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Evaluation of antihyperglycemic activity of Buni (*Antidesma bunius* L. spreng) fruit in two groups of Streptozotocin-Induced Diabetic Wistar Rats

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Abstract

This study investigated the antihyperglycemic potential of Buni (Antidesma bunius L.spreng) fruit extract in two groups of streptozotocin (STZ)-induced diabetic Wistar rats. Male rats (250-300 grams, 6-10 weeks old) were injected with STZ (35 mg/kgBW or 45 mg/kgBW) to induce diabetes, followed by treatment with Buni fruit extract at doses of 100 mg/kgBW or 300 mg/kgBW for six weeks. Fasting blood glucose levels were monitored throughout the study. Results show that buni fruit extract at 100 mg/kgBW significantly reduced fasting blood glucose levels in the STZ-45 mg/kgBW group compared to the untreated diabetic control group ($p<0.05$). However, the 300 mg/kgBW dose did not exhibit a statistically significant effect in either STZ-induced group ($p>0.05$). Buni fruit extract demonstrates dose-dependent antihyperglycemic activity in STZ-induced diabetic Wistar rats. The 100 mg/kgBW dose effectively lowered fasting blood glucose levels, suggesting the potential for Buni fruit as a natural therapeutic option for managing diabetes.

Keywords: Buni fruit, Antidesma bunius L., Fasting blood sugar, STZ

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1. Introduction

In 2045, the International Diabetes Federation (IDF) predicts that there will be 693 million individuals globally suffering from diabetes, and in the twenty-first century, this is a top health concern [1].

For the management of DM, the American Diabetes Association (ADA) suggests medical nutrition therapy (MNT) and physical activity [2]. Micronutrients are crucial for controlling macronutrients including proteins, lipids, and carbs. Micronutrients and other bioactive substances can function on their own or in concert with other substances. Polyphenols, which have an impact on carbohydrate metabolism, are one of them. The most prevalent antioxidants in the average person's diet are polyphenols [3]–[5].

The Buni fruit (Antidesma bunius) is one of the fruits that is rich in polyphenols [6]. This fruit contains three different types of flavonoids, which are compounds found in plants that act as protection against pathogens or climatic change [7], [8]. Buni fruit (A. bunius (L.)Spreng) contains flavonoids with the percentage of n-hexane extractconcentration by 10.72%, the ethyl acetate extract of 7.9% and the ethanolextract of 3.56% counted towards or as rutin [9].

It is a challenge to clarify how different polyphenol metabolic structures that have a hypoglycemic effect relate to one another, therefore this is the context in which researchers will examine whether delivering Buni fruit extract affects fasting blood sugar levels. This study investigated the antihyperglycemic potential of Buni (Antidesma bunius L.spreng) fruit extract in two groups of streptozotocin (STZ)-induced diabetic Wistar rats.

2. Materials and methods

In this interventional/quasi-experimental investigation, Buni fruit extract was the therapy, and a pre-post interventional study design with a control group was used. Male Wistar rats (Rattus norvegicus L.), weighing 250–300 grams and aged 6–10 weeks, served as the study's subjects. then put in a room with air conditioning (AC) that has a 12-hour light-dark cycle and a temperature of 25–20^0 C. The meal fed to experimental animals contains 80% crude protein and they have full access to water.

Forty experimental animals have been used in this study, and they were split into two treatment groups. Streptozotocin (STZ) was administered to the first group at a dose of 35 mg/kg body weight, and to the second group at a dose of 45 mg/kg body weight. Streptozotocin (STZ) was administered intraperitoneally to rats in the hyperglycemia group using 0.5 cc of B-Braun disposable syringe, starting at dose 35 and 45 mg/kg body weight, to achieve the desired hyperglycemia with a GDS range of > 200 mg/dl.

The experimental animals received 2% sucrose for 48 hours after the injection to help with the hypoglycemic phase. Experimental mice classified as diabetic had fasting blood glucose levels (GDP) 126 mg/dL. The Ethics Committee gave their approval to the experimental protocol.

Extraction of the buni fruit, accomplished by the subsequent steps: Fresh Buni fruit, which have been taken from the stalks, washed, drained, and packaged in plastic bags weighing 100 grams each with the packaging date on them, are dark red and purple in color. After being packaged, buni fruit is chilled at -20^0 C until extraction is needed. Furthermore, 1000 grams of frozen buni fruit were immediately extracted with 70% ethanol in a glass container covered in aluminum foil to keep out light (pH 4.9) and acidified with 0.01% citric acid. The goal of this additives is to keep the anthocyanin content of the buni fruit stable. Since organic acids are easily removed during the solvent evaporation process, citric acid was chosen as an acidifier.

The extraction process was conducted for 6 hours at 260°C. The dregs were then extracted three more times after the extract had been filtered. A thick extract is created when the extraction liquid is fan-evaporated, and it is subsequently dried using the freeze-drying method [10].

Each animal model received a sonde injection of buni fruit extract at a dosage of 100 mg or 300 mg. The entire course of treatment lasted for six weeks. The experimental animals were fasted for the entire night in order to produce Fasting Blood Glucose, which was then quantified using a glucometer (*Accu Chek Instant*) after blood was drawn from a vein in the tail. Following the administration of buni fruit extract for six weeks, this fasting blood sugar check is performed every week.

3. Results and Discussions

Table 1 show that Buni fruit extract administered to the STZ-induced group dose 35 mg/kgBW comes out to have a p value > 0.05, indicating that the outcome was not statistically significant.

Table 2 shows the p-value for each group in this table of fasting blood glucose. Group 3 has a p-value <0.05 (p-value = 0,026), indicating significant changes in fasting blood sugar. The group of wistar rats that received a dose of STZ of 45 mg/kg body weight and a dose of Buni fruit extract of 100 mg/kg BW showed significant outcomes when the two groups of data are compared.

The purpose of this study was to support the wide availability of Antidesma bunius (L.) spreng. fruit in traditional medicine and as food. The pharmacological effects of this herb in an animal model of diabetes have not been well studied. Therefore, in order to support their traditional use for treating diabetes, fruit extract from Antidesma bunius was investigated for its antidiabetic properties in the current study. The fruit extract displayed an antihyperglycemic effect in the present investigation by dramatically lowering blood glucose levels when it was repeatedly administered to rats at a dose of 100 mg/kg orally, once daily, for six weeks. The others results of the identification of secondary metabolites using TLC showed that green and red buni fruit extract contains flavonoid, phenolic and alkaloid compounds. The results of the α-glucosidase enzyme inhibition test showed that the red buni fruit extract had the highest activity compared to green buni fruit extract with an IC_{50} value of 85.27 ppm [11].

This is consistent with the study by P. Chowtivannakul (2015), however slightly different at a dose of 250 mg/kg body weight that has been found to lower fasting blood glucose. It has been documented that *A. bunius* has anti-diabetic properties. When compared to the positive control (given Metformin), its fruit ethanolic extract (500 mg extract/kg body weight) was found to be beneficial at reducing the FBG levels in alloxanized ICR mice. [12], [13].

Table 1: Fasting Blood Sugar of STZ-induced Wistar Rats dose 35 mg/kgBW

Group	Fasting Blood Glucose		
	Pre-Intervention	Post-Intervention	p* value
Normal Control	97.667 ± 11.039	102 ± 8.72	0.387
Sick Control	281.20 ± 53.49	320.60 ± 100.32	0.467
DM + Extracts 100 mg/kgBW	347.33 ± 32.08	355.67 ± 128.34	0.904
DM + Extracts 300 mg/kgBW	306.20 ± 75.08	321.80 ± 106.99	0.740

Table 2: Fasting Blood Sugar of STZ-induced Wistar Rats dose 45 mg/kgBW

Group	Fasting Blood Glucose		
	Pre-Intervention	Post-Intervention	p* value
Normal Control	98.86 ± 5.98	103.14 ± 8.67	0.044
Sick Control	385.33 ± 80.87	600 ± 0.00	0.001
DM + Extracts 100 mg/kgBW	425.00 ± 51.11	230.83 ± 117.79	0.026
DM + Extracts 300 mg/kgBW	419.00± 68.46	358.71 ± 268.91	0,372

This finding is supported by additional study, particularly that of El-Tantawy et al. (2015) who examined the hypoglycaemic effects of methanolic extract of A. bunius in rats with alloxan-induced diabetes. After 28 days of treatment with the methanolic extract of A. bunius, the fasting blood glucose level was significantly reduced in comparison to the diabetic rat, but there was no significant change in the fasting blood glucose level in the control group, further supporting the extract's anti-diabetogenic effects. [14]. *Antidesma bunius* fruit extract (ABE) exhibits antioxidant activity and inhibits carbohydrate digestive enzymes, including intestinal maltase and sucrase. ABE may be a promising ingredient that helps suppress carbohydrate digestion and prevent monosaccharide-mediated protein glycation, oxidation, and aggregation [15].

Another finding from this study is the use of STZ as a medication to cause hyperglycemia in lab animals. When applying STZ as a model to generate experimental diabetic rats, the findings by Qinna and Badwan (2015) highlight the significance of choosing appropriate and consistent basal glucose levels. Since STZ has been shown to cause several forms of diabetes mellitus in animals, it is strongly advised that experimental methods evaluating diabetic medication include a specified glucose level. Because STZ has the potential to change the normal glucose homeostasis, caution must be used while investigating the effects of different antidiabetic drugs on STZ diabetic animals.[16]

Between before and after STZ induction, the two treatment groups with various STZ dosages demonstrated a very significant increase in fasting blood sugar. Goyal et al. (2016) examined into variations in the outcomes of STZ induction in several research employing STZ as an animal model for diabetes [17]. A high-fiber diet with a dose of STZ of 35 mg/kg body weight were used in Srinivasan's (2005) study, which revealed a stable hyperglycemia status [18]. This supports the previous study's findings that the increase in fasting blood glucose was not significantly greater at a dose of 35 mg/kg BW of STZ compared to a dose of 45 mg/kg body weight [19].

4. Conclusions

Administration of buni fruit extract can lower Wistar rats' fasting blood glucose levels after STZ 45 mg/kg body weight induction

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