Original Article

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Effect of zinc oxide nanoparticles on the pancreas functions in albino mice

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Abstract

The study was conducted on 40 male Swiss albino mice that were obtained from the Research and Development Authority of the Ministry of Industry and Minerals in Baghdad to determine the effect of zinc oxide nanoparticles (ZnO-Nps) on the. pancreas The animals were divided into five groups, each group containing eight mice, which were treated orally with 0.1 ml once daily of zinc oxide nanoparticles at two concentrations of 100 and 200 mg/kg for two periods of 7 and 14 days, while the control group received water and diet only. After completing the two dosage periods, the body weights were recorded, and the blood samples were collected from the treated and control animals; then the animals were sacrificed in order to study the functional, morphological and histological changes of (pancreas) that occurred as a result of treatment with zinc oxide nanoparticles.

Keywords:

Nanoparticles, zinc oxide, pancreas, Amylase, Lipase.

Introduction

The areas of using nanoscience have expanded significantly in recent times due to the development of nanoscience technology [1], which has led to an increase in its importance in all applied, medical, engineering, cosmetic, electronic and biological sciences [2], and for this reason this science is one of The important sciences of the twenty-first century, and nanoscience can be defined as the science that is concerned with studying and characterizing nanomaterials, determining their chemical, physical, and mechanical properties, and studying the associated phenomena arising from minimizing their sizes, [3] Nanomaterials differ in their chemical, biological and physical properties according to their manufacturing methods.

Among the materials involved in the manufacture of nanomaterials are metals (gold, silver, iron, aluminum, cobalt, etc.) and metal oxides (titanium dioxide, zinc oxide, zinc dioxide, silicon dioxide, Iron oxide, zinc oxide [4]. Many experiments and studies have shown that when these materials reach the ecosystem, they negatively affect living organisms [5]

(The small size of zinc nanoparticles increases their surface area, giving them a high ability to penetrate cell membranes and accumulate them, which affects their tissue structure and functional performance. [6] There are multiple ways in which the organism's body is exposed to nanoparticles that differs according to the route through which they pass, such as inhalation through the respiratory system, blood through the skin, food and drink through the digestive system. The pancreas is one of the important organs in the digestive system, whose main function is to regulate the level of sugar. blood and any disorder or tissue damage in it leads to an imbalance in the level of sugar in the blood and its functional performance, and this is what I explained [7] When the rats were injected with two doses (100,300 mg/kg) of zinc oxide nanoparticles, its accumulation in the endocrine cells of the islets of Langerhans in the pancreatic gland led to damage and necrosis with a decrease in insulin secretion and an increase in the level of sugar in the blood.

Materials and Methods

Animal collection and studied groups characteristics:

The study was carried out using 40 white mice of (Balb/C Strain) which obtained from

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the Industrial Research and Development Authority. The average weight of animals ranged between (30-35) gram, and their age ranged between (8-12) weeks, and the animals were in good health. Then, the animals were transferred to the animal house of a private laboratory and placed in plastic cages with metal mesh covers. The cages were covered with sawdust, which was replaced every two days, and the cages were cleaned and sterilized during the experiment period. All animals were placed throughout the study period under standardized laboratory conditions in terms of lighting (12 hours of darkness/12 hours of light), temperature (20-30 °C) and ventilation; they were also given their diet and water. Zinc oxide nanoparticles produced by Zhengzhou Dongyao Nano Materials Co., LTD were used, and their specifications were as follows: particle purity reached 99.99%, average particle size was 50 nanometers, cubic shape, and it was as white powder. In addition, the purity of the powder was confirmed using the Energy Dispersive X Ray Spectroscopy (SDX) device at Al-Nahrain University/College of Science/Department of Physics/Electron Microscope Laboratory, where the purity was 100% as shown in (Figure 1). While the shape and size of the studied nanoparticles were detected through using of Transmission Electron Microscopy (TEM) located at Al-Nahrain University/College of Medicine, where the particles appeared in cubic shapes and some in the form of clusters (Figure 2); these results were almost identical to the manufacture company's specifications.

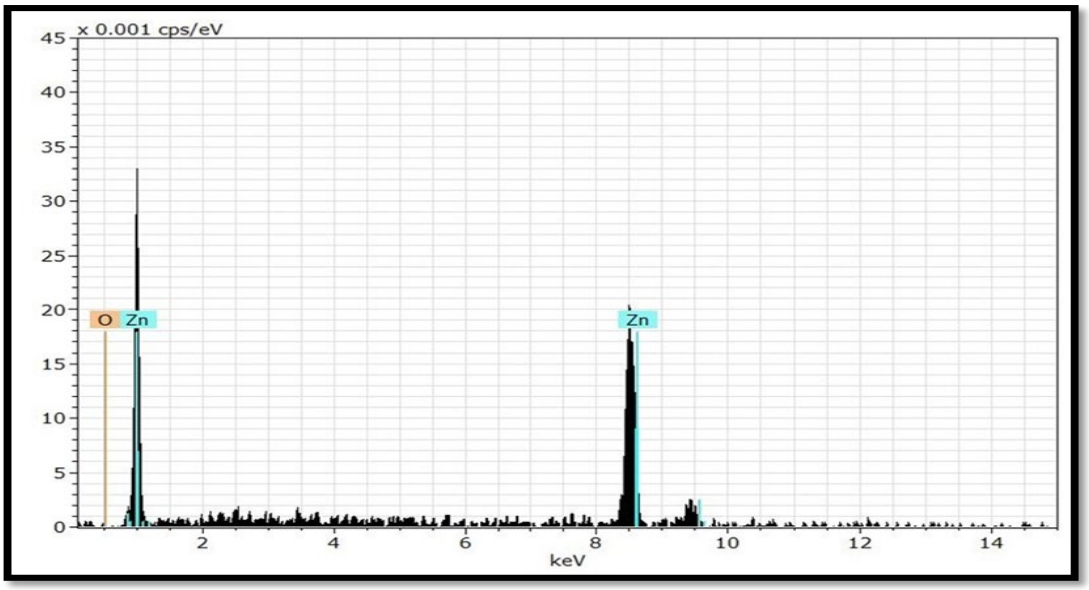

Figure (1): Shows the purity of zinc oxide nanoparticles using SDX device

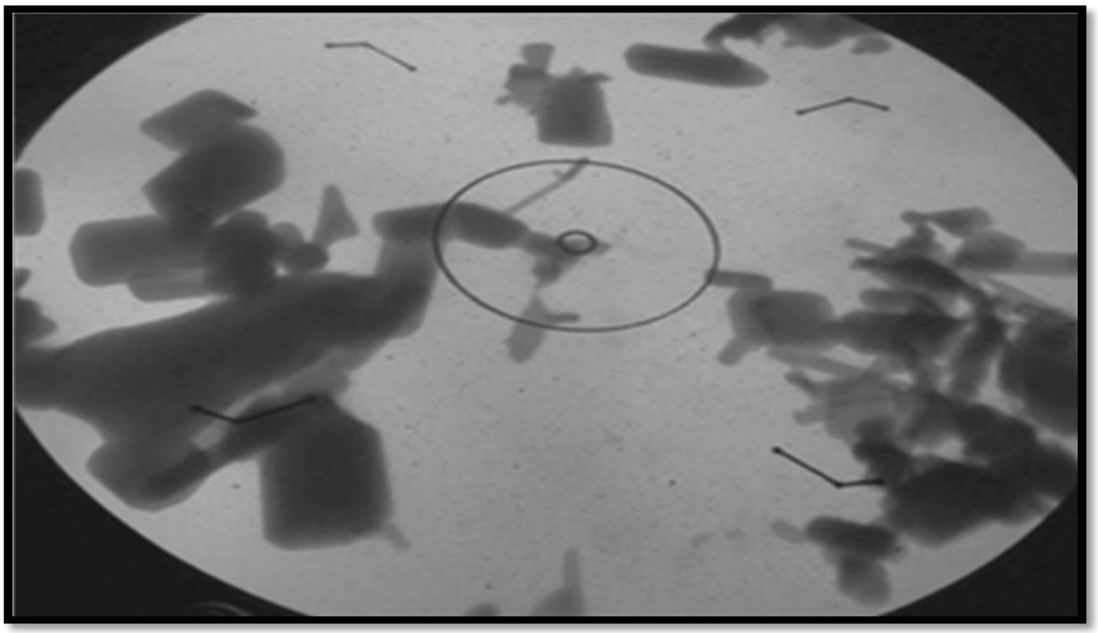

Figure (2): Shows the cubic shapes of zinc oxide nanoparticles using TEM microscope.

The dosing solution of ZnO-NPs powder was prepared with two concentrations of 100 and 200 mg/kg, by dissolving 325 and 650 mg of this powder in 13 ml of distilled water respectively. Then, the mixture for each concentration was placed in a storage bottle Vial Tube Container, then the tube was placed on a magnetic stirrer for half an hour to mix the material well, and after that it was placed in an ultrasonic device for 15 minutes to prevent agglomeration of the material. The solution of ZnO- NPs for each concentration is mixed daily before dosing it to the animals by placing it on a magnetic stirrer for 15 minutes, then it is given to the animals orally using a plastic tube at a rate of 0.1 ml of prepared solution from each concentration of ZnO-NPs once a day and during the two treating periods 7 and 14 days as following: -

1. The first group: it included 8 male white mice who were treated with 0.1 ml of distilled water. This group was considered as control animals
2. The second group: it included 8 male white mice treated with 0.1 ml of 100 mg/kg of ZnO-NPs for 7 days.
3. The third group: it included 8 male white mice who were treated with 0.1 ml of 100 mg/kg of ZnO-NPs for 14 days.
4. The fourth group: it included 8 male white mice who were treated with 0.1 ml of 200 mg/kg of ZnO-NPs for 7 days.
5. The fifth group: it included 8 male white mice who were treated with 0.1 ml of 200 mg/kg of ZnO NPs for 14 days.

Biochemical analysis and histological sections preparation

After 14 days of the experiment, the animal was anaesthetized using chloroform, and the blood samples were collected by cardiac puncture. The blood samples were gathered into tubes containing a gelatinous substance (Gel tube), and the serum was separated at 5000 rpm for 5 minutes by centrifugation and the separated serum was used for determination. the activity of pancreas enzymes including. (amylase and lipase). Then, the animals were killed by causing paralysis using the cervical dislocation method, and the pancreas was immediately excised and washed with normal saline (0.9%). The colorimetric enzymatic methods (Biodiagnostic kits) were used for the measurement the activity of Plasma pancreas using spectrophotometer (Milton Roy Spectronic 1201). The excided pancreas was fixed in formalin solution (10%) for 48 hours, then the fixative was removed from the pancreas by washing it with tap water for several times, after which it was preserved in ethyl alcohol (70%) for preparing the histological sections. All prepared slides for the histological study of the pancreas were examined using a light microscope with a magnification of 10 and 40X. Then, photographs of some histological sections of the pancreas were taken using an Olympus compound microscope and an Omax USB Camera (3.7) (China) which connected to a laptop.

Statistical analysis

All data were analyzed using SPSS (V.24) program using One Way ANOVA test by obtaining Least Significant Differences (LSD) between the means of studied groups. The data were presented as Mean±S.E, and the $p \leq 0.05$ was considered as significant differences.

Results

-1 Animal body weights

The statistical analysis of the resulted that value of ($p<0.0001$) means that there are significant differences between the studied groups and for the two periods (14 and 7 days) and for the two concentrations (100, 200) mg/kg of ZnO-NPs. The results showed significant differences in the body weights of animals treated with ZnO-NPs at a concentration of 100 mg/kg and for 7 days at average of (-2.03±0.08) and animals treated with a concentration of 200 mg/kg and for 7 days at average of (-4.87±0.46) as compared to control group for a period of 7 days with average (1.48±0.27).

Furthermore, the results also showed significant differences between the treated animals at a concentration of 100 mg/kg and for 14 days with average (-3.97±0.59), and a concentration of 200 mg/kg and for 14 days with average (0.26 ± -5.36) in comparison to control group for 14 days with average (2.26±0.39). There were also significant differences in the body weight of animals treated with a concentration of 100 mg/kg treated with ZnO-NPs for 7 days with animals treated at a concentration of 100 and 200 and for 14 days, where the less body weight was associated with increasing the concentration and duration of treatment (Table 1).

Table (1): The body weights of animals before and after treatment with 100 and 200 mg/kg ZnO-NPs for 7 and 14 days.

Groups treated with ZnO-NPs	Weight gain (Mean±S.E.)	P Value
Control (7 days)	1.48±0.27	<0.0001***
ZnO-NPs (100 mg/Kg) 7 days	-2.03±0.08 [a]	
ZnO-NPs (200 mg/Kg) 7 days	-4.87±0.46 [ac]	
Control (14 days)	2.26±0.39	
ZnO-NPs (100 mg/Kg) 14 days	-3.97± 0.59 [be]	
ZnO-NPs (200 mg/Kg) 14 days	-5.36 ±0.26 [bde]	

* Significant differences between all groups
a Significant difference vs. control (7 days)
b Significant differences vs. control (14 days)
c Significant differences vs. conc. 100 (7 days)
d Significant differences vs. conc. 100 (14 days)
e Significant differences vs. conc. 100 (7 days) & 14 days (100&200)

-2 Histological changes of the pancreas

The microscopic examination of the cross sections in the pancreas in control group, which were stained with

Hematoxylin-Eosin, detected a normal histological structure, consisting of lobules with various sizes and shapes, separated by septa and linked together by delicate connective tissue. These lobules are interspersed with blood vessels and ducts, and each lobe consists of acini from the outer part and the Islets of Langerhans; these islets consist of a group of endocrine cells with capillaries in the middle (Fig. 3, 4). While the cross sections of the pancreas of mice treated with 100 mg/kg of ZnO-NPs for 7 days, it showed histological changes, which were represented in congestion in blood vessels, infiltration of inflammatory cells, an increase in the thickness of some septa between the lobes, and the fusion of some acini (Fig. 5) [8].In contrast, increasing the period of exposure of mice to 14 days, this caused an increase in the thickness of the septa between the acini, hypertrophy of the external endocrine ducts, an increase in zymogen granules, and an increase in pancreatic juice, as well as changes in the shapes of Langerhans islets to oval and blood congestion (Figure 6) as compared to the normal tissue of control group (Fig. 3, 4) [9]. In addition, the cross sections of the pancreas in mice treated with a concentration of 200 mg/kg of ZnO-NPs for 7 days using Hematoxylin-Eosin stain, noticed increasing blood congestion and infiltration of inflammatory cells with an increase in the thickness of the septa between the lobes (Fig. 7). Whereas the increasing the exposure period to 14 days, it caused cell necrosis, hypertrophy of the external endocrine ducts, acini fusion, tissue fibrosis and increasing of inflammatory cells infiltration in comparison to the duration of exposure of ZnO-NPs for 7 days (Fig. 8)

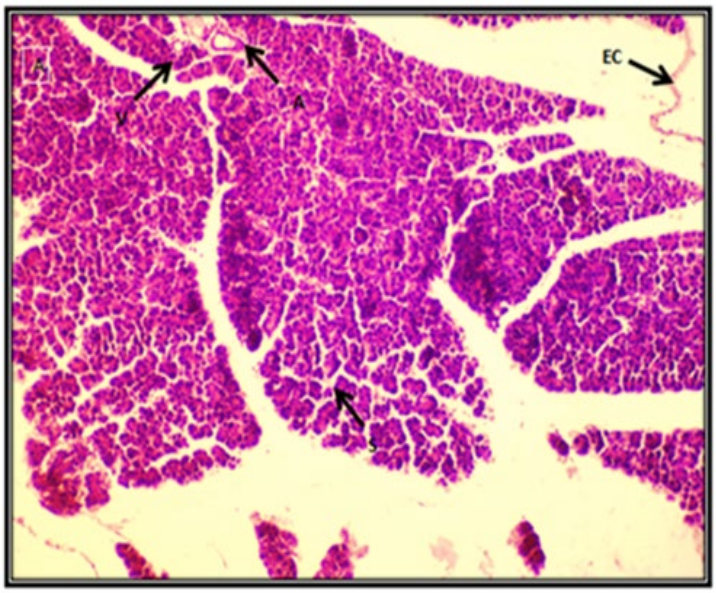

Figure (3): A cross section in the pancreas of albino rats of the control group showing (V) the vein, (A) the artery, (EG) the columnar epithelium, and (S) stroma. Hematoxylin-eosin stain (100X).

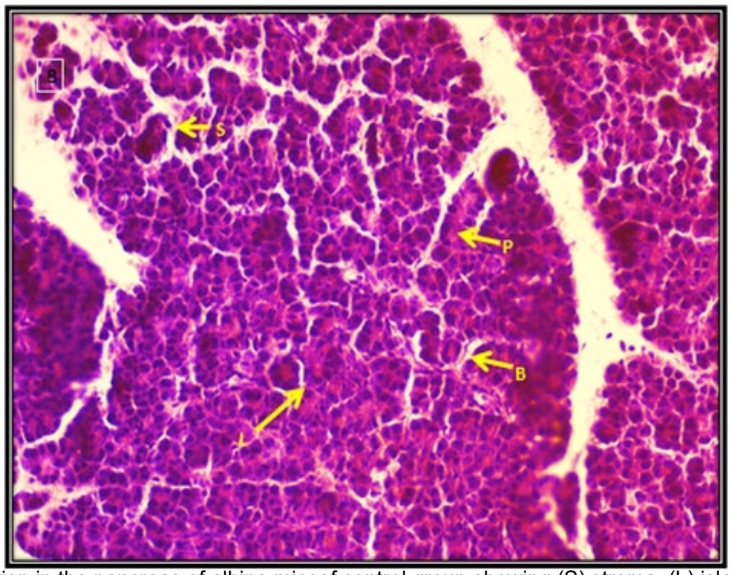

Figure (4): A cross-sectional section in the pancreas of albino miceof control group showing (S) stroma, (L) islets of Langerhans, (B) capillaries, and (P) pancreatic duct. Hematoxylin-eosin stain (400X).

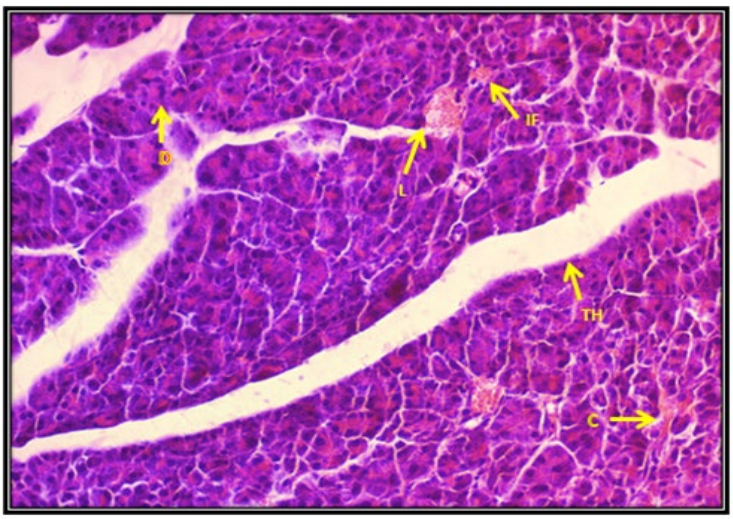

Figure (5): A cross section in the pancreas of albino mice of the group dosed at a concentration of 100 mg/kg of ZnO-NPs for 7 days showed histopathological changes represented by (C) blood hyperemia, (IF) infiltration of inflammatory cells, (D) fusion of some acini, (TH) increase The thickness of the segmental interlobular septa, (L) islets of Lanker-Hans. Hematoxylin-eosin stain (400X).

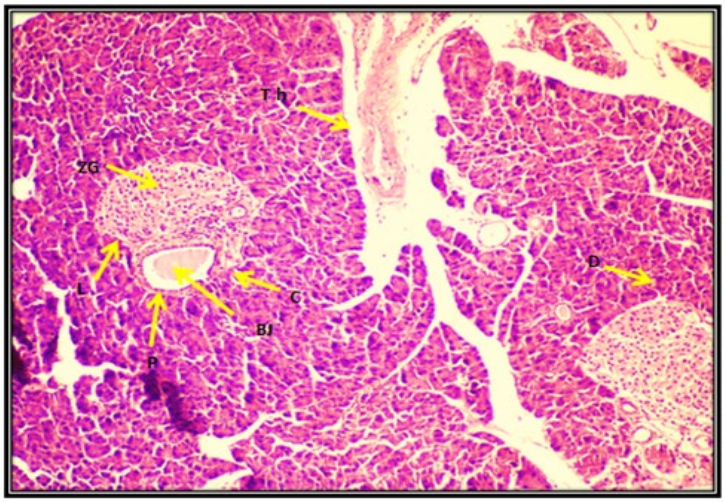

Figure (6): A cross-sectional section of the pancreas of albino rats of the group dosed at a concentration of 100 mg/kg for a period of 14 days showed histological changes represented by (C) hyperemia, (ZG) non-secretory zymogen granules, (D) dentate fusion, (TH) increase thickness of the interlobular septa, (P) widening of the pancreatic duct, (BJ) increased pancreatic juice, (L) change in the shape of the islet of Langerhans. Hematoxylin-Eosin stain (100X).

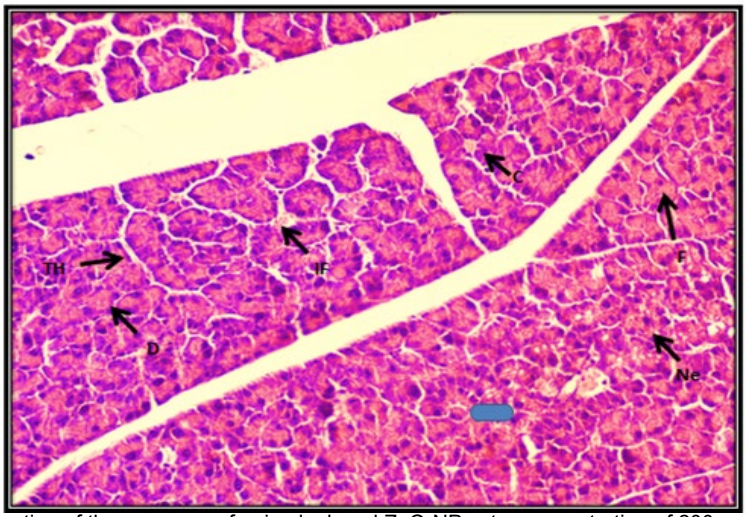

Figure (7): A cross-sectional section of the pancreas of animals dosed ZnO-NPs at a concentration of 200 mg/kg for7 days. It shows (C) an increase in blood congestion, (D) an increase in acini fusion, (TH) an increase in the thickness of the septa between the lobes, (IF) infiltration of inflammatory cells, (Ne) necrosis of dentate cells, ( ) hyperplasia of the exocrine ducts, (F) fibrosis. Hematoxylin-Eosin stain (400X)

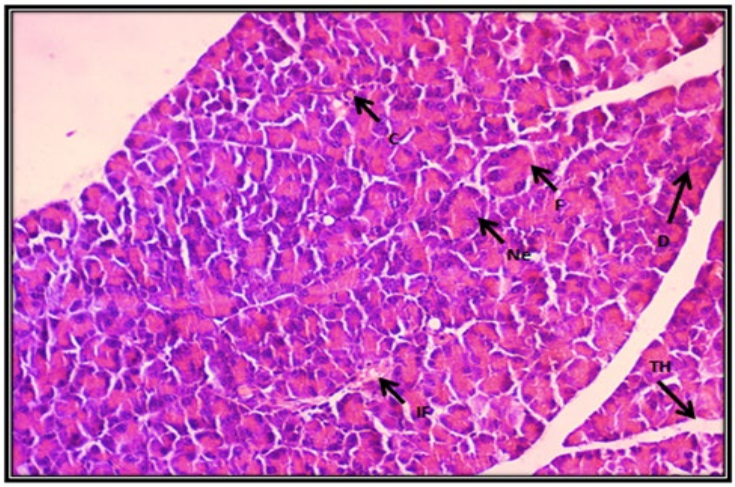

Figure (8): cross-sectional section of the pancreas of animals dosed with zinc nanoparticles at a concentration of 200 mg/kg for 14 days, showing (D) fusion of most dentures, (Ne) necrosis of dentate cells, (F) fibrosis, (TH) an increase in the thickness of the cross-sectional barriers between Lobules, (C) congestion of blood vessels, (IF) increased infiltration of inflammatory cells. Hema Toxlin-Eosin (400X)

The enzymes activity

-1 Amylase activity

The Amylase activity was illustrated in table (2), as the statistical analysis found a significant difference (p=0.002) in the Amylase activity in the studied groups for 7 and 14 days after treatment.

Interestingly, a significant effect was detected in amylase enzyme in the group of animals treated with ZnO-NPs (100 and 200 mg/kg) for 7 days and in the group of animals treated with a concentration of (200 mg/kg) for 14 days in comparison to control group (Table 2).

However, there were no significant differences between the control group and the group of treated animals with a concentration of (100 mg/kg) for 14 days but showed a significant difference with the rest of the groups. Moreover, a significant difference in amylase activity was found between the two groups of animals treated with my concentration (100 and 200 mg/kg) for 7 days, as well as significant differences in the two groups of animals treated with (100 and 200 mg/kg) for 14 days (Table 2).The mean of the amylase activity in control group was (1457.13±163.58), (2051.50±219.05) in treated animal with ZnO-NPs at 100 mg/Kg for 7 days, (1940.25±243.87) in treated animal with ZnO-NPs at 100 mg/kg for 14 days, (2659.88±127.60) in treated animal with ZnO-NPs at 200 mg/Kg for 7 days and (2540.38±260.56) in treated animal with ZnO-NPs at 200 mg/kg for 14 days (Table 2).

Table (2): The activity of Amylase before and after treatment with 100 and 200 mg/kg ZnO-NPs for 7 and 14 days.

Groups treated with ZnO-NPs	Amylase activity (mg/dL) (Mean±S.E.)	P Value
Control	1457.13±163.58	0.002**
ZnO-NPs (100 mg/Kg) 7 days	2051.50±219.05 [a]	
ZnO-NPs (100 mg/ Kg) 14 days	1940.25±243.87 [d]	
ZnO-NPs (200 mg/ Kg) 7 days	2659.88±127.60 [ab]	
ZnO-NPs (200 mg/ Kg) 14 days	2540.38±260.56 [ac]	

* Significant differences between all groups
a Significant difference vs. control
b Significant differences vs. conc. 100 & 200 (7 days)
c Significant differences vs. conc. 100 & 200 (14 days)
d Significant differences vs. conc. 100 (14 days)

-2 Lipase activity

The results of the current study revealed the presence of significant differences (p<0.0001) in the activity of lipase between the studies groups, as the activity of enzyme the groups treated with (100 and 200 mg / kg) of ZnO-NPs for 7 and 14 days significantly increased as compared to control group. the means were (21.13±3.72), (23.45± 2.59), (35.63± 4.77), (32.05±2.87), (54.36± 5.76) in control, ZnO-NPs at (100 mg/kg) for 7 days, ZnO-NPs at (100 mg/kg) for 14 days, ZnO-NPs at (200 mg/kg) for 7 days and ZnO-NPs at (200 mg/kg) for 14 days respectively (Table 3). Although, no significant difference was found between control group and animal treated at a concentration of (100 mg/kg) for 7 days. In addition, significant differences were also found between the animals treated with concentration (100 and 200 mg/kg) for 7 days as

well as for 14 days. Furthermore, there is a significant difference between the two groups of animals treated with concentrations (100 and 200 mg/kg) for 14 days with those treated with a concentration (100 mg/kg) for 7 days, as well as significant differences between the group of (200 mg/kg) for 14 days and the animals treated with a concentration (200 mg/kg) for 7 days as shown in Table (3).

Table (3): The activity of Lipase before and after treatment with 100 and 200 mg/kg ZnO-NPs for 7 and 14 days.

Groups treated with ZnO-NPs	Lipase activity (mg/dL) (Mean±S.E.)	P Value
Control	21.13±3.72	
ZnO-NPs (100 mg/Kg) 7 days	23.45± 2.59	
ZnO-NPs (100 mg/ Kg) 14 days	35.63± 4.77 [ad]	
ZnO-NPs (200 mg/ Kg) 7 days	32.05±2.87 [ab]	
ZnO-NPs (200 mg/ Kg) 14 days	54.36± 5.76 [acde]	<0.0001***

* Significant differences between all groups
a Significant difference vs. control
b Significant differences vs. conc. 100 & 200 (7 days)
c Significant differences vs. conc. 100 & 200 (14 days)
d Significant differences vs. conc. 100 (7 days)
e Significant differences vs. conc. 200 (7 days)

Biochemical Test

The levels of Sugar

As shown in table (4), the statistical analysis showed that there was a significant difference ($p<0.0001$) in the sugar level between the studied groups, as it was significantly increased in the groups of animals treated with ZnO-NPs at (100, 200) mg/kg for 7 days and 14 days, except at 200 mg/kg for 14 days, in comparison to control group. In addition, mice treated with 200 mg/kg for 14 days, the sugar level significantly decreased as compared to those treated with 100 and 200 mg/kg for 7 days. These observations suggested that the duration play a major role in influencing on the level of sugar.

The mean was in control group (71.58±6.34), (149.66±19.80) in treated animal with ZnO-NPs at 100 mg/Kg for 7 days, (112.69±13.26) in treated animal with ZnO-NPs at 100 mg/Kg for 14 days, (143.89±11.85) in in treated animal with ZnO-NPs at 100 mg/Kg for 7 days and (92.39±12.34) in treated animal with ZnO-NPs at 200 mg/Kg for 14 days.

Table (4): The sugar levels before and after treatment with 100 and 200 mg/kg ZnO-NPs for 7 and 14 days.

Groups treated with ZnO-NPs	Sugar level (mg/dL) (Mean±S.E.)	P Value
Control	71.58±6.34	
ZnO-NPs (100 mg/Kg) 7 days	149.66±19.80 [a]	
ZnO-NPs (100 mg/ Kg) 14 days	112.69±13.26 [a]	
ZnO-NPs (200 mg/ Kg) 7 days	143.89±11.85 [a]	
ZnO-NPs (200 mg/ Kg) 14 days	92.39±12.34 [bc]	<0.0001***

* Significant differences between all groups
a Significant difference vs. control
b Significant differences vs. conc. 200 (7 days)
c Significant differences vs. conc. 100 (7 days)

Discussion

Weight changes

1-Animal body weights

The current study detected the harmful effect of ZnO-NPs on the body weights of animals before and after treatment, where it was noticed that there were no significant differences in the average body weights of animals in control group, whereas the body weights of animals showed general significant differences between the studied groups. The animal weights significantly decreased with an increases in the concentration of ZnO-NPs to reach their lowest average at the highest concentration (200 mg /kg) and also with an increase in the duration of treatment from 7 to 14 days, which affected the animal body structure [10]. The reason for the decrease in weight of animals is due to the accumulation of ZnO-NPs in the digestive organs, which affected the vital activities taking place inside these organs, causing loss of appetite or diarrhea in treated animals, and then the stored fat is consumed [11].

The findings of the current study are in agreement Tabish et al. [12] study, where it was found that the injecting of rat intraperitoneally with graphene nanoparticles (GNPs) at a concentration of 5 and 15 mg/kg for 27 days, caused decrease in the rate body weights and this effect was increased with increasing the concentration. Moreover, the results of Koster et al [13] found that when a rat was dosed with ZnO-NPs for 14 days [14], it led to a decrease in the body weights of

animals due to loss of appetite resulting from the accumulation of ZnO-NPs in the stomach and intestine, which caused a disruption in the digestive system functions, which led to weight loss [8].

2-Histopathological changes in the pancreas

The results of microscopic examination of pancreatic tissue sections stained using Hematoxylin-Eosin stain for animals dosed with ZnO-NPs at concentrations of 100 and 200 mg/kg for 7 and 14 days showed a histological changes represented by cell necrosis, acini fusion, increased thickness of septa, vascular congestion, increased zymogen granules, infiltration of inflammatory cells and dilatation of the ducts; these changes increase with increasing concentration and duration in comparison to control group of animals that retain their normal histological structure. It is believed that the reason for necrosis, acini fusion and infiltration of inflammatory cells is due to the accumulation of ZnO-NPs in the membranes of endocrine cells, causing toxicity to them, which leads to the formation of reactive oxygen species by lipid peroxide, resulting in the destruction of the plasma membrane of the cell and disturbance of osmotic balance, and this change in osmosis causes cell necrosis [9].

The results of this study are consistent with the study of Ali et [7] where it was found that when injected the rats with two concentrations ZnO-NPs (100 and 300 mg/kg) for 30 days, it caused necrosis and damage to the endocrine cells of Langerhans islets and their contraction. The reason can clarified by that the mechanism of lipid peroxidation and reactive oxygen species production, which is produced as a result from the toxic effect ZnO-NPs accumulation on the endocrine glands and acini, which leads to the destruction of the cell's plasma membrane and disturbance of the permeability pressure, which consequently causes a disturbance in the cell balance, eventually causing necrosis [15]. In addition, the results of this study also are in agreement with the study of Sewelam et al [16] which observed that the injecting ZnO-NPs into peritoneum of adult rats at two concentrations (250 and 700 mg /kg) for a period of 14 days led to the exposure of pancreatic tissue to cellular damage, represented by congestion of blood vessels, ducts expansion and infiltration of inflammatory cells. These harmful effects are explained due to the dissolving of ZnO-NPs and releasing of zinc ions as is a heavy metal that leads to pancreatic toxicity. While the expansion of the ducts caused by the accumulation of ZnO-NPs, it may be caused by blocking the main duct or by a mild injury to the ductal cells.

Furthermore, the microscopic examination of the histological sections in pancreas of animals dosed with ZnO-NPs for 7 and 14 days detected the occurrence of fibrosis in pancreatic tissues, which increases with increasing duration and concentration. The reason is may due to the occurrence of oxidative stress, which affects the activity of pancreatic cells and increases the production of collagen fibers where their deposition leads to fibrosis. The results of the current study are consistent with the results of Abd El-Haleem and Mohamed [17] study, where it was found that pancreatic fibrosis may due to the deposition of collagen fibers resulting from the activity of astrocytes in the pancreas containing fat. These cells during its differentiation lose fat droplets and look like fibroblasts capable of synthesizing collagen types, which are stimulated by oxidative stress, and therefore this fibrosis leads to a distortion in the cellular engineering of the acini[18].

3-Changes in the level of sugar

The current study revealed that there was an increase in the sugar level in animals treated with ZnO-NPs at a concentration of 100 and 200 mg /kg and for periods 7 and 14 in comparison to control group, however the sugar level showed the highest rate in the two groups of animals dosed at a concentration of 100 and 200 mg kg for 7 days, while it levels recorded a decrease in the two groups of animals dosed at a concentration of 100 and 200 mg/kg for 14 days. The stimulation of the hyperglycemic response is observed depending on the dose and method of administration, as ZnO-NPs reach the maximum peak in the first days of treatment and then sugar levels begin to decrease. The reason is may due to the rapid elimination of waste through defecation, which leads to difficulty in the distribution and accumulation of ZnO-NPs in the liver cells as it is known that the liver is one of the main organs generating free glucose, as the higher the dose, the hyperglycemia increases because its rise causes an increase in the concentration of zinc ions in the liver cells, and thus an increase in glucose levels through the breakdown of glycogen[19], causing a decrease in insulin. The observation of this study is in agreement with Virgen-Ortiz et al [20] results via treatment of rats with ZnO-NPs at concentrations of 10 and 100 mg/kg and in two different ways of administration, injection into the peritoneum and orally, for the same period. It was found that the sugar peak level was observed in the short term of orally administered animals[21], where the peak

concentration of nanoparticles in the blood is reached after six hours and then begins to decrease; unlike the intraperitoneal injection, the concentration is kept high after 74 hours of administration and the effect increases with increasing concentration.

4-Enzymatic Changes in Pancreas

The results of this study showed that the amylase and lipase levels was increase in pancreas of mice dosed with ZnO-NPs at concentrations of 100 and 200 mg / kg for 7 and 14 days, and the levels elevated with increasing concentration and time in comparison control group. This may explained by intracellular dissolution of ZnO-NPs causing the production of Zn^{2+} ions as a major mechanism leading to pancreatic toxicity, where elevated Zn^{2+} has a cytotoxic effect [22], or it may due to elevation in lipid peroxidation resulting from oxidative stress and generation of excess ROS (lipid peroxidation is a molecular mechanism by which cellular oxidation of lipid molecules can be accelerated). The results of current study are consistent with Sewelam and Amin [16], which found that the injection intraperitoneal of rat with 200 and 700 mg/kg of concentration of ZnO-NPs with a size of 35 nm for 14 days, caused an elevation in the levels of amylase and lipase enzymes in the pancreas due to pancreatic poisoning as a result of the decomposition of ZnO-NPs and the release of zinc ions, the increase of which is an indicator of pancreatic toxicity, in addition to intracellular oxidative stress that causes excess ROS release, which triggers a cascade of proinflammatory cytokine releasing.

Conclusions

The findings of the current study revealed that the treatment of adult white mice with ZnO-NPs at two concentrations of 100 and 200 mg/kg for two periods of 7 and 14 days, it had negative effects on the organs of the digestive system. These effects increased with increasing the higher concentrations of ZnO-NPs and prolonged duration of the oral administration, as their effects were evident, both on the morphological appearance of the cells Pancreas and changes in the functional changes and Pancreas histological structure of the. Therefore, it was suggested to conduct other studies using lower concentrations of ZnO-NPs to find out the safe concentration limits for these particles, because as it has many uses in humans and animal's life.

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