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RESEARCH ARTICLE

PHARMACOLOGY

HEPATOPROTECTIVE ACTIVITY OF FRUITS OF "*PRUNUS DOMESTICA*"

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ABSTRACT

Extract of Methanol:ethanol (70:30) of *Prunus domestica* was prepared and tested for its hepatoprotective effect against Paracetamol and CCl_4 induced hepatitis in rats . Alteration in the levels of biochemical markers of hepatic damage like SGPT, SGOT, ALP,Total bilirubin, direct bilirubin and tissue LPO, GSH, catalase and SOD were tested in both treated and untreated groups. Paracetamol (2 g/kg) and CCl_4 (1.5ml/kg) has enhanced the SGPT, SGOT, ALP, Total bilirubin and direct bilirubin and tissue level of GSH. Treatment with extract of *P. domestica* fruits (150 mg/kg and 300 mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner.

KEYWORDS

Prunus domestica ; Paracetamol;CCl_4; Hepatoprotective

INTRODUCTION

The liver is a vital organ of paramount importance involved in the maintenance of metabolic functions and detoxification from the exogenous and endogenous challenges, like xenobiotics, drugs, viral infections and chronic alcoholism. If during all such exposures to the above mentioned challenges the natural protective mechanisms of the liver are overpowered, the result is hepatic injury.

Liver damage is always associated with cellular necrosis, increase in tissue lipid peroxidation and depletion in the tissue GSH levels. In addition serum levels of many biochemical markers like SGOT, SGPT, bilirubin, alkaline phosphatase, are elevated [1,2].In this phenomenal growth of modern medicine, there are no synthetic drugs available for the treatment of hepatic disorders. However there are several herbal formulations claimed have possess beneficial activity in treating hepatic disorders. In one of our field surveys we found that plant *P. domestica* which was claimed to possess hepatoprotective Flavonoids, Glycosides, Alkaloids, Phenolics Compound, Terpinoids, Protien and Amino Acids . There are reports showed that possess Plum pox virus[3], antioxidant[4],colon carcinoma[5], inflammation on neurologic processes properties.. However there are no scientific basis or reports in the modern literature regarding its usefulness as hepatoprotective agent. Thus the present study was conducted to evaluate the hepatoprotective activity of the extract of *P. domestica* fruits by using Paracetamol, CCl_4 induced hepatic injury in rats.

MATERIAL AND METHOD

Plant

The fruits of *Prunus Domestica* were collected from Bhopal (M.P.). The plant was authenticated by Dr. Zia-ul Hasan Department of Botanical, Safia College of Science Bhopal (M.P.). The voucher specimen no. (137/BOT./SAFIA/2010) was deposited in the herbarium of the Department of Botanical, Safia College of Science Bhopal (M.P.).

Extraction by Maceration

For maceration, the material was placed in an Erlenmeyer flask, the corresponding amount of solvent was added [(70:30) Methanol : Acetone] and left to macerate for 5 days at room temperature with regular stirring at regular interval.

Animals

Albino Wistar rats (100-150gm) of either sex were used for this study and these animal were obtained from animal house [CPCSEA Reg. No.1283/c/09/CPCSEA], PINNACLE BIOMEDICAL RESEACH INSTITUTE, Bhopal (M.P.). Throughout the experiment, the animals were housed, four animal per cage, maintained at ambient temperature of (25º±2); 30-60% humidity, under 12 hr. light-dark cycle. They were fed with standard pellet diet and water *ad libitum*. The animals were habituated to laboratory conditions for 48 hr. prior to the experimental protocol to minimize any non specific stress.

HEPATOPROTECTIVE ACTIVITY USING PARACETAMOL MODEL

The extract of *Prunus domestica*, paracetamol, vehicle, silymarin were given with the help of oral feeding cannula.

Five groups of rats each containing six received:

Group-1: Normal control, given water daily for 7 days.

Group-2: Paracetamol control, given water daily for 7 days followed by single dose of paracetamol (2g/kg body weight, i.p.) on 7th day.

Group-3: Extract (150 mg/kg body weight) + Paracetamol (2g/kg body weight) single i.p. dose on 7th day.

Group-4 : Extract (300mg/kg body weight) + Paracetamol (2g/kg body weight) single i.p. dose on 7th day.

Group-5 : Standard-Paracetamol (2g/kg body weight) + Silymarin (100mg/kg body weight).

Group 1 was normal control group received only normal food and water ad libitum and Group 2 was treated only vehicle for 7 days and Group 3-4 was treated with extract for 7 days and Group 5 was also treated with vehicle for 7 days. The paracetamol was administered on 7th day after administration of the extract and vehicle to all five groups. In Group 5 after treated paracetamol standard drug sylimarin was also given [126]

HEPATOPROTECTIVE ACTIVITY USING CCL4 MODEL

The extract of *Prunus domestica*, carbontetrachloride, vehicle, silymarin were given with the help of oral feeding cannula.

Five groups of rats each containing six received:

Group-1: Normal control, given water daily for 7 days.

Group-2: CCl4 control, given water daily for 7 days followed by single dose of CCl4 (1.5ml/kg body weight, i.p.) on 7th day.

Group-3: Extract (150 mg/kg body weight) + CCl_4 (1.5ml/kg body weight) single i.p. dose on 7th day.

Group-4 : Extract (300mg/kg body weight) + CCl_4 (1.5ml/kg body weight) single i.p. dose on 7th day.

Group-5 : Standard-CCl_4 (1.5ml/kg body weight) + Silymarin (100mg/kg body weight)

Group 1 was normal control group received only normal food and water ad libitum and Group 2 was treated only vehicle for 7 days and Group 3-4 was treated with extract for 7 days and Group 5 was also treated with vehicle for 7 days. The CCl_4 was administered on 7th day after administration of the extract and vehicle to all five groups. In Group 5 after treated CCl4 standard drug sylimarin was also given.

Preparation of Samples for Biochemical Studies

The experiment on the 8th day, the rats was be fasted overnight. On the 8th day, the fasted rats were sacrificed under diethyl ether anesthesia and blood samples collected into plain sample bottles. Blood samples will be obtained by orbital puncture with glass capillary.The blood was kept for 30 minutes without disturbing. The clot was dispersed with glass rod and then centrifuged for 15-20 minutes at 2000 rpm to separate serum. The serum of each animal of all groups was estimated for SGOT, SGPT, ALP and Total Bilirubin and tissue homogenate of animal was estimated for LPO, GSH, SOD, and catalase.

Statistical Analysis

The mean value ± SEM were calculated for each parameter. Results were subjected to statistical analysis using one-way ANOVA followed by Dunnett' test.

RESULTS

PARACETAMOL INDUCED HEPATOTOXICITY

SGOT, SGPT, ALP and bilirubin these are mostly used in liver function test as it is

relevant that any truamatic injury, any disease affecting structures of tissu ,acute myocardial infarction and liver diseases . which may be due to intoxication shows elevated level of SGOT, SGPT, ALP and bilirubin.

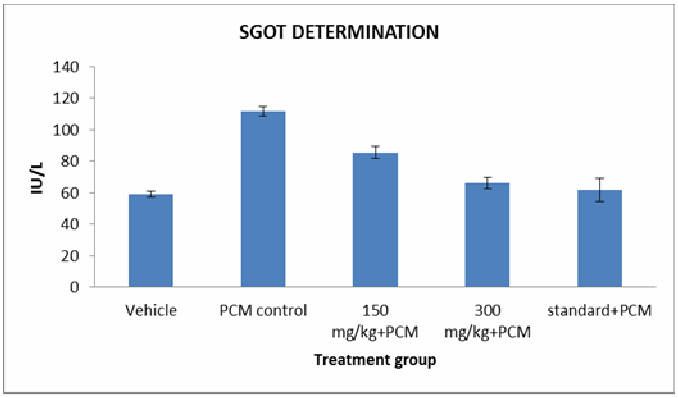
Table 1
Effect of P. domestica extract on serum enzymes and bilirubin

Treatment Group	SGOT	SGPT	ALP	BILIRUBIN	
				TOTAL	DIRECT
Vehicle	58.5±3.7	28.3±8.4	26.7±12.8	0.66±0.08	0.11±0.04
Paracetamol	111.7±6.2[a]	102.3±5.2[a]	91.5±5.2[a]	2.2±0.3[a]	0.55±0.08[a]
EXTRACT 150mg/kg	85.6±7.7[c a]	65.9±6.3[c]	63.4±10.6[c]	1.05±0.18[c d]	0.43±0.10[b a]
EXTRACT 300mg/kg	66.1±7.0[c]	45.4±13.3[c]	40.1±12.5[c d]	1.33±0.5[c]	0.22±0.07[c d]
Salymarin	61.74±14.9[c]	38.0±5.5[c d]	36.07±6.3[c]	0.66±0.16[c d]	0.1±0.01[d]

Each group consist of six animals
[a] *Significant increase (p<0.05) as compared to vehicle treated group*
[b] *Nonsignificant protection against paracetamol induced toxicity (p>0.05)*
[c] *Significant protection against paracetamol induced toxicity (p<0.05)*
[d] *Nonsignificant as (p>0.05) compared to vehicle treated group*

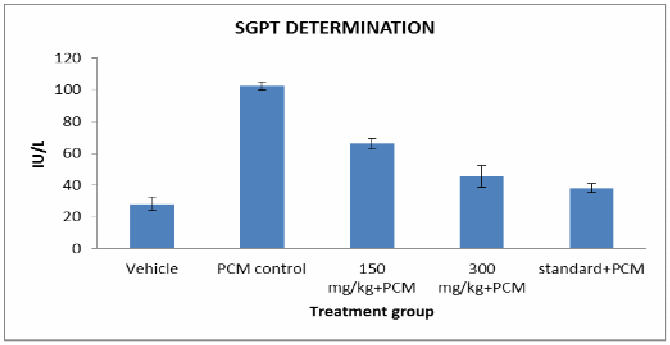
SGOT:- Serum glutamic oxaloacetic transaminase
SGPT:- Serum glutamic pyruvic transaminase
ALP:- Alkaline phosphatase
PCM:- Paracetamol

Graph no. 1



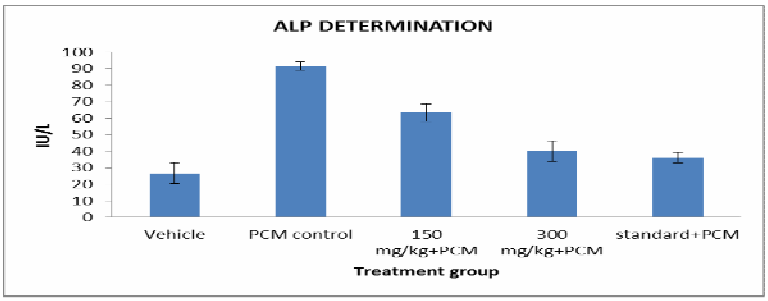
In table no.3 the SGOT level is revealed and that paracetamol produces significant increase in SGOT level up to 111.7±6.2 (P<0.05 as compared to vehicle treated group).Extract 150mg/kg and 300mg/kg decrease SGOT level significantly (P<0.05)as compared to paracetamol group. Silymarin also produced significant production against paracetamol induced hepatotoxicity. SGOT test also known as AST test majors the amount of protein enzyme called glutamic oxaloacetic transaminase occurring in our blood an it is a tool to major whether any risk liver function is present .Thus our extract is showing sgnificnt protection in these case.

Graph No. 2



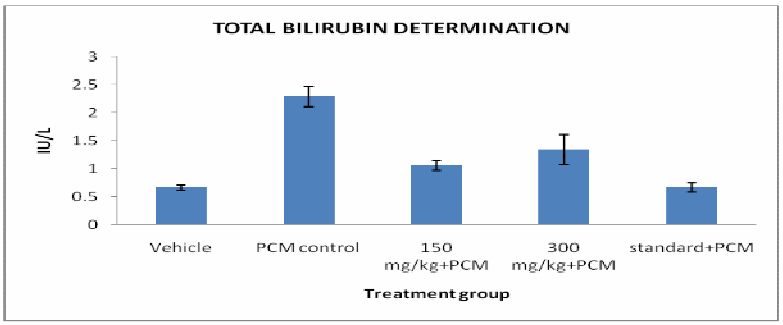
In the case of SGPT level in normal animal (vehicle treated) was found to 28.3±8.4. which was very high in paracetamol treated group that is 102.3±5.2 animals who where provide extract 150mg/kg where found to be protected as SGPT level. In tese case was 65.9±6,3 and45.4±13.3 for 300mg/kg and both of this values where significantly less than value of paracetamol treated animals.Serum glutamate pyruvate transaminase is an enzyme that is normaly present in liver nd heart cell. SGPT is released in to blood when liver and heart are damage. The blood SGPT level are thus elevated with liver damage from below table .It was observed that extract is decreasing these elevated SGPT level.

Graph No. 3



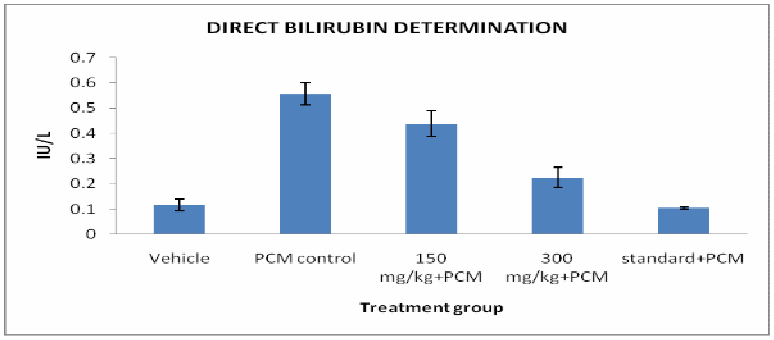
In these case ALP is revealed that paracetamol produces significant increase in ALP level up to 91.5±5.2 ($p<0.05$) as compared to vehicle treated and the normal animal (vehicle treated) was found to 26.7±12.8 and than the extract of P. domestica 150mg/kg group of animal show that 63.4±10.6 and extract 300mg/kg level 40.1±12.5 was significant decreases as compared to paracetamol group. Silymarin also produced significant production against paracetamol induced hepatotoxicity.

Graph No. 4



In graph no. 4 indicate that total bilirubin level in that graph the level of total bilirubin in vehicle treted was found to 0.66±0.08 and the paracetamol produces significantly increase total bilirubin level as 2.2±0.3 as compare to vehicle group and the extract of 150mg/kg was found to be total bilirubin level was 1.05±0.18 significant protection against paracetamol induced toxicity ($p<0.05$) and nonsignificant as ($p>0.05$) compared to vehicle treated group and extract of 300mg/kg found to be 1.33±0.5 was significant protection against paracetamol induced toxicity ($p<0.05$) .

Graph no. 5



In graph 5 indicate direct bilirubin .The vehicle group was found 0.11±0.027 and the paracetamol group 0.55±0.08 was significant increase as compared to vehicle treated group. And the extract of 150mg/kg was found significant protection against paracetamol induced toxicity and significant increase as compare to vehicle treated group and silymarin group was found significant protection against paracetamol induced toxicity.

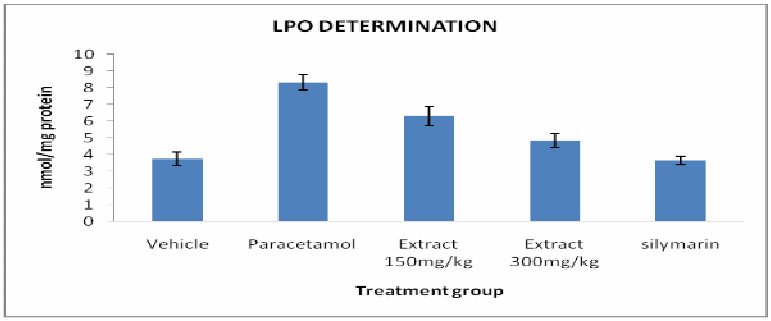
(Table no.5)

Treatment Group	LPO	GSH	CATALASE	SOD
Vehicle	3.75±0.79	0.58±0.184	35.65±1.12	106.2±10.8
Paracetamol	8.31±0.90[a]	0.099±0.024[a]	22.188±0.90[a]	50.85±4.22[a]
EXTRACT 150mg/kg	6.30±1.14[c a]	0.21±0.076[b a]	24.935±1.36[c a]	65.32±6.04[c a]
EXTRACT 300mg/kg	4.84±0.89[c d]	0.38±0.106[c a]	29.742±1.98[c a]	88.45±9.38[c a]
Silymarin	3.65±0.515[c d]	.0495±0.036[c d]	32.376±1.44[c a]	95.78±5.06[c d]

** Each group consist of six animals*
[a] Significant increase ($p<0.05$) as compared to vehicle treated group
[b] Nonsignificant protection against paracetamol induced toxicity ($p>0.05$)
[c] Significant protection against paracetamol induced toxicity ($p<0.05$)
[d] Nonsignificant as ($p>0.05$) compared to vehicle treated group.

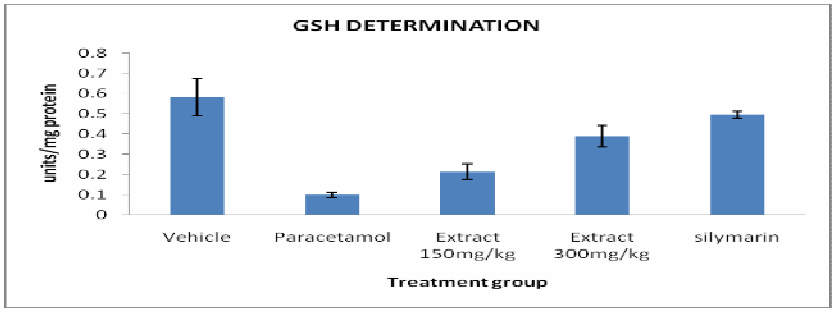
LPO:- Lipid peroxidation
GSH:- Glutathione
SOD:- Superoxide dismutase

Graph No. 6



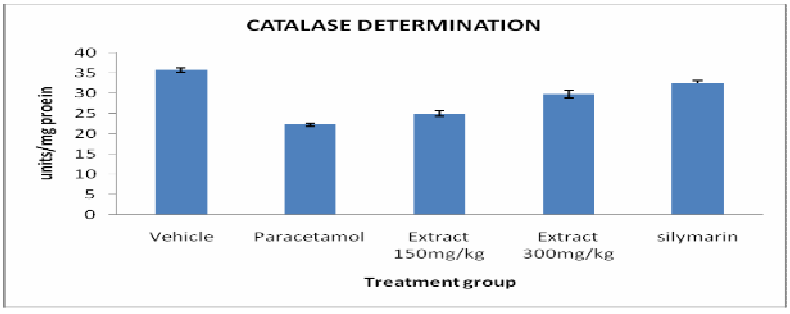
Lipid Per Oxidation ,in these case paracetamol group was found to 8.31±0.902 significant increase as compared to vehicle group 33.75±.791 and the extract of 150mg/kg found to be protected as LPO level in this case was 6.305±1.147 significant protection against paracetamol induced toxicity and significant increase as compared to vehicle treated group the extract of 300mg/kg was 4.84±.89 significant protection against paracetamol group and nonsignificant as compared vehicle treated group and silymarin group of animal given LPO level was 3.657±.515. significant decrease as compared to paracetamol group.

Graph No. 7



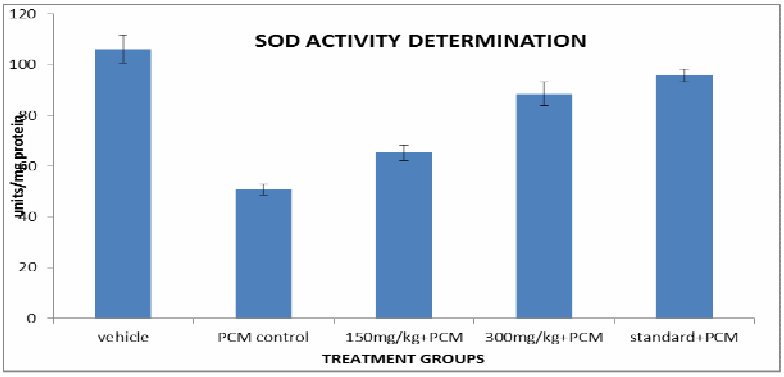
In case of GSH level in vehicle group was found to .58±.18 than the paracetamol group was .09±.02 which was significant as compared to vehicle. The extract of 150mg/kg was .71±.07 nonsignificant protection against paracetamol induced toxicity group and significant as compared to vehicle treated group and 300mg/kg extract was .38±.10 significant protection against paracetamol toxicity and significant increase as compared to vehicle treated group. Salymarin was .495±.03 produced significant protection against paracetamol induced hepatotoxicity.

Graph No. 8



In case of catalase the vehicle was found to 35.6±1.12 that the paracetamol group 22.18±.9 which was significant as compared to vehicle .The extract of 150mg/kg and 300mg/kg was 24.93±13.6 and 29.7±1.98 as significant protection against paraceytamol induced toxicity and significant increase as compared to vehicle treated .Silymarin also produce 32. 37±1.44 significant protected against paracetamol and significant increase as compared to vehicle treated group.

Graph No. 9



In case of SOD level vehicle group was found to 106.2±10.8 that the paracetamol group was found to 50.85±4.22 which was significant increases as compared to vehicle group. The extract of 150mg/kg 65.32±6.04 and extract of 300mg/kg 88.45±9.38 was found significant protection against paracetamol induced toxicity and significant increases compared to vehicle treated group.

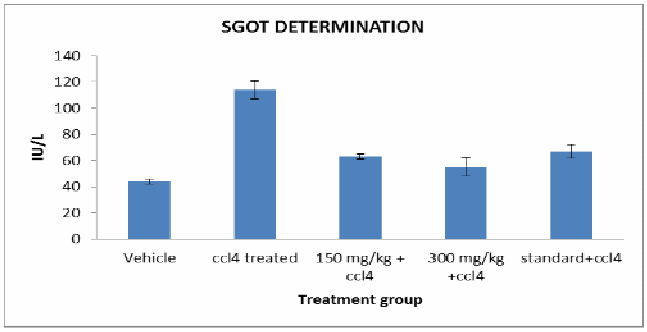
CCl_4 INDUCED HEPATOTOXICITY

(Table no.6)

Treatment Group	SGOT	SGPT	ALP	BILIRUBIN	
				TOTAL	DIRECT
Vehicle	44.05±3.92	33.57±3.59	26.86±6.84	0.66±0.17	0.11±0.04
CCl_4	113.79±13.68[a]	111.50±5.64[a]	111.6±10.25[a]	1.70±0.12[a]	0.80±0.14[a]
150mg/kg EXTRACT+CCl_4	63.12±4.12[c a]	58.30±19.08[c a]	79.74±5.95[c a]	1.06±0.13[c a]	0.48±0.15[c a]
300mg/kg EXTRACT+CCl_4	55.00±14.46[c d]	52.12±8.45[c a]	60.82±4.348[c a]	0.93±0.081[c a]	0.27±0.14[c d]
Silymarin+CCl_4	66.94±10.70[c a]	30.11±6.71[c d]	46.58±6.39[c a]	0.54±0.08[c d]	0.10±0.01[c d]

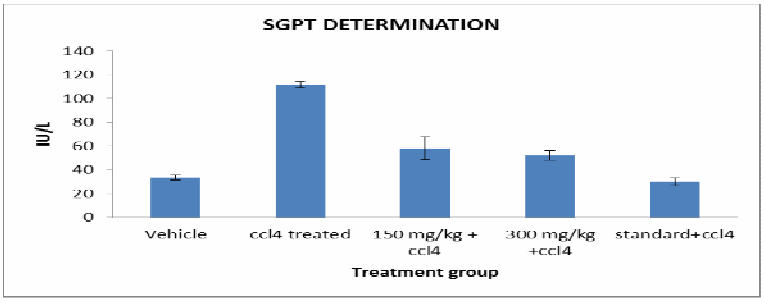
** Each group consist of six animals*
[a] Significant increase ($p<0.05$) as compared to vehicle treated group
[b] Nonsignificant protection against CCl_4 induced toxicity ($p>0.05$)
[c] Significant protection against CCl_4 induced toxicity ($p<0.05$)
[d] Nonsignificant as ($p>0.05$) compared to vehicle treated group

Graph no. 10



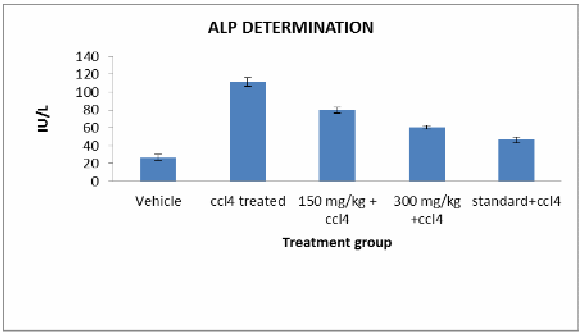
In table no. 6 it is revealed that CCl4 produced significant increase in SGOT level up to 113.79±13.68 as compared to vehicle treated group.Extract 150mg/kg decrease SGOT level significant as comparwed to ccl4 group and it significant increase as compared to vehicle treated group and the extract of 300mg/kg SGOT level 55±14.46 also decrease as compared to ccl4 group and it was nonsignificant as compared to vehicle treated group.Silymarin 66.94±10.70 also produce significant protection against ccl4 and vehicle treated group.

Graph No. 11



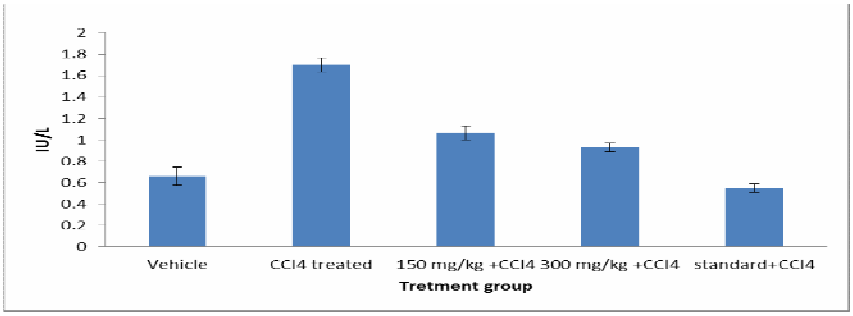
In SGPT level vehicle treated was found to 33.57±3.59 which was very high in ccl4 treated group that is 111.50±5.64 significant increase of these group as compared to vehicle.animal who where provide extract 150mg/kg and 300 mg/kg found to be protected as SGPT level in this case was 58.30±19.08 and 52.18±8.45 significant protection against ccl4 induced hapatotoxicity and significant increase as compared to vehicle treated group. In silymarin group was 30.11±6.71 significant protection against ccl4 induced hapatotoxicity and significant increase as compared to vehicle treated group.

Graph no. 12



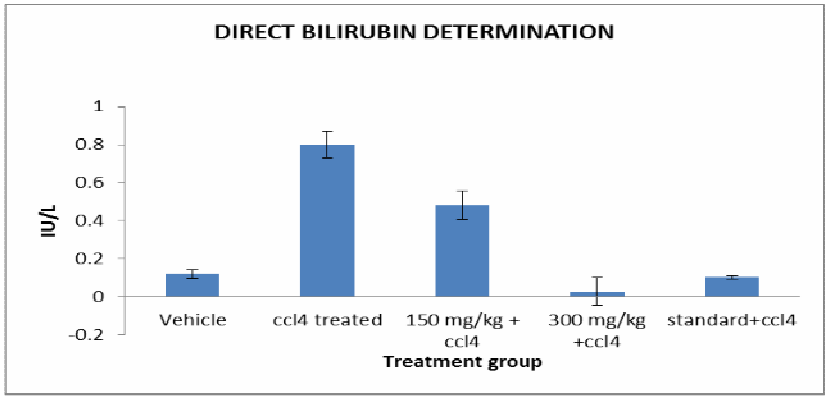
ALP level was found in vehicle group 76.86±6.84 and the ccl4 induced group was high significant increase 111.6±10.25 as compared to vehicle treated gtoup. The extract dose of 150mg/kg and 300mg/kg was 79.74±5.95 and 60.82±4.348 significant protection against ccl4 induced hepatotoxicity and significant increase as compared to vehicle group.In case of silymarin was 46.58±6.39 also significant protection against ccl4 induced group and significant increase as compared to vehicle group.

Graph no. 13



In bilirubine case the total bilirubin level of vehicle was .66±.17 and ccl4 induced hepatotoxicity level 1.70±.12 significant increase as compared to vehicle. The extract of 150mg/kg and 300mg/kg was significant protection against ccl4 induced hepatotoxicity and significant as compared to vehicle treated group . The silymarin was found the level .54±.08 significant protection against ccl4 induced toxicity and nonsignificant as campared to vehicle group.

Graph no. 14



The direct bilirubin level found in vehicle group was .11±.04 .ccl4 group was .80±.14 was significantincrease as compared to vehicle .Extract 150mg/kg was found .48±.15 significant protection against ccl4 and significant as compared to vehicle.The extract of 300mg/kg was found .27±.14 significant against ccl4 group and non significant as compared to vehicle treated group. Silymarin was .10±.01 significant protection against ccl4 and nonsignificant as compared to vehicle.

Table no.6

Effect of P. domestica extract on carbontetrachloride induced changes in enzyme levels

Treatment Group	LPO	GSH	CATALASE	SOD
Vehicle	1.42±0.09	0.62±0.184	35.65±1.12	106.23±10.86
Control CCl_4	4.21±0.19[a]	0.16±0.112[a]	23.49±0.97[a]	39.98±5.18[a]
150mg/kg EXTRACT+CCl_4	2.92±0.60[c a]	0.27±.024[b a]	26.54±1.39[c a]	56.21±9.10[c a]
300mg/kg EXTRACT+CCl_4	2.17±0.65[c a]	0.39±.062[c a]	30.83±1.90[c a]	78.63±6.22[c a]
Standard Silymarin+CCl_4	1.54±0.10[c d]	0.51±.096[c d]	33.31±1.64[c d]	89.88±6.23[c a]

** Each group consist of six animals*

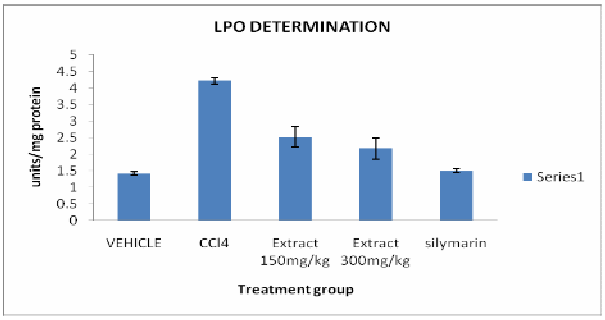
[a] *Significant increase (p<0.05) as compared to vehicle treated group*

[b] *Nonsignificant protection against CCl_4 induced toxicity (p>0.05)*

[c] *Significant protection against CCl_4 induced toxicity (p<0.05)*

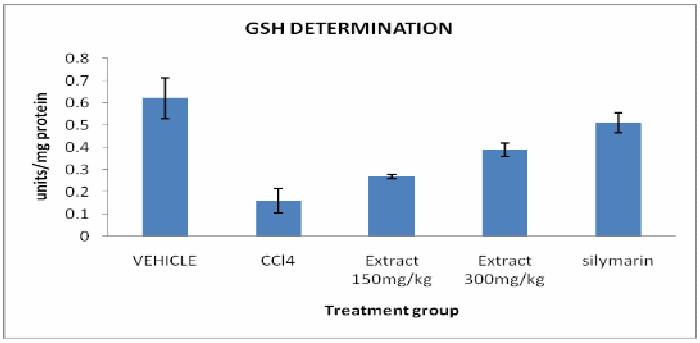
[d] *Nonsignificant as (p>0.05) compared to vehicle treated group*

Graph no. 15



The LPO level of vehicle was 1.42±0.094 and ccl4 induced group LPO level was 4.21±.194 significant increase as compared to vehicle. Extract 150mg/kg and 300mg/kg was found 2.921±.605 and 2.174±.651 significant protection against ccl4 induced toxicity and significant increases as compared to vehicle and the silymarin also significant protection against ccl4 induced toxicity and nonsignificant compared to vehicle.

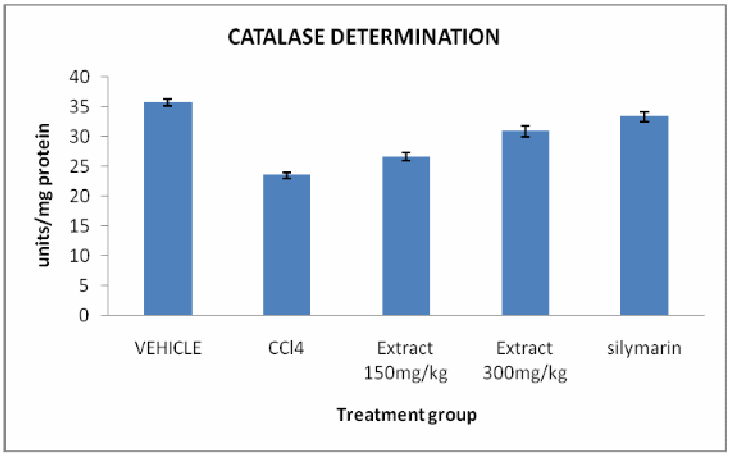
Graph no. 16



In case of GSH level in vehicle group was found to .623±.184 that the ccl4 group was .165±.112 which significant as compared to vehicle treared group. The extract of 150mg/kg was

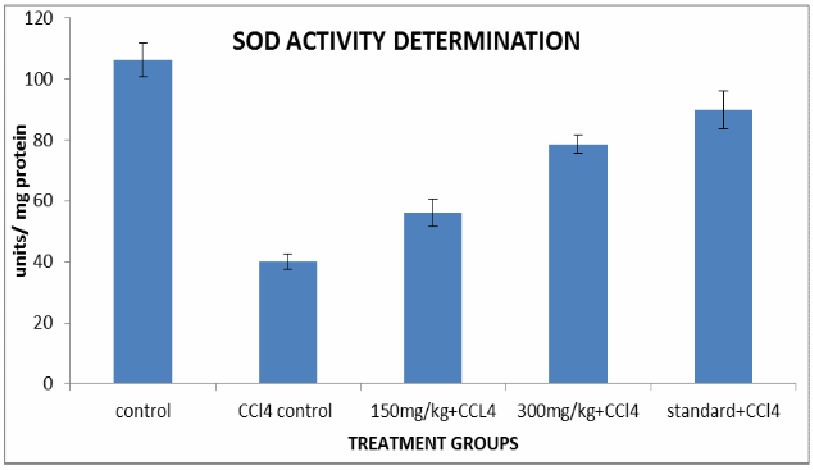
.27±.024 ,nonsignificant protection against ccl4 induced hepatotoxicity and significant increases as compared to vehicle. Extract 300mg/kg was .398±.062 significant protection against ccl4 induced toxicity and significant as compared to vehicle group and the silymarin was found to .518±.096 it produce significant protection against ccl4 induced toxicity nonsignificant as compared to vehicle.

Graph no. 17



In case of catalase which was found to 35.65±1.126 that the ccl4 group 23.49±.97 which was significant as compared to vehicle group and extract of 150 mg/kg and extract 300mg/kg was 26.54±1.396 and 30.831±1.906 significant protection against ccl4 induced toxicity and significamt increase as compared to vehicle group.silymarin was 33.312±1.642 significant against ccl4 group and nonsignificant as compared to vehicle group.

Graph no. 18



In case of SOD level ,vehicle group was found 106.23±10.86 that the ccl4 group was 39.98±5.18 which was significant as comoared to vehicle.and extract of 150 mg/kg and 300 mg/kg was 56.21±9.10 and 78.63±6.22 significant protection against ccl4 induced toxicity and significant increase as compared to vehicle. Silymarin was also significant as vehicle and ccl4 group.

DISCUSSION

Liver plays an important role in metabolism of drug and nutrients. Because of its central role in drug metabolism, it is the most vulnerable tissue for drug toxicity. According to the reports published by USFDA, more than 900 drugs, toxins, and herbs have been reported to cause liver injury, and drugs account for 20-40% of all instances of hepatic failure. Approximately 75% of the idiosyncratic drug reactions result in liver transplantation or death. Drug-induced hepatic injury is the most common reason cited for withdrawal of an approved drug. Physicians must be vigilant in identifying drug-related liver injury because early detection can decrease the severity of hepatotoxicity if the drug is discontinued. The manifestations of drug-induced hepatotoxicity are highly variable, ranging from asymptomatic elevation of liver enzymes to fulminant hepatic failure. Knowledge of the commonly implicated agents and a high index of suspicion are essential in diagnosis.

The cytochrome P-450 enzymes catalyze phase 1 reactions. Most of these intermediate products are transient and highly reactive. These reactions may result in the formation of metabolites that are far more toxic than the parent substrate and may result in liver injury. As an example, the metabolite of acetaminophen is *N* -acetyl-p-benzoquinone-imine (NAPQI) and is produced with ingestion of high doses. NAPQI is responsible for the liver injury in cases of toxicity. Cytochrome P-450 enzymes are hemoproteins located in the smooth endoplasmic reticulum of the liver. At least 50 enzymes have been identified, and based on structure, they are categorized into 10 groups, with groups 1, 2, and 3 being the most important in drug metabolism. Each P-450 enzyme can metabolize many drugs. Drugs that share the same P-450 specificity for biotransformation may competitively inhibit each other, resulting in drug interactions. Several drugs can induce and inhibit the P-450 enzyme.

Phase 2 reactions may occur within or outside the liver. They involve conjugation with a moiety (ie, acetate, amino acid, sulfate, glutathione, glucuronic acid) that further increases solubility. Subsequently, drugs with high molecular weight may be excreted in bile, while the kidneys excrete the smaller molecules. Drugs that induce and inhibit the P-450 enzymes are phenobarbital, phenytoin, carbamazepine primidone, ethanol, glucocorticoids, rifampin, griseofulvin, quinine, omeprazole, etc.

Paracetamol toxicity is caused by excessive use or overdose of the analgesic drug paracetamol. Mainly causing liver injury, paracetamol toxicity is one of the most common causes of poisoning worldwide. It is the most common cause of acute liver failure. With progressive disease, signs of liver failure may develop; these include low blood sugar, low blood pH, easy bleeding, and hepatic encephalopathy. Some will spontaneously resolve, although untreated cases may result in death.

Damage to the liver, or hepatotoxicity, results not from paracetamol (PCM) itself, but from one of its metabolites, *N*-acetyl-*p*-benzoquinoneimine (NAPQI). NAPQI depletes the liver's natural antioxidant glutathione and directly damages cells in the liver, leading to liver failure. Risk factors for toxicity include excessive chronic alcohol intake, fasting or anorexia nervosa, and the use of certain drugs such as isoniazid.

Paracetamol, an analgesic and antipyretic, is assumed to be safe in recommended doses; overdoses, however, produce hepatic necrosis. Small doses are eliminated by conjugation followed by excretion, but when the conjugation enzymes are saturated, the drug is diverted to an alternative metabolic pathway, resulting in the formation of a hydroxylamine derivative by cytochrome P-450 enzyme. The hydroxylamine derivative, a reactive electrophillic agent, reacts non-enzymatically with glutathione and detoxifies. When the hepatic reserves of glutathione depletes, the

hydroxylamine reacts with macromolecules and disrupts their structure and function. Extensive liver damage by paracetamol itself decreases its rate of metabolism and other substrates for hepatic microsomal enzymes. Induction of cytochrome P-450 or depletion of hepatic glutathione is a prerequisite for paracetamol-induced Toxicity. [11] The ethanol extract of *Prunus domestica* reduced the elevated levels of all the biochemical parameters by paracetamol and CCl_4. Paracetamol-induced liver necrosis was inhibited significantly by *prunus domestica* extract, which confirms the protective action of the methanolic:acetonic (7:3) extract of P*runus domestica* against experimentally induced liver damage in rats. SGOT SGPT, ALP, TBL, DBL,LPO GSH,Catalase AND SOD are the most sensitive tests employed in the diagnosis of hepatic disease. The elevated levels of these parameters were significantly reduced by the treatment of *Prunus domestica* extract. It can be concluded from this investigation that fruits of *Prunus domestica* possess hepatoprotective activity. It is well documented that the compounds quercetin, rutin, Vitamins C and E are strong antioxidants.

Decrease the level of SGOT SGPT ALP and BILIRUBIN after treatment with extract in liver damage indicates the affectiveness of the extract in normal functional status of the liver.

Various environmental toxicants and clinically useful drugs, like acetaminophen and gentamicin, can cause severe organ toxicities through the metabolic activation to highly reactive free radicals including the superoxides and oxygen reactive species [12]. One of the most extensively studied of the environmental toxicants is carbon tetrachloride (CCl_4). CCl_4 is known to undergo reductive metabolism by CYP2E1 into a highly reactive trichloromethyl radical (.CCl_3) and phosgene that initiates lipid peroxidation, disrupts membrane integrity and causes cell death [13, 14, 15]. Evidence suggests that various enzymatic and non-enzymatic systems have been developed by the cell to cope with the oxidative stress that is associated with reactive oxygen species (ROS) and other free radicals generated.

This effect may be due to the presence of polyphenols and other antioxidants in the extract, as the toxicity produced by Paracetamol and CCl_4 is due to oxidative stress.

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