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EVALUATION OF HEPATOPROTECTIVE ACTIVITY OF AQUEOUS EXTRACT OF SWERTIA CHIRAYITA IN WISTAR RATS

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Abstract:

In this study we investigated the in vivo Hepatoprotective activity of aqueous extract of Swertia chirayita in induced hepatotoxicity using Wistar rats of either sex as model. Hepatotoxicity was induced by the administration of 3% CMC per 100g body weight). Swertia chirayita extract at different dose levels (200 and 400mg/kg, p.o.) showed the dose dependent hepatoprotective effect and was compared with well-known standard hepatoprotective Silymarain (100mg/kg).

The rats were divided into five groups with three rats in each for three models. Group I (Control) served as normal and received the vehicle alone (Sterile distilled water, 10 ml/kg, p.o.) for 21 days. Group II (control and 40% ethanol) animals on the 21 days. Group III Received 40% ethanol v/v (2.0ml/l00g body wt, p.o.) for 21 days and standard drug silymarin (25 mg/kg. p.o.) for 21 days once daily and IV were treated with 40% ethanol and aqueous extract Swertia chirayita (400 mg/kg) 21 days once daily. Group V was treated with Received 40% ethanol and aqueous extract of Swertia chirayita (200 mg/kg) 21 days once daily the animals were sacrificed 48 h after the last injection of hepatotoxic drugs under mild ether anesthesia. The blood was collected and allowed to stand for 30 min at 37°C and then centrifuged to separate the serum to estimate various biochemical parameters.

In hepatoprotective studies, the toxicity elevated levels of serum marker enzymes Total Bilirubin ALT, AST, ALP, SGOP and SGPT levels. Ethanol induced hepatotoxicity was significantly prevented by pretreatment ethanolic extract of leaves. Decrease in wet liver weight, reduction in elevated biochemical parameter levels like serum SGPT, SGOT, and total bilirubin, after treatment with aqueous extract of Swertia chirayita 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.

The data obtained from animal experiments are expressed as mean ± SEM (standard error of mean). For statistical analysis data were subjected to analysis of variance (ANOVA) followed by Student's t-test. Values are considered statistically significant at $p < 0.01$ for ANOVA and $P < 0.05$ for t-test.

Keywords: *Swertia chirayita, Hepatoprotective activity, Alkaline Phosphate, Aspartate amino trasferase, Alanine amino transferase.*

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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.

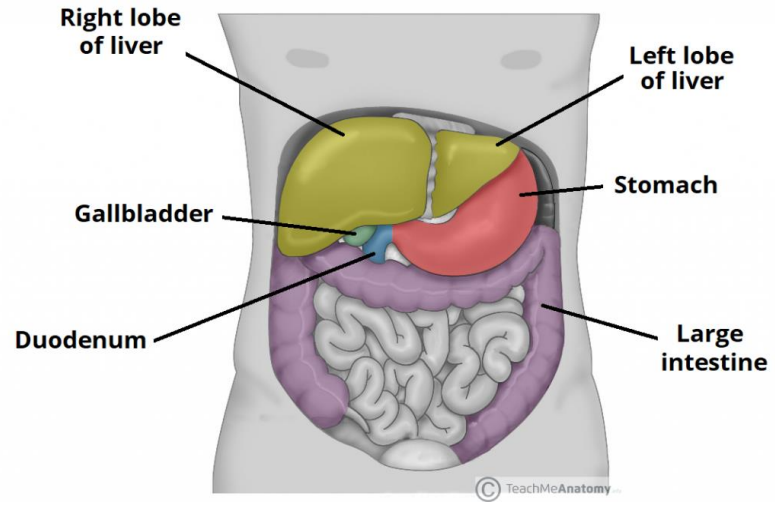

Figure : 1: Anatomical position of liver

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.

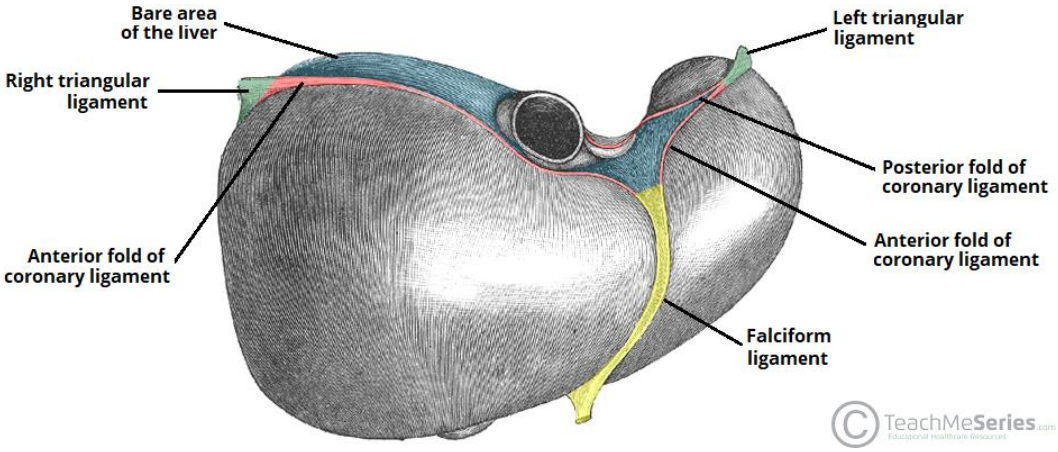

Fig 2 – Diaphragmatic surface of the liver, demonstrating the three main ligaments. The bare area of the liver lies between the anterior and posterior folds of the coronary ligament.

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.

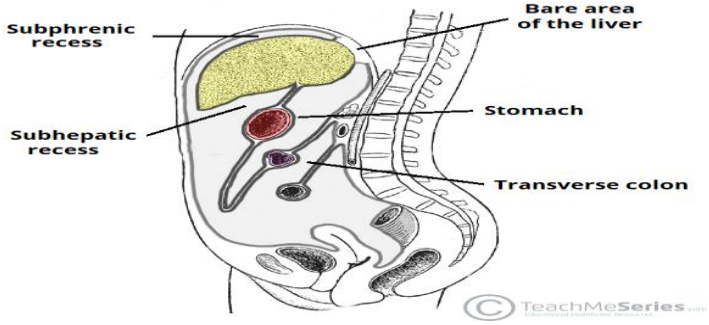

Fig 3 – The subphrenic and subhepatic recesses.

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.

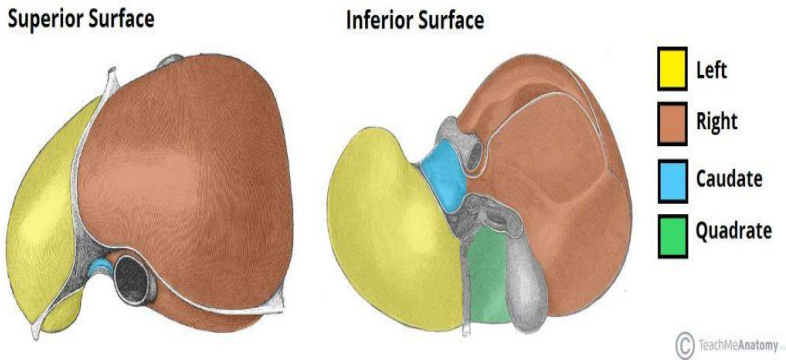

Fig 4 – The anatomical lobes of the liver.

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.

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 Ethanolic extract to identify different Phyto-constituents.

3.1. Alkaloids

The crude powder and aqueous extract of *Swertia chirayita* was 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.

3.2. Flavonoids

3.2.1. Shinoda test

The presence of flavonoids was estimated by Shinoda test. The crude powder and aqueous extract of *Swertia chirayita* were treated with few drops of concentrated HCl and magnesium ribbon. The

appearance of pink or tomato red Colour within few minutes indicated the presence of flavonoids.

3.2.2. Alkaline reagent test
The crude powder and aqueous extract of *Swertia chirayita* was 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.

3.3. Cardiac glycosides
Keller-kiliani test was performed for the presence of cardiac glycosides. The crude powder and aqueous extract of *Swertia chirayita* was 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.

3.4. Plobotannins
The crude powder and aqueous extract of *Swertia chirayita* was boiled with 1% aqueous HCl. Deposition of red precipitate was taken as evidence for the presence of phlobatanins.

3.5. Saponins
The presence of saponins was determined by Frothing test. The crude powder and aqueous extract of *Swertia chirayita* was vigorously shaken with distilled water and were 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.

3.6. Steroids
Liebermann-Burchard reaction was performed for the presence of steroids. Achloroformic solution of the crude powder and aqueous extract of *Swertia chirayita* was 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.

3.7. Tannins
The crude powder and aqueous extract of *Swertia chirayita* was treated with alcoholic ferric chloride ($FeCl_3$) reagent. Blue color indicated the presence of tannins.

3.8. Triterpenes
Chloroform extract of the crude powder and aqueous extract of *Swertia chirayita* was 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).

Stimulation of Liver Regeneration:
One of the mechanisms to explain the ability of silymarin to stimulate the regeneration of hepatic tissue is the increase in protein synthesis in damaged livers. In both *in vivo* and *in vitro* experiments, significant increases in the formation of ribosome and DNA synthesis were measured in addition to the increase in protein synthesis. Interestingly, the increased protein synthesis was only measured in damaged livers (partial hepectomy), not in controls. The mechanism of increased protein synthesis is currently not known but some authors speculate silymarin imitates a physiologic regulator, so the silybin fits into a specific binding site on the polymerase, thus stimulating ribosome formation. (Schopen RD et al; 1969).
The potential for stimulation of protein synthesis by silymarin was investigated in malignant liver tissue, and no increases in protein synthesis, ribosome formation, or DNA synthesis were found in malignant cell lines. (Sonnenbichler J et al; 1986).

Alcohol hepatotoxicity
Alcohol is one of the main causes of end-stage liver disease worldwide In the United States, alcoholic liver disease is the second most common reason for liver transplantation (Mandayalu Jamal et al 2004). The Dionysus Study, a cohort study of the prevalence of chronic liver disease in an Italian population showed that 21% of the population studied was at risk for developing liver damage. Of these, only 5.5 % of the individuals at risk showed actual Signs of liver damage.

About 50 years ago it was believed that alcohol in itself was not toxic, rather that the nutritional deficiencies often accompanying it mere the actual causes of liver damage. However, It was shown by Lieber and De Carli that in rats, alcoholic liver damage developed despite sufficient nutrition (De Carli and Lieber; 1967). The toxicity of alcohol was later on shun to be related to its metabolism by alcohol dehydrogenases (ADHs) and also to the metabolism by CYP2E1. There is also a component of metabolism by catalase (Zilna, Fialova et al. 2001) The main pathway for ethanol (EtOH) oxidation in

die liver IS ADH to acetaldehyde, which is associated with the reduction of NAD to NADH increases in xanthine oxidase activity, which elevates production of superoxide Fialova et al 2001). Metabolism of EtOH by alcohol dehydrogenase Influences the redox status of the liver also in other ways. Enhanced acetaldehyde production after EtOH metabolism decreases hepatic glutathione (GSH) content. The decrease in GSH both due to an increased loss, as well as a lower rate of synthesis (Speisky, MacDonald et al 1985). The absolute majority of EtOH oxidation is by ADH to acetaldehyde and by aldehyde dehydrogenase to acetic acid. However, there is a slight of P450 dependent inducible EtOH oxidation due to the CYP2E1 component. Also, CYP1A2, CYP3A4 and CYP2B families may contribute to EtOH oxidation (Johansson, Ekstrom et al. 1988; Lieber 2004).

The first indication that not only alcohol dehydrogenases participate the metabolism of ethanol came in the early 1970's, when it was discovered that microsomal membrane fractions were capable of catalyzing the oxidation of ethanol. These reactions required NADPH and were inhibited by CO, properties that are distinct from those of alcohol dehydrogenases (Liber. Rubin et al;1970). It was then discovered that this activity was due to CYP2E1 and that the enzyme was inducible by ethanol in rats (Ryan Koop et al. 1986; Johansson Ekstrom et al. 1988)

Free radicals have been implicated in alcoholic liver disease in various ways. Mechanism that are thought to be Involved are impairment of antioxidant defenses, as well as production of reactive oxygen by flie mitochondria and the CYP2E1 enzyme, and by activated phagocytic cells. Oxidative compounds then may lead to activation of immune cells to express pro-fibrotic and pro-Lnflam matoly cytokines. Macrophages produce TNTa In various conditions that cause oxidative stress (Ahmed, Aronson et al. 2000), as well as IL-1 and IL-6 (Meng and Lowell 1997). Also, oxidative stress leads to the generation of lipid peroxidation products and protein adducts (Ekstrom and Inge1man-Sundberg 1989; Dupont, Lucas et al 1998; Johansson and Inge1man-Sundberg 1985; Albano, French et al 1999), which eventually stimulate a break in self-tolerance and all immune reaction associated with hepatitis (Albano 2006). CYP2E1 Inhibitors have been shown to reduce the formation of lipid peroxidation products (Inge1manSundberg Johansson et al 1993). CYP2E1 has also been should be elevated in non-alcoholic steatohepatltis (Weltman, Farrell et al. 1998). Furthermore, it has been shown that the increase m cellular oxidative stress by even moderate alcohol consumption may be one of the mechanisms by which alcoholism progression of chronic hepatitis C, as antibodies towards albumin adducted with lipid peroxidation products were greater in consumers (Riga-monti, Mottaran et al; 2003).

It was suggested that CYP2E1 may play a role in alcoholic liver damage as it has been shovm that during ethanol oxidation CYP22E1 produces O2 -and H202 as a result of uncoupling of oxygen consumption with NADPH oxidation (ingeman-Sundberg and Johansson 1984). In the presence of iron catalysts, even more reactive oxygen species (ROS) can be formed, such as the hydroxyl radical, superoxide and hydrogen peroxide(Ingeman-Sundberg and Johansson 1984; Gonzalez 2005; Cederbaum 2006 and Ingeman-Sundberg 1989); Kou Galeotti et al. 1991). These reactive oxygen species (ROS) may lead to elevated levels of lipid peroxidation products, that in turn adducts with cellular proteins. Adducts may also be formed with nucleic acids. Eventually, this will result In cell damage (Cederbaum 2006) It has been shown that the vanous lipid peroxidation products formed lead to an Immune response in human alcoholics, which worsens as disease progresses (Mot-taraw Stewart et al. 2002). Lipid peroxidation products have also been shown to play a part in fibrosis, by able to activate the stellate cells of die liver to increase their production of collagen which has been particularly studied for the lipid aldehyde malondi aldehyde(MDA) (Maher, Tzagarakis et al. 1994).

Liver injury is often zonated within the liver this is the case for many hepatotoxins that primarily damage the perivenous region and also true in the case of ethanol. Notably, ChQ2E1 is particularly induced in regions by ethanol (Johansson Lindros et al. 1990; Fang, Lindros et al. 1998). vitro studies using HepG2 cells transfected to express CYP2E1, both stably and transiently, have shown signs of DNA fragmentation and cell death in transfected cells, which is not seen in controls. EtOH-induced apoptosis was prevented by an Inhibitor of ethanol oxidation Via CP2E1, and also by an antioxidant that prevents lipid peroxidation (wuand Cederbaum 1999) In this cell model it was also noted that glutathione levels were lowered (Wu and Cederbaum 2004).

Although alcohol is undoubtedly a hepatotoxicity still only approximately 20% of heavy drinkers (males) develop alcoholic cirrhosis (Lelbach 1975). Cirrhosis is most often preceded by hepatitis, generally defined by the following morphologic features; hepatocyte necrosis, neutrophil polymorph Infiltrate fatty changes and usually also Mallory bodies

(accumulations of hyaline material in damaged hepatocytes). The series of events preceding cirrhosis are commonly; fatty accumulating hepatitis, fibrosis and finally cirrhosis.

8. RESULTS

PRELIMINARY PHYTOCHEMICAL ANALYSIS

The results of qualitative phytochemical analysis of the crude powder and the aqueous extract of *Swertia chirayita* are shown in Table.

Table ---: Preliminary qualitative phytochemical analysis of *Swertia chirayita*

Phytochemical	Test	aqueous 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 aqueous extract maximum amount of tannins, alkaloids, Flavonoids, phlobotannins, saponins and triterpenes were present. Cardiac glycosides and steroids were absent.

RESULTS AND DISCUSSION

Table 1: Effect of extracts of aqueous extracts *Swertia chirayita* on SGOT

GROUP	SGOT level mean ± SEM
Control	1352±2.01
Negative Control	1825.03± 1.102**a
Standard	1402.01±1.1**b
Swertia chirayita 200mg/kg	1400.10±1.05 *b
Swertia chirayita 400mg/kg	1591.14±2.10 ***b

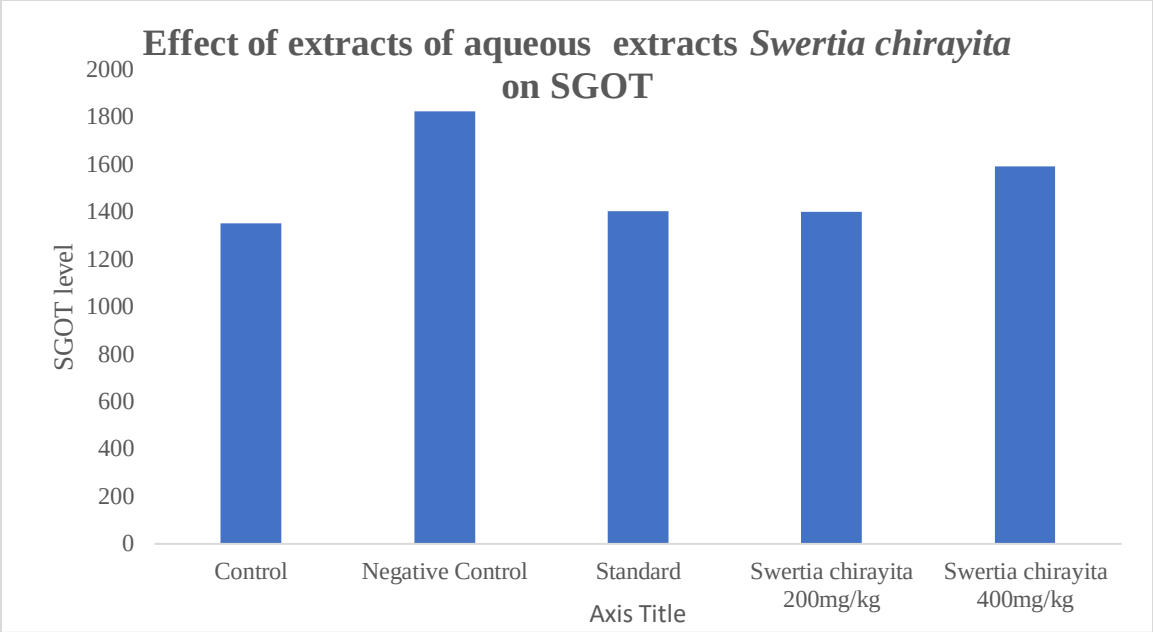

Figure1: Graphical representation of Effect of *Swertia chirayita* on SGOT

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 *SWERTIA CHIRAYITA* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 2: Effect of extracts of aqueous extracts *Swertia chirayita* on SGPT

GROUP	**SGPT level mean ± SEM**
Control	1525±1.16
Negative Control	1892.10± 1.05**a
Standard	1520.02±1.02**b
Swertia chirayita 200mg/kg	1510.10±1.10 *b
Swertia chirayita 400mg/kg	1911.16±1.06 ***b

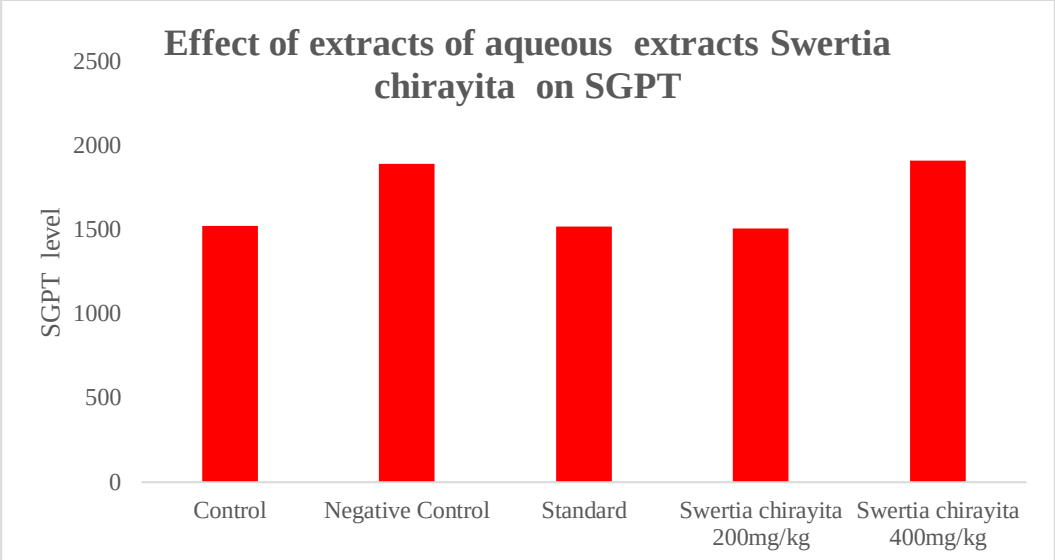

Figure2: Graphical representation of Effect of *Swertia chirayita* on SGPT

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 *SWERTIA CHIRAYITA* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 3: Effect of extracts of Ethanolic extracts *Swertia chirayita* on Bilirubin

GROUP	**Total Bilirubin mean ± SEM**
Control	1.16±0.05
Negative Control	2.19 ± 0.12***a
Standard	1.15 ± 0.05*b
Swertia chirayita 200mg/kg	1.36 ± 0.01 **b
Swertia chirayita 400mg/kg	1.30 ± 0.06 **b

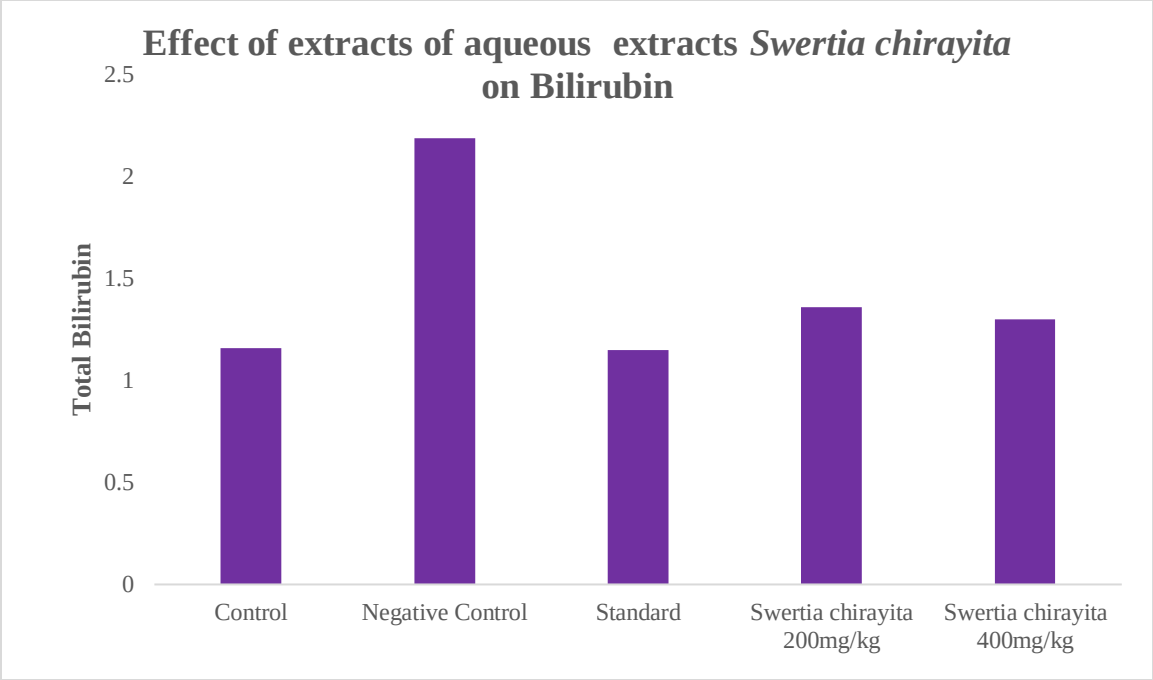

Figure3: Graphical representation of Effect of *Swertia chirayita* on Bilirubin

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 *SWERTIA CHIRAYITA* 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 *Swertia chirayita* treated group at a dose of 200mg/kg/po when compared to control group. There was significant (p<0.001) decrease in Bilirubin in *Swertia chirayita* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 4: Effect of extracts of aqueous extracts *Swertia chirayita* on ALP

GROUP	**ALP level mean ± SEM**
Control	42.01±0.02
Negative Control	51.6±0.05*a
Standard	37.0±0.03**b
Swertia chirayita 200mg/kg	45±6.01***b
Swertia chirayita 400mg/kg	42.1±0.10*b

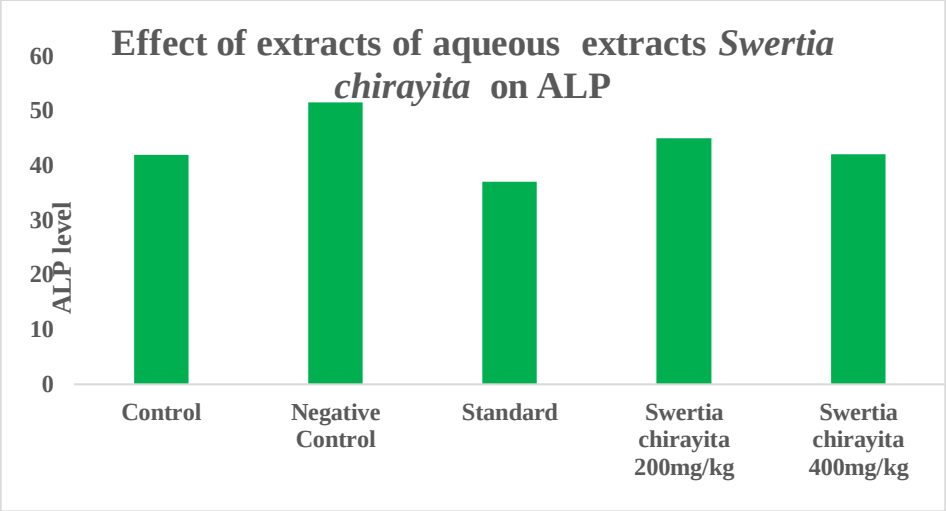

Figure4: Graphical representation of Effect of *Swertia chirayita* on ALP

EFFECT OF *SWERTIA CHIRAYITA* 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 *Swertia chirayita* 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 *Swertia chirayita* 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 *Swertia chirayita* at a dose of 200mg/kg/p.o showed a significant ($p<0.001$) decrease in ALP when compared to Ethanol induced group. The *Swertia chirayita* 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 ethanol aqueous treated groups shows intact architecture, few regenerative hepatocytes, sinusoidal congestion and scattered mononuclear inflammatory cells which is similar to silymarin treated group.

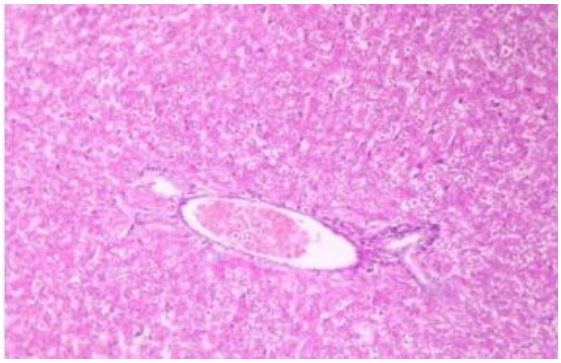

Fig 5: Normal Control group, showing normal hepatocytes

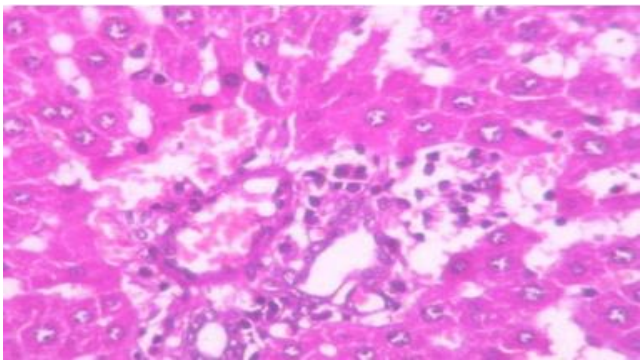

Fig 6: Ethanol treated animal group shows that hepatic cells damage and congestion of the liver.

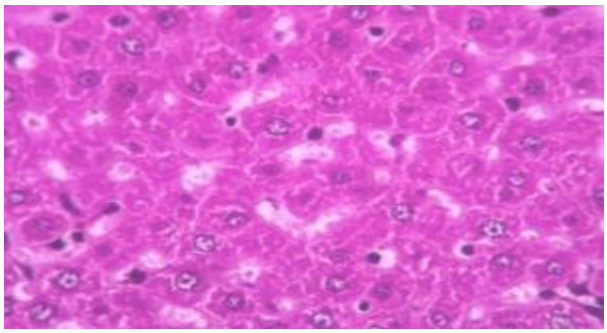

Fig 7: Hepatocytes in group treated with Standard (Silymarin 200 mg/kg)

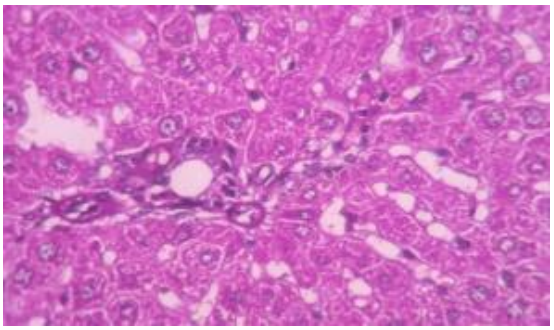

Fig 8: *Swertia chirayita* of 400 mg/kg shows that few regenerative hepatocytes, sinusoidal congestion and scattered mononuclear inflammatory cells

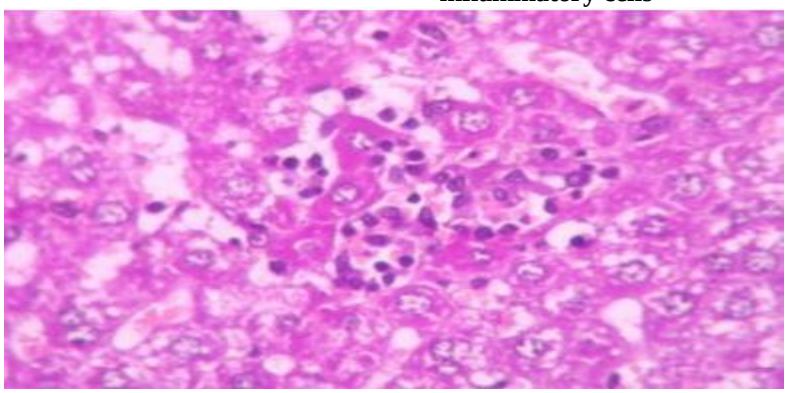

Fig 9: *Swertia chirayita* of 200 mg/kg shows that few regenerative hepatocytes, sinusoidal congestion and scattered mononuclear inflammatory cells

CONCLUSION:

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.

In order to investigate the medicinal use of *Swertia chirayita* 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 aqueous extract of *Swertia chirayita* 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 aqueous extract of *Swertia chirayita* 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 aqueous extract of *Swertia chirayita* (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.

Aqueous extract *Swertia chirayita* 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 *Swertia chirayita*, 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.

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