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"Effects of iron oxide nanoparticles on male rats' thyroid and kidney functions"

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Abstract:

Iron oxide nanoparticles (Fe2O3 NPs) are commonly used in a variety of applications, including wastewater treatment, paints, cosmetics, drug delivery, imaging, and targeted therapy such as anticancer and antimicrobial drugs, as well as industrial food dyes. The purpose of this study was to examine the impact of Fe2O3 nanoparticles on male rats' thyroid and kidney functions considering exposure duration and dose. Fifty-four male Sprague-Dawley rats were used in this research in three groups, each group consisting of 18 rats. Each group was divided into three subsections of 6 mice that were exposed as follows: Animals in Group 1 were used as controls, and Groups 2 and 3 received oral treatments at 250 and 1000 mg/kg Fe2O3 NPs, respectively, for different periods of 15 days, 30 days, and 45 days and every animal had blood samples taken to measure the level of thyroid hormones, creatinine, and urea. The results of the current study showed a high significant increase ($P \leq 0.01$) in creatinine and urea levels which was an indicator of a malfunction in kidney function. Also, the TSH hormone level showed a high significant increase($P \leq 0.01$) and a high significant decrease ($P \leq 0.01$) in the T3 and T4 hormone levels after exposure to different doses (250, 1000 mg/kg) of iron oxide nanoparticles for 15, 30 and 45 days, which had an effect on the function of the thyroid gland and caused hypothyroidism and this led to a decrease in the metabolism process.

Keywords: Iron oxide nanoparticles, thyroid hormone, rat, creatinine, urea.

Introduction:

Nanoparticles (NPs) are defined as small particles that are 100 nm or smaller in at least one dimension. Nanoparticles have attracted great interest due to their small size and high surface area leading to their extraordinary electronic, chemical, optical, mechanical, and magnetic properties (Selmani

et al., 2022). One of the most important metal oxide nanoparticles is iron oxide nanoparticles (Fe2O3 NPs), It is used in multiple fields due to its unique electrical, magnetic, and optical properties. Iron oxide nanoparticles have been used in drug delivery and anti-cancer, anti-viral, and anti-microbial applications and bio imaging, hyperthermia, photo ablation therapy, biosensors, and therapeutic applications (Attia *et al*., 2022). In addition, Fe2O3 NPS is employed in several industries like ceramics, dyes, and wastewater treatment to eliminate various contaminants such heavy metals, dyes, and pharmaceuticals, which are also utilized in cosmetics (Bibi *et al*., 2019). Also, iron oxide nanoparticles(Fe2O3) are widely used as industrial food dyes to color sweets, olives, or cheese rinds (EFSA, 2015). Therefore, iron oxides are classified as food additives by the European Union and assigned the code E172 (Voss *et al*., 2020). Nanoparticles (NPs) can interfere with cellular function by penetrating cytoplasmic membranes due to their small size (Radhi and Al-Bairuty, 2019). Depending on these applications, it is very important to focus on their potential toxic and harmful effects on growth, survival, and reproduction in cells and organisms (Omidi *et al*., 2015). Long-term exposure to iron oxide nanoparticles may affect thyroid hormones (T3 and T4) and TSH levels and cause endocrine system dysfunction. An essential component of the endocrine system are thyroid gland which crucial to maintaining homeostasis, growth, and development, as well as for the cardiovascular, reproductive, and neurological systems to work normally. It also governs several other cellular functions, including metabolism. T3 and T4 hormones both produce from thyroid gland (Zhou *et al*., 2022).The main organ that are responsible for blood filtration, electrolyte and water balance, and blood pressure maintenance in the bloodstream are kidney (Vart *et al*., 2016). Biomarkers such as creatinine and urea are often used to diagnose the efficiency of the kidneys in their excretion capacity, Urea is the first renal sign that increases when the kidney suffers from any damage or injury (Chew and DiBartola, 1989).

Previous Studies:

Previous studies conducted on rats or mice reported mixed results on the effect of iron oxide, as kidney toxicity was reported after administration of Fe2O3 NPs (Reddy *et al*., 2017), while other studies did not report toxicity (Ghasempour *et al*., 2015).

This study aimed to assess the impact of Fe2O3 NPs on the function of the kidney through calculation urea and Creatinine levels, and Thyroid-

stimulating hormone (TSH), triiodothyronine (T3), and thyroxin (T4) levels in male rats to assess thyroid gland function.

Material and methods

Ethical consent

An ethical consideration agreement surrounding the use of animals in research has been signed by reference. No.: BCSMU/1023/ 0036Z . This procedure has been authorized by (the College of Science's Licensing or Ethics Committee /Al-Mustansiriya University, Iraq) to conduct experiments on animal models.

Preparation of Fe2O3 NP Solutions

iron oxide nanoparticles utilize in this investigation were generated from the Sky spring Nanomaterial firm; the features of this product are Appearance: red powder, purity: 99%. Particle diameters range from 20 to 40 nm, and 40–60 m2/g is the specific surface area. The density in bulk is 1.20 g/cm3., while the true density is 5.24 g/cm3.

The varied doses of Fe2O3 nanoparticles employed in this investigation were created by mixing the powder of Fe2O3 nanoparticles with deionized water and vortexing for 10 minutes, then dosing each rat with 1ml of the solution via oral gavage, dosing dependent on its weight. Two different concentrations of Fe2O3 nanoparticle solution were made: (low dose) 250 mg/kg and (high dose) 1000 mg/kg (Kumari *et al*., 2012).

Animal care

54 mature male Rattus norvegicus Sprague Dawley rats, (200–225) grams in weight and aged between 6 and 8 weeks. They were acquired from the Biotechnology Research Center at Al Nahrain University. Animals were then housed in the Biotechnology Research Center, AL Nahrain University, it were kept for 15 days to allow for adaption before beginning the experiment below a regulated degree situation of 25°C and a 12-hour light/dark cycle. To feed and drink, the animals were given pellets and tap water.

Design experimental

Three groups of animals were created at random, two of which served as treatments and one control and each group was split into 3 subgroups based on the duration of exposure (15, 30, 45) days twice a week, orally, and six rats per group, as showed in the details that follow:

■Groups (1, 2, and 3) as control animals

animals were given deionized water orally twice a week, throughout different periods of 15, 30, and 45 days.

■Groups (4, 5, and 6) (animals received a low concentration of Fe2O3 nanoparticles).

animals were given a low concentration (250 mg/kg body weight) of Fe2O3NPs suspension orally twice a week, for 15, 30, and 45 days.

■Groups (7, 8, and 9) (animals received a high concentration of Fe2O3 nanoparticles).

animals were given a high concentration (1000 mg/kg body weight) of Fe2O3NPs suspension orally twice a week, for 15, 30, and 45 days.

Blood Samples collection

Following the experiment is over, the rats are weighed and then For a few minutes, diethyl ether fully sedated them. blood samples from the cardiac puncture totalling 4ml were collected and placed in the clot activator gel tubes, and before centrifuging, let samples to clot for thirty minutes at room temperature, Centrifugation was utilized to separate the serum for the hormonal and biochemical testing at (3000) rpm for (15) minutes, and maintained at -20ºC until analysis.

Hormonal Analysis:

Thyroid function

The Cobas e 411 analyzer measured thyroid hormones (T4, T3, and TSH). The German-based Roche/Hitachi firm invented and produced this device. This device requires a small amount of serum, up to 25 µl, and can obtain test results in as little as 9–18 minutes.

Biochemical Analysis:

Kidney Functions

The urea and creatinine levels was measured by using an automated analyzer instrument (Cobas c111)

Analytical statistics

The Statistical Analysis System (SAS) (2012) program was used to determine the effect of the different factors on all study parameters. and analysis of variance (ANOVA) was conducted and the least significant difference (LSD) test was determined, which compares the means of the research values to ascertain whether there are any significant effects where the difference is considered highly significant when ($P \leq 0.01$) and significant when ($p \leq 0.05$).

Results and Discussion:

1-The impact of Fe2O3 NPs on the function of thyroid hormones

The findings from the statistical examination of the impact of Fe2O3 NPs on thyroid hormones, which involve (T3, T4, and TSH) in Tables (1, 2, and 3),

show at day 15 as opposed to control groups (1.35 ± 0.004) nmol/L, the values of T3 (nmol/L) revealed a significant drop (P≤0.01) in both groups receiving treatment (250, 1000) mg/kg (1.28 ±0.002), (1.02 ±0.003) nmol/L respectively, and at 30 day, in contrast to control groups (1.35 ±0.002) nmol/L at same concentrations (1.23 ±0.005), (0.887 ±0.03) nmol/L. Furthermore, following 45 days of exposure to Fe2O3 NPs, there was a significant reduction (P≤0.01) in T3 hormone levels at concentrations (250, 1000 mg/kg) (0.89 ±0.03), (0.665 ±0.01) nmol/L, in compared with control groups (1.34 ±0.004) nmol/L. as indicated by Table 1.

Table 1: The impact of Fe2O3 NPs in two doses (250 and 1000 mg/kg) on T3 level (nmol/L) of rats during different exposure periods

Concentration (mg/kg)	Mean ±SE of T3 (nmol/L)			LSD value
	15 Day	30 Day	45 Day	
0	1.35 ±0.004 A a	1.35 ±0.002 A a	1.34 ±0.004 A a	0.0144 NS
250	1.28 ±0.002 B a	1.23 ±0.005 B a	0.89 ±0.03 B b	0.0662 **
1000	1.02 ±0.003 C a	0.887 ±0.03 C b	0.665 ±0.01 C c	0.0591 **
LSD value	0.0276 **	0.057 **	0.0635 **	---
Means that the presence of distinct large characters in same column and small letters in same row vary considerably. ** (P≤0.01).				

(A,B,C) represent the significant difference between groups when time is a fixed factor and concentration is a variable factor .

(a,b,c) represent the significant difference between groups when time is a variable factor and concentration is a fixed factor .

In contrast to the group under control (42.70 ±0.09) nmol/L, the value of T4 hormone (nmol/L) for the animals treated with Fe2O3 NPs at both concentrations (250 and 1000 mg/kg) during 15 days was found to be significantly lower (P≤0.01) (36.55 ±0.19), (32.49 ±0.13) nmol/L similarly, all animals treated with Fe2O3 NPs for 30 days at the same concentrations (30.36 ±0.14) and (26.13 ±0.18) nmol/L, respectively, appear a extremely noteworthy decrease (P≤0.01) inT4 levels compared with control (42.73 ±0.11) nmol/L. Finally, the study found a significant reduction (P≤0.01) in

T4 levels in groups treated to (Fe2O3 NPs) at different concentrations (250, 1000) mg/kg for 45 days (24.67 ±0.14) and (18.56 ±0.17) nmol/L, compared to the groups under control (42.80 ±0.05) nmol/L. as indicated by Table 2.

Table 2: The impact of Fe2O3 NPs in two doses (250 and 1000 mg/kg) on T4 level (nmol/L) of rats during different exposure periods

Concentration (mg/kg)	Mean ±SE of T4 (nmol/L)			LSD value
0	42.70 ±0.09 A a	42.73 ±0.11 A a	42.80 ±0.05 A a	0.194 NS
250	36.55 ±0.19 B a	30.36 ±0.14 B b	24.67 ±0.14 B c	0.478 **
1000	32.49 ±0.13 C a	26.13 ±0.18 C b	18.56 ±0.17 C c	0.492 **
LSD value	0.454 **	0.478 **	0.389 **	---
Means that the presence of distinct large characters in same column and small letters in same row vary considerably. ** (P≤0.01).				

(A,B,C) represent the significant difference between groups when time is a fixed factor and concentration is a variable factor .

(a,b,c) represent the significant difference between groups when time is a variable factor and concentration is a fixed factor .

Table 3's results indicate that statistically significant rise (P≤0.01) showed in TSH (µIU /mL) for all groups subjected to 250 and 1000 mg/kg of Fe2O3NPs for 15 days (1.924 ±0.01) and (2.031 ±0.004) µIU /mL in comparison with the control animals (1.78 ±0.002) µIU /mL . The results as well showed after 30 days at the same concentrations (2.10 ±0.04) and (2.45 ±0.008) µIU /mL, respectively, in comparison to the control (1.78 ±0.002) µIU /mL . In addition, a significant rise (P≤0.01) in TSH hormone levels at two doses (250, 1000 mg/kg (2.62 ±0.01) and (3.07 ±0.02) µIU /mL in compared to the control animals (1.78 ±0.01) µIU /mL after 45 days of exposure to Fe2O3 NPs.

Table 3: The impact of Fe2O3 NPs in two doses (250 and 1000 mg/kg) on TSH level (µIU /ml) of rats during different exposure periods

Concentration (mg/kg)	Mean ±SE of TSH (µIU /ml)			LSD value
	15 Day	30 Day	45 Day	
0	1.78 ±0.002 C a	1.78 ±0.002 C a	1.78 ±0.01 C a	0.0049 NS
250	1.924 ±0.01 B c	2.10 ±0.04 B b	2.62 ±0.01 B a	0.0682 **
1000	2.031 ±0.004 A c	2.45 ±0.008 A b	3.07 ±0.02 A a	0.017 **
LSD value	0.0193 **	0.0652 **	0.0184	---
Means that the presence of distinct large characters in the same column and small letters in the same row vary considerably.. ** (P≤0.01).				

(A,B,C) represent the significant difference between groups when time is a fixed factor and concentration is a variable factor .
(a,b,c) represent the significant difference between groups when time is a variable factor and concentration is a fixed factor .

2- the impact of Fe2O3 nanoparticles on the function of kidney

In the current study, kidney function was calculated by measuring the amount of Creatinine and urea after exposure of each animal to Fe2O3 nanoparticles for(15, 30, and 45) days.

A highly significant rise (p≤0.01) was revealed by statistical analysis in the creatinine (mg/dl) level after exposure to Fe2O3 nanoparticles at a concentration (250 and 1000 mg/kg) (1.21 ±0.004) and (1.32 ±0.002) mg/dl respectively, in contrast to the animals under control (0.826 ±0.01) mg/dl through 15 days. Additionally, showed an extremely notable rise (p≤0.01) in Creatinine levels after exposure to both doses of Fe2O3 NPs (1.61 ±0.02), (1.83 ±0.003) mg/dl respectively, during 30 days compared to the group under control (0.829 ±0.01) mg/dl. Eventually, there was a large and noteworthy rise (p≤0.01) in animals after exposure to the same doses of Fe2O3 NPs (250 and 1000 mg/kg) (1.92 ±0.01), (2.76 ±0.01) mg/dl respectively, for 45 days in compared with the control (0.827 ±0.01) mg/dl .as the table 4

Table 4: The impact of Fe2O3 NPs in two doses (250 and 1000 mg/kg) on Creatinine (mg/dl) level of rats during different exposure periods

Concentration (mg/kg)	Mean ±SE of Creatinine (mg/dl)			LSD value
	15 Day	30 Day	45 Day	
0	0.826 ±0.01 C a	0.829 ±0.01 C a	0.827 ±0.01 C a	0.019 NS
250	1.21 ±0.004 B c	1.61 ±0.02 B b	1.92 ±0.01 B a	0.0313 **
1000	1.32 ±0.002 A c	1.83 ±0.003 A b	2.76 ±0.01 A a	0.0085 **
LSD value	0.0096 **	0.0293 **	0.0109 **	---
Means that the presence of distinct large characters in the same column and small letters in the same row vary considerably. ** (P≤0.01).				

(A,B,C) represent the significant difference between groups when time is a fixed factor and concentration is a variable factor .
(a,b,c) represent the significant difference between groups when time is a variable factor and concentration is a fixed factor .

Whereas, the results of evaluating the urea(mg/dl) level recorded a high significant increase (P≤0.01) within 15 days after exposure to various concentrations (250 and 1000 mg/kg) of Fe2o3 NPs (46.44 ±0.53),(53.22 ±0.93) mg/dl respectively, compared to the control group (38.54 ±0.24) mg/dl, also the results of animals that were exposed to Fe2O3 NPs at the same concentrations for 30 days showed a high significant rise (P≤0.01)(67.65 ±0.28)and(75.61 ±0.34) mg/dl respectively, in comparison to control group (38.31 ±0.20) mg/dl. Furthermore, a highly noteworthy rise (P≤0.01) in the urea level of animals exposure for 45 days with two doses (250, 1000 mg/kg) of Fe2O3 NPs (85.76 ±0.34) and (112.07 ±0.71) mg/dl respectively, compared to the control group (38.02 ±0.32) mg/dl .as show in table 5

Table 5: The impact of Fe2O3 NPs in two doses (250 and 1000 mg/kg) on Urea (mg/dl) level of rats during different exposure periods

Concentration (mg/kg)	Mean ±SE of Urea (mg/dl)			LSD value
	15 Day	30 Day	45 Day	
0	38.54 ±0.24 C c	38.31 ±0.20 C a	38.02 ±0.32 C a	0.372 NS
250	46.44 ±0.53 B c	67.65 ±0.28 B b	85.76 ±0.34 B a	1.215 **
1000	53.22 ±0.93 A c	75.61 ±0.34 A b	112.07 ±0.71 A a	2.125 **
LSD value	1.947 **	0.839 **	1.483 **	---
Means having with the different big letters in same column and small letters in same row differed significantly. ** (P≤0.01).				

(A,B,C) represent the significant difference between groups when time is a fixed factor and concentration is a variable factor .
(a,b,c) represent the significant difference between groups when time is a variable factor and concentration is a fixed factor .

Discussion

In the current investigation, the levels of (T3, T4, and TSH) were measured to determine if the thyroid was hyperthyroid or hypothyroid.

The thyrotropin-releasing hormone is produced by the hypothalamus (TRH) and the anterior pituitary gland produces TSH, which controls the thyroid gland. triiodothyronine (T3) and thyroxine (T4). are the two primary hormones that the thyroid gland produces. The thyrotropin-releasing hormone, T4, and TSH operate together in synchrony to maintain homeostasis and normal feedback of mechanisms (Mullur *et al*.,2014). The investigation finding a highly significant reduction in T3, T4 levels. as well as a highly significant rise in level of TSH.

These results corroborated those of a prior study conducted by(Assadi *et al*., 2016) which found that rats receiving an intraperitoneal injection of MoO3 NPs (5 mg/kg) for 28 days had significant reduction in T3 and T4 levels and a rise in TSH levels in their serum. Another previous study showed that whereas the TSH level did not significant change across all concentrations and time periods, intraperitoneal ZnO NP treatment at doses of (30 and 60 mg/kg) in 3 various time durations (7, 14, and 28) days resulted from a high significant reduction in T3 and T4 levels(Luabi *et al*., 2019). Furthermore, a

study conducted by (Sakr and Steenkamp, 2021) observed a noteworthy reduction in T3, T4, and TSH levels in 24 male rats exposure to ZnO NPs 200 mg/kg Via gavage daily for 30 days when compared to the control group. Another study (Hassanin *et al*., 2013) found that following intraperitoneally injection daily at a concentration of (0.5 mg/kg) for five days, showed that SeNPS significantly reduced T4 and T3 levels in their serum. According to a different earlier study, rats given daily intraperitoneally injections of MgONPs (80 mg/kg) for 14 and 28 days experienced a highly substantial an increase in thyroid stimulating hormone (TSH) levels and reduction in T3, T4(Obaid *et al*., 2022). However, this study contradicted a previous study by (Yousefi Babadi *et al*., 2013) which gave male rats three different doses of iron oxide NPs (20, 50, and 150) µg/kg for fifteen days. The findings revealed rise in the levels of T4 in high dosage group and a significant reduction in TSH at 50 and 150 µg/kg groups. An investigation showed that giving rats oral Fe2O3NPs at 5 mg/kg dose and (IP) of AgNPs at 50 mg/kg dose combination every day for 79 days significant increase in T3, T4, and TSH levels (Ahmed *et al*., 2020). Another study found that giving oral CuO/ZnO nanoparticles at doses of 0, 5, 10, 20, and 40 mg/L to female rats for 30 days in a row significantly increased the amount of T4 in the serum and significantly reduced TSH concentrations at the tested doses(Mohammed *et al*., 2023). Other study by (Sulaiman *et al*., 2018) showed non-significant altered TSH and T3 hormones level while decrease in T4 level after long-term intraperitoneal injection by Ag NPs at doses (12.5, 25, and 50 mg/kg) for (10,20 and 30) days.

The decrease in these hormone levels could be attributed to the direct cytotoxicity of the NPs that damages thyroid follicular and Para-follicular cells (Pani and Pani, 2017).

Thyroid follicular cells' mitochondrial activity is compromised by NPs in the oxidative state, which lowers the energy needed for the production and release of thyroid hormones (Sakr and Steenkamp, 2021)

A primary role of kidney is removal and excretion of plasma constituents including nanoparticles, into the urine in order to remove ions and excess waste products from blood, for this reason, they are considered one of the mostly important secondary target organs (Puntes *et al*., 2019).

Urea is the first renal sign that increases when the kidney suffers from any damage or injury, also an increase in creatinine in the blood is considered a renal marker to evaluate the glomerular filtration rate. Creatinine increases

only when approximately (70-80%) of the functional capacity of the kidneys is lost (Chew and DiBartola, 1989).

The current study investigated how nanoparticles effect on kidney enzymes are in line with other research despite the differences in doses, duration, methods of administration. (Ajadi *et al*., 2019) reported that exposure intraperitoneal to different concentrations of iron oxide nanoparticles Fe2O3 (5, 25, and 50 mg/kg) for 14 days significantly rise in the level of urea and creatinine in contrast to the control animals and showed histological changes in kidney tissue. A study conducted by (Mohammed *et al*., 2020) revealed that kidney damage occurred as a result of exposure to iron oxide nanoparticles at dose of 20 mg/kg intraperitoneally daily for a week, resulting an increase in kidney enzymes level creatinine, urea in comparison with control group, and this indicates the presence of a defect in kidney function. Also, Inhalation of silica nanoparticles (Si NPs) by adult male mice at two doses (500 and 1000 ppm) caused an increase in creatinine and urea at 1000 ppm after 28 days in comparison with the treated group (500 ppm Si NPs) and with the control group (Azouz and Korany, 2021). Another study investigate that exposure to TiO2 NPs at dose 50 and 200mg/kg led to increase urea , creatinine and total protein levels after 1,2 and 4 weeks (Luaibi and Mohammed, 2023).

While another study reported that injected intraperitoneally male rats with magnetite nanoparticles Fe3O4 daily at 40 mg/kg of body weight for 14 days, no discernible difference in the levels of urea and creatinine when compared to the control group (Rahdar *et al*., 2018). Also, this study contradicts a previous study that reported that there were no changes in the level of kidney enzymes after injecting rats with different concentrations of 50,100,150 mg/kg from iron oxide nanoparticles through 15 and 30 days (Salehi *et al*., 2017). On the other hand, a study found that administering Al2O3 NPs orally to male Swiss albino mice given concentrations of 15,30, and 60 mg/kg for five days showed no discernible changes in (total protein, urea, and creatinine) levels in these animals' serum as opposed to the control group (De *et al*., 2020). Also, there is a previously reported rise in urea and Creatinine levels in patients with thyroid disorders (Bolkiny *et al*., 2019).

Several studies demonstrated that metal oxide nanoparticles may produce oxidative stress by producing ROS and free radicals, and the kidneys' antioxidant defense mechanisms shield animals against metal-induced oxidative stress (Jorgensen, 2010). research has also shown that

hypothyroidism increases the production of ROS and lipid peroxidation which ultimately results in oxidative stress (Das *et al*., 2022).

Conclusion:

The current study's findings indicate a drop in T3 and T4 levels and an increase in TSH hormone levels after exposure to Fe2O3NPs, on the other hand, led to an increase in the levels of creatinine and urea in comparison to the control group. Long-term exposure to the nanomaterial may have created oxidative stress that led to necrosis of kidney cells and apoptosis, Therefore this results in the inhibition of secretion, which raises the blood levels of urea and creatinine due to the disruption in renal function.

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تأثير جزيئات أكسيد الحديد النانوية على وظائف الغدة الدرقية والكلى لدى ذكور الجرذان

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مستخلص البحث:
تُستخدم جسيمات أكسيد الحديد النانوية (Fe2O3 NPs) بشكل شائع في مجموعة متنوعة من التطبيقات، بما في ذلك معالجة مياه الصرف الصحي، والدهانات، ومستحضرات التجميل، وتوصيل الأدوية، والتصوير، والعلاج الموجه مثل الأدوية المضادة للسرطان والمضادة للميكروبات، وكذلك الأصباغ الغذائية الصناعية. كان الغرض من هذه الدراسة هو دراسة تأثير جزيئات Fe2O3 النانوية على وظائف الغدة الدرقية والكلى لدى ذكور الجرذان مع الأخذ في الاعتبار مدة التعرض والجرعة. تم استخدام أربعة وخمسون من فئران سبراغ داولي الذكور في هذا البحث في ثلاث مجموعات، كل مجموعة تتكون من 18 فأرا. تمت معالجة كل مجموعة لمدة متفاوتة 15 يومًا و30 يومًا و45 يومًا. تم تقسيم كل مجموعة إلى ثلاثة أقسام فرعية مكونة من 6 فئران تم تعريضها على النحو التالي: تم استخدام الحيوانات في المجموعة 1 كعناصر تحكم، وتلقت المجموعتان 2 و3 علاجات عن طريق الفم بجرعة 250 و1000 ملجم/كجم من Fe2O3 NPs، على التوالي، لفترات مختلفة من 15 يومًا، و30 يومًا، و45 يومًا، وتم أخذ عينات دم من كل حيوان لقياس مستوى هرمونات الغدة الدرقية والكرياتينين واليوريا. أظهرت نتائج الدراسة الحالية ارتفاعاً معنوياً عالياً ($P\leq0.01$) في مستويات الكرياتينين واليوريا وهو مؤشر على وجود خلل في وظائف الكلى، كما أظهر مستوى هرمون TSH ارتفاعاً معنوياً عالياً ($P\leq0.01$) وانخفاضاً معنوياً عالياً ($P\leq0.01$) في مستوى هرموني T3 وT4 بعد التعرض لجرعات مختلفة (250، 1000 ملغم/كجم) من جسيمات أكسيد الحديد النانوية لمدة 15 و30 و45 يوماً مما كان له تأثير على وظيفة الغدة الدرقية وتسبب في قصور الغدة الدرقية وهذا أدى إلى انخفاض في عملية التمثيل الغذائي.

الكلمات المفتاحية: جزيئات أكسيد الحديد النانوية، هرمون الغدة الدرقية، الجرذان، الكرياتنين، اليوريا
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