Egypt.J.Chem. **Vol. 62**, No. 10. pp. 1771 - 1783 (2019)

Egyptian Journal of Chemistry
http://ejchem.journals.ekb.eg/

Evaluation of Zinc-oxide Nanoparticles Effect on Treatment of Diabetes in Streptozotocin-induced Diabetic Rats

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TO produce unique products with novel properties, to manipulate materials at the nano-scale level. Nanoparticles demonstrate novel or improved characteristics that are supported with specific properties such as size and distribution. The effect of zinc oxide nanoparticles (ZnONPs) on diabetic rats induced by streptozotocin- were evaluated in this study. Forty male albino rats with weight 180-200 gm were used in this study and grouped as follows: Group A: non-diabetic animals (n=10) negative control; Group B1: Diabetic animals that did not received any treatment (n=10) positive control; Group B2: the Diabetic animals (n = 10) who received ZnONPs (10 mg / kg body weight oral daily); Group B3: the Diabetic animals (n=10) who received Diamicron (10 mg / kg body weight oral daily). Intraperitonial injection of streptozotocin by a single dose (60 mg/kg body weight) was used to induce diabetes. After 7 days from the induction, the samples were taken by capillary from fasting rats to measure glucose and insulin (Initial) and after 21 days. At the end of experiment the blood glucose, serum insulin and HbA1c levels were determined for all studied groups. Tissues samples from liver and pancreas were taken to determine the histopathology and gene expression for insulin and insulin receptor. The results indicated high level of blood glucose and low level of insulin in diabetic rats as compared to the -ve control, while their levels were significantly modified in rats that administrated ZnONPs and Diamicron and this results will be confirmed by the gene expression. zinc oxide nanoparticles act as potent antidiabetic agent through decreasing blood glucose and increasing serum insulin.

Keywords: ZnONPs, Diamicron, Nanotechnology, Diabetes.

Introduction

The DM (Diabetes mellitus) is a number of different disorders characterized by hyperglycaemia and glucose intolerance, due to deficiency of insulin, disturbed insulin action, or both. The complexity of diabetes appears due to disruption in the regulatory systems for the storage and the fuels of metabolic mobilization including the carbohydrates anabolism and catabolism, proteins, and lipids emanating from the disturbed secretion of insulin and action of insulin [1].

World Health Organization (WHO) estimated that there are 422 million adults suffering from diabetes mellitus worldwide, according to the latest 2016 data. The persons suffering from diabetes need the improvement of some drugs with several methods of action. Some articles indicated that certain metals play a crucial role in the metabolism of glucose and the effect of their deficiency on the development of diabetes as chromium [2], vanadium [3] magnesium [4], and zinc [5]. Moreover, these metals were reported to have an important function in the maintenance of

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Received 4/4/2019; Accepted 23/4/2019
DOI: 10.21608/ejchem.2019.11350.1735

blood glucose levels and have been used in the treatment of diabetes. Zinc (Zn) is ordered as the second abundant trace element, after iron, in all human tissues and tissue fluids. Several biological activities such as cell division, epithelial cell integrity, immune response regulation, and the proper function of more than three hundred enzymes are tightly correlated with zinc. Previous studies elucidated the precise role of zinc in the pathophysiology of DM. They indicated that the insulin molecule forms complexes and polymers with zinc in the β cell granules. Furthermore, Zn plays a significant role in insulin excretion. Anti-diabetic and insulin-like effects of Zn have been confirmed in numerous studies in vivo & in vitro. Previous researches demonstrated that Zn may interact with certain components of insulin signalling pathways and hence regulated the metabolism of blood sugar. In addition, Zn can also promote the B subunit insulin receptor phosphorylation [6]. Improvement a Zn-based medication for the treatment of both types of diabetes and their associated complications thus become an appealing suggestion. In diabetes, an important role of zinc has been involved by the zinc supplies studies in diabetic rats [7]. Alkaladi et al. [8] informed the anti-diabetic effects of ZnONPs on gene expression of insulin induction, insulin receptor and glucose metabolizing enzymes. In the same way Umrani and Paknikar [9] reported that the ZnONPs capability for controlling of blood sugar level in rats with diabetes. These two studies are only applied for monitoring the ZnONPs effect on rats with diabetes.

This work was aimed to demonstrate the curative effect of zinc oxide nano-particles on diabetic rats that induced with streptozotocin as well as their compared effect to Diamicron therapy.

Material and Methods

This study was conducted on male forty Wistar rats weighing 180–200 gm were obtained from the National Research Centre (Cairo, Egypt); and according to the ethical committee of National Research Centre no (16-207).

Rats were housed in separate metal cages, fresh and clean drinking water was supplied adlibitum through specific nipple. Rats were kept at constant environmental and nutritional conditions during the course of the experiment. Cleaning and changing water and food was done for all animals twice daily. The animals were left 7 days for acclimatization before the beginning of the experiment. The rats were handled according to the Guidelines for the Care and Use of Laboratory Animals from the National Institutes of Health, USA.

Diabetes Induction:

The rats had been fasted for 12 hours before induction of diabetes by using streptozotocin (STZ). The rats received a single intraperitioneal (I.P) injection of 60 mg/Kg of freshly prepared STZ and dissolved in 0.05 M citrate buffer, pH 4.5. Rats with serum glucose levels of 200 mg/dl after 2 h of glucose intake (2 g/kg body weight, orally) were considered diabetic and chosen for the subsequent studies [10].

Experimental design:

The rats were randomly divided into three groups 7 days after the induction of diabetes:

Group A: non-diabetic animals (n=10) negative control;

Group B1: Diabetic animals that not received any treatment (n=10) positive control;

Group B2: the Diabetic animals (n =10) who received ZnONPs (10 mg / kg body weight oral daily) [10].

Group B3: the Diabetic animals (n=10) who received Diamicron (10 mg / kg body weight oral daily [11].

Sampling

- 1st blood samples were taken by capillary at the start of experiment to measure the glucose and insulin.

- 2nd venous blood samples were taken after 21 days of treatment, rats were anesthetized, blood samples were collected from the abdominal vena cava to measure the glucose, insulin, HbA1C and liver and kidney functions.

- The pancreas and liver tissues were quickly collected and divided into two parts for gene expression and histopathological analysis.

Methods:

Zinc Oxide Nanoparticles (ZnONPs):

In the present study, ZnO nanoparticles (ZnONPs) were prepared Using Pechini method [12]. In this technique, stoichiometric amounts of Zn (NO3)2.6H2O were weighed and well mixed, with distilled water and ethylene glycol. This mixture was then transferred on a magnetic stirrer with a hot plate until drying, after that, an autoignition takes places resulting in a fluffy white yellowish powder then grinded. This powder was

collected and then heated at 500 o C in Lenton Furnace UAF 16/5.

High resolution transmission electron micrograph shows clear platelets with hexagonal shape, slightly agglomerated in a chain like network. Homogeneous size and distribution with average particle size 47 nm. This result agrees well with that calculated from XRD.

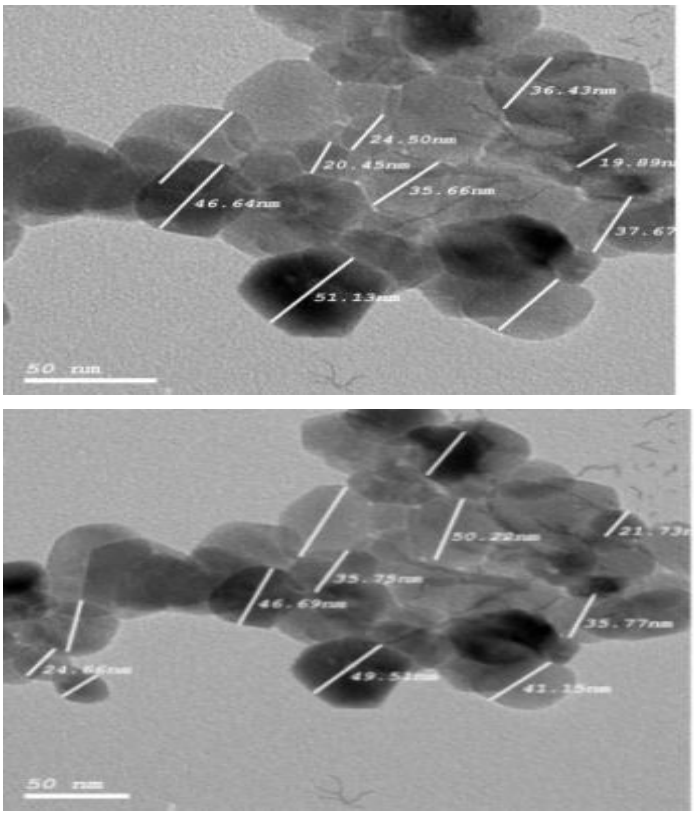
Biochemical investigation:

- Blood glucose level (mg/dL) was estimated by glucose oxidase method using by Trinder [13].
- The serum insulin levels were assayed by sandwich ELISA using according to the method of [14] using kit purchased from DRG international, Inc. (NJ, USA).
- The blood glycated Hb levels were determined using a commercial assay kit obtained from intermedical, Italy [15].
- Urea measure by Urease method [16] & Creatinine were determined by using colorimetric Enzymatic Jaffe method [17].

- SGPT and SGOT were determined by using Enzymatic Kinetic method [18].

Total RNA extraction:

TRIZOL reagent (Invitrogen, Germany) was used to extract the total RNA, from liver tissues of male rats according to the manufacturer's instructions. The concentration for extracted RNA was detected using Nano-drop2000 spectrophotometer (Thermo Fisher Scientific, USA). Eluted RNA was stored in -80°C till further processing. Secondly, PCR quantitation experiments were performed by using qRTPCR. Master Mix Kit, (Fermentas, Germany) to determine the expression of insulin and insulin receptor gene and housekeeping gene -actin (used as an endogenous control) for normalization. The working master mix was prepared according to manufacturer's protocol. Fluorescence measurements were made in every cycle and the thermal profile used as follows: An amount of total RNA (5 µg) was used with a master mix. The RT reaction was carried out at 25°C for 10 min, followed by 1 h at 42°C, and finished with a denaturation step at 99°C for 5 min. Afterwards the reaction tubes containing RT preparations were flash-cooled in an ice chamber until being used for cDNA amplification through quantitative Real Time- polymerase chain reaction (qRT-PCR) [19]. PCR was performed in one step:



3 min pre incubation at 95°C, followed by 40 cycles of 95°C for 1 sec; at 55°C for 30 sec; and at 72°C for 30 sec. The samples were measured in duplicated.The forward insulin primer: F-CCT GTT GGT GCA CTT CCT AC, reverse insulin primer: R-TGC AGT AGT TCT CCA GCT GC, The forward insulin receptor primer:

F-TTCATTCAGGAAGACCTTCGA, reverse insulin receptor primer:

R-AGGCCAGAGATGACAAGTGAC, The forward□-actinprimer:

F-GGTATGGAATCCTGTGGCATCCATGAAA, reverse□-actin primer:
R-GTGTAAAACGCAGCTCAGTAACAGTC-CG

The data was assayed using the comparative ΔΔCT method.

Liver and Pancreatic tissues for the histopathological study:

Autopsy samples of the pancreas and liver were prepared for the histopathological examination and stained with hematoxylin and eosin according to the method reported by [20].

Statistical analysis:

All calculations will be performed using SPSS version 18.0 (SPSS, Chicago, IL) statistical package. Descriptive parameters are presented as mean ± standard deviation. Comparisons between groups of means were performed using analysis of variance. P value will be considered as significant P<0.05.

Results

Serum glucose:

The glucose levels in serum were significantly increased in group B1 (diabetic group) compared with group A (-ve control). After therapy with ZnoNPs (group B2) and Diamicron (group B3) induced a significant decrease in the serum glucose levels in these treated groups compared with group B1 (diabetic group), while they induced a significant increase compared with the group A. There was no significant difference between group B2 and group B3 (Table 1, Fig. 1).

The insulin level:

The levels of insulin in serum were a decreased significantly in group (B1) liken with the group A. The rats treated with ZnoNPs (group B2)

TABLE 1. The glucose (mg / dl) level in different studied groups

Groups	Glucose level (mg / dl)		P-value
	Start	Final	
Group A	106.7 ± 8.06	104.3 ± 4.64	0.459
Group B_1	245.2 ± 11.49	350.1 ± 10.32	<0.001
Group B_2	243.8 ± 5.85	151.7 ± 4.57	<0.001
Group B_3	243.9 ± 5.86	149.4 ± 5.19	<0.001

p<0.05 considered significant

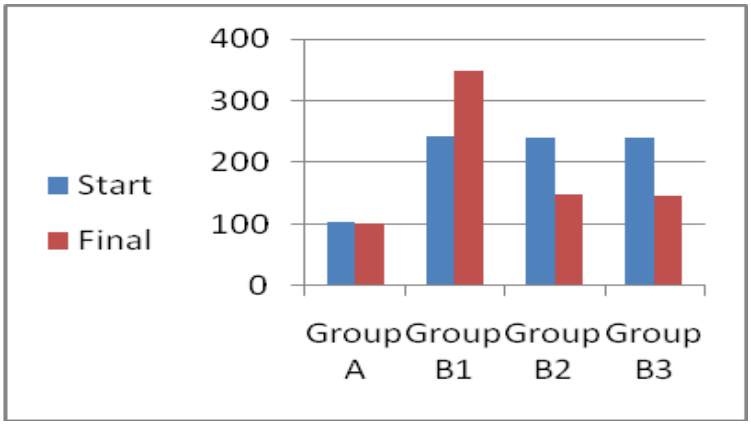


Fig. 1. Glucose level in different studied groups.

and Diamicron (group B3) showed significantly increase in the levels of insulin in serum liken with the group (B1), while they were appeared a decrease significantly compared to the group A. There was no significant difference between group B2 and group B3.

Glycated hemoglobin (HbA1-C):

The level of hemoglobin glycation was increased significantly in group B1 liken with the group A. The rats were treated with ZnoNPs (group B2) and Diamicron (group B3) induced a significant decrease in the level of HbA1-C liken with the group B1 and show an increase significantly liken with the group A (Table 3, Fig. 3).

Gene expression:

In this study, the insulin and insulin receptor genes were decreased significantly in the rats of group B1 liken with group A in their pancreas and liver tissues. Treatment with ZnoNPs (group B2) and Diamicron (group B3) induced a significant increase in the insulin and insulin receptor gene levels compared to the diabetic group (B1) in pancreas and liver tissues (Tables 4, 5, Fig. 4, 5).

The study of histopathological:

The pancreatic structural (control pancreas) histologically is formed from closely packed lobules of pancreatic acini. They are created by

TABLE 2. The insulin level (mg / dl) in different studied groups

Groups	Insulin Level (mg/dl)		P-value
	Start	Final	
Group A	15.25 ± 0.20	15.62 ± 0.28	0.018
Group B_1	11.04 ± 0.22	9.95 ± 0.51	<0.001
Group B_2	11.39 ± 0.26	13.23 ± 0.26	<0.001
Group B_3	11.23 ± 0.28	13.1 ± 0.22	<0.001

p<0.05 considered significant

TABLE 3. The HbA1-C level in different studied groups

Groups	HbA1-C%	P-value
Group A	5.75±0.35	<0.001
Group B_1	8.76±0.28	<0.001
Group B_2	7.08 ±1.07	<0.001
Group B_3	7.28±1.22	<0.001

p<0.05 considered significant

TABLE 4. The insulin receptor gene in different studied groups

Group A	**0.04**	**1.95**
Group B_1	0.02	0.66
Group B_2	0.03	1.65
Group B_3	0.02	1.19

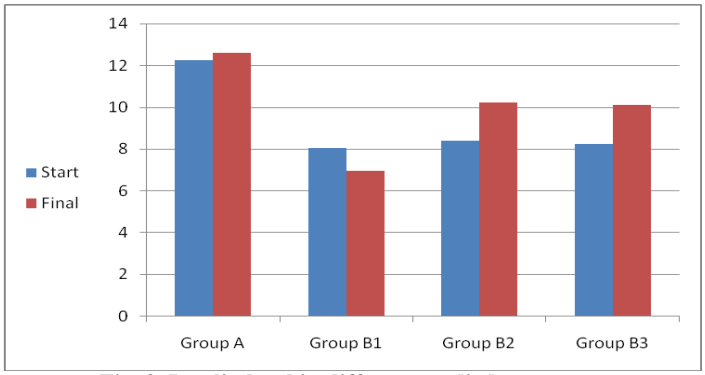


Fig. 2. Insulin level in different studied groups

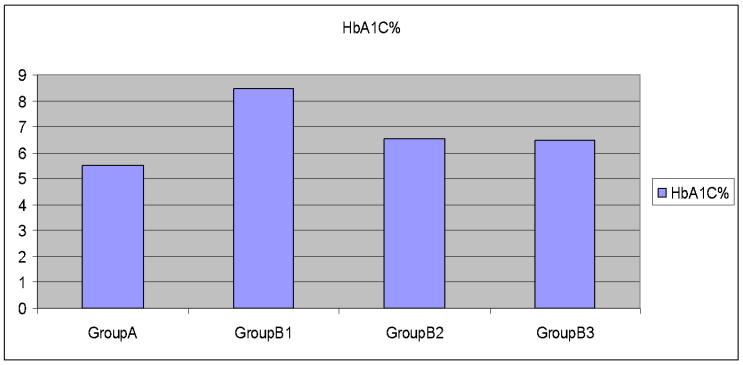


Fig. 3. HbA1-C level in different studied groups

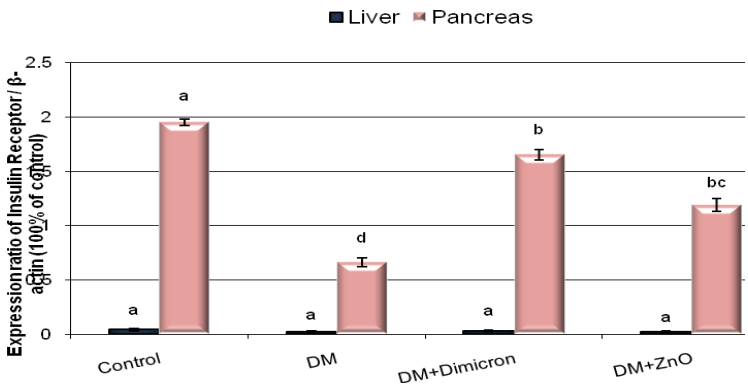


Fig. 4. Insulin receptor in different studied groups

TABLE 5. The insulin gene in different studied groups

Groups	Insulin	
	Liver	Pancreas
Group A	0.07	1.74
Group B_1	0.03	0.48
Group B_2	0.04	1.39
Group B_3	0.04	0.97

pyramidal cells with basal nuclei and an apical acidophilic cytoplasm. The islets of Langerhans were embedded within the exocrine portions (Fig. 6). The diabetic rat's pancreas (group B1) appeared marked reduction in islets of Langerhans (IL) with marked degenerative changes and necrotic tissue of all the islets, the acini showed marked atrophy with degenerative and vaculation changes (Fig. 8). The pancreas of Diamicron treated group (group B3) showed restoration of the normal size of Islets of Langerhans (IL) with normal endocrine cell distribution with mild necrotic tissue and central vaculation showing appearance and distribution of Beta cells (Fig. 10). Pancreas of nano-Zinc Oxide treated rats (group B2) showed restoration of normal size of islets of Langerhans (IL) with marked peripheral hyperplasia and mild central vaculation and necrotic changes with clear appearance and distribution of Beta cells (Fig. 12).

The histological structure of the control liver showed normal liver parenchyma, hepatocytes with normal liver sinusoids and canaliculi with normal

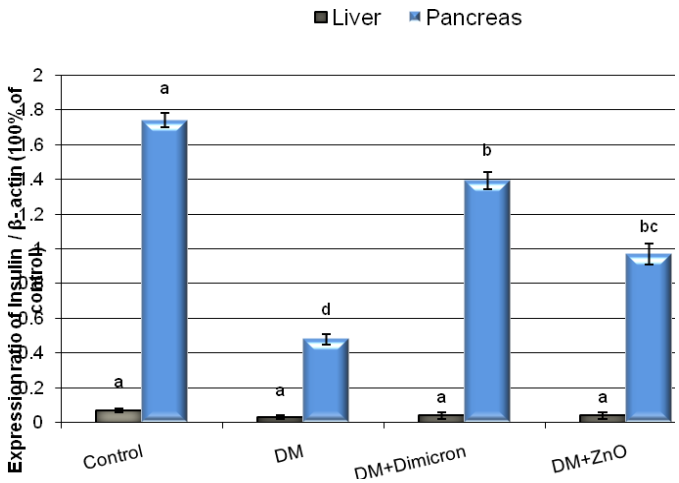


Fig. 5. Insulin in different studied groups

Pancreatic tissue

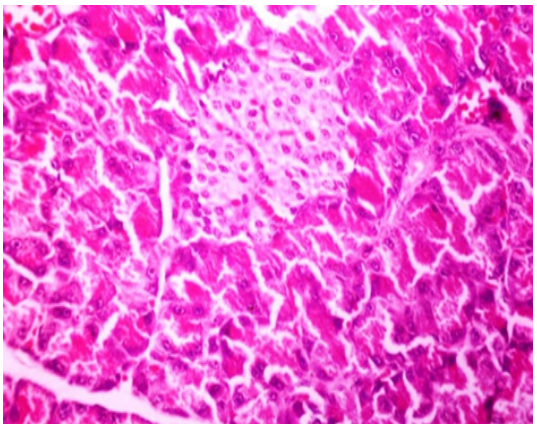


Fig. 6. A photomicrograph showing the normal histological architecture of the control rat pancreas, for both endocrine and exocrine portions normal acinar structure with normal islets (x400).

Liver tissue

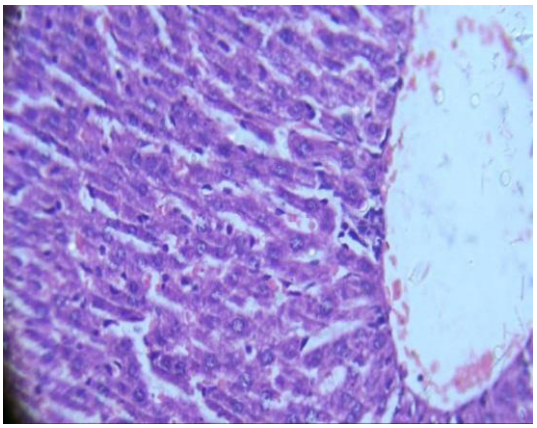


Fig. 7. Liver of normal rat (Negative control) with normal Blood sinusoids (BS) and normal histoarchtexture and hepatic cords (HC) with normal appearance and distribution of Kuppfer cells (KC) and normal caliber of central vein (CV). H&E X 40.

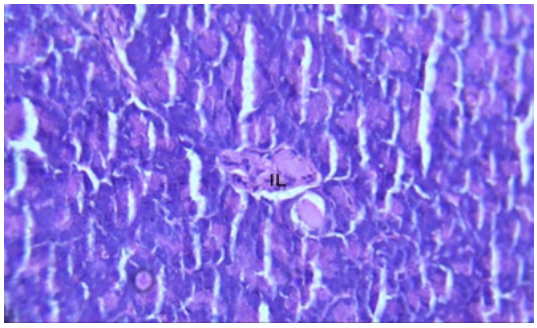


Fig. 8. Pancreas of Positive control group induced diabetic model with STZ. Showing marked reduction in islets of langerhans (IL) with marked degenerative changes and necrotic tissue of all the islets, acini showing marked atrophy degenerative and vaculation changes. H&E X 40.

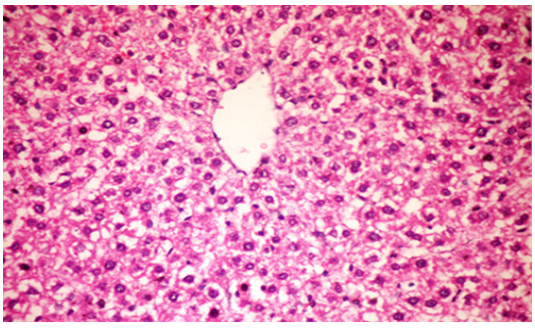


Fig. 9. A photomicrograph of liver of diabetic rat showed Kupffer cells activation and cytoplasmic vacuolization of hepatocytes, dilatation of liver sinusoids and some necrotic changes of liver tissue with marked fatty changes (FC) some hebatocytes showed apoptotic changes nuclear pyknosis (PN) H&E X 40.

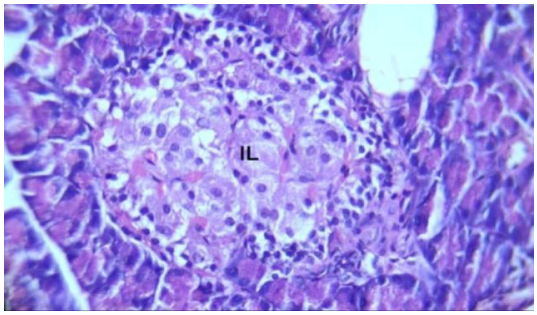


Fig. 10. Pancreas of Diamicron treated group showing restoration of normal size of Islets of Langerhans (IL) with normal endocrine cell distribution α and β cells with mild necrotic tissue and internal vaculation, swelling pyramidal cells of acini. H&E X 40.

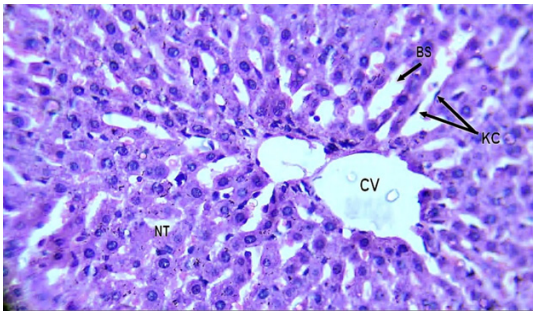


Fig. 11. Liver of Diamicron treated group showing marked dilated blood sinusoids (BS) with mild increased of Kupfer cells (KC), mild necrotic changes, normal tissue histoarchetexture, normal hepatic cords. H&E X 40.

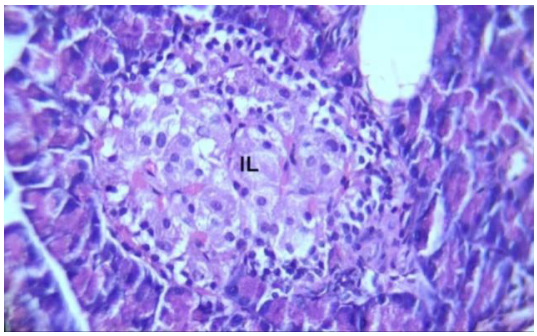


Fig. 12. Pancreas of Zinc Oxide treated rats showing restoration of normal size of islets of Langerhans (IL) with marked peripheral hyperplasia with mild central vaculation and necrotic changes (NT), normal distribution of endocrine cells α and β cells (βC) and (αC) with mild inflammatory cells (INF) and normal connective tissue (CT) septum interlobular septum (ILS). H&E X 40.

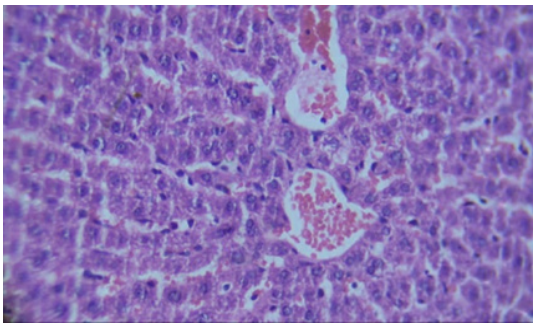


Fig. 13. Liver of Zinc Oxide treated group showing normal tissue histoarchitecture with mild dilated blood sinusoids (BS) and normal number and distribution of Kuppfer cell (KC) with congested central vein (CCV) and hemorrhagic changes (HcH) and infiltration of inflammatory cells (INF), some apoptotic changes and neuclearpyknosis (PC). H&E X 40.

hepatic cords and normal tissue histoarchitecture, normal appearance and distribution of Kupfer cells with a normal central vein (Fig. 7). The liver of positive diabetic control rats showed Kupffer cells activation and cytoplasmic vacuolization of hepatocytes, dilation of liver sinusoids and some necrotic changes of liver tissue with marked fatty changes (FC) some hepatocytes showed apoptotic changes expressed in nuclear pyknosis (PN) (Fig. 9) Liver of Diamicron treated rats showed marked dilataion of liver sinusoids and swelling of hepatocytes with normal frequency of Kupfer cells and normal hepatic cords (Fig. 11). Liver of nano-ZnO treated rats showed a moderate CV congestion with hemorrhagic changes, moderate increase of Kupfer cells and inflammatory cells infiltration with mild dilatation of liver sinusoids and mild swelling of hepatocytes, some hepatocytes showed mild apoptotic changes and nuclear pyknosis (Fig. 13).

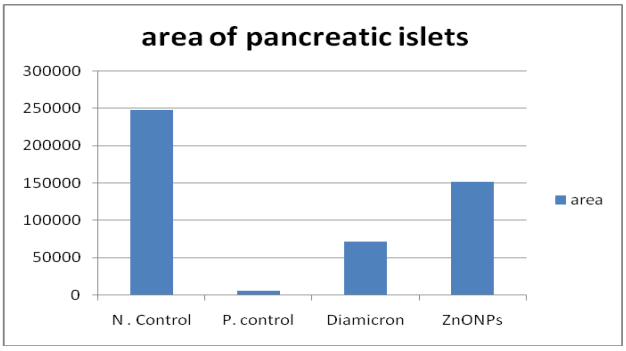
Discussion

The DM is a worldwide metabolic trouble distinguished with the rise in blood sugar levels [21]. The persons suffering from diabetes would need the multiple medications evolution with several methods of action [8].

The objective of this work is to develop a powerful and safe natural anti-diabetic agent using nanotechnology. This can be fulfilled via studying the effect of zinc oxide nanoparticles (ZnONPs), in treating diabetic rats that induced with STZ. Our results showed significantly increase in blood glucose and a decrease significantly in serum insulin levels in rats with diabetes compared with group A (control group). In agreement with our results, Gupta et al. [22] showed an increase significantly in the sugar of blood in rats with diabetes. This is because of the pancreatic β cells destruction by STZ, promoting the event that the induction of diabetes by STZ, may be through the oxygen free radicals generation. The glucose elevation in rats treated with STZ is because of oxidative stress production in the pancreas, which resulted in a single strand break in DNA of the pancreatic islets [23]. Naturally, the production of hepatic sugar is inhibited by insulin. This is with decreasing glucose-6-phosphatase and fructose-1,6-bisphosphatase enzyme activities [24]. The increased blood glucose level following STZ-injection could also be explained according to the fact that due to insulin deficiency in diabetic rats, the glucose-6-phosphatase is activated which is a serious enzyme for the gluconeogenesis final step where it catalyzes the hydrolysis of glucose-6-phosphate to phosphate and glucose. The sugar is transported out of the liver to increase blood sugar concentration [25].

Morphometric analysis:

Group	**Pancreatic islet area/um**
Negative control	24863
Positive control	6456
Diamicron treated	71977.21
ZnONPs treated	151859



The significant increase in blood glucose level following STZ injection in the diabetic group is associated with a significant decrease in serum insulin level. Aziz et al. [26] reported that insulin deficiency is due to diabetes is the consequence of autoimmune-mediated destruction of pancreatic beta-cells.

Our result showed that glycated hemoglobin (HbA1-C) was significantly increased in the diabetic group compared with the control group. Erythrocyte hemoglobin glycation is measured by glycated hemoglobin, ever after the life span of erythrocytes is one hundred and twenty days, HbA1-C reflects intend glycaemic rate for the previous weighted to the most recent months (three months). It supplies a number of information about the concentration of immediate blood sugar. Earlier studies have reported glycosylated hemoglobin to be used as a diagnostic test for Type 2 Diabetes instead of relying only on blood glucose levels [27].

After treatment, the results showed a decrease significantly in blood sugar level and an increase significantly in the level of serum insulin in diabetic groups treated with the ZnONPs and the Diamicron in comparison to diabetic group rats. Glycated hemoglobin was significantly decreased in groups treated with ZnONPs and Diamicron groups compared to diabetic group. In agreement with our results, Alkaladi et al. [8] showed a decrease significantly in sugar of blood and an increase significantly in the level of insulin in rats with diabetic which were treated with ZnONPs. This introduced a great anti-diabetic activity of those nanoparticles. The Zinc (Zn) has been illustrated to be a powerful metal that develops utilization and metabolism of glucose by means of its efficient effect on the hepatic glycogenesis enhancement by actions on the pathway of signaling of the insulin. Jansen et al. [28] declared that zinc improves insulin signaling by increasing phosphorylation of insulin receptor, glycogen synthase kinase-3 inhibition and stimulation of PI3K activity. The decrease in the blood glucose and increased in insulin level following ZnONPs injection could be explained according to Meyer and Spence [29] who reported the decreasing in pancreatic zinc may reduce in the islet β-cells ability that produces and secretes insulin.

Our results pointed out that the mRNA expression level of pancreatic insulin and insulin receptor genes increased in ZnO NPs and Diamicron treated groups if compared with the non-treated group of diabetic rats. In the same way, Akaladi et al. [8]; reported the ability of ZnONPs for the induction of insulin and IR gene expression in STZ-diabetic rats, they reported that antidiabetic effects of ZnONPs occur through insulin induction, IR and the gene expression of metabolizing glucose enzymes. In the same way, Umrani and Paknikar [9] manifested the ZnONPs ability in blood sugar controlling in rats with diabetes; as it acts as a potent antidiabetic through decreasing of blood glucose and increasing of serum insulin as well as inhibition of lipid and protein free radicals. Also, they denoted that ZnONPs therapy produce in the inhibition of a glucosidase enzyme in the intestine and thereby reduce the sugar absorption.

Regarding histopathological examination, our result was in agreement with Alkaladi et al. [8] who stated that ZnONP treated rats reporting several normal Langerhans islets with someone destructed in between normal duct and acini in the pancreas.

Also, the same results were obtained by Umrani et al. [30] who reported that ZnONP therapy was not showed any changes in histological of the kidney and liver tissue. The necrosis of B-cell was seen in a pancreatic portion of rats with Type 2 diabetes. ZnONP therapy showed that increasing the mass of β-cell in the pancreas, suggesting proliferative effects that are in agreement with our histopathological results that the treatment with ZnONPs restores the histological structure and of islets of Langerhans and increase the number and distribution of B-cells.

The histopathological results of Diamicron treated rats in the present study were in according with Muzammil et al. [31] results who showed that the diabetic rats Pancreas treated with gliclazide revealed vacuolations of some cells of islets of Langerhans.

The histopathological effect of the STZ-treated group on the liver tissue were in according with Hamadi et al. [32] results who showed that the obtained from the group treated with the fatty change exhibited of STZ, ballooning declination, some of the hepatic parenchyma necrosis. The CV in the portal veins, as well as hepatic parenchyma and the portal area bile ducts, were dilated, there were diffuse□mononuclear leucocytes inflammatory cells infiltrations as well as distribute Kupffer cells proliferation in between the degenerated and fatty changed hepatocytes.

The histopathological changes of ZnONPs on liver tissue in the present study was in agreement with the results of Muzammil et al. [31] who stated that zinc-oxide oral administration promoted pathological effects significantly on the liver and heart. Some hepatocytes nuclei in the liver exhibited degrees of chromatin condensation and fragmentation as a result of apoptosis. Some degree of hemorrhages and focal necrosis was apparent as well infiltration of lymphocyte was also present within the tissue of liver group B3 treated with ZnONPs oral administration at the dose of body weight (400 mg/kg).

In conclusion, ZnO NPs and Diamicron have effects of synergistic on diabetes treatment. ZnONPs are promising as anti-diabetic agents, along with the standard antidiabetic agent Diamicron, as they restore the function and the β cells structure. In the stage of pre-diabetic, the supplementation of ZnONP may stop diabetes type2 progression.

Acknowledgement

This work was supported by National Research Centre fund through Grant project {No; 11010184}.

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تقييم تأثير جزيئات أكسيد الزنك المتناهية الصغر في علاج السكر فى الجرذان المصابة بداء السكري المستحث بالستربتوزوتوسين

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نحتاج إلى معالجة المواد على مستوى النانو لإنتاج منتجات فريدة بخصائص جديدة. تعرض الجسيمات النانو خصائص جديدة و متطوره مدعومة بخصائص فريدة مثل الحجم والتوزيع.

ومن ثم تم تقييم تأثير جسيمات أكسيد الزنك النانو عليعلاج مرض السكري في الفئران المستحثة بالستربتوزوتوسين في هذه الدراسه. تم استخدام أربعين من ذكور الجرذان البيضاء وزنها يتراوح بين ١٨٠-٢٠٠ جم، ثم تم تقسيمها الى ثلاث مجموعات بشكل عشوائي بعد سبعة ايام من حقن الماده المسببه لمرض السكري، وذلك بالاضافه الى المجموعة (أ): الحيوانات غير المصابة بالسكري وكل مجموعة تحتوي على عشر جرذان، المجموعة ب ١: الحيوانات المصابة بالسكري والتي لم تاخذ اى علاج، المجموعة ب٢: المجموعة المصابة بالسكرى وتستقبل ١٠ ملي جرام من علاج الديناميكرون، المجموعة ب ٣: المجموعة المصابه بالسكرى وتستقبل ١٠ ملى جرام من جزيئات اكسيد الزنك النانو. بعد ٢١ يوم من العلاج تم تحديد مستويات الجلوكوز ومستوى الهيموجلوبين السكري ومستوى الانسولين في الدم. واشارت النتائج الى زياده فى مستوى الجلوكوز والهيموجلوبين السكرى فى الدم ونقص فى مستوى الانسولين فى الجرذان المصابة بمرض السكرى بينما حدث العكس في الجرذان التى تم معالجتها بالديناميكرون وجزيئات اكسيد الزنك النانو. وتبين مما سبق ان جزيئات اكسيد الزنك تعمل كمضاد قوى لمرض السكرى من خلال خفض نسبه الجلوكوز وزياده مستوى الانسولين فى الدم.