

Study of the effect of *Moringa oleifera* leaves powder in Southwestern Algerian diabetic patients: a pilot clinical trial

Sarra HENOUDA^{1*}, Saida KAROUCHE², Amina ATTOU¹,
Ahmed BOULAL¹

¹University of Ahmed Draia, Faculty of Science and Technology, Laboratory of Saharan Natural Resources, Adrar 01000, Algeria; sarra.henouda@univ-adrar.edu.dz (*corresponding author); ami.attou@univ-adrar.edu.dz; ahm.boulal@univ-adrar.edu.dz

²Larbi Ben M'Hidi University, Department of Natural and Life Sciences, Laboratory of Natural Substances, Biomolecules and Biotechnological Applications, Oum El Bouaghi, Algeria; saidabmc86@yahoo.fr

Abstract

Moringa oleifera Lam. leaves are commonly used for diabetes worldwide. To date, there has been no research study done to investigate its effect on lipid and carbohydrate profile in Algerian diabetic patients. This pilot clinical study aimed to evaluate its long term-effect on lipid and carbohydrate profile in Algerian diabetic patients in preparation for a larger trial. 44 diabetic patients from Adrar city were administrated with 3600 mg of MO leaves powder twice a day at breakfast and at 7 p.m. for a period of 90 consecutive days, along with their regular hypoglycemic medications, in order to evaluate their serum lipid (TC, C-HDL, C-LDL and TG) and carbohydrate profile (blood sugar and HbA1c), weight, BMI and blood pressure, across five time-points (on days 0, 3, 7, 30, and 90). The results showed that oral administration of *Moringa oleifera* powder had a statistically significant effect on blood sugar (HbA1c), LDL-C, HDL-C levels in diabetic patients ($p < 0.05$). *Moringa oleifera* leaf powder seemed reduced LDL-C, and HbA1c and elevated HDL-C, in diabetic patients. No side effect was reported by any participant. However, it did not have a statistically significant effect on weight, BMI and blood pressure. The data from the present clinical trial provide persuasive, although preliminary evidence supporting the therapeutic potential of *Moringa oleifera* leaf powder for managing chronic hyperglycemia and dyslipidemia in Algerian patients with diabetes. A more extensive trial is necessary to determine the *Moringa oleifera* leaf powder optimal dose and evaluate if its effect results into long-term advantages. In addition, further investigations are required to clear the underlying mechanisms involved with these effects.

Keywords: Algeria; diabetic; leaves powder; *Moringa oleifera*

Abbreviations: 95% CI: 95% Confidence Interval; BG: Blood Glucose; BMI: Body Mass Index; HbA1c: Hemoglobin A1c; HDL-C: High-density lipoproteins; IDF: International Diabetes Federation; LDL-C: Low Density Lipoproteins; MO: *Moringa oleifera*; SBP/DBP: systolic/diastolic blood pressure; SD: Standard Deviation; TC: Total Cholesterol; TG: Triglycerides; W: Weight.

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Introduction

Diabetes is a chronic metabolic disorder that affects lipid, carbohydrate, and protein functions, resulting in persistent hyperglycemia, arising from abnormal insulin secretion, insulin action, or both, causing slow damage (Weyer *et al.*, 1999), which leads over time to severe damage to the heart, blood vessels, eyes, kidneys and nerves (WHO, 2023). The incidence of diabetes has increased exponentially over the years and is projected to rise above 783 million by 2045 in adults between the age of 20-79 (vs. 463 and 537 million in 2019 and 2021, respectively), likewise, the mortality death was found to increase and approximately 6.7 million adults are estimated to have died as a result of diabetes or its complications in 2021 (Saeedi *et al.*, 2019; IDF 2021). According to the IDF (2021), the prevalence of diabetes in Algeria has been increased to 7.4% in 2021 in adults aged 20-79 years. In addition, Algeria is one of the top ten countries in the world for both the number of children with type 1 diabetes and the number of new cases of type 1 diabetes. Algeria ranks among the top ten countries globally in terms of both the number of children with type 1 diabetes and the number of new cases of type 1 diabetes. Therefore, enhancing the management of diabetes is still a major public health concern at the national level.

The WHO appraised that more than 80% of people worldwide are estimated to use traditional medicine (WHO, 2023). In the last years, the high cost of prescription medications, particularly for impoverished populations, especially in developing countries, and in particular, their detrimental side effects have led to an increase in herbal medicine use (Nicolle *et al.*, 2011; Yuan *et al.*, 2016). In rural areas, financial barriers to accessing medications and to achieving optimal health are even greater; most of the population in the Adrar region cannot easily access modern medicines and prefer to use herbal medicine as the first line treatment. Therefore, there will always be the need to search for cost-effective and efficient hypoglycemic agents with fewer side effects.

MO (Family: Moringaceae) (Olson, 2002) is one of the medicinal plant widely used in recent years. Various parts of this plant such as the leaves, roots, seed, fruit have been extensively studied for their many therapeutic potential such as antitumor, antiuroliathatic, antifertility, hypotensive, analgesic, antipyretic, antiepileptic, hypocholesterolaemic, antifungal, antibacterial, antifungal, aphrodisiac, cholagogue, antioxidant, hepatoprotective, immunomodulators, cardiogenic and as cardiac and circulatory stimulants (Karadi *et al.*, 2006; Martín *et al.*, 2013; Al-Asmari *et al.*, 2015; Saini *et al.*, 2016; Mabrok and Mohamed, 2019). Furthermore, MO is used worldwide (in Bangladesh (Kadir *et al.*, 2012), South Africa (Semenya *et al.*, 2012), Senegal (Dièye *et al.*, 2008; Yousefian, 2012), Nigeria (Popoola and Obembe, 2013), Ugandan rural (Kasolo *et al.*, 2010) as a popular remedy for diabetes.

The leaves are the most explored part of the tree due to the presence of various nutrients such as essential amino acids, minerals, vitamins and carbohydrates (Vergara-Jimenez *et al.*, 2017). They are also characterized by a low calorific value, which makes them suitable for the diet of overweight people (Gopalakrishnan *et al.*, 2016). Bioactive compounds that are present in its leaves are alkaloids, flavonoids, phenolic compounds, tannins, saponins, lignin, amides, glycosides, carotenoids (Kashyap *et al.*, 2022), which play an important role in stabilizing blood pressure and BG levels in diabetic patients (Padayachee and Bajjnath, 2020).

MO leaves non-toxicity *in vivo* has been confirmed in many studies (Mbikay, 2012). No acute or sub-acute toxicity was reported following treatment with MO leaves, even at doses of 2000 mg/kg (Adedapo *et al.*, 2009), According to Barichella *et al.* (2019), a daily dose of 14 g was safe and well accepted. Hence, the plant is relatively safe both for nutritional and medicinal uses (Adedapo *et al.*, 2009). No report contradicting this evidence was found in the scientific literature. In addition, it should be noted that the plant is already used as food.

Medicinal plants local knowledge remains poorly documented in scientific literature. MO one of these medicinal plants which is used for antidiabetic purpose in the area. The present study is a scientific approach to reestablish the traditional uses of MO in Algerian South Eastern and to evaluate its hypoglycemic,

hypolipidemic, hypotensive and weight-loss potentialities. We aimed to conduct a pilot approach of the MO leaves powder effect on the lipid (TC, C-HDL, C-LDL and TG) and carbohydrate profile (BG and HbA1c) among Algerian South Eastern diabetic patients. Another objective of the present study was to test whether it was possible to recruit and retain patients to such a study for further studies.

Materials and Methods

Collection and preparation of plant materials

Moringa is the most popular plant found in southern Algeria (Boulal *et al.*, 2019; Boulal *et al.*, 2020). The *Moringa oleifera* L. leaves used in our study, which were identified by botanists from our university, were collected from mid-March to early April 2021-2022 from the Adrar region, located in the central part of the Sahara in southwestern Algeria (Figure 1). They were washed with tap water, shade dried, milled and ground into powder with the help of a mixer. The measured powder (3600 mg/day for each patient) was stored in hermetically sealed glass jars and kept in a dry place.

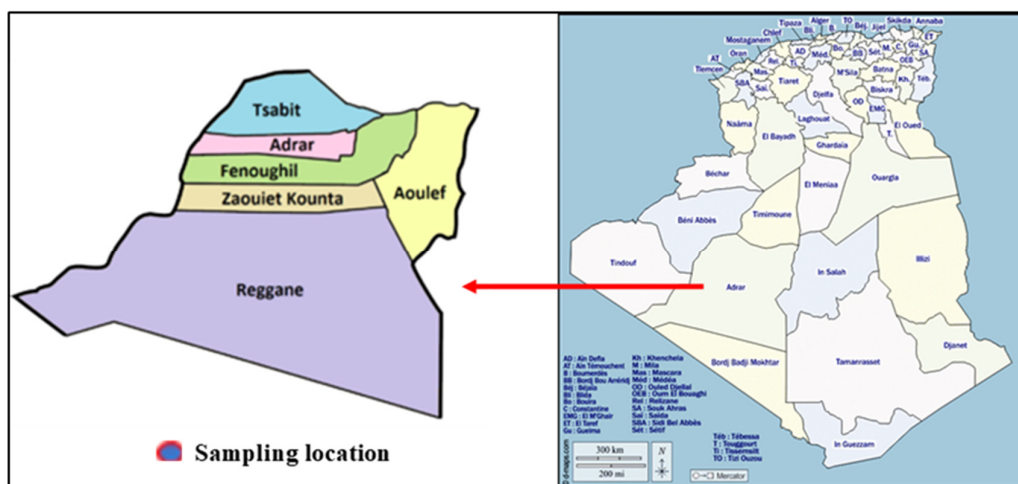


Figure 1. Presentation of the MO leaves collection site (Boulal *et al.*, 2021)

Patients and ethical issues

We recruited 44 diabetic volunteers from Adrar city, 1200 km south of Algeria. Diabetic patients were excluded if they had any major cardiac, respiratory, renal, liver or mental disease; or if they had any allergy to MO leaves powder. Eligible patients had to be ≥ 18 years old. All patient detailed data regarding personal and medical history of diabetes were gathered on individual interview. Clinical characteristics were collected from medical records. All selected patients were informed about study objectives and allowed an opportunity to ask questions, they were ensured of the confidentiality of information, and then they gave their signed informed consent for inclusion before participating in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the hospital where the participants were recruited. The study was carried out from February 2021 to June 2022.

Study on long-term effect of MO on serum biochemical parameter levels, weight, BMI, and blood pressure

Diabetic patients were asked to take 3600 mg of MO leaves powder twice a day, in the morning with breakfast and in the evening at 7 p.m. for 90 days. Participant's hypoglycemic medications were not altered and they were instructed to maintain their usual nutritional habits throughout the study. On days; 0, 3, 7, 30, and 90 the blood samples were collected in order to assess the lipid (TC, C-HDL, C-LDL and TG) and

carbohydrate profile (BG and HbA1c). The body weight, BMI and HTA of each patient were also measured. Patients were asked about any symptoms.

Assay of serum biochemical parameters levels

Fasting BG, C-HDL, C-LDL and TG were determined using automated chemistry analyzer/Mindray® BS-240.

Assay of HbA1c levels

HbA1c was determined using automated HPLC method/MEDCONN® (MQ-2000 PT).

Statistical analysis

Data were analysed using SPSS 26 (IBM). Continuous variables are presented as means and standard deviations, whereas categorical variables are presented as numbers and frequencies. Normality and homogeneity checks were carried out on the residuals using Shapiro-Weilk test and Levene/Bartlett test. Repeated measures ANOVA or Freidman test were used to determine the effect of MO powder on serum biochemical parameters levels, weight, BMI and HTA across time-points (D_0 , D_3 , D_7 , D_{30} , and D_{90}) according to application condition, then post-hoc comparisons were used to determine the source of significant differences where appropriate.

Dependent Sample t-Test was used to compare the effect of MO powder on HbA1c rate. $p < 0.05$ was considered statistically significant with 95% confidence intervals (CIs).

Results

Participants

A total of 44 diabetic patients were enrolled in this study. Sociodemographic characteristics of diabetic participants are summarized in Table 1. The current study diabetic group included more women (sex ratio; 0.375). The mean age of the women was higher than that of the men (52.41 ± 14.895 vs. 47.50 ± 14.463 years). Furthermore, the percentage of subjects currently smoking or having previously smoked was low compared to those who never smoked (6.8 % vs. 93.2%, respectively). Smoking habits did not appear to be a significant contributor to variations in serum biochemical parameters levels of lipid (TC, C-HDL, C-LDL and TG) and carbohydrate profile (BG and HbA1c), and to variations in weight, BMI and BP, on D_0 , D_3 , D_7 , D_{30} , and D_{90} , in this cohort ($p > 0.05$). The percentage of patients who never attended school was relatively high compared to those who were schooled (18.2% vs. 81.8%, respectively). However, it was feasible to recruit and retain patients to this study, even if it was not easy, despite the high number of participants with a low educational level (≤ 9 years of school: 75%), but they participated significantly in the group. No major side effects were reported by any subject except for some gastric issues seen during the first few days of treatment.

Effect of MO powder on BG

BG of diabetic participants was on average about 0.29 g/L lower after 90 days of MO powder administration, the results are summarized in Table 2. However, the results for the repeated measures ANOVA indicate that no significant time effect of MO leaves powder on BG levels for diabetic patients (BG_{D_0} : $1.89 \pm 0,652$ (0.90-3.56 g/L) vs. $BG_{D_{90}}$: 1.60 ± 0.573 (0.71-2.99 g/L) $p > 0.05$).

Effect of MO powder on HbA1c rate (%)

Table 2 shows the differences among baseline measurement of HbA1c diabetic patients, which was taken at the start of the study (D_0) and a final reading that was taken on the ninetieth day (D_{90}) ($HbA1c_{D_0}$: 10.03 ± 2.187 (6.20 - 15.10) vs. $HbA1c_{D_{90}}$: 9.20 ± 1.702 (6.5-13.10), $p=0.000$). MO powder leaves has a

statistically significant effect on HbA1c values of diabetic patients. The present results indicate that long-term administration of MO powder leaves decreases hyperglycemia in diabetic patients.

Effect of MO powder on TC

In the present study group, TC values progressed downwardly over time, but the change was not statistically significant. Thus, MO powder leaves administration has no statistically significant effect on patients' serum TC levels (TC_{D0}: 1.71 ± 0.454 (0.92-3.09) vs. TC_{D90}: 1.67 ± 0.398 (1.03-3.01), $p > 0.05$) (Table 2).

Table 1. Participant's characteristics

| | |
|----------------------------|--|
| Mean age in years (SD) | 51.07 ± 14.776 (29-84) |
| Gender | |
| Men N, (%) | 12 (27.3) |
| Women N, (%) | 32 (72.7) |
| Sex ratio | 0.375 |
| Family status, N (%) | Married 36 (81.8) Single 1 (2.3) Divorced 2 (4.5) Widow 5 (11.4) |
| Profession, N (%) | Active 19 (43.18) Inactive 25 (56.81) |
| Regular Exercise, N (%) | Yes 12 (27.3) No 32 (72.7) |
| Education level, N (%) | Never attended school 8 (18.2) Mosque 7 (15.9) Primary/middle school 18 (40.9) Secondary 7 (15.9) University 4 (9.1) |
| Smoking status, N (%) | Never smoking 93.2% Ever smoking 2.3% Current smoking 4.5% |
| Diabetes duration (months) | 78.55 ± 58.668 (2-300) |
| Side effect, n (%) | Yes 5 (11.36) gastric problem (nausea) No 39 (88.63) |

Table 2. Effect of MO powder leaves on day 90 serum biochemical parameters levels in diabetic subjects

| Biochemical parameters (g/L) | | | | | | |
|------------------------------|------------------------------|-----------------------------|-------------------------------|------------------------------------|-----------------------------|---|
| Days | Blood sugar (0.6-1.10) r | TC (< 2.00) r | LDL-C (< 1.50) r | HDL-C (> 0.55) r | TG (0.35-1.35) r | HbA1c (%) ND < 6 CD < 7 UD > 8 |
| D0 | 1.89 ± 0.652 (0.90-3.56) | 1.71 ± 0.454 (0.92-3.09) | 0.97 ± 0.364 (0.30-1.89) | 0.43 ± 0.139 (0.17-0.99) | 1.16 ± 1.121 (0.32-6.75) | 10.03 ± 2.187 (6.20-15.10) |
| D3 | 1.82 ± 0.581 (0.73- 3.27) | 1.64 ± 0.393 (0.91-2.66) | 1.04 ± 0.383 **(0.24-2.30) | 0.37 ± 0.134 (0.13-0.90) | 1.06 ± 0.926 (0.26-5.30) | / |
| D7 | 1.78 ± 0.628 (0.70-3.15) | 1.68 ± 0.439 (0.62-2.80) | 0.87 ± 0.429 * (0.05-2.35) | 0.41 ± 0.199 (0.06-0.93) | 1.15 ± 0.882 (0.26-5.18) | / |
| D30 | 1.80 ± 0.640 (0.71-3.09) | 1.63 ± 0.383 (0.82-2.45) | 0.63±0.399 A (0.01-1.34) | 0.68±0.422 abc (0.17-2.17) | 1.11±0.789 (0.14-4.80) | / |
| D90 | 1.60±0.573 (0.71-2.99) | 1.67 ± 0.398 (1.03-3.01) | 0.81 ± 0.423 (0.01-1.64) | 0.55 ± 0.234 def (0.30-1.37) | 1.33 ± 0.676 (0.58-4.00) | 9.20 ± 1.702 *** (6.5-13.10) |

R: reference values; ND: Non-diabetic; CD: controlled diabetes; UC: Uncontrolled diabetes.

LDL-C (A, D₃ vs D₃₀ p = 0.001**; B, D₇ vs D₃₀ p = 0.027*; D₀ vs D₃₀ p = 0.002**.

HDL-C (a, D₃ vs D₃₀ p = 0.002**; b, D₇ vs D₃₀ p = 0.027*; c, D₀ vs D₃₀; p = 0.01*; d, D₃ vs D₉₀; p = 0.000***; e, D₇ vs D₉₀; p = 0.006**; f, D₀ vs D₉₀; p = 0.03*)

*p < 0.05; ** p < 0.01; *** p < 0.0001

Effect of MO powder on LDL-C

During the twelve weeks MO powder leaves treatment, LDL-C levels of diabetic patients were measured on D₀, D₃, D₇, D₃₀, and D₉₀, and the results are summarized in Table 2. Normality checks were carried out on sample data, which were normally distributed. Repeated-measures ANOVA with a Greenhouse-Geisser correction showed that mean LDL-C concentrations differed significantly across five time points [F(3.179, 111.256) = 8.683, p = 0.000] (LDL-C_{D0}: 0.97 ± 0.364 (0.30-1.89) vs. LDL-C_{D90}: 0.81 ± 0.423 (0.01-1.64)). Post hoc analysis using the Bonferroni correction revealed that LDL-C values were statistically significantly decreased by 0.414 g/L between D₃ and D₃₀ (95% CI, p = 0.001), then reduced by 0.239 g/L between D₇ and D₃₀ (95% CI, p = 0.027), finally decreased by an additional 0.341 g/L on D₃₀ (95% CI, p = 0.002). No other differences are significant.

Effect of MO powder on HDL-C

Diabetic participants used MO powder leaves for 90 consecutive days. Their HDL-C was measured before the special diet, after 3, 7, 30 and 90 days. Normality checks were carried out on data, which were approximately normally distributed. A repeated measures ANOVA with a Greenhouse-Geisser correction was performed to compare the effect of MO powder leaves on HDL-C values of diabetic participants. The results (Table 2) show that there was a statistically significant effect of MO powder leaves on HDL-C concentrations (F(ddl=1.65, 61.061)=10.402, p = 0.000) (HDL-C_{D0}: 0.43 ± 0.139 (0.17-0.99) vs. HDL-C_{D90}: 0.55 ± 0.234 (0.30-1.37)). Post hoc test using the Bonferroni correction showed an increased HDL-C levels between the initial assessment (D₀) and follow-up assessment 30 days later by an average of 0.253 g/L (0.43 ± 0.139 vs 0.68±0.422, p = 0.01 respectively) and then increased by 0.123 g/L between D₀ and D₉₀ (p = 0.03). Therefore, we can conclude that the results of repeated measures ANOVA indicate a significant temporal effect of treatment with MO powder leaves on increasing HDL-C levels of diabetic patients.

Effect of MO powder on TG

The MO powder leaves treatment has no statistically significant effect on serum TG levels in diabetic patients (TG_{D0}: 1.16 ± 1.121 (0.32-6.75 g/L) vs. TG_{D90}: 1.33 ± 0.676 (0.58-4.00 g/L), p>0.05 (=0.052) (Table 2). It should be noted that diabetic patients with moderate to severe hypertriglyceridemia at D₀ had significantly decreased serum TG levels with MO powder administration by the end of the study (TG_{D0}: 4.06 vs. TG_{D90}: 1.86 and TG_{D0}: 6.75 vs. TG_{D90} 4 g/L, respectively).

Effect of MO powder on weight

Change in body weights in diabetic patients is shown in Table 3. MO powder leaves has no statistically significant effect on patients' weights (W_{D0}: 74.69 ± 12.044 (45-105 kg) vs. W_{D90}: 73.69 ± 11.839 (50-101kg), p>0.05). However, administration of MO powder leaves for 90 days improved the weight gain in diabetic patients who were underweight.

Effect of MO powder on BMI

The study cohort showed a non-statistically significant BMI reduction at the end of the study, following oral administration of MO leaves powder (BMI_{D0}: 28.47 ± 4.701 (16.53-39.45) vs. BMI_{D90}: 28.07 ± 4.487 (18.37-38.21) p>0.05) (Table 3).

Effect of MO powder on blood pressure

Patients in this cohort presented non-significant SBP/DBP reductions, following oral administration of MO leaf powder, at the end of the study (BP_{D0}: 134.87 ± 22.927/78.46 ± 11.130 (100-190/60-100 mm Hg) vs. BP_{D90}: 126.41 ± 15.302/97.18 ± 11.7315 (90-160/50-800 mm Hg), p>0.05, Table 3).

Table 3. Effect of MO on day 90 weights, BMI and HTA in diabetic patients

| | Wight (kg) | BMI (kg/m ²) | HTA (mm Hg) |
|-----|----------------------------|--------------------------------|--|
| D0 | 74.69 ± 12.044 (45-105) | 28.47 ± 4.701 (16.53-39.45) | 134.87 ± 22.927/78.46 ± 11.130 (100-190/60-100) |
| D3 | 74.72 ± 12.087 (45-105) | 28.48 ± 4.737 (16.53-39.86) | 131.54 ± 20.843/76.67 ± 11.773 (100-190/50-100) |
| D7 | 73.79 ± 12.254 (45-105) | 28.12 ± 4.736 (16.53-39.45) | 131.79 ± 22.580/76.67 ± 10.345 (100-190/50-100) |
| D30 | 73.51 ± 11.573 (49-101) | 28.01 ± 4.473 (18-39.04) | 128.97 ± 21.126/74.36 ± 10.207 (100-190/60-100) |
| D90 | 73.69 ± 11.839 (50-101) | 28.07 ± 4.487 (18.37-38.21) | 126.41 ± 15.302/97.18 ± 11.7315 (90-160/50-800) |

Discussion

We successfully enrolled and maintained participation of diabetic patients in a trial that explored the effects of MO leaves powder on serum biochemical parameters levels and also on weight, BMI and blood pressure, for 90 days across five time points (D₀, D₃, D₇, D₃₀, and D₉₀). The choice of the posology (Sissoko *et al.*, 2020) and the duration of its administration was based on scientific evidence, the advice of the diabetologists following the diabetic participants as well as the traditional healers in the region. No adverse effects were reported. Based on various searches, this is the first scientific report evaluating the potential of MO leaves powder as antidiabetic, hypolipidemic, weight loss and antihypertensive agent originated from Algeria.

Hypoglycemic effect

At 90-day follow-up, treatment with MO leaves powder resulted in a lower glycemic response in diabetic patients, with no statistically significant differences. There was a trend, though not significant, toward a difference in reducing the rise in BG. These data, stemming mainly from the results of small sample study, suggest information on the hypoglycemic potential of MO leaf powder, require larger sample size to confirm this effect. A larger study of diabetic patients is needed to confirm this effect, and to investigate whether a larger dose would have a greater effect. However, daily administration of MO leaf powder for a period of 90 days had a statistically significant effect on HbA1c values ($p = 0.000$), indicating that MO medication can induce with time better carbohydrate balance. It would also be interesting to evaluate its effect on postprandial BG levels in diabetic patients.

Several studies in diabetic rats have shown that MO leaf extracts have antidiabetic effect (Kar *et al.*, 2003; Momoh *et al.*, 2013), which might be mediated through the stimulation of insulin release leading to enhanced glucose uptake and glycogen synthesis (Olayaki *et al.*, 2015). Among the MO leaves investigated compounds, alpha glucosidase inhibitor is a very crucial one in regulating carbohydrate and lipid metabolism (Raptis and Dimitriadis, 2001; Adisakwattana and Chanathong, 2011). Moreover, qualitative phytochemical analysis of MO leaves has shown that they are also composed of proteins, dietary fibers, micro-minerals, flavonoids and triterpenoids, which are very effective in reducing blood sugar (Leone *et al.*, 2015). A daily intake of MO leaves powder may help to prevent hyperglycemia and hyperlipidemia.

Hypolipidemic effect

The results of this study showed that the administration of MO powder leaves (3600 mg, twice a day) to diabetic patients for a period of 90 days seemed decrease the serum LDL-cholesterol values ($p=0.004$), which exhibited significant hypolipidemic effect on the 3rd, 7th, 30th days after treatment, suggesting that the MO powder leaves has role in management of hyperlipidemia on chronic administration that does not reach three months. But not those of total cholesterol and TG, this could be due to the reduced number of patients compared to studies which have confirmed its important role in the reduction of these two lipid parameters. However, treatment of diabetic patients with MO powder leaves in the present study showed a significant increase in HDL levels. Hypercholesterolemia is one of the major risk factors for coronary and cardiovascular diseases in diabetic patients (Ravi *et al.*, 2005). In spite of the availability of several anti-hyperlipaemic agents, there is increase in their incidence and risk of congestive heart failure. Therefore, there is still considerable interest in the evaluation of new synthetic and herbal anti-hyperlipidemic agents. Preclinical studies suggest that MO powder leaves may have a lipid-lowering activity (Ghasi *et al.*, 2000; Mehta *et al.*, 2003), which could reduce this risk. Increased HDL values are one of the required criteria of a good cholesterol-lowering agent that associated with a lower risk of heart disease. The hypolipidemic effect of MO leaves is due to the presence of the sterols, particularly β -sitosterol that appears to be a bioactive leaf phytoconstituent responsible for its hypolipidemic potential (Rajanandh and Kavitha, 2010). β -sitosterol lowers the cholesterol level by lowering plasma LDL concentration and by inhibiting the cholesterol reabsorption from endogenous sources in association with simultaneous increase in its excretion into faeces in the form of neutral steroids (Ghasi *et al.*, 2000). For the more, the MO leaves contain vitamin C, flavonoids and triterpenoids that are very effective to regulate lipogenesis in liver and control BG and cholesterol levels (Leone *et al.*, 2015). The change in the lipid profile with MO powder leaves treatment may contribute to the decreased incidence of atherosclerosis, cardiovascular and coronary heart disease. Further investigations are needed to confirm these results and to specify the appropriate dose and duration of treatment to have its ideal cholesterol-lowering effect. In addition, exploration of circulating biochemical inflammatory markers should be performed, as the balance of pro and anti-inflammatory cytokines could assess the risk of complications, monitor disease progression, and guide treatment decisions of both diabetes and atherosclerosis (Barbu *et al.*, 2022).

MO leaves are particularly interesting as a potential dietary intervention for diabetic patients with no risk of toxicity. Giving MO leaf powder in capsules might be more convenient. Pending the results of further research, it is best to encourage diabetic patients to incorporate MO into their daily diet if they are not already doing so.

Limitations

This was a small pilot study due to logistical difficulties and the mentality of patients in the region because they are not used to participating in this type of study. This is the first pilot study in the Adrar region.

Conclusions

The results of this study concluded that MO leaves powder, administered twice a day, seemed to reduce serum biochemical parameters levels in diabetic patients, particularly it had a significant effect in lowering long-term high blood sugar levels (HbA1c rate). It seems that the MO leaf powder has long-term effect in diabetic patients. Further investigations and clinical studies should be done with more diabetic patients to confirm the results obtained, and studying other parameters influencing the lipid and glycemic profile as well as the study of the reduction of long-term complications of diabetes. Intervention to prevent diabetes should target both abnormalities defects in insulin secretion and insulin action. Additionally, the bioactive constituent should also be identified.

Authors' Contributions

Conceptualization: SH, SK and AB; Data curation: SH and AA; Formal analysis: SH and AA; Funding acquisition: SH; Investigation: SH and AA; Methodology: SH, SK, AA and AB; Project administration: SH and AB; Resources: SH and AB; Supervision: SH, SK, AA and AB; Validation; Visualization: SH, SK and AB; Writing - original draft: SH, SK and AA; Writing - review and editing: SH, AA and AB. All authors read and approved the final manuscript.

Ethical approval (for researches involving animals or humans)

This study received approval no. 61/2021 from the Ethics Committee of Tililane hospital.

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Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

References

- Adedapo AA, Mogbojuri OM, Emikpe, BO (2009). Safety evaluations of the aqueous extract of the leaves of *Moringa oleifera* in rats. *Journal of Medicinal Plants Research* 3:586-591.
- Adisakwattana S, Chanathong B (2011). Alpha-glucosidase inhibitory activity and lipid-lowering mechanisms of *Moringa oleifera* leaf extract. *European Review for Medical and Pharmacological Sciences* 15(7):803-808.
- Al-Asmari AK, Albalawi SM, Athar MT, Khan AQ, Al-Shahrani H, Islam M (2015). *Moringa oleifera* as an anti-cancer agent against breast and colorectal cancer cell lines. *PloS One* 10:e0135814. <https://doi.org/10.1371/journal.pone.0135814>
- Barbu E, Popescu MR, Popescu AC, Balanescu SM (2022). Inflammation as a precursor of atherothrombosis, diabetes and early vascular aging. *International Journal of Molecular Sciences* 23(2):963. <https://doi.org/10.3390/ijms23020963>
- Barichella M, Pezzoli G, Faierman SA, Raspini B, Rimoldi M, Cassani E, ... Cereda E (2019). Nutritional characterization of Zambian *Moringa oleifera*: acceptability and safety of short-term daily supplementation in a group of malnourished girls. *International Journal of Food Sciences and Nutrition* 70(1):107-115. <https://doi.org/10.1080/09637486.2018.1475550>
- Boulal A, Atabani AE, Mohammed MN, Khelaf M, Uguz G, Shobana S, Bokhari A, Kumar G (2019). Integrated valorization of *Moringa oleifera* and waste *Phoenix dactylifera* L. dates as potential feed stocks for biofuels production from Algerian Sahara: An experimental perspective. *Biocatalysis and Agricultural Biotechnology* 20(101234):101234. <https://doi.org/10.1016/j.bcab.2019.101234>
- Boulal A, Kalloum S, Bekouche H, Boulahya K (2020). Microbiological treatment of domestic wastewater with *Moringa oleifera* seeds from the city of Adrar-Algeria. *Fascicula Biologie* 27(2):209-214.
- Boulal A, Ouafiane A, Oubiri M, Ladjel S (2021). Study of the antibacterial and antioxidant capacities of fixed oil of *Moringa oleifera* L. cultivated in the Southwest of Algeria. *Asian Journal of Dairy and Food Research* 40(4):415-421. <https://doi.org/10.18805/ajdfr.DR-219>
- Dièye AM, Sarr A, Diop SN, Ndiaye M, Sy GY, Diarra M, ... Faye B (2008). Medicinal plants and the treatment of diabetes in Senegal: survey with patients. *Fundamental & Clinical Pharmacology* 22(2):211-216. <https://doi.org/10.1111/j.1472-8206.2007.00563.x>
- Ghasi S, Nwobodo E, Ofili J (2000). Hypocholesterolemic effects of crude extract of leaf of *Moringa oleifera* Lam in high-fat diet fed Wistar rats. *Journal of Ethnopharmacology* 69(1):21-25. [https://doi.org/10.1016/s0378-8741\(99\)00106-3](https://doi.org/10.1016/s0378-8741(99)00106-3)
- Gopalakrishnan L, Doriya K, Kumar DS (2016). *Moringa oleifera*: a review on nutritive importance and its medicinal application. *Food Science and Human Wellness* 5:49-56. <https://doi.org/10.1016/j.fshw.2016.04.001>
- Mabrok HB, Mohamed MS (2019). Induction of COX-1, suppression of COX-2 and pro-inflammatory cytokines gene expression by *Moringa* leaves and its aqueous extract in aspirin-induced gastric ulcer rats. *Molecular Biology Reports* 46(4):4213-4224. <https://doi.org/10.1007/s11033-019-04874-9>
- International Diabetes Federation (2021). IDF Diabetes Atlas. 10th edition. Brussels, Belgium. Retrieved 2021 from <https://www.diabetesatlas.org>
- Kadir MF, Bin Sayeed MS, Shams T, Mia MM (2012). Ethnobotanical survey of medicinal plants used by Bangladeshi traditional health practitioners in the management of diabetes mellitus. *Journal of Ethnopharmacology* 144(3):605-611. <https://doi.org/10.1016/j.jep.2012.09.050>
- Kar A, Choudhary BK, Bandyopadhyay NG (2003). Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. *Journal of Ethnopharmacology* 84(1):105-108. [https://doi.org/10.1016/s0378-8741\(02\)00144-7](https://doi.org/10.1016/s0378-8741(02)00144-7)

- Karadi RV, Gadge NB, Alagawadi KR, Savadi RV (2006). Effect of *Moringa oleifera* Lam. root-wood on ethylene glycol induced urolithiasis in rats. Journal of Ethnopharmacology 105(1-2):306-311. <https://doi.org/10.1016/j.jep.2005.11.004>
- Kashyap P, Kumar S, Riar CS, Jindal N, Baniwal P, Guine RPF, Correia PMR, ... Kumar H (2022). Recent advances in drumstick (*Moringa oleifera*) leaves bioactive compounds: composition, health benefits, bioaccessibility, and dietary Applications. Antioxidants 11(2):402. <https://doi.org/10.3390/antiox11020402>
- Kasolo JN, Bimenya GS, Ojok L, Ochieng J, Ogwal-Okeng JW (2010). Phytochemicals and uses of *Moringa oleifera* leaves in Ugandan rural communities. Journal of Medicinal Plants Research 4(9):753-757.
- Leone A, Spada A, Battezzati A, Schiraldi A, Aristil J, Bertoli S (2015). Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of *Moringa oleifera* leaves: An overview. International Journal of Molecular Sciences 16(6):12791-12835. <https://doi.org/10.3390/ijms160612791>
- Martín C, Martín G, García A, Fernández T, Hernández E, Puls J (2013). Potenciales aplicaciones de *Moringa oleifera*. Una revisión crítica [Potential applications of *Moringa oleifera*. A critical review]. Pastos Forrajes 36:137-149.
- Mbikay M (2012). Therapeutic potential of *Moringa oleifera* leave sin chronic hyperglycemia and dyslipidemia: a review. Frontiers in Pharmacology 3:24. <https://doi.org/10.3389/fphar.2012.00024>
- Mehta K, Balaraman R, Amin AH, Bafna PA, Gulati OD. Effect of fruits of *Moringa oleifera* on the lipid profile of normal and hypercholesterolaemic rabbits. Journal of Ethnopharmacology 86(2-3):191-195. [https://doi.org/10.1016/s0378-8741\(03\)00075-8](https://doi.org/10.1016/s0378-8741(03)00075-8)
- Momoh MA, Chime SA, Kenchukwu FC (2013). Novel drug delivery system of plant extract for the management of diabetes: an antidiabetic study. Journal of Dietary Supplements 10(3):252-263. <https://doi.org/10.3109/19390211.2013.822454>
- Nicolle E, Souard F, Faure P, Boumendjel A (2011). Flavonoids as promising lead compounds in type 2 diabetes mellitus: molecules of interest and structure activity relationship. Current Medicinal Chemistry 18(17):2661-2672. <https://doi.org/10.2174/092986711795933777>
- Olayaki LA, Irekpa JE, Yakubu MT, Ojo OO (2015). Methanolic extract of *Moringa oleifera* leaves improves glucose tolerance, glycogen synthesis and lipid metabolism in alloxan-induced diabetic rats. Journal of Basic and Clinical Physiology and Pharmacology 26(6):585-593. <https://doi.org/10.1515/jbcpp-2014-0129>
- Olson ME (2002). Combining data from DNA sequences and morphology for a phylogeny of Moringaceae (Brassicales). Systematic Botany 27(1):55-73. <http://dx.doi.org/10.1043/0363-6445-27.1.55>
- Padayachee B, Baijnath H (2020). An updated comprehensive review of the medicinal, phytochemical and pharmacological properties of *Moringa oleifera*. South African Journal of Botany 129:304–316. <https://doi.org/10.1016/j.sajb.2019.08.021>
- Popoola JO, Obembe OO (2013). Local knowledge, use pattern and geographical distribution of *Moringa oleifera* Lam. (Moringaceae) in Nigeria. Journal of Ethnopharmacology 150(2):682-691. <https://doi.org/10.1016/j.jep.2013.09.043>
- Rajanandh MG, Kavitha J (2010). Quantitative estimation of β -sitosterol, total phenolic and flavonoids compounds in the leaves of *Moringa oleifera*. International Journal of PharmTech Research 2(2):1409-1414.
- Raptis SA, Dimitriadis GD (2001). Oral hypoglycemic agents: insulin secretagogues, alpha-glucosidase inhibitors and insulin sensitizers. Experimental and Clinical Endocrinology & Diabetes 109(2):S265-287. <https://doi.org/10.1055/s-2001-18588>
- Ravi K, Rajasekaran S, Subramanian S (2005). Antihyperlipidemic effect of *Eugenia jambolana* kernel on streptozotocin-induced diabetes in rats. Food and Chemical Toxicology 43(9):1433-1439. <https://doi.org/10.1016/j.fct.2005.04.004>
- Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N ... IDF Diabetes Atlas Committee (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Research and Clinical Practice 157:107843. <https://doi.org/10.1016/j.diabres.2019.107843>
- Saini RK, Sivanesan I, Keum YS (2016). Phytochemicals of *Moringa oleifera*: a review of their nutritional, therapeutic and industrial significance 3 Biotech 6(2):203. <https://doi.org/10.1007/s13205-016-0526-3>

- Semenya S, Potgieter M, Erasmus L (2012). Ethnobotanical survey of medicinal plants used by Bapedi healers to treat diabetes mellitus in the Limpopo Province, South Africa. *Journal of Ethnopharmacology* 141(1):440-6445. <https://doi.org/10.1016/j.jep.2012.03.008>
- Sissoko L, Diarra N, Nientao I, Stuart B, Togola A, Diallo D, Willcox ML (2020). *Moringa oleifera* leaf powder for type 2 diabetes: a pilot clinical trial. *African Journal of Traditional, Complementary and Alternative Medicines* 17(2):29-36. <https://doi.org/10.21010/ajtcam.v17i2.3>
- Vergara-Jimenez M, Almatrafi MM, Fernandez ML (2017). Bioactive components in *Moringa oleifera* leaves protect against chronic disease. *Antioxidants* 6(4):91. <https://doi.org/10.3390/antiox6040091>
- Weyer C, Bogardus C, Mott DM, Pratley RE. The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. *The Journal of Clinical Investigation* 104(6):787-6794. <https://doi.org/10.1172/JCI7231>
- World Health Organization (2023). Retrieved 2023 February 10 from: <https://www.who.int/initiatives/who-global-centre-for-traditional-medicine>
- Yousefian N (2012). The *Moringa oleifera* tree in Senegal: ethnobotany, markets and nutrition. Master's dissertation. University of California, Davis.
- Yuan H, Ma Q, Ye L, Piao G (2016). The traditional medicine and modern medicine from natural products. *Molecules* 21(5):559. <https://doi.org/10.3390/molecules21050559>



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