Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2023.52.008249

Clinical Evidence of Moringa Leaves on Glycemic Control: A Review of Animal and Human Studies

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ARTICLE INFO

Received: August 14, 2023

Published: August 22, 2023

Citation: Amina Faheem, Sanaullah Iqbal and Umer Faheem. Clinical Evidence of Moringa Leaves on Glycemic Control: A Review of Animal and Human Studies. Biomed J Sci & Tech Res 52(3)-2023. BJSTR. MS.ID.008249.

ABSTRACT

The incidence of type 2 diabetes has been increased substantially in the last two decades. Improving diet and lifestyle along with functional foods can prevent the increasing incidence of diabetes. Moringa is a functional food that contains flavonoids mainly quercetin, kaempferol and chlorogenic acid which are responsible for hypoglycemic effects. Moreover, moringa is gaining popularity regarding its health benefits as a super food among Asian population but the scientific evidence is still lacking. The present review aims to present the existing literature published regarding the role of moringa leaves in glycemic control in various animal models and human studies limited to time frame from 2007 to 2022. Numerous research had emphasized on the role of biologically active components present in moringa leaves in the prevention of various diseases such as non-insulin dependent diabetes mellitus. In the conducted studies, large number of animal trails has reported antihyperglycemic activity of moringa. In humans, there is limited evidence regarding hypoglycemic effect of moringa. It is difficult to reach a conclusion and hence, there is a need to conduct well designed clinical trials of appropriate duration regarding the effect of moringa leaf powder supplementation on glycemic control in humans.

Keywords: Moringa Oleifera; Moringa Leaf; Diabetes; Glycemic Control; Animal Models; Effect; Mechanisms

Abbreviations: ORAC: Oxygen Radical Absorbance Capacity; SGLT1: Sodium Glucose Linked Type 1 Transporters; ERK: Extracellular Signal-Regulated Kinase; ROS: Reactive Oxygen Species; MESH: Medical Subject Headings; GK: Goto-Kakizaki; STZ: Streptozotocin; HFD: High Fat Diet

Introduction

Globally, diabetes mellitus is a major public health problem. There are two types of diabetes. Type 1 diabetes which is also known as insulin dependent diabetes is characterized by lack of insulin secretion due to autoimmune destruction of pancreatic beta cells. It accounts for 5 to 10% of all diabetic cases (Kharroubi and Darwish, [1]). Type 2 diabetes mellitus is also known as non-insulin dependent diabetes. Around 90 to 95% of diagnosed cases of diabetes are of type 2 diabetes. It is a chronic metabolic disorder characterized by insulin resistance, deficiency of insulin secretion from pancreas and increased plasma glucose levels. Type two diabetic individuals are at increased risk of developing serious complications such as dyslipidemia and cardiovascular complications leading to mortality and morbidity (Galicia-Garcia, et al. [2]). The incidence of type 2 diabetes has been increased substantially in the last two decades (Danaei, et al. [3]). Around 415 million people worldwide are living with diabetes. In developing countries, such as Pakistan, prevalence of diabetes mellitus is reported to be 17.1% around 148% higher than previously stated (IDF, [4]).

South Asians have increased risk for the development of non-communicable diseases such as diabetes and cardiovascular diseases. Due to urbanization, dietary patterns have shifted towards increased con-

sumption of refined carbohydrates, sweets, desserts, sugary drinks, fat and animal foods with a decrease in the intake of fiber thus increasing the incidence of non-communicable diseases including diabetes (Faheem, et al. [5,6]). Improving diet and lifestyle along with functional foods can prevent the increasing incidence of diabetes. In recent years, functional foods have gained popularity regarding health benefits beyond basic nutritional value among South Asians (Alissa, et al. [7]). Numerous researches had emphasized on the role of biologically active components present in functional foods in the prevention of various diseases such as non-insulin dependent diabetes mellitus. Regular consumption of functional food can reduce the occurrence of diabetes mellitus by improving insulin sensitivity, lipid profile and antioxidant status of body. Moreover, functional foods are cost effective and without side effects as compared to pharmacological interventions (Alkhatib, et al. [8]).

Moringa Nutritional Composition

Moringa is also known as a drumstick tree among Asian population. Moringa is a functional food that has been widely used as a medical herb to treat hyperglycemia and diabetes (Leone, et al. [9]). Moringa tree have numerous nutritional as well as medicinal health benefits. Moringa is a miracle plant with extraordinary nutritional, therapeutic and antioxidant properties. It is an excellent source of protein, vitamins, minerals and phytochemicals, containing 92 nutrients, 46 anti-oxidants and 36 anti-inflammatory compounds. This composition makes it a "Super Food". Many studies had shown that moringa leaves are a rich source of macronutrients, micronutrients and other bioactive components which are essential for proper functioning of the human body (Islam, et al. [10]). The leaves of moringa are consumed raw or as a powder, as they are rich in minerals (calcium, iron, potassium, and magnesium) as well as beta-carotene, b-complex vitamins, vitamin C and E, polyphenols and antioxidants (Falowo, et al. [11]). Chromium, magnesium and zinc present in moringa multiplies the effect of insulin to reduce blood sugar level.

The B-vitamins, antioxidants and omega-3 fatty acids present aids in diabetes control. Being super anti-oxidant, moringa reduces oxidative stress and control free radicals. Free radicals are unstable compounds, produced during metabolism in body. These must be controlled otherwise damage cellular and mitochondrial membranes resulting oxidative stress, early aging and atherosclerosis / heart diseases. Moringa is the queen of anti-oxidants, has highest Oxygen Radical Absorbance Capacity (ORAC) value among plants. It has 46 different anti-oxidants which modulate enzymatic activity, facilitate detoxification and promote anti-tumoral activities. Moringa contains important flavonoids like catechins, polyphenols, beta-sitosterol, quercetin and vitamin K reduce that fat deposits in blood vessels and act as cardio-protector, preventing one the major complication associated with diabetes mellitus. It aids in wound healing due to presence of high amount of vitamin C. Due to vitamin A and plenty of anti-oxidants, Moringa not only reduce the rate of the aging process but also improves the condition of hair, skin as well as eyes. Thus, it also reduces the risk of diabetes complications such as retinopathy.

Mode of Action of Moringa Leaves in Improving Glycemic Control

Moringa leaf contains flavonoids mainly quercetin, kaempferol and chlorogenic acid which are responsible for hypoglycemic effects in different animal models. These compounds reduce the intestinal absorption of glucose by inhibiting sodium glucose linked type 1 transporters (SGLT1) present in the mucosa of small intestine (Singh, et al. [12]). Quercetin provides protection to beta cells (pancreas) from oxidative damage and stimulates insulin secretion via phosphorylation of extracellular signal-regulated kinase (ERK) 1/2 pathway (Youl, et al. [13]). Existing evidence from studies has shown that chlorogenic acid in moringa decreases glycogenolysis and gluconeogenesis by inhibiting glucose-6-phosphate translocase (Mbikay,[14]). Epidemiological researches have reported certain insulin-like proteins in moringa that contribute to the hypoglycemic effect (Vargas-Sanchez, et al. [15]). The flavonoids and polyphenols present in moringa leaves exhibit hypoglycemic effects by inhibiting the activity of enzymes such as α-glucosidase and α-amylase which are responsible for the hydrolysis of starch (Adisakwattana, et al. [16]). Bioactive components present in moringa leaves such as kaempferol, gallic acid, quercetin, ellagic acid and chlorogenic acid, act as a protective agent against Reactive Oxygen Species (ROS). These compounds prevents proteins, lipids and DNA from free radical oxidation. These reactive oxygen species causes oxidative damage to beta cells and thus lead to insulin resistance (Sangkitikomol, et al. [17]). Considering the current evidence, moringa contains flavonoids and isothiocynates which are responsible for its anti-inflammatory effects (Xu, et al. [18]). (Figure 1) represents the role of active ingredients moringa leaves in glycemic control.

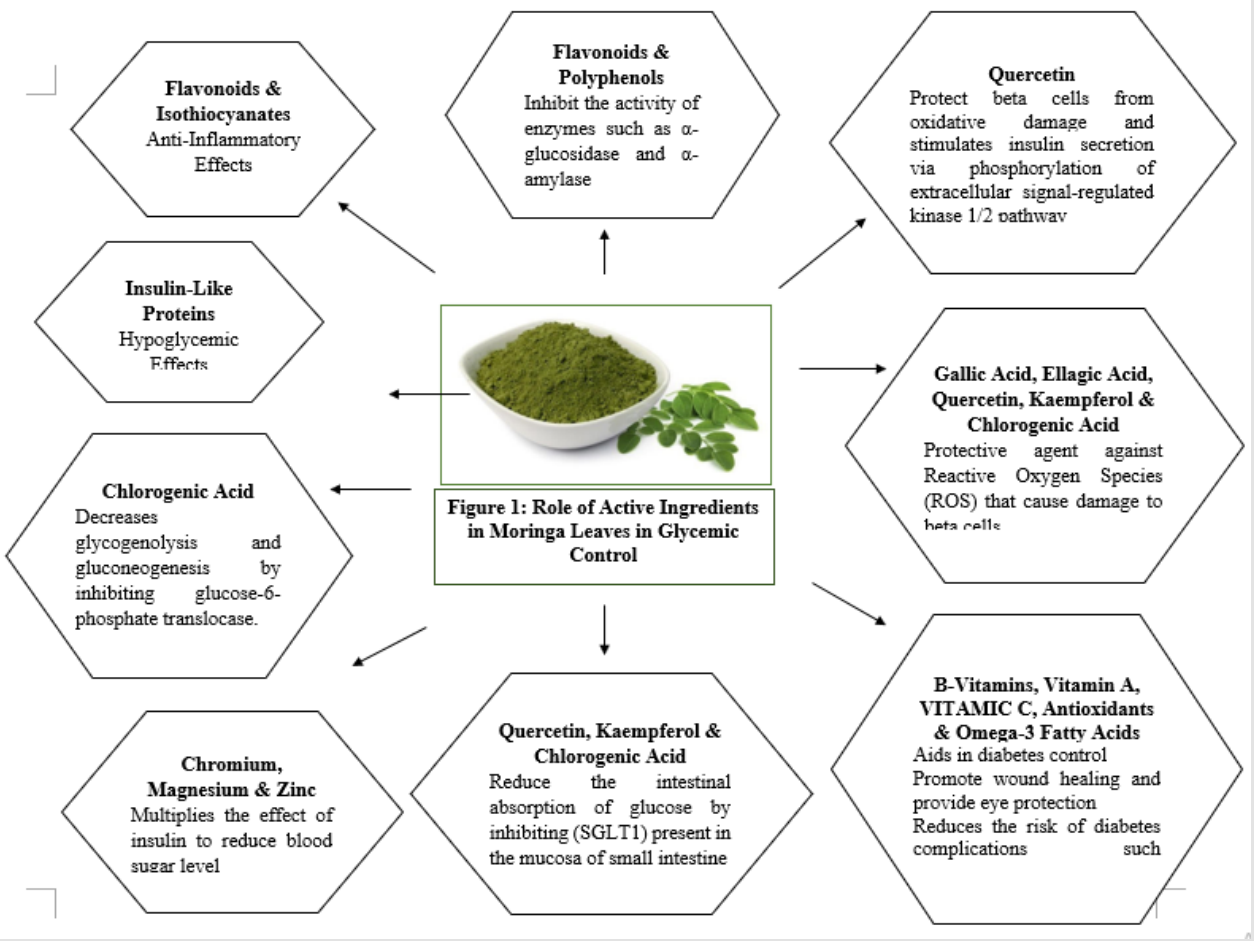

Figure 1: Role of Active Ingredients in moringa Leaves in Glycemic Control.

Materials and Methods

Search Strategy

This review of literature reviews all papers published regarding effect of moringa leaves on blood glucose levels. A thorough search was done using multiple databases and manual tracking of citations in selected articles was also performed. Google Scholar, PubMed, Science Direct, Cochrane Library, Food Science and Technology Abstracts, MEDLINE and Scopus were the search engines used to find articles limited to time frame 2007 to 2022. Boolean operators were used for more focused and productive search and to avoid unnecessary interruption.

Keyword and MeSH Terms

The search strategy followed departs from the more general aspects like the nutritional profile of moringa and progressively moves the focus of interest towards the main study object, which is hypoglycemic effect of moringa leaves in various animal models and human studies. The search involved the following key words: moringa oleifera, moringa leaf, diabetes, glycemic control, animal models, effect, and mechanisms. These keywords were also used as Medical Subject Headings (MeSH).

Inclusion and Exclusion Criteria

The present review included peer reviewed articles in the English language within time frame 2007 to 2022 fulfilling the criteria described below.

- Studies that used moringa leaf powder and moringa leaves extract as an intervention in humans.
- Studies that used moringa leaf powder and moringa leaves extract as an intervention in animal models.

Studies that used seeds, bark and parts other than leaves of moringa tree as a intervention. Studies which were not in English language and those with intervention period less than two days in different rodent models were excluded from the review. Editorials, letters, conference abstracts and unpublished studies were excluded.

Results

This present systematic review was conducted according to the PRISMA guidelines. The flowchart of our literature search is shown in (Figure 2). A total of 200 articles were searched through multiple databases. After removal of duplicate articles, there were 65 articles screened for included in the review. Majority of studies were excluded because they failed to report plasma glucose levels. Therefore, the present review included 25 studies (20 in animal model and 5 in humans).

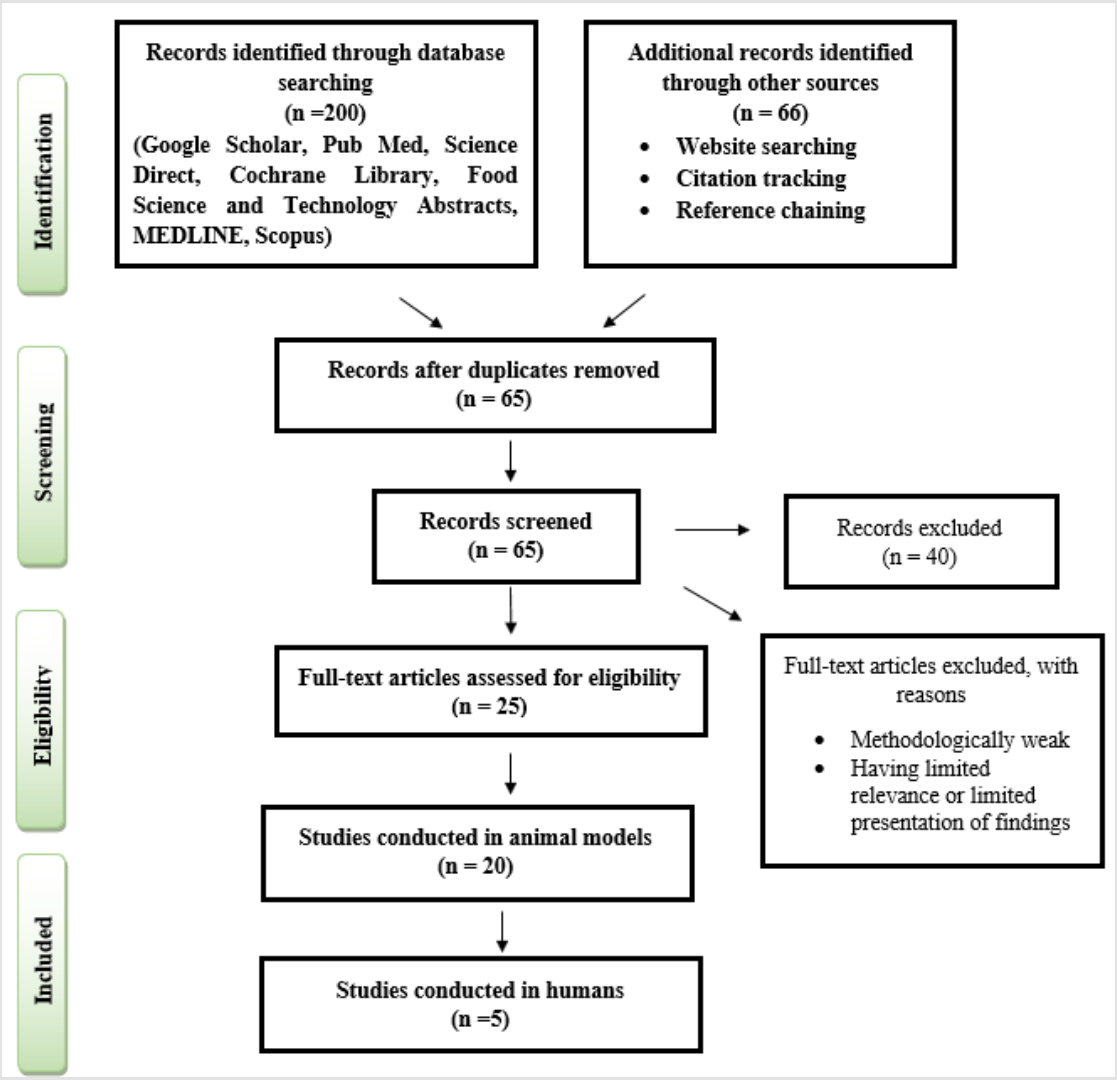

Figure 2: Search Strategy (Articles).

Clinical Evidence of Moringa on Glycemic Control

Recently, functional foods are gaining popularity regarding prevention of diabetes because of the bioactive components present in them and limited side effects as compared to pharmacological interventions (Abd El Latif, et al. [19]). Moringa leaves had been studied for antidiabetic, anti-inflammatory and antioxidant effects. Several animal trails have investigated moringa mechanism of action and its role in various disease models such as diabetes mellitus. Many animal trails have reported anti hyperglycemic effects of moringa. But there are few clinical trials regarding hypoglycemic effect of moringa in humans (Vargas-Sánchez, et al. [15]).

Clinical Trials in Humans

To investigate the effect of moringa on plasma glucose levels, ten healthy participants within the age group 20 to 40 years were selected. After every 2 weeks the selected participants received moringa

leaf powder capsules at an increasing dosage of 1 gram, 2 gram and 4 grams. Insulin and blood glucose levels were measured at baseline and 0.5, 1, 1.5, 2, 4, and 6 hours after moringa capsule ingestion. The results concluded that there was no reduction in plasma glucose levels. The current study reported significant improvement in insulin levels of the subjects. Authors reported no negative effects after moringa ingestion (Anthanont, et al. [20]). A single oral dose of 500 mg moringa aqueous leaf extract was given to healthy volunteers. The study reported no significant reduction in blood glucose levels of the subjects after moringa ingestion. There was a significant improvement in antioxidant markers (Ngamukote, et al. [21]). A single oral dose of 20 g of moringa leaf powder supplemented with meal was given to diabetic patients. There was a specific meal for the participants comprising 80 gram of rice and 160 gram of camel meat stew. Authors reported significant reduction in blood glucose levels of the subjects at 90, 120 min and 150 min after moringa ingestion. Postprandial glucose response peaked earlier with lower increments at 90-, 120-, and 150-min. authors also reported significant reduction alpha amylase activity (Leone, et al. [9]). The three studies with single dose administration are shown in (Table 1).

Table 1: Human Studies with Single Dose Administration (Moringa Leaf Powder).

Authors (Year)	Moringa Treatment (Dosage & Duration)	Result (Blood Glucose)
Anthanont, et al. [20]	0 g, 1 g, 2 g and 4 g	No significant changes in plasma glucose Mean plasma insulin increased.
Ngamukote, et al. [21]	500 mg	No significant changes in blood glucose levels. Significant increase in antioxidant capacity.
Leone, et al. [9]	20 grams once with meal	Significant reduction in glycemic control to 150 min after intake. Postprandial glucose response peaked earlier with lower increments at 90, 120, and 150 min. Significant reduction in α-amylase activity.

A study was conducted to evaluate the antihyperglycemic effect of moringa. Treatment group was administered 8 gram moringa leaves powder in three divided doses for one month. The study concluded significant reduction in fasting and post prandial plasma glucose levels of the subjects in experimental group receiving moringa supplementation. The authors reported no adverse effects after moringa ingestion (Kumari, et al. [22]). A randomized controlled clinical study was conducted to evaluate the effect of moringa leaf capsules and placebo in type 2 diabetes mellitus patients. There were 16 participants in both groups. Experimental group received 8 gram moringa leaf powder per day (4 gram moringa leaf powder capsules, twice daily) for one month. The results concluded that there was no significant reduction in fasting plasma glucose levels and HbA1C levels between groups. After moringa leaf powder ingestion, there were no changes reported in individuals' creatinine, blood urea nitrogen (BUN), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels. There was no adverse effect regarding consumption of moringa leaf powder (Taweerutchana, et al. [23]). These clinical trials of short duration are shown in (Table 2).

Table 2: Short Duration Human Trial of Moringa Leaf Powder (Only one month & HBA1c Parameter was not accurately measured).

Authors (Year)	Moringa Treatment (Dosage & Duration)	Result (Blood Glucose)
Kumari, et al. [22]	8-gram moringa leaves powder in three divided doses for 1 month	Significant reduction in fasting blood glucose and post prandial blood glucose levels ($p<0.05$) Significant improvement in the mean blood lipid levels
Taweerutchana, et al. [23]	4-gram moringa leaf powder capsules, twice daily for 1 month	No significant changes in Fasting Plasma Glucose (FPG)

Clinical Trials in Animals

A study conducted on diabetic male Goto-Kakizaki (GK) rats and nondiabetic male Wistar rats showed improved in plasma glucose levels after moringa leaf powder ingestion. The control groups orally received 2 gram/kg body weight of single dose of glucose. Experimental group received 200 mg moringa leaf powder per kg body weight with 2 gram/kg body weight of glucose solution. Plasma glucose levels were measured at 10, 20, 30, 45, 60, 90 and 120 min from the tail vein using blood glucose meter. Moringa leaf powder significantly reduced plasma glucose levels at 20, 30, 45 and 60 min in GK rats. Moringa significantly decreased stomach emptying (Ndong, et al. [24]). A three week supplementation of moringa leaf powder in metabolic syndrome induced wistar rats reported improvement in blood glucose level. 700 mg/kg/day of moringa leaf powder was administered orally via a gavage for 3 weeks. The present study reported significant reductions in abdominal circumference and in triglyceride levels. The authors reported no significant improvement in blood pressure and total cholesterol levels (Lopez, et al. [25]).

A clinical trial was conducted on thirty healthy male sprague dawley rats (180–200 g) to evaluate the effect of moringa leaf powder on blood glucose levels. Diabetes was induced by 150 mg/kg of alloxan monohydrate in rats. Experimental group received 50 mg/day of moringa leaf powder orally using cannula needle for 2 months. The diabetic group receiving moringa leaf powder reported increase in body weight and significant reductions in blood glucose levels as compared to control group (Villarruel-Lopez, et al. [26]). Studies regarding mo-

ringa leaves powder supplementation in animal model are represented in (Tables 3-6). Moringa aqueous extract was administered orally by a gavage at an increasing dosage of 100 mg, 200 mg, and 300 mg/kg body weight for three weeks in streptozotocin (STZ) induced diabetic rats. Different doses of moringa extract improved glycemic control in diabetic rats (Jaiswal, et al. [27]). A study conducted on diabetic rats showed reduction in fasting plasma glucose levels after moringa extract ingestion. Experimental group orally received 400mg of moringa extract for 28 days. Diabetes was induced by intraperitoneal dose of 100 mg/kg of alloxan monohydrate in rats. The control group was given distilled water without moringa extract. Moringa leaf extract significantly reduced cholesterol and glucose levels treatment group (Oyedepo, et al. [28]). Female alloxan-induced diabetic wistar rats at intraperitoneal dosage of 100 mg/kg body weight receiving moringa aqueous leaf extract showed significant reduction in glycemic levels together with improvement in lipid profile. In addition, also normalized the mRNA expression of gluconeogenic enzyme pyruvate carboxylase in hepatic tissues (Abd El Latif, et al. [19]).

Table 3: Clinical Trials of Moringa Leaf Powder in Animal Model.

Authors & Year	Animal Model	Moringa Treatment (Dosage & Duration)	Result (Blood Glucose)
Lopez, et al. [25]	Wistar rats with metabolic syndrome (MS) induced with high-fat diet	700 mg/kg/day for 3 weeks	Reduction in fasting glucose levels and Oral Glucose Tolerance Test. Significant improvement in glucose tolerance, abdominal circumference and in triglyceride levels
Villarruel-Lopez, et al. [26]	Alloxan-induced diabetic Sprague-Dawley rats	50 mg/day for 2 months	Significant reductions in blood glucose levels and increase in body weight Prevented weight loss. No effect on lipid profile. No histopathology observation. No change in enumeration of lactic acid bacteria.
Ndong M, et al. [24]	Goto-Kakizaki (GK) diabetic rats and nondiabetic Wistar rats used as controls	glucose 2 g/kg + 200 mg/kg moringa (single dose)	Significant reduction in postprandial level at 20, 30, 45 and 60 min. Moringa significantly decreased stomach emptying ($p<0.05$)

Table 4: Macronutrients and Micronutrients in 100 Gram Dried Moringa Leaves.

Nutrient	Amount in 100 g
Energy (Kcal) [1]	304 +/- 87 kcal
Moisture (mg) [1]	7.4 +/- 2.89
Protein (g) [1]	24 +/- 5.8
Carbohydrates (g) [2]	36 +/- 9.2
Fat (g) [2]	6 +/- 2.5
Fiber, total dietary (g) [2]	20.6 – 28.6
Ca (mg) [1]	1897 +/- 748.4
P (mg) [1]	297 +/- 149.0
Mg (mg) [1]	473 +/- 429.4
Fe (mg) [1]	32.5 +/- 10.78
Zn (mg) [1]	2.4 +/- 1.12
Na (mg) [3]	220 +/- 180.0
K (mg) [3]	1467 +/- 636.7
Vitamin A (µg RAE) [4]	3639 +/- 1979.8
Thiamin (mg) [5]	2.6
Riboflavin (mg) [5]	1.29 – 20.5
Niacin (mg) [5]	8.2
Folate (µg) [6]	540
Vitamin C (mg) [6]	172 +/- 37.7
Vitamin E (mg) [5]	56 – 113

Note: Nutritional Composition of Moringa Leaves (Dried).

Table 5: Phytochemical Analysis of Moringa Leaves.

Phytochemicals	Amount
Chlorogenic Acid (mg/g) [7]	50.69 +/- 0.03
Caffeic Acid (mg/g) [7]	6.28 +/- 0.03
Ellagic Acid (mg/g) [7]	33.15 +/- 0.02
Gallic Acid (mg/g) [7]	32.42 +/- 0.02
Quercitrin (mg/g) [7]	29.74 +/- 0.01
Quercetin (mg/g) [7]	18.23 +/- 0.01
Isoquercitin (mg/g) [7]	64.53 +/- 0.03
Kaempferol (mg/g) [7]	47.91 +/- 0.01
Catechin (mg/g) [7]	9.98 +/- 0.01
Saponin (%) [8]	5
Total Phenol (mg/GAE g) [7]	29.20 +/- 0.40
Total flavinoid (mg/GAE g) [8]	17.48 +/- 0.18

Table 6: Clinical Trials of Moringa Leaf Extract in Animal Model.

	Animal Model (Induction)	Moringa Treatment (Dosage & Duration)	Result (Blood Glucose)
Jaiswal, et al. [27]	Streptozotocin induced diabetic rats. 55mgkg^{-1} in 0.1M citrate buffer (pH 4.5)	100, 200, 300 mg/day for 3 weeks	Author & Year
Oyedepo, et al. [28]	Alloxan-induced diabetic rats. 100 mg/kg	400 mg/day for 28 days	Significant reduction in plasma glucose & cholesterol levels.
Abd El Latif, et al. [19]	Alloxan-induced diabetic rats	100 mg/kg body weight	Normalized the elevated serum levels of glucose, triglycerides, cholesterol, and malondialdehyde, and normalized mRNA expression of the gluconeogenic enzyme pyruvate carboxylase in hepatic tissues. Increased liver body weight gain and normalized the reduced mRNA expression of fatty acid synthase.
Fahmy, [29]	Alloxan-induced diabetic rats. 120 mg/kg	150 mg/day for 21 days	Significant improvement in glycemic levels Restored the normal histological structure of the pancreas
Olayaki, et al. [30]	Alloxan-induced diabetic rats. intraperitoneal dose of 120 mg/kg	300 mg/kg body weight for 6 weeks	Significantly improved glucose tolerance, and increased serum insulin levels. Reduced serum concentrations of triglyceride, total cholesterol, and low-density lipoprotein (LDL)-cholesterol and enhanced serum level of high-density lipoprotein (HDL)
Toma A, et al. [31]	Streptozotocin induced diabetic rats. 40 mg/kg body	500 mg/day for 14 days	Significant improvement in glycemic levels Improved serum lipid profiles, liver enzymes and kidney functions. Improved damage of islet of Langerhan's
Khan, et al. [32]	Streptozotocin induced diabetic rats. 45 mg/kg, intraperitoneal	100 mg/kg body weight for 3 weeks	Fasting blood glucose, lipid profile, liver marker enzyme level were significantly restored. Inhibited the activity of α-amylase and α-glucosidase and it displayed improved antioxidant capacity, glucose tolerance and rate of glucose uptake
Olurishe, et al. [33]	Alloxan-induced diabetic rats' intraperitoneal dose of 150 mg/kg	300mg/kg body weight for 42 days	Reductions in fasting blood glucose (FBG) levels and random blood glucose (RBG) levels. No significant difference was seen in mean serum levels of insulin and body weight across groups
Abdeldaim, et al. [34]	Alloxan-induced diabetic rats 150mg/kg	250/kg body weight for 18 days	Decreased blood glucose Prevented organ changes and significantly restored all measures. Normalized the expression of apoptotic, gluconeogenic, and glycogenic genes in hepatic tissue.
Azad, et al. [35]	Alloxan-induced diabetic rats 90 mg/kg	500 mg (single dose)	Reduced plasma glucose levels at 30 min. α-amylase action was inhibited by the extract
Omodanisi, et al. [37]	Streptozotocin induced diabetic rats 55 mg/kg	250 mg/day for 6 weeks	Significant improvement in glycemic levels High antioxidant capacities of moringa extract and improved serum biochemical markers protective action against diabetic-induced renal damage, reactive oxygen species (ROS) and inflammation and could therefore reducing diabetic complications,

Paula, et al. [38]	Alloxan-induced diabetic rats 150 mg/kg	300 and 500 mg/kg of body weight (single dose)	Significant reductions in plasma glucose levels Effective in reducing the oxidative stress in diabetic mice by a decrease in malondialdehyde level and increase in catalase activity.
Azevedo, et al. [39]	Streptozotocin induced diabetic rats intraperitoneal dose of 145 mg/kg body weight	100 mg for 10 days	Significant improvement in blood glucose level
Bamagous, et al. [40]	Streptozotocin induced diabetic rats 55 mg/kg	200 mg/day for 30 days	Reversed the manifestation of streptozotocin on the levels of serum glucose & insulin, lipid profile, hepatic damage markers
Hidayati et, al. [41]	Streptozotocin induced diabetic rats 60 mg/kg	50 mg/day for 10 days	Significantly decreased blood glucose , cholesterol and LDL levels.
Answer, et al. [42]	Streptozotocin induced diabetic rats 40 mg/kg	100 mg, 200 mg, and 400 mg/kg body weight For 21 days	Reduced the levels of glucose, insulin and cytokines. Significant decrease in glucose AUC.
Irfan, et al. [43]	Metabolic syndrome induced rats (High at Diet-20% Fructose)	1000 mg/kg/day for 4 weeks	Significant improvement in glycemic control, insulin resistance and visceral fat. Provided the mitigation against metabolic syndrome features

A significant improvement in blood glucose levels was reported in male rats treated with moringa leaf extract (150 mg/kg of body weight for 21 days) with alloxan-induced diabetes at a intraperitoneal dose of 120 mg/kg. The authors also stated that moringa leaves possess potent antihyperglycemic activity (Fahmy, et al. [29]). A significant decrease in blood glucose levels was reported in male wistar rats treated with moringa methanolic leaf extract (300 mg/kg of body weight) with alloxan-induced diabetes at a intraperitoneal dose of 120 mg/kg. The authors also stated improvement in insulin levels and lipid profile in experimental group with moringa methanolic leaf extract as compared to control group (Olayaki, et al. [30]). A study conducted on diabetic rats showed significant reduction in blood glucose levels after moringa ethanol extract ingestion via oral gavage. Diabetes was induced by intraperitoneal dose of 40 mg/kg body weight of streptozotocin in male rats. Treatment group orally received 500 mg/kg of moringa extract for 14 days. Authors reported significant improvement in lipid profile in experimental group with moringa leaf extract. The ethanolic extract also improved islet of Langerhan's in pancreas in treatment group. (Toma A, et al. [31]). A recent study reported significant improvements in glycemic levels in female wistar rats with streptozotocin (45 mg/kg, intraperitoneal) induced diabetes and in high-fat diet induced female diabetic mice, treated with moringa leaf extract. After diabetes induction, streptozotocin induced rats received 100 mg/kg of body weight of moringa leaf extract orally for 3 weeks. The diabetic mice were administered 200 mg/kg of body weight of moringa leaf extract. There was significant improvement in high density lipoprotein levels with significant reduction in total cholesterol and triglyceride levels in both diabetes induced mice and rats (Khan, et al. [32]).

Authors reported that forty-two days administration of 300 mg/kg of body weight moringa ethanolic leaf extract along with sitagliptin (an oral hypoglycemic used for type 2 DM) reported significant reduction in fasting plasma glucose levels in alloxan-induced (intraperitoneal dose of 150 mg/kg) diabetic wistar rats. The study concluded no improvements in insulin levels diabetic rats treated with moringa extract (Olurishe, et al. [33). An oral dose of 250 mg/kg of body weight moringa aqueous leaf extract was given to 150mg/kg of alloxan-induced diabetic rats for 18 days. The study reported significant reduction in blood glucose levels after moringa ingestion. There was a significant improvement in antioxidant markers and normalized the expression of apoptotic, gluconeogenic, and glycogenic genes in hepatic tissue (Abdeldaim, et al. [34]). A study conducted on diabetic rats showed reduction in plasma glucose levels after moringa extract ingestion. Experimental group orally received 500mg of moringa extract was suspended in distilled. The control group was given equal volume of distilled water without moringa extract. Moringa leaf extract significantly reduced plasma glucose levels at 30 min in treatment group (Azad, et al. [35]). Previous researches had showed an antihyperglycemic effect of moringa in different animal models. Strongest hypoglycemic effects in diabetic models (animals) were reported at the doses between 200 and 300 mg/kg (Wang, et al. [36]). A recent study reported significant improvements in glycemic levels in rats with streptozotocin (55 mg/kg, intraperitoneal) induced diabetes treated with moringa leaf extract. After diabetes induction, streptozotocin induced rats received 250 mg/kg of body weight of moringa leaf extract orally for six weeks. High antioxidant capacities of moringa extract and improved serum biochemical markers (Omodanisi, et al. [37]).

A protein isolate (Mo-LPI) from moringa leaves was studied in 150 mg/kg of alloxan-induced diabetic mice. A single protein isolate dose of 300 and 500 mg/kg of body weight reported significant reduction blood glucose level in diabetic mice. The hypoglycemic effect of the extract was abolished after heating at 98 °C. The authors reported no significant improvement in insulin levels (Paula, et al. [38]). A study conducted on male diabetic rats showed reduction in blood glucose levels after moringa extract ingestion. Diabetes was induced by intraperitoneal dose of 145 mg/kg body weight of streptozotocin in male rats. Experimental group orally received 100mg/kg of moringa extract for 10 days. Authors reported significant improvement in glycemic control in treatment group with moringa leaf extract (Azevedo, et al. [39]). A ethyl acetate extract fraction from moringa leaves was studied in 55 mg/kg streptozotocin-induced diabetic mice. 200 mg/kg of body weight ethyl acetate extract fraction from moringa leaves for 30 days reported significant reduction blood glucose level in diabetic rats.Moringa extract reversed the manifestation of streptozotocin on` the levels of serum glucose & insulin, lipid profile, hepatic damage markers (Bamagous, et al. [40]).

Another study was conducted on thirty male rats to investigate the antihyperglycemic effect of moringa leaf extract. Diabetes was induced by 60 mg/kg of streptozotocin in rats. Experimental group received 50 mg/day of moringa leaf extract orally for 10 days. The diabetic group receiving moringa leaf extract reported significant reductions in blood glucose and cholesterol levels (Hidayati, et al. [41]). High fat diet (HFD) fed rats were administered 40 mg/kg of streptozotocin to induce type 2 diabetes. Treatment group received moringa leaf extract at an increasing dosage of 100 mg, 200 mg, and 400 mg/kg body weight. The study showed significant reduction in plasma glucose levels of the subjects in experimental group treated with moringa as compared to control group (Answer, et al. [42]). A four-week supplementation of moringa leaf extract in metabolic syndrome induced rats reported improvement in plasma glucose level. 1000 mg/kg/day of moringa leaf extract were administered orally for 4 weeks. The authors also reported significant improvement in insulin resistance and visceral fat after moringa supplementataion (Irfan, et al. [43-56]).

Conclusion

In the present review, many animal trials (twenty studies) had reported antihyperglycemic activity of moringa. All these studies reported significant improvement in blood glucose levels along with lipid profile. Strongest hypoglycemic effects in diabetic models (animals) were reported at the doses between 200 and 300 mg/kg. In humans, there is limited evidence regarding hypoglycemic effect of moringa. Only five studies are reported in humans. Three of them were with single dose administration and postprandial blood glucose measurement. Among them, only one study (20 g moringa leaf powder once with meal) reported significant improvement in post prandial blood glucose levels. The remaining were two clinical trials with 8-gram moringa leaf powder supplementation of short duration around one month. Secondly, the HbA1C parameter was not accurately measured in these two studies. Moreover, one study reported significant reductions in blood glucose level while the other study reported no significant improvement in glycemic control in diabetic patients. Hence, considering the current evidence, it is difficult to reach a conclusion that moringa can be used as an anti-hyperglycemic agent and there is a need to conduct a clinical trial of appropriate duration in humans.

References

1. Kharroubi AT, Darwish HM (2015) Diabetes mellitus: The epidemic of the century. World J Diabetes 6(6): 850-867.
2. Galicia Garcia U, Benito Vicente A, Jebari S, Larrea Sebal A, Siddiqi H, et al. (2020) Pathophysiology of Type 2 Diabetes Mellitus. Int J Mol Sci 21(17): 6275.
3. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, et al. (2011) Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose) National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2•7 million participants. Lancet 378(9785): 31-40.
4. (2019) International Diabetes Federation. IDF Diabetes Atlas 2019.
5. Faheem A, Raza Q, Iqbal S, Batool R, Faheem U (2022) Sex Differences in Nutritional Status and Associated Risk Factors among Cardiovascular Disease (CVD) Patients in Lahore, Pakistan; A Cross-Sectional Descriptive Study. Preprints 2022: 2022050295.
6. Siegel KR, Patel SA, Ali MK n (2014) Non-communicable diseases in South Asia: contemporary perspectives. Br Med Bull 111(1): 31-44.
7. Alissa EM, Ferns GA (2012) Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases. J Nutr Metab 2012: 569486.
8. Alkhatib A, Tsang C, Tiss A, Bahorun T, Arefanian H, et al. (2017) Functional Foods and Lifestyle Approaches for Diabetes Prevention and Management. Nutrients 9(12): 1310.
9. Leone A, Spada A, Battezzati A, Schiraldi A, Aristil J, et al. (2015) Cultivation, Genetic, Ethnopharmacology, Phytochemistry and Pharmacology of Moringa oleifera Leaves: An Overview Int J Mol Sci 16(6): 12791-12835.
10. Islam Z, Islam SMR, Hossen F, Mahtab Ul Islam K, Hasan MR, et al. (2021) Moringa oleifera is a Prominent Source of Nutrients with Potential Health Benefits. Int J Food Sci 11.
11. Falowo AB, Mukumbo FE, Idamokoro EM, Lorenzo JM, Afolayan AJ, et al. (2018) Multi-functional application of Moringa oleifera Lam. in nutrition and animal food products: A review Food Res Int 106: 317-334.
12. Singh BN, Singh BR, Singh RL, Prakash D, Dhakarey R, et al. (2009) Oxidative DNA damage protective activity, antioxidant, and anti-quorum sensing potentials of Moringa oleifera. Food Chem Toxicol 47(6): 1109-1116.
13. Youl E, Bardy G, Magous R, Cros G, Sejalon F, et al. (2010) Quercetin potentiates insulin secretion and protects INS-1 pancreatic β-cells against oxidative damage via the ERK1/2 pathway. Br J Pharmacol 161(4): 799-814.
14. Mbkiay M (2012) Therapeutic Potential of Moringa oleifera Leaves in Chronic Hyperglycemia and Dyslipidemia: A Review. Front Pharmacol 3: 24.
15. Vargas Sánchez K, Garay Jaramillo E, González Reyes RE (2019) Effects of Moringa oleifera on Glycaemia and Insulin Levels: A Review of Animal and Human Studies. Nutrients 11(12): 2907.

16. Adisakwattana S, Chanathong B (2011) Alpha-glucosidase inhibitory activity and lipid-lowering mechanisms of Moringa oleifera leaf extract. Eur Rev Med Pharmacol Sci 15(7): 803-808.

17. Sangkitikomol W, Rocejanasaroj A, Tencomnao T (2014) Effect of Moringa oleifera on advanced glycation end-product formation and lipid metabolism gene expression in HepG2 cells. Genet Mol Res 13 (1): 723-735.

18. Xu YB, Chen GL, Guo MQ (2019) Antioxidant and Anti-Inflammatory Activities of the Crude Extracts of Moringa oleifera from Kenya and Their Correlations with Flavonoids. Antioxidants (Basel) 8(8): 296.

19. Abd El Latif A, El Bialy Bel S, Mahboub HD, Abd Eldaim MA (2014) Moringa oleifera leaf extract ameliorates alloxan-induced diabetes in rats by regeneration of β cells and reduction of pyruvate carboxylase expression. Biochem Cell Biol 92(5): 413-419.

20. Anthanont P, Lumlerdkij N, Akarasereenont P, Vannasaeng S, Sriwijitkamol A (2016) Moringa oleifera leaf increases insulin secretion after single dose administration: a preliminary study in healthy subjects. J Med Assoc Thail 99: 308-313.

21. Ngamukote S, Khannongpho T, Siriwatanapaiboon M, Sirikwanpong S, Dahlan W, et al. (2016) Moringa Oleifera leaf extract increases plasma antioxidant status associated with reduced plasma malondialdehyde concentration without hypoglycemia in fasting healthy volunteers. Chin J Integr Med 29: 1-6.

22. Kumari DJ (2010) Hypoglycaemic effect of Moringa oleifera and Azadirachta indica in type 2 diabetes mellitus. Bioscan 5(20): 211-214.

23. Taweerutchana R, Lumlerdkij N, Vannasaeng S, Akarasereenont P, Sriwijitkamol A (2017) Effect of Moringa oleifera Leaf Capsules on Glycemic Control in Therapy-Naïve Type 2 Diabetes Patients: A Randomized Placebo Controlled Study. Evid Based Complement Alternat Med 2017: 6851390.

24. Ndong M, Uehara M, Katsumata S, Suzuki K (2007) Effects of Oral Administration of Moringa oleifera Lam on Glucose Tolerance in Goto-Kakizaki and Wistar Rats. J Clin Biochem Nutr 40(3): 229-233.

25. Lopez M, Ríos Silva M, Huerta M, Cárdenas Y, Bricio Barrios JA, et al. (2018) Effects of Moringa oleifera leaf powder on metabolic syndrome induced in male Wistar rats: a preliminary study. J Int Med Res 46(8): 3327-3336.

26. Villarruel López A, López de la Mora DA, Vázquez Paulino OD, Puebla Mora AG, Torres Vitela MR, et al. (2018) Effect of Moringa oleifera consumption on diabetic rats. BMC Complement Altern Med 18(1): 127.

27. Jaiswal D, Rai K, Kumar A, Mehta S, Watal G (2009) Effect of Moringa oleifera Lam. leaves aqueous extract therapy on hyperglycemic rats. J Ethnopharmacol 123(3): 392-396.

28. Oyedepo T, Babarinde S, Ajayeoba A (2013) Evaluation of anti-hyperlipidemic effect of aqueous leaves extract of Moringa oleifera in alloxan induced diabetic rats. International journal of biochemistry research & review 3(3): 162.

29. Fahmy T, Hassan NS, Abdrabou RR (2015) Potential activity of Moringa oleifera leaf extract and some active ingredients against diabetes in rats. Int J Sci Eng Res 6(5): 1490.

30. Olayaki LA, Irekpita E, Yakubu MT, Ojo O (2015) Methanolic extract of Moringa oleifera leaves improves glucose tolerance, glycogen synthesis and lipid metabolism in alloxan-induced diabetic rats. J Basic Clin Physiol Pharmacol 26(6): 583-593.

31. Toma A, Makonnen A, Adisakwattana S (2015) Antidiabetic activities of aqueous ethanol and n-butanol fraction of Moringa stenopetala leaves in streptozotocin-induced diabetic rats. BMC 15(1): 1-8.

32. Khan W, Parveen R, Chester K, Parveen S, Ahmad S (2017) Hypoglycemic potential of aqueous extract of Moringa oleifera leaf and in vivo GC-MS metabolomics. Front Pharmacol 8: 577.

33. Olurishe C, Kwanashie H, Zezi A, Danjuma N, Mohammed B (2016) Chronic administration of ethanol leaf extract of Moringa oleifera Lam. (Moringaceae) may compromise glycaemic efficacy of Sitagliptin with no significant effect in retinopathy in a diabetic rat model. J Ethnopharmacol 194: 895-903.

34. Abdeldaim M, Shaban E, Abd Elaziz S (2017) An aqueous extract from Moringa oleifera leaves ameliorates hepatotoxicity in alloxan-induced diabetic rats. Biochem Cell Biol 95: 524-530.

35. Azad SB, Ansari P, Azam S, Hossain SM, Shahid MI, et al. (2017) Anti-hyperglycaemic activity of Moringa oleifera is partly mediated by carbohydrase inhibition and glucose-fibre binding. Biosci Rep 37(3): 30.

36. Wang F, Zhong HH, Chen WK, Liu QP, Li CY, et al. (2017) Potential hypoglycaemic activity phenolic glycosides from Moringa oleifera seeds. Nat Prod Res 31(16): 1869-1874.

37. Omodanisi E, Aboua Y, Chegou N, Oguntibeju O (2017) Hepatoprotective, Antihyperlipidemic, and Anti-inflammatory Activity of Moringa oleifera in Diabetic-induced Damage in Male Wistar Rats. Pharmacogn 9: 182-187.

38. Paula PC, Sousa DO, Oliveira JT, Carvalho AF, Alves BG, et al. (2017) A Protein Isolate from Moringa oleifera Leaves Has Hypoglycemic and Antioxidant Effects in Alloxan-Induced Diabetic Mice. Molecules. 22(2): 271.

39. Azevedo IM, Araújo Filho I, Teixeira MMA, Moreira C, Medeiros AC (2018) Wound healing of diabetic rats treated with Moringa oleifera extract. Acta Cir Bras 33(9): 799-805.

40. Bamagous GA, Al Ghamdi SS, Ibrahim A, Mahfo A, Afify M, et al. (2018) Antidiabetic and antioxidant activity of ethyl acetate extract fraction of Moringa oleifera leaves in streptozotocin-induced diabetes rats via inhibition of inflammatory mediators. Asian Pac J Trop Biomed 8(6): 320.

41. Hidayati S, Sulistyawati R, Nurani H (2018) Regulation of ethyl acetate fraction from Moringa oleifera leaves to improve lipid metabolism and insulin sensitivity in type 2 diabetes. Int J Pharm Pharm Sci. 10: 78-82.

42. Anwer T, Makeen HA, Alshahrani S, Siddiqui R, Moni S, et al. (2021) Antidiabetic potential of Moringa oleifera Lam. leaf extract in type 2 diabetic rats, and its mechanism of action. Trop J Pharm Res 20(1): 95-103.

43. Irfan HM, Khan NAK, Asmawi MZ (2022) Moringa oleifera Lam. leaf extracts reverse metabolic syndrome in Sprague Dawley rats fed high-fructose high fat diet for 60-days. Arch Physiol Biochem 128(5): 1202-1212.

44. Amir AH, Ul Haq Z, Mahar SA, Qureshi FM, Ahmad I, et al. (2019) Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. Br Med J 9(2): e025300.

45. Hostalek U (2019) Global epidemiology of prediabetes - present and future perspectives. Clin Diabetes Endocrinol 5: 5.

46. Kushwaha S, Chawla P, Kochhar A (2014) Effect of supplementation of drumstick (Moringa oleifera) and amaranth (Amaranthus tricolor) leaves powder on antioxidant profile and oxidative status among postmenopausal women. J Food Sci Technol 51 (11): 3464-3469.

47. Nova E, Redondo Useros N, Martínez García RM, Gómez Martínez S, Díaz Prieto LE, et al. (2020) Potential of Moringa oleifera to Improve Glucose Control for the Prevention of Diabetes and Related Metabolic Alterations: A Systematic Review of Animal and Human Studies. Nutrients 12 (7): 2050.

48. Tabak AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M (2012) Prediabetes: a high-risk state for diabetes development. Lancet 379(9833): 2279-2290.

49. Yameogo CW, MD Bengaly, A Savadogo, Philippe Augustin Nikiema, Sabadenedyo Alfred Traore, et al. (2011) Determination of chemical composition and nutritional values of Moringa oleifera leaves. Pakistan Journal of Nutrition 10(3): 264-268.

50. Sanchez Machado D, J Nunez Gastelum, C Reyes Moreno, Benjamin Ramirez Wong, Jerardo Cervantes, et al. (2010) Nutritional quality of edible parts of Moringa oleifera. Food Analytical Methods 3: 175-180.

51. Juliani HR, Y Fonseca, D Acquaya, H Malumo, Malaïny Diatta, et al. (2010) Nutritional assessment of moringa (Moringa spp) from Ghana, Senegal and Zambia, Chapter 25. In: African Natural Plant Products: New discoveries and challenges in chemistry and quality. Washington, DC: American Chemical Society 1021: 469-484.

52. Nambiar VS, S Seshadri (2001) Bioavailability trials of beta-carotene from fresh and dehydrated drumstick leaves (Moringa oleifera) in a rat model. Plant Foods for Human Nutrition 56(1): 83-95.

53. Fuglie LJ (2001) The miracle tree. Moringa oleifera: Natural nutrition for the tropics training manual. New York: Church World Service.

54. Shishankaran D, S Girumurthy, SH Kehoe (2011) Chapter 12. Developing micronutrient-rich snacks for pre-conception and antenatal health: The Mumbai maternal nutrition project (MMNP). In Thompson B, Amoroso L., Eds. Combating Micronutrient Deficiencies: Food-based Approaches. Wallingford, UK: CAB International and Food and Agriculture Organization of the United Nations.

55. Jimoh (2018) Enzymes inhibitory and radical scavenging potentials of two selected tropical vegetable (Moringa oleifera and Telfairia occidentalis) leaves relevant to type 2 diabetes mellitus. Revista brasileira de farmacognosia 28: 73-79.

56. Okah, Reminus, Walter Cornelius (2019) Phytochemical analysis of moringa oleifera (leaves and flowers) and the functional group. Global Scientific Journal 7(60): 41-51.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.52.008249

Sanaullah Iqbal. Biomed J Sci & Tech Res