ORIGINAL ARTICLE

Methanol Extract of *Basella Alba* Leaf Enhances Glucose Utilization in Nicotine Treated Male Wistar Rats

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Abstract

Background: Nicotine has been reported to exert adverse effects on insulin sensitivity, predispose individuals to metabolic syndrome, and induce decreased functionality of the pancreas. The present study evaluated the influence of methanol extract of *Basella Alba* leaf on glucose utilization in nicotine treated male Wistar rats.
Methods: Twenty male rats, weighing 200-240g were divided into four groups of five animals each as follows; Healthy Control (H-C) rats, which were given no treatment but placebo, Nicotine Control (N-C), which received 1.0 mg/kg of nicotine, Low Dose Nicotine + *Basella Alba* group (LDN-Ba), which received 0.5 mg/kg nicotine and 200mg/kg of MeBa, and High Dose Nicotine + *Basella Alba* group (HDN-Ba) that were given 1.0 mg/kg of nicotine and 200 mg/kg of MeBa.
Results: Following acute nicotine exposure, FBG levels were significantly higher ($p < 0.05$) in NC, LDN-B and HDN-B rats when compared to H-C. Likewise, OGTT showed a significant ($p < 0.05$) derangement in N-C and HDN-B when compared to HC and LDN-B groups. Body weight, weight and relative weight of pancreas were significantly decreased ($p < 0.05$) in all nicotine treated groups when compared to the healthy control group. Histopathology also revealed general distortion of pancreatic histoarchitecture in the nicotine control rats. A significant decrease ($p < 0.05$) in the blood glucose level and improved OGTT was observed in LDN-B rats after four weeks treatment with *Basella Alba* compared with N-C.
Conclusion: The findings revealed that the dysfunction in glucose metabolism caused by nicotine toxicity is dose dependent and the administration of methanol extract of *Basella Alba* leaf ameliorate these effects to a greater extent in low dose than in high dose nicotine group.

Key Words: Methanol Extract; *Basella Alba*; Glucose Utilization; Nicotine

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INTRODUCTION

Tobacco is a known leading cause of lung cancer from which nicotine was first extracted by German physicians Wilhelm Heinrich Posselt and Karl Ludwig Riemann [1]. Despite an increasing public awareness from numerous health initiatives, nicotine addiction remains a major challenge worldwide [2]. Nicotine is a strong alkaloid and a tertiary amine composed of a pyridine and pyrolidine ring and it is a clear liquid with a characteristic odor in its pure form [3]. Nicotine is reported to be the main addictive constituent of tobacco cigarette and despite the enormity of health hazards associated with tobacco use, one third of total world's population is still believed to consume tobacco products [4].

A number of experimental and clinical studies suggest that smoking decreases insulin sensitivity, and consequently results in a compromise of glucose utilization. In diabetic patients, it appears that cigarette smoking tend to worsen the metabolic control. A larger dose of insulin is usually needed to attain similar metabolic control in smoking patients than in non-smokers [5]. Nicotine has adverse effects on insulin resistance and can predispose individuals to developing metabolic syndrome [6]. Additionally, exposure to nicotine has been identified to induce morphological alterations in the pancreas, which may result in apoptosis of pancreatic beta cells and abnormal glucose tolerance. The consequent reduction in beta cells mass thus leads to decreased functionality of the pancreas and dysfunctional glucose utilization.

Concerning the cure of human diseases, medicinal plants have remained major sources of therapeutic agents since ancient times. The last few decades has however witnessed an upsurge in technological processing of medicinal plants into therapeutic agents due to the increasing interest in the use of natural products, which is said to be growing worldwide at a rate between 7 to 15% yearly [7]. Notwithstanding the dominant status of modern medicine, the invention of alternative therapeutic agents and new drugs from natural substances remains pivotal in medical practices. The

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development of traditional medicine via exploration of various local medicinal agents has been encouraged by World Health Organization (WHO) since 1980 [8], following reports of involvement by approximately 80% of the total world's population. It is therefore imperative to continue to exploit this field of research to a greater extent.

Phytochemicals such as alkaloids, terpenoids, glycosides, and flavonoids have been found to be an essential components of plants that are used in the treatment and management of metabolic disorders [9]. Among the plants that possess these phytochemicals is *Basella Alba* [10]. *Basella Alba* belongs to the family *Basellaceae*, native to tropical Asia and believed to originate from India and/or Indonesia. It is a fast growing vegetable that is able to tolerate heat significantly. *Basella Alba* is grown in the tropics as a perennial plant, but suffice in warmer regions as an annual crop. It is low in calories by volume and high in protein per calories [11]. It has been reported to reduce fasting blood glucose level in animals to an extent that is comparable to standard drugs [10, 12].

Tobacco usage has been identified as the leading cause of preventable cancers in humans. An estimated 1.27 billion people are reported by WHO to use nicotine in one way or another worldwide. Tobacco consumption is claimed to be solely responsible for the death of almost 5.4 million people annually with a projection of up to one billion deaths in the 21st century if current consumption rate of tobacco is unchecked [13].

Nicotine contributes to the development of many clinical conditions including some pancreatic pathologies [14, 15, 16]. A study by Chowdhury *et al.*, 1998 [17] showed that the administration of nicotine to rodents induced morphological pancreatic alterations and the mechanism by which nicotine relays its effects was suggested to be mediated by nicotinic acetylcholine receptors [18]. Juvenile Wistar rats that were exposed to nicotine during gestation showed apoptosis of pancreatic beta cells and abnormal glucose tolerance [6, 19]. These findings, all generally suggest a reduced functionality of the pancreas and dysfunctional carbohydrate metabolism. Exposure to nicotine has also been found to alter pancreatic islets gene expression of different transcription factors specific for endocrine cells and hormones, such as insulin and glucagon [19]. As a consequence of these altered genetic parameters, the normal physiological control of glucose homeostasis is also altered considerably [20].

Natural food substances and nutraceuticals play very important roles in both the primary and complimentary treatment of various diseases. Furthermore, there has been no satisfactory therapeutic measure or treatment for the management of nicotine induced dysfunction in glucose utilization. *Basella Alba* contains phytochemicals such as alkaloids, terpenoids, glycosides, and flavonoids, which are essential components of plants that have been used effectively in the treatment of diabetes mellitus. This formed the basis for hypothesizing an enhanced glucose utilization following *Basella Alba* administration in nicotine treated rats. The paucity of information on the euglycemic potential of *Basella Alba* leaf in nicotine-induced dysfunctional glucose utilization, provided the motivation for carrying out this study.

METHODS

Experimental Animals

Twenty male Wistar rats with weight ranging from 200 to 240g were procured from the animal facility of the College of Health Sciences, Bowen University, Iwo Osun State, Nigeria for this study. The animals were kept in clean cages under standard conditions (i.e. temperature at 25±2˚C and a 12 hourly light/dark cycle) in a separate room in the animal house of the Physiology Department, Faculty of Basic Medical and Health Sciences, Bowen University Iwo, Osun State, Nigeria. All the animals were fed with normal rat feed and water *ad libitum,* unless during overnight fast for fasting blood glucose analysis. After random selection into various experimental groups, the rats were allowed a period of two weeks in the new environment for acclimatization before initiation of experimental treatments. The use of animals throughout this study was in accordance with the guidelines and principles for research involving use of animals as recommended by the declaration of Helsinki and the Guiding principles in the care and use of animals [21].

Preparation of Study Plant Material

Fresh *Basella Alba (B. Alba)* leaves from traditional settlements of western Nigeria were identified and authenticated in the department of Botany, University of Ibadan with voucher number (UIH-22391). The leaves were removed from the stems, washed in clean water and air-dried at room temperature. The dried leaves were then grinded into fine powder and 110g of the powdered leaves was mixed with 1000 ml of methanol using the method described in earlier work by Arokoyo et al., 2019 [22]. After keeping in water bath at a temperature of 40˚C for 1 hour, the mixture was then stirred repeatedly at room temperature for a further 72 hours. The mixture was filtered with the aid of a cheese cloth and the filtrate concentrated to dryness by evaporation in a rotary evaporator (Hei-VAP Core). A solid mass was obtained with the yield being 22.45%. The extract was dissolved in normal saline and administered by oral gavage during the study.

Preparation of Nicotine and Dosage

Nicotine (Alchem Inc., Minnesota, USA) was dissolved in normal saline to get an initial dilute stock solution from which further dilutions were freshly prepared daily as required. The nicotine dosage for each group of animals was delivered orally by gavage at 0.5mg/kg body weight (low dose) and 1.0 mg/kg body weight (high dose) [23]. Dilutions were done on a daily basis to maintain freshness and nicotine stock was kept constantly refrigerated at – 20 ^{0} C.

Experimental Design

The twenty male Wistar rats were randomly divided into four groups of five rats per group. Each group was kept in different cages and treated as follows:

Group I: Healthy control (H-C) - Rats were neither given nicotine nor given *B. alba,* but had equivalent normal saline throughout the experiment.

Group II: Nicotine Control (N-C) – Rats were given nicotine at high dose (1.0 mg/kg) without *B. Alba* extract

treatment throughout the experiment.

Group III: Low Dose Nicotine + Ba Treatment (LDN-Ba) – Rats were given nicotine at low dose (0.5 mg/kg) and also given methanol extract of *B. Alba* (200 mg/kg) daily as treatment [10].

Group IV: High Dose Nicotine + Ba Treatment (HDN-Ba) – Rats were given nicotine at high dose (1.0 mg/kg) and also given methanol extract of *B. Alba* (200 mg/kg) daily as treatment.

Both Nicotine and *B. Alba* were administered via oral gavage with the aid of an oropharyngeal canular. The drugs were administered for a period of four weeks.

Measurement of Fasting Blood Glucose (FBG) Level

Baseline fasting blood glucose was recorded after two weeks of acclimatization in all rats and weekly in all animals from the four experimental groups after an overnight fast. The blood samples for FBG were collected from the tail capillaries by pricking the tip of the tail with a sterile lancet and expressing one or two drops of blood. This was applied in an appropriate manner to a glucometer (On Call Plus II) strip to determine the FBG levels.

Measurement of Oral Glucose Tolerance

Baseline oral glucose tolerance test (OGTT) was recorded after two weeks of acclimatization in all rats, then after acute exposure to nicotine and at the end of four weeks treatment with methanol extract of *B. Alba*. The blood samples for OGTT were collected from the tail capillaries by pricking the tip of the tail with a sterile lancet and expressing one or two drops of blood. This was applied in an appropriate manner to a glucometer (On Call Plus II) strip to determine the FBG levels. The rats were starved for 10 hours but were given enough water before the commencement of OGTT. The FBG was first checked which was recorded as 0 minute. The rats were then given an oral load of 80% glucose solution via oral gavage after which timing begins. The blood glucose level was tested at 30, 60, 90 and 120 minutes.

Collection of Pancreas Samples for Analysis

After the treatment period, all the animals were anaesthetized using diethyl ether and euthanized via exsanguination. The pancreas was carefully excised, weighed, and immediately fixed in 10% formalin solution. The tissues were processed and histopathological slides prepared from all samples. The prepared slides were examined microscopically and digital photomicrographs obtained and interpreted at the histology laboratory of the Department of Anatomy, College of Health Sciences, Bowen University, Iwo, Osun State Nigeria.

Estimation of Body Weight, Pancreas Weight and Relative Weight of Pancreas

All the animals were weighed weekly with the aid of a digital weighing balance. After being euthanized and dissected, the animals' pancreas was excised, cleaned, and weighed immediately. The relative pancreas weight was calculated by dividing the weight of pancreas by the final body weight of the corresponding animal before euthanization.

Ethical Considerations

Strict adherence to study design guidelines in the use of nicotine and all other materials was observed in accordance to the ethical approval granted by the research ethics committee of Bowen University Teaching Hospital (BUTH/REC-379; NHREC/12/04/2012)

Statistical Analysis

The data obtained from each group were expressed as mean ± standard error of mean (SEM). Statistical analysis was done using GraphPad Prism Version 5.0 (GraphPad Software, Inc. USA). More specifically, one way analysis of variance (ANOVA) was used to compare differences, followed by Newman-Keuls post-hoc test. Differences in the results were considered significant at $p < 0.05$.

RESULTS

Effects of Treatments on Fasting Blood Glucose (FBG) Levels

Fasting blood glucose levels of all experiment groups before the commencement of treatments showed no significant difference and was recorded as baseline readings for each group. After the first and second weeks of treatment with nicotine and *Basella Alba* as required in the design, there was a significant increase in the FBG levels of N-C, LDN-Ba, and HDN-Ba groups when compared to the H-C group ($p < 0.05$) (Table 1).

Table 1. Table showing the effect of Methanol Extract of *Basella Alba* Leaf on Fasting Blood Glucose Levels in Nicotine Treated and Control Wistar rats.

	FBG (mg/dl)			
	H-C	**N-C**	**LDN-Ba**	**HDN-Ba**
Baseline	56.63 ± 2.42	58.50 ± 2.43	51.75 ± 2.04	50.50 ± 2.36
Week 1	45.67 ± 1.45	66.88 ± 3.56[a]	58.40 ± 3.47[a]	64.25 ± 2.12[a]
Week 2	48.14 ± 3.62	66.20 ± 5.67[a]	69.17 ± 3.23[a]	72.25 ± 4.05[a]
Week 3	52.14 ± 3.26	55.50 ± 2.33	57.33 ± 3.28	57.00 ± 2.00
Week 4	54.33 ± 3.74	61.75 ± 2.87	59.00 ± 3.54	58.67 ± 3.38

- Values expressed as mean ± (SEM), n = 5
- 'a' signifies a significant difference when compared to H-C ($p < 0.05$)
- mg/dl = Milligram per deciliter

After the third and the fourth week of treatment, the differences observed in FBG levels of animals from groups N-C, LDN-Ba and HDN-Ba showed no statistical significance when compared to readings from H-C group (Table 1).

Effects of Treatments on Oral Glucose Tolerance

Before the commencement of treatment, oral glucose tolerance test curve appeared to follow normal trend in all four experimental groups (Figure 1a). There was no significant difference in the blood glucose levels recorded at 0, 30, 60, 90 and 120 minutes post glucose load in rats from N-C, LDN-Ba and HDN-Ba when compared to H-C group (Figure 1a).

After two weeks of exposure to the various experimental treatments in each group, OGTT curve was significantly deranged in N-C, LDN-Ba and HDN-Ba groups when compared to the healthy control (H-C) group's curve. Readings obtained after 30, 60, 90 and 120 minutes post glucose load were significantly higher ($p < 0.05$) in all three treatment groups when compared to H-C group's readings (Figure 1b).

At the end of four weeks of treatment with nicotine and methanol extract of *Basella alba*, blood glucose readings obtained after 30, 60, 90 and 120 minutes post glucose load were significantly higher ($p < 0.05$) in N-C and HDN-Ba groups when compared to H-C group. Additionally, blood glucose levels did not subside significantly in both groups after 120 minutes post oral glucose load. However, readings from LDN-Ba rats showed no significant difference when compared to those from H-C rats (Figure 1c), and OGTT curve followed a normal pattern.

Effects of Treatments on Body Weight, Pancreas Weight, and Relative Weight of Pancreas

There was no statistically significant difference in the body weights of the animals in all four experimental groups before the commencement of treatments. However, after four weeks of treatment, there was a significant decrease in the body weights of N-C, LDN-Ba and HDN-Ba groups when compared to H-C group ($p < 0.05$). However, there was no significant difference in the body weights of animals in the three nicotine groups (i.e. N-C, LDN-Ba and HDN-Ba groups). The final body weight was significantly increased when compared to the initial body weight for animals in H-C group but significantly decreased for animals in N-C, LDN-Ba and HDN-Ba groups ($p < 0.05$) as shown in figure 2.

There was a significant decrease in the weight of pancreas of animals in N-C, LDN-Ba, HDN-Ba groups when compared to H-C group ($p < 0.05$). However, pancreas weight was not significantly different when HDN-Ba and LDN-Ba groups were compared and when both groups were compared to N-C group (Figure 3a)

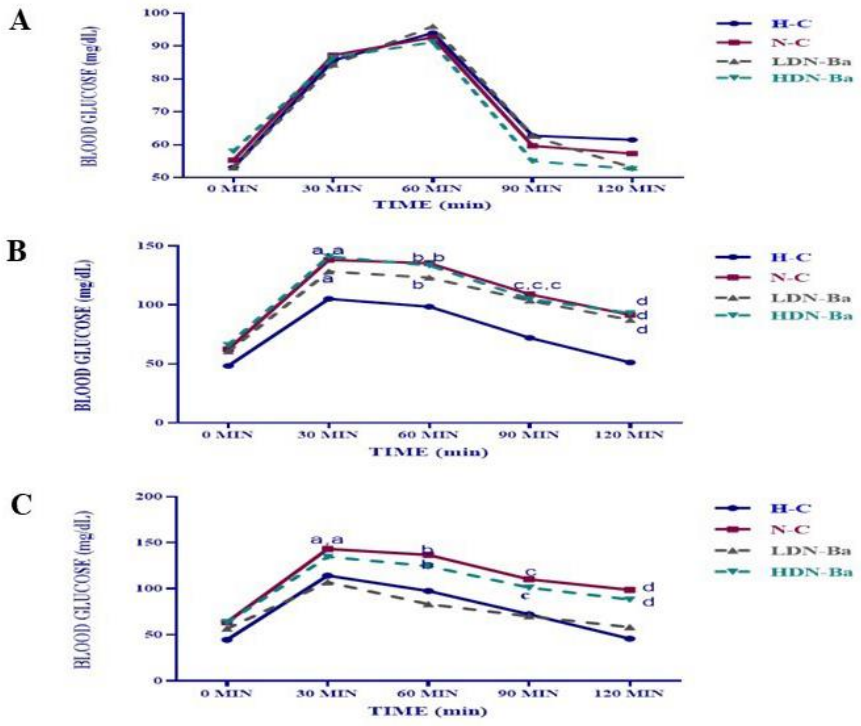

Figure 1. Oral glucose tolerance test curves of control and nicotine plus/minus Basea alba-treated rats before (A), during (B) and after (C) treatments

- 'a' = significant difference when compared with H-C reading at 30 win ($p < 0.05$)
- 'b' = significant difference when compared with H-C reading at 60 win ($p < 0.05$)
- 'c' = significant difference when compared with H-C reading at 90 win ($p < 0.05$)
- 'd' = significant difference when compared with H-C reading at 120 win ($p < 0.05$)
- H-C = Health control, N-C = Nicotine Control, LDN-Ba = Low Dose Nicotine + B. alba, EDN-Ba = High Dose Nicotine + B. alba

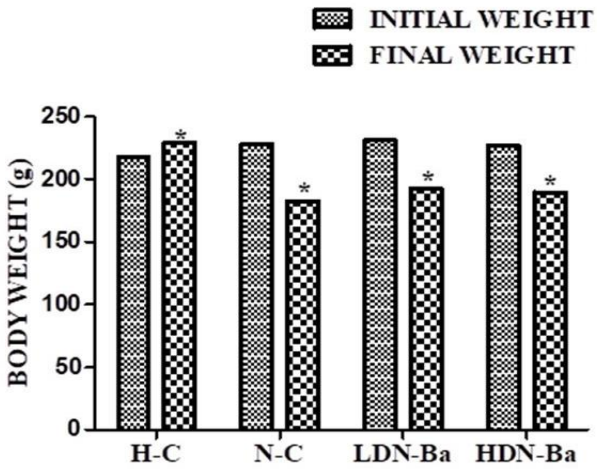

Figure 2. Effect of nicotine and methanol extract of Basella alba leaf on weight of Wistar rats after four weeks of treatment

- '*' = significant difference when compared to initial weight ($p < 0.05$)
- H-C = Health control, N-C = Nicotine Control, LDN-Ba = Low Dose Nicotine + B. alba, HDN-Ba = High Dose Nicotine + B. alba

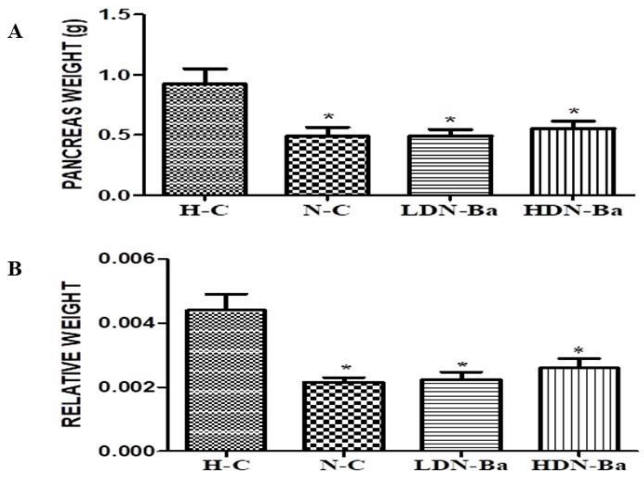

Figure 3. Effect of Methanol Extract of *Basella alba* Leaf on pancreas weight (A) and relative weight (B) in Nicotine Treated and Untreated Wistar rats.

- '*'= Significant difference when compared to H-C ($p < 0.05$)
- H-C = Health control, N-C = Nicotine Control, LDN-Ba = Low Dose Nicotine ± B. alba, HDN-Ba = High Dose Nicotine ± B. alba.

Likewise, relative weight of pancreas was significantly decreased in N-C, LDN-Ba, HDN-Ba groups when compared to H-C group ($p < 0.05$), but showed no significant difference when HDN-Ba and LDN-Ba groups were compared and when both groups were compared to N-C group (Figure3b)

Histopathology of the Pancreas

The effect of methanol extract of *Basella Alba* leaf on histological features of the pancreas of nicotine treated rats are shown in Figures 4 and 5. The histology slide from healthy control (H-C) group shows normal pancreatic structure with apparently intact islet of Langerhans and normal interlobular ducts when compared to slides from N-C, LDN-Ba and HDN-Ba groups (Figures 4 & 5). The slide from N-C group shows distortion in pancreatic histoarchitecture as characterized by necrotic islets of Langerhans (red arrow) and abnormally enlarged interlobular

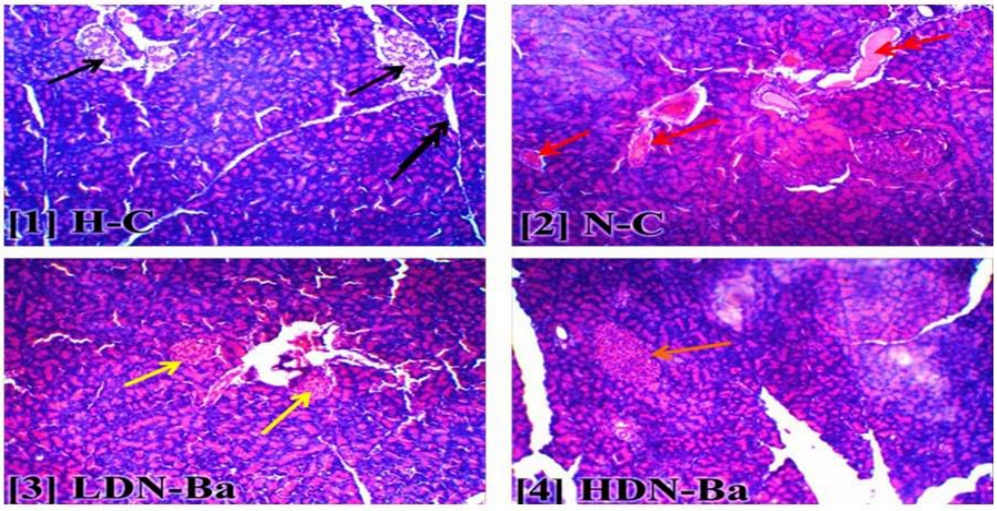

Figure 4. Photomicrograph of Pancreas Sections showing the effect of Methanol extract of *Basella alba* leaf on the Histopathology of the Pancreas of Nicotine treated male Wistar rats (H & E stain, X100 Mag.)

[1] Healthy control rat with apparently intact islet of Langerhans (black arrow) with normal interlobular duct (double black arrow head);
[2] Nicotine control rats with general distortion of pancreatic histoarchitecture characterized by evidence of necrotic islet of Langerhans (red arrow) with abnormally sized interlobular duct (double red arrow head);
[3] LDN-Ba rat showing evidence of shrunken islet of Langerhans (yellow arrow) with apparently intact interlobular ducts. There is evidence of improved pancreatic histoarchitecture when compared with nicotine control group;
[4] HDN-Ba rat showing improved pancreatic islet of Langerhans with normal-appearing size (orange arrow) when compared with the healthy control as well as the nicotine control groups.

- H-C = Health control, N-C = Nicotine Control, LDN-Ba = Low Dose Nicotine + B. alba, HDN-Ba = High Dose Nicotine + B. alba.

duct (double headed red arrow) (Figure 4). Slides from LDN-Ba and HDN-Ba groups show evidence of shrunken islet of Langerhans with apparently intact interlobular ducts and improved acinar arrangement, indicating an improved pancreatic histoarchitecture when compared to N-C (See arrows, Figures 4 and 5).

DISCUSSION

The findings reported in this study demonstrated the fact that nicotine has deleterious effects on glucose utilization of male Wistar rats and that these effects are dose dependent and ameliorated by treatment with methanol extract of *Basella alba*. The observed nicotine-induced dysfunctions with regard to glucose utilization is in absolute conformity with earlier reports by Benowitz in 2013 [24] that nicotine reduces sensitivity to insulin and may either aggravate or precipitate diabetes mellitus and contribute to endothelial dysfunction. This present study revealed a significant elevation of fasting blood glucose following acute exposure to nicotine, which appeared worse in the group of rats treated with high dose nicotine. This is a confirmation that the effect of nicotine on fasting blood glucose levels is dose dependent as reported by Willi *et al.*, 2007 [25] and that the initiation of diabetes mellitus or the worsening of existing cases may be largely dependent on the rate of cigarette consumption, rather than the mere act of cigarette smoking.

The derangement observed in oral glucose tolerance curve of rats after acute exposure to nicotine may be an indication of reduced insulin sensitivity. The blood glucose levels recorded in the high dose nicotine groups remained significantly high even after 120 minutes post glucose load with or without *Basella Alba* treatment, but returned back to normal fasting range in the low dose nicotine group after sufficient treatment with *Basella Alba* extract. This further confirms that the effects of nicotine on blood glucose levels is dose dependent [26] and response to interventions may be less positive with higher doses of nicotine. Alberto and coworkers in a bid to reach this conclusion, reported a diminished insulin sensitivity index (ISI) and hence tissue sensitivity to insulin that was more prominent in chronic smokers than in non-smokers who were only exposed to acute smoking. This offers a tenable explanation for the dose dependent derangement in OGTT curve observed in this present study since ISI has been used as a practical measure of insulin resistance and by implication, glucose utilization [27, 28].

Furthermore, nicotine is known to stimulate an increased energy expenditure in the body along with decreased energy generation from reduction in appetite [29, 30].The decrease in body weight, pancreas weight and relative pancreas weight observed with acute exposure to nicotine can be partly attributed to these as well as to the direct injurious impact of nicotine on the pancreatic tissue [31]. Nicotine can therefore be seen as being capable of inducing and/or speeding up catabolic processes in body tissues of users thereby resulting in massive loss in both organ weight and body weight.

The anti-hyperglycemic potentials of *Basella Alba* have been widely reported in previous studies. Bamidele *et al.*, 2010 [32] and Nirmala *et al.*, 2011 [12], reported that aqueous extract of *Basella Alba* leaves reduced blood glucose level in alloxan diabetic Wistar rats. These studies failed to demonstrate the mechanism(s) through which this effect is achieved and it was not clear whether or not the effect translates into an improvement in glucose utilization. The rich presence of antioxidant phytochemicals within the plant material have been stressed out in more recent studies as being responsible for this beneficial attribute of *Basella Alba* [33, 34]. The possibility of the various phytochemicals inherent in this plant scavenging and/or reducing the generation of reactive oxygen species (ROS) as already suggested [35, 32, 12], is further corroborated in the findings reported in this study, which indicate a generally improved health in nicotine treated rats after the administration of *Basella Alba* extracts. Nicotine causes multiple cellular injuries via numerous unexplained mechanisms, but surely involving increased generation of free radicals like superoxide anions and hydrogen peroxide by causing disruptions in mitochondrial respiration [36]. This is one possible explanation for the histopathological effects observed in the pancreas of nicotine treated rats in this study and the resultant rise in FBG and deranged OGTT. *Basella Alba* appears to induce a protective effect against these nicotine-induced injurious processes and even stimulate regeneration of damaged islet cells as similarly observed in the study by Arokoyo et al., 2018 [37], where the islet cell injury was streptozotocin induced. It may therefore suffice to infer that *Basella Alba* has both protective and regenerative effects on the islet cells irrespective of the primary source of assault. The anti-oxidant phytochemicals in the plant, apart from scavenging free radicals produced by oxidative damage, may also decrease blood glucose via suppression of peroxidation and apoptosis in beta islet cells by increasing glycogen deposit in liver and muscles through the activation of hepatic glucokinase, hexokinase and phosphofructokinase [38]. Quantitative evaluation of these enzymes will go a long way in confirming this suggestion and will be a key focus of future studies. Additionally, it may be important to highlight the fact that the anti-hyperglycemic effect of *Basella Alba* was rather insignificant in the first two weeks of treatment during this study and minimal even at the end of four weeks treatment. This is an indication that the mechanism(s) involved as already suggested require a longer duration of administration to be fully effective which will also be a major consideration in subsequent investigations.

The OGTT curve is a reliable indicator of how well the body tissues respond to post-prandial blood glucose. Glucose utilization in insulin-dependent tissues like skeletal muscles and fat cells, which are rich in insulin-responsive glucose transporters (GLUTs) is often mediated via a well-defined response to blood glucose and insulin peak after food ingestion [39, 40]. This study demonstrated a derangement in this response following weeks of nicotine administration which was worse with high dose nicotine and to an extend ameliorated by *Basella Alba*. It is possible, therefore, that *Basella Alba* either upregulates the expression of some GLUT receptors, improves their sensitivity to insulin, enhances insulin release from islet cells in response to rising blood glucose, or even a combination of all these effects. The

limited scope of this study is not sufficient to completely unravel this line of thinking, but it is however clear from the histological findings that islet cells appear to be improved both quantitatively and qualitatively with the administration of *Basella Alba,* which suggests an enhanced insulin production and release.

CONCLUSION

In conclusion, this study revealed that exposure to nicotine causes dysfunction in glucose utilization and induces a pro-diabetes state, which is dependent on the dose of nicotine administered. However, the administration of methanol extract of *Basella Alba* leaf ameliorates the effects of nicotine toxicity on glucose metabolism to a greater extent in low dose nicotine as against high dose. The protective effect of *Basella Alba* on nicotine toxicity with regards to glucose utilization is hereby demonstrated and this is largely due to its therapeutic effects on damaged pancreatic islet of Langerhans, which is both functional and morphological.

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