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Effects of Aqueous Root Extract of *Jatropha curcas* on Hyperglycaemic and Haematological Indices in Alloxan-induced Diabetic Rats

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Abstract

Hypoglycaemic potentials of aqueous root extract of *Jatropha curcas* (250 and 450 mg/kg body weight of rats) was investigated in alloxan-induced diabetic rats. Effect of the extract on some haematological parameters was also investigated. Thirty albino rats (*Rattus norvegicus*) of mean weight 165.0 ± 2.50 g were randomly selected into normal and diabetic groups, each with six rats. Diabetic treated rats were placed on 14.2 mg/kg body weight glucophage (reference drug), 250 mg/kg and 450 mg/kg body weight of extract. All treatments were administered orally, once daily for fifteen days. The blood glucose levels were monitored and the haematological parameters like haemoglobin (Hgb), red blood cell (RBC) count, white blood cell (WBC) count, packed cell volume (PCV), percentage lymphocytes (LYM) and neutrophils (NEUT) were also analyzed. A significant ($p < 0.05$) reduction in fasting Blood Glucose Levels (BGL) was observed in alloxan-induced diabetic rats treated with the extract. There was a significant ($p < 0.05$) reduction in Hgb, PCV, RBC and WBC and its differentials of the diabetic untreated rats while administration of glucophage, 250 and 450 mg/kg body weight of the aqueous extract (Jc250 and Jc450) to diabetic rats significantly ($p < 0.05$) increase all these parameters. These results suggested that the aqueous root extract of *Jatropha curcas* possesses hypoglycaemic activity and also improved the aberrations in the blood parameters of alloxan-induced diabetic rat.

Keywords: *Jatropha curcas*, root, aqueous extract, diabetic rats, hypoglycaemic, haematology

Introduction

Diabetes mellitus (DM) is a disease characterized by inability to regulate blood glucose caused by relative or absolute deficiency in insulin. The disease may occur as a result of pancreatic β -cells impairment, leading to reduction in insulin secretion. It could also occur when the insulin receptors are resistant to the functions of circulating insulin (ADA, 2010). Recurrent or persistent hyperglycemia during diabetes causes glycation of body proteins, which

in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries (Sharma, 1993). Glycosylation and stiffening of red blood cells, may be responsible for, or associated with, large vessel disease in diabetes (Guthrie and Guthrie, 2002). In diabetes, reduced haemoglobin has been reported (Mansi, 2006) which may be accompanied by a fall in the red blood cell count and packed cell volume

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(Moss, 1999; Muhammad and Oloyede, 2009).

Pharmacological treatment of DM is based on oral hypoglycemic agents and insulin which have many side effects (Andreoli *et al.*, 1990). In diabetes, the causes and sites of intervention in biochemical process are diverse (Larner, 1985) and high serum total triglyceride level, high level of transaminase; creatinine kinase and urea have been implicated (Anaja, 1995). The evaluation of medicinal plants used traditionally in treating diabetes is of growing interest (Holman and Turner, 1991; Williams and Pickup, 1991). The World Health Organization also recommended and encouraged this practice especially in countries where access to conventional treatment of diabetes is inadequate (WHO, 1980). It however emphasized the fact that safety should be the over-riding criteria in the selection of herbal medicine for use in healthcare.

Another major factor, besides hyperglycaemia, which complicates diabetic state and results in death is hyperlipidaemia (Nabel, 2003; Nagappa *et al.*, 2003). Developing countries are the most affected because of expensive and inadequate treatments (Djrolo *et al.*, 1998), coupled with the side effects associated with these drugs. Alternative strategies to the current modern pharmacotherapy of diabetes mellitus are urgently needed, because of the inability of existing therapies to control all the pathological aspects of the disorder, as well as the enormous cost and poor availability for many rural populations in developing countries (WHO, 2002). Although the use of plants as an alternative therapy for diabetes is encouraged and recommended (WHO, 1980), some of them are without scientific scrutiny.

Jatropha curcas (Linn) or physic nut is a perennial poisonous shrub, which grows up to 5 m high and belongs to the family Euphorbiaceae (Gadekar, 2006). The plant originated from Central America but has spread to other tropical and subtropical countries mainly in Asia and Africa. The leaves are usually green to pale green in colour; the flowers are unisexual but occasionally hermaphrodite. The fruits are produced mainly during rainy seasons and the seeds are mature when the capsule changes from

green to yellow (Dehygan and Webster, 1997). In traditional medicine, this plant has been applied since the earliest times for the cure of various ailments ranging from simple fevers to infectious diseases including sexually transmitted diseases in many African and Asian countries (Thomas, 1989; Burkill, 1994). In Nigeria, the fruits of *J. curcas* and the stem bark of *Cochlospermum planchonii* are combined for the treatment of diabetes mellitus (Igoli *et al.*, 2005). *J. curcas* is also used traditionally for the treatment of pains in the South Eastern part of Nigeria. The use of aqueous extract of the seeds and nuts as contraceptive has been reported (Gonasekera *et al.*, 1995). The leaf extract has also been shown to have a potent cardiovascular action (Fojas *et al.*, 1986). Other applications include the use of the seeds for making soap, candles, detergents, lubricants and dyes. The bark is used as fish poison and the oil from the seed is used as biodiesel (Achten *et al.*, 2008). The sap from the stem is used to stop bleeding from wound and the plant is also used as living fence to protect garden and fields from animals (Gadekar, 2006).

Evaluation of the anti-diabetic potential of *J. curcas* becomes necessary to provide scientific proof and justify its use in ethno-medicine. This research was therefore designed to study the effect the aqueous root extract of *J. curcas* on blood glucose level and haematology of diabetic rats.

Materials and methods

Plant Materials

The roots of *Jatropha curcas* were collected from a garden at Elega's compound in Oke-Oyi, Ilorin-East Local Govt Area of Kwara State, Nigeria and authenticated at the Herbarium of the Department of Plant Biology, University of Ilorin, Ilorin, Nigeria, where a voucher specimen was deposited.

Chemicals and Drugs

Alloxan was obtained from Sigma Chemical Company, St Louis, Mo, U.S.A. All the other chemicals used were of analytical grade and prepared in glass distilled water.

Animals

Thirty (30) albino rats of both sexes (135±25 g weight) were obtained from the small Animal Breeding Unit of the Department of Biochemistry, University of Ilorin, Ilorin. They were maintained on standard animal pellets and water *ad libitum*.

Methods

Preparation of Extract

Based on simulation from the method of preparation of the extract locally, a decoction of *J. curcas* root was prepared by boiling a 1 kg weight portion of the fresh root in 5 L of distilled water for 30 min. The extract was filtered and the resulting filtrate was concentrated using a Rotary Evaporator. The concentrate was then reconstituted using distilled water.

Phytochemical screening

Chemical tests described by Wall *et al.* (1952, 1954); Harborne (1973); Odebiyi and Sofowora (1980); and Trease and Evans (1989) were carried out on the extract to identify the constituents.

Induction of Diabetes

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared Alloxan (150 mg/kg body weight) in ice cold 0.9% NaCl solution. The animals were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycemia. Control (normal) rats were not injected with alloxan and were placed on normal saline alone. After 24 h, rats with moderate diabetes having hyperglycemia (blood glucose level above 180 mg/dL) were considered as diabetic and used for the experiment. The aqueous root extract was administered orally at concentrations of 250 and 450 mg/kg body weight rats⁻¹ day⁻¹ for 15 days.

Experimental Design

The animals were divided into 5 groups of 6 animals each for the evaluation of anti-diabetic activity.

Group I: Non-diabetic rats administered normal saline for 15 days (Normal-NDDW).

Group II: Diabetic control rats administered

normal saline for 15 days (DNT).

Group III: Diabetic rats given *Glucophage* (14.2 mg/kg/rat/day) in aqueous solution orally for 15 days (DTSD).

Group IV: Diabetic rats administered *J. curcas* aqueous root extract (250 mg/kg/rat/day) orally for 15 days (DJc250).

Group V: Diabetic rats administered *J. curcas* aqueous root extract (450 mg/kg/rat/day) orally for 15 days (DJc450).

Determination of Blood Glucose Level

Fasting blood glucose levels were determined with ONE TOUCH BASIC® Glucometer (LIFESCAN, Inc 2001 Milpitas, CA 95035, USA). The fasting Blood Glucose Levels (BGL) was monitored at two days interval for 15 days by tail tipping method.

Determination of Haematological Parameters

After two weeks treatment with the two extracts, blood samples were obtained through cardiac puncturing of the rats for the determination of the haematological parameters: Red blood cells (RBC), packed cell volume (PCV), haemoglobin concentration (Hb), white blood cell count (WBC) and its differential counts, using the method of Dacie and Lewis (1991).

Statistical Analysis

All data were statistically analysed with Students't-test and two-way ANOVA, followed by Tukey Kramer post test. Values of $p < 0.05$ were considered significant.

Results and Discussion

Table 1 shows the phytochemicals present in the aqueous root extract of *Jatropha curcas*. Flavonoids, tannins, saponin and phlobatannin were detected. Flavonoids of different plant origin showed a promising anti-diabetic activity, as demonstrated in diabetic animal models (Zarzuelo *et al.*, 1996; Nojima *et al.*, 1998; Kim *et al.*, 2004). Saponins are glycosides of triterpenes, steroids or alkaloids. Previous researchers have demonstrated the hypoglycemic activity of triterpenoid glycosides (Reher *et al.*, 1991; Kako *et al.*, 1997). Thus the phytochemical constituents

Table 1: Phytochemical Constituents of the Aqueous Root Extracts of *J. curcas*

Phytochemicals	<i>Jatropha curcas</i>
Alkaloids	-
Flavonoids	+
Cardiac glycosides	-
Tannins	+
Saponins	+
Phlobatannins	+

- = Not detected; + = Detected

indicate that the aqueous root extract of *J. curcas* could have potentials to be an antidiabetic agent.

Dose dependent reduction in BGL was observed in alloxan-induced diabetic rats treated with aqueous root extract of *J. curcas*. In this study, the extract produced a sustained significant ($p < 0.05$) reduction in blood glucose level of the diabetic rats compared to non-diabetic rats (Table 2). Evaluation of hypoglycaemic activity of antidiabetic agents using alloxan-induced hyperglycaemia model has been described to be very useful (Szkudelski, 2001). Alloxan selectively destroys the pancreatic insulin secreting beta cells; leaving the less active cells thus resulting in a diabetic state (Kamtchoung *et al.*, 1998; Szkudelski, 2001). Glucophage can be used as a standard drug to compare the efficacy of the hypoglycaemic agents in alloxan-induced diabetes.

Medicinal plant extracts have been valuable antidiabetic agents and may involve one or more active components responsible for blood glucose reduction (Marles and Farnsworth, 1995; Grover *et al.*, 2002). Thus the hypoglycaemic effect of *J. curcas* in this study may be linked to the presence of flavonoids and terpenes in the extracts. These compounds have been implicated in the anti-diabetic activities of many plants (Shimizu *et al.*, 1984; Ivorra *et al.*, 1989; Reher *et al.*, 1991; Okokon *et al.*, 2006). In this study, the hypoglycaemic action of the aqueous root extract of *J. curcas* may be by potentiating the insulin effect, either by increasing the pancreatic secretion of insulin from the cells of islets of langerhans or its release from bound insulin (Pari and Armanath, 2004).

In diabetic untreated rats, significant ($p < 0.05$) reductions in Hb, RBC, PCV, WBC, LYM and

NEUT were observed during the analysis of the haematological parameters (Table 3). Appreciable elevation in the levels of RBC and WBC occurred upon administration of the extracts and values obtained were not significantly ($p > 0.05$) different from that of glucophage. The same trend was observed in the levels of Hb and PCV in the treated rats, however they were significant ($p < 0.05$) lower to that of the reference drug. There was a significant ($p < 0.05$) increase in the level of the LYM and NEUT of the diabetic treated rats on 250 and 450 mg/kg body weight of the extract which compared well with the reference drug.

Blood examination is a good way of assessing the health status of animals as it plays a vital role in physiological, nutritional and pathological status of organisms (Kakade *et al.*, 1972; Muhammad *et al.*, 2000). Assessment of haematological parameters can be used to determine the extent of deleterious effect on blood constituents of an animal (Ashafa *et al.*, 2009; Mohammed *et al.*, 2009). It can also be used to explain blood relating functions of chemical compounds/plant extract (Yakubu *et al.*, 2007). During diabetes the excess glucose present in blood reacts with haemoglobin to form glycosylated haemoglobin. The present study thus revealed that alloxan-induced diabetic untreated rats showed abnormalities in the haematological parameters. Some of these abnormalities might be due to destruction of matured red blood cells leading to the low Hb counts accompanied by the fall in the RBC and PCV (Moss 1999; Muhammad and Oloyede, 2009). Very low reading of RBC, Hb and haematocrit could indicate anaemia (Muhammad and Oloyede, 2009). Also, selective immune modulatory effect and localized toxicity could occur as recorded in the lymphocytes and neutrophils of the diabetic untreated rats. Administration of the extract elicits a positive change in the haematological parameters of the diabetic rats. Thus, increase in RBC by the extract is an indication of its ameliorative effect on alloxan-induced anaemia while the change in level of LYM by the extract may indicate an anti-infection activity (Muhammad *et al.*, 2009).

Table 2: Effect of *J. curcas* on blood glucose levels of alloxan-induced diabetic rats during treatment

Day	Normal	DNT	DTSD	DJc250	DJc450
Day 0	83.70 ± 1.26 ^a	80.00 ± 3.04 ^a	80.50 ± 3.57 ^a	82.30 ± 0.76 ^a	81.70 ± 1.58 ^a
Day 1	95.70 ± 1.58 ^a	314.70 ± 1.52 ^a	316.70 ± 2.25 ^b	310.30 ± 1.31 ^c	315.50 ± 1.57 ^b
Day 3	78.20 ± 1.54 ^a	310.00 ± 1.65 ^b	240.80 ± 1.17 ^c	294.50 ± 1.23 ^d	286.00 ± 2.67 ^e
Day 5	61.80 ± 1.58 ^a	311.80 ± 2.70 ^b	87.20 ± 2.56 ^c	207.80 ± 1.17 ^d	277.00 ± 5.42 ^e
Day 7	67.70 ± 1.41 ^a	227.30 ± 0.56 ^b	80.50 ± 2.11 ^c	194.50 ± 0.56 ^d	215.80 ± 0.91 ^e
Day 9	111.00 ± 0.86 ^a	230.70 ± 2.33 ^b	116.20 ± 1.38 ^c	144.30 ± 1.91 ^d	187.00 ± 2.04 ^e
Day 11	112.50 ± 1.54 ^a	304.50 ± 2.31 ^b	104.80 ± 1.14 ^c	173.70 ± 2.99 ^d	185.80 ± 3.75 ^e
Day 13	80.00 ± 0.97 ^a	293.20 ± 2.09 ^b	94.80 ± 1.17 ^c	105.80 ± 0.40 ^d	160.20 ± 3.17 ^e
Day 15	89.30 ± 2.03 ^a	221.70 ± 1.23 ^b	95.30 ± 1.45 ^c	105.70 ± 1.26 ^d	118.2 ± 1.40 ^e

Values are expressed as mean of six replicates ± SEM

Values with different superscripts (within rows) are statistically different (p < 0.05).

Table 3: Effect of oral administration aqueous root extracts of *J. curcas* on haematological parameters in alloxan-induced diabetic rats

Parameter/ Group	Normal	DNT	DSTD	DJc250	DJc450
Hb (g/dL)	21.00±1.65 ^a	11.30±0.43 ^b	20.90±0.66 ^a	16.90±0.96 ^c	12.50±0.48 ^d
PCV%	62.00±4.88 ^a	33.20±1.30 ^b	61.80±1.96 ^a	50.70±1.20 ^c	47.30±3.11 ^c
RBC (×10 ¹² μ/L)	3.70±0.06 ^a	3.10±0.04 ^b	3.60±0.07 ^a	3.60±0.03 ^a	3.40±0.13 ^c
PLATELETS(×10 ⁹ /L)	846.67±27.23 ^a	296.67±33.63 ^b	760.00±25.22 ^c	681.67±29.03 ^d	559.83±43.27 ^e
WBC (×10 ¹² μ/L)	7.90±0.81 ^a	5.20±0.89 ^b	7.70±1.08 ^a	7.20±2.65 ^a	6.00±1.01 ^c
NEUT%	38.00±6.59 ^a	10.00±5.60 ^b	31.80±4.96 ^c	29.50±5.24 ^a	25.30±3.25 ^c
LYMPH%	90.00±1.71 ^a	62.00±6.60 ^b	79.50±4.40 ^c	74.70±3.25 ^c	73.70±3.32 ^c

Values are expressed as mean of six replicates ± SEM.

Values with different superscripts along the column are statistically different (p<0.05).

Conclusion

The results from this study showed that aqueous root extract of *J. curcas* exerted hypoglycaemic action and ameliorate anaemic condition in alloxan-induced diabetic rats. Further studies need be carried out, however, to isolate and identify the active principle(s) in the extract as well as elucidate its mode of action and toxicological effect.

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