Anti –diabetic activity of Murraya koenigii – A comprehensive review

ABSTRACT

Diabetes mellitus, one of the noncommunicable illnesses, is a severe problem worldwide as one of the leading causes of death. Because existing synthetic medications have various drawbacks, researchers are still looking for better anti-hyperglycemic treatments. Plants have been used in ancient medicine for thousands of years. India is the biggest producer of medicinal plants and is aptly regarded as the "World's Botanical Garden." Murraya koenigii Linn, also known as Meethi neem, is a Rutaceae plant. Curry trees are unique to India and likely found almost everywhere else on the subcontinent, except in the Himalayan highlands. For centuries, curry leaves were used as an antiemetic, diarrhea remedy, febrifuge, and blood purifier. Curry leaves are useful as an antioxidant, anti-diabetic, antibacterial, antihypertensive, cytotoxic, and in treating bronchial respiratory problems. Traditionally, the leaves were utilized as a spice in curries as well as other dishes. It includes coumarins and derivatives, alkaloids, flavonoids, phenolic compounds, and essential oil. Numerous studies have found that these phytochemicals have a significant effect on type 2 diabetes. This review focuses on this plant's anti-diabetic action and concludes that it has the potential to be evaluated as a candidate for developing a new diabetes mellitus medication.

Keywords: Medicinal plants, *Murraya koenigii*, Diabetes mellitus

Introduction

Diabetes mellitus, among the most frequent endocrine and metabolic illnesses, has caused enormous morbidity and death as a result of microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular (heart attack, stroke, and peripheral vascular disease) effects. In human bodies, anti-oxidative processes, both enzymatic and non-enzymatic, contribute to the reduction of reactive oxygen species, which are linked to a number of degenerative disorders, including diabetes [Ponnulakshmi et al., 2019]. The sickness is spreading swiftly over the world and is impacting people in every country. Diabetes patients have elevated blood glucose levels due to insulin insufficiency [Ponnusamy et al., 2011]. Type 2 diabetes, also called the non

diabetic Mellitus, has to be the most common type of diabetes, accounting for 90 percent to 95 percent of instances in which the body fails to make sufficient insulin or use it properly [Li et al., 2004]. According to the World Health Organization, the diabetes population will reach 300 million or more by 2025 [GY et al., 2005]. Insulin and various oral anti-diabetic medications, including sulfonylureas, biguanides, and glinides, are currently available for diabetes treatment. Many of them have a variety of significant side effects; as a result, one of the most critical areas of research is the search for more effective and safer hypoglycemic agents[Saxena et al., 2004]. The hypoglycemic impact of various plants used as anti-diabetic agents has been established, and the mechanisms underlying this effect are being researched. This article discusses natural compounds with anti-diabetic characteristics that operate as insulin-mimetic or secretagogues. Traditional remedies derived from commonly available medicinal plants hold considerable promise for developing new anti-diabetic medications [Jung et al., 2006].

Certain medicinal herbs have recently been described to be effective in the treatment of diabetes throughout the world, and they have been used empirically in anti-diabetic and antihyperlipidemic drugs. Plants' anti-hyperglycemic action is mainly related to their capacity to restore pancreatic tissue function by increasing insulin secretion, inhibiting glucose absorption in the intestine, or facilitating metabolites in insulin-dependent activities. Even though literature lists over 400 plant species with hypoglycemic action, hunting for new anti-diabetic medications from natural plants remains appealing since they contain chemicals that have alternative and harmless effects on diabetes mellitus.

Plant-derived active components that have shown action as in treatment of diabetes include alkaloids, glycosides, galactomannan gun, polysaccharides, peptidoglycans, hypoglycin, guanidine, steroids, sugars, glycopeptides, terpenoids, amino acids, and inorganic ions [Grover et al.,2002].

Curry leaves are Murraya koenigii (M. koenigii) (L) Spreng of the Rutaceae family. M. koenigii is found all across the world's tropical and subtropical regions. [Wojdyo et al.,2007]. Only two Murraya species, M. koenigii and M. paniculate are found in India, out of 14 worldwide. M. koenigii is more important because of the wide range of traditional therapeutic characteristics it possesses. This plant has been utilized in various ways for millennia and is known as "krishnanimba" in Indian Ayurvedic medicine [Ahluwalia et al., 2004]. M. koenigii's leaves,

roots, bark, and fruit have been demonstrated to support a range of biological activities. Even after drying, aromatic bioactive components in M. koenigii leaves retain their flavor and other properties [Amna et al.,2019]. The leaves of M. koenigii have a slightly bitter taste, a pungent odor, and are somewhat acidic. They are used as antihelminthics, analgesics, digestives, and appetizers in Indian cuisine [Desai et al., 2012]. Piles, inflammation, itching, fresh cuts, diarrhea, bruising, and edema are treated using M. Koenig's green leaves. To some extent, the roots are purgative. They are stimulating and are used to treat aches and pains in the body.The bark can be used to treat snakebites [Gajaria et al., 2015]. The essential oil obtained from M. koenigii leaves has been proven in animal models to have anti-oxidative and hepatoprotective properties [Ma et al., 2016] antibacterial, antifungal, anti-inflammatory, and nephroprotective effects [Tripathi et al., 2018]. Several chemical elements of distinct carbazole alkaloids and other significant metabolites, such as terpenoids, flavonoids, phenolics, carbohydrates, carotenoids, vitamins, and nicotinic acid, have been attributed to the therapeutic qualities of M. koenigii from various regions of the plant.

M. koenigii has received increased interest in traditional medicines and home cures in recent years. On the other hand, few research have been undertaken to assess M. koenigii's pharmacological and therapeutic usefulness in improving health and healing sickness[Dar et al.,2017]. This review aims to present previous and existing major studies on *M. koenigii* activity in diabetics.

Traditional Uses of M. koenigii

M. koenigii essential oils and fresh leaf powder can be used to season foods and make ready-to-eat meals. The essential oil from leaf extracts can also be employed as a perfume, and taste agent in traditional practise due to its increased antibacterial activity [Erkan et al.,2012]. Fresh curry leaves are cooked with coconut oil until they have been crushed to a black residue to make a great hair tonic for restoring normal hair tone and promoting hair development. Curry leaves have long been used as an antidiarrheal, antifungal, blood purifying, anti-inflammatory, and anti-depressant medication, either whole or in little amounts. [Joshi et al.,2018].

Medicinal Uses of M. koenigii

Different plant parts, like the leaves, roots, and bark, could be used as tonics to induce digestion and flatulence or as antiemetics [Adebajo et al.,2006]. The leaves turn unpleasant to the taste after infusion and are useful in lowering fever. The root's juice is used to treat kidney pain [Tembhurne et al., 2009]. The leaves and roots can be used as an antihistamine, analgesic, piles treatment, body heat reducer, and thirst quencher, as well as to relieve inflammation and irritation. They're also suitable for treating leucoderma and blood problems. The green leaves can be consumed raw to treat diarrhea, and the paste made from boiling the leaves in milk can be used to treat toxic bites and eruptions. [Sim et al.,2011].

Phytochemistry of M. koenigii

The leaves, roots and stem bark of M. koenigii have been used to isolate a variety of phytochemicals. Alkaloids, flavonoids, terpenoids, and polyphenols have been found in M. koenigii extracts of leaves, roots, stem bark, fruits, and seeds. Moisture is 63.2 percent, protein is 8.8%, carbohydrate is 39.4%, total nitrogen is 1.15 percent, fat is 6.15 percent, total sugars are 18.92 percent, starch is 14.6 percent, and crude fiber is 6.8 percent in the plant leaves. Vitamin A (B-carotene): 6.04 0.02 mg/100 g; vitamin B3, (niacin): 2.73 0.02 mg/100 g; vitamin B1 (thiamin): 0.89 0.01 mg/100 g; calcium: 19.73 0.02 mg/100 g; magnesium: 49.06 0.02 mg/100 g; sodium: 16.50 0.21 mg/100 g [Igara et al.,2016] The alcohol-soluble extract has a value of 1.82 percent, ash has a value of 13.06 percent, acid-insoluble ash has a value of 1.35 percent, cold water (20 °C) extractive has a value of 27.33 percent, and maximum of hot-water-soluble extractive has a value of 33.45 percent. Carbazole alkaloids, essential oils, terpenoids, and flavonoids all play important functions in the human body.

Antidiabetic Activity of *M. koenigii*

Because of their low cost, medicinal plants are particularly useful in managing diabetes mellitus in developing countries. Diabetes mellitus, a metabolic disorder, is rapidly being a major public health concern. In recent years, numerous phytochemicals with anti-diabetic properties have been found in plants. M. koenigii leaf alkaloids were examined and found to inhibit the aldose reductase enzyme, glucose consumption, and other enzyme systems, potentially extending anti-diabetic benefits[Patel et al., 2012]. The -glucosidase inhibitory property of M. koenigii was examined, and it was discovered to inhibit glycosidase. Patients with type 2 diabetes are

commonly treated with alpha-glucosidase inhibitors [Gul et al., 2012]. According to one study, an ethanolic extract of M. koenigii reduced blood glucose levels significantly, and this action of M. koenigii reducing blood glucose is mediated by antioxidant properties and insulin-mimetic effects. M. koenigii also demonstrated a high antioxidant effect, lowering MDA levels, increasing GSH levels, and significantly lowering the homeostatic model assessment (HOMA)-insulin resistance index. Overall, M. koenigii appears to have anti-diabetic and antioxidant properties in rats. [Husna et al.,2018].

Hypoglycemic activity:

The hypoglycemic effect can be achieved by increasing insulin production from [beta]-cells of Langerhans islets in the pancreas or emancipating insulin from its bound state [Gautam et al., 2012]. The antioxidant defence system of plasma and pancreas, as well as the probable protective impact of M. koenigii leaf extract against -cell damage, were examined in streptozotocin-induced diabetic rats. It was determined that M. koenigii therapy protects against diabetes by lowering oxidative stress and pancreatic-cell damage.

The effects of M. koenigii leaves were researched by Arulselven and Subramanian. Streptozotocin-induced diabetic rats were used in the experiment, and they were given 200 mg [kg.sup.-1] M. koenigii leaves for 30 days. M. koenigii dramatically reduced blood glucose and glycosylated hemoglobin levels while significantly increasing insulin and liver glycogen levels, according to the findings. It also decreased lactate dehydrogenase, glucose-6-phosphatase, fructose-1,6-diphosphatase, and glycogen phosphorylase activities while increasing hexokinase and pyruvate kinase activities. The effects of M. koenigii fruit juice were researched by Tembhurne and Sakarkar [Tembhurne et al.,2009]. They used alloxan-induced diabetic mice treated for 15 days with 2.5 and 5.0 ml/kg M. koenigii fruit juice...

The hypoglycaemic effect of M koenigii leaf extracts, as well as the number of spices employed, was investigated, proving that they can be utilized as an effective anti-diabetic diet [Srinivasan et al.,2015].

M. koenigii leaf extract reduced blood glucose levels by 13.1, 16.3, and 21.4 percent and 3.2, 5.58, and 8.21 percent for mild and moderate diabetes produced by alloxan in rats fed the extract as a meal, demonstrating its potential as an antihyperglycaemic agent[Yadav et al., 2004].

The effect of an aqueous extract of M. koenigii leaves on hypoglycaemic activity in normal and alloxan-induced diabetic rabbits was compared to the impact of a common hypoglycemic medication, tolbutamide. In both normal and diabetic rats, a single treatment of varied dose levels (200, 300, and 400 mg/kg) of the aqueous extract resulted in a reduction in blood glucose levels [Kesari et al., 2005].

Curry leaf extract has been shown to lower blood cholesterol and blood glucose levels in diabetic rats, as well as reduce body weight after therapy [Xie et al.2006].

For 30 days, oral administration of an ethanolic extract of M. koenigii to Streptozotocin-induced diabetic rats dramatically reduced blood glucose, glycosylated hemoglobin, urea, uric acid, and creatinine levels in the diabetic treatment group of animals[Aruselvan et al.,2006].

For a brief period of 6 hours, the aqueous extract of M. koenigii had a favorable effect in reducing the severity of diabetes in alloxan and normal induced diabetic rabbits48.

M. koenigii considerably reduced blood glucose levels, according to the findings. Many types of research [Harve et al.,2004] examined flavonoids, quercin, metformin, quinolizidine, anthocyanin, catechin, flavone, phenylpropanoids, lipoic acid, and coumarin as the most phytochemical compounds having anti-diabetes activity.

Traditional or alternative therapy, in addition to mainstream pharmaceuticals, plays a crucial part in the treatment of diabetes mellitus. It must understand how to use it and what phytochemical ingredients are present. The goal of this review study was to compile the new medicinal plant, M. paniculata, as the therapy of choice. All of this data will aid researchers in their investigation of the scientific evidence.

Conclusions

The present review discusses M. koenigii's medicinal uses, phytochemical constituents, and pharmacological qualities, with a focus on its anti-diabetic properties. M. koenigii contains alkaloids, polyphenols, terpenoids, and flavonoids, among other bioactive substances. M. koenigii and its substances appear to have anticarcinogenic, proapoptotic, antiangiogenic, antimetastatic, immunomodulatory, and antioxidant properties. The broad activity of M. koenigii and its derivatives in cell signalling pathways at multiple levels in various illnesses illustrates the

molecular processes behind these activities. M. koenigii and its derivatives reduce oxidative stress, neurotoxicity, neuroinflammation, neuronal loss, and cognitive dysfunctions.. However, like other polyphenols, M. koenigii's actions are restricted to some extent by its bioavailability, and in such cases, increased efficiency should be pursued. As a result, future research should involve additional experimental studies on improving bioavailability and efficiency in clinical trials.

References

1. Patel DK, Kumar R, Prasad SK, Sairam K, Hemalatha S. Antidiabetic and *in vitro* antioxidant potential of *Hybanthus enneaspermus* (Linn) F. Muell in streptozotocin-induced diabetic rats. Asian Pac J Trop Biomed. 2011;1(4):316–322.
2. Ponnulakshmi R, Shyamaladevi B, Vijayalakshmi P, Selvaraj J. In silico and in vivo analysis to identify the antidiabetic activity of beta sitosterol in adipose tissue of high fat diet and sucrose induced type-2 diabetic experimental rats. Toxicol Mech Methods. 2019 May;29(4):276-290. doi: 10.1080/15376516.2018.1545815. Epub 2019 Jan 15. PMID: 30461321.
3. Ponnusamy S, Ravindran R, Zinjarde S, Bhargava S, Kumar AR. Evaluation of traditional Indian antidiabetic medicinal plants for human pancreatic amylase inhibitory effect *in vitro*. Evid Based Complement Alternat Med. 2011;2011:515647.
4. Li WL, Zheng HC, Bukuru J, De Kimpe N. Natural medicines used in the traditional Chinese medical system for therapy of diabetes mellitus. J Ethnopharmacol. 2004;92(1):1–21

5. Sy GY, Cissé A, Nongonierma RB, Sarr M, Mbodj NA, Faye B. Hypoglycaemic and antidiabetic activity of acetonic extract of *Vernonia colorata* leaves in normoglycaemic and alloxan-induced diabetic rats. J Ethnopharmacol. 2005;98(1–2):171–175
6. Saxena A, Vikram NK. Role of selected Indian plants in management of type 2 diabetes: a review. J Altern Complement Med. 2004;10(2):369–378
7. Jung M, Park M, Lee HC, Kang YH, Kang ES, Kim SK. Antidiabetic agents from medicinal plants. Curr Med Chem. 2006;13(10):1203–1218.
8. Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol. 2002;81(1):81–100.
9. Wojdyło A., Oszmiański J., Czemerys R. Antioxidant activity and phenolic compounds in 32 selected herbs. Food Chem. 2007;105:140–149.
10. Ahluwalia V., Sisodia R., Walia S., Sati O.P., Kumar J., Kundu A. Chemical analysis of essential oils of *Eupatorium adenophorum* and their antimicrobial, antioxidant and phytotoxic properties. J. Pest Sci. (2004) 2014;87:341–349
11. Amna U., Halimatussakdiah P.W., Saidi N., Nasution R. Evaluation of cytotoxic activity from Temurui (*Murraya koenigii* [Linn.] Spreng) leaf extracts against HeLa cell line using MTT assay. J. Adv. Pharm. Technol. Res. 2019;10:51–55
12. Desai S.N., Patel D.K., Devkar R.V., Patel P.V., Ramachandran A.V. Hepatoprotective potential of polyphenol rich extract of *Murraya koenigii* L.: An in vivo study. Food Chem. Toxicol. 2012;50:310–314.
13. Gajaria T.K., Patel D.K., Devkar R.V., Ramachandran A.V. Flavonoid rich extract of *Murraya koenigii* alleviates in-vitro LDL oxidation and oxidized LDL induced apoptosis in raw 264.7 Murine macrophage cells. J. Food Sci. Technol. 2015;52:3367–3375.
14. Ma Q.G., Xu K., Sang Z.P., Wei R.R., Liu W.M., Su Y.L., Yang J.B., Wang A.G., Ji T.F., Li L.J. Alkenes with antioxidative activities from *Murraya koenigii* (L.) Spreng. Bioorg. Med. Chem. Lett. 2016;26:799–803
15. Tripathi Y., Anjum N., Rana A. Chemical Composition and In vitro Antifungal and Antioxidant Activities of Essential Oil from *Murraya koenigii* (L.) Spreng. Leaves. Asian J. Biomed. Pharm. Sci. 2018;8:6–13
16. Rautela R., Das G.K., Khan F.A., Prasad S., Kumar A., Prasad J.K., Ghosh S.K., Dhanze H., Katiyar R., Srivastava S.K. Antibacterial, anti-inflammatory and antioxidant effects of Aegle marmelos and *Murraya koenigii* in dairy cows with endometritis. Livest. Sci. 2018;214:142–148
17. Dar R.A., Shahnawaz M., Qazi P.H., Qazi H. General overview of medicinal plants: A review. J. Phytopharm. 2017;6:349–351
18. Erkan N., Tao Z., Vasantha Rupasinghe H.P., Uysal B., Oksal B.S. Antibacterial activities of essential oils extracted from leaves of *Murraya koenigii* by solvent-free microwave extraction and hydro-distillation. Nat. Prod. Commun. 2012;7:121–124.

19. Joshi T., Jain T., Mahar R., Singh S.K., Srivastava P., Shukla S.K., Mishra D.K., Bhatta R.S., Banerjee D., Kanojiya S. Pyranocarbazoles from *Murraya koenigii* (L.) Spreng. as antimicrobial agents. Nat. Prod. Res. 2018;32:430–434.
20. Adebajo A.C., Ayoola O.F., Iwalewa E.O., Akindahunsi A.A., Omisore N.O.A., Adewunmi C.O., Adenowo T.K. Anti-trichomonal, biochemical and toxicological activities of methanolic extract and some carbazole alkaloids isolated from the leaves of *Murraya koenigii* growing in Nigeria. Phytomedicine. 2006;13:246–254
21. Tembhurne S.V., Sakarkar D.M. Hypoglycemic effects of fruit juice of *Murraya koenigii* (L) in alloxan induced diabetic mice. Int. J. PharmTech Res. 2009;1:1589–1593
22. Sim K.M., Teh H.M. A new carbazole alkaloid from the leaves of Malayan *Murraya koenigii*. J. Asian Nat. Prod. Res. 2011;13:972–975
23. Igara C., Omoboyowa D., Ahuchaogu A., Orji N., Ndukwe M. Phytochemical and nutritional profile of *Murraya koenigii* (Linn) Spreng leaf. J. Pharmacogn. Phytochem. 2016;5:7–9
24. Patel D.K., Kumar R., Laloo D., Hemalatha S. Natural medicines from plant source used for therapy of diabetes mellitus: An overview of its pharmacological aspects. Asian Pac. J. Trop. Dis. 2012;2:139–150.
25. Gul M.Z., Attuluri V., Qureshi I.A., Ghazi I.A. Antioxidant and α-glucosidase inhibitory activities of *Murraya koenigii* leaf extracts. Pharmacogn. J. 2012;4:65–72.
26. Husna F., Suyatna F.D., Arozal W., Poerwaningsih E.H. Anti-Diabetic Potential of *Murraya koenigii* (L) and its Antioxidant Capacity in Nicotinamide-Streptozotocin Induced Diabetic Rats. Drug Res. (Stuttg) 2018;68:631–636.
27. Gautam, M.K., A. Gupta, C.V. Rao and R.K. Goel, 2012c. Antihyperglycemic and antioxidant potential of Murraya paniculata Linn. Leaves: a preclinical study. Journal of Pharmacy Research, 5: 1334-1337.
28. Arulselven, P. and S. Subramanian, 2007. Effect of Murraya koenigii leaf extract on carbohydrate metabolism studied in streptozotocin induced diabetic rats. International Journal of Biological Chemistry, 1: 21-28.
29. Tembhurne, S.V. and D.M. Sakarkar, 2009. Hypoglycemic effects of fruit juice of Murraya koenigii (L) in alloxan induced diabetic mice. International Journal of PharmTech Research, 1: 1589-1593.
30. Srinivasan K. plant foods in the management of Diabetes Mellitus, spices as beneficial antidiabetic food adjuncts. Int. J. Food Sci. Nutr 2005; 56(6): 399- 414
31. Yadav SP, Vats V, Ammini AC, Grover JK. Brassica juncea significantly the development of insulin resistance in rats fed fructose enriched diet. J Ethnopharmacol 2004; 93(1): 113-116.
32. Kesari AN, Gupta RK, Watal G. Hypoglycaemic effects of Murraya koenigii on normal and alloxan diabetic rabbits. J. Ethnopharmacol 2005; 97(2): 247-51

33. Xie JT, Chang CZ, Mehendale SR, Ambihipahar R, Ambihipahar U, Fong HH et al. curry leaf reduces blood glucose and blood cholesterol level in ob/ob mice. Am J Chin Med 2006; 34(2):279-84.
34. Aruselvan P, Senthil KGP, Satish KD, Subramanian S. Antidiabetic effect of Murraya koenigii leaves on streptozotocin induced diabetic rats. Pharmazie 2006; 61(10): 874-7.
35. Harve G, Kamath V. larvicidal activity of plant extrats used alone and in combination with known synthetic larvicidal agents against Aedes Aegypti. Ind J Exp. Biol 2004; 42(12): 1216-9.