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RESEARCH ARTICLE

HEPATOPROTECTIVE ACTIVITY OF SCHISANDRA GRANDIFLORA AGAINST PARACETAMOL INDUCED HEPATOTOXICITY IN WISTAR RATS.

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Abstract

Aim: Paracetamol (PCM) overdose induces Hepatotoxicity in humans and experimental animals. The present study aims to evaluate Hepatoprotective activity of *Schisandra grandiflora* against paracetamol induced hepatotoxicity.

Method: In this experimental study wistar albino Rats were selected and Hepatotoxicity induced by paracetamol (PCM) p.o, 3g/kg body weight. On 7th day after the administration of plant extract and silymarin (50mg/kg) the plant extract of *Schisandra grandiflora* was administered orally at doses of 100mg/kg & 200mg/kg body weight daily for 7 days.Several serum makers, Serum glutamate pyruvate transaminase (SGPT), Serum glutamate oxaloacetate transaminase (SGOT), alkaline phasphatase (ALP), bilirubin total protein was measured to assess the effect of the extract on paracetamol Induced hepatic damage. A comparative histopathological study exhibited almost normal result as compared as control group.

Introduction:-

Liver is a vital organ in the body it is responsible for detoxification by removing toxins and wastes. The liver diseases are one of the most fatal diseases it affects over 10% of the world population. It includes hepatitis, cirrhosis, hemochromatosis, fibrosis, fatty liver, alcoholic liver disease, drug induced liver disease Most of hepatotoxic chemicals damage liver cells primarily by producing reactive species. Excessive exposure to poisonous chemicals leading to hepatic damageAcetaminophen (paracetamol) is widely used antipyretic, and analgesic it is generally considered safe at therapeutic doses, which produces acute liver damage if over dose are consumed. Paracetamol is metabolized mainly in the liver excretes glucuronide and sulphate conjugates. At toxic doses of paracetamol, the normal metabolic pathways become saturated, causing N-acetyl p-benzoquinone imine (NAPQI) to be formed and hepatic glutathione to be rapidly depleted. Paracetamol toxicity is caused by the reaction metabolite N-acetyl p-benzoquinoneimine which is partly metabolized by cytochrome P-450. It causes severe oxidative damage & glutathione depletion leads to liver necrosis. Introduction of cytochrome or depletion of hepatic glutathione is a precondition for paracetamol induced hepatotoxicity.

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In current situations many newly developed drugs are used in the liver disease treatment which possess harmful side effects for that reason further research on plants and herbs potentially added the chemical based drugs are vital as medicinal agents it exhibits hepatoprotective properties.

Silymarin has been used in clinical practice for the treatment of liver diseases extracted from the seed and fruit of the plant silybum marianum, also called milk thistle. It can cause allergic skin reactions, decreased platelets, and high bilirubin in blood. In this study silymarin used as positive control against Paracetamol induced acute hepatic damage in rats.

Materials and methods:-

Drugs and chemicals:

Paracetamol was obtained from the Ranbaxy laboratory limited, serum glutamic oxaloacetate transaminase (SGOT) Excel diagnostics Pvt. Ltd, Serum glutamic pyruvic transaminase (SGPT) Excel diagnostics Pvt. Ltd, alkaline phosphatase (ALP) Excel diagnostics Pvt. Ltd, Hyderabad. Bilirubin other chemicals used in this research were also of analytical grade.

Plant material:

The fruits of Schisandra grandiflora plant were collected from Himalayas and Authenticate by Central Research Institute of Unani Medicine, Hyderabad (Authentication no: SMPU/CRI-Hyd 13195).

Preparation of extracts:

The fresh fruits were collected shade dried and then powdered. The dried coarse powder of the fruit was extracted by using soxhlet apparatus to perform ethanolic extractions. After the extracts were preserved by placing in sample bottles closed with aluminum foil and kept at 4°C. Extracts were exposed to preliminary phytochemical investigation. Extracts were dissolved in water for injection; paracetamol suspension prepared by using 40% sucrose solution and exposed for hepatoprotective activity against paracetamol induced liver damage.

Phytochemical analysis:

The ethanolic extracts were subjected to the phytochemical analysis using predictable procedure like alkaloids, carbohydrates, flavonoids, glycosides, saponins, proteins, amino acids, tannins.

Experimental animals:

The study evaluated by using wistar albino rats (150-200gm) obtained from the animal house, sainath agencies, bapujinagar, musheerabad, Hyderabad. The animals were grouped and housed in cages not more than six animals under laboratory conditions temperature 25±2°C with dark and light by 12h. Animals fed with standard pellet diet and libitum and acclimatized for 7 days. The study protocol was approved by Institutional Animal Ethics Committee (IAEC) Approval No: vcp/cology/001/11/2017) which was constituted in accordance with the rules and guidelines of the committee for the purpose of control and supervision of Experimental on Animals, India.

Acute oral toxicity:

The acute oral toxicity study was carried out by the OECD guidelines, revised guidelines423, received from CPCSEA.

Evaluation of hepatoprotective activity:

Animals were divided in to 4 groups, each group contains 6 animals

1. Group 1: which served as normal control received saline water 5ml/kg p.o. for seven days.
2. Group 2: This served as toxicant control administration of paracetamol 1g/kg p.o. for seven days
3. Group 3: served as standard. Silymarin is used as standard drug 50mg/kg p.o.
4. Group 4: group four served as test control animals treats with Schisandra grandiflora ethanolic plant extract 100mg/kg & 200mg/kg p.o. for seven days.

The animals were sacrificed on the 8^{th} day under light anesthesia. Blood collected from the each rat by retro orbital plexus under anesthesia for investigation of biochemical parameters such as SGOT, SGPT, ALP, and Bilirubin.
Serum was separated by the centrifugation of blood at 10000rpm for 15 min at 40°C supernatants were collected which are further used in the study of biochemical parameters. All the animals are sacrificed and liver of experimental animals was removed processed immediately for histological investigation.

Histopathological studies:
The livers were excised quickly and fixed in 10% formalin and paraffin embedded. Liver sections of about 4-6µm stained with haemotoxylin and eosin. Thick sections of paraffin embedded rat liver were dewaxed with distill water for 2 min. then the sections stained with haemotoxylin for 5min at room temperature. After 15min the sections were counterstained with eosin for 2min. dehydrate with alcohol and washed with xylene & blocked by eosin observed under microscope.

Statistical analysis:-

All the results were expressed as mean ± SD analyzed by one way ANOVA, followed by dunett't' test between group using graphpad instat. Results of all the extracts including standard compared with result produced by normal control.
*p<0.05, **p<0.01 vs. paracetamol treated group

Results:-

Phytochemical study of ethanolic extract of Schisandra grandiflora shows the presence of alkaloids, terpenoids, steroids, tannins, glycosides, saponins, flavonoids.

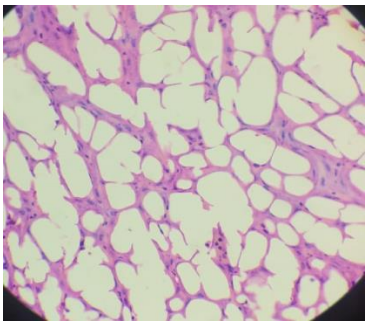
Acute toxicity:
ethanolic extract did not show any signs and symptoms of toxicity & mortality up to 2000mg/kg.

Hepatoprotective activity:
The hepatoprotective activity of ethanolic extract of Schisandra grandiflora on paracetamol treated rat's shows increase in the serum hepatic enzyme levels such as SGOT, SGPT, ALP, ALT, Bilirubin when compared to normal control indicates the marked increase value.

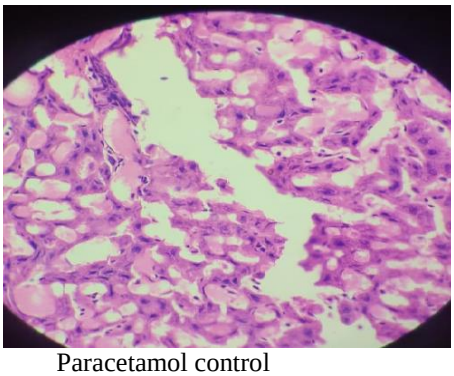
Biochemical assessment for the paracetamol induced hepatic injury:

s.no	groups	SGOT	SGPT	ALP	T.B	D.B
1	Control	55.71± 0.491	53.22±1.25	61.61± 0.0204	0.0445± 0.0031	0.12± 0.002
2	Paracetamol control (1gm/kg)	123.75± 1.64	121.23±2.73	169.07± 1.806	0.696± 0.358	0.66± 0.001
3	Standard silymarin (50mg/kg)	101.41± 0.691**	96.32±2.85**	103.37± 1.681**	0.837± 0.0368**	0.31± 0.01**
4	Schisandra extract (100mg/kg)	90.08± 0.764**	84.52±1.502**	89.63± 1.682**	0.795± 0.015**	0.14± 0.001**
5	Schisandra extract (200mg/kg)	63.125± 0.92***	62.825±0.978***	63.187± 1.964***	0.679± 0.0080***	0.10± 0.01***

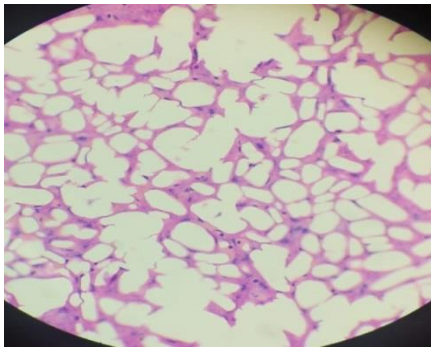
Histopathological study:
The hepatic architecture was present in normal control group. Normal structures were absent in toxic control group. The histopathological profile of the rat liver treated with ethanolic extract intoxicated with paracetamol showed moderate hepatoprotective activity while the standard group treated with silymarin & intoxicated with paracetamol showed less degeneration of hepatocytes indicating the regeneration activity.



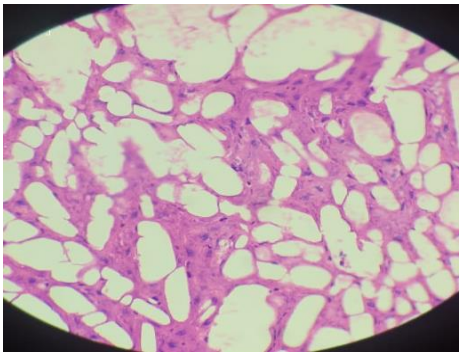
Normal control



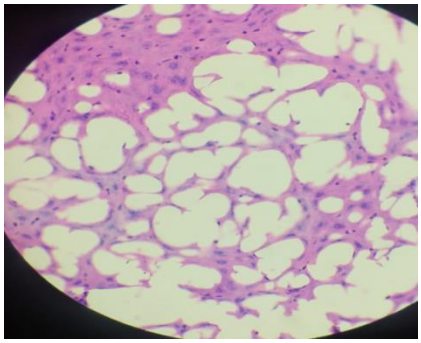
Paracetamol control



Paracetamol + Silymarin



Paracetamol + S.grandiflora (100mg/kg)



Paracetamol + S.grandiflora (200mg/kg)

Paracetamol control animals exhibited extensive disturbance in the liver heavy inflammation of fat dewdrops, sternly relapsed hepatocytes, congested sinusoids and injured central vein due to progress of highly combative radicals because of oxidative menace initiated by paracetamol.

Paracetamol treated animals showed necrosis congested sinusoids. Animals treated with Schisandra grandiflora (100mg/kg, 200mg/kg) shows substantial dose dependent liver protection against toxicant. Liver sections of rats treated with Silymarin it used as standard drug and similar to the control developed histopathological changes have been achieved the anti-oxidant effects of Silymarin it moderate hepatic damage.

Discussion:-

Schisandra grandiflora contains many active Constituents terpenoids, flavonoids, volatile oils, steroids, proteins, glycosides, and tannins shows various pharmacological actions consequently this study was assumed to examine whether S.grandiflora protects against Paracetamol persuaded hepatotoxicity. Treatment with ethanolic extract of Schisandra grandiflora 100mg/kg, 200mg/kg reduced these prominent serum markers indicating the activity of plant extract against Paracetamol induced liver damage and compared with Silymarin standard drug.

Conclusion:-

By the overall experiment research serum biochemical parameters like SGOT, SGPT, ALP, and Bilirubin in both test drug and reference standard drug it shows presence of good anti- hepatotoxic effect. Analysis of the histopathological study data indicates both test and reference drugs show the good cytoprotective activity against paracetamol induced toxicity. Hence the trial drug Schisandra grandiflora can be used as an anti-hepatotoxic drug.

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