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Dr. S Bhavani MD(S)
Research Officer (Siddha),
Siddha Central Research Institute, Arumbakkam,
Chennai, Tamil Nadu, India

Correspondence
DR. S Bhavani MD(S)
Research Officer (Siddha),
Siddha Central Research Institute, Arumbakkam,
Chennai, Tamil Nadu, India

Hepato-protective herbs & medicines in siddha system of medicine-A review

Dr. S Bhavani MD(S)

Abstract
Siddha medicine has huge array of medicine for liver wellness and illness. This sphere is one of the accentuating and conspicuous strength of Siddha medicine. Causes for liver toxicity ranges from wide range of xenobiotics, chemicals, drugs and toxins. Around hundred of hepato-protective herbs mentioned in Siddha literature. In this review, exploring few most commonly used herbs & Siddha medicines in practice for Liver morbidity.

Keywords: Hepatotoxicity, hepato- protective herbs, Siddha medicine in liver morbidity.

1. Introduction
Liver is the second largest gland in the body. It performs many vital functions related to digestive, metabolic, detoxification, immunity, store house of nutrients and hence maintains the homeostasis of the body. The central role executed by liver in the clearance and transformation of xenobiotics, chemicals, toxins etc., makes it susceptible to liver injury. Blood from the gastro-intestinal tract passes through the hepatic portal circulation, the hepatocytes of the liver, surveil the contents of the blood & remove many potentially toxic substances. More than 900 drugs & toxins have been reported to cause liver injury[1]. Though liver has its capacity to regenerate its tissues. The updated data confirmed that hepatotoxicity was the most commonly reported adverse drug reaction leading to drug withdrawal worldwide.Paradigm shift in search of hepato-protectives drug moiety tracing back to ethnopharmacological background offers great scope. This review article throws light upon hepato-protectives used in Siddha system of medicine.

2. Aquilaria Agallocha
The hepato-protective effect of ethanolic extract of Aquillaria agallocha leaves (EEAA) induced by CCl4 induced hepatotoxicity in rat model was done by Rahman *et al*., estimated serum hepatic enzyme levels & histopathological study of liver tissues [2]. Reported remarkable decrease in serum ALT, AST & ALP levels in treated groups which increased due to CCl4 induced liver damage when compared with standard drug.
At the doses of 200 & 400 mg/kg the ethanolic extract of Aquillaria agallocha leaves (AAE) lowered the AST, ALP, ALT, LDH, Cholesterol & bilirubin in the PCM [3] (Paracetamol intoxicated rats) significantly ($p<0.05$ to $p<0.01$). The histopathological findings such as centri-lobular hepatic necrosis, cell degeneration & infiltrating lymphocytes in PCM intoxicated group was not seen in rats pre-treated with the ethanolic extract AAE. The anti-oxidant property of the phytochemicals in AAE is probably that offers the hepato-protection.

3. Indigofera tinctoria
The pre-treatment with Indigofera tinctoria extract improves hepatic enzymic & non-enzymic antioxidant status and decreases the levels of lipid peroxides in rats treated with toxic doses of D-galactosamine & endotoxin [4].
Treatment of rats with Indigofera tinctoria (250,500 mg/kg b.wt) in paracetamol treated rats show significant lowering of serum levels of AST, ALT, ALP, GGT, LDH, Bilirubin, cholesterol against paracetamol induced liver toxicity, whereas protein level increased [5]. The anti- hepatotoxic efficacy of the Indigofera tinctoria extract demonstrated by reduction in the extent of necrosis, degree of degeneration & fatty accumulation in the central vein significantly.

4. Tinospora cordifolia
The treatment with T. cordifolia extract (100 mg/kg bwt for 15 days) in CCl4 intoxicated rats

was found to protect the liver, by significant reduction in serum levels of SGOT, SGPT, ALP, Bilirubin observed following CCl4 intoxication[6]. The results of experiment also suggested that the T. cordifolia extract may protect against immunosuppression caused by CCl4 induced toxicity.

The effect of T. cordifolia on kupffer cell activity in a model of chronic liver damage [7] is evaluated by decoction made by mixing 100 mg powdered stem of T. cordifolia. Prevention of deterioration of kupffer cell activity appears to be due to its macrophage activating property against any suppressant influences on kupffer cells.

T. cordifolia prevents hepatic damage induced by antitubercular drugs and bile salts [8]. Inactivating property against hepatitis B and E surface antigens in 48 to 72 hours is exhibited by the Tinospora cordifolia extract *in vitro* [9].

5. Phyllanthus niruri

The hepato-protective potential of Phyllanthus niruri extracts was evaluated in rats by inducing liver damage by CCl4 with pre-treatment [10] reduced CCl4 induced changes in the SGOT, SGPT, well known markers for hepatic injury. The chemical constituents of Phyllanthus niruri namely phyllanthus & hypophyllanthus (Shamasundar *et al*., 1985) probably protects against cytotoxicity of CCl4 in an isolated hepatocyte culture.

The hepato-protective activity of Phyllanthus niruri in paracetamol induced liver damage is demonstrated in rats showed marked improvement in suppression of elevated liver markers. Also, hepatic catalase activity is decreased by paracetemol induced liver damage, & this activity is reversed by Phyllanthus niruri [11].

Studies on Phyllanthus amarus/niruri against hepatitis B virus Thyagarajan *et al* [12]. Have shown anti-viral properties against HBV by the whole plant extract of Phyllanthus niruri. The potential of Phyllanthus amarus in treating Hep. B virus, is explained by disruption of

HBV polymerase activity, mRNA transcription & replication [13]. This occurs by a mechanism of interactions between HBV enhancer I & C/EBP transcription factors[14].

Jayaram and Thyagarajan [15] reported *in vitro* inhibition of HBsAg secretion by PLC/PRF/5 (Alexander) cell line for 48 hr when the cell line was treated with 1mg/ml concentration of Phyllanthus amarus as a single dose.

Phyllanthus amarus is reported to be safe and non-toxic to mice in a dose of 10mg/kg

b.w. A 20% aq. extract of Phyllanthus niruri is effective as an oral pre-treatment at 0.2 ml/100 mg b.w against CCl4 induced hepatotoxicity in rats. The hexane extracted compounds, phyllanthin & hypophyllanthin were found to reduce CCl4 or galactosamine- induced cyto-toxicity of cultivated rat hepatocytes [16]. The compound Triacontanal was protective against galactosamine induced toxicity only.

In a clinical trial in acute viral hepatitis (AVH) patients, Jayanth *et al*. [17] used P. niruri & compared it with other herbal medicines. A significantly greater diminish in transaminase levels after 2 wks treatment with P.niruri in both HBsAg +ve & -ve groups was observed. In another study, P. amarus treatment improved liver functions significantly faster in both acute hepatitis A & B, with a higher rate of HBsAg clearance.

In a clinical trial [18], on Chronic HBV carriers, HBsAg clearance is the Phyllanthus amarus treated group was 59% versus 4% in the placebo group. The second open trial in 1990 showed 20% HBsAg clearance and 63.6% loss of infectivity by HBeAg sero-conversion.

6. Eclipta alba

Eclipta alba significantly counteracted CCl4 induced inhibition of the hepatic, microsomal drug metabolising enzyme amidopyrine N-demethylase & membrane bound glucose-6-phosphatase. The loss of hepatic lysosomal acid phosphatase & alkaline phosphatase by CCl4 was restored to normal by Eclipta alba in rats at subcellular levels [19].

The active constituents of the plant, Coumestans such as Wedelolactone & demethylwedelolactone are responsible for the potent anti-hepatotoxic activities in CCl4, galactosamine & phalloidin induced liver damage in rats [20]. Wedelolactone has been reported to be a potent anti-hepato-toxic & selective 5-lipoxygenase inhibitor with an IC50 of 2.5 & it does by oxygen radical scavenging mechanism.

Wedelolactone exhibits trypsin inhibitory effect (Samiulla *et al*; 2002; Syed *et al*; 2003). It was useful in the treatment of Cirrhosis of liver & Infectious Hepatitis (Murphy *et al*, 1979) [21].

7. Indigofera aspalathoides

The methanol extract of Indigofera aspalathoides decreased the elevated serum enzyme levels in CCl4 induced hepato-toxicity in rats [22]. Probably, the extract preserve the structural integrity of the hepatocellular membrane that is evident from the marked reduction in liver markers in serum of rats due to the prevention of leakage of the intracellular enzymes by its membrane stabilizing activity.

8. Terminalia chebula

The 95% ethanolic extract of Terminalia chebula fruit (Tc extract) which was chemically characterized on the basis of chebuloside 2 as a marker, was investigated for hepato-protective activity against anti-tuberculosis (anti-TB) drug-induced toxicity. Tc extract was found to prevent the hepato-toxicity caused by the administration of Rifampicin (RIF), Isoniazid (INH) and Pyrazinamide (PZA) in combination in a sub-chronic mode (12wks) [23]. The hepato-protective effect of Tc extract could be attributed to its prominent anti- oxidative and membrane stabilizing activities. The biochemical observational changes were supported by histological profile.

9. Tribulus terrestris

Tribulusamides A & B, New lignanmides comprising 2 cinnamic amide parts united in 9 cis configuration were isolated from the fruits of Tribulus terrestris. And together with other known compounds such as N-trans-feruloytyramine, terrestriamide, N-trans coumaroyltyramine & beta sitosterol 24. These compounds added to primary cultured mouse hepatocytes markedly prevented cell death induced by D-galactosamine TNF-alpha.

10. Cassia fistula

Hepato-cellular membrane damage, consequent to administration of CCl4 was evident by a 16 fold increase in the LPO & 50% reduction in the activities of CAT (catalase) & GR in the liver tissue [25]. Pre-treatment of ethanolic extract for 7 days prior to CCl4 administration completely inhibited the elevated levels of lpo & reversed the decrease in the levels of CAT & GR towards normalcy in the liver tissue. This clearly demonstrates the antioxidant & hepato-protective effect by various phytochemical principles i.e., flavonoids, saponins, alkaloids & tannins that are present in the ethanolic leaf extract.

DEN (Diethylnitrosamine) is reported to be a well-known

hepatotoxin & hepatocarcinogen. It is observed that administration of a single dose of DEN to rats produced a significant increase in the activities of all the 3 marker enzymes, the increase being 2 fold for AST & ALP, whereas it was 3 fold for ALT when compared to control rats. Treatment with ELE for 30 days after DEN administration significantly reduced the altered activities of these enzymes back to normalcy [26].

Treatment with ELE (ethanolic leaf extract) for 30 days after DEN administration markedly decreased the levels of MDA (Malondialdehyde). There was a significant decrease in the activity of both SOD (Superoxide dismutase) 60% & CAT (Catalase) 40% upon administration of DEN in the liver tissue, which was ameliorated treatment with ELE for 30 days. It can be hypothesised that the ELE might have scavenged & detoxified the superoxide anions & hydroxyl radicals released during the metabolic activation of DEN, hence improving the activity of hepatic markers & antioxidant enzymes [27].

11. Terminalia bellerica

The experiment was done to evaluate the protective effect of Terminalia bellerica fruit extract & its active principle gallic acid (3, 4, 5, trihydroxy benzoic acid) at different doses against ccl4 in toxicity [28]. Treatment with Terminalia bellerica extract (200, 400 & 800 mg/kg, p.o) showed dose-dependent recovery in depleted glutathione level, elevated SGOT, SGPT, Alkaline phosphatase after CCl4 toxicity but the effect was more obvious with gallic acid. Hence concluded that 200mg/kg dose of gallic acid was found to be effective against CCl4 induced liver & kidney damage [29].

12. Phyllanthus emblica

Aqueous extract of Phyllanthus emblica (100-200 mg/kg) increased cell viability of rat hepatocytes being treated with paracetamol (2g). That is pre-treatment of rats with Phyllanthus emblica at oral doses of 100-200mg/kg, 4hrs before paracetamol administration lowered the hepato-toxicity [30]. The tannins & flavonoids present in Phyllanthus emblica fruit extract has very potent anti-oxidant & hepato-protective properties. The study also indicates that animals administered with paracetamol (2g) alone showed higher hepatotoxicity.

13. Asteracanthus longifolia

Methanolic extract of the seeds exhibits hepato-protective activity against paracetamol & thioacetamide intoxication in rats (Singh & Handa, 1999). Ahmed *et al*. (2008) studied the activity of seeds against chemically induced hepato-carcinogenesis in wistar rats [31]. Methanol extract of seed showing anti-tumor promoting potential inhibit hepato-carcinogenesis in rats, increase GPX, CAT & ODC. (Shivasanghari *et al*, 2004) studied the protective efficacy of Asteracantha longifolia on acetaminophen induced liver damage in rats.

Shanmugasundaram & Venkataraman (2006) experimented the aqueous extract of the roots for hepato-protective in CCl4 induced liver toxicity in rats & *in vitro* (FTC) & thiobarbituric acid (TBA) methods [32]. Shailajan *et al* (2005) showed the whole plant of Asteracantha longifolia was hepatoprotective against CCl4 induced liver dysfunction in rats [33]. The aq.extract & ethanolic extract of whole plant powder showed hepato-protective effect against galactosoamine induced hepatotoxicity (Shailajan *et al*, 2007).

14. Ricinus communis

Ricinus communis leaf extract was evaluated for hepato-protective, choleretic & anti- cholestatic activity [34]. In a preliminary test with albinorats, an ethanol extract showed significant protection against galactosamine induced hepatic damage. On fractionation of the ethanol extract, yielded 2 pure compounds-Ricinine & N-dimethyl ricinine was found to be more active and it reversed the biochemical changes produced by galactosamine at a dose of 6 mg/kg for 7 days.

Ricinus communis leaves ethanolic extract 250/500 mg/kg body weight possesses hepato-protective activity due to their inhibitory activities of an increase in the activities of serum transaminases and the level of lipid peroxidation, protein, glycogen in the liver induced by CCl4. It also treated the depletion of glutathione level & adenosine triphosphate activity which was observed in the CCl4-induced rat liver [35]. The presence of flavonoids in ethanol extract of Ricinus communis pronounces this beneficial effect by the membrane stabilizing & anti-oxidative effects. Hence, the Ricinus communis increase the regenerative & reparative capacity of the liver due to the presence of flavonoids & tannins. The whole leaves of Riccinus communis showed the protective effect against liver necrosis as well as fatty changes induced by CCl4 while the glycoside & cold aqueous extract provide protection only against liver necrosis & fatty changes respectively.

15. Evolvulus alsinoides

The hepato-protective activity of ethanolic extracts of Evolvulus alsinoides Linn (EAEE) were screened in rats [36]. Test groups received 100mg/kg b.w.p.o of the selected fractions i.e., TF-EAEE, BNF-EAEE & BLF-EAEE, by oral route for 7 days, followed by paracetamol (3.0g/kg.b.w) in 1% w/v gum acacia on the 8th day. Biochemical parameters such as SGPT, SGOT, ALP, TB, TP & Cholesterol levels were estimated. Pre-treatment of rats with 100mg/kg of the three test fractions (TF-EAEE 100, BLF-EAEE 100 & BNF-EAEE 100) resulted in a significant protection against paracetamol induced alteration in the serum levels.

16. Allium sativum

Allicin (diallythiosulfinate) is the main biologically active component of freshly crushed garlic (*Allium sativum* Linn.) cloves. It is produced by the interaction of the non- protein aminoacid alliin with the enzyme allinase (alliinylase, EC4.4.1.4). D-galactosamine highly sensitizes the host response of the experimental animal to endotoxin (lipopolysaccharide) & causes fulminant hepatitis within 8 hr after administration. In D- galactosamine /lipopolysaccharide (D-GaIN/LPS)-induced hepatitis in rats, a significant increase of lipid peroxidation and decreased liver antioxidant enzyme levels are observed [29]. Pre-treatment with allicin, the active component of freshly crushed garlic cloves, prevented these alterations [37].

In another experiment, on wistar rats treated with lead (Pb), the toxicity due to it altered serum AST, ALT levels. When supplemented with garlic & vit. C significantly reduced exhibiting hepato-protective activity [38].

17. Smilax chinensis

The methanol extract of the rhizomes of Smilax chinensis L. were evaluated for hepato-protective activity in rats by inducing liver damage by CCl4 [39]. The methanol extract at an oral dose of 200 & 400 mg/kg/p.o showed a significant P(<0.05) protective effect by lowering serum levels of SGOT, SGPT, Alkaline phosphatase & bilirubin & increasing the

levels of total protein levels as compared to Silymarin used as the control.

The ethylacetate fraction of Smilax chinensis Linn. shows pronounced hepato-protective activity by its phenolic content, as powerful antioxidant [40].

18. List of herbs used in siddha medicine [41]:

Botanical Name	Tamil name	Taste	Parts used
Ricinus communis	Erandam	Bitter	Young leaf
Eclipta alba	Karisalai	Bitter	Whole plant
Wedelia chinenensis	Manjal karisalai	Bitter	Whole plant
Rhus succedanea	karkadagasingi	Astringent	Galls
Andrographis paniculata	Nilavembu	Bitter	Leaves, stem
Azadirachta indica	Vembu	Bitter	Leaf, bark
Erythrina indica	Kalyana murungai	Bitter, Pungent	Leaf, flower, seeds, bark
Aquillaria agallocha	Agil	Pungent, bitter, mild sweet	Stem bark
Cassia fistula	Sarakkonrai	Astringent, mild bitter	Leaf, flower, bark
Emblica officinalis	Nelli	Astringent	Fruit
Glycyrhiza glabra	Adhimathuram	Sweet	Root bark
Terminalia chebula	Kadukkai	Astringent	Fruit
Terminalia bellerica	Thanrikkai	Astringent	Fruit
Indigofera aspalathoides	Avuri	Bitter	Leaf
Smilax chinensis	Parangipattai	Sweet	Root tuber
Phyllanthus amarus	Keezhanelli	Bitter	Whole herb
Strychnos potatorum	Thettran	Bitter	Seed
Tinospora codifolia	Seendhil	Bitter	Stem, leaf, root tuber
Tribulus terrestris	Nerunjil	Astringent, sweet	Whole herb
Asteracantha longifolia	Neermulli	Sweet, mild bitter	Whole plant
Momordia charantia	Paagal	Bitter	Leaf, fruit, seed.
Indigofera tinctoria	Avuri	Bitter	Whole herb
Piper nigrum	Milagu	Pungent	Fruit
Cuminum cyminum	Seeragam	Pungent, sweet	Seed
Asparagus racemosus	Satavari	Sweet	Root tuber
Zingiber officinale	Inji	Pungent	Rhizome
Piper longum	Thippili	Pungent	Fruit
Allium sativum	Poondu	Pungent	Bulb
Allium cepa	Vengayam	Pungent	Bulb
Curcuma longa	Manjal	Bitter, Pungent	Rhizome
Ferula asafoetida	Perungayam	Bitter	Gum
Thespesia populnea	Poovarasu	Bitter, Astringent	Leaf, Bark, Flower
Boerrhavia diffusa	Mookirattai	Bitter	Whole plant
Tricosanthes dioica	Pudalai	Sweet	Leaf, stem
Alternanthera sessilis	Ponnankanni	Sweet	Leaf
Acalypha indica	Kuppaimeni	Bitter, Pungent	Whole plant
Santalum album	Sandhanam	Bitter, mild astringent	Wood
Amaranthus tricolor	Mulaikeerai	Sweet	Leaves
Piper cubeba	Milagu	Bitter, Pungent	Seed, stem
Costus speciosus	Koshtam	Bitter	Root
Elaettaria cardamomum	Elam	Pungent	Fruit
Evolvulus alsinoides	Vishnukirandhi	Bitter,mild pungent	Whole herb
Coccinia grandis	Kovai	Sweet	Leaf, fruit
Aegle marmelos	Vilvam	Astringent, Bitter	Leaf
Solanum nigrum	Manathakkali	Bitter	Leaf
Solanum trilobatum	Thoothuvalai	Mild bitter, Pungent	Leaf
Vitis vinifera	Drakshai	Sweet	Fruit
Ocimum basilicum	Thiruneetrupachilai	Pungent	Leaves
Raphanus sativus	Mullangi	Pungent	Leaves
Luffa acutangula	Peypirkku	Bitter	Fruit
Picrorhizza kurroa	Kadugurohini	Bitter, Pungent	Root
Tephrosia purpurea	Kozhunji	Pungent	Leaf
Hemidesmus indicus	Nannari	Sweet, mild bitter	Root
Aristolochia indica	Eechuramooli	Bitter	Leaf, Root
Premna tomentosa	Pidangunaari	Pungent	Leaf
Aloe vera	Kumari	Mild bitter	Root, Juice
Stereospermum chelonoides	Pathiri	Astringent	Leaf, root, bark
Sida cordifolia	Sittramutti	Astringent	Whole plant
Alstonia scholaris	Ezhilaipalai	Bitter	Bark
Apium graveolens	Sathaguppai	Sweet, pungent	Seeds
Berberis aristata	Maramanjal	Bitter	Bark
Cassia occidentalis	Peyavarai	Bitter, astringent	Leaf, Root
Cassia tora	Oosi thagarai	Bitter, salt	Leaf, Root

Momordia charantia	Paagal	Bitter	Leaf, fruit, seeds
Trigonella foenum graceum	Vendayam	Bitter	Seeds
Lawsonia inermis	Maruthonri	Astringent	Leaves
Foeniculum vulgare	Sombhu	Pungent, sweet	Seeds, Root
Solanum nigrum	Manathakkali	Bitter	Leaves
Solanum indicum	Siruvazhudunai	Bitter, Astringent	Leaf, root
Mentha piperita	Pudhina	Pungent, Astringent	Leaves
Fumaria parviflora	Thara	Bitter, Astringent	Leaf
Garcinia mangostana	Mangustan	sweet	Fruit, leaf
Nelumbo nucifera	Thamarai	Sweet, Astringent	Flower, seed, Tuber
Sphaeranthus indicus	Kottaikarandhai	Bitter	Leaf
Crataeva religiosa	Maavilingapattai	Bitter	Leaf, Bark
Embelia ribes	Vayvilangam	Bitter	Seeds
Vernonia anthelmintica	Kaatuseeragam	Bitter	Seeds
Cissusquadrangularis	Pirandai	Pungent	Root, Stem

19. Siddha Drugs used in Liver diseases [42]

1. Karisalai karkam
2. Keezhanelli karkam
3. Sivanarvembu karkam
4. Kadukkai karkam
5. Nerunjil karkam
6. Sarakonrai flower/leaf/bark karkam
7. Avuri ilai karkam
8. Avarai verpattai karkam
9. Mullangi leaf juice
10. Siru aamanakku kozhunthu
11. Neermulli kudineer
12. Mandoorathi adai kudineer
13. Ayabringharaja karpam
14. Ayasambeera karpam
15. Vediuppu chunnam
16. Muthuchippi parpam
17. Karpoora silasathu parpam
18. Pavala parpam
19. Palagarai parpam
20. Sangu parpam.
21. Aya parpam
22. Annabedhi chenduram
23. Arumuga chenduram
24. Navachara chenduram
25. Ayakandha chenduram
26. Lohamandoora chenduram
27. Kantha chenduram
28. Vediannabedhi chenduram
29. Ayaveera chenduram
30. Keezhanelli Nei
31. Karisalai Nei.
32. Santhachandrodaya mathirai
33. Thalisathi choornam
34. Amukkra choornam

20. External Therapy

1. Keezhanelli thailam
2. Karisalai thailam
3. Kaiyan Nellikkai thailam
4. Vetiver thailam
5. Arakku thailam
6. Mahachandanaadhi thailam.

21. Conclusion

Extensive resources of herbs & formulations in Siddha for hepato-protection was formulated wisely as a single herb therapy to various combination that a single herb only may not be effective in different needs as in toxicity of drugs, viral infections, fatty liver disease, alcoholic fatty liver disease, cirrhosis, etc., Also, it is worth to be mentioned that in Siddha, external therapy was also prescribed auxillary to internal medicine to treat holistically.

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23. References

1. Drug-induced liver injury: Towards early prediction & risk stratification. World J Hepatol. 2017; (1):30-37.
2. Alam. An insight of pharmacognostic study & phytopharmacology of Aquillaria agallocha. Journal of Applied Pharmaceutical Sciences. 2015; 5(08):173-181.
3. J Alam. Journal of Traditional and Complementary Medicine. Hepatoprotective potential of ethanolic extract of Aquillaria agallocha leaves against paracetamol induced hepatotoxicity in SD rats, 2017, 9-13.
4. M Sreepriya, T Devaki, K Balakrishna, T Apparanantham. Effect of Indigofera tinctoria Linn on liver antioxidant defense system during D-galactosamine/endotoxin-induced acute hepatitis in rodents. Indian Journal of Experimental Biology. 2001; 39:181-184.
5. M Muthulingam. Antihepatotoxic efficacy of Indigofra tinctoria (Linn.) on paracetamol induced liver damage in rats. Int J Pharm Biomed Res. 2010; 1(1):13-18.
6. B Bishayi. Hepatoprotective & Immunomodulatory properties of Tinospora cordifolia in CCl4 intoxicated mature albino rats. The Journal of Toxicological Sciences. 2002; 27(3):139-146.
7. Nagarkatti DS, Rege NN, Desai NK, Dahanukar SA. Modulation of Kupffer cell activity by Tinospora cordifolia in liver damage. J Postgrad Med 40:65.
8. Avnish K Upadhyay, Kaushal Kumar, Arvind Kumar, Hari S. Mishra Tinospora cordifolia (Willd.) Hook. f. and Thoms. (Guduchi) – Validation of the Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res. 2010; 1(2):112-121.
9. Avnish K Upadhyay, Kaushal Kumar, Arvind Kumar, Hari S Mishra. Tinospora cordifolia (Willd.) Hook. f. and Thoms. (Guduchi) – validation of the Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res. 2010; 1(2):112-121.
10. R Harish, T Shivanandappa. Antioxidant activity & hepatoprotective potential of Phyllanthus niruri. Food chemistry. 2006; 95:180-185.
11. SM Sabir, JBT Rocha. Water extractable phytochemicals

from Phyllanthus niruri exhibit distinct *in vitro* antioxidant and *in vivo* hepatoprotective activity against paracetamol-induced liver damage in mice. Food chemistry. 2008; 111:845-851
12. SP Thyagarajan, S Jayaram, V Gopalakrishnan, R Hari, P Jeyakumar, V Gopalakrishnan *et al*. Herbal medicines for Liver Diseases in India. Journal of Gastroenterology & Hepatology. 2002; 17:s370-s376.
13. Lee CD, Ott M, thyagarajan SP, Shafritz DA, Burk RD, Gupta S. *Phyllanthus amarus* down-regulates hepatitis B virus mRNA transcription and replication. European Journal of Clinical Investigation, doi:10.1046/j.1365-2362.1996.410595.x 1996; 26:1069-1076.
14. Ott M, Thyagarajan SP, Gupta S. *Phyllanthus amarus* suppresses hepatitis B virus by interrupting interactions between HBV enhancer I and cellular transcription factors. European Journal of Clinical Investigation, doi:10.1046/j.1365- 2362.1997.2020749.x. 1997; 27: 908-915.
15. Jayaram S, Thyagarajan SP. Inhibition of HbsAg secretion from Alexander cell line by Phyllanthus amarus. Indian Journal of Pathol. Microbial. 1996; 39:211-15.
16. Kodakandla Venkata Syamsundar, Bikram Singh, Raghunath Singh Thakur, Aktar Husain, Yoshnobu, Kiso *et al*. Anti-hepatotoxic principles of Phyllanthus niruri. Journal of Ethnopharmacology. 1985; 14(1):41-44.
17. Thyagarajan SP, Jayaram S, Paneerselvam A. Effect of Phyllanthus amarus, an Indian medicinal plant on healthy carriers of Hepatitis B virus. Results of six clinical trials. Indian Journal of Gastroenterology. 1990-1996-1999; 18 (uppl.1):s26.
18. SP Thyagarajan, T Thirunalasundari, S Subramanian, PS Venkateswaran, BS Blumberg. Ef fect of Phyllanthus amarus on chronic carriers of Hepatitis B virus.The Lancet. 1988; 332(8614):764-766.
19. AK Saxena, B Singh, KK Anand. Hepato-ptotective effects of Eclipta alba on subcellular levels in rats. Journal of Ethnopharmacology. 1993; 40(3):155-161.
20. VM Jadhav. Chemical composition, pharmacological activities of Eclipta alba. Journal of Pharmacy Research. 2009; 2(8):1229-1231.
21. Sunita Dalal, Sudhir K Kataria, KV Sastry, SVS Rana. Phytochemical Screening of methanolic extract & anti-bacterial activity of active principle of hepato-protective herb, Eclipta lba. Ethnobotanical Leaflets. 2010; 14:248-58.
22. M Gupta. Hepatoprotective activity of Indigofera aspalathoides extract against CCl4 induced liver damage. Oriental Pharmacy & Experimental Medicine. 2004; 4(2):100-103.
23. Gupta. Biological & Pharmacological properties of T.chebula Retz. (Haritaki)-An overview. Int Journal of Pharm, pharm Sci, 4, 362-68.
24. Jian-Xin Li, Qin Shi, Quan-Bo Xiong, Jeevan Kumar Prasain, Yasuhiro Tezuka, Toru Hareyama *et al*. Tribulusamide A and B, New Hepatoprotective Lignanamides from the Fruits of *Tribulus terrestris*: Indications of Cytoprotective Activity in Murine Hepatocyte Culture. Natural products chemistry. www.http:/thieme-connect.com.
25. Kannampalli Pradeep. Effect of Cassia fistula Linn extract on diethylnitrosamine induced hepatic injury in rats. Chemico-Biological Interactions. 2007; 167:12-18.
26. Kannampalli Pradeep. Effect of Cassia fistula Linn extract on diethylnitrosamine induced hepatic injury in rats. Chemico-Biological Interactions. 2007; 167:12-18.
27. Kannampalli Pradeep. Effect of Cassia fistula Linn extract on diethylnitrosamine induced hepatic injury in rats. Chemico-Biological Interactions. 2007; 167:12-18.
28. Anjana Jadon, Monika Bhadauria, Sangeeta Shukla. Protective effect of Terminalia bellerica Roxb. And gallic acid against carbon tetrachloride induced damage in albino rats.
29. Shirish S Pingale. Hepatoprotective action of Terminalia bellerica on CCl4 induced hepatic disorders. Der Pharma Chemica. 2011; 3(1):42.
30. HL Vidhya Malar, S Mary Mettilda Bai. Hepatoprotective activity of Phyllanthus emblica against paracetamol induced hepatic damage in Wistar albino rats.African Journal of Basic & Applied Sciences. 2009; 1(1-2):21-25.
31. Nagendra Singh Chauhan, VK Dixit. Asteracantha longifolia Nees, Acanthaceae: chemistry, traditional & medicinal uses and its pharmacological activities.-a review. Brazilian journal of pharmacognosy.
32. Nagendra Singh Chauhan, VK Dixit. Asteracantha longifolia Nees, Acanthaceae: chemistry, traditional & medicinal uses and its pharmacological activities.-a review. Brazilian journal of pharmacognosy.
33. Mariappan. *In vivo* investigation of Hepatoprotective activity of Asteracantha longifolia Nees. On CCl4 induced hepatotoxicity in wistar albino rats. Asian Journal Pharm Clin Res. 2015; 8(6):218-222.
34. PKS Visen. Hepato-protective activity of Ricinus communis leaves. International journal of pharmacognosy. 1992; 30(4):241-250.
35. Evan Sabina Prince. Iranian journal of pharmaceutical sciences. Autumn. 2011:7(4):269-278.
36. Thatipelli Ravi Chander. Hepatoprotective activity of Evolvulus alsinoides Linn. on paracetamol induced rats. Journal of pharmaceutical and scientific Innovation. 2014.
37. V Vimal, T Devaki. Hepato-protective effect of allicin on defense system in galactosamine/endotoxin challenged rats, Journal of ethnopharmacology, 2004.
38. GO Ajayi, TT Adeniyi, DO Babayemi. Hepato-protective & some haematological effects of Allium sativum & vit. C in lead exposed wistar rats. International Journal of Medicine & Medical sciences. 2009; 1(3):064-067.
39. Venkidesh R. Hepatoprotective activity of Smilax chinensis L.in CCl4 induced hepatotoxicity in rats.International Journal of Biological & Pharmaceutical Research. 2010; 1(2):72-75.
40. Mandal. Hepatoprotective and antioxidant activities of Smilax chinensis L.Root. Parmacologyonline. 2008; 2:529-535.
41. KS Murugesa Mudaliar, Siddha Materia Medica. 9th edition, Indian Medicine & Homeopathy Department Publication, 2013.
42. KN Kuppusamy, Mudaliar. Siddha Maruthuvam, Tamilnadu Siddha medical council publication, 1987.