CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.22719261

Available online at: http://www.iajps.com Research Article

PHARMACOLOGICAL EVALUATION OF HEPATOPROTECTIVE ACTIVITY OF ETHANOLIC EXTRACT OF FOENICULUM VULGARE STEMS IN ALBINO RATS

Ch Ramya*[1], Sasanam Neeraja[2], Md.Asma[2], Bollempally Pavani[2], W Om Rao [2]

[1]Assistant Professor, Department of Pharmacology, St. Mary's College of Pharmacy, St. Francis Street, Hyderabad, Telangana - 500025, India.

[2]Student, Mary's College of Pharmacy, St. Francis Street, Hyderabad, Telangana - 500025, India.

Abstract:

The present study evaluated the hepatoprotective and antioxidant activities of the ethanolic stem extract (EEFV) of Foeniculum vulgare against Paracetamol-induced hepatotoxicity in albino rats. Hepatotoxicity was induced by administering Paracetamol (3 g/kg, p.o.) for 14 days. Animals were divided into five groups: normal control, toxic control, standard (Silymarin 100 mg/kg), and two test groups receiving EEFV at 250 and 500 mg/kg, respectively, one hour after Paracetamol administration.

Paracetamol treatment significantly elevated serum AST, ALT, ALP, and total bilirubin levels while reducing total protein and albumin, along with loss of body weight and increased liver weight, confirming severe liver damage. In addition, Paracetamol induced marked oxidative stress, evidenced by significant reductions in superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) levels, accompanied by a significant increase in malondialdehyde (MDA), a marker of lipid peroxidation. Treatment with Silymarin markedly restored these altered biochemical and antioxidant parameters toward normal values.

EEFV treatment produced dose-dependent hepatoprotective and antioxidant effects. Both doses significantly reduced serum liver marker enzymes and bilirubin levels while improving total protein and albumin concentrations. Furthermore, EEFV significantly increased SOD, CAT, and GSH levels and decreased MDA levels compared with the toxic control group, indicating enhancement of the endogenous antioxidant defense system and protection against oxidative liver damage. The higher dose (500 mg/kg) showed effects comparable to the standard drug Silymarin. Histopathological observations supported the biochemical findings by demonstrating restoration of normal hepatic architecture and reduced cellular degeneration in the treated groups.

The study concludes that the ethanolic stem extract of Foeniculum vulgare possesses significant hepatoprotective and antioxidant activities against Paracetamol-induced liver injury. The protective effects may be attributed to its antioxidant phytoconstituents, which scavenge free radicals, inhibit lipid peroxidation, and stabilize hepatocellular membranes. Therefore, Foeniculum vulgare may serve as a promising natural therapeutic agent for the prevention and management of liver disorders associated with oxidative stress.

Keywords: *Foeniculum vulgare, hepatoprotective activity, Paracetamol-induced, Silymarin*

Corresponding author:

Ch Ramya,

Department of Pharmacology, St. Mary's College of Pharmacy, Hyderabad, Telangana - 500025, India.

QR CODE

Please cite this article in press ***Ch Ramya*** *et al.,* ***Pharmacological Evaluation Of Hepatoprotective Activity Of Ethanolic Extract Of Foeniculum Vulgare Stems In Albino Rats.,****. Indo Am. J. P. Sci, 2026; 13(09).*

1. INTRODUCTION:

Medicinal plants play a key role in human health care. About 80% of the world population relies on the use of traditional medicine which is predominantly based on plant materials [1]. The traditional medicine refers to a broad range of ancient natural health care practices, including folk/tribal practices as well as Ayurveda, Siddha, Amchi and Unani. These medical practices originated from time immemorial and developed gradually, to a large extent, by relying or based on practical experiences without significant references to modern scientific principles. These practices incorporated ancient beliefs and were passed on from one generation to another by oral tradition and/or guarded literature. Although herbal medicines are effective in the treatment of various ailments very often these drugs are unscientifically exploited and/or improperly used.

Therefore, these plant drugs deserve detailed studies in the light of modern science. It is estimated that about 7,500 plants are used in local health traditions in, mostly rural and tribal villages of India. Out of these, the real medicinal value of over 4,000 plants is either little known or hitherto unknown to the mainstream population. The classical systems of medicine such as Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants [2]. A detailed investigation and documentation of plants used in local health traditions and pharmacological evaluation of these plants and their taxonomical relatives can lead to the development of invaluable plant drugs for many dreaded diseases. Random screening of plants has not proved economically effective [3]. Liver diseases and medicinal plants: The Liver has a pivotal role in the regulation of physiological processes. It is involved in several vital functions such as metabolism, secretion and storage. Furthermore, detoxification of a variety of drugs and xenobiotics occurs in liver. The bile secreted by the liver has, among other things, an important role in digestion. Liver diseases are among the most serious ailments.

They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatosis (non-inflammatory diseases), and cirrhosis (a degenerative disorder resulting in fibrosis of the liver). Liver diseases are mainly caused by toxic chemicals (certain antibiotics, chemotherapeutics, peroxidised oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc.), excess consumption of alcohol, infections, and autoimmune/disorders. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damage in the liver. Enhanced lipid peroxidation produced during the liver microsomal metabolism of ethanol may result in hepatitis and cirrhosis. It has been estimated that about 90% of acute hepatitis is due to viruses. The major viral agents involved are Hepatitis B, A, C, D (delta agents), E, and G. Of these, Hepatitis B infection often results in chronic liver disease and cirrhosis of the liver. Primary liver cancer has also been shown to be produced by these viruses. It has been estimated that approximately 14- 16 million people are infected with this virus in South East Asia region and about 6% of the total population in the region are carriers of this virus. A vaccine has become available for immunization against Hepatitis B virus. Hepatitis C and Hepatitis E infections are also common in countries of South East Asia region [3].

Liver

The liver is the largest organ of the human body that performs multiplicity of vital metabolic functions . Anatomically, the liver is located slightly beneath the diaphragm and anterior to the stomach. It is involved in maintenance of glucose homeostasis, secretion of lipoproteins, and excretion of bile. It synthesizes albumin, prothrombin, fibrinogen and binding protein for iron, copper and vitamin A. Liver parenchyma serves as a storage organ for glycogen, fat and fat soluble vitamins, iron and copper. Catabolically, it is involved in breakdown of various hormones, serum protein, and detoxification of drugs, chemicals and products of bacterial metabolism [4].

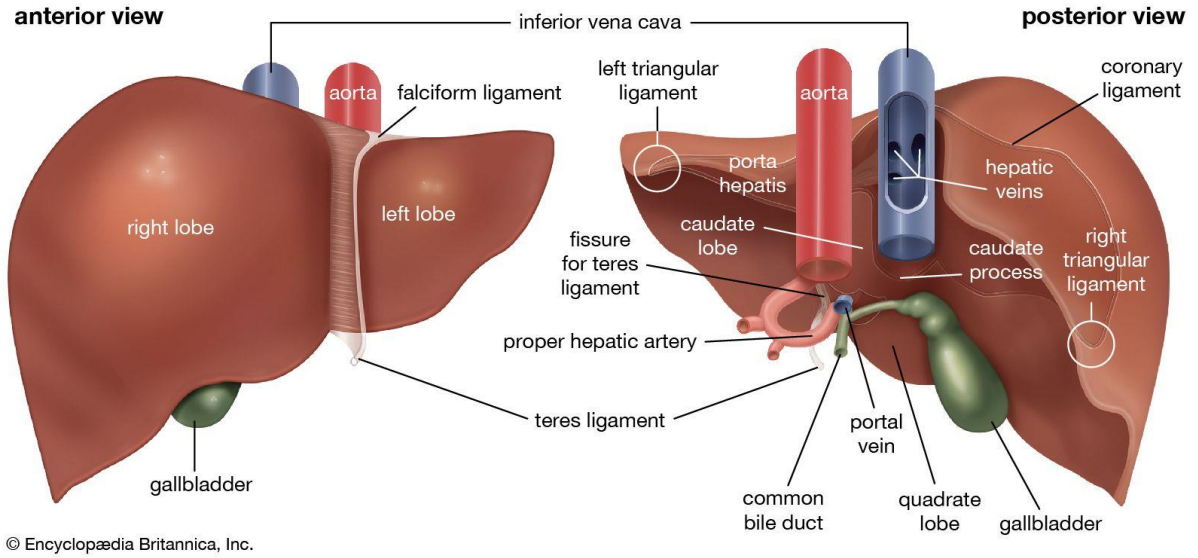
Despite its complex functions, the liver has a remarkable ability to regenerate after injury. However, it is susceptible to various diseases, such as hepatitis, fatty liver disease, cirrhosis, and liver cancer, which can impair its function. Liver function tests (LFTs) are commonly used to assess its health and detect any underlying issues. Maintaining liver health is crucial for overall well-being, as liver dysfunction can affect multiple organ systems.

Structure of liver

The liver weighs approximately 1500g and accounts for approximately 2.5% of adult body weight . The surface of the liver is smooth and dome shaped, where it is related to the concavity of the inferior surface of the diaphragm. The liver lies mainly in the right upper quadrant of the abdomen where it is hidden and protected by the thoracic cage and diaphragm. The normal liver lies deep to the ribs 7 – 11 on the right side and crosses the midline towards the left nipple [5].

The liver is divided into 4 lobes: right, left, caudate, and quadrate. The right and left lobes are the largest, while the caudate and quadrate are smaller and located posteriorly. Two ligaments are visible

anteriorly. Superiorly, the falciform ligament separates the right and left lobes. Inferior to the falciform ligament is the round ligament, which protrudes from the liver slightly. Also visible anteriorly on the most inferior portion of the right lobe is the gallbladder. Posteriorly, many more interesting structures are visible. That the caudate lobe is located superiorly, approximately between the right and left lobes. Adjacent to the caudate lobe is the sulcus for the inferior vena cava. Just inferior to the caudate lobe is the porta hepatis, where the hepatic artery and hepatic portal vein enter the liver. The portal vein carries nutrient laden blood from the digestive system. Inferior to the porta hepatis is the bile duct which leads back to the gallbladder. That the hepatic vein, where post-processed blood leaves the liver, is found inferior and adjacent to the sulcus for the inferior vena cava. The liver is held on place by a system of mesenteries posteriorly, and is also attached to the diaphragm via the falciform ligament. Additionally, most of the liver is covered by visceral peritoneum [5-7].



© Encyclopædia Britannica, Inc.

Origin of the Liver

The cells that will eventually make up the adult liver originated during embryogenesis from the ventral foregut definitive endoderm 7. The different developmental stages of the liver involves establishment of competence for liver formation, after which liver specification, hepatic bud formation, growth and finally differentiation will occur . During the development of the liver, as well as certain duration after partus, the metabolic profile of the young liver is far from that of the adult phenotype. Prior to birth, and shortly thereafter, many metabolic changes occur in the liver . These allow the organism to adapt to uptake of nutrients from food, but also change its ability to metabolize xenobiotics. As the organism matures, with duration an adult pattern of metabolic enzymes develops. During the development of the hepatocellular carcinoma, frequently the gene expression pattern of the hepatocytes reverts to a more fetal-like stage [9]. In certain cases this leads to the expression of metabolic enzymes otherwise found only during embryogenesis. This partly fetal-like expression pattern is also noticeable in many human hepatoma cell lines that are often used for in vitro toxicology studies [10-15] .

MATERIALS AND METHODS:

COLLECTION AND IDENTIFICATION OF PLANT MATERIAL

The *Foeniculum vulgare* stems are collected and identified. The stems were collected from local areas of Tirupati and Authenticated by Dr. K. Madhava Chetty, Assistant professor, Department of Botany S.V University Tirupati. Andhra Pradesh.

Extraction of plant material

Stems of *Foeniculum vulgare* are collected and shade dried for one week, the dried stems are pulverized by a mechanical grinder reduced to coarse powder and around 50g of powder material was subjected to successively hot continuous extraction .a weight quantity of the plant powdered material was extracted by soxhlet with ethanol of 250ml for 6-8 hours with intermediate heating at 40 ^{0} c after that the residues were extracted the extract was filtered using Whatmann filter paper and then the extract was evaporated in a rota evaporator and further dried under vacuum.

Pharmacological Study of *Foeniculum vulgare*

Animals

30 Wistar Rats, all around 60 days old, was utilized in this study, which was conducted from Jeeva life

sciences, Hyderabad. Upon their arrival, a random sample of animals was selected and weighed to verify that they complied with the specified age requirement. Rats weighed between 180 and 200 grams on average. The animals were accommodated in metabolic enclosures (55 x 32.7 x 19 cm), lined with pine litter, with a maximum of five animals of the same sex per cage. A period of seven days was allocated for the observation and acclimatization of all animals from the moment they were received until the commencement of treatment. A veterinary surgeon examined the animals during this time period to ensure they met the necessary health requirements to commence the study. The experimental groups were allocated the samples utilizing a random distribution technique. By utilizing this methodology, the initial bodyweights can be approximately equalized, and participants can be randomly assigned to experimental groups bearing the CPCSEA REG.

Acute Oral Toxicity Study [16]

Acute toxicity investigations utilized healthy Wistar rats (180-220 g) of both sexes by OECD guidelines 425. Following an overnight fast, the rodents were separated into three groups, with five rats in each group. The oral (p.o) administration of extracts consisted of 100, 500, and 2000 mg/kg body weight. Behavioral and autonomic profiles of the rodents were continuously monitored for two hours, and for forty-eight hours for any indications of toxicity or mortality. Ingestion of the test substance was performed. The vehicle (distilled water) was administered in the same volume to the rodents comprising the control group as to the rats in the other treatment groups. Oral administration was conducted at a volume of 10 ml/kg. The determination of the amount of the test substance to be administered to each animal was based on its body weight on the testing day.

Induction of Hepatotoxicity [17]

Pre-treatment Group

With the exception of the control group, all pre-treated groups of rats were administered daily doses of Paracetamol (3g/kg of body weight), Silymarin (100mg/kg), and ethanolic Extract of *Foeniculum Vulgare* (250 and 500mg/kg) for 14 days.

Group I Distilled water (Control) 10 mL/kg, p.o.
Group II Paracetamol only 3 g/kg, p.o.
Group III Paracetamol + Silymarin Paracetamol 3 g/kg, then Silymarin 100 mg/kg after 1 hr, p.o.
Group IV Paracetamol + EEFV (Low dose) Paracetamol 3 g/kg, then EEFV 250 mg/kg after 1 hr, p.o.
Group V Paracetamol + EEFV (High dose) Paracetamol 3 g/kg, then EEFV 500mg/kg after 1 hr, p.o.

Measurement of Body weight

Daily body weight monitoring of the animals was conducted with precision using an electrical balance. All measurements were conducted daily, specifically between 8.30 and 9.15 hours, before the administration of distilled water (as the control) and the drug paracetamol.

Body weight changes [18]

Body weight is an important physical parameter in hepatoprotective studies using Paracetamol, as liver injury commonly leads to anorexia, impaired metabolism, weakness, and consequent loss of body weight in the toxic control group. In contrast, animals in the normal control group show a gradual increase in body weight over the study period. When treated with a hepatoprotective agent such as extracts from Foeniculum vulgare, prevention of weight loss or restoration toward normal weight gain is observed. Thus, maintenance or recovery of body weight in treated groups indicates improvement in general health and supports the hepatoprotective effect alongside biochemical.

Liver weight

After completion of the experimental period, animals are fasted overnight and anesthetized. Blood is collected for biochemical analysis, and the abdomen is opened through a midline incision. The liver is carefully excised, freed from surrounding connective tissue, and washed gently with normal saline to remove adhering blood. The liver is then blotted dry with filter paper and weighed immediately using a digital analytical balance to obtain the absolute liver weight. The relative liver weight (liver index) is calculated using the formula:

$$\text{Liver Index} = \frac{\text{Liver weight (g)}}{\text{Body weight of animal (g)}} \times 100$$

An increase in liver weight is observed in the toxic control group due to inflammation and cellular swelling caused by Paracetamol-induced damage, while normalization of liver weight in treated groups (e.g., with extracts of Foeniculum vulgare) indicates hepatoprotective activity.

Antioxidant parameters

Estimation of Superoxide Dismutase (SOD) [19]

Superoxide dismutase (SOD) activity was estimated according to the method of Kakkar P et al. Liver tissue was homogenized in ice-cold phosphate buffer (0.1 M, pH 7.4) to prepare a 10% homogenate and centrifuged at 10,000 rpm for 15 minutes at 4°C. The reaction mixture consisted of sodium pyrophosphate buffer, phenazine methosulfate (PMS), nitro blue tetrazolium (NBT), NADH, and tissue supernatant. After incubation at 30°C for 90 seconds, the reaction was terminated by the addition of glacial acetic acid. The color intensity was measured spectrophotometrically at 560 nm. The activity of SOD was expressed as units per milligram of protein (U/mg protein).

Estimation of Catalase (CAT)

Catalase activity was determined by the method described by Aebi H. Liver homogenate was prepared in phosphate buffer and centrifuged to obtain the supernatant. The reaction mixture contained phosphate buffer, hydrogen peroxide (H_2O_2), and the tissue supernatant. Catalase activity was measured by monitoring the decomposition of hydrogen peroxide through the decrease in absorbance at 240 nm using a UV-visible spectrophotometer. The enzyme activity was expressed as units per milligram of protein (U/mg protein).

Estimation of Reduced Glutathione (GSH)

Reduced glutathione (GSH) levels were estimated using the method of Ellman GL. Liver homogenate was mixed with 10% trichloroacetic acid (TCA) and centrifuged to precipitate proteins. The supernatant was then treated with phosphate buffer and Ellman's reagent (5,5′-dithiobis-(2-nitrobenzoic acid), DTNB). GSH present in the sample reacted with DTNB to produce a yellow-colored chromogen. The absorbance was measured at 412 nm, and the results were expressed as micrograms of GSH per milligram of protein (µg/mg protein).

Estimation of Lipid Peroxidation (MDA)

Lipid peroxidation was assessed by measuring malondialdehyde (MDA) levels according to the method of Ohkawa H et al. Liver homogenate was mixed with sodium dodecyl sulfate (SDS), acetic acid, and thiobarbituric acid (TBA) reagent. The mixture was heated in a boiling water bath for 60 minutes, cooled, and extracted with n-butanol:pyridine solution. After centrifugation, the absorbance of the resulting pink-colored thiobarbituric acid reactive substances (TBARS) complex was measured at 532 nm. MDA levels were expressed as nanomoles per milligram of protein (nmol/mg protein) and served as an index of lipid peroxidation and oxidative stress.

Serum Biochemical [20]

AST (SGOT)

AST (SGOT) is estimated by the Reitman–Frankel method based on the transamination reaction where aspartate and α-ketoglutarate form oxaloacetate and glutamate. In this procedure, 0.5 mL of substrate reagent (containing L-aspartate and α-ketoglutarate in buffer, pH ~7.4) is mixed with 0.1 mL of serum and incubated at 37 °C for 60 minutes; a control is prepared using distilled water instead of serum. After incubation, 0.5 mL of 2,4-dinitrophenylhydrazine (DNPH) is added and allowed to stand for 20 minutes at room temperature for color development. Then, 5.0 mL of 0.4 N NaOH is added, mixed well, and the solution is kept for 10 minutes. The absorbance of the test and control is measured at 505 nm using a spectrophotometer. The AST activity is calculated using the absorbance values and expressed in IU/L; an elevated AST level indicates hepatocellular damage, while reduction toward normal after treatment suggests hepatoprotective activity.

ALT (SGPT) [21]

ALT (SGPT) is estimated by the Reitman–Frankel method based on the transamination reaction in which alanine and α-ketoglutarate form pyruvate and glutamate. In this procedure, 0.5 mL of substrate reagent (containing L-alanine and α-ketoglutarate in buffer, pH ~7.4) is mixed with 0.1 mL of serum and incubated at 37 °C for 60 minutes, while a control is prepared using distilled water instead of serum. After incubation, 0.5 mL of 2,4-dinitrophenylhydrazine (DNPH) is added and allowed to stand for 20 minutes at room temperature for color development. Then 5.0 mL of 0.4 N NaOH is added, mixed well, and kept for 10 minutes. The absorbance is measured at 505 nm using a spectrophotometer, and ALT activity is calculated from the absorbance values and expressed in IU/L. Elevated ALT indicates hepatocellular injury, while a decrease toward normal after treatment reflects hepatoprotective activity.

ALP [22]

Alkaline phosphatase (ALP) is a membrane-bound enzyme concentrated in the bile canaliculi and biliary epithelium of the liver; its rise in serum mainly indicates cholestasis or biliary obstruction during hepatotoxicity. In liver injury models (e.g., paracetamol), damage to the biliary system and hepatocyte membranes releases ALP into circulation, making it an important parameter in hepatoprotective studies. ALP is commonly estimated by the Kind–King method, where ALP hydrolyzes disodium phenyl phosphate to liberate

phenol in an alkaline medium; the phenol formed reacts with 4-aminoantipyrine in the presence of an oxidizing agent (potassium ferricyanide) to produce a red-colored complex measured spectrophotometrically at 510 nm. Increased ALP levels indicate biliary damage and impaired liver function, while reduction toward normal after treatment suggests hepatoprotective effect. Results are expressed in IU/L.

Total Bilirubin [23]

Total bilirubin is a key indicator of the liver's excretory function and reflects the sum of conjugated (direct) and unconjugated (indirect) bilirubin in serum. In hepatotoxicity (e.g., with Paracetamol), impaired uptake, conjugation, and excretion by damaged hepatocytes leads to a rise in serum bilirubin, often accompanied by jaundice. It is commonly estimated by the Malloy–Evelyn (diazo) method, where bilirubin reacts with diazotized sulfanilic acid to form a pink-colored azobilirubin measured spectrophotometrically at 540 nm. Elevated total bilirubin indicates hepatic dysfunction and cholestasis, while a reduction toward normal after treatment signifies hepatoprotective activity.

Total Protein [24]

Total protein in serum reflects the liver's synthetic capacity, as most plasma proteins (especially albumin) are produced by hepatocytes. In hepatotoxicity induced by agents such as Paracetamol, impaired protein synthesis leads to a decrease in serum total protein levels. It is commonly estimated by the Biuret method, in which peptide bonds of proteins react with copper sulfate in an alkaline medium to form a violet-colored complex measured spectrophotometrically at 540 nm. A reduction in total protein indicates compromised liver function, while restoration toward normal after treatment suggests hepatoprotective activity. Results are expressed in g/dL.

Albumin

Albumin is the major plasma protein synthesized exclusively by the liver and serves as a sensitive marker of the liver's synthetic function. During hepatotoxicity induced by agents such as Paracetamol, hepatocellular damage impairs protein synthesis, leading to a decrease in serum albumin levels. Albumin is commonly estimated by the Bromocresol Green (BCG) dye-binding method, where albumin binds with BCG in an acidic medium to form a green-colored complex measured spectrophotometrically at 630 nm. Reduced albumin indicates compromised liver function, while restoration toward normal after treatment reflects hepatoprotective activity.

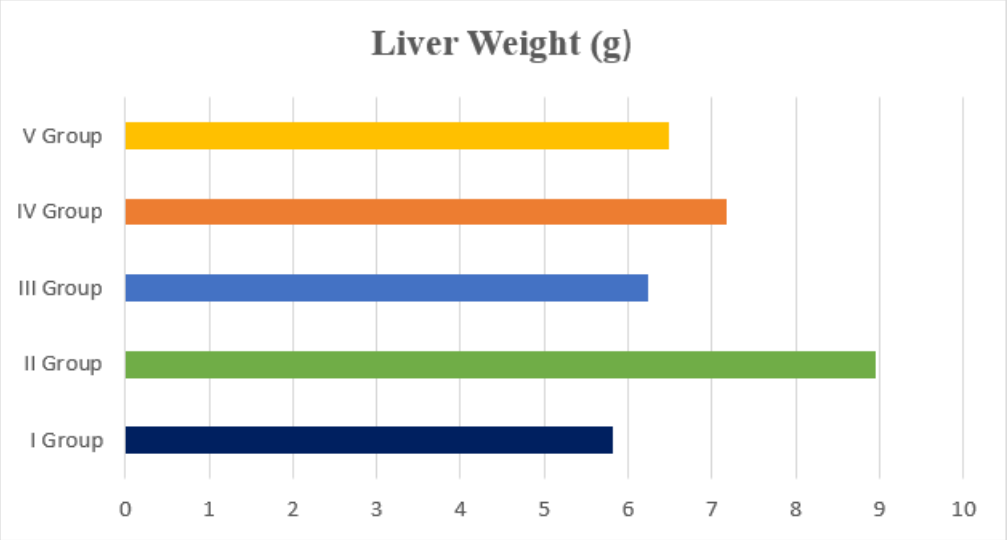
Body Weight

Group	Initial Body Weight (g)	Final Body Weight (g)	Change (g)
Group I -Control	178.4 ± 3.2	196.6 ± 3.8	18.2
Group II - Paracetamol	180.1 ± 3.5	158.3 ± 3.1	−21.8
Group III - Para + Silymarin	179.6 ± 3.1	191.2 ± 3.6	11.6
Group IV - Para + EEFV 250	181.3 ± 3.4	176.5 ± 3.2	−4.8
Group V - Para + EEFV 500	177.9 ± 3.0	189.8 ± 3.5	11.9

EEFV stands for the ethanolic extract of stems of *Foeniculum vulgare*. The stems are dried, powdered, and subjected to extraction using ethanol as the solvent, which efficiently dissolves a wide range of phytoconstituents such as flavonoids, phenolic compounds, tannins, and volatile components. This extract is used as the test sample in the study to evaluate its hepatoprotective potential against Paracetamol-induced liver damage in rats. The presence of antioxidant and bioactive phytochemicals in the ethanolic extract is believed to contribute to membrane stabilization, reduction of oxidative stress, and restoration of normal liver function parameters.

Liver weight

Group	Treatment	Liver Weight (g)
I Group	Control (Distilled water)	5.82 ± 0.14
II Group	Paracetamol (3 g/kg)	8.96 ± 0.21
III Group	Paracetamol + Silymarin (100 mg/kg)	6.24 ± 0.16
IV Group	Paracetamol + EEFV 250 mg/kg	7.18 ± 0.18
V Group	Paracetamol + EEFV 500 mg/kg	6.48 ± 0.15

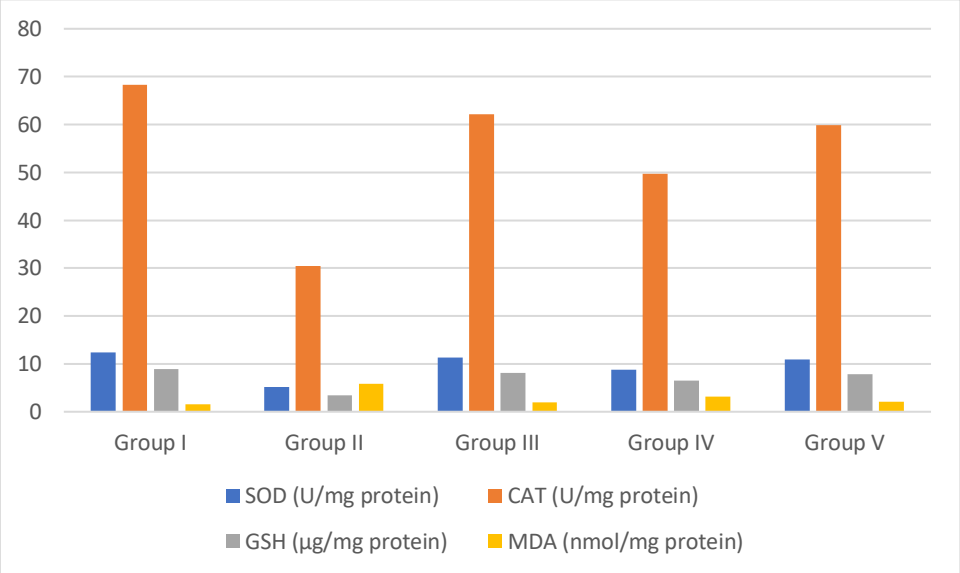


Paracetamol treatment led to a significant rise in liver weight in the toxic group, reflecting hepatomegaly from inflammation and tissue injury. Silymarin treatment brought the liver weight back near normal. The EEFV-treated groups showed dose-dependent improvement, and the higher dose (500 mg/kg) produced liver weights comparable to the standard, indicating strong hepatoprotective effect.

Antioxidant parameters

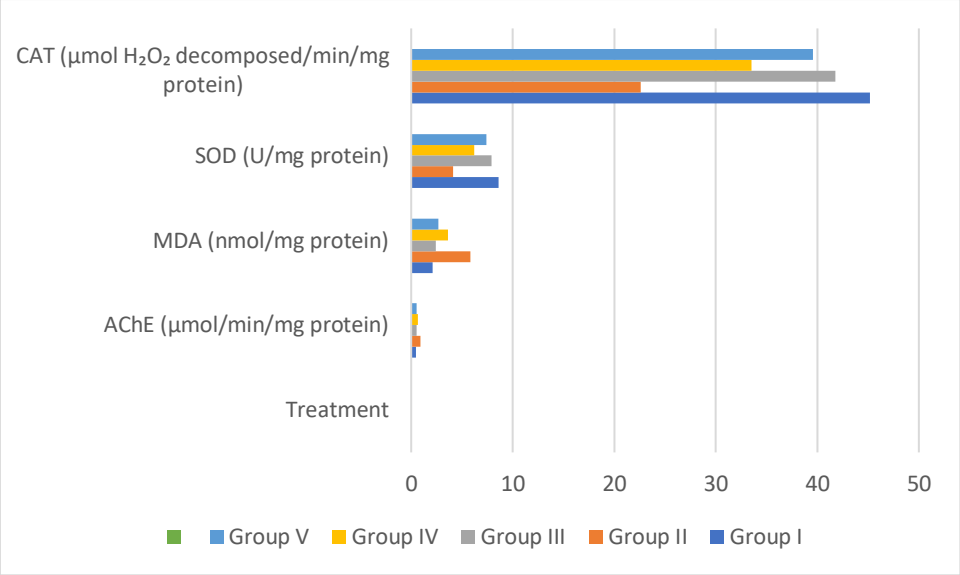
Group	**Treatment**	**SOD (U/mg protein)**	**CAT (U/mg protein)**	**GSH (µg/mg protein)**	**MDA (nmol/mg protein)**
Group I	Distilled water (Control)	12.45 ± 0.42	68.32 ± 2.11	8.95 ± 0.31	1.52 ± 0.08
Group II	Paracetamol only	5.21 ± 0.28***	30.45 ± 1.54***	3.42 ± 0.17***	5.86 ± 0.21***
Group III	Paracetamol + Silymarin (100 mg/kg)	11.36 ± 0.37###	62.18 ± 1.85###	8.12 ± 0.28###	1.89 ± 0.09###

Group IV	Paracetamol + EEFV (250 mg/kg)	8.84 ± 0.31###	49.76 ± 1.68###	6.47 ± 0.24###	3.18 ± 0.15###
Group V	Paracetamol + EEFV (500 mg/kg)	10.92 ± 0.35###	59.84 ± 1.79###	7.85 ± 0.27###	2.14 ± 0.11###



Biochemical parameters

Parameter	Group I Control	Group II Paracetamol	Group III Para + Silymarin	Group IV Para + EEFV 250	Group V Para + EEFV 500
AST (IU/L)	62.4 ± 2.1	148.6 ± 4.3	74.2 ± 2.8	96.5 ± 3.1	79.8 ± 2.6
ALT (IU/L)	48.7 ± 1.9	132.4 ± 3.8	58.6 ± 2.2	82.3 ± 2.7	63.1 ± 2.4
ALP (IU/L)	102.5 ± 3.6	228.7 ± 6.2	118.4 ± 4.1	146.2 ± 4.8	124.6 ± 3.9
Total Bilirubin (mg/dL)	0.46 ± 0.03	1.92 ± 0.08	0.62 ± 0.04	0.94 ± 0.05	0.71 ± 0.04
Total Protein (g/dL)	7.21 ± 0.12	4.82 ± 0.10	6.88 ± 0.11	6.12 ± 0.13	6.74 ± 0.12
Albumin (g/dL)	4.42 ± 0.09	2.96 ± 0.07	4.18 ± 0.08	3.62 ± 0.09	4.05 ± 0.08



The biochemical results clearly demonstrate successful induction of hepatotoxicity by Paracetamol in Group II, as evidenced by a marked elevation in serum AST, ALT, ALP, and total bilirubin along with a significant reduction in total protein and albumin levels compared to the normal control. These changes indicate severe hepatocellular damage, impaired biliary function, and reduced synthetic capacity of the liver. Treatment with the standard hepatoprotective agent Silymarin in Group III significantly restored all altered biochemical parameters toward normal values, confirming the validity of the experimental model.

Administration of the ethanolic stem extract of Foeniculum vulgare (EEFV) in Groups IV and V showed a dose-dependent hepatoprotective effect. The 250 mg/kg dose produced moderate improvement, while the 500 mg/kg dose demonstrated near-normalization of enzyme levels and protein parameters, comparable to the standard drug. The reduction in transaminases and ALP suggests protection of hepatocyte membranes and biliary structures, whereas normalization of bilirubin, total protein, and albumin indicates restoration of liver excretory and synthetic functions.

DISCUSSION:

Hepatotoxicity produced by Paracetamol is a well-established experimental model characterized by oxidative stress, hepatocellular necrosis, and impairment of liver function. In the present study, repeated administration of paracetamol significantly elevated serum AST, ALT, ALP, and total bilirubin levels while reducing total protein and albumin, confirming severe liver damage in the toxic control group. The marked loss in body weight and increase in liver weight and liver index further supported the occurrence of hepatomegaly, inflammation, and metabolic distress.

Paracetamol intoxication also induced pronounced oxidative stress, as evidenced by a significant decrease in endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), along with a marked increase in malondialdehyde (MDA), a marker of lipid peroxidation. These findings indicate excessive generation of reactive oxygen species (ROS) and depletion of the hepatic antioxidant defense system, which contribute to hepatocellular injury.

Treatment with the standard hepatoprotective agent Silymarin significantly restored all altered biochemical, antioxidant, and physical parameters toward normal values, validating the reliability of the experimental model. The ethanolic stem extract (EEFV) of *Foeniculum vulgare* demonstrated notable hepatoprotective activity in a dose-dependent manner. The 250 mg/kg dose produced moderate protection, whereas the 500 mg/kg dose showed near-normalization of liver enzymes, bilirubin, protein levels, body weight, liver weight, and antioxidant markers comparable to the standard group.

The extract-treated groups exhibited significant increases in SOD, CAT, and GSH levels together with a reduction in MDA concentration compared with the paracetamol-treated group, indicating attenuation of oxidative stress and inhibition of lipid peroxidation. The higher dose (500 mg/kg) produced a more pronounced antioxidant effect than the lower dose, suggesting superior free radical scavenging and cytoprotective activity.

The hepatoprotective effect of the extract may be attributed to the presence of phytoconstituents such as flavonoids, phenolic compounds, tannins, and other bioactive antioxidants that stabilize hepatocyte membranes, neutralize free radicals, inhibit lipid peroxidation, and promote regeneration of damaged liver tissue. Reduction in transaminases and ALP indicates protection of hepatocellular and biliary architecture, while improvement in bilirubin, total protein, and albumin suggests restoration of excretory and synthetic liver functions. Furthermore, the restoration of antioxidant enzyme levels and suppression of MDA formation confirm that the hepatoprotective activity of EEFV is closely associated with its antioxidant potential, thereby protecting the liver against paracetamol-induced oxidative damage.

CONCLUSION:

The present study demonstrates that repeated administration of Paracetamol successfully induced hepatotoxicity in albino rats, as evidenced by significant elevations in serum AST, ALT, ALP, and total bilirubin along with reductions in total protein and albumin, decreased body weight, and increased liver weight and liver index. These alterations confirmed severe hepatocellular damage and impaired liver function. In addition, Paracetamol administration caused marked oxidative stress, characterized by significant decreases in hepatic antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), along with a significant increase in malondialdehyde (MDA), indicating enhanced lipid peroxidation and oxidative damage to liver tissues.

Treatment with the standard drug Silymarin effectively restored the altered biochemical, antioxidant, and physical parameters toward normal values, validating the experimental model. The ethanolic stem extract (EEFV) of *Foeniculum vulgare* showed significant hepatoprotective and antioxidant activities in a dose-dependent manner. The extract significantly increased SOD, CAT, and GSH levels while reducing MDA levels compared with the toxic control group, thereby strengthening the endogenous antioxidant defense system and protecting hepatocytes from oxidative injury. The higher dose (500 mg/kg) produced results comparable to the standard drug, indicating strong protective potential.

the ethanolic stem extract of *Foeniculum vulgare* possesses potent hepatoprotective and antioxidant activities against paracetamol-induced liver injury. The protective effects are likely mediated through its ability to scavenge free radicals, inhibit lipid peroxidation, stabilize hepatocellular membranes, and restore normal liver function. Therefore, *Foeniculum vulgare* may serve as a promising natural therapeutic agent for the prevention and management of liver disorders associated with oxidative stress and hepatocellular damage.

REFERENCES:

1. WHO, Regional Office For The Western Pacific, Research Guidelines For Evaluating The Safety And Efficacy Of Herbal Medicines, Manila, WHO, 1993.
2. Pushpangadan P. Role of Traditional Medicine in Primary Health Care. In: Iyengar PK, Damodaran VK, Pushpangadan P, Editors. Science for Health. Published By State Committee On Science, Technology And Environment, Govt. Of Kerala, 1995.
3. Domitrović R, Potočnjak I. A comprehensive overview of hepatoprotective natural compounds: mechanism of action and clinical perspectives. Archives of toxicology. 2016 Jan;90(1):39-79..
4. Arika WM Nyamai DW Osano KO Ngugi MP Njagi ENM. Biochemical Markers of In vivo Hepatotoxicity.Journal of Clinical Toxicology. 2016;6(2):1.
5. J. Ozougwu, "Physiology of the liver", International Journal of Research in Pharmacy and Biosciences, vol. 4, no. 8, pp. 13-24, 2017
6. Allen SE.*The liver: Anatomy, Physiology, Disease and Treatment*. 2002 North Eastern University Press, USA
7. 4 Watt AJ, Zhao R, Li J, Duncan SA. Development of the mammalian liver and ventral pancreas is dependent on GATA4. *BMC Developmental Biology* 2007, 7: 37 - 45.
8. Burke ZD, Thowfeequ S, Tosh D. Liver specification: a new role for rats in liver development. *Current Biology 2006*, 16(17): 688 - 690.
9. Nardone G, Romano M, Calabro A, Pedone PV, De Sio I, Persico M.. Activation of fetal promoters of insulin like growth factors II gene in hepatitis C virus-related chronic hepatitis, cirrhosis and hepatocellular carcinoma. *Hepatology* 1996, 23(6): 1304 - 1312.
10. Bhargav Bhongiri[1] , Vadivelan Ramachandran[*1] , Raju Bairi[1] , Tharani Mohanasundaram1 , Vaishnavi Munnangi .In Vivo Evaluation Studies For Isoflavones Loaded Nanodroplets For Diabetic Encephalopathy,Afr.J.Bio.Sc. 6(9) (2024).
11. Grisham JW. Cell type in rat liver cultures: their identification and isolation. *Molecular and Cellular Biochemistry 1983,* 53(2): 23 – 33.
12. Kmiec Z. Co-operation of liver cells in health and diseases. *Advances in Anatomy, Embryology and Cell Biology 2001*, 161: 3 – 12.

13. Sirica AE, Pitot AC. Drug metabolism and effects of carcinogens in cultural hepatic cells. *Pharmacological Review 1979*, 31(3): 205 – 228
14. Friedman SL. Hepatic satellite cells: Protein, multifunctional and enigmatic cells of the liver. *Physiological Review 2008*, 88(1): 125 – 17
15. TY - JOUR AU - Krishnan, Siva PY - 2019/01/01 SP - 1385 EP - 1395 T1 - LIVER DISEASES-AN OVERVIEW VL - 8 D
16. Julie Polson, Robert, Ezmina Lalani et al., Acetaminophen-induced acute liver failure: Results of a United States multicentre, prospective study. Hepatology., 2005; 42(6):1364–1372.
17. Shah AH, Qureshi S, Ageel AM, Ageel AM. *Toxicity studies in mice of ethanol extracts of Foeniculum vulgare fruit and Ruta chalepensis aerial parts.* J Ethnopharmacol. 1991;34(2-3):167-172.
18. Mitchell JR, Jollow DJ, Potter WZ, Gillette JR, Brodie BB**.** Acetaminophen-induced hepatic necrosis. I. Role of drug metabolism. *J Pharmacol Exp Ther*. 1973;187(1):185-194.
19. Reitman S, Frankel S. A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases. *Am J Clin Pathol*. 1957;28:56–63.
20. Kind PRN, King EJ. Estimation of plasma phosphatase by determination of hydrolyzed phenol with amino-antipyrine**.** *J Clin Pathol.* 1954; 7:322–326.
21. Malloy HT, Evelyn KA. The determination of bilirubin with the photoelectric colorimeter**.** *J Biol Chem.* 1937; 119:481–490.
22. Gornall AG, Bardawill CJ, David MM. Determination of serum proteins by means of the biuret reaction. *J Biol Chem.* 1949; 177:751-766.
23. Doumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromocresol green. *Clin Chim Acta.* 1971; 31:87-96.
24. Mitchell JR, Jollow DJ, Potter WZ, Gillette JR, Brodie BB. Acetaminophen-induced hepatic necrosis. I. Role of drug metabolism. *J Pharmacol Exp Ther*. 1973; 187:185-194.
25. Hinson JA, Roberts DW, James LP. Mechanisms of acetaminophen-induced liver necrosis. *Handb Exp Pharmacol.* 2010; 196:369-405.