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Research

Hepatic Protective Activity Hemidesmus Indicus

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Abstract

Hemidesmus indicus root (Family Apocynaceae). In the present study a pharmacognostic evaluation of the root was undertaken. In addition to the evaluation of physicochemical characteristics; preliminary phytochemical parameters and pharmacological activities of Ethanolic extracts has been carried out. The aim of the present study was carried out with the objective of phytochemical screening and to evaluate the hepatoprotective activity of Ethanolic extract of *Hemidesmus indicus.* Liver diseases (like jaundice) are the common ailments affecting mankind, though no remedy is available in allopathic at present. In the recent past years many medicinal plants are screened for their hepatoprotective activity and quite a few of they are already successful in entering the market, Hence the present study is planned to find out the hepatoprotective activity of *Hemidesmus indicus* drug induced hepatotoxicity methods.

Keywords: *Hemidesmus indicus,* Hepatoprotective activity, Alkaline Phosphate, Aspartate amino trasferase, Alanine amino transferase.

INTRODUCTION

Liver

Liver is the most important organ, which plays a pivotal role in regulating various physiological processes in the body. It is involved in several vital functions, such as metabolism, secretion and storage. It has great capacity to detoxicate toxic substances and synthesize useful principles [1].

Anatomical Position

The liver is predominantly located in the right hypochondrium and epigastric areas and extends into the left hypochondrium. When discussing the anatomical position of the liver, it is useful to consider its external surfaces, associated ligaments, and the anatomical spaces (recesses) that surround it.

Liver Surfaces: The **external surfaces** of the liver are described by their location and adjacent structures. There are two liver surfaces – the diaphragmatic and visceral

Diaphragmatic surface: the anterosuperior surface of the liver.
It is smooth and convex, fitting snugly beneath the curvature of the diaphragm. The posterior aspect of the diaphragmatic surface is not covered by visceral peritoneum, and is in direct contact with the diaphragm itself (known as the 'bare area' of the liver).

Visceral surface: the posteroinferior surface of the liver. With the exception of the fossa of the gallbladder and porta hepatis, it is covered with peritoneum. It is moulded by the shape of the surrounding organs, making it irregular and flat. It lies in contact with the right kidney, right adrenal gland, right colic flexure, transverse colon, first part of the duodenum, gallbladder, oesophagus and the stomach.

Ligaments of the Liver
There are various ligaments that attach the liver to the surrounding structures. These are formed by a double layer of peritoneum.

Falciform ligament: this sickle-shaped ligament attaches the anterior surface of the liver to the anterior abdominal wall and forms a natural anatomical division between the left and right lobes of the liver. The free edge of this ligament contains the ligamentum teres, a remnant of the umbilical vein.

Coronary ligament (anterior and posterior folds): attaches the superior surface of the liver to the inferior surface of the diaphragm and demarcates the bare area of the liver The anterior and posterior folds unite to form the triangular ligaments on the right and left lobes of the liver.

Triangular ligaments (left and right): The left triangular ligament is formed by the union of the anterior and posterior layers of the coronary ligament at the apex of the liver and attaches the left lobe of the liver to the diaphragm. The right triangular ligament is formed in a similar fashion adjacent to the bare area and attaches the right lobe of the liver to the diaphragm.

Lesser omentum: Attaches the liver to the lesser curvature of the stomach and first part of the duodenum. It consists of the hepatoduodenal ligament (extends from the duodenum to the liver) and the hepatogastric ligament (extends from the stomach to the liver). The hepatoduodenal ligament surrounds the portal triad. In addition to these supporting ligaments, the posterior surface of the liver is secured to the **inferior vena cava** by hepatic veins and fibrous tissue. The bare area of the liver lies between the anterior and posterior folds of the coronary ligament.

Hepatic Recesses
The **hepatic recesses** are anatomical spaces between the liver and surrounding structures. They are of clinical importance as infection may collect in these areas, forming an abscess.

Subphrenic spaces – located between the diaphragm and the anterior and superior aspects of the liver. They are divided into a right and left by the falciform ligament.

Subhepatic space – a subdivision of the supracolic compartment (above the transverse mesocolon), this peritoneal space is located between the inferior surface of the liver and the transverse colon.

Morison's pouch – a potential space between the visceral surface of the liver and the right kidney. This is the deepest part of the peritoneal cavity when supine (lying flat), therefore pathological abdominal fluid such as blood or ascites is most likely to collect in this region in a bedridden patient.

Anatomical Structure
The structure of the liver can be considered both macroscopically and microscopically.

Macroscopic: The liver is covered by a fibrous layer, known as **Glisson's capsule**. It is divided into a right lobe and left lobe by the attachment of the **falciform ligament.** There are two further 'accessory' lobes that arise from the right lobe, and are located on the visceral surface of liver:

Caudate lobe: located on the upper aspect of the visceral surface. It lies between the inferior vena cava and a fossa produced by the ligamentum venosum (a remnant of the fetal ductus venosus).

Quadrate lobe: located on the lower aspect of the visceral surface. It lies between the gallbladder and a fossa produced by the ligamentum teres (a remnant of the fetal umbilical vein).

Separating the caudate and quadrate lobes is a deep, transverse fissure – known as the **porta hepatis**. It transmits all the vessels, nerves and ducts entering or leaving the liver with the exception of the hepatic veins.
Microscopically, the cells of the liver (known as hepatocytes) are arranged into **lobules**. These are the structural units of the liver. Each anatomical lobule is hexagonal-shaped and is drained by a **central vein**. At the periphery of the hexagon are three structures collectively known as the portal triad:

Arteriole: a branch of the hepatic artery entering the liver.
Venule: a branch of the hepatic portal vein entering the liver.
Bile duct: branch of the bile duct leaving the liver. The portal triad also contains **lymphatic vessels** and **vagus nerve** (parasympathetic) fibres.

Arterial Supply and Venous Drainage
The liver has a unique dual blood supply:

Hepatic artery proper (25%): supplies the non-parenchymal structures of the liver with arterial blood. It is derived from the coeliac trunk.

Hepatic portal vein (75%): supplies the liver with partially deoxygenated blood, carrying nutrients absorbed from the small intestine. This is the dominant blood supply to the liver parenchyma, and allows the liver to perform its gut-related functions, such as detoxification.
Venous drainage of the liver is achieved through hepatic veins. The central veins of the hepatic lobule form collecting veins which then combine to form multiple hepatic veins. These hepatic veins then open into the **inferior vena cava**.

MATERIALS AND METHODS

Chemicals
Ethanol Absolute
Petroleum ether
Silymarin
SGOT enzyme Kit (Giri diagnostic kit pvt ltd)
SGPT enzyme kit (Giri diagnostic kit pvt ltd)
Chloroform (Central drug house pvt ltd) New Delhi

Phytochemical analysis
Preliminary chemical tests were carried out for methanolic extract to identify different Phyto-constituents.

Alkaloids
The crude powder and methanol extract of *Hemidesmus indicus* Rootwas dissolved in 2 N HCl. The mixture was filtered and the filtrate was divided into 3equal portions. One portion was treated with few drops of Mayer's reagent; one portion was treated with equal amount of Dragondroff's reagent and the other portion was treated with equal amount of Wagner's reagent. The creamish precipitate, orange precipitate and brown precipitate indicated the presence of respective alkaloids. A (+) score was recorded if the reagent produced only a slight opaqueness; a (++) score was recorded if a definite turbidity but no flocculation was observed and a (+++) score was recorded if heavy precipitate or flocculation was observed.

Flavonoids
Shinoda test
The presence of flavonoids was estimated by Shinoda test. The crude powder and methanol extract of *Hemidesmus indicus* Rootwere treated with few drops ofconcentrated HCl and magnesium ribbon. The appearance of pink or tomato red colour within few minutes indicated the presence of flavonoids.

Alkaline reagent test
The crude powder and methanol extract of *Hemidesmus indicus* Rootwas treated with few drops of diluted sodium hydroxide (NaOH) separately. Formation of intense yellow color which turned colorless on addition of few drops of diluted HCl indicated presence of flavonoids.

Cardiac glycosides

Keller-kiliani test was performed for the presence of cardiac glycosides. The crude powder and methanol extract of *Hemidesmus indicus* Rootwas treated with 1 ml mixture of 5% $FeCl_3$ and glacial acetic acid (1:99 v/v). To this solution, few drops of concentrated H_2SO_4 were added. Appearance of greenish blue color within few minutes indicated the presence of cardiac glycosides.

Plobotannins

The crude powder and methanol extract of *Hemidesmus indicus* Rootwas boiled with 1% aqueous HCl. Deposition of red precipitate was taken as evidence for the presence of phlobatanins.

Saponins

The presence of saponins was determined by Frothing test. The crude powder and methanol extract of *Hemidesmus indicus* Rootwas vigorously shaken with distilled water and was allowed to stand for 10 min and classified for saponin content as follows: no froth indicates absence of saponins and stable froth for more than 1.5cm indicated the presence of saponins.

Steroids

Liebermann-Burchard reaction was performed for the presence of steroids. Achloroformic solution of the crude powder and methanol extract of *Hemidesmus indicus* Rootwas treated with acetic anhydride and few drops of concentrated H_2SO_4 were added down the sides of test tube. A blue green ring indicated the presence of steroids.

Tannins

The crude powder and methanol extract of *Hemidesmus indicus* Rootwas treated with alcoholic ferric chloride ($FeCl_3$) reagent. Blue color indicated the presence of tannins.

Riterpenes

Chloroform extract of the crude powder and methanol extract of *Hemidesmus indicus* Rootwas treated with concentrated sulphuric acid (H_2SO_4). Appearance of reddish brown ring indicated the presence of triterpenes.

Mechanism of Action of silymarin

The mechanisms which provide silymarin hepatoprotective effects are many and varied, and include antioxidation, anti-lipid peroxidation, enhanced detoxification, and protection against glutathione depletion. (Halim AB et al; 1997)

RESULTS

Preliminary phytochemical analysis

The results of qualitative phytochemical analysis of the crude powder and the methanol extract of *Hemidesmus indicus* root are shown in Table.

Table 1: Preliminary qualitative phytochemical analysis of *Hemidesmus indicus root*

Phytochemical	Test	Methanolic extract
Alkaloids	Dragandroffs test	+
	Mayers test	+
	Wagners test	+
Flavonoids	Shinoda test	+
	Alkaline reagent test	+
Cardiac glycosides	Keller-kilianni test	-
Phlobotannins	HCl test	+
Saponins	Frothing test	+
Steroids	Libbermann-Burchard test	-
Tannins	$FeCl_3$ test	+
Triterpenes	H_2SO_4 test	+

(-): absent, (+): present.

In methanol extract maximum amount of tannins, alkaloids, Flavonoids, phlobotannins, saponins and triterpenes were present. Cardiac glycosides and steroids were absent.

RESULTS AND DISCUSSION

Table 2: Effect of extracts of Ethanolic extracts *Hemidesmus indicus* root on SGOT

GROUP	SGOT level mean ± SEM
Control	1414±1.06
Negative Control	1824.01± 2.241**a
Standard	1464.24±1.10**b
HI 200mg/kg	1431.61±1.25 *b
HI 400mg/kg	1624.14±2.05 ***b

*Values are expressed as Mean ± SEM, n=6; Comparison: a -Group I vs. Group II b- Group II vs. Group III, IV & V; NS Non significant; *P<0.05, **P<0.01;***P<0.001; One way ANOVA followed by Dunnet"s "t" Test*

Effect Of Hemidesmus Indicus On Sgot

There was significant (p<0.001) increase in serum SGOT in Ethanol induced group when compared to control group. There was significant (p<0.001) decrease in serum SGOT in Silymarin treated group when compared to control group. There was significant (p<0.001) decrease in serum SGOT in *Hemidesmus indicus* treated group at a dose of 200mg/kg/p.0 when compared to control group. There was significant (p<0.001) decrease in serum SGOT in *Hemidesmus indicus* treated group at a dose of 400mg/kg/p.o when compared to control group. There was a significant (p<0.01) decrease in serum SGOT level in Silymarin treated rats when compared to ethanol induced. The *Hemidesmus indicus* at a dose of 200mg/kg/p.o showed a significant (p<0.010) decrease in serum SGOT level when compared to ethanol induced group. The *Hemidesmus indicus* at a dose of 400 mg/kg/p.o showed a significant (p<0.001) decrease in serum SGOT level when compared to Ethanol induced group. The results were shown in the Table no.1 and Graph no.2.

Table 3: Effect of extracts of Ethanolic extracts *Hemidesmus indicus* root on SGPT

GROUP	SGOT level mean ± SEM
Control	1512±1.14
Negative Control	1951.36± 2.204**a
Standard	1559.42±2.60**b
Hemidesmus indicus 200mg/kg	1524.21±1.60 *b
Hemidesmus indicus 400mg/kg	1924.56±2.45 ***b

Graphical representation of Effect of Hemidesmus indicus on SGPT; Values are expressed as Mean ± SEM, n=6
*Comparison: a -Group I vs. Group II b- Group II vs. Group III, IV & V; NS Non significant; *P<0.05, **P<0.01;***P<0.001; One way ANOVA followed by Dunnet"s "t" Test*

Effect of *hemidesmus indicus* on SGPT

There was significant (p<0.01) increase in serum glutamic pyruvate transaminase level in Ethanol induced rats when compared to control group. There was significant (p<0.05) decrease in SGPT in ethanol treated group when compared to control group. There was significant (p<0.01) decrease in serum SGPT in *Hemidesmus indicus* treated group at a dose of 200mg/kg/p.0 when compared to control group. There was significant (p<0.01) decrease in serum SGPT in *Hemidesmus indicus* treated group at a dose of 400mg/kg/p.o when compared to control group. There was a significant (p<0.01) decrease in serum SGPT level in Silymarin treated rats when compared ethanol induced group. The *Hemidesmus indicus* at a dose of 200mg/kg/p.o showed a significant (p<0.01) decrease in serum SGOT level when compared to Ethanol induced group. The *Hemidesmus indicus* at a dose of 400 mg/kg/p.o showed a significant (p<0.001) decrease in serum SGOT level when compared to Ethanol induced group.

Table 4: Effect of extracts of Ethanolic extract *Hemidesmus indicus* root on Bilirubin

GROUP	Total Bilirubin mean ± SEM
Control	1.14±0.01
Negative Control	2.42 ± 0.10***a
Standard	1.15 ± 0.02*b
Hemidesmus indicus 200mg/kg	1.24 ± 0.02 **b
Hemidesmus indicus 400mg/kg	1.14 ± 0.01 **b

*Values are expressed as Mean ± SEM, n=6 Comparison: a -Group I vs Group II b- Group II vs Group III, IV & V; NS Non significant; *P<0.05, **P<0.01;***P<0.001 One way ANOVA followed by Dunnet"s "t" Test*

Effect of *hemidesmus indicus* on total bilirubin

There was significant ($p<0.01$) increase in Bilirubin level in Ethanol induced group when compared to control group. There was significant ($p<0.01$) decrease in Bilirubin in Silymarin treated group when compared to control group. There was significant ($p<0.05$) decrease in Bilirubin in *Hemidesmus indicus* treated group at a dose of 200mg/kg/po when compared to control group. There was significant ($p<0.001$) decrease in Bilirubin in *Hemidesmus indicus* treated group at a dose of 400mg/kg/p.o when compared to control group. There was a significant ($p<0.01$) decrease in Bilirubin in Silymarin treated rats when compared ethanol treated. The *Hemidesmus indicus* at a dose of 200mg/kg/p.o showed a significant ($p<0.05$) decrease in serum bilirubin when compared to ethanol induced group. The *Hemidesmus indicus* at a dose of 400 mg/kg/p.o showed a significant ($p<0.001$) decrease in Bilirubin when compared to Ethanol induced group.

Table 5: Effect of extracts of Ethanolic extract *Hemidesmus indicus* root on ALP

GROUP	ALP level mean ± SEM
Control	44.02±0.01
Negative Control	48.2±0.02*a
Standard	38.4±0.01**b
Hemidesmus indicus 200mg/kg	44±1.71***b
Hemidesmus indicus 400mg/kg	40.6±0.10*b

Effect of *hemidesmus indicus* on alp

There was significant ($p<0.01$) increase in ALP in ethanol induced group when compared to control group. There was significant ($p<0.01$) decrease in ALP in Silymarin treated group when compared to control group. There was significant ($p<0.05$) decrease in ALP in *Hemidesmus indicus* treated group at a dose of 200mg/kg/p.0 when compared to control group. There was significant ($p<0.001$) decrease in Alp in *Hemidesmus indicus* treated group at a dose of 400mg/kg/p.o when compared to control group. There was a significant ($p<0.05$) decrease in ALP in Silymarin treated rats when compared ethanol treated. The *Hemidesmus indicus* at a dose of 200mg/kg/p.o showed a significant ($p<0.001$) decrease in ALP when compared to Ethanol induced group. The *Hemidesmus indicus* at a dose of 400 mg/kg/p.o showed a significant ($p<0.05$) decrease in ALP when compared to Ethanol induced group.

Histopathological studies of the liver in paracetamol induced hepatotoxicity

The histopathological evaluation of paracetamol toxicity in all the groups was examined and shown in figure. The description is as follows, Section of rat liver treated with vehicle control group shows liver parenchyma with intact architecture which is the normal appearance. Section of liver in toxicant control group shows partially effaced architecture. Some of the hepatocytes show apoptotic changes, perivenular mononuclear inflammatory infiltration, scattered inflammatory infiltration within the parenchyma which is due to toxicity. Section of liver in silymarin treated group shows liver parenchyma with intact architecture. Some of the central veins show congestion with diffuse congestion of sinusoids.

Section of liver in test drug ethanolqueous treated groups shows intact architecture, few regenerative hepatocytes, sinusoidal congestion and scattered mononuclear inflammatory cells which is similar to silymarin treated group.

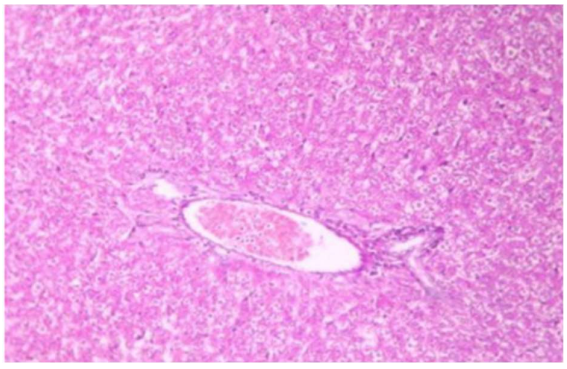

Fig 1: Normal Control group, showing normal hepatocytes

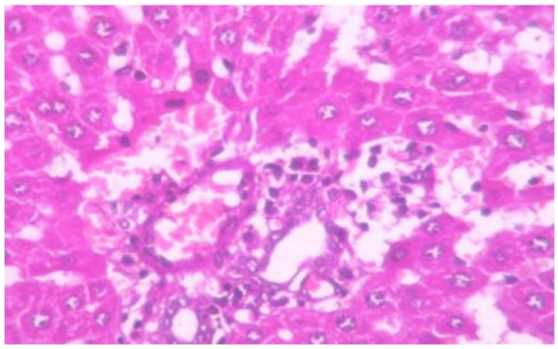

Fig 2: Ethanol treated animal group shows that hepatic cells damage and congestion of the liver

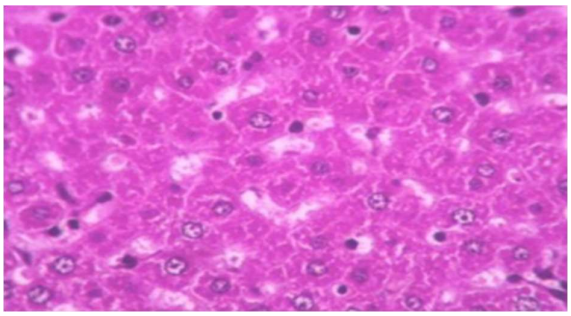

Fig 3: Hepatocytes in group treated with Standard (Silymarin 200 mg/kg)

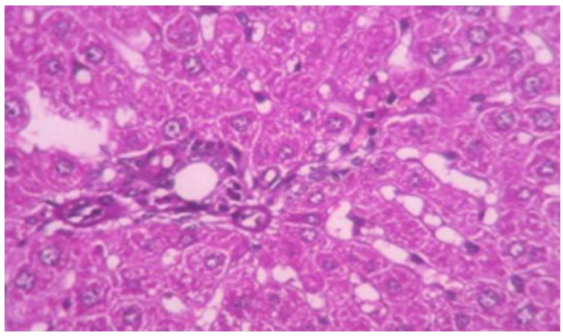

Fig 4: *Hemidesmus indicus* of 400 mg/kg shows that few regenerative hepatocytes, sinusoidal congestion and scattered mononuclear inflammatory cells

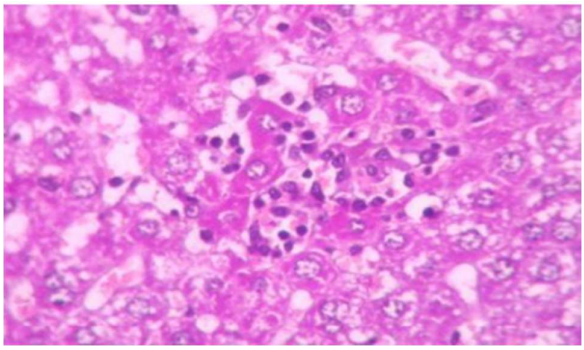

Fig 5: *Hemidesmus indicus* of 200 mg/kg shows that few regenerative hepatocytes, sinusoidal congestion and scattered mononuclear inflammatory cells

DISCUSSIONS

There are many factors which are responsible for the liver damage or injuries such as chemicals and drugs. In the present study ethanol was used to induce Hepatotoxicity, since it is clinically relevant. Ethanol produces a constellation of dose related deleterious effects in the liver (Leo et al., 1982). The majority of ethanol is metabolized in the liver and individuals who abuse alcohol by routinely drinking 50-60 g (about 4 to 5 drinks) of ethanol per day are at risk for developing alcoholic liver disease. In addition, both acute and `chronic ethanol administration cause enhanced formation of cytokines, especially TNF-alpha by hepatic Kupffer cells, which have a significant role in liver injury. Besides the development of fatty liver (steatosis), another early sign of excessive ethanol consumption is liver enlargement and protein accumulation, both of which are common findings in alcoholics and heavy drinkers.

Hemidesmus indicus are commonly used in the native system of medicine. Various parts of the plant like root and roots are medicinally important.

In order to investigate the medicinal use of *Hemidesmus indicus* in hepatoprotective, we evaluated crude extract for its Hepatoprotective activity using different *in vitro* assays and *in vivo* rat model of Hepatoprotective activity.

Elevated levels of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) are indications of hepatocellular injury. In the present study AEOC and AQEOC at a dose of 500 mg/kg, p.o caused a significant inhibition in the levels of SGOT and SGPT towards the respective normal range and this is an indication of stabilization of plasma membrane as well as repair of hepatic tissue damage caused by ethanol.

On the other hand suppression of elevated ALP activities with concur-rent depletion of raised bilirubin level and an increase in the total plasma protein content suggests the stability of biliary dysfunction in rat liver during hepatic injuries with toxicants. These results indicate that AEHI and AQEHI preserved the structural integrity of the hepatocelluar membrane and liver cell architecture damaged by ethanol which was confirmed by histopathological examination.

On examining the liver function tests of ethanol induced animals, the SGOT, SGPT, ALP, Total bilirubin has significantly increased After treatment with the ethanolic extract of *Hemidesmus indicus* (200 mg/kg and 400 mg/kg) the excretion of has SGOT, SGPT, ALP, Total Bilirubin significantly decreased Although the low dose was more potent than the high dose when compared with silymarin treated group, which is a standard.

Ethanolic extract *Hemidesmus indicus* of has shown promising *invitro* efficacy on Hepatoprotective activity, we have observed increase in the absorbance indicating the inhibition of Nucleation and Aggregation of calcium oxalate in *invitro* studies.

For the in vivo Hepatoprotective activity, of *Hemidesmus indicus*, Ethanol-induced hepatotoxicity rat model of was used. Since the liver damage inducing treatment, Ethanol, was given orally, therefore, the extract was given p.o. in order to prevent any potential interaction of Ethanol with plant constituents inside gut, interfering with absorption of either of the two. Administration of Ethanol resulted in the increased toxicity, which might be due to the Hepatotoxicity, as evident by increase in SGOT, SGPT, and ALP as compared to normal.

SUMMARY

The present study was aimed to assess the hepatoprotective activity and diuretic activity of Ethanolic extract of *Hemidesmus indicus* root. LD50 studies were conducted in albino rats with aqueous and Ethanolic extract of *Hemidesmus indicus* root according to OECD guideline No.425 and was found safe up to the dose level of 4 gm/kg confirming its non-toxic nature. The hepatoprotective activity was studied in ethanol induced hepatotoxic animal model. The Physical parameter wet liver weight, Biochemical parameters like serum SGPT, SGOT, and total Bilirubin levels, and histopathology of livers were considered as major parameters of study. Ethanol induced hepatotoxicity was significantly prevented by pretreatment ethanolic extract of root. Decrease in wet liver weight, reduction in elevated biochemical parameter levels like serum SGPT, SGOT, and total bilirubin, after treatment with Ethanolic extract of *Hemidesmus indicus* root confirmed the hepatoprotective effect of extract under study. In liver injury models in rats restoration of hepatic cells with minor fatty changes and absence of necrosis after treatment with extract was observed, indicating satisfactory hepatoprotection. Based on improvement in serum marker enzyme levels, physical parameters, and histopathological studies it was concluded that ethanol extract of *Hemidesmus indicus* root possesses significant hepatoprotective activity in the doses used. The hepatoprotective activity was studied in ethanol induced hepatotoxic animal model. The Physical parameter wet liver weight, Biochemical parameters like serum SGPT, SGOT, and total Bilirubin levels, and histopathology of livers were considered as major parameters of study.

CONCLUSION

The hepatoprotective effect of Ethanolic extract of *Hemidesmus indicus* root was confirmed by the following measures: The isolated livers from the toxicant (ethanol) treated animals exhibited increase in wet liver weight. Indeed, extract treated animals exhibited decrease in the values of above physical parameters as an indication of hepatoprotection. Serum marker enzymes such as SGPT, SGOT and total Bilirubin, showed marked increase. The same is observed in liver diseases in clinical practice and hence are having diagnostic importance in the assessment of liver function. In the present study, the methanolic and aqueous extract of *Hemidesmus indicus* root significantly reduced the elevated levels of above mentioned serum marker enzymes. Hence, at this point it is concluded that the methanolic and aqueous extract of *Hemidesmus indicus* root possesss hepatoprotective activity. Finally based on improvement in serum marker enzyme levels, physical parameters, functional parameters and histopathological studies, it is concluded that the Ethanolic extract of *Hemidesmus indicus* root possesses hepatoprotective activity and thus supports the traditional application of the same under the light of modern science.

REFERENCES

1. Shanmugasundaram P, Venkataraman S. 2006. Hepatoprotective and antioxidant effects of Hygrophila auriculata (K. Schum) Heine Acanthaceae root extract. Journal of Ethnopharmacology 104: 124-128.
2. Saleem TSM, Chetty CM, Ramkanth S, Rajan VST, Kumar KM, Gauthaman K. 2010. Hepatoprotective herbs - a review. International Journal of Research in Pharmaceutical Sciences 1: 1-5.
3. Kaplowitz N, Tsukamoto H. 1996. Oxidative stress and liver disease. Progress in Liver Diseases. 14:131-59.
4. Ajith TA, Hema U, Aswathy MS. 2007. Zingiber officinale Roscoe prevents acetaminophen-induced acute hepatotoxicity by enhancing hepatic antioxidant status.
1. Food and Chemical Toxicology 45: 2267-2272.
5. Timbrell J, 2001. Introduction to Toxicology. 3rd ed. Taylor and Francis, New York, pp. 57-71.
6. Kohen R, Nyska A, 2002. Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods for their quantification. Toxicologic Pathology 30: 620-650.
7. Gupta AK, Misra N. 2006. Hepatoprotective activity of aqueous ethanolic extract of Chamomile capitula in paracetamol intoxicated albino rats. American Journal of Pharmacology and Toxicology 1: 17-20.
8. Negi AS, Kumar JK, Luqman S, Shanker K, Gupta MM, Khanuja SPS (2008). Recent advances in plant hepatoprotectives: A chemical and biological profile of some important leads. Medicinal Research Reviews 28: 746-772.
9. Kohle C, Schwarz M, Bock KW; 2008. Promotion of hepatocarcinogenesis in humans and animal models. Archives of Toxicology 82: 623-631.
10. Miyoshi H, Rust C, Roberts PJ, Burgart LJ, Gores GJ. 1999. Hepatocyte apoptosis after bile duct ligation in the mouse involves Fas. Gastroenterology 117: 669-677.
11. Seki S, Kitada T, Sakaguchi H. 2005. Clinicopathological significance of oxidative cellular damage in non-alcoholic fatty liver diseases. Hepatology Research 33: 132-134.
12. Kitase A, Hino K, Furutani T, Okuda M, Gondo T, Hidaka I, Hara Y, Yamaguchi Y, Okita K. 2005. In situ detection of oxidized n-3 polyunsaturated fatty acids in chronic hepatitis C: correlation with hepatic steatosis. Journal of Gastroenterology 40: 617-624.
13. Albano E, Mottaran E, Occhino G, Reale E, Vidali M. 2005. Role of oxidative stress in the progression of non-alcoholic steatosis. Alimentary Pharmacolcology and Therapeutics 22: 71-73.
14. Lee WM. 2003. Acute liver failure in the United States. Seminars in Liver Disease 23: 217-226.
15. Cullen JM, Miller RT. 2006. The role of pathology in the identification of druginduced hepatic toxicity. Expert Opinion on Drug Metabolism and Toxicology 2: 241-247.