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Research Article

Evaluation of Hepatoprotective Effect of *Pistacia lentiscus L*. Fatty Oil in Rats Intoxicated by Carbon Tetrachloride.

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ABSTRACT
The aim of the present study was the evaluation of hepatoprotective effect of *Pistacia lentiscus* fatty oil in rats intoxicated by carbon tetrachloride (CCL4). The study was conducted on 24 Wistar rats divided randomly to 4 groups. The first served as negative control (normal or CRL), the second intoxicated with CCl4 (CCl4 group), the 2 other groups were intoxicated by CCL4 and treated orally by 2ml/kg or 5ml/kg of PLFO (PLFO1 and PLFO2 groups). The results showed a significant elevation of ALT and AST enzymes in CCl4 group. PLFO2 recorded an aggravation of transaminases when compared to CCl4. However, PLFO1 has shown a significant decrease of AST with comparison to CCl4.
We conclude that the use of PLFO to prevent hepatotoxicity has resulted in a partial activity by decreasing significantly ALT enzyme with the dose of 2ml/kg. However, the dose of 5ml/kg was found to aggravate the hepatic alterations by increasing significantly both of ALT and AST enzymes.

Keywords: Hepatoprotective effect, Pistacia lentiscus L., CCl4, rats.

INTRODUCTION

Although several synthetic medicines are recommended for liver therapy but most of them are immunosuppressive[1]. Facing this problem, studies have focused medicinal plants in the hope to look for novel molecules most effective with low adverse effects. *Pistacia lentiscus* fatty oil is a vegetable oil extracted from fruits of this plant belonging to Anacardiacae family. It is a well known traditional remedy in east of Algeria. In previous studies, we have evaluated scientifically some pharmacological and toxicological properties of this oil. This vegetable oil has shown a healing property in dermal burns[2-4], anti hypercholesterolemic effect[5], some toxicological studies were also undertaken[6,7]. The present study was carried out to assess hypatoprotective effect of *P. lentiscus* vegetable oil against carbon tetrachloride induced toxicity.

MATERIALS AND METHODS

The study was carried out in Pharmaco-toxicology laboratory, Institute of Veterinary Sciences, University of Constantine1, Algeria.

Animals and housing conditions

The experimental animals were male Wistar rats weighing between 240 - 260g from the animal husbandry of the University Constantine 1. The rats were randomly divided into 4 groups of 6 each, and were kept in standard cages for acclimation period (two weeks) before being used in the different experiments. During this period the animals have free access to food and water and were kept at a constant temperature (22 ± 2) °C with a 12/12h light/dark cycle.

Tested drugs

Fruits of *Pistacia lentiscus L.* were collected in the region of El Milia (North of Algeria) and the oil was extracted by a traditionnal method and was conserved until use.

CCl4: Chemical products were obtained from Faculty of Natural Sciences and Life of the above cited university.

Experimental protocol

The rats were divided into four groups of six rats each and were kept in the same conditions.

Group I: healthy control (CRL), which receives orally 2 ml of distilled water for 15 consecutive days.

Group II or PLFO1 group: These rats received daily 2ml/Kg of *P. lentiscus L.* vegetable oil (PLFO) and carbon tetrachloride (CCl4) every 3 days at a dose of 1.5ml/Kg for 15 days via oral route.

Group III or PLFO2 group: These animals received daily oral dose of 5ml/kg of PLFO and CCl4 every 3 days at a dose of 1.5ml/Kg for 15 days.

Group IV or groupe CCl4: These rats were gaved every 3 days by CCl4 at a dose of 1.5ml/Kg for 15 days.

The administration of CCl4 was performed 60 min after oral gavage of rats with PLFO. Treated groups were gaved using a stomach tube.

Clinical changes and body weight

The rats were evaluated clinically, the first day every 60 minutes during the first 8 hours, and every day once at the same time for a period of 15 days. During the observation period, the deaths and symptomatology disorders were

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Table 1: Evolution of body weights of rats of different groups.

Animal groups	Body weights in g (Mean±SD)*		
	I	II	III
PLFO1	239.528±28.194	250.996±26.606	274.177±17.381
PLFO2	235.996±20.036	234.14±55.440	259.256±22.546
CCL4	255.47±29.570	273.45±31.910	276.3±33.714
Normal control (CRL)	254.248±33.717	261.285±47.369	316.622±48.218

*No significant changes.

Table 2: Biochemical parameters of rats of different groups.

	ALT (IU/L)		AST (IU/L)		GLU (g/L)		CREA (mg/L)		UREA (mg/L)		Uric acid (mg/L)	
Groups	M N	Var	MN	Var	MN	Var	MN	Var	MN	Var	MN	Var
CRL	45.25	10.91	150.75	7.56	0.94	0.013	6.25	10.92	0.32	0.0092	16.8	140.7
CCl4	93.40	5.85	178.6	8.58	1.05	0.303	6.4	3.80	0.174	0.0024	8.83	17.77
PLFO 1	91.25	0.96	150	9.20	1.5	0.192	4.5	3.00	0.178	0.0015	10.20	45.20
PLFO 2	108	27.20	236	2.00	1.02 6	0.146	5.5	3.7	1.04	2.057	10.25	65.58
CRL versus CCl4		S		S		NS		NS		NS		NS
CCl4versus PLFO1		NS		S		NS		NS		NS		NS
CCl4 versus PLFO2		S		S		NS		NS		NS		NS
PLFO1versusPLFO2		S		S		NS		NS		NS		NS

MN : Mean, MN : Moyenne ; Var : variance ; S :significant $p<0.05$; NS : non significant $p>0.05$.

noted. The evolution of weight in rats of different experimental groups was investigated each 7 days throughout the experimental period.

Biochemical analysis

Rats of control group and treated animals that survived until 15th day were anesthetized on the 16th day with ether and blood samples were collected by cardiac puncture into sterile heparin tubes and centrifuged at 3000 rpm for 10 min to collect serum in sterile tubes. The biochemical analysis was performed at the Laboratory of Biochemistry, Ain Smara Polyclinic, Constantine. The parameters tested were : ALT, AST, creatinine, urea , uric acid and glucose.

Statistical Analysis

The results were statistically analyzed using one-way ANOVA to identify differences between treated groups and controls. Data were considered significant at $p < 0.05$.

RESULTS

During the experimental period, no mortality was observed in rats that were available for evaluation.

Clinical changes and body weight

All animals in the experimental groups (PLFO1, PLFO2, and CCl4, control group (CRL) were clinically normal during the experimental period, despite some common clinical signs such as anorexia, hypoactivity, which are reversible and appeared in rats for a short period. Daily administration of PLFO at different doses and CCl4 did not disturb the body changes in rats (Table 1). Weight gain obtained after 15 days was 34.64 ± 10.82 g / rat in PLFO1 group, it was 23.26 ± 2.51g/rat in PLFO2 group, it was 20.83 ± 4.14 in the CCl4 group and 62,374 ± 14.50g/rat for control rats.

Biochemical analysis

The effects of vegetable oil of *Pistacia lentiscus L*. on liver enzymes (ALT and AST) in CCl4 intoxicated rats are summarized in table 2. The results showed a significant increase in ALT and AST in groups of rats intoxicated by CCl4 compared to control group rats (CRL). The treatment of rats with this vegetable oil at a dose of 2ml/Kg (PLFO1) showed a non-significant decrease in ALT, but a significant decrease in AST compared to the control group and intoxicated rats by CCl4. However, the rats treated by vegetable oil at a dose of 5ml/kg (PLFO2) showed a significant increase ($p < 0.05$) of the two liver enzymes (ALT and AST) compared to control group and also the rats intoxicated with CCl4. In addition, PLFO2 group showed a significant increase in transaminases compared to animals treated with a dose of 2ml/Kg (PLFO1 group). The treatment of rats with oil at the dose of 5ml/kg (PLFO2) showed no hepato-protective effect as evidenced by elevated liver parameters. The results showed also no significant changes in blood glucose and indicators of kidney (Creatinine, urea and uric acid).

DISCUSSION

The liver is a vital organ that plays a major role in the metabolism of xenobiotics in the body. Liver damage or liver dysfunction is a major health problem that concerns not only health professionals but also the pharmaceutical industry and drug regulator[8]. Biochemical changes are complex, hepato-toxicants act by different mechanisms. Carbon tetrachloride (CCl4) is the most used to induce experimental hepato-toxicity[9] because it induces pathological conditions encountered in clinical: lesions of steatosis, hepatocyte necrosis and even cirrhosis[10]. In body, CCl4 converts in microsomes (oxidation by

cytochrome P 450) in CCl 3; a trichloromethyl radical which binds covalently with protein and unsaturated lipids and induces lipid peroxidation followed by a series of biochemical disturbances such triglyceride accumulation due to blockage in the synthesis of the lipoprotein, polyribosomiale disintegration, depression of protein synthesis, high levels of serum markers enzymes (ALT, AST and ALP), glutathione depletion, increased lipid oxidation, membrane breakdown and cell death[11]. Cell membranes rich in unsaturated fats are very sensitive to these alterations that may be the cause of their failure, which will result in the presence in the serum of many enzymes released from the cytosol and subcellular organelles (mitochondria, lysosomes, nuclei) after liver injury. This hepatocellular damage with the subsequent distruption of the plasma membrane allows leakage of intracellular enzymes such as ALT and AST into the bloodstream [12].

Hepato protective ability of a drug to reduce the injurious effects or to preserve the normal hepato- physiological mechanism that has been disrupted by a hepatic toxin is the index of its protective effects. The estimation of enzymes (ALT and AST) as serum markers may make an assessment of liver function. In our study, there was a significant increase of ALT and AST in rats intoxicated with CCl4 compared with those of normal group. Treatment with vegetable oil of *Pistacia lentiscus* L. showed a significant increase in AST and ALT in the PLFO2 group compared to PLFO1 group. A non significant decrease in ALT, but a significant decrease of AST were recorded in PLFO1 (dose of 2ml/kg) when compared to CCL4 group. For ALT, the comparative results showed a significant increase in PLFO2 in comparison with CCl4 group and also a significant increase in PLFO2 as compared to PLFO1. In contrast, the results showed a decrease but not significant in PLFO1 compared to CCl4 group. The dose of 2ml/kg of oil has restored levels of AST near normal range in PLFO1 group. But the dose of 5ml/kg of oil (PLFO2) has caused aggravation and therefore damage to the liver. The parallel increase in AST and ALT reflects the extent of hepatic cytolysis in infectious viral or toxic hepatitis, cirrhosis and cholestasis syndrome. In our study, the dose of 2ml/kg may be suggested to help in preventing hepatotoxicity at least by decreasing ASP. In a study of Janakat et al. (2002)[13], the unboild aqueous extract of *Pistacia lentiscus* L. flowers has proved an anti-hepatotoxic activity, by reducing significantly the four parameters (ALT, AST, ALP and bilirubin).

CONCLUSION

In conclusion, the use of *Pistacia lentiscus* fatty oil to prevent hepatotoxicity has resulted in a partial activity by decreasing significantly AST enzyme with the dose of 2ml/kg. However, the dose of 5ml/kg was found to aggravate the hepatic alterations by increasing significantly both of ALT and AST enzymes.

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