

# Hypoglycaemic and coronary risk index lowering effects of *Bauhinia thoningii* in alloxan induced diabetic rats

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## Abstract

**Background:** Disease, one of humanity's greatest adversaries, has in recent times showed an intimidating increase in numerical and pathological strength. This stretched the available medications to the limit thereby necessitating the need for the discovery of new and alternative medications to combat the menace of disease. Diabetic mellitus is one disease condition for which ideal synthetic drugs are yet to be discovered. To this end, pharmaceuticals are looking in the direction of medicinal plants.

**Objective:** This work aimed at screening *Bauhinia thoningii* (leaves) for its hypoglycaemic effect. The effect of the extract on lipid profile as a Coronary Risk Index (CRI) was also evaluated.

**Methods:** Aqueous crude extract of the plant was administered orally to alloxan induced diabetic rats and fasting blood glucose monitored over a period of 7 days. Blood samples collected from the rats were assayed for full lipid profile and the CRI calculated.

**Results:** *Bauhinia thoningii* caused 81.37% reduction in blood glucose of the experimental animals over a period of 7 days from an initial 365 mg/dl to 68 mg/dl. The plant extract was also observed to have the capacity to ameliorate diabetic complications like cardiovascular disorders. The extract reduced the Low Density lipoprotein (LDL) and reduced the CRI.

**Conclusions:** Results from this study confirmed the hypoglycaemic efficacy of the extract and ability to ameliorate coronary diabetic complications. Further study is required to purify the plant extract to identify the fraction(s) that are responsible for the hypoglycaemic effects observed. This will also help to isolate the active components and elucidate the likely mechanism of action of the plant extract.

**Key words:** *Bauhinia thoningii*, diabetes, coronary risk index

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## Introduction

Disease has been one of humanity's greatest enemies. As human populations witness an upsurge so does the magnitude of prevailing global ailments. One of such diseases, Diabetes Mellitus (DM) has plagued mankind with a global epidemiology 171 million people in 2000 and a projected figure of 342 million by the year 2030.<sup>1</sup> It is characterised by hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism.<sup>2</sup> There are two principal types of diabetes. Type 1 or insulin dependent diabetes which is due to a deficiency of insulin caused

by autoimmune destruction of pancreatic beta cells. Type 2 or non-insulin dependent diabetes mellitus is due to reduced secretion of insulin or to peripheral resistance to the action of insulin. Obesity is one of the factors associated with insulin resistance. Diabetics are prone to complications such as hyperglycaemia hyperosmolar state, diabetic ketoacidosis, oxidative stress resulting from elevated glucose concentration<sup>3</sup>, microvascular (retinopathy, albuminuria, and neuropathy) and impaired immune response (making diabetics prone to respiratory infections). These no doubt rank the condition as one of the worst metabolic diseases. Before the advent of insulin therapy, starvation diets and traditional plant treatments were the cornerstone of antidiabetic therapies.<sup>4</sup> The search for drugs in combating this 'wasting disease' yielded some dividend over the years. Of note are drugs like insulin and oral hypoglycaemics (sulfonylureas, biguanides, thiazolidinediones). Insulin administration is required in Type 1 DM. Type 2 diabetics often

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require administration of oral hypoglycaemic drugs or insulin.

However, modern pharmaceuticals cannot effectively treat this condition and or the accompanying complications. For instance neither insulin injections nor oral hypoglycaemic agents reinstate a normal pattern of glycaemic control, whether used alone or in combination, and whether administered as a standard or intensive regimen.<sup>5</sup> Also some drugs have unwanted side effects. Hypoglycaemia, or abnormally low blood glucose, is an acute complication of several diabetes treatments. It is rare otherwise, either in diabetic or non-diabetic patients. Furthermore, low income earners of the developing nations where the prevalence has been predicted to be more and who are unable to access formal health systems due to financial or logistic reasons, are especially dependent on herbal medicine.

It is against this background that the pharmaceutical industry is re-discovering a rich resource of nature's plant wealth which has been waiting to be exploited.<sup>6</sup>

With this tremendous increase in the global use of medicinal plants for the treatment of this condition, several concerns regarding the efficacy and safety of the herbal medicines have also been raised.<sup>7</sup> Hence it has become necessary to standardize the efficacy and safety measures so as to ensure supply of medicinal plant materials with good quality. Since the aim of treatment is to achieve the best possible control of blood glucose concentration and prevent or minimize complications, this study sought to evaluate the hypoglycaemic effect of extract of *Bauhinia thonningii* alloxan induced diabetic rats. The plant is a pan-African tall shrub with twisted stem, reaching 6 m in height, very branched; sometimes bears off-shoots. The folklore medicinal uses of the leaves include antipyretic, expectorant, anthelmintic, antidiarrhoea and antimalaria.<sup>8</sup>

## Methods

### Animals

Adult healthy Wistar albino rats weighing 100-250g of both sexes were used for this study. They were kept under standard conditions in the animal house of the Faculty of Veterinary Medicine, University of Ibadan, Nigeria. The animals were acclimatized for 14 days before the beginning of each experiment. They were fed normal rat chow (Guinea Feed, Nigeria) and potable water throughout the experiment, unless when otherwise stated. Animals

were handled according to the recommendations of the Institution's Ethics committee.

### Plant collection and preparation

Fresh *Bauhinia thonningii* leaves were collected from the Department of Wild life and Fisheries, University of Ibadan, Nigeria. The confirmatory identification of the plant was done at Forestry Research Institute of Nigeria (Voucher number FHI 108866). The leaves were rinsed with potable water and 10% crude aqueous extract of the fresh plant prepared by milling 10g of the fresh plant material with the aid of an electrical grinder. As prescribed for use locally, the milled plant material was extracted with 100ml of distilled water (for crude aqueous extract) at room temperature. This was then filtered using a Buckner funnel and Whatman's No. 1 filter paper. It was the filtrate that was administered to the animals in the course of this study fresh for a maximum of two days after which fresh extract was prepared

### Induction of experimental diabetes

Experimental diabetes was induced in rats by intraperitoneal injection of 5% alloxan monohydrate (5g/100ml normal saline) at a dose of 120mg/kg.<sup>9</sup> 72 hours after administration, animals having blood glucose level of 200mg/dl and above were considered diabetic. The rats so induced were divided into three groups of 5 animals per group. Group I (control) received distilled water throughout the experimental period of 7 days. Animals in group 2 were administered 500mg/kg of the plant extract. Group 3, which is the positive control group, received 10mg/kg of glibenclamide as a reference drug. Oral administration to the animals was done once every 24 hours. Another set of 5 rats (Non diabetic group) were not induced for diabetes and served as baseline for comparison of parameters. This group received distilled water throughout the period of the experiment. The animals were fasted overnight for 12 hours. Between 7.00- 9.00 hours the fasting blood glucose of all the animals was measured using electronic glucometer (ACUU) check Advantage, Roche diagnostic GmbH<sup>10</sup>, from the tail snips of the rats. The first fasting glucose level from the rats was considered as the baseline (Day 0). On the last day of the experiment (Day 7) blood was obtained from the experimental animals from the retro orbital plexus using plain capillary tubes into plain bottles. The plain bottles were placed in a slanting position

to obtain serum for serum for analysis of full lipid profile.

### Determination of lipid profile

Full lipid profile was determined by colorimetric method.<sup>11,12</sup> Coronary Risk Index (CRI) was calculated by dividing the Total Cholesterol (TC) by High density lipoprotein (HDL).<sup>13,14</sup>

### Statistical analysis

Data obtained were expressed as mean  $\pm$  standard error of mean. Significant difference was set at  $P < 0.05$  using the student's t-test (SPSS computer software, version 10.0).

### Results

Table 1 shows the fasting blood glucose of Non diabetic, diabetic, diabetic treated with oral hypoglycaemic (reference) and diabetic administered aqueous extracts rats. Day 0 was the start of the experiment. The oral hypoglycaemic agent and

extracts were administered for the first time after the baseline blood glucose concentration was measured.

The non diabetic rats showed normal blood glucose between 78.60 – 79.60 mg/dl throughout the period of the experiment.

The diabetic untreated rats showed fluctuating blood glucose concentration which was high throughout the period of the experiment.

The group of rats administered oral hypoglycaemic agent-glibenclamide (positive control group) shows a steady reduction in the blood glucose from the first day after administration to the 7<sup>th</sup> day. From a high glucose concentration depicting diabetes (316.33) to 95.33. The percentage difference between the 1<sup>st</sup> day of administration to the 7<sup>th</sup> day was 69.87%.

*Bauhinia thonningii* caused a steady decrease in the blood glucose concentration from 365.00 (day 0) to 68.00 (day 7) amounting to 81.37% difference.

**Table 1: Effect of 500mg/kg aqueous crude extract of *Bauhinia thonningii* (leaves) on fasting blood glucose concentration in alloxan-induced diabetic rats**

Treatment	Glucose(mg/dl) Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7 %*
Non Diabetic	81.00 $\pm$ 3.00	79.60 $\pm$ 40.00	77.50 $\pm$ 3.60	78.80 $\pm$ 4.20	77.70 $\pm$ 3.90	77.40 $\pm$ 3.70	78.60 $\pm$ 4.10	79.20 $\pm$ 4.00 2.22%
Diabetic control	548.33 $\pm$ 57.5	474.33 $\pm$ 22.3	417.33 $\pm$ 19.7	503.33 $\pm$ 46.6	508.00 $\pm$ 27.2	461.00 $\pm$ 57.6	499.00 $\pm$ 27.3	500.67 $\pm$ 19.0 8.69%
Positive control	316.33 $\pm$ 79.9	242.00 $\pm$ 100.9	244.67 $\pm$ 96.2	137.00 $\pm$ 36.5	97.33 $\pm$ 14.2	92.00 $\pm$ 11.0	96.33 $\pm$ 4.1	95.33 $\pm$ 4.6 <sup>o</sup> 69.87%
<i>Bauhinia thonningii</i>	365.00 $\pm$ 3.4	194.00 $\pm$ 15.5	157.33 $\pm$ 0.8 <sup>2</sup>	153.00 $\pm$ 1.7	146.00 $\pm$ 3.4	135.00 $\pm$ 2.8	125.00 $\pm$ 2.8	68.00 $\pm$ 2.8 <sup>o</sup> 81.37%

<sup>o</sup>Superscripted items indicate statistically significant ( $P < 0.05$ ) difference exist between mean value of rats in the group on Day 0 and Day 7

\*% Difference between Day 0 & Day 7

Table 2 shows the lipid profile and CRI (Coronary Risk Index) of Diabetic Untreated (DC), Positive control (PC) (administered oral hypoglycaemic agent) and Diabetic administered extract rats.

A statistically significant decrease in TC, TG (Triglyceride), LDL (Low density lipoprotein), LDL/HDL and CRI, compared with the DC was also observed.

**Table 2: Effect of 500mg/kg aqueous crude extract of *Bauhinia thonin* (leaves) on lipid profile alloxan-induced diabetic of rats**

Treatment	Total Cholesterol (TC)mg/dl	Triglyceride (TG)mg/dl	High density lipoprotein (HDL)(mg/dl)	Low density lipoprotein (LDL)(mg/dl)	LDL/HDL	Coronary risk index (CRI) TC/HDL
Non diabetic	84.60±0.56	69.20±4.50	30.00±0.00	16.00±0.50	0.53±0.00	2.82±0.13
Diabetic control	95.67±2.85	166.00±54.37	26.67±3.33	43.33±7.69 <sup>2</sup>	1.62±0.17 <sup>2</sup>	3.69±0.41
Positive control	73.33±1.76 <sup>1</sup>	64.33±1.20 <sup>1</sup>	27.33±4.06	17.67±5.61 <sup>1</sup>	0.41±0.26 <sup>1</sup>	2.80±0.38
<i>Bauhinia thonin</i>	67.33±3.76 <sup>1</sup>	59.33±7.22 <sup>1</sup>	31.00±0.58	25.00±1.73 <sup>1</sup>	0.81±0.04 <sup>1</sup>	2.17±0.08 <sup>1</sup>

Superscripted items indicate statistically significant (P<0.05) exist between mean value of rats and: <sup>1</sup>-diabetic control and <sup>2</sup>-positive control.

## Discussion

Results obtained from the alloxan – induced diabetic rats (Table 1) showed that in the diabetic untreated group, the blood glucose concentration remained very high confirming the total destruction of beta cells and non stimulation of insulin secretion.

Results of glibenclamide treated diabetic rats indicated a gradual and progressive decline over the period of the experiment. A significant decrease in blood glucose concentration was noticed by day 7 (Table 1), a percentage reduction of 69.8. This indicates stimulation of insulin release from the pancreas.

Diabetic conditions can be classified into two groups: Insulin –dependent diabetes mellitus (IDDM) which results from degeneration of the pancreatic beta cells, and which requires treatment with insulin, and non – insulin dependent diabetic mellitus (NIDDM) which can be treated with oral hypoglycaemic agents. Alloxan monohydrate has been shown to destroy the beta cells thus inducing type 1 or IDDM.<sup>15,16</sup> The increase in blood glucose concentration was proposed by Bansal *et al*<sup>17</sup> to be due to the toxic effect of alloxan on the beta cells of the pancreas. The report further stated that alloxan and the product of its reduction, dialuric acid, establishes a redox cycle with the formation of superoxide radicals. These radicals undergo dismutation to hydrogen peroxide and the action of the reactive oxygen species with a simultaneously massive increase in cytosolic calcium concentration causes rapid destruction of the beta cells. This destruction results in the inability of the pancreas to synthesize and secrete adequate amount of insulin necessary for the metabolism of carbohydrate.

Usually treatment of type 1 diabetic mellitus may involve insulin and / or oral hypoglycaemic agents such as Sulphonylureas (glibenclamide) and Biguanides (metformin). Sulphonylureas act in three

ways: by stimulating the release of insulin from the pancreas (the main action), weakly inhibiting the process of gluconeogenesis (forming glucose from amino acids and fatty acids) in the liver and increasing the number of insulin receptors on target cells.

It was observed that *Bauhinia thonin* caused a steady decline in the blood glucose over the same time lapse. The overall reduction amounted to 81.37%. The pattern of hypoglycaemic effect looked similar to that of glibenclamide and can be postulated to act by the same mechanism. Studies by Aderibigbe *et al*.<sup>18</sup> and; Emudianughe and Aderibigbe<sup>19</sup> on some other plants have shown similar effect. It was postulated that apart from having inhibitory effect on glucose absorption, it is probable that other mechanisms such as direct stimulation of glycolysis in peripheral tissues, reduced hepatic gluconeogenesis and reduction of plasma glucagon levels may be in operation.

The biochemistry of the movement of lipids is in the blood stream and the factors that increase lipid deposition in arteries is extremely complex. As far as cholesterol is concerned, the two lipoproteins most concerned with its transport are the high density lipoproteins (HDL) and the low density lipoproteins (LDL). LDL transports cholesterol to the cells where it is deposited even though it may not be required and is therefore associated with atherosclerosis. HDL, on the other hand, transports cholesterol to the liver where it can be removed from the body. A ratio of HDL to LDL indicates this condition.<sup>20</sup> Normally, it is found that high cholesterol levels are associated with high LDL levels, but having a high HDL may compensate for this.

Khan showed a strong relationship between high level of total cholesterol concentration in the blood and cardiovascular diseases. Furthermore diabetics have an increased risk of coronary disease.

In this study, the plant extracts caused a significant reduction in the ratio of HDL to LDL compared with the diabetic rats. This points to the ability of this extract to reduce atherosclerosis, a complication of diabetes.

## Conclusion

Diabetes mellitus is a syndrome or a group of disease leading to prolonged hyperglycaemic state and other grievous physiological complications with multifocal root cause.

Results from this study have confirmed the hypoglycaemic efficacy of extract of *Bauhinia thoninjjii*. The plant extract was also observed to have the capacity to ameliorate diabetic complications like cardiovascular disorders.

Purification and fractionation of the crude extracts will help to further know the active fractions with a view to postulating the likely mechanism of action of the plant extract.

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