

“Economic Impact On Sufferers of Diabetes Mellitus through Natural Treatment: A Brief Review”

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Abstract

Diabetes is known as a group of metabolic disorders in which a patient has increased blood sugar level, either the reason is insulin deficiency in body or either because body's cells were not responding to that insulin forming in patient's body. It is a leading cause of death. Traditional medicines are being looked up once again for its treatment; the WHO also recommended its further investigation. Diabetes is also a multifactorial disease leading to several complications. It is now the reason of economic loss to its patients and their families and of course to health care system and national economy. In this review, plants and their pharmacological activity in natural treatment is explored. Phytomedicine used in natural treatment present an exciting opportunity for the development of new types of therapeutics for diabetes mellitus with a holistic approach.

A list of medicinal plants with proven antidiabetic and related beneficial effects and of herbal drugs used in treatment of diabetes is compiled.

This review is done to emphasize research-

ers to conduct further research keeping in focus not only on natural treatments of diabetes to relieve the patient but also to reduce economical burdens.

Keywords:

Diabetes, Economy, Metabolic Disorder, Natural Treatment.

1. INTRODUCTION

Diabetes is one of the five leading causes of death. Diabetes mellitus (DM) is a metabolic disorder, complex in nature, resulting in either insulin insufficiency or insulin dysfunction. It is of two types, that is, Type I diabetes (insulin dependent) and Type II diabetes (noninsulin dependent), constituting 90% of the diabetic population. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and expected to be 4.4% in 2030 (W.H et al., 2016).

Diabetes has become more common in the past few decades due to the stress of growing population, ecological disturbances, and

rapid changing lifestyles. When diabetes is not properly managed, it has serious consequences on the patient's health and well-being. All of its types can affect major parts of the body and can also cause an increase in overall risk of death of patient prematurely (Wild et al., 2004). Common possible complications of the disease include heart attack, kidney failure, leg amputation, nerve damage, stroke, and vision loss (Seuring et al., 2015). While in pregnancy, fetal death and other complications may appear due to uncontrolled diabetes (ibid).

Diabetes is a costly disease to manage in low- and middle- income countries and should be priority for the global health community seeking to achieve universal health coverage. Globally, in 2014 an estimated 422 million people (adults) had diabetes, compared to estimated number in 1980 which was 108 million (Ettaro L et al., 2004). Since 1980 global prevalence (age-standardized) has almost doubled. It is rising from 4.7% to 8.5% in the adult population (Ng CS et al., 2014). This reflects an increase in associated risk factors such as being overweight or obesity. Over the past decade, diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries (ibid).

In 2012 approximately 1.5 million deaths were seen due to diabetes. Increased level of glucose than optimal caused further 2.2 million of deaths, and from this total 3.7 million deaths, 43% of people died before 70 years of their age (ibid). Investigation shows that deaths occurring before age 70 is unfortunately higher in middle and low income countries as compared to high income. It has been expected that diabetes prevalence in 2030 would be doubled and would approximately reach to 366 million in elderly people of more than 65 years of age (Saeedi P et al., 2019). In addition to morbidity and mortality, diabetes causes sub-

stantial economic burden for individuals, households and health systems.

In 2017 millions of deaths were observed due to diabetes and global health expenditure was also estimated in same year as USD 727 billion (ibid).

Different anti-diabetic medicines are available in the market for controlling blood glucose level include insulin analogues, α -glucosidase inhibitors, biguanides, dipeptidyl peptidase-4 inhibitors, sulphonylureas, thiazolidiones etc. whereas all these work differently in the body to counteract increased glucose level in blood with different side effects. Long term use of these agents demands some safe, effective and affordable treatment of this lifestyle disease (ibid).

To overcome this demand, scientists are now looking towards hypoglycemic agents of natural or plant origin. Herbal treatment for diabetes is not new. However, further research is required to meet the demand of patients to build their confidence in use of such affordable drugs derived from natural origin.

People of developing countries have lack of access to basic healthcare services, there is also lack of health insurance and welfare schemes for underprivileged people. These people often cannot bear the expenses of healthcare services so most of the time they are diagnosed late when acute and chronic complications become more threatening. Similarly, in Pakistan more than 11% of adult population has diabetes mellitus. According to IDF 6.6 million people of age between 20-79 in Pakistan are diabetics (ibid). Estimated average cost for diabetes management in Pakistan is about 5542 rupees while total cost is Rs 36,577,200,000 per month and it can increase if the hospitalization cost is added. These types

of research studies giving information about cost of particular disease on the individual as well as society are beneficial for nations to decide funding priorities. Now Pakistan have to take measures to control this crippling disease and so the economic burden could also be bearable for patients as well as the country. However, still there is need of researches that not only to help in lowering the cost of treatment but also to improve the health status of diabetic patients.

Due to least toxicity, cheap prices and easy availability of herbal drugs, now they are widely used.

2. MATERIALS AND METHOD

There are many plants that have anti-diabetic potential, abundantly distributing among families including: Araliaceae, Asteraceae, Cucurbitaceae, Lamiaceae, Leguminosae, iliaceae, Moraceae and Rosaceae. They are being used by different purpose (Table 1).

Table 1: Some commonly used plants with anti-diabetic activity are as follows:

S. No.	Anti-Diabetic Plant	Local Name	Breif discription	Pictures
1.	<i>Cinnamomum verum</i>	Daar chini	Tropical evergreen tree and has properties like Insulin. Inner bark has ability to decrease the levels of blood glucose, triglycerides and cholestrol.	
2.	<i>Pterocarpus marsupium</i>	Indian Kino Tree	Large deciduous tree and it is believed to reduces the absorption of glucose from GIT and also improve insulin & Proinsulin. It has effects on beta cell regeneration.	
3.	<i>Momordica charantia</i> (seeds)	Bitter Gourd/ Bitter Melon/ Karela	Researchers isolated various compounds from bitter melon including charantin and polypeptide-P (Insulin like protein) or plant insulin. Bitter melon acts on pancreatic and non pancreatic cells like muscle cells and lowers the concentration of blood glucose level. stimulates pancreatic insulin secretion.	

4.	<i>Gynema sylvestre</i>	Gurmar boti	It is also used as over the counter drug for weight loss and as blood sugar balancing formulae. In India it is used to treat Type I and Type II diabetes.	
5.	<i>Allium cepa</i>	Onion/piyaz	Allylpropyl disulphide found in onion prevents the insulin breakdown by liver and also stimulates production of insulin by the pancreas.	
6.	<i>Trigonella foenum graecum</i>	Fenu greek seeds/Methi dana	Fiber rich portion of its seeds lowers the blood sugar and to some extent also lowers the cholesterol levels in blood.	
7.	<i>Vaccinium myrtillus</i>	Bilberry	It helps in clearing out extra sugar of blood.	
8.	<i>Panax ginseng:</i>	Ginseng	In traditional Chinese medicines it is used for treatment of diabetes. It enhances the insulin release from pancreas and number of insulin receptors. It also directly lowers the blood sugar level.	

9.	<i>Ginkgo biloba</i>	Ginkgo	Its extract has been proven in the prevention and also treatment of early stages of diabetic neuropathy. Research also suggest its use in the prevention of diabetic retinopathy.	
10.	<i>Acacia arabica</i>	Babool	Its extract acts as secretagogue to insulin release and so use as antidiabetic agent (in control rats). Also used in induced-hypoglycemia (normal rabbits) initiating release of insulin from pancreatic beta cells.	
11.	<i>Aegle marmelos</i> (Fruits and Leaves)	Bael giri	Leaves extract reduces blood sugar level and also prevents sugar level at one hour in the test of oral glucose tolerance.	
12.	<i>Allium sativum</i>	Lahsan	Allicin present in garlic is actually responsible for its hypoglycemic effect by increasing hepatic metabolism, increasing release in insulin from pancreatic cells and therefore there is decrease in fasting blood glucose level and triglycerides levels in blood.	
13.	<i>Aloe vera and Aloe barbadensis</i>	Ailwa/ Ghekwar	Extracts increase glucose tolerance in both normal and diabetic rats, hypoglycemic (alloxanized diabetic rats). (Bitter principle) showed hypoglycemic effect in diabetic rats through stimulation of synthesis and/or release of insulin from pancreatic beta cells, anti inflammatory activity (improves wound healing in diabetic mice).	

14.	<i>Azadirachta indica</i>	Neem	Antihyperglycemic activity (STZ treated rats) because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm, anti-bacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects.	
15.	<i>Eugenia jambolana</i>	Jaman	Kernels decoction is commonly used household remedy for cure of diabetes. Extracts showed hypoglycemic action and also inhibition of enzyme insulinase effects. In type 2 diabetes (glycemic rats) return to normal levels within 3–6 months in 75% of cases particularly in obese patients.	
16.	<i>Mangifera indica</i> (Leaves and Seeds)	Aam	Aqueous extract of leaves of <i>Mangifera indica</i> possesses hypoglycemic effect which may be due to reduction in intestinal glucose absorption.	
17.	<i>Ocimum sanctum</i>	Tulsi	Research showed remarkable reduction in fasting glucose level, amino acid, cholesterol, triglycerides, lipid and uric acid levels from tulsi.	
18.	<i>Phyllanthus amarus</i>	Amla	Traditionally it has been used in the diabetes therapeutics, methanolic extracts showed reduction in blood glucose level in alloxanized diabetes. Also decreases lipid peroxidation and antioxidant.	

19.	<i>Rosa damascena</i>	Gule Surkh	Rosa damascene R. damascena was found to be a potent inhibitor of the α -glucosidase enzyme, anti-diabetic effect may be mediated by inhibition of α -glucosidase that suppress carbohydrate absorption from the small intestine and reduced the postprandial glucose level.	
20.	<i>Tinospora cordifolia</i> (Willd) Miers (Roots and Stem)	Gilo	Stem Hypoglycemic and a hypolipidemic activity (alloxan diabetic rats) decreases the blood glucose level and increases glucose tolerance (rodents).	
21.	<i>Swertia chirayita</i>	Chirayita	Stimulates insulin release from islets. Methanolic leaf extracts contain significant antibacterial & antidiabetic potential, methanolic root has potential antioxidant activity.	
22.	<i>Artemisia absinthium</i>	Afsanteen	Ethanol extract of Artemisia absinthium in alloxan-induced diabetic rats was given in a dose 250, 500, and 1000 mg/kg body weight in distilled water i/p, for 10 days	

3. RESULTS AND DISCUSSION:

Diabetes is an important human ailment affecting many from various walks of life. It is proving to be a major health problem, though there are various approaches to reduce the ill effects of diabetes and also to overcome the economic burden of Pakistan.

Now this is the demand of society for the

incorporation of natural origin products for treatment and management of diabetes because extensive use of insulin orally is not feasible and burden on patient's pocket while undesirable adverse effects of synthetic drugs and their contraindications making people uncomfortable in using such drugs.

Active principles useful in diabetes are present in plants, such as dietary fibers, alkaloids, flavonoids, saponins, amino acids, steroids, peptides, and others. These drugs produce potent hypoglycemic, anti-hyperglycemic, and glucose suppressive activities. Effects from the natural treatment may be achieved by either insulin release from pancreatic β -cells, inhibited glucose absorption in gut, stimulated glycogenesis in liver or increased glucose utilization by the body.

Numerous physicians of the modern system of medicine are prescribing natural drugs containing flavonoids and polyphenols and other important components not only for their antioxidant potential but also improving the formation of beta insulin cells, oxidative stress playing important role in damaging the insulin-producing cells of the pancreas and diabetic complications in DM.

There is tremendous scope in natural treatment in the comprehensive management of diabetes as these compounds also exhibited antioxidant and hypolipidemic activity, restored enzymatic functions, repair, and regeneration of pancreatic islets and the alleviation of liver and renal damage as evident by the review.

This research review depicted the claims on variety of common medicinal plants (Table 1) and their antidiabetic potentials, which also scientifically proved for the treatment of diabetes as safe, efficacious and economical.

Moreover, they have powerful immune boosting properties due to possessing energetic essential chemical agents, which cover and cure the diabetic complication (neuropathy, nephropathy, retinopathy etc). However, this study fills the gap between the use of antidiabetic medicinal plants in relation to diseases and restoration of health in the cheapest way, which overcomes the complications of diseases, minimi-

izes sign and symptoms, boosts immunity and most importantly reduces the economic burden from diabetic patients of the poor population of Pakistan.

Therefore, some of the medicinal plants are preferred as they affect the outcome and the management of this disease due to lesser side effects and low cost. A list of medicinal plants which are commonly used in the treatments of diabetes is compiled (Table 1).

4. CONCLUSION

The present research review based on antidiabetic effects of some herbs or medicinal plants, which are commonly being used for culinary purposes, they have safe, prompt action and are cost effective. Therefore, after detailed research findings from the literature survey, consideration of the use of these medicinal herbs should be obvious in not only to control diabetes and complication but also to minimize the economic burden due to day-by-day increasing diabetes sufferers from every social class of society.

5. REFERENCES

1. Organization, W.H., Global report on diabetes: executive summary. 2016, World Health Organization.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes care*. 2004 May 1;27(5):1047-53.
3. Seuring T, Archangelidi O, Suhrcke M, The economic costs of type 2 diabetes: a global systematic review. *Pharmacoeconomics* 2015;33:811–31.
4. Ettaro L, Songer TJ, Zhang P, Cost-of-illness studies diabetes mellitus. *Pharmacoeconomics* 2004;22:149–64.
5. Ng CS, Lee JY, Toh MP. Cost-of-illness studies of diabetes mellitus: a systematic review. *Diabetes Res Clin Pract* 2014;105:151–63.
6. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala

- AA, Ogurtsova K, SB Cosgrove Shaw JE. Global and regional diabetes prevalence estimates for 2019; and projections for 2030 and 2045: Results from the International Diabetes of Federation Diabetes Atlas. *Diabetes research and clinical practice*. 2019 Nov 1;157:107843.
7. Choudhury H, Pandey M, Hua CK, Mun CS, Jing JK, Kong L, Ern LY, Ashraf NA, Kit SW, Yee TS, Pichika MR. An update on natural compounds in the remedy of diabetes mellitus: A systematic and review. *Journal of traditional and complementary medicine*. 2018 Jul 1;8(3):361-76.
 8. Hussain M, Naqvi SB, Khan MA, Rizvi M, Alam S, Abbas A, Akram MU. Direct cost of treatment of diabetes mellitus type 2 in Pakistan. *Int J Pharm Pharm Sci*. 2014;6(11):261-4.
 9. Khowaja LA, Khuwaja AK, Cosgrove P. Cost of diabetes care in out-patient clinics of Karachi, Pak. *BMC health services research*. 2007 Dec; 7(1):189.
 10. Kaur V, Valecha V. Diabetes and antidiabetic herbal formulations: an alternative to Allopathy. *European Journal of Medicine*. 2014(4):226-40.
 11. Al-Rowais NA. Herbal medicine in the treatment of diabetes mellitus. *Saudi medical journal*. 2002 Nov 1;23(11):1327-31.
 12. Joseph B, Jinni D. Insight into hypoglycemic effect of traditional Indian herbs used in the treatment of diabetes. *Res J Med Plants* 2011;5:352-76.
 13. Makheswari MU, Sudarsanam D. Phytomedicine for diabetes mellitus. An Overview. *Res.. Pharm* 2011;1:28-37.
 14. Akter S, Rahman MM, Abe SK, Sultana P. Prevalence of diabetes and prediabetes and their risk factors among Bangladeshi adults: A nation wide survey. *Bull World Health Organ* 2014;92:204-13, 213A.
 15. Kahkashan Z, Rehman SZ, Tajuddin N, Latif A, Jahan N. Hypoglycemic activity of Berg-e-Arusa and Shoneez. *Indian J Tradit Knowl* 2009;8:410-2.
 16. Havsteen BH. The biochemistry and medical significance of the flavonoids. *Pharm Ther* 2002;96:67-202.
 17. Tiwari AK, Prashad P, Thelma BK, Kumar KM, Ammini AC, Gupta A, et al. Oxidative stress path way genes and chronic renal insufficiency in Asian Indians with Type 2 diabetes. *J Diabetes Complications* 2009;23:102-11.
 18. Anzar MA. Drugs indicated for the management of ziaabetes shakri diabetes mellitus in unani med. An overview. *Int J Pharm India* 2013;1:460-74.
 60. Achrekar S, Kaklij GS, Pote MS, Kelkar SM. Hypoglycemic activity of Eugenia jambolana and Ficus bengalensis: Mechanism of action. *In Vivo* 1991; 5:143-7.
 19. Patel DK, Prasad SK, Kumar R, Hemalatha SM. An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pac J Trop Biomed*. 2012;2:320-30.
 20. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS, Hamiduddin, et al.: Anti-diabetic formulations in a Unani medicine *International Journal of Green Pharma • Oct-Dec 2018 (Suppl) • 12 (4) | S783* Systematic review of herbs and dietary supplements for glycemic control in diabetes. *Diabetes Care* 2003;26:1277-94.
 21. Wadkar KA, Magdum CS, Patil SS, Naikwade NS.; Antidiabetic potential and Indian medicinal plants. *J. Herbal Med Toxicol* 2008;2:45-50.
 22. Ribes G, Sauvaire Y, Baccou JC, Valette G, Chenon D, Trimble ER, et al. Effects of fenugreek seeds on endocrine pancreatic secretions in dogs. *Ann Nutra Metab* 1984;28:37-43.
 23. Riyad MA, Abdul-Salam SA, Mohammad SS. Effect of fenugreek and lupine seeds on the development of experimental diabetes in rats. *Planta Med* 1988;54:286-90.
 24. Alarcon-Aguilara FJ, Roman-Ramos R, Perez Gutierrez S, Aguilar-Contreras A, Contreras Weber CC, FloresSaenz JL et al. Study of the anti hyperglycemic effect of plants used as antidiabetics. *J. Ethnopharmacol* 1998;61:101-10.
 25. Mostafa S, El-Shenawy A. Biological activities of Eugenia jambolana (Family Myrtaceae). In: Preedy VR, Watson RR, Patel VB. *Nuts and Seeds in Health and Disease Prevention*. San Diego, CA: Academic Press; 2011. p. 688.
 26. Anzar MA. Drugs indicated for the management of ziaabetes shakri (diabetes mellitus) in unani medicine An overview. *Int J Pharm India* 2013;1:460-74. 60. Achrekar S, Kaklij GS, Pote MS, Kelkar SM. Hypoglycemic activity of Eugenia jambolana and Ficus bengalensis: Mechanism of action. *In Vivo* 1991;5:143-7.
 27. Stark A, Madar Z. The effect of an ethanol extract derived from fenugreek (*Trigonella foenum-graecum*) on bile acid absorption and cholesterol levels in rats.

- Br J Nutr 1993;69:277-87.
28. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. J Clin Biochem Nutr 2007; 40: 163-73.
 29. Sharma RD. Hypoglycemic effect of gum acacia in healthy human subjects. Nutr Res 1985;5:1437-41.
 30. Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pac J Trop Biomed 2012;2:320-30.
 31. Achrekar S, Kaklij GS, Pote MS, Kelkar SM. Hypoglycemic activity of Eugenia jambolana and Ficus on bengalensis: Mechanism of action. In Vivo 1991; 5: 5:143-7.
 32. Shukla R, Sharma SB, Puri D, Prabhu KM, Murthy PS. Medicinal plants for treatment of diabetes mellitus. Indian J Clin Biochem 2000;15:169-77.
 33. Petchi RA, Parasuraman S, Vijaya C, Darwhekar DG. Antidiabetic effect of kernel seeds extract of Mangifera indica (Anacardiaceae). Int J Pharm Bio Sci 2011;2: 385-93.
 34. Boskabady MH, Shafei MN, Saberi Z, Amini SM.; Pharmacological effects of Rosa damascena. Iran J.; Basic Med Sci 2011;14:295-307.
 35. Roy P, Abdulsalam FI, Pandey DK, Bhattacharjee A, Eruvaram NR, Malik T, et al. Evaluation of antioxidant, antibacterial, and antidiabetic potential of two traditional medicinal plants of India: Swertia of cordata and Swertia chirayita. Pharm Res 2015;7:S57-62.
 36. Haytham MD, Abas MM. Mohammad MA, Jaffar MM. Antidiabetic effect of Artemisia absinthium in extracts on alloxan induced diabetic rats. Comp Clin Pathol 2014;23:1733-42.
 37. Al-Waili NS. Treatment of diabetes mellitus by Artemisia herba-alba extract: Preliminary study. Clin . Exp Pharmacol Physiol 1986;13:569-73.