

Azadirachta Indica - A Review as a Potent Anti- Diabetic Drug

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Abstract

Diabetes mellitus (DM) is a stern metabolic disease which has several complications including diabetic nephropathy, coronary heart disease, and hypertension. Natural product based compounds and there analogs thereof from various medicinal plants have provided numerous clinically useful drugs. Neem consists of several chemical constituents such as tannins, saponins, sterols, flavonoids, terpenoids, anthraquinones, and alkaloids which mainly assist in management of diabetes. Neem constituents like rutin and quercetin have been shown to have anti-hyperglycemic effects too. In this review article, the main focus is on the potential of neem (*Azadirachta indica*), which acts as the most valuable traditional plant in India that has been explored towards an antidiabetic application.

Keywords: Antidiabetic, *Azadirachta indica*, Diabetes Mellitus, Neem, Type I, Type II.

Introduction

Diabetes Mellitus (DM) is a complex metabolic disorder of carbohydrates, proteins and fats. DM is a common non-communicable disease in developing as well as developed countries (Singh N *et al.*, 2016 and Okur M *et al.*, 2017) affecting approx. 100 million people worldwide (Deshmukh C *et al.*, 2015). It is mainly of 2 types: Type I i.e. insulin dependent diabetes mellitus (IDDM) and Type II i.e. non-insulin dependent diabetes mellitus (NIDDM) (Okur M *et al.*, 2017). It results in the abnormal levels of glucose in the bloodstream and can cause brain damage, heart diseases (stroke), cardiovascular problems, angina, and nerve damage (neuropathy) (Riaz S 2009 and Piero M *et al.*, 2014). Type I diabetes is mainly due to lack of functional β -cells causing insulin insufficiency and therefore require insulin from exogenous source. Type II is common type of DM in which patient is unable to respond to insulin. The common symptoms are: -

- ✚ High levels of sugar in the blood
- ✚ Unusual thirst

- ✚ Frequent urination
- ✚ Extreme hunger and loss of weight
- ✚ Blurred vision
- ✚ Nausea and vomiting
- ✚ Extreme weakness and tiredness
- ✚ Irritability

An extensive literature search was done that concludes that various parts of the plants such as leaves, root, bark, fruit, seeds, stem, flower and the whole plant in some cases are used for treatment of DM (Ahmad S 2012). Neem (*Azadirachta indica*) is a versatile medicinal plant with anti-inflammatory, antipyretic (Okpanvi S *et al.*, 1981), anti-microbial, antidiabetic, immunomodulatory, antiulcer, antibacterial, antimalarial, and antioxidant, antimutagenic and anticarcinogenic properties (Hossain M *et al.*, 2011 and Chattopadhyay *et al.*, 1987).

Table 1: Taxonomic position of Neem

1.	Order	Rutales
2.	Suborder	Rutinae
3.	Family	<i>Meliaceae</i>
4.	Subfamily	Melioideae
5.	Tribe	Melieae
6.	Genus	<i>Azadirachta</i>
7.	Species	<i>Indica</i>

Each part of neem plant has some medicinal and biological properties and is a valuable source for the formulation of various medicines (Haque.S *et al.*, 2016).Some important uses of neem and its parts are mentioned in the Table 2 below.

Table 2: Uses of Different Parts of Neem

Part	Medicinal uses
Leaf	Eye problem, intestinal worms, skin ulcers, leprosy
Bark	Analgesic, antipyretic
Flower	Treat intestinal worms, reducing bile, controlling phlegm
Fruit	Haemorrhoids, intestinal worms, bloody nose, UTIs, low sperm

	levels, asthma, eye problem, piles
Seed oil	Leprosy, intestinal worms, for birth control
Root	Astringent, treat head lice, skin ulcers, diuretic

Antidiabetic Effect of Various Parts of *Azadirachta indica*:

Table 3: Anti-diabetic Activity of Neem & its Parts

Plant part	Finding of the study	Reference
Leaves	Neem leaves extract showed significant anti-diabetic activity in diabetic rats	Fattah A <i>et al.</i> , 2020
Leaves and twigs	The aqueous extract of neem leaves and twigs significantly ameliorate hyperglycemia, endothelial dysfunction.	Pingali U <i>et al.</i> , 2020
Root bark	Neem root bark extract (NRE) was given in the dose of 800 mg/kg showed significant reduction in blood sugar level. But in comparison to glibenclamide it was not showing significant result.	Patil P <i>et al.</i> , 2013
Flower	The flowers of <i>Azadirachta indica</i> contain atleast two constituents which are responsible for the hypoglycaemic activity.	Waliullah S <i>et al.</i> , 2008
Leaf extract & seed oil	Pretreatment with neem leaf extract and seed oil administration, started 2 weeks prior to alloxan in rabbits, partially prevented the rise in blood glucose levels as compared to control diabetic animals.	Khosla P <i>et al.</i> , 2000

Fttah A. E. *et al.*, 2020 reported that neem leaves extract supplementation in diabetic rats showed a significant elevation in body weight gain and antidiabetic activity due to the enhancement of glucose metabolism. Diabetic rats treated with neem leaves extract showed elevation in insulin which showed its hypoglycaemic properties.

Pingali U. *et al.*, 2020 reported that the aqueous extract of neem leaves and twigs significantly ameliorate hyperglycemia, endothelial dysfunction, and systemic inflammation, as metformin can do. The extract significantly decreased the oxidative stress as compared to placebo.

Gupta S. et al., 2004 reported that petroleum ether extract of neem seed kernel and husk showed a significant protection against the oxidative damage induced by Streptozotocin in heart and erythrocytes of rats. They act as cardioprotective but renal and hepatic toxicity was not prevented by them.

Satyanarayana K. et al., 2015 reported that the oral effective dose of *A. indica* leaf extract (400 mg/Kg body weight) in high-fat-induced rats normalized the altered levels of blood glucose & serum insulin. It plays a significant role in management of Type2 DM.

Purohit. A et al., 1991 reported that neem barks and neem flower possess active hypoglycaemic constituents.

Martinez N. et al., in the year 2014 reported that the aqueous extract of neem leaves produce hypoglycaemic effect observed through the determination of glucose in normoglycemic medium.

Nagashayana G. et al., 2014 reported that neem seed oil has hypoglycaemic properties. Rats were used as animal models to study the antidiabetic effects of neem. Diabetes were induced in rats by alloxan monohydrate, and assessment was done by fasting blood glucose levels and the results indicated that neem oil has got potential to reduce blood glucose levels within a short period of time.

Waliulah S. et al., 2008 reported that the flowers of *Azadirachta indica* contain at least two constituents which are responsible for the hypoglycaemic activity. It is effective in reducing the enhanced blood glucose level under their experimental conditions.

Conclusion

It is concluded in this review that with some potential evidences and facts shows that neem has hypoglycaemic property. Different parts of neem plant i.e. leaves, bark, flower, seed, oil, roots have very significant antidiabetic action by lowering blood glucose level. The extract of seed and leaf can be used to treat diabetes and can be formulated as a dosage form to treat DM.

References

- Ahmad, S. (2012). Lokaj Chikitsay Vesaja Udvid (Traditional Treatments and Medicinal Plants). *Anupam Prokashni*: 1-775.
- Chattopadhyay, R.R., Chattopadhyay, R. N., Poddar, G. and Maitra S. K. (1987). Preliminary Report on Antihyperglycemic Effect of Fresh Leaves of *Azadirachta indica* (Beng neem). *Bulletin of Calcutta School of Tropical Medicine*. **35**: 29-33.

- Deshmukh, C. D. and Jain, A. (2015). Diabetes Mellitus: A Review. *International Journal of Pure & Applied Bioscience*. **3(3)**: 224-230.
- Fattah, A. E., Naga, A. M., Habibi E. M. and Shams, S. E. (2020). Ameliorative role of Neem (*Azadirachta indica*) Leaves Ethanolic Extract on Testicular Injury of Neonatally Diabetic Rats Induced by Streptozotocin. *Egyptian Journal of Basic and Applied Sciences*. **7(1)**: 202-207
- Gupta, S., Kataria, M., Gupta, P. K., Murganandan, S. and Yashroy R. C. (2004). Protective Role of Extracts of Neem Seeds in Diabetes Caused by Streptozotocin in Rats. *Journal of Ethnopharmacology*. **90**: 185-189.
- Haque, S. E. and Sreenivasulu, M. (2016). *Azadirachta indica* and Its Antidiabetic Potential- A Review. *International Journal of Pharmacognosy*. **3(7)**: 288-294.
- Hossain, M. A., Shah, M. D. and Sakari, M. (2011). Gas Chromatography- Mass Spectrometry Analysis of Various Organic Extracts of *Merremia borneensis*. *Asian Pacific Journal of Tropical Medicine*. **4**: 637-641.
- Khosla, P., Bhanwra, S., Seth, S., Singh, J. and Srivastva, R.K. (2000). A Study of Hypoglycemic Effects of Neem in Normal and Alloxan Diabetic Rabbits. *Indian Journal of Physiology and Pharmacology*. **44(1)**: 69-74.
- Nagashayana, G., Jagadeesh, K. and Revankar, S. P. (2014). Evaluation of Hypoglycemic Activity of Neem (*Azadirachta indica*) in Albino Rats. *IOSR Journal of Dental and Medical Sciences*. **13(9)**: 4-11.
- Nubilde, M., Ybarra, L. M. and Requena D. (2014). A Study of Hypoglycemic Effects of Neem in Human Blood Cells. *Emirates Journal of Food and Agriculture*. **26(7)**: 623-629.
- Oberlay, L. W. (1988). Free Radicals and Diabetes. *Free Radical Biology & Medicine*. **5**: 113-124.
- Okpanyi, S. N. and Ezeukwu, G. C. (1981). Anti-Inflammatory and Antipyretic Activities of *Azadirachta indica*. *Planta Media*. **4(1)**: 34-39.
- Okur, M. E., Karantas, I. D. and Sifaka, P. (2017). Diabetes Mellitus: A Review on Pathophysiology, Current Status of Oral Medications and Future Perspective. *Acta Pharmaceutica Scientia*. **55(1)**: 61-82.
- Patil, P., Patil, S., Mane, A. and Verma, S. (2013). Antidiabetic Activity of Alcoholic Extract of Neem (*Azadirachta indica*) Root Bark. *National Journal of Physiology, Pharmacy and Pharmacology*. **3**: 142-146.

- Piero, M. N., Nzaro, G. M. and Njagi, J. M. (2014). Diabetes Mellitus- A Devastating Metabolic Disorder. *Journal of Biomedical and Pharmaceutical Sciences*, Asian. **4(40)**: 1-7
- Pingali, U., Ali, M. A. and Nutalapati C. (2020). Evaluation of the Effect of An Aqueous Extract of *Azadirachta indica* (Neem) Leaves and Twigs on Glycemic Control, Endothelial Dysfunction and Systemic Inflammation in Subjects with Type 2 Diabetes Mellitus- A Randomized, Double-Blind, Placebo-Controlled Clinical Study. *Dove Medical Press*. 13.
- Purohit, A. and Dixit, V. P. (1991). Hypoglycemic Effect of Neem Bark and Flower on Streptozotocin- Induced Diabetes in Mice. *Ancient Science of Life*. 11(1 & 2): 28-30.
- Riaz S. (2009). Diabetes Mellitus. *Scientific Research and Essay*. **4(5)**: 367-373.
- Satyanarayana, K., Sravanthi, K., Shaker, I. A. and Ponnulakshmi, R. (2015). Molecular Approach to Identify Antidiabetic Potential of *Azadirachta indica*. *Journal of Ayurveda and Integrative Medicine*. **6(3)**: 165-173.
- Singh, N., Kesharwani, R., Tiwari, A. K. and Patel, D. (2016). A Review on Diabetes Mellitus. *The Pharma Innovation Journal*. **5(7)**: 36-40.
- Waliullah, S., Javed, K., Jafri, M. A. and Singh, S. (2008). Effect of *Azadirachta indica* Flower Extract on Basal and Experimentally Elevated Blood Glucose in Rats. *Oriental Pharmacy and Experimental Medicine*. **8(3)**: 302-310.

