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The Role of Ileum in the Absorption of Glucose in Normal and Alloxan-Induced Diabetic Rats Treated with Kolaviron

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Abstract: Kolaviron (KV) is an established antihyperglycemic agent in both normal and experimental diabetic rats. The role of ileum in glucose uptake in KV-treated normal and diabetic rats was investigated. Rats (150–180 g) were used and grouped into 4 (n=5/group). Groups 1 and 2 are the control (non-diabetic) and untreated diabetics respectively while groups 3 and 4 were treated with 200 mg/kg KV and 5mg/kg Glibenclamide (GB) orally respectively. Diabetes was induced by 120 mg/kg of alloxan. Before each phase, rats fasted for 12 h with free access to water. Phase 1 assessed the effect of treatments on blood glucose levels while Phases 2 and 3 investigated the route of glucose utilization following treatments. Rats were anaesthetized before laparotomy in Phases 2 and 3 following which 4 ml of modified Krebs solution was infused between 2 ligated ends of the ileum. Glucose concentration was determined by the glucose oxidase method. Data were analyzed and considered significant at $P < 0.05$. Fasting blood glucose of KV-treated and GB-treated decreased significantly compared to the Control and Diabetic after 2 h of KV administration. The A-V study recorded a 14.1%, 27.6%, and 19.3% decrease in A-V difference of blood glucose concentration in the untreated diabetics, KV-treated and GB-treated respectively compared to the control after 2 h. The ileum glucose absorption (mg/dl/cm) increased significantly in the KV-treated (12.67±1.2; 18.12±1.6) and GB treated (10.41±0.8; 16.51±1.1) when compared with the control (8.66±0.9; 11.61±1.6) and untreated diabetic (9.91±0.8; 11.13±0.9) after 90 and 120 minutes respectively. The mode of improved absorption into the enterocytes was not elucidated in this study. The role of the surviving pancreatic β-cells should be investigated.

Keywords: Kolaviron, Ileum, Glucose Absorption, Rats, Antihyperglycemic, Diabetes

1. Introduction

The gastrointestinal system has been reported to play a significant role in glucose homeostasis [1–3], and several studies have demonstrated an increased rate of glucose absorption, especially in experimental diabetic animals [4]. It is known that experimental diabetes produced by alloxan markedly increases intestinal sugar absorption and that hyperglycemia itself can enhance intestinal sugar transport [5, 6]. Several theories have been published to explain these changes. Among the tactics receiving attention in reducing postprandial hyperglycemia and probable management of hyperglycemia is to reduce the amount of glucose available for absorption at the intestinal level [7].

Major resection of the intestine can cause significant malabsorption syndrome known as short bowel syndrome (SBS) [8]. This may cause a major absorption problem for the gut and its role in glucose homeostasis may be impaired, more so in glucose metabolic impairments such as diabetes gut. This might provide the ileum as the major part of the gut spared and its efficiency to modify its role in such a situation is not well established especially in glucose deranged states.

The ileum is not a decent site for glucose absorption in normal humans and animals due to the reduced number of

hexose transmembrane transporters SGLT1 and GLUT2 which makes glucose absorption difficult [9]. Certain earlier reports have demonstrated that bypass surgeries such as small bowel resection in rats could attain important absorptive tissue for glucose in normal animals by hyperplasia and not necessarily due to increased expression of the transporting genes of SGLT1 and GLUT 2 [9]. It is a belief that glucose accumulates in the distal ileum in normal individuals as a result of a possible reduction in SGLT1 and as a result of the missed absorption in the resected gut in bariatric surgery [10].

Kolaviron, a biflavonoid complex of Garcinia kola seeds has been reported for its action on glucose utilization by the gut [11, 12] among several other important influences on inflammation, diarrhea and ulcer healing [13–15]. However, the effect of kolaviron, a reported potent antihyperglycemic agent on the ileum of experimental diabetic rats has not received adequate attention. The role of the ileum in glucose management in diabetic rats was investigated in this study.

2. Material and Methods

2.1. Animals

Adult female Wister strain albino rats (150 - 180 g) were used for this study.

2.2. Plant Material

Seeds of Garcinia kola were obtained locally in Ibadan, Nigeria, and certified by a Botanist at the University of Ibadan.

2.3. Test Material

Kolaviron was isolated according to Iwu *et al* (1990) [16].

2.4. Experimental Procedure

The experiments were performed in three phases and grouped into 4 of 5 animals each. Group I represents the control rat treated with normal saline, groups II was the untreated diabetic while groups III and IV were treated with 200 mg/kg of KV (D+KV) and 5mg/kg of Glibenclamide (D+GB) respectively. The animals fasted for 12 hours before the start of the experiment.

Phase I - Blood samples were taken from the tails of all animals at 0 hours, 1 hour, and 2 hours post-treatment.

Phase II - The intestinal segments 15-20cm long were identified for consistency. The segments were then filled with 4ml of the modified Krebs's bicarbonate solution containing 2g of glucose. Samples for glucose concentrations were collected for analysis at intervals of 90 and 120 minutes from each animal. Glucose absorbed per length was then determined.

Phase III - Two hours post-treatment, blood samples were obtained from the abdominal aorta and mesenteric vein of the rats and were quickly determined using the method above.

2.5. Histology of Pancreas

The pancreas was isolated via laparotomy, weighed and fixed in 10% formalin in a labeled bottle. Tissue processing was carried out by auto-technic on 5µm thick sections and was mounted on slides and stained with Gomori's Chrome Alum Hematoxylin and Phloxine Eosin. Stained sections were evaluated and the microphotograph was taken using an Acuscope microscope.

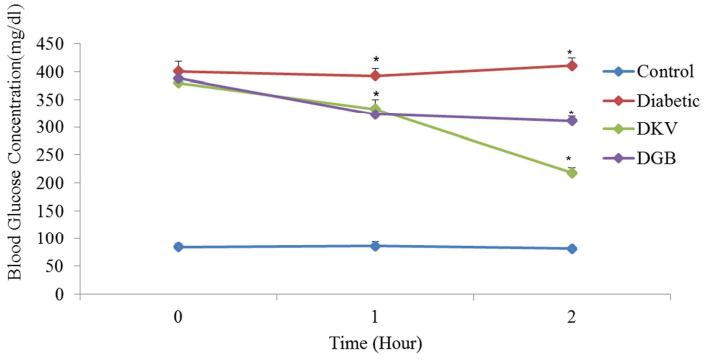
2.6. Statistical Analysis

Unpaired student t-test and ANOVA using Microsoft excel software version 2010. Differences were considered significant at $P< 0.05$.

3. Results

3.1. Effects of Kolaviron on Fasting Blood Glucose (FBG) and After Kolaviron Treatment

The rats were tested for their fasting blood glucose (mg/dL) before the commencement of the study. The FBG increased significantly in all diabetic groups compared to the control. One hour after treatment with kolaviron and glibenclamide, figure 1 shows the blood glucose of the Diabetic treated with Kolaviron (DKV) (333.0±21.2) and Diabetic treated with glibenclamide (DGB) (323.0±20.1) reduced significantly compared to the diabetic untreated (393.0±18.8). Two hours after the treatments DKV (218.0±9.8), DGB (311.0±8.7) compared to the diabetic untreated (413.0±18.7), figure 1.

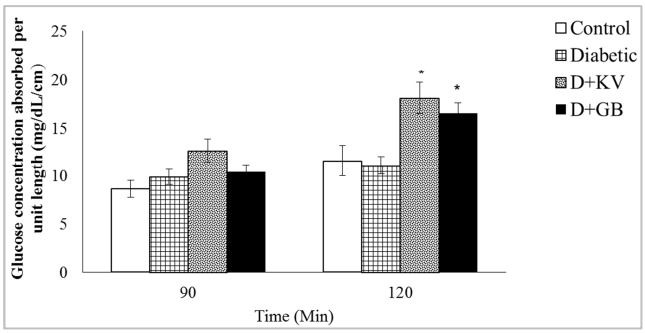


*significant compared to control

Figure 1. *Blood Glucose Concentration of Rats treated with Kolaviron.*

3.2. Effects of Kolaviron on Luminal Glucose Absorption in Vivo of Diabetic Rats

The luminal glucose absorption per unit ileum length (mg/dL/cm) was reported in Figure 2. The significant absorption was observed at 120 min. after the commencement of the experiment. The luminal glucose absorption increased significantly in the DKV (18.12±2.51) and DGB (16.51± 2.13) groups compared to Diabetic untreated (11.13±1.94) and control (11.61±2.51).

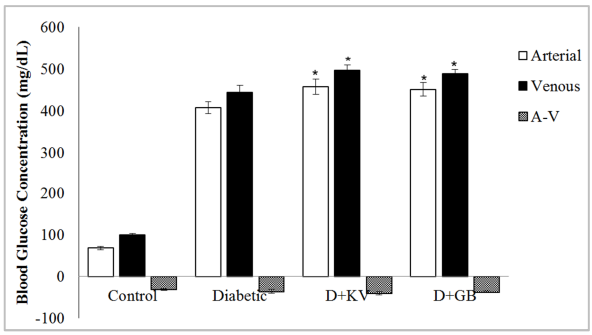


*significant compared to control

Figure 2. *Luminal Glucose Absorption by the Ileum in the different diabetic groups.*

3.3. Effects of Kolaviron on the Arterio-venous Blood Glucose Differences in Diabetic Rats

The arteriovenous differences (mg/dL) were not significantly different when compared in all the groups. However, figure 3 shows a significant increase in the arterial and venous components of the DKV (457.3±21.3; 497.2 ± 10.8), DGB (451.2±22.1; 488.5±11.2), compared to the diabetic untreated (407.9±18.6; 443.6±12.6) and control (68.2±6.1; 99.5±4.3), respectively.



*significant compared to control

Figure 3. *Arterial-Venous Blood Glucose Concentration Differences.*

3.4. Histopathologic Findings on the Pancreas

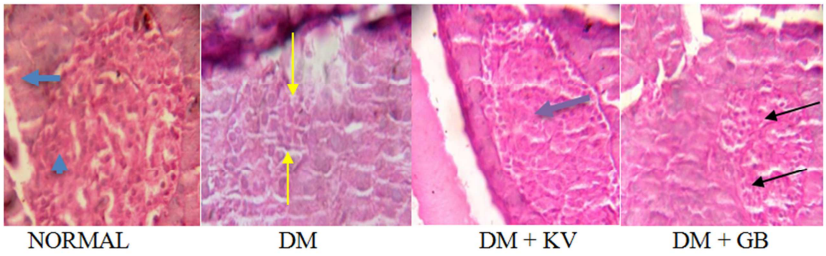


Figure 4. *Representative Photomicrograph of the Pancreas (Gomori's Chrome Alum Hematoxylin and Phloxine Eosin Magx400): NORMAL: several numbers of beta cells appear blue/ dark blue (slender arrow), and other few cells appear pink/red. DM: enlarged beta cells within shrunk islet of Langerhan (slender arrow). DM + KV: moderate numbers of beta cells appearing blue/ dark blue (slender arrow), other few cells appearing pink/red appear to be the alpha cells. DM + GB: mildly depleted beta cells within islet of Langerhan (slender arrow).*

4. Discussion

It is understood from previous studies that the enterocytes' absorption of glucose is via the carrier-mediated transport of glucose from the luminal end [17, 18]. The ileum is not a major site for glucose absorption but its adaptively involved with better glucose absorption in the face of resection of the proximal end of the gut [19, 20]. The role of ileum in the handling of diabetic-like states with the use of kolaviron treatment was investigated in this study.

The fasted glucose was substantially high in the diabetic groups to warrant for recruitment of animals into the diabetic-like group from the definition of our inclusion criteria. In this study, we reported a significant increase in glucose absorption rate of the diabetic treated groups (either with kolaviron or glibenclamide) compared to the absorption from the ileum of control and non-treated diabetic rats. This buttresses the reports that there is increased intestinal glucose absorption in experimental diabetics [2, 5, 6]. The mucosal-to-serosal movement of glucose molecules was augmented, this was observed after 2 h of glucose infusion into the ileum. It has been reported earlier that hyperglycemia alone without diabetes could facilitate increased absorption of glucose by the intestine [6] and the role of the ileum in luminal glucose absorption by the gut was reported to increase in normal rats in the presence of kolaviron compared to without kolaviron [11].

The arterial-venous glucose differences consistently show an increase in the venous end compared to the arterial with a negative difference in all the groups. The important finding from this aspect of the study described further increased

uptake of glucose away from the mucosa. Although there was an increase on both ends of the arterial and venous in the treated diabetic groups, this is by no means comparable to the control and the diabetic untreated groups with a similar arterial-venous difference. This further portrays kolaviron as a potent antihyperglycemic agent that potentiated uptake of glucose from the luminal glucose in the ileum. A similar study on rat brain increased glucose uptake following treatment with kolaviron by the brain cells [12].

The role of diabetic ileum in the increasing uptake of glucose in the absence or presence of kolaviron as observed in this study could be due to the possible inhibitory effect of kolaviron on pancreatic alpha-amylase activities [11]. Though all the diabetic groups had better ileal glucose uptake compared to the control, the groups with kolaviron treatment performed much better than untreated diabetics. Thus showing the increasing adaptability of the diabetic ileum to regulate glucose better compared to the control. A previous report by Fujita et al [4], described the role of SGLT1 in the improved glucose absorption in the diabetic intestine. The adaptability of modalities involved in these tendencies was not elucidated in the current study.

5. Conclusion

We concluded that the increase in the ileum glucose absorption rate seen in Diabetic treated groups may suggest modulatory activities on pancreatic β cells left out among other routes as buttressed by increased ileum glucose absorption reported in both diabetics alone and diabetics treated. Future emphasis should be on the role of GLUT 2 and SGLT 1 as well as verify the impact of the pancreatic alpha-amylase and insulin.

Conflict of Interest

The authors declare that they have no competing interests**.**

References

[1] Alada AR, Oyebola DD. Evidence that the gastrointestinal tract is involved in glucose homeostasis. *Afr J Med Med Sci* 1996; 25: 243–249.

[2] Alada AR, Falokun PO, Oyebola DD. Intestinal glucose uptake in normal, untreated and insulin-treated diabetic dogs. *Afr J Med Med Sci* 2005; 34: 147–156.

[3] Alada AR, Oyebola DD. The role of adrenergic receptors in the increased glucose uptake by the canine gut. *Afr J Med Med Sci* 1997; 26: 75–78.

[4] Fujita Y, Kojima H, Hidaka H, et al. Increased intestinal glucose absorption and postprandial hyperglycaemia at the early step of glucose intolerance in Otsuka Long-Evans Tokushima Fatty rats. *Diabetologia* 1998; 41: 1459–1466.

[5] Caspary WF. Increase of active transport of conjugated bile salts in streptozotocin-diabetic rat small intestine'. *Gut* 1973; 14: 949–955.

[6] Csaky TZ, Fischer E. Intestinal sugar transport in experimental diabetes. *Diabetes* 1981; 30: 568–574.

[7] Inzucchi SE. Oral antihyperglycemic therapy for type 2 diabetes: scientific review. *JAMA* 2002; 287: 360–372.

[8] O'Keefe SJD, Buchman AL, Fishbein TM, et al. Short bowel syndrome and intestinal failure: consensus definitions and overview. *Clin Gastroenterol Hepatol* 2006; 4: 6–10.

[9] Iqbal CW, Fatima J, Duenes J, et al. Expression and function of intestinal hexose transporters after small intestinal denervation. *Surgery* 2009; 146: 100–112.

[10] Jurowich CF, Otto C, Rikkala PR, et al. Ileal Interposition in Rats with Experimental Type 2 Like Diabetes Improves Glycemic Control Independently of Glucose Absorption. *J Diabetes Res*; 2015. Epub ahead of print 2015. DOI: 10.1155/2015/490365.

[11] Odukanmi OA., Oluwole FS. and Olaleye SB. *Effects of Kolaviron, a Garcinia Kola biflavonoid, on Rat Intestinal Glucose Absorption and Alpha Amylase Inhibitory Activities*. 2014.

[12] Salau VF, Erukainure OL, Bharuth V, et al. Kolaviron stimulates glucose uptake with concomitant modulation of metabolic activities implicated in neurodegeneration in isolated rat brain, without perturbation of tissue ultrastructural morphology. *Neurosci Res* 2021; 169: 57–68.

[13] Odukanmi OA, Salami AT, Ashaolu OP, et al. Kolaviron attenuates ischemia/reperfusion injury in the stomach of rats. *Appl Physiol Nutr Metab* 2018; 43: 33–37.

[14] Salami A, Morakinyo O, Odukanmi O, et al. Kolaviron modulates intestinal motility and secretion in experimentally altered gut functions of Wistar rats. *J Complement Med Res* 2018; 9: 55–62.

[15] Ajayi SA, Odukanmi OA, Ojo, GB. The Protective Effects of Kolaviron on the Renal Functions Journal of Pharmaceutical and Scientific Innovation THE PROTECTIVE EFFECTS OF KOLAVIRON ON THE RENAL FUNCTIONS OF FEMALE WISTAR RATS TREATED WITH CLOMIPHENE CITRATE. *J Pharm Sci Innov* 2012; 1: 102–107.

[16] Iwu MM, Igboko OA, Elekwa OK, et al. Prevention of thioacetamide-induced hepatotoxicity by biflavanones of Garcinia kola. *Phyther Res*. Epub ahead of print 1990. DOI: 10.3/JQUERY-UI.JS.

[17] Zheng Y, Sarr MG. Translocation of transfected GLUT2 to the apical membrane in rat intestinal IEC-6 cells. *Dig Dis Sci* 2011; 57: 1203–1212.

[18] Kellett GL, Brot-Laroche E, Mace OJ, et al. Sugar absorption in the intestine: the role of GLUT2. *Annu Rev Nutr* 2008; 28: 35–54.

[19] Rubin DC, Levin MS. Mechanisms of intestinal adaptation. *Best Pract Res Clin Gastroenterol* 2016; 30: 237–248.

[20] Tappenden KA. Intestinal adaptation following resection. *JPEN J Parenter Enteral Nutr* 2014; 38: 23S-31S.