

# Original Research Article

## Effects of *Moringa Oleifera* Leaves Extract on Alloxan- Induced Diabetic Albino Rats

### ABSTRACT

*Moringa oleifera*, popularly known as “miracle tree” belongs to the family, Moringaceae. It is a medicinal plant in which the leaves are the most nutritious part, being a significant source of vitamins and protein among others. This study was conceived and designed based on the gaps in the research that has been performed and what is known about the plant. In this study, the effect of *Moringa oleifera* leaves extract on alloxan induced diabetes in Wistar albino rats was investigated. A total of forty five (45) rats were acclimatized for a period of two weeks, then randomly divided into five (5) groups (1, 2, 3, 4, and 5) of nine (9) rats each and fed with standard feed and water. Group 1 which is the control was fed with just water and standard feed while Hyperglycemia was induced in groups 2, 3, 4, & 5 intra-peritoneally after an over-night fasting using alloxan at a concentration of 130mg/kg b.w. and allowed for 48hours which resulted in a high blood glucose level between 300mg/dl and 600mg/dl. Group 2 was not given any treatment while Groups 3, 4, & 5 were treated with doses 100mg/kg b.w., 200mg/kg bw, and 400mg/kgbw of *Moringa oleifera* leaf extract respectively for a period of three weeks. A glucometer was used to check the blood glucose level of the animals before and after treatment. The results of Groups 3, 4, & 5 ( $172.0 \pm 4.75$ mg/dl,  $142.9 \pm 47.25$ mg/dl,  $70.6 \pm 24.46$ mg/dl respectively) showed a significant decrease ( $p < 0.05$ ) in blood glucose level of the induced rats when compared with Group 2 ( $316 \pm 47.17$ mg/dl) which was induced only alloxan. It can therefore be concluded that this study has shown that the extract of *Moringa oleifera* leaves offers an anti-diabetic effect in Wistar albino rats.

Keywords: (*Moringa oleifera*, Diabetic Rats, Hyperglycemia Alloxan)

## 30 INTRODUCTION

31

32 Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic disorders in  
33 which there are high blood sugar levels over a prolonged period [1]. Symptoms of high blood  
34 sugar include frequent urination (polyuria), glycosuria (presence of glucose in urine) and  
35 hyperglycemia (glucose rate on an empty stomach higher than 1.2g/l in plasma blood and  
36 confirmed in at least two occasions) increased thirst, and increased hunger [2].

37 Basically, there are two major clinical classes of diabetes; type 1 diabetes *mellitus* and type 2  
38 diabetes *mellitus*. If left untreated, diabetes can cause many complications. Acute complications  
39 can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term  
40 complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and  
41 damage to the eyes [1]. Diabetes is due to either the pancreas not producing enough insulin or  
42 the cells of the body not responding properly to the insulin produced [3].

43 According to the International Diabetes Federation [4] 2014 updates, out of the world seven  
44 billion population, 387million people, aged 20–79 years worldwide are diabetic, giving a  
45 comparative prevalence of 8.3%, while 46.3% cases are undiagnosed. In every 7 seconds, a  
46 person dies of diabetes, 4.9 million deaths was recorded in 2014 [4]. Seventy seven percent  
47 (77%) of people with diabetes live in low and middle-income countries. Africa has recorded  
48 cases of 2,150,274 (5.05%) diabetic patients with over 13 million undiagnosed cases. In Nigeria,  
49 there are estimated 374,651 diabetic cases, with another 172,339 undiagnosed cases. These  
50 figures account for about 4.64% Nigerian adults between ages 20-79 living with diabetes. An  
51 estimated 105,090 Nigerians died in 2014 as a result of diabetes [4]. An average diabetic  
52 Nigerian spent about 43527.16 naira (US \$178.39) in 2014 due to diabetes treatment [4]. With

53 this alarming prevalence rate, *diabetes mellitus* poses a major challenge globally and accounts  
54 for a number of disabilities and deaths globally.

55 Medicinal plants have been identified and used throughout human history [5]. Medicinal plants  
56 are plants which can be used for therapeutic purposes or which are precursors for the synthesis of  
57 useful drugs [6]. Many important drugs used in healthcare today are directly derived from plants  
58 due to its bioactive constituents such as; alkaloids, tannins, steroids, etc [5]. Medicinal Plant  
59 materials have been shown to have various chemicals also known as phytochemical at various  
60 concentrations. These phytochemicals play vital roles in the medicinal and otherwise properties  
61 of the plant materials. Plants may act on blood glucose through different mechanisms. Some  
62 plants may contain insulin-like substances [7], inhibit insulinase activity or increase beta  $\beta$ -cells  
63 in the pancreas by activating the regeneration of these cells [8;9] or some may serve as  
64 antioxidants by reducing the oxidative stress due to free radicals in the pancreas [10;11].

65 *Moringa oleifera* is one of the most widely distributed species of the Moringaceae family  
66 throughout the World, especially in Asian countries, having a remarkable range of  
67 pharmacological properties in addition to significant nutritional value. *Moringa* derives from the  
68 Tamil word, '*murungai*', referring to a twisted pod found in young fruit [12]. *M. oleifera* is a  
69 fast-growing, deciduous tree that can reach a height of 10–12 m (32–40 ft) and trunk diameter of  
70 45 cm (1.5 ft). The bark has a whitish-grey color and is surrounded by thick cork while the  
71 shoots have purplish or greenish-white, hairy bark. The tree has an open crown of drooping and  
72 fragile branches. The flowers are fragrant and bisexual, surrounded by five unequal, thinly  
73 veined, yellowish-white petals. The fruit is a hanging, three-sided brown capsule of 20-45 cm  
74 size which holds dark brown, globular seeds with a diameter around 1 cm. The seeds have three  
75 whitish papery wings and are dispersed by wind and water [13].

76 The leaves are the most nutritious part of the plant, being a significant source of B vitamins,  
77 vitamin C, pro-vitamin A as beta-carotene, vitamin K, manganese, and protein, among other  
78 essential nutrients [14]. The therapeutic use of *M. oleifera* leaves has been evaluated in diabetes  
79 because of their possible capacity to decrease blood glucose concentrations after ingestion  
80 because they contains polyphenols such as quercetin-3-glycoside, rutin, kaempferol and  
81 glycosides [15; 16;17]

82 Several biological activities of the *Moringa oleifera* leaves have been reported such as anti-  
83 septic, antioxidant, antihypertensive, larvicidal, fungicidal, hypolipidemic amongst others [18].  
84 Several studies have shown that *Moringa oleifera* leaves presented anti-diabetic properties [17;  
85 19; 20; 21]. Other parts of the plant such as the pods and seed have also shown to exhibit anti-  
86 diabetic property [22].

87 At the moment, there are a growing researches on herbal remedies considered to be less toxic  
88 and have negligible side effect for the management of diabetes mellitus, especially in countries  
89 where access to conventional treatment of the disease is inadequate [23]. The present study  
90 evaluates the anti-diabetic effect of the leaf extracts of *M. oleifera* on alloxan- induced wistar  
91 albino rats with a view to providing more information on the clinical treatment of diabetes.

92

## 93 **MATERIALS AND METHODS**

### 94 **Sample collection and Preparation;**

95 Fresh large quantity of leaves of *Moringa oleifera* plant was gotten from a farm in Elele, River  
96 State, Nigeria. The botanic identification and authentication (MU/PHGSY/05/001) was done in  
97 faculty of pharmacy Madonna University, Elele campus. *Moringa oleifera* leaves were dried  
98 under room temperature and ground with manual grinder. Cold extraction was carried out by

99 soaking 400g of *M. oleifera* leaf powder in 2L of methanol for 72hrs. The mixture was  
100 subsequently filtered using **Whatman** filter paper. The residue was re-extracted in 2L of  
101 methanol for 48hrs and then concentrated using the rotator evaporator and dried. The extract was  
102 stored at -20°C until use.

### 103 **Animal Experiment**

104 A total of 45 albino rats weighing between 120-180g were obtained from the animal house of  
105 Madonna University, Elele, Nigeria and used for the study. They rats were housed in a  
106 photoperiod cycle of 12h:12h (Light and dark), at room temperature (28°C) and fed with  
107 standard laboratory diet and distilled water for a period of two weeks for acclimatization.

108 Groups 2, 3, 4, and 5: were induced with diabetes by the intraperitoneal (IP) injection 130mg/kg  
109 body weight of alloxan monohydrate solution. They rats were assigned into five (5) groups of  
110 nine (9) rats per group as shown below;

111 Group 1: Normal Untreated rats (negative control)

112 Group 2: received Untreated Diabetic rat (positive control)

113 Group 3: Diabetic rats treated with 100mg/kg of leaf extract.

114 Group 4: Diabetic rats treated with 200mg/kg of leaf extract.

115 Group 5: Diabetic rats treated with 400mg/kg of leaf extract

### 116 **INDUCTION OF DIABETES**

117 The baseline blood glucose levels of the rats were determined before they were induced with  
118 diabetes by intraperitoneal (IP) injection of 130mg/kg body weight of alloxan monohydrate  
119 solution [24]. After a period of 48hours, the rats were tested to ascertain the onset of **diabetes**.

120 The blood glucose levels of the animals were determined using an Acc-Check glucometer. The  
121 blood glucose levels of the rats were determined on a weekly basis for four (4) weeks of

122 administration of the extracts. The body weights of the rats before induction, after induction and  
123 at intervals during the extract administration were noted. The treatment was withdrawn after a 28  
124 days regime.

## 125 ADMINISTRATION OF EXTRACTS

126 With the aid of a gavage tube, the prescribed doses of plant extracts were orally administered to  
127 the rats daily, for 28 days of experiment.

## 128 RESULTS

129 The results obtained from the study were expressed as mean  $\pm$  standard deviation and  
130 comparison of differences in their various groups were done using one-way analysis of variance.

131 **Table 1: The mean value of the weight (g) of all the rats treated throughout the**  
132 **experimental period.**

Group	WEEK 1	WEEK 2	WEEK 3	WEEK 4	P-VALUE
1	129.77 $\pm$ 20.52	131.77 $\pm$ 12.09	139.0 $\pm$ 12.86	148.0 $\pm$ 16.59	P>0.05
2	140.77 $\pm$ 18.97	127.33 $\pm$ 5.26	119.5 $\pm$ 10.94	74.77 $\pm$ 14.62	P<0.05
3	119.67 $\pm$ 14.20	110.23 $\pm$ 17.50	110.4 $\pm$ 17.55( $\uparrow$ 0.15)	111.4 $\pm$ 11.30( $\uparrow$ 0.91)	P<0.05
4	124.56 $\pm$ 14.37	116.2 $\pm$ 20.40	117.6 $\pm$ 11.70( $\uparrow$ 1.20)	120.0 $\pm$ 25.36( $\uparrow$ 2.04)	P<0.05
5	119.57 $\pm$ 10.40	108.8 $\pm$ 14.20	112.0 $\pm$ 8.47( $\uparrow$ 2.94)	113.8 $\pm$ 11.90( $\uparrow$ 1.61)	P<0.05

134 Mean  $\pm$  SD. Figures in parenthesis indicate percentage decrease $\downarrow$  or increase $\uparrow$  in body weights.  
135 P<0.05=Significant, p>0.05=Not significant.

136

137 **KEY;** Group 1: Normal Untreated rats (negative control)

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141 Group 5: Diabetic rats treated with 400mg/kg of leaf extract

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143 **Table 2: The mean value of the glucose concentration (mg/kg) of all the rats treated**  
144 **throughout the experimental period.**

Group	Week 1	Week 2	Week 3	Week 4	p-value
1	73.2±8.26	68.2±7.41	71.4±3.67	74.8±14.62	p>0.05
2	70.8±5.12	465.2±79.7	394.2±56.6	316.1±47.17	P<0.05
3	66.3±7.57	460.4±74.46	275.3±92.63(↓40.20)	172.0±45.75(↓37.52)	P<0.05
4	70.9±5.99	477.8±80.75	357.2±140.16(↓25.24)	142.9±47.25(↓59.99)	P<0.05
5	67.7±6.78	495.2±56.19	190.2±63.77(↓61.59)	70.6±24.46(↓62.88)	P<0.05

145 Mean ± S.D. P<0.05=Significant, p>0.05=Not significant. Figures in parenthesis indicate  
146 percentage decrease↓ or increase↑ in blood glucose level within the weeks.

147

148 **KEY;** Group 1: Normal Untreated rats (negative control)

149 Group 2: received Untreated Diabetic rat (positive control)

150 Group 3: Diabetic rats treated with 100mg/kg of leaf extract.

151 Group 4: Diabetic rats treated with 200mg/kg of leaf extract.

152 Group 5: Diabetic rats treated with 400mg/kg of leaf extract

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156 **DISCUSSION**

157 Results from Table 1 shows that the weight of the animals after the induction with alloxan and  
158 during the treatment with *Moringa oleifera* leaf extract revealed that there was no significant  
159 difference between the initial body weights ( $P < 0.05$ ).

160 Whereas the normal rats (group 1) gained weights, the untreated diabetic rats (group 3). This  
161 weight loss could be attributed to the action of diabetes. The ability of alloxan induced diabetes  
162 to induce weight loss in diabetic untreated rats mimics what is commonly observed in clinical  
163 diabetes [1].

164 Within the *Moringa oleifera* treated groups (groups 3, 4 and 5), it would be noticed that there  
165 was an initial loss of weight amongst these groups of rats probably as a result of onset of diabetes  
166 (week two). However, as treatment was introduced, it could be noticed that they rats showed  
167 little weight gain. This suggests a possible short-term positive effect of the extracts on body  
168 weight of diabetic rats. At this point, it could be noticed that group 5 with the highest extract  
169 dose exerted the highest percentage weight gain (2.94%), while group 3 with the lowest extract  
170 dose presented the lowest percentage gain (0.15). This suggests a possible dose dependent  
171 weight gain. It seems that as the dose of *Moringa* was increased, the weight gained increased.

172 At week four, the treated groups continued to gain weight, however the trend in earlier week  
173 didn't continue. Group 4 with the middle extract dose scored the highest percentage weight gain  
174 (2.04%), while group 3 still maintained its lowest percentage weight gain (0.91%). This suggests  
175 that in the long run, a more moderate extract dose would exert a better effect on weight gain.

176 Thereby, suggesting a possible deleterious effect of increased dosage on weight in the long run.

177 The restoration of body weight by *Moringa* seems to be due to its lowering blood sugar  
178 property by increased glucose metabolism, and this may be due to the protective effect of the  
179 extract in controlling muscle wasting, by reversal of gluconeogenesis [25].



180 Diabetic *M. oleifera* treated rats increased in body weight. This result is consistent with previous  
181 studies. Olayaki *et. al.*, [25] observed that oral administration of extract of *M. oleifera* inhibits  
182 weight loss in alloxan induced diabetic rats.

183 Table 2 shows that there is no significant difference ( $p > 0.05$ ) in the glucose levels in all the  
184 groups before diabetes was induced. This implies that the blood Glucose level in all groups  
185 before induction of diabetes is comparable.

186 The blood glucose level at week 1 shows that there is no significant difference in the mean  
187 glucose levels ( $p > 0.05$ ) among the Groups. Group 2 and Group 4 had near same blood glucose  
188 levels ( $70.8 \pm 5.12$  mg/kg and  $70.9 \pm 5.99$  mg/kg respectively), while Group 3 and 5 had similar  
189 glucose levels ( $66.3 \pm 7.57$  mg/kg and  $67.7 \pm 6.78$  mg/kg respectively). Group 1 had the highest  
190 blood glucose level ( $73.2 \pm 8.26$  mg/kg).

191 At week two, there is a significant different between Group 1 and the other groups signifying  
192 diabetes. Within the diabetic Group, there is no significant difference between them.

193 At the end of week three, within the diabetic Groups, Group 2 indicated the highest mean blood  
194 glucose level ( $394.2 \pm 56.6$  mg/kg). All rats treated with *Moringa Oleifera* presented an  
195 appreciable level of percentage decrease in their blood glucose showing a possible anti-diabetic  
196 effect. Within the *Moringa oleifera* treated Groups, from table 2, Group 5 presented the highest  
197 percentage decrease in blood glucose level ( $\downarrow 61.59$ ). This probably indicates that higher doses of  
198 *Moringa oleifera* can reduce blood glucose more than lower doses, indicating a dose dependant  
199 relationship.

200 At the end of the fourth weeks of treatment (tab.2), there is no significant difference ( $p > 0.05$ )  
201 between Groups 1 and 5 ( $74.8 \pm 14.62$  mg/kg and  $70.6 \pm 24.46$  mg/kg). Within the diabetic Groups,  
202 Group 2 indicated the highest mean blood glucose level ( $316.1 \pm 47.17$  mg/kg). Groups 3, 4, and 5

203 treated with *Moringa oleifera* presented percentage decrease in their blood glucose (↓37.52,  
204 ↓59.99 and ↓62.88 respectively) showing an anti-diabetic property of the plant sample. Within the  
205 *Moringa oleifera* treated Groups, from table 2, Group 5 presented the highest percentage  
206 decrease in blood glucose level (↓62.88), while Group 3 with lowest dose showed the smallest  
207 percentage decrease (↓37.52). This pattern tends to show that as the dose is reduced, the anti-  
208 diabetic property of the leaf is reduced.

209 As shown in the Table above, *Moringa oleifera* exerted an blood glucose lowering activity on  
210 diabetic rats. Groups with higher doses presented a better percentage decrease showing the  
211 possibility that higher doses can reduce blood glucose more than the smaller doses.

212 The hypoglycemic effect of *Moringa Olifera* leaf observed in the present study agrees with  
213 results of earlier studies.

214 This finding collaborates with the report of Sai *et al* [27] which clearly revealed that aqueous  
215 extract of *M. oleifera* leaf possesses potent antihyperglycemic and antihyperlipidemic effect in  
216 both insulin resistant and insulin deficient rat models. Similarly, after treating diabetic rats with  
217 both aqueous and ethanolic extracts of *Moringa* leaf for 14 days, Ezeigbo *et al* [19], reported a  
218 percentage reduction of 45.2% and 33.7% respectively in blood glucose of the diabetic rats.

219 In another study by Olayaki *et al.*, [26], they observed that oral administration of extract of *M.*  
220 *oleifera* significantly reduces blood glucose concentration. Studying the effect of the  
221 consumption *Moringa* by diabetic rats, Villarruel-López *et al* [21] reported that consumption of  
222 the leaves showed a hypoglycemic effect in diabetic rats. A further research by Lopez *et al*  
223 showed that the tested doses revealed no lethal dose and no significant differences in  
224 genotoxicity parameter. Another study by Basyony *et.al.*, [20] suggested that *Moringa oleifera*  
225 seeds extract was able to reverse the inhibit ion of insulin secretion from the pancreatic beta cells

226 and reduced the blood glucose level. Furthermore, Ghiridhari *et. al.* [28] reported that medication  
227 with *M. oleifera* gives diabetic patients better glucose tolerance by increasing treatment time.

228 The anti-diabetic effects of *Moringa* leaf extracts indicate the presence of hypoglycaemic agents  
229 in the plant. *M. oleifera* contains three classes of phytochemicals, that is, glucosinolates such as  
230 glucomoringin, flavonoids such as quercetin and kaempferol, and phenolic acids such as  
231 chlorogenic acid; all of these classes have medicinal benefits [29;30]. These three  
232 phytochemicals of *Moringa* possess antioxidant, hypoglycemic, hypotensive, antidyslipidemic,  
233 anticancer, and anti-inflammatory properties [31; 32; 33]. Hypoglycemic effect of *Moringa* leaf  
234 may probably be due to contents of elements such as calcium, magnesium, potassium, sodium,  
235 zinc, chromium [34]. These elements play role in blood glucose homeostasis by regulating the  
236 key enzymes involved in gluconeogenesis in the liver e.g. glucose-6- phosphatase, fruitcose-1, 6-  
237 bisphosphatase and phosphoenolpyruvate carboxykinase, thereby blocking gluconeogenesis  
238 and enhancing glucose utilization in the body [34]. The leaf may also contain certain  
239 hypoglycemic agents such as phytochemicals like tannins. It might also contain insulin  
240 stimulatory substances such as insulin receptors substrate (IRS), glycogen synthase, the  $\beta_3$   
241 adrenergic receptor, glucose dependent insulinotropic polypeptide (GIP) receptor [34].  
242 However, the mechanism by which the extract lowered the blood glucose level in alloxan  
243 induced diabetic rats is still unclear. It could be by stimulating peripheral utilization of glucose  
244 by inhibiting absorption in the gastrointestinal tract (GIT), increasing glucose metabolism, or  
245 regenerating the pancreatic tissue or potentiating the insulin secretion by the surviving B- cells  
246 [35]. It has been established that alloxan monohydrate destroys the pancreatic  $\beta$ -cells [36, 37]  
247 hence, *M. oleifera* leaf extract might exhibit anti-diabetic property by the regeneration of  $\beta$ -cells

248 to release insulin [38; 39]. This ameliorates the effect of the alloxan and thereby normalizes the  
249 elevated serum level of glucose [38].

250 Reports from several studies have also shown that diabetes can be managed by herbal approaches  
251 with results comparable with the result obtained in the present study. A 2018 study on  
252 hypoglycaemic and biochemical effects of the aqueous and methanolic extract of *Persea*  
253 *americana* seeds on alloxan-induced albino rats by Ejiofor *et al* [40] concluded that The effects  
254 of different doses (200mg/bw, and 300/bw) of both water and methanol extracts of *P.*  
255 *americana* seed were comparable to those of a reference drug, insulin. About 94% seed diet of  
256 *Acacia arabica* showed hypoglycemic effect in rats through release of insulin. *Acacia arabica*  
257 seed powder at 2, 3 and 4g/kg. b.wt., exerted a significant hypoglycemic effect in normal rabbits  
258 by stimulating the release of insulin from pancreatic beta cells [41]. Plants such as *Gallega*  
259 *officinalis* [42; 43; 44] *Syzygium cumini* [45; 46], are reported to have anti diabetic properties.  
260 Interestingly, these studies were carried out with different parts of the plants such as seed, leaves  
261 and even flower. Anti hyperglycemic activity of *Allium sativum* (garlic) was reported to be most  
262 potent when administered at 0.25 mg/kg b.wt dose level which was due to increased insulin-like  
263 activity [47]. Oral administration of the juice, ethanol extract, and oil of *A. sativum* has  
264 remarkably blood sugar lowering effect in normal and alloxan-induced diabetic rats or rabbit  
265 suggesting stimulation of insulin secretion from parital cells of pancreas [48].

## 266 **CONCLUSION**

267 Results from this study indicate indicates that extracts of *M. oleifera* leaf exerts significant anti-  
268 diabetic property in rats. These observations provide a pharmacological basis for the traditional  
269 use of *M. oleifera* leaf in the management of diabetes mellitus. However, further studies are

270 required to identify the active ingredient responsible for the anti-diabetic properties of the leaf  
271 extract.

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