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Hepatoprotective Effect of *Opuntia Ficus-Indica* Aqueous Extract against Carbon Tetrachloride-Induced Toxicity in Rats

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Abstract: The present study was undertaken to evaluate the hepatoprotective activity of *Opuntia ficus-indica*L. aqueous extract. About 24 Wistar male rats were divided randomly to 4 groups of 6 each. The 1st was given distilled water and served as normal control (CRL). The 2nd was intoxicated orally with carbon tetrachloride at a dose of 1.5 mL/kg each 72 h (CCl4 group) for a period of 15 days. 2 other groups were intoxicated as CCl4 group and treated once daily by aqueous extract of *Opuntiaficus-indica L.* at doses of 2 mL/kg or 5 mL/kg respectively (OFI1 and OFI2 groups). The results showed a significant elevation of Aspartate Amino Transferase (AST) (ANOVA, $p<0.001$) and Alanine Amino Transferase (ALT) (ANOVA, $p<0.05$) in CCl4 group compared to control. Treatment of rats with cactus aqueous extract at 2 mL/kg has resulted in significant reduction of AST (ANOVA, $p<0.001$) compared to CCl4 group. In OFI2 group, AST and ALT were increased but non significantly compared to CCl4 group. The other tested parameters (Urea, creatinine and uric acid) have not recordered significant changes between all groups. The study concluded that *Opuntiaficus-indica* L. aqueous extract may exert hepatoprotective effect at 2 mL/kg against CCl4-induced toxicity at least by decreasing AST enzyme activity.

Keywords: *Opuntiaficus-Indica* L., Aqueous Extract, CCl4, Hepatoprotective Effect

Introduction

Liver is the vital organ of metabolism and excretion. About 20000 deaths found every year were due to liver disorders. In addition, hepatocellular carcinoma is one of the ten most common tumors in the world with over 250000 new cases each year (Gupta and Misra, 2006). In spite of tremendous strides in modern medicine, there are hardly any drugs that stimulate liver function, offering protection to the liver from damage and helping regeneration of hepatic cells (Goyal and Sharma, 2012). Consecutively, several scientific studies have focused medicinal plants used in the different traditional systems, in the hope to find more potent drugs with minimum adverse effects.

Opuntia ficus-indica L. is a tropical or subtropical plant belonging to the Cactaceae family and is mainly used for fruit production (De Cortázar and Nobel, 1992). It can be used also as a vegetable forage resource for livestock feed in arid and semiarid lands during periods of drought and shortage of herbaceous plants (Felker *et al*., 2006). In the majority of scientific medicinal researches involves the leaves (cladodes) rather than the fruit (El-Kossori *et al*., 1998). The cladodes are utilized, in traditional medicine, for the management of ulcers, wounds, rheumatic pain and fatigue. Experimental studies showed that cactus pear could reduce glucose and cholesterol levels in human blood (Frati *et al*., 1990; Stintzing *et al*., 2001). Chemopreventive effect on oxidative stress and genotoxicity was also recently investigated (Brahmi *et al*., 2011a). The chemical composition of cactus cladodes has been investigated in various studies. It is characterized by a high value of water (85-92%), 4-6% of carbohydrates, 1% proteins, 0.2% fats, minerals (1%), vitamin C (12.7 mg/100 g) and ß-carotene

(12.9 µg/100 g) (El-Kossori *et al*., 1998; Rodriguez-Felix and Cantwell, 1988).

The aim of the present study is to evaluate the possible hepatoprotective effect of aqueous extract from cactus cladodes against carbon tetrachloride.

Materials and Methods

Animals

The study was conducted on 24 male Wistar rats (180-230 g weight). The animals were randomly divided on 4 groups of 6 each and were kept in standard cages for an acclimation period of 15 days with laboratory conditions. Food and water were provided *adlibitum* and a temperature of 22±2°C with a 12/12 h light/dark cycle were maintained.

Tested Drugs

Cladodes of *Opuntia ficus-indica* were collected in the region of Tamalous (East of Algeria) and the aqueous extract was prepared each 4 days.

CCl4 and ether were obtained from Faculty of Natural Sciences and Life of Constantine University.

Experimental Protocol

Four groups were formed, one control and 3 experimental lots, as follows:

- Group I: Normal control (CRL), received 2 mL of distilled water orally for 15 consecutive days
- Group II or CCl4: These rats were gaved every 3 days by CCl4 at a dose of 1.5 mL/kg for 15 days
- Group III or OFI1: These rats received daily 2 mL/kg of *Opuntia ficus-indica* aqueous extract and carbon tetrachloride (CCl4) every 3 days at a dose of 1.5 mL/kg for 15 days via oral route
- Group IV or OFI2: These animals received daily oral dose of 5 mL/kg of *Opuntia ficus-indica* aqueous extract and CCl4 every 3 days at a dose of 1.5 mL/kg for 15 days

The administration of CCl4 was performed 60 min after oral gavage of rats with the aqueous extract of *Opuntia ficus-indica*. All animals were given using a stomach tube. The experimental procedures involving the handling and treatment of animals were approved by the ethical committee of the institute of veterinary sciences, University of Constantine 1, Algeria.

Biochemical Analysis

All survived rats until 15th day were anesthetized on the following day with ether and blood samples were collected by cardiac puncture into heparinized tubes and centrifuged at 3000 rpm for 10 min to collect sera. The biochemical analysis was performed in Biochemistry Laboratory (Polyclinic of Ain Smara, Constantine) including: ALT, AST, creatinine, urea and uric acid.

Statistical Analysis

All results were expressed as mean with variance. Data were analyzed using one-way ANOVA. The differences between groups were considered significant at $p<0.05$.

Results

The results recorded in Table 1 and Figs. 1 and 2 showed a significant elevation of ALT ($p<0.05$) and AST ($p<0.001$) enzymes in Group II due to CCl4 application compared with normal animals with no alliteration of other measured parameters. The administration of *Opuntia ficus-indica* at a dose of 2 mL/kg has resulted in a significant reduction of AST ($p<0.001$) in OFI1 group when compared to CCl4 group with no significant impact on the other tested parameters Figs. 3-5. However, the application of the aqueous extract at a dose of 5 mL/kg has accentuated the elevation of AST and ALT but nonsignificantly in the OFI2 group compared to CCl4 group.

Table 1. Biochemical parameters of the different rat groups

	AST (IU/L)		ALT (IU/L)		Urea (mg/L)		Creatinin (mg/L)		Uric Acid (mg/L)	
	Mn	Var.	Mn	Var.	Mn	Var.	Mn	Var.	Mn	Var.
CRL	74.0	28.00	45.66	12.33	0.25	0.0004	6.25	10.91	16.66	25.33
CCl4	250.33	960.33	59.33	32.33	0.19	0.0015	6.40	3.80	10.20	8.20
OFI1	116.00	15.33	60.50	387.00	0.20	0.0004	5.50	3.60	14.25	231.58
OFI2	187.25	1294.25	144.00	12474.60	0.20	0.0026	5.50	3.00	22.00	247.30
Statistical data										
CCl4 Vs CRL	$p<0.001$		$p<0.05$		NS		NS		NS	
OFI1 Vs CCl4	$p<0.001$		NS		NS		NS		NS	
OFI2 Vs CCl4	NS		NS		NS		NS		NS	
OFI1 Vs OFI2	NS		NS		NS		NS		NS	

Mn: Mean, Var.: Variance; NS: Nonsignificant ($p>0.05$)

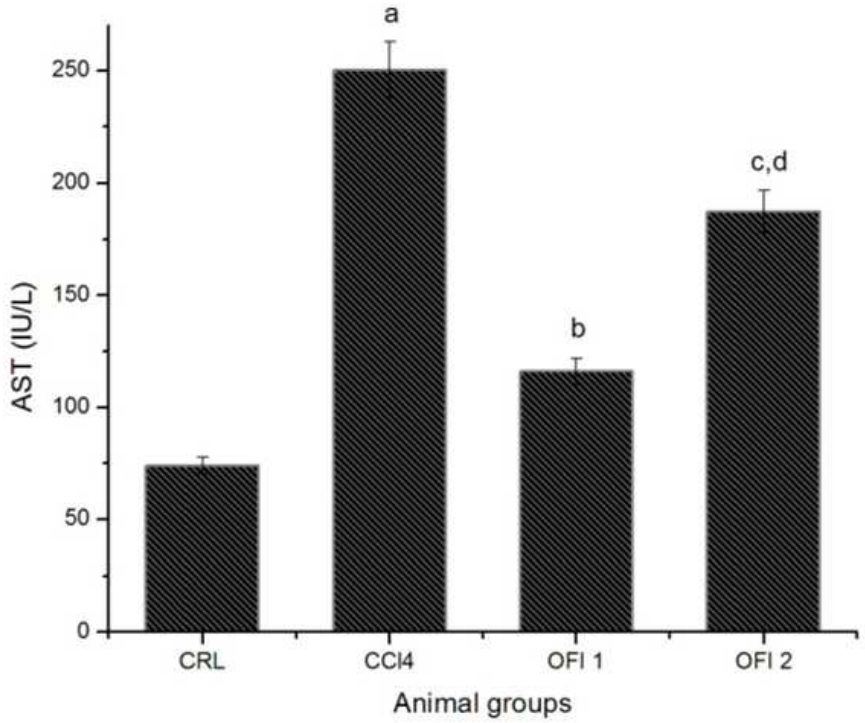

Fig. 1. AST variations in the different rat groups. CRL: normal control, CCl4: Carbontetrachloride intoxicated group, OFI1: *Opuntia Ficus-Indica* treated rats (2 mL/kg), OFI2: *Opuntia ficus-indica* treated rats (5 mL/kg), NS: nonsignificant, a: CCl4 Vs CRL ($p<0.001$), b: OFI1 Vs CCl4 ($p<0.001$), c: OFI2 Vs CCl4 (NS), d: OFI1 Vs OFI2 (NS)

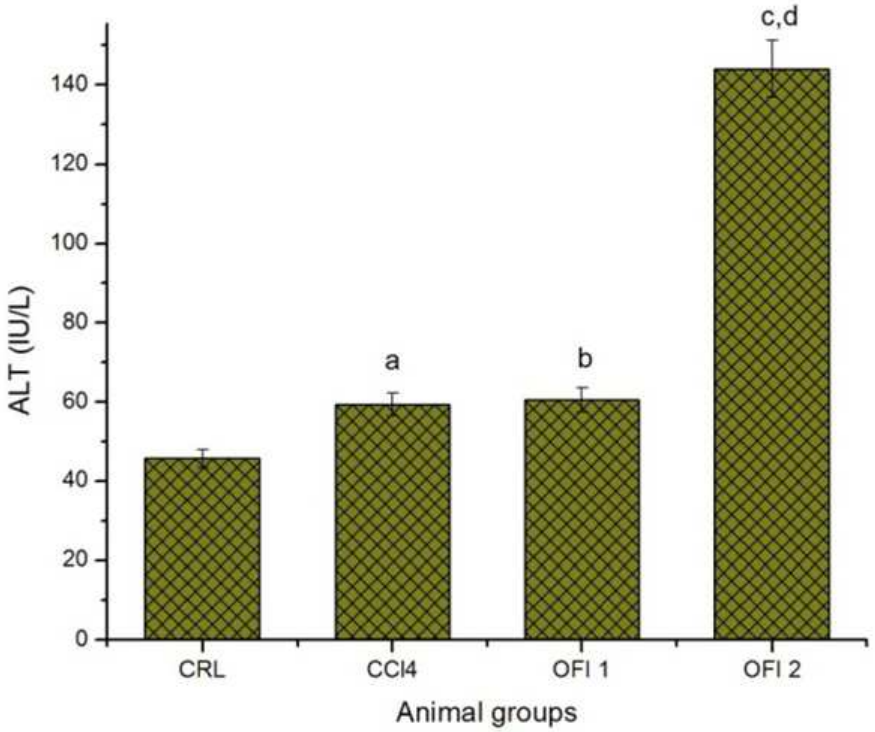

Fig. 2. ALT variations in the different rat groups. CRL: Normal control, CCl4: Carbontetrachloride intoxicated group, OFI1: *Opuntia ficus-indica* treated rats (2 mL/kg), OFI2: *Opuntia ficus-indica* treated rats (5 mL/kg), NS: Nonsignificant, a: CCl4 Vs CRL ($p<0.05$), b: OFI1 Vs CCl4 (NS), c: OFI2 Vs CCl4 (NS), d: OFI1 Vs OFI2 (NS)

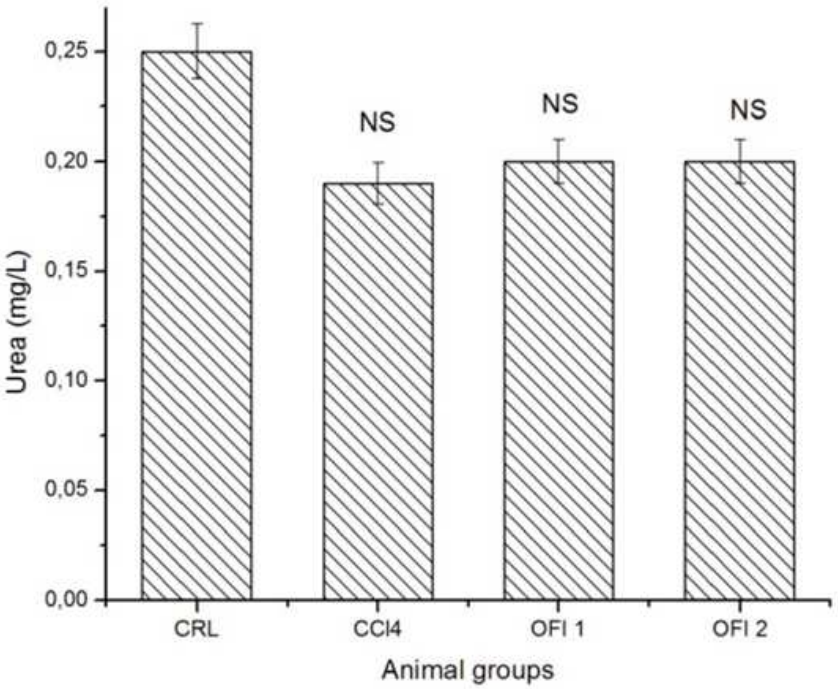

Fig. 3. Values of urea in the control and treated groups. CRL: Normal control, CCl4: Carbontetrachloride intoxicated group, OFI1: *Opuntia ficus-indica* treated rats (2 mL/kg), OFI2: *Opuntia ficus-indica* treated rats (5 mL/kg), NS: Nonsignificant difference between all groups

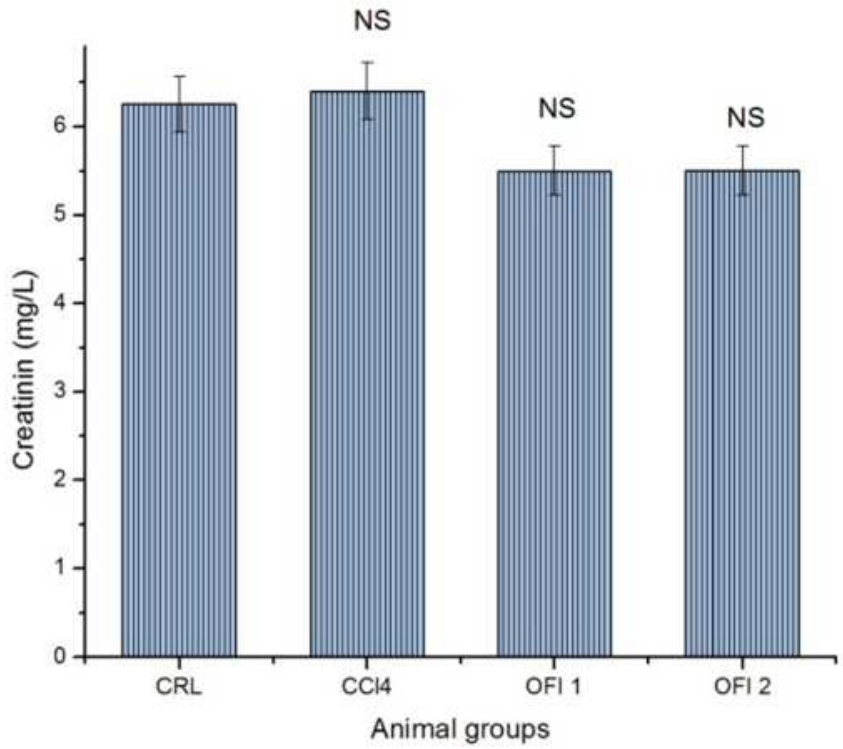

Fig. 4. Values of creatinine in the control and treated groups. CRL: Normal control, CCl4: Carbontetrachloride intoxicated group, OFI1: *Opuntia ficus-indica* treated rats (2 mL/kg), OFI2: *Opuntia ficus-indica* treated rats (5 mL/kg), NS: Nonsignificant difference between all groups

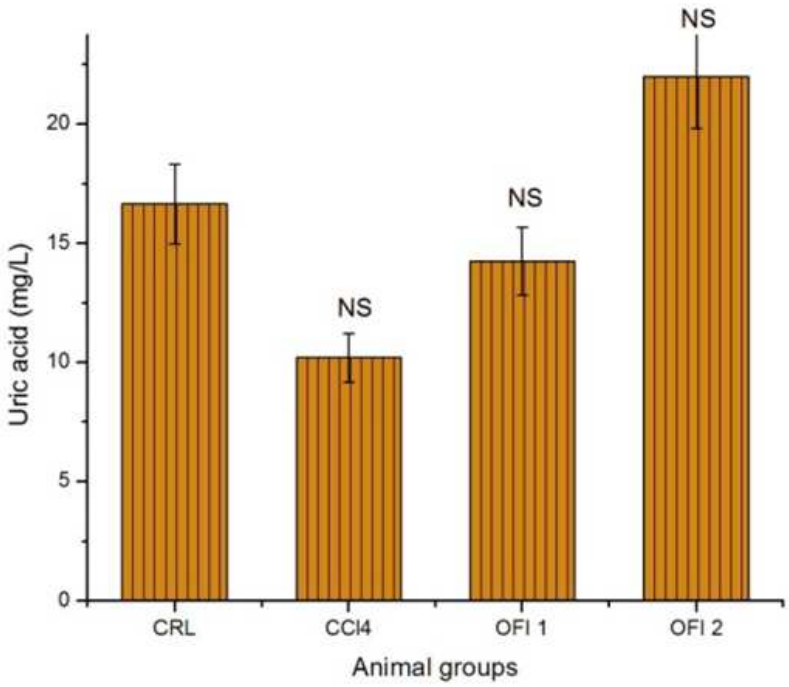

Fig. 5. Values of uric acid in the control and treated groups. CRL: Normal control, CCl4: Carbontetrachloride intoxicated group, OFI1: *Opuntia Ficus-Indica* treated rats (2 mL/kg), OFI2: *Opuntia ficus-indica* treated rats (5 mL/kg), NS: Nonsignificant difference between all groups

Discussion

Carbon tetrachloride is a well documented hepatotoxic drug used to induce hepatic cirrhosis model for scientific research (Gutiérrez and Solís, 2009; Karandikar *et al*., 1963; Recknagel, 1983). In the present study, we have applied this toxic product via oral route each 3 days for a period of 15 days to ovoid a high rate of mortality. A study of Jang *et al*. (2008) has compared some experimental protocols to induce liver cirrhosis in mice and rats via intra peritoneal and oral routes using 3 hepatotoxic products. They have shown that livers from animals administered CCl4 orally twice a week for 10 weeks was the most effective to achieve sufficient fibrosis and greatest reproducibility with acceptable animal survival.

In the present study, the dose of 2 mL/kg of cactus aqueous extract has shown a hepatoprotective effect in term of AST decrease. However, the dose of 5 mL/kg has accentuated the hepatic lesions which suggest that this dose is very high and may be toxic for tested animals. In a review of Feugang *et al*. (2006), were investigated the phytochemical composition and the medicinal uses of cactus. This vegetable has shown anti cancer, anti viral, anti diabetic (type 2 diabetes), anti hyperlipidemic and anti hypercholesterolemic effects, anti oxidant properties, anti-inflammatory activity and hepatoproptective effect against CCl4-induced hepato-toxicity in rats. In a study of Brahmi *et al*. (2011b) conducted on mice, cactus cladode extract has proven effective activity in the protection against benzo (α) pyrene which is a widespread environmental genotoxin classified as probably carcinogenic in human inducing liver injury. A double-lind, placebo controlled, crossover trial of Wiese *et al*. (2004), conducted on 64 healthy volunteers, has concluded that *Opuntia ficus-indica* extract has a moderate effect reducing hangover symptoms, apparently by inhibiting the production of inflammatory mediators. Finally, a study of Ncibi *et al*. (2008) has shown that cactus stem extract protects the liver and decrease the toxicity induced by chlorpyrifos (organophosphorous pesticide).

Conclusion

In view of the present results, it may be concluded that *Opuntia ficus-indica* aqueous extract at a dose of 2 mL/kg exerted a hepatoprotective effect against carbon tetrachloride-induced toxicity in rats at least by decreasing AST activity.

Acknowledgment

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Author's Contributions

Zouhir Djerrou: Designed the research plan and organized the study, participated in all experiments, coordinated the data-analysis and has drafted the article.

Zineb Maameri: Participated in all experiments and data analysis.

Sihem Halmi: Participated in all experiments and acquisition of data.

Hadria Djaalab and Foulla Riachi: Participated in all experiments.

Loubna Benmaiza: Participated in data analysis.

Youcef Hamdipacha: Participated in analysis and interpretation of data.

Conflict of Interest

The authors have no conflict of interest to declare.

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