Research paper

Comparative hepatoprotective potential of *Tinospora cordifolia*, *Tinospora sinensis* and *Neem-guduchi*

Bhagashri Nagarkar, MSc[1], Rohan Kulkarni, MSc[1], Prashant Bhondave, MPharm[2], Deepak Kasote, PhD[3], Omkar Kulkarni, MD (Ay)[1], Abhay M. Harsulkar, PhD[2], Suresh D. Jagtap, PhD[1]

[1]Interactive Research School for Health Affairs (IRSHA), Bharati Vidyapeeth University, Pune Satara Road, Pune, Maharashtra, India.

[2]Department of Pharmaceutical Biotechnology, Poona College of Pharmacy, Bharati Vidyapeeth University, Erandwane, Pune, Maharashtra, India

[3]S. N. Arts, D. J. M. Commerce and B. N. S. Science College Sangamner, Pune, Maharashtra, India.

Corresponding Author:

Suresh D. Jagtap

Interactive Research School for Health Affairs (IRSHA)

Bharati Vidyapeeth Deemed University,

Pune Satara Road, Pune, Maharashtra, India

Abstract

***Objectives*:** The objective of this study was to evaluate the comparative efficacy of *Tinospora cordifolia* (Willd.) Miers ex Hook. F., *Tinospora sinensis* (Lour.) Merrill and *T. cordifolia* growing on *Neem* (*Azadirachta indica* A. Juss.) called *Neem-guduchi.* They have been widely used in the traditional medicine systems in various dosage forms to treat liver disorders. They are of common occurrence and are being used as substitutes to each other. There is no such comparative study yet published.

***Design*:** *Guduchi-Satwa*, a well-known dosage form was prepared according to the traditional procedure. Hepatoprotective potential was assessed using paracetamol-induced hepatotoxicity model in rats and evaluated by using biochemical parameters viz. alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (BIL).

***Results*:** Both *T. cordifolia* and *T. sinensis Satwa* significantly reduced the paracetamol induced elevated levels of serum ALT, AST, ALP and total bilirubin at dose of 200 mg/kg, i.p. as compared to *Neem-guduchi.*

***Conclusions*:** *Satwa* preparation form of *T. sinensis* offers exploitable level of hepatoprotection potential.

Keywords: *Tinospora cordifolia*; *Tinospora sinensis*; Hepatoprotective; *Guduchi*

Introduction

Liver diseases are a worldwide health problem. In India use of medicinal plants and their formulations are common for the treatment of liver diseases.[1] Liver injuries can be caused by prescription drugs, toxic chemicals, alcohol consumption and viral infections.[2] Most of the liver damage instances are associated with redox imbalance and oxidative stress.[3] Due to paucity of a reliable hepatoprotective drugs in modern medicine, herbal drugs are being recommended for the treatment of liver diseases.[4] However, no scientific evidence is available to support these claims and for their mechanism of action.

Guduchi is one of the most commonly practiced herbs being prescribed for various disorders for its curative as well as preventive role. In Indian sub-continent, four different species of *Tinospora* are found, viz. *T. cordifolia* (Willd.) Miers ex Hook. F. & Thoms, *T. sinensis* (Lour.) Merr., *T. crispa* (L.) Miers ex Hook. f. & Thoms and *T. glabra* (Burm f.) Merrill. The plant is locally known as *Amrita, Amritavalli, Chinnobhava, Chakralakshanika, Guduchi, Gulvel, Gurch, Kaduvel, Kundalini, Madhuparni, Sudarsana Tantrika, Vatsadani* etc. Out of these four species, *T. cordifolia* and *T. sinensis* are described as medicinal species.[5,6]

Most practitioners believe that *Guduchi* as described in *Ayurveda* is *T. cordifolia*, although, the description matches very well with both, moreover, better with *T. sinensis*. They are a large, glabrous, perennial, deciduous, climbing shrub of family Menispermaceae [5,7,8] and widely used in folk and *Ayurvedic* systems of medicine.[9,10]

Tinospora cordifolia (Willd.) Miers ex Hook. F. & Thoms:

T. cordifolia is distributed throughout the tropical and subtropical Indian subcontinent and China. In India, it is fairly common inhabitant of deciduous and dry forests, growing over hedges and small trees. It is one of the major constituent of several *Ayurvedic* preparation used preferably for general debility, dyspepsia, fever and urinary diseases.[11,12] Apart from other studies, hepato-protective potential validated with respect to *T. cordifolia* by scientific

research includes a clinical study for normalization of altered liver functions[13]; antihepatotoxic activity in CCL_4 induced liver damage, normalizing liver function in goats[14]; significant increment in the functional capacities of rat peritoneal macrophages.[15] As preventive antitubercular drug[16,17] and bile salts induced hepatic damage[6]; for jaundice[18] and activity against hepatitis B and E.[19] The chemical constituent reported in *T. cordiofolia* belongs to different classes such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides.[6]

***T. sinensis* (Lour.) Merrill (syn. *Tinospora malabarica*)**

T. sinensis is native of south and Southeast Asia, Nepal, Srilanka and Bengal. In India it occurs in Assam, Bihar, Orissa, Maharashtra, Andhra Pradesh, Karnataka, Kelala and Tamilnadu.[20] The mature stem of *T. sinensis* has been used to treat fever, jaundice and burning sensation.[21] In china, the fresh leaves and stem is used in the treatment of chronic rheumatism[22], for treatment in piles and ulcerated wounds.[23] The scientific validation studies on *T. sinensis* reported to possess anti-inflammatory[23] and anti-diabetic[24] activities but there is no report on its hepatoprotective potential.

In *Ayurvedic* practice, both *T. cordifolia* and *T. sinensis* are used as "*Guduchi*" often mixed together in various proportions. As *T. cordifolia* is easily available and used in major proportion. Interestingly however, it was observed that the description of *Guduchi* as described in *Ayurvedic* literature matches accurately with *T. sinensis* rather than with *T. cordifolia.* In *Ayurvedic* literature, it is also mentioned that *Guduchi* that grows on *Neem* tree has a better potential and preferentially used in treatment of certain diseases, presumably due to close vicinity to *Neem*.[5,25]

Considering these contexts, the present study was designed to evaluate comparative hepatoprotective potential of *T. cordifolia, T. sinensis* and *Neem-guduchi.* We have prepared *Ayurvedic* formulation known as "*Guduchi Satwa*" following procedure described in

Ayurveda and compared their biological activity using Paracetamol intoxication induced hepatotoxicity model in rats. It is of utmost interest to identify *Guduchi* that is described in *Ayurvedic* literature as well as validate the claim about *Neem-guduchi* having better biological activity.

Materials and Methods

Collection of Plant material

Stems of *T. cordifolia, T. sinensis* and *Neem-guduchi* were collected during November 2011 from Pune, India. The plants were identified and voucher specimen has been deposited at the herbarium of Medicinal Plants Conservation Center, Pune *Tinospora_cordifolia* (Willd.) Miersex Hook. F. & Thoms (MPCC 3464), *Tinospora sinensis* (Lour.) Merr. (MPCC 3525) and *Neem-guduchi* (*T. cordifolia* (Willd.) Miers ex Hook. F. & Thoms) (MPCC 3526).

Preparation of *Guduchi Satwa*

Fresh stems of selected three variants of *Tinospora* sp. were used for the preparation of *Guduchi Satwa*. The preparation was defined in *Ayurvedic* literature as sediment extract, which is predominantly starchy in nature. In brief, freshly collected stem parts were washed with water and cut into small pieces. They were hand-macerated in water and left overnight to sediment. Next morning, the water was decanted, solid part that remained was then air dried for couple of days, when completely dried, made into find powder, which was collected as *Guduchi Satwa.*[26] This *Satwa* was re-suspended in water at the time of oral administration.

Experimental animals

The study was carried out on male Wistar rats (150–250 g). Animals were maintained under standard husbandry conditions (temperature 25±2 ◦C, 12-h light: 12-h dark cycle) and fed with standard pellet diet (Amrut, Sangali, M.S., India) and water *ad-libitum.* All animal experiments were handled according to the international guidelines for the care and use of

laboratory animals of National Research Council (1996). This study was carried out in accordance with CPCSEA guidelines (Committee for the purpose of control and supervision of experimental animals). The study was approved by institutional animal ethical committee (1153/ac/07/CPCSEA) of Amrutvahini College of Pharmacy, Sangamner.

Paracetamol-induced hepatic damage

Comparative hepatoprotective potential of *T. cordifolia*, *T. sinensis* and *Neem- guduchi* was studied against paracetamol-induced hepatotoxicity, according to method described by Sadashivan et al.[27] Animals were randomly divided into eight groups (n=6) and received feed and water normally throughout the study. Paracetamol (Crocin, Remidix Pharma Pvt. Ltd., India) was suspended in 2 ml of water and administered p.o., at a dose of 2.5 g/kg to induce hepatic toxicity in all groups except Healthy control on day 3, 30 min after drug administration. Group I, was the Healthy control group maintained without paracetamol and without any formulation. Group II, was the paracetamol control group and did not receive any drug. In group III and IV animals received *Satwa* of *T. cordifolia* (suspended in water) at a dose 200 and 400 mg/kg p.o. respectively, for 4 days. Similarly, Group V and VI received *Satwa* of *T. sinensis* (suspended in water) at doses 200 and 400 mg/kg p.o. respectively for 4 days. Group VII and VIII received *Satwa* of *Neem-guduchi* (suspended in water) at doses 200 and 400 mg/kg p.o. respectively for 4 days. The animals were sacrificed 48 h after paracetamol administration by mild ether anesthesia. Blood from all animals were collected by retro-orbital puncture, allowed to clot and serum was separated at 3500 rpm for 15 min and used for biochemical studies.

Blood biochemical markers assay

Activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and total bilirubin were estimated using standard kits (Merck Specialties

Pvt. Ltd. India) according to instruction of the manufacturer with an autoanalyzer (Nihon Kohden, Japan).

Histopathological studies

For histopathological analysis, liver specimens fixed in 10% formalin were embedded in paraffin, sliced 5-µm thick, stained with hematoxylin and eosin (H and E). The liver sections then assessed for pathological changes.[28]

Statistical analysis

The statistical analysis was one-way ANOVA followed by Dunnette comparison test using graphpad prism 5.00 for Windows, GraphPad Software, San Diego California USA. All values are expressed as Mean ± S.E.M.

Results

In the present study, comparative hepatoprotective potential of *T. cordifolia*, *T. sinensis* and *Neem-guduchi Satwa* were evaluated by assessing activities of serum enzymes AST, ALT, ALP and total bilirubin. The animals of paracetamol treated group showed significant elevated levels of AST, ALT, ALP and bilirubin, as compared with Healthy control group (Table 1). The results of comparative hepatoprotective potential of *T. cordifolia*, *T. sinensis* and *Neem-guduchi Satwa* on paracetamol treated rats are also summarized in Table 1. *T. cordifolia Satwa* pretreated groups exhibited significantly decreased, paracetamol intoxication elevated activities of serum enzymes AST, ALT and total bilirubin at dose 200 mg/kg, p.o. *T. cordifolia Satwa* at dose 200 mg/kg, p.o. shows 92.2%, 83.2% and 76.9% recovery of AST, ALT and total bilirubin respectively. However surprisingly, activities of serum enzymes ALT, ALP along with total bilirubin were found to be further elevated at dose 400 mg/kg, p.o. Similarly, group pretreated with *T. sinensis Satwa* at dose, 200 mg/kg, p.o. showed significant decrease in levels of AST, ALT, ALP and total bilirubin, increased by paracetamol

intoxication at dose 200 mg/kg, p.o. It shows 104%, 84%, 110% and 84.6% recovery of AST, ALT, ALP and total bilirubin accordingly (Table 1). But, group treated with *T. sinensis Satwa* at dose 400 mg/kg, p.o. showed non-significantly decreased activities of ALT, ALP and total bilirubin, when compared with paracetamol control group. Interestingly, the groups of animals treated with *Neem-guduchi Satwa* at doses, 200 mg/kg and 400 mg/kg, p.o., exhibited non-significant decreases in paracetamol intoxication elevated levels of AST, ALT, ALP and total bilirubin (Table 1).

The results of microscopic examination of liver sections of animals from Healthy control group showed normal liver architecture (Figure 1a). The liver sections of paracetamol intoxicated group rats exhibited infiltration of macrophages and ballooning degeneration in liver parenchymal cells. Lesions of necrosis, pyknosis and nuclear degeneration were evident (Figure 1b). Liver sections of rats treated with *T. sinensis* showed near-normal liver architecture (Figure 1c). Treatment of *T. cordifolia* was found to be effective in restoring paracetamol induced hepatic damage when compared with healthy control as it restored near-normal cellular architecture (Figure 1d). Contrary to expectations, treatment of *Neem-guduchi* showed limited recovery form disturbed cellular architecture in which lesions of nuclear degeneration could be seen (Figure 1e).

Discussion

Serum biochemical markers are generally employed to assess liver function. The estimation of serum bilirubin associated normal liver function. On other hand, estimation of serum enzymes AST, ALT and ALP is the quantitative marker for the determination of type of liver diseases. In the present study, comparative hepatoprotective potential of *T. cordifolia, T. sinensis* and *Neem-guduchi Satwa* were evaluated by using paracetamol-induced hepatotoxicity. Paracetamol produces hepatic necrosis at higher doses. Several studies have

192 demonstrated that induction of hepatocellular damage or necrosis by higher doses of
193 acetaminophen in experimental animals and humans.[29] For screening of hepatoprotective
194 agents, paracetamol-induced hepatotoxicity has been used as a reliable and reproducible
195 method. Paracetamol is metabolized primarily in the liver and eliminated by conjugation with
196 sulfate and glucuronide and then excreted through kidney. PCM is activated and converted
197 by cytochrome P450 enzymes to toxic metabolite NAPQI (N-acetyl-p-benzoquinoneimine)
198 that causes oxidative stress and glutathione (GSH) depletion.[29,30] Paracetamol and carbon
199 tetrachloride (CCl_4) are well-known hepatotoxins, had been used to study hepatoprotective
200 activity by several investigators.[31-33] An obvious sign of hepatic injury is leakage of cellular
201 enzymes into plasma.[34-36] AST predominantly found in mitochondria of the hepatocytes. ALT
202 is more specific to liver and thus is a reliable parameter for detecting liver injury. Serum ALP
203 and bilirubin are also known to be associated with liver cell damage. The activities of ALT,
204 AST and ALP and level of serum bilirubin are largely used as most common biochemical
205 markers to evaluate liver injury.[37] Administration of paracetamol caused a significant
206 elevation of enzymes level such as AST, ALT, ALP and bilirubin level and has been
207 attributed to the damage structural integrity of liver, because they are cytoplasmic in location
208 and released into circulation after cellular damages indicating development of
209 hepatotoxicity.[38,39]

210 The results of present study indicated that administrations *Satwa* of *T. cordifolia* and *T.*
211 *sinensis* at dose 200 mg/kg, i.p. found to significantly reduce the increased activities of serum
212 marker enzymes AST, ALT, ALP and total bilirubin level. However, there is no report so far
213 on possible hepatoprotective mechanism of aqueous stem extract of both species. We
214 assumed that it could be mediated through the modulation of glutathione detoxification and/or
215 suppressing free radicals. Furthermore, result of present study also exhibits *T. sinensis Satwa*
216 have more hepatoprotective potential than *T. cordifolia Satwa*, which supports the view about

this being potent alternative for guduchi. However, in the present study both *T. cordifolia* and *T. sinensis Satwa* found to have reversed to hepatotoxic activity at dose 400 mg/kg, o.p. that could be due to the toxic effect of *Satwa* at higher doses. *T. cordifolia* growing on *Neem* tree (*Azadirachta indica*) hence called *Neem-guduchi* was believed to be more medicinally potent than *T. cordifolia* growing on any other tree as emphesized in the ancient *Ayurvedic* literature.[5,25] However, result of present study revealed that *Neem-guduchi Satwa* did not significantly affect the paracetamol intoxicated elevated levels of ALT, AST and ALP and total bilirubin at selected doses. Thus, the result of present study does not support the claim of *Neem-guduchi* as far as hepatoprotective potential is concerned. The histological findings also supported the results of biochemical markers. Rats treated with *T. sinensis* and *T. cordifolia* showed almost normal hepatic cellular architecture similar to that of control. This confirmed the protection offered to hepatic structural integrity.

Conclusions

In conclusion, the result of hepatoprotective study indicated that *Satwa* of *T. sinensis* has comparatively higher hepatoprotective activity than *T. cordifolia*, although both formulations could have significant protection against paracetamol induced hepatic toxicity. Both the plants therefore may be used as *guduchi* as described in *Ayurvedic* literature. Our data on hepatoprotection however, could not support the claim about *Neem-guduchi*. Finally, it has been suggested that further comparative characterization of chemical constituents of each species is essential to reveal the potent Hepatoprotective components along with their proportionate combination.

Acknowledgements

Authors are thankful to Principal, Amrutvahini College of Pharmcy, Sangamner, India for providing animal house facility.

Disclosure Statement

No competing financial interests exist.

References

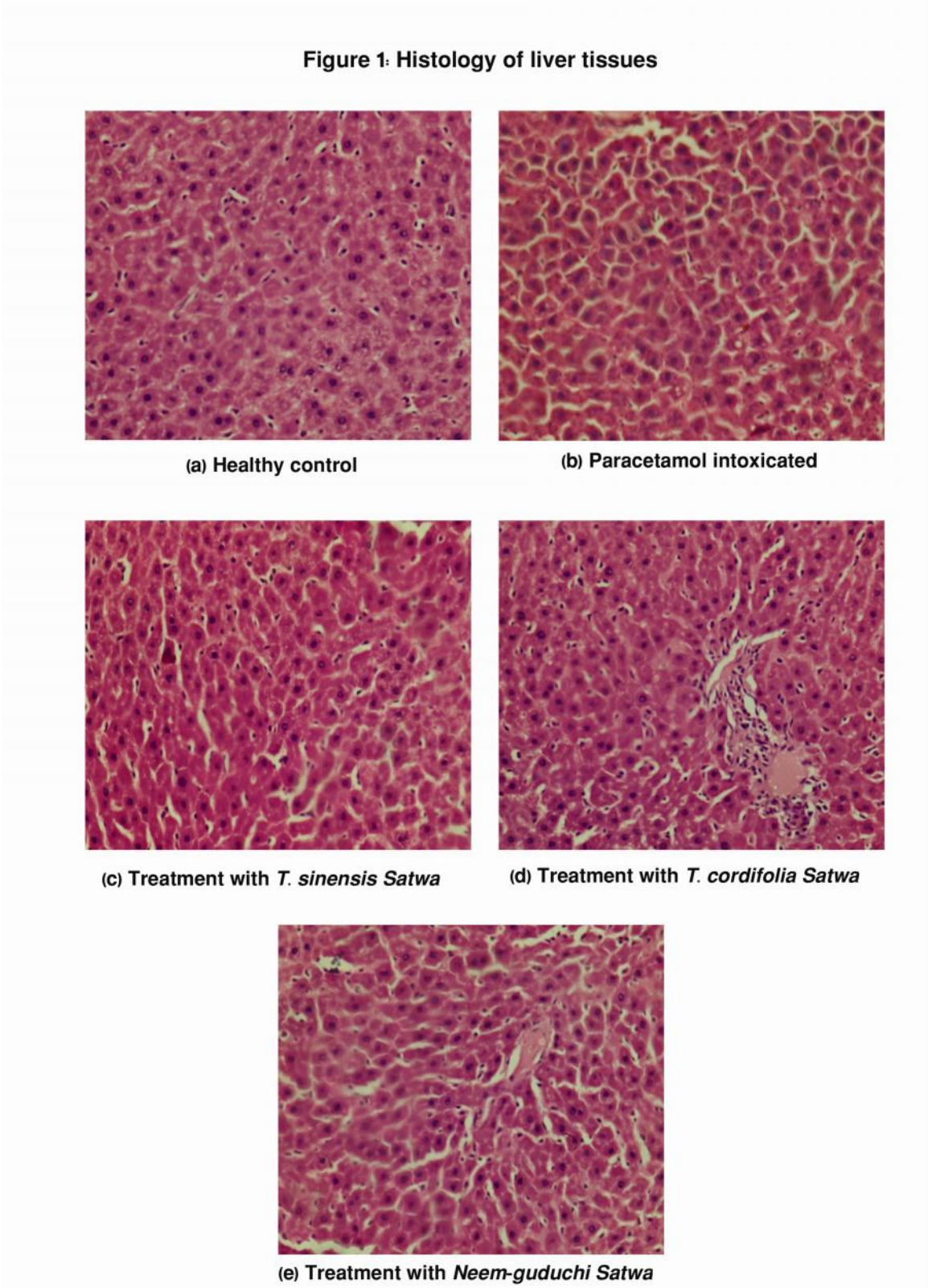
1. Sethuraman MG, Lalitha KG, Rajkapoor B. Hepatoprotective activity of *Sarcostemma brevistigma* against carbon tetrachloride-induced hepatic damage in rats. Current Sci 2003;84:1186-1187.
2. Lee CP, Shih PH, Hsu CL et al. Hepatoprotection of tea seed oil (*Camellia oleifera* Abel.) against CCl_4-induced oxidative damage in rats. Food Chem Toxicol 2007;45:888-895.
3. Vrba J, Modriansky M. Oxidative burst of kupffer cells: Target for liver injury treatment. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2002;146:15-20.
4. Sharma N, Shukla S. Hepatoprotective potential of aqueous extract of *Butea monosperma* against CCl4 induced damage in rats. Exp Toxicol Pathol 2011;63:671-676.
5. Anonymous. Wealth of India: A dictionary of Indian Raw Materials and Industrial Products. New Delhi, India: CSIR, 2003;X:251.
6. Upadhyay A, Kumar K, Kumar A et al. *Tinospora cordifolia* (Willd.) Hook. f. and Thoms. (*Guduchi*)–validation of the Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res 2011;1:112-121.
7. Amia RK. Pictorial Guide to Plants. Dehradun, India: Natraj Publishers, 2003;454-455.
8. Vaidya DB. Materia Medica of Tibetan medicine. Delhi, India: Sri Satguru Publications, 1994:163.
9. Nadkarni KM, Nadkarni AK. Indian Materia Medica. Mumbai, India: M/S Popular Prakasan Pvt Ltd, 1976;1.
10. Kirtikar KR, Basu BD. Indian Medicinal Plants. New Connaught Place, Dehra Dun, India: M/S Bishen Singh, Mahendra Pal Singh, 1975;1.

11. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi, India: CSIR, 1956;246.
12. Chopra RN, Chopra LC, Handa KD et al. Indigenous Drugs of India. Kolkata, India: M/S Dhar VN & Sons, 1982.
13. Karkal YR, Bairy LK. Safety of aqueous of *Tinospora cordifolia* (Tc) in healthy volunteers: A double blind randomized placebo controlled study. Iranian J pharmacol Therap 2007;6:59-61.
14. Nagarkatti DS, Rege NN, Desai NK et al. Modulation of Kupffer cell activity by *Tinospora cordifolia* in liver damage. J Postgrad Med 1994;40:65-67.
15. Bishayi B, Roychowdhury S, Ghosh S et al. Hepatoprotective and immunomodulatory properties of *Tinospora cordifolia* in CCl_4 intoxicated mature albino rats. J Toxicol Sci 2002;27:139-146.
16. Adhvaryau MR, Reddy N, Vakharia BC. Prevention of hepatotoxicity due to anti tuberculosis treatment: A novel integrative approach. World J Gastroenterol 2008;14:4753-4762.
17. Panchabhai TS, Ambarkhane SV, Joshi AS et al. Protective effect of *Tinospora cordifolia, Phyllanthus emblica* and their combination against antitubercular drugs induced hepatic damage: An experimental study. Phytother Res 2008;22:646-650.
18. Rege NN, Bapat RD, Koti R et al. Immunotherapy with *Tinospora cordifolia*; A new lead in the management of obstructive jaundice. Indian J Gastroenterol 1993;12:5-8.
19. Mehrotra R, Katiyar CK, Gupta AP. Hepatoprotective compositions and composition for treatment of conditions related to hepatitis B and E infection. 2000; US Patent 749296.
20. Udayan PS, George S, Tushar KV et al. *Tinospora sinensis* (Lour.) Merr. from Sickupara, Kolli Hills forest, Namakkal District, Tamil Nadu. ZOOS' print Journal 2004;19:1622-1623.

21. Pimpriker RB, Patil VVK, SinthalKumar et al. Hypoglycemic Activity of *Tinospora sinensis* (Linn) leaves, J Pharm Res 2009;2:729-730.
22. Parrota John A. Healing plants of peninsular Indian Herb. CSBI publication, 2001;507.
23. Li RW, Lin GD, Myers SP et al. Anti-inflammatory activity of Chinese medicinal vine plants. J Ethnopharmacol 2003;85:61-67.
24. Yonemitsu M, Fukuda N, Kimura T. Studies on the constituents of *Tinospora sinensis* separation and structure of new phenolic glycoside tinosinen. Planta Med 1993;59:552-553.
25. Watt GA. Dictionary of Economic Products of India. Delhi, India, 1972;6:63.
26. Ramnarayan S. Vaidya Ramnarayan Sharma- A great benefactor to Ayurvedic development. Sachitra Ayurved 1985;38:3-4.
27. Sadashivan S, Latha PG, Sasikumar JM et al. Hepatoprotective studies on *Hedyotis corybosa* (L) Lam. J Ethnopharmacology 2006;106:245-249.
28. Kasote DM, Badhe YS, Zanwar AA et al. Hepatoprotective potential of ether insoluble phenolic components of n-butanol fraction (EPC-BF) of flaxseed against CCl(4) -induced liver damage in rats. J Pharm Bioallied Sci 2012;4:231-235.
29. Vermeulen NPE, Bessems JGM, Vande Streat R. Molecular aspects of paracetamol-induced hepatotoxicity and it mechanism based prevention. Drug Metab Rev 1992;24:367-407.
30. Cohen SD and Khairallah EA. Selective protein arylation and acetaminophen-induced hepatotoxicity. Drug Metab Rev 1997;29:59-77.
31. Visen PKS, Shukla B, Patnaik GK et al. Andrographolide protects rat hepatocytes against paracetamol-induced damage. J Ethnopharmacol 1993;40:131-136.

32. Singh A, Handa SS. Hepatoprotective activity of *Apium graveolens* and *Hydrophila auriculata* against paracetamol and thioacetamide intoxication in rats. J Ethnopharmacol 1995;49:119-126.
33. Ahmed MB, Khater MR. Evalution of the protective potential of *Ambrosia maritime* extract on acetaminophen-induced liver damage. J Ethnopharmacol 2001;75:169-174.
34. Wilkinson JH. An Introduction to Diagnostic Enzymology. Edward Arnold, London: 1962;84.
35. Schmidt E, Schmidt F. Guide to Practical Enzyme Diagnosis. Boehringer Manaheion Gmbh, West Germany 1967;15.
36. Schmidt E, Schmidt FW, Mohr J et al. Liver Morphology and enzyme release. Further studies in the isolated perfused rat liver. In: keppler (Ed.) Pathogenesis and Mechanism of liver cell Necrosis. Medical and Technical publishing Co. Ltd., Lancaster 1975;147.
37. Kozer E, Evans S, Barr J et al. Glutathione, glutathione-dependent enzymes and antioxidant status in erythrocytes from children treated with high-dose paracetamol. Br J Clin Pharmacol 2003;55:234-240.
38. Gutierrez RMP, Solis RV. Hepatoprotective and Inhibition of Oxidative Stress in Liver of *Prostechea michuacana*. Rec Nat prod 2009;3:46-51.
39. Sallie R, Tredger J M, William R. Drugs and the liver part 1: Testing liver function. Biopharm Drug Disp 1991;12:251-259.

340 **FIGURE 1**- HISTOLOGY OF LIVER TISSUES



341

TABLE 1- COMPARATIVE HEPATOPROTECTIVE EFFECT OF AQUEOUS STEM EXTRACT OF *T. CORDIFOLIA*, *T. SINENSIS* AND *NEEM-GUDUCHI* ON SERUM AST, ALT, ALP AND TOTAL BILIRUBIN AGAINST PARACETAMOL INTOXICATION

Sr. No.	Groups	AST (IU/ml)	ALT (IU/ml)	ALP (IU/ml)	Total bilirubin (mg/dl)
I.	Normal control	156.0±12.3***	81.3±6.18***	448.0±26.9**	0.27±0.016**
II.	Paracetamol control	440.0±23.1	302.0±22.0	859.0±107	0.40±0.006
III.	*T. cordifolia* (200mg/kg p.o.)	178.0±13.5[c] (92)	118.3±9.1[b] (83)	511.0±54.7	0.30±0.007[a] (77)
IV.	*T. cordifolia* (400 mg/kg p.o)	254.0±52.5[b] (65)	207.0±26.2	871.0±41.5	0.37±0.007
V.	*T. sinensis* (200 mg/kg p.o)	143.0±3.1[c] (104)	125.0±24.3[b] (80)	404.0±52.3[b] (110)	0.29±0.006[a] (85)
VI.	*T. sinensis* (400mg/kgp.o)	230.0±36.9[c] (74)	174.0±28	756.0±103	0.33±0.017
VII.	*Neem-guduchi* (200 mg/kg p.o)	328.0±46.8	193.0±52.2	637.0±81.7	0.35±0.034
VIII.	*Neem-guduchi* (400mg/kg p.o)	306.0 ±19.9	207.0±26.2	637.0±81.7	0.37±0.028

Values are mean ± S.E.M., n=6 animals per group.

Values in the parenthesis indicate percent protection in individual biochemical parameters from their elevated values.

The percentage of the protection is calculated as 100 × (values of paracetamol control − values of sample)/(values of paracetamol control – values of control).

**, P < 0.05, **, P < 0.01, ***, P < 0.001, Normal control compared to paracetamol control.*

[a], P < 0.05, [b], P < 0.01, [c] , P < 0.001, All groups expect normal control compared to paracetamol control