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The Interaction of Activated Vitamin D3 In Rats Exposed to Experimentally Induced Type I or II Diabetes Mellitus

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Abstract

THE current study was conducted to evaluate the interaction of activated vitamin D3 with rats exposed to type I or type II diabetes mellitus Rats' models of both type I and II diabetes mellitus were conducted using a single dose of streptozotocin (60mg/ kg.b.wt) and 40% dietary fructose, respectively. After the induction of both types of diabetes mellitus, rats were supplemented with activated vitamin D3 (1µg/ kg . b.wt). At the end of the experiment, plasma blood glucose level, serum blood insulin level, lipid profile, antioxidant status markers (MDA, GSH, and CAT), and hepatic adiponectin, galectin, and VDR gene expression analysis were estimated. Serum blood insulin, Plasma blood glucose, lipid profile (LDL, HDL, cholesterol, TAG), and redox state markers, as well as hepatic gene expression of adiponectin, galectin, and vitamin D receptor, showed significant deteriorations in the type I diabetic group and type II diabetic group which were improved significantly in the treated groups It can be concluded that supplementation of activated vitamin D3 can improve glycemic status, serum lipid profile and antioxidant status in rats exposed to type I or type II diabetes mellitus.

Keywords: Diabetes mellitus; vitamin D; Adiponectin; Galectin-3; VDR; STZ.

Introduction

Diabetes mellitus (DM) is defined as a group of metabolic diseases characterized by hyperglycemia caused by deficiencies in insulin production, insulin sensitivity or both [1]. It is well known that diabetes is divided into two types: insulin-dependent (IDDM, type I) and non-insulin-dependent (NIDDM). It is worth mentioning that, a naturally occurring broad-spectrum antibiotic, cytotoxic, and anti-cancer molecule called streptozotocin (STZ) are particularly harmful to mammalian pancreatic beta cells, which produce insulin [2]. Ultraviolet radiation stimulates the skin to create vitamin D derived from 7-dehydrocholesterol. Since photosynthesis in the skin was the natural supply of vitamin D during the evolution of vertebrates and primates, vitamin D cannot be called a real vitamin but rather a prohormone [3]. The dual hydroxylation reactions of vitamin D are crucial for its activation in both the liver and kidneys. The first hydroxylation happens in the liver where 25-hydroxylases turn it into 25-hydroxyvitamin D. The second hydroxylation step takes place in the kidney where 1-hydroxylase transforms 1, 25-dihydroxyvitamin D into the bloodstream. Vitamin D binding protein (DBP) is a carrier protein that helps transport vitamin D and its metabolites through the bloodstream. Vitamin D metabolites are catabolized by another multifunctional hydroxylase [4]. Rodents and rabbits have shown that pancreatic insulin release is impacted by vitamin D deprivation, demonstrating that vitamin D is required for the endocrine pancreas to operate properly [5].Hepatic adiponectin is a bioactive protein that is secreted into the circulation by adipocytes. Adiponectin, the most prevalent circulating protein produced exclusively in adipose tissue, acts as a hormone with anti-inflammatory, anti-diabetic, and insulin-sensitizing properties, and is known to play a significant role in several metabolic processes, including glucose control and fatty acid catabolism [6]. Adiponectin improves fat metabolism, controls insulin sensitivity, manages

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glucose tolerance, and improves homeostasis in diabetic individuals [7], Adiponectin is thought to be one of the most potent markers of type II diabetes mellitus[8]. Widely expressed lectins that bind galactosidase are known as galectins [9], Mammalian galectins can recognize galactoside residues and form complexes that crosslink glycosylated ligands thanks to one or two highly conserved carbohydrate recognition domains (CRDs) [9]. The insulin resistance homeostasis model assessment (HOMA-IR) is connected to galectin-3 levels. Galectin-3 levels are inversely associated with HOMA-IR and HbA1c levels. Still, they are positively linked to glucose disposal rate (GDR) and insulin sensitivity index (ISI) in individuals suffering from diabetes mellitus [10].The nuclear receptor superfamily includes the vitamin D receptor (VDR). The binding of 1, 25-dihydroxyvitamin D to the VDR improves its activation [11]. Studies on microarray expression profiles have contributed to a better knowledge of vitamin D physiology, and a lot of these observations are explained by the VDR's role as a gene transcription regulator [12]. A good candidate for NIDDM vulnerability is the vitamin D receptor gene [13]. The vitamin D receptor (VDR) gene has also been implicated in the pathophysiology of IDDM type I in numerous investigations. In certain research, it has also been hypothesized that vitamin D insufficiency is linked to the autoimmune destruction of beta cells and the start of IDDM (type I), which is brought on by a breakdown in immunological control. For IDDM (type I), vitamin D is protective [14]. From this point, the current study aimed to assess the potential protective effect of vitamin D supplementation on the gene expression profiles of adiponectin, galectin-3, and vitamin D receptors, as well as the hepatic antioxidant profile, serum lipid profile, and atherogenic indices in rats exposed to both NIDDM and IDDM.

Material and Methods

Experimental animals

Sixty male Wistar rats weighing 80±5 g and aged 14±3 days were employed. They were housed in Mansoura University's Department of Biochemistry, Faculty of Veterinary Medicine, and were kept on a 12-hour light-dark cycle under strict sanitary circumstances. All rats were fed a basal diet (protein 21.5%, fats 3.48%, fibers 2.39%, and energy of at least 3000 kcal/kg diet) with an unlimited water supply [15], Throughout the trial, rats were housed in separate cages and subjected to constant dietary and environmental settings. The rats will be acclimatized for 15 days before the start of the trial. Diabetes and normal animals will be maintained in separate metabolic cages, with a stocking density of 5 rats per 1.2 m^2 [16]**.**

Animal grouping

After acclimation, rats were separated into six equal groups, the first group was serving as the control group (C) and being fed the basal diet. The second group, (VD) was fed a basal diet with oral vitamin D supplementation of one microgram per kg of the rats' body weight (b.wt) **[**17**].** The third group was made up of experimentally induced diabetes mellitus (IDDM) with intraperitoneal injection of STZ (dissolved in citrate buffer 0.1 mol/L, pH 4.2) at a concentration of 60 mg/kg b.wt [18]. Rats were thought to have diabetes if their blood glucose concentrations exceeded 200 mg/dl. To promote insulin resistance before the onset of diabetes, the fourth group (NIDDM) was given a regular diet in addition to an oral 40% fructose solution for 4 weeks [19], followed by STZ induction of type II diabetes (40 mg/kg b.w.t.) [20]. The fifth group (IDDM/VD) of rats was exposed to IDDM and was given vitamin D supplementation orally, while the sixth group (NIDDM/VD) of rats with type II diabetes was given a normal diet and vitamin D supplementation orally.

Collection of blood samples

Rats were fasted for 8 hours after 8 weeks of experimental diabetes induction, and anesthesia was conducted and maintained with sodium thiopental (Pharco, Co, Egypt) (20 mg/kg body weight) [21]. After complete sedation, blood was drawn from the heart of rats using a cardiac puncture and divided into two parts: one part was used to measure fasting plasma glucose collected in a sodium fluoride tube while the other was stored in a dry, clean, sterile, and sealed tube that was left to clot and a clear serum sample was aspirated and transferred to a clean Eppendorf tube to measure serum insulin concentration [22], serum total cholesterol (TC) concentration [23], serum HDL-cholesterol (HDL-c) concentration [24], serum LDL-cholesterol (LDL-c) concentration [25] and serum triacylglycerol (TAG) concentration [26].

Collection of pancreas and liver specimens

The sedated animals were euthanized via cervical dislocation, and the animals were dissected to obtain pancreas and liver tissues. Liver samples were divided into three compartments. The tissues were submerged in neutral buffered formalin (10%) to determine histological alterations in the first compartment. The second portion was kept in phosphate-buffered saline (pH 7.4) to determine reduced glutathione levels, catalase activity, and malondialdehyde levels. The final compartment was stored in Trizol reagent (Invitrogen, Lithuania) for gene expression analysis of hepatic adiponectin, galectin, and vitamin D receptors against glyceraldehyde 3 phosphate dehydrogenase (GAPDH) as a housekeeping gene. Tissue from the pancreas was also collected and stored in neutral

buffer formalin (10%) for the determination of histopathological changes in each rat.

Following the dissection, each rat was placed in a plastic bag and buried underground under the methods of [27].

Histopathological examination of liver and pancreas tissues

The liver and pancreatic tissues were paraffin-embedded, and 3-µm thick slices were cut and stained with hematoxylin and eosin before being studied under a light microscope [28].

Measurement of MDA levels, CAT activity, and GSH levels in liver tissues

Using a mortar and pestle, 100 mg of liver tissues were homogenized in 900 µl of ice-cold buffer (phosphate buffer saline), then centrifuged at 4,000 xg for 15 minutes at 4 °C. The supernatant was stored at - 20 °C until it was used for oxidant and antioxidant analysis. Liver oxidative stress was determined with measurements of malondialdehyde (MDA) levels (as the index for lipid peroxidation) [29], as well as Catalase (CAT) activity [30], and reduced glutathione (GSH) levels were determined [31]. The manufacturer's recommendations (Bio-Diagnostics, Dokki, Giza, Egypt) for the colorimetric method were used to measure these markers in the supernatant of liver homogenates.

Gene expression analysis of hepatic adiponectin, galectin, and vitamin D receptors

Gene expression analysis was conducted using a quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) for the genes that encode adiponectin, galectin, and vitamin D receptors in hepatic tissues (Table 1). The application of real-time PCR for amplification of desired genes was conducted using a Step-One Real-time PCR machine (Thermo Fisher Scientific, UK), where RNA was extracted from hepatic tissues using Trizol reagent (Thermo Fisher Scientific, UK), according to the manufacturer manual and cDNA synthesis was conducted using TOPreal premix cDNA synthesis kit (Enzynomics, South Korea) using the following cycling conditions: initial denaturation at 94^{o}C for 9 minutes, then followed by 35 cycles of 95 ^{o}C for 30 seconds, 59 ^{o}C for 30 seconds and 72 ^{o}C for 40 seconds, and then the reaction was completed by final elongation step at 72 ^{o}C for 8 minutes. All the desired genes were amplified against GAPDH and the fold expression was calculated using $2^{-\Delta\Delta ct}$ method.

Histopathological examination of liver and pancreas tissues

The liver and pancreatic tissues were paraffin-embedded, and 3-µm thick slices were cut and stained with hematoxylin and eosin before being studied under a light microscope [28].

Statistical analysis

The data in SPSS version 20 were examined using one-way analysis of variance. Tukey was used as a post hoc test to discover significant differences between means at a significance level of 0.05. The data were presented as mean and standard error [36].

Results

Antioxidant status and oxidative stress markers

Oxidative stress damage markers in liver homogenate (MDA) were significantly higher in groups IDDM and NIDDM when compared to the control group (p=0.0001), while MDA levels significantly decreased after vitamin D supplementation in groups IDDM/VD and NIDDM/VD (p=0.002). On the other hand, group IDDM and NIDDM had decreased antioxidant enzyme activities of catalase and reduced glutathione due to the induction of diabetes mellitus(p=0.012) and (p=0.005), respectively when compared with the control group, which began to improve significantly after supplementation with vitamin D in both IDDM/VD and NIDDM/VD (p=0.019) and (p=0.009), respectively when compared with the corresponding diabetic group (Fig.1).

Serum lipid profile and atherogenic indices in rats exposed to type I and type II diabetes mellitus

LDL-C significantly increased in groups IDDM (p=0.09) and NIDDM (p=0.001), when compared to control group C, which started to decrease significantly in treated groups with vitamin D in both IDDM/VD (p=0.034) and NIDDM/VD (p=0.001). On the contrary, HDL significantly increased in both diabetic groups supplemented with vitamin D (IDDM/VD and NIDDM/VD) compared to groups IDDM (p=0.0001) and NIDDM (p=0.04), which was significantly decreased compared with control group C.

Surrogate marker of insulin resistance values there is insignificant changes in groups (IDDM/VD and NIDDM/VD) in comparison with groups IDDM and NIDDM after vitamin D supplementation. Atherogenic index (AI) significantly decreased in the treated group (IDDM/VD and NIDDM/VD) in comparison with groups IDDM and NIDDM, which was significantly increased in comparison with control group C. Atherogenic coefficient (AC) showed an insignificant increase in group (NIDDM) and treated group (NIDDM/VD) when compared to the control group and Group IDDM showed non-significant change when compared to control group C but there was a significant increase in treated group IDDM/VD when compared to the control group. Castelli's risk index-1 (CR1) showed a significant increase in group (NIDDM) when compared to the control group but there was non-significant increase in group IDDM in comparison with control group while treated groups (IDDM/VD

and NIDDM/VD) showed no significant changes (Fig.2).

Glycemic status in rats subjected to type I and type II diabetes mellitus

Plasma glucose concentration levels demonstrated a substantial increase in Groups IDDM and NIDDM when compared to the control group C. Serum insulin levels revealed a significant decrease in Groups IDDM and NIDDM compared to the control group C, HOMO-IR value revealed a significant increase in both Groups IDDM and NIDDM compared to control group C. At the same time, Vitamin D supplementation showed considerable changes in plasma glucose concentration, serum insulin levels, and HOMO-IR values when compared to untreated groups, levels of plasma glucose concentration decreased considerably in treated groups with vitamin D IDDM/VD and NIDDM/VD in comparison with untreated groups IDDM and NIDDM, serum insulin levels were significantly increased in treated groups IDDM/VD and NIDDM/VD) in comparison with groups IDDM and NIDDM. In contrast, HOMO-IR decreased considerably in treated groups (NIDDM/VD) in comparison with group NIDDM but insignificantly decreased in treated group IDDM/VD in comparison with group IDDM (Fig.3).

Gene expression analysis in rats exposed to type I and type II diabetes mellitus

Hepatic adiponectin showed a significant decrease in both Group IDDM and NIDDM compared to the control group C which increased significantly after vitamin D supplementation in groups IDDM/VD, but insignificantly in treated group NIDDM/VD ($P > 0.05$), Hepatic Galectin showed a significant increase in both Group IDDM and NIDDM compared to control group ($P > 0.05$) which decreased significantly after vitamin D supplementation in groups IDDM/VD and NIDDM/VD and Hepatic VDR decreased considerably in Groups IDDM and NIDDM compared to the control group ($P< 0.05$), but increased insignificantly after vitamin D treatment in Groups IDDM/VD and NIDDM/VD ($P>0.05$) (Fig.4).

Histopathological examination in rats exposed to type I and type II diabetes mellitus

Microscopic images of H&E stained pancreatic sections in the control group and group VD showed normal histological pictures of islets of Langerhans and pancreatic acini while diabetic rats in the control group showed ill-defined and shrunken atrophied islets of Langerhans with less numerous cells.

Group IDDM showed an increase in the size of the Langerhans islets with preservation of architecture along with a large number of normal pancreatic α and β-cells with focal sporadically vacuolated cells in the center of the islets, while the pancreatic section of group NIIDM showed shrunken islets of Langerhans with fewer cells and some that are vacuolated.

The pancreatic section of group NIIDM/VD showed preservation of architecture of the islets of Langerhans along with a large number of normal pancreatic α and β-cells with focal sporadically vacuolated cells, the exocrine portion appeared normal. (Fig.5).

Microscopic images of H&E stained liver sections in group C and CD showed normal histological pictures of hepatic lobules, central veins (CV), and sinusoids.

liver sections of diabetic rat (IDDM) group showed lymphohistiocytic exudate around the central vein replacing the hepatocytes, Round cell infiltration replacing the hepatic parenchyma, focal hepatocytes necrosis represented by nuclear karyolysis and congestion in the portal vessels along with fibrinocollagenous proliferation.

Liver sections of NIIDM group showed diffuse vacuolization of the hepatocytes with congested vessels along with few perivascular inflammatory cell infiltration coagulative necrotic of hepatocytes represented by nuclear pyknosis and eosinophilic cytoplasm along with extensively congested and dilated sinusoids, while liver sections of NIIDM/VD group showed an improvement in the hepatocytes appearance and absence of vacuolization with individual hepatocyte necrosis. Liver sections of IIDM/VD showed normal hepatocytes with occasional hepatocyte necrosis (Fig. 6).

Discussion

Diabetes mellitus (DM) or induced DM significantly deteriorates pancreatic functions and pancreatic and hepatic morphology and disrupts the balance between antioxidant activities and reactive oxygen species (ROS) levels in hepatic tissues by increasing MDA and decreasing CAT activity and GSH concentrations. Vitamin D supplementation significantly improved all studied parameters compared to diabetic, non-treated groups.

Blood glucose levels were elevated significantly as a result of STZ, while insulin levels also dropped significantly. The current result revealed that the level of plasma glucose concentration values revealed a significant increase in both diabetic groups IDDM and NIDDM in comparison with the control group C. The obtained result was supported by [37] who reported a significant increase in plasma glucose levels after induction of diabetes by STZ injection. While there was a significant decrease in plasma glucose concentration in treated groups by vitamin D supplementation, the obtained result was supported by [38] who reported that Vitamin D significantly decreased fasting plasma glucose in both types of diabetes.

Serum insulin level values revealed a significant decrease in both diabetic Groups IDDM and NIDDM in comparison with the control group C, the obtained result was supported by [38], while insulin levels were significantly decreased in treated groups (IDDM/VD and NIDDM/VD) with vitamin D supplementation in comparison with groups IDDM and NIDDM, the obtained result was supported by [38].

HOMA-IR a biomarker of insulin resistance quantification revealed a significant increase in both diabetic groups IDDM and NIDDM in comparison with the control group C **[**39**]** They noted that both diabetes and the swim-trained diabetic groups displayed considerably higher resistance in HOMA-IR tests, while HOMA-IR insignificantly decreased in treated groups (IDDM/VD) with vitamin D in comparison with group IDDM, but significantly decreased in treated group (NIDDM/VD) in comparison with groups NIDDM, the obtained results was supported by [40] who reported that vitamin D supplementation significantly reduced the HOMA-IR diabetic resistant group.

Free radical overproduction associated with diabetes mellitus has been linked to numerous pathways, including hyperglycemia and antioxidant status, leading to oxidative stress. This oxidative stress accelerates the onset, progression, and consequences of diabetes. Both type I and type II diabetes exhibit excessive free radical generation, and their insufficient clearance damages cellular proteins, membrane lipids, and nucleic acids [41], Malondialdehyde, a marker of lipid peroxidation (MDA) was increased significantly in IDDM and NIDDM when compared with the control group, the obtained results were supported by [42] who reported that existence of lipid peroxidation disorders in diabetic patients. After vitamin D supplementation, the level of MDA was decreased**.** As a result of diabetes mellitus development, antioxidant enzymatic activity of catalase and glutathione levels were also lowered, that was started to improve significantly after supplementation with vitamin D, the obtained results were supported by [43].

LDL significantly increased in IDDM and NIDDM in comparison with the control group C, the obtained results were supported by [44] who reported that there was a significant increase in the lipid profile except HDL was decreased, LDL started to decrease significantly in treated Groups with vitamin D (IDDM/VD and NIDDM/VD), the obtained results were supported by **[**45] who reported that LDL levels were significant decrease in ovariectomized rats, while HDL significantly increased in the treated group (IDDM/VD and NIDDM/VD) in comparison with groups IDDM and NIDDM which was significantly decreased, the obtained results were supported by [46]**.**

Gene expression analysis of adiponectin showed significant downregulation in both groups exposed to IDDM and NIDDM, which increased significantly after supplementation with vitamin D (IDDM/VD). Adiponectin constitutes an essential link between obesity and insulin resistance, where lower adiponectin expression levels are associated with higher glucose levels [47]**.** It is recorded that adiponectin is decreased dramatically in animals suffering from diabetes mellitus

Galectin-3 is implicated in developing obesity and diabetes by regulating glucose levels in adipose tissue and pancreatic islet levels [48]. Hepatic Galectin revealed a significant increase in both Group IDDM and NIDDM in comparison with the control group, the obtained results supported by [49] who reported that Galectin levels were significantly increased in obesity and type 2 diabetes. In addition, supplementation with vitamin D in groups IDDM/VD and NIDDM/VD revealed a significant decline in hepatic galectin expression that was supported by [50], who reported that vitamin D suppresses Galectin-3 gene in ovarian cancer cells.

Conclusion

Supplementation of the activated form of vitamin D achieved a marked improvement of glycemic status and serum lipid profile through improving the gene expression of galectin 3 and adiponectin with marked improvement in glycemic status in rats exposed to both IDDM and NIDDM.

Declarations

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interests

All authors declare no conflict of interest in relation to the manuscript.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request, despite that all data were given during submission process

Ethical approval

The current study complies with national and international guidelines. The current study was approved by the research ethics committee at Mansoura University (M/78).

TABLE 1. sequence of primers used in gene expression analysis

Primer	Sequence	Reference
Hepatic vitamin D receptor	F: GCCCCTCATAAAGTTCCAGGTG	[32]
	R: GGATAGGCGGTCCTGAATGG	
Hepatic galectin-3	F: ATCCTGCTACTGGCCCCTTT	[33]
	R: GCGATGTCGTTCCCTTTCTT	
Hepatic adiponectin	F: AATCCTGCCCAGTCATGAAG	[34]
	R: CATCTCCTGGGTCACCCTTA	
Glyceraldehyde 3 phosphate dehydrogenase	F: GCATCTTCTTGTGCAGTGCC	[35]
	R:TACGGCCAAATCCGTTCACA	

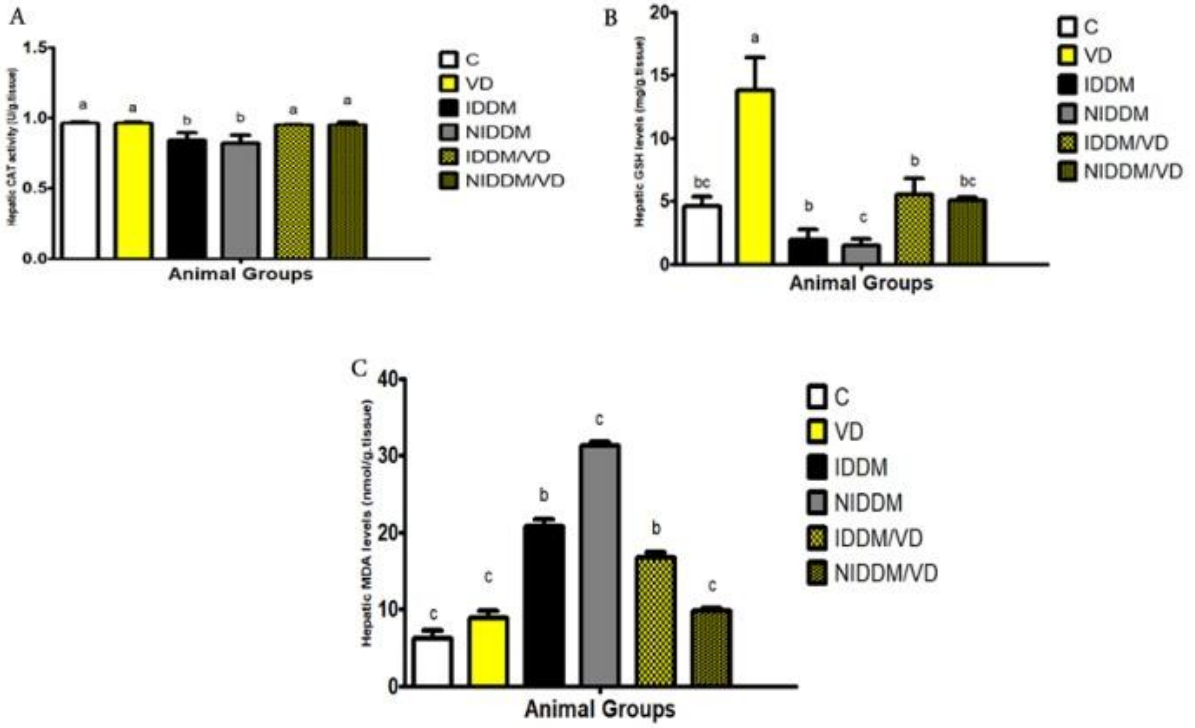

Fig. 1. Activated vitamin D improved antioxidant status in rats exposed to both IDDM and NIDDM: A. Hepatic CAT activity; B. Hepatic GSH levels; C. Hepatic MDA levels. Values were expressed as Mean±SE, where the means carried the same lowercase letter indicated a non-significant change. Mean contained the same letter, indicating a non-significant change.

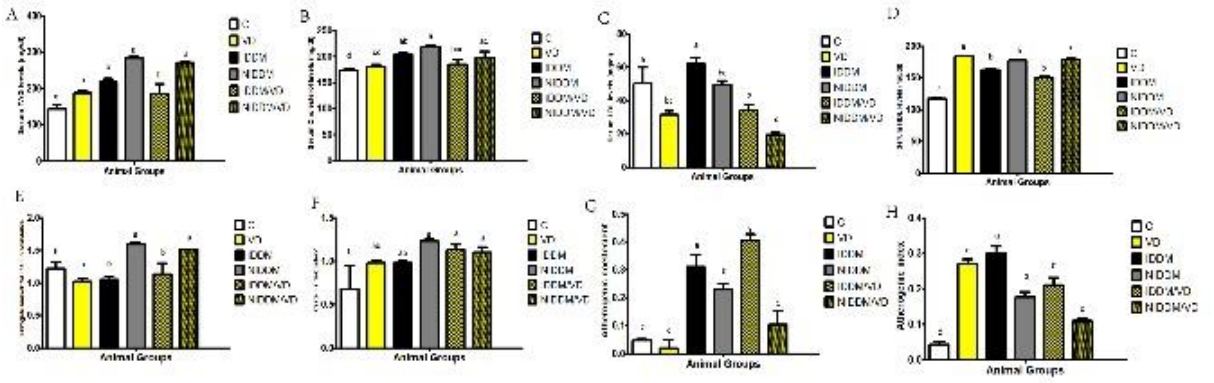

Fig. 2. Activated vitamin D improved serum lipid profile and atherogenic indices in rats exposed to Both IDDM and NIDDM. A. Seum TAG levels; B. Serum total cholesterol levels; C. Serum LDL-C levels; D. Serum HDL-C levels, E. Surrogate marker for insulin resistance; F. Castelli's risk index; G. Atherogenic coefficient; H. Atherogenic index. Values were expressed as Mean±SE, where the means carried the same lowercase letter indicating a non-significant change. Mean contained the same letter, indicating a non-significant change.

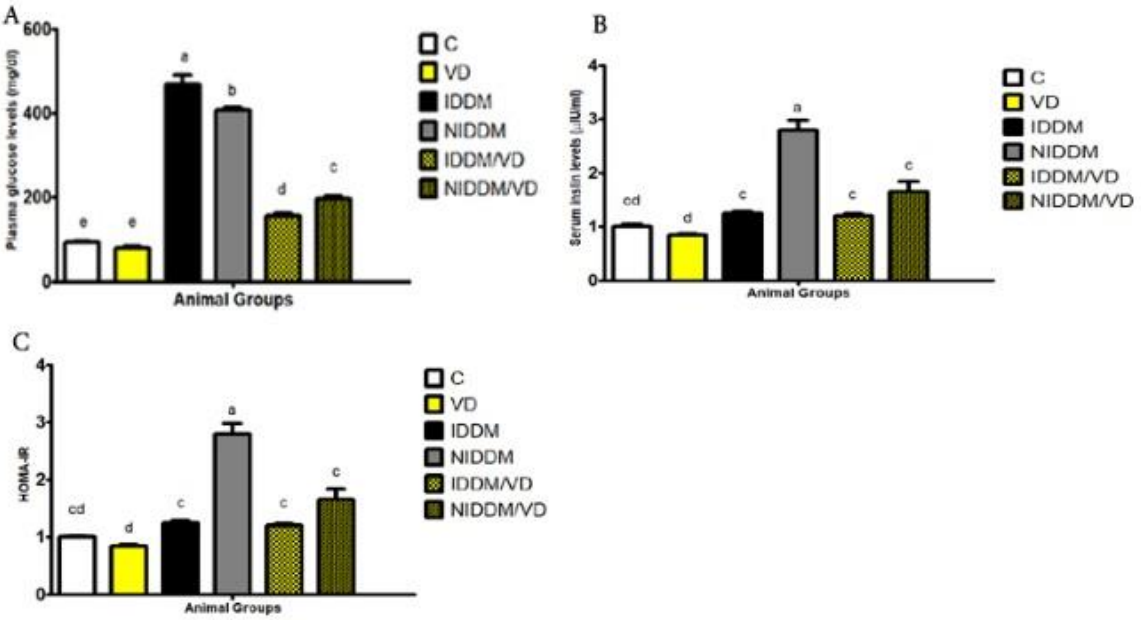

Fig. 3. Activated vitamin D improved glycemic status in rats exposed to both IDDM and NIDDM: A. Plasma glucose levels; B. Serum insulin levels; C. HOMA-IR. Values were expressed as Mean±SE, where the means carried the same lowercase letter indicating a non-significant change. Mean contained the same letter, indicating a non-significant change.

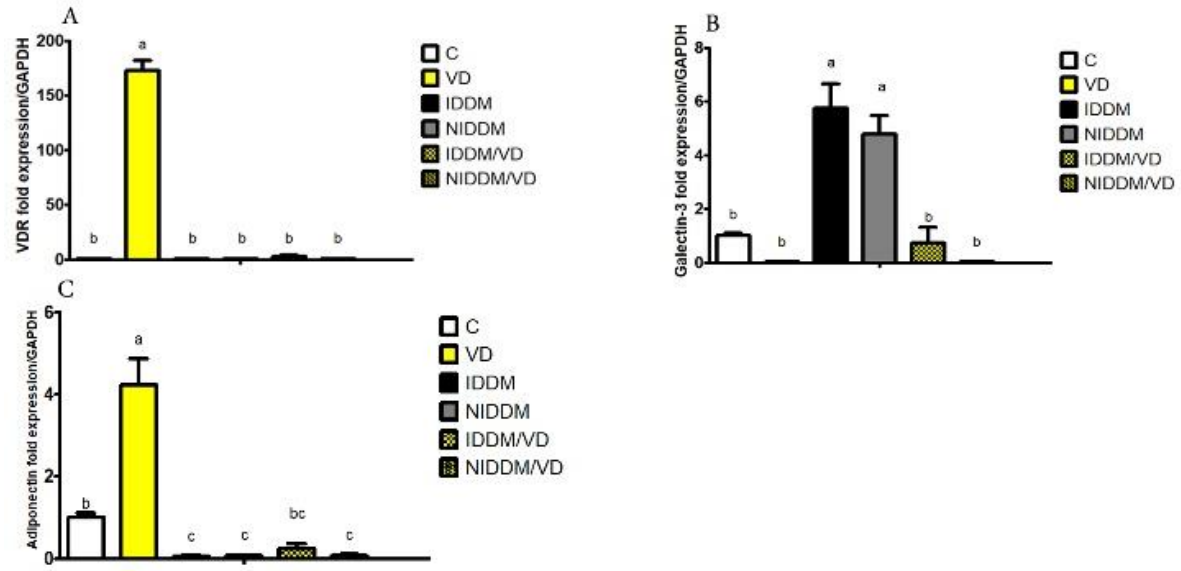

Fig. 4. Gene expression analysis of A. VDR; B. Galectin-3 ; and C. Adiponectin of rats exposed to both IDDM and NIDDM and supplemented with activated vitamin D. Values were expressed as Mean±SE, where the means carried the same lowercase letter indicating a non-significant change.

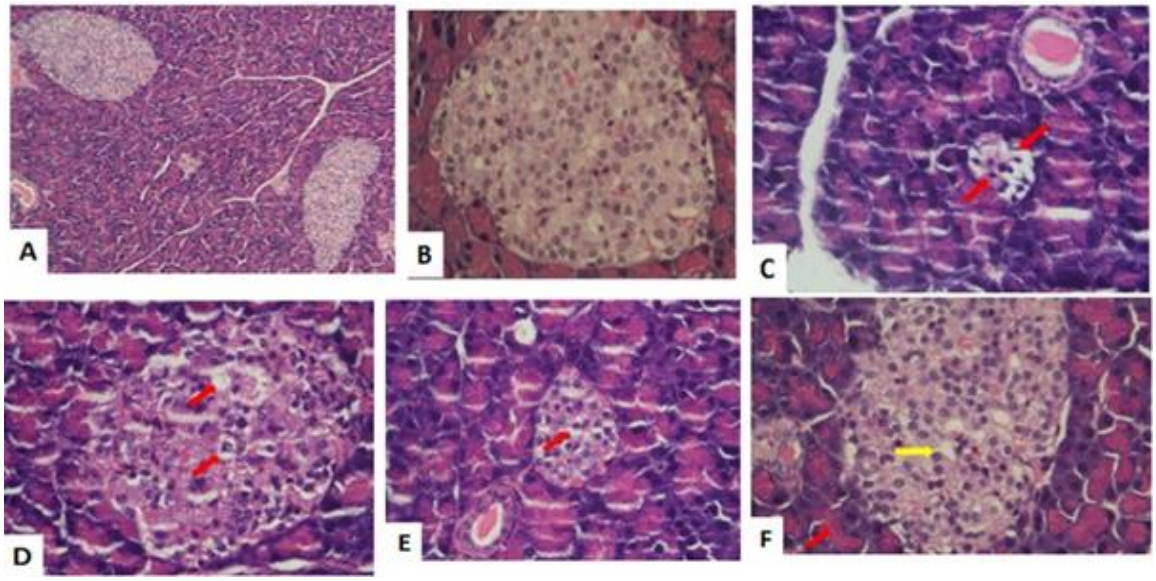

Fig. 5. Microscopic images of H&E stained pancreatic sections in control and Vit.D groups showing normal histological pictures of islets of langerhans and pancreatic acini X:100, X:400. (C): pancreatic sections of diabetic rats (type I) showing ill-defined and shrunken atrophied islets of langerhans with less numerous cells (red arrows) X:400. (D): pancreatic section of diabetic (type I) rat treated with Vit.D showing increase in the size of the islets of Langerhans with preservation of architecture along with large number of normal pancreatic α and β-cells with focal sporadically vacuolated cells (red arrows) in the center of islets of langerhans X:400. (E): pancreatic section of diabetic rat (type II) showing shrunken islets of langerhans with less numerous cells and some are vaculated (red arrow).

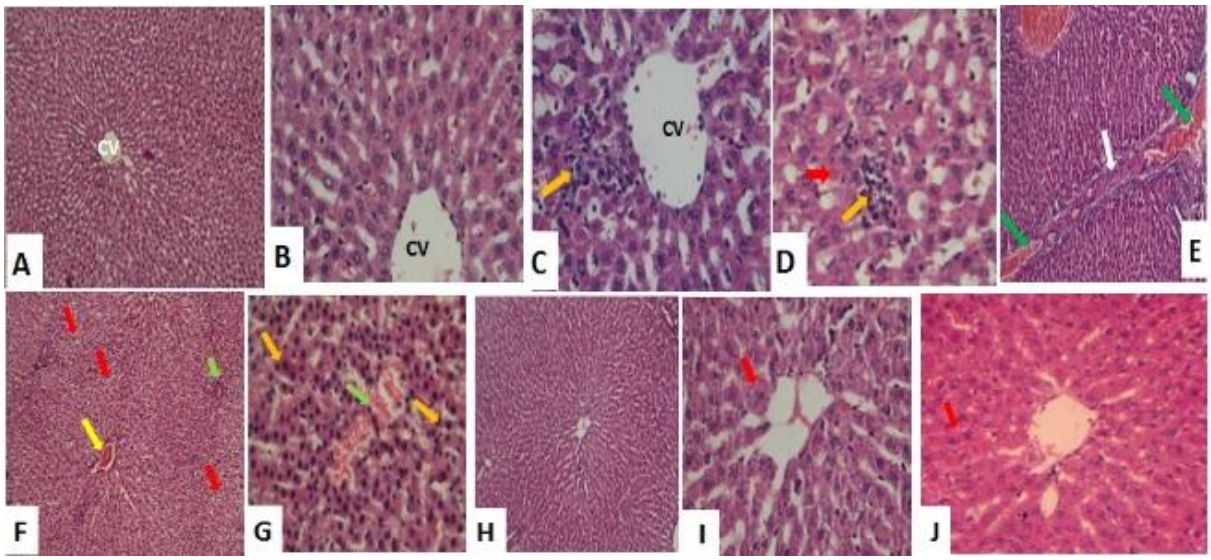

Fig. 6. Microscopic images of H&E stained liver sections in control and Vit.D groups showing normal histological pictures of hepatic lobules, central veins (CV) and sinusoids X:100, X:400. (C,D,E): liver sections of diabetic rat (type I) showing (C): lymphohistocytic exudate around the central vein replacing the hepatocytes (yellow arrow) X:400, (D): Round cell infiltration replacing the hepatic parenchyma (yellow arrow), focal hepatocytes necrosis represented by nuclear Karyolysis (red arrow) X:400, (E): Congestion in the portal vessels (green arrows) along with fibrinocollagenous proliferation (white arrow) X:100. (F,G): liver sections of diabetic rat (type II) showing (F): diffuse vacuolization of the hepatocytes (red arrows) with congested vessels (yellow arrow) along with few perivascular inflammatory cell infiltration (green arrow) X:100, (G): coagulative necrotic of hepatocytes represented by nuclear pyknosis and eosinophilic cytoplasm (yellow arrows) along with extensively congested and dilated sinasoid (green arrow) X:400. (H,I) liver sections of diabetic rats (type II) treated with Vit.D showing improvement in the hepatocytes appearance and absence of vacuolization with individual hepatocyte necrosis (red arrows) X:100, X:400. (J): liver sections of diabetic rats (type I) treated with Vit.D showing normal hepatocytes with occasional hepatocytes necrosis (red arrow) X:400.

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تفاعل فيتامين د3 النشط في الفئران المصابة بداء السكري من النوع الأول أو الثاني المستحدث تجريبياً

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الملخص

أُجريت الدراسة الحالية لتقييم تأثير فيتامين D3 النشط على الفئران المصابة تجريبيًا بداء السكري من النوع الأول أو الثاني. تم إحداث داء السكري من النوع الأول باستخدام حقنة واحدة من مادة الستربتوزوتوسين (60 ملغ/كغ من وزن الجسم)، بينما تم إحداث داء السكري من النوع الثاني من خلال التغذية على حمية غنية بالفركتوز بنسبة 40%. عقب إحداث كلا النوعين من داء السكري، تم إعطاء الفئران جرعة من فيتامين D3 النشط (1 ميكروغرام/كغ من وزن الجسم). في نهاية فترة التجربة، تم تقدير مستويات كل من: غلوكوز البلازما، إنسولين المصل، مؤشرات الدهون (الكوليسترول الكلي، الدهون الثلاثية، البروتينات الدهنية عالية ومنخفضة الكثافة)، إضافةً إلى مؤشرات حالة مضادات الأكسدة (المالون ثنائي الألدهيد MDA، الغلوتاثيون GSH، وإنزيم الكاتالاز CAT)، وكذلك التعبير الجيني الكبدي لكل من الأديبونكتين والجالكتين ومستقبل فيتامين D. أظهرت النتائج وجود اضطرابات ملحوظة في مستويات الغلوكوز والإنسولين، ملامح الدهون، حالة التوازن التأكسدي، والتعبير الجيني الكبدي في مجموعتي السكري من النوع الأول والنوع الثاني، والتي تحسنت بشكل ملحوظ في المجموعات المعالجة بفيتامين D3 النشط. يمكن الاستنتاج أن مكملات فيتامين D3 النشط قد تسهم في تحسين السيطرة على سكر الدم، صورة الدهون، الحالة المضادة للأكسدة، والتعبير الجيني الكبدي في الفئران المصابة بداء السكري من النوع الأول أو الثاني

الكلمات الدالة: داء السكري؛ فيتامين د؛ أديبونيكتين؛ غاليكتين-3؛ VDR؛ STZ.