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Virgin olive oil ameliorates deltamethrin-induced nephrotoxicity in mice: A biochemical and immunohistochemical assessment

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ABSTRACT

Objective: A major class of synthetic pyrethroid insecticide, deltamethrin (DM), can elicit pathophysiological effects through oxidative stress in non-targeted organisms such as mammals. There is accumulating evidence that virgin olive oil (VOO), a rich source of polyphenolic components, have anti-oxidant, anti-inflammatory, and anti-apoptotic properties. This study aimed to determine the protective and ameliorative effects of VOO against DM-induced nephrotoxicity.
Methods & materials: Mice were randomly divided into four equal groups: DM group, DM plus VOO group, VOO group, and vehicle group. Five weeks after gavaging, kidney samples were taken for biochemical assessment of malondialdehyde (MDA), glutathione (GSH) and catalase (CAT), and for immunohistochemical assessment of caspase-3, cyclooxygenase-2 (cox-2) and poly (ADP-ribose) polymerase (PARP).
Results: The MDA level in kidney was increased in the DM group, which was significantly decreased after VOO administration in the DM plus VOO group. The GSH level and CAT activiy in kidney were decreased in the DM group, which were significantly increased after VOO administration in the DM plus VOO group. Greater expression of caspase-3, cox-2, and PARP could be detected in the DM group, which was significantly attenuated in the DM plus VOO group. Also, the histopathological changes which were detected in the DM group attenuated after VOO consumption.
Conclusion: Virgin olive oil exerted protective effects against deltamethrin-induced nephrotoxicity, which might be associated with its anti-apoptotic, anti-inflammatory, and anti-oxidative properties.

1. Introduction

Comparatively safe insecticides, pyrethroids, have been classified as type I or type II based upon their chemical structure and clinical manifestations of acute exposure [1]. Deltamethrin is a type II synthetic pyrethroid insecticide with relatively low mammalian toxicity which is used worldwide as a major class of insecticides in agriculture [2]. Studies have shown that deltamethrin is readily absorbed through contaminated water and food [2], and it is bioavailable in feces and urine [3]. In spite of its rapid metabolism and low toxicity, numerous studies documented that chronic exposure to deltamethrin have some of side effects in non-targeted organisms, including neurotoxicity [4], genotoxicity [5], haemolysis [6], reproductive damages [7], pulmonary disorders [8], and hepatotoxicity [9]. Recently, it was also reported that exposure to deltamethrin can elicit nephrotoxicity and cause degenerative changes in kidney tissue [10,11]. Production of free radicals, induction of lipid peroxidation, disturbance of the total body's antioxidant capacity, inflammation, and apoptosis account the main mechanisms for the deltamethrin toxicity in non-targeted organisms [10,12]. Therefore, it seems that the use of antioxidant supplements is essential to subside the side effects. Within the previous decades, a rapidly growing number of natural polyphenols, secondary metabolites of plants, with anti-oxidant, anti-inflammatory, and anti-apoptotic effects have been described. One of the main sources of these molecules is olive oil. Olive oil is a rich source of polyphenolic components which have many beneficial health effects in human [13]. There is accumulating evidence that attributed the beneficial effects of olive oil to a variety of biological activities such as free radical scavenging actions which is mediated by chelating of metal ions and providing of hydroxyl group for quenching and neutralization of free radicals

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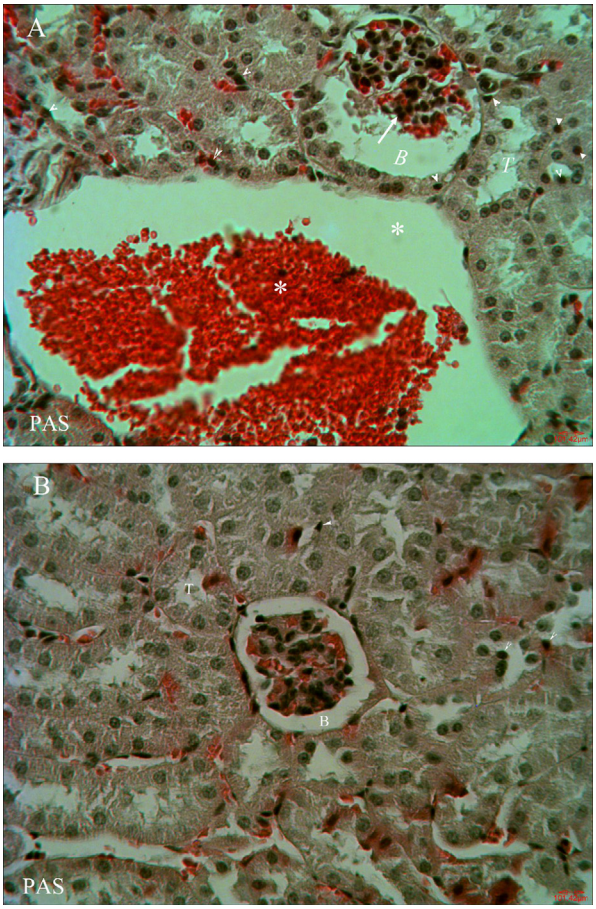

Fig. 1. Photomicrographs of kidney sections of DM group and DM plus VOO group (stained with PAS, × 400). Sections of kidney of DM treated rats (1A, 1B) showing enlarged and congested renal vein (asterisks), swelling of renal tubules (T), atrophied glomeruli (arrow) and dilatation of the bowman capsule (B), and pyknotic nuclei of renal epithelium (arrowheads). Sections of kidney of DM + VOO group (1C) showing mild dilation of the bowman capsule (B) and renal tubules (T), and focal nuclear pyknosis of renal epithelium (arrowheads).

[14,15], anti-inflammatory potency which is mediated by attenuation of anti-inflammatory mediators, and anti-apoptotic properties which is mediated by inhibition of proapoptotic and induction of anti-apoptotic proteins [16,17]. Meanwhile, olive oil consumption increases total plasma antioxidant activity [18].

Accordingly, in the present study, we investigated the protective effects of virgin olive oil consumption against deltamethrin induced-nephrotoxicity.

2. Methods & materials

2.1. Virgin olive oil

Virgin olive oil purchased from Giah Essence Phytopharm Co. (Iran). The Chemical composition of the oil is shown in the table below (taken from the Company's website, www.giahessence.com).

Major phenolics and fatty acids	
Phenolics (mg/kg)	Hydroxytyrosol (0.48 ± 0.02)
	Tyrosol (0.96 ± 0.30)
	Vanilic acid (1.01 ± 0.18)
	Cinamic acid (0.92 ± 0.41)
Fatty acid (%)	Linoleic acid (3.69 ± 0.16)
	Linolenic acid (0.43 ± 0.03)
	Stearic acid (2.24 ± 0.29)
	Oleic acid (75.17 ± 2.66)
	Palmitic acid (16.80 ± 2.55)
	Palmitoloeic acid (1.35 ± 0.37)

2.2. Animals

Adult male mice (25 ± 3.0 g) were used (laboratory animal research center, Sari, Iran) in this study. They were kept in the laboratory under constant conditions of temperature (23 ± 2 °C) and light/dark cycle (12 h/12 h) for at least one week before and through the experimental work. All procedures were done according to the guidelines of the university's animal care codes (code; Amums.rec.1392.135) to minimize the animal's suffering and were fed a standard mice chow and drinking water ad libitum throughout the study period.

2.3. Grouping

The animals were randomly allocated in four groups, each containing 5 mice: (1) Deltamethrin (DM) treated group, which received DM (Sigma-Aldrich, Germany) diluted in dimethyl sulfoxide (Sigma-Aldrich, Germany) (at 5 mg/kg/day for a period of five weeks by gavages [19]; (2) DM plus virgin olive oil (VOO) treated group, which received 0.4 mL of VOO by gavages for five weeks after 2 h of DM administration [20]; (3) VOO treated group, which received 0.4 mL of VOO by gavages for five weeks; (4) Vehicle group, which received 2.5% diluted DMSO by gavages for five weeks. At the end of the experiment, all mice were euthanized with an injection of sodium pentobarbital and then kidneys were harvested for biochemical, histopathological, and immunohistochemical assessments.