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Medicinal Effects of Moringa Species *(M. oleifera* and *M. stenopetala)*

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Abstract: Moringa is a plant that is a native to parts of Africa and Asia, is the sole genus in the flowering plant family Moringaceae. Both *M. stenopetala* and *M. oleifera* are commonly known Moringa species that are grown in the tropics and sub-tropics. It is endemic to East Africa mainly present in northern Kenya and southern part of Ethiopia. All parts of the tree except the wood are edible, providing a highly nutritious food for both humans and animals. *Moringa oleifera* Lam. is the most widely known species. It is the most widely cultivated species, is a multipurpose tree native to the foothills of the Himalayas in northwestern India and cultivated throughout the tropics. This multipurpose tree has been introduced to Ethiopia over the last few years and is grown at nursery sites parallel to *M. stenopetala* in southern parts of the country. It grows abundantly in Southwestern Ethiopia where the leaves are eaten as vegetable. For centuries, people all over the world, including traditional healers have utilized different parts of the *Moringa* tree as traditional medicine. The medicinal uses are numerous and have been long recognized in the traditional systems of Medicine. *M. stenopetala* with its related species of the *M. oleifera* are commonly used in folk medicines. It has a multipurpose effects of anti-hyperglycemic, anti-cancer, anti-cholesterolic, hypotensive and against to bacteria, fungus and viral pathogens.

Key words: Moringa, Anti-hyperglycemic effect, Anti-cancer effect, anti aging effect

INTRODUCTION

Moringa is a plant that is a native to parts of Africa, Asia and Arabia, is the only genus in the flowering plant family Moringaceae. It contains 13 species from tropical and subtropical climates that range in size from tiny herbs to massive trees. The most widely cultivated species are *Moringa oleifera*, native to India and the *Moringa stenopetala*, an East African species[1]. *Moringa* spps. are one of the most useful tropical trees with a multiple array of uses. All plant parts of this genus are used in the indigenous systems of human medicine for the treatment of a variety of ailments. All parts of the tree except the wood are edible, providing a highly nutritious food for both humans and animals. *Moringa* spp. are rich sources of various phytochemical compounds including glucosinolates; However, there are only detailed profiles for *M. oleifera* and *M. stenopetala*[1].

MEDICINAL EFFECTS OF MORINGA SPECIES

Moringa oleifera is the most widely known species. It is the most widely cultivated species, is a multipurpose tree native to the foothills of the Himalayas in northwestern India and cultivated throughout the tropics. *M. oleifera* is grown for its nutritious pods, edible leaves and flowers and provides many beneficial properties including its use as a source of food, medicine, cosmetic oil, forage for livestock and water coagulant. It is commonly known by regional name as drumstick tree and a rapidly growing tree that is widely cultivated and has now become naturalized in Afghanistan, Florida and East and West Africa [1].

Almost all parts of this plant: root, bark, gum, leaf, fruit (pods), flowers, seed and seed oil have been used for treating various ailments such as skin infections, anemia, coughs, diarrhea swelling, headaches, gout, acute rheumatism, hysteria, cholera, heart complaints, fevers, respiratory disorders, inflammation, digestive disorders, asthma, intestinal complaints, diabetes and rheumatism in the indigenous system of medicine[2].

Specific parts of *M. oleifera* also exert many pharmacological activities such as: hypoglycemic and antihyperglycemic effect[3-6]; Hypolipidemic effect[7,8]; Antibacterial activity[9] and anti-cancer effects[10,11].

The different parts of *M. oleifera* are known to be good sources of phytochemicals compounds. These phytochemicals contribute to the healing properties of *M. oleifera* [1]. This multipurpose tree has been introduced to Ethiopia over the last few years and is grown at nursery sites parallel to *M. stenopetala* in southern parts of the country [12].

***Moringa stenopetala* (Baker f.) Cufodontis:** *Moringa stenopetala* is also belongs to the family Moringaceae. It is a branched tree[13] that grows 6 to 10 m . It is endemic to East Africa mainly present in northern Kenya and southern part of Ethiopia[1,14]. It grows abundantly in Southwestern Ethiopia where the leaves are eaten as vegetable. The species is known by different vernacular names such as "*Shiferaw*" in Amharic, "*Aleko*" in Wollaytegna and “Cabbage tree” in English. It grows widely at an altitude range of 1000 to 1800 meter above sea level. The leaves are one of the best vegetable foods that can be found in the locality[13]. The flowers are good nectar sources for honey; the seeds are used in clearing muddy water; the wet or dried root part chopped and mixed with water is also used to treat malaria[1].

M. stenopetala is well adapted to semi-arid areas of 500 mm annual rainfall and continued to grow during the exceptionally long dry season. It is a multipurpose tree that is cultivated both for human food and animal feed in Southern Ethiopia [12].

M. stenopetala, although not as studded as *M. oleifera* for its medicinal properties, it offers a wide range of traditional medicinal benefits, for instance, the bitter-tasting water left over after cooking the leaves is consumed for several medicinal purposes by the traditional communities of Ethiopia. The leaves and roots, mixed with the water are used to treat malaria, hypertension, stomach disorders, asthma and diabetes. The Gidole and Burji people use it for the treatment of digestion problems and dysentery. The bark is used by the Njemp people in Kenya to treat coughs. The leaves and roots are also used in many areas of Ethiopia to treat malaria, hypertension, colds, asthma, stomach problems and diabetes[1].

In Arba Minch area, the leaves are used to treat hypertension and diabetes[1]. The presence of different phytochemical constitutes of *M. stenopetala* found to exert many biological activities, such as anti-cancer activity[1]; hypotensive effect [15]. and other effects. The Konso-speaking natives in southern Ethiopia use the leaves to prevent colds and anaemia, and the roots to treat epilepsy. Moreover, the fractions isolated from the aqueous extract of the plants were also shown to have both hypoglycemic and antidiabetic effect in mice [16,17]. The leaves of moringa have medicinal values for stomach pain and to expel retained placenta following birth. It is also used as a food [13]. *M. stenopetala* is a promising tree for nutrition, water purification and herbal medicine and it has many beneficial qualities, similar to those found in *M. oleifera*[1].

For centuries, people all over the world, including traditional healers have utilized different parts of the *Moringa* tree as traditional medicine. The medicinal uses are numerous and have been long recognized in the traditional systems of Medicine. *M. stenopetala* and its related species (*M. oleifera)* are commonly used in folk medicines as anti-hypertensive, as anti-diabetic, as anti-cholesterol, as anti-cancer, as anti-asthmatic, as anti aging and etc. So, the objective of this paper was to review the above remedies effects of moringa tree[18].

Anti-hyperglycemic effect: Medicinal plants with various active principles and properties have been used from ancient times by physicians and laymen to treat a great variety of human diseases such as diabetes, coronary heart disease, cancer and others. The beneficial multiple activities of plants used traditionally in DM like manipulating carbohydrate metabolism by various mechanisms, preventing and restoring the integrity and function of β-cells, releasing insulin activity, improving glucose uptake and utilization, and the antioxidant properties present in medicinal plants, offer an exciting opportunity to develop them in to therapeutics[17]. Moringa is one of the medicinal plants which is widely used for antidiabetic purpose. The ant hyperglycemic activity of *moringa* may be attributed to one or more of the aforementioned mechanisms. Some authors investigated that, Moringa contains several active principles which might contribute for the antidiabetic effect. According to these different authors, the ant hyperglycemic effect of ethanol fraction, chromatographic fractions and butanol fraction of the plant confirms the presence of some of the active components[16, 17, 19].

Different experimental studies reported that, *moringa* leaves significantly decrease blood glucose concentration in Wistar rats and Goto-Kakizaki rats. The effective ness of the plant increases as dose and time of exposure increases[20,21]. As a mechanistic model for antidiabetic activity of *Moringa*, it has been indicated that dark chocolate polyphenols and other polyphenols are responsible for hypoglycemic activity. *Moringa* leaves are potent source of polyphenols, including quercetin-3- glycoside, rutin, kaempferol glycosides, and other polyphenols[20]. Thus, potential anti- diabetic activity of *Moringa* can be commercialized through the development of suitable technology with achieving anti-diabetic activity up to conventional drugs. In addition to that, as it has rich source of ascorbic acid it helps the diabetic patients to control their blood glucose level [20].

In another study, which conducted in diabetic animals, *M. olifera* exhibited significant blood glucose lowering activities. In normal rats, *M. olifera* leaf extract also decreased the blood glucose level. The effects were greater in diabetic rats than in normal rates. In diabetic animals, a significant reduction was found in urine sugar and urine protein levels. In similar study, the aqueous extracts of the leaves has hypoglycemic effects in non-diabetic rabbits. It was found to exert a dose-dependent decrease in blood glucose concentration, although it was less potent than the anti-diabetic drug glibenclamide[3,6,.].

A number of investigators have shown that coumarin, flavonoid, terpenoid and a host of other secondary plant metabolites including arginine and glutamic acids possess hypoglycemic effects in various experimental animals[22]. Hypoglycemic and antihyperglycemic activity of the leaves of *M. oleifera* may be probably due to the presence of terpenoids, which appears to be involved in the stimulation of the β-cells and the subsequent secretion of preformed insulin. One or more of the other chemical constituents of the plant especially flavonoid is also likely to have played a crucial role in the hypoglycemic action of the plant extract[22].

In another study, the oral daily administered dose of 400 mg/ kg body weight of the *M. oleifera* aqueous extract led to significant decrease in hyperglycemia (**Figure 1**.) and **(Table 1**.)[3,6].

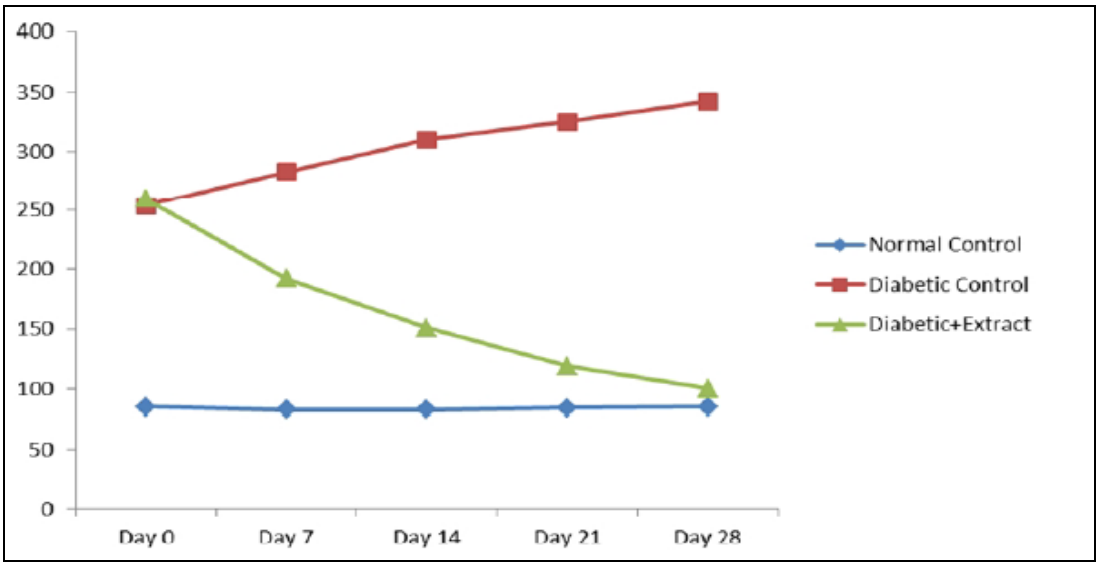

Figure 1: Effect of aqueous extract of *M. oleifera* leaves on blood glucose in diabetic rats adopted from[3,6].

An aqueous extract of *Moringa* leaves normalizes the high blood glucose level in diabetic rats by the 28th day of the experiment. Some authors suggest that, the mechanisms of actions could be either by increasing the tissue utilization of glucose, by inhibiting hepatic gluconeogenesis or absorption of glucose into the muscles and adipose tissues[6]. After the 28 days treatment, there was a significant reduction in fasting blood glucose levels for the groups treated with plant extracts. The reduction was comparable with that obtained with the standard hypoglycaemic drug (glibenclamide)[4]. The phytochemical screening of aqueous extract of

M. Olifera revealed the presence of alkaloids, flavonoids, gallic tannins, phenols, saponins and catecholic compounds and steroids indicating the presence of pharmacologically important phytochemicals[3].

Table 1: Effect of aqueous extract of *M. oleifera* leaves on blood glucose in diabetic rats adopted from6**.**

Groups	Blood glucose (mg/dl)				
	0 Day	7 Day	14 Day	21 Day	28 Day
Normal control	85 ± 1.22	84 ± 1.12	84 ± 0.09	83 ± 2.44	85 ± 1.02
Diabetic control	255 ± 2.80	285 ± 2.87	312 ± 2.66	324 ± 4.22	344 ± 2.55
Diabetic + extract	262 ± 2.11	190 ± 2.11*	153 ± 2.80*	121 ± 3.23**	102 ± 1.23**

All values are expressed as mean ± SEM (n=8), *: P<0.05, **: P<0.01 as compared to diabetic control.

As further noted, the leaves have distinctive strong, mustard-like taste, contain calcium, iron and other trace minerals, and are eaten as a supplement to the major staple foods. The raw leaves of it contain minerals such as potassium, iron, zinc, phosphorus and calcium in significant amount. The presence of these minerals may also contribute to the antihyperglycemic effect of the plant[7].

The presence of phytochemicals in plant products gives a great potential for balancing metabolic disturbances. Several phytomolecules including flavonoids, phenolic compounds, alkaloids, glycosides, saponins, glycolipids, dietary fibres, polysaccharides, peptidoglycans, carbohydrates, amino acids and others obtained from various plant sources have been reported as potent hypoglycemic agents. Flavonoids are a heterogeneous group of ubiquitous plant polyphenols, which exhibit a variety of pharmacological activities, including the antiatherogenic as well as antihyperglycemic effects, lipoprotein oxidation, blood platelet aggregation and vascular reactivity. A high content of phytochemicals especially total polyphenolic compounds and total flavonoids may contribute to the pleiotropic effects of *Moringa* leaves that support the use of the plant for different metabolic disorders[23].

Another important point is that, it is well known that inhibition of intestinal α-glucosidase and pancreatic α-amylase activity results in delaying carbohydrate digestion of absorbable monosaccharides, causing reduction of postprandial hyperglycemia. The Moringa extract showed a weaker pancreatic α-amylase activity compared to intestinal α-glucosidase activity. α- glucosidase inhibitors delay intestinal carbohydrate absorption and slow the sharp rise in blood sugar levels that diabetic patients typically experience after snacks. Study reports showed that, hydroalcoholic leaf extract of *M. stenopetala* has a potent inhibitor of α-glucosidase activity, and therefore suggests that, extracts of *Moringa* could be an attractive source of alternative treatment. In conclusion, they demonstrate that the inhibition of intestinal α-glucosidase by extracts of *Moringa* may contribute to antihyperglycemic activity[23].

Anti-cholesterolic effect: Besides hyperglycemia, diabetes mellitus is highly characterized by elevated levels of triglycerides and cholesterol in the blood highly associated with a modern lifestyle and increase consumption of a high fat diet[23]. Reducing absorption of free fatty acids and free cholesterol by inhibiting pancreatic lipase and pancreatic cholesterol esterase reduces hyperlipidemia associated with diabetes mellitus. The antihyperlipidemic effects of M. stenopetala may be due to the inhibition of pancreatic lipase

and pancreatic cholesterol esterase. Therefore, the extracts of Moringa show antihyperlipidemic activity due to the inhibition of lipase and cholesterol esterase enzymes. Thus plant material of Moringa could be used for prevention/treatment of hyperglycemia and hyperlipidemia [23].

Moreover, *Moringa* leaves also contain bioactive phytoconstituent, (that is, β-sitosterol) with cholesterol lowering effect[20]. The study conducted on crude extract of *Moringa* leaves show that, a significant cholesterol lowering action in the serum of high fat diet fed rats which might be attributed to the presence of a bioactive Phytoconstituents, i.e. β- sitosterol. *Moringa* fruit also has been found to lower the serum cholesterol, phospholipids, triglycerides, low density lipoprotein (LDL), very low density lipoprotein (VLDL), cholesterol to phospholipid ratio, atherogenic index lipid and reduced the lipid profile of liver, heart and aorta in hypercholesteremic rabbits and increased the excretion of fecal cholesterol[21,24].

Table 2: Effect of aqueous leaf extract of *M. oleifera* on lipid profile of alloxan induced diabetic rats adopted from[6].

Variable	Normal Control	Diabetic Control	Diabetic + Extract
Total cholesterol (mmol/L)	4.62±0.254	6.01±0.188*	4.77±0.356**
Triglycerides (mmol/L)	0.97±0.102	1.70±0.065*	1.25±0.412**
HDL (mmol/L)	1.54±0.212	1.25±0.198	1.60±0.320
LDL (mmol/L)	2.77±0.153	4.12±0.102*	3.43±0.226**

*Values are expressed as mean ±SEM (n=8), * P> 0.05 when compared to control, **significantly reduced when compared to diabetic control group.*

The total cholesterol level and Triglycerides level was significantly increased in the diabetic group when compared with the normal control group while there was no significant difference in the cholesterol level of the *M. oleifera*-treated diabetic group and the control group. Though there was no significant difference in the HDL level of the three groups, the diabetic control group had a significantly higher LDL when compared with the normal control while there was no difference in the LDL level of the *M. oleifera* -treated group and the normal control group as shown above in (**Table 2 and 3.)**[3]

Diabetes-induced hyperlipidemia has been attributed to excess mobilization of fat from the adipose due to underutilization of glucose[6].This hypolipidemic effect of *Moringa* could be related to its chemical composition, which shows the presence of alkaloids, flavonoids, saponin and cardiac glycosides. All these components are known to reduce serum lipid level in animals. Saponins may lower cholesterol by binding with cholesterol in the intestinal lumen, preventing its absorption, and/or by binding with bile acids, causing a reduction in the enterohepatic circulation of bile acids and increase in its fecal excretion. The increased bile acid excretion is offset by enhanced bile acid synthesis from cholesterol in the liver and consequent lowering of the plasma cholesterol[6].

A study conducted on the methanolic extract of *M. oleifera* (150, 300 and 600 mg/kg) and simvastatin (4 mg/kg) along with hyperlipidemic diet were administered to Albino Wistar rats for 30 days in order to observe hypolipidaemic effect. It was found that the serum cholesterol, triacylglyceride, VLDL, LDL, and atherogenic index were reduced by *Moringa* and simvastatin. *M. oleifera* was also found to increase the

excretion of fecal cholesterol. Thus, it can be concluded that *Moringa* possesses a hypolipidemic effect. Besides administration of M. *stenopetala* at 600, 750 and 900 mg/kg significantly decreases cholesterol [25,26]. A study carried out on butanol fraction of *M. stenopetala* leaves on serum total cholesterol and triglyceride levels showed significantly higher serum total cholesterol and triglyceride levels in the diabetic control group than in the normal control group. TG and TC levels were significantly decreased with butanol fraction administration of *M. stenopetala* [17].

Table 3: Effect of butanol fraction of *M. stenpetala* in TG and TC after chronic administration in alloxan induced diabetic mice adopted from[17]**.**

Treatment groups	Total cholesterol(mg/dl)	Triglyceride(mg/dl
Normal control	184±7.48***	172.0±4.90***
Diabetic control	228.0±4.93	220.0±6.33
Glibenclamide	212.0±4.88	188.0±4.89**
Butanol fraction	192.0±4.94**	184.0±4.90***

***P < 0.01, ***P < 0.001verses Diabetic controls Mean ± Standard error of deviation.*

Similarly, mice treated with doses of 600, 750 and 900 mg/kg of *M. stenopetala* aqueous leaf extract had significantly decreased their blood cholesterol level from 134.60 ± 15.09 to 119.60 ± 9.10, 118.60 ±8.50 and 113.20 ± 5.07, respectively, in a dose dependant-manner. This study is similar with the study reported for *M. oleifera* leaf extract that showed hypocholesterolemic activity. It was reported that the mechanism of cholesterol reduction is thought to be through the lowering of plasma concentrations of LDL by β-sitosterol, the bioactive phytoconstituent isolated from *M. oleifera*. Therefore β-sitosterol or a similar constituent in the leaves of *M. stenopetala* may be responsible for this effect as well[27].

Hypotensive effect: Blood pressure (BP) is the pressure exerted by circulating blood on the walls of blood vessels. Blood pressure tends to rise with age. Following a healthy lifestyle helps some people delay or prevent this rise in blood pressure.

- High blood pressure increases the chance for getting:
- Heart disease, kidney disease, stroke and congestive heart failure

The important nutrients needed by a person suffering from high blood pressure are Calcium, Magnesium, Potassium, Zinc, Vitamin C and Vitamin E. Moringa contains these entire nutrient in it. Moringa contains Vitamin C helps support the body's production of nitric oxide, which is critical to normal functioning of blood vessels. The better your blood vessels work, the lower the risk of hypertension. Calcium is needed for smooth muscle relaxation and contraction; It is also needed for blood coagulation [24]. Moringa contains calcium which is 17 times that of milk. It was noted that increased calcium intake will decline the incidence of hypertension. Increased consumption can have a direct effect on blood vessels. *Potassium* also play an important role against the hypertension as sodium retention in the blood is restricted. High potassium tends to lower the sodium content. Potassium is thought to act by increasing sodium excretion in the urine, which helps blood vessels dilate. Moringa also contains Magnesium, Zinc, and Vitamin E, which help smoothen

and relax the muscles of blood vessels, which takes part in decreasing the blood pressure along with other nutrients[24].

In addition to that, Moringa leaves contain several bio active compounds, they exert direct effect on blood pressure, and thus these can be used for stabilizing blood pressure. Moringa compounds leading to blood pressure lowering effect includes nitrile, mustard oil glycosides and thiocarbamate glycosides present in Moringa leaves[24]. Bioassay guided fractionation of the active ethanol extract of Moringa leaves led to the isolation of four pure compounds, niazinin A, niazinin B, niazimicin and niazinin A + B which showed a blood pressure lowering effect in rats mediated possibly through a calcium antagonist effect[21,24].

Another studies investigated that, the hypotensive activity of the ethanolic and aqueous extracts of *M. oleifera* whole pods and their parts, namely, coat, pulp, and seed. It was found that the ethyl acetate phase of the ethanolic extract of pods was found to be the most potent fraction at the 30 mg/kg dose. Its bioassay-directed fractionation led to the isolation of thiocarbamate and isothiocyanate glycosides which were also the hypotensive principles of the pods as observed in case of Moringa leaves. Two new compounds, O-[2'-hydroxy-3'-(2''-heptenyloxy)]-propyl undecanoate and O-ethyl-4-[(alpha-L-rhamnosyloxy)-benzyl] carbamate along with the known substances methyl p-hydroxybenzoate and beta-sitosterol have also been isolated in the studies. The results of the studies reported that, the latter two compounds and p-hydroxybenzaldehyde showed promising hypotensive activity[25].

Studies conducted on *in vivo* and *in vitro* hypotensive effect of aqueous extract of *M. stenopetala* also stated that, administration of aqueous leaf extract of *M. stenopetala* at doses of 10, 20, 30 and 40 mg/kg showed statistically significant reduction of SBP, DBP and MABP. On the other hand the decline in pulse pressure was statistically significant only at the dose of 40 mg/kg (**Table 4**.) [15,28].

Table 4: The effects of iv infusion of different doses of *M. stenopetala* aqueous extract in anaesthetized guinea pigs on systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and mean arterial blood pressure (MABP) adopted from[15, 28]

Doses of *M. Stenopetala*	SBP	DBP	PP	MABP
control	81.91 ± 2.73	53.16± 2.70	28.74± 2.29	62.74± 2.49
5mg/kg	76.69 ± 2.59	48.22± 2.40	28.46± 2.43	57.71± 2.18
10mg/kg	60.89 ± 3.95**	38.73±3.19**	22.15 ± 2.44	46.12±3.27**
20mg/kg	54.65 ± 3.73**	32.62 ± 2.51**	22.02 ± 2.59	3.97±2.71**
30mg/kg	47.79 ± 3.02**	24.89 ± 2.13**	22.89 ± 2.44	32.52±2.18**
40mg/kg	39.26 ± 3.10**	20.79 ± 1.56**	18.47 ± 2.37**	26.94±1.89**

*Data are expressed as Mean ± SEM (n=12). ** P < 0.05*

According to the authors, the duration of action was longer; that is, about 10 minutes as compared to the one minute action of acetylcholine[15, 28]

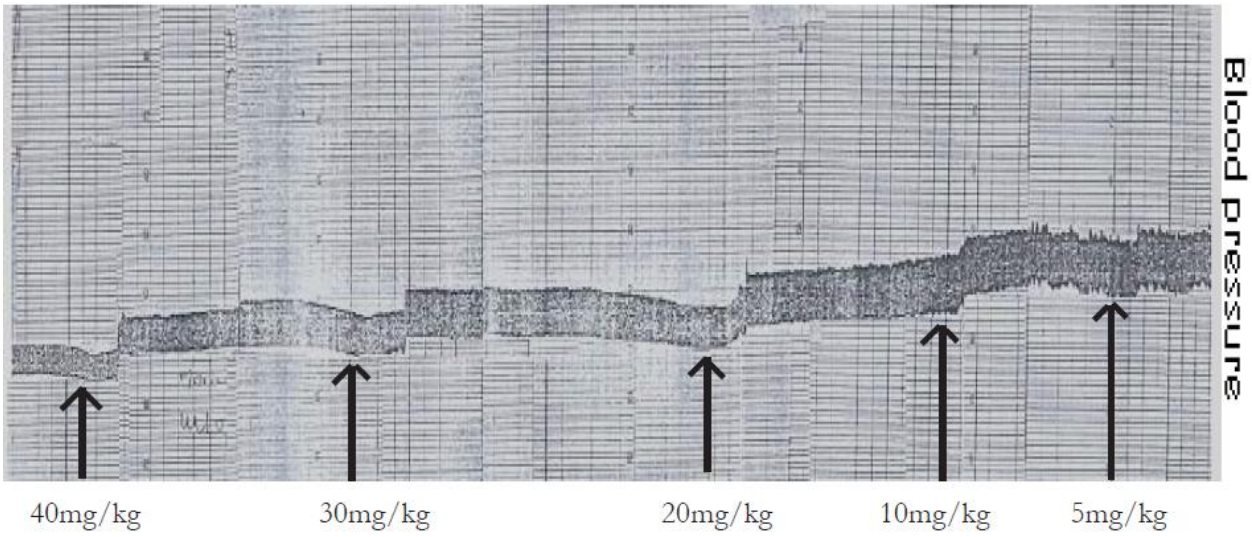

Figure 2: The hypotensive effect of *M. stenopetala* crude extract in anaesthetized guinea pig. Arrows indicate the point at which the test extracts were administered Modified from [15, 28]Acetylcholine at a dose of 1 µg/kg produced a considerable drop in blood pressure and pretreatment of animals with atropine (1 mg/kg), the muscarinic blocker of acetylcholine, abolished the effect of acetylcholine on blood pressure. However, atropine pretreatment did not alter the hypotensive effect of the aqueous leaf extract of *M. stenopetala* in anaesthetized guinea pig (Figure 3.) [15, 28]

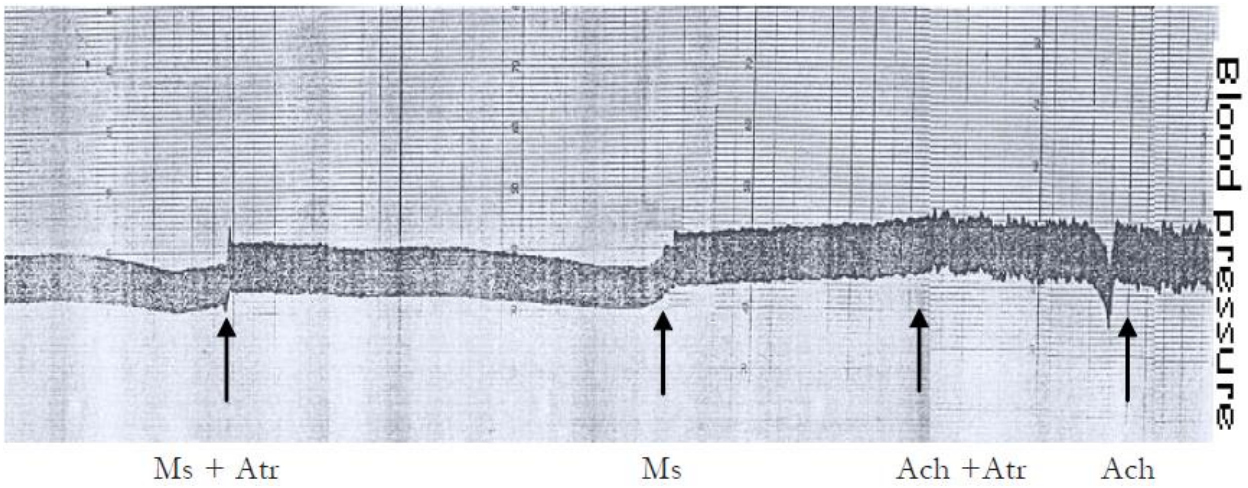

Figure 3: The non-muscarinic mechanism of action of *M. stenopetala* in inducing hypotensive effect in anaestehetized guinea pig. Ms = Moringa stenopetala; Atr = Atropine; Ach = Acetylcholine adopted from[15, 28]

Moreover, another studies show that, *Moringa* roots, leaves, flowers, gum and the aqueous infusion of seeds have been also found to possess diuretic activity and such diuretic components are likely to play a complementary role in the overall blood pressure lowering effect of this plant[20,24]. In addition to that, some studies reported diuretic activity from hot water infusions of *Moringa* shows increased urine out put in rates

[29, 30]. Similar study shown that, the aqueous leaf extract of *M. stenopetala* did not exhibit any vasoconstrictor activity on the resting baseline of guinea pig aorta[15,28]. Therefore, the widespread combination of diuretic along with lipid and blood pressure lowering constituents make this plant highly useful in cardiovascular disorders[24].

Blood Parameter effect: Study investigation revealed that, there was no significant change in the body weight of mice treated with doses of 600 and 750 mg/kg of Moringa extract. According to them, no significant change in the weight of liver and kidney was observed in the entire group. They also added that, there was no significant difference in the hematological composition of the blood parameters[27] between the control group treated with 600 mg/kg, 750 mg/kg and 900 mg/kg . This might suggest that, the non-toxic effect of the extract. The rate of food and water intake of the mice given 600, 750 and 900mg/kg doses of M. stenopetala aqueous leaf extract was comparable with those of the control group. Similar to the other experiments it was established that M. stenopetala was not toxic even at higher doses[27].

Table 6: Hematological analysis of mice after treatment with *M. stenopetala* extract adopted from**[27].**

Hematological parameters	Control (diss. water)	Treatment groups (mg/kg bw)		
		600	750	900
WBC x 10^3/µl	4.40 ± 0.21	5.10 ± 0.23	5.10 ± 0.71	5.66 ± 0.53
RBC x 10^6/µl	7.91 ± 0.92	8.52 ± 0.49	8.09 ± 0.52	8.55 ± 0.28
Platelets x 10^3/µl	396.75 ± 27.02	397.05 ±12.05	389.07 ± 120.05	399.06 ± 112.67
HCT (%)	48.22 ± 1.58	48.62 ± 1.41	48.44 ± 1.96	48.04 ± 1.25
HGB (g/dl)	10.70 ± 1.00	10.62 ± 0.93	10.50 ± 0.60	10.80 ± 0.32
MCV (fl)	84.10 ± 1.47	82.56 ± 0.88	82.42 ± 0.51	85.78 ± 1.70
MCH (pg)	28.24 ± 0.55	28.20 ± 0.54	28.80 ± 0.22	28.70 ± 0.24
MCHC (g/dl)	32.74 ± 1.42	32.38 ± 1.10	33.44 ± 0.48	32.80 ± 0.39
Lymphocytes (%)	40.74 ± 3.70	39.74 ± 2.95	44.66 ± 3.42	46.18 ± 2.91

Values are mean ± SEM. P<0.05, N=5/group

Keys: WBC, white blood cell; RBC, red blood cell; HCT, hematocrit; HGB, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.

But in other similar studies investigated that, blood parameters namely: PCV, WBC counts, differentiation of WBC, hemoglobin (Hb) and platelets (PLT) were found to be positively affected by using this plant[31].Dietary components of *M. oleifera* were reported to have measurable effect on blood constituents. With the exception of MCHC, Hb, RBCs and platelets in rats and PCV, RBCs and platelets in rabbits, the other blood parameters did not change significantly with inclusion of *M. oleifera* leaf extract in rats and fresh leaves in rabbits. However, in all of these experiments stated that, the mean values of each blood parameter were within the normal range [31].

Anti-cancer effect: Other amazing effects of Moringa were reported as anticancer effect. Since Moringa species have long been recognized by folk medicine practitioners as having value in tumor therapy, some author examined the compounds for their cancer preventive potential[2]. Recently, these compounds were shown to be potent inhibitors of phorbol ester (TPA)-induced Epstein-Barr virus early antigen activation in

lymphoblastoid (Burkitt's lymphoma) cells. In this study, he investigated that, the inhibited tumor promotion in a mouse two-stage DMBA-TPA tumor model. In the same study he observed that, skin tumor prevention following ingestion of drumstick (Moringa seed pod) extracts. In this mouse model, which included appropriate positive and negative controls, a dramatic reduction in skin papillomas was demonstrated. Thus, traditional practice has long suggested that cancer prevention and therapy may be achievable with native plants[2].

Different scholars: found that, Moringa leaves to be a potential source for antitumor activity. *O*-Ethyl-4-(α-L-rhamnosyloxy) benzyl carbamate together with 4(α-L-rhamnosyloxy)-benzyl isothiocyanate , niazimicin and 3-*O*-(6′-*O*oleoyl- β-D-glucopyranosyl)- β-sitosterol have been tested for their potential antitumor promoting activity using an *in vitro* assay which showed significant inhibitory effects on Epstein– Barr virus early antigen. Niazimicin has been proposed to be a potent chemopreventive agent in chemical carcinogenesis [21, 24]. It has been found that niaziminin, a thiocarbamate from the leaves of *Moringa*, exhibits inhibition of tumor-promoter-induced Epstein–Barr virus activation. On the other hand, among the isothiocyanates, naturally occurring 4- [(4′-*O*-acetyl-α-i-rhamnosyloxy) benzyl], significantly inhibited tumor-promoter induced Epstein–Barr virus activation, suggesting that the isothiocyano group is a critical structural factor for inhibiting tumor-promoter induced Epstein–Barr virus activity[2, 21, 24].

Moringa contains benzyl isothiocyanate which have anti-cancer and chemo protective capabilities. The chemo protective aspect is critical for those who are battling cancer; this helps strengthen cells so that they can tolerate chemotherapy. Antioxidants are also involved in the prevention of cellular damage; the common pathway for cancer, aging, and a variety of diseases[2].

In another study showed that, the presence of glucosinolates determined as 4(á-lrhamnosyloxy) benzyl isothiocyanate in the seeds of *M. stenopetala* found to exert many biological activities, such as anti-cancer activity due to their ability to kill cancer cells by inducing apoptosis, depleting ATP and leading the cells to oxidative stress[1]. On the other hand, the major secondary metabolites in the tissues of *M. stenopetala* and determined the presence of low amounts of 4-monoacetyl-4-(R-Lrhamnopyranosyloxy)-benzylglucosinolate isomers, but significant amounts of 4-(R-L rhamnopyranosyloxy)-benzylglucosinolate and benzylglucosinolate are found in the stem tissue. The root tissues found to contained both 4-(R-Lrhamnopyranosyloxy)-benzylglucosinolate and benzylglucosinolate. The leaves of *M. stenopetala* contained quercetin 3-*O*-rhamnosylglucoside (rutin) and traces of quercetin 3-*O*-glucoside[32].

Moringa has been found as a potent anticancer plant and several bioactive compounds with significant antitumor activity have been discovered from *Moringa*. Among bioactive compounds from *Moringa*, niazimicin, a *Moringa* leaves thiocarbamate was found to have potent anticancer activity. Furthermore, niazimicin also shows the inhibition of tumor promoter teleocidin B- 4-induced Epstein-Barr virus (EBV) activation. Another study involving 11 plants used in Bangladeshi folk medicine, *Moringa* was considered as potential source of anticancer compounds. The study indicated that the potential cytotoxic effects of *Moringa* leaf extract on human multiple myeloma cell lines. Beside leaves, *Moringa* seed extracts also have anticancer activity through its effects on hepatic carcinogen metabolizing enzymes, antioxidant parameters and skin papillomagenesis in mice[20, 24].

Anti-aging effect: The cellular turnover cycle that was 28 days in the youth expands to close to 35 days by the 40s. With new skin equaling younger-looking skin. A more natural way to support skin health by regenerating new skin cells without the dermabrasion and chemical peels of topical agents is with

Cytokinins. Cytokinins are plant hormones that promote cellular growth and delay the aging process. Cytokinins stimulate cell division, delay the aging and destruction of tissues, protect against cell oxidation, and postpone cell death. When the diet includes these plant nutrients, the body as a whole can fight aging, starting at the cellular level[2].

The most potent Cytokinin is Zeatin. Zeatin is a plant hormone derived from the purine adenine. It is a member of the plant growth hormone family known as cytokinins. Moringa is jammed with a cytokinin called zeatin. Zeatinis found in most plants, it is more abundant in Moringa plant than any other. zeatin has been reported to have several *in vitro* anti-aging effects on human skin fibroblasts[2,33]. Zeatin is the most powerful of all cytokinins. zeatin helps promote small cell size, a key component to more youthful skin. It also influences the structural and functional integrity of the cell, and prevents accumulation of macromolecular damage in the cell. The study found that zeatin increases the activity of some antioxidant enzymes, counteracting the free radical-induced oxidative damage incurred during cell aging. By preventing damage, antioxidants allow the skin to focus on building new collagen and other tasks (such as getting rid of old skin cells) that keep it looking young. Cytokinins have proven to delay biochemical modifications associated with aging in culture human cells. Zeatin protects the skin [2]. When human skin cells are nourished with Zeatin, they retain their functions longer and are more resistant to environmental stresses[33].

Moringa not only contains thousands of times more zeatin than any other known plant, it is also the most nutritious plant discovered to date, with over 90 nutritional compounds, including 46 antioxidants and 36 anti-inflammatories[33]. Moringa could be the new anti-aging alternative. Because of its high content of vitamins A, C, and E, which are very potent antioxidants, Moringa is a very good quencher of unstable free radicals that can react with the damage of molecules that cause aging[2, 33].

Anti-asthmatic effect: It has been reported a long time ago that *Moringa* plant alkaloid closely resembles ephedrine in action and can be used for the treatment of asthma. Alkaloid moringine relaxes bronchioles. The seed kernels of *Moringa* also showed promising effect in the treatment of bronchial asthma, during a study to analyze efficacy and safety of seed kernels for the management of asthmatic patients. The study showed significant decrease in the severity of asthma symptoms and also concurrent respiratory functions improvement[20]. In addition to that the alcoholic extracts of *Maringa* seed kernels were found spasmolytic in acetylcholine, histamin and 5HT induced bronchospasm[30].

Effect on ocular diseases : Vitamin A deficiency is a major cause of blindness, which ranges from impaired dark adaptation to night blindness. Consumption of *Moringa* leaves, and pods and leaf powder which contain high proportion of vitamin A can help to prevent night blindness and eye problems in children. Ingesting drumstick leaves with oils can improve vitamin A nutrition and can delay the development of cataract. In fact the use of *Moringa* as a supplementary food was highly accepted for integrated child development scheme supplementary food (ICDS-SFP) for its potential as vitamin A source[20].

Acute and/or Subchronic toxicity: Another important investigation about Moringa were its acute oral toxicity. In acute oral toxicity studies M. olifera extract did not show any mortality and toxic effects up to the dose of 2000 mg/kg body weight. So one-fifth of the safe dose is used for the experiments[6]. Not only that but also, the acute toxicity of M. stenopetala studies by different authors revealed that, the administration of graded doses of different fraction (up to a dose of 5000 mg/kg) did not produce significant changes in behaviors such as alertness, motor activity, breathing, restlessness, diarrhea, convulsions, coma and appearance of the animals[15, 17, 19, 28]. Some scholars reported that, no clinical signs or deaths or no observed

fatality related to extract administration were observed. According to them, some clinical observations noted was included, general state of the animals including the dynamics of body weight changes, skin abrasions, minor hair loss, appetite, motor activity and behavior of the animals[16, 17]. They added that, the incidences of these signs were similar in control and 300 mg/kg and 600 mg/kg extract administered mice. Another authors also added that, there was no mortality in group mice that received oral dose of 1 g/kg, 5 g/kg and 10 g/kg, respectively in the 24 hrs of regular observation [15, 28].

No death was observed up to the dose of 5 g/kg body weight indicating that the medium lethal dose (LD50) is greater than 5 g/kg body weight in mice. They also added that, the relative safety of the fraction of *M. stenopetala* leaves at the graded dose of up to 5000 mg/kg. According to them, any compound or drug with the oral LD50 estimate greater than 1000 mg/kg could be considered low toxic and safe. Arising from this fact, the fraction of *Moringa* at an oral dose of 5000 mg/kg could be considered relatively safe on acute exposure[17, 19].

The observation that the fraction did not show any toxic manifestations or lethality up to the dose level of 50 g/kg indicates the wide safety margin of the extract and supports the traditional use of the leaves of *Moringa* for its food value or in both types of diabetes mellitus or there was no significant treatment-related effect on food consumption[16,19].

Table 7: Acute toxicity of ethanol extract of *M. stenopetala* in mice modified from **[19].**

Group	Dose (g/kg)	Number of deaths	Death (%)	Probit value
1	10	0/6*	0.0	-
2	15	0/6*	0.0	-
3	20	0/6*	0.0	-
4	30	0/6*	0.0	-
5	50	0/6*	0.0	-
6	Control	0/6*	0.0	-

Values with superscript (*) are not significantly different as compared to the control at $P < 0.05$.

CONCLUSION

Different literatures revealed that, the different fraction of *Moringa* species has ant hyperglycemic, antihyperlipedemic, hypotensive effects and so on with wide safety margin[15- 19.]

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