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Ameliorative effect of *Urtica dioica* root extract on CdCl₂- induced hepatotoxicity in rats

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Abstract

Different parts of *Urtica dioica* are known for its antioxidant compounds having various applications in the health and nutritional products. The aim of this study was to elucidate the antioxidant properties of dried root extracts against CdCl₂ induced acute liver damage by monitoring the hepatic biochemical markers at dose 250 mg/kg/day for 4 days and were subsequently exposed to a single dose Cd (4 mg/kg) intraperitoneally (i.p.) 12 hours after the last extract/ vehicle treatment.

CdCl₂ induced hepatotoxicity was evident from the increased activities of serum hepatic marker enzymes and total bilirubin along with reduction in total protein and albumin levels. Administration of *Urtica dioica* root extract at dose 250 mg/kg daily significantly reversed the enzyme activities and total bilirubin to their near normal and T. protein and albumin were increased significantly back to normal.

Keywords: Cadmium, *Urtica dioica* extract, Hepatic markers, antioxidant

1. Introduction

Many plant derived natural products have the potential to be hepatoprotective against various toxic chemicals and drugs; therefore they can be used to treat acute and chronic liver disease. The challenge is to identify the most promising compounds and evaluate their protective mechanism^[1].

Urtica dioica L. belongs to the family Urticaceae which is an annual herb growing in Europe, Asia, northern Africa, and western North America and often called (common nettle, stinging nettle). *Urtica dioica* L. has medicinal properties and its extract have been used for hundreds of years in world traditional medicine for treating diseases such as eczema, digestion and sexual disorders, joints pain and anemia^[2]. Also, it is used to treat disorders of the kidneys and urinary tract^[3], gastrointestinal tract, skin, cardiovascular system^[4], hemorrhage, bronchitis, rheumatism, gout^[5, 6], and some of autoimmune diseases^[7]. From current pharmaceutical studies, additional pharmaceutical applications of *U. dioica* have revealed antioxidant, hepatoprotective^[8, 9], anti-inflammatory, antiulcer^[10], antiviral^[11], anticancer^[12], and antibacterial, antifungal^[13, 2].

Different parts of *U. dioica* plant are known to be rich in many phytochemical compounds such as flavonoids, tanins, volatile compounds and phytosterols which found to possess wide pharmacological actions especially potent free radical scavenging^[14, 11]. Three smooth-muscle stimulating substances including acetylcholine, histamine, and 5-hydroxytryptamine (5-HT) have been identified in *U. dioica*^[15]. Carvacrol (38.2%), carvone (9.0%), naphthalene (8.9%), (E)-anethol (4.7%), hexahydrofarnesyl acetone (3.0%), (E)-geranyl acetone (2.9%), (E)-β-ionone (2.8%) and phytol (2.7%) are characterized as the main components of *U. dioica* essential oil^[14]. Rhizomes of *U. dioica* contain other biological active compounds such as scopoletin, sterols, fatty acids, polysaccharides and isolectins^[11].

Cadmium is one of the most dangerous occupational and environmental toxins. It is found in drinking water, atmospheric air and even in food. Cadmium is reported to be very toxic to biological systems^[16]. The liver, kidney and heart are the most important target organs when considering Cd-induced toxicity because this heavy metal accumulates in these organs. For this reason many researches are carried out to find natural compounds that help in the protection against Cd-induced toxicity with fewer or no side effects^[17, 18].

The objective of present study is designed to evaluate the hepatoprotective activity of dried root extract of *Urtica dioica* against toxicity induced by cadmium chloride (CdCl₂).

2. Materials and Methods

2.1 Preparation of plant root extracts

Dried root of *Urtica dioica* was obtained from herbal store-Amman. The sample of the plant specimen was identified by a Botanist from Biological Sciences, University of Jordan/Amman.

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The dried roots were ground into fine powder using an electric dry mill. A total of 100 g of the ground powder was soaked in 500 ml of distilled water for 24 hours at 40 °C. The mixture was filtered with watman filter paper No.1. The filtrate was dried at temperature 40 °C. The yield of *Urtica dioica* was around 20%.

Appropriate concentration of the extract was then subsequently made by dilution with distilled water into 250 mg/kg body weight and administered to the animals. The 250 mg/kg extract was more effective than 500 mg/kg in hepatic function which was well comparable with standard drug silymarin (25 mg/kg).

2.2 Animal Models

A total of 18 healthy adult male albino rats weighing between (160-180 g) obtained from the animal house- University of Applied Sciences- Amman were used. The animals were maintained under standard conditions of humidity 50%, temperature (25 ± 1 °C) with a 12 h light/12 h dark cycle. All rats were allowed free access to food and water *ad libitum*. The animals were divided randomly into three groups of six rats each as follows:

- **Group I:** Served as olive oil treated vehicle with saline-control
- **Group II:** Rats were administered CdCl₂ 4 mg/kg body weight in normal saline subcutaneously to induce acute liver injury.
- **Group III:** Rats were treated with 250 mg/kg body weight of *Urtica dioica* extract for four days and subsequently exposed to a single injection of CdCl₂ 12 hour after the last (*U. dioica* extract /vehicle) treatment.

All experimental animals were handled according to the guidelines of the institutions animal ethical committee. All

chemicals used were of analytical grade, purchased locally.

2.3 Blood Collection

At the end of the experimental period, animals were subjected to ether anaesthesia, blood was collected by cardiac puncture. The blood was transferred into EDTA anti-coagulant tube and allowed to clot at room temperature for 30 minutes. Serum was thereof obtained by centrifugation using bench top centrifuge (Germany) for 10 minutes at 3000 rpm.

2.4 Biochemical Assays

The serum enzymes; aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), total proteins, total bilirubin and albumin assays were carried out on the same day according to the procedures described by Randox Lab. Ltd-UK. diagnostic kits.

2.5 Statistical Analysis

Data were presented as mean ± standard error of the mean. Statistical analysis was by the one way analysis variance (ANOVA) using the spss version 10 softwares, and a p-value 0.05 was considered significant.

3. Results

3.1 Hepatic marker enzymes

The activity of ALT, AST, and ALP in the serum of the control and experimental animals is presented in table (1). The activity of these enzymes were elevated significantly ($p < 0.05$) after CdCl₂ injection (group II) when compared to control rats. The administration of the *Urtica dioica* extract to the CdCl₂ (group III) intoxicated rats resulted in significant lowering ($p < 0.05$) of the enzyme levels at all intervals measured.

Table 1: Effect of *Urtica dioica* extract on serum hepatic enzymes in different subjected groups

Parameter	Group I (contol)	Group II (CdCl ₂)	Group III (CdCl ₂ + <i>U. dioica</i> extract)
ALT	30.21 ± 1.94*	73.10 ± 2.37*	49.70 ± 3.98*
AST	55.85 ± 1.22*	110.57 ± 2.45*	69.40 ± 3.38*
ALP	44.32 ± 3.32*	92.82 ± 3.11*	50.40 ± 4.82*

*Results are given as means ± S.E. for six rats. Units are in IU/L. Statistical significance at $p < 0.05$.

3.2 Blood marker proteins

The levels of total bilirubin, total proteins and albumins in the serum of control and experimental animals are shown in table (2). A similar increase in the concentration of T. bilirubin, on the other hand a decreased in T. proteins and albumins was observed in rats serum after injection of CdCl₂ (group II) when compared to control rats. *U. dioica* extract treatment (group III) markedly decreased the level of T. bilirubin significantly ($p < 0.05$), the values of T. protein and albumin were significantly increased ($p < 0.05$) in rats toward normally when compared to CdCl₂ intoxicated rats.

Parameter	Group I (contol)	Group II (CdCl ₂)	Group III (CdCl ₂ + <i>U. dioica</i> extract)
T. bilirubin	0.42 ± 0.20*	0.64 ± 0.45*	0.48 ± 0.36*
T. proteins	6.20 ± 0.47*	3.90 ± 0.11*	5.98 ± 0.32*
Albumins	5.38 ± 0.82*	3.26 ± 0.47*	4.89 ± 0.16*

*Results are given as means ± S.E. for six rats. Units are in mg/dl. Statistical significance at $p < 0.05$.

3.3 Biochemical blood markers

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4. Discussion

Numerous evidences suggest that CdCl₂-induced liver damage is more associated with biochemical changes that contribute to liver cytotoxicity. Hence the role of oxidative damage has been strongly documented in the pathogenesis of CdCl₂-induced toxicity in different tissues [19, 20, 16]. Enormous reports suggest that oxidative stress, depletion of hepatic antioxidant system and increase in lipid peroxidation are the possible mechanisms of CdCl₂ [21, 22, 1].

In the present study, the rats treated with CdCl₂ showed a significant liver damage, as elicited by the increase activities of hepatic marker enzymes (ALT, AST, and ALP) and total bilirubin (Tables 1, 2). Decline in the concentrations of total proteins and albumins (Table 2) also serve as indicator of

liver function. It has been reported that when the liver is damaged with the introduction of toxic chemicals, alcohol, drugs or infectious virus, a significant increase in the levels of hepatic marker enzymes and bilirubin. Those markers were used as biochemical markers to indicate hepatic injury [23-25].

Serum ALT, AST, ALP and Bilirubin are the most sensitive markers used in the diagnosis of hepatic injury because these are located in the cytoplasm and are released into blood circulation after cellular damage [26]. Elevated activity of hepatic enzymes in serum observed in this study might be due to the release of these enzymes from cytoplasm into the blood circulation rapidly after rupture of cell plasma membrane. Moreover, it has been well established that CdCl₂ administration causes a marked elevation in the activities of aminotransferases and alkaline phosphatase during hepatotoxicity [27, 1], which strongly support our present observation.

Urtica dioica extract co-supplementation in our study significantly restored the activities of hepatic marker enzymes to considerable extent (Table 1). This protective action might possibly be due to its effect on preserving the cellular membrane of hepatocytes from breakage by reactive metabolites, thereby restoring the status of these enzymes. Also *U. dioica* extract treatments had a markedly protective effect against CdCl₂ treated animals (Table 2), because these parameters (T. bilirubin, T. proteins, Albumins) are synthesized in the liver and are used to monitor the liver function [28].

The phytochemical analysis of *U. dioica* root extract have been studied extensively and found to contain many active constituents such as: Flavonoids, phytosterols, pentacyclin triterpenes, coumarins, ceramides, Lignans, hydroxyl fatty acids, and some polysaccharides were isolated from the hydrophilic fraction, and are considered to be very important pharmacological findings [29, 4]. As in literature, these phytochemical have shown to be a very effective antioxidants that have high potentiate to fight the free active oxidative radicles that are produced by the oxidative stress upon the treatment of toxic chemicals such as CdCl₂ [30-32].

Urtica dioica has shown a protective effect against oxidative damage in isolated rat hepatocytes [33]. Furthermore, *U. dioica* has antioxidant activity by suppressing the chemiluminescence in phagocytes [34]. Recently, it is observed that *U. dioica* has a significant hepatoprotective effect in CCl₄-administration by decreasing the lipid peroxidation and increasing the antioxidant defense system activity in rabbits³⁵ and rats⁸ emphasizing its antioxidant potential. However, it is found that *U. dioica* can prevent liver fibrosis and cirrhosis, suggesting that this plant protects liver against fibrosis possibly through immunomodulator and antioxidant activities [36, 37].

5. Conclusion

It can be concludes from the data observed in the present study that dried root extract of *Urtica dioica* might have scavenged, detoxified the free radicals and improve the activities of hepatic markers and antioxidant status. Therefore, *Urtica dioica* root extract could be useful as a hepatoprotective agent against chemicals-induced liver damage in vivo.

6. Acknowledgement

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7. References

- Mirani N, Ashraf NJ, Siddque J, Rub A. Protective effect of Rutin against cadmium-induced hepatotoxicity in swiss albino mice. *J Pharmacol Toxicol.* 2012; 7(3):150-157.
- Cowan MM. Plant products as antimicrobial agents. *Clin Microbiol Rev.* 1999; 12(4):564-82.
- Wagner H, Willer F, Samtleben R, Boos G. Search for the antiprostatic principle of stinging nettle (*Urtica dioica*) roots. *Phytomedicine*, 1994; 1:213-224.
- Asgarpanah J, Mohajerani R. Phytochemistry and pharmacologic properties of *Urtica dioica* L., *J Med Plant Res.* 2012; 6:5714-9.
- Davis PH. Flora of Turkey and East Aegean Islands. University Press, Edinburg. 1982, 7.
- Sezik E, Yeşilada E, Honda G, Takaishi Y, Takeda Y, Tanaka T. Traditional medicine in Turkey X. Folk medicine in Central Anatolia. *J Ethnopharmacol.* 2001; 75(2-3):95-115.
- Musette P, Galelli A, Chabre H *et al.* *Urtica dioica* agglutinin, a V beta 8.3-specific superantigen, prevents the development of the systemic lupus erythematosus-like pathology of MRL lpr/lpr mice. *Eur J Immunol.* 1996; 26:1707-1711.
- Kanter M, Coskun O, Budancamanak M. Hepatoprotective effects of *Nigella sativa* L. and *Urtica dioica* L. on lipid peroxidation, antioxidant enzyme systems and liver enzymes in carbon tetrachloride-treated rats. *World J Gastroenterol.* 2005; 11:6684-8.
- Mavi A, Terzi Z, Ozgen U, Yildirim A, Coskun M. Antioxidant properties of some medicinal plants: *Prangos ferulacea* (Apiaceae), *Sedum sempervivoides* (Crassulaceae), *Malva neglecta* (Malvaceae), *Cruciata taurica* (Rubiaceae), *Rosa pimpinellifolia* (Rosaceae), *Galium verum* subsp. *verum* (Rubiaceae), *Urtica dioica* (Urticaceae). *Biol. Pharm. Bull.* 2004; 27(5):702-705.
- Gülçin I, Küfrevioğlu OI, Oktay M, Büyükköroğlu ME. Antioxidant, antimicrobial, antiulcer and analgesic activities of nettle (*Urtica dioica* L.). *J Ethnopharmacol.* 2004; 90:205-15.
- Krystofova O, Adam V, Babula P, Zehnalek J, Beklova M, Havel L *et al.* Effects of various doses of selenite on stinging nettle (*Urtica dioica* L.). *Int. J. Environ. Res. Public Health*, 2010; 7:3804-3815.
- Koch E. Extracts from fruits of saw palmetto (*Sabal serrulata*) and roots of stinging nettle (*Urtica dioica*): Viable alternatives in the medical treatment of benign prostatic hyperplasia and associated lower urinary tracts symptoms. *Planta Med.* 2001; 67:489-500.
- Nisha AT, Garg S, Guatam N, Kumar R. *In vitro* antifungal potency of plant extracts against five phytopathogens. *Braz Arch Biol Technol.* 2011; 54:1093-8.
- Gul S, Demirci B, Başer KH, Akpulat HA, Aksu P. Chemical composition and in vitro cytotoxic, genotoxic effects of essential oil from *Urtica dioica* L. *Biol. Pharm. Bull.* 2005; 18(5):523-527.
- Collier HO, Chesher GB. Identification of 5-hydroxytryptamine in the sting of the nettle (*urtica dioica*). *Br J Pharmacol Chemother.* 1956; 11(2):186-9.
- Buchet JP, Lauwerys R, Roels H, Bernard A, Bruaux P, Claeys F *et al.* Renal effects of cadmium body burden on the general population. *Lancet.* 1990; 336:699-702.
- Godt J, Scheidig F, Grosse-Siestrup C, Esche V, Brandenburg P, Reich A *et al.* The toxicity of cadmium

- and resulting hazards for human health. *J Occup Med Toxicol.* 2006; 1:22.
18. Hyder O, Chung M, Cosgrove D, Herman JM, Li Z, Firoozmand A *et al.* Cadmium exposure and liver disease among US adults. *J Gastrointest Surg.* 2013; 17(7):1265-73.
 19. Hare L, Tessier A. Predicting animal cadmium concentrations in lakes. *Nature.* 1996; 380:430-432.
 20. Swiergosz-Kowalewska R. Cadmium distribution and toxicity in tissues of small rodents. *Microsci Res Tech.* 2001; 55:208-222.
 21. Sarkar S, Yadav P, Trivedi R, Bansal AK, Bhatnagar D. Cadmium-induced lipid peroxidation and the status of the antioxidant system in rat tissues. *J Trace Elem Med Biol.* 1995; 9(3):144-149.
 22. Renugadevi J, Prabu SM. Cadmium-induced hepatotoxicity in rats and protective effect of naringenin. *Exp Toxicol Pathol.* 2010; 62(2):171-181.
 23. Al-Kubaisy K, Al-Noaemi M. A protective role of *Nigella sativa* oil against the harmful effect of CCl₄ on liver cells. *The Inter J Nut & Wellness,* 2007; 3(1).
 24. Hussein JS, Oraby FS, El-Shafey N. Antihepatotoxic effect of garlic and onion oils on ethanol-induced liver injury. *J App Sci Res,* 2007; 3(11):1527-1533.
 25. Al-Kubaisy K, El-Essa LY, Shawagfeh MT, Al-Groom R, Jamain H. Hepatoprotective activity of *Teucrium polium* against CCl₄-induced hepatotoxicity in male albino rats. *Inter J Endogenous Med Plants.* 2013; 46(2):1206-1210.
 26. Sallie R, Tredeger JM, William R. Drugs and the liver." *Biopharm Drug Dispos.* 1991; 12:251-259.
 27. Lee JR, Park SJ, Lee HS, Jee SY, Seo J, Kwon YK *et al.* Hepatoprotective activity of licorice water extract against cadmium-induced toxicity in rats. *Evid Based Complement Alternat Med.* 2009; 6(2):195-201.
 28. Friedmann RB, Anderson RE, Entine SM, Hirshberg SB. Effect of disease on clinical lab tests. *Clin Chemi.* 1980; 26(4):1-476.
 29. Haj Said A, El-Othmani I, Derfoufi S, Benmoussa A. Highlights on nutritional and therapeutic value of stinging nettle (*Urtica dioica*) *International Journal of Pharmacy and Pharmaceutical Sciences,* 2015; 7(10).
 30. Bubols GB, Vianna Dda R, Medina-Remon A, von Poser G, Lamuela-Raventos RM, Eifler-Lima VL *et al.* The antioxidant activity of coumarins and flavonoids. *Mini Rev Med Chem.* 2013; 13(3):318-34.
 31. Wang T, Hicks KB, Moreau R. Antioxidant activity of phytosterols, oryzanol, and other phytosterol conjugates, *Journal of the American Oil Chemists' Society,* 2002; 79(12):1201-1206
 32. Pietta PG. Flavonoids as antioxidants. *J Nat Prod.* 2000; 63(7):1035-1042.
 33. Daba MH, Abdel-Rahman MS. Hepatoprotective activity of thymoquinone in isolated rat hepatocytes. *Toxicol. Lett.* 1998; 95:23-29.
 34. Haq A, Abdullatif M, Lobo PI, Khabar KS, Sheth KV, Al-Sedairy ST. *Nigella sativa*: effect on human lymphocytes and polymorphonuclear leukocyte phagocytic activity. *Immunopharmacol.* 1995; 30:147-155.
 35. Turkdogan MK, Ozbek H, Yener Z, Tuncer I, Uygan I, Ceylan E. The role of *Urtica dioica* and *Nigella sativa* in the prevention of carbon tetrachloride-induced hepatotoxicity in rats. *Phytother. Res.* 2003; 17:942-946.
 36. Turkdogan MK, Agaoglu Z, Yener Z, Sekeroglu R, Akkan HA, Avci ME. The role of antioxidant vitamins (C and E), selenium and *Nigella sativa* in the prevention of liver fibrosis and cirrhosis in rabbits: new hopes. *Dtsch. Tierarztl Wochenschr,* 2001; 108:71-73.
 37. Kataki M, Murugamani V, Rajkumari A, Mehra P, Awasthi D, Yadav R. Antioxidant, Hepatoprotective, and Anthelmintic Activities of Methanol Extract of *Urtica dioica* L. Leaves. *Pharmaceutical Crops,* 2012; 3:38-46.