*Research Article*

# Histological study on the Effect of Selenium Nanoparticles on Cadmium-induced Thyrotoxicity in Adult Male Albino Rat

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## Abstract
**Back ground:** Cadmium is a widespread and serious material that leads to different harmful cellular changes up to death. Se is a well-known element for its antioxidant role in living systems of humans and animals. Selenium nanoparticles have the ability to act as an antioxidant with reduced risk of ordinary selenium toxicity. **Aim of work:** is to investigate the effect of Selenium nanoparticles on cadmium induced thyrotoxicity in adult male albino rats. **Material and methods:** A total of 38 adult male albino rats were divided into four groups. The control group (8 rats) was given only distilled water for 35 days; the cadmium-treated group was given CdCl2 in their drinking water for 35 days; the nanoselenium-treated group was given $Na_2SeO_3$ in their drinking water for 35 days and the nanoselenium-cadmium-treated group was given $Na_2SeO_3$ and CdCl2 in their drinking water for 35 days. The animals of all groups were sacrificed at the same time and their thyroid glands were rapidly dissected out. The specimens of each group were processed for light and immunohistochemical studies. They were stained with hematoxylin and eosin, masson's trichrome, and inducible nitric oxide synthase. Quantitative morphometric, and statistical studies were performed. **Results:** Picture of cytotoxicity was visible in cadmium-treated thyroid sections in the form of disorganized follicles of varying diameters, with a predominance of smaller follicles. The follicular epithelial cells appeared to be enlarged and had a vacuolated cytoplasm. In addition to reduced or absent colloid. The thyroid gland of nanoselenium–cadmium-treated animals showed a nearly normal follicular structure.
**Conclusion:** In experimental animal the administration of nanoselenium in response to an increased risk of exposure to cadmium compounds has a protective effect against their harmful effects.
**Keywords**: cadmium, rats, nanoselenium, thyroid gland.

## Introduction
The thyroid is an essential endocrine gland and its secretions are metabolically pertinent as T3&T4[1]. Cadmium (Cd) is a widespread heavy metal pollutant, which can be discharged into the environment during industrial production, including the production of batteries, metal plating, pigments and plastics[2]. Human exposure to Cd occurs chiefly through inhalation or ingestion. Ten to fifty percent of inhaled cadmium dust and about five to ten percent of ingested Cd is absorbed depending on its particle size[3]. Cd is unique among other metals because of its toxicity at a very low dosage, long biologic half-life and its low rate of excretion from the body[4]. Its inability to undergo metabolic degradation to less toxic metabolites makes its exposure a serious health concern[5]. There is increasing concern about its contamination of soil and water as it bioaccumulate in the food chain, particularly in regions of inadequate exposure-control. Unlike most heavy metals, exposures to cd can induce disruptions in a number of biological activities and systems at relatively lower doses[6]. Selenium (se) is known for its antioxidant role in living systems that is considered an essential element for humans and animals[7]. Se is an important trace mineral of fundamental importance for human health especially function of the immune system[8]. Se supplementation shows promising potential for enhancing glutathione peroxidase (GPx) and other selenoprotein activity in various pathological conditions. The efficacy of selenium supply frequently depends on the bioavailability of the used compounds selenomethionine (SeMet) possesses excellent bioavailability and lower toxicity, and therefore it is more applicable for long-term administration[9]. Nanotechnology has enabled researchers to synthesize nanosize particles that possess

increased surface areas. Compared to conventional microparticles, it has resulted in increased interactions with biological targets[10]. Nano-selenium has potent effects on upregulation of GPx, and it yields more efficacious results in the induction of glutathione S-transferase over the short term, but it causes less oxidative stress[11].The size of nano-selenium plays an important role in its biological activity, as 5–200 nm nano Se can directly scavenge free radicals in vitro in a size-dependent fashion. 12 several methods, including γ-irradiation and laser ablation, have been applied to synthesize selenium nanoparticles, but the most used synthetic approach for preparing selenium nanoparticles is chemical reduction[12]. The aim of this work is to investigate the histological effect of selenium Nanoparticles on cadmium-induced thyrotoxicity in adult male albino rats.

## Material and Methods

The study was conducted at the animal house, Faculty of Veterinary medicine, Beni-suef University.

**Drugs and Chemicals:** Cadmium (cadmium chloride) particles were obtained from analytical chemistry department, Faculty of Pharmacy, Beni-Suef University, Egypt. Selenium nano-particles (320 nm particle size) were obtained from the Nanotechnology Unit, Faculty of Pharmacy, Beni-Suef University, Egypt. Ketamine andxylazine were obtained from pathology department, Faculty of Veterinary medicine, Beni-Suef University, Egypt.

**Animals:** Thirty eight male albino rats 5–6 months old, weighing 200–220 g were used in this study. Male rats only were included in this work to avoid the effect of female hormones on the thyroid function. Each group was housed in a separate cage in a constant temperature (22–24°C) and light-controlled room on an alternating 12:12 h light-dark cycle and had free access to food. Rats were fed a standard commercial pellet diet and were kept for one week before beginning the experiment for acclimatization. Animals were treated according to animal rights committee.

**Experimental design:** Rats were divided into four groups, Group I (8 rats): served as control and were given only distilled water for 35 days[13]. Two of them will be sacrificed with each experimental group, group II (10 rats) (cadmium-treated group): each rat received 200 parts per million (ppm) Cd (as $CdCl_2$) in their drinking water for 35 days[13], group III (10 rats) (Nano selenium-treated group): each rat

received 0.1 ppm Se (as $Na_2SeO_3$) in their drinking water for 35 days[14], group IV(10 rats) (experimental group): each rat was given Cd at the same dose, period and route of administration of the group II concomitantly with nano selenium at the same dose and route of group III for 35 days[13] &[14]. On the last day of the experiment, rats were sacrificed by ether over dose followed by opening the neck through an upper midline incision and specimens were taken from both thyroid lobes which were removed and separated from trachea. The obtained specimens were fixed immediately in 10% formol saline then washed and dehydrated in ascending grades of alcohol (70, 90, and 100%). This was followed by clearing in xylene. Embedding was done and paraffin blocks were obtained. Then 5-6 µm thick serial sections were cut and mounted on charged slides to prevent section loss. For immunohistochemical studies, sections were mounted on poly L-lysine coated slides.

**Paraffin sections**

were subjected for the following staining procedures H and E to demonstrate the histological changes[15], Masson's trichrome stain to demonstrate stromal changes in collagen deposition[15] and Immunohistochemical study, inducible Nitric Oxide Synthase (iNOS) to detect cellular oxidative stress[7].

**Morphometric study** [10]

Thyroid gland morphometry was performed to determine the thyroid gland activity of control versus treated rats. Data were obtained using "Leica Qwin 500 C" image analyzer computer system Ltd. (Cambridge, England) in histology department, faculty of medicine, Cairo University. Images were captured live on to the screen from sections under light microscope with video camera. The image analyzer consisted of a color video camera, Olympus microscope, colored monitor, hard disc of IBM personal computer connected to the microscope and controlled by "Leica Qwin 500 C" software. The image analyzer was first calibrated in

order to automatically convert the measurement units (pixels) produced by the image analyzer program into actual micrometer units. These parameters were measured, cell height, area percentage of collagen fibers deposition and area percentage of iNOS positive immunostaining

**Statistical analysis**[16]

All data were expressed as mean ± SD. A histogram was constructed, and statistical analysis was performed with a Student t-test to compare the means between the different groups. The P-value was calculated using the Graph Pad Software program (San Diego, California, USA), and the level of significance was considered as follows: P greater than 0.05, nonsignificant; P of up to 0.05, significant.

## Results

### Histopathological changes

The results of examination of the thyroid gland sections of the control group (group I) and Nano-Se treated group (group III) by light microscope were similar to the normal structure. Results of group II showed significant histopathological changes in the thyroid gland. H and E stained sections showed loss of the normal architecture of the thyroid follicles. There was absence of colloid in some follicles, desquamated epithelial cells in the lumens of thyroid follicles, increased epithelial cell height, cytoplasmic vacuolations, large interfollicualar space and congested blood vessels. Masson's trichrome sections showed increased collagen deposition.

The immunohistochemical stained sections showed strong iNOS immunoreaction. In group IV, concomitant treatment with Se-NPs effectively inhibited the Cd induced thyroid damage and succeeded in restoring the thyroid integrity induced by cadmium. H and E stained sections showed follicles of different diameters filled with colloid, with a predominance of larger follicles. There were decrease in the interfollicular space, apparent decrease in the follicular epithelial cell height but congested blood capillaries were still present. Masson's trichrome sections showed significant decrease in collagen deposition. The immunohisto-chemical stained sections showed weak iNOS immunoreaction.

Group I
Hematoxylin and Eosin stained sections

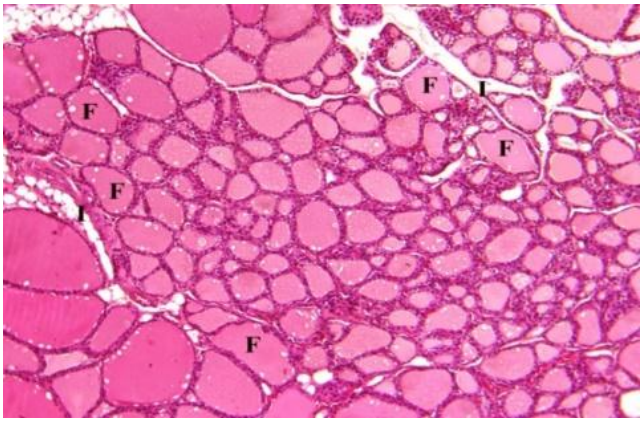



**Fig (1): A photomicrograph of a section of the thyroid gland of control group (group I) displaying normal thyroid follicles (F) and interlobular C.T. (I). (H. & E., x100)**

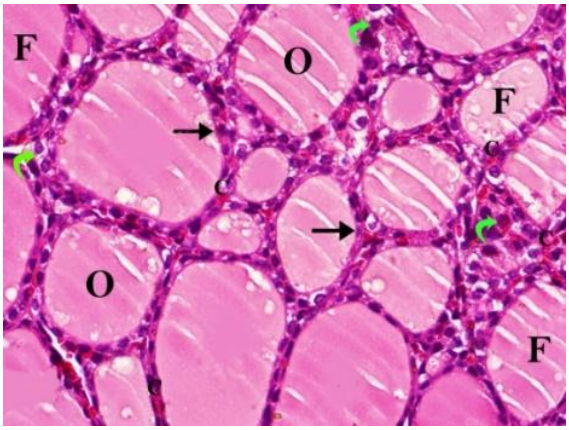



**Fig (2): A photomicrograph of a section of the thyroid gland of control group (group I) displaying follicles (F) filled with acidophilic colloid (O) and lined by simple cubical epithelium (arrows) and parafollicular cells (curved arrows). Simple cubical epithelium was formed of cubical cells with central rounded nuclei. Parafollicular cells were large with paler cytoplasm and present between the basement membrane and the follicular cells but they did not reach the follicular lumen. Note: inter follicular blood capillaries (C). (H. & E., x400)**

Masson's trichrome stained sections

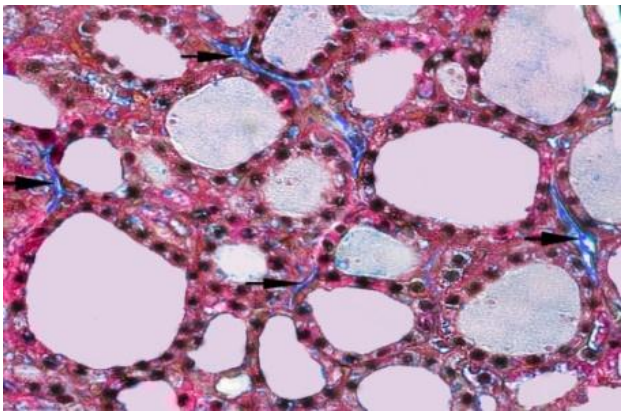


**Fig (3): A photomicrograph of a section of thyroid gland of the control group (group I) displaying minimal collagen distribution in the interfollicular C.T. (arrows) (Masson's trichrome., x400)**

Immunohistochemical study (iNOS) of thyroid gland sections

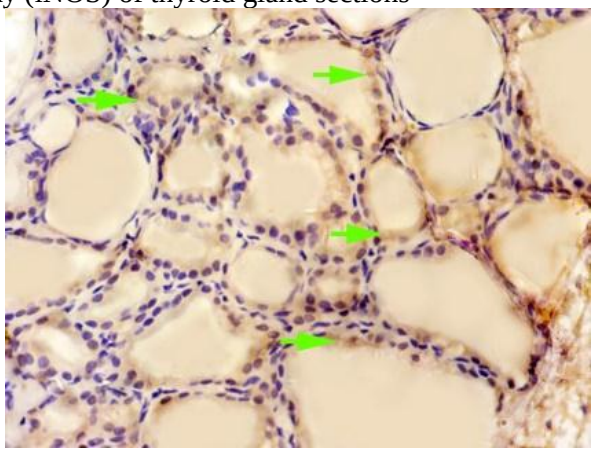


**Fig (4): A photomicrograph of a section of thyroid gland of the control group (group I) displaying weak iNOS cytoplasmic immunoexpression in the follicular epithelial cells (arrows). (iNOS immunostaining., x400)**

Group III
Hematoxylin and Eosin stained sections:

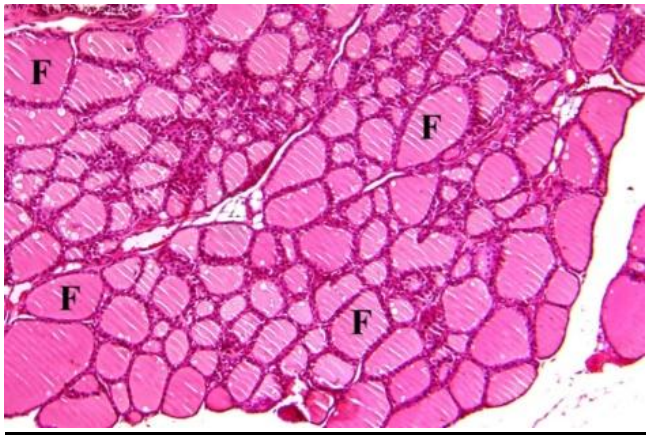



**Fig (5): A photomicrograph of a section of the thyroid gland of the nano selenium-treated group (group III) displaying normal thyroid follicles (F) (H. & E., x100)**

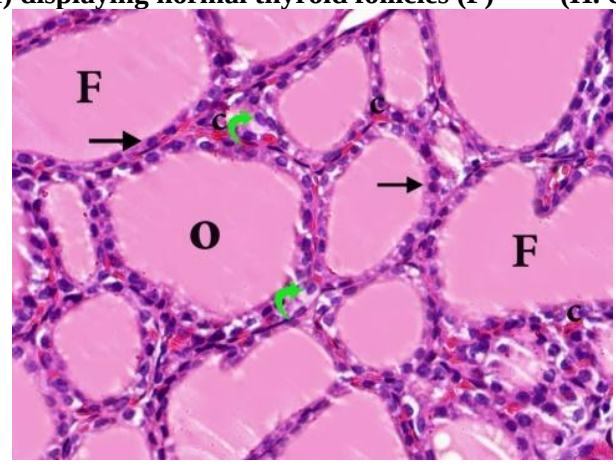



**Fig (6): A photomicrograph of a section of the thyroid gland of the nano selenium-treated group (group III) displaying follicles (F) filled with acidophilic colloid (O) and lined by simple cubical epithelium (arrows) and parafollicular cells (curved arrows). Simple cubical epithelium was formed of cubical cells with central rounded nuclei. Parafollicular cells were large with paler cytoplasm and present between the basement membrane and the follicular cells but they did not reach the follicular lumen. Note: inter follicular blood capillaries (C). (H. & E., x400)**

Masson's trichrome stained sections

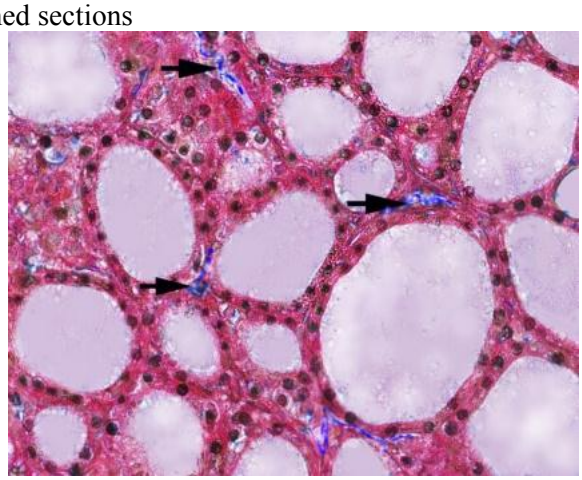


**Fig (7): A photomicrograph of a section of thyroid gland of the nano selenium-treated group (group III) displaying minimal collagen distribution in the interfollicular C.T. (arrows). (Masson's trichrome., x400)**

Immunohistochemical study (iNOS) of thyroid gland sections

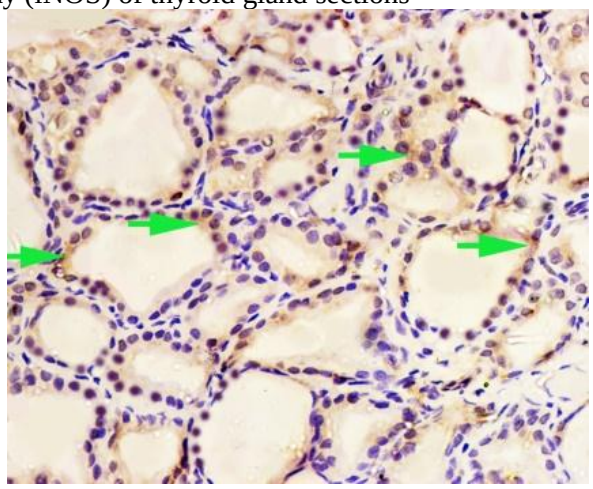


**Fig (8): A photomicrograph of a section of thyroid gland of the nano selenium-treated group (group III) displaying weak iNOS cytoplasmic immunoexpression in the follicular epithelial cells (arrows). (iNOS immunostaining., x400)**

Group II

Hematoxylin and Eosin stained sections:

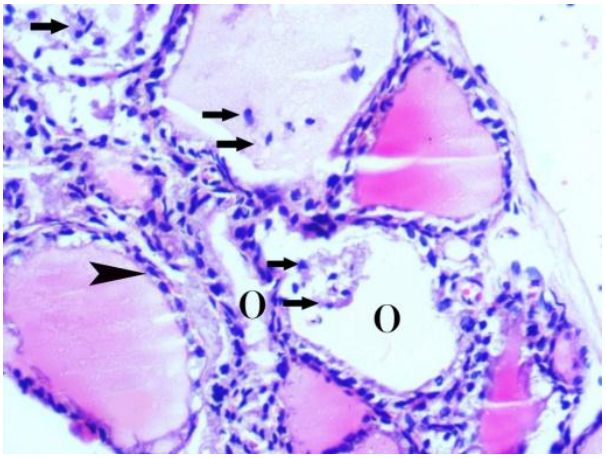



**Fig (9):A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying detached epithelial cells in the lumen of thyroid follicles (arrows), follicular epithelium is squamous (arrow head) and absence of colloid in some follicles (O). (H. & E., x400)**

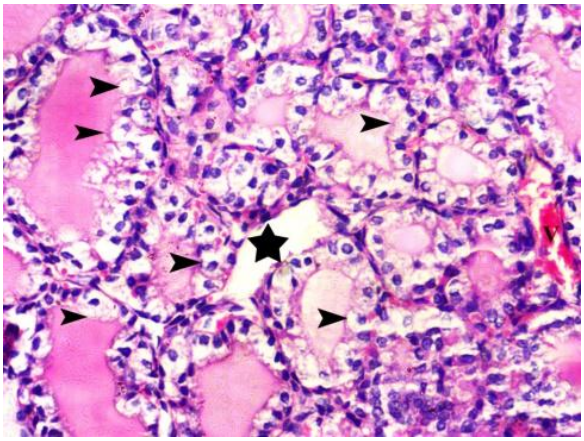


**Fig (10): A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying increased height of the follicular epithelial cells with vacuolations in their cytoplasm (arrow heads). There is dilated and congested blood vessel (V) and wide interfollicular space (star). (H. & E., x400)**

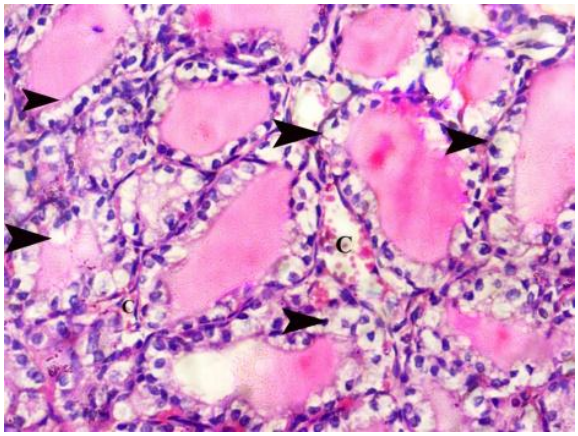



**Fig (11): A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying increased height of the follicular epithelial cells with vacuolations in their cytoplasm (arrow heads). Also there are dilated and congested interfollicular blood capillaries (C). (H. & E., x400)**

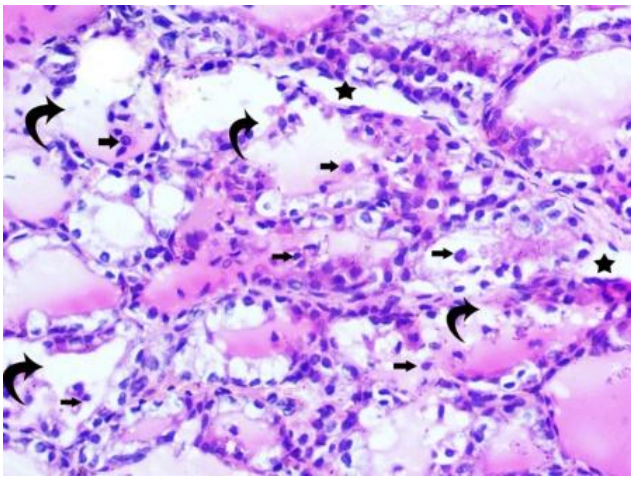


**Fig (12): A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying loss of normal architecture of the thyroid follicles (curved arrows), detached epithelial cells in thyroid follicles lumens (arrows) and wide interfollicular space (star). (H. & E., x400)**

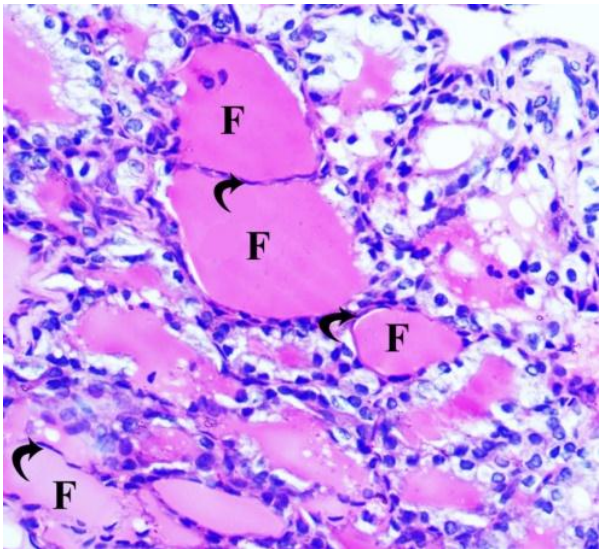



**Fig (13): A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying flattened follicular epithelial cells (curved arrows) lining thyroid follicles (F). (H. & E., x400)**

Masson's trichrome stained sections

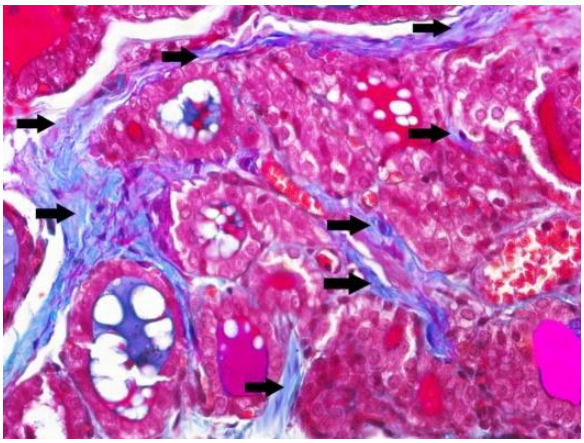


**Fig (14): A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying massive collagen deposition in the interfollicular C.T.(arrows) compared with those of group I. (Masson's trichrome., x400)**

Immunohistochemical study (iNOS) of thyroid gland sections

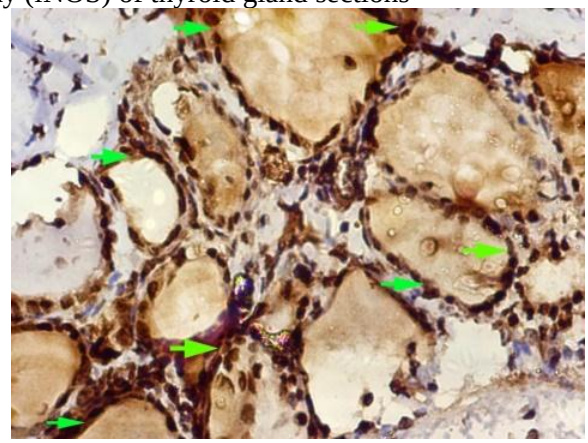


**Fig (15): A photomicrograph of a section of thyroid gland of the cadmium-treated group (group II) displaying strong iNOS cytoplasmic immunoexpression in the follicular epithelial cells (arrows). (iNOS immunostaining., x400)**

Group VI

Hematoxylin and Eosin stained sections:

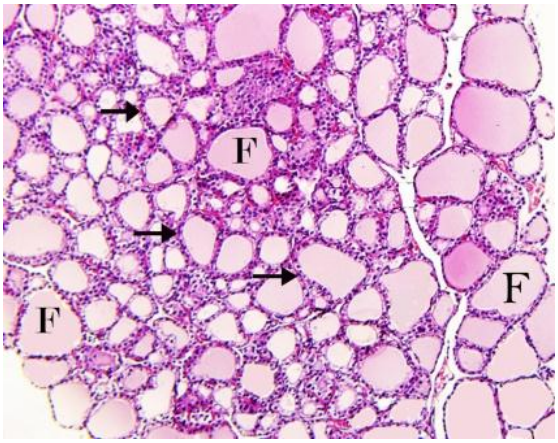



**Fig (16): A photomicrograph of a section of the thyroid gland from the nano-selenium and cadmium-treated group (group IV) displaying apparently normal follicles (F) lined with simple cubical epithelium (cubical cells with central rounded nuclei) (arrows). (H. & E., x100)**

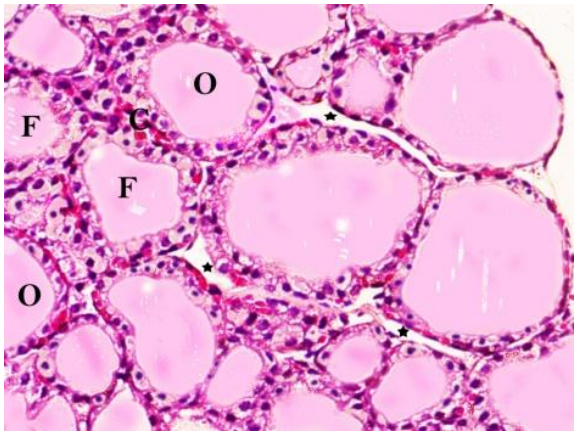



**Fig (17): A photomicrograph of a section of thyroid gland of the nano-selenium and cadmium-treated group (group VI) displaying apparently normal thyroid follicles (F) of different diameters. Follicles are filled with colloid (O). There is narrowing in the interfollicular spaces (star) but congested blood capillaries (C) are still present. (H. & E., x400)**

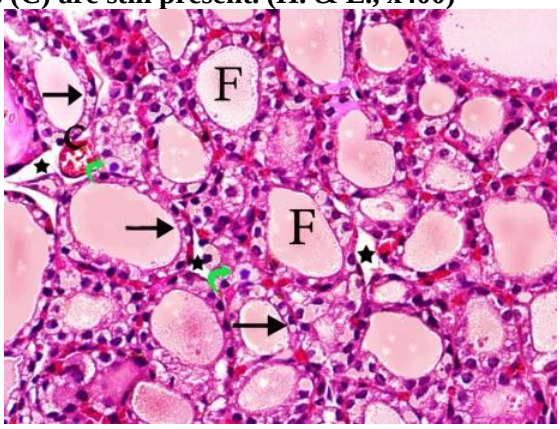



**Fig (18): A photomicrograph of a section of thyroid gland of the nano-selenium and cadmium-treated group (group VI) displaying apparently normal follicles (F) lined with simple cubical epithelium (cubical cells with central rounded nuclei) (arrows). Parafollicular cells were large with pale cytoplasm & present between the basement membrane and the follicular cells but they did not reach the follicular lumen (curved arrows).There is narrowing in the interfollicular spaces (star) but congested blood capillaries (C) are still present. (H. & E., x400)**

Masson's trichrome stained sections

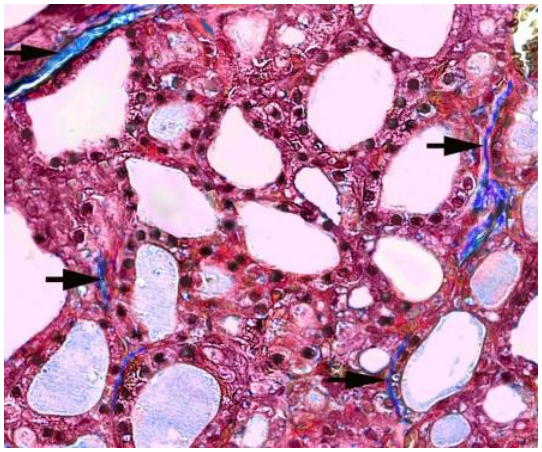


**Fig (19): A photomicrograph of a section of thyroid gland of the nano-selenium cadmium-treated group (group VI) displaying moderate collagen deposition in the interfollicular C.T. (arrows) compared with those of group II. (Masson's trichrome., x400)**

Immunohistochemical study (iNOS) of thyroid gland sections

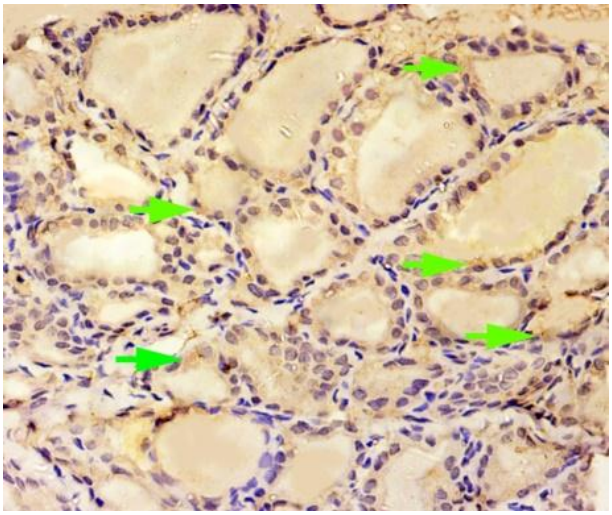


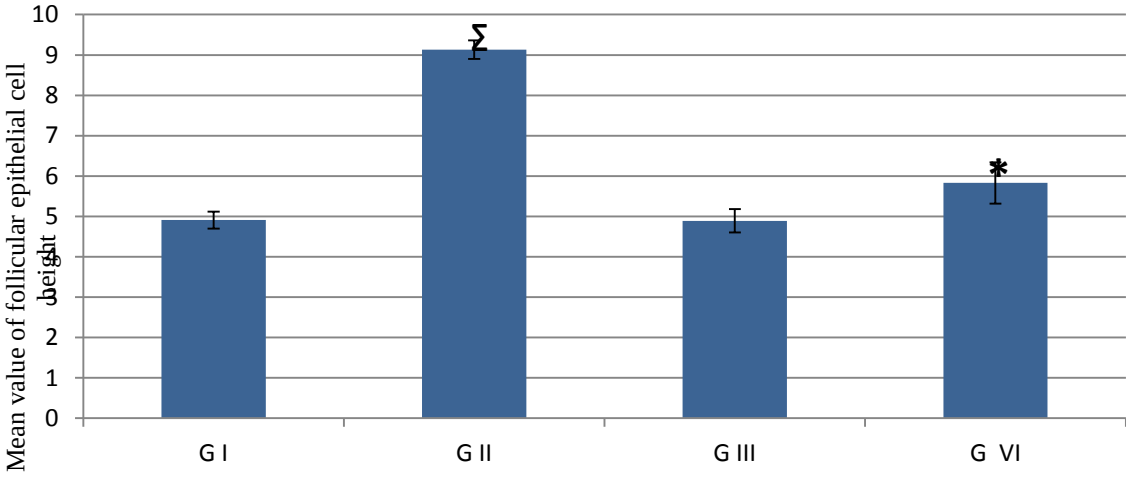
**Fig (20): A photomicrograph of a section of thyroid gland of the nano-selenium and and cadmium-treated group (group VI) displaying weak iNOS cytoplasmic immunoexpression in the follicular epithelial cells (arrows). (iNOS immunostaining., x400)**

**Morphometric and Statistical results**

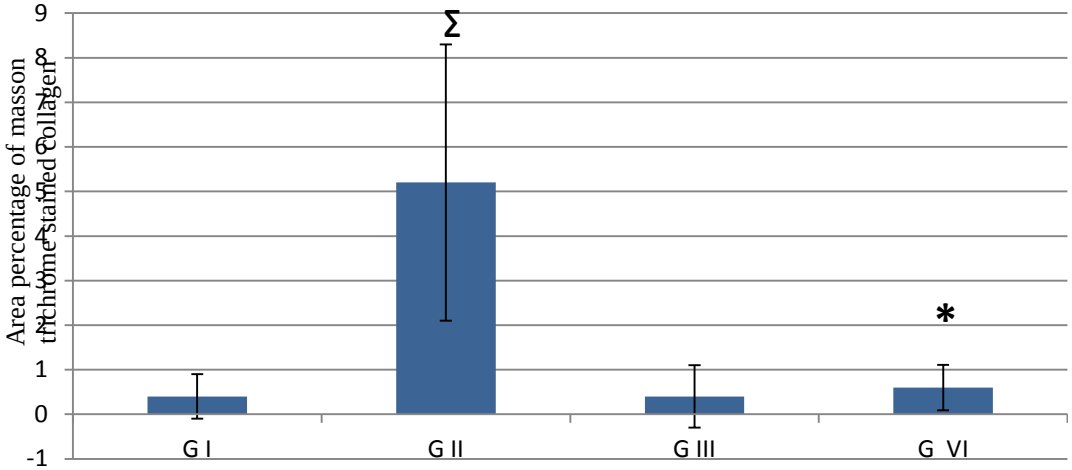
**Table (1): Mean ± SD of the morphometrical parameters of the thyroid glands of the four experimental groups.**

| Morphometrical parameters | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| 1) Follicular epithelial cell height | 4.91±0.21 | 9.13±0.23 ∑ | 4.89±0.29 | 5.83±0.51 * |
| 2) Area percentage of masson's trichrome stained collagen | 0.4±0.5 | 5.2±3.1 ∑ | 0.4±0.7 | 0.6±0.7 * |
| 2) Area percentage of iNOS positive immunostaining | 1.1±0.1 | 3.5±0.29 ∑ | 1.1±0.3 | 1.3±0.7 * |

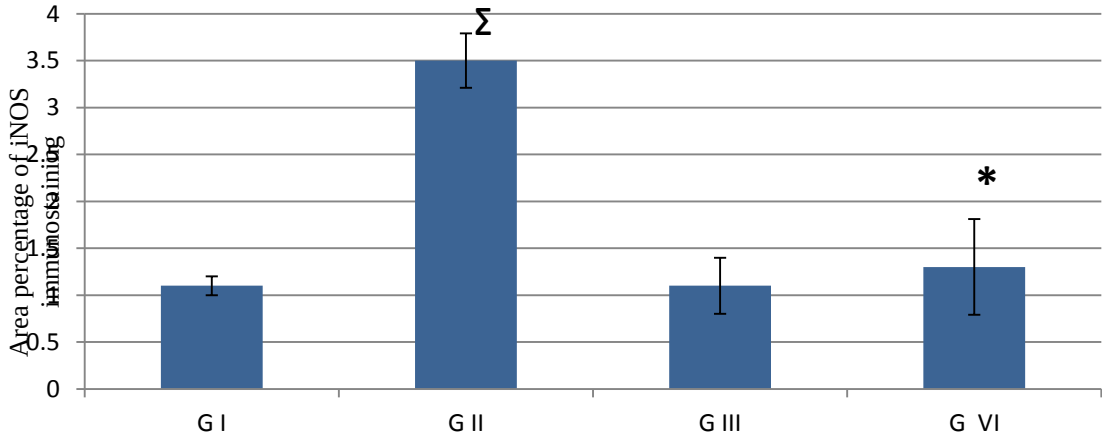
There was a significant increase in the mean follicular epithelial cell height in group II, in comparison with group I. Also, there was a significant decrease in the mean follicular epithelial height in group IV in comparison with group II. There was a significant increase in the area percentage of masson's trichrome-stained collagen in group II, in comparison with group I. Also, there was a significant decrease in the area percentage of masson's trichrome-stained collagen in group IV in comparison with group II. There was a significant increase in the area percentage of iNOS staining in group II, in comparison with group I. Also area percentage of iNOS staining in group IV in comparison with group II.




Histogram (1): Mean values of follicular epithelial cell height of the four tested groups, ∑ = Significant change compared to group I (P value < 0.05).* = Significant change compared to group II (P value < 0.05).




Histogram (2): Area percentage of trichrome-stained collagen of the four tested groups, ∑ = Significant change compared to group I (P value < 0.05).* = Significant change compared to group II (P value <0.5)




Histogram (3): Area percentage of iNOS staining of the four tested groups ∑ = Significant change compared to group I (P value < 0.05). * = Significant change compared to group II (P value < 0.05).

## Discussion

Examination of the sections of the thyroid gland by light microscope did not show substantial differences among rats in the control group (group I) and Nano-Se treated group (group III) and their results were similar to the normal structure. On the other hand, Cd administration induced histological changes in the thyroid gland of group II. H and E stained sections showed follicles of varying diameters. Some follicles contained desquamated epithelial cells in their lumens and others showed absence of colloid. There was loss of the normal architecture of the thyroid follicles. The follicular epithelial cell height was increased with cytoplasmic vacuolations but also squamous follicular epithelial cells were present in some follicles. There were dilated and congested blood vessels. Also wide interfollicular spaces were found. These findings were confirmed by the morphometrical and statistical results; there was a significant increase in the mean follicular epithelial cell height in group II, in comparison with group I. Cd exposure can lead to numerous health hazards in many organs such as liver, kidney, testes and thyroid gland[17]. Recent evidence suggests that Cd induced toxicity occurs as a result of oxidative stress and increased generation of ROS. Increased production of ROS depletes reduced glutathione and enhances lipid peroxidation in tissues. Cd induces a cascade of inflammatory reactions with increased production of pro-inflammatory cytokines, particularly tumor necrosis factor-α (TNF-α) which is responsible for further tissue injury[18]. Cd causes Se depletion and leads to reduction in 5- deiodinase enzyme (5'-D) in liver and kidney, which converts T4 to T3 resulting in hypothyroidism. On the other hands, the decrease in Se leads to decrease in Glutathione peroxidase "GPx", which is one of the body antioxidants and its decrease leads to increase in reactive oxygen and hydrogen peroxide, which damage the thyroid gland[19]. There were similar findings detected by[20] who found squamous follicular epithelium, desquamation of epithelial cells inside the follicles. They attributed these changes to metal accumulation in the mitochondria of thyroid follicular epithelial cells influencing the oxidative phosphorylation of these organelles. Similarly,[21] found desquamated epithelial cells inside the follicles and enlarged follicular epithelial cells with vacuolated cytoplasm. They suggested that the mechanism of Cd toxicity was due to interference in the synthesis and secretion of T4 as a result of destruction of thyroid follicular cells, decrease transformation rate of the T4 to T3 in the peripheral tissue by inhibiting the activity of (5'-D) and interference with pituitary or hypothalamus glands. Also, they stated that the severity of the disturbances increases with the time of exposure.[22] recruited cytoplasmic vacuolations and necrosis in thyroid sections. They explained these changes due to Cd exposure which decreases the total level of iodine in the thyroid gland and serum and disrupts the metabolism of thyroid hormones. As a result of iodine deficiency, there was a decreased production of thyroid hormones, which leads to morphological and functional changes in the thyroid gland. In agreement with results of the current study,[23] made a study to detect the effect of Cd on the thyroid gland of Chinese toads and stated that there were severe loss of the normal architecture. They suggested that accumulation of high Cd concentrations may cause damage of organs that favor normal growth, such as the thyroid gland.

Thyroid damage was due to Cd induced oxidative stress which increased the antioxidant enzyme activity and both apoptosis- and antiapoptosis-related gene messenger ribonucleic acid (mRNA) transcript expressions changed in order to protect the body against damage.[24] reported that there was damage in the structure of the follicular epithelial cells of the thyroid gland, desquamated cells in follicular lumens and congested blood vessels. They attributed these changes to Cd accumulation in the mitochondria of thyroid follicular epithelial cells that leads to inhibition of the synthesis and release of thyroid hormones influencing the oxidative phosphorylation of these organelles. Also, there were similar findings detected by[25] who made a study to detect the Cd effect on liver and found histopathological changes in hepatic tissue in the form of necrosis, vacuolated cytoplasm, congested blood vessels and thickened wall of the central vein. They mentioned another mechanism of Cd induced tissue damage. They reported that this necrosis occurred due to ischemia resulting from endothelial cell dysfunction after accumulation of Cd in the wall of the endothelium of the

blood vessels. But, large Interfollicular spaces which may be either as a result of collapse of some follicles or due to necrosis of the other cells, leaving empty spaces[7]. As regard Masson's trichrome stain, in the present study thyroid glands of rats exposed to Cd (group II) showed massive deposition of collagen in the interfollicular C.T.

These findings were confirmed by the morpho-metrical and statistical results; there was a significant increase in the area percentage of trichrome-stained collagen in group II, in comparison with group I. There were similar findings detected by[20] and [22] who detected increased interstitial fibrous tissue between thyroid follicles. In the present study, immune-histochemical reaction of the thyroid glands exposed to cadmium (group II) showed strong iNOS immunoexpression, in comparison with weak iNOS expression in the control group.

These findings were confirmed by the morphometrical and statistical results; there was a significant increase in the area percentage of iNOS staining in group II, in comparison with group I. Similar findings were detected by[7] who detected strong immunoexpression of iNOS in the thyroid tissue.[26] , [18] & [27] explained these changes due to TNF-α which increased the expression of iNOS enzyme leading to production of a large amount of nitric oxide (NO) that involved in the pathogenesis of cadmium -mediated cytotoxicity. On the other hand, results of group IV (rats receiving both Nano-Se and cadmium) in the present work showed that Nano-Se succeeded in restoring the thyroid integrity by lowering oxidative stress induced by cadmium. As there was almost no histolopathological changes observed in thyroid tissues as Nano-Se attenuated the development of the changes observed after exposure to Cd. H and E stained sections of group IV showed large and small follicles filled with colloid and there was narrowing of the interfollicular space.

Also, there were apparent decrease in the follicular epithelial cell height and these findings were confirmed by the morphometrical and statistical results. There was a significant decrease in the mean follicular epithelial cell height in group IV, in comparison with group II. Congested blood capillaries were still present. In agreement with the results obtained in this study,[10]&[7] detected near-normal follicular structure and interfollicular conne-ctive tissue. Large and small follicles were filled with colloid and reduction of interfollicular space. The blood capillaries were still congested. They stated that administration of selenium nanoparticles to rats inhibited the development of changes observed in the thyroid gland after heavy metal induced thyroid damage. They explained the protective effect of Se-NPs due to significant increase in hepatic antioxidant activities (GSH & GST) and depletion of MDA. They also stated that the most important metabolic roles of selenium in mammalian cell are due to its function in the active site of many antioxidant enzymes; like GPx and thioredoxine reductase.

Also,[28] reported that nano-Se administration produced a significant increase in antioxidant enzyme activity, preventing the induction of oxidative stress and enhancing the antioxidant defenses involving SOD and GSH-dependent enzymes which can be attributed to the free radicals scavenging ability of Nano-Se. Cellular antioxidant defenses involving the enzymes SOD, CAT, and GPX play an important role against ROS generation during oxidative stress and protect tissues from oxidative damage. Masson's trichrome stained thyroid sections of group IV showed moderate deposition of collagen in the interfollicular C.T. These findings were confirmed by the morphometrical and statistical results; there was a significant decrease in the area percentage of collagen in group IV, in comparison with group II. In agreement with these results obtained in this study,[10] detected the protective role of Se-NPs on the thyroid gland. Nano-Se succeeded in reduction of collagen deposition in the interfollicular C.T.[29] stated that Se succeeded in reduction of collagen deposition by inhibiting α-smooth muscle actin (α-SMA) synthesis and increasing the mRNA expression of matrix metalloproteinase 9 (MMP9). But, [30] stated that Se can protect the cells from the harmful effects of free radicals and acts the part of the active site of the selenoenzyme.

Also, Se has anti-inflammatory properties involving the cyclooxygenase and lipoxygenase cascade. Immunohistochemical reaction of thyroid glands of group IV in the current study showed weak iNOS immunoexpression in the

cytoplasm of follicular epithelial cells, in comparison with strong iNOS expression in group II. These findings were confirmed by the morphometrical and statistical results; there was a significant decrease in the area percentage of iNOS staining in group IV, in comparison with group II. In agreement with these results, [7] stated that Nano-Se succeeded in protection of the thyroid gland from heavy metal induced oxidative stress. They found weak iNOS expression in the follicular epithelial cells of the thyroid gland of rats treated with chromium and Nano-Se. They explained this protective role due to the function of Nano-Se in the active site of many antioxidant enzymes, like thioredoxin reductase and GPx. Also, they stated that Se at nanoparticle size has a comparable efficacy in upregulating selenoenzymes and tissue selenium levels. In conclusion, antioxidants like GSH is considered an important line of defense and protect the cells against oxidative stress mediated cellular injury either by scavenging free radicals or by converting the toxic radicals to non-toxic end products [31]. The activity of antioxidant enzymes such as SOD, catalase (CAT) and GPx is very important to protect against oxidative stress. SOD catalyzes dismutation of the superoxide anion to $H_2O_2$ and $O_2$. The harmful $H_2O_2$ is further detoxified to water by CAT and GPx[32]. Administration of Cd significantly reduces the level of GSH and also inhibits the activities of these antioxidant enzymes SOD, CAT, and GPx in the thyroid gland indicating pronounced oxidative stress [31]. Nano-Se administration produced a significant increase in antioxidant enzyme activity such as SOD, CAT, and GPx to protect against ROS generation during oxidative stress and protect tissues from oxidative damage[28]. Also Se reduces the content of Cd in tissues by forming compounds and antagonizing Cd-induced oxidative stress[29].

## Conclusion

Finally, the administration of Nano-Se under the exposure to Cd prevented Cd induced oxidative stress in the thyroid gland and offered significant protection against histopathological changes in this organ. The studies mentioned before provide confirmation of the present hypothesis that Se-NPs may be good candidates for investigation of their possible prophylactic use in humans exposed to Cd.

## References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