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Evaluation of Hepatoprotective Activity of *Argemone mexicana* Aerial Part Extracts on CCL_4 Induced Liver Damage in Wistar Rats

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Abstract: This study is carried out on Wistar rats to evaluate the hepatoprotective activity of *Argemone mexicana* L aerial part extracts against CCL_4 induced acute liver damages. The areal part of the plant was extracted by methanol and water using soxhlet, rotary evaporator and freeze drying apparatus. Hepatic injury was achieved by injecting 3 mL/kg s.c. of CCL_4 in equal volume proportion with olive oil. The aqueous and methanol extracts of *Argemone mexicana* areal part were given at different doses, 100, 200, 400 mg/kg/day Methanol extract, and 400 mg/kg/day orally of aqueous extract for 5 days under CCL_4 induction at 3rd day. The significance of differences between means was compared among the groups using Independent-sample T-test with probability value. The methanol extract at 100 mg/kg offered significant hepatoprotective activity ($p<0.05$) by reducing the serum marker enzyme, like Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyrovate Transaminase (SGPT) and Alkaline Phosphatase (ALP). Histopathlogical studies further confirmed the hepatoprotective activity of 100 mg/kg methanol extract. *Argemone mexicana L.* at dose 100 mg/kg indeed has a reasonable potential in healing liver parenchyma and regeneration of liver cells hence it may acts as a potent liver tonic. The results obtained were compared with silymarin (70 mg/kg.oral), the standard drug, which shown recovery toward normalization almost like that of silymarin, therefore, we recommend for further studies to isolate the pure component and the mechanism that displayed the hepatoprotective activity for making standard drug.

Key words: Hepatotoxicity, papaveraceae, phyllanthus species, silymarin, soxhlet

INTRODUCTION

Liver is one of the most important organs in human body dealing with metabolism and detoxification of external and internal substances, many toxin targets the liver can cause hepatotoxic effects which become serious health problems particularly in the rural area and the war affected regions where the hepatitis and hepatosis are common due to viral, parasite, alcohols and toxic substances. More over the discovery and appearance of the cancer disease and its fast progress that widely spread over the world is thought to be some drugs represent one of its main causative agents (Dimopoulos and Eluthreakis, 2004).

Thus, in the absence of reliable liver protective drugs, medicinal plants play important role in management of liver disorders. Medicinal plants sector has traditionally occupied an important position in the socio-cultural, spiritual and medicinal aspect of rural and tribal lives of Sudan. Medicinal plants being the effective source of both traditional and modern medicines are genuinely useful for primary health care. Such plants should be investigated thoroughly to determine their structural and functional properties, as well as the efficiency of various parts (Santos *et al*., 1995).

Some Hepatoprotective function is achieved by herbal medicines based on Phyllanthus species but these are declared as endangered plants by Sudanese Society of Medicines unless the claim had supported with scientific report. Therefore, the aim of the present context is to evaluate the hepatoprotective potential of the Argemone mexicana extract in a conventional animal model.

The plant *Argemone mexicana Linn* (family papaveraceae), locally known as khash-khash, is a widely distributed plant throughout the subtropical and tropical regions of the world. It contains alkaloids as berberine, protopine, sarguinarine, optisine, and chelerytherine, the seed oil contains myristic, palmitic, oleic, and linoleic acids (Dymock *et al*., 1982) The whole plant is analgesic, antispasmodic, possibly hallucinogenic and sedative and contains alkaloids similar to those in the opium poppy (*P. somniferum*) and so can be used as a mild pain-killer (Usher, 1974) The fresh yellow, milky acid sap is known to contain protein dissolving substances which can be

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used in the treatment of warts, cold sores, cutaneons affections, skin diseases, itches. The root is known to be alterative and can be used in the treatment of chronic skin diseases. They are expectorant and can be used in the treatment of coughs and other chest complaints. The seeds are known to be demulcent, emetic expectorant and laxative. An infusion, in small quantities can be used as sedative for children, but caution is advised since the oil in the seeds is strongly purgative, the seed can also be used as an antidote to snake poisoning (Lesley, 2001). The methanol extract, the partially purified fraction, and the pure compounds isolated from *A. mexicana* significantly and in a concentration-dependent manner reduced the morphine withdrawal. Since the pure compounds were identified as protopine and allocryptopine, the observed effects could be related to these compounds (Capasso *et al*., 1997).

The present study has been done to make an evaluation of hepatoprotective activity of *Argemone mexicana* L aerial part extracts on CCl_4 induced liver damage in laboratory Wistar rats.

MATERIALS AND METHODS

Plant materials: Areal part of *Argemone mexicana* for the proposed study was collected from Hillet Kuku, North Khartoum, in March, 2009. The plant was cleaned, shade-dried, ground coarsely by mechanical grinder and the methanol and aqueous extracts were used in the present study.

Preparation of the extracts: The method was performed by using Soxhlet, rotary evaporator and freeze drying apparatus. The air-dried areal part of the plant was triturated to coarse powder, 100 g of the powder was weighed precisely using sensitive electric analytical balance, and subjected to extraction with 250 mL methanol (99.8%) for 2 h, then, the extract was separated from solvent using rotary evaporator, air dried and yield was recorded (17% w/w from starting row materials - methanol extract). The plant residues were further dried, weighted and extracted with distilled water over night at room temperature, filtered with whatman paper and further, dried by freeze drier and the yield was recorded (13.5% w/w from starting row materials -aqueous extract (Suftness and Douras, 1979).

Experimental animals: Forty-two Wistar rats of both sexes, 30 days old and of 90±10 g average body weight were used. The rats were clinically healthy and housed within the premises of Medicinal and Aromatic Plants Research Institute (MAPRI), National Center for Research(NCR), Khartoum, Sudan and fed on rat diet (flour 75.3%, meat 15%, edible oil 7.5%, sodium chloride 1.5% and vitamins and minerals 0.7) and water provided *ad. Libitum*.

Experimental design: Animals were divided into seven groups, each group containing six animals. Group1 represent normal control, received distilled water for 5 days. Group 2 represent induction control, received Carbon Tetra Chloride (CCL_4) 3 ml/kg, subcutaneously (s.c), 1:1dilution with olive oil on 3rd day. Group 3 received Silymarin (70 mg/kg/day orally) for 5 days and CCL_4 induction on 3rd day. Groups 4, 5, and 7 received (100, 200 and 400 mg/kg/day orally) methanol extract of the plant respectively for 5 days and CCL4 induction on 3rd day (s.c). Group 6 received 400 mg/kg aqueous extract for 5 days orally, and CCL_4 induction on 3rd day (s.c). Clinical signs, average body weight and body weight gain were reported for each group. On the 6th day, animals were killed under diethyl ether anesthesia and blood samples for hematological and serobiochemical parameters were immediately collected. The serobiochemical parameters considered are Asparate Transaminase (AST), Alanine aminotransferase (ALT), alkaline phosphatase (ALP), Serum albumin and total protein. The Haematological parameters considered were: Hemoglobin (Hb), Packed Cell Volume (PCV), Red Blood Cells (RBCs), white blood cells (WBCs) and differential WBCs counts, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH) and Mean Corpuscular Haemoglobin Concentration (MCHC) were determined. At necropsy, all rats were examined to identify gross lesion. And the specimen of the liver was quickly removed after autopsy and fixed in 10% formalin for histopathological study.

Statistical analysis: Statistical Package for Social Science (SPSS) was used for the analysis of the data. The significance of differences between means was compared among the groups using Independent-sample T-test (Snedecor and Cochran, 1989).

RESULTS

Clinical findings: In rats of groups 2 to 7, in appetence, intermittent diarrhea, emaciation, erection of hair and weakness of the fore and hind limbs are the prominent manifestations. These signs appear on 3rd, 4th and 5th days after CCL_4 induction and are more severe in rats of groups 2 and 6, with slight to moderate in groups 3, 4, 5 and 7. In the postmortem observation, the liver and kidneys of rats in groups 2-7 showed severe to moderate fatty change, necrosis, and/or congestion. Severe necrosis of liver and kidney are observed in rats of groups 2, 6 and 7. There are no lesions in the control-undosed rats (Group 1).

Growth changes: Body weight and body weight gain of rats given daily oral doses of *A. mexicana*.L areal part

Table 1: Body weight and body weight gain in rats orally given *A.mexicana* extracts for 6 days

Groups	Parameters	
	Body weight (g) 0 day	Body weight gain (g) 6 day
6 Days		
1. Control (Normal diet)	93.0±1.2	10.2±1.3
2. CCL_4 control	92.5±3.3	7.8±1.4*
3. Silymarin control	85.8±2.7	9.3±2.7^{NS}
4. 100 mg/kg/day (per os) methanolic extract	87.5±2.8	8.1±1.0*
5. 200 mg/kg/day (per os) methanolic extract	85.0±1.2	7.0±1.2*
6 400 mg/kg/day (per os) methanolic extract	92.1±1.0	4.0±0.78*
7. 400 mg/kg/day (per os) aqueous extract	90.0±1.8	6.0±0.96*

Values are expressed as mean±S.E.; NS: Not significant; *: Significant at ($p<0.05$)

Table 2: Heamatological change of rats given *A. mexicana* methanol and aqueous extracts orally for 6 days under CCL_4 induction at 3rd day

Parameters	Groups						
	1. Normal control (normal diet)	2. CCL_4 (control)	3. Silymarin (control)	4. *A. mexicana* (100 mg/kg methanol extract)	5. *A. mexicana* (200 mg/kg methanol extract)	6. *A. mexicana* (400 mg/kg aqueous extract)	7. *A. mexicana* (400 mg/kg methanol extract)
6 Days							
Hb (g/dl)	16.9±0 .6	29.5±0.4*	16.3±1.4 ^{NS}	18.7±2.2 ^{NS}	16.3±0.3 ^{NS}	16.0±2.0 ^{NS}	15.3±0.5 ^{NS}
RBC ($X10^6mm^3$)	10.6±0.5	9.40±0.58	9.30±0.35 ^{NS}	11.9±0.5 *	9.20±0.3 ^{NS}	9.56±1.2 ^{NS}	10.4±0.9 ^{NS}
PCV (%)	64.9±1.9	60.2±1.2*	59.4±1.4*	55.1±1.1 ^{NS}	60.7±1.6 ^{NS}	60.7±1.2 ^{NS}	64.6±5.4 ^{NS}
MCV (mm^3)	66.0±0 .9	62.5±0.88*	64.2±0.5 ^{NS}	63.6±0.7 ^{NS}	64.0±1.1 ^{NS}	62.7±0.7*	62.0±0.8*
MCH (pg)	16.2±0.4	32.5±5.7*	15.4±0.66 ^{NS}	16.6±0.6 ^{NS}	17.4±0.2 ^{NS}	16.5±0.3 ^{NS}	15.2±1.8 ^{NS}
MCHC (%)	28.4±3.4	51.6±3.2 *	24.2±1.2 ^{NS}	25.6±0.6 ^{NS}	26.9±0.2 ^{NS}	24.5±0.7*	24.5±1.8 ^{NS}
WBC ($\times10^3mm^3$)	8.90±0.7	14.9±1.3*	9.30±0.78 ^{NS}	9.24±2.4 ^{NS}	13.8±0.8*	13.9±0.5*	12.2±0.6*
Lymphocytes (%)	54.7±6.9	40.2±2.3 *	41.5±0.4*	51.8±3.2 ^{NS}	39.1±0.4*	46.9±0.3*	49.3±0.5*
Granulocytes (%)	47.2±0.5	59.8±0.5 *	58.4±0.4*	48.2±3.2 ^{NS}	60.9±0.4*	53.1±0.5*	50.6±4.7 ^{NS}

Values are expressed as mean±S.E; NS: Not significant; *: Significant at ($p<0.05$)

Table 3: Serobiochemical analysis of rats given *A. mexicana* methanol and aqueous extracts orally for 6 day under CCL_4 induction at 3rd day

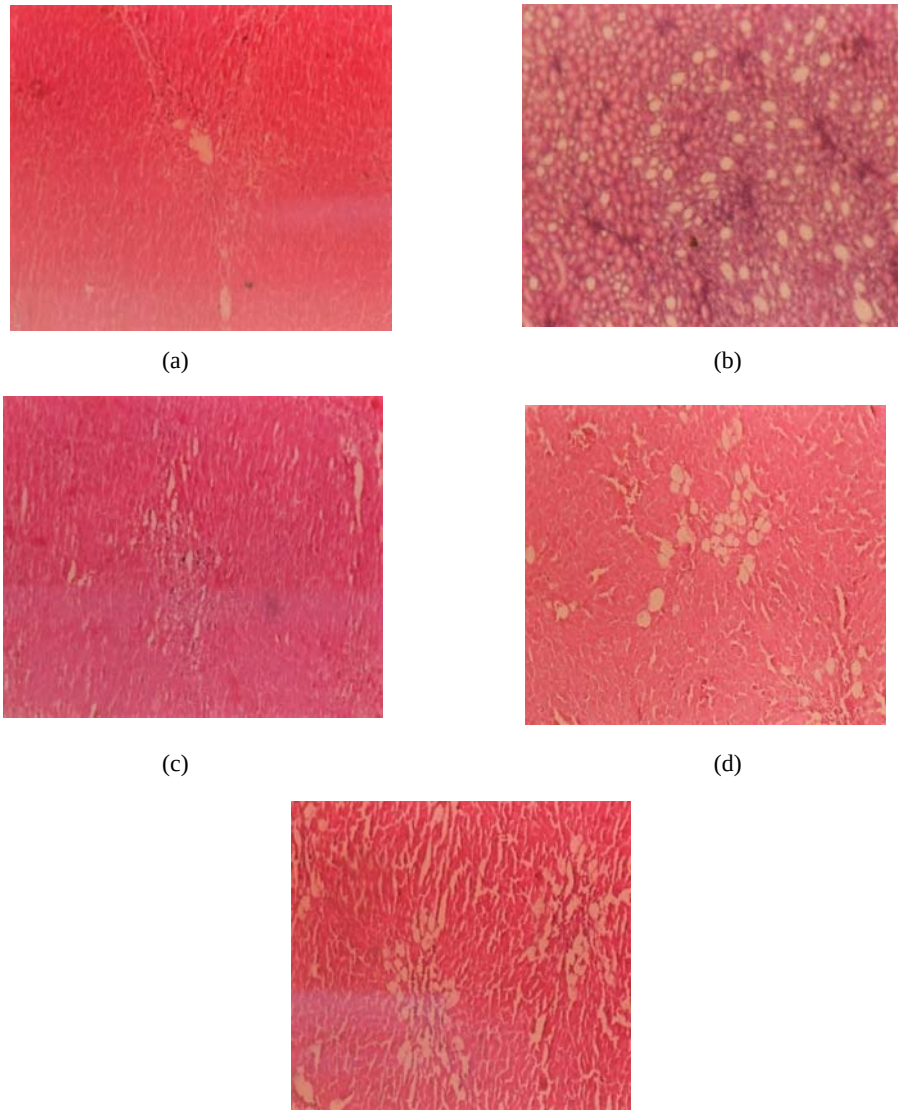
Parameters	Groups						
	1.Normal control (normal diet)	2. CCL_4 (control)	3. Silymarin (control)	4. *A. mexicana* (100 mg/kg methanol extract)	5. *A. mexicana* (200 mg/kg methanol extract)	6. *A. mexicana* (400 mg/kg aqueous extract)	7. *A. mexicana* (400 mg/kg methanol extract)
AST (iu)	9.5±0.7	45.7±0.7 *	20.7±3.3 *	11.6±2.5 *	30.8±1.4 *	52.0±1.1*	48.2±1.7 *
ALT (iu)	8.4±5.6	20.6±2.5 *	14.3±4.2 *	15.8±4.6 *	16.8±1.4 *	14.4±5.9 *	9.0±4.6 ^{NS}
ALP (iu)	44.4±6	094.4±1.4 *	31.0±6.6 *	48.6±1.5 *	74.8±1.9 *	85.0±1.5 *	53.6±1.1 *
Total protein (g/dL)	7.4±0.3	7.0±0.6^{NS}	7.2±0.6 ^{NS}	8.5±0.7 *	6.6±0.2 ^{NS}	6.4±0.9 *	6.6±0.9 ^{NS}
Albumin (g/dL)	4.9±0.2	4.3±0.5^{NS}	5.0±0.5^{NS}	4.3±0.5 ^{NS}	5.2±0.5 ^{NS}	2.7±0.2 *	3.1±0.4 *
Globulin (g/dL)	3.4±0.5	2.5±0.2 *	2.7±0.5 ^{NS}	4.1±0.6 *	1.4±0.5 *	3.5±0.8 ^{NS}	3.7±0.4 ^{NS}
Bilirubin (mg/dL)	0.42±0.1	1.3±0.8 *	1.2±0.2 *	1.2±0.7 *	0.6±0.4 ^{NS}	0.8±0.2 ^{NS}	0.6±0.5 ^{NS}

Values are expressed as mean±S.E; NS: Not significant; *: Significant at ($P<0.05$)

extracts at different doses for five days under CCL_4 induction at 3rd day on rats are presented in Table 1. The normal control (Group1), which received normal diet for 5 days, had a higher ($p<0.05$) body weight gain than groups 2, 4, 5, 6 and 7 at 6th day after treatment, but no significant change with group 3 (Silymarin control). Two rats, one from group 2 and the other from group 5, died during experiment.

Hematological findings: The hematological data are presented in Table 2 after 6 days of treatment with methanol and aqueous extract which represents a comparison of treated groups (2 to 7) with the normal control (Group 1). The value of RBCs in group 2, PCV in groups 2, 3 and 4, and MCH in group 2, 6 and 7 were lower ($p<0.05$) than normal control (Group 1) and other groups. MCH and MCHC in group 2, WBCs in groups 2, 5, 6 and 7, and granulocytes in groups 2, 3, 5, 6, and 7 were higher ($p<0.05$) than normal control.

Serobiochemical findings: The effect of both methanol and aqueous extracts of *A. mexicana* L for 6 days on Serobiochemical parameters under CCl_4-induced liver injury in rats, are presented in Table 3, 4 and 5. Table 3 shows a comparison of treated groups with normal control. The activity of AST were higher ($p<0.05$) in groups 2-7 (highest in groups 2, 6 and 7), ALT in groups 2-6 (highest in group 2) and bilirubin in groups 2, 3 and 4 than normal control. And the concentration of total protein in group 6, Albumin in groups 6 and 7 and ALP were higher ($p<0.05$) in all groups except in group were lower, and Globulin in groups 2, 4 and 5 were lower than normal control. Table 4 represents a comparison of treated groups with CCl_4-control. The activity of AST in groups 4 and 5 (lower in group 4) and ALT lower in groups 4, 5 and 6 (lowest in group 6), ALP in groups 4-7; Albumin in groups 6 and 7; and Globulin and bilirubin in groups 5, 6 and 7 were lower ($p<0.05$) than CCl_4-control. Table 5 represents a comparison of treated groups with Silymarin



(a) (b) (c) (d) (e)

Fig. 1: Shows a comparison of liver damages in different doses of plant extracts (a) represents liver of normal rat, (b) represents CCl_4 control, (c) represents 100 mg/kg methanol extract (d) represents 400 mg/kg aqueous extract, and (e) represents 400 mg/kg methanol extract (H & E) ×100

Table 4: Serobiochemical analysis of rats given *A. mexicana* methanol and aqueous extracts orally for 6days under CCL_4 induction at 3rd day

	Groups				
Parameters	2. CCL_4 (control)	4. *A.mexicana* (100 mg/kg methanol extract)	5.*A. mexicana* (200 mg/kg methanol extract)	6 . *A. mexicana* (400 mg/kg aqueous extract)	7. *A. mexicana* (400 mg/kg methanol Extract)
AST (iu)	45.7±0.7	11.6±2.5 *	30.8±1.4 *	52.0±1.1 *	48.2±1.1 *
ALT (iu)	20.6±2.5	15.8±0.6 *	16.8±1.4 *	14.4±0.9 *	19.0±4.6 NS
ALP(iu)	94.4±1.5	48.6±1.1 *	74.8±1.9 *	85.0±1.7 *	53.6±1.1 *
Total protein (g/dL)	7.0±0.2	8.5±0.7 *	6.6±0.3 NS	6.4±0.9 NS	6.67±0.9 NS
Albumin (g/dL)	4.3±0.5	4.3±0.8 NS	5.2±0.5 NS	2.7±0.2 *	3.10±0.4 *
Globulin (g/dL)	2.5±0.8	4.1±0.60 *	1.4±0.5 *	3.5±0.8 *	3.70±0.6 *
Bilirubin (mg/dL)	1.3±0.28	1.2±0.7 NS	0.6±0.1 *	0.8±0.2 *	0.6±0.5 *

Values are expressed as mean±S.E; NS: Not significant; *: Significant at ($p<0.05$)

Table 5: Serobiochemical analysis of rats given *A.mexicana* methanol and aqueous extract orally for 6 days under CCL_4 induction at 3rd day

	Groups				
Parameters	3. Silymarin (control)	4. *A. mexicana* (100 mg/kg/day methanol extract)	5. *A. mexicana* (200 mg/kg/day methanol extract)	6. *A. mexicana* (400 mg/kg/day aqueous extract)	7.*A. mexicana* (400 mg/kg/day methanol extract)
AST (iu)	20.7±3.3	11.6±2.5 *	30.8±1.4 *	52±1.3 *	48.2±1.7 *
ALT (iu)	14.3±4.2	15.8±4.6 NS	16.8±1.4 *	14.4±5.9 NS	9.0±4.6 *
ALP(iu)	31.0±6.6	48.6±1.1 *	74.8±1.9 *	85±1.5 *	53.6±1.1 *
Total protein	7.2±0.6	8.5±0.7 *	6.6±0.2 *	6.4±0.9 *	6.6±0.9 *
Albumin (g/dL)	5.0±0.5	4.3±0.8 *	5.2±0.5 NS	2.7±0.2*	3.1±0.4 *
Globulin (g/dL)	2.2±0.5	4.1±0.6 *	1.4±0.4 *	3.5±0.8 *	3.7±0.6 *
Bilirubin (mg/dL)	1.2±0.2	1.2±0.7 NS	0.6±0.4 *	0 .8±0.2*	0.6 ±0.5 *

Values are expressed as mean±S.E; NS: Not significant; *: Significant at ($p<0.05$)

control. The value of AST activity in group 4; Total protein and Bilirubin in groups 5, 6 and 7; were lower ($p<0.05$) and Globulin in groups 6 and 7 were higher than control than control. And there are increase ($p<0.05$) in AST activity in groups 5, 6 and 7; ALT in group 5 and lower in group 7; and ALP in groups 4, 5, 6 and 7.

Histopathological findings: Results of histopathological studies provided supportive evidence for biochemical analysis. Histology of liver section of normal control animal (group 1) exhibited normal hepatic cells each with well defined cytoplasm, prominent nucleus, and nucleolus and well brought out central vein (Fig. 1a), whereas that of CCl_4 intoxicated group animal showed total loss of hepatic architecture with centrilobular hepatic necrosis, fatty changes, vacuolization and congestion of sinusoids, kupffer cell hyperplasia, crowding of central vein and apoptosis (Fig. 1b). Treatment with methanol extract of plant, at a dose of 100 and 400 mg/kg body weight (b.wt) showed moderate to weak activity in protecting the liver cells from CCl_4-injury (Fig. 1c and e), respectively.

Treatment with aqueous extract of plant at a dose of 400mg/kg b.wt showed a good result than corresponding dose of methanol extract (Fig. 1d). Among the plant extracts, treatment with methanol extract of plant, at a dose of 100 mg/kg b.wt extract returned the injured liver to quite normal. So it could be decided that the hepatoprotective activity was dose dependent.

DISCUSSION

Nowadays, Liver disorders become a serious health problem worldwide due to many toxins and microorganism, but in medicinal practices, reliable liver protective drugs are not available therefore, in this scheme, we attempt to evaluate the hepatoprotective activity of *Argemone mexicana* L. on CCL_4 Induced liver damage Since the changes associated with CCL_4 induced liver damages are similar to that of acute viral hepatitis (Suja *et al*., 2004), CCL_4 mediated hepatotoxicity was chosen as the experimental model. The ability of hepatoprotective drug to reduce the injurious effect or to preserve the normal hepatic physiological mechanisms that have been disturbed by hepatotoxin, is the index of its hepatoprotective effects (Yada and Dixit, 2003) CCl_4 has a direct destructive effect on membranes of the hepatocyte and on consequent interface with cellular metabolism and transport. It damages the membranes of the hepatocyte causing leakage of the enzymes present in the cell. These results in elevation of the levels of plasma tramaminases (Ashok *et al*., 2002) it leads to fat decomposition in the liver due to blockage of secretion of hepatic triglycerides into plasma. The toxicity of CCl_4 depends upon the cleavage of C-Cl bond to generate a trichloro methyl- a free radical (CCl_3O_2); this cleavage occurs in the endoplasmic reticulum and is mediated by the cytochrome p-450 mixed function oxidase system. The product of the cleavage binds irreversibly to hepatic proteins and lipids. The metabolism of CCl_4 releases CCl_3 a free radical, which initiates per oxidation and cleavage of fatty acids in the membranes. The CCl_4 derived free radicals initiates the process of peroxidations by attacking Methylene Bridge of unsaturated fatty acid side chains of microsomal lipids (Ashok *et al*., 2002) a single dose of CCl_4 leads to centrilobular necrosis and fatty liver. Within a few minutes, there is injury to the endoplasmic reticulum lending to functional defects of the Hepatocyte and multiple biochemical manifestations of hepatic injury. CTC causes accumulations of fat in the liver especially by interfering with the transfer of triglycerides from the liver into the plasma. Many clinical conditions that cause an increase in cholesterol levels also cause increase in triglycerides enzymes sensitive to cytotomic injury are serum Alanine amino transferase (ALT) and serum Asparatate amino transferase (AST). Asparatate and Alanine amino transferases are present in high concentration in liver (Ashok *et al*., 2002). Due to hepatocytes necrosis or abdominal membrane permeability, the serum marker enzymes (AST, ALT and ALP) are released from the cells and their levels in the blood increase (Pingale Shirish, 2010) ALT is a sensitive indicator to acute liver damage and elevation of this enzyme in no hepatic disease is unusual. Alkaline phophatase, although is not a liver specific enzyme, the liver is major source of this enzyme. Bilirubin levels in blood also increase in liver diseases (Ashok *et al*., 2002) the present study revealed a significant increase in the activities of these enzymes level on exposure to CCL_4

indicating considerable hepatocellular injury. Administration of plant extract at 100 mg/kg attenuate the elevated level of enzymes (AST, ALT and ALP) produced by CCL_4 and caused subsequent recovery toward normalization almost like that of silymarin (known hepatoprotectant). All the values were compared with those of the control animals and the conclusion was obtained based on general and abnormal behavior, biochemical parameters and food and water consumptions. The observations of biochemical assay of group I (normal control) and group 4 (100 mg/kg plant extract) showed a good matching which indicates best recovery (Pingale *et al*., 2008) this finding agree with Fakhrul who demonstrated that Oral supplementation of aqueous extract of *A. mexicana* stem and leave show the protective effect on the brain and liver (Fakhrul, 2002) furthermore Pingale confirmed that *Argemone mexicana* L indeed has a high potential in healing liver parenchyma and regeneration of liver cells hence it may act as a potent liver tonic.

This finding is further confirmed with histopathiological studies which showed the hepatoprotective activity of the plant extracts in dose dependant manner. Group 2 showed increased secretions indicating liver damage due to CCl_4, Groups 5, 6 and 7 also showed more values of all biochemical parameters and group 3 showed some recovery due to Silymarin hepatoprotectant. The observations of the higher dosed groups (Groups 5, 6 and 7) from intermittent diarrhea to body weight loss may attribute to gastroenteritis or to the parasymy-pathomimtic cholinergic effect of the plant constituents as El Gamal (1995) said the toxicity effect of high doses may related to Argemone alkaloid protopine, allocryptopine sanguinarine and chelerthrine which cause proteinuria (specifically loss of albumin) occurs, with a resultant edema as would occur in nephrotic syndrome. Other symptoms are bilateral pitting edema of extremities headache, loose bowels, erythema and breathlessness (Sharma *et al*., 1999).

CONCLUSION AND RECOMMENDATION

From above observations of biochemical parameters it was demonstrated that *Argemone mexicana* L. at dose 100 mg/kg indeed has a reasonable potential in healing liver parenchyma and regeneration of liver cells hence it may acts as a potent liver tonic. But the active ingredients and the mechanism by which *A. mexicana* displays the hepatoprotectivity is not known yet, therefore, further investigations are needed to be carried out to isolate the pure components which have an effect, and to know the mechanism by which it act for the benefits of human being.

REFERENCES

Ashok, K., S. Somayaji and K. Bairy, 2002. Hepatoprotective effect of Ginkgo biloba. Indian J. Pharmacol., 33: 260-266.

Capasso, A., S. Piacente, C. Pizza, N. Tommasi, C. Jativa and L. Sorrentino, 1997. Isoquinoline alkaloids from Argemone mexicana reduce morphine withdrawal in guinea pig isolated ileum. Plant Med., 63: 326-328.

Dimopoulos, M.A. an P. Eluthreakis, 2004. Adverse effects of thalidomide aministration in pateint with neoplastic disease. J. Clino. Onco., l: 15-20.

Dymock, A.H. W.G. Warden and A.U. Hooper, 1982. Photochemical screening of Mexican poppy. Ethnobotany., 5: 120-126.

El Gamal, A.A., 1995. Phytochemistry, Pharmacology and Toxicicology of Argemone mexicana L. Ph.D. Thesis, Faculty of Pharmacy, University of Khartoum, Sudan.

Fakhrul, R.G., 2002. Studies On the Neurotoxicology Of Argemone oil. Central Council of Research in Unani Medicine (CCRUM).

Lesley, H.A., 2001. Weeds and Invasive Plants, South Africa Handbook Smith, A.C., Flora vitiensis nova. A new Flora of Fiji, National Tropical Botanical.

Pingale, S., 2010. Hepatoprotection study of leaves powder of *Azadirachta indica* A. JUSS. Int. J. Pharm. Sci. Rev. Res., 3(2): 37-42.

Pingale, S., D.P. Raghunath and S. Mugdha, 2008. Standrization of herdal drugs as potent livertonicepartment pharmacologyonline. Maharashtra India, 1: 13-19.

Santos, P.R.V., A.C.X. Oliveria and T.C.B. Tomassini, 1995. Controle microbiogico de products fitoterapicos. Rev. Farm. Bioquim., 31: 35-38.

Sharma, B.D., S. Malhotra, V. Bhatia and M. Rathee, 1999. Epidemic dropsy cuased by *argemone mexica*. India. Postgrad Med. J., 75: 657-661.

Snedecor, G.W. and WC. Cochran,1989.Statistical Method, 8th end Iowa State University Press, Ames, Iowa.

Suftness, M. and J. Douras, 1979. Drugs of Plant Origin in Methods in Cancer Research. Academic Press, New York, pp: 548.

Suja S.R., P.G. Latha, P.Pushpangadan and S. Rajasekharan, 2004. Hepatoprotective effect of *heliminthstaches* zylanica. J. Ethnopharmacol., 92: 61-66.

Usher, G.A., 1974. Dictionary of Plants used by Man. Constable, Lodon.

Yada, N.P. and V.K. Dixit, 2003. Hepatoprotective effect of leafe of *Kalanchoe penniata*. J. Ethnopharmacol., 86: 197-202.