



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Moringa Oleifera : An Overview Phytochemical Constituents , Activity

1Abhishekh Hazgude, 2Sneha Kanase

1Student, 2Asst.Proff

1Arihant College of Pharmacy,

2Arihant College Of Pharmacy

Abstract :

Moringa oleifera is one of the popular plants that have shown significant health benefits. Certainly, preclinical evidence (predominantly from animal models) summarized in the current review supports the beneficial effects of Moringa oleifera leaf extracts in combating the prominent characteristic features of diabetes mellitus. This includes effective control of blood glucose or insulin levels, enhancement of insulin tissue sensitivity, improvement of blood lipid profiles, and protecting against organ damage under sustained conditions of hyperglycemia. Interestingly, as major complications implicated in the progression of diabetes, including organ damage, Moringa oleifera leaf and seed extracts could efficiently block the detrimental effects of oxidative stress and inflammation in these preclinical models. Notably, these extracts (especially leaf extracts) showed enhanced effects in strengthening intracellular antioxidant defences like catalase, superoxide dismutase, and glutathione to lower lipid peroxidation products and reduce prominent pro-inflammatory markers such as tumor necrosis factor- α , interleukin (1L)- β , IL-6, monocyte chemoattractant protein-1 and nitric oxide synthase. From animal models of diabetes, the common and effective dose of leaf extracts of Moringa oleifera was 100–300 mg/kg, within the treatment duration of 2–8 weeks. Whereas supplementation with approximately 20 g leaf powder of Moringa oleifera for at least 2 weeks could improve postprandial blood glucose in subjects with prediabetes or diabetes. Although limited clinical studies have been conducted on the antidiabetic properties of Moringa oleifera, current findings provide an important platform for future research directed at developing this plant as a functional food to manage diabetic complications

Keywords : diabetes complications, oxidative stress, inflammation, moringa (Moringa oleifera), therapeutic targets

Introduction :

According to the World Health Organization (WHO), diabetes is one of the top ten causes of mortality and morbidity worldwide (World Health Organization, 2022). Diabetes mellitus is a metabolic disorder characterized by a hyperglycemic state that occurs with dysregulation of insulin levels and, in some cases, coincides with overweight and obesity (International Federation of Diabetes Mellitus, 2021). In fact, excess body fat or obesity remains a major cause of the development of type 2 diabetes (T2D), the main form of diabetes (International Federation of Diabetes Mellitus, 2021). The rapid increase in the incidence of diabetes, especially T2DM, is a cause for concern and highlights the urgent need for research into effective treatments for this disease (Ahmad et al., 2019). Cumulative research focuses on understanding the pathophysiological mechanisms involved in the development of diabetes-related complications, which is important for discovering effective treatments that can improve metabolic function and prevent multiple organ failure in people suffering from diabetes. (King and Brownlee, 1996; Fowler, 2007; Wei et al., 2020). As a representative example, inflammation and oxidative stress, which usually result from abnormal proinflammatory responses or increased free radical production, are increasingly recognized as major disorders associated with the development and acceleration of diabetes-related complications. (King and Brownlee, 1996). In particular, oxidative stress is associated with activation of protein kinase C (PKC), which typically corresponds to disruption of insulin signaling and tissue damage in experimental models of diabetes (King and Brownlee, 1996). Importantly, this supports Randle et al.'s (1963) hypothesis that altered uptake and metabolism of glucose and free fatty acids may be an important process in the pathogenesis of insulin resistance, a key feature of T2DM. In fact, the development of T2DM involves a variety of biochemical mechanisms beyond inflammation and oxidative stress or PKC activation (King and Brownlee, 1996). The literature suggests that effective modulation of energy metabolism and insulin signaling through modulation of the AMP-activated protein kinase (AMPK) or phosphoinositide 3-kinase/protein kinase B (PI3K/AKT) pathways reverses some of the devastating effects of diabetes. I suggest that it appears to be ordered. Zirat)., 2006; Hwang et al., 2018; Mazibuko-Mbeje et al., 2018). Indeed, plants and related bioactive compounds are increasingly being tested for their antidiabetic properties. Several natural plants have demonstrated anti-diabetic properties by lowering blood sugar levels and regulating the AMPK/PI3K/AKT pathway (Francini et al., 2019 ; Mazibuko-Mbeje et al., 2019 ; Costa et al., 2020). Our group is continuously reviewing the literature on the effects of plants such as *Camellia sinensis* and *Aspalathus lineis*, including known bioactive compounds of some plants such as gallic acid and isoorientin, for their ameliorative effects on metabolic complications (Dludla et al., 2019; Zikubu et al., 2020; Dludla et al., 2021). *Moringa oleifera* is a medicinal plant that has received much attention due to its diverse biological properties. Evidence reviewed showed that plants enhance biological performance and protect against complications associated with heart disease, cancer, fatty liver disease, and diabetes (Paikra et al., 2017; Vergara-Jimenez et al., 2017; Abd Rani et al., 2017). al., 2018). For example, a previously published review identified the positive effects of *Moringa oleifera* leaves on improving glycemic control in experimental models of diabetes (Ahmad et al., 2019). In particular, this review identified a limited number of studies reporting the potential beneficial effects of this plant, including the fact that the literature summarized was primarily conducted in animals using preclinical in vitro and in vivo models. However, data on the important biochemical mechanisms involved in the antidiabetic effects of *Moringa oleifera* have not been critically analyzed, even though such information already supports the hypoglycemic potential of this medicinal plant. Recently, Louise et al. demonstrated the effectiveness of *Moringa oleifera* in cardiovascular or metabolic disorders by reducing harmful pro-inflammatory responses and suppressing oxidative stress by mediating molecular mechanisms such as inhibiting translocation or enhancing translocation of nuclear factor kappa B (NF- κ B). supported the potential benefits of . Nuclear factor-erythroid factor 2-related factor 2 (Nrf2) antioxidant response in various preclinical models (Louisa et al., 2022). Therefore, there is a need to better understand the intracellular response of *Moringa oleifera* in diabetes or related metabolic complications. This study provides a brief overview of the medicinal plant *Moringa oleifera* and its therapeutic mechanisms in controlling various complications of diabetes. The focus is on understanding the modulating effects of this medicinal plant on inflammation and oxidative stress mechanisms in diabetes. The current review includes evidence obtained from searches (up to the end of December 2021) in major search engines such as PubMed, Google Scholar and ScienceDirect. A systematic search was performed using the Medical Subject Headings (MeSH)

terms “Moringa oleifera,” “diabetes,” “glucose metabolism,” “insulin resistance,” “oxidative stress,” and “inflammation” and their relevant synonyms. EndNote20 desktop software (Elsevier, Amsterdam, The Netherlands) was used to reference and identify duplicate studies. This review included preclinical and clinical studies reporting the mechanisms of action of Moringa oleifera in models of diabetes and related metabolic syndrome. However, review articles and encyclopedias were excluded but screened for primary results. In particular, to better understand the potential benefits of Moringa oleifera, important information is provided regarding the plant parts being evaluated and the effective treatment doses and experimental models used in the study.

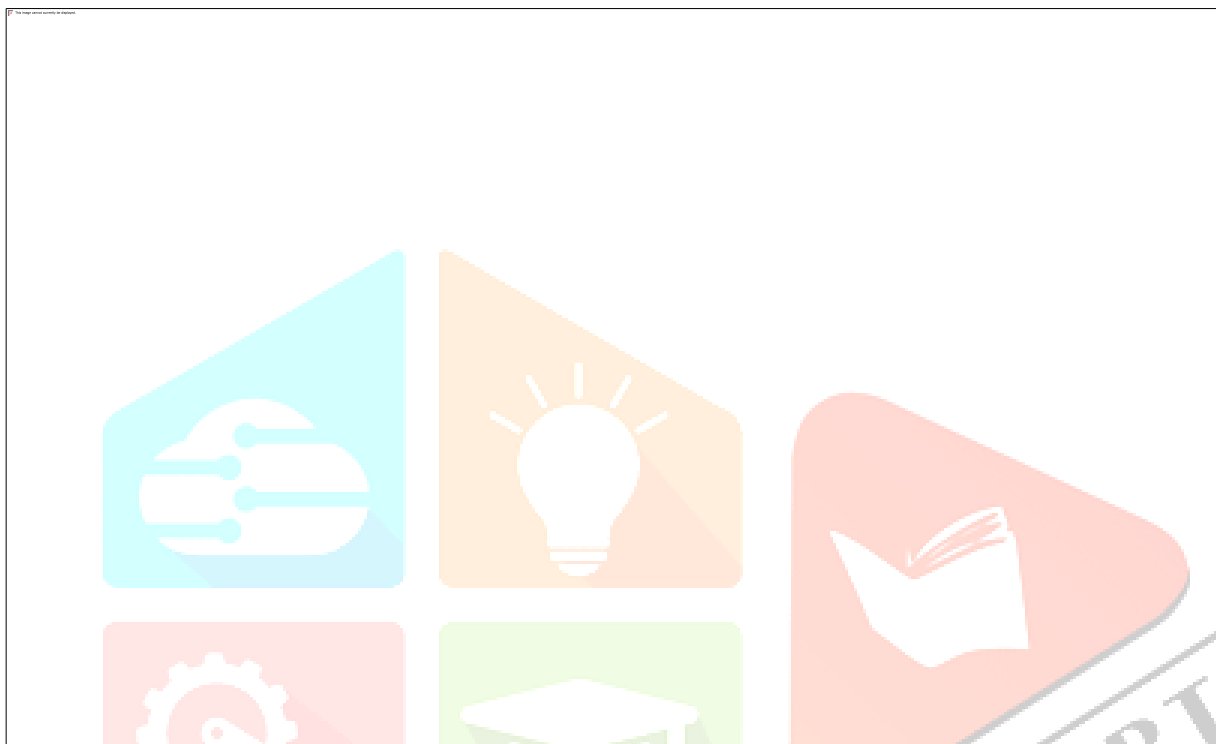


Fig 1 . Moringa Oleifera

Diabetes mellitus (DM) is a life-threatening metabolic disorder in populations worldwide, causing hyperglycemia, which is a major cause of diabetes complications such as retinopathy, nephropathy, and neuropathy [1 , 2]. Diabetic nephropathy (DN) is a structural abnormality manifested by hypertrophy of both glomerular and tubular elements. Signs of diabetic nephropathy also include increased thickness of the glomerular basement membrane, progressive accumulation of extracellular matrix components, early increase in glomerular filtration rate due to intraglomerular hypertension, subsequent proteinuria, systemic hypertension, and possible loss of renal function. Moringa oleifera lamac (Moringa) is a cultivated species of the genus Moringa in the Moringaceae family. Several health benefits have been reported with the addition of moringa leaves or seeds or their extracts [4-6]. middle. Oleifera has been described as a miracle tree, a tree of life, and a gift from God to man. Moringa root reduced the increase in urinary oxalate levels and the deposition of stone-forming substances in the kidneys of stone-prone rats after treatment with ethylene glycol [8]. Moringa has been used to improve nutrition, enhance food security, promote rural development, support sustainable land management and livestock nutrition [9]. Moringa alleviated liver fibrosis in rats, reduced liver damage and liver fibrosis symptoms, reduced CCl4-induced increases in serum aminotransferase and globulin levels, and increased hydroxyproline and myeloperoxidase activities in the liver. has decreased. [5]. The antioxidant and antidiabetic activities of the aqueous extract of Moringa leaves indicate its potential benefit as a potent antidiabetic agent in albino rats with streptozotocin-induced diabetes. Raw moringa extract is also an excellent nitric oxide radical scavenger and a potential source of natural antioxidants [10]. Moringa is also used for nutraceutical purposes and is used to treat hypercholesterolemia and hyperglycemia, and as a dietary supplement, it can be prescribed as a dietary

supplement along with existing medications for patients with coronary artery disease [11]. Moringa also accelerated the healing of normal wounds, and dexamethasone inhibited wounding in rats [12]. Despite moringa's medical benefits, it has been shown to have toxic effects on mice and rats at high concentrations.

Drug Profile :

Taxonomical Classification

Kingdom – Plantae

Sub kingdom – Tracheobionta

Super Division – Spermatophyta

Division – Magnoliophyta

Class – Magnoliopsida

Sub class – Dilleniidae

Order – Capparales

Family – Moringaceae

Genus – Moringa

Species – oleifera

Herbs and their components play an important role in various medical systems such as Unani, Siddha, Yoga, Homeopathy, Naturopathy and Ayurveda. More than 70% of the population uses this non-homeopathic medicine system. Moringa oleifera is also known as horseradish and drumstick. On the photo. Figure 1 shows a Moringa oleifera Lam plant. The Moringa oleifera (Munga) plant, a member of the Moringaceae family, is native to the sub-Himalayan regions of India, Pakistan, Bangladesh and Afghanistan. It is a small, fast-growing evergreen or deciduous tree. It usually grows to a height of 10 to 12 m [1]. The mung bean plant contains a large and rare combination of zeatin, quercetin, beta-sitosterol, chemopherol, and caffeoylginic acid. The major minerals present in Moringa oleifera include iron, potassium, calcium, copper, zinc, magnesium, manganese, etc. Other most important and valuable species of Moringa plant are M. oleifera, M. arborea, M. drouhardii, M. ovalifolia, M. Longituba, M. Rivae, M. Borgiana, M. Korkanensis, M. Hildebrandti, M. Ruspoliana, M. stenopetala, M. peregrine falcon, M. pygmaea. Various parts of the plant such as bark, leaves, seeds, flowers, roots and immature pods contain large amounts of important plant components such as terpenoids, alkaloids, tannins, steroidal aglycones and reducing sugars. The leaves of the plant contain essential amino acids needed to build a strong and healthy body. Moringa oleifera leaves have been used for centuries in traditional and Ayurvedic medical systems related to the treatment or prevention of diseases due to their water-holding capacity, water-purifying ability, and high nutritional value. The leaves of the plant are small and difficult to collect. Take advantage of the leaves' rich nutritional content, including vitamins, minerals, and essential amino acids. 100 grams of dried Moringa oleifera leaves contain 9 times more vitamin A than carrots, 15 times more potassium than bananas, 17 times more calcium than milk, 12 times more vitamin C than oranges, and 25 times more iron than spinach. Rich in antioxidants, mung bean leaves contain a variety of antioxidants, including beta-carotene, vitamin C, quercetin, and chlorogenic acid. Chlorogenic acid has been shown to lower blood sugar levels [2]. Leaves and seeds of Moringa oleifera Lam. This may protect against some of the effects of arsenic toxicity, which is especially important in light of the news. Arsenic contamination of groundwater has also become a global public health problem. Moringa oleifera seeds have

been found to be much more capable of purifying water [3]. The digestive system contains a plant called Moringa oleifera Lam. Because of its very high fiber content, it acts like a rag in the intestines, removing all the excess debris left behind from a high-fat diet, and is famous for its isothiocyanates, which have beneficial antibacterial activity. Eliminates Helicobacter pylori (H. pylori), the bacteria that causes gastritis and stomach cancer, from the body.



Synonyms

Latin – Moringa oleifera

Sanskrit – Subhanjana,

Hindi – Saguna, Sainjna

Gujarati – Suragavo

Tamil – Mulaga, Munaga

Malayalam – Murinna, Sigru

Punjabi – Sainjna, Soanjna

Unani – Sahajan

Ayurvedic – Haritashaaka, Raktaka, Akshiva

Arabian – Rawag,

French – Morungue

Spanish – Angela, Ben, Moringa

Chinese – La ken



English - Drumstick tree, Horseradish tree

Morphology :

Moringa oleifera is a small, fast-growing evergreen or deciduous tree that typically grows to 10–12 m in height. It has spreading brittle branches, feathery trefoil leaves, and whitish-gray bark [4].

leaf

The leaves are 2-pinnate or usually 3-lobed, up to 45 cm long, and the leaflets are pubescent, green, and have little hair on the upper surface. The branches are pubescent, green and have compound leaves with leaflets 1-2 cm long.

flowers

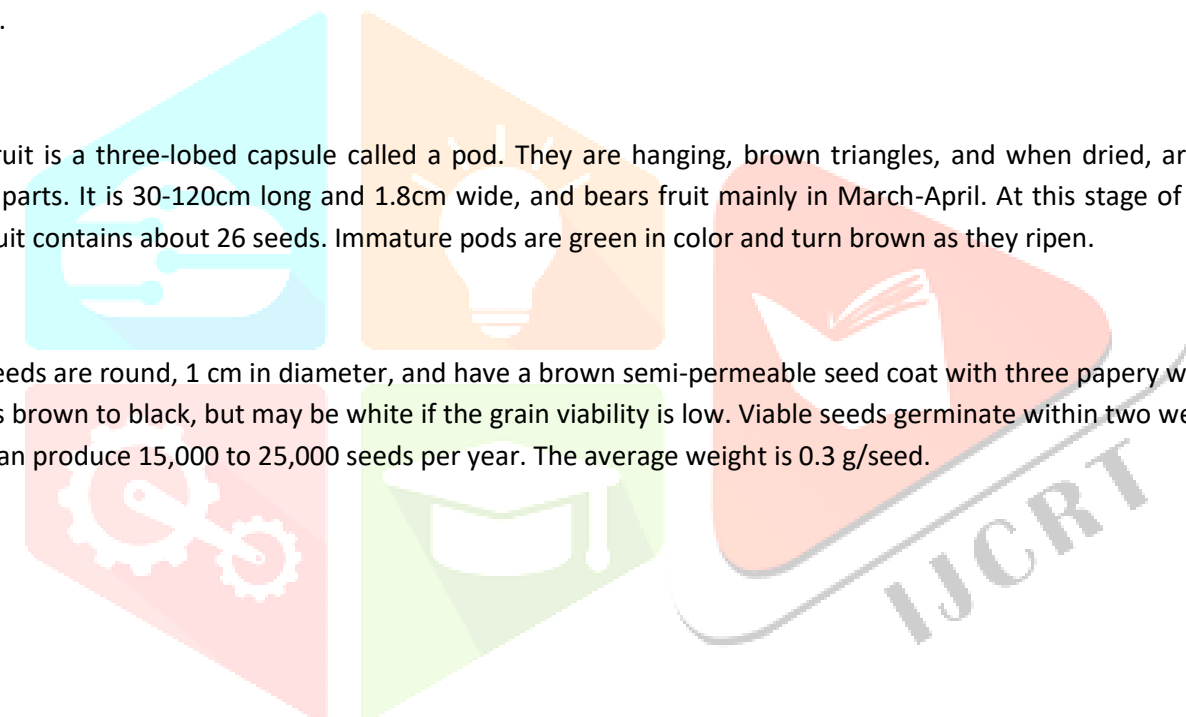
The fragrant bisexual, yellow-white flowers appear on hairy stems in spreading or drooping axillary panicles 10 to 25 cm long. Individual flowers are about 0.7 to 1 cm long and 2 cm wide, consisting of five uneven yellow-white, finely veined, spatula-shaped petals, five stamens with five small sterile stamens, a unicellular ovary and a slender style. It has a pistil. .

fruit

The fruit is a three-lobed capsule called a pod. They are hanging, brown triangles, and when dried, are divided into three parts. It is 30-120cm long and 1.8cm wide, and bears fruit mainly in March-April. At this stage of development, the fruit contains about 26 seeds. Immature pods are green in color and turn brown as they ripen.

seed

The seeds are round, 1 cm in diameter, and have a brown semi-permeable seed coat with three papery wings. The seed coat is brown to black, but may be white if the grain viability is low. Viable seeds germinate within two weeks, and each tree can produce 15,000 to 25,000 seeds per year. The average weight is 0.3 g/seed.



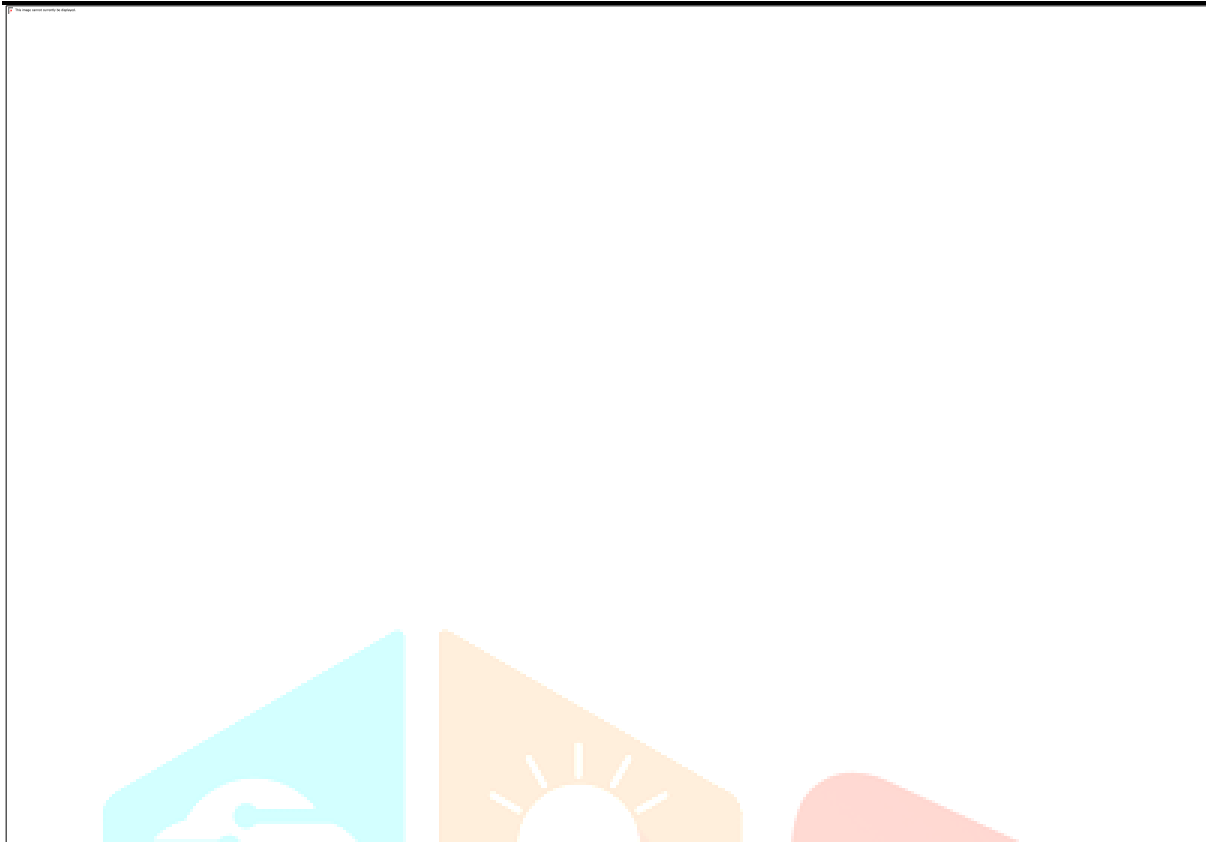


Fig 2 : Morphology Of Moringa Oleifera

Therapeutic properties of *M. oleifera* organs :

M.oleifera has many therapeutic properties. he has Painkillers, anti-inflammatory agents, antipyretics, anticancer agents, Antioxidants, nootropics, hepatoprotectors, gastrointestinal protectors, Anti-ulcer drugs, cardiovascular drugs, anti-obesity drugs, anti-epileptic drugs, anti-stone drugs, diuretics, local anesthetics, anti-allergy drugs, Anthelmintic, wound healing, antibacterial, Immunomodulatory and anti-diarrheal properties (Bhattacharya et al., 2018). The juice of the leaves was considered a cleanser. and anti-thrombotic agents; Relieve seizures in children, Treatment of headaches and conjunctivitis (West Africa) World Health Organization (WAHO), 2013). fresh leaves Applying a poultice by pressing on the abscess ripen and expedite expulsion Foreign body. Poultice made from heated leaves Used to treat syphilitic ulcers. (Fortin et al., 2009). The leaves are boiled and used. Treatment of high blood pressure and erectile dysfunction (Diop, 2014), and is also used as an antipyretic (Sèye, 2014). A decoction of flowers has an antifungal and therapeutic effect. For male infertility and sexual dysfunction women (Fortin et al., 2009). The fruit has been used in: Treatment of inflammatory diseases, asthma, rhinitis (Guy, 2011). Seed powder was used. Hypertension (Diop, 2014). Seeds have also been used for: treatment of splenomegaly; Wound treatment. they also It is helpful in treating hyperthyroidism and rheumatism. Processed *M. oleifera* seed meal can be used to treat malnutrition. Issues (West African Health Organization (WAHO); 2013). Moringa bark contains two alkaloids. Moringin and Moringinine (Kerharo, 1969). It is used for Treatment of heart problems, yellow fever and Toothache relief with a massage using crushed roots It has a beneficial effect on rheumatism and joint pain. root, It is administered nasally in powder form and can be used as an antipyretic. Headache and neuralgia (Guye, 2011).

Anti-diabetic activity :

The water-soluble extract of *Moringa oleifera* leaves exhibits anti-diabetic activity and regulates diabetes, providing glycemic control [8]. An in vitro study was conducted on the antioxidant and in vivo antidiabetic effects of methanolic extract of *Moringa oleifera* pods in streptozotocin (STZ)-induced diabetic albino rats. After administering 150 or 300 mg/kg of the extract to diabetic rats for 21 days, the anti-diabetic effect was evaluated by measuring changes in biochemical indicators in serum and pancreatic tissue. After treatment with the extract, the progression of diabetes was significantly reduced. In treated rats, both doses of the extract significantly reduced serum glucose and nitric oxide levels with a concurrent increase in serum insulin and protein levels [9]. The antidiabetic activity of two doses of moringa seed powder, 50 and 100 mg/kg, was studied in male rats with STZ-induced diabetes. The diabetes positive control group showed increased IL-6 levels, increased lipid peroxidation, and decreased antioxidant enzymes in serum and kidney tissue homogenate compared to the negative control group [10].

The antidiabetic activity of *Moringa oleifera* has been demonstrated. Several studies conducted in sub-Saharan Africa have reported Other parts of the world. *M. oleifera* leaves are suitable. Sources of Green Leafy Vegetables to Reduce Diabetes Complications in diabetic patients (Giridhari et al., 2011). The aqueous extract inhibits the activity of α -amylase and α -glucosidase; Antioxidant ability, glucose improvement Tolerance and glucose uptake rate in yeast cells. The aqueous extract can be used as an herbal remedy. For the treatment of diabetes when used as a supplement or separately (Khan et al., 2017). Ethnobotanical findings were accepted. It is possible to catalog the abundance of antidiabetic medicinal plants from sub-Saharan Africa. Community interest in these remedies. In Senegal A study conducted on Fulani herdsmen ViduTiengoli, Tessekere municipality, Iferlo; The Niore du Rip and Tiwanouan departments showed: Population and traditional customs widely used *Moringa oleifera* for the treatment of diabetes (Delattre et al.) al., 2001; Geez, 2016; Diop, 2014; Say, 2014). Additionally, other ethnobotanical studies were also conducted. Africa shows the presence of medicinal plants in everyday life. Community-Based Diabetes Management The case of Mali (Kone, 2017; Razinge, 2010) Chad (Etuk and Mohammed, 2009); Species vary depending on the ethnic group. *M. oleifera* is It was cited as a standard in all his reviews. Antidiabetic medicinal plant due to its efficacy. Results of ethnobotanical studies on use Medicinal plants as alternative treatments Diabetes has identified 112 plant species belonging to 51 species. families in Togo (Ayeni et al., 2016); 168 tradition Herbal medicine from Tanzania (Luniera et al., 2016); and A total of 24 species of plants belonging to 20 families. South Africa (Semenya et al., 2012). Methods of preparation of traditional medicine In the form of decoction, maceration, infusion or infusion. Adding leaf or seed powder to food. in According to a study conducted in Tanzania Traditional medicine used in people with diabetes It was 77.1% (Luniera et al., 2016). use of plants It was related to availability (cost) and efficiency. Lowers blood sugar levels and reduces or eliminates classic signs of disease; But others also said the opposite. Access to health care, especially for chronic conditions; In rural areas, medicines remain a serious problem.

Plants play an important role in the health of society system. However, the World Health Organization (WHO) Encouraged research into traditional medicine. Treatment of these chronic non-communicable diseases (Sante Peace Organization, 2013). many There is nothing specific about the preparation of this drug Dosages that can be dangerous if toxic In some plants. Doses ranging from 100 to 800 mg were used in the bioassay. Animal testing was conducted. Extracts (aqueous, methanolic and ethyl acetate) at a dose of 200 mg/kg was most frequently used. work (Figure 4). Criteria for including animals Biological assays depend on blood sugar levels. Causes diabetes. Streptozotocin and Various doses of Alloxan have been used as follows: Experimental model for inducing diabetes in the laboratory Animals under study. They trigger insulin-producing cells. The pancreas is destroyed, causing necrosis. Most studies use metformin or tolbutamide as the drugs. Reference drug. Studies have shown that aqueous extracts *M. oleifera* leaves showed dose-dependent hypoglycemia. The activity of alloxan-induced diabetic rats was almost It is as effective as standard medications (tolbutamide, metformin). Aqueous extract at doses of 100 and 200 mg/kg *M.oleifera* helps improve fasting blood sugar levels. Increases HDL cholesterol and reduces LDL levels Induction of cholesterol and triglyceride levels in diabetic rats Streptozotocin or alloxan. Methanolic extract of *M. oleifera* leaves is available at doses of 300 and 600 mg/kg. Alloxan-induced hypoglycemic effect in diabetic rats, Improved glucose tolerance,

glycogen and lipid synthesis Metabolism (Olayaki et al., 2015). therapy Water-soluble extract of leaves (7 days) and seeds (28 days) *M. oleifera* at a dose of 400 mg/kg for alloxan challenge. Diabetic rats showed hypoglycemic activity (Adeeyo et al., In 2013; Oyedepo et al., 2013). Application of aqueous extract of *M. oleifera* leaves Doses of 250 and 800 mg/kg for alloxan induction. Satisfactory hypoglycemic activity was observed in diabetic rats; Not only does it improve pancreatic function in mice, (Omodanisi et al., 2017; Aja et al., 2013). oral- Administration of leaf extract reduces plasma lipid levels Diabetes-related imbalances, mechanisms It may increase blood sugar utilization by inhibiting hepatic glucose production or uptake of glucose by the liver. muscle and adipose tissue (Oyedepo et al., 2013). However, HDL levels are high and LDL levels are reduced. Concentration after administration of *M. oleifera* extract May play a protective role in development Atherosclerosis and cardiovascular complications Diabetes (Olayaki et al., 2015). wealth of africa Flora of medicinal plants, adaptation of *M. oleifera* to the Sahelian climate and its use as daily food; Decision-makers should be encouraged to support research. This so-called miracle plant. This can be done by: Funding and institutional support for clinical research Treat patients with diabetes according to ethical standards. Oxidative stress is suspected to be a cause of chronic non-communicable diseases, especially: diabetes. This causes insulin to decrease. Secretion and reduction of Langerhans cells Condition worsens due to low blood sugar hormones Insulin Resistance in Type 2 Diabetes Profile (Delatre et al., 2001). phytochemical composition *M. oleifera* has a protective effect against oxidation. Preventing or slowing down the oxidation of others due to stress molecule. This is usually done through free capture. Reduces radical and inflammation occurrence Cytokines due to high phenol content (Omodanisi et al.) al., 2017). The hypoglycemic activities of *M. oleifera* are as follows: Because it contains antioxidants such as flavonoids Quercetin and kaempferol, polyphenols and vitamins, and other parts of the plant (Adeeyo et al., 2013). Quercetin significantly increases liver activity. Insulin-like glucokinase. The leaves contain terpenoids. It appears to be involved in beta cell stimulation. Subsequent secretion of preformed insulin (Konmy et al. al., 2016). Other compounds found in *Moringa oleifera*. Leaves like isothiocyanates appear to reduce insulin levels Resistance and hepatic glucose production. The organs of *Moringa oleifera* also contain flavonoids. Tannins, alkaloids, saponins, and terpenoids (Abdulkadir et al., 2016; Hafiz et al., 2016). Phytochemical analysis of roots Powder extract containing methanol Some secondary metabolites, namely alkaloids, tannins, Flavonoids, cardiac glycosides, saponins, triterpenes and Steroids (Umar et al., 2018). The healing effect of *M. oleifera* on diabetic wounds can be explained as follows. Presence of tannin, a polyphenol component Tissue regeneration and infection control properties (Donggok et al., 2018). *M. oleifera* is also used in many treatments. Diseases such as high blood pressure and obesity This can be explained by the presence of β -sitosterol. leaf. Using underground components may result in the following hazards: Type (if there is no recovery mechanism) Biodiversity conservation by local communities

Materials and Methods: 2

.1 Extract preparation:

MO fruits, leaves and flowers were obtained from the field and herbarium. The leaves were submitted to the Department of Botany, Maharaja Sayajirao University, Baroda, for species. test. MO was dried in an oven at a temperature of 50°C to obtain dry powder. 100g each dry powder. The components were extracted with 500 ml of methanol for 48 h in a Soxhlet apparatus. The methanol extract is It was dried in a water bath at 55°C. Plant yield percentages were 9.8%, 6.3%, and 7.7% for fruit; leaves and flowers respectively. Plant extracts were lyophilized and stored at -70°C. working solution It is prepared by dissolving the extract in physiological solution. 2.2

Experimental model:

Healthy adult female Wistar rats (80–90 days old) were housed in sockets. Ventilated room with temperature control on a 12-hour light:12-hour dark schedule. Rats were fed standard food Balanced rat pellets (Baroda, India) and drinking water were provided ad libitum. The mice were isolated. Categorized into the following groups: (i) Control (C) (ii) Streptozotocin-induced diabetes (STZ) (iii) Ovariectomy (OVX) (iv) Streptozotocin-induced diabetic ovariectomy (STZ-OVX) (v) STZ-OVX plant extract. each group It consists of 6 rats. The control group was provided only with a car. Group V was divided into three groups. Group treated with leaf, flower and fruit extract at 200 mg/kg body weight (LD50 = 400 mg/kg) B.V.). 2.3 Biochemical tests. Animals were sacrificed after 30 days. Blood sugar levels, ALP and TRAcP activity Serum was assessed using commercially available kits (Reckon Diagnostics, India). 2.4

Statistical analysis:

One-way analysis of variance was performed followed by multiple comparisons of the obtained data. using Graph Pad 5 (a p value <0.05 was considered significant).

Safety and toxicity profile of *Moringa oleifera*

It is now recognized that many people rely on medicinal plants for the treatment of various diseases, largely due to genetic knowledge (Palhares et al., 2015; Muvhulawa et al., 2022). Therefore, general interest in the use of medicinal plants to treat various diseases has increased over the years (Rakotoarivelo et al., 2015; Michel et al., 2020). Therefore, it is important to evaluate the toxicity of plants to know how safe they are for humans. Accumulated studies have shown that *Moringa oleifera* exhibits many important biological properties, such as antioxidant, anti-inflammatory, and antihyperglycemic properties, and has recently been proven to be a good plant for use as an alternative treatment for diabetes (Omodanisi et al., 2017b; Gothai et al., 2017; Paula et al., 2017; Abd et al., 2020; Xiong et al., 2021). In vitro and in vivo studies have shown that this plant does not produce lethal doses and is safe to use. In fact, a study by Villarruel-López and others showed that the use of *Moringa oleifera* at doses varying from 100 to 500 mg/kg was not toxic to rats (Villarruel-López et al., 2018). Albrahim and Binobead also used mice to show that *Moringa oleifera* reduces becin-induced cytotoxicity as measured by changes in liver function, oxidative stress, DNA damage, and liver damage (Albrahim and Binobead, 2018a). Analysis of data by Asare and colleagues showed that *Moringa oleifera* is genotoxic at supplementation doses above 3000 mg/kg body weight, and supplementation is generally considered safe at levels below 1000 mg/kg body weight (Asare et al., 2012). However, other studies have shown that although the existing literature is very promising (Awodele et al., 2012; Ajibade et al., 2013; Stohs and Hartman, 2015; Patriota et al., 2020; Siddiqui et al., 2021; Teshome et al., 2021)., 2020; al., 2021), further clinical studies (in humans) to obtain standardized extracts of this plant.

Conclusion :

As diabetes continues to spread rapidly, there is an urgent need to find new and more effective treatments for this chronic disease (International Diabetes Federation, 2021). Metformin and insulin, commonly used as antidiabetic drugs, clearly extend the lifespan of diabetic patients (Joya-Galeana et al., 2011; Foretz et al., 2014; Bailey, 2017). Therefore, although diabetes can be controlled through other effective interventions such as exercise and calorie restriction (Nyawo et al., 2021; Shakoor et al., 2021; Mthembu et al., 2022), consistent compliance with these interventions is difficult. Yes. Few people have it. Intensive intervention. In addition to lowering glucose levels or improving insulin sensitivity, there was a need to find treatments that could target both oxidative stress and inflammation, key dysregulations associated with diabetes development (Vikram et al., 2014; Mahlangu et al. 2014). , 2020;Mokgalaboni et al., 2021b). It is also used on rooibos (*Aspalathus Linearis*) and broccoli (*Brassica oleracea var. italica*). It has rich antioxidant properties that combat metabolic complications such as oxidative stress and inflammation (Hwang and Lim, 2014; Dlodla et al., 2017a; Orlando et al.). , 2022). Plants have been studied for their therapeutic properties and are cheaper, more accessible, and safer than synthetic traditional medicines (Ahmad et al., 2019). There is growing evidence that plants are used not only as a food source, but also as medicine, nutraceuticals, and more. (Alegbelee, 2018). It also contains polyphenols, vitamins, flavonoids, alkaloids and other important phytochemicals. *Moringa oleifera* has been shown to reduce insulin resistance through activation of insulin-independent PI3K/AKT and AMPK pathways in skeletal muscle and improve oxidative metabolism in skeletal muscle through NAD-dependent deacetylase (SIRT1).).)-PPAR α as well as by improving fatty acid peroxidation (Bao et al., 2020; Duranti et al., 2021). Indeed, compelling evidence summarized in this review supports the beneficial effects of *Moringa oleifera* in improving blood glucose levels, lipid profile and insulin sensitivity and preventing liver or kidney damage in preclinical (animal) models of T1DM/T2DM. Table No. 1). and 2).2). Interestingly, these extracts enhance intracellular antioxidants such as CAT, SOD, GSH and GST, reduce lipid peroxidation products MDA/TBARS, and reduce the expression levels of pro-inflammatory markers such as TNF- α , 1L- β and IL. I order it. The effect of Shiki has been improved. -6, manual transmission. -1, COX-2 and nitric oxide synthase. Figure 3 summarizes some of the therapeutic effects of protection against oxidative stress and inflammation associated with *Moringa oleifera* extract in preclinical models of diabetes. Additionally, a review of the current literature revealed that *Moringa oleifera* leaf extract is widely used at doses ranging from 100 to 300 mg/kg with an initial treatment period of 2 to 8 weeks (Tables (Tables1, 2). . It also establishes a platform for future research (currently limited) aimed at developing *Moringa oleifera* as a functional food for the treatment of diabetes. It is important to note that further clinical trials are needed to evaluate whether *Moringa oleifera* leaf extract can serve as an important biomarker of oxidative stress and inflammation to confirm preclinical results.

References

- Abd Eldaim M. A., Shaban Abd Elrasoul A., Abd Elaziz S. A. (2017). An Aqueous Extract from *Moringa Oleifera* Leaves Ameliorates Hepatotoxicity in Alloxan-Induced Diabetic Rats. *Biochem. Cell. Biol.* 95, 524–530. 10.1139/bcb-2016-0256 [PubMed] [CrossRef] [Google Scholar]
- Abd H. H., Ahmed H. A., Mutar T. F. (2020). *Moringa Oleifera* Leaves Extract Modulates Toxicity, Sperms Alterations, Oxidative Stress, and Testicular Damage Induced by Tramadol in Male Rats. *Toxicol. Res. (Camb)* 9, 101–106. 10.1093/toxres/tfaa009 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- Abd Rani N. Z., Husain K., Kumolosasi E. (2018). *Moringa* Genus: A Review of Phytochemistry and Pharmacology. *Front. Pharmacol.* 9, 108. 10.3389/fphar.2018.00108 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- Ahmad J., Khan I., Blundell R. (2019). *Moringa Oleifera* and Glycemic Control: A Review of Current Evidence and Possible Mechanisms. *Phytother. Res.* 33, 2841–2848. 10.1002/ptr.6473 [PubMed] [CrossRef] [Google Scholar]

Ajibade T. O., Arowolo R., Olayemi F. O. (2013). Phytochemical Screening and Toxicity Studies on the Methanol Extract of the Seeds of *Moringa Oleifera*. *J. Complement. Integr. Med.* 10. 10.1515/jcim-2012-0015 [PubMed] [CrossRef] [Google Scholar]

Aju B. Y., Rajalakshmi R., Mini S. (2020). Corrigendum to "Protective role of *Moringa oleifera* leaf extract on cardiac antioxidant status and lipid peroxidation in streptozotocin induced diabetic rats" [*Heliyon* 5, (12), (December 2019), e02935]. [*Heliyon* 56 (12), e02935e03146. 10.1016/j.heliyon.2019.e03146 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Aju B. Y., Rajalakshmi R., Mini S. (2019). Protective Role of *Moringa Oleifera* Leaf Extract on Cardiac Antioxidant Status and Lipid Peroxidation in Streptozotocin Induced Diabetic Rats. *Heliyon* 5, e02935. 10.1016/j.heliyon.2019.e02935 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Al-Malki A. L., El Rabey H. A. (2015). The Antidiabetic Effect of Low Doses of *Moringa oleifera* Lam. Seeds on Streptozotocin Induced Diabetes and Diabetic Nephropathy in Male Rats. *BioMed Res. Int.* 2015, 13. 10.1155/2015/381040 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Albrahim T., Binobead M. A. (2018a). Roles of *Moringa Oleifera* Leaf Extract in Improving the Impact of High Dietary Intake of Monosodium Glutamate-Induced Liver Toxicity, Oxidative Stress, Genotoxicity, DNA Damage, and PCNA Alterations in Male Rats. *Oxidative Med. Cell. Longev.* 2018, 1–11. 10.1155/2018/4501097 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Alegbeleye O. O. (2018). How Functional Is *Moringa Oleifera*? A Review of its Nutritive, Medicinal, and Socioeconomic Potential. *Food Nutr. Bull.* 39, 149–170. 10.1177/0379572117749814 [PubMed] [CrossRef] [Google Scholar]

Rena G., Pearson E. R., Sakamoto K. (2013). Molecular mechanism of action of metformin : old or new insights. *Diabetologia* 56, 1898–1906. 10.1007/s00125-013-2991-0 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Roep B. O., Thomaidou S., Van Tienhoven R., Zaldumbide A. (2021). Type 1 diabetes mellitus as a disease of the β -cell (Do Not blame the immune system?). *Nat. Rev. Endocrinol.* 17, 150–161. 10.1038/s41574-020-00443-4 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Rose B. A., Force T., Wang Y. (2010). Mitogen-activated protein kinase signaling in the heart: angels versus demons in a heart-breaking tale. *Physiol. Rev.* 90, 1507–1546. 10.1152/physrev.00054.2009 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Saini R. K., Sivanesan I., Keum Y. S. (2016). Phytochemicals of *Moringa oleifera*: a review of their nutritional, therapeutic and industrial significance. *3 Biotech.* 6, 203. 10.1007/s13205-016-0526-3 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Shakoore H., Apostolopoulos V., Feehan J., Ali H. I., Ismail L. C., Al Dhaheri A., et al. (2021). Effect of calorie restriction and exercise on type 2 diabetes. *Pril. Makedon. Akad. Nauk. Umet. Odd. Med. Nauki* 42, 109–126. 10.2478/prilozi-2021-0010 [PubMed] [CrossRef] [Google Scholar]

Sharma P., Jha A. B., Dubey R. S., Pessarakli M. (2012). Reactive oxygen species, oxidative damage, and antioxidative defense mechanism in plants under stressful conditions. *J. Bot.* 2012, 26. Article ID 217037. 10.1155/2012/217037 [CrossRef] [Google Scholar]

Siddiqui S., Upadhyay S., Ahmad I., Hussain A., Ahamed M. (2021). Cytotoxicity of *Moringa oleifera* fruits on human liver cancer and molecular docking analysis of bioactive constituents against caspase-3 enzyme. *J. Food Biochem.* 45, e13720. 10.1111/jfbc.13720 [PubMed] [CrossRef] [Google Scholar]

Sierra-Campos E., Valdez-Solana M., Avitia-Domínguez C., Campos-Almazán M., Flores-Molina I., García-Arenas G., et al. (2020). Effects of *Moringa oleifera* leaf extract on diabetes-induced alterations in paraoxonase 1 and catalase in rats analyzed through progress kinetic and blind docking. *Antioxidants* 9, 840. 10.3390/antiox9090840 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Singh G., Passari A. K., Leo V. V., Mishra V. K., Subbarayan S., Singh B. P., et al. (2016). Evaluation of phenolic content variability along with antioxidant, antimicrobial, and cytotoxic potential of selected traditional medicinal plants from India. *Front. Plant Sci.* 7, 407. 10.3389/fpls.2016.00407 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Sissoko L., Diarra N., Nientao I., Stuart B., Togola A., Diallo D., et al. (2020). *Moringa Oleifera* leaf powder for type 2 diabetes: A pilot clinical trial. *Afr. J. Traditional Complementary Altern. Med.* 17, 29–36. 10.21010/ajtcam.v17i2.3 [CrossRef] [Google Scholar]

Stanford K. I., Goodyear L. J. (2014). Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. *Adv. Physiol. Educ.* 38, 308–314. 10.1152/advan.00080.2014 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Steinmetz K. L., Spack E. G. (2009). The basics of preclinical drug development for neurodegenerative disease indications. *BMC Neurol.* 9 (Suppl. 1), S2. 10.1186/1471-2377-9-S1-S2 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Stohs S. J., Hartman M. J. (2015). Review of the safety and efficacy of *Moringa oleifera*. *Phytother. Res.* 29, 796–804. 10.1002/ptr.5325 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Tail J., Clerc P., Gauvin-Bialecki A., Gonthier M.-P. (2020). Medicinal plant polyphenols attenuate oxidative stress and improve inflammatory and vasoactive markers in cerebral endothelial cells during hyperglycemic condition. *Antioxidants* 9, 5731–5827. 10.3390/antiox9070573 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Tang Y., Choi E. J., Han W. C., Oh M., Kim J., Hwang J. Y., et al. (2017). *Moringa oleifera* from Cambodia ameliorates oxidative stress, hyperglycemia, and kidney dysfunction in type 2 diabetic mice. *J. Med. Food* 20, 502–510. 10.1089/jmf.2016.3792 [PubMed] [CrossRef] [Google Scholar]

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. Altern. Med.* 2017, 6581390. 10.1155/2017/6581390 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Teodoro J. S., Nunes S., Rolo A. P., Reis F., Palmeira C. M. (2018). Therapeutic options targeting oxidative stress, mitochondrial dysfunction and inflammation to hinder the progression of vascular complications of diabetes. *Front. Physiol.* 9, 1857. 10.3389/fphys.2018.01857 [PMC free article] [PubMed] [CrossRef] [Google Scholar]