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Eruca sativa Essential Oil Protects upon Hyperthyroidism Induced Damages in Rat

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Abstract

The study was conducted to evaluate the protective effects of *Eruca sativa* oil upon hyperthyroidism induced damages to thyroid, kidney and brain of male Wistar rats. Our experimental conditions revealed an obvious increase in the serum FT4, creatinine, urea and calcium levels together with significant decrease in TSH, proteins and uric acid. In addition, hyperthyroidism treatment triggered an oxidative stress in thyroid, brain and kidney as revealed by an increased level of lipid peroxidation, an increase of superoxide dismutase activity in kidney and brain and a decrease of glutathione peroxidase and catalase activities in thyroid, kidney and brain functions. When *Eruca sativa* oil was added, all this parameter was significantly shifted to more normal values. In conclusion, *Eruca sativa* oil displays beneficial effects upon thyroid dysfunction, nephrotoxicity, neurotoxicity and oxidative stress in hyperthyroidism treated animals. This property could be attributed to the presence of antioxidant components determined by GC-MS. The experimental protocol was performed according to the European convention for the protection of vertebrate animals used for experimental and other scientific purposes (Council of Europe No 123, Strasbourg) and approved by the ethics committee for research on laboratory animal use of our institution.

Keywords: Hyperthyroidism; *Eruca sativa*; Wistar rats; Thyroid; Neurotoxicity

Introduction

Thyroid hormones, tri-iodothyronine (T3) and tetraiodothyronine (T4) are crucial in regulating the growth and the differentiation of many tissues and organs such as the maturation and function of the nervous system [1]. Several reports have been published on the relation between hyperthyroidism and oxidative stress. In fact, high concentrations of thyroid hormones stimulate free radical formation in mitochondria by affecting oxygen metabolism [2]. Although reactive oxygen species play an important role in physiological mechanisms extremely reactive oxygen radicals can cause severe oxidative damage to molecules [3].

Hyperthyroidism is known to stimulate ROS generation and induce oxidative stress in many tissues by disturbing the endogenous pro-oxidant/anti-oxidant equilibrium [4]. Others *in vivo* and *in vitro* studies indicate that thyroid hormones have a considerable impact on oxidative stress. Similarly, Xing et al. show that hyperthyroidism increased MDA (malondialdehyde) and glutathione (GSH) levels in cerebral, hepatic and cardiac tissues of rat [5]. Indeed, hyperthyroidism accelerates several physiologic processes, a fact which is reflected in the increased renal blood flow, hypertrophic and hyperplastic tubuli, and increased glomerular filtration rate [6]. Other findings reported that hyper metabolism due to hyperthyroidism is associated with an increase in formation of free radicals and lipid peroxide levels in many organs [7]. It is reported that not only hyperthyroidism but also hypothyroidism lead to changes in oxidant and antioxidant systems [8,9]. The action of thyroid hormones (thyroxine, T4; triiodothyronine, T3) on brain development and function is gaining renewed interest. In fact, mammalian brain maturation was stimulated by thyroid hormones [9]. For several years, a special attention was paid to the dietary regimen and more particularly to natural products (fruits, vegetables) for their capacities to reduce oxidative damages induced by various medicals terms as hypo and hyperthyroidism, as medicinal plant we find *Eruca sativa*. This plant is an annual and biannual herb and is one of the varieties of mustard. The plant originated in the Mediterranean region but is presently found round the world. This plant has a wide spread medicinal use. Traditionally, its use as astringent, diuretic, digestive, emollient, tonic, depurative, laxative, rubefacient and stimulant is well- documented [10,11].

Eruca sativa has several antioxidant constituents including glucosinolates, flavonoides, carotenoids [12]. Several reports are found in the literature about the antifungal activity of these compounds on postharvest pathogens [13,14].

In this study, we aimed to investigate whether a dietary regimen enriched for 7 weeks of *Eruca sativa* oil, could prevent hyperthyroidism induced by levothyroxin injection as a synthetic thyroid hormone that is chemically identical to thyroxine (T4) in male rat. Serum levels of TSH, FT4, calcium, creatinine, urea, proteins and uric acid and activities of antioxidant enzymes (Superoxide-dismutase, catalase, glutathione peroxidase) in thyroid, kidney and brain were measured.

Materials and Methods

Essential oil extraction of *Eruca sativa*

The essential oils were extracted by hydrodistillation of dried plant material (100 g of *Eruca sativa*) in 500 ml of distilled water) using a Clevenger-type apparatus for 4.5 h as described in the European

Pharmacopeia. The essential oil was collected, dried under anhydrous sodium sulphate and stored at 4°C until used [15].

Experimental design

3-month-old Wistar male rats, about 160 g body weight, fed on 15% proteins food pellets (SNA, Sfax, Tunisia), were kept in a breeding farm, at 22°C, with a stable hygrometry, under constant photoperiod.

The rats were divided into 4 batches: (C) was control group, (L) levothyroxin treated animals injected (i.p) (20 mg/kg), (ES) was a group treated with *Eruca sativa* oil during 7 weeks by forcible feeding and (ES+L) was a group previously treated with *Eruca sativa* oil by forcible feeding and injected (i.p) by levothyroxin for 3 days.

At the end of this experimental period, all animals were rapidly sacrificed by decapitation in ordrer to minimize the handling stress. Blood serum was obtained by centrifugation (1500 xg, 15 min, 4°C). Thyroid, kidney and brain were stored at -80°C until use.

The experimental protocol was performed according to the European convention for the protection of vertebrate animals used for experimental and other scientific purposes (Council of Europe No 123, Strasbourg) and approved by the ethics committee for research on laboratory animal use of our institution.

Biochemical assay

Levels of FT4, TSH, calcium, creatinine, urea, proteins, urea and acid uric in serum were determined by kit methods Spinreact.

The level of lipid peroxidation was measured as thiobarbituric acid reactive substances (TBARS), according to Yagi's method [16]. For the assay, 125 µl of supernatant (S1) were mixed with 175 µl of 20% trichloroacetic acid containing 1% butyl-hydroxytoluene and centrifuged (1000 xg, 10 min, 4°C). Then, 200 µl of supernatant (S2) was mixed with 40 µl of HCl (0.6 M) and 160 µl of thiobarbituric acid (0.72 mM) and the mixture was heated at 80°C for 10 min. The absorbance was measured at 530 nm. The amount of TBARS was calculated using an extinction coefficient of 156 mM^{-1} cm^{-1} and expressed as n moles/mg protein.

The total superoxide-dismutase (SOD) activity was determined by measuring its ability to inhibit the photoreduction of nitrobluetetrazolium (NBT) [17]. One unit of SOD represents the amount inhibiting the photoreduction of NBT by 50%. The activity is expressed as units/mg protein, at 25°C.

Glutathione-peroxidase (GPX) activity was assayed according to the method of Flohe and Gunzler. [18]. The activity at 25°C was expressed as µ moles of GSH oxidized/min/g protein.

Catalase (CAT) activity was measured according to Aebi [19]. The reaction mixture (1 ml) contained 100 mM phosphate buffer (pH=7), 100 mM H_2O_2 and 20 µl (about 1-1.5 mg of protein) of liver. H_2O_2 decomposition was followed at 25°C by measuring the decrease in absorbance at 240 nm for 1 min. Besides, the enzyme activity was calculated using an extinction coefficient of 0.043 mM^{-1} cm^{-1} and expressed in international units (I.U.) i.e., in µ moles H_2O_2 destroyed /min/mg protein.

Protein content in tissue extracts was determined according to Lowry's method [20] using bovine serum albumine as standard.

Gas chromatography-mass chromatography (GC-MC)

The essential oils were analysed using an Agilent-Technologies 6890 N Network GC system equipped with a flame ionization detector and HP-5MS capillary column (30 m × 0.25 mm, film thickness 0.25 µm; Agilent-Technologies, Little Falls, CA, USA). The injector and detector temperatures were set at 220 and 290°C, respectively. The column temperature was programmed from 80 to 220°C at a rate of 4°C/min, with the lower and upper temperatures being held for 3 and 10 min, respectively. The flow rate of the carrier gaz (Helium) was 1.0 ml/min. A sample of 1.0 µl was injected, using split mode (split ratio, 1:100). All quantifications were carried out using a built-in data-handling program provided by the manufacturer of the gas chromatograph. The identity of the components was assigned by comparison of their retention indices, relative to n- alkanes indices and GC-MS spectra from a home-made library, constructed based on the analyses of reference oils, laboratory-synthesized components and commercial available standards [21,22].

Results

As shown in Figure 1, hyperthyroidism induced a significant decrease of TSH and a significant increase of FT4 in serum respectively by 66% and +148% (Figure 1) as compared to controls. In the same group our data show a significant increase by +31% in calcitonine level as other biomarkers of thyroid dysfunction.

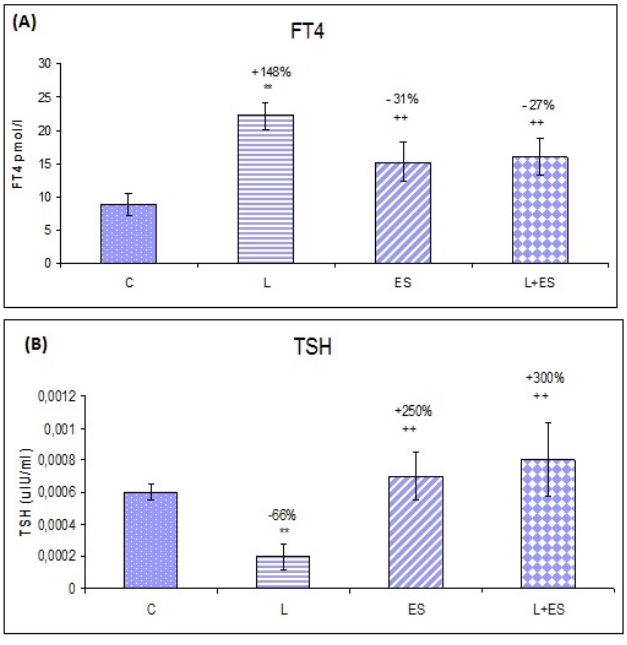

Figure 1: Plasma free thyroxin (FT4) (pmol/l) (A) and TSH levels (uIU/ml) (B) after 7 weeks and 3 days of treatment in: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ ES). Values are the mean of 6 measurements ± SD. ** Significant difference as compared to control rats (C) ($p \leq 0.01$). ++ Significant difference when comparing (L+ ES) groups to L group.

As compared to controls, levothyroxin affected kidney function which is evidenced by an increase levels of creatinine and urea levels

by +50% and +72%, respectively and a decrease levels of proteins and acid uric by -29% and -23% respectively in serum (Figures 2 and 3).

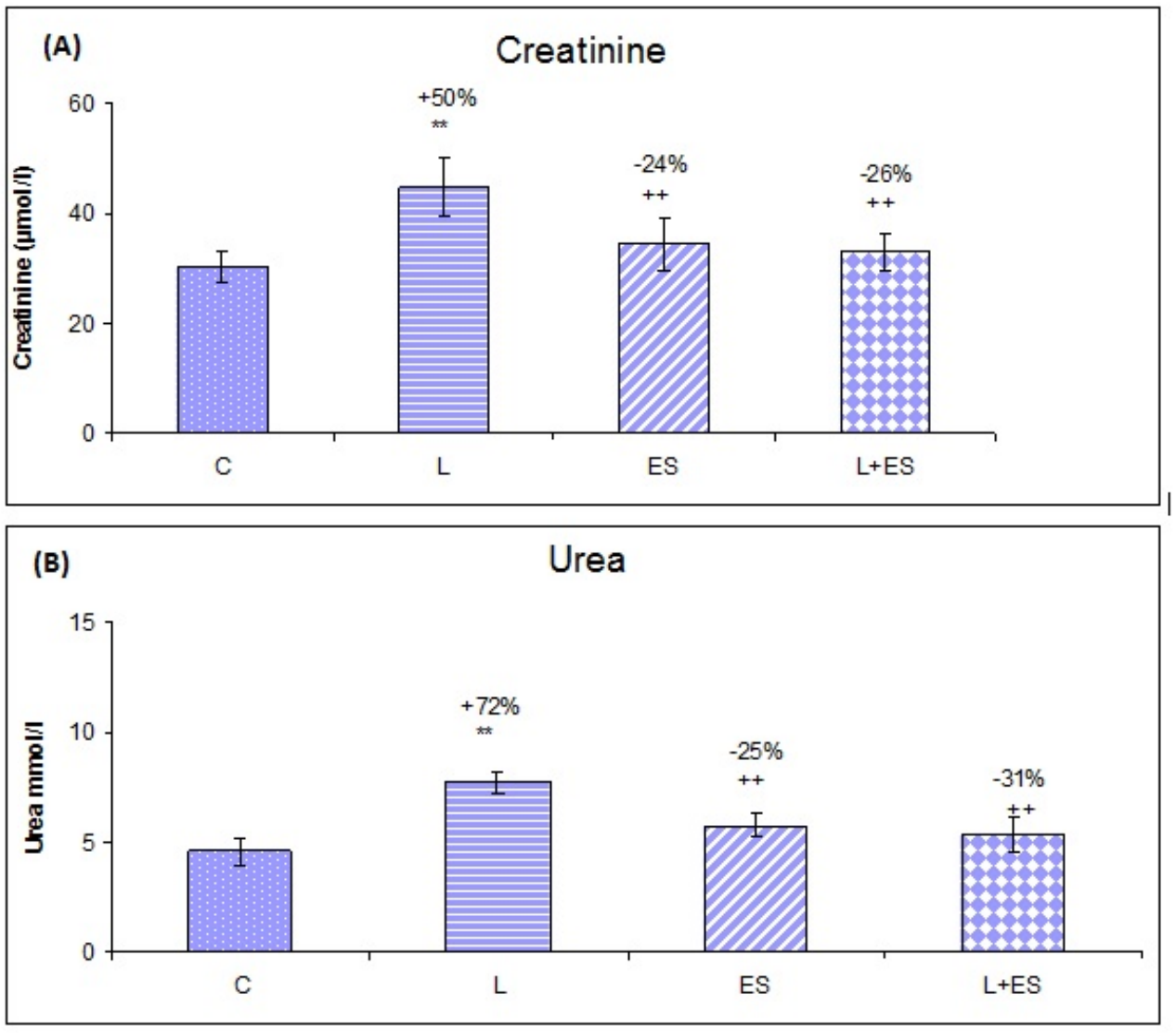

Figure 2: Serum creatinine (µmol/l) (A), Urea mmol/l (B) levels after 7 weeks and 3 days of treatment in: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ ES). Values are the mean of 6 measurements ± SD. ** Significant difference as compared to control rats (C) ($p \leq 0.01$). ++ Significant difference when comparing (L+ ES) groups to L group.

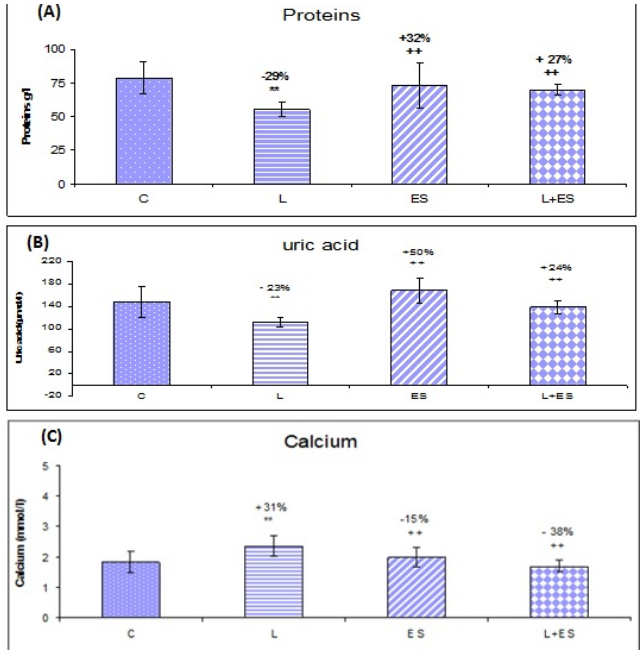

Figure 3: Serum proteins (g/l) (A), uric acid (µmol/l) (B) and calcium(mmol/l) (C) levels after 7 weeks and 3 days of treatment in: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ ES). Values are the mean of 6 measurements ± SD. ** Significant difference as compared to control rats (C) ($p \leq 0.01$). ++ Significant difference when comparing (L+ ES) groups to L group.

Interestingly, these adverse effects of levothyroxine were much alleviated in animals previously treated with *Eruca sativa* oil.

The TBARS level in thyroid, kidney and brain increased in levothyroxin-treated rats as compared to controls by +87%, +133% and +69% respectively (Tables 1 and 2). SOD activities in kidney, brain and thyroid were significantly decreased by 91%, 80% and by 48% respectively. Again, when rats were previously treated with the *Eruca sativa* oil this effect of levothyroxin poisoning was much reduced. Activities of GPX and CAT were found to be respectively reduced (by 50% and 54% respectively) in thyroid and (by 77% and 44%, respectively) in kidney and by 66% and 48% in brain of levothyroxin-treated rats, as compared to controls (Tables 3 and 4). These changes were alleviated when the rats were previously treated with *Eruca sativa* oil.

Group	Thyroid	Brain	Kidney
C	0.84 ± 0.02	0.65 ± 0.023	0.32 ± 0.01
L	1.5 ± 0.17**	1.1 ± 0.03**	0.73 ± 0.06**
ES	0.5 ± 0.05	0.52 ± 0.012	3 ± 0.0360
L+ES	0.7 ± 0.06++	0.44 ± 0.06++	0.32 ± 0.06++

Table 1: TBARS (nmol/mg protein) levels in thyroid, brain and kidney after 7 weeks and 3 days of treatmentin: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ES). Values are the mean of 6 measurements ± SD. ** Significant difference as compared to control rats (C) ($p \leq 0.01$). ++ Significant difference when comparing (L+ES) groups to L group. ($p \leq 0.01$).

Group	Thyroid	Brain	Kidney
C	3.8 ± 0.8	1.6 ± 0.2	4.9 ± 0.6
L	1.95 ± 0.6**	0.32 ± 1.85**	0.42± 3.2**
ES	3.42 ± 0.7	1.84 ± 0.2	4.9± 0.6
L+ES	4.12 ± 0.5++	2 ± 0.21++	5±0.42++

Table 2: SOD (U/mg protein) levels in thyroid, brain and kidney after 7 weeks and 3 days of treatment in: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ES). Values are the mean of 6 measurements ± SD. ** Significant difference as compared to control rats (C) ($p \leq 0.01$). ++ Significant difference when comparing L+ES groups to L group. ($p \leq 0.01$).

Group	Thyroid	Brain	Kidney
C	0.84 ± 0.05	0.3 ± 0.03	0.09 ± 0.005
L	0.4 ± 0.05**	0.1 ± 0.01**	0.02 ± 0.002**
ES	0.7 ± 0.08	0.4 ± 0.006	0.02 ± 0.12
L+ES	0.65 ± 0.07++	0.33 ± 0.02++	0.12 ±0.03++

Table 3: GPX (U/mg protein) levels in thyroid, brain and kidney after 7 weeks and 3 days of treatment in: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ES). Values are the mean of 6 measurements ± SD. **Significant difference as compared to control rats (C) ($p \leq 0.01$). ++ Significant difference when comparing L+ES groups to L group. ($p \leq 0.01$).

Group	Thyroid	Brain	Kidney
C	28.9 ± 0.4	23.6 ± 2.3	30. 9 ± 1.7
L	13.1 ± 3.4**	12.1 ± 2.04**	17.66 ± 4.4**
ES	27.5 ± 4.4	24.8 ± 3.6	30 ± 4.123
L+ES	6.33 ± 2.06++	26.5 ± 2.6++	27.127 ± 5.03++

Table 4: CAT (U/mg protein) levels in thyroid, brain and kidney after 7 weeks and 3 days of treatment in: controls (C), Levothyroxin-treated rats (L), *Eruca sativa* given rats (ES) and rats previously given *Eruca sativa* then treated by Levothyroxin (L+ES).

GC/MS analysis: The results obtained with the GC/MS analysis of the oil are depicted in Table 5 that shows the identified constituents, the percentage composition, retention time and retention index. The essential oil was found to contain 32 constituents representing 98.87% of the total essential oil while minor constituents (1.13%) of the oil remained unidentified. The main constituents were found, 2-Phenylethyl, isothiocyanate (30.59%), Methyl stearate (20.31%),

Eucalyptol (15.61%), 5-methylthiopentanonitrile (6.87) and Camphor (6.34%).

No	TRb	Compound	KIa	Composition
1	504	1,3,6-Octatriene	864	0.0082
2	5088	3-Carene	904	0.0158
3	5362	Cis-13-Eicosenoic acid	936	0.0028
4	5403	Camphene	976	0.0072
5	5904	Beta-Phellandrene	996	0.0124
6	6056	Beta-Pinene	1023	0.0015
7	6598	(+)-4-Carene	1042	0.0024
8	6778	tert-Butylbenzene	1256	0.0041
9	6832	Cyclohexene	1276	0.0064
10	6926	Eucalyptol	1465	0.1561
11	737	1,4-Cyclohexadiene	1488	0.0056
12	7886	Cyclohexene	1512	0.0015
13	8195	No Match	1589	0.0013
14	9178	Camphor	1609	0.0634
15	9587	3-Cyclohexene-1-methanol	1628	0.0014
16	9654	Borneol	1677	0.0116
17	9741	3-Cyclohexen-1-ol	1681	0.0052
18	10036	3-Cyclohexene-1-methanol	1683	0.0094
19	10361	Bicyclo[3.1.1]hept-3-en-2-one	1693	0.0012
20	11504	Aceticacid, 1,7,7-trimethyl	1711	0.0076
21	13719	Caryophyllene	1752	0.005
22	1407	Allylisothiocynate	1767	0.0047
23	14287	Methylstearate	1772	0.2031
24	16444	DiethylPhthalate	1808	0.0057
25	21338	5-methylthiopentanonitrile	1820	0.0687
26	22591	2Phenylethylisothiocyanate	1851	0.3059
27	23308	Ethyl oleate	1863	0.0017
28	2609	Heneicosanoicacid	1877	0.0074
29	26839	Methyl 20-methyl-heneicosanoate	1900	0.003
30	27451	2,3-Dihydroxypropyl cis-13-d	1920	0.0158
31	28461	Sulforaphane	1985	0.0267
32	28545	No Match	2001	0.0064
33	28636	No Match	2012	0.0044

Table 5: GC/MS chromatogram of *Eruca sativa* essential oil. TR[b]: Retension Time (min) KI[a]: Retention Index (kovats).

Discussion

The thyroid gland is an organ that contribute in regulating the body's metabolism and other body functions and maintain body homeostatic. This means, high concentrations of thyroid hormones play an important role in inducing oxidative stress in many organs by stimulating free radical formation in mitochondria, affecting oxygen metabolism and the antioxidant defence system [23]. In our study, the injection of levothyroxine, as a synthetic thyroid hormone that is chemically identical to thyroxine (T4) and is naturally secreted by the follicular cells of the thyroid gland, was used to induce hyperthyroidism. The effectiveness of levothyroxine administration in inducing hyperthyroidism was confirmed by significant increase in FT4 together with obvious decrease in TSH circulating levels. Also, an increase in lipid peroxidation in thyroid was also signaled after this treatment. This is can be explained in the light of previous findings by the considerable impact of thyroid hormones on oxidative stress and that thyroid hormones act on mitochondria by regulating energy metabolism, and mitochondria are a major source of intracellular free radicals [24]. Moreover, this thyroid dysfunction can be also associated with hyper-metabolic state which caused mainly by oxidative stress which induced damage to molecules, then affected many organs. It seems that when thyroid hormones increase metabolic systems of the body in general, the resulting increase in reactive oxygen types inevitably leads to lipid peroxidation [25]. On the other hand, hyperthyroidism leads to changes in both oxidant and antioxidant systems. In this finding, a significant elevation of lipid peroxidation, together with the decrease of SOD, GPX and CAT activities in levothyroxin treated animals compared to controls was reported, showing that the increase in free radicals signaled by could not be overcame by antioxidant system which affected thyroid and others organs.

Because hyperthyroidism affect also nutrient absorption and use by the body, an increase level of calcium was detected in this finding.

Levothyroxin damage also kidney by reducing glomerular filtration rate, an increase level of creatinine and urea and a decrease level of proteins in blood were noted. As other renal markers we find in blood of treated rats, a decrease of uric acid level, as the end product of purine catabolism, exerts antioxidative properties and may participate to the defense against an oxidative stress by scavenging various ROS [26]. Many findings reported that when the thyroid is either hyper-or hypo-functioning, changes in different clinical renal parameters such as glomerular filtration rate, urinary protein, creatinine ratio and markers of tubular function can occur. Vice versa, kidney disease influences circulating thyroid hormones [27]. Besides, an increase of lipid peroxidation level and superoxide dismutase activity together with reduction of CAT and GPX activities in kidney were reported in this data which contribute to the worsening of the oxidative stress. Our results are supported by others findings which recorded that hyperthyroidism increases glomerular filtration rate up to 18% in hyperthyroid rats [28]. According to Xing [29], renal failure progresses in hyperthyroidism due to the damage caused by glomerulosclerosis, proteinuria and oxidative stress. Levothyroxine induced also oxidative stress in brain, because thyroid hormones are essential for brain maturation, and for brain function. This data show also that oxidative stress in brain is evidenced by the increase level in lipid peroxidation and the inhibition of the enzymatic defense system mainly that brain is a large consumer of oxygen and being poor in anti-oxidant defense systems. Thyroid hormone deficiency, even of short duration may lead to irreversible brain damage, the consequences of which depend on the specific timing of onset and duration of thyroid hormone deficiency [30]. Many studies have linked oxidative stress to thyroid cancer by showing its association with abnormally regulated oxidative or antioxidative molecules [31]. The data obtained in the present study showed *Eruca sativa* oil to have a potent antioxidant activity and protect against levothyroxine induced damages in thyroidal state, kidney and brain. We found that *Eruca sativa* oil treatment was able to restore TSH, FT4, creatinine, urea, proteins, uric acid and calcitonin levels in plasma. Similar results were reported in mercuric chloride treated rats by Abassi et al. [32] who emphasized the alleviating effect of *Eruca sativa* on renal damage by reducing creatinine, urea and lipid peroxidation in blood. *Eruca sativa* effects could be able to reduce lipid peroxidation and restored the levels of SOD, CAT and GPX activities in thyroid, kidney and brain. The possible factors behind the protective effects of *Eruca sativa* is related to its contents of bioactive substances such as glucosinolates, flavonoids, carotenoids, vitamin C and phenolic compounds [33,34].

Tabert et al. [35] indicated the main antioxidant in *E. sativa* seed extract to be glucoerucin. The antioxidant activity of glucoerucin plausibly implicates free radical scavenging activity and an ability to induce phase-II metabolizing enzymes [36]. *Eruca sativa* oil, with its potent free radical scavenging ability was expected to protect the biomolecules from free radical induced damage. This latter might also be expected to exclude Fe^{3+} as a strategy to control ROS. Consistent to report of Khoobchandani [37], our study also indicated that the beneficial effects of *Eruca sativa* oil can be attributed to scavenging free radical's properties. It is important to note that the curative and preventive properties of medicinal plants are perhaps due to the presence of various secondary metabolites such as alkaloids, flavonoids, glycosides, phenols, saponins, sterols and phospholipids all known to be efficient radical scavengers [38]. As for the second reason, our research, demonstrate the presences of 32 compounds identified in the essential oil of *Eruca sativa*, accounting 98.87% of the total essential oil and contributed beneficial effects against hypertroidism [39,40].

Furthermore, Bansal et al. [41] have proven that the antioxidant activity of the essential oil could be attributed in part to the presence of compounds such as 3-Cyclohexene-1-methanol and camphor and its ability to decompose free radicals by quenching reactive oxygen species and trapping radicals before reaching their cellular targets [42].

Conclusion

Eruca sativa oil prevent thyroid, kidney and brain from damage induced by levothyroxin by scavenging ROS by its antioxidants major components. Obtained by GC-MS. Further studies on the isolation of more of antioxidants are in progress.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Alam MS, Kaur G, Jabbar Z, Javed K, Athar M (2007) *Eruca sativa* seeds possess antioxidant activity and exert a protective effect on mercuric chloride induced renal toxicity. Food Chem Toxicol 45: 910-920.
2. Hanafi EM, Hegazy EM, Riad RM, Amer HA (2010) Bio-protective effect of *Eruca sativa* seed oil against the hazardus effect of aflatoxin B1 in male-Rabbits. Int J Academ Res 2: 67-74.
3. Barillari J, Canistro D, Paolini M, Ferroni F, Pedulli GF, et al. (2005) Direct antioxidant activity of purified glucoerucin, the dietary secondary

metabolite contained in rocket *(Eruca sativa Mill)* seeds and sprouts. J Agric Food Chem 53: 2475-2482.

4. Rodriguez S, Maria SVG, Maria CM, Murray PM, et al. (2006) *Diplotaxis tenuifolia* (L) DC a source of a potentially antifungal essential oil containing nitrile. Biochem Systemat Ecol 4: 353-355.
5. Hassan WA, Rahman TA, Aly MS, Shahat AS (2011) Alterations in monoamines level in discrete brain regions and other peripheral tissues in young and adult male rats during experimental hyperthyroidism. Int J Devl Neurosci 31: 311-318.
6. Sewerynek E, Wiktorska J, Lewinski A (1999) Effects of melatonin on the oxidative stress induced by thyrotoxicosis in rats. Neuro Endocrinol Letters 20: 157-161.
7. Karbownik M, Lewinski A (2003) The role of oxidative stress in physiological and pathological processes in the thyroid gland; possible involvement in pineal-thyroid interactions. Neuro Endocrinol Letters 24: 293-303.
8. Mogulkoc R, Beltaci AK, Oztekin E, Aydin L, Sivrikaya A (2006) Melatonin prevents oxidant damage in various tissues of rats with hyperthyroidism. Life Sci 79: 311-315.
9. Kobori H, Ichihara A, Miyashita Y, Hayashi M, Saruta T (1998) Mechanism of hyperthyroidism-induced renal hypertrophy in rats. J Endocrinol 159: 9-14.
10. Fernandez V, Videla LA (1996) Hepatic glutathione biosynthetic capacity in hyperthyroid rats. Toxicol Letters 89: 85-89.
11. Kumar A, Sinha RA, Tiwari M, Singh R, Koji T, et al. (2007) Hyperthyroidism induces apoptosis in rat liver through activation of death receptor-mediated pathways. J Hepatol 46: 888-898.
12. Fernandez V, Tapia G, Varela P, Castillo I, Mora C, et al. (2005) Redox up-regulated expression of rat liver manganese superoxide dismutase and Bcl-2 by thyroid hormone is associated with inhibitor of kappa B-alpha phosphorylation and nuclear factor-kappa B activation. J Endocrinol 186: 539-547.
13. HoekI Vand, Daminet S (2009) Interactions between thyroid and kidney function in pathological conditions of these organ systems. Gen Comparative Endocrinol 160: 205-215.
14. Kumar A, Sinha RA, Tiwari M, Singh R, Koji T, et al. (2007) Hyperthyroidism induces apoptosis in rat liver through activation of death receptor-mediated pathways. J Hepathol 46: 888-898.
15. Hussein J, Salah A, Oraby F, Deen E, Khayat ANE (2010) Antihepato toxic effect of *Eruca sativa* extracts on alcohol induced liver injury in rats. J American Sci 11: 381-389.
16. Yagi K (1976) A simple fluorometric assay for lipoperoxide in blood plasma. Biochem Med 15: 212-216.
17. Sun Y, Oberley LW, Li Y (1988) A simple method for clinical assay of superoxide dismutase. Clin Chem 34: 497-500.
18. Flohe L, Gunzler WA (1984) Assays of glutathione peroxidase. Methods Enzymol 105: 114-121.
19. Aebi H (1984) Catalase in Vitro. Meth Enzymol 105: 121-126.
20. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ (1951) Protein measurement with the Folin phenol reagent. J Biol Chem 193: 265-275.
21. Adams RP (2005) Identification of essential oil components by gas chromatography/quadrupole mass spectrometry, Allured Publishing Corporation, Carol Stream, USA.
22. Lagowski JJ (1981) Qualitative analysis of flavor and fragrance volatiles by glass capillary gas chromatography. J Chem Educ 58: 381.
23. Messaraha M, Boulakouda MS, Boumendjelb A, Abdennoura C, Fekic El (2007) The impact of thyroid activity variations on some oxidizing-stress parameters in rats 330: 107-112.
24. Das K, Chaing GB (2004) Thyroid hormone influence antioxidant defense system in adult rat brain. Neurochem Res 29: 1755-1766.
25. Videla LA, Fernández V, Cornejo P, Vargas R (2012) Metabolic basis for thyroid hormone liver preconditioning: Upregulation of AMP-activated protein kinase signaling. Scient World J, PP: 475-479.
26. Mahera N, Shaikh Al, Tala AL, Abdul W, Sahar H, et al. (2014) Hypothyroidism induced by carbimazole in diabetic mice and its Management Using Parsley and *Eruca sativa* oil. J Pharma Biol Sci 9: 24-27.
27. Li F, Lu S, Zhu R, et al. (2011) Heme oxygenase-1 is induced by thyroid hormone and involved in thyroid hormone preconditioning-induced protection against renal warm ischemia in rat. Mol Cellul Endocrinol 339: 54-62.
28. Xing M (2012) Oxidative stress: a new risk factor for thyroid cancer. Endocr Relat Cancer 19: 7-11.
29. Warner A, Mittag J (2012) Thyroid hormone and the central control of homeostasis. J Mol Endocrinol 49: 29-35.
30. Hsia SH, Hsia SV (2014) A cohort historical analysis of the relationship between thyroid hormone malady and alpha-human herpes virus activation. J Steroids Horm Sci PP: 5-133.
31. Paulsen SR, Gammon SR, Mustard KJ, Hardie DG, Winder WW (2002) Effects of thyroid state on AMP-activated protein kinase and acetyl-CoA carboxylase expression in muscle. J Appl Physiol 93: 2081-2088.
32. Abbasi BH, Ali M, Ali M, Zia S, Bokhari A, et al. (2011) Free radical scavenging activity in *in vitro* derived tissues of *Eruca sativa*. Pak J Bot 43: 1351-1359.
33. Braverman LE, Utiger RD (1996) Introduction to thyrotoxicosis. Werner and Ingbar's The Thyroid. Philadelphia, USA, PP: 522-524.
34. Mogulkoca R, Oztekinb EA, Aydina L, Sivrikayab N (2006) Melatonin prevents oxidant damage in various tissues of rats with hyperthyroidism. Life Sci 79: 311-315.
35. Tabert J, Kevers C, Pincemail J, Defraigne JO, Dommes J (2009) Comparative antioxidant capacities of phenolic compounds measured by various tests. Food Chem 113: 1226-1233.
36. Hussein J, Salah A, Oraby F, Amany NElD, Zakarya ElK (2016) Antihepato toxic effect of *Eruca sativa* extracts on alcohol induced liver injury in Rats. J Ame Sci 6: 381-389.
37. Khoobchandani M, Ganesh N, Gabbanini S, Valgimigli L, Srivastava MM (2011) Phytochemical potential of *Eruca sativa* for inhibition of melanoma tumor growth. Fitoterapia 82: 647-53.
38. Shaikh MNAl, Wahab TAA, Kareem SHA (2014) Hypothyroidism induced by carbimazolein diabetic mice and its management using parsley and *Eruca sativa* oil. J Pharma Bio Sci 9: 24-27.
39. Ahmed DF (2014) Role of *Eruca sativa* oil treatment on profenofos supplemented female albino rats. Egypt J Exp Biol (Zool) 10: 137-143.
40. Gulfraz M, Sadiq A, Tariq H, Rahmatullah Q, Zenat A (2010) Phytochemical analysis and antibacterial activity of *Eruca sativa* seed. Pak J Bot PP: 240-243.
41. Bansal PS, Medhe N, Ganesh M, Srivastava MM (2015) Antimelanoma potential of *Eruca sativa* seed oil and its bioactive principles. Ind J Pharma Sci 77: 208-217.
42. Lertsatitthanakorn P, Taweechaisupapong S, Aromdee C, Khunkitti W (2006) *In vitro* bioactivities of essential oils used for acne control. IJA 16: 43-49.