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Some Histological Changes in the Intestines of Alloxan Induced Diabetic Mellitus Albino Rats

*Kebe E. Obeten, Ubom, K. Samuel, Charles C. Mfem
*Department of Anatomy, University of Calabar, Calabar
Department of Physiology, University of Calabar, Calabar
Corresponding author: Kebe E. Obeten
Email: fredobeten@yahoo.com

Abstract
Changes in intestinal histology of the Albino rats with alloxan induced diabetes mellitus was investigated using fifteen (15) albino rats. The rats were divided into 3 groups A, B, C. Group A served as the control group, group B served as the experimental low dose treated with 100mg/bw of Alloxan, while group C served as the experimental high dose was treated with 200mg/bw of Alloxan. The small intestines were removed and passed through routine tissue processing. The results in the rat of the control group A showed the mucosa, sub-mucosa, muscle and serious layer, luminar surfaces of the villi were lined by simple columnar cells. The brunner glands were also seen in the submucosa. While in rat of group B (low dose); the brunner glands appear to have decreased in size and number of goblet cells appeared more columnar. The histology of the layer was almost as similar to that of the control group. Group C (high dose); whereas in rats in group C was degeneration of the brunner glands characterized by pale staining cytoplasm; the nuclei of the columnar cells of the villi appear pykonotic; there was also loss of villi; the sub-mucosa coat appears to have undergone fibrotic changes; and, the various layers appear indistinct. Our results suggest that high dose of alloxan causes degeneration of the various layers of the duodenum.
Keywords: Alloxan, Diabetes mellitus, Wistar rats, Histological changes

Introduction

The chemical induction of diabetes appears to be the most popularly used procedure in inducing diabetes mellitus in experimental animals. The foremost drug-induced diabetic model is the alloxan diabetes that is capable of inducing type I diabetes mellitus in experimental animals. The surgical and genetic methods of diabetes induction are associated with a high percentage of animal morbidity and mortality. Hence, alloxan induced diabetes model appears to be the most reliable and easily reproducible method of inducing diabetes mellitus in experimental animals. So, efforts should be made towards upbringing and uplifting the model of alloxan induced diabetes mellitus in the experimental animals.

Diabetes mellitus has been considered as one of the major health concerns all around the world today. Experimental nimal models are one of the best strategies for the understanding of pathophysiology of any disease in order to design and develop the drugs for its treatment (Ress, 2005; Chatzigeorgiou, 2009). Numerous animal models have been developed for the past few decades for studying diabetes mellitus and testing anti-diabetic agents that include chemical, surgical and genetic manipulations (Srinivasan, 2007; Etuk, 2010). One of the most potent methods to induce experimental diabetes mellitus is chemical induction by Alloxan (Etuk, 2010). It is a well- known diabetogenic agent that is used to induce Type I diabetes in experimental animals. Alloxan is a urea derivative which causes selective necrosis of the β- cells of pancreatic islets. In addition, it has been widely used to produce experimental diabetes in animals such as rabbits, rats, mice and dogs with different grades of disease severity by varying the dose of alloxan used (Etuk, 2010; Iranloye, 2011). As it has been widely accepted that alloxan selectively destroys the insulin-producing beta-cells found in the pancreas, hence it is used to induce diabetes in laboratory animals. The toxic action of alloxan on pancreatic beta cells involve oxidation of essential sulphydryl (-SH groups), inhibition of glucokinase enzyme, generation of free radicals and disturbances in intracellular calcium homeostasis (Szkudelski, 2001, Dhanesha, 2012).

Alloxan (2,4,5,6-tetraoxypyrimidine;2,4,5,6- pyrimidinetetrone) is an oxygenated pyrimidine derivative which is present as alloxan hydrate in aqueous solution. Brugnatelli originally isolated alloxan in 1818 and the name was given by Wohler and Liebig in 1838 (Wohler, 1848). Moreover, the compound was discovered by von Liebig and Wohler in 1828 and has been regarded as one of the oldest named organic compounds that exist. The name Alloxan emerged from the merging of two words, i.e., Allantoin and Oxaluric acid. Allantoin is a product of uric acid excreted by the foetus in the allantois and oxaluric acid has been derived from oxalic acid and urea that is found in urine. Additionally, the alloxan model of diabetes induction was first described in rabbits by Dunn, Sheehan and McLetchie in 1943 (Dunn, 1943)

Alloxan-induced diabetes has been commonly employed as an experimental model of insulin dependent diabetes mellitus. The mechanism of alloxan action has been thoroughly studied which currently can be characterized quite well. Several experimental studies have demonstrated that alloxan evokes a sudden rise in insulin secretion

in the presence or absence of lucose which appeared just after alloxan treatment (Szkudelski, 1998; Lachin, 2012). This particular alloxan-induced insulin release occurs for short duration followed by the complete suppression of the islet response to glucose even when high concentrations of glucose were used (Kliber, 1996). Further, the alloxan action in the pancreas is preceded by its rapid uptake by pancreatic beta cells that have been proposed to be one of the important features determining alloxan diabetogenicity. Moreover, in pancreatic beta cells, the reduction process occurs in the presence of different reducing agents like reduced glutathione (GSH), cysteine, ascorbate and protein-bound sulfhydryl (-SH) groups (Lenzen, 1991 ; Zhang, 1992). Alloxan reacts with two -SH groups in the sugar binding site of glucokinase resulting in the formation of the disulfide bond and inactivation of the enzyme. As a result of alloxan reduction, dialuric acid is formed which is then re-oxidized back to alloxan establishing a redox cycle for the generation of reactive oxygen species (ROS) and superoxide radicals. (Munday 1988) The superoxide radicals liberate ferric ions from ferritin and reduce them to ferrous and ferric ions. In addition, superoxide radicals undergo dismutation to yield hydrogen peroxide (H_2O_2) in the presence of superoxide dismutase. As a result, highly reactive hydroxyl radicals are formed according to the Fenton reaction in the presence of ferrous and H_2O_2.

Materials and methods

Fifteen (15) young Wistar rats weighing an average of 90-180g were gotten from the animal house of the Department of Physiology, Faculty of Basic Medical Science, University of Calabar, Calabar. The rats were maintained under normal laboratory conditions of temperature, humidity and light for a period 2 weeks in the animal holdings of the Department of Human Anatomy, University of Calabar, Calabar, Nigeria, before commencement of experiment.

Alloxan which is a uric acid derivative, induces diabetes by initiating free radical damage of DNA in the beta-cells of the pancreas, causing the cells to malfunction and die. When these cells fail to operate normally, they no longer produce enough insulin, resulting in a variety of type 1 or Juvenile-onset diabetes (IDDM).

Discussion

Results from this research work reveals that at high dose of alloxan there is a degeneration of intestinal glands especially in the duodenum where the brunner glands were destroyed and there was pyknosis in the nuclei of goblet cells indicating cell death.

The GIT epithelium is said to be covered by a protective mucosa gel composed predominantly of mucin glycol-proteins that are synthesized and secreted by goblet cells. Hence a decrease in the number of goblet cells would indicate possible reduction mucous to help rid it of the irritant of causative factor.

The sole function of the villi is that of absorption, the villi absorbs nutrients from digested food into the blood stream. Hence, when there is villous erosion, it points towards decrease absorption of nutrients through the epithelial lining and lacteals of the villous. Continuous intake may predispose the individual to mal-absorption.

Earlier studies showed that Alloxan and product of its reduction establishes a redox cycle with the formation of superoxide redicals resulting in the formation of highly reactive hydroxyl radicals within the tissues brining about acidosis and subsequent death of some animals, (Szku-delski, 2001).

Result

Control group A: Four distinct layers are seen, the mucosa, sub mucosa, serous layers and luminar surfaces of the villi are lined by simple columnar cells. Interspaced amongst the columnar cells are goblet cells. Brunner glands are also there in the sub-mucosa.

Group B: The low dose, here the Brunner glands appeared to be decreased in size and number. Goblet cells appear more in columnar epithelial cells. The histology of the layer was almost as similar to that of the control.

Group C: High dose, here there was degeneration of the Brunner glands characterized by pale staining cytoplasm, the nuclei of the columnar cells of the villi appear pkykonotic, there is also loss of villi. The sub mucosa coat appears to have undergone fibrotic and the various layers appear indistinct.

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PLATES

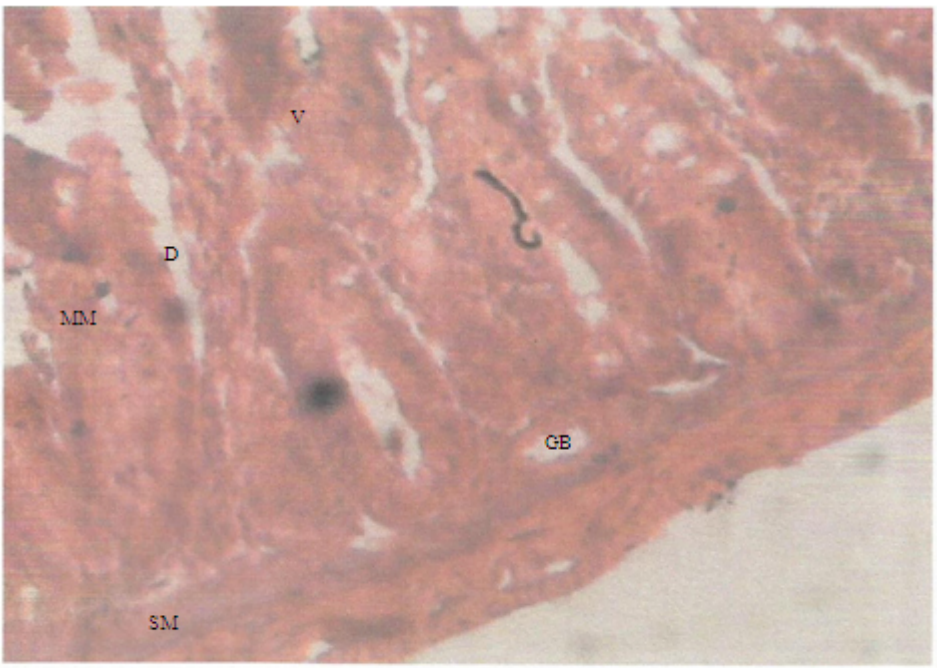

Plate 1: Photomicrograph of control group A showing normal Muscularis mucosae (MM), duct (D), Villi (V), Glands of Brunner (GB)

V

D

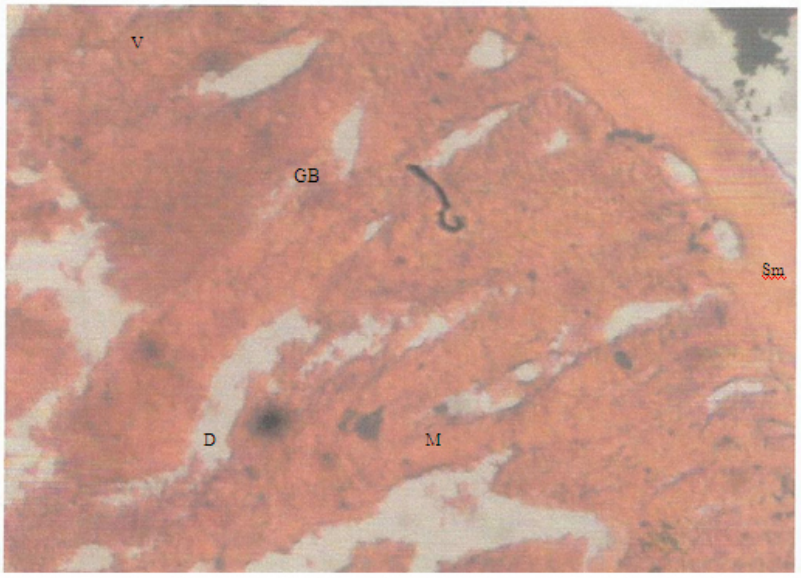

Plate 2: Photomicrograph of group B (Low dose) showing decreased Gland of Brunner (GB), Mucosa (M), Sub mucosa (Sm), Villi (V), Duct (D)

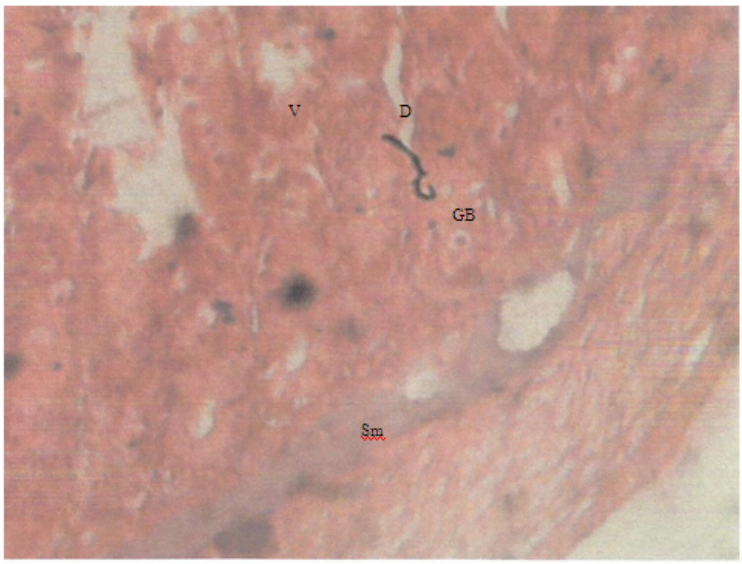

Plate 3: Photomicrograph of group C (High dose) showing the Sub mucosa (Sm), Gland of Brunner (GB), Duct (D) and Villi (V)

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