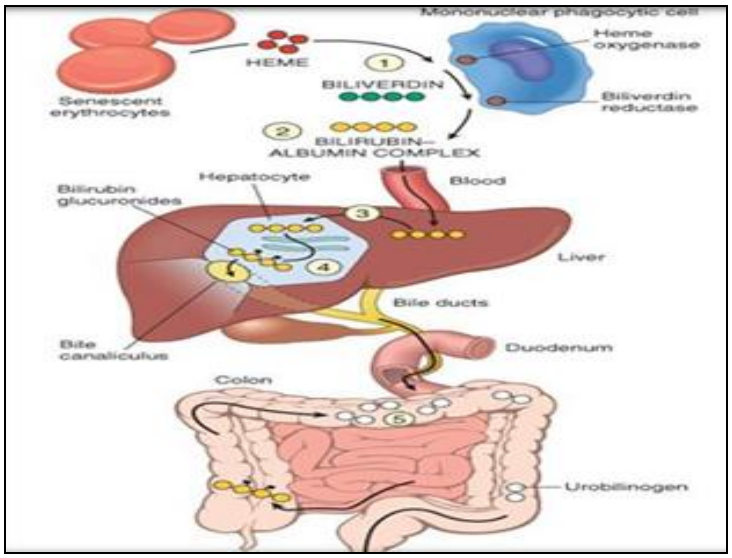

FIG. 2: THE PRODUCTION AND METABOLISM OF BILIRUBIN ARE SHOWN IN FIGURE [1]

4. Post-hepatic / Cholestatic: [9]

Echinococcosis: It is a parasitic tapeworm infectious disease that affects the lungs, liver, brain, *etc.* [11]. It is spread contaminated animal faeces with tapeworm eggs, through the contaminated food and water. And the spreading process of the disease is known as hydatid, hydatidosis [12]. The life cycle of echinococcosis is shown in **Fig. 3**.

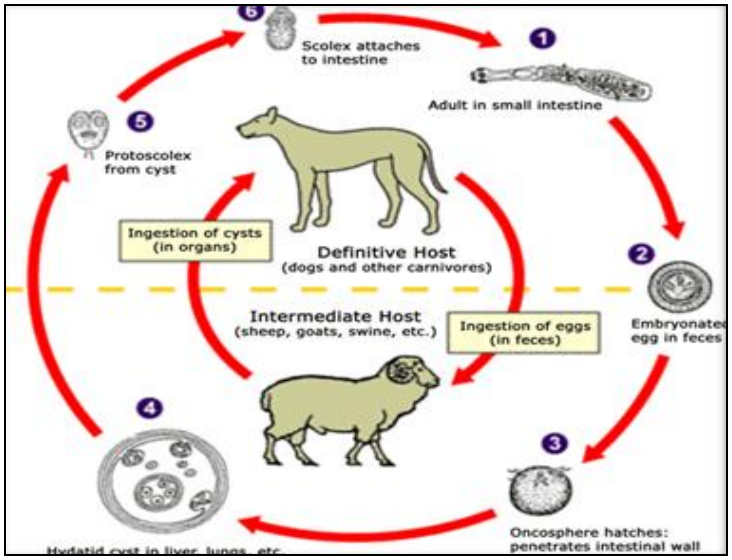

FIG. 3: ECHINOCOCCOSIS LIFE CYCLE

5. Cholangitis: Cholangitis is an inflammation of the bile duct usually caused by bacteria upside from its junction [13] in case of ascending cholangitis the bile duct are infected by bacteria [14]. Symptoms of cholangitis are yellow discoloration of the skin or whites of the eyes, abdominal pain, confusion, low blood pressure and so on [15] and it is shown in **Fig. 4.**

6. Cholelithiasis: Cholelithiasis refers to the formation of gallstones in the gallbladder16. Gallstones are mainly composed of bilirubin, calcium salts, cholesterol, and small amounts of protein and other materials [17]. The Gallstone blocks the biliary fluid, as a symptom, a cramp-like pain in the upper part of the abdomen is found called gallbladder attack [18,] and it is shown in **Fig. 4**.

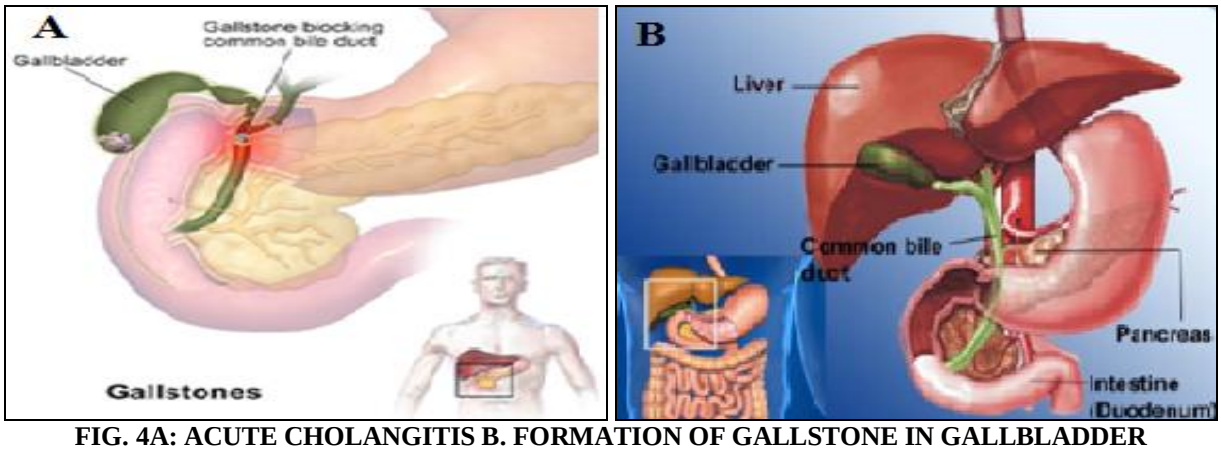

FIG. 4A: ACUTE CHOLANGITIS B. FORMATION OF GALLSTONE IN GALLBLADDER

Role of Natural Products as Hepatoprotective Drug: Till now the synthetic drug play the important role in the treatment of hepatotoxicity. From the clinical report and the various adverse effects such as of these drugs such as excessive bleeding, hemorrhage and difficulty breathing, dry mouth, dementia, and so on, since the present day, the developing countries people gradually move the herbal drug for the treatment of the toxicity [20]. Herbs/medicinal plant/homemade remedies are less expensive than synthetic drugs, and majority peoples in rural/backward areas have blind faith in them. They are right because they can treat any disease by using them without any lethal side

effects [21]. Although herbal medicines are less potent in comparison to synthetic drugs in some cases, but these are still considered less toxic or having less side effects in contrast to synthetic drugs [22]. The ultimate norm for any medicine (human madeor natural) is their non-toxicity, effectiveness, specificity, stability, and potency [23-26]. For the various literature surveys, it is clear that the terpenoids are the potent bioactive compounds for the treatment of ulcers. Terpenoids are the naturally occurring hydrocarbon compounds, and they are oxygenated derivatives like alcohols, aldehydes, ketones, and the terpenoids are called isoprenoids. Terpenoids are the derivative of polymers of isoprene unit (C_5H_8) [27]. Terpenoids is found in all volatile oils, resins combination of plant or animal origin. Terpenoids have the prevention and curative poverty for the of several diseases such as cancer, antimicrobial, antifungal, anti-parasitic, antiviral, anti-allergenic, hepato-protective, antispasmodic, antihyperglycemic, anti-inflammatory, immune-modulatory properties and so, on [28-31] the classification of terpenoids is given in **Table 1**. Various plants and polyherbal formulations are used in the treatment of liver disease. Some herbal plants are providing protection from liver damage caused by toxic chemicals and screening models of the drugs, oxidative mechanisms and so on. Screening plants for anti-hepatitis activity such as P. Kurroa, *Glycyrrhiza glabra*, A. Paniculata are likely to be active against in hepatitis virus and liver toxicity.

A combination of different herbal extracts is likely to provide desired activities to cure severe liver disease. To the importance of their use, we reviewed some popular herbal plants having hepatoprotective potential. The development of such medicines with the standard of safety and efficacy can revitalize treatment of liver disorders, and hepatoprotective activity of the medicinal plants is shown in **Table 2**.

TABLE 1: CLASSIFICATION OF TERPENOIDSO

Name of Terpenoids	Unit of Terpenoids	Examples of Terpenoids
Hemiterpenoids	(C_5H_8)	Prenol
Monoterpenoids	($C_{10}H_{16}$)	Geraniol, limonene
Sesquiterpenoids	($C_{15}H_{24}$)	A-Bisabolbol, Dehydrocostuslactone
Diterpenoids	($C_{20}H_{32}$)	Andrographis paniculata,Oridonin
Sesterterpenoids	($C_{25}H_{40}$)	Geranylfarnesol
Triterpenoids	($C_{30}H_{48}$)	Actein, Ginsenoside
Tetraterpenoids (carotenoids)	($C_{40}H_{64}$)	B-Carotene, Lycopene
Polyterpenoids	$(C_5H_8)_n$	Natural rubber

TABLE 2: HEPATOPROTECTIVE ACTIVITY OF THE MEDICINAL PLANTS

S. no.	Common Name	Botanical Name	Family	Model of Hepatoprotective Drug	Active Constituent	Plant Part used
1	Indian Rhododendron [35]	*Melastoma malabathricum L.*	(Melastomataceae)	Paracetamol-induced liver toxicity in rats.	Flavonoids, phenolic components	Leaves
2	Mimosa catechu, catechu, cachou, cutch tree, black cutch [36]	*Acacia catechu*	(Fabaceae)	Liver Damage Induced by Iron overload in mice	Saponins, tannins, flavonoids, phenols, alkaloidal	Heart wood
3	Kalmegh [37]	*Andrographis paniculata*	(Acanthaceae)	Against galactosamine or paracetamol induced hepatotoxicity in rats.	Terpenoids	Extract of the plant
4	Kutaki [38]	*Picorrhiza kurroa*	(Scrophulariace)	Liver against CCl4 intoxicated rats	Iridoid Glycosides	Extract of the plant
5	Sweet neem leaves, curry leaves [39]	*Murraya koenigii L*	(Rutaceae)	CCl_4 treated hepatotoxic rats	Polyphenol, girinimbine	Leaf
6	Tulsi [40-42]	*Ocimum sanctum*	(Lamiaceae)	O.sanctum, against paracetamol, CCl_4 and lead induced liver damage	Phenolic components, anti-oxidant, oleanolic acid, urosolic acid.	Whole plant
7	Haridra, Haldi [43-47]	*Curcuma longa*	Zingiberaceae	hepatoprotective activity against CCl_4 and TAA induced toxicity	Diarylheptanoids, curcumin, zingiberene, germacrone	Different extracts of C. longa, rhizomes, stems
8	Punarnava [48-52]	*Boerhavia diffusa,*	(Nyctaginaceae)	induced by paracetamol and acetaminophen	Isoflavonoids, flavonoids, flavonoid glycosides, xanthene, purine nucleoside, lignans, steroids	Roots

9	Himalayan mayapple[53]	*Podophyllum hexandrum*	(Berberidaceae)	CCl4-induced hepatotoxicityin rats	Tannins, terpenoids, alkaloids, flavonoids, phenols, steroids	Rhizome
10	Milkvetch, goat's thorn, locoweed [54]	*Astragalus kahiricus*	(Fabaceae)	Ethanol-induced liver apoptosis in rats	flavonoids, phenolic compounds	Roots
11	Wild marjoram [55]	*Origanum vulgare*	(Lamiaceae)	Carbon tetrachloride-induced hepatotoxicity in rats	Terpenoids, tannin, phenolic compounds flavonoids, saponins	Leaves
12	Cup shaped sori, little cup, cyathea[56]	*Cyathea gigantean*	(Cyatheaceae)	Paracetamol induced hepatotoxicity in rats	Phenolic compounds, tannins & flavonoids	Leaves
13	Pineapple guava, guavas teen[57]	*Feijoasellowiana*	(Myrtaceae)	3, 4-methylene dioxymethamphetamine (MDMA or ecstasy) induced liver damage	Polyphenols, carbohydrates, vitamin A	Fruits peel
14	Kokum [58]	*Garcinia Indica*	(Clusiaceae)	Ethanol-induced hepatotoxicity in rats	Xanthones, flavonoids, benzophenones, lactones & phenolic acids	Fruit rind
15	sacred fig, Bo-Tree, Pippal[59]	*Ficus religiosa*	(Moraceae)	Isoniazid rifampicin& paracetamol-induced hepatotoxicity	Flavonoids	Leaves
16	Sunset musk mallow, sunset hibiscus, hibiscus Manihot[60]	*Abelmoschus Manihot (L.) Medic*	(Malvaceae)	Carbon tetrachloride (CCl_4) induced hepatocyte damage	Total Flavonoids	Flowers
17	Gum Arabic tree, Babul, Kikar[61]	*Acacia nilotica Linn*	(Fabaceae)	Acetaminophen-induced hepatic damage in Wistar rats	Carbohydrate cardiac glycoside, saponin, tannins	Aerial parts
18	wild carrot, bird's nest, bishop's lace, Queen [62]	*Daucus carota*	(Apiaceae)	Thioacetamide induced Oxidative stress in rat liver	Monoterpenoids, flavonoids, quercetin, limonene	Seeds
19	Lelom leaves, Lelompata[63]	*Premna esculenta Roxb.*	(Verbenaceae)	CCl_4-induced liver toxicity in rats.	Polyphenols, flavonoids	leaves
20	Veldt Grape or Devil's Backbone [64]	*Cissus quadrangularis*	(Vitaceae)	Rifampicin-induced hepatotoxicity in rats.	β-carotene	Stem
21	Oleander [65]	*Nerium oleander*	(Apocynaceae)	$CCl_{(4)}$-induced hepatotoxicity in rats	Terpenoids, cardiac glycosides, tannin, flavonoids, saponins, phenolic	Flower
22	Rose mallow, bharadwaji, bankapas [66]	*Hibiscus vitifolius Linn.*	(Malvaceae)	Anti-tubercular drug-induced hepatotoxicity in rats	Flavonoids, phenolic compounds	Roots
23	Sweet neem leaves, curry leaves [67]	*Murraya koenigii L.*	(Rutaceae)	CCl_4 treated hepatotoxicity in rats	Polyphenol	Leaf
24	Yellow Berried Nightshade [68]	*Solanum xanthocarpum*	(Solanaceae)	CCl_4-induced liver injury in rats.	Steroidal alkaloid, Solasonine, fatty & resinous substances	Fruits
25	Chiretta [69]	*Swertiachirayita*	(Gentianaceae)	Paracetamol induced hepatotoxicity in Swiss albino mice	Tannins, glycosides	Whole plant
26	Cilantro, Chinese parsley or dhania [70]	*Coriandrum sativum (Linn.)*	(Apiaceae)	carbon tetrachloride (CCl_4) induced hepatotoxicity	Alkaloids, phenolic compound, flavonoids, isoquercetin, quercetin	Whole plant
27	Conkerberry or Bush Plum, Currant Bush [71]	*Carissa opaca*	(Apocynaceae)	CCl_4-induced damage in rat	Flavonoids,tannins, terpenoids, alkaloids, anthraquinones & cardiac glycosides	Leaves
28	GendaPhul (Marigold) [72-73]	*Tageteserecta Linn*	(Compositae)	Targetserecta against Carbon tetrachloride-induced hepatic damage in rats	Quercetagetin, glucoside, quercetagetin,Phenolics, syringic acid, methyl-3,5-dihydroxy-4-Methoxy benzoate, quercetin, thienyl and ethyl gallate	Flower
29	Arar [74]	*Juniperusprocera*	Cupressaceae	Against carbon tetrachloride	Diterpenes,	Bark and

				induced liver injury.	sesquiterpenes	leaves
30	Hadidi [75-77]	*Fagonia schweinfurthii*	(Zygophyllacea)	Carbon tetrachloride(CC_{l4}) induced hepatotoxicity in HepG2 cell line and rats.	Flavonol glycosides and terpenoid glycosides	Whole plant
31	Almecega, breubranco[78-80]	*Protium heptaphyllum*	(Burseraceae)	Against acetaminophen-induced liver injury in mice	triterpenoids like oleanolic acid, ursolic acid, hederin, and glycyrrhizin	trunk wood resin
32	Bee Sting Bush 81	*Azima tetracantha*	(Salvadoracaee)	Paracetamol induced	Flavonoids, triterpenoids	Leaves
33	Bitter leaf [82-84]	*Vernonia amygdalina*	(Compositae)	Against acetaminophen-induced hepatotoxicity and oxidative stress in mice *in-vivo.*	Terpenoids	Leaf extract
34	Christmas tree [85]	*Alchornea cordifolia*	(Euphorbiaceae)	Carbon tetra chloride-induced hepatic damage in rats	Alkaloids, flavonoids, saponins and tannins	Leaves
35	Abuta, velvet leaf[86]	*Cissampelos pareira*	(Menispermacea e)	Carbon-tetra chloride induced hepatic damage	Alkaloids, essential oil, sterol, leno	Roots
36	Sweetgum [87-88]	*Liquidambar styraciflua L.*	(Altingiaceae)	CCl_4-induced hepatic damage in rats,	Triterpenoids	Leaves
37	Celery [89-91]	*Apium graveolens L.*	(Umbelliferae)	against $CC1_4$-induced hepatotoxicity in albino rats.	flavonoids, phenolic compounds, betacarotene, vitamin C, sesquiterpene	Seeds
38	Sickle bush, Bell mimosa, Chinese lantern tree [92]	*Dichrostachys cinerea*	(Fabaceae)	CCL_4 induced hepatotoxicity	Flavonoids, polyphenols, tannins	Leaves
39	Grains of Paradise, Melegueta pepper [93]	*Aframomummele gueta*	(Zingiberaceae)	Ethanol-induced Liver toxicity in male Wistar rats	Alkaloids, tannins, saponin, steroids, cardiac glycoside, flavonoid, terpenoids	Whole plant
40	Jiwanti[94]	*Leptadenia reticulata (Retz.)*	(Asclepiadacea)	Carbon tetrachloride-induced hepatotoxicity in rats	Glycosides, flavonoids, tannins, phytosterols, phenolic	Stems

Active Compound Terpenoids used for Hepatoprotective Activity:

1. C-Methylflavone: It is obtained from the dried herb *Boerhavia diffusa* belongs to the family (Nyctaginaceae). It contains the phenolic compounds, anthocyanin, antho-xanthin, flavonoids, and so on. Flavones have been shown to have a wide range of biological and pharmacological activities are *in-vitro* studies. Examples include are anti-bacterial, antifungal, anti-viral, antioxidant, anti-microbial, anti-cancer, anti-diarrheal, hepato-protective, antiinflam-matory, anti-allergic activities [95-96]. The structure of C- Methyl flavone is given in **Fig. 1**.

2. Borhavine: It is obtained from the *Boerhavia diffusa* belongs to the family (Nyctaginaceae). It is used in Ayurveda of anti-diabetic, diuretic, anti-fibrinolytic agent, anti-inflammation, jaundice, dyspepsia, and diuretic properties [97]. The structure of Borhavine is given in **Fig. 2.**

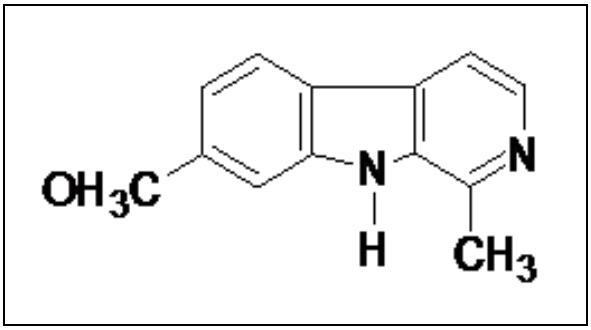

FIG. 1: CHEMICAL STRUCTURE OF BORHAVINE

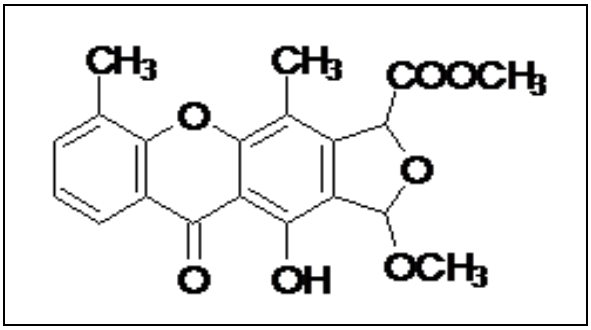

FIG. 2: CHEMICAL STRUCTURE OF C-METHYLFLAVONE

3. Kutkoside: The drug found dried roots and rhizomes of *Picrorhiza kurroa* Royle belongs to the family (Scrophulariaceae). Uses of these drugs are hepatoprotective activity, anti-inflammatory, bitter tonic, stomachic, purgatives preparations, jaundice, hepatitis, and picrorhiza as an antidote for dog-bite [98]. The structure of kutakoside is given in **Fig. 3.**

4. Kutkin: It is obtained from the *Picrorhiza kurroa* belongs to the family (Plantaginaceae). It contains a bitter glycoside that contains two C-9 iridoid glycosides Picrosidei and kutakoside. It is used in the treatment of digestive problems, liver damage, cirrhosis, wound healing, vitiligo, and so on. The structure of kutkin is given in **Fig. 4**.

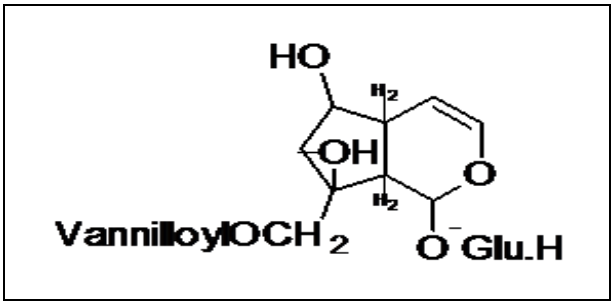

FIG. 3: CHEMICAL STRUCTURE OF KUTKOSIDE

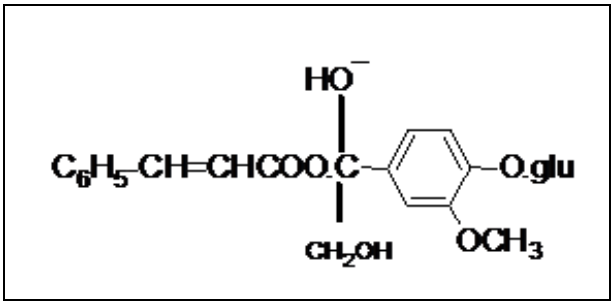

FIG. 4: CHEMICAL STRUCTURE OF KUTKIN

5. Beta-Eudesmol: It is the dried rhizome of Atracyclodeslanceae that belongs to the family (Asteraceae) [99]. β. Eudesmol consists of monoterpenoids, phenolic acids, steroids, and the major constituents include are atractylodin (14%), Beta- eudesmol (6%), hinesol (1%). Other minor constituents include are atractyloside, atractyloquinone, atractylochromene [100-101]. Uses of the β. Eudesmol is hepatoprotective, night blindness, optic atrophy, to relieve stagnant liver, reducing stress and relieving depression. The structure of beta-eudesmol is given in **Fig. 5**.

6. Andrographolide: Andrographolide consists of leaves or entire aerial parts of *Andrographis paniculata* Nees. Belongs to the family (Acanthaceae). It consists a diterpene lactone, andrograpanin, flavonoids, and phenols. And the roots of kalmegh consist of monohydroxy-trimethyl flavone, panicolin, 5-hydroxy tetra-methoxy flavone, and it is used in febrifuge, anthelmintic, astringent, anodyne, and it is useful in debility, cholera, piles, immune-modulator and jaundice [102]. The structure of andrographolide is given in **Fig. 6.**

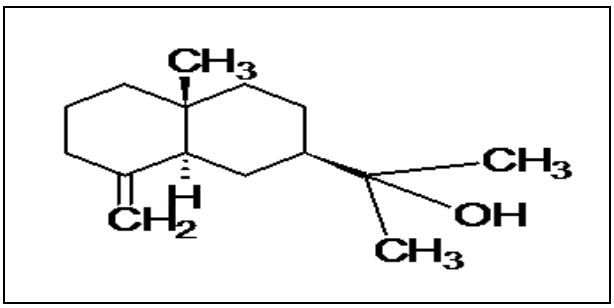

FIG. 5: CHEMICAL STRUCTURE BETA-EUDESMOL

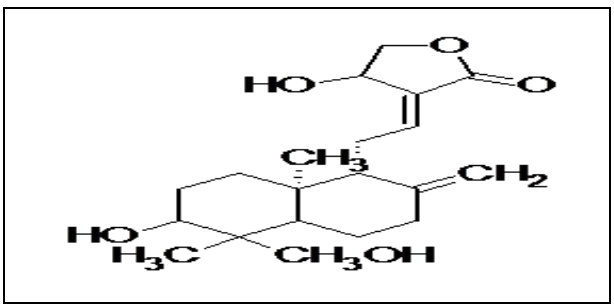

FIG. 6: CHEMICAL STRUCTURE OF ANDROGRAPHOLIDE

7. Andrograpanin: Andrograpanin is a minor compound of *Andrographis paniculata* belong to the family (Acanthaceae).

Andrograpanin consists of diterpene lactone, poly-phenols, flavonoids, triacylglycerol's, lupeol and it is used in the anti-inflammatory, anti-infectious function, cold, fever, and diarrhea. The structure of andrograpanin is given in **Fig. 7**.

8. *Lindera strychnifolia*: It is obtained from the roots of *Lindera aggregate* belonging to the family (Lauraceae). L. strychnifolia consists of sesqui-terpenes lactones, hydrocarbons, alkaloids, hydroxyi sogerma furen olide, lindenone, lauro-litsine. It is used in the hepatoprotective, anti-inflammatory, antioxidant, anti-cancer activity for lungs [103]. The structure of lindera strychnifolia is given in **Fig. 8.**

9. Cucurbitacin: It is obtained from the fruit of Cucurbita pepobelong to the family (Cucurbitaceae). It consists of triterpenes, alkaloids, flavonoids, palmitic, oleic acid and linoleicacid, 5-hydroxytryptophan, cucurbitacin. These are useful in the anti-inflammatory, analgesic, urinary disorders, anti-ulcer, hepato-protection, anti-oxidant, antidiabetic [104-105]. The structure of cucurbitacin is given in **Fig. 9.**

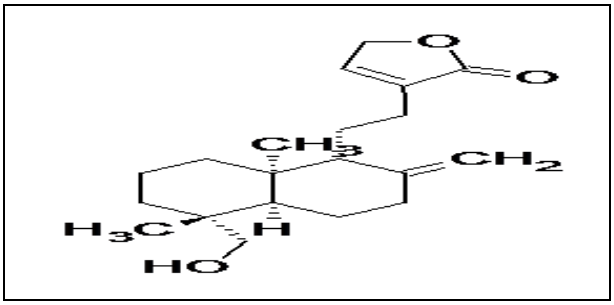

FIG. 7: CHEMICAL STRUCTURE OF ANDROGRAPANIN

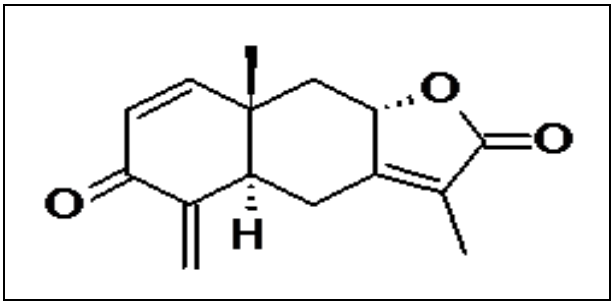

FIG. 8: CHEMICAL STRUCTURE OF *LINDERA STRYCHNIFOLIA*

10. Secologanin: It is obtained from the genus of flowering plant Ecballium elaterium belong to the family (Cucurbitaceae). Secologanin consists of triterpenoids glycosides, proteins, lipids, glycosyl cucurbitacin. It is used in the treatment of epilepsy, treatment of malaria, rhinosinusitis, prevention of CCl_4-induced hepato-toxicity, abortifacient, immunomodulator. The structure of Secologanin is given in **Fig. 10**.

11. Ursolic Acid: Ursolic acid is present in many plants such as Mirabilis Jalapa belongs to the family (Nyctaginaceae). It consists of pentacyclic triterpenoids hydroxy monocarboxylic acid, oleanolic acid, betulinic acid.

It is used in beneficial effects, which include anti-inflammatory, anti-oxidant, anti-apoptotic, anti-carcinogenic.

Ursolic acid can be used in the treatment and prevention of obesity, diabetes, cardiovascular disease, brain disorder, and liver disease. The structure of ursolic acid is given in **Fig. 11.**

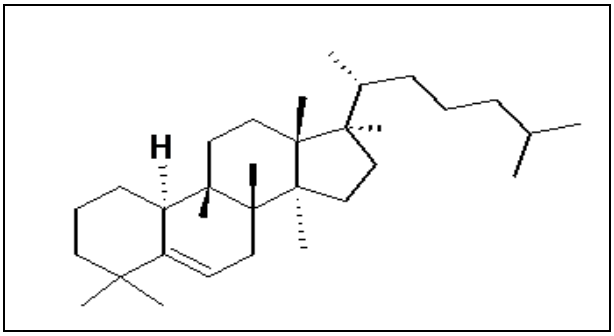

FIG. 9: CHEMICAL STRUCTURE OF CUCURBITACIN

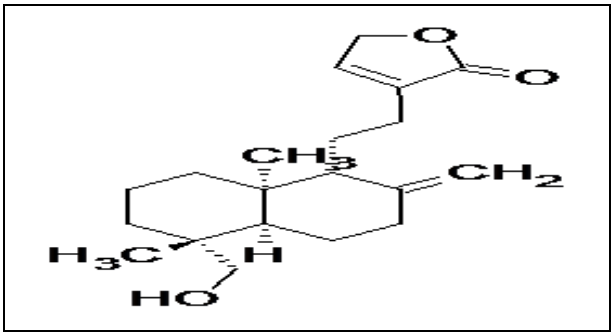

FIG. 10: CHEMICAL STRUCTURE OF SECOLOGANI

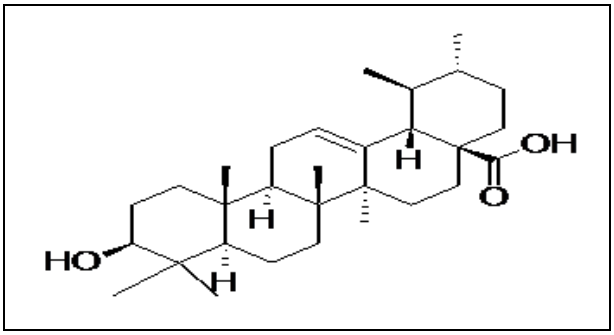

FIG. 11: CHEMICAL STRUCTURE OF URSOLIC ACID

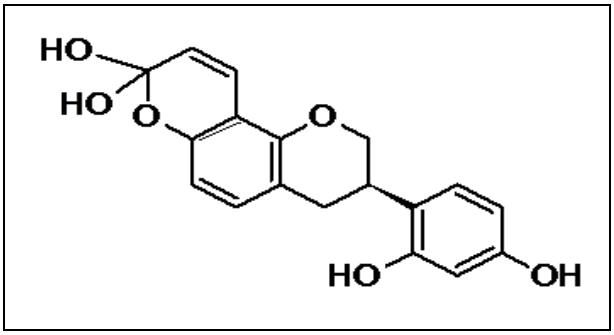

FIG. 12: CHEMICAL STRUCTURE OF GLABRIDIN

12. Glabridin: It is obtained from the extract of the unpeeled root of *Glycyrrhiza glabra* belong to the family (Leguminosae). It consists of triterpenoids, saponin glycosides, coumarins, flavonoids, isoliquiritigenin, and it is used in the demulcent, expectorant, anti-inflammatory, spasmolytic agent, hepatitis C and psoriasis [111-112]. The structure of glabridin is given in **Fig. 12.**

13. Glabrene: It is obtained from the roots of *Glycyrrhiza glabra* belong to the family (Fabaceae). Glabrene is used in the treatment of hepatitis C, Eczema, stomach infection and ulcers and so on. The structure of glabrene is given in **Fig. 13**.

14. Harmine: It is obtained from seeds of *Peganum harmala* L. belongs to the family (Zygophyllaceae). It consists of triterpenoids, flavonoids, monoamine oxidase inhibitors, alkaloids. It is used in the psychoactive effect, inhibits the formation of bone-resorbing cells, antitumor, antidiabetic, hepatoprotective, Parkinson's disease, anti-microbial [113-115]. The structure of harmine is given in **Fig. 14**.

15. Harmaline: It is an alkaloid from *Passiflora incarnate* belong to the family (Nitrariaceae).It consists of alkaloids, Beta-carbolines, saturated fatty acid, tetra decanoic acid, tridecanoic acid, hexadecanoic acid, and so on. Harmaline is used in the analgesic, emmenagogue, abortifacient and anthelminthic, anti-tumor. The structure of harmaline is given in **Fig. 15**.

16. Iridomyrmecin: It is obtained from the plant of *Actinidia polygama* belong to the family (Actinidiaceae). Iridomyrmecin consists of alkaloids, iridoids, crocetin, glycosides.

It is used as an antioxidant, to reduce swelling, constipation, gallbladder diseases, high cholesterol, high blood pressure, bladder infection, wound healing, swelling of the pancreas, rheumatoid arthritis [116]. The structure of Iridomyrmecin is given in **Fig. 16**.

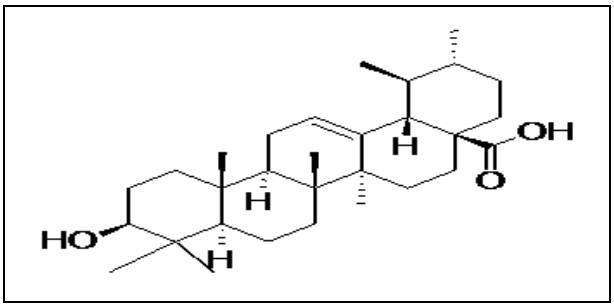

FIG. 13: CHEMICAL STRUCTURE OF GLABRENE

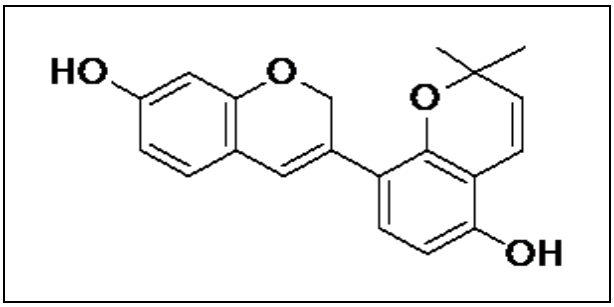

FIG. 14: CHEMICAL STRUCTURE OF HARMIN

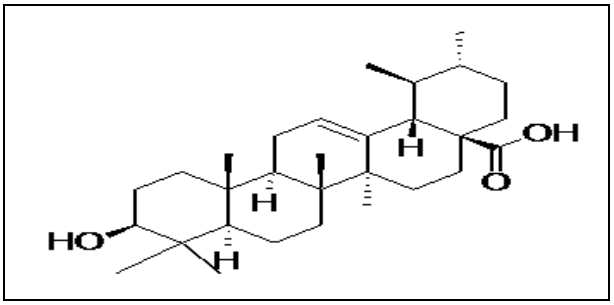

FIG. 15: CHEMICAL STRUCTURE OF HARMALINE

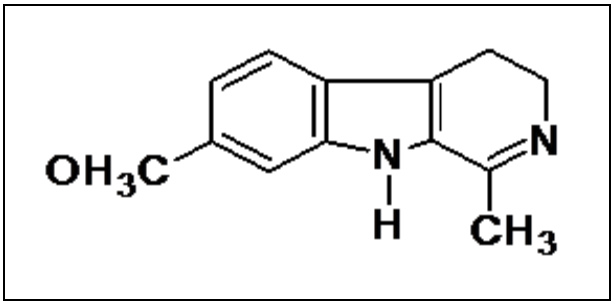

FIG. 16: CHEMICAL STRUCTURE OF IRIDOMYRMECIN

17. Genipin: It is obtained from the fruit of Gardenia jasminoides belong to the family (Rubiaceae). Genipin is an excellent natural cross-linker for proteins, collagen, and gelatin, and it is used in the treatment of cholestasis and hepatitis, wound dressing, jaundice, and so on [117] the structure of Genipin is given in **Fig. 17**.

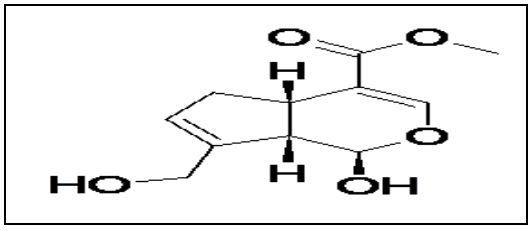

FIG. 17: CHEMICAL STRUCTURE OF GENIPIN

CONCLUSION: The present study synthesized the most accurate evidence for the hepatoprotective effects of some plants, fruits, and natural resin against different toxic compounds that cause hepatic damage. In general, this article identified and provided evidence of some phytochemicals with hepato-protective activity; the mechanism of action was related to their antioxidant potential and evaluated to determine their safety of the hepatoprotective activity. Now a day terpenoids get very important in the field of phytochemistry. Terpenoids act as antioxidants, and allopathic agents are used in hepatoprotection. Several leads obtained from terpenoids containing plants potential hepatoprotective agents, andro-grapholide, silymarin, oleander, Daucus carota, wild marjoram have been established to have potent hepatoprotective properties. Andro-grapholide is very effective on the treatment of hepatitis, jaundice, liver failure. Despite inspiring data on the possibility of discoveries in the future, evidence on the treatment of chronic liver diseases by natural medications is not sufficient. Therefore, medications discovered from natural sources should recommend to conducted more clinical trials. More confidence, better training, and little bit awareness for the natural medicine are necessary for both patients and physicians.

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