Scholars Academic Journal of Pharmacy (SAJP) **ISSN 2320-4206 (Online)**
Sch. Acad. J. Pharm., 2014; 3(2): 162-177 **ISSN 2347-9531 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Review Article

Phytochemical and Pharmacological Accounts of Some Reviewed Plants with Antidiabetic Potential

Kharjul Mangesh[1]*, Kharjul Ashwini[2], Bhairy Srinivas[2], Gupta Shivram[2], Kale Aaditi[2]
[1]Research Scholar, Department of Pharmacy, JJT University, Vidhya Nagari, Jhunjhunu-Churu Road, Chudela, Jhunjhunu- 333001, Rajasthan, India
[2]Department of Pharmacognosy, Shivajirao S. Jondhle College of Pharmacy, Asangaon, Thane-421601, Maharashtra, India

***Corresponding author**
Kharjul Mangesh
Email: kharjulmangesh@gmail.com

Abstract: With increased morbidity and mortality, diabetes mellitus is emerging as major health problem. 69% adults of developing countries and 20% of developed countries are susceptible to diabetes. Insulin therapy is suggested only when diet or oral hypoglycemic fails to control blood glucose levels and in case of postpancreatectomy. Insulin analogues are advantageous with low risk of hypoglycemia particularly nocturnal hypoglycemia. Drawbacks of insulin therapy are like local pain, inconvenience of multiple injections, insulin edema, lipohypertropy, insulin allergy, resistance and above all of this are weight gain. Oral hypoglycemic agents like Sulphonylureas (Glibenclamide, Glipizide, Gliclazide), Non-Sulphonylureas (Nateglinide, Repaglinide), Alpha-glucosidase inhibitors (Acarbose, Miglitol), Dipeptidylpeptidase(DPP) IV inhibitors (Sitagliptin, Linagliptin, Alogliptin, Dutogliptin, Gemiglaptin) are used for treatment of diabetes but they have their own limitations due to selective mechanism of action. WHO in 1976 officially recognized importance of traditional medicine as source of primary health care by globally addressing its traditional medicine programme. India being the botanical garden of the world, is the largest producer of medicinal herbs. 21,000 plants are listed by WHO, used for medicinal purposes around the world. This review covers phytochemical and pharmacological accounts of some plants with antidiabetec potential. Herbal drugs are the oldest known healthcares available to mankind, enlisted in naturopathic, ayurvedic, homeopathic and other medicine systems obtained from natural sources. Herbal drugs becomes advantageous over allopathic drugs due to their safety, low cost, complete accessibility with enhance tolerance.There is more preclinical research warranted for exploration of antidiabetic potential of new plants/herbs whichever is not yet studied and there is also need of clinical establishment of antidiabetic plants which are already found promising in their preclinical evaluation.
Keywords: diabetes mellitus, Oral hypoglycemic agents, phytochemical, Herbal drugs

INTRODUCTION

Diabetes Mellitus (DM)

As per WHO diabetes mellitus referred as diabetes, characterized by hyperglycemia is a chronic disease, which occurs when pancreas produces insufficient insulin or there is decreased insulin sensitivity in cells [1, 2] by the year 2025,300 million people worldwide will be affected by most common endocrine disorder i.e. diabetes [3]. 69% adults of developing countries and 20% of developed countries are susceptible to diabetes [4]. With increased morbidity and mortality, diabetes mellitus is emerging as major health problem [5-7].

Types of DM

Type -I or Insulin Dependent Diabetes Mellitus (IDDM)/ juvenile-onset /ketone-prone diabetes

It is immune mediated or idiopathic diabetes mellitus, characterized by destruction of beta cells of pancreas by T- cell mediated immune attack and life span of pancreatic cell is decreased by one third along with ketoacidosis in body tissues and fluid [1, 4, 8].

Type-II or Non-insulin Dependent Diabetes Mellitus (NIDDM)/ adult-on-set diabetes

Lack of insulin secretion in response to blood glucose levels demonstrates NIDDM. Reduced insulin sensitivity is predominant abnormality, leading to hyperglycemia which can be reversed by drugs improving insulin sensitivity or reducing glucose production by liver [1, 8].

Gestational Diabetes Mellitus (GDM)

In a non-diabetic pregnant woman, gestational diabetes develops near the end of the 3rd trimester or beginning of 4th trimester. It is characterized by carbohydrate intolerance due to body's inability to use

insulin as a result of pregnancy induced hormonal changes. 4% of pregnancies are affected by gestational diabetes, which disappears after child birth [3, 9, 10].

TREATMENT OF DIABETES MELLITUS

Allopathic treatment (insulin therapy)

Insulin

It is an endocrine hormone released from β cells of pancreas, obtained from biological origin and classified as rapid acting, short acting, intermediate acting or long acting. In 1992, insulin was introduced for clinical use before each main meal and one injection in the night, usually at 1 a.m. insulin is a small protein with a molecular weight of 5808. It contains 51 amino acids arranged in two chains A and B linked by disulphide bridges [11-14].

Pharmacodynamics of Insulin

Initial dose: 0.5-1.0 units/ kg per day and maintenance dose Adjust doses to achieve premeal and bedtime glucose level of 80-140 mg/dl. Insulin facilitates glucose entry into adipose tissues, muscles, and liver by stimulating several enzymatic reactions that start at the insulin receptors. The stimulation of an intrinsic tyrosine kinase of the insulin receptor results in an increase in membrane phosphorylation that consequently increases the membrane permeability to glucose through a complicated cascade of intracellular events and by inhibiting hepatic glucose production [13,15].

Table 1: Pharmacokinetics of Insulin [15]

Biosynthesis and release	Distribution.	Metabolism	Excretion
Proinsulin is precursor of insulin, biosynthesized in pancreas and certain proteolytic enzymes breaks down it into active form i.e. insulin.	Insulin doesn't shows plasma protein binding, hence it is rapidly distributed throughout the extracellular fluid, once releases from pancreas.	Liver is a principle site for insulin metabolism where aspartially it is metabolized in muscles tissues and kidneys. With a short half life (about 5-6 minutes), 50% of circulating insulin is deactivated by the liver.	About 98% of unchanged insulin is reabsorbed in the proximal tubules for further action.

Advantages and disadvantages of Insulin

Insulin therapy is suggested only when diet or oral hypoglycemic fails to control blood glucose levels and in case of postpancreatectomy. Insulin analogues are advantageous with low risk of hypoglycemia particularly nocturnal hypoglycemia. Drawbacks of insulin therapy are like local pain, inconvenience of multiple injections, insulin edema, lipohypertropy, insulin allergy, resistance and above all of this are weight gain [15-18].

ALLOPATHIC TREATMENT (ORAL HYPOGLYCAEMIC THERAPY)

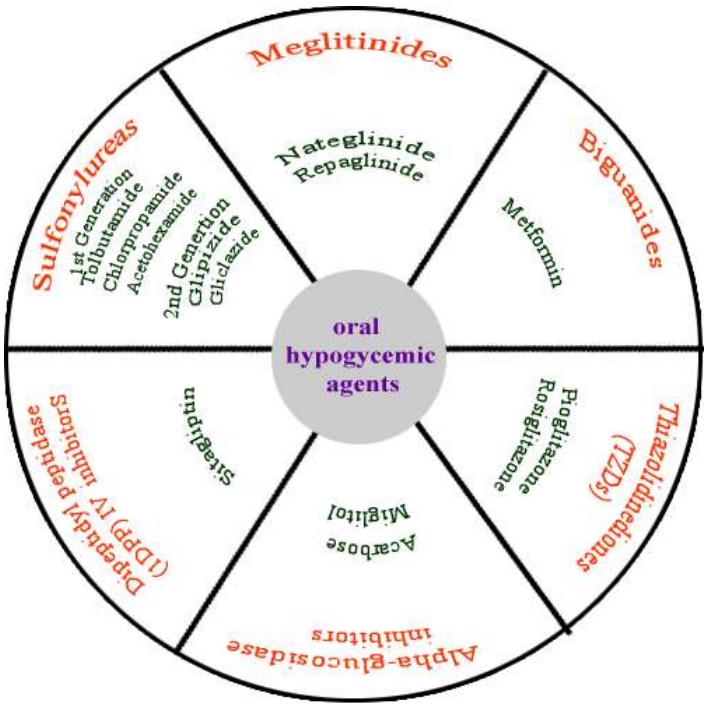


Fig. 1: Classification of allopathic antidiabetic medicines

Sulphonylureas

Sulphonylureas derivatives of sulfonic acid and urea, are time tested oral hypoglycemic from last 50 years [19, 20] Second generation (Glibenclamide, Glipizide, Gliclazide) sulphonylureas are clinically used today were as First generation(Tolbutamide, Chlorpropamide, Acetohexamide, Tolazamide) sulphonylureas is outdated [21, 22].

Non-Sulphonylureas

(Meglitinides)Nateglinide and Repaglinide represents non sulphonylureas as meglitinides where former isbenzoic acid derivatives and later is phenylalanine derivatives [23].

Alpha-glucosidase inhibitors

Acarbose and Miglitol are luminally acting oral hypoglycemics acts by inhibiting enzyme Alpha-glucosidase [22].

Dipeptidylpeptidase (DPP) IV inhibitors

Sitagliptin and linagliptin are worldwide registered DPP-IV inhibitors. Alogliptin, dutogliptin, and gemiglaptin, are recently developed [24].

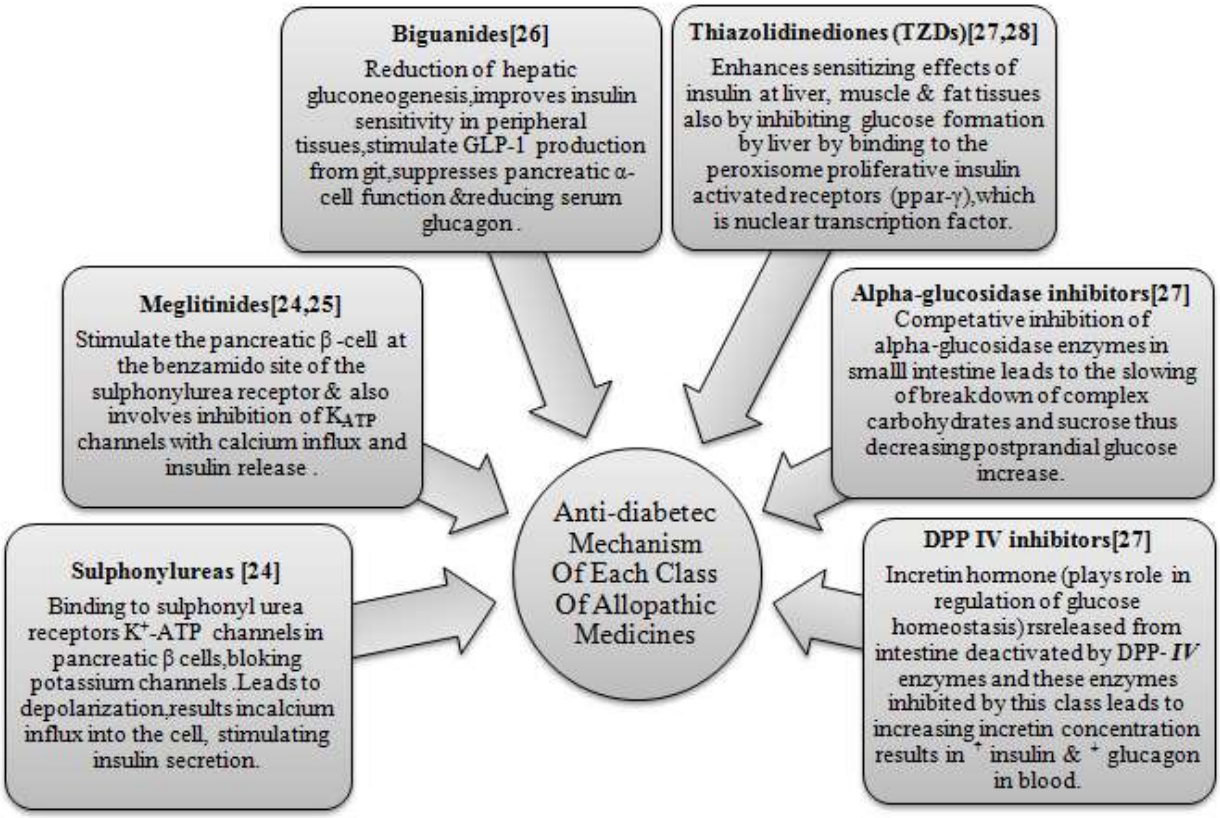


Fig. 2: Antidiabetec Mechanism of Allopathic Medicines

Table 2: Simplified comparative data of oral hypoglycemic agents [3,4,13,27]

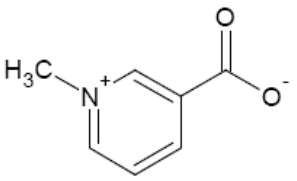
DRUG CLASS	Individual drugs	Dose of drugs(mg/day)		Advantages	Disadvantages	Most common ADR
		Initial dose	Maintainance dose			
Sulfonylureas	Acetohexamide	250	1500	Inexpensive, improved lipid profile by lowering Triglycerides	Weight gain, and rarebut severe hypoglycemia	Hypoglycaemia, Rare allergies, SIADH can be caused by first generation and disulfiram reaction with alcohol, cardio-vascular effects
	Glipizide	5	20			
	glyburide	2.5	08			
	Glimepride	1-2	-			
(Meglitinides)	Nateglinide	180-480	120	Lower triglycerides,	Weight gain similar to	Experience limited, hypersensitivity

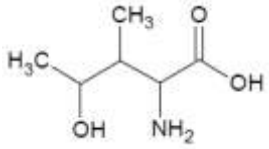
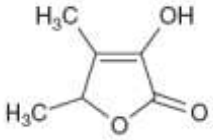
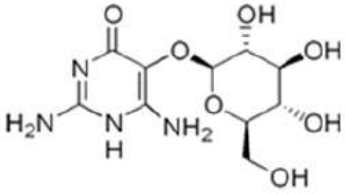
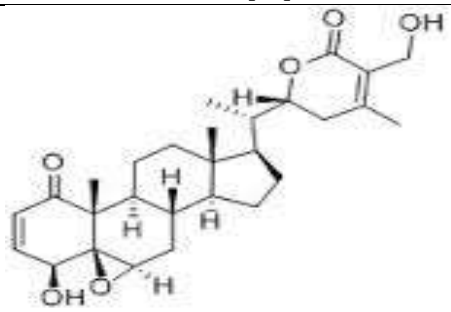
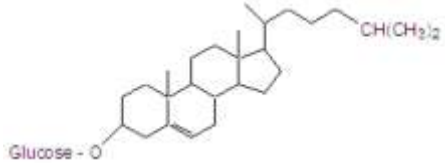
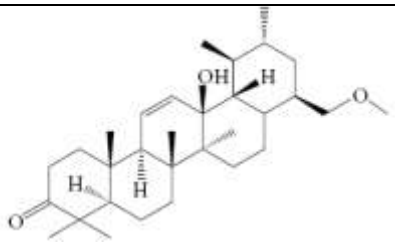
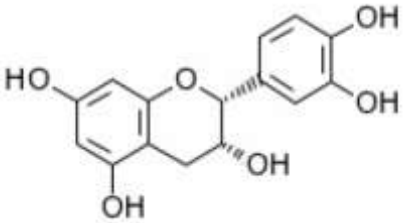
	Repaglinide	0.5-2	16	uncommon hypoglycemia	hypoglycemia	reactions including pruritus, rashesandurticaria.
Biguanides	Metformin	500mg b.i.d	2550	Metformin is only FDA approved oral diabetic in children more or =to 10 years. Lowers TG and total cholesterol, No hypoglycemia, No weight gain	Minimal effect on HDL, used as monotherapy does not sustain HbA1C reductions	Gastrointestinal side effect (Diarrhea) minimized by XR form. Lactic acidosis occurs rarely , abdominal discomfort, and metallic taste
Thiazolidinediones (TZDs)	Pioglitazone	15-30	45	Lower TG, and raises HDL, No hypoglycemia effect	Weight gain, elevated ALT levels, and edema noted.	Gastrointestinal adverse effects at elevated dosages, rare liver failure,
	Rosiglitazone	4-8	8mg/day or 4mg b.i.d			
Alpha-glucosidase inhibitors	Acarbose	NA	25-100mg t.i.d	Lower TG, No hypoglycemia noted, as well as absence of weight gain	Minimal effect on total cholesterol andHDL levels	Gastrointestinal adverse effects such as bloating, and flatulence.
	Miglitol	NA	25-100mg t.i.d			
Dipeptidyl Peptidase (DPP) IV inhibitors	Sitagliptin	NA	100mg once with/ without food	Neutral effect On weight, No hypoglycemia, No drug interactions	Minimal effect on total cholesterol and HDL	Upper respiratory tract infection, headache.

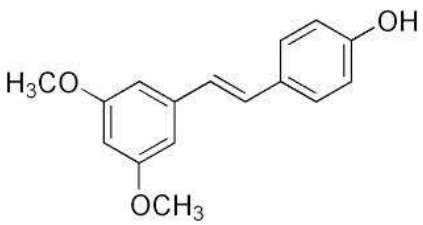
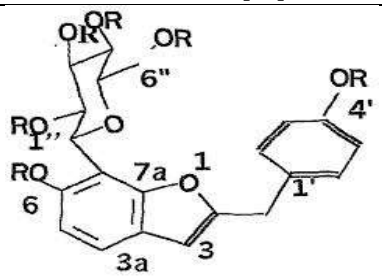
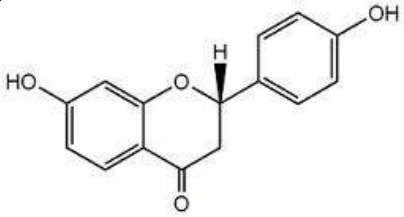
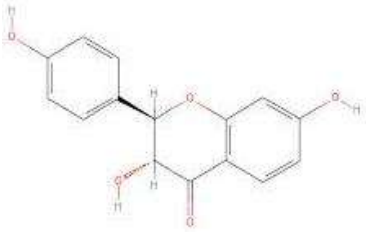
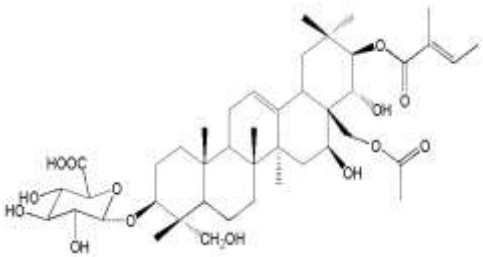
TRADITIONAL & ANCIENT USE OF ANTIDIABETIC HERBAL MEDICINES

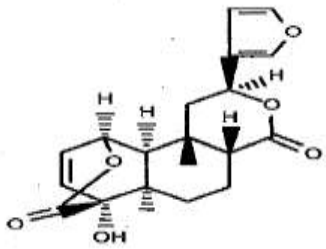
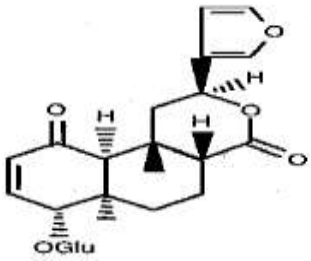
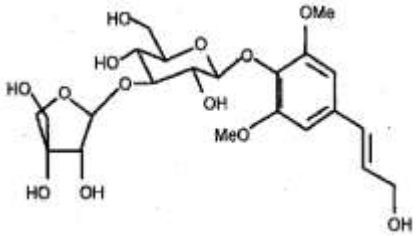
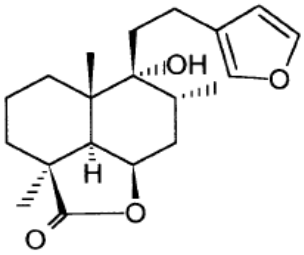
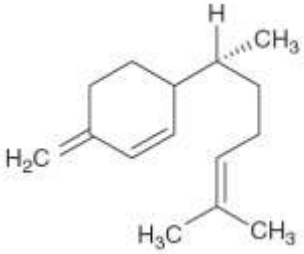
WHO in 1976 officially recognized importance of traditional medicine as source of primary health care by globally addressing its traditional medicine programme [29]. India being the botanical garden of the world, is the largest producer of medicinal herbs. 21,000 plants are listed by WHO, used for medicinal purposes around the world [30]. This review covers phytochemical and pharmacological accounts of some plants with antidiabetec potential. Herbal drugs are the oldest known healthcares available to mankind, enlisted in naturopathic, ayurvedic, homeopathic and other medicine systems obtained from natural sources. Herbal drugs becomes advantageous over allopathic drugs due to their safety, low cost, complete accessibility with enhance tolerance [31].

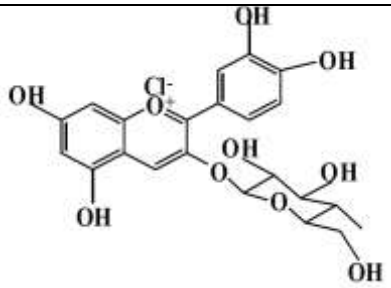
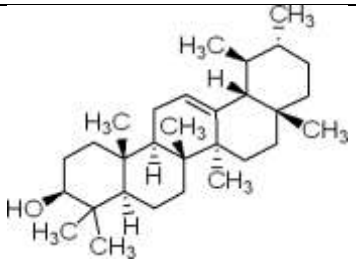
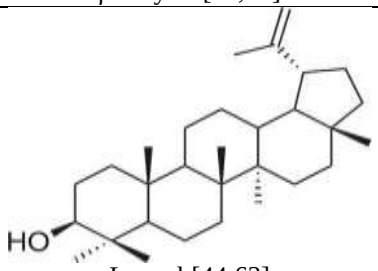
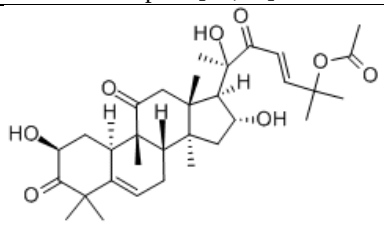
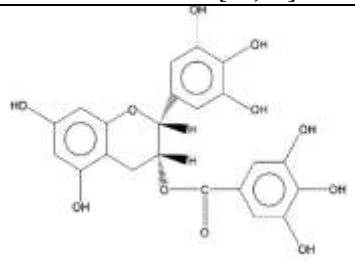
Table 3: Phytochemistry of herbal antidiabetic medicinal plants

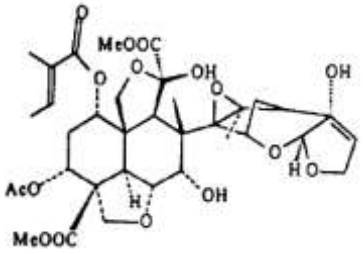
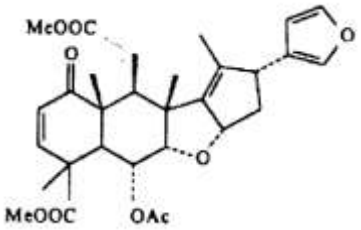
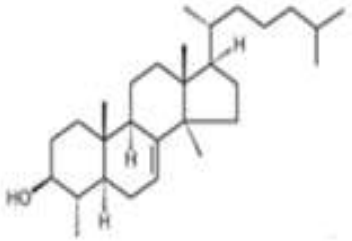
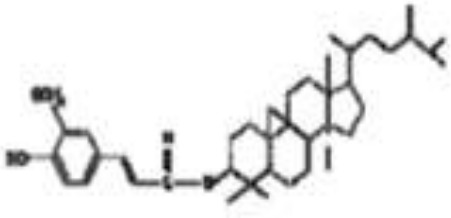
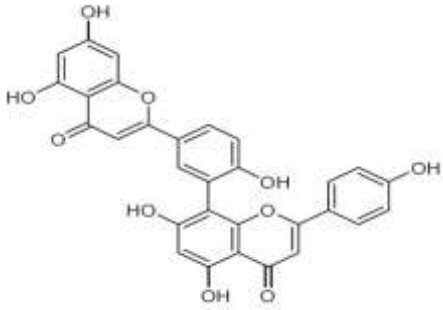
Botanical name of plant	General (local) name	Plant part used	Active (antidiabetec) chemical constituents with their structure
Trigonellafoenum graecum [32]	Methi [33] Fenugreek [34] (English vernacular)	Seeds [33]	 Trigonelline (1-methylpyridinium-3-carboxylate) [35-36]

			 4-hydroxyisoleucine (2-amino-4-hydroxy-3-methylpentanoic acid)[35,36]
			 Sotolon [35,37]
			 Vicine [38]
			 withaferin-A [38]
Momordica charntia [39] 	Bitter gourd, Balsam pear, Bitter melon, Bitter cucumber [40]	Fruits, seeds [39]	 Charantin [39,41]
			 Momordicin [42]
Pterocarpus marsupium [43]	Indian kino, Bijasal [43]	Heart wood, leaves, flowers, bark, & gum [44]	

			(-)-Epicatechin [45]
			 Pterostilbene [46]
			 Marsupin [47]
			 Liquiritigenin [47]
			 Isoliquiritigenin [47]
Gymnema sylvestre [48] 	Gurmar, mera-singi [48]	Leaves [49]	 Gymnemic acid [50]

Tinospora cordifolia [51] 	Guduchi, Giloy or Amrita [51]	Stem [52]	 Columbin [53]
			 Tinosporaside [53]
			 Cordifolioside A [53]
Marrubium vulgare L. [54] 	Horehound [54]	Leaf, roots [39]	 Marrubiin [39,55]
Zingiber officinale [56] 	Ginger [56], Adark [57]	Rhizome [57]	 Sesquiterpene [37,57] (β-Sesquiphellandrene)

*Grewiaasiatica*L.[58] 	Phalsa [58]	Fruit[58]	 cyanidin 3- glucoside [59,60]
Cocciniaindica [61] (Cocciniagrandis, Cocciniacordifolia) 	Kundaru Ki Bel (Hindi) Ivy Gourd (English) [61]	Fruit, leaf, root, whole plant [62]	 β-amyrin [44,63]
			 Lupeol [44,63]
			 cucurbitacin B [44,63]
Camellia sinensis(L.) [64] 	Chha [64]	Leaf [65]	 Epigallocatechingallate [66,67]

Azadirachtaindica [68] 	Neem [68]	Bark, Leaf, Seed [62]	 Azadirachtin [68,69]
			 Nimbin [69,70]
Aloe vera [71] 	Goddess, Kumari, Guarpatha [71]	Leaves [72]	 Lophenol (phytosterols) [73]
			 4-Methylenecycloartanol [73]
Biophytumsensitivum [74] 	Life plant, little tree plant, sensitive plant [74]	Leaves [75]	 Amentoflavone [76,77]

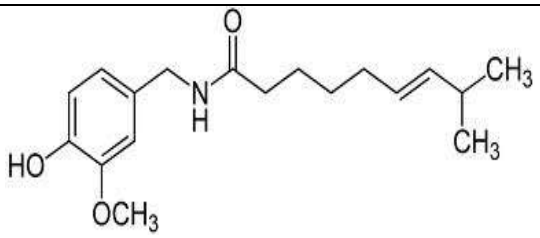
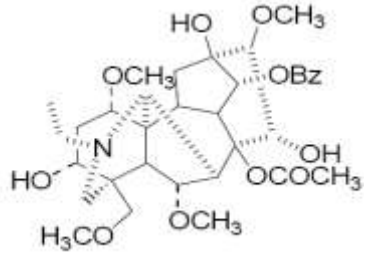
Capsicum annum [78] 	Chilli pepper[78]	Fruit [78]	 Capsaicin[79,80]
Acontium carmichaeii [78] 	Pinyn [78]	Root [78]	 Aconitine [81,82]

Table 4: Mechanism of action, available dose and dosage form of antidiabetic plants

Plant name	Antidiabetic mechanism of action	Dose	Dosage form
Trigonellafoenum graecum	It diminishes the carbohydrate metabolism by inhibiting intestinal enzyme alpha-amylase. It stimulates glucose dependant insulin secretion from pancreatic beta cells to induce hypoglycemia.[83]	10-15 grams per day in divided doses with meals. [35]	Seed powder. [83]
Momordica charntia	It mimics insulin activity by stimulating muscle cells glucose and aminoacid uptakes, decreases hepatic gluconeogenesis. [84, 85]	Fresh juice- 57-113 gm daily, Tincture- 1.3 ml/ twice/ daily, Juice extract- 300-600 mg.[10]	Crude drug, extracts, fruit juice and tablets.[77]
Pterocarpus marsupium	It exerts protective, restorative, regenerative effects in diabetic beta cells. Insulin releasing activity is correlated to potential increase in the cyclic adenosine monophosphate (cAMP) in pancreatic islets, along with significant convertion of proinsulin to insulin [86]	Wood extract (pterostilbene) – 10 mg/ kg, Bark decoction- 1 gm/ 100 mg body weight for 10 days [10]	The wood extract & bark decoction [10]
Gymnema sylvestre	Hypoglycemic activity of gymnemic acid isdue to regeneration of islet cells, stimulation of insulin release , increase glucose uptake by cells, inhibition of glucose absorption, and suppression of gluconeogenic enzymes and sorbitol dehydrogenase [87]	Powder leaf- 2-4 mg/daily, Water soluble acidic solution- 400 mg/day [10]	It is used as water soluble acidic solution &as powered leaf [10]

Tinospora cordifolia	Decreased blood glucose by level and increased glucose tolerance is correlated with regeneration of beta cells of islets of langerhans [88]	aqueous extract at a dose of 400 mg/kg,its effect is equivalent to only one unit/kg of insulin [89]	the hydro alcoholic and chloroform extract of t.cordifolia stem [90]
Marrubium vulgare L	Promotes insulin release from beta cells of islets of langerhans or and inhibit processs of insulin breakdown [91]	the aqueous extract at 200 and 300 mg/kg/ twice daily for 2 weeks [91]	Decoction.[92]
Zingiber officinale	By improving insulin sensitivity it reduces fasting blood glucose and improves serum insulin level [65]	3–10 g fresh ginger, or 2–4 g dry ginger, 1–3 ×/day [93]	Fresh ginger juice [93]
*Grewia asiatica*L	Hypoglycemic effect is mainly result of improving glucose utilization by cells [94]	1 kg sugar, 1 glass of water and 2 teaspoon of ghee are heated to make sheera. Then 1 kg crushed fruit of Grewiais mixed with it and strained through a fine cloth. 2-3 teaspoon strained mixture is used With one glass of water twice a day [95]	Syrup (One kg fruit is crushed with fingers in 1 liter of water and then strained. Sugar is added to the strained juice to make syrup. The syrup is taken according to the need) [95]
Coccinia indica	Glucose synthesis is inhibited by suppression of gluconeogenic enzymes like glucose-6- phosphatase and fructose-1, 6-bisphosphatase. Activates glucose-6-phosphate dehydrogenase thre by promoting glucose oxidation. Hypoglycemic effect is also due to insulin secretagogue activity [96]	Dried extract (500 mg/kg p.o., for 6 weeks), 3–6 g powder of Whole plant and 5–10 ml juice [96]	Bimb or Kanturi [97]
Camellia sinensis(L.)	Inhibits development of insulin resistance, hypoglymia and other metabolic effects .also decreases glucose absorption from intestine [64, 98]	1.5 g/body of green tea promoted glucose metabolism in healthy human volunteers [99]	Tea [97]
Azadirachta indica	Improves peripheral glucose uptake by inhibiting action of epinephrine on glucose metabolism [100]	Aq. Leaf extract is taken at a dose of 2-3 tea spoons daily in empty stomach.[68] and Capsule- 1-2 capsules/ twice daily [10]	decoction and juice of leaves[101] & capsules [10]
Aloe vera	Maintains glucose homeostasis by interfering with carbohydrate metabolizing enzymes. Increases production and release of insulin [44]	Aloe vera gel at 200 mg/kg possesses significant antidiabetic activity[102]	gel extract [71]
Biophytumsensitivum	Possess insulotrophic effects i.e. improvement in synthesis and release of insulin from the beta cells of langerhans [89]	200 mg/kg body weight is optimum for hypoglycaemia [89]	-
Capsicum annum	Insulin producing cells are protected from autoreactive T cells. Anti-inflammatory effects of capsaicin results due to binding of capsaicin to the VR1 receptors which activates pancreatic macrophages [103]	1g and 2g Capsicum frutescence supplemented diet [104]	-
Acontium carmichaeii	Improvement in peripheral glucose uptake is due to activation of opioid μ receptors of peripheral tissues, thereby lowering plasma glucose levels [81]	-	-

CONCLUSION

Biologically obtained insulin, insulin analogues and oral hypoglycemic agents are used for treatment of diabetes but they have their own limitations due to selective mechanism of action. India being the botanical garden of the world, is the largest producer of medicinal herbs. 21,000 plants are listed by WHO, used for medicinal purposes around the world. This review covers phytochemical and pharmacological accounts of some plants with antidiabetec potential. Herbal drugs are the oldest known healthcares available to mankind, enlisted in naturopathic, ayurvedic, homeopathic and other medicine systems obtained from natural sources. Herbal drugs becomes advantageous over allopathic drugs due to their safety, low cost, complete accessibility with enhance tolerance. There is more preclinical research warranted for exploration of antidiabetic potential of new plants/herbs whichever is not yet studied and there is also need of clinical establishment of antidiabetic plants which are already found promising in their preclinical evaluation.

REFERENCES

1. Vidyasagar K, Shivakrishna N, Sripathi BN, Tejasruthi PVR, Ramanareddy K, Sunitha P, Srikanth P; beneficial effect of ethonolic extract of bael fruit in combination with metformin HCl in normal rabbits. International journal of research in pharmacy and chemistry, 2011; 1(3): 528-534.
2. Diabetes mellitus from world health organization (WHO). Available from http://www.who.int/topics/diabetes_mellitus/en/
3. Bastaki S; Diabetes mellitus and its treatment. International Journal Diabetes & Metabolism, 2005; 13: 111-134.
4. SatheeshMadhav NV, Bhattacharya S, Uniyal SN, Nautiyal A; A Detailed Review on Diabetes Mellitus And Its Treatment In Allopathic And Alternative Systems. Pharmanest An International Journal of Advances in Pharmaceutical Sciences, 2013; 4(1): 16-43.
5. Patel B, Oza B, Patel KP, Malhotra SD, Patel VJ; Pattern of antidiabetic drugs use in type-2 diabetic patients in a medicine outpatient clinic of a tertiary care teaching hospital. International Journal of Basic & Clinical Pharmacology, 2013; 2(4): 485-491.
6. Dr.Mullaicharam AR, Hosni ASA; Comparative Study of Alternative Medicines And Allopathic Medicines For Treatment Of Diabetes Mellitus. International Journal of Institutional Pharmacy And Life Sciences, 2012; 2(1): 250-258.
7. Mondal P, Bhuyan N, Das S, Kumar M, Borah S, Mahato K; Herbal Medicines Useful For The Treatment Of Diabetes In North-East India. International Journal of Pharmacy and Biological Sciences, 2013; 3(1): 575-589.
8. Mohana LS, Rani KSS, Reddy UKT; A Review On Diabetes Milletus And the Herbal Plants Used For Its Treatment. Asian Journal of Pharmaceutical and Clinical Research, 2012; 5(4): 15-21.
9. Murugesh S, Mani D; A Brief Overview of Diabetes. International Journal of Pharmacy and Pharmaceutical Sciences, 2011; 3(4): 22-27.
10. Gupta PD, De A; Diabetes Mellitus and its Herbal Treatment. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012; 3(2): 706-721.
11. Joshi SR, Parikh RM, Das AK; Insulin - History, Biochemistry, Physiology and Pharmacology. Journal of the associations of physicians of India, 2007; 55: 19-25.
12. Bangstad H-J, Danne T, Deeb LC, Jarosz-Chobot P, Urakami T, Hanas R; Insulin treatment in children and adolescents with diabetes. Pediatric Diabetes, 2009; 10(12): 82–99.
13. Mane PB, Antre RV, Oswal RJ; Antidiabetic Drugs: An Overview. International Journal of Pharmaceutical and Chemical Sciences, 2012; 1(1): 301-306.
14. TasneemTs.S; Newer Insulins. International Journal of Pharmaceutical, Chemical and Biological Sciences, 2013; 3(2): 242-246.
15. Mehanna AS; Insulin and Oral Antidiabetic Agents. American Journal of Pharmaceutical Education, 2005; 69(5): 1-11.
16. Kinesh VP, Neelam DP, Punit BP, Bhavesh SB, Pragna KS; Novel Approches for Oral Delivery of Insulin and Current Statuus Of Oral Insulin Products. International Journal of Pharmaceutical Sciences And Nanotechnology, 2010; 3(3): 1057-1064.
17. Davis T, Edelman SV; Insulin Therapy in Type 2 Diabetes. The Medical Clinics of North America, 2004; 88: 865–895.
18. Kaur J, Badyal DK; Newer Insulins. JK Science Journal of Medical Education & Research, 2008; 10(3): 107-111.
19. Zanchia A, Lehmannb R, Philippec J; Antidiabetic drugs and kidney disease. The European Journal of Medical Sciences, 2012; 142: 1-8.
20. Patidar D, Dwivedi SK; Diabetes Mellitus: An Update. International Journal of Pharmaceutical & Research sciences, 2012; 1(4): 259-276.
21. Wadkar KA, Magdum CS, Patil SS, Naikwade NS; Anti-diabetic potential and Indian medicinal plants. Journal of Herbal Medicine and Toxicology, 2008; 2 (1): 45-50.
22. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet, 1998; 352: 837-853.
23. Cheng AYY, Fantus IG; Oral antihyperglycemic therapy for type 2 diabetes Mellitus. Canadian medical association journal, 2005; 172 (2): 213-226.

24. Davis S; Oral hypoglycaemic drugs for the, treatment of type 2 diabetes mellitus. South African Pharmaceutical Journal, 2012; 79(3): 22-24.
25. Keidan B, Hsia J, Katz R; Plasma Lipids and Antidiabetic Agents A Brief Overview. The British Journal of Diabetes and Vascular Disease, 2002; 2(1): 40–43.
26. Joshi P, Joshi S; Oral hypoglycaemic drugs and newer agents use in Type 2 diabetes mellitus. South African Family Practice, 2009; 51(1): 10-16.
27. Ibrahim R; Diabetes mellitus type II: review of oral treatment options. International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(1): 21-30.
28. Feig DS, Briggs GG, Koren G; Oral Antidiabetic Agents in Pregnancy and Lactation A Paradigm Shift?. Annals of Pharmacotherapy, 2007; 41(7): 1174-1180.
29. Maurya R, Gupta CM; Traditional herbs for modern medicine. Tech monitor, 2006; 23-36.
30. Joseph, Jini D; Insight into the Hypoglycaemic Effect of Traditional Indian Herbs used in the Treatment of Diabetes. Research Journal of Medicinal Plant, 2011; 5(4): 352-376.
31. Pathak K, Das RJ; Herbal Medicine- A Rational Approach in Health Care System. International Journal of Herbal Medicine, 2013; 1(3): 86-89.
32. Yadav R, Kaushik R, Gupta D; The health benefits of *Trigonellafoenum graecum*: a review. International Journal of Engineering Research and Applications, 1(1): 032-035.
33. Maurya U, Srivastava S; Traditional Indian Herbal Medicine Used As Antipyretic, Antiulcer, Anti-Diabetic And Anticancer: A Review, International Journal Of Research In Pharmacy And Chemistry, 2011; 1(4): 1152-1159.
34. Charles SV; Fenugreek: a natural, prototype oral hypoglycaemic agent used in Malta. Malta Medical Journal, 2009; 21(02): 42-44.
35. Jonathan K; Herbs that Lower Blood Sugar. The Online Journal of the American Association of Integrative Medicine, 2006; 1-5.
36. Conclusion on the Peer Review of the Pesticide Risk Assessment of the Active Substance Fenugreek Seed Powder (Fen 560), European Food Safety Authority; Conclusion on Pesticide Peer Review. European Food Safety Authority Journal, 2010; 8(3): 1-50.
37. Villupanoor AP, Bhageerathy C, John TZ, Leela NK, Shafeekh KM; Chemistry of Spices. CABI publishers, British Library, London, UK, 2008: 78, 242-259.
38. Gauttam V, Kalia AN; High Performance Thin Layer Chromatography Method for Simultaneous Estimation of Vicine, Trigonelline and Withaferin-A in A Polyherbal Antidiabetic Formulation. International Journal of Pharmacy and Pharmaceutical Sciences, 2013; 5(2): 367-371.
39. Saravanamuttu S, Sudarsanam D; Antidiabetic Plants and Their Active Ingredients: A Review. International Journal of Pharmaceutical Sciences and Research, 2012; 3(10): 3639-3650.
40. Behera TK, Behera S, Bharathi LK, John KJ, Simon PW, Staub JE; Bitter Gourd: Botany, Horticulture, Breeding. Horticultural Reviews, 2010; 37: 101-141.
41. Haque ME, Alam MB, Hossain MS; The Efficacy of Cucurbitane Type Triterpenoids, Glycosides And Phenolic Compounds Isolated From *Momordica charantia*: A Review. International Journal of Pharmaceutical Sciences and Research, 2011; Vol. 2(5): 1135-1146.
42. Chang CLT, Lin Y, Bartolome AP, Chen YC, Chiu SC, Yang WC; Herbal Therapies for Type 2 Diabetes Mellitus: Chemistry, Biology, and Potential Application of Selected Plants and Compounds. Evidence-Based Complementary and Alternative Medicine, 2013; 1-33.
43. Rao GS, Khan Md; Anti-Diabetic Plant Profiles:- A Review. International Journal of Innovative Pharmaceutical Sciences and Research, 2013; 1(3): 322-333.
44. Radhika S, Senthilkumar R, Arumugam P; A review on ethnic florae with anti hyperglycemic efficacy. International Journal of Herbal Medicine, 2013; 1 (4): 55-62.
45. Gupta R, Kumar GB, Johri S, Saxena AM; An Overview Of Indian Novel Traditional Medicinal Plants With Antidiabetic Potentials. African Journal Traditional, Complementary and Alternative Medicines, 2008; 5 (1): 1–17.
46. Pterostilbene Monograph. Alternative Medicine Review, 15(2): 159-163.
47. Waghmare AS, Pawar RG, Grampurohit ND, Gadhave MV, Gaikwad DD; *Pterocarpus marsupium* Roxb – Phytochemistry and Pharmacological Activity. International Journal of Institutional Pharmacy and Life Sciences, 2012; 2(2): 400-411.
48. Triveni KB, Lakshmi VK, Shashidhara S, Anitha S; *Gymnema sylvestre*: A Comprehensive Review. Pharma Science Monitor an International Journal of Pharmaceutical Sciences, 2012; 3(4): 2402-2420.
49. Matheka DM, Alkizim FO; Complementary and Alternative Medicine for type 2 diabetes mellitus: Role of medicinal herbs. Journal of Diabetes and Endocrinology, 2012; 3(4), 44-56.
50. Tahira A, Ziaul H; *Gymnema sylvestre* Plant Used by Peoples of Vidisha District for The Treatment of Diabetes. International Journal of Engineering Science Invention, 2013; 2(6): 98-102
51. Devprakash, Srinivasan KK, Subburaju T, Suhas G, singh S; *Tinospora cordifolia*: A Review on Its Ethnobotany, Phytochemical & Pharmacological Profile. Asian Journal of Biochemical and

Pharmaceutical Research, 2011; 1(4) 2011: 291-302.
52. Meena AK, Bansal P, Kumar S; Plants-herbal wealth as a potential source of Ayurvedic drugs. Asian Journal of Traditional Medicines, 2009; 4 (4): 152-170.
53. Handa SS, Mundkinajeddu D, Mangal AK; Indian Herbal Pharmacopoeia. Volume-1, A Joint Publication Of Regional Research Laboratory-Jammu & Indian Drug Manufacturers Association, Mumbai, 1998: 156-164.
54. Tahseen MA, Mishra G; Ethnobotany and Diuretic Activity of Some Selected Indian Medicinal Plants: A Scientific Review. The Pharma Innovation – Journal, 2013; 2(3): 109-121.
55. Knoss W, Reuter B, Zapp J; Biosynthesis of the Labdane Diterpene Marrubiin in Marrubium Vulgare via A Non-Mevalonate Pathway. Biochemical Journal, 1997; 326: 449-454.
56. Singh K, Verma B; Role of Ayurvedic Herbs on Madhumeha (Diabetes Mellitus). International Journal of Ayurvedic & Herbal Medicine, 2013; 3(2): 1136-1144.
57. Mishra SB, RaoCh.V, Ojha SK , Vijayakumar M, Verma A; An Analytical Review Of Plants For Anti Diabetic Activity With Their Phytoconstituent& Mechanism Of Action. International Journal of Pharmaceutical Sciences and Research, 2010; 1(1): 29-46.
58. Semwal A, Kumar R, Singh R; Nature's Aphrodisiacs - A Review of Current Scientific Literature. International Journal of Recent Advances in Pharmaceutical Research, 2013; 3(2): 1-20.
59. Goyal PK; Phytochemical and Pharmacological Properties of the Genus Grewia- A Review. International Journal Of Pharmacy And Pharmaceutical Sciences, 2012; 4(4): 72-78.
60. Zia-Ul-Haq M, Stanković MS, Rizwan K, De Feo V; Grewiaasiatica L., a Food Plant with Multiple Uses. Molecules, 2013; 18: 2663-2682.
61. Kumar M, Alok S, Jain SK, Verma A, Alok M, Sabharwal M; Morphology, pharmacological activity, pharmaceutical preparation, doses and side effect of *Coccinia indica* (Wight &Arn.): An overview. Journal of Coastal Life Medicine, 2013; 1(4): 330-336.
62. Ocvirk S, Kistler M, Khan S, Talukder SH, Hauner H; Traditional Medicinal Plants Used For The Treatment Of Diabetes In Rural And Urban Areas Of Dhaka, Bangladesh – An Ethnobotanical Survey. Journal of Ethnobiology and Ethnomedicine, 2013; 9(43): 1-8.
63. Sharma R, Arya V; A Review on Fruits Having Anti-Diabetic Potential. Journal of Chemical and Pharmaceutical Research, 2011; 3(2): 204-212.
64. Parmar N, Rawat M, Kumar JV; *Camellia sinensis* (Green Tea): A Review. Global Journal of Pharmacology, 2012; 6(2): 52-59.
65. Behera B, Yadav D; Current Researches on Plants Having Antidiabetic Potential-An Overview. Research and Reviews: Journal of Botanical Sciences, 2013; 2(2): 4-17.
66. Patel DK, Prasad SK, Kumar R, Hemalatha S; An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific Journal of Tropical Biomedicine, 2012; 2(4): 320-330.
67. Sutherland BA, Rosanna MAR, Appleton I; Mechanisms of action of green tea catechins, with a focus on ischemia-induced neurodegeneration. Journal of Nutritional Biochemistry, 2006; 17: 291– 306.
68. Swargiary A, Boro H, Brahma BK, Seydur R; Ethno-Botanical Study of Anti-Diabetic Medicinal Plants used by the Local People of Kokrajhar District of Bodoland Territorial Council, India. Journal of Medicinal Plants Studies, 2013; 1(5): 51-58.
69. Kumar PS, Mishra D, Ghosh G, Panda CS; Biological Action and Medicinal Properties Of Various Constituent Of *Azadirachta indica* (Meliaceae)" An Overview. Scholars Research Library Annals Of Biological Research, 2010; 1(3): 24-34.
70. Chawla R, Thakur P, Chowdhry A, Jaiswal S, Sharma A, Goel R *et al.*; Evidence based herbal drug standardization approach in coping with challenges of holistic management of diabetes: a dreadful lifestyle disorder of 21st century. Journal of Diabetes & Metabolic Disorders, 2013; 12(35): 1-16.
71. Uma MM, Sudarsanam D; Phytomedicine for Diabetes mellitus: An overview. Research in Pharmacy, 2011; 1(4): 28-37.
72. Dixit PK, Mittal S; A Comprehensive Review on Anti-Diabetic Agents of Herbal Origin. International Journal of Pharmacy And Pharmaceutical Sciences, 2013; 5(2): 29-32.
73. Noor A, Bansal VS, Vijayalakshmi MA; Current Update on Anti-Diabetic Biomolecules From Key Traditional Indian Medicinal Plants. Current Science, 2013; 104(6): 721-727.
74. Sri KT, Ushasri S, Shalemurani M, Nirmala PY, Anjaneyulu P; Biophytumsensitivum Dc – An Overview. International Journal of Pharmacological Screening Methods, 2013; 3(2): 69-79.
75. Bnouham M, Ziyyat A, Mekhfi H, Tahri A, Legssyer A; Medicinal plants with potential antidiabetic activity - A review of ten years of herbal medicine research (1990-2000). International Journal Diabetes & Metabolism, 2006; 14: 1-25.
76. Varghese KJ, Anila J, Nagalekshmi R, Resiya S, Sonu J; Dasapushpam: The Traditional Uses and the Therapeutic Potential of Ten Sacred Plants of Kerala State in India. International Journal of

Pharmaceutical Sciences and Research, 2010; 1(10): 50-59.
77. World Health Organization, Spain, WHO monographs on selected medicinal plants. 2009; 4: 269.
78. Labu ZK, Jahan K, Rahman F; Current Official Status of Traditional Medicine and Their Used As In Chronic Diseases: Bangladesh. Journal of Drug Discovery and Therapeutics, 2013; 1(3): 93-104.
79. Tripathi AK, Bhoyar PK, Baheti JR, Biyani DM, Khalique M, Kothmire MS *et al.*; Herbal Antidiabetics: A Review. International Journal of Research in Pharmaceutical Sciences, 2011; 2(1): 30-37.
80. Aggarwal BB, Surh YJ, Shishodia S; The molecular targets and therapeutic uses of curcumin in health and disease. Advances in experimental medicine and biology, 2007; 595: 489.
81. Hao D, Xiaojie Gu, Xiao P, Lijia Xu, Peng Y; Recent advances in the chemical and biological studies of Aconitum pharmaceutical resources. Journal of Chinese Pharmaceutical Sciences, 2013; 22(3): 209–221.
82. Shyaula SL; Phytochemicals, Traditional Uses and Processing of Aconitum Species in Nepal. Nepal Journal of Science and Technology, 2011; 12: 171-178.
83. Akbari M, Rasouli H, Bahdor T; Physiological and pharmaceutical effect of fenugreek: a review. IOSR Journal of Pharmacy, 2012; 2(4): 49-53.
84. Başar A; Bitter Melon (*Momordica charantia*) and the Effects of Diabetes Disease. Journal Of Agriculture Faculty Of Uldag University, 2012; 26(2): 65-69.
85. Panara JR; A Short Review on Antidiabetic Activity of Bitter Gourd. International Journal Of pharmaceutical Research and Bio-Science, 2013; 2(4): 333-336.
86. Saxena A, Naval KV; Role of Selected Indian Plants in Management of Type 2 Diabetes: A Review. The Journal of Alternative and Complementary Medicine, 2004; 10(2): 369–378.
87. Saneja A, Sharma C, Aneja KR, Pahwa R; *Gymnema sylvestre* (Gurmar): A Review. Scholars Research Library, Der Pharmacia Lettre, 2010; 2(1): 275-284.
88. Patel P, Harde P, Pillai J, Darji N, Patel B; Antidiabetic Herbal Drugs A Review. Pharmacophore: An International Research Journal, 2012; 3(1): 18-29.
89. Rawat M, Parmar N; Medicinal Plants with Antidiabetic Potential - A Review. American-Eurasian Journal of Agricultural & Environmental Sciences, 2013; 13 (1): 81-94.
90. Patil R, Patil R, Ahirwar B, Ahirwar D; Current status of Indian medicinal plants with antidiabetic potential: a review. Asian Pacific Journal of Tropical Biomedicine, 2011; S291-S298.
91. Boudjelal A, Henchiri C , Siracusa L, Sari M, Ruberto G; Compositional analysis and in vivo anti-diabetic activity of wild Algerian *Marrubium vulgare* L. infusion. Fitoterapia, 2012; 83: 286–292.
92. Azzi R, Djaziri R, Lahfa F, Sekkal FZ, Benmehdi H, Belkacem N; Ethnopharmacological survey of medicinal plants used in the traditional treatment of diabetes mellitus in the North Western and South Western Algeria. Journal of Medicinal Plants Research, 2012; 6(10): 2041-2050.
93. Duke JA, Bogenschutz-Godwin MJ, Ducellier J, Duke PAK; Handbook of Medicinal Herbs. 2nd edition, CRC Press, Washington, D.C, 2002: 328-329.
94. Wadkar KA, Magdum CS, Patil SS, Naikwade NS; Anti-Diabetic Potential and Indian Medicinal Plants. Journal of Herbal Medicine and Toxicology, 2008; 2 (1): 45-50.
95. Khan SM, Rehman FU, Khan MA, Mushtaq A, Muhammad Z, Said G; Medicinal Folk Recipes Used As Traditional Phytotherapies In District Dera Ismail Khan, Kpk, Pakistan. Pakistan Journal of Botany, 2011; 43(3): 1453-1462.
96. Pandey M, Vijayakumar; Nutraceutical Supplementation for Diabetes: A Review. International Journal of Pharmacy and Pharmaceutical Sciences, 2011; 3(4): 33-40.
97. Amreen F, Agrawal P, Singh PP; Herbal option for diabetes: an overview. Asian Pacific Journal of Tropical Disease, 2012; 2(1): S536-S544.
98. Malvi R, Jain S, Khatri S, Patel A, Mishra S; A Review on Antidiabetic Medicinal Plants and Marketed Herbal Formulations. International Journal of Pharmaceutical & Biological Archives, 2011; 2(5): 1344-1355.
99. Ogle N; Green tea *Camellia sinensis*. Australian Journal of Medical Herbalism, 2009; 21(2): 44-48.
100. Donga JJ, Surani VS, Sailor GU, Chauhan SP, Seth AK; A Systematic Review on Natural Medicine Used For Therapy of Diabetes Mellitus of Some Indian Medicinal Plants. Pharma Science Monitor an International Journal of Pharmaceutical Sciences, 2011; 2(1): 36-72.
101. Pradhan P; Antihyperglycemic Effect of Various Medicinal Plants of Sikkim Himalayas- A Review. International Journal of Research in Phytochemistry and Pharmacology, 2011; 1(3): 124-130.
102. Kavishankar GB, Lakshmidevi N, Murthy SM, Prakash HS, Niranjana SR; Diabetes and medicinal plants-A review. International Journal of Pharmaceutical and Biomedical Sciences, 2011; 2(3): 65-80.
103. Nevius E, Srivastava PK, Basu S; Oral ingestion of Capsaicin, the pungent component of chili pepper, enhances a discreet population of macrophages and confers protection from autoimmune diabetes. Mucosal Immunol., 2012; 5(1): 76-86.

104. Ojieh EA, Adegor CE, Ewhre OL; Regulated Effects of *Capsicum frutescens* Supplemented Diet (C.F.S.D) On Fasting Blood Glucose Level, Biochemical Parameters and Body Weight in Alloxan Induced Diabetic Wistar Rats. British Journal of Pharmaceutical Research, 2013; 3(3): 496-507.