



Evaluation of anti-diabetic effect of two local herbal medicinal preparations containing *Cordyline fruticosa* (L.) A. Chev in Rivers State, Nigeria

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GSC Biological and Pharmaceutical Sciences, 2025, 30(02), 195-202

Publication history: Received on 29 December 2024; revised on 10 February 2025; accepted on 13 February 2025

Article DOI: <https://doi.org/10.30574/gscbps.2025.30.2.0049>

Abstract

Diabetes half-shot (Dhs) and Thirst Excessive half shot (TEhs) are liquid herbal formulations used in Rivers State and some part of Nigeria by some traditional medicine for the treatment of diabetes mellitus. This study aimed at evaluating the phytochemical constituents and anti-diabetic potential of the herbal formulations in alloxan induced diabetic rats. The up and down OECD protocol was employed for assessing acute toxicity. Hyperglycemia was induced intraperitoneally with 150 mg/kg of alloxan and treated with 0.5 and 1.0 ml of Dhs and TEhs respectively for the period of 21 days. The fasting blood glucose levels, serum lipid parameters were recorded on day 3, 7, 14 and 21 respectively. Qualitative phytochemical analysis was carried out on the formulations using standard prescribed methods. Whereas at a dose of 3 ml per rat no visible sign of toxicity was observed, at a much higher dose of 9 ml per rat, mortality was recorded and when step down to a dose of 6 ml per rat no visible sign of toxicity was observed. After day 3, a quick onset hypoglycemic effect with a decrease in the fasting blood glucose levels of 57.89 and 95.23% were observed for the 0.5 and 1.0 ml per rat doses respectively which fluctuated on day 7 and 14 but later stabilized to > 76.56 % reduction on the day 21. A similar trend was also observed for the TEhs. However, a 100 % mortality was recorded after day 3 for the 1.0 ml higher dose which could be associated with sub-chronic toxicity. Both Dhs and TEhs showed the presence of carbohydrates, triterpenoids and protein. These results demonstrate significant antidiabetic potential of the two herbal formulations justifying the use of these herbals in the indigenous system of medicine. Further studies for investigating the specific compound(s) responsible for such beneficial role in diabetes, pre-clinical and clinical activities.

Keywords: Diabetes half shot; Thirst Excessive half shot; Liquid Herbal Preparations; Diabetes Mellitus; Standardization

1. Introduction

Diabetes, known as 'Diabetes mellitus' describes a metabolic disorder characterised by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, action or both [1]. Diabetes mellitus is a disorder that affects the body's ability to make or use insulin. It is frequently associated with the development of micro and macro vascular diseases which include neuropathy, nephropathy, cardiovascular and cerebrovascular diseases [2]. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs. Diabetes mellitus may present with characteristic symptoms such as thirst, polyuria, blurring of vision,

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and weight loss. In its most severe forms, ketoacidosis or a non-ketotic hyperosmolar state may develop and lead to stupor, coma and, in absence of effective treatment, death. Often symptoms are not severe, or may be absent, and consequently hyperglycaemia sufficient to cause pathological and functional changes may be present for a long time before the diagnosis is made.

Plants are the primary health care resource in many communities around the world [3]. The use of plants in traditional medicine practice for healing and prevention of illnesses is as old as man. Methods of folk healing throughout the World commonly used herbs as part of their tradition [4]. The chemical entities formed as a result of metabolism in plants have been used as sources for the discovery and development of drugs in orthodox medicine practice and as agents of industrial and agrochemical uses [5]. Herbal preparations considered in this study are sold in Port Harcourt Metropolis, Rivers State by a herberal practioner purposely for the treatment of diabetes to diabetes patients. Therefore, there is need to validate the claim of the usage of some medicinal plants in the folk through scientific investigations and possibly develop a more refine drugs from them. The purpose of this research is to investigate the claim that Diabetes half short and Thirst Excessive half shot that are used in treating diabetes for phytochemical constituents, safety and therapeutic potentials.

2. Materials and methods

2.1. Sample Collection and Identification

The two anti-diabetic herbal preparations were collected from traditional medicine practitioner through River State Traditional Medicine Board and were identified as liquid preparation named Diabetes half-shot (Dhs) and Thirst Excessive half shot (TEhs).

2.2. Phytochemical Screening

The herbal preparations shall be subjected to phytochemical screening using standard methods [6],[7].

2.3. Experimental Animals (Rats)

For this investigation, about fifty (50) Wister rats weighing 100 to 150 kg were employed. The rats were purchased from the Department of Experimental Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences' animal house and transported to the Faculty of Basic Medical Sciences' animal house. The rats were acclimatized for two weeks prior to the study with free access to water and feeding, *adlibitum*.

2.4. Acute Toxicity

This test was evaluated using the Organization for Economic Co-operation and Development (OECD 425) – Up and Down procedure. The rats were weighed and fasted before the implementation of the protocol. Two groups of five (5) Wister rats with average weight of 216.9g (0.217kg) were given a dose progression for each sample; 14ml/kobo (3 ml), 28ml/kg bw (6 ml) and 42 ml/kgbw (9 ml) (determined by the residue on dryness of the herbal preparation) for a period of 14 days. The animals were examined with extra care during the first four hours and every other day. Their weight was assessed at least once each week.

2.5. Induction of Diabetes

In vivo anti-diabetic effects of the herbal formulations were assessed as described [8]. The rats were weighed and fasted before the implementation of the protocol. Animals were grouped into A – G. Group B – G were given a single dose (150 mg/kg) of alloxan intraperitoneally and observed for 72 hours for sustained hyperglycemia development [9]. Animals with blood glucose level of greater than 200 mg/dl were considered diabetic and then regrouped and received daily treatment. Group A (normal rats supplied with distilled water), Group B (induced rats given distilled water), Group C (induced rats receiving 75 mg/ml of metformin), Group D (induced rats treated with 3.5 ml/kg of TEhs), Group E (induced rats treated with 7 ml/kg of TEhs), Group F (induced rats treated with 3.5 ml/kg of Dhs) and Group G (induced rats treated with 7 ml/kg of Dhs). On days 0, 3, 7, 14, and 21 of the trial, fasting blood sugar (FBS) levels were measured using a glucometer (Accucheck, Germany).

2.6. Biochemical analysis

Three weeks after the treatment, blood was collected into EDTA tubes through the jugular venipuncture of the rats and analyzed for biochemical variables; total cholesterol, triglycerides, High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL).

3. Results and discussion

Table 1 Physical Characteristics of the two Herbal preparations

Character	State
State	Liquid
Colour	Reddish brown
Odour	Aromatic

Table 2 Residue/ Yield on drying of the two herbal preparations

Herbal preparations	Ave. weight (g/ml)
Diabetes Half shot (<i>Dhs</i>)	0.016
Thirst Excessive Half shot (<i>TEhs</i>)	0.016

Values are mean from the two samples in triplicates of pre-weighed crucibles each at 1ml

Table 3 Acute toxicity (LD₅₀) of the two herbal preparations (OECD -425)

Test seq.	Animal ID	Dose (ml/kgbw)	Number of rats per dose (each sample)	Mortality
1	R1	14 ml/kgbw (3ml)	1	0
2	R2	42 ml/kgbw (3ml)	1	X
3	R3	28 ml/kgbw (3ml)	1	0
4	R4	28 ml/kgbw (3ml)	1	0

(0 = survival, X = death) » Toxicity level > 28ml/kgbw

Table 4 Phytochemical screening of the two herbal preparations

Test	Diabetes Half Short	Excessive Half Short
Alkaloids	-	-
Anthraquinones	-	-
Cardenolides	-	-
Cyanogenic glycosides	-	-
Phenolics	-	-
Saponins	-	-
Tannins	-	-
Triterpenoids	+	+
Carbohydrates	+	+
Fixed oils	-	-
Proteins	+	+

(+):- positive; (-):- negative

Table 5 Result of the Thirst Excessive Halfshot (TEhs) on postprandial fasting blood glucose (FBG) concentrations in rats with diabetes brought on by alloxan

Treatment Group	Fasting Blood Glucose Level(mmol/L)					
	Baseline	0min	30min	60min	90min	120min
TEhs 3.5ml/kgbw	4.35 ± 0.18	16.65 ± 0.35	7.65 ± 0.05 (54.05)	6.35 ± 0.45 (61.86)	4.50 ± 0.10 ^a (72.97)	3.85 ± 0.55 ^a (76.88)
TEhs 7ml/kgbw	5.36 ± 0.33	19.76 ± 1.09*	15.16 ± 2.49 (23.28)	13.94 ± 4.17 (29.45)	7.45 ± 1.21 ^a (62.30)	7.40 ± 1.57 (62.55)
Metformin (10mg/kg)	5.10 ± 0.40	23.10 ± 2.70	21.20 ± 2.10 (8.22)	21.20 ± 1.90 (8.22)	19.60 ± 0.50 (15.15)	18.95 ± 0.35 (17.97)
Diabetic untreated	4.67 ± 0.18	13.34 ± 1.21	19.18 ± 2.49	20.8 ± 3.38	20.85 ± 5.04	20.0 ± 4.69
Normal control	5.66 ± 0.27	ND	ND	ND	ND	ND

Notes: Values are mean ± SEM, n = 5. *Significantly different from negative control, ^aSignificantly different from Positive control, ^bSignificantly different from both controls, p < 0.05, Values in parenthesis indicates % fall in BGL as compared to the postprandial

Table 6 Result of the Thirst Excessive Halfshot (TEhs) of fasting blood glucose (FBG) concentrations in rats with diabetes brought on by alloxan

Treatment Group	Fasting Blood Glucose Level(mmol/L)					
	Baseline	0min	Day 3	Day 7	Day 14	Day 21
TEhs 3.5ml/kgbw	4.35 ± 0.18	16.65 ± 0.35	4.15 ± 0.05 ^b (75.08)	9.85 ± 1.05* (40.84)	7.70 ± 1.80* (53.75)	7.90 ± 0.10 (52.55)
TEhs 7ml/kgbw	5.36 ± 0.33	19.76 ± 1.09*	4.30 ± 0.19 ^b (78.24)	6.55 ± 0.95* (66.85)	5.25 ± 0.45* (73.43)	5.10 ± 1.70* (74.19)
Metformin (10mg/kg)	5.10 ± 0.40	23.10 ± 2.70	15.30 ± 1.70 (33.77)	10.55 ± 1.25* (54.33)	7.95 ± 0.45* (65.58)	6.70 ± 0.60 (71.0)
Diabetic untreated	4.67 ± 0.18	13.34 ± 1.21	23.25 ± 0.25	23.67 ± 1.07	23.3 ± 1.00	13.77 ± 1.37
Normal control	5.66 ± 0.27	ND	5.42 ± 0.32	5.66 ± 0.27	5.52 ± 0.20	5.78 ± 0.39

Notes: Values are mean ± SEM, n = 5. *Significantly different from negative control, ^aSignificantly different from Positive control, ^bSignificantly different from both controls, p < 0.05, Values in parenthesis indicates % fall in BGL as compared to the postprandial

Table 7 Result of the Diabetes Halfshot (Dhs) on postprandial fasting blood glucose (FBG) concentrations in rats with diabetes brought on by alloxan

Treatment Group	Fasting Blood Glucose Level(mmol/L)					
	Baseline	0min	30min	60min	90min	120min
Dhs 3.5ml/kgbw	4.28 ± 0.11	20.18 ± 1.25*	18.00 ± 1.69 (10.80)	17.12 ± 2.87 (15.16)	9.90 ± 0.60 ^a (50.94)	16.43 ± 4.71 (18.58)
Dhs 7ml/kgbw	3.84 ± 0.32	27.82 ± 2.05*	23.28 ± 2.99 (16.32)	20.86 ± 3.29 (25.02)	21.30 ± 4.18 (23.44)	19.36 ± 3.30 (30.41)
Metformin (10mg/kg)	5.10 ± 0.40	23.10 ± 2.70	21.20 ± 2.10	21.20 ± 1.90	19.60 ± 0.50	18.95 ± 0.35

			(8.22)	(8.22)	(15.15)	(17.97)
Diabetic untreated	4.67 ± 0.18	13.34 ± 1.21	19.18 ± 2.49	20.8 ± 3.38	20.85 ± 5.04	20.0 ± 4.69
Normal control	5.66 ± 0.27	ND	ND	ND	ND	ND

Notes: Values are mean ± SEM, n = 5. *Significantly different from negative control, ^aSignificantly different from Positive control, ^bSignificantly different from both controls, p < 0.05, Values in parenthesis indicates % fall in BGL as compared to the postprandial

Table 8 Result of the Diabetes Halfshot (*Dhs*) of fasting blood glucose (FBG) concentrations in rats with diabetes brought on by alloxan

Treatment Group	Fasting Blood Glucose Level(mmol/L)					
	Baseline	0min	Day 3	Day 7	Day 14	Day 21
Dhs 3.5ml/kgbw	4.28 ± 0.11	20.18 ± 1.25*	5.16 ± 0.72 ^b (74.43)	5.50 ± 0.10* (72.75)	4.35 ± 0.05* (78.44)	5.25 ± 0.64* (73.98)
Dhs 7ml/kgbw	3.84 ± 0.32	27.82 ± 2.05*	2.73 ± 0.47 ^b (90.19)	20.95 ± 1.35 (24.69)	26.00 ± 0.00 (6.54)	14.80 ± 0.00 (46.80)
Metformin (10mg/kg)	5.10 ± 0.40	23.10 ± 2.70	15.30 ± 1.70 (33.77)	10.55 ± 1.25* (54.33)	7.95 ± 0.45* (65.58)	6.70 ± 0.60 (71.0)
Diabetic untreated	4.67 ± 0.18	13.34 ± 1.21	23.25 ± 0.25	23.67 ± 1.07	23.3 ± 1.00	13.77 ± 1.37
Normal control	5.66 ± 0.27	ND	5.42 ± 0.32	5.66 ± 0.27	5.52 ± 0.20	5.78 ± 0.39

Notes: Values are mean ± SEM, n = 5. *Significantly different from negative control, ^aSignificantly different from Positive control, ^bSignificantly different from both controls, p < 0.05, Values in parenthesis indicates % fall in BGL as compared to the postprandial

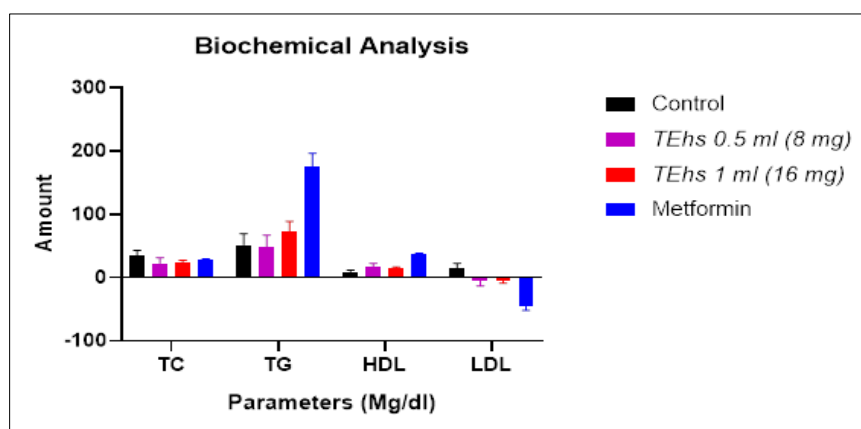


Figure 1 The effect of the Thirst Excessive Half-shot on the lipid profile of the experimented rats as compared with the controls

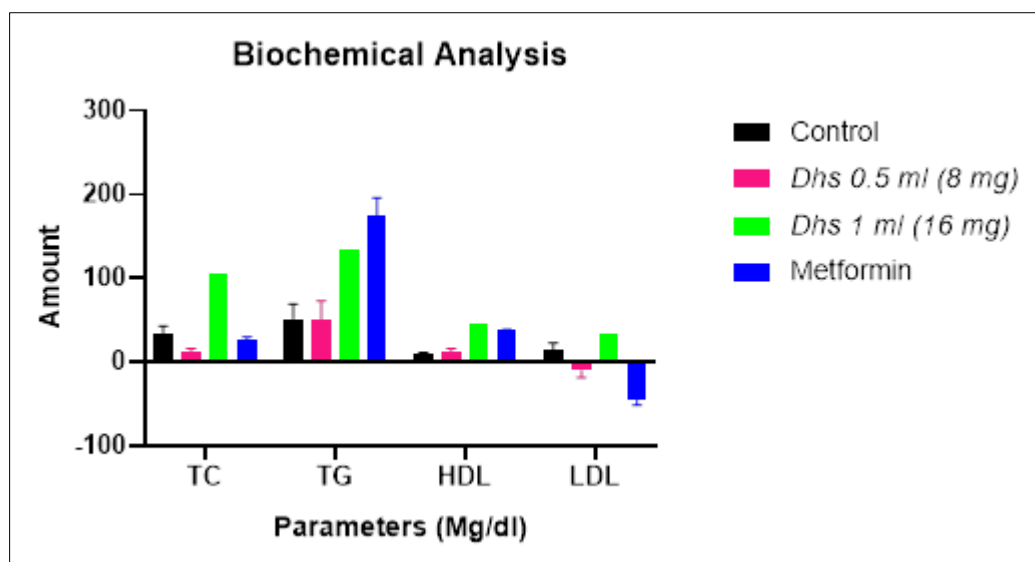


Figure 2 The effect of the Diabetes Half-shot on the lipid profile of the experimented rats as compared with the controls

Herbal medications are increasing in demand as complementary treatments. The usage of medicinal herbs is regrettably not strictly regulated in Nigeria, which renders them freely accessible and potentially open to abuse by end users [10]. Although there is widespread support for herbal combinations in Nigeria, little is known regarding the potential hazard associated with ongoing use. Herbal therapies have the potential to be both therapeutically beneficial and harmful. Additionally, many herbal treatments lack the scientific evidence needed to support their claimed medicinal values. To achieve synergistic benefits, polyherbal formulations are widely utilised in the conventional medical system to control diabetes.

This research sought to determine the anti-diabetic effectiveness of two polyherbal preparations; Dhs and TEhs in alloxan induced diabetic rats. One of the experimental ways to examine the effects of hypoglycemic drugs is alloxan-induced diabetes. Alloxan, a β -cytotoxin, severely destroys β -cells in the Islet of Langerhans, impairing their capacity to make and release insulin. Hyperglycemia results from the inhibition of the insulin system's function. Diabetes brought on by alloxan is marked by a reduction in body weight and elevated calorie consumption. Protein waste as a result of improper glucose metabolism and excessive tissue protein breakdown may be the cause of weight loss [11].

The two polyherbal formulations contained proteins, triterpenoids, and carbohydrates, according to the phytochemical examination. Table 3 shows that other phytochemicals such as alkaloids, flavonoids, saponins, glycosides, cardiac glycosides, anthraquinones, phlobatanins, phenolics, and tannins are absent.

Examination of the safety profile of the two herbal formulations using albino rats showed mortality at a dose higher than 28 ml/kg (Table 3). According to the LD₅₀ data, two separate dosages of 3.5 ml/kg and 7 ml/kg of the formulations were selected and used for the anti-diabetic activity study.

The elevation in the rats' blood sugar concentrations showed that diabetes had been successfully established in the rats. A remarkable decline ($p < 0.05$) in the blood glucose concentration of the diabetic rats was found for the various treated groups as observed in Table 5 to 8.

Following therapy with both herbal remedies and the common medicine (metformin) for 120 minutes postprandial, a considerable reduction in fasting blood sugar concentrations was recorded. Day 21's FBS revealed that the blood sugar concentrations approached normal (with the range of $\pm 3 - 10$ mmol/L), when compared to the blood glucose level of the normal control group.

From table 5, it was observed that the two doses (3.5 and 7 ml/kg) of TEhs showed a remarkable reduction in blood glucose from 30 minutes after administration with a significant reduction of 76.88% and 62.55% at 120 minutes of day one. Consequently, the reduction progresses as observed in Table 6 where there was no significant difference between the treatment groups and the normal control group on day 14 and 21. The 7 ml/kg showed a higher percentage reduction than metformin (10 mg/kg) on day 21 even though they both exhibited significant reduction in Table 6.

In Diabetes half-shot (Dhs) treatments, there was no significant reduction within the observed minutes on day 1 in Table 7. However, 3.5ml/kg of Dhs in Table 8 exhibited a steady stable blood glucose that has no significant difference from the normal control group that were not induced diabetes. The effect is more significant than metformin as the percentage reduction of Dhs were all higher than metformin, notable in Table 8.

Diabetes enhances Total Cholesterol (TC), Triglycerides (TG) and Low-Density Lipoprotein (LDL) values by way of its decreasing effect of High-Density Lipoprotein (HDL) value. Effect of the herbal preparations and Metformin on the Lipid profile showed that for TEhs 3.5ml/kg (0.5ml), Triglycerides (TG) and Total Cholesterol (TC) were decreased, and when juxtaposed to the normal control, there was a substantial rise ($p < 0.05$) in High Density Lipoprotein and a decrease in Low Density Lipoprotein. TEhs 7ml/kg (1ml) showed reduction in TC and significant variations ($p < 0.05$) on increasing Low-density lipoprotein compared to the normal control, low density lipoprotein (Fig 1). In Fig 2, significant variations ($p < 0.05$) were observed on Dhs 3.5ml/kg compared to metformin on the reduced values of Total Cholesterol and LDL. With the TEhs (3.5ml/kg and 7ml/kg) and Metformin dosages, a statistically significant rise ($p < 0.05$) in HDL value was seen. LDL values for the herbal preparations and Metformin were found to be decreasing remarkably in comparison to the normal control group's value in Fig 1 and 2. It takes a sizable rise in HDL for the body to transport cholesterol from other organs back to the liver to be eliminated from the body (MedlinePlus: U.S. National Library of Medicine, HDL: The "Good" Cholesterol).

4. Conclusion

The two herbal medicinal preparations containing *Codyline fruticosa* were found to be safe with effective antidiabetic activity as claimed by the vendor in Rivers State, Nigeria.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest

Statement of ethical approval

The study was carried out with the approval of Research and Ethic Committee of the University of Port Harcourt.

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