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## Histopathological evaluation of diabetic rats treated with nano vanadium

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### Abstract

Diabetes mellitus, a heterogeneous metabolic disorder characterized by hyperglycemia with disturbances in carbohydrate, lipid and protein metabolism. Vanadium in the form of nanoparticles has been known to exert better action as an anti-diabetic agent. This study was aimed to assess the histological changes in the liver, kidney and pancreas of STZ-induced diabetic rats following treatment with vanadium pent oxide nanoparticles. Histopathological studies on the tissues of liver, kidney and pancreas in diabetic animals showed degenerative changes and treatment with Nano vanadium was able to partially restore the degenerative changes indicating the protective effect of vanadium by normalizing biochemical and histological abnormalities in diabetic rats.

**Keywords:** Histopathology, nano vanadium, diabetic rats,  $\beta$  cells

### Introduction

Diabetes mellitus (DM) is a heterogeneous metabolic disorder resulting from a defect in insulin secretion, insulin action and/or both (Pareek *et al.*, 2009) <sup>[1]</sup>. It is characterized by hyperglycemia with disturbances in carbohydrate, lipid and protein metabolism (Patel *et al.*, 2012) <sup>[2]</sup>. Chemically induced diabetic models are common in elucidating the possible role of environmental factors involved in the endocrine pancreatic destructive processes in the development of diabetes (Srinivasan and Ramarao) <sup>[3]</sup>. Alloxan (ALX) and streptozotocin (STZ), the cytotoxic analogues, are the two most prominent diabetogenic agents used for inducing diabetes in mammals (Szkudelski *et al.*, 2001; Szkudelski *et al.*, 1998) <sup>[4-5]</sup>.

To treat diabetes mellitus, several types of insulin preparations and oral hypoglycemic drugs have been developed and are in clinical use. However, there are several problems concerning the insulin use, such as physical pain and mental apprehension due to daily insulin injections. Since, the currently available oral hypoglycaemic drugs lack desired properties of an ideal drug, there is an immediate need for an effective, safe and less expensive drug (Patel *et al.*, 2012) <sup>[2]</sup>.

A number of transitional and other metal compounds like vanadium, zinc, chromium, molybdenum and cobalt complexes have all been proposed as possible adjuncts in the treatment of diabetes mellitus (Thompson *et al.*, 1999; Rehder *et al.*, 2002) <sup>[6-7]</sup>. Vanadium is the most thoroughly studied and efficacious insulin-enhancing transition metal. A wide variety of vanadium containing complexes has been tested as a potential candidate for anti-diabetic treatments (Crans *et al.* 2003; Sakura *et al.*, 1999) <sup>[8-9]</sup>.

Vanadium complexes have been demonstrated to exert various insulin-mimetic and anti-diabetic effects without apparent signs of toxicity. When administered in the form of nanoparticles, it exerts better action as an anti-diabetic agent and antioxidant than administering as a vanadium complex (Keyshams *et al.*, 2013; Vijay *et al.*, 2018; Vijay *et al.*, 2019) <sup>[10-12]</sup>. The aim of this study was to assess histological changes in the liver, kidney and pancreas of STZ-induced diabetic rats treated with vanadium pent oxide nanoparticles.

### Materials and Methods

#### Experimental animals

Male Wistar rats, weighing about 150-200 g were obtained from Laboratory Animal Medicine Unit, Tamil Nadu Veterinary and Animal Sciences University, Chennai - 51, India. The animals were maintained on standard rat feed supplied by Provimi Animal Nutrition India Private Limited, Bangalore, India. All animals were housed in cages with 12/12 hours light/dark cycle.

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The animals were fed *ad libitum* feed and water throughout the experimental period. The animals were acclimatized for three weeks prior to the start of the experiment. The animal experiments were carried out after prior approval of Institutional Animal Ethical Committee (IAEC), MVC, Chennai - 7.

### Experimental design

This study was conducted for thirty days. Twenty four male Wistar rats were randomly divided into three groups, each consisting of eight animals. Group I served as untreated control. Group II served as streptozotocin induced diabetic control. Groups III was diabetic rats treated at the dose rate of 5 mg/kg b.wt with vanadium pentoxide nanoparticles.

### Diabetes induction

Before induction, the blood glucose level was assessed by MYLIFE PURA glucometer to rule out spontaneous diabetes in the rats. Those animals, showing normal blood glucose levels of 80-110 mg/dL, were selected for the study.

The selected animals were fasted overnight and a single intraperitoneal injection of a freshly prepared solution of STZ (45 mg/kg b.wt) in 0.1 M cold citrate buffer (pH 4.5) was given to induce diabetes. The animals were allowed to access five per cent glucose solution overnight, to prevent hypoglycemia induced by STZ by massive pancreatic insulin release. After 72 hours, rats showing blood glucose above 250 mg/dL were considered as diabetic and rats of Group III were treated with vanadium pentoxide nanoparticles (5 mg/kg b.wt) daily for 30 days.

### Sample Collection

Animals were sacrificed at the end of the experiment, tissue

samples of liver, kidney and pancreas were collected in the formal saline for histopathological studies.

### Histopathology

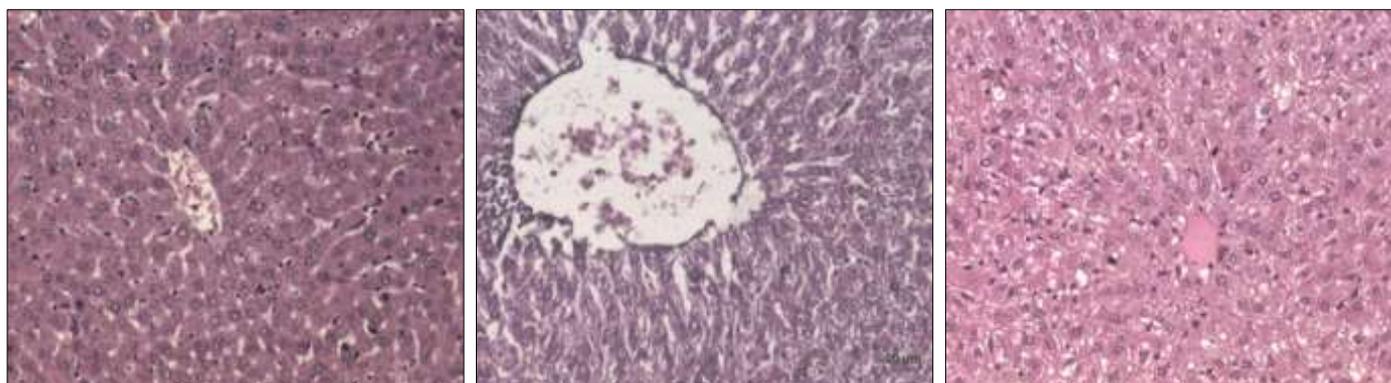
After the tissues were fixed completely in 10 per cent formalin, all the collected tissue samples were embedded in paraffin. Serial sections were cut and stained with haematoxylin and eosin. The sections were examined under high power microscope (200X) and photomicrographs of tissues picture were taken.

### Results and Discussion

#### Effect of Nano Vanadium on Histopathology of Liver

Effect of vanadium on histopathology of liver is shown in figure-1. In the present study, normal hepatic lobule and central venule with radiating cells of normal shape and size were observed in the liver of control rats. STZ-induced diabetic rats showed degeneration of hepatocyte, dilatation of sinusoids, venous congestion and vacuolar degeneration of hepatocytes. On treatment with Nano vanadium pentoxide, decreased intensity of degeneration and dilatation of sinusoids was observed, which indicates that vanadium prevents the damage in the liver of STZ- induced diabetic rats

Koyuturk *et al.* (2005) <sup>[13]</sup> reported that a normal histological appearance was observed in the liver of normal control rats. While vacuolization, nuclei-containing perichromatin material, pyknotic nuclei, large cytoplasmic granules, rupture in the epithelium of vein, hyperaemia and dilatations in sinusoids were observed in hepatocytes of diabetic rats. The hepatocytes of nano vanadium treated diabetic rats had exhibited lesser degenerative changes with less vacuolization and pycnotic nuclei when compared to diabetic control rats.



a. Normal Control

b. Diabetic control

c. Nano vanadium treatment

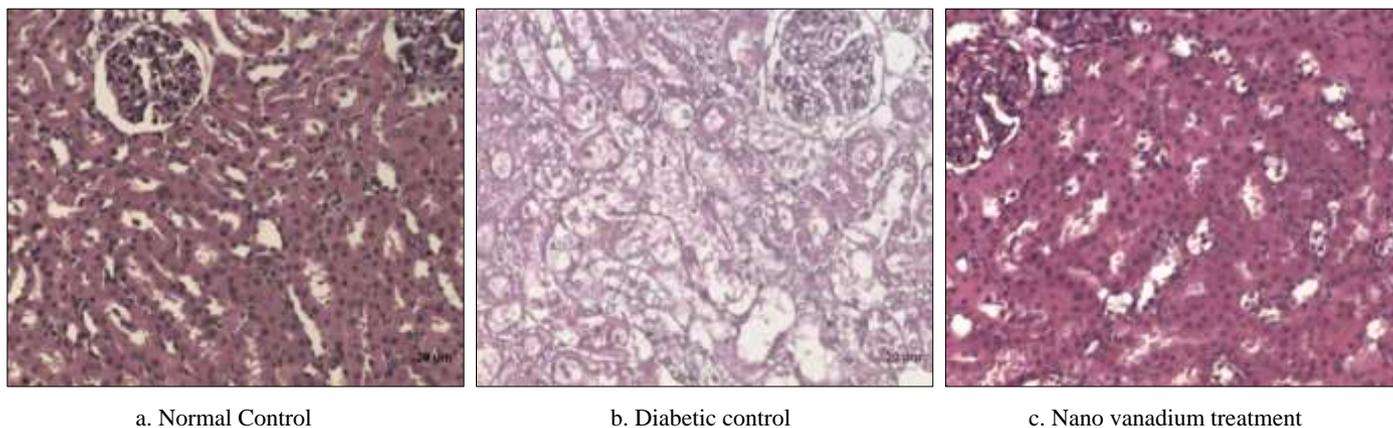
**Fig 1:** Histological changes in liver of control and treatment group

#### Effect of nano Vanadium on Histopathology of Kidney

Effect of nano vanadium on histopathology of kidney is shown in Figure-2. Kidney of normal control rats showed normal architecture and normal glomerular structure. Histopathological examination of kidney tissue of STZ-induced diabetic control rats showed marked changes like tubular epithelial cell degeneration and necrosis which is expressed by eosinophilic deposits with vacuolations in glomeruli tuft, mild mesangial cells hyperplasia, and cystic

dilatation of tubules. Treatment with Nano vanadium pentoxide reduced the intensity of degeneration and no cystic dilatation of tubules was observed, which indicates the protective nature of vanadium on the kidney tissue.

Similarly, Saad and Najjar, (2005) <sup>[14]</sup> reported that histopathological evaluation of kidneys revealed that STZ-induced diabetes exhibited glomerular hypertrophy, tubular dilation, intra-tubular hyaline casts and interstitial inflammatory cell infiltration.



a. Normal Control

b. Diabetic control

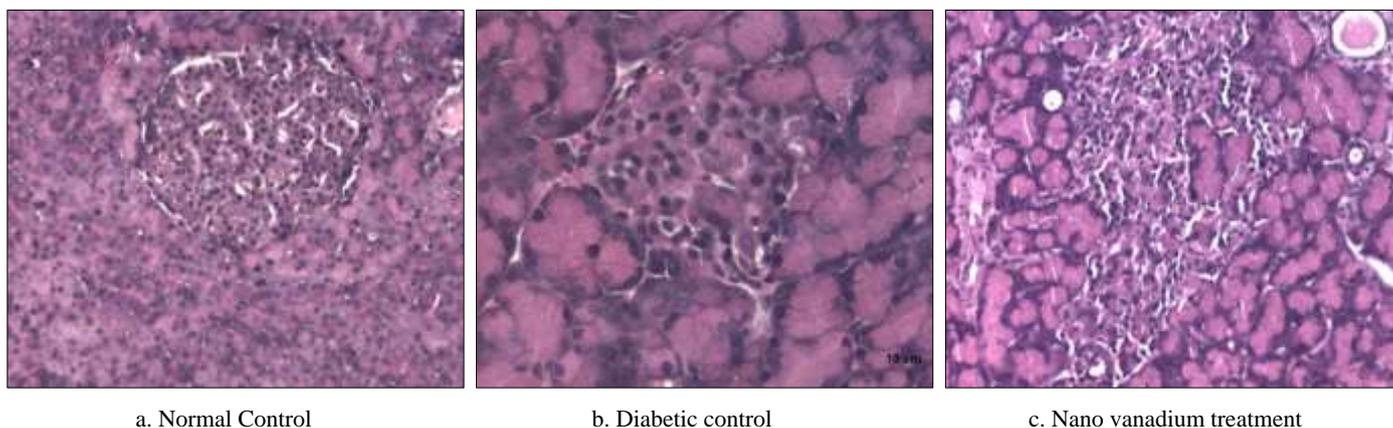
c. Nano vanadium treatment

**Fig 2:** Histological changes in kidney of control and treatment group

### Effect of nano Vanadium on Histopathology of Pancreas

Effect of nano vanadium on histopathology of pancreas is shown in Figure-3. In the present study, normal acinar architecture and pancreatic islets showing predominant beta cells and few eosinophilic alpha cells were observed in normal control rats. Pancreatic section of STZ-induced diabetic control rats showed degeneration of islets of

Langerhans with the areas of eosinophilic amorphous deposits within islets, suggesting cellular necrosis. There was also a decrease in population of islets when compared to that of diabetic control rats. In diabetic rats treated with Nano vanadium pentoxide decline in the degeneration of islets of Langerhans with normal pancreatic acinar cell structure when compared to that of diabetic control rats.



a. Normal Control

b. Diabetic control

c. Nano vanadium treatment

**Fig 3:** Histological changes in pancreas of control and treatment group

Similarly, Ahmadi *et al.*, (2002) <sup>[15]</sup> observed that in diabetic rats the sizes of islets were smaller than normal and islets showed necrotic cells with pyknotic nuclei and dense eosinophilic cytoplasm, while in vanadium treated diabetic rats pancreatic islet cells did not show any obvious changes as compared to normal rats.

Cam *et al.*, (1997) <sup>[16]</sup> stated that the partial preservation of pancreatic  $\beta$  cells is critical for a long-term reversal of the diabetic state. The vanadium induced amelioration of the diabetes may be the result of preserving a functional portion of pancreatic  $\beta$  cells that initially survived STZ toxicity, induction of islet neogenesis from undifferentiated precursor cells or Trans differentiation from other kinds of unknown cells (Sjoholm, 1996; Bertelli and Bendyan, 1997) <sup>[17-18]</sup>.

In conclusion, histopathological studies on the tissues of liver, kidney and pancreas in diabetic animals showed degenerative changes. Nano vanadium pentoxide treatment was able to partially restore the degenerative changes indicating the protective effect of vanadium.

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