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Evaluating the effectiveness of *Moringa oleifera* leaf capsules in controlling glycemic and hypertension levels in type 2 diabetes patients

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Abstract: *Moringa oleifera* (MO) phytochemicals and therapeutic properties improve hyperglycemia and treat type 2 diabetes. Thus, this study examined the effects of MO leaf capsules on blood glucose management in type 2 diabetic mellitus (T2DM) and hypertension and their safety. A prospective placebo-controlled experiment randomly assigned 24 patients to receive 3g and 6g of MO leaf capsules twice a day or a placebo for three months. Pre- and post-study lab and clinical outcomes were assessed. The placebo control group and 3g MO leaf showed a minor change, whereas 6g and control placebo showed a considerable drop in examined features. MO usage was safe. In T2DM patients, MO leaves lowered blood pressure, requiring further study. MO leaves may help T2DM patients manage blood pressure and blood sugar, according to the study. MO's therapeutic components need more research.

Keywords: *Moringa oleifera*, type 2 diabetes, systolic blood pressure.

INTRODUCTION

Public health is threatened by T2DM. Insulin resistance and pancreatic insulin secretion cause T2DM, making therapy and management difficult and expensive. Herbal treatments for type 2 diabetes are available (Gomes *et al*., 2021). The drumstick tree, MO is a traditional herb. In Western Asia, several portions of the plant have been used as antihypertensive medicines, thyroid hormone regulators, laxatives, and antibiotics (Thurber & Fahey, 2009). MO seed is a staple in Asian cuisine. As industrialists bought its leaves and seeds for raw materials, many families started cultivating it. Farmers have removed the plant (Kasolo *et al*., 2010). MO is grown worldwide, although its origins in the sub-Himalayan regions of India, Pakistan, Bangladesh, and Afghanistan, where it has been utilized in folk medicine (Santos *et al*., 2015). Due to its nutritional, medicinal, and industrial uses, MO is known as a "miracle tree" or "wonder tree" (Jain *et al*., 2021).

MO leaf has been shown to lower plasma and urine glucose levels and enhance glucose tolerance test outcomes in diabetic and non-diabetic rat models (Nova *et al*., 2020). MO leaf fiber decreases intestinal glucose uptake and slows gastric emptying, which may explain its hypoglycemic effects (Leone *et al*., 2018). In a 2016 trial of 10 healthy volunteers, a single dose of 4 grams of MO leaf powder capsules increased insulin secretion without affecting liver or kidney function (Anthanont *et al*., 2016). Although there is a substantial amount of evidence supporting the positive effects of MO on plasma glucose levels in animal models and healthy individuals, there is still a lack of data regarding its effects on type 2 diabetes. Although a small number of studies (Nova *et al*., 2020; William *et al*., 1993) have assessed the effectiveness and safety of MO in individuals with type 2 diabetes, these studies were not randomized. As a result, this study was conducted as a randomized, placebo-controlled investigation to determine whether the use of MO leaf capsules could enhance glucose control in patients with type 2 diabetes mellitus (T2DM), as well as to assess its safety.

MATERIALS AND METHODS

Participants individual

The eligible candidate patients were enrolled in the study, and participants were required to meet certain criteria:

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having type 2 diabetes for less than 5 years, aged between 25 and 65 years, recording fasting plasma glucose (FPG) less than normal (200mg/dl), and hemoglobin (HbA1C) less than 9% recorded.

Moringa leaf capsule and placebo

The MOL were purchased from local market and identified by Botanist Dr. Nishat from the University of Agriculture, Faisalabad. The dried MOL (150 mg) was dissolved in 1 mL of cold (4°C) water, vortexed rapidly for 30 seconds, and then chilled for five minutes to twenty-four hours. At room temperature, the suspension was violently vortexed once again for one minute. The suspension was centrifuged twice (12,000 rpm, 10 min each time), and the water-insoluble components were eliminated. The supernatants were then collected using membrane filtration (0.2-m filter). For further examination, the obtained MOL extracts were lyophilized and kept at 20°C. The lyophilized MOL extracts were resuspended in DW for the tests at a final protein concentration of 20 mg/mL.

With the help of the co-worker of a batch of MO leaf powder capsules. The manufacturing process followed good practice guidelines, which involved cleaning and drying the leaves before grinding them into a powder. The resulting powder was then encapsulated, and 500 mg powder received MO leaf active ingredients. Similarly, placebo capsules were also made at the same place as the control. These capsules were made to look and feel the same as the MO leaf capsules, with matching size and color. However, the placebo capsules contained only plain powder, magnesium stearate, and talcum with no active ingredient. To ensure the accuracy of the study, placebo capsules were produced alongside the MO leaf capsules at the same manufacturing unit. These capsules had the same appearance as the active capsules but contained only inert substances.

Study duration

From April 2022 to November 2022, a prospective randomized placebo-controlled study was carried out. The study received ethical approval from the Health Research Ethics Review Committee of Health Sciences. All volunteer patients gave written authorization to apply the placebo moringa pill to type 2 diabetes. A one-month screening period preceded a 12-week randomized treatment period. All participants visited the diabetes unit for medical history review, physical examination (including body weight and blood pressure), and laboratory tests (FPG, HbA1C, creatinine, and liver function tests) during screening. They also learned 9-point plasma glucose (PG) monitoring and behavioral counseling to manage diabetes. The 9-point plasma glucose (PG) profile measured PG levels in the morning of day 1, before each meal, 2 hours after each meal, before bedtime on day 2, and before breakfast on day 3. Participants took 6 or 12 MO leaf capsules (3 or 6 grams) or a placebo before breakfast and dinner for 12 weeks. The previous studies used one dose for one month (Taweerutchana *et al*., 2017), while we used the two doses to check the efficacy of MO leaves capsules for three months. The reason for choosing a three-month period was to more accurately assess the average HbA1C level, which reflects the past three months of glucose control and liver function results. After completion of the 12-week study, all participants were requested to return to the diabetes unit for medical history review, physical examination, and blood collection to measure FPG, HbA1C, creatinine, and liver function tests. The follow-up period for this study was three months, with an anticipated dropout rate of 15%. Thus, each group was required to have 24 participants to ensure an adequate sample size.

Exclusion criteria

Participants who met the inclusion criteria and did not satisfy the exclusion criteria were randomly assigned in a 1:1 ratio to receive either MO leaf capsules or a placebo of equivalent appearance using a table of random numbers. Excluded from the study were people with type 1 or other types of diabetes, those who had used glycemic-lowering agents within 2 months prior to enrollment, those with a creatinine clearance of less than 60 ml/min/1.73 m2, those with elevated levels of alanine or aspartate aminotransferases greater than 2 times the upper limit of the normal range, and those with a history of heart disease or other cardiovascular diseases.

Ethical approval

The ethical approval from the Health Research Ethics Review Committee of University of Health Sciences and its reference No.321.

STATISTICAL ANALYSIS

For all statistical analyses, the SPSS version (v28.0) software was used. Continuous variables were presented as either mean ± standard deviation, or as median with minimum and maximum values as appropriate. Categorical variables were displayed as frequencies and percentages. The independent t-test was applied to analyze continuous variables, while categorical variables were analyzed using either the Chi-square. The means were compared at a 5% probability level for significance level.

RESULTS

The study included two groups of participants: one group received 3g of MO leaf, while the other group received a placebo capsule, while the second group received 6g of MO leaf to optimize the effective results of hypertension and type 2 diabetes patients. The study measured the outcomes for both groups. The group that received 3g of

Table 1: Parameters of MO leaf and Placebo group at the initial stage of experiment

Variables	MO Leaf (3 g) *	Placebo capsules *	MO leaf (6 g)	Placebo capsule
Age	57±9.2	54±8.3	52±11.3	56±7.8
Body weight	73±10	70±9.2	78±11.2	76±13.4
BMI	27±7	28±8.2	28.5±	
Family history	18	15	17	18
Hypertension	11	15	9	13
Lipid-lowering agents	7	10	9	12
Fasting Plasma Glucose mg/dl	140±9	138±10	135±11	137±12
HbA1c	7.1±9	6.9±11	7.0±12	7.0±11

Table 2: Clinical and glucose parameters were evaluated under MO leaf and placebo groups.

		MO leaf 3 (g) *	Placebo *	MO leaf 6 (g) leaf	Placebo
	Body weight (kg)				
1	Baseline	70.81±9	68.6±12	69.39±9	66.88±10
2	Second month	70.81±11	68.6±11	69.39±7	66.88±9
3	Third month	69.84±10	67.62±10	68.4432±9	65.92±10
	Systolic Blood Pressure (mmg)				
1	Baseline	129.01±10	125.44±10	126.42±8	122.304±7
2	Second month	129.01±10	123.48±9	126.42±7	120.393±7
3	Third month	124.16±9	127.4±8	121.67±9	124.21±6
	Diastolic Blood Pressure (mm HG)				
1	Baseline	82.45±11	74.48±7	80.80±7	72.61±8
2	Second month	79.54±10	74.48±10	77.94±10	72.61±7
3	Third month	76.63±7	77.42±11	75.09±10	75.48±10
	Fasting Plasma Glucose (mg/dl)				
1	Baseline	133.86±10	129.36±9	131.18±8	126.12±11
2	Second month	126.1±9	126.42±11	123.57±11	123.25±10
3	Third month	131.92±10	123.48±10	129.28±10	120.39±9
	Hemoglobin A1C				
1	Baseline	6.9258±11	7.007±7	6.78±8	6.83±9
2	Second month	6.79±10		6.65±9	
3	Third month	6.984±10	6.7326±8	6.84±10	6.56±8

MO leaf had higher scores than the placebo group in both males and females (fig. 1).

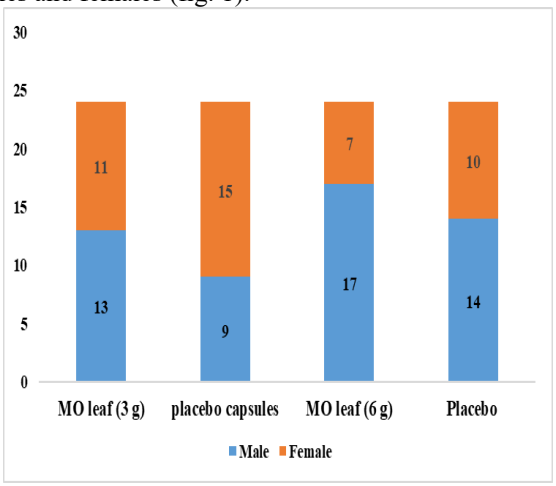

Fig. 1: Gender distribution studied the MO leaf and placebo treatments.

The table shows the results of a study that investigated the effects of MO leaf on various health parameters at the initial stage. The group that received 6g of MO leaf had higher scores than the placebo group in males but not in females (fig. 1). There was a trend towards decreasing age with increasing doses of MO leaf. There was a trend towards increased body weight with increasing doses of MO leaf. There were no significant differences in family history, hypertension, or lipid-lowering agents between the two groups. Fasting plasma glucose was slightly lower in the group that received 3g of MO leaf compared to the placebo group, but there was no significant difference between the group that received 6g of MO leaf and the placebo group at the initial stage of the experiment.

The table presents the detailed results of a clinical trial comparing the effects of two doses of MO leaf extract (3g and 6g) with a placebo on various health markers over three months. The first set of data shows the participants' body weight in kilograms.

The baseline body weight for all groups was similar, with an average of around 70.81kg, except for the placebo group, which had a slightly lower baseline weight of 68.6kg. Over the course of the trial, the participants in all groups showed a slight decrease in weight, with the highest dose group (6mg) showing the most significant change, with an average weight of 68.44kg at the end of the trial.

The second set of data shows the systolic blood pressure (SBP) in mm Hg. At baseline, the SBP for all groups was similar, with an average of around 126-129mm Hg. Over the three months of the trial, the SBP remained stable for the placebo group, while the highest dose group (6 mg) showed a significant decrease in SBP, from 126.42 to 121.67mm Hg. The third set of data shows the diastolic blood pressure (DBP) in mm Hg. At baseline, the DBP for all groups was similar, with an average of around 74-82 mm Hg. Over the course of the trial, the DBP decreased slightly in all groups, with the highest dose group (6 mg) showing the most significant change, with an average DBP of 75.09mm Hg at the end of the trial (table 2).

The fourth set of data shows the fasting plasma glucose (FPG) in mg/dL. At baseline, the FPG for all groups was similar, with an average of around 126-133mg/dL. Over the three months of the trial, the FPG decreased slightly in all groups, with the highest dose group (6g) showing the most significant change, with an average FPG of 129.28 mg/dL at the end of the trial.

The last set of data shows the hemoglobin A1C levels. At baseline, the hemoglobin A1C levels for all groups were similar, with an average of around 6.7-7.0. Over the course of the trial, the highest dose group (6mg) showed a slight decrease in hemoglobin A1C, with an average level of 6.84 at the end of the trial. However, the placebo group showed a slight increase in hemoglobin A1C (HbA1C), with an average level of 6.73 at the end of the trial (table 2). The safety of MO leaf capsule with two concentrations in patients with therapy-naive type 2 diabetes was evaluated. The study found no incidence of hypoglycemia in either treatment group, and there were no significant differences in BUN, Cr, AST, and ALT between the baseline and the end of the study. Among patients in the MO group, 15% experienced transient diarrhea, which resolved within a few days. The results indicate that high doses of MO leaf powder did not have any adverse effects.

DISCUSSION

The first clinical research to evaluate MO leaf capsules to a placebo in type 2 diabetic patients without prior treatment is this one. At 3g MO leaves, hemoglobin A1C levels decreased little, while at 6g and in placebo groups, they decreased considerably. Plasma glucose levels before and after meals were similar in both groups. MO leaves have no side effects. Interestingly, the MO leaf group demonstrated a small decrease in systolic blood pressure relative to control, but a substantial reduction was obtained at 6g MO leaf and placebo. John & Chellappa (2005) and William *et al*. (1993) found that MO leaves lowers glucose levels in animals and humans. However, another study found identical results without the same effect. In conclusion, *Moringa oleifera*'s glucose-lowering properties as medication were not replicated in this investigation (Taweerutchana *et al*., 2017). Similarly, a previous study (Anthanont *et al*., 2016) conducted research on healthy individuals and demonstrated that a single dose of 4g of MO leaf powder capsules resulted in a significant increase in insulin secretion by 74%. Therefore, the lack of impact on plasma glucose levels observed in the current study cannot be attributed to an inappropriate dosage (Anthanont *et al*., 2016). In summary, the results indicate that while a single dose of MO leaf powder capsules increased insulin secretion in a previous study, it did not have a similar effect on plasma glucose levels in the current study.

The second group shows SBP in mm Hg. All groups exhibited baseline SBPs of 126-129mm Hg. Over three months, the placebo group's SBP remained stable, while the highest dose group (6g) saw a significant decline from 126.42 to 121.67mm Hg. The third group shows DBP in mm Hg. All groups had baseline DBPs of 74-82mm Hg. The highest dose group (6 g) ended the research with an average DBP of 75.09mm Hg, whereas all other groups witnessed a slight drop. The placebo group may have improved plasma glucose through self-monitoring. The study suggests that the raw material's low bioactive phytochemical concentration and blood glucose self-monitoring may have affected the outcomes. Hyperglycemia, HbA1C, and systolic blood pressure improved over three months. After 12 months, self-monitoring of blood glucose (SMBG) reduced glycemic control and HbA1C by 0.1% compared to the control group. SMBG helps patients control their glucose levels by providing feedback and encouraging healthy lifestyle changes (Ahmad *et al*., 2019). The study examined MO leaf's efficacy and safety. High doses of MO leaves cause transaminitis and weight gain in animals (Todorović Vukotić *et al*., 2021). However, liver and renal function in study subjects was unaffected. 25% of patients who took MO leaf powder had diarrhea, but it went away. This study, like others on MO leaves, found no side effects (Taweerutchana *et al*., 2017).

CONCLUSION

To summarize, the current study found a significant impact of MO leaf on glycemic control in patients with type 2 diabetes at a higher (6g MO leaf) dose relative to a lower dose (3g). However, the use of MO was deemed

safe and did not have any harmful effects. Additionally, the study revealed a potential trend towards reduced blood pressure among type 2 diabetes patients, although further long-term duration investigation is required to confirm more detailed results of MO leaf as a miracle plant for curing hypertension and type 2 diabetes.

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