

## 'Shasha'(Delonixregia) in the treatment of Diabetes mellitus.

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**Abstract:** This paper reports on the use of the seed solution of the plant 'Sha sha' (*Delonix regia*) as a therapeutic agent in the treatment of diabetes mellitus and its associated liver challenges. Seventy-two experimental albino rats were divided into eight groups with the first group as control, and others made diabetic with streptozotocin (60 mg/kg body weight of rat). The diabetic rats were treated with distilled water, 0.2g/kg, 0.4g/kg, 0.6g/kg of Sha sha seed solution, Glucophage (500mg/kg), Vitamin C (20mg/kg) and Glucophage+Vitamin C (500 and 20mg/kg) respectively for groups 2-8, for three weeks. Streptozotocin significantly increased glucose levels from 122.00± 2.04 to 162.00± 4.61mg/dl after three days of intra peritoneal injection and also caused significant increases in the serum concentrations of the liver enzymes like AST (121.67±7.26 (U/L)), which was reduced to 100.00±3.00, ALT from 55.33±1.76 to 50.00±1.15(U/L), and ALP (335.67±1.45) reduced to 158.00±6.35 (U/L). Glucophage, Vitamin C and Glucophage with Vitamin C in combination produces significant reduction for AST(100±3.00, 91.00±2.00, 70.00±3.00), ALT 27.00±1.15, 27.00±2.00, 36.00±4.04) and Alkaline Phosphatase (202.00±12.70, 199.67±11.26, 146.67±3.18) respectively. The plant seed solution and the standard drugs also caused significant decreases (p<0.05) in the levels of the enzymes, which reduced as the concentration of the plant solution increased. Hyperglycemia and oxidative stress management was effectively achieved by the combination therapy as observed. This plant solution mimicked the standard drugs (Glucophage and Vitamin C) causing decreases in glucose level in the diabetic rats. The plant solutions and the standard drugs in the verified concentrations proved to be suitable therapy though vitamin C seems to be more effective in the management of diabetes and its associated liver damage.

**Keywords:** Diabetes mellitus, Glucophage, 'Shasha'(Delonixregia), Streptozotocin, Vitamin C,

### I. INTRODUCTION

The plant botanically called *Delonix regia* is known as 'Sha sha' in Urhobo community of Delta State of Nigeria. It is a tropical tree that is native to Madagascar but has been widely planted around the world in tropical and semi-tropical areas. It is generally called flamboyant or royal poinciana [1], Krishnachura, Gulmohar or Malinche [2] and Tabachine [3]. The flowers give way to flattened bean-like fruit pods (each to 24" long) [1]. The pods contain the 'Sha sha' seeds that look like beans.

*Delonix regia* (Fabaceae) leaves and seeds are used in folk medicine of Bangladesh for the treatment of diabetes in traditional medicine which plays important roles in health services around the globe with about three-quarters relying on plants and plant products for health care. The rationale behind the designs of novel drugs are gotten from traditional medicine that offers new proposal in modern healthcare [4]. Many plants from Fabaceae family have been used heavily as liver detoxifying or cleansing agents and for management of diabetes. Prominent examples are *Clitoria ternatea* Linn. [5], *Pongamia pinnata*, *Tephrosia villosa*, *Trigonella foenumgraecum* [6], *Albizia moleuccana*, *Arachis hypogaea*, *Butea monosperma*, *Tamarindus indica* [7] for diabetes and *Glycyrrhiza glabra* [8] for liver detoxification.

'Sha sha' is therefore implicated in the treatment of diabetes mellitus (DM) - an endocrine chronic disease characterized by hyperglycemia, hyperlipidemia, negative nitrogen balance and sometimes ketonemia [9]. DM is also a known risk factor of hepatocarcinoma [10, 11], oxidative stress, inflammation, and insulin resistance [12]. Its incidence is increasing with western way of living. Report estimated that 323 million adults are affected and 5.1 million deaths recorded [13, 14] currently in the world. In spite of the best currently available hypoglycemic agents, the management of the disease has not shown to be improved [14]. In DM, high

levels of glucose can lead to oxidative stress via glucose auto-oxidation and can damage various organs including the liver [13] which are kept in check by complex network of antioxidant defense and repair systems [15]. Many people have reported the use of Vitamin C in the management of diabetes induced oxidative stress. Antioxidant like Vitamin C could be used either in combination or singularly to manage diabetes and its associated liver problems. The ability of a therapeutic agent to restore glycemic balance in hyperglycemic condition is an index of its anti-diabetic property [16].

This work intends to see if DM and its associated liver damage could be managed using 'Sha sha' seed solution. Since the 'Sha sha' leaf has been reported to have maximum hypoglycemic activities compared to standard drug Glibenclamide in hyperglycemic mice [2]. The plant decoction is used for gastric problems, body pains and rheumatic pains of joints while the ethanolic extracts has anti-inflammatory, antibacterial, antimalarial effects; and known to contain proteins, flavonoids, tannins, phenolic compounds, glycerol, sterols and triterpenoids [4].

## II. MATERIALS AND METHODS.

### 2.1. Animals

Seventy-two albino rats, weighing 125 - 145g were bred in the animal house of Physiology Department in Madonna University. The animals were kept under standard laboratory conditions with water and feed (Bendel feeds and Flour mill Ltd.) *ad libitum*.

### 2.2. Drugs used

Glucophage, Vitamin C and Streptozotocin were purchased from Merk Pharmaceuticals, Emzor Pharma Industries and Capino pharmacy respectively.

### 2.3 Preparation of Plant Extract

The seeds of 'Shasha' were dried by sunlight and pulverized into a fine powder. The powder was sieved and 10g dissolved in water, boiled for 10 minutes and cooled. Three doses of 0.2, 0.4 and 0.6g/Kg body weight were prepared from this stock using distil water as a vehicle.

### 2.4 Animal treatment and drug administration

The rats were divided into eight groups of nine (9) rats per group. Groups II to VIII were made diabetic by using intraperitoneal injection of 60 mg/kg body weight of rat. Group I served as normal control and was given only feed and water. Group II served as Diabetic control and was not treated either with the plant or drugs; Groups III-V received the three different doses of 'Shasha' seed solution; while Groups VI-VIII received 500, 20 and 500 plus 20 mg/kg body weight of Glucophage, Vitamin C and Glucophage/Vitamin C combination respectively. The treatment was done daily and at weekly interval, the rats were sacrificed and blood was collected for analysis. The experimental design is further explained below

Group I: Normal Control; Non – diabetic and No Treatment

Group II: - Diabetic control - Diabetic and No Treatment

Group III - Diabetic and Treated with Extract (0.2g/kg body weight of rat)

Group IV: - Diabetic and treated with Extract (0.4g/kg body weight of rat)

Group V:- Diabetic and treated with Extract (0.6g/kg body weight of rat)

Group VI: - Diabetic and treated with Glucophage(500mg/kg body weight of rat)

Group VII: - Diabetic and treated with Vitamin C(20 mg/kg body weight of rat)

Group VIII: - Diabetic and treated with Glucophageand Vitamin C(500mg+ 20mg body weight of rat)

### 2.5 Collection of blood sample

The rats were sacrificed painlessly under chloroform anesthesia. Blood was collected at weekly intervals by cardiac puncture, centrifuged at 3000rpm for 10minutes and serum was collected for further analysis.

### 2.6 Determination of biological variables

The serum activities were determined using the spectrophotometric methods of Monica [17], for Glucose; Reitman and Frankel [18] for Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST); GSCC [19] method for Alkaline phosphatase (ALP).

### 2.7 Statistical Analysis

The data obtained were expressed as Mean + Standard Error of Mean ( $M \pm SEM$ ). The significance of difference among the various treated groups and control group were analyzed by means of one-way Analysis of Variance ANOVA followed by Dennett's multiple comparison test (San Diego, CA.USA). The level of significance was set at  $p < 0.05$ .

## III. RESULTS

Table 1 shows the effects of 'Sha asha' (*Delonix regia*) seed solution on glucose level in streptozotocin-induced diabetes. There was a significant increase ( $p < 0.05$ ) in glucose level after 72hrs of

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streptozotocin induction from a normal level of 122.00±2.04 to 162.00±4.61mg/dl. Group III glucose level were significantly (p <0.05) changed within a range of 158.00± 6.35 to 160.67± 6.93when compared to the normal level. In the other groups there were reductions in glucose level close to the normal level, though not significant. The level of glucose was seen to be significantly reduced (p <0.05) as the concentration of the extract was increasing and also as the time in weeks, increased, hence 0.2g/kg and 0.6g/kg body weight significantly reduced the glucose level from 158.00± 6.35mg/dl to 125.67± 10.10mg/dl respectively in d third week. The 'Sha asha' seed solution at 0.4 and 0,6g/kg was able to reduce the glucose level below those of Glucophage and vitamin C, though not significant Glucophage alone reduced glucose level more than Vitamin C alone or in combination.

**Table 1. Effects of 'Sha sha', seed solution, Glucophage and Vitamin C treatments, of glucose level (mg/dl)in streptozotocin-induced Wister rats after 3 weeks(21 days)**

Treatment	WEEK 1	WEEK 2	WEEK 3
Group I-Normal control	122.00±2.04 <sup>ad</sup>	123.00±4.04 <sup>ad</sup>	122.00±4.04 <sup>a</sup>
Group II- Steptozotocin-induced	162.00± 4.61 <sup>ac e</sup>	161.00± 4.61 <sup>ace</sup>	162.00± 4.61 <sup>acde</sup>
Group III- Extract (0.2g/kg)	160.67±6.93 <sup>abc</sup>	159.33± 6.64 <sup>abc</sup>	158.00± 6.35 <sup>abcd</sup>
Group IV- Extract (0.4g/kg)	140.00± 1.45 <sup>e</sup>	133.67± 2.02 <sup>be</sup>	126.67± 2.60 <sup>be</sup>
Group V- Extract (0.6g/kg)	129.33± 13.48 <sup>bde</sup>	127.67± 11.89 <sup>be</sup>	125.67± 10.10 <sup>be</sup>
Group VI- Glucophage 500mg/kg	135.67± 0.33 <sup>ce</sup>	129.67± 0.33 <sup>c</sup>	123.67± 0.33 <sup>ce</sup>
Group VII- Vitamin C 20mg/kg	153.00± 6.80 <sup>ade</sup>	147.00± 6.80 <sup>acd</sup>	137.67± 3.75 <sup>de</sup>
Group VIII- Metformin+VitaminC 520mg/kg	143.33± 3.52 <sup>e</sup>	138.00± 9.81	132.00± 9.81 <sup>e</sup>

Result Represents Mean ±SEM of Triplicate Sample. Values were considered significant at p<0.05 and superscripts in the same row with the same letters are significant.

<sup>a</sup> = Significant Difference when each all the groups were compared with Group I

<sup>b</sup> = Significant Difference when Group III was compared with all the groups.

<sup>c</sup> = Significant Difference when Group VI was compared all the groups.<sup>d</sup>=Significant Difference when Group VII was compared with all the groups.

<sup>e</sup> =Significant Difference when Group II was compared with all the groups.

Table 2 shows the effects of 'Sha sha', seed solution, Glucophage and Vitamin C treatments on AST level( mg/dl) in streptozotocin-induced Wister rats after 3 weeks (21 days). There were significant increases in AST level in all the groups as a result of streptozotocin-induction of diabetes. There were decreases in AST levels in Groups V (40.00± 1.00 U/L), IV (44.00± 1.73U/L) and III (89.00±5.20U/L) as concentration of 'Sha sha', seed solution increases. Glucophage reduced the AST level significantly in second week from 106.00±2.66 to 72.00±2.64(U/L). Vitamin C reduced the AST level more than the Glucophage and Vitamin C/Glucophage combination.

**Table 2. Effects of 'Sha sha' seed solution, Glucophage and Vitamin C treatments on Aspartate Aminotransferase(AST) (U/L) Level of streptozotocin-induced Albino rats after 3 weeks of treatment,**

Treatment	WEEK 1	WEEK 2	WEEK 3
Group I-Normal control	93.67±4.66 <sup>acd</sup>	93.67± 4.67 <sup>acd</sup>	93.67± 4.67 <sup>a</sup>
Group II- Steptozotocin-induced	118.00± 6.26 <sup>acd</sup>	106.00±2.66 <sup>acd</sup>	121.67± 7.26 <sup>acd</sup>
Group III- Extract (0.2 g/kg)	89.00± 5.20 <sup>bcd</sup>	93.67± 1.86 <sup>bdc</sup>	90.33± 1.33 <sup>b</sup>
Group IV- Extract (0.4g/kg)	44.00± 1.73 <sup>ab</sup>	87.67± 1.33 <sup>bcd</sup>	93.00± 2.30 <sup>b</sup>
Group V- Extract (0.6g/kg)	40.00± 1.00 <sup>a</sup>	82.67±3.75 <sup>acd</sup>	100.00±3.00
Group VI- Glucophage 500mg/kg	46.33± 0.66 <sup>a</sup>	72.00±2.64 <sup>acd</sup>	100.00±2.00
Group VII- Vitamin C 20mg/kg	44.00±1.73 <sup>a</sup>	55.67±2.03 <sup>acd</sup>	91.00±2.00
Group VIII- Glucophage+VitaminC 520mg/kg	30.00±1.00 <sup>acd</sup>	75.00±1.00 <sup>acd</sup>	70.00± 3.00 <sup>acd</sup>

Result Represents Mean ±SEM of Triplicate Sample. Values were considered significant at p<0.05 and superscripts in the same row with the same letters are significant.

<sup>a</sup> = Significant Difference when each all the groups were compared with Group I

<sup>b</sup> = Significant Difference when Group III was compared with all the groups.

<sup>c</sup> = Significant Difference when Group VI was compared with all the groups.

<sup>d</sup> =Significant Difference when Group VII was compared with all the groups.

<sup>e</sup> =Significant Difference when Group II was compared with all the groups.

Table 3 shows the effects of 'Sha sha' seed solution, Glucophage and Vitamin C treatment on Alanine Aminotransferase (ALT) of streptozotocin- induced Wister rats. The first week of treatment resulted in reduction of ALT level all in U/L, from the diabetic level of 55.33±1.76 to 50.00±1.15, 28.00±1.00, 27.00 ±1.15. 36.67±1.47, 27. 67±1.33 and 28.33±0.67 U/L for groups III to VIII respectively. In week 2, Group V

(7.33±0.67U/L) was significantly lowered (p<0.05) from the diabetic level of 41.33±2.60. The same was observed for groups III (19.00±1.15), IV (14.67±1.45), Glucophage (25.67±0.67) and Vitamin C (19.00±1.15). In week 3, the ALT level {U/L} of Groups III (36.67±1.45), IV (27.00±1.15), VI (23.67±1.20) and VIII (36.00±4.04) were significantly lowered (p<0.05) from the diabetic level of 47.00±1.73U/L.

**Table 3. Effects of 'Sha sha' seed solution, Glucophage and Vitamin C treatment on Alanine Aminotransferase (ALT) (U/L) of streptozotocin-induced Wister rats after 3 weeks(21 days)**

Treatment	WEEK 1	WEEK 2	WEEK 3
Group I-Normal control	38.67±2.60 <sup>aebc</sup>	38.67±2.60 <sup>aebc</sup>	38.67±2.60 <sup>ab</sup>
Group II- Steptozotocin-induced	55.33±1.76 <sup>aebc</sup>	41.33±2.40 <sup>aebc</sup>	47.00±1.73 <sup>aebc</sup>
Group III- Extract (0.2gg/kg)	50.00±1.15 <sup>aebc</sup>	19.00±1.15 <sup>aebc</sup>	36.67±1.45 <sup>aebc</sup>
Group IV- Extract (0.4g/kg)	28.00±1.00 <sup>aebc</sup>	14.67±1.45 <sup>aec</sup>	27.00±1.15 <sup>aeb</sup>
Group V- Extract (0.6g/kg)	27.00±1.15 <sup>aebc</sup>	7.33±0.66 <sup>aebc</sup>	23.67±1.20 <sup>aeb</sup>
Group VI- Glucophage 500mg/kg	36.67±1.45 <sup>aebc</sup>	25.67±0.66 <sup>aebc</sup>	27.00±1.15 <sup>aeb</sup>
Group VII- Vitamin C 20mg/kg	27.67±1.33 <sup>aebc</sup>	21.00±4.00 <sup>ae</sup>	27.00±2.00 <sup>aeb</sup>
Group VIII- Glucophage+VitaminC 520mg/kg	28.33±0.67 <sup>aebc</sup>	19.00±1.15 <sup>aec</sup>	36.00±4.04 <sup>aec</sup>

Result Represents Mean ±SEM of Triplicate Sample. Values were considered significant at p<0.05 and superscripts in the same row with the same letters are significant.

<sup>a</sup> = Significant Difference when each all the groups were compared with Group 1

<sup>b</sup> = Significant Difference when Group III was compared with all the groups.

<sup>c</sup> = Significant Difference when Group VI was compared with all the groups.

<sup>d</sup> = Significant Difference when Group VII was compared with all the groups.

<sup>e</sup> = Significant Difference when Group II was compared with all the groups.

Table 4 shows the effects of 'Sha sha' extract, Glucophage and Vitamin C treatment on Alkaline Phosphatase of streptozotocin - induced Wister rat after 3 weeks. Week 1 treatment showed that only groups IV (102.67±18.19), V (80.00±32.91) and VIII (44.00±2.89) had their ALP(U/L) level significantly reduced from the diabetic level of 289.00±42.02. As the duration of treatment was increasing, the ALP level was increasing in Groups III to VIII. Significant reductions (p<0.05) were observed for Groups V, VII and VIII indicating that high concentration of 'Sha sha' seed solution, Vitamin C and Glucophage/Vitamin C combination were able to reduce the ALP level(U/L) ,

**Table 4. Effects of 'Sha sha' ,Glucophage and Vitamin C treatment on Alkaline Phosphatase of streptozotocin-induced Wister rats after 3 weeks(21 days)**

Treatment	WEEK 1	WEEK 2	WEEK 3
Group I-Normal control	235.67±1.45	235.67±1.45 <sup>aebcd</sup>	235.67±1.45 <sup>aebcd</sup>
Group II- Steptozotocin-induced	289.00±42.02	428.33±46.93 <sup>aecd</sup>	335.67±2.03 <sup>aebcd</sup>
Group III- Extract (0.2gg/kg)	152.00±49.07	381.67±13.02 <sup>aebccd</sup>	289.33±10.34 <sup>aebcd</sup>
Group IV- Extract (0.4g/kg)	102.67±18.19 <sup>e</sup>	199.67±11.26 <sup>aebcd</sup>	176.67±3.17 <sup>aebcd</sup>
Group V- Extract (0.6g/kg)	80.00±32.91 <sup>e</sup>	105.00±13.28 <sup>aebcd</sup>	158.00±6.35 <sup>aebcd</sup>
Group VI- Glucophage 500mg/kg	146.00±5.77	304.00±8.66 <sup>aebcd</sup>	202.00±12.70 <sup>aebcd</sup>
Group VII- Vitamin C 20mg/kg	131.67±5.49	115.67±3.76 <sup>aeb</sup>	199.67±11.26 <sup>aebcd</sup>
Group VIII- Glucophage+VitaminC 520mg/kg	44.00±2.89 <sup>e</sup>	155.00±8.08 <sup>aebd</sup>	146.67±3.18 <sup>aebcd</sup>

Result Represents Mean ±SEM of Triplicate Sample. Values were considered significant at p<0.05 and superscripts in the same row with the same letters are significant.

<sup>a</sup> = Significant Difference when each all the groups were compared with Group 1

<sup>b</sup> = Significant Difference when Group III was compared with all the groups.

<sup>c</sup> = Significant Difference when Group VI was compared with every all the groups.

<sup>d</sup> = Significant Difference when Group VII was compared with all the groups.

<sup>e</sup> = Significant Difference when Group II was compared with all the groups.

#### IV. DISCUSSION

In this study, the mean glucose level (mg/dl) of untreated diabetic rat (diabetic control) (162± 4.62) increased significantly, (p<0.05) in all the three weeks compared to the normal rats (122.00± 4.04). This confirms the necrosis of pancreatic beta cell by streptozotocin[20]. It could be inferred that 'Sha sha' had ameliorating effect on hyperglycemic glucose level as the concentration increases, when compared with the standard drug Glucophage (135.67 ±0.33), diabetic group(162.00 ±4.62) and normal rats(122.00± 4.04). It was also observed that 0.6g/kg concentration of 'Sha sha' solution (129.33± 13.48) lowered glucose level significantly (p<0.05) [21]. It is speculated that Sterols, triterpenoids or glycosides presents in the plant extracts may be responsible for the observed activities [22].

Delaney *et. at.* [23] reported the hepatic toxicity and membrane labializing effect on organ of *Delonix regia*. In this study there was significant (p<0.05) elevation in the untreated diabetic rats in the level of liver



enzymes (AST, ALT, and ALP) across the weeks compared to the normal rats and other groups respectively. This is in conformity with the report of literature [23]

The 'Sha sha' solution shows that at 0.6g/kg concentration of solution ( $40.00 \pm 0.00$ ), Vitamin C ( $44.00 \pm 1.73$ ) and Glucophage+ Vitamin C ( $30.00 \pm 1.00$ ) for weeks 1, 2 and 3 shows significant decrease compared to other groups. This inferred that 'Sha Sha' at 0.6g/kg concentration has ameliorating effects on liver hepatotoxicity. This is in conformity with the report by Dakhale *et al* [14], indicating that the decreased Plasma AA levels in patients with type 2 diabetes was reversed significantly after treatment with vitamin C along with glucophage compared to placebo with Glucophage, showing better outcome in glycemic control with vitamin C supplementation, and provided a simple means of preventing and ameliorating the complications of diabetes [24]. The combination of vitamin C with Glucophage has been reported to be more effective in reducing the risk of diabetic related long term complications in diabetic mellitus[25]. The presence of flavonoids may be responsible for piloting these activities [1, 4, 23]. A report by Videla [26], indicated a rapid mobilization of liver-ALP in blood, resulting increase serum levels at early stages of liver damage.

Similarly, the extract administration decreases the elevated Alanine Transferase Level. This is attributed to the ability of the antioxidant supplement to balance off free radicals generated hence preventing peroxidation of the lipid components of the cell membrane. Disruption of membrane integrity is a common causative factor attributed to increase release or leakage of cellular contents [27]. This finding is consistent with the reports of Li *et al.* [28].

## V. CONCLUSION

'Sha sha'(Delonix regia) was shown to possess anti diabetic properties and able to ameliorate liver hepatotoxicity effects. Its use especially with vitamin C in the treatment of diabetes mellitus will therefore be beneficial to diabetic patients.

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### Conflict of interest

No conflict of interest associated with this work.

### Contribution of authors

The authors declare that work was done by the authors named in this article and all liabilities pertaining to the claims relating to the content of this article will be borne by the authors.

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