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Moringa oleifera: A review of its supplemental effect on human health with regards to blood glucose, malnutrition and anemia.

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Abstract

Moringa oleifera, grown mainly in the tropical and subtropical regions of the world is commonly known as 'drumstick leaves' or 'horseradish leaves'. Leaves, as well as all other part of the Moringa tree are edible and they form traditional diets in any countries. Because of its high nutritive value, every part of the tree is suitable for either nutritive or commercial purposes. The leaves are found to be rich in minerals, vitamins and other essential phytochemicals that can be used to treat malnutrition, control blood glucose and prevent anemia. This review explores the use of moringa leaves across disciplines for its medicinal values and deals with its supplemental effect on blood glucose, malnutrition and anemia.

Keywords: *Moringa oleifera*, malnutrition, blood glucose, anemia

1. Introduction

Moringa oleifera is the best known of the thirteen species of the genus Moringacae. It was believed to be originated from India in some 5000 years ago. Moringa is mainly grown in the tropical and sub-tropical regions of the world. Moringa grows well in the dry sandy soils but it also tolerates poor soils, including coastal areas. Leaves are eaten fresh by the local people in the tropical regions of Asia, Africa and South America. Besides leaves, the fruits, flowers and immature pods of this tree are edible and they for a part of traditional diets in many countries of the tropics and sub-tropics (Siddhuraj and Becker, 2003)

English common names include: Moringa, drumstick tree (from the appearance of the long, slender, triangular seed-pods), horse radish tree (from the taste of the roots, which resembles horse radish), ben oil tree, or benzoil tree (from the oil which is derived from the seeds. Moringa is known by various vernacular names-Drumstick tree, Radish tree, Horse radish tree, Mother's Best Friend, *West Indian ben* (English), *Tella Munaga, Sajana* (Telugu), *Murungai, Sigru, Moringa, Murinna, Morunna* (Tamil), *Saragavo, Midho saragavo, Suragavo, Saragvo* (Guajarati), *Mungaara, Shajmah, Shajna, Segra* (Hindi),

Mungaara, *Sojna, Sajna, Sujana* (Bengali), *Nugge* (Kannada), *Sigru, Moringa, Muringa, Murinna, Morunna* (Malayalam), *Sujna, Shevga, Shivga* (Marathi), Shobhanjana, *Danshamula, SigruShobhanjan, Sobhanjana* (Sanskrit) *Munigha, Sajna* (Oriya), *Sanjina, Soanjana* (Punjabi) *Lal Sahinjano* (Rajasthan). The seeds can be used as a flocculent to clarify water and as a source of non-drying and very stable oil, known as Ben oil (Seewu *et al.*, 2010).

All parts of *Moringa oleifera* are consumed as food. The plant produces leaves during the dry season and during times of drought, and is an excellent source of green vegetable when little other food is available. Leaves, pods, roots and flowers can be cooked as vegetables. The roots have been used as a substitute for horseradish but may be slightly toxic. The leaves are very nutritious and rich in protein, vitamins A, B and C and minerals. They are highly recommended for pregnant and nursing mothers as well as young children. M. oleifera seeds contain about 30-40% of edible oil (ben oil), which is resistant to rancidity and provides substantial amounts of oleic acid, sterols and tocopherols (FAO, 2014).

The tree is claimed to have potential to improve nutrition, increase food security, and encourage rural development. Drumstick leaves are alternate, oddly tripinnate, compounded and triangular in outline. They are 20-70 cm long and are spirally arranged on the twig. Leaflets are quite plae when young but become richer in colour with maturity (Chauhan and Pandey, 2014). The leaves are packed with nutritional properties and are 100 % edible. They are rich source of nutrients like protein, carbohydrate, fiber, Beta-carotene, vitamin C and minerals like calcium, potassium, iron and phosphorus (Joshi and Mehta, 2010).

Vitamins like beta carotene of vitamin A, vitamin B such as folic acid, pyridoxine and nicotinic acid, vitamin C, D and E are also present (Mbikay 2012). In fact, moringa is said to provide 7 times more vitamin C than oranges, 10 times more vitamin A than carrots, 17 times more calcium than milk, 9 times more protein than yogurt, 15 times more potassium than bananas and 25 times more iron than spinach (Rockwood *et. al.*, 2013).

Potential application of *M. Oleifera* leaves as an ingredients in different foods such as soups, in weaning foods, chocolates, herbal biscuits & cakes, yoghurt, Khakra, fortified ice milk, and muffins. Thus, it is an excellent source of macro and micro nutrients with enormous potential uses but is very less explored. It can be utilized to make foods that could be a step towards curbing malnutrition (Sahay *et al.*, 2017). The leaves contain various types of antioxidant compounds such as ascorbic acid, flavonoids, phenolic compounds and carotenoids and act as a natural antioxidant (Anwar *et. al.*, 2007). *M. Oleifera* leaves have significant medicinal uses like as antibiotics, anti-inflammatory, for skin treatment, blood pressure regulation, anemia treatment and diabetes. It is also known to have various biological activities, including antitumor, anticancer, prevention of cardiovascular diseases and antioxidant. (Ananias, 2015). It has also been used traditionally to treat constipation. (Anwar *et. al.*, 2007).

Table: 1 Nutritional composition of Moringa leaves (Per 100 g)

Components		
	Raw leaves ^a	Dried leaves ^b
Energy (kcal)	64	304 ± 87
Water (g)	78.66	0.0074 ± 0.0029
Protein (g)	9.40	24 ± 5.8
Total lipid (g)	1.40	6 ± 2.5
Carbohydrate, by difference (g)	8.28	36 ± 9.2
Vitamin A (RAE) (μg)	378	3639 ± 1979.8
Thiamin (mg)	0.257	2.6
Niacin (mg)	2.220	8.2
Pantothenic acid (mg)	0.125	_
Vitamin B-6 (mg)	1.200	2.4
Vitamin C, total ascorbic acid (mg)	51.7	172 ± 37.7
Folate total (µg)	40	540
Sodium (mg)	9	220 ± 180.0
Potassium (mg)	337	1467 ± 636.7
Calcium (mg)	185	1897 ± 748.4
Phosphorus (mg)	112	297 ± 149.0
Magnesium (mg)	42	473 ± 429.4
Iron (mg)	4.00	32.5 ± 10.78
Zinc (mg)	0.60	2.4 ± 1.12
Copper (mg)	0.105	0.9 ± 0.48
Manganese (mg)	1.063	-
Selenium (µg)	0.9	-

^aInformation obtained from United States department of agriculture nutrient database

M. Oleifera leaves are eaten as a nutritious vegetable. Leaves can be eaten fresh, cooked or stored as dried powder for several months. Leaves particularly when dried are easy to handle and store as they have a very good shelf life. Also, after drying, the nutrients are more concentrated, thereby making them even richer and more valuable. Hence, M. Oleifera leaves can be preserved for a long time without loss of nutrients. Inclusion of M. Oleifera in diet to supplement daily nutrient needs could help to prevent many diseases (Sharma et al., 2012). An overdose of M. Oleifera may cause high accumulation of iron. High iron can cause gastrointestinal distress and haemochromatosis. Hence, a daily dose of 70 g of M. Oleifera is suggested to be good and prevents over accumulation of nutrients (Asiedu-Gyekye et al., 2014).

It is the purpose of this review to provide a brief overview of the plethora of research regarding the supplemental effect of *M. Oleifera* leaves. Due to the extent of the literature, we have chosen to focus on the benefits associated with some common health conditions and on benefits in healthy people rather than to review the extensive literature related to cancer and other disease states.

^bAverage values and standard deviation published by Witt (2013)

2. Mechanism of action

2.1 Effect on Blood glucose

Glucose, a major fuel for animal cells is supplied to the organism through dietary carbohydrates and endogenously through hepatic gluconeogenesis and glycogenolysis. Variety of neuronal signals and enterohormones (incretins), as well as meal consumption and intestinal flora regulates glucose absorption from the intestinal tract. Glucose homeostasis reflects a balance between glucose supply and its utilization. Physiologically, this balance is determined by the level of circulating insulin and tissue responsiveness to it. Insulin, secreted by pancreatic islet β cells stimulates the glucose uptake and utilization by tissues, especially by liver, skeletal muscle, and adipose tissue. It also suppresses gluconeogenesis in hepatocytes, while stimulating lipogenesis and inhibiting lipolysis in adipocytes (Gerich, 2000). An individual is diagnosed as diabetic when his blood glucose level is chronically ≥ 126 mg/dL after an overnight fast and ≥ 200 mg/dL 2 hour after an oral glucose load of 75g (Alberti and Zimmet, 1998). M. Oleifera has been used in folk medicine for the treatment of diabetes (Dieye et al., 2008). Several studies aimed at verifying these properties using leaves were identified.

Kumara (2010) examined the hypogluceic effect of M. Oleifera leaf dietary consumption over a period of 40 days in T2DM patients, 30-69 years of age, not on anti-hyperglycemic medication. The experimental group included 46 subjects, 32 men and 14 women. In the control group 9 subjects were included 4 men and 5 women. Daily meals were comparable agong these groups in terms of relative content of food types (cereals, green leafy vegetables, fruits etc) and nutrients (energy, protein, fat, fiber, minerals etc). The experimental group received a daily dose of 8 gm M. Oleifera powder. Fasting Plasma Glucose (FPG) and Post prandial plasma glucose (PPPG) at the end of th protocol were compared to baseline levels. Final values did not differ uch from the baseline in the control group, however, the levels in the experimental group were significantly reduced (FPG: -28%, P<0.01; PPPG: -26%, P<0.05). Ghiridhari, (2011) also revealed also the reduction on post prandial blood glucose in a group of 60 T2DM patients in the age group 40 to 58 years, BMI 20 to 25 kg/m^2 , on sulfonylurea medication and a standardized calorie-restricted diet with consumption of M. oleifera leaf powder. The patients were equally divided into a control and experimental groups, patients in the experiental group were prescribed two M. Oleifera leaf powder constituted 98% (w/w) of the tablet content. Blood glycated hemoglobin (HbA1c) was measured before and after the regien. Post prandial glucose was determined before the regimen and every 30 days afterward. In the control group, (HbA1c) and post prandial glucose progressed downwardly with time, but with non-significant change. The results showed that post prandial blood glucose of experimental group initially was 210 mg/dl and it reduced to 191, 174 and 150 mg/dl respectively after the first, second and third month of supplementation (9%, 17%, 29% respectively). Glycated hemoglobin in experimental group was initially 7.81 and decreased to 7.4 per cent after the supplementation period; but in the control group it decreased to 7.36 from the initial value of 7.38 per cent. The results indicated that drum stick leaves are suitable source of green leafy vegetable to reduce the diabetic complications in diabetic patients.

Anthanont et al., (2016) observed that M. oleifera leaf powder consumption also helped increase insulin secretion in healthy subjects. In this study ten healthy volunteers were enrolled in this study (mean age 29 ± 5 years; BMI 20.6 ± 1.5 kg/m2; FPG 81 ± 5 mg/dl). After an overnight fast and every two weeks, subjects received an oral dose of M. oleifera at increasing dosages of 0, 1, 2, and 4 g. Plasma glucose (PG) and insulin were collected at baseline and at 0.5, 1, 1.5, 2, 4, and 6 hours after each M. oleifera dosage administration. Insulin secretion rate was measured using area under the curve (AUC) of insulin and AUC of insulin/glucose ratio. After doses of 0, 1, 2, and 4 g M. Oleifera, mean plasma insulin increased (2.3 \pm 0.9, 2.7 ± 1.0 , 3.3 ± 1.4 , and 4.1 ± 1.7 μ U/ml, respectively) despite there being no differences in mean PG (77 \pm 6, 78 ± 5 , 79 ± 6 , and 79 ± 5 mg/dl, respectively). AUC of insulin was greater after high-dose M. oleifera (4) g) than after baseline or low-dose MO capsule (1 g) (24.0 \pm 3.5 vs. 14.5 \pm 1.8 or 16.1 \pm 2.0, respectively; p = 0.03), while there was no difference in AUC of glucose. Accordingly, insulin secretion rate represented by AUC of insulin/glucose ratio after high-dose M. oleifera was significantly increased by 74% (P = 0.041), as compared with that of baseline suggesting that high-dose (4 g) M. oleifera leaf powder capsules significantly increased insulin secretion in healthy subjects. These results suggest that M. oleifera leaf may be a potential agent in the treatment of type 2 diabetes. (Leone et al., 2018) evaluated the effect M. Oleifera leaf powder on postprandial glucose response by randomly administering, on 2 different days, a traditional meal supplemented with 20 g of M. oleifera leaf powder to 17 diabetics (experimental) and none to 10 healthy subjects (control). Capillary glycaemia was measured immediately before the meal and then at 30 min intervals for 3 h. In the diabetic subjects the postprandial glucose response peaked earlier with supplementation compared to that of control group and with lower increments at 90, 120, and 150 min. The mean glycemic meal response of the experimental group was lower than of the control group. The healthy subjects showed no differences. Thus, M. Oleifera leaf powder could be a hypoglycemic herbal drug. However, given the poor taste acceptability of the 20 g M. Oleifera meal, lower doses should be evaluated..

2.2 Malnutrition

Ideally, good nutrition should be assured by a varied diet rich in meat, root, grain, fruit and vegetable foods. In reality, for a majority of the world's population such variety in food is unaffordable or seasonally unavailable. Elsewhere in the tropics, meals are generally built around one staple food rich in carbohydrates but very poor nutritionally. In this context, M. Oleifera is a very simple and readily available solution to the problem of malnutrition. The edible leaves of the M. Oleifera tree are already an occasional food source throughout the tropics and sub-tropics (Dhakar et al., 2011). Acceptance of M. Oleifera as a nutritional supplement or a food additive in undernourished populations is compatible in those cultures that currently use green leafy plant sources in traditional dishes. Rural populations, and those populations who rely heavily on subsistence farming, may find using M. Oleifera leaves more compatible than purchasing non-locally produced food. Because households can produce their own M. Oleifera or find it in local markets, they are able to use it just as they would with other locally grown foods such as grains, legumes, root and/or tuber vegetables (Thurner and Fahey, 2009).

Traditional dishes around the world include green leafy plant sources which can be substituted or augmented with *M. Oleifera* leaves. An Indian study evaluated food attitudes in children and infants, where they were given 30 g and 15 g respectively of *M. Oleifera* leaves mixed with 10 g of legumes and the dish was found to be coarse and bitter (Gopaldas et al., 1973). Acceptance of *M. Oleifera* as a nutritional supplement or a food additive in undernourished children is compatible in some cultures and countries but the lack of robust clinical trials data increases the uncertainty regarding *M. oleifera* nutritional benefits in undernutrition. Protein energy malnutrition (PEM) is a major public health problem in developing countries (Bhutia, D.T (2014).

A study of using *M. Oleifera* as therapeutic option for malnutrition in Africa was conducted by Saleh and Salam, (2014) to investigate the effect of *M. Oleifera* powder for treating mild and moderate malnutrition among sample of children in pediatric age group. A ready prepared *M. Oleifera* powder (10g) was added to 1 cup fruit juice as directed by pharmaceutical company was taken twice daily between meals was prescribed for 40 days. Growth was monitored and recorded before and after intake of *M. Oleifera* powder. After intervention, cases gained more weight than controls yet, it was not statistically significant (P 0.07). Also, there was no statistical difference between cases and controls regarding weight after intervention and BMI after intervention (P 0.89 and 0.93) respectively. There was dietary inadequacy regarding total caloric intake with high intake of protein, CHO and adequate intake of fat. Regarding micro nutrients there was inadequate intake of vitamin A, vitamin D, vitamin C, calcium and zinc with adequate intake of Iron.

Srikanth et al., (2014) conducted a study to identify children with Protein Energy Malnutrition, give nutritional intervention in the form of Moringa Oleifera powder for 2 months and to reassess the nutritional status after the nutritional intervention at the end of 2 months for sixty children, thirty in the intervention group and thirty in the control group. Nutritional Intervention was given in the form of Moringa oleifera leaf powder 15 g twice daily for two months. Reassessment of the nutritional status following the intervention showed that 70% children with grade II PEM improved to grade I, and 60% children with grade I PEM had shown significant (P < 0.01) improvement in their nutritional status. Thus, concluding that Moringa Oleifera is a good malnutrition combatant and needs to be promoted in the community. Another trail of study investigates the effect of *Moringa* chocolate cookies (Morichoco) on body weight in adolescent girls with malnutrition was conducted by Fadiyah et al., (2018). A total of 36 adolescent girls with malnutrition were randomly divided into three groups: 12 in the control group (C) were only given chocolate cookies, 12 in the treatment group (T1) were given chocolate cookies fortified with 4 g Moringa oleifera leaf powder (MOLP), and 12 in the T2 group who were given chocolate cookies fortified with 8 g MOLP. The treatment was performed for 60 days. Their body weight was measured before, during, and after treatment. Before treatment, mean body weight of the C group (38.24±5.00 kg) was slightly lower than the T1 (39.63±3.75 kg) and T2 groups (38.41±3.90 kg). After 30 days treatment, the mean body weight only increased in the C and T2 group (38.53±5.59 and 38.53±3.21 kg). At the end of treatment, the mean body weight of the T1 group remained stable and adolescent girls in the C and T2 groups had mean body weights of 38.95±5.27 kg and

 38.73 ± 3.56 kg, respectively. Dose and duration of Morichoco administration did not significantly affect body weight (p > 0.05). In conclusion, administration of Morichoco was unable to increase body weight of adolescent girls with malnutrition.

A research work concerning the "Acceptability and safety of short-term daily supplementation in a group of malnourished girls" assessed the use, acceptability and safety of *M. Oleifera* on children (girls) in Zambia (Barichella et al. 2019). With regards to safety concerns, supplementation of 14 g per day of *M. Oleifera* powder was deemed safe for children and adolescents both in the short and long term. This research also noted that mild nausea was reported in 20% of the children at various age groups when meals were supplemented with 20 g of *M. Oleifera* daily showing to be still an inadequate and symptomatic dose in children.

2.3 Anemia

Common methods used to fight against nutritional anemia include iron supplementation and food-based approaches. Iron supplements are commonly distributed in the form of highly concentrated tablets or syrup, consisting of a single or multiple nutrients, to the highly affected individuals or high-risk groups as a quick and short-term solution to IDA. Food-based approaches include food fortification, use of multiple micronutrient powders (commonly known as "sprinkles"), and dietary diversification (WHO & FAO, 2006). The majority of families, especially those in rural communities, consume most of their food directly from their own farms. Therefore, dietary diversification through promoting locally available food products with high nutrient density continues to be a long-term, cost-effective, and sustainable solution to iron deficiency (Caulfield et al., 2006). Dietary diversification within a minimum recommended number of meals is important to ensure adequate micronutrient supply (WHO & FAO, 2006), especially among poor communities who cannot access fortified processed food products. Sindhu et al., (2013) conducted a study with the intention of finding efficient substitutes in the form of non-haem iron of vegetable origin i.e. M. Oleifera leaves (drumstick) and jaggery to treat anaemia in 60 women belonging to lower socio-economic strata in suburban/rural Bangalore aged 15-45 as the target group. In this study, 30 women were assigned to the intervention group and 30 to the control group. The intervention group was then given a therapy which consisted of 100gm of M. Oleifera and jaggery (dry weight) in a ratio of 80:20 for thirty days. At the end of the supplementation period (30 days), the women in intervention group showed an increase in haemoglobin level with highly significant result, t=4.109 (P=<0.001) indicating that M. Oleifera with jaggery has significantly improved haemoglobin levels of anaemic women. This can be promoted in the community for women with iron deficiency anaemia. The effect of M. Oleifera leaf extract for anemia prevention was determined by (Nadimin et al., 2015). Two groups received supplementation of M. Oleifera leaf extract and folic iron (60mg Fe and 0.25 mg folic). Hb levels of pregnant women in a group of M. Oleifera leaf extract before intervention (11.283 + 0.78 g/dL) increased to (11.754 +1.09 g/dL) after intervention. Hb levels of pregnant women in folic iron group also increased between before and after intervention (p=0.002). The

amount of increase in haemoglobin concentration of pregnant women in folic iron group of $(0.9986 \pm 1.7638 \text{ g/dL})$ was higher than *M. Oleifera* leaf extract group (0.4771 + 1.3051 g/dL), but a large increase in hemoglobin levels between the two groups was not significant (p=0.168).

Similar to the study, the effect of *M. Oleifera* extract on anemia patients was conducted by Suzana *et al.*, (2017). It was a randomized, double-blind, placebo-controlled study in 35 anemic women (16 to 49 years) in which the water extract of *M. Oleifera* leaves was examined as an add-on therapy in the subject treated with ferrous sulfate (200mg/ tablet). The subjects were divided into 17 of *M. Oleifera* leaves and 18 of control. The extract of *M. Oleifera* leaves of 1400 mg was formulated in capsules and was administrated daily for 3 weeks. The result showed there were significantly increase of mean of hemoglobin (0.794±0.81 g/dL), ferritin (29.378±42.48 ng/mL), MCHC (Mean Corpuscular Haemoglobin Concentration) (2.459±2.86 g/dL), RDW (Red Distribution Wide) (1.4±2.07 %) and decreased of platelets (36529.41±59024.48 /uL). The control groups were significantly increased of mean of the hemoglobin (0.644± 0.83g/dL), erythrocytes (0.475±0.523 Tpt/L), hematocrit (2.189±14.08 %), MCV (Mean Corpuscular Volume)(4.756±8.91 fL), MCH (2.183±2.47 pg) dan RDW (2.844±2.80%). The hematocrit (3.14±1.47%), MCH (Mean Corpuscular Hemoglobin) (3.495±1.33 pg), MCHC (3.264±0.96 g/dL) values of *M. Oleifera* leaves were significantly higher whereas the platelets count (55251.63±23404/uL) of moringa leaves were significantly lower (p<0.05) than those of control group. Thus it can be concluded that *M. Oleifera* leaves extract could improve iron deficiency anemia in women.

Shija *et al.*, (2019) investigated the effect of *M. oleifera* leaf powder supplementation on reducing anemia among children below 2 years comprising of 95 anemic children who were followed for 6 months. The intervention communities received *M. oleifera* leaf powder and nutrition education, while control communities only received nutrition education. After 6 months, anemia prevalence significantly decreased in the intervention group by 53.6% (100%–46.4%; p < 0.001) compared to 13.6% (100%–86.4%; p = 0.005) in control community. The effect was also observed in the reduction of the prevalence of moderate and severe anemia in the intervention communities by 68.2% and 77.9%, respectively, and by 23.3% and 56.9%, respectively, in the control communities. Increasing amount and time of using *M. oleifera* supplementation resulted to significant reduction in anemia cases therefore can be used as complementary solution in addressing anemia among children especially when the use of infant formulas and fortified food product is very poor.

The effect of giving *M. Oleifera* leaves extract plus royal jelly supplement on increasing erythrocyte index was studied in anaemia pregnant women by (Hastuty *et al.*, 2020). Sixty three anemic pregnant women were included and divided into three groups- 21 subjects of *M. Oleifera* Leaf Extract plus Royal Jelly (MLERJ) group with the intervention of 1 capsule in the morning with a dose of 500 mg MLE + 10 mg RJ, 21 subjects of *M. Oleifera* Leaf Extract (MLE) with the intervention 1 capsule in the morning with a dose of 500mg MLE and the Placebo group 21 received no intervention. There was an increase in the erythrocyte

index levels (MCV, MCH and MCHC) of the three study groups. suggesting that *M. Oleifera* can be used as an alternative treatment to treat anemia.

3. Conclusion

Collectively, the studies described in this review provide compelling, albeit very preliminary, experimental evidence of a therapeutic potential of *M. oliefera* leaves in treating high blood glucose, malnutrition and anemia. No report contradicting this evidence was found in the scientific literature. In conclusion, based on the available experimental evidence, *M. Oleifera* leaves powder holds some therapeutic potential for treating various ailments. Despite there being a lot of scientific evidence and feeding studies which have reported the nutritional potential of this knowledge is not tapped into poor countries that are highly affected by malnutrition. Therefore, sharing of best practices and study findings should not end in scientific, academic platforms such as journals and books, but more efforts should be invested to spread the information to the general public. The effect of environmental factors affecting the nutrient levels of *M. Oleifera* leaves grown across the globe also require further analysis.

Author contribution

All the authors equally contributed to the background research, writing, and reviewing of this manuscript.

Conflicts of Interest

The authors declare no conflict of interest

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