3. REVIEW OF LITERATURE
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Though liver diseases are among the important diseases affecting mankind, no remedy is available for the majority of them at present. However, a number of medicinal plant preparations have been advocated in traditional systems of medicine, especially in ayurveda for treating liver diseases. Their usage has been in vogue for centuries and they are often claimed to offer significant relief. In spite of such widespread use, interest in hepatoprotective activity kindled, especially outside India, only after the publication of the report\textsuperscript{126,127}, on the isolation of silymarin, a flavonolignan, from \textit{Silybum marianum} and its efficacy as a hepatoprotective agent.

\textit{Cynara scolymus} in the form of a decoction was used in the middle ages against jaundice and dropsy. The chief active constituent, cynarin, was isolated and identified as 1,5 dicafeoylquinic acid by Pannizzi and Scarpati\textsuperscript{123}. In fact, in the plant it is present as 1,3 dicafeoylquinic acid, which becomes transesterified to the 1,3 decaffeoyl isomer during extraction\textsuperscript{128}. According to Gaudin\textsuperscript{129}, \textit{Cynara} extract possesses antihepatotoxic activity, which is why it was recommended by Oudot\textsuperscript{130} as a preventive against liver damage. Maros\textsuperscript{131} \textit{et al} proved that an aqueous leaf extract accelerated the increase in weight of the liver, showed pronounced hyperaemic activity, and caused a significant increase in the number of binuclear hepatocytes and the RNA level. In addition, cynara extract is choleric, diuretic and antilipaemic.

Adzet\textsuperscript{132} \textit{et al} have reported hepatoprotective activity in cynarin, a polyphenolic compound, isolated from \textit{Cynara scolymus} against \textit{CCl}_4 and Gal-N induced cytotoxicity in primary cultured rat hepatocytes.

The bark of \textit{Aphanamyxis polystachya} is claimed to be useful in liver and spleen
diseases, tumors and for abdominal complaints, in the indigenous system of medicine\textsuperscript{133}. It is one of the components of many marketed preparations for liver diseases in India\textsuperscript{134}. The ethyl acetate soluble fraction of the alcoholic extract of \textit{A. polystachya} stem bark was studied for its antihepatotoxic action after CCl\textsubscript{4} challenge in rats. This fraction (0.6g/kg oral) induced a marked reversal of liver injury to the normal state, monitored by measurement of enzyme levels and histopathological studies\textsuperscript{135}.

\textit{Eclipta alba} (L) Hassk. is principally used as a tonic and deobstruent in hepatic and splenic enlargements, and in various chronic skin diseases\textsuperscript{136}. As an ayurvedic drug it has been reported to be promising in the treatment of infective hepatitis in adults and children\textsuperscript{137}. A liquid extract from the fresh leaves of \textit{E. alba} has been shown to be effective in preventing CCl\textsubscript{4} induced liver damage in guinea pigs\textsuperscript{138}. The coumestans wedelolactone and desmethyl wedelolactone isolated from this plant exhibited antihepatotoxic activity in assays employing CCl\textsubscript{4}, galactosamine and phalloidin induced cytotoxicity in rat hepatocytes\textsuperscript{139}. The fine powder from the dried aerial parts of this plant has also been reported to possess antiinflammatory and antihepatotoxic activity in rats\textsuperscript{140}. An alcoholic extract of freshly collected \textit{Eclipta alba} exhibited dose dependent (62.5-500 mg/kg) and significant hepatoprotective activity against CCl\textsubscript{4} induced liver injury in rats and mice\textsuperscript{141}.

The herb of \textit{Phyllanthus niruri} (Fam. Euphorbiaceae) is reported to possess astringent, deobstruent, stomachic, diuretic, febrifugal and antiseptic properties\textsuperscript{142}. Phyllanthin and hypophyllanthin from hexane extract of \textit{P. niruri} were reported to prevent CCl\textsubscript{4} and galactosamine liver damage in primary cultured rat hepatocytes\textsuperscript{143}.

The fresh juice of the leaves of \textit{R. communis} is reported to be used as an emetic, in narcotic poisoning and is considered useful in jaundice\textsuperscript{144}. The crude extract and its
butanol soluble fraction has been reported to afford significant protection to rats against Gal-N induced hepatic damage\textsuperscript{145}. Subsequent chromatographic fractionation led to the isolation of two active fractions which in turn yielded two pure compounds, ricinine and N-demethyl ricinine. The latter was found to be more active as it reversed the biochemical changes produced by galactosamine at a dose of 6 mg/kg for 7 days. It demonstrated an anticholestatic effect against paracetamol induced cholestases\textsuperscript{145a}.

From a pharmacological and clinical standpoint, the best studied plant substances are the flavonolignans of Silybum marianum. The antihepatotoxic constituent, silymarin, is a mixture consisting chiefly of silybin, with silydianin and silychristin\textsuperscript{118-122}. The three compounds are isomeric and differ only in the linkage of the taxifolin moiety to coniferyl alcohol. Since the compounds of the silymarin complex show a high specificity for the liver, several attempts have been made to synthesize the main component, silybin\textsuperscript{146-148}. Silymarin and silybin have been tested in a large number of model liver damage systems\textsuperscript{149,150}. In almost all systems, the protective effect was highly significant. Particularly impressive was the demonstration of an antagonism against $\alpha$-amanitin and phalloidin, the otherwise fatal toxins of the death cap fungus\textsuperscript{151,152}. When administered prophylactically before phalloidin poisoning silymarin is 100\% effective in preventing the toxicity of phalloidin. Even when administered upto 10 minutes after phalloidin, silymarin can completely counteract the toxic effects. The same antagonising effect was also observed with $\alpha$-amanitin. Thus silymarin is hitherto the only known "broad spectrum antiamanitic" being active against phallotoxins and amatoxins\textsuperscript{153}. The action of silymarin is due to the protection of intact liver cells or cells not yet irreversibly damaged by acting on the cell membrane and the stimulation of protein synthesis, which causes an increase in the production of new liver cells\textsuperscript{154}.
(+)-Catechin is another antihepatotoxic natural product introduced for therapeutic purposes. There are two different stereoisomeric and diastereoisomeric pairs of catechin\textsuperscript{155}. Cyanidanol - 3 (+) catechin, at a dose level of 100 mg/kg, completely antagonizes paracetamol induced liver damage in rats whereas (-) catechin does not have the same effect. This action is thought to be due to the inhibition of paracetamol binding to liver microsomal protein and a direct inactivation of the acylating activity of paracetamol. In animal experiments, catechin increases the liver ATP level or prevents the decrease of liver ATP, following the action of the liver poisons, malonic acid or DL-ethionine\textsuperscript{156}. Catechin also appears to be capable of influencing the course of alcoholic intoxication, since it largely normalizes the biochemical parameters that are affected by alcohol\textsuperscript{157}. Certain parallels can be drawn between the molecular mechanism of activity of catechin and silymarin\textsuperscript{158}.

Chinese chemists have isolated a series of lignans from the fruits of \textit{Schizandra chinensis} BAIIV and \textit{Schizandra splenanthera} of the Magnoliaceae which were used in traditional Chinese medicine as tonics and sedatives\textsuperscript{124}. These compounds contain hitherto unknown bisbenzocyclooctadiene systems, and they include the schizandrins, gomisins, schisantherins, stegans and kadsurins. For schisantherin A, however no protective effect against phalloidin poisoning could be found\textsuperscript{159,160}. Of all these compounds, schizandrin B from \textit{Schizandra chinensis}\textsuperscript{160} has been submitted to the most thorough pharmacological investigation. When administered orally before or after CCl\textsubscript{4} intoxication, it decreases the elevated SGPT value. It also markedly increases the resistance of mice against the toxic effects of digoxin and indomethacin and in partially hepatectomized mice, it leads to a rapid regeneration of the liver tissue. Two further Chinese studies showed a lowering of raised SGOT values by similarly structured schizandrins and were wuweizins A-C from \textit{Schizandra chinensis}\textsuperscript{161}. Liu\textsuperscript{162} has reported
the presence of significant hepatoprotective activity against CCl₄ induced liver injury in
a group of lignans belonging to dibenzocycloocteno group isolated from the alcoholic
extract of the kernels of *Fructus Schizandrae*.

A different lignan with similar activity has been isolated from *Thujopsis dolabrata*
(Cupressaceae)¹⁶³. The leaves of this tree were used in folk medicine as a remedy for
jaundice. This lignan is a deoxypodophyllotoxin. Both extracts and the pure compound
have been studied for their protective effect in the model CCl₄ liver damage system.

Hikino et al have screened a number of plant extracts and active principles for
hepatoprotective activity utilizing CCl₄ and galactosamine induced cytotoxicity tests in
primary cultured rat hepatocytes. In some of the studies they have attempted to elucidate
the probable mechanism of hepatoprotective activity noted with some of the isolates¹⁶⁴.
This group has reported hepatoprotective activity in desoxypodophyllotoxin isolated
*Dianthus superbus, Varcalamus herb*¹⁶⁶, glycyrrhizin analogues isolated from *Glycyrrhiza
glabra*, curcuminoids from *Curcuma longa*¹⁶⁸, extracts of *Atractylodes rhizome*,
atractylon, β-eudesmos and hinesol¹⁶⁹, methanol extract of *Wedelia chinensis herb*¹⁷⁰
and capillarisin, arcapillin, quercetin and isorhamnetin isolated from buds of *Artemisia
capillaries*¹⁷¹. In all these studies the test compounds have been studied against CCl₄
and Gal-N induced cytotoxicity in primary cultured hepatocytes.

Korean pharmacologists¹⁷² reported antihepatotoxic activity for saikosaponins
from *Bupleurum falcatum* L. in the model galactosamine liver damage system. SGOT
and SGPT values were lowered by 20 mg/kg saikosaponin both before or after injection
of D-galactosamine.

Two iridoid glycosides from *Picrorrhiza kurroa*, benzoyl and vanilloylcatalpol,
showed protective effects against liver intoxication of mice with CCl\textsubscript{4} and in choleretic activity in rats\textsuperscript{173,174}. Studies in animal models\textsuperscript{175-178} have indicated that the hepatoprotective factors are the iridoid glycosides namely kutkin present in the alcoholic extract of the root and rhizome\textsuperscript{179}. Picroliv is a standardized fraction of \textit{Picrorhiza kurroa} containing mainly a mixture of two iridoid glycosides, picroside-I and kutkoside in a fixed ratio of 1:1.5. Picroliv was identified as the active hepatoprotective constituent of the plant which possessed marked activity against a wide range of hepatotoxins including \textit{Plasmodium berghei} infection\textsuperscript{180-186}. Picroliv showed a significant dose dependent protective activity against galactosamine\textsuperscript{187} and thioacetamide induced hepatic damage in the rat, evaluated on isolated hepatocytes preparation. It enhanced the percentage of viable hepatic cells. Picroliv also antagonized the changes in the enzymes SGOT, SGPT and alkaline phosphatase produced by thioacetamide both in the isolated hepatocyte suspension as well as in serum. It was found to be more potent than silymarin, a known hepatoprotective agent\textsuperscript{188}.

Alcoholic and ether extracts of \textit{Luffa echinata} were found to protect rats against CCl\textsubscript{4} induced injury\textsuperscript{189,190}.

Anand\textsuperscript{191,192} and co workers have carried out detailed evaluation of alcoholic extract of the aerial part of \textit{Indigofera tinctoria}. The extract was found to afford significant protection to mice, rats and rabbits against CCl\textsubscript{4} induced hepatic injury.

Mangiferin, a xanthone isolated from \textit{Canscora decussata} protected rats against CCl\textsubscript{4} induced liver injury\textsuperscript{193}.

According to Singh\textsuperscript{194} \textit{et al} petroleum ether extract of \textit{Nympheastellata} provides significant protection to rats against CCl\textsubscript{4} induced functional, histopathological and morphological changes. The extract was found to promote parenchymal tissue
regeneration.

*Ocimum sanctum* also protected rats against CCl₄ induced liver injury¹⁹⁵.¹⁹⁶. It is reported to contain ursolic acid, apigenin, luteolin, apigenin-7-O-glucuronide, luteolin-7-O-glucuronide, orientin and molludistin¹⁹⁷. However, no study has been attempted to evaluate these isolates for hepatoprotective activity. The ethanol extract of *Ocimum sanctum* leaf has been reported to possess hepatoprotective effect against paracetamol induced liver damage in rats¹⁹⁸. The extract prevented paracetamol induced alterations in serum transaminase and acid phosphatase activities and in liver glutathione content. Histopathological studies confirmed the presence of hepatoprotective activity.

*Tinospora cordifolia* is reported to be effective in preventing fibrous changes in liver injury induced by CCl₄¹⁹⁹.

Kokate *et al* studied the antihepatotoxic activity of *Phyllanthus niruri*, *Tinospora cordifolia* and *Ricinus communis* in albino rats intoxicated with CCl₄. The ethanol extract of *P. niruri* exhibited statistically significant antihepatotoxic activity in terms of reduction in SGPT, SGOT and serum bilirubin contents of the CCl₄ damaged group²⁰⁰.

Alcoholic extract of the leaves of *Withania somnifera* was found to significantly inhibit the CCl₄ induced alterations in transaminase activity and pentobarbitone sleeping time thus revealing its hepatoprotective activity. This was confirmed through histopathological studies²⁰¹. A withanolide, 3-β-hydroxy-2, 3-dihydrowithanolide F, isolated from *Withania coagulans* fruits also showed significant hepatoprotective activity against CCl₄ induced liver injury. The activity was assessed by measuring pentobarbitone sleeping time, serum transaminase activity and through histopathological studies²⁰².

Lin²⁰³ *et al* have reported hepatoprotective activity in solasodine, solamargine,
solasonine and ursolic acid isolated from the fruit of *Solanum incanum* as assessed by noting their effect on CCl₄ induced alterations in pentobarbitone sleep prolongation and elevation of transaminase activity. Carpesterol, another isolate, completely prevented pentobarbitone sleeping besides lowering transaminase activity to almost normal level.

Lin and Tome²⁰⁴ found significant hepatoprotective activity with sambuculin A, isolated from *Sambucus formosana*. In the same plant β-amyrin and oleanolic acids were also isolated. A mixture of α-amyrin and β-amyrin palmitates exhibited a strong hepatoprotective effect against CCl₄ induced liver injury.

The pure active principle of the *Piper* species is the alkaloid piperine which is known to possess several pharmacological actions like antifertility effects, CNS depression, antiinflammation, inhibition of hepatic drug metabolism and enhancement in drug bioavailability²⁰⁵. Piperine, obtained from *Piper longum* and *Piper nigrum*, was evaluated for its antihepatotoxic potential in order to validate its use in traditional therapeutic formulations. This plant principle exerted a significant protection against tert-butyl hydroperoxide and CCl₄ hepatotoxicity by reducing both *in vitro* and *in vivo* lipid peroxidation, enzymatic leakage of SGPT and alkaline phosphatase, and by preventing the depletion of GSH and total thiols in the intoxicated mice. Silymarin, a known hepatoprotective drug was tested simultaneously for comparison. Piperine showed a lower hepatoprotective potency than silymarin²⁰⁶.

Kolaviron, a mixture of bioflavonoids, isolated from *Garcinia kola* was found to produce significant hepatoprotective effect against CCl₄ induced liver injury²⁰⁷. Iwu²⁰⁸ *et al* have evaluated kolaviron, and kolaflavonone, obtained from *Garcinia kola* against thioacetamide induced liver toxicity in rats by measuring thiopental induced sleeping time. Both were found to significantly shorten thiopental sleeping time indicating
significant hepatoprotective activity. Besides, they were also found to alter serum microsomal enzyme levels.

The ethanol extract of the above ground parts of *Salsola collina*, was found to provide significant protection against CCl₄ induced changes in metabolic functions and liver cytoarchitecture²⁰⁹.

Pretreatment with an aqueous extract of *Hypoestes triflora* leaves prevented CCl₄ induced prolongation of duration of barbiturate sleep revealing its presence of hepatoprotective activity. The active principle responsible for the hepatoprotective activity was reported to be benzoic acid. It prevented CCl₄ induced elevation in transaminase activity in mice²¹⁰.

Brevifolin, hyperin, ellagic acid and 3, 3', di-O-methyl-ellagic acid isolated from *Canarium album* and *Euphorbia nematocypha* were found to possess significant hepatoprotective activity. The hepatoprotective activity in these compounds has been ascribed to their antioxidative effects²¹¹.

Ethanol extract of the leaves of *Withania frutescens* has been reported to prevent CCl₄ induced alterations in pentobarbitone sleep, biochemical parameters studied and in the derangement of liver cytoarchitecture²¹².

Avadhoot²¹³ *et al* have reported significant hepatoprotective effect in the alcoholic extract of *Vitex negundo* seeds. The extract was found to significantly reverse CCl₄ induced changes in morphological, biochemical and functional parameters studied.

Chakraborti²¹⁴ *et al* have evaluated different extracts of root of *Boerhaavia repanda* for hepatoprotective activity in rats against hepatotoxicity induced by CCl₄, galactosamine (Gal-N) and paracetamol. Petroleum ether, chloroform and methanol
extracts showed significant activity against \( \text{CCl}_4 \) induced liver injury. Chloroform and methanol extracts were found to be effective against Gal-N induced hepatotoxicity. However, both extracts failed to inhibit paracetamol induced liver injury. None of the extracts of the aerial part exhibited any hepatoprotective activity against \( \text{CCl}_4 \) induced liver damage. The authors have studied both biochemical and histopathological parameters to assess hepatoprotective activity. The same workers have also reported significant hepatoprotective activity in chloroform and methanol extracts of roots and aerial parts of \textit{Boerhaavia diffusa} against \( \text{CCl}_4 \) induced liver injury\textsuperscript{215}.

Patel\textsuperscript{216} \textit{et al} have screened eleven medicinal plants for hepatoprotective activity against \( \text{CCl}_4 \) induced liver damage. Ethanol extracts of \textit{Vanda roxburghii}, flowers of \textit{Calotropis gigantea}, fruits of \textit{Quercus infectoria} and rhizomes of \textit{Curcuma longa} were found to afford significant protection.

Investigations carried out on the leaf extracts of \textit{Gymnosporia montana}\textsuperscript{217} and \textit{Paederia foetida}\textsuperscript{218} revealed the presence of hepatoprotective activity.

The hepatoprotective activity of an ethanol : water (1:1) extract of \textit{Lawsonia alba} has been studied against \( \text{CCl}_4 \) induced liver toxicity. The effects of the extract on hexobarbitone induced sleep, bromosulphalein clearance and on certain biochemical parameters indicated its protective role\textsuperscript{219}.

The alcoholic extracts of the leaves of \textit{Gymnema sylvestre} and nodular roots of \textit{Curcuma zedoaria} were found to possess hepatoprotective activity against \( \text{CCl}_4 \) induced liver damage\textsuperscript{220}.

In another set of studies, hepatoprotective activity has been reported\textsuperscript{221} in 20 (S) ginsenoside RH\textsubscript{2}, 20(R) ginsenoside RG3 and 20(S) ginsenoside -RS against \( \text{CCl}_4 \) induced cytotoxicity, 20(S) ginsenoside -RH\textsubscript{1} prosapogenin of 20(S) ginsenoside -RS.
against Gal-N induced cytotoxicity.

(-) Kaur-16-en-19-oic acid and mixture of three kaurenoids (34-angeloyloxy, 34-tiglinoxyloxy and 34-senicioyloxy-kaur-16-en-19-oic acid), isolated from *Wedelia chinensis* has exhibited significant hepatoprotective activity against cytotoxicity in primary cultured rat hepatocytes produced by both CCl₄ and Gal-N. Lignoceric acid, another isolate, produced cytotoxicity but was found inactive against the Gal-N induced cytotoxicity222.

Hepatoprotective activity has been reported in the constituents of garlic (*Allium sativum*) namely alliin, the volatile oil, S-allylmercaptocysteine and S-methyl mercaptocysteine. Hepatoprotective activity has also been reported in betulonic acid, an isolate from the fruit of *Liquidambar formosana*223.

Lauhers224 et al have reported the presence of significant hepatoprotective effect in dried hydroalcoholic extract of *Peumus boldus* against tert-butylhydroperoxide induced cytotoxicity in isolated rat hepatocytes. It also protected mice against CCl₄ intoxication (*in vitro*). Boldine the main alkaloid in the plant has been implicated for the hepatoprotective activity.

Phalloidin, a flavonoid isolated from *Baccharis trimera* was also found to possess hepatoprotective activity225.

Handa226 et al have confirmed that andrographolide, isolated from *Andrographis paniculata* possesses hepatoprotective activity. Andrographolide *per se* produces a significant dose (1.5 - 12 mg/kg) dependent choleretic effect (4.8 - 73%) as evidenced by increase in bile flow, bile salts and bile acids in conscious rats and anaesthetized guinea pigs. The paracetamol induced decrease in volume and contents of bile was
prevented significantly by andrographolide pretreatment. It was found to be more potent
than silymarin, a clinically used hepatoprotective agent\textsuperscript{39}.

Sharma\textsuperscript{227} \textit{et al} have also found hepatoprotective effect in \textit{Tephrosia purpurea}.

Roy\textsuperscript{228} and workers have reported that the aqueous extract of \textit{Phyllanthus emblica} fruit could prevent the toxic effect of lead nitrate and aluminium sulphate on liver parenchymal cells.

In an interesting study Mehrotra\textsuperscript{229} \textit{et al} have reported hepatitis B virus inactivating activity in the alcoholic extract of \textit{Phyllanthus amarus} in an \textit{in vitro} test system.

The effect of aqueous extract of carrot (\textit{Daucus carota}) was evaluated to get insight into hepatocellular antioxidant defence mechanism and lipid peroxide formation in CCl\textsubscript{4} induced acute liver injury in mice. The CCl\textsubscript{4} induced increased lipid peroxidation and decreased glutathione level were reversed towards normalization in a dose related manner following pretreatment with the extract. The extract also dose dependently reduced catalase, glutathione peroxidase, and glutathione S-transferase activity with a simultaneous elevation in the activity of glutathione reductase that were otherwise altered remarkably due to CCl\textsubscript{4} induction. These results indicate a possible hepatoprotective role of carrot extract against oxidative damage\textsuperscript{230}.

The protective effect of \textit{R. sativus} (radish) juice against paracetamol hepatotoxicity was investigated by Popovic\textsuperscript{231} \textit{et al}. Combined treatment with radish juice and paracetamol induced decrease of body temperature, hematocrit, glutathione content, and lipid peroxidation in comparison to the radish juice pretreatment. Radish juice pretreatment did not significantly change the examined parameters. However, some beneficial effects of radish juice in acute liver injury caused by paracetamol can
be assumed.

The free radical scavenger, antihepatotoxic and membrane stabilising activities of the ethanol extract and fractions of *Rosmarinus tomentosus* were studied. Pretreatment with an ethanol extract of *R. tomentosus* caused an important decrease in the CCl₄ induced toxicity in rat liver, made evident by its effects on the levels of SGPT and bilirubin in the serum and the malondialdehyde concentration in the liver. These effects are similar to those produced by silymarin. The chloroform fraction showed the greatest antihepatotoxic activity and the ethyl acetate fraction the greatest free radical scavenger activity.

Rusu et al studied the effects of *Chrysanthemum balsamita* hydroalcoholic extract administered to CCl₄ intoxicated rats, for a period of seven days. The extract produced some positive effects, such as decrease of liver steatosis and of serum transaminase levels.

The methanol fraction of the extract of *Pluchea indica* roots exhibited significant hepatoprotective activity against experimentally induced hepatotoxicity by CCl₄ in rats and mice. The extract caused significant reduction of the elevated serum enzyme levels (AST, ALT, LDH and serum alkaline phosphatase) and serum bilirubin content in acute liver injury. A significant increase of reduced serum, total protein, albumin and albumin globulin ratio was also observed on treatment with the extract. The extract significantly reduced the prolonged pentobarbitone induced sleeping time and also caused a significant reduction of plasma prothrombin time in comparison with CCl₄ treated animals. The extract caused significant reduction of the increased bromosulphalein retention by CCl₄ treatment. These findings are suggestive of a potent hepatoprotective effect of the extract.
The methanol extract of the roots of *Ampelopsis brevipedunculata* var. hancei exhibited marked protective activity against CCl₄ and D- galactosamine induced liver damage in primary cultured rat hepatocytes. Ampelopsin-E and cis ampelopsin-E obtained by fractionation showed antihepatotoxic activity²³⁵.

The liver protective effects of the water extracts of the aerial parts of *Tithonia diversifolia* and *Dicliptera chinensis* against acute hepatic damage induced by CCl₄ were determined in rats. The results indicated that treatment with a water extract of the aerial part of *T. diversifolia* decreased the SGOT, SGPT level elevation caused by CCl₄. The pathological changes of hepatic lesions caused by CCl₄ were improved by treatment with the drug extracts mentioned above²³⁶.

The aqueous extract of the leaves of *Combretum glutinosum* has been reported to be active against hepatic disease and hepatitis B²³⁷.

The effect of the *Mikania cordata* (chloroform root extract of) was evaluated in mice. Single administration of CCl₄ was used as a model for liver injury. Total lipids in liver, triglyceride content in serum and liver and cholesterol level in serum and its different lipoprotein fractions were used as markers for functional efficacy of the liver cells. Results indicated that the *M. cordata* root extract seemed to show some promising activities in recovering the damage caused in liver tissue by CCl₄²³⁸.

Hepatoprotective effect of the ethanol extract of the aerial parts of *Tridax procumbens* and its chloroform soluble and insoluble fractions were studied in acute hepatitis induced in rats by a single dose of CCl₄. Hepatoprotective activity was monitored by estimating serum transaminases, serum alkaline phosphatase, serum bilirubin and serum albumin. Only the ethanol extract and the chloroform insoluble fraction exhibited activity²³⁹.
Plate-1: *Thespesia populnea*, a large compact evergreen tree found in the coastal areas.

Plate-2: *Thespesia populnea*, a branch showing yellow flowers
Plate-3: *Lagenaria siceraria*, a creeper with long petioled 5-lobed leaves and bottle-shaped fruits.

Plate-4: *Capparis spinosa*, a loosely spreading spiny shrub or bush.
Plate-5: *Solanum nigrum*, a herbaceous or suffrutescent weed.
THESPESIA POPULNEA

Thespesia\textsuperscript{240} Soland. ex Correa (Malvaceae) consists of a small genus of trees and shrubs, distributed in the tropics of the world.

T. Populnea Soland. ex Correa also known as the Portia Tree, Umbrella Tree, Indian Tulip Tree, False Rosewood is a compact quick-growing, evergreen tree, 18 m in height and 1.2 m in girth, with 2.5 m clear bole, commonly found on the coasts of India and the Andamans. Bark grey to brown, fissured, often knobby, fibrous, about 4 mm thick; leaves cordate-ovate, dark green, 7-15 cm long; flowers yellow with purple base, completely changing to purple when about to wither, 5-7.5 cm; capsules brown, globose or oblong, 2.5 cm x 4 cm, with persistent calyx; seeds pilose or powdery on the surface, flat, egg-shaped.

The tree is largely cultivated for ornament and shade, and it blooms throughout the year in the tropics. It can grow everywhere including saline soils, except in hilly areas, but prefers light and porous soils. It thrives in moist and warm situations, but can withstand temperatures as low as -4°C.

The bark, leaves, flowers and fruits are reported to be useful in cutaneous affections, such as scabies, psoriasis, ringworm, guineaworm and eczema. The yellow juice of fruits is employed in treating certain herpetic diseases. A decoction of the bark is given internally in the diseases of skin, and that of the fruits as an antidote for poisoning. The fruits contain a principle which is active against both Gram-positive and Gram-negative bacteria; this principle is remarkably active against enterobacteria, and is promising for exploitation as a cure in intestinal disturbances. The seeds yield a deep-red, thick fatty oil which is also used in cutaneous diseases. A compound oil of the bark and capsule is useful in urethritis and gonorrhoea. The astringent bark, roots
and fruits are stated to be used in dysentery, cholera and haemorrhoids; the mashed bark is employed as a poultice or hot fomentation for wounds.

The young buds and leaves have a pleasant taste and along with the flowers are eaten either raw, cooked or fried in butter. The leaves are reported to be employed as a local application to inflamed and swollen joints. The extracts of leaves are active against *Micrococcus pyogenes* var. *aureus* and *Escherichia coli*. The root is reported to be toxic. The seeds possess purgative properties. The plant has been shown to be effective in malaria. The pollen may cause allergy.

The ethanol extract of fruits showed activity against Ranikhet disease virus and also anticancer activity against Lewis lung-carcinoma in mice.

The flowers of *Thespesia populnea* have been investigated many times in the past with reference to the polyphenolic components present\(^{241-243}\). When the material is extracted in succession with petroleum ether, acetone and alcohol, the flavonoids as aglycones and glycosides are found largely in the alcoholic extract\(^{244}\). The isolation of the glycoside populnin (kaempferol 7-glucoside), its aglycone populnetin (kaempferol) and a third pigment, identical with herbacetin has been reported earlier from the petals and flowers\(^{245,246}\). However another report mentions the complete absence of herbacetin or gossypetin from the flowers, but the presence of quercetin, quercetin-3-glucoside, kaempferol-5-glucoside, kaempferol-7-glucoside, kaempferol-3-rutinoside and rutin\(^{244}\).

The petroleum ether extract of the flowers contains dextrorotatory gossypol as its main constituent\(^{247}\). Other components isolated from this fraction include nonacosane, lupenone, myricyl alcohol, lupeol, \(\beta\)-sitosterol and \(\beta\)-sitosterol \(\beta\)-D-glucoside\(^{248}\).
LAGENARIA SICERARIA

Lagenaria\textsuperscript{249} Ser. (Cucurbitaceae) is a monotypic genus found growing wild in the warmer parts of the world. It is cultivated in India for its fruits which are used as vegetables.

\textit{L. siceraria} (Mol.) Standl. syn. \textit{L. leucantha} Rusby; \textit{L. vulgaris} Ser. Bottle Gourd or Calbash Gourd is a large pubescent, climbing or trailing herb, with stout 5-angled stems and bifid tendrils, found throughout India, either wild or cultivated. The leaves are long-petioled, 5-lobed with large, white, solitary, monoecious or dioecious flowers; fruits are large, upto 1.8 m long, usually bottle or dumb-bell-shaped and are almost woody when ripe; the seeds are numerous, long, white, smooth, 1.6-2 cm long and horizontally compressed with a marginal groove.

\textit{L. siceraria} is a popular vegetable grown almost all the year round, particularly in frost-free areas. It can be cultivated in all kinds of soil, but thrives best in heavily manured loams. It requires a warm humid climate or plenty of watering when grown during dry weather.

The young and tender fruits are eaten as vegetable. The flesh is soft, spongy and insipid when young; it is somewhat bitter when old. Analysis of the edible portion of the fruit gave the following values: moisture 96.3; protein 0.2; fat (ether extract) 0.1; carbohydrates 2.9; mineral matter 0.5; calcium 0.02; and phosphorus <0.01%. Other mineral elements reported to be present are: iron (0.7 mg/100g) sodium (11 mg/100g), potassium (86 mg/100g) and iodine (4.5 \(\mu\)g/kg). Glucose and fructose have been detected. The amino acid composition of the fruit is as follows: leucine 0.8; phenylalanine 0.9; valine 0.3; tyrosine 0.4; alanine 0.5; threonine 0.2; glutamic acid 0.3; serine 0.6; aspartic acid 1.9; cystine 0.6; cysteine 0.3; arginine 0.4; and proline 0.3
The fruit is a good source of B vitamins and a fair source of ascorbic acid. The edible portion contains: thiamine 44 μg; riboflavin 23 μg; niacin 0.33 mg; and ascorbic acid 13 mg/100 g.; it contains 16.02 mg/g (dry basis) of choline.

The fruit is rich in pectin. Bitter fruits yield 0.013% of a solid foam containing cucurbitacins B, D, G and H, mainly cucurbitacin B (C_{32}H_{48}O_{8}, m.p. 184-186°C); these bitter principles are present in the fruit as aglycones. Leaves contain cucurbitacin B, and roots, cucurbitacins B, D and traces of E. The fruit juice contains β-glycosidase (elaterase). An investigation has been made of elaterase, a relatively specific enzyme for the hydrolysis of the bitter principle glycosides of the Cucurbitaceae. A comparative study covering 33 different species showed that this enzyme is widely spread in this family. Elaterase has been isolated from the fruit and its action on various other glycosides was determined.2\textsuperscript{50}

The seeds are edible. They are reported to contain a saponin. \textsuperscript{13}CNMR spectroscopy of the sterols isolated from the seeds of bottle gourd has demonstrated the co-occurrence of the C-24 epimers spinasterol and chondrillasterol.\textsuperscript{251} The sterol constituents of 32 seeds and mature plant (leaves and stems, pericarp of the fruit and roots) materials from the 12 genera of the Cucurbitaceae were investigated and 44 sterols were identified or newly characterised. Plants which yield non-bitter fruits contain no bitter principles or elaterase.

The presence of steroidal sapogenins in leaves has been reported from Philippines\textsuperscript{249}. The fruit pulp around the seeds is considered emetic as well as purgative; it is given to horses. It is cooling, diuretic and antibilious and applied externally in delirium. The juice of the fruit mixed with lime juice is used as an
application for pimples; boiled in oil it is used for rheumatism; the leaf juice is used for baldness. The seeds are used in dropsy and as an anthelmintic; the root is also used in the treatment of dropsy. The seed oil is applied externally in headaches. The prickly cortex of the vine and flowers are regarded as counterpoisons.

**CAPPARIS SPINOSA**

*Capparis* Linn. (Capparidaceae) consists of a large genus of about 270 species of trees and erect, prostrate or climbing shrubs, distributed throughout the warm regions of the earth. About 40 species occur in India of which a few are of economic importance.

*C. spinosa* Linn., the Caper Bush is a small, prostrate shrub found on rocky and hilly localities in the Deccan peninsula, Rajputana and north western India.

Commercial European capers are the flower buds of *C. spinosa*. They have an acrid, burning taste, and are considered useful in scurvy. In India the buds, and also the fruits, are similarly used. The flower-buds contain a glycoside, rutin (m.p., 188°C), which on acid hydrolysis gives rhamnose, dextrose and quercetin. On hydrolysis by the enzyme rutinase it yields the sugar rutinoside, C\(_{12}\)H\(_{23}\)O\(_{10}\) and quercetin. The former on acid hydrolysis gives rhamnose and dextrose. The flower buds contain about 4% pentosans on dry weight basis. They also contain rutic acid, pectic acid, a substance with garlic odour, a volatile emetic constituent and saponin. Caper seeds yield 34 to 36% of a pale yellow oil. The component acids of the oil are palmitic and stearic 7-9; oleic 42-46; and linoleic 45-51%; acid val. 7.1-44.1; and iod. val. 115-125. The root bark contains rutic acid and a volatile substance of garlic odour. The bark is used as bitter, aperient, diuretic, expectorant, emmenagogue and tonic. It is used in rheumatism, paralysis, tooth ache, affections of liver and spleen, and tubercular glands.
The bruised leaves are used as a poultice in gout.

The homologous polyprenols, cappaprenol-12, cappaprenol-13 and cappaprenol-14 with 12, 13 and 14 isoprene units respectively were isolated by preparative HPLC from alcoholic extracts of the leaves of *Capparis spinosa*\(^\text{254}\). In addition to these components, the occurrence of indole glucosinolates, glucobrassicin, neoglucobrassicin and 4-methoxyglucobrassicin in the roots of *Capparis* has also been demonstrated by HPLC and mass spectral methods\(^\text{255}\).

The alkaloid stachydrine (C\(_7\)H\(_{13}\)O\(_2\)N), isolated from the rind of the root of *Capparis spinosa* has been found to shorten the bleeding time and also to reduce the loss of blood\(^\text{256}\).

A new flavonol glycoside, quercetin-7-O-β-D-glucopyranoside-β-L-rhamnopyranoside was isolated from the concentrated ethanol extract of aerial parts of *Capparis spinosa*\(^\text{257}\).

**SOLANUM NIGRUM**

*Solanum*\(^\text{258}\) *Linn.* (Solanaceae) consists of a large genus of herbs, shrubs and rarely trees, found throughout the temperate and tropical parts of the world. Over 50 species have been recorded in India and a few ornamental exotics have been introduced into the gardens. The genus is economically very important, as several species are sources of food, fodder and drugs.

Several species of *Solanum* produce glycoalkaloids which on hydrolysis and removal of sugar residues yield steroidal alkaloids with 27 carbon atoms. Solanine (now resolved into six glycoalkaloids with common aglycone), and solasonine are widely distributed among the members of the genus. The aglycones of these two glycoalkaloids
are respectively solanidine (C_{27}H_{13}NO) and solasodine (C_{27}H_{13}NO_2). The latter occurs as the aglycone of solamargine and solanigrine (α- and β-solanigrine). The *Solanum* glycoalkaloids are toxic to animals when injected. Like the saponins, they are surface-active and haemolytic, and possess antifungal and cytostatic properties. *Solanum* alkaloids have close structural and configurational relationships with steroidal sapogenins and many interconversions between alkaloids and steroids and steroidal sapogenins have been accomplished.

*S. nigrum* Linn. (Black Nightshade) is a herbaceous weed, 30-45 cm high, found throughout India in dry parts, up to an elevation of 2,100 m. Leaves are ovate or oblong, sinuate-toothed or lobed, narrowed at both ends; flowers white, in drooping umbel-like 3-8-flowered clusters; berries red, yellow or black, round; seeds discoid, smooth, yellow, minutely pitted.

*S. nigrum* herb has antiseptic and antidysenteric properties. An infusion of the plant is used as an enema in infants having abdominal upsets. It is a household remedy for anthrax pustules and is applied locally. The plant is also credited with emollient, diuretic and laxative properties and its decoction is regarded as an antispasmodic and narcotic. The freshly prepared extract of the plant is effective in the treatment of cirrhosis of the liver, and also serves as an antidote to opium poisoning. An alcoholic extract of the leaves is active against *Staphylococcus aureus* and *Escherichia coli*.

The leaves are used in the treatment of scrofulous dyscrasias, and are said to produce diaphoresis when in overdose; they also cause nausea, purging and nervous disturbances. In China, the leaves are applied to wounds and sores. The juice of fresh leaves is reported to produce dilatation of the pupil.

The leaves and tender shoots of *S. nigrum* are boiled in the same way as spinach.
and eaten in many parts of India, especially by patients suffering from dropsy. Ripe fruits are used in pies and preserves; they are sometimes used as a substitute for raisins in plum puddings. Fruits make a delightful jam.

Berries are considered to possess tonic, diuretic and cathartic properties and are useful in heart diseases. They are a domestic remedy for fevers, diarrhoea, ulcers and eye troubles. Aqueous extracts of the ripe fruit inhibit cholineesterase activity of human plasma.

Fruits contain glucose and fructose (15-20%), vitamin C and \( \beta \)-carotene. Green unripe fruits, however, contain glycoalkaloids and their eating is a toxic hazard to human beings as well as livestock. Ripe fruit contains very little alkaloids and can be consumed without ill effects.

Members of the *Solanum* species (Solanaceae) have been studied in the past and found to be a rich source of the steroidal alkaloids, solanine, solamargine, solasonine and \( \alpha \) and \( \beta \) solanirine, all of which yield solasodine as the aglycone\(^{259-261}\). A survey of the solasodine content in five spp. of *Solanum* (*S. mammosum, S. nigrum, S. aviculare, S. pseudocapsicum, S. khasianum*) grown in Pakistan showed that the leaves contain 0.3 to 2.3\%, while the fruits contain 1.37 to 5.2\% of the compound\(^{262}\).

Roberg, M.\(^{263}\) and Marker\(^{264}\) et al have reported the presence of saponins in some *Solanum* species.

Varshney and Sharma\(^{261}\) have reported the presence of a steroidal sapogenin, tigogenin in the form of saponin in *Solanum nigrum* berries from Uttar Pradesh.

One spirostanol glycoside and two furostanol glycosides have been isolated from a methanol extract of the stems and roots of *Solanum nigrum* and identified as 3-O
(β-lycotetraosyl) - (25 R) - 5α - Spirostan - 3β-ol (Ultronin A), 3-O -(β lycotetraosyl) - 26 - O - (β-D-glycopyranosyl) - (25 R) - 22α - methoxy - 5α -furostane - 3β, 26 - diol (Ultroside A) and 3-O-(β-lycotetraosyl) -26-O-(β-D-glucopyranosyl) - (25 R) - 5α-furostane - 3β, 22α, 26 - Triol (Ultroside B). A new spirostanoside, Ultronin B was isolated from the roots and stems.

Diosgenin, a major raw material for commercial steroid production, occurs in many spp. of Solanum. Solasodine and sapogenins have been reported from Solanum nigrum.

Flavonoid glycosides, quercetin 3-glucosyl (1→6) galactoside, 3-gentiobioside, 3-galactoside and 3-glucoside have been found to occur in the leaves of Solanum nigrum. Two new quercetin glycosides have been identified from the leaves of Solanum nigrum, namely, quercetin 3-O-(2-Gal-α-rhamnosyl)-β-glucosyl (1→6) -β-galactoside and quercetin 3-O-α-rhamnosyl (1→2) -β-galactoside.

The anthocyanin, petanin has been isolated from the berries of Solanum nigrum var. guineense.