Role of *Moringa oleifera* seed consumption on the levels of glucose, serum adipokines and bone function markers in patients with type 2 diabetes mellitus

Hazhar M. Balaky\(^1\), Ismail S. Kakey\(^2\)

\(^1\)Department of Chemistry, Faculty of Science, Soran University, Erbil, KRG, Iraq  
\(^2\)Department of Biology, Faculty of Science and Health, Koya University, Koya KOY45, Erbil, KRG, Iraq

**ABSTRACT**

The current study was conducted to investigate the impact of consumption of *Moringa oleifera* seed on the levels of glucose, bone function markers and adipokines, in diabetes males. This study involved (47) diabetes male patients aged (40-59) years that have been classified into (Group 1): diabetes male under the treatment of *Moringa oleifera* seed (n=15) and (Group 2) diabetes male under the treatment of synthetic drugs (n=32). In addition to (15) apparently healthy subjects as a control group. Diabetes male patients consumed every day the *Moringa oleifera* seed at dose of 70 mg (one teaspoon) for 6 months. Blood samples were collected from both group to determine serum lipid profile, adipokines, bone function markers. Results indicate that consumption of *Moringa oleifera* seed induced a remarkable decrease in the levels of glucose and HbA1c, with accompanying increases in the levels of leptin and adiponectin. Furthermore, the use of *Moringa oleifera* seed increased vitamin D and inorganic phosphorus levels with concomitant decreases in the levels of osteoprotegerin and serum total calcium. These results show that consumption of *Moringa oleifera* seeds has a hypoglycemic effect, improving bone function markers and increasing adipokine levels in diabetic patients by improving biochemical indicators.

**INTRODUCTION**

Plants and their derivatives have been used for the treatment of DM for thousands of years and are often thought to be less toxic and less adverse than their synthetic equivalents. For this reason, medicinal plants have long been consumed as a therapeutic substance for diabetes mellitus worldwide. Medicinal herbs, including *Moringa oleifera*, have attracted attention for their curative effect and controlling of diabetes. The antihypertotoxicity, antidysslipidemic, and anti-inflammatory action of *Moringa oleifera*, as well as its capability to regulate essential hepatic enzymes and biochemical markers, were assessed in experimentally induced diabetic rats (Kumar *et al.*, 2015). Current glucose-lowering administration agents have a little disadvantage in comparison to synthetic agents. However, they have side effects like a disorder of the skin, haematological disorders and increased activities of hepatic enzymes. Despite the development of pharmacological agents to treat diabetes, the use of therapeutic plants is considered a complementary remedy for this disease. The herbal treatment methods used in the treatment of diseases have been transferred through gener-
The specialised agency of the United Nations responsible for international public health has proposed the progression of oral glucose-lowering agents from medicinal herbals as a natural herbal medicament to treat patients with diabetes attribute to their being cost-powerful and safe (Singh et al., 2008). *Moringa oleifera* arose from India and is now grown across the world. So, individuals in many economically developing countries have been consuming *Moringa oleifera* to treat and prevent the symptoms of diabetes for years. This is primarily due to its natural advantages. *Moringa oleifera* has been revealed to naturally improve the immune system, which usually becomes impaired in those who suffering from diabetes mellitus. *Moringa oleifera* has also been indicated to possess various essential anti-inflammatory effects. There are no adverse side effects linked with the utilisation of *Moringa oleifera*, considering that it is a safe, natural way for an individual to regulate their blood glucose and other complications correlated with diabetes.

*Moringa oleifera* (MO), is an Asian herb also called Drumstick tree which has high medicinal value and can be cultivated in the north and south regions of the world. It is usually grown and cultivated in Pakistan and is also known as Sohanjana. Maximum height of its tree is up to 10 m. Its leaves, seeds, pods and roots are also used in treating lung diseases, hypertension and skin infection. MO leaves contain vital proteins, essential amino acids, trace elements, phenolic compounds, antioxidants, bioactive compounds, tannins that making it ideal against specific health problems (Nasir et al., 2017).

It is also plentiful in vitamins and minerals that mostly resides in leave parts in the form of vitamin B6, provitamin A as β-carotene, magnesium, calcium (Bharali et al., 2003), phosphorous, potassium, vitamin A and D as well as various antioxidants as vitamin C and flavonoids (Mbikay, 2012). The antioxidant and antihyperglycemic activity of aqueous extract of *Moringa oleifera* leaves have emerged as a potent antihyperglycemic in streptozotocin-induced diabetic albino rats (Al-Malki and Rabey, 2015).

**MATERIALS AND METHODS**

**Study population and study design**

**Group 1**

Composed of 15 diabetic male patients (under the consumption of *Moringa oleifera* seed: 70 mg (one teaspoon) every day for six months).

**Group 2**

Composed of 32 diabetic male patients (under treatment with synthetic drugs).

**Group 3**

(Normal Control) Composed of 15 healthy males.

**Sample collection and evaluation**

Blood specimens were collected from the study subjects (patients and healthy individuals) after 10-12 hours of fasting. The samples were preserved in Gold-top serum separator tubes (SST) and EDTA tubes before centrifugation process. The specimens were centrifuged at 3500 rpm for 10 min, and the resulting serum and plasma samples were separated and preserved in Eppendorf tubes. After the collection of all samples were completed, the serum and plasma samples were dissolved to be ready for biochemical analyses.

**Biochemical assays**

The circulating glucose level was determined by the enzymatic colourimetric method, using BIO-LABO kit (France). Also, the HbA1c (Hemoglobin A1c) in whole blood was measured by the colourimetric method involving (fluorescence immunoassay (FIA) using Boditech Medkit. The serum leptin was determined by sandwich enzyme-linked immunosorbent assay (ELISA) technique using the Human Leptin (LEP) ELISA kit manufactured by SunLong Biotech, China. Furthermore, the serum adiponectin was determined by sandwich enzyme-linked immunosorbent assay (ELISA) technique using the human adiponectin (ADP) ELISA kit manufactured by SunLong Biotech, China. Serum Osteoprotegerin was estimated by sandwich enzyme-linked immunosorbent assay (ELISA) technique using the human Osteoprotegerin (OPG) ELISA kit manufactured by Sun Long Biotech, China. The serum 25-OH Vitamin D Concentration was assessed by solid-phase sequential enzyme immunoassay (EIA) technique using a kit made by Monobind, USA. The determination of serum inorganic phosphorous and serum calcium were performed by using the enzymatic colourimetric method using BIO-LABO kit (France).

**Statistical Analysis**

SPSS version 21 and GraphPad prism version 8 computer programs were used for statistical data analysis. Analytical test results and Bar graphs were performed expressed as Mean±SE. Unpaired T-test (Man-Whitney U) test was used for comparing the study parameter means between patient and control groups.
RESULTS AND DISCUSSION

Comparison the effect of M. oleifera seeds with synthetic antidiabetic drugs on the levels of glucose & HbA1c

The result of oral consumption seed of Moringa oleifera on the levels of glucose & HbA1c indiabetic male patients with age range (40-59) is shown in Table 1. The results uncover the presence of statistically significant difference of glucose (P=0.0153) & HbA1c levels (p=0.0114) in diabetic male, who were under the herbal treatment of M. oleifera seeds (195.4±3.13 mg/dL and 7.24±0.22 %) respectively in comparison to diabetic patients who were under the treatment of synthetic drugs (245.1±14.74 mg/dL and 9.06±0.38 %) respectively.

The observed results in the current study indicate that dietary supplementation of Moringa oleifera seed has a positive blood sugar effects by reducing FBG, which is high-risk health factor for diabetic patients. It has been revealed that a considerable decrease in blood glucose levels over some time in treated samples was caused by Moringa oleifera (MO) extract. This decrease may result from increased releasing of insulin (by the action of MO) from pancreatic β-cells (Rafiau and Luka, 2015). Thus, diminished in the current glucose level declares the capability of extract to minimise hyperglycemia. Increase in the fall of blood glucose over time may be due to the components in the extract, which remains in the body for a long time and prevents DM. The capability of the seed extract of moringa oleifera to remarkably decrease high glucose level may attribute to significant plant constituents seed like micronutrient and phytochemical. The most important phytochemical constituent of the Moringa oleifera extract that has been recorded is flavonoids, which has been further identified by both structure and functional relation as; flavans, flavanonones, flavones, flavanols, flavonons, and isoflavones. Bioflavonoids are best known for their multi-purpose biological activities, including its ability to act as glucose-lowering effects (Szkudelski, 2001). Also, the Moringa oleifera contains many potent antioxidant phytochemicals, especially quercetin and kaempferol. Kaempferol has been known to have glucose-lowering activities. Also, the mode of action could be either by an increase in the tissue utilisation of glucose by Moringa oleifera blocking hepatic biosynthesis of glucose from the non-carbohydrate substance or through absorption of glucose into the muscles and adipose tissues (El-Desouki et al., 2015). The effect of Moringa oleifera seed on glycosylated haemoglobin levels (HbA1c) is presented in Table 1. The majority of metabolic disorders has been reported to increase HbA1c level in diabetic animals and to decrease serum insulin. HbA1c is used to monitor glycemic control in diabetic patients and is considered to be an essential biomarker for the progression and improvement of chronic diabetic complications (Katare et al., 2018). In this study, the HbA1c levels in diabetic patients under the treatment of herbal (seed of Moringa oleifera) showed a significant decrease, and this may be due to the positive effect of the seed extract on glucose metabolism, resulting in improved glycemic control.

The results of the current study are in line with (Shanker et al., 2019), who reported that mean glucose and HbA1c levels were reduced significantly in diabetic patients who used Moringa oleifera seed. Plants with anti-diabetic activity employ various mechanisms in living organisms (increasing insulin sensitivity and secretion, stimulating regeneration in Langerhans islets and preventing free radicals). Previous animal studies reported that Moringa oleifera seed extract has a lowering effect on blood glucose levels in diabetic rats. The antihyperglycemic impact of Moringa oleifera may be caused by stimulating the releasing of insulin from β-cells via prevention of the formation of free radicals (Bamagous et al., 2018). Several polyphenols are found in Moringa oleifera. Amongst the most powerful are the flavonoids quercetin and kaempferol, caffeoylquinic acid. These compounds appear to converse anti-diabetic properties, acting as a competitive blocker of the sodium-glucose linked transporter type 1, thus decreasing the intestinal absorption of glucose (Vargas-Sánchez et al., 2019).

However, absorption of glucose involves other mechanisms such as the glucose transporter 2, which can be engaged towards small intestine mem-

| Parameters | Herbal treatment | Synth. treatment | P-Value |
|------------|-----------------|------------------|---------|
| Glucose mg/dL | 195.4±3.13 | 245.1±14.74 | 0.0153 |
| HbA1c % | 7.24±0.22 | 9.06±0.38 | 0.0114 |

The value expressed mean ± SE
increasing insulin secretion and release (reformative characteristic on pancreatic beta-cells, been examined upon their protective function and et al. in the number of OH groups on the B ring, (to presence of a 2,3-double bond and to an increase kaempferol, have been biochemically described due impacts of flavonoids, including quercetin and haemoglobin A1C (HbA1C). These preventative a diminish in post-prandial high glucose level and caused by the blocking of these enzymes, causes 2 diabetes, the capacity of the small intestine to receive glucose is increased, as a result of an elevation in the expression of glucose transporter type 2 and sodium-glucose linked transporter type 1 (Dyer et al., 2002). This forms a new problem on the diabetic patients, further complicated because of consumption of anti-diabetic drugs such as sulfonylureas, biguanides or thiazolidinediones, that have principle targets on organs other than the intestines (Meneses et al., 2015). Moringa oleifera has been studied as an antihyperglycemic agent due to its actions on the lowering of glucose concentration. One of the suggested mechanisms contributed is quercetin, as this substance can act as a blocker of glucose transporter type 2. However, it does not affect glucose transporter type 5 or sodium-glucose linked transporter type 1.

Nevertheless, quercetin has also been revealed to phosphorylate adenosine monophosphate-activated protein kinase, to elevation glucose uptake through stimulation of glucose transporter type 4 in skeletal muscle, and to diminishing the formation of glucose through negatively regulation of phosphoenolpyruvate carboxykinase and glucose-6-phosphatase in the liver. Moringa oleifera aqueous leaf extract has been shown to block the activity of α-glucosidase, pancreatic α-amylase, and intestinal sucrase, involving anti-diabetic properties (Vargas-Sánchez et al., 2019). These preventative effects are the possible advantage of phenols, flavonoids, and tannins present in Moringa oleifera. A delay in digestion of carbohydrate, caused by the blocking of these enzymes, causes a diminish in post-prandial high glucose level and haemoglobin A1C (HbA1C). These preventative impacts of flavonoids, including quercetin and kaempferol, have been biochemically described due to presence of a 2,3-double bond and to an increase in the number of OH groups on the B ring, (Tadera et al., 2006). Besides, these compounds have been examined upon their protective function and reformative characteristic on pancreatic beta-cells, increasing insulin secretion and release (Latif et al., 2014). Quercetin causes insulin production through phosphorylation of extracellular signal-regulated kinase 1/2 pathway and protection of pancreatic beta-cells against oxidative stress (Youl et al., 2010). Glucose lowering activity in the bioassay due to the presence of phytochemicals, that act as bioactive compounds with an antioxidant property that has been linked with a protective effect versus chronic regressive diseases. These glucose lowering impacts have been examined with doses of seed powder (50–100 mg/kg body weight) in diabetic patients, wherein diminishes in fasting blood sugar and circulating haemoglobin A1c compared with controls have been recorded (Olayaki et al., 2015). Previous researches proposes that kaempferol enhances glucose uptake via the PI3K and PKC pathways in the rat soleus muscle. Orally consumed kaempferol, remarkably diminished fasting blood glucose and serum HbA1c concentrations while ameliorating insulin insensitivity. Quercetin blocks the transport of fructose and glucose by glucose transporter type 2 in the brain and stimulates glucose transporter type 4 expression in skeletal muscle (Sherein et al., 2014). This could describe the affinity towards lower blood glucose concentrations in the diabetes group treated with Moringa oleifera compared to the positive control group. The glucose-lowering effect of Moringa oleifera leaf (8 g/day) by dietary administration in a period time of 40-days in type 2 diabetic patients in the age range (30-60) years of age without pharmacological treatment was examined and revealed a remarkably decreased glucose response in comparison to the patients not taken Moringa oleifera leaf (Kumari, 2010). Another study showed that a group of type 2 diabetic patients, with age range 40-58 years given Moringa oleifera leaf tablets/day for 90 days exhibited that the blood glucose response developeddescendingly with time while HbA1C showed lowering direction but not remarkably (Ghiridhari et al., 2011).

**Comparison the effect of M. oleifera seeds with synthetic antidiabetic drugs on the levels of adipokines**

Table 2 revealed, highly remarkable (P=0.0276) increase in circulating concentration of leptin in diabetic males who were under the treatment of herbal (seed of Moringa oleifera) which was (134.6±26.87

| Parameters         | Herbal treatment | Synthetic treatment | P-Value |
|--------------------|------------------|---------------------|---------|
| Leptin (pg/mL)     | 134.6±26.87      | 113.3±34.47         | 0.0276  |
| Adiponectin (ng/mL)| 3.08±1.09        | 0.67±0.18           | 0.0029  |

Values expressed Mean±SE.
pg/mL) as compared to diabetic patients. The latter was under the treatment of synthetic drugs (113.3±34.47 pg/mL). On the other hand, the results in Table 2 also showed a remarkable increase (P=0.0029) in mean serum level of adiponectin in diabetic males who were under the treatment of herbal (seed of Moringa oleifera) which was (3.08±1.09 ng/ml) as compared to diabetic patients who were under the treatment of synthetic drugs (2.05±0.22 ng/mL).

The results in this study revealed a remarkable increase in serum leptin concentration in herbal treated patients when compared to patients which used synthetic anti-diabetic drugs. At the same time, a non-significant increase of adiponectin level was seen in herbal treated patients in comparison to patients which used synthetic anti-diabetic drugs. Body fat that is stored within the abdominal cavity is considered as the direct association between various metabolic disorder and obesity, such as type 2 diabetes, hypertension and atherosclerosis, which are classified under the clinical signs of the metabolic disorder. Previous work (Ahmed et al., 2014) established the benefit of ethanolic extract of Moringa oleifera in ameliorating obesity and hyperlipidemia take place in female obese rats after a long period of therapy with HCD. Also, Moringa oleifera exhibited a beneficial effect in improving high serum level of leptin and low level of adiponectin. The direct potential mechanism for the describing of the curative role of Moringa oleifera in ameliorating the reported metabolic disturbance is the nature of M. oleifera as an antioxidant substance. The hypoglycemic effect of Moringa oleifera due to presence of various active elements like vitamins, minerals, amino acids, carotenoids, alkaloids, and flavonoids and contains phenolic compounds (such as zeatin, quercetin, isoquercetin, kaempferol, apigenin and rutin) (Yassa and Tohamy, 2014). Several studies showed that in the fatty tissue of obese rats, the gene expression of leptin was elevated. In contrast, the gene expression of adiponectin was diminished compared to the expression observed in the control rats.

The treatment with Moringa oleifera extracts negatively-regulated leptin mRNA expression while it positively-regulated adiponectin mRNA expression. Reduction in the leptin gene expression upon medicament with M. oleifera provided the principle pathway in the ameliorating of adiposity. Previous researches proposed a two-way correlation between serum leptin level and leptin mRNA in fatty cells and adiposity level (de Queiroz et al., 2014; de Azevedo Melo Luvizotto et al., 2013). de Azevedo Melo Luvizotto et al. (2013) recorded that utili-

sation of high-fat meals for an extended period resulted in increased expression of leptin which due to the elevated mass of adipose tissue (de Queiroz et al., 2014). In his study demonstrated that the hyperleptinemia as a result of leptin mRNA and protein positively-regulation enhanced rats to show a high index of adiposity after feeding a diet high in sucrose (de Queiroz et al., 2014).

Furthermore, positively-regulation of adiponectin mRNA exhibited ameliorating in the fatty cell of the obese rat. Adiponectin mRNA negatively-regulation is a symptom of fatty cell precipitation in obese rats and mice and a defect of insulin sensitivity (Choi et al., 2016). Additionally, Moringa oleifera might act as an insulin sensitizer as it act in a similar track to anti-resistin antibody, which promote insulin-mediated uptake of glucose in a fatty cell (Ye et al., 2013). The additional significant role of positively-regulation of adiponectin gene expression upon treatment with Moringa oleifera was the decrease in the abnormalities of metabolic pathway occurred in obese rats. Adiponectin is an antiatherogenic agent that reduce cardiovascular risk, which may be due to its anti-inflammatory properties. It blocks dysfunction of the endothelial cell, because it inhibits the expression receptors of low-density lipoprotein scavenger on macrophages, thus decreasing low-density lipoprotein uptake and formation of plaque. Contrary to leptin, adiponectin ameliorates insulin sensitivity, and its level in serum is negatively proportional to adiposity concentration. Obese patients with a decreased level of adiponectin progressed pattern of leptin resistance followed by insulin insensitivity, hyperlipidemia and heart disease (Metwally et al., 2017).

Gene expression analysis supplied a mechanistic curative role of ethanolic extract of M. oleifera in the controlling of obesity and reduction of abnormalities of metabolic pathways that occurred in cardiac muscle, resulting from high cholesterol diet (HCD) in female rats. Moringa oleifera extract worked directly on the fat mass and improved the defect of mRNA expression of leptin and adiponectin genes. Thus, it exhibits ameliorating in body mass index, atherogenic hyperlipidemia and insulin resistance. Therefore, Moringa oleifera could provide potent phytotherapy in the ameliorating of high levels of cholesterol, hardening of arteries and type 2 diabetes but without complications.

Comparison the effect of M. oleifera seeds with synthetic antidiabetic drugs on the levels of bone function markers

Table 3, revealed a remarkable reduction (P=0.0478) in mean serum concentration of
osteoprotegerin in diabetic males who were under the treatment of herbal (seed of *Moringa oleifera*) (300.1±36.43 pg/mL) as compared to diabetic patients who were under the treatment of synthetic drugs (496.3±61.46 pg/mL). While there was a remarkable increase (P=0.0105) in mean serum concentration of vitamin D in diabetic males who were under the treatment of herbal (seed of *Moringa oleifera*) which was (13.86±3.01 ng/mL) as compared to diabetic patients who were under the treatment of synthetic drugs (5.78±1.30 ng/mL). On the other hand, this study observed that there was significantly increasing (p<0.0001) in mean serum concentration of inorganic phosphorus in diabetic males who were under the treatment of herbal (seed of *Moringa oleifera*) which was (7.56±0.43 mg/dL) in comparison to diabetic patients who were under the treatment of synthetic drugs (4.34±0.27 mg/dL). While there was a remarkable decrease (p=0.0343) in mean serum concentration of total calcium in diabetic males who were under the treatment of herbal (seed of *Moringa oleifera*) which was (9.34±0.22 mg/dL) in comparison to diabetic patients who were under the treatment of synthetic drugs (11.10±0.46 mg/dL).

The findings in the current research are in line with (Habib and Al-Moalem, 2018; Srikanta, 2011). Type II DM is a disorder of carbohydrate metabolism linked with several complications, including a defect in the process of healing of the bone fracture. Bone is considered as an important skeletal structure in the body, is influenced by diabetic status, especially during the process of fracture healing. Bone is a tissue that undergoes frequent repairing and has a high magnitude for reformation. Disturbance in the balance between bone resorption and new bone formation leads to bone loss (He et al., 2004). Bone loss has also been linked with diabetes mellitus. Several studies have recorded that type 1 diabetes changes bone repairing by decreasing the synthesis of new bone, causing weakness of bone. This has been described by a reduction in mineral density of the bone in humans and variation in the production of new bone in animal researches. Several studies have confirmed the efficacy of medicinal plants in ameliorating bone health. The literature study of osteoporosis reveals that vitamin D, calcium and garlic oil, in ovary removed rats with low bone mass has been achieved by (Holick et al., 2008). From the previous studies, it can be seen that there are many medicinal plants for DM and fragile bone. Still, very little are having a positive impact both on carbohydrate as well as mineral metabolism. One of such plant is *Moringa oleifera* (MO), which has been labelled as a “wonder tree” as the advantages of MO is abundant: each part of the tree is advantageous in several ways. *Moringa oleifera* leaves are a great source of minerals (calcium, iron), protein and vitamins (especially Vitamin A, B and C). They are used to fighting malnutrition, hypertension, blindness, diabetes mellitus, anaemia, renal stones, to enhance lactation in nursing women, and as a disinfectant. *Moringa oleifera* plant has been confirmed to possess the strength of against bone damage. It has already been established that flavonoids content of *Moringa oleifera* (MO), have anti osteoclastic activity. As the flower is rich in these flavonoids, one can understand the potent effect of flower extract on this osteoclastic function marker.

It has been reported that *Moringa oleifera* is an excellent source of phenolic phytochemicals and variety of curative properties. Phenolic phytochemicals are now indicated to have a possible role in controlling various diseases associated with chronic oxidation; one of them is type 2 DMs (Patel et al., 2015; Farooq, 2012). Reported that powder of *Moringa oleifera* contains a sufficient amount of protein, minerals, phenols, vitamins and different phytoneutrients. This making the *Moringa oleifera* to act as a therapeutic substance for various illnesses. Kane et al. (2017) and Gopalakrishnan et al. (2016) reported that *Moringa oleifera* is one of the most extravagant plant wellsprings of minerals, such as Calcium, Copper, Iron, Potassium, Magnesium, Manganese and Zinc. Both protective and therapeutic role of *Moringa oleifera* in fight-

| Parameters                        | Herbal treatment | Synthetic treatment | P-Value |
|-----------------------------------|------------------|---------------------|---------|
| Osteoprotegerin (pg/mL)           | 300.1±36.43      | 496.3±61.46         | 0.0478  |
| Vitamin D (ng/mL)                 | 13.86±3.01       | 5.78±1.30           | 0.0105  |
| Inorganic Phosphorous (mg/dL)     | 7.56±0.43        | 4.34±0.27           | <0.0001 |
| Total calcium (mg/dL)             | 9.34±0.22        | 11.10±0.46          | 0.0343  |

Values expressed mean ±SE
ing human illnesses due to their content of minerals. For example, calcium is a multi-purpose supplement essential to the body digestion, while deficiency of calcium causes loss of bone mass. In this way, *Moringa oleifera* is showed the best solution for the treatment of fragile porous bones (Habib and Al-Moalem, 2018).

Additionally, administration the ethanolic extract of *Moringa oleifera* seeds was observed to diminish the circulating concentration of mediators of inflammation, the volume of paw oedema, and to prevent cytotoxic T-lymphocyte cells that cause anterior pituitary destruction, also to reduce the destruction of bone and cartilage erosion in the synovial joint, following to the progression of arthritis in rats. Furthermore, seeds of *Moringa oleifera* assist in treating joint inflammation, stiffness, arthritis, anti-inflammatory agents and cramp (Habib and Al-Moalem, 2018). Several studies have been published, describing the role of *Moringa oleifera* as a potent pharmaceutical agent, one of which was presenting its role in the protection bones from mass loss in rats with removed ovaries (Burali et al., 2010). It has been reported that *Moringa oleifera* having cell forming bone property, as it augmented all the indicators of osteoblast activity. Remarkable osteoblast activity of *Moringa oleifera* attribute to the presence of fruit and flower extract. In a study by Vali et al. (2007), it was revealed that bone formation in vitro due to the significant action of many flavonoids. *Moringa oleifera* plays a crucial role in stimulating osteoblastic cells because MO is rich in various flavonoids. It has been reported that *Moringa oleifera* fruit extract was shown to be having a significant effect on bone loss; it was also shown to be having a significant impact on calcium homeostasis (Patel, 2013). Furthermore, Rangrez et al. (2011) revealed that *Moringa oleifera* could inhibit the loss of bone mass in ovaries removed promote bone loss.

**CONCLUSIONS**

The data obtained from the present study have established the hypoglycemic effect of *Moringa oleifera* seed consumption by the improvement of the glucose & HbA1c levels. The current findings suggested utilising *Moringa oleifera* seeds as an excellent anti-osteoporotic activity. Furthermore, seeds of *Moringa oleifera* have ameliorating adipokine action.

**ACKNOWLEDGEMENTS**

We thank all staff at Laila Qasim Diabetes Centre in Erbil, and also thanks for the Research Center in Soran University for their help and collaboration to this work.

**Conflict of interest**

The authors declare no conflict of interest during this study.

**Funding Support**

The authors declare that they have no funding support for this study.

**REFERENCES**

Ahmed, H. H., Metwally, F., Rashad, H., Zaaza, A., Ezzat, S., Salama, M. 2014. *Moringa oleifera* offers a multi-mechanistic approach for management of obesity in rats. *International Journal of Pharmaceutics Review and Research*, 29(2):98–106.

Al-Malki, A. L., Rabey, H. A. E. 2015. The Antidiabetic Effect of Low Doses of *Moringa oleifera* Lam. Seeds on Streptozotocin Induced Diabetes and Diabetic Nephropathy in Male Rats. *BioMed Research International*, 2015:1–13.

Bamagus, G., Ghamdi, S. A., Ibrahim, I. A., Mahfoz, A., Aify, M. A., Alsugoor, M., Shammah, A. A., Arulselvan, P., Rengarajan, T. 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 Pacific Journal of Tropical Biomedicine*, 8(6):320–320.

Bharali, R., Tabassum, J., Azad, M. R. H. 2003. Chemo-modulatory effect of *Moringa oleifera*, Lam, on hepatic carcinogen metabolising enzymes, antioxidant parameters and skin papilloma genesis in mice. *Asian Pacific Journal of Cancer Prevention : APJCP*, 4(2):131–139.

Burali, S. C., Kangralkar, V., Sravani, O. S., Patil, S. L. 2010. The beneficial effect of ethanolic extract of *Moringa oleifera* on osteoporosis. *Int J Pharmaceutical Appl*, 1(1):50–58.

Choi, B. K., Park, S. B., Lee, D. R., Lee, H. J., Jin, Y. Y., Yang, S. H., Suh, J. W. 2016. Green coffee bean extract improves obesity by decreasing body fat in high-fat diet-induced obese mice. *Asian Pacific Journal of Tropical Medicine*, 9(7):635–643.

de Azvedo Melo Luvizotto, R., Nascimento, A. F., Imaiuzumi, E., Pierine, D. T., Conde, S. J., Correa, C. R., Yeum, K.-J., Ferreira, A. L. A. 2013. Lycopene supplementation modulates plasma concentrations and epididymal adipose tissue mRNA of leptin, resistin andIL-6in diet-induced obese rats. *British Journal of Nutrition*, 110(10):1803–1809.

de Queiroz, K. B., Guimarães, J. B., Coimbra, C. C.,...
Rodovalello, G. V., Carneiro, C. M., Evangelista, E. A., Guerra-Sá, R. 2014. Endurance Training Increases Leptin Expression in the Retroperitoneal Adipose Tissue of Rats Fed with a High-Sugar Diet. *Lipids*, 49(1):85–96.

Dyer, J., Wood, I. S., Palejwala, A., Ellis, A., Shirazi-Beechey, S. P. 2002. Expression of monosaccharide transporters in intestine of diabetic humans. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 282(2):G241–G248.

El-Desouki, N. I., Basyony, M. A., Hegazi, M. M., El-Aama, M. S. 2015. Moringa oleifera leaf extract ameliorates glucose, insulin and pancreatic beta cells disorder in alloxan-induced diabetic rats. *Research Journal of Pharmaceutical Biological and Chemical Sciences*, 6(3):20–20.

Farooq, F. 2012. Medicinal properties of Moringa oleifera: An overview of promising healing. *Journal of Medicinal Plants Research*, 6(27):4368–4374.

Ghiridhari, V. V. A., Malhati, D., Geetha, K. 2011. Anti-diabetic properties of drumstick (Moringa oleifera) leaf tablets. *Int. J. Health Nutr*, 2(1):1–5.

Gopalakrishnan, L., Doriya, K., Kumar, D. S. 2016. *Moringa oleifera* plant extract. *Journal of Diabetes Mellitus*, 5(2):10–17.

Habib, M., Al-Moalem, M. 2018. Effect of Moringa Leaves and Seeds on Osteoporosis in Rats. *Journal of Food and Dairy Sciences*, 2018(0):129–135.

He, H., Liu, R., Desta, T., Leone, C., Gerstenfeld, L. C., Graves, D. T. 2004. Diabetes Causes Decreased Osteoclastogenesis, Reduced Bone Formation, and Enhanced Apoptosis of Osteoblastic Cells in Bacteria Stimulated Bone Loss. *Endocrinology*, 145(1):447–452.

Holick, M. F., Biancuzzo, R. M., Chen, T. C., Klein, E. K., Young, A., Bibuld, D., Reitz, R., Salameh, W., Ameri, A., Tannenbaum, A. D. 2008. Vitamin D2 is as Effective as Vitamin D3 in Maintaining Circulating Concentrations of 25-Hydroxyvitamin D. *The Journal of Clinical Endocrinology & Metabolism*, 93(3):677–681.

Kane, F. C., Tounkara, L. S., Kimsassoum, D., Guewofokeng, M., Diop, A. T., Wilfred, F. M. 2017. Nutritional value of a dietary supplement of Moringa oleifera and Pleurotus ostreatus. *African Journal of Food Science*, 11(6):171–177.

Katare, D. P., Sharma, G., Asshar, M. U., Aeri, V. 2018. Effect of ethanolic extract of Euphorbia hirta on chronic diabetes mellitus and associated cardiorenal damage in rats. *International Journal of Green Pharmacy (IJGP)*, (03):191–199.

Kellett, G. L., Brot-Laroche, E. 2005. Apical GLUT2: A Major Pathway of Intestinal Sugar Absorption. *Diabetes*, 54(10):3056–3062.

Kumar, R., Arora, V., Ram, V., Bhandari, A., Vyas, P. 2015. Hypoglycemic and hypolipidemnic effect of Allopolyherbal formulations in streptozotocin induced diabetes mellitus in rats. *International Journal of Diabetes Mellitus*, 3(1):45–50.

Kumari, D. J. 2010. Hypoglycemic effect of Moringa oleifera and Azadirachta indica in type 2 diabetes mellitus. *Bioscan*, 5(20):211–214.

Latif, A. A. E., Bialy, B. E. S. E., Mahboub, H. D., Eldaim, M. A. A. 2014. Moringa oleifera leaf extract ameliorates alloxan-induced diabetes in rats by regeneration of β cells and reduction of pyruvate carboxylase expression. *Biochemistry and Cell Biology*, 92(5):413–419.

Mbibay, M. 2012. Therapeutic Potential of Moringa oleifera Leaves in Chronic Hyperglycemia and Dyslipidemia: A Review. *Frontiers in Pharmacology*, 3.

Meneses, M., Silva, B., Sousa, M., Sá, R., Oliveira, P., Alves, M. 2015. Antidiabetic Drugs: Mechanisms of Action and Potential Outcomes on Cellular Metabolism. *Current Pharmaceutical Design*, 21(25):3606–3620.

Metcally, F. M., Rashad, H. M., Ahmed, H. H., Mahmoud, A. A., Raouf, E. R. A., Abdalla, A. M. 2017. Molecular mechanisms of the anti-obesity potential effect of Moringa oleifera in the experimental model. *Asian Pacific Journal of Tropical Biomedicine*, 7(3):214–221.

Nasir, M., Ahmed, A., Aslam, A., Mehmood, K. 2017. Effect of different concentration of Moringa oleifera leaves on the serum profile and organs of the induced diabetic rats. 2:24–30.

Olayaki, L. A., Irekpita, J. E., Yakubu, M. T., Ojo, O. O. 2015. Methanolic extract of Moringa oleifera leaves improves glucose tolerance, glycogen synthesis and lipid metabolism in alloxan-induced diabetic rats. *Journal of Basic and Clinical Physiology and Pharmacology*, 26(6):585–593.

Ota, A., Ulrich, N. P. 2017. An Overview of Herbal Products and Secondary Metabolites Used for Management of Type Two Diabetes. *Frontiers in Pharmacology*, 8.

Patel, C. 2013. The anti-osteoporotic effect of Moringa oleifera on osteoblastic cells: SaOS 2. *IOSR Journal of Pharmacy and Biological Sciences*, 5(2):10–17.

Patel, C., Ayaz, Parikh, P. 2015. Studies on the osteoprotective and anti-diabetic activities of Moringa Oleifera plant extract. *IOSR Journal of Pharmacy and Biological Sciences*, 5(5):19–22.
Raϐiu, A. A., Luka, C. D. 2015. Effect of Aqueous Extract of Moringa Oleifera Seed on Some Biochemical Parameters In Alloxan-Induced Diabetic Rats. *Journal of Biological Sciences and Bioconservation*, 7:1–1.

Rangrez, A. Y., Balakrishnan, S., Parikh, P. H. 2011. Osteoprotective effect three anti-inflammatory plants in ovariectomised Wistar rats. pages 675–84.

Shanker, U., Prasad, K., Kumar, A., Gari, M., Kunj, M., Kapur, S., Rana, R. 2019. Effects of Moringa oleifera Leaf Extract on Blood Sugar Parameters in Type2 Diabetic Patients: A Comparative Observational Study. *EAS Journal of Pharmacy and Pharmacology*, 1(2):32–39.

Sherein, I. A. E.-M., El-Badawi, A., Omer, H. 2014. Assessment of antimicrobial effect of moringa: In vitro and in vivo evaluation. *African Journal of Microbiology Research*, 8(42):3630–3638.

Singh, S. K., Rai, P. K., Jaiswal, D., Rai, D., Sherma, B., Watal, G. 2008. Protective effect of Cynodon dactylon against STZ induced hepatic injury in rats. *Journal of Ecophysiology and Occupational Health*, 8:195–199.

Srikanta, P. 2011. The anti-osteoporotic activity of methanolic extract of an Indian herbal formula NR/CAL/06 in ovariectomised rats. *Journal of Chinese Integrative Medicine*, 9(10):1125–1132.

Szkudelski, T. 2001. The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. *Physiological Research*, 50(6):537–546.

Tadera, K., Minami, Y., Takamatsu, K., Matsuoka, T. 2006. Inhibition of ALPHA-Glucosidase and ALPHA-Amylase by Flavonoids. *Journal of Nutritional Science and Vitaminology*, 52(2):149–153.

Vali, B., Rao, L., Elsohemy, A. 2007. Epigallocatechin-3-gallate increases the formation of mineralized bone nodules by human osteoblast-like cells. *The Journal of Nutritional Biochemistry*, 18:341–347.

Vargas-Sánchez, K., Garay-Jaramillo, E., González-Reyes, R. E. 2019. Effects of Moringa oleifera on Glycaemia and Insulin Levels: A Review of Animal and Human Studies. *Nutrients*, 11(12):2907–2907.

Yassa, H. D., Tohamy, A. F. 2014. Extract of Moringa oleifera leaves ameliorates streptozotocin-induced Diabetes mellitus in adult rats. *Acta Histochemica*, 116(5):844–854.

Ye, H., Zhang, H. J., Xu, A., Hoo, R. L. C. 2013. Resistin Production from Adipose Tissue Is Decreased in db/db Obese Mice, and Is Reversed by Rosiglitazone. *Plos One*, 8(6):e65543–e65543.