



Antihyperglycemic and Anti-hyperlipidemic Effect of Herbamed, A Herbal Formulation in Alloxan-Induced Diabetic Rats



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Abstract

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and its occurrence is increasing fast in most of the countries. Herbal medicine derived from plant extracts have been utilized increasingly for the treatment of various disorders like diabetes mellitus. The present study was designed to evaluate the anti diabetic activity of 'Herbamed', a herbal formulation composed of *Vernonia amygdalina*, *Ocimum gratissimum*, *Zingiber officinale* and *Allium sativum* in alloxan-induced diabetic rats model. Alloxan (150mg/kg) was used to induce diabetes in rats and the blood glucose levels were estimated by using glucometer. The herbal formulation known as 'Herbamed' was administered to diabetic rats for 7 days at 0.5 and 1.0mL (250mg/kg rat). The herbal formulation produced a significant reduction ($P<0.05$) of blood glucose levels in diabetic rats at both doses tested. It also showed a beneficial effect on the lipid profile and liver function test in alloxan induced diabetic rats. These results showed that 'Herbamed' exhibits antihyperglycemic and antihyperlipidemic activities in diabetic rats.

Keywords: Diabetes mellitus; Herbal medicine; Antihyperglycemic; Alloxan; Antihyperlipidemic

Introduction

Diabetes mellitus (DM) is the most common degenerative disease and has been shown to affects about 10% of the world population [1]. DM is a metabolic disorder characterized by hyperglycaemia, abnormal lipid and protein metabolism along with specific long-term complications affecting the brain, liver, retina and kidney [2]. Hyperglycaemia has been implicated in the development and progression of the complications of diabetes mellitus. The pathogenesis of DM is managed by insulin and oral administration of anti-diabetic drugs such as metformin, acarbose, sulfonylureas and biguanides. Unfortunately, all these drugs have a number of side effects and some of the oral synthetic hypoglycaemic agents have been successful in controlling long-term microvascular and macrovascular complications. Hence, recent research focuses on medicinal plants with little/or no side effects.

For some decades now, diabetics have been treated with medicinal plants based on traditional medicine information. Several plant species have been discovered to possess hypoglycemic effects [3-5]. Despite the presence of anti-diabetic medicines in the market,

the search for more effective and safer hypoglycemic agents has continued to be an important area of research. Many traditional plant drugs and herbal formulation are frequently considered to be less toxic and freer from side effects than synthetic one. Based on the WHO 1980 recommendations, hypoglycaemic agents of plant origin used in traditional medicine are important. In the traditional system of Indian medicine, plant formulation and combined extracts of plants are used as drug of choice rather than individual. Various herbal formulations such as diamed are well known for their anti-diabetic effects [6,7].

'Herbamed' is a polyherbal drug composed of four medicinal plants (Table 1). There is no report available in the literature for the anti-diabetic effect of 'herbamed' in alloxan-induced diabetic rats. The present investigation was undertaken to study the antihyperglycemic effect of 'herbamed', a herbal formulation, on changes in blood glucose, plasma lipid profile and hepatic function test in alloxan-induced diabetic rats. The effects produced by this formulation on different parameters were compared with metformin, an anti-diabetic drug.

Table 1: 'Herbamed' composition and parts used

S/N	Botanical Name	Common Name	Family	Part Used
1	<i>Vernonia amygdalina</i>	Bitter leaf	Asteraceae	Leaves
2	<i>Ocimum gratissimum</i>	Clove basil	Lamiaceae	Leaves
3	<i>Zingiber officinale</i>	Ginger	Zingiberaceae	Rhizome
4	<i>Allium sativum</i>	Garlic	Amaryllidaceae	Root

Materials and Methods

Drugs and chemicals

Drugs and chemicals used such as Alloxan, metformin, Tris-HCl buffer and sodium chloride were obtained from Sigma-Aldrich (St. Louis, MO, USA). Except stated otherwise, all other chemicals and reagents were of analytical grades and the water was glass distilled. Kits used for this experiment were purchased from RANDOX Laboratories Ltd., Crumlin, County Antrim, UK). Alloxan was dissolved in saline solution for intraperitoneal administration and metformin was dissolved in distilled water for oral administration.

Plant samples

Vernonia amygdalina, *Ocimum gratissimum*, *Zingiber officinale* and *Allium sativum* were collected freshly from Afe Babalola University (ABUAD) farms, Ado-Ekiti, Nigeria. Voucher specimens were deposited at the herbarium of the Botany Department, Ekiti State University, Ekiti State, Nigeria.

'Herbamed' preparation

'Herbamed' was prepared on the basis of an ayurvedic anti-diabetic formulation proposed by Pandey et al. [8]. One hundred grams (100g) of *Vernonia amygdalina* and *Ocimum gratissimum* as well as ten grams (10g) of *Zingiber officinale* and *Allium sativum* were blended in 20mL of distilled water and filtrate was collected by the method of continuous cold extraction.

Experimental animals

Male albino Wistar rats (180-250g) bred in the Central Animal House, College of Medicine, Afe Babalola University, were used. The animals were fed on a standard pellet diet (ABUAD Farms, Nigeria) and water was freely available.

Experimental induction of diabetes

The rats were injected intraperitoneally with alloxan

monohydrate dissolved in sterile normal saline at a dose of 150mg/kg. After three days, the rats which had developed moderate diabetes and hyperglycaemia with a blood glucose range ≥ 250 mg/dL, were used for the experiment. Blood was collected from the eyes (venous pool).

Experimental design

In this experiment a total of 30 rats (24 diabetic surviving rats, 6 normal rats) were used. Diabetes was induced in rats before the start of the experiment. The rats were divided into five groups (n=6) after the induction of diabetes. Group 1 was the normal untreated rats. Group 2 was the diabetic untreated rats. Group 3 was the diabetic rats given 'Herbamed' (0.5mL (0.25g)kg⁻¹) in aqueous solution daily using an intragastric tube for 7 days. Group 4 was the diabetic rats given 'Herbamed' (1.0mL (0.25g)kg⁻¹) in aqueous solution daily using an intragastric tube for 7 days. Group 5 was the diabetic rats given metformin (500mg/kg) in aqueous solution daily using an intragastric tube for 7 days. After the end of the experiment, the rats were killed by decapitation. Blood was collected in an anti-coagulant tube containing EDTA and the serum obtained was used for the estimation of some biochemical parameters.

Biochemical assays

For the determination of biochemical assays, the serum obtained was used for the determination of lipid profile (Total cholesterol, LDL-C and Triglycerides) using commercial available kits from RANDOX Laboratories Ltd., Crumlin, County Antrim, UK.

Statistical analysis

All data were expressed as mean \pm standard error of mean (S.E.M.). The statistical analysis used was one-way ANOVA, followed by the post hoc Tukey's test, p<0.05 was considered to represent a significant difference in both analyses used.

Results

Effect of 'herbamed' on blood glucose level in alloxan-induced diabetic rats

Table 2: Change in blood glucose level.

Experimental Groups	Initial Glucose Level (mg/dl)	Final Glucose Level (mg/dl)	Decrease in Glucose Level (%)
Group 1	111.2 \pm 1.6	106.7 \pm 6.7	3.03 \pm 0.02
Group 2	347.3 \pm 14.3	400.1 \pm 12.0	-15.3 \pm 2.1
Group 3	281.0 \pm 8.1	256.3 \pm 6.3	8.78 \pm 1.4
Group 4	309.1 \pm 9.9	189.7 \pm 8.7	38.6 \pm 4.1
Group 5	310.5 \pm 10.5	217.7 \pm 11.7	29.9 \pm 3.4

Values represent mean \pm SEM (n=6).

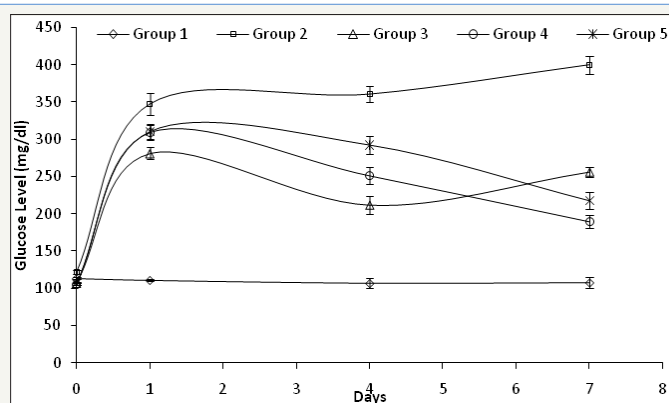
Key:

Group 1-control

Group 2-diabetic untreated rats.

Group 3-diabetic rats given Herbamed (0.5mL (0.25g)kg⁻¹)Group 4-diabetic rats given Herbamed (1.0mL (0.25g)kg⁻¹)

Group 5-diabetic rats given metformin (500mg/kg)

**Figures 1:** Effect of herbamed on blood glucose level in alloxan-induced diabetic rats**Key:**

Group 1-control

Group 2-diabetic untreated rats.

Group 3-diabetic rats given Herbamed (0.5mL(0.25g)kg⁻¹)Group 4-diabetic rats given Herbamed (1.0mL(0.25)kg⁻¹)

Group 5-diabetic rats given metformin (500mg/kg)

(Figure 1) represents the effect of 'herbamed', an herbal formulation on blood glucose level in alloxan-induced diabetic rats. The result revealed that alloxan caused a significant ($P < 0.05$) increase in blood glucose level when compared with the control. However, the herbal formulation as well as the anti-diabetic drug (metformin) prevented this alteration by causing a significant ($P < 0.05$) decrease in blood glucose level in a dose-dependent manner when compared with the diabetic control group. Taking into consideration the change in blood glucose level in (Table 2), our herbal formulation at higher dose compare favorably with the anti-diabetic drug (metformin) tested in this experiment.

Discussion

Alloxan, a beta-cytotoxin, has been demonstrated to induce 'chemical diabetes' (alloxan diabetes) in a wide variety of animal species by damaging the insulin-secreting cells of the pancreas [9]. This damages a large number of beta-cells, resulting in decrease in endogenous insulin release. Alloxan administered rats therefore become hyperglycaemic in a short period of time, followed by a hepatic glucose over production. In the present study, we observed

a significant increase in blood glucose levels after alloxan injection of the rats. Etuk et al. & Adeyi et al. [10,11] attributed this increase in glucose levels to the reactive oxygen species induced by alloxan; in conjunction with a simultaneous massive increase in cytosolic calcium concentrations that led to a rapid destruction of pancreatic islet cells and a concomitant reduction in synthesis/release of insulin.

Interestingly, treatment with our herbal formulation resulted in a significant decrease in blood glucose level in a dose-dependent manner (Figure 1). The possible contributing mechanism is hypothesized to be due to the potentiation of insulin secretion from β -islet cells and consequent enhanced transport of blood glucose to peripheral tissues. The ameliorative and preventive effect of herbamed against alloxan-induced diabetic rat may be attributed to the synergistic effect of the various phytochemicals present in the herbal mixtures. This findings support the traditional use of herbal formulation as an anti-diabetic herbal medicine. However, further studies should be carried out to confirm its exact mechanism of action and phytochemistry. Hypercholesterolemia is well-known as one of the most important risk factors of diabetes mellitus [12].

Table 3: Effect of herbamed on serum lipid profile in alloxan-induced diabetic rats.

Experimental Groups	Total Cholesterol	Triglyceride	LDL-Chol
Group 1	26.7±2.6a	53.4±6.7a	10.6±1.2a
Group 2	41.9±1.3b	121.1±9.7b	24.3±4.1b
Group 3	27.4±2.1a	54.3±6.3a	10.8±1.4a

Group 4	28.3±2.4a	45.1±3.1a	11.3±4.1a
Group 5	37.9±5.4a	51.5±4.4a	10.3±2.4a

Values represent mean±SEM (n = 6).

Values with the same superscript letter along the column are not significantly different at P< 0.05

Key:

Group 1-control

Group 2-diabetic untreated rats.

Group 3-diabetic rats given Herbamed (0.5mL (0.25g)kg⁻¹)

Group 4-diabetic rats given Herbamed (1.0mL (0.25g)kg⁻¹)

Group 5-diabetic rats given metformin (500mg/kg)

It has been shown that hypercholesterolemia increases oxidative stress and leads to lipid peroxidation. It has been suggested that lowering circulating cholesterol levels can reduce the risk of cardiovascular diseases and diabetes mellitus. In the present study, we observed that alloxan treatment altered lipid profile in diabetic rats as shown by a significant (P<0.05) increase in total cholesterol, triglyceride and LDL-cholesterol levels when compared with the control (Table 3). However, our herbal formulation tested caused a significant (p<0.05) decrease in total cholesterol, triglyceride and LDL-cholesterol levels when compared with the induced group. The hypocholesterolemic effect of the herbal formulation could be due to high polyphenols in the herbal constituents. It is well-known that plasma cholesterol concentration can be regulated by cholesterol biosynthesis, cholesterol removal from the circulatory system, the absorption of dietary cholesterol, and its excretion via bile and feces [13].

Conclusion

In the present study, our results demonstrated that 'herbamed', an herbal formulation composed of *Vernonia amygdalina*, *Ocimum gratissimum*, *Zingiber officinale* and *Allium sativum* exhibit antihyperglycemic and antihyperlipidemic properties in alloxan-induced diabetic rats model. This finding supports the traditional use of herbal formulation as an anti-diabetic herbal medicine. However, further studies should be carried out to confirm its exact mechanism of action and phytochemistry.

Conflict of Interest

No conflict of interest to be stated for any of the authors.

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