



Modulating efficacy of foeniculum vulgare mill. essential oil in rats exposed to oxidative stress

A. S. Nada¹, O. M. Ahmed², E. S. Abdel-Reheim¹, N. E. Amin¹ and M. M. Ali¹.

**Drug Radiation Research Department, National Centre for Radiation Research and Technology (NCRRT), Atomic Energy Authority, P. O. Box: 29 Nasr City, Cairo, Egypt.*

*** Zoology Department, Faculty of Science, Beni-Suif University*

E-mail: Ashnada59@hotmail.com

Received:03/11/2010.

Accepted:29/12/2010.

ABSTRACT

This study was conducted to evaluate the modulating efficacy of prolonged oral administration of *Foeniculum vulgare* Mill. essential oil (FEO) against gamma irradiation-induced oxidative stress in male rats. To achieve the ultimate goal of this study, 32 male Swiss Albino rats were divided into 4 groups, each consists of 8 rats: Group 1 was normal control group, group 2 irradiated with a single dose (6.5 Gy), and sacrificed 7 days irradiation, group 3 received FEO (250 mg/kg body wt) for 28 successive days by intra-gastric gavages and group 4 received treatment of FEO for 21 days, then was exposed to gamma-radiation (6.5Gy), followed by treatment with FEO 7days later to be 28 days as group 3. Sacrifice of all animals was performed after 28 days from the beginning of the experiment. Liver and kidney glutathione (GSH) contents; lipid peroxidation (TBARS) and metallothioneins (MTs) levels were determined. In addition, levels of some trace elements (Fe, Cu, Zn and Se) in liver and kidney tissues were also estimated. Rats exposed to gamma radiation exhibited a profound elevation in TBARS and MTs level of liver and kidney tissues. Noticeable drop in liver and kidney glutathione contents were also observed. Tissue organs displayed some changes in trace element concentrations. Rats treated with fennel oil before and after whole body gamma irradiation showed significant modulation in the activity of antioxidants (GSH, MTs). FEO was also effective in minimizing the radiation-induced increase in TBARS as well as trace elements alteration in some tissue organs comparing with irradiated control rats. It could be concluded that FEO exerts a beneficial protective potential against radiation-induced biochemical perturbations and oxidative.

Keywords: *Fennel oil, oxidative stress, trace elements, γ -rays, rats.*

INTRODUCTION

Ionizing radiations are known to induce oxidative stress through the generation of reactive oxygen species (ROS) resulting in an imbalance in the pro-oxidant, antioxidant status in the cells ⁽¹⁾. Multiple processes may lead to cellular damage under irradiation but the generation of oxygen free radicals followed by TBARS may be one of the key components in this cascade of events. Radiation generates ROS that interact with cellular molecules, including DNA, lipids, and proteins ⁽²⁾. Because of the lipid component in the membrane, TBARS is reported to be particularly susceptible to radiation damage ⁽³⁾. In addition, cell TBARS is related to radiation-induced cell death, changes in membrane fluidity ⁽⁴⁾ and in the activities of some membrane enzymes ⁽⁵⁾. Furthermore, it has been shown that irradiation causes a marked change in the plasma total antioxidant capacity and total body irradiation is known to cause a pronounced decrease in antioxidant capacity and large increase in oxidant stress ⁽⁶⁾.

Natural antioxidants can protect the human body from free radicals and retard the progress of many chronic diseases as well as retard lipid oxidative rancidity in foods ^(7, 8). Plant tissue is the main source of α -tocopherol, ascorbic acid, carotenoids and phenolic compounds ⁽⁹⁾. Flavonoids and other plant phenolics have been reported to have multiple biological effects such as antioxidant activity, anti-inflammatory action, inhibition of platelet aggregation and antimicrobial activity ^(10, 11).

Fennel is an annual, biennial or perennial aromatic herb employed in culinary preparations for flavoring bread and pastry, in candies and in alcoholic liqueurs as well as in cosmetic and medicinal preparations ⁽¹²⁾. Trans-anethole, fenchone and estragole are the most important volatile components of *Foeniculum vulgare* volatile oil ^(13, 14). It has been reported that FEO-induced hepatoprotective effects ⁽¹⁵⁾; exhibited inhibitory effects against acute and sub acute inflammatory diseases and allergic reactions and showed a central analgesic effect ⁽¹⁶⁾, produced antioxidant activities including the radical scavenging effects, inhibition of hydrogen peroxides H₂O₂ and Fe²⁺ chelating activities ⁽¹⁷⁾, have estrogenic activities, increase milk secretion, promote menstruation, facilitate birth, alleviate the symptoms of the male climacteric, and increase libido ⁽¹⁸⁾. It also have properties for the prevention and therapy of cancer ^(19, 20), antitumor activities in human prostate cancer ⁽²¹⁾, and antimicrobial properties ⁽²²⁾. Furthermore, fennel has a bronchodilatory effect ⁽²³⁾ as well as

immunomodulatory activities by enhancing natural killer cell functions, the effectors of the innate immune response^(24, 25). Singh *et al.*⁽²⁶⁾ showed that both volatile oil and extract showed strong antioxidant activity. Toda⁽²⁷⁾ revealed that several aromatic herbs including *Foeniculi Fructus* have inhibitory effects on TBARS or protein oxidative modification by copper. Tognolini *et al.*⁽²⁸⁾ stated that FEO and its main component anethole, demonstrate a safe antithrombotic activity that seems due to their broad spectrum antiplatelets activity, clot destabilizing effect and vaso-relaxant action.

Copper, Iron, zinc and selenium are essential metalloelements. These essential metalloelements as well as essential amino acids, essential fatty acids and essential cofactors (vitamins) are required by all cells for normal metabolic processes but can't be synthesized *de novo* and dietary intake and absorption are required to obtain them⁽²⁹⁾. Copper, iron, manganese and zinc dependent enzymes have roles in protecting against accumulation of ROS as well as facilitating tissue repair⁽³⁰⁾. These essential trace elements are involved in multiple biological processes as constituents of enzyme system including superoxide dismutase (Cu, Zn, Mn, SODs), oxide reductase, glutathione (GSHpx, GSH, GST), MTs *etc.*⁽³¹⁾. These metals increased the antioxidant capacities, the induction of metalloelements dependent enzymes, these enzymes play an important role in preventing the accumulation of pathological concentration of oxygen radicals or in repairing damage caused by irradiation injury⁽³²⁾. The highly content of essential trace elements in FEO may offer a medicinal chemistry approach to overcoming radiation injury⁽³¹⁾.

In view of these considerations, the present study was carried out to evaluate the possible modulator effects of prolonged administration of FEO against gamma irradiation-induced oxidative stress and trace elements changes in liver and kidney of male rats.

MATERIALS AND METHODS

Experimental animals

Male Swiss albino rats (Sprague Dawely strain), weighting 120-150g, were obtained from the Egyptian Organization for Biological Products and Vaccines. They were kept for about 7 days, before the onset of the experiment, under observation to exclude any intercurrent infection and to acclimatize the laboratory conditions. The animals were kept in metal cages with good aerated covers at normal atmospheric temperature (25+ 5°C) and at normal daily 12 h dark/light cycles. They were fed commercial food pellets and provided with tap

water *adlibitum*.

Radiation processing

Whole body gamma irradiation was performed with a Canadian gamma cell 40-Cesium, ^{137}Cs biological sources, belonging to NCRRT, at Cairo, Egypt. The radiation dose level was 6.5 Gy.

Treatment

FEO purchased from local market (EL CAPTAIN pharmaceutical Co.) was supplied to animals as a single dose (250 mg/ kg body wt) according to Özbek *et al.*⁽³³⁾ by intragastric gavages.

Experimental design

After an adaptation period of one week, the animals were divided into four groups, each of 8 rats. **Group 1:** normal control group. **Group 2:** the animals were subjected to a single dose of whole body gamma irradiation (6.5 Gy), and were sacrificed after 7 days of irradiation. **Group 3:** the animals received FEO (250 mg/ kg body wt) for 28 consecutive days, through oral administration by intra-gastric gavages. **Group 4:** the animals received treatment FEO for 21 days, then were exposed to gamma radiation (6.5Gy), followed by treatment with FEO 7 days later to be 28 days as group 3. Rats were sacrificed after 7 days of gamma irradiation, liver and kidney were taken for biochemical analysis.

Biochemical analysis

GSH reduced was determined according to the method of Beutler *et al.*⁽³⁴⁾. The lipid peroxidation products were estimated as TBARS according to Yoshioka *et al.*⁽³⁵⁾. MTs determined according to the method described by Onosaka and Cherian³⁶.

Instrumentation

Trace elements were determined in plants and animals tissue samples. After digestion in pure concentrated nitric acid and hydrogen peroxide at 5:1 ratio (IAEA³⁷), sample digestion was carried out using Milestone MLS-1200 Mega, High performance Microwave Digestor Unit, Italy. The selected elements were estimated using UNICAM939 Atomic Absorption Spectrometry, England, equipped with deuterium back ground correction. All solutions were prepared with ultra pure water with a specific resistance $18\Omega\text{cm}^{-1}$, obtained from ELGA, Ultra Pure Water Station, England. The biochemical

assay was achieved using Herios γ UV/VIS Spectrophotometers, Japan.

Statistical analysis

The data were analyzed using one-way analysis of variance (ANOVA) followed by LSD test to compare various groups with each others using PC-STAT program (University of Georgia) coded by Rao *et al.*⁽³⁸⁾. Results were expressed as mean \pm standard error (S.E.) and values of $P>0.05$ were considered non-significantly different, while those of $P<0.05$ and $P<0.01$ were considered significant and highly significant, respectively. F probability expresses the general effect between groups.

RESULTS

In Table 1, a highly significant increase ($P<0.01$) in the activity of metallothioneins and TBARS concentration in the liver homogenate of irradiated rats were determined with percentage change of 59.83% and 29.35 %, respectively. While irradiation produced significant depletion in reduced glutathione (-29.27%) concentration ($P< 0.01$), when compared with control rats. Treatment with FEO caused non-significant changes in liver reduced GSH, levels of TBARS and a highly significant ($P<0.01$) increase in MTs compared to normal control group recording percentage changes of 0.33%, 5.63% and 40.82%, respectively. Administration of fennel oil before and after irradiation produced a highly significant ($P<0.01$) increase in GSH compared to irradiated group, recording percentage change from -29.27 to -14.56% from control group, while a marked modulation in TBARS was observed and a decrease in the levels of TBARS was recorded compared with the irradiated rats (<0.01). FEO treatment minimized the percentage of TBARS from 29.35% to 8.83%. However, a significant decrease of MTs from 59.83 to 35.33% was recorded, in comparison with irradiated group.

Table 1: Effect of *Foeniculum vulgare* essential oil (FEO) on antioxidant status in liver fresh tissues of different animal groups.

Groups	GSH (mg/ g tissue)	TBARS (nmol/ g tissue)	MTs (mg/ g tissue)
Control	74.92 \pm 2.096	36.25 \pm 1.46	27.34 \pm 0.45
Irradiated	52.99 \pm 0.87*	46.89 \pm 0.76*	43.7 \pm 1.025*
% Change	-29.27	29.35	59.83
Treated	74.67 \pm 1.14	38.29 \pm 0.86	38.50 \pm 0.72*
% Change	0.33	5.63	40.82
IRR+ FEO	64.01 \pm 1.31*#	39.45 \pm 0.99*#	37 \pm 0.77*#
% Change	-14.56	8.83	35.33

The % change of control.

Values are expressed as mean \pm S.E of 8 observations.

*Significant difference when comparing with the corresponding value of control rats.

#Significant difference when comparing with the corresponding value of irradiated rats.

In Table 2, a single dose (6.5 Gy), resulted in a highly significant increase ($P < 0.01$) in metallothioneins and TBARS concentrations in the kidney homogenate of irradiated rats ($P < 0.001$), with percentage change of 67.27% and 61.14%, respectively. On the other hand, a highly significant depletion in GSH was observed as compared to control group ($P < 0.01$) recording percentage change of -53.36%. Group (3) treated with FEO showed non-significant changes in kidney levels of reduced glutathione (GSH), TBARS, and MTs, recording percentage changes of -2.48%, 3.42% and -4.76% of the control level, respectively. Administration of fennel oil to irradiated rats produced a highly significant increase in kidney GSH level as compared to the irradiated group; the values returned toward normal level to be -20.37% of the normal control instead of -53.36% for irradiated group. On the other hand, TBARs and MTs levels were highly significantly decreased as compared to irradiated group; with a percentage change of 32.77% and 8.79% instead of 61.14% and 67.27%, respectively.

Table 2: Effect of Foeniculum vulgare essential oil (FEO) on antioxidant status in kidney fresh tissues of different animal groups.

Groups	GSH (mg/ g tissue)	TBARS (nmol/ g tissue)	MTs (mg/ g tissue)
Control	66.55 ± 0.88	43.51±0.98	22.06 ± 0.66
Irradiated	31.04 ± 0.83*	70.11±1.04*	36.9 ± 1.02*
% Change	-53.36	61.14	67.27
Treated	64.90± 1.52	45.00 ± 0.7	21.01 ± 0.56
% Change	-2.48	3.42	-4.76
IRR+ FEO	52.99 ± 0.95*#	57.77±0.41*#	24 ± 0.47#
% Change	-20.37	32.77	8.79

Legends are as in Table (1)

Concerning the concentration levels of Zn in different tissue organs, it was observed that whole body gamma irradiation at 6.5 Gy induced-significant elevation ($P < 0.01$) in Zn concentration levels in liver with percentage change of 14.05% and significant decrease ($P < 0.01$) in kidney (-8.17%). Treatment with fennel oil induced non-significant change in zinc levels in liver (4.11%) and significant increase kidney (6.13%) in comparison with the control. The combined treatment of irradiation and fennel oil, induced-significant retention of zinc in liver (15.92%) and non-significant changes were recorded in kidney (-2.16%) in comparison with control group. While, in comparison with irradiated group there was significant increase in kidney and non-significant

increase in liver, Table 3.

Table 3: Concentration levels of Zn ($\mu\text{g/g}$ fresh tissue) in liver and kidney tissues of different animal groups.

Groups	Liver	Kidney
Control	29.46 \pm 0.43	30.97 \pm 0.71
Irradiated	33.6 \pm 0.65*	28.44 \pm 0.6*
% Change	14.05	-8.17
Treated	30.76 \pm 0.56	32.87 \pm 0.56*
% Change	4.11	6.13
IRR+ FEO	34.15 \pm 0.56*	30.3 \pm 0.55#
% Change	15.92	-2.16

Legends are as in Table (1)

Concerning the concentration levels of copper, irradiation induced significant reduction ($P < 0.01$) in copper levels in liver and kidney with percentage change of -22.48% and -16.61%, respectively. Treatment with fennel oil induced non-significant ($P > 0.05$) increase in copper levels in kidney with percentage change of 9.82% and non significant decrease in liver -7.49%. While in irradiated treated animals there were non-significant ($P > 0.05$) changes in copper levels in liver 4.13% and significant decrease in kidney -24.10% in comparison with control group while in comparison with irradiated group, there was a significant increase in liver and non significant change in kidney, Table 4.

Table 4: Concentration levels of Cu ($\mu\text{g/g}$ fresh tissue) in liver and kidney tissues of different animal groups.

Groups	Kidney	Liver
Control	3.87 \pm 0.14	5.60 \pm 0.30
Irradiated	3 \pm 0.05*	4.67 \pm 0.18*
% Change	-22.48	-16.61
Treated	3.58 \pm 0.09	6.15 \pm 0.19
% Change	-7.49	9.82
IRR+ FEO	4.03 \pm 0.12#	4.25 \pm 0.11*
% Change	4.13	-24.10

Legends are as in Table (1)

In Table 5, the levels of iron were significantly increased in liver of irradiated group with percentage changes of 128.8%, while it insignificantly decreased in kidney (-3.09%). Fennel treatment induced non significant change in liver (3.86%) and kidney (0.52%). Fennel treatment with irradiation induced significant increase of iron levels in kidney (12.09%) in comparison with the control. In liver, (115.22%) Fe concentration was significantly increased in comparison with normal control group and was significantly decreased when

compared to irradiated group.

Table 5: Concentration levels of Fe ($\mu\text{g/g}$ fresh tissue) in liver and kidney tissues of different animal groups.

Groups	Kidney	Liver
Control	80.01 \pm 0.70	76.58 \pm 1.30
Irradiated	183.07 \pm 3.1*	74.21 \pm 3.01
% Change	128.81	-3.09
Treated	83.1 \pm 0.73	76.98 \pm 0.92
% Change	3.86	0.52
IRR+ FEO	172.2 \pm 3.9* [#]	85.84 \pm 1.7* [#]
% Change	115.22	12.09

Legends are as in Table (1)

The concentration levels of selenium were significantly increased ($P < 0.01$) in liver (25.81%) and non-significantly decreased in kidney (-4.77%) as a result of whole body gamma irradiation. Fennel oil treatment induced a significant increase in liver (85.80%) and kidney (12.48%) compared to control group. The combined treatment and irradiation induced more selenium retention in liver (26.48%) and non significant increase in kidney (7.99%) in comparison with control while in comparison with irradiated rats; there was significant increase in kidney and non significant increase in liver, Table 6.

Table 6: Concentration levels of Se (ng/g fresh tissue) in liver and kidney tissues of different animal groups.

Groups	Kidney	Liver
Control	126.7 \pm 4.08	495.32 \pm 16.9
Irradiated	159.4 \pm 6.16*	471.7 \pm 14.94
% Change	25.81	-4.77
Treated	235.42 \pm 8.4*	557.14 \pm 16.55*
% Change	85.80	12.48
IRR+ FEO	160.25 \pm 6.9*	534.9 \pm 22.5 [#]
% Change	26.48	7.99

Legends are as in Table (1)

Table 7: Concentration levels of Fe, Cu, Zn, Mn, Ca, and Mg ($\mu\text{g/g}$) and Se (ng /g) dry wt in fennel plants.

Groups	Concentration	Element	Concentration
Fe	128.77 \pm 1.24	Ca	4073.4 \pm 83.91
Cu	12.14 \pm 0.08	Mg	(151.37 \pm 0.94) \times 10 ²
Zn	32.5 \pm 0.99	Se	695.7 \pm 7.28
Mn	65.3 \pm 2.33		

Each value represents the mean of 8 samples recorded \pm S.E.

DISCUSSION

In the present study, gamma irradiation (6.5 Gy) induced significant increase in the oxidation of lipid, associated with depletion in GSH content. The significant acceleration in TBARS content, is attributed to the peroxidation of the membrane unsaturated fatty acids due to free radical propagation concomitant with the inhibition in bio-oxidase activities⁽³⁹⁾. Moreover, Chen *et al.*⁽⁴⁰⁾ attributed the increase in TBARS level after irradiation to inhibition of antioxidant enzymes activities. Ionizing radiations produced peroxidation of lipids leading to structural and functional damage to cellular membranous molecules directly by transferring energy or indirectly by generation of oxygen derived free radical (OH), superoxide (O₂⁻) and nitric oxide (NO) which are the predominant cellular free radicals^(41, 42). The polyunsaturated fatty acids present in the membranes phospholipids are particularly sensitive to attack by hydroxyl radicals and other oxidants. In addition to damaging cells by destroying membranes, TBARS can result in the formation of reactive products that themselves can react with and damage proteins and DNA⁽⁴³⁾. Oxidative stress leads to over production of NO, which readily reacts with superoxide to form peroxynitrite (ONOO⁻) and peroxynitrous acid which can initiate lipid peroxidation⁽⁴⁴⁾.

Also, the present results revealed a significant depletion in glutathione after radiation exposure, which might resulted from diffusion through impaired cellular membranes and/or inhibition of GSH synthesis. Pulpanova *et al.*⁽⁴⁵⁾ explained the depletion in GSH content by irradiation by the diminished activity of GSR and to the deficiency of NADPH which is necessary to change oxidized glutathione to its reduced form. These data are consistent with the previous reports of Osman⁽⁴⁶⁾ and Ramadan *et al.*⁽⁴⁷⁾. The depletion in glutathione and increase in TBARS are in agreement with those recorded by Bhatia and Jain⁽⁴⁸⁾ and Koc *et al.*⁽⁴⁹⁾ who reported a significant depletion in the antioxidant system accompanied by enhancement of lipid peroxides after whole body gamma-irradiation.

Results also indicate that MTs were increased after treatment with gamma-irradiation. These data are in agreement with those reported by Koropatnick *et al.*⁽⁵⁰⁾ and Nada and Azab⁽⁵¹⁾ who stated that the induction of metallothioneins by irradiation appears to be due to an increased synthesis of their MTs. Metallothioneins are also involved in protection of tissues against various forms of oxidative stress⁽⁵²⁾. Induction of MTs biosynthesis is involved

in a protective mechanism against radiation injuries ⁽⁵³⁾.

The accumulation of certain metals in the organs could be attributed to the disturbance in mineral metabolism after radiation exposure ⁽⁵⁴⁾. Radiation also induced significant alterations in the levels of MTs in different tissue organs. Concerning the concentration levels of zinc in different tissue organs, it could be observe that irradiation induced increases in zinc in liver. Similar observations were obtained by Yukawa *et al.* ⁽⁵⁵⁾ and Smythe *et al.* ⁽⁵⁶⁾ who found that whole body gamma-irradiation induced an elevation of zinc in different organs. Okada ⁽⁵⁷⁾ recognized that lymphoid organs as spleen, lymph nodes and bone marrow are extremely radiosensitive. He explained that zinc derived from these tissues that were damaged by irradiation could accumulate in liver or kidney, thus stimulating the induction of MTs. Sasser *et al.* ⁽⁵⁸⁾ reported that the injury produced by the radiation was probably responsible for the increased uptake of zinc by erythrocytes. The injury may have caused a shift of plasma proteins affecting the availability of zinc to the erythrocytes or caused erythrocytes to have an altered affinity for zinc.

In the present study, a depression in the copper levels of liver and kidney were recorded in the tissue of irradiated animals. Similar observations were obtained by many investigators ^(54, 55, 56, 59) who recorded that irradiation induced decrease in copper in liver and kidney. Cuproenzymes are able to reduce oxygen to water or to hydrogen peroxide. Cuproenzymes possess high affinity for oxygen, depending on the number of incorporated copper atoms ⁽⁶⁰⁾, these may explain the decreases in copper due to excess utilization of cuproenzymes after irradiation, or may be due to *de novo* synthesis of Cu-SODs and catalase which prevent the formation of O₂ and hydroxyl radical associated with irradiation ⁽⁶¹⁾.

Radiation induced a significant increase of iron in liver while in kidney there was a non significant change. These results are in full agreement with Ludewig and Chanutin ⁽⁶²⁾ Olson *et al.* ⁽⁶³⁾, Beregovskaia *et al.* ⁽⁶⁴⁾ and Nada *et al.* ⁽⁵⁹⁾ who reported that the increase in value of iron may be related to the inability of bone marrow to utilize the iron available in the diet and released from destroyed red cells. While in the kidney, the changes in the iron contents were comparatively small. The kidney is capable of forming ferritin from iron released from hemoglobin. Increased iron level may be due to oxidative stress inducing proteolytic modification of ferritin ⁽⁶⁵⁾ and transferring ⁽⁶⁶⁾. Iron overload is associated with liver damage, characterized by massive iron

deposition in hepatic parenchymal cells, leading to fibrosis and eventually to hepatic cirrhosis.

The results of the present study showed a significant increase of selenium level in liver of irradiated group and a non-significant decrease in kidney. The increases of Se in liver may be attributed to the re-synthesis of glutathione (*de novo* synthesis). Yukawa *et al.*⁽⁵⁵⁾ and Smythe *et al.*⁽⁵⁶⁾ recorded a decrease in Se concentration after irradiation at doses of 4, 5.5 and 6 Gy. The decrease of selenium might indirectly contribute to the decrease of GSH content and its related antioxidant enzymes namely glutathione peroxidase⁽⁶⁷⁾. This idea is supported by the well known fact that Se is present in the active site of the antioxidant enzyme GSH-Px⁽⁶⁸⁾ and that Se deficiency decreased GSH-px in response to radiation treatments⁽⁶⁹⁾. It has been reported that selenium plays important roles in the enhancement of antioxidant defense system^(70, 71); increases resistance against ionizing radiation as well as fungal and viral infections⁽⁷²⁾.

On the other hand, the present study revealed that long term pretreatment of FEO for 28 days to irradiated animals; induced a significant amelioration in radiation-induced changes of the tested parameters. It means that FEO has a physiologic antioxidant role. Essential oils, as natural sources of phenolic component attract investigators to evaluate their activity as antioxidants or free radical scavengers. The essential oils of many plants have proven a radical-scavenging and antioxidant properties in the 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical assay at room temperature⁽⁷³⁾. The phenolic compounds are very important plant constituents because of their scavenging ability due to their hydroxyl groups⁽⁷⁴⁾. The phenolic compounds may contribute directly to antioxidative action⁽⁷⁵⁾.

Fennel essential oil possess physiologic antioxidant activities including the radical scavenging effect, inhibition of hydrogen peroxides H₂O₂ and Fe chelating activities where it can minimize free radicals which initiate the chain reactions of TBARS. The antioxidant effect is mainly due to phenolic compounds which are able to donate a hydrogen atom to the free radicals thus stopping the propagation chain reaction during TBRS process^(76, 77). These may explain the significant amelioration of TBRS induced by irradiation.

Administration of FEO protects against the endogenous GSH depletion resulting from irradiation. The increased GSH level suggested that protection of FEO may be mediated through the modulation of cellular antioxidant levels.

These results suggested that FEO has a free radical scavenging activity. Many investigators showed that FEO has strong antioxidant effect^(78, 26, 79) through its phenolic compounds. Reicks and Crankshaw⁽⁸⁰⁾ stated that D-limonene increases the concentration of GSH in the liver. The antioxidant species such as anethole, β -myrcene and D-limonene present in fennel as mentioned earlier might also interact with ROS and neutralize them leading to chemo-preventive effect. An increase in the antioxidant enzyme activity and a reduction in the TBARS by *Foeniculum vulgare* may result in reducing a number of deleterious effects due to the accumulation of oxygen radicals, which could exert a beneficial action against pathological alterations⁽¹⁶⁾.

Regarding the main principal constituents of *Foeniculum vulgare* plants, considerable concentrations of essential trace element were identified. These essential trace elements are involved in multiple biological processes as constituent of enzyme systems including SOD, oxido-reductases, GPx and MTs^(81, 82). Sorenson⁽³¹⁾ has found that iron, selenium, manganese, copper calcium, magnesium and zinc-complex prevent death in lethal irradiated mice due to facilitation of *de novo* synthesis of essentially metalloelemets-dependent enzymes especially MTs. These enzymes play an important role in preventing accumulation of pathological concentration of oxygen radicals or in repairing damage caused by irradiation injury.

On the basis of the present observation it could be suggested that FEO essential oil which contains a mixture of bioactive compounds as well as essential trace elements could be of value to stimulate the body self defense mechanisms against oxidative stress by the induction of MTs and the maintenance of glutathione contents in addition to minimization of TBARS and trace element alteration.

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القدرة الوقائية لزيت نبات الشمر فى الجرذان المعرضة للإجهاد التاكسدى

أحمد شفيق ندا * أسامة محمد احمد* * إيمان صلاح عبد الرحيم ** نور الدين أمين محمد * ، مها محمود على*

* قسم البحوث الدوائية الإشعاعية، المركز القومي لبحوث وتكنولوجيا الإشعاع- هيئة الطاقة الذرية ، ص.ب. 29. مدينة نصر، القاهرة ، مصر.
** قسم علم الحيوان ، كلية العلوم، جامعة بنى سويف

تهدف هذه الدراسة إلى تقييم الدور الوقائي لزيت نبات الشمر ضد التغيرات البيوكيميائية التي تحدث نتيجة للتعرض للإشعاع. ولتحقيق ذلك تضمنت هذه الدراسة استخدام عدد (32) من ذكور الجرذان البيضاء التى يتراوح وزنها من 120-150 جرام وقسمت إلى أربع مجموعات وتحتوى كل مجموعة على (8 جرذان): المجموعة الأولى/ جرذان المجموعة الضابطة، المجموعة الثانية / جرذان تم تعرضها إلى جرعة مفردة من أشعة جاما (6.5 جراى) و تم ذبحها بعد 7 أيام من التشيع ، المجموعة الثالثة / جرذان تمت معالجتها بزيت نبات الشمر (250 مللي جرام/كجم) لمدة 28 يوما متتالى عن طريق الفم ، المجموعة الرابعة / جرذان تمت معالجتها بزيت نبات الشمر (250 مللي جرام/كجم) لمدة 21 يوما ثم تم تعرضها لأشعة جاما (6.5 جراى) ثم عولجت مرة أخرى بزيت نبات الشمر لمدة 7 أيام لتكمل 28 يوما (كما فى المجموعة الثالثة). وفى نهاية التجربة تم ذبح الجرذان وقد تم قياس بعض الدلالات المضادة للأكسدة (محتوى الجلوتاثيون المختزل والميتالوثيونين) وكذلك دراسة التغيرات التى تحدث فى مستوى الدهون فوق مؤكسدة (المواد المتفاعلة مع حمض الثيوبوربيتيورك) فى الكبد والكلى مع تقدير معدلات بعض العناصر الشحيحة (الحديد ، النحاس ، الزنك والسيلينيوم) فى أنسجة كل من الكبد والكلى. وتشير النتائج إلى أن الجرذان التى تعرضت للإشعاع (6.5 جراى) قد أظهرت ارتفاعا فى دهون فوق مؤكسدة (المواد المتفاعلة مع حمض الثيوبوربيتيورك) والميتالوثيونين التى تمت دراستها وانخفاض ملحوظا فى مستوى الجلوتاثيون فى كلا من أنسجة الكبد والكلى ومصاحب بتغيرات طفيفة فى العناصر الشحيحة نتيجة الإجهاد التاكسدى لأشعة جاما. وأسفرت هذه الدراسة إلى أن المعالجة بزيت نبات الشمر (250 مللي جرام /كيلو جرام من وزن الجرذ) قبل وبعد التعرض للإشعاع أدى إلى تحسن فى القياسات الكيميائية الحيوية المختلفة وزيادة فى مضادات الأكسدة (الجلوتاثيون والميتالوثيونين) وانخفاض نسبة الدهون فوق مؤكسدة وتقليل الخلل الذى يحدث فى بعض العناصر الشحيحة. خلصت الدراسة إلى أن المعالجة بزيت الشمر له دور وقائى ضد الإشعاع المحفز لبعض التغيرات البيوكيميائية والإجهاد التاكسدى.