Diabetes mellitus and use of medicinal plants for its treatment

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ABSTRACT

Diabetes mellitus is one of the most common non-communicable diseases globally. It is not a single disease but is a group of metabolic disorder affecting a huge number of population in world. Oral hypoglycemic agents like biguanides and sulphonylureas are still play important role in the management of the Diabetes mellitus but it have some side effect so there are an increasing number of people seeking alternative therapies that may have less severe or no side effects. Several medicinal Plants such as *Allium cepa, Anacardium occidentale, Andrographic paniculata, Momordica charantia, Azadirachtha indica, Brassica oleraccia, Cinnamomum tamala* and *Withania sominifera* have been used to control diabetes in the traditional medicinal systems of many cultures worldwide. In this review gives information about scientific name, family and the parts of the plant used to treat diabetes.

KEY WORDS: Diabetes mellitus, medicinal plant, antidiabetics, insulin, hyperglycemia.

1. INTRODUCTION

Diabetes Mellitus is a metabolic disorder characterized by hyperglycemia due to defect in insulin secretion, insulin action or both. Over the last century human life style and food habits have drastically changed which lead to various chronic diseases. Diabetes milletus is one such disease which is causing serious problems to human health[1]. The number of people suffering with diabetes worldwide is increasing at alarming rate. It is predicted that the number of diabetes person could reach up to 366 million by the year 2030[2]. Without enough insulin, the cells of the body cannot absorb sufficient glucose from the blood; hence blood glucose levels increase, which is termed as hyperglycemia. If the glucose level in the blood remains high over a long period of time, this can result in long term damage to organs, such as the kidneys, liver, eyes, nerves, heart and blood vessels. Complications in some of these organs can lead to death[3]. The practice of traditional medicine using medicinal plants is as old as the origin of man. This type of healthcare was described as Herbalism or Botanical medicine[4]. Diabetes and herbs have a long relation from the past. Thus, plants are a potential source of anti-diabetic drugs which can be proved by the ethnobotanical information reports about 800 plants that may possess anti-diabetic potential. Although, synthetic oral hypoglycemic agents/insulin are the mainstream treatment of diabetes and are effective in controlling hyperglycaemia, they have prominent side effects and fail to significantly alter the course of diabetic complications. This forms the main reason for an increasing number of people finding alternating therapies that may have less severe or no side effects[5,6]. Globally, sales of herbal medicines are growing by about 10% annually. Over 25% of our common medicines contain at least some compounds obtained from plants. In less developed countries the World Health Organization estimates that 75-80% of the people rely on plant based medicines for primary health care. The use of traditional medicine has increased in developed countries also, mainly due to the failure of modern medicine to provide effective treatment for chronic diseases and emergence of multi drug resistant Bacteria and Parasites. The adverse effect of chemical drugs, questioning of the approaches and assumptions of allopathic medicine, their increase in costs and greater public access to information on traditional has also lead to an increase in interest in alternative treatment [7].

1.1. Classification of diabetes: The first widely accepted classification of diabetes mellitus was published by WHO in 1980 [8] and, in modified form, in 1985. The 1980 and 1985 classifications of diabetes mellitus and allied categories of glucose intolerance included clinical classes and two statistical risk classes. The 1980 Expert Committee proposed two major classes of diabetes mellitus and named them, IDDM or Type 1, and NIDDM or Type 2. In the 1985 Study Group Report the terms Type 1 and Type 2 were omitted, but the classes IDDM and NIDDM were retained, and a class of Malnutrition–related Diabetes Mellitus (MRDM) was introduced. In both the 1980 and 1985 reports other classes of diabetes included Other Types and Impaired Glucose Tolerance (IGT) as well as Gestational Diabetes Mellitus (GDM). These were reflected in the subsequent International Nomenclature of Diseases (IND) in 1991, and the tenth revision of the International Classification of Diseases (ICD–10) in 1992. The 1985 classification was widely accepted and is used internationally [9,10]. This classification is summarized in Table no.1.

Table.1.Classification of diabetes

Class name	Characteristics
Insulin-dependent diabetes mellitus (IDDM)	* Low or absent levels of circulating endogenous insulin and dependent on injected insulin to prevent ketosis and sustain life. * Onset predominantly in youth but can occur at any age. * Associated with certain HLA and GAD antigens. * Abnormal immune response and cell antibodies are frequently present at diagnosis. * Etiology probably only partially, as only 35% of monozygotic twins are concordant for IDDM.
Non-insulin-dependent diabetes mellitus (NIDDM)	* Insulin levels may be normal,elevated, or depressed; hyperinsulinemia and insulin resistance. * Characterize most patient; insulinopenia may develop as the disease progresses. * Not insulin-dependent or ketosis-prone undernormal circumstances, but may use insulin for treatment of hyperglycemia. * Onset predominantly after age 40 years but can occur at any age. * Approximately 50% of men and 70% of women are obese * Etiology probably strongly genetic as 60%-90% of monozygotic twins are concordant for NIDDM.
Gestational diabetes(GDM)	* Glucose intolerance that has its onset or recognition during pregnacy. * Associated with older age, obesity, family history of diabetes. *Conveys increased risk for the women for subsequent progression to NIDDM. * Associated with increased risk of macrosomia.
Other type of diabetes, including diabetes secondary to or associated with * Pancreatic disease * Hormonal disease * Drug or chemical exposure * Insulin receptor abnormalaties * Certain genetic syndromes	* In addition to the presence of the specific condition, hyperglycemia at a level diagnostic of diabetes is also present. * Causes of hyperglycemia are known for some condition e.g. pacreatic disease; in other cases an etiologic relationship between diabetes and the other condition is suspencted.

1.2. Pathophysiology of diabetes mellitus: Diabetes mellitus is divided into 2 main types:

a. **Type I (insulin-dependent Diabetes mellitus or IDDM)**: It occurs due to insulin insufficiency because the body does not generate any insulin and patients entirely depend on an exogenous supply of insulin. IDDM is more pronounced in children and young adults [11]. It causes severe damage to the pancreatic β-cells. It is categorized as autoimmune (immune mediated) Diabetes (type 1A) or idiopathic Diabetes with β - cell destruction (type 1B), although the precise description of the later is still unknown [12].

b. Type II (non -insulin -dependent Diabetes mellitus or NIDDM): Type 2 diabetes mellitus is one of the most common diseases of the western world and is associated with cardiovascular disease [13]. Patients suffering from NIDDM are unable to respond to insulin and can be treated with exercise, diet management and medication. Mostly, its onset is in adulthood, largely occurring in obese people over 40 years of age. It indicates a condition with disturbed carbohydrate and fat metabolism. Hypertension, hyperlipidemia, hyperinsulinemia and atherosclerosis are often allied with Diabetes.

Both the types demonstrate some frequent symptoms like high blood sugar levels, unusual thirst, extreme hunger, frequent urination, extreme weakness, blurred vision etc. Although the pathophysiology of Diabetes is not entirely understood, many studies indicate the participation of free radicals in the pathogenesis of Diabetes [14] and its complications [15-17]. Free radicals are proficient enough of damaging cellular molecules, proteins, lipids and DNA, leading to alternation of cell functions. In fact, the abnormalities in lipids and proteins are one of the key reasons for the development of diabetic complications. During Diabetes, free radicals oxidize the lipoproteins, and various irregularities of lipoprotein metabolism also occur in very low-density lipoprotein (VLDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) in Diabetes [18]. Different extracellular proteins are also modified into glycoprotein due to high blood glucose, which is associated with severe diabetic complications [19]. Reactive oxygen species (ROS) are being reported to be formed in different tissues in Diabetes [20-21] by various sources such as the nonenzymatic glycosylation reaction, [22] the electron transport chain in mitochondria [23] and membrane -bound

NADPH oxidase [24-25] ROS are also involved in the progression of insulin resistance as well as pancreatic β-cell dysfunction [26]. Also, advanced glycation end products (AGEs) are produced by non -enzymatic glycosylation of proteins, which tends to mount up on long -lived molecules in tissues creating abnormalities in cell and tissue functions [27-28]. AGEs also play a role in improved vascular permeability in both micro- and macro-vascular structures by sticking to specific macrophage receptors, which leads to free radical production and endothelial dysfunction. AGEs, produced on nucleic acids, may also lead to altered gene expression and mutation. In Diabetes, oxidative stress coexists along with decrease in the antioxidant status, which can lead to the detrimental effects due to free radicals [29]. Vitamins C and E, the natural antioxidants, have been reported to decrease the oxidative stress in experimental Diabetes [30]. Numerous plant products have been reported to have a significant antioxidant activity, which may be of some benefit in Diabetes [31,11].

1.3. General mechanism of action of medicinal plants with antidiabetic property: Different mechanisms of action of medicinal plants with anti-diabetic have been extensively described. These include inhibition of renal glucose reabsorption [32], stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes, reduction in insulin resistance [33] regenerating and/or repairing pancreatic beta cells with increasing the size and number of cells in the islets of Langerhans [34]. Stimulation of insulin secretion [35] and stimulation of glycogenesis and hepaticglycolysis [36] with antidiabetic plants is well established. Also, protective effect on the destruction of the beta cells and improvement in digestion along with reduction in blood sugar urea has been documented [37]. Prevention of pathological conversion of starch to glucose, and inhibition of β-galactocidase, α-glucocidase and alpha-amylase with concomitant capacity to lower cortisol has also been reported [38-39]. Antioxidant activity of antidiabetic plant against oxidative stress which is involved in pancreatic ß-cell dysfunction has been reported as one of the mechanisms of action of antidiabetic plants [40].

1.4. Treatment of diabetes mellitus: India has an officially recorded list of 45,000 plant species and a various estimation of 7500 species of medicinal importance [41]. Raw onion bulb (A//ium cepa) and cloves of garlic (A//ium sativum) have long been used as dietary supplement for traditional treatment of diabetes. Former is used as stimulant, diuretic and expectorant [42]. Concentrated extract of onion bulbs exerted a week hypoglycemic action in healthy and altoxan diabetic animals [43]. Some other medicinal plant used for treatment of diabetes are given in Table no.2.

Table.2. Some medicinal plants used for diabetes

Plant name	Family	Parts used	Activity	Reference
Brassssica juncea	Cruciferae	Seed	Hypoglycemic	[44]
Alangium lamarcku	Alangiaceae	Leaves	Antidiabetic	[45]
Caesalpinia digyna	Fabaceae	Root	Antidiabetic	[46]
Albizia odoratissima	Mimosaceae	Bark	Antidiabetic	[45]
Berberis vulgaris	Berberidaceae	Root	Hypoglycaemic	[47]
Catharanthus roseus	Apocynaceae	Leaf	Hypoglycemic	[48]
Centaurium erythrea	Gentianaceae	Leaf	Antidiabetic	[49]
Costus speciosus	Costaceae	Rhizome	Antidiabetic	[50]
Chaenomeles sinensis	Rosaceae	Friuts	Antidiabetic	[51]
Embelia ribes	Myrsinaceae	Berries	Antidiabetic	[52]
Cocos nucifera	Arecaceae	Leaf	Antihyperglycemic	[53]
Cyclocarya paliurus	Cyclocaryaceae	Bark	Hypoglycemc	[54]
Dillenia indica	Dilleniaceae	Leaves	Antidiabetic	[55]
Hybanthus enneaspermus	Violaceae	Whole plant	Antidiabetic	[56]
Axonopus compressus	Poaceae	Leaves	Antidiabetic	[57]
Lippa nodiflora	Verbenaceae	Whole Plant	Antidiabetic	[58]
Marrubium vulgare	Lamiaceae	Aerial part	Hyperglycemia	[59]
Lithocarpus polystachyus	Fagaceae	Leaves	Hypolipidemic	[60]
Ocimum sanctum	Lamiaceae	Aerial part	Antidiabetic	[61]
Opuntia streptacantha	Cactaceae	Leaves	Antihyperglycemia	[62]
Psidium guajava	Myrtaceae	Fruits	Antihyperglycemic	[63]
Ophiopogon japonicus	Asparagaceae	Root	Antihypoglycemic	[64]
Setaria italica	Poaceae	Seed	Antihyperglycemic	[65]
Semecarpus anacardium	Anacardiaceae	nut	Antidiabetic	[66]
Solanum torvum	Solanaceae	Friut	Antihyperglycemic	[67]
Zygophyllum album	Zygophyllaceae	Whole plant	Antidiabetic	[68]

Vitex negundo	Lamiaceae	Leaves	Antihyperglycemic	[69]
Viscum schimperi	Viscaceae	aerial parts	Antihyperglycemic	[70]
Cassia auriculata	Caesalpiniacae	Leaves	Antihyperglycemic	[71]
Symplocos cochinchinensis	Symplocaceae	Leaves	Hypolipidaemic, Antidiabetic	[72]
Vaccinium arctostaphyls	Ericaceae	Fruit	antidiabetic	[73]
Solanum xanthocarpum	Solanaceae	Leaves	Antihyperglycemic	[74]
Prosopis glandulosa	Fabaceae	Whole plant	Antidiabetic	[75]
Enicostemma littorale	Gentianaceae	Whole plant	Antidiabetic	[76]

2. CONCLUSION

Diabetes Mellitus is a metabolic disorder characterized by hyperglycemia due to defect in insulin secretion, insulin action or both. Allopathic medicines are not effective in treating the disease leading to various adverse effects. Hence medicinal plants are the best alternative for the treatment of diabetes milletus. The plant species have proved their efficacy in reducing blood glucose levels. This paper has presented various anti-diabetic plants that have been pharmacologically tested and shown to be of some value in treatment of Diabetes Mellitus. In near future herbal plants will play a crucial role in modern system of medicine.

REFERENCES

1. Kumar PJ, Clark M, Textbook of Clinical Medicine, Pub: Saunders (London), 2002, 1099-1121.

2. Oyedemi SO, Adewusi EA, Aiyegoro OA, Akinpelu DA, Antidiabetic and haematological effect of aqueous extract of stem bark of *Afzelia africana* (Smith) on streptozotocin-induced diabetic Wistar rats, Asian Pac.J.Trop. Biomed., 1, 2011, 353-358.

3. Pari L, Saravanan R, Antidiabetic effect of *diasulin*, a herbal drug, on blood glucose, plasma insulin and hepatic enzymes of glucose metabolism in hyperglycaemic rats, Diabetes, Obesity and Metabolism, 6, 2004, 286–292.

4. Evans WC, Trease and Evans, Pharmacognosy 15th ed., W.B Saunders, Edinburgh, 2002, 585.

5. Rao MU, Sreenivasulu M, Chengaiah B, Reddy KJ, Chetty CM, Herbal Medicines for Diabetes Mellitus: A Review, International Journal of Pharm.Tech.Research, 2(3), 2010, 1883-1892.

6. Evans WC, Trease and Evans Pharmacognosy, Saunders Company Ltd., 13, 2008, 137.

7. WHO, Traditional Medicine Strategy, World Health Organization, Geneva, 2002.

8. WHO Expert Committee on Diabetes Mellitus, Second Report, Geneva: WHO, Technical Report Series, 1980, 646.

9. National Diabetes Data Group, Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance, Diabetes, 28, 1979, 1039–57.

10. World Health Organization, Diabetes Mellitus: Report of a WHO Study Group, Geneva: WHO, Technical report Series, 1985, 727.

11. Vasim Khan, Abul Kalam Najmi, Mohd Akhtar, Mohd Aqil, Mohd.Mujeeb, Pillai KK, A pharmacological appraisal of medicinal plants with antidiabetic potential, J.Pharm.Bioallied Sci., 4(1), 2012, 27–42.

12. Alberti KG, Zimmet PZ, Definition, diagnosis and classification of Diabetes mellitus and its complications, Part 1: Diagnosis and classification of Diabetes mellitus provisional report of a WHO consultation, Diabet.Med., 15, 1998, 539–53.

13. Psallas M, Manes C, Incretins in type 2 diabetes mellitus: cardiovascular and antiatherogenic effects beyond glucose lowering, Hippokratia Medical Journal, 16(2), 2012, 100-105.

14. Mattecci E, Giampietro O, Oxidative stress in families of type I diabetic patient, Diabetes Care, 23, 2000, 1182–6.

15. Oberlay LW, Free radicals and Diabetes, Free Radic.Biol.Med., 5, 1988, 113–24.

16. Baynes JW, Thorpe SR, Suzanne R, The role of oxidative stress in diabetic complications, Curr.Opin. Endocrinol., Diabetes Obes., 3, 1996, 277–84.

17. Diabetes Complications, 15, 2001, 203–10.

18. 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., 40, 2007, 163–73.

19. Glugliano D, Ceriello A, Paolisso G, Oxidative stress and diabetic vascular complications, Diabetes Care, 19, 1996, 257–67.

20. Baynes JW, Thorpe SR, Role of oxidative stress in diabetic complications: A new perspective on an old paradigm, Diabetes, 48, 1999, 1–9.

21. Dandona P, Thusu K, Cook S, Snyder B, Makowski J, Armstrong D, Oxidative damage to DNA in Diabetes mellitus, Lancet, 347, 1996, 444–5.

22. Sakurai T, Tsuchiya S, Superoxide production from non enzymatically glycated protein, FEBS Lett., 236, 1988, 406–10.

23. Brownlee M, Biochemistry and molecular cell biology of diabetic complications, Nature, 414, 2001, 813–20.

24. Harrison D, Griendling KK, Landmesser U, Hornig B, Drexler H, Role of oxidative stress in atherosclerosis, Am.J.Cardiol., 91, 2003, 7–11.

25. Mohazzab KM, Kaminski PM, Wolin MS, NADH oxidoreductase is a major source of superoxide anion in bovine coronary artery endothelium, Am.J.Physiol., 266, 1994, H2568–72.

26. Evans JL, Goldfine ID, Maddux BA, Grodsky GM, Oxidative stress and stress-activated signalling pathways: A unifying hypothesis of type 2 Diabetes, Endocr.Rev., 23, 2002, 599–622.

27. Brownlee M, Advanced protein glycosylation in Diabetes in Diabetes and ageing, Annu.Rev.Med., 46, 1996, 223–34.

28. Elgawish A, Glomb M, Friendlander M, Monnier VM, Involvement of hydrogen peroxide in collagen cross-linking by high glucose *in vitro* and *in vivo*, J.Biol.Chem., 271, 1999, 12964–71.

29. Collier A, Wilson R, Bradley H, Thomson JA, Small M, Free radical activity is type 2 Diabetes, Diabet.Med., 7, 1990, 27–30.

30. Garg MC, Bansal DD, Protective antioxidant effect of vitamins C and E in streptozotocin induced diabetic rats, Indian J.Exp.Biol., 38, 2003, 101– 4.

31. Anjali P, Manoj KM, Same comments on Diabetes and herbal therapy, Anc.Sci.Life, 15, 1995, 27–9.

32. Eddouks M, Maghrani M, Lemhadri A, Ouahidi ML, Jouad H, Ethno pharmacological survey of medicinal plants used for the treatment of diabetes mellitus, hypertension and cardiac diseases in the south-east region of Morocco, Journal of Ethnopharmacology, 82, 2002, 97-103.

33. Pulok KM, Kuntal M, Kakali M, Peter JH, Leads from Indian medicinal plants with hypoglycemic potentials, Journal of Ethnopharmacology, 106, 2006, 1–28.

34. Mohamed B, Abderrahim Z, Hassane M, Abdelhafid T, Abdelkhaleq L, Medicinal plants with potential antidiabetic activity – A review of ten years of herbal medicine research. International Journal of Diabetes Metabolism, 14, 2006, 1-25.

35. Esmaeili MA, Yazdanparast R, Hypoglycaemic effect of Teucrium polium: studies with rat pancreatic islets, Journal of Ethnopharmacology, 95, 2004, 27-30.

36. Miura T, Itoh C, Iwamoto N, Aato M, Kawai M, Park SR, Suziki I, Hypoglycemic activity of the fruit of the *Momordica charantia* in Type 2 diabetic mice, Journal of Nutrition Science & Vitaminology (Tokyo), 47, 2001, 340-4.

37. Kim MJ, Ryu GR, Chung JS, Sim SS, Min DS, Rhie DJ, Yoon SH, Hahn SJ, Kim MS, JoYH, Protective effects of epicatechin against the toxic effects of streptozocin on rat pancreatic islets: *in vivo* and *in vitro*, Pancreas, 26, 2003, 292-299.

38. Gholap S, Kar A, Hypoglycaemic effects of some plant extracts are possibly mediated through inhibition in corticosteroid concentration, Pharmazie, 59, 2004, 876-878.

39. Heidari R, Zareae S, Heidarizadeh M, Extraction, Purification, and Inhibitory Effect of Alpha-Amylase Inhibitor from Wheat (*Triticum aestivum Var. Zarrin*). Pakistan Journal of Nutrition, 4, 2005, 101-105.

40. Hideaki K, Taka-aki M, Yoshihisa N, Dan K, Munehide M, Yoshimitsu Y, Oxidative Stress and the JNK Pathway in Diabetes, Current Diabetes Reviews, 2005, 65-72.

41. Ashis P, Khan M L, Arunachalam A and Arunachalam K, Biodiversity and conservation of rhododendrons in Arunachal Pradesh in the Indo-Burma biodiversity hotspot, Curr.Sci., 89, 2005, 623.

42. Medicinal Plants of India, Ed. Satyavati G.V, Raina MK. and Sharma M, Indian Council of Medical Research, New Delhi, Vol.I, 1976.

43. Jain R.C and Vyas C.R, Hypoglycemic action of onion on rabbits, Brit.Med.J., 2, 1974, 730.

44. Thirumalai T, Therasa VS, Elumalai EK, David E, Hypoglycemic effect of *Brassica juncea* (seeds) on streptozotocin induced diabetic male albino rat, Asian Pac.J.Trop.Biomed, 4, 2011, 323-325.

45. Kumar D, Kumar S, kohli S, Arya R, Gupta J, Antidaibetic activity of methanolic bark extract of *Albizia odoratissima Benth* in alloxan induced diabetic albino mice, Asian Pac.J.Trop.Med., 4, 2011, 900-903.

46. Rajesh Kumar, Dinesh Kumar Pate, Satyendra Kuldip Prasad, Kirshnamurthy Sairam, Siva Hemalatha, Antidiabetic activity of alcoholic leaves extract of *Alangium lamarckii Thwaites* on streptozotocin-nicotinamide induced type 2 diabetic rats, Asian Pac.J.Tropical Med., 2011, 904-909.

47. Meliani N, Amine Dib ME, Allali H, Tabti B, Hypoglycaemic effect of *Berberis vulgaris* L. in normal and streptozotocin induced diabetic rats, Asian

Pac.J.Trop.Biomed, 6, 2011, 468-471.

48. Ohadoma SC, Michael HU, Effects of co-administration of methanol leaf extract of Catharanthus roseus on the hypoglycemic activity of metformin and glibenclamide in rats, Asian Pac.J.Trop.Med., 2011, 475-477.

49. Sefi M, Fetoui H, Lachkar N, Tahraoui A, Lyoussi B, Boudawara T, *Centaurium erythrea* (Gentianaceae) leaf extract alleviates streptozotocin-induced oxidative stress and cell damage in rat pancreas, J.Ethnopharmacol., 135, 2011, 243-250.

50. Eliza J, Diasy P, Ignacimuthu S, Duraipandiyan V, Antidiabetic and antilipidemic effect of eremanthin from Costus speciosus (Koen.)Sm., in STZ-induced diabetic rats, Chem Biol.Interact, 182, 2009, 67-72.

51. Sancheti S, Sancheti S, Seo SY, Antidiabetic and antiacetyl cholinesterase effects of ethyl acetate fraction of *Chaenomeles sinensis* (Thouin) Koehne fruits in streptozotocin-induced diabetic rats, Exp.Toxicol. Pathol., 65(1-2), 2011, 55-60.

52. Mahendran S, Badami S, Maithili V, Evaluation of antidiabetic effect of embelin from Embelia ribes in alloxan induced diabetes in rats, Biomed Preventive Nutr., 1, 2011, 25-31.

53. Naskar S, Mazumder UK, Pramanik G, Gupta M, Sureshkumar RB, Bala A, Evaluation of antihyperglycemic activity of *Cocos nucifera* Linn. on streptozotocin induced type 2 diabetic rats, J.Ethnopharmacol., 138, 2011, 769-773.

54. Li S, Li J, Guan XL, Li J, Deng SP, Li LQ, Hypoglycemic effects and constituents of the barks of *Cyclocarya paliurus* and their inhibiting activities to glucosidase and glycogen phosphorylase, Fitoterapia, 82, 2011, 1081-1085.

55. Kumar S, Kumar V, Om Prakash, Antidiabetic, hypolipidemic and histopathological analysis of *Dillenia indica* (L.) leaves extract on alloxan induced diabetic rats, Asian Pac.J.Trop.Med., 2011, 347-352.

56. 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.Med., 4, 2011, 316-322.

57. Ibeh BO, Ezeaja MI, Preliminary study of antidiabetic activivty of the methanolic leaf extract of *Axonopus compressus* (P.Beauv) in alloxan induced diabetic rats, J.Ethnopharmacol., 138, 2011, 713-716.

58. Balamurugan R, Ignacimuthu S, Antidiabetic and hypolipidemic effect of methanol extract of *Lippia nodiflora* L. in STZ induced diabetic rats, Asian Pac.J.Trop.Biomed., 1, 2011, S30-36.

59. Elberry AA, Harraz FM, Ghareib SA, Gabr SA, Nagy AA, Sattar EA, Methanolic extract of *Marrubium vulgare* ameliorates hyperglycemia and dyslipidemia in streptozotocin-induced diabetic rats, Int.J.Diabetes Mellitus, 2011.

60. Hou SZ, Chen SX, Huang S, Jiang DX, Zhou CJ, Chen CQ, The hypoglycemic activity of *Lithocarpus polystachyus Rehd*. leaves in the experimental hyperglycemic rats, J.Ethnopharmacol., 138, 2011, 142- 149.

61. Patil R, Patil R, Ahirwar B, Ahirwar D, Isolation and characterization of anti- diabetic component (bioactivity guided fractionation) from *Ocimum sanctum* L. (Lamiaceae) aerial part, Asian Pac.J.Trop.Med., 2011, 278-282.

62. Cetto AA, Wiedenfeld H, Anti-hyperglycemic effect of *Opuntia streptacantha* Lem., J.Ethnopharmacol., 133, 2011, 940-943.

63. Huang CS, Yin MC, Chiu LC, Antihyperglycemic and antioxidative potential of *Psidium guajava* fruit in streptozotocin-induced diabetic rats, Food Chem.Toxicol., 41, 2011, 2189 2195.

64. Chen X, Jin J, Tang J, Wang Z, Wanga J, Jin L, Extraction, purification, characterization and hypoglycemic activity of a polysaccharide isolated from the root of *Ophiopogon japonicas*, Carbohydrate Polymers, 83, 2011, 749-754.

65. Sireesh Y, Kasetti RB, Nabi SA, Swapna S, Apparao C, Antihyperglycemic and hypolipidemic activities of *Setaria italica* seeds in STZ diabetic rats, Pathophysiology, 18, 2011, 159-164.

66. Hedayathullah Khan HB, Vinayagam KS, Palanivelu S, Panchanatham S, Anti-diabetic effect of *Semecarpus anacardium* Linn nut milk extract in a high fat diet STZ-induced type 2 diabetic rat model, Comp.Clin.Pathol., 21(6), 2012, 1395-1400.

67. Gandhi GR, Ignacimuthu S, Paulraj MG, Sasikumar P, Antihyperglycemic activity and antidiabetic effect of methyl caffeate isolated from *Solanum torvum Swartz* fruit in streptozotocin induced diabetic rats, Eur.J.Pharmacol., 670, 2011, 623-631.

68.Ghoul JE, Boughanmi NG, Attia MB, Biochemical study on the protective effect of ethanolic extract of *Zygophyllum album* on streptozotocin induced oxidative stress and toxicity in mice, Biomed.Preventive Nutr., 1(2), 2011, 79-83.

69. Sundaram R, Naresh R, Shanthi P, Sachdanandam P, Antihyperglycemic effect of iridoid glucoside, isolated from the leaves of *Vitex negundo* in streptozotocin-induced diabetic rats with special reference to glycoprotein components, Phytomedicine, 19(3-4), 2012, 211-216.

70. Sattar EA, Elberry AA, Harraz FM, Ghareib SA, Nagy AA, Gabr SA, Antihyperglycemic and hypolipidaemic effects of the methanolic extract of *Saudi mistletoe (Viscum schimperi Engl*.), J.Adv.Res., 2, 2011, 171-177.

71. Gupta S, Sharma SB, Singh UR, Bansal SK, Salutary effect of *Cassia auriculata* L. leaves on hyperglycemia-induced atherosclerotic environment in streptozotocin rats, Cardiovasc.Toxicol., 11, 2011, 308-315.

72. Sunil C, Ignacimuthu S, Agastian P, Antidiabetic effect of *Symplocos cochinchinensis* (Lour.) S. Moore. in type 2 diabetic rats, J.Ethnopharmacol., 134, 2011, 298-304.

73. Feshani AM, Kouhsari SM, Mohammadi S, Vaccinium arctostaphylos, a common herbal medicine in Iran: Molecular and biochemical study of its antidiabetic effects on alloxan-diabetic Wistar rats, J.Ethnopharmacol., 133, 2011, 67-74.

74. Poongothai K, Ponmurugan P, Syed Zameer Ahmed K, Senthil Kumar B, Sheriff SA, Antihyperglycemic and antioxidant effects of *Solanum xanthocarpum* leaves (field grown & in vitro raised) extracts on alloxan induced diabetic rats, Asian Pac.J.Trop.Med., 2011, 778-785.

75. Georgea C, Lochnera A, Huisamen B, The efficacy of Prosopis glandulosa as antidiabetic treatment in rat models of diabetes and insulin resistance, J.Ethnopharmacol., 137, 2011, 298-304.

76. Sonawane RD, Vishwakarma SL, Lakshmi S, Rajani M, Padh H, Goyal RK, Amelioration of STZ-induced type 1 diabetic nephropathy by aqueous extract of *Enicostemma littorale Blume* and *swertiamarin* in rats, Mol.Cell Biochem., 340, 2010, 1-6.