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The possible ameliorative effect of *Olea europaea L.* oil against deltamethrin-induced oxidative stress and alterations of serum concentrations of thyroid and reproductive hormones in adult female rats

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ABSTRACT

This study aimed to verify whether *Olea europaea* L. (olive) oil (OEO) exerted a protective effect against oxidative stress induced by deltamethrin (DM) and alterations of pituitary, thyroid and gonadal hormones in adult female rats. DM (0,00256 g/kg body weight),OEO (0,6 g/kg body weight) and DM with OEO were administered to rats orally for 28 days. Volatile compounds present in olive oil were analysed by GC-MS. Estradiol (E_2), Thyroxine (T4),Thyroid Stimulating Hormone (TSH), Triiodothyronine (T3), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Progesterone (Pg) were measured in serum using Chemiluminescent Microparticle Immunoassay (CMIA). Lipid peroxidation (LPO), protein carbonyls (PCs), reduced glutathione (GSH) levels along with superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST) and glutathione peroxidase (GPx) activities were determined in thyroid and ovarian tissues. Sesquiterpenes, (E,E)-α-farnesene (16.45%) and α-copaene (9,86%), were analysed as the main volatile compounds of OEO. The relative weight of ovaries and thyroid and body weight significantly decreased in rats treated with DM. DM caused significant alterations in TSH, T4, FSH, Pg and E_2 levels while T3 and LH concentrations remained unchanged when compared to control. DM also increased significantly LPO and PCs levels. In addition, GSH reserves as well as CAT, GPx, SOD and GST activities were suppressed in DM-received rats. The presence of OEO with DM returned the levels of oxidative stress markers, thyroid and reproductive hormones at the control values. Our results indicate that OEO is a powerful agent able to protect against DM oxidative stress and endocrine changes.

1. Introduction

Millions of human and animal lives have been saved by insecticides since their synthesis data and use. Insecticides for their important role of control against insect pests of crops and vector-borne diseases have revolutionized the field of agriculture and human health (Ansari et al., 2014). Pyrethroids, synthetic analogs of pyrethrins, have been obtained starting from the natural compounds through isosteric modifications resulting more stable and efficacy and are now the new and most important class of crop protection chemicals (Casida, 1980). Their use as wide-spectrum insecticides is largely increased over the years and this is due in particular to the high level of activity as insecticides, to the low frequency of resistance development in insects, to the low level of acute toxicity in mammals and to the rapid breakdown in the environment (Eraslan et al., 2006). Pyrethroids may be classified into two types, type I and type II on the basis of the chemical structure and toxicity.

Deltamethrin (DM), [(S)-&-cyano-3-phenoxybenzyl-(1R,cis)-2,2-dimethyl-3-(2,2 dibromovinyl)-cyclopropane-1-carboxylate], a type II synthetic pyrethroid, has become an insecticide of choice extensively used in agriculture and other domestic applications. Although initially considered to be safe, recent data on DM exposure has raised suspicions about its association with neurotoxicity, biochemical alterations, metabolic disruptions, genotoxic effects and endocrine perturbations via excessive production of free radicals leading to oxidative stress on cells from various organs in intoxicated animals (Gabbianelli et al., 2002; Eraslan et al., 2006; Nasuti et al., 2007; Desai et al., 2016).

The potential of synthetic pyrethroids to provoke endocrine disruption is an area of increasing concern. According to the Environmental Protection Agency (EPA), endocrine disruptor chemicals (EDCs) are defined as exogenous chemicals or chemical mixtures that

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affect endocrine system structure or function causing adverse effects. They are molecules present in the environment and in food that interfere with normal hormone regulation. DM has been closely reported to affect thyroid gland by reducing hormone levels or inducing DNA damage and histopathological changes (Abdul-Hamid and Salah, 2013; Şekeroğlu et al., 2014). On the other hand, it has been found that DM is able to inhibit the secretion of pituitary hormones; luteinizing hormone (LH) and follicle stimulating hormone (FSH) (Ekaluo et al., 2013; Desai et al., 2016). Moreover, DM exposure has been reported to reduce progesterone (Pg) serum levels and affect adversely the ovarian architecture and the follicular growth in female rats (Belhadj et al., 2014). Hence, each treatment, which mitigated ROS excessive production, could ameliorate DM harmful effects on adult endocrine system.

Within the previous decades, a rapidly growing number of natural compounds have been described to have a powerful anti-apoptotic and free radical scavenging/antioxidant effects. One of the main sources of these molecules is olive oil. Khalatbary et al. (2015) reported that pre-exposure to the main polyphenolic component oleuropein (OE) in olive oil, provided the molecular evidence for the protective activity against DM induced apoptosis that is mediated by altered expression of P53, Bax, Bcl-2, and caspases in the neuronal cells of rat cerebral cortex. Furthermore, previous studies have demonstrated that the use of olive oil may have a potential role in decreasing the risk to develop different neoplasms malignant, especially breast, stomach, ovary, colon and endometrium cancers (Al-Seeni et al., 2016). In addition, extra virgin *Olea europaea* L. oil first pressed has appreciable amounts of unsaponifiable matter that has a high content of α-dl-tocopherol and polyphenolic derivatives which exhibit antioxidant properties (Litridou et al., 1997; Covas et al., 2006). It has been observed that olive oil added to the rat's diet seems effective in inhibiting oxidative liver damage (El-Kholy et al., 2014). In this context, the study of De La Lastra et al. (2002) provided evidence that dietary extra virgin olive oil supplementation not only reduces in rats gastric oxidative damage induced by indomethacin but also enhances the antioxidant defense system of glutathione. Manna et al. (2002) reported the protective effect of different extra virgin olive oils against oxidative injuries mediated by ROS in intestinal (Caco-2) cells and in erythrocytes.

Based on the above studies and since there are no published data that have investigated the ameliorative role of extra virgin *Olea europaea* L. oil against DM induced hormonal alterations, our current study aimed to evaluate the protective effect of OEO on hormonal imbalance and oxidative damages in thyroid and ovaries of adult female rats subjected to DM intoxication.

2. Materials and methods

2.1. Chemicals and reagents

Test chemical deltametrin in the commercial formulation Decis 25 EC, denotes 2.8% of technical grade deltametrin in emulsifiable concentrate containing 1% of Tetrapropylene benzene sulfonic acid, 1% of Methylpropanol and 25% of Light aromatic solvent naphtha (petroleum). Pyrethroid insecticide was purchased from Bayer Crop Sciences (Spain). All the other chemicals and reagents used in this study were of analytical grade and purchased from Sigma chemicals (Aldrich Chemical Company).

2.2. Olea europaea L. oil extraction procedure

Healthy *Olea europaea* L. fruits were collected from Ouedjana region (Jijel, Northeastern Algeria) during the harvesting period 2016/2017 at the stage of full maturation. The taxonomical identification of olive sample was confirmed by the department of Environment and Agronomy Sciences of the University of Jijel. The oil was extracted from the fruits by traditional first cold pressure extraction in various phases. The fruits were ground into a paste, mixed for 30 min, spread on fibre disks and then pressed. To increase the filtration of the oil, cold water was run down the sides of the disks. The liquids were then separated by decantation. After this step, extra virgin OEO was produced. The obtained extra virgin olive oil was filled in glass bottles and stored at a temperature ranging from 15 to 20 °C until use (Djerrou et al., 2010).

2.3. Simultaneous distillation extraction (SDE) of oil volatile compounds

The volatile compounds of OEO were extracted with Likens–Nickerson apparatus as described by Kesen et al. (2013). 40 ml of olive oil were mixed with 100 ml of water and 25 ml NaCl 30% into a 500 ml distillation flask; 40 ml dichloromethane was put into the other 100 ml distilled flask. Both flasks were placed in a heater and the extraction was done for approximately 3 h. The pooled organic extract was dehydrated by adding anhydrous sodium sulfate and then concentrated to 5 ml in a Kuderna Danish concentrator and then reduced to 200 µl under a gentle flux of pure nitrogen. Two microliters of this extract were injected in the gas chromatograph set in the split mode (1: 20).

2.4. Gas chromatography–mass spectrometry (GC-MS) analysis of volatile compounds

Volatile profile of OEO was established using a Shimadzu QP 2010 (Shimadzu, Kyoto, Japan) gas chromatograph coupled with a GC-MS–QP2010 quadrupole mass spectrometer (Shimadzu, Kyoto, Japan) operating in the electron impact mode (70 eV) and equipped with National Institute of Standards and Technology (NIST) libraries. Capillary column SE 30 (30 m × 0.25-mm × 0.25 µm thickness) of 100% dimethylpolysiloxane was utilized.

The initial column temperature was 80 °C increased at a rate of 3.0 °C min^{-1} to 250 °C, hold for 1 min and then at a rate of 25 °C min^{-1} increased from 250 to 300 °C and hold for 5 min. The injector and detector temperatures were 200 and 300 °C, respectively. The retention indices for all components were determined using n-alkanes as standard. The unknown compounds were identified: i) by comparison of their GC retention indices (RI) with those reported in the literature, ii) by comparison of their patterns of mass spectral fragmentation with those stored in the MS database (NIST 05). Compounds were quantified as area percentages of total volatiles.

2.5. Animals and experimental design

Thirty healthy and sexually mature female of Wistar albino rats strain weighing between 150 and 200 g provided from Pasteur institute (Algiers, Algeria) were used for the experiments. At the arrival, animals were randomized into treated and control groups and caged separately. Rats were exposed to a 12 h light/dark cycle, at a room temperature of 18–22 °C and relative humidity of 40–50%, and were fed a standard laboratory diet and water *ad libitum*. Animals were quarantined for 10 days prior to the beginning of treatment. All experimental procedures were carried out in accordance with the Guide for the Care and Use of Laboratory Animals issued by the U.S. National Academy of Sciences. The tested concentration of DM was calculated from the percentage of active ingredient of commercial formulation. Adequate dilutions were made with corn oil to achieve the DM test dose level of 0,00256 g/kg body weight (1/50 of LD50) (Arora et al., 2016). Additionally, a ternary mixture of solvents (TMS) DM free was prepared in adjusted volume of 2 ml/kg with a view to assess potential solvent-related effects. Target exposure doses of Tetrapropylene benzene sulfonic acid, Methylpropanol and Light aromatic solvent naphtha were respectively 0.00091 g/kg bw, 0.00091 g/kg bw and 0.02285 g/kg bw. The dose level of OEO was taken from a study of Al-Attar et al. (2016). Dosages of DM, solvent mixture and OEO were adjusted weekly for body weight changes. Animals were randomly divided into five groups of six rats each (n = 6). Group 1 (untreated rats) served as control. Group 2 treated with solvent