Sundaraganapathy et al. / International Journal of Pharmacy & Therapeutics, 6(4), 2015, 242-246.

e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

IJPT

HEPATOPROTECTIVE ACTIVITY OF *Plectranthus vettiveroides* AGAINST PARACETAMOL AND D-GALACTOSAMINE INDUCED HEPATIC TOXICITY

***R.Sundara Ganapathy [1], S.Mohan[2], S.Kameshwaran [3], C.Dhanapal[4]**

[1]Dean, Faculty of Pharmacy, Karpagam Academy of Higher Education (Deemed to be University), Eachanari Post, Coimbatore, Tamilnadu, India.
[2] Principal, Karpagam College of Pharmacy, Othakkalmandapam, Coimbatore, India
[3] Department of Pharmacology, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham University, AIMS, Ponekkara P.O, Kochi, Kerala, India.
[4] Departmentof Pharmacology, JKK Munirajah College of Pharmacy, Kumarapalaym, Namakkal, Tamilnadu, India.

ABSTRACT

The present study was to evaluate the protective effect of ethanolic extract of *Plectranthus vettiveroides* (EEPV) roots against paracetamol and D-galactosamine induced hepatic toxicities in Wistar rats. Two different experiments of 10 and 14 days against paracetamol and D-galactosamine, respectively. Six group of animals. The control group received normal saline, a toxicant group in two experiments received paracetamol 750 mg/kg p.o. every 72 h for 10 days and D-galactosamine 400 mg/kg i.p. single dose. The EEPV was used at the two dose levels of 120 and 240 mg/kg/day. Treatment groups treated with it also administered with D-galactosamine, finally blood was withdrawn from the animals for serum estimation of serum glutamate oxaloacetate transferase (SGOT), serum glutamate pyruvate trasnferase (SGPT), albumin, bilirubin, and alkaline phosphatase (ALP), animals was sacrificed, and liver tissue was excised for estimation of thiobarbituric acid reactive substances (lipid peroxidation, malondialdehyde), tissue glutathione (GSH) and histopathological studies. It was evident from the biochemical estimation that both paracetamol and galactosamine caused hepatotoxicity in the toxicant groups. However, treatment with EEPV significantly ($P < 0.001$, vs. toxicant) reduced the levels of SGOT, SGPT, serum bilirubin, and ALP, as well as decreased lipid peroxidation. In addition, treatment with test formulation also significantly ($P < 0.001$, vs. toxicant) elevated serum albumin and GSH levels compared to toxicant groups. On the basis of these studies and comparative evaluation it can be concluded that the extract showed hepatoprotective activity against paracetamol and D-galactosamine at 120 mg/kg and 240 mg/kg.

Key Words:- Hepatoprotective, liver disease, EEPV.

INTRODUCTION

Liver disorders are one of the major causes of morbidity and mortality all over the world. Drug-induced hepatic toxicity is one of the main causes of liver diseases, and accounts for increasing number of hospital admissions (Døssing, 1993). Natural plant products have been globally used for the prevention and treatment of hepatic disorders and scientifically proven for their medicinal efficacy (Handa *et al.*, 1986). *Plectranthus vettiveroides* is also known as coleus vettiveroides, coleus zeylanicus,

Corresponding Author

R. Sundaraganapathy
Email:- sgpram2000@gmail.com

plectranthus zeynanicus (Lamiaceae). The main phytochemical constituents of the genus Plectranthus are diterpenoids ,essential oils and phenolics. About 140 diterpenoids were identified from the coloured leaf – glands of plectranthus species. The main constituents of essential oils of plectranthus are mono and sesquiterpenes. Flavonoides seem to be rare in plectranthus, only two flavonoides were identified ,4',7-dimethoxy -5,6- identified, vone in plectra thus ambigns and chrysosplevetin from p.marruboides. Traditionally it has been used as an antibacterial, deodorant, cooling agent and also used against eye burning head ache and fever. Therefore,The present study was undertaken to evaluate the hepatoprotective potential of EEPV against paracetamol and D‑galactosamine induced hepatic toxicity in Wistar rats (Chatterjee and Sil, 2006).

MATERIALS AND METHODS

Animals

Male Wistar albino rats weighing 200–250 g were used for the study. The animals were maintained under standard laboratory conditions and were allowed free access to food pellets and water ad libitum.

Paracetamol induced hepatic toxicity

Animals were randomly divided into six groups (n = 6/group) and treated as follows: Group 1 (control): Normal saline, 1 ml/kg for 10 days, Group 2 (toxicant): Paracetamol 750 mg/kg p.o. every 72 h for 10 days, Group 3: Liv52 p.o. for 10 days along with paracetamol 750 mg/kg p.o. every 72 h for 10 days, Group 4: Livfit p.o. for 10 days along with paracetamol 750 mg/kg p.o. every 72 h for 10 days, Group 5: EEPV 120 mg/kg p.o. for 10 days, along with paracetamol 750 mg/kg p.o. every 72 h for 10 days, Group 6: EEPV 240 mg/kg p.o. for 10 days along with paracetamol 750 mg/kg p.o. every 72 h for 10 days.

D‑galactosamine induced hepatic toxicity

Animals were randomly divided into six groups (n = 6/group) and treated as follows: Group I (control): Normal saline, 1 ml/kg for 14 days, Group II (toxicant): D‑galactosamine 400 mg/kg i.p. single dose, Group III: Liv52 p.o. for 14 days, D‑galactosamine 400 mg/kg i.p. the single dose was co‑administered on 14th day, Group IV: Livfit p.o. for 14 days, D‑galactosamine 400 mg/kg i.p. the single dose was co‑administered on 14th day, Group V: EEPV 120 mg/kg p.o. for 14 days, D‑galactosamine 400 mg/kg i.p. the single dose was co‑administered on 14th day Group VI: EEPV 240 mg/kg p.o. for 14 days, D‑galactosamine 400 mg/kg i.p. the single dose was co‑administered on 14th day.

Biochemical and histopathological evaluation

Blood was collected from the tail vein of animals 48 h after the completion of the treatment, allowed to coagulate and centrifuged to collect serum at 27°C. Following these animals were sacrificed, and liver tissue was removed for estimation of lipid peroxidation and glutathione (GSH) levels and histopathological studies. Biochemical estimation of serum glutamate oxaloacetate transferase (SGOT), serum glutamate pyruvate transferase (SGPT), albumin, bilirubin, and alkaline phosphatase (ALP) levels was carried out using commercially available kits.

RESULTS AND DISCUSSION

Paracetamol induced hepatic toxicity

The effect of various treatments on hepatic biochemical parameters is shown in Table 1. Paracetamol caused hepatic toxicity in the toxicant group as evident from significantly ($P < 0.001$, vs. toxicant) elevated levels of SGOT, SGPT, serum bilirubin, and ALP, as well as increased lipid peroxidation and significantly reduced ($P < 0.001$, vs. toxicant) level of serum albumin and tissue GSH compared to toxicant. However, both the standard drugs (Liv52 and Livfit) significantly ($P < 0.001$) improved these parameters showing positive shifts of values toward control groups compared to toxicants [Table 1].

Treatment with EEPV at 120 mg/kg and 240 mg/kg showed significant reduction ($P < 0.001$) of serum SGOT and SGPT levels in comparison to the toxicant group. Improvement in serum SGOT level was comparatively better ($P < 0.001$) at 240 mg/kg than 120 mg/kg dose. Similarly, treatment with EEPV at doses of 120 and 240 mg/kg also reduced increased serum ALP and bilirubin levels significantly ($P < 0.001$ vs. toxicant). Treatment with paracetamol significantly reduced serum albumin and tissue GSH levels compared to control group ($P < 0.001$ vs. control), whereas, animals treated with EEPV showed significant improvement ($P < 0.001$ vs. toxicant) in serum albumin and tissue GSH level. Lipid peroxidation was evident from significantly increased ($P < 0.001$) malondialdehyde (MDA) level in hepatic tissue of the paracetamol (toxicant) treated groups were significantly higher ($P < 0.001$ vs. control) compared to normal animals. However, treatment with EEPV significantly reduced ($P < 0.001$ vs. toxicant) elevated MDA level. These results histopathological evaluation [Figure 1] were in accord with biochemical parameters.

D-galactosamine induced hepatic toxicity

The results of biochemical estimations of various treatment groups treated against D-galactosamine induced hepatic toxicity are shown in Table 2. Estimation of biochemical parameters showed that D-galactosamine caused hepatic in the toxicant group as evidenced from significantly ($P < 0.001$, vs. toxicant) elevated SGOT, SGPT, serum bilirubin, and ALP levels, as well as significantly reduced ($P < 0.001$, vs. toxicant) level of serum albumin. D-galactosamine also caused increased lipid peroxidation and reduced GSH levels in treated animals. Treatment with standard 1 and standard 2 (i.e., Liv52 and Livfit, respectively) significantly ($P < 0.001$) reduced the elevated levels of SGOT, SGPT, serum bilirubin, ALP, and tissue MDA. EEPV significantly reduced ($P < 0.001$) SGOT and SGPT levels in comparison to toxicant group at both 120 mg/kg and 240 mg/kg. Improvement in both SGOT and SGPT levels were comparatively better ($P < 0.001$) at the dose of 240 mg/kg vs. 120 mg/kg. Similarly, treatment with EEPV at doses of 120 and 240 mg/kg also reduced increased serum ALP and bilirubin levels significantly ($P < 0.001$ vs. toxicant). Comparatively better reduction in the bilirubin levels was observed at the higher dose (240 mg/kg) of EEPV. Further treatment with EEPV significantly improved ($P < 0.001$ vs. toxicant) the levels of albumin and GSH in serum and tissue, respectively. Elevated Lipid peroxidation measured as liver tissue MDA level showed significant reduction after treatment with EEPV ($P < 0.001$ vs. toxicant) at 120 and 240 mg/kg doses. Histopathological observations were found in concurrence with the results of biochemical estimations. EEPV contains different phytoconstituents which are potentially reduces elevated levels of hepatic biomarkers, indicating that the extract could inhibit the induction of fibrosis in rats. Protective effects of EEPV have been shown on microsomal lipid peroxidation and triglycerides in the liver suggest a restorative effect in the process of liver damage also the phytoconstituents shows hepatoprotective activity by reduced the lipid content liver more significantly the standard dose of the known hepatoprotective silymarin (Bishayi *et al.*, 2002). All these reports are suggestive of strong hepatoprotective activity of EEPV against the two toxicants.

Table 1. Results of estimation of hepatic biomarkers in different treatment groups against paracetamol-induced hepatic toxicity

Parameters	Control	Toxicant	LIV 52	LIVFIT	EEPV 120 mg/kg	EEPV 240 mg/kg
SGOT (IU/L)	136.4±1.4	46.4±2.45a	161.2±2.45b	158.3±2.14b	328.4±1.2c,d	172.15±1.58b,h
SGPT (IU/L)	141.25±1.25	588.1±2.86a	286.85±0.25b	244.51±2.74b	333.01±1.74b,d,i	227.1±5.41b,c
Albumin (mg/dL)	5.94±2.74	23.7±0.1a	36±2.1b	4.99±2.86b	3.87±0.35b,d	4.89±0.21b
Bilirubin (mg/dL)	0.78±0.01	2.00±1.25a	1.04±1.2b	1.1±0.04b	1.42±0.1b,c	0.74±0.03b,h
ALP (IU/L)	160.21±6.41	377.12±1.23a	218.26±3.21b	235±2±1.24b	231.25±1.1b	219.7±1.5b
GSH (nmol/mg)	7.30±0.21	5.63±0.1a	6.90±0.12b	6.97±0.13b	6.52±0.1b	6.97±0.2b
MDA (nmol/mg)	0.16±0.01	0.80±0.01a	0.18±0.01b	0.19±0.02b	0.22±0.1b	0.20±0.11

a*P*<0.001 versus control, b*P*<0.001 versus toxicant, c*P*<0.001 versus Liv52, d*P*<0.001 versus Livfit, h*P*<0.001 versus EEPV (120 mg/kg), i*P*<0.001 versus EEPV (240 mg/kg). SGOT: Serum glutamate oxaloacetate transferase, SGPT: Serum glutamate pyruvate transferase, ALP: Alkaline phosphatase, GSH: Glutathione, MDA: Malondialdehyde

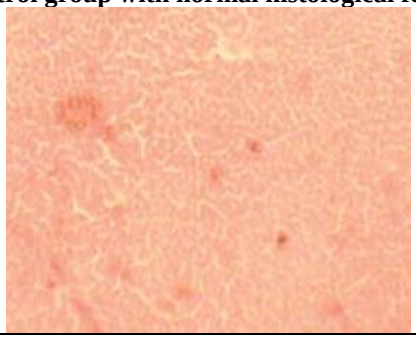
Table 2. Results of estimation of hepatic biomarkers in different treatment groups against D-galactosamine induced hepatic toxicity

Parameters	Control	Toxicant	LIV 52	LIVFIT	EEPV 120 mg/kg	EEPV 240 mg/kg
SGOT (IU/L)	135.2±1.41	454.25±2.41a	210.21±2.0b	205±12.7b	297.21±1.85c,d,i	203±12.84b
SGPT (IU/L)	140.25±2.31	619.52±2.14a	277±2.41b	249.25±12.1b	397.1±2.74b,c,d,i	201.5±2.41b,c,d
Albumin (mg/dL)	5.22±1.42	3.15±2.15a	5.09±2.51b	4.57±0.1b	3.87±2.41b,c,d	4.13±2.1c
Bilirubin (mg/dL)	0.78±1.25	2.30±1.45a	0.89±1.52b	1.10±2.54b	1.39±2.16b,c,i	0.93±1.85b
ALP (IU/L)	160.25±2.54	419.58±1.21a	232±5.84b	264.56±1.21b	290±2.84b	241±1.25b
GSH (nmol/mg)	7.21±0.20	4.75±0.24a	6.17±0.2b	6.31±0.21b	5.87±0.12b,i	6.81±0.29b
MDA (nmol/mg)	0.15±0.10	0.87±0.06a	0.21±0.02b	0.23±0.12b	0.19±0.1b	0.19±0.52b

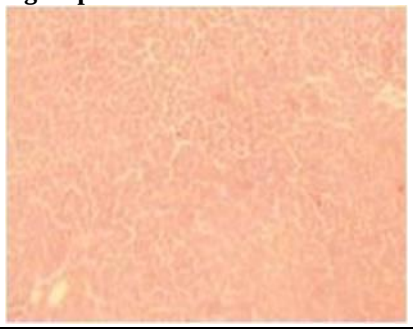
a*P*<0.001 versus control, b*P*<0.001 versus toxicant, c*P*<0.001 versus Liv52, d*P*<0.001 versus Livfit, h*P*<0.001 versus EEPV (120 mg/kg), i*P*<0.001 versus EEPV (240 mg/kg). SGOT: Serum glutamate oxaloacetate transferase, SGPT: Serum glutamate pyruvate transferase, ALP: Alkaline phosphatase, GSH: Glutathione, MDA: Malondialdehyde

Figure 1. Histology of hepatic tissue of different treatment groups against paracetamol-induced hepatic toxicity.

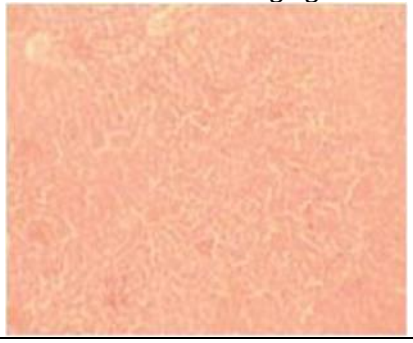
(i) Control group with normal histological features,



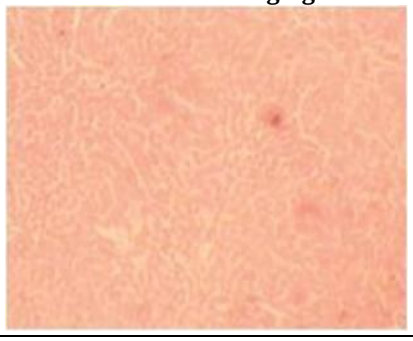
(ii) toxicant group necrotic areas and vacuole formation,



(iii) showing almost normal histology after treatment with EEPV at 120 mg/kg



(iv) showing almost normal histology after treatment with EEPV at 240 mg/kg.



(v) Normal architecture of hepatic tissue in animals treated with standard silymarin

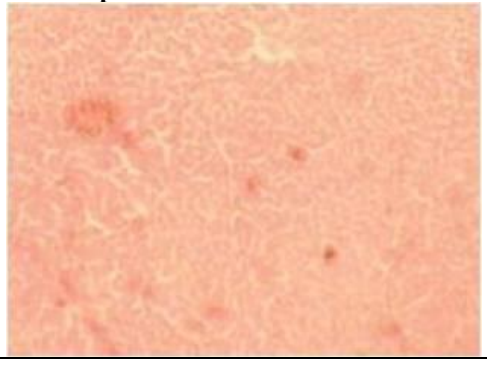
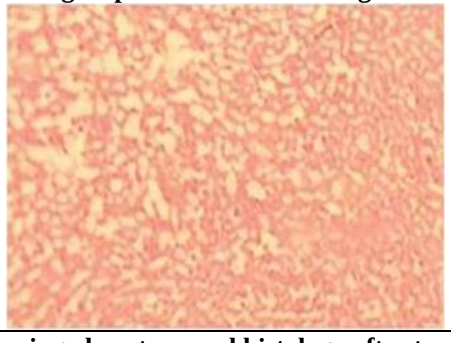
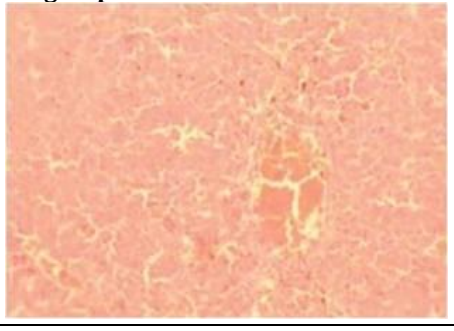


Figure 2. Histology of hepatic tissue of different treatment groups against D-galactosamine induced hepatic toxicity

(i) Control group with normal histological features,



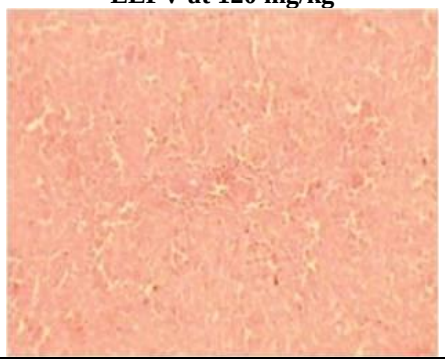
(ii) toxicant group necrotic areas and vacuole formation,



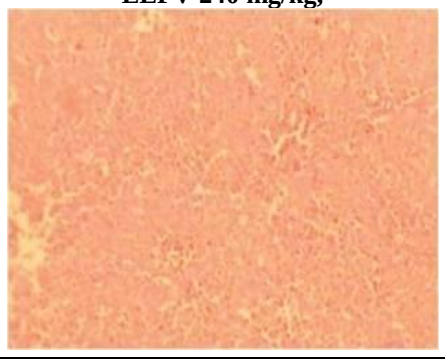
(iii) showing almost normal histology after treatment

(iv) showing almost normal histology after treatment with

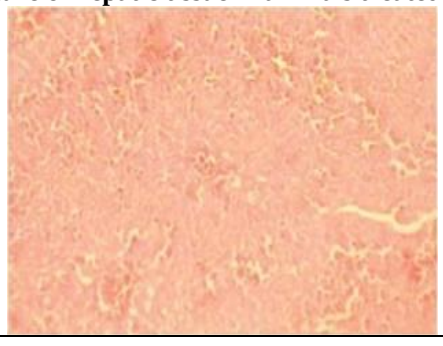
EEPV at 120 mg/kg



EEPV 240 mg/kg,



(v) The normal architecture of hepatic tissue in animals treated with standard silymarin



CONCLUSION

EEPV possesses significant hepatoprotective activity at the dose dependent manner, the hepatoprotective nature of the plant is mainly due to the various phytoconstituents present in the extract, if further isolation of active constituents responsible for the hepatoprotective avtivity is and clinical trial is carried out a new potent hepatoprotective agent might be developed.

ACKNOWLEDGEMENT: None

CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

REFERENCES

Bishayi B, Roychowdhury S, Ghosh S, Sengupta M. Hepatoprotective and munomodulatory properties of *Tinospora cordifolia* in CCl4 intoxicated mature albino rats. *J Toxicol Sci*, 27, 2002, 139‑46.

Chatterjee M, Sil PC. Hepatoprotective effect of aqueous extract of *Phyllanthus niruri* on nimesulide‑induced oxidative stress *in vivo*. *Indian J Biochem Biophys*, 43, 2006, 299‑305.

Døssing M, Sonne J. Drug‑induced hepatic disorders. Incidence, management and avoidance. *Drug Saf*, 9, 1993, 441‑9.

Handa SS, Chakraborty KK, Sharma A. Antihepatotoxic activity of some Indian herbal formulations as compared to silymarin. *Fitoterapia*, 57, 1986, 307.