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International Journal of Clinical Biochemistry and Research

Journal homepage: https://www.ijcbr.in/

Original Research Article

Protective effect of *Ageratum conyzoides* against carbon tetrachloride –induced hepatic damage in rats

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ARTICLE INFO

Article history:
Received 12-05-2023
Accepted 11-09-2023
Available online 25-10-2023

Keywords:
Hepatoprotective
Antioxidants
Histopathpology
Carbon tetrachloride
Hepatotoxicity

ABSTRACT

Aim & Background: The present study was conducted toexamine the Hepatoprotective activity against the carbon tetrachloride toxicity in Wister rats.
Materials and Methods: The Petroleum ether, ethyl acetate and methanol extract of *Ageratum canyzoides* was prepared and evaluated for phytochemical screening. The serum level of glutamic oxaloacetate transaminase (SGOT) Glutomicpyruvate transaminase (SGPT) and bilirubin were investigated for the assessment of hepatoprotective activity of ethyl acetate of extract *Ageratum conyzoides*.
Results: Additionally, the histological changes in liver were studied. The primary phytochemical investigation of the extract of *Ageratumcanyzoides* revealed the presence of Flavonoids, tannins, and carbohydrates. Pretreatment with ethyl acetate extract of *Ageratumconyzioide* showed a significant ($P<0.05$) decrease in serum SGOT, SGPT and bilirubin when compared to control group rats treated with CCl_4 in dose dependent manner.
Conclusion: The outcomes of histology study revealed that there was significant reversal of histological functions of liver. In conclusion, the findings of study validated that the *Ageratum canyzoides* can improve CCl_4–induced hepatic toxicity.

1. Introduction

Liver regulates various important metabolic functions and damage is associated with distortion of their metabolic function. Today liver damage is a very common ailment in the world resulting in serious disabilities ranging from severe metabolic disorders to even mortality.[1]

Antioxidants such as GSH, ascorbic acid, and Vitamin E and enzymes such as SOD catalase and GPX act against oxidative process. Hepatocytes which make most of the liver structure are very active in the metabolism of exogenous chemicals and is one of the major reasons. Carbon tetra methyl chloride is one of the most commonly used hepatotoxins in the experimental study of liver diseases.[2–4]

2. Materials and Methods

2.1. Preparation of plant material

The whole plant *Ageratum conyzoides* was collected from the local surroundings of Bhopal region, during the month of August - October 2020. The plant was identified by Dr. Jagrati Tripathi - Professor of Botany, Govt. College Khemlasha Sagar. The voucher specimens are kept in the P.G. Department of Zoology, Career College, Bhopal. The whole plant was washed thoroughly under running tap water, the dried plant Material Collagenase powdered and subjected to extraction.

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https://doi.org/10.18231/j.ijcbr.2023.040

2.2. Preparation of extract

The extract was done by maceration using petroleum ether, ethyl acetate and methanol. The extract obtained was evaporated in rotary evaporator to get a powder. The extract then subjected to phytochemical analysis to detect the chemical constitution present in each extract.[5]

2.3. Animals

Male wister rats (135-108g) were used for evaluation of hepatoprotective activity. The animals were housed in polypropylene cages at 25°C±1C with the relative humidity of 55±5% under 12h/12h light /dark cycle. They received a standard chow, water and labium throughout the experiments, according to the International ethical guidelines for the care of laboratory animals.[6,7] The study protocol was approved by the Institutional Animal Ethical committee.

CCl_4 induced hepatotoxicity- Assessment of hepatoprotective activity was carried on albino rats. The animals were segregated in four groups consisting of six animals each.

Group I served as normal control receiving 5% CMC (10 ml / kg).

Group II received (1ml/ kg ip) equal volume of olive oil(50%v/v) for two successive days and were maintained as CCl_4 group.

Group III animals were treated orally for seven days with suspension of ethyl acetate extract (100mg/kg).

Group IV animals were treated with CCl_4 and ethyl acetate extract (100mh/kg).

After the treatment the blood samples were collected via retro orbital and the serum was separated by centrifugation at 2500 rpm for 15 min for the estimation of biochemical enzyme. After collecting the blood, the liver was separated and weighted (20-25g).[8]

2.4. Biochemical determination

Biochemical parameters such as serum glutamate oxaloacetate transaminase (SGOT) serum glutamate pyurvate transaminase (SGPT) and serum bilirubin were determined.

Histopathpology: Liver was excised quicklyand fixed in 10% buffered neutral formalin and processed for paraffin embedding following the standard micro techniques. Section of liver is stained with alumhaematoxylin and eosin were observed microscopically for histopathology changes.

2.5. Statistical analysis

The results are expressed as mean ± SEM of six animals from each group. The data was evaluated by one way ANOVA followed by Turkeys multiple comparison tests. P values <0.05 were considered statistically significant.

3. Results and Discussion

3.1. Phytochemicals Screening of Ageratum conyzoides

Presence of secondary metabolites might be a useful indicator of both efficacy and potential toxicity: hence test for the presence of phytochemical classes with known bioactivity was done with preliminary phytochemical investigation of the extracts of whole plants. The treatment with ethyl acetate extracts of *Ageratum conyzoides* at dose (100mg/kg) has decreased. Thus, the activity of SGOT, SGPT and total billlirubin in CCl_4 treated rats was examined.

4. Discussion

According to Gillette[9] herbal remedies are becoming increasingly popular as complementary medications for the treatment and prevention of a wide range of illnesses, most of which are caused by exposure to stress or pollutants. A number of plant components have the ability to reduce the liver damage brought on by various chemical agents. It has also been demonstrated in several experiments that *A. conyzoides* various sections cannot be extracted using aqueous or alcoholic methods. The liver's membrane stability and ability to operate is preserved by extracts.[10,11]

This biochemical restoration by plant extracts may be caused by cytochrome P-450 inhibition, promotion of its glucuronidation of toxic metabolites, or directly scavenging activity of reactive intermediate molecules responsible for the hepatocytes insert. Yellow pigment bilirubin (unconjugated) is created when heme is catabolized. Prior to being secreted into bile, hepatocytes conjugate bilirubin with glucuronic acid (conjugated bilirubin) to make it water soluble and so readily excretable.[12]

Hepatocytes failure to perform the conjugation process under exposure to hepatotoxicants led to an increase in the levels of unconjugated bilirubin.[13] The pretreatment group that had been given acetone and n-hexane extracts of *A. conyzoides* had considerably lower levels of these enzymes than the group that had been exposed to APAP, demonstrating that the extracts continue to maintain the liver's ability to operate. Another well-known very effective hepatoprotective compound is silymarin, a standardised extract of Silybum marianum (Compositae). The liver damage caused by carbon tetra chloride, D-galN, and APAP in rat models was averted by this compound, which reverses hepatotoxin-induced abnormalities in biochemical parameters.[14] This compound has thus far undergone the most extensive investigation of all plant compounds.

Similar findings on acetaminophen-induced liver damage were previously reported by Hattori et al. (1990)[15] The elevated levels of BUN and CR in the APAP-treated group might be attributed to protein metabolism. Albumin, transferin, and transthyretin are examples of the negative acute-phase proteins, whose production and secretion are

Table 1: Effect of methanolic extract of *A.conyzoidesisolated* compound on biochemical parameters of liver in rats against CCl_4 administration

S. No.	Treatment	Dose	SGOT/AST(IU/L)	SGPT/ALT (IU/L)	ALP (IU/L)	Bilirubin (IU/L)
1	VehicleSaline	10 ml/kg	32.1±4.845	28.8±3.746	105.4±8.016	0.76±0.048
2	Control (CCl_4)	-	136.6±5.680*	132.6±2.581*	302.3±9.872*	1.81±0.111*
3	Silymarine	100 mg/kg	44.1±3.920**	38.5±8.336**	125.1±7.833**	0.80±0.054**
4	MEEA	200 mg/kg	84.6±4.226**	78.6±6.377**	223.5±9.027**	1.08±0.057**
5	MEEA	400 mg/kg	69.1±4.792**	63.1±6.177**	161.8±5.344**	0.93±0.031**

Each group consists of six animals (N=6).
MEEA = Methanolic extract of *A.conyzoides**P<0.001 as compared to vehicle treated group
** P<0.001 as compared to CCl_4 treated group

Table 2: Effect of isolated compound on biochemical parameters of liver in rats against CCl_4 administration

S. No.	Treatment	Dose	SGOT/ AST(IU/L)	SGPT/ALT (IU/L)	ALP (IU/L)	BILIRUBIN (IU/L)
1	VehicleSaline	10 ml/kg	32.1±4.845	28.8±3.746	105.4±8.016	0.76±0.048
2	Control (CCl_4)	-	136.6±5.680*	132.6±2.581*	302.3±9.872*	1.81±0.111*
3	Silymarine	100 mg/kg	44.1±3.920**	38.5±8.336**	125.1±7.833**	0.80±0.054**
4	Isolated fraction	100 mg/kg	75.36±4.313**	61.76±5.243**	197.5±7.152**	0.902±0.042**
5	Isolated fraction	200 mg/kg	56.1±3.654**	52.4±4.231**	141.1±3.253**	0.877±0.021**

*P<0.001 as compared to vehicle treated group

lowered. According to the study's findings, groups of rats administered APAP alone had lower levels of albumin and total protein than control groups. Administration of *Ageratum conyzoides* extracts, however, reduced the impact, reestablish the levels of SGPT, SGOT, LDH, and bilirubin as a sign that the plasma membrane has stabilised and that the hepatic tissue damages brought on by APAP have been repaired.

5. Conclusion

Our study indicated that the alcoholic extract of *Ageratum conyzoides* isolated compound could be beneficial as hepatoprotective agents and showed significant result.

These results suggest that the application of Ageratum conyzoide extract in CCl_4 induced toxicity can be reversed. However extensive research is required to explore for safer use of herbal preparation.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Sharma M, Soni M, Gupta A. Protective effect of *Ageratum conyzoides* against carbon tetrachloride –induced hepatic damage in rats. *Int J Clin Biochem Res* 2023;10(3):228-231.