IJPSR (2010), Issue 1, Vol. 1 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received 14 December, 2009; received in revised form 23 December, 2009; accepted 29 December, 2009

AN ANALYTICAL REVIEW OF PLANTS FOR ANTI DIABETIC ACTIVITY WITH THEIR PHYTOCONSTITUENT & MECHANISM OF ACTION

S. B. Mishra *[1], CH. V. Rao [2], S. K. Ojha [2], M. Vijayakumar [2], A. Verma [3] and S. Alok [4]

Department of Pharmacognosy, Roorkee College of Pharmacy *[1], Roorkee (Uttarakhand), India

Ethnopharmacology Division, National Botanical Research Institute [2], Lucknow (U.P.), India

Department of Pharmaceutical Sciences, College of Health Sciences [3], AAIDU, Allahabad (U.P.), India

Institute of Pharmacy [4], Bundelkhand University, Jhansi (U.P.), India

Keywords:

Diabetes,

Hypoglycemic,

Mechanism of action,

Phytoconstituents

***Correspondence for Author**

Shanti Bhushan Mishra

Lecturer

Roorkee College of Pharmacy

9th milestone, Roorkee-Dehradun highway, Roorkee, Uttarakhand, India

Email: shantipharma15@gmail.com

Ph: +919452060202

ABSTRACT:

Diabetes and its different types is an age old disease for clinicians since centuries. Many aspects of Diabetes needs to be explored with respect to physiological actions of insulin and the various clinical features of this disease such as tissue complication , since this is life style disease , so proper treatment in relation to diet and anti diabetic agents is emphasized In fact, herbal treatment for diabetes is not new. Plants and plant extracts were used to combat the disease as early as 1550 B.C., with as many as 400 "prescribed" before the development earlier this century of effective medications to control diabetes. In this paper an attempt has been made to give an overview of certain Indian plants with their phytoconstituents and mechanism of action which have been studied for their antidiabetic activity.

INTRODUCTION: Herbal medicine is the oldest form of healthcare known to mankind. Herbs had been used by all cultures throughout history. It was an

integral part of the development of modern civilization. Primitive man observed and appreciated the great diversity of plants available to him. The plants provided food, clothing, shelter, and medicine. Much of the medicinal use of plants seems to have been developed through observations of wild animals, and by trial and error. As time passes off, each tribe added the medicinal power of herbs in their area to its knowledge base. They methodically collected information on herbs and developed well-defined herbal pharmacopoeias. Indeed, well into the 20th century much of the pharmacopoeia of scientific medicine was derived from the herbal lore of native peoples. Many drugs commonly used today are of herbal origin. Indeed, about 25 percent of the prescription drugs dispensed in the United States contain at least one active ingredient derived from plant material. Some are made from plant extracts; others are synthesized to mimic a natural plant compound.

The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine for some aspect of primary health care. Herbal medicine is a major component in all indigenous peoples' traditional medicine and a common element in Ayurvedic, homeopathic, naturopathic, traditional oriental, and Native American Indian medicine. WHO notes that of 119 plant-derived pharmaceutical medicines, about 74 percent are used in modern medicine in ways that correlated directly with their traditional uses as plant medicines by native cultures. Major pharmaceutical companies are currently conducting extensive research on plant materials gathered from the rain forests and other places for their potential medicinal value. This article has an objective to collect scattered scientific information on the herbs of hypoglycemic activity and to provide present status of plants on which antidiabetic activity has been done,

MATERIAL AND METHOD: The information on the plants having antidiabetic activity was collected from different web sites Journal and books available. These were further studied specifically to analyze the phyto-constituent and different mechanism which can alter the blood glucose metabolism. Based upon the hypothesis plants belong to specific family may have similar type of chemical composition and similar type of mechanism of action. The screening has been done on 83 Indian journals and 13 international journals containing 99 plants 45 families 7 basic phytoconstituent and 8 mechanism of action. After compilation of data the method has been opted from generalization to specification. Table 1 contains List of plants having Antidiabetic activity with their chemical constituents and mode of action; where as Constituent Vs Mode of Activity has been described in Table 2. To understand the mechanism of action fig-1 has been provided along with figures of phytoconstituent in fig-2.

TABLE-1 LIST OF PLANTS HAVING ANTI-DIABETIC ACTIVITY

Botanical Name	Local Name*	Family	Parts used	Mechanism of action	Chemical Constituents
Abies pindrow Royle[1]	Morinda / Rodha	Pinaceae	Entire plant	Insulin secretagogue activity	Volatile oil
***Abroma augusta* Linn**[2]	Devil's cotton	Sterculiaceae	Roots & Leaves	Lowering blood sugar	Fixed oil, Alkaloid
***Acacia arabica* willd**[3]	Babool	Leguminosae	Seed	Initiate release of insulin	arabin
***Achyranthus aspera L*.**[4]	chirchiri	Amaranthaceae	Entire plant	Decrease blood sugar	
***Agrimony eupatoria* L.**[5]		Rosaceae	Leaves	Insulin releasing & insulin like activity	
***Ajauga iva* wall.ex.Benth**[6]	Bugle weed	Labiatae	Entire plant	Decrease plasma glucose level	
***Allium sativum* Linn.**[7]	Lehsun	Liliaceae	Roots	Antihyperglycemic and antinociceptive effect	v.oil, Allin, Allicin
***Allium cepa* Linn.**[8]	Pyaz	Liliaceae	Bulb	Stimulating effects on glucose utilization and antioxidant enzyme	Protein, carbohydrate, vit. A,B,C, Allyl propyldisulphide
***Aloe vera* Tourn. ex. Linn.**[9, 10, 11]	Gheequar	Liliaceae	Entire plant		Aloin glycoside
Aloe barbadensis Miller[12]	Gheequar	Liliaceae	Leaves	Stimulating synthesis and/or release of insulin	Barbaloin, isobarbaloin, resin
***Amaranthus spinosus* Linn.**[13]	Kataili chaulai	Amaranthaceae	Stem		
***Anacardium occidentale* Linn**[14]	Kaju	Anacardiaceae	Entire plant		Flavonols, terpenoid, caumarin, phenolic compound,essential oil
Andrographis paniculata Nees [15, 16]	Kalmegh	Acanthaceae	Entire plant	Increase glucose metabolism	Diterpenoid lactone andrographoloid
Annona squamosa[17]	Sharifa	Annonaceae	Leaves	Hypoglycemic and antihyperglycemic activities of ethanolic leaf-extract, Increased plasma insulin level	Acetogenins- squamosin B, squamosamide,reticulatain -2,isosquamosin
Artemisia pallens Wall[18]	Davana	Compositae	Aerial parts	Hypoglycemic, increases peripheral glucose utilization or inhibits glucose reabsorption	Essential oil, davanone
Averrhoa bilimbi[19, 20]	Bilimbi	Oxalidaceae	Leaves	increase serum insulin level	
***Azadirachta indica* A.juss.**[21]	Neem	Meliaceae	Leaves	Glycogenolytic effect due to epinephrine action was blocked	Nimbidin, Nimbin, Nimbidol, Nimbosterol
***Beta vulgaris* Linn**[22]	chukandar	Chenopodiaceae	Leaves	Reduce blood glucose level by regeneration of β cells	
Bidens pilosa[23]		compositae	Aerial parts		Polyacetylenic glucoside
Bixa orellana L.[24]	Annotta	Bixaceae	Entire plant	Increase plasma insulin conc. & increase insulin binding on insulin receptor	Oleo-resin
Boerhaavia diffusa L. [25]	Punarnava	Nyctaginaceae	Leaves & Entire plant	Increase in hexokinase activity,decrease in glucose-6-phosphatase and fructose bis-phosphatase activity, increase plasma insulin level	Alkaloid punarnavaine, punarnavoside
Brassica juncea	Rai	Cruciferae	Leaves	Food adjuvants for diabetic	Isothiocyanate glycoside

L. [26]			& seed	patients	singrin, protein, fixed oil
***Caesalpinia bonducella* Flem.** [27]	Karanju	Leguminose	Seed kernels	Free radicle scavenging	Fatty oil
Camellia sinensis [28]	Green tea (chai)	Theaceae	Leaves	Increase insulin secretion	Polyphenolic constituents (EGCG)
***Capparis deciduas* Edgew** [29]	Karer	Capparidaceae	Powder	Hypoglycemic,antioxidant, hypolipidaemic	
***Capsicum frutescens* Linn.** [30]	Mirch	Solanaceae	Entire plant	Increase insulin secretion & reduction of insulin binding on the insulin receptor	Capsaicin,pritein
***Carum carvi* Linn.** [31]	Shia jira	Umbelliferae	Fruits		V.oil, resin, carvone, fixed oil
Cassia alata [32]	Ringworm senna	Caesalpiniaceae	Leaves		
Cassia auriculata [33]	Tarwar	Caesalpiniaceae	Flower	Increase utilization of glucose through increase glycolysis	
***Catharanthus roseus* G.Don** [34]	Sadabahar	Apocynaceae	Leaves, twig & flower	Increase metabolisation of glucose	Indole alkaloid, vincristine vinblastin
Cinnamomum zeylanicum Nees [25]	Dalchini	Lauraceae	Bark	Elevation in plasma insulin	V.oil, tannin, mannitol, ca.oxalate,
***Clausena anisata* Burm.f.** [36]		Rutaceae	Roots	Stimulate secretion of insulin	
***Coriandrum sativum* Linn.** [37]	Dhania	Umbelliferae	Seed		V.oil, fixed oil, protein
Coscinium fenestratum Calebr [38]	Jharhaldi	Menispermaceae	Stem	Increase enzymatic antioxidants	Barberine ,glycoside,saponin
Croton cajucara Benth [39]	Jamalgota	Euphorbiaceae	Bark		Fixed oil
***Cryptolepis sanguinolenta* R.** [40]	Anantmul	Asclepidaceae	Entire plant	Increase glucose uptake by 3T3-L1 cells	Cryptolepine
***Eclipta alba* Linn.** [41]	Bhringraj	Compositae	Leaves	Decrease activity of glucose-6-phosphatase& fructose-1-6,bisphasphatase	Ecliptin alkaloid
Embellica officinalis Gaertn. [42]	Amla	Euphorbiaceae	Fruits	Reduce 5-hydroxymethylfurfural,creatinine albumin level	Vit.C, tannin
Enicostemma littorale Blume [43, 44, 45]	Chhota chirayata	Gentianaceae	Entire plant	Decrease glycosylated Hb & glucose 6 phosphatase	Swertiamarine glycoside
***Eugenia jambolana* Lam.** [46, 47, 48]	Jamun	Myrtaceae	Seed, fruit , leaves, kernel	Lowers plasma glucose level	
***Eucalyptus globulus* Labill.** [49]	Eucalyptus	Myrtaceae	Leaves	Increase insulin secretion from clonal pancreatic beta line (BRIN-BD 11)	Essential oil , cineol
Euphrasia officinale [50]	Eyebright	Scrophulariaceae	Leaves		
***Ficus religiosa* Linn.** [51]	Peepal	Moraceae	Entire plant	Initiating release of insulin	Tannin
***Ficus bengalensis* Linn.** [52]	Bargad	Moraceae	Bark	Rising serum insulin	Tannin
Ficus carica [53]	Anjir	Moraceae	Leaves		

***Gymnema montanum* hook f.** [54]		Asclepiadaceae	Leaves	Antioxidant& antiperoxidative	
***Gymnema sylvestre* R.** [55, 56, 57, 58,	Gudmar	Asclepiadaceae	Leaves	Lowers plasma glucose level	Gymnemic acid, quercital
***Gentiana olivier*Griseb.** [59]		Gentianaceae	Flowers	Lowers plasma glucose level	Iso-orientin C-glycoside
***Glycerrhiza glabra* Linn.**[60]	Mulethi	Leguminosae	Root	Lowers plasma glucose level	Triterpenoid,saponin, glycerrhizin
Gynura procumbens [61]		Compositae	Leaves	Lowers plasma glucose level	
***Hibiscus rosa sinensis* Linn.**[62]	Gudhal (china rose)	Malvaceae	Entire plant	Stimulate insulin secretion from beta cells	Vit.B,C, Fat,
***Helicteres isora* Linn.**[63]	Indian screw tree	Sterculiaceae	Root	Decrease plasma triglyceride level & insulin sensitizing activity	Saponin ,tannin, lignin
Hordeum vulgare [64]	Jau	Graminaeae	Barley seed		
Hovenia dulcis Thunb[65]	Sicka	Rhamnaceae	Entire plant		flavonoids
***Ipomoea aquatica* Forsk.**[66]	Kalmisag	Convolvulaceae	Leaves	Reduce fasting blood sugar level & serum glucose level	Carotene
***Ipomoea batata* Linn.**[67]	Shakarkand	Convolvulaceae	Tubers	Reduce insulin resistance & blood glucose level	
***Juniperus communis* Linn.**[68]	Hauber	Pinaceae	Fruits	Increase peripheral glucose consumption & induce insulin secretion	
***Lupinus albus* Linn.**[69]	Turmas	Fabaceae	Seed	Lower serum glucose level	Alkaloid , fatty oil, asparagines
***Luffa aegyptiaca* Mill.**[70]	Ghiatori	Cucurbitaceae	Seed	Lactigogue activity	Fatty oil
Leucas lavandulaefolia Rees[71]	Kumbha	Labiatae	Entire plant	Reduce blood glucose level	
Lagerstronemia speciosa[72]	Jarul	Lythraceae	Leaves		
Lepidium sativum[73]	Halim, hurf	Cruciferae	Seeds		
***Mangifera indica* Linn.**[74]	Mango	Anacardiaceae	Leaves	Reduction of intestinal absorption of glucose	Mangiferin
Myrtus communis L.[75]	Vilayati mendhi	Myrtaceae	Leaves	Lower blood glucose level	V.oil mirtii oleum
Memecylon umbellatum Burm[76]	Anjani	Melastomataceae	Leaves	Lower serum glucose	
Momordica cymbalania Fenzl ex naud in [77]	kadavanchi	Cucurbitaceae	Fruit powder	Reduce blood glucose level	
Mucuna pruriens L.[78]	Kiwach	Leguminosae	Seed	Reduce blood glucose level	
***Musa sapientum* Linn.**[79]	Banana	Musaceae	Flower	Reduce blood glucose &glycosylated Hb	
***Momordica charantia* Linn.** [80]	Karela	Cucurbitaceae	Fruit	Reduce blood glucose level	Momordicine alkaloid, ascorbic acid
Morus indica L. [81]	Shehtoot	Moraceae	Leaves	Increase glucose uptake	
Murraya koeingii (L)spreng[82]	Curry leaf	Rutaceae	Leaves	Increase glycogenesis , decrease glycogenolysis & gluconeogenesis	

***Nelumbo nucifera* Gaertn.** [82]	Lotus	Nymphaeaceae	Rhizome	Reduce blood sugar level	Nuciferin, nornuciferin
***Ocimum sanctum* Linn.** [84]	Tulsi	Labiatae	Leaves	Lowering blood sugar level	V.oil, phenol, aldehyde, fixed oil, alkaloid, tannin, ascorbic acid
***Olea europia* Linn.**[85]	Olive	Oleaceae	Leaves	Potentiation of glucose , induced insulin released , & increase peripheral uptake of glucose	Oleuropeoside
Opuntia Ficus indica Mill[86]	Indian fig	Cactaceae	Stem		
***Pandanus odorus* Linn.**[87]	Kevra	Pandanaceae	Root	Decrease plasma glucose level	Essential oil
***Panax ginseng* Mey.**[88]	Pannag	Araliaceae	Root & entire plant	Lowering blood sugar level	Glycans, panaxans I,J,K & L
Punica granatum Linn[89]	Anar	Punicaceae	Seed	Reduce blood sugar level	Vit.C, protein, tannin, gallic acid, pelletierine
Picrorrhiza kurroa Royle ex. Benth[90]	Katuka	Scrophulariaceae	Entire plant	Decrease serum glucose	Picrorrhizin, kutkin
Phyllanthus amarus [91]	Bhui amla	Euphorbiaceae	Entire plant	Decrease blood glucose level	Alkaloids
Phaseolus vulgaris [92, 120]	Lobia	Papilionaceae	Pod, seed, whole plant	Hypoglycemic, hypolipidemic, inhibit alpha amylase activity,antioxidant.	
Salacia oblonga [93]	Chundan	Celastraceae	Root	inhibition of alpha glucosidase activity	
***Salacia reticulata* Wight.**[94]	Anukudu chettu	Celastraceae	Stem & root	inhibition of alpha glucosidase activity	
***Swertia chirayata* Roxb.ex.Flem**[95]	Chirayata	Gentianaceae	Entire plant	Stimulates insulin release from islets	Zanthone mangiferin, gentianine, swerchirin
Syzygium cumini Linn[96]	Jamun	Myrtaceae	Seed	Decrease blood glucose level	
***Scoparia dulcis* Linn.** [97]	Mithi patti	Scrophulariaceae	Leaves	Decrease glycosylated Hb & Inc. total Hb, Insulin-secretagogue activity	
Trigonella foenum graceum[98]	Methi	Leguminosae	Seed	Decrease blood glucose concentration	Protein, fat, V.oil, fixed oil, carbohydrate
***Tribulus terrestris* Linn.**[99]	Gokhru	Zygophyllaceae	Saponin	Decrease serum glucose	Harmine
***Tinospora crispa* Linn.**[100]	Giloe	Menispermaceae	Stem	Anti-hyperglycemic, stimulates insulin release from islets	
***Tinospora cardifolia* Willd.**[101]	Giloe	Menispermaceae	Root	Decrease blood glucose & brain lipid	Berberine, starch
***Tamarindus indica* Linn.**[102]	Imli	Caesalpimiaceae	Seed		
***Teramnus labialis* (Roxb) Benth**[103]	Mashoni	Fabaceae	Aerial parts		Caumarin -fraxidin
***Urtifca dioica* Linn.**[104]	Bichhu booti	Urticaceae	Leaves	Increase insulin secretion	Fatty oil

***Viscum album* Linn.**[105]	Vadank	Loranthaceae	Entire plant	Alpha glucosidase inhibitor	
Vinca rosea [106]	Sadabahar	Apocynaceae	Leaves	Beta cell rejuvenation, regeneration, & stimulation	Vincristine , vinblastine
***Withania somnifera* Dunal**[107]	Ashwagandha	Solanaceae	Root	Decrease blood sugar level	Withanine, somnine, withaferine, withanolides
Xanthium strumarium[108]	Chhota gokhru	Compositae	Fruits	Increase glucose utilization	Phenolic compound ,caffeic acid
Zingiber officinale Roscoe [109]	Adrak	Zingiberaceae	Rhizome	Increase insulin level & decrease fasting glucose level	Sesquiterpene
Zizyphus sativa Gaertn[110]	Pitni-ber	Rhamnaceae	Leaves	Dose dependent reduction in blood glucose level	Tannin

TABLE-– 2 CONSTITUENTS Vs MODE OF ACTIVITY

Constituents	Mode of Activity
Alkaloids[113]	**Inhibit alpha-glucosidase and decrease glucose transport through the intestinal epithelium**
Imidazoline compounds[114]	**Stimulates insulin secretion in a glucose-dependent manner.**
Polysaccharides[115]	**Increased the levels of serum insulin, reduce the blood glucose levels and improve tolerance of glucose**
Flavonoids[116]	**Suppressed the glucose level, reduced plasma cholesterol and triglycerides significantly and increased their hepatic glucokinase activity probably by enhancing the insulin release from pancreatic islets**
Dietary fibers[117]	**Effectively adsorbed glucose, retard glucose diffusion and inhibit the activity of alpha-amylase and may be responsible for decreasing the rate of glucose absorption and concentration of postprandial serum glucose**
Saponin, (Triterpenoid +steroidal glycosides) [118]	**Stimulates the release of insulin and blocks the formation of glucose in the bloodstream,**
Ferulic acid[119]	**Stimulatory effects on insulin secretion**

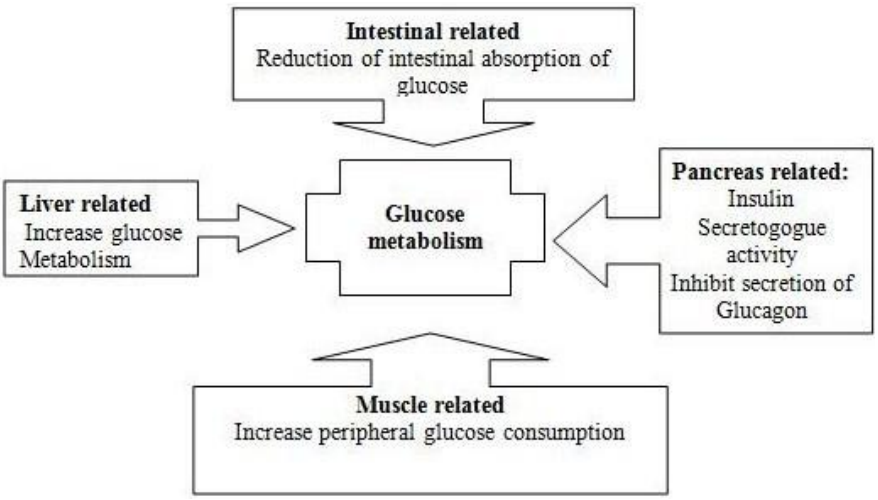
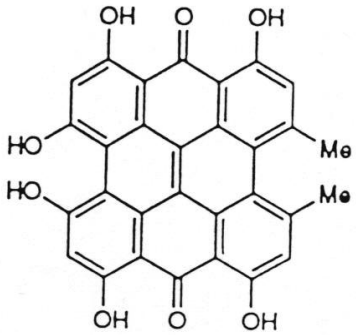
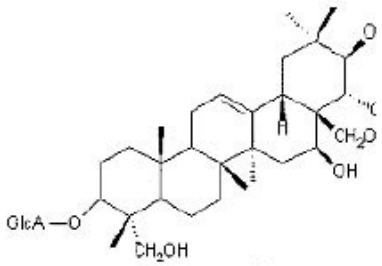


Fig 1: Explaining Mechanism of action to control Glucose metabolism

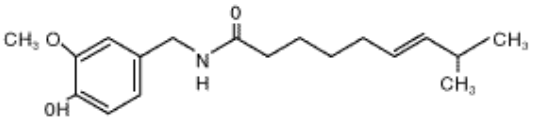


Hypericine

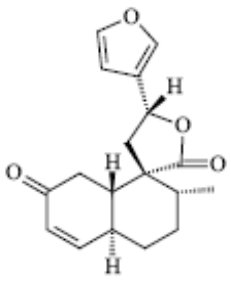


Gymnemic acid

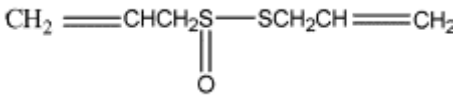
	R_1	R_2
Gymnenic acid 2:	2-Methylbutyloyl	Ac
Gymnemic acid 3:	2-Methylbutyloyl	H
Gymnemic acid 4:	Tigloyl	H



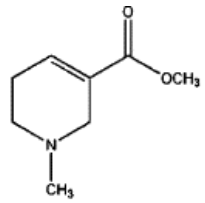
Capsaicin



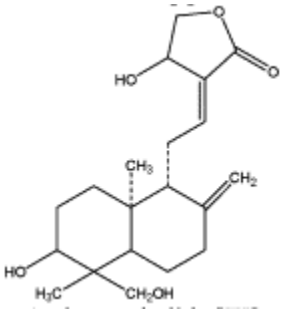
trans-dehydrocrotonin



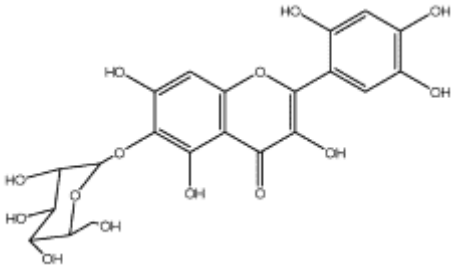
Allicin



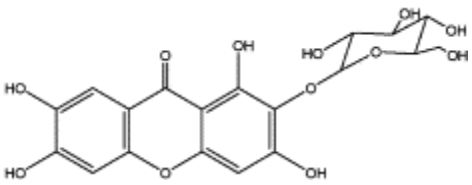
Arecoline



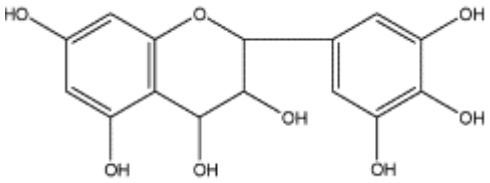
Andrographolide



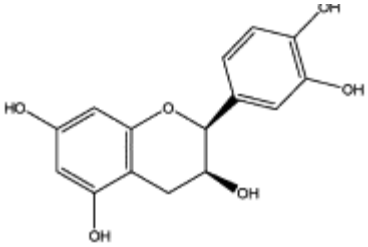
Shamimin



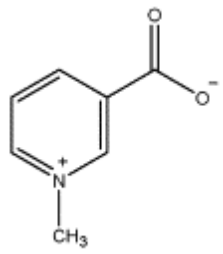
Mangiferin (IX)



Leucodelphidin **(**X)



(-) Epicatechin



Trigonellin

Fig-2: Structures of chemical constituents belong to hypoglycemic activity

CONCLUSION: Diabetes is a disorder of carbohydrate, fat and protein metabolism attributed to diminished production of insulin or mounting resistance to its action. Herbal treatments for diabetes have been used in patients with insulin-dependent and non-insulin-dependant diabetes, diabetic retinopathy, diabetic peripheral neuropathy, etc. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level.

There are several plants known for their antidiabetic activity, with different mode of action and phytoconstituents. This is an effort to streamline the phytoconstituents of specific family with specific mode of action to reduce plasma glucose. Keeping in view from the reports on their potential effectiveness against diabetes, it is assumed that the botanicals have a major role to play in the management of diabetes, which needs further exploration for necessary development of drugs and nutraceuticals from natural resources[111-11].

REFERENCES:

1. Hussain Z, Waheed A, Qureshi RA, Burdi DK, Verspohl EJ, Khan N and Hasan M: The effect of medicinal plants of Islamabad and murree region of Pakistan on insulin secretion from INS-1 cells. Phytotherapy Research 2004;18(1):73-77
2. Halim EM: Lowering of blood sugar by water extract of azadirachta indica and abroma augusta in diabetic rats. Indian Journal of Experimental Biology 2003;41(6):636-640
3. Wadood A, Wadood N and Shah SA: effect of acacia arabica and caralluma edulison blood glucose level of normal and alloxan diabetic rabbits. Journal of Pakistan Medical Association 1989;39(8):208-212
4. Mohammad S.A. and Javed I: evaluation of hypoglycemic effect of Achyranthus aspera in normal and alloxan diabetic rabbit. Journal of Ethanopharmacology 1991; 31(1):49-57
5. Gray AM and Flatt PR: Action of the traditional antidiabetic plant Agrimony eupatoria (agrimony) effect on hyperglycemia, cellular glucose metabolism, and insulin secretion. British Journal of Nutrition 1998; 80(1):109-114
6. Hilaly JE and Lyoussi B: Hypoglycemic effect of the lyophilized aqueous extract of Ajuga ivain normal and streptozotocin diabetic rats. Journal of Ethanopharmacology 2002; 80(2-3):109-113
7. Kumar GR and Reddy KP: Reduced nociceptive responces in mice with alloxan induced hyperglycemia after garlic (*allium sativum*) treatment. Indian Journal of Experimental Biology 1999; 37(7):662-666
8. Kumari K and Augusti KT: Antidiabetic and antioxidant effect of S-methyl cysteine sulfoxide isolated from onion (*Allium sepa* Linn) as compared to standard drug in alloxan diabetic rats. Indian Journal of Experimental Biology 2002; 40(9):1005-1009
9. Chithra P, Sajithlal GB and Chandrakasan G: Influence of aloe vera on the healing of dermal wounds in diabetic rats. Journal of Ethanopharmacology 1998; 59(3):195-201
10. Okyar A, Can A, Akav N, Baktir G and Sutlupinar N: Effect of Aloe vera leaves on blood glucose level

in type 1 and type 2 diabetic rat models. Phytotherapy Research 2001; 15(2): 157-161
11. Rajasekaran S, Sivaghanam K, Ravi K and Subramanian S: Hypoglycemic effect of *Aloe vera* gel on streptozotocin induced diabetes in experimental rats. Journal of Medicinal food 2004; 7(1): 61-66
12. Ajabnoor MA: Effect of aloe on blood glucose leveling normal and alloxan diabetic mice. Journal of Ethanopharmacology 1990; 28(2):215-220
13. Sangameswaran B and Jayakar B: Antidiabetic, antihyperlipidemic, & spermatogenic effect of amaranthus spinosus linn on streptozotocin induced diabetic rats. Natural Medicine (Tokyo) 2008; 62(1):79-82
14. Kamt Chouing P, Sokeng SD, Moundipa PF, Watcho P, Jatsa HB and Lontsi D: Protective role of anacardium occidetaleextract against streptozotocin induced diabetes in rats. Journal of Ethnopharmacology 1998;62 (2): 95-99
15. Zhang XF and Tan BK: Antidiabetic property of ethanolic extract of andrographis paniculata in streptozotocin diabetic rats. Acta Pharmacologia Sin 2000; 21(12):1157-1164
16. Yu BC, Hung CR, Chen WC and Cheng JT: Antihyperglycemic effect of andrographolide in streptozotocin induced diabetic rats. Planta Medica 2003; 69(12): 1075-1079
17. Annie shirwaikar, Rajendran K and Kumar DC: Oral antidiabetic activity of annona squamosa leaf alcohol extract in NIDDM rats. Pharmaceutical Biology (formerly Int.J. of Pharmacology) 2004; 42(1): 30-35
18. Subramoniam A, Pushpangadan P,Rajasekharan S and Valsaraj R: Effect of *Artemisia pallens* wall on blood glucose level in normal and alloxan induced diabetic rats. Journal of Ethnopharmacology 1996; 50(1):13-17
19. Pushparaj P, Tan CH and Tan BK: Effect of *Averrhoa bilimbi* leaf extract on blood glucose and lipids in streptozotocin diabetic rats. Journal of Ethnopharmacology *2*000;72(1-2): 69-76
20. Pushparaj P, Tan CH and Tan BK: The mechanism of hypoglycemic action of the semipurified fraction of averhoa bilimbi in streptozotocin diabetic rats. Life Science 2001; 70(5): 535-547
21. Chatopadhyay RR: Possible mechanisms of antihyperglycemic effect of Azadirachta indica leaf extract part 4. General Pharmacology 1996; 27(3):431-434
22. Bolkent S, Yanardag R, Tabakoglu-oguz A and Ozsoy-sacan O: Effect of chard (*Beta vulgaris* L.var.cicla) extract on pancreatic beta cell in streptozotocin diabetic rats:a morphological and biochemical study. Journal of Ethnopharmacology 2000; 73:251-259
23. Ubillas RP, Mendez CD, Jolad SD, Luo J, King SR, Carlson TJ and Fort DM: Antihyperglycemic acetylenic glucoside from *Bidens pilosa*. Planta Medica 2000; 66(1): 82-83
24. Russel KRM, Morrison EA and Ragoobirsingh D: The effect of annatto on insulin binding properties in the dog. Phytotherapy Research 2005;19(5): 433-436
25. Satheesh MA, Pari L: Antioxidant effect of *Boerhaavia diffusa* L. in

tissue of alloxan induced diabetic rat. Indian Journal of Experimental Biology 2004; 42(10):989-992
26. Grover JK, Yadav SP and Vats V: Effect of feeding *Murraya koeingii* & *Brassica juncea* diet kidney function and glucose level in streptozotocin diabetic mice. Journal of Ethanopharmacology 2003; 85:1-5
27. Parameshwar S, Srinivasan KK and Mallikarjuna rao C: Oral antidiabetic activity of different extract of *caesalpinia bonducella* seed kernels. Pharmaceutical Biology 2002; 40(8):590-595
28. Koyama Y, Abe K, Sano Y and Shizaki L: Effect of green tea on gene expression of hepatic gluconeogenic enzyme *in vivo*. Planta Medica 2004; 70(11): 1100-1102
29. Yadav P, Sarkar S, Bhatnagar D: Action of *capparis decidua* against alloxan induced oxidative stress and diabetes in rat tissues. Pharmacological Research 1997; 36(3): 221-228
30. Talan I, Ragoobirsingh D and Morrison EY: The effect of capsaicin on blood glucose plasma insulin leveland insulin binding in dog models. Phytotherapy Research 2001;15(5):391-394
31. Eddouks M, Lemhadri A and Michel JB: Caraway & caper potential antihyperglycemic plants in diabetic rats. Journal of Ethanopharmacology 2004; 94(1):143-148
32. Palanichamy S, Nagarajan S and Devasagayam M: Effect of *Cassia alata* leaf extract on hyperglycemic rats. Journal of Ethanopharmacology 1988; 22(1): 81-90
33. Latha M and Pari L: Antihyperglycemic effect of cassia auriculata in experimental diabetes and its effect on key metabolic enzyme involved in carbohydrate metabolism. Clinical and experimental pharmacology and physiology 2003; 30(1-2): 38
34. Singh S, Vats P, Suri S and MML Radhe: Effect of an antidiabetic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats. Journal of Ethanopharmacology 2001; 76:269-277
35. Eugen JV and Katrim B and Eckhard N: Antidiabetic effect of *Cinnamomum cassia & Cinnamomum zeylanicum in vivo & in vitro*. Phytotherapy Research 2005; 19(3):203-206
36. Ojewole JA:Hhypoglycemic effect of C*lausena anisata* willd. hook metanolic root extract in rats. Journal of Ethanopharmacology 2002; 81(2):231-237
37. Swanston-Flatt SK, Day C, Bailey CJ and Flatt PR: Traditional plant treatment for diabetes studies in normal and streptozotocin diabetic mice. Diabetologia 1990;33(8):462-464
38. Shirwaikar A, Rajendran K and Punitha IS: Antidiabetic activity of alcoholic stem extract of *Coscinium fenestratum* in streptozotocin nicotinamide induced type 2 diabetic rats. Journal of Ethanopharmacology 2005; 97(2):369-374
39. Farios RA, Rao VS, Viana GS, Silveira ER, Maciel MA and Pinto AC: Hypoglycemic effect of trans-dehydrocrotonin anor- clerodane diterpene from croton cajucara. Planta Medica 1997; 63(6):558-560

40. Luo J, Fort DM and Carlson TJ: *Cryptolepis sanguinolenta*: an ethanobotanical approach to drug discovery and isolation of a potentially useful new antihyperglycemic agent. Diabetic Medicine 1998; 15(5):367-374
41. Ananthi J, Prakasam A and Pugalendi KV: Antihyperglycemic activity of eclipta alba leaf on alloxan induced diabetic rats. Yale Journal of Biology and Medicine 2003; 76(3):97-102
42. Rao TP, Sakaguchi N, Juneja LR, Wada E and Yokojawa T: Amla (*Embellica officinalis* Gaertn) extract reduce oxidative stress in streptozotocin induced diabetic rats. Journal of Medicinal Food 2005; 8(3): 362-368
43. Maroo J, Vasu VT and Gupta S: Dose dependent hypoglycemic effect of aqueous extract of enicostemma littorale Blume in alloxan induced diabetic rats. Phytomedicine 2003,10(2-3):196-199
44. Upadhyay UM and Goyal RK: Efficacy of Enicostemma littorale in type 2 diabetic patient. Phytotherapy Research 2004; 18(3): 233-235
45. Vijayvargia R, Kumar M and Gupta S: Hypoglycemic effect of aqueous extract of *Enicostemma littorale* Blume (Chhota chirayata) on alloxan induced diabetes mellitus in rats. Indian Journal of Experimental Biology 2000; 38(8): 781-784
46. Sharma SB, Nasir A, Prabhu KM, Murthy PS and Dev G: Hypoglycemic and hypolipidemic effect of ethanolic extract of seeds of *Eugenia jambolana* in alloxan induced diabetic rabbits. Journal of Ethanopharmacology 2003;85(2-3):201-206
47. Grover JK, Vats V, Rathi SS: Antihyperglycemic effect of *Eugenia jambolana* and *Tinospora cardifolia* in experimental diabetes and their effects on key metabolic enzyme involved in carbohydrate metabolism. Journal of Ethnopharmacology 2000; 73: 461-470
48. Rave K, Sivagnanam K, Subramanian S: Antidiabetic activity of *Eugenia jambolana* seed kernels on streptozotocin induced diabetic rats. Journal of medicinal food 2004; 7(2): 187-191
49. Gray AM and Flatt PR: Antihyperglycemic action of *Eucalyptus globulus* (eucalyptus) is associated with Pancreatic & extra pancreatic effects in mice. Journal of Nutrition 1998; 128(12):2319-2323
50. Porchezhian E, Ansari SH and Shreedharan NK: Antihyperglycemic activity of *Euphrosia officinale* leaves. Fitoterapia 2000; 71(5) : 522-526
51. Wadood N, Wadood A and Nisar M: Effect of *Ficus religiosa* on blood glucose level and total lipid level of normal and alloxan diabetic rabbits. Journal of Ayub Medical College, Abbottabad 2003; 15(4):40-42
52. Cherian S and Augusti KT: Antidiabetic effect of a glycoside of leucopelargonidin isolated from *Ficus bengalensis* Linn. Indian Journal of Experimental Biology 1993; 31(1): 26-29s
53. Perez C, Dominguez E, Ramiro JM, Ramero A, Campillo JE and Torres MD: A study on the glycemic balance in streptozotocin diabetic rats treated with an aqueous extract of *Ficus carica* (fig tree)

leaves. Phytotherapy Research 1998; 10(1): 82-83
54. Ananthan R, Latha M, Ramkumar KM, Pari L, Bhaskar C and Narmatha bai V: Modulatory effect of *Gymnema montanum* leaf extract on alloxan induced oxidative stress in wistar rats. Nutrition 2004; 20:280-285
55. Ghalap S and Kar A: Effect of *Innula racemosa* root and *Gymnema sylvestre* leaf extract in the regulation of corticosteroid induced diabetes mellitus: involvement of thyroid harmone. Pharmazie 2003; 58: 413-415
56. Ghalap S and Kar A: Gymnemic acid from Gymnema sylvestre potentially regulates dexamethasone induced hyperglycemia in mice. Pharmaceutical Biology 2005; 43(2): 192-195
57. Shanmugasundaram KR, Panneerselvam C, Samudram P and Shanmugasundaram ER: Enzyme changes and glucose utilization in diabetic rabbits :The effect of *Gymnema sylvestre* R. Br. Journal of Ethanopharmacology 1983; 7(2):205-34
58. Sugihara Y, Nojima H, Matsuda H, Murakami T, Yoshikawa M and Kimura I: Anti hyperglycemic effect of gymnemic acid IV a compound derived from *Gymnema sylvestre* leaves in streptozotocin diabetic mice. Journal of Asian Natural Product Research 2000, 2(4):321-327
59. Ekrem sezika, Mustafa aslana, Erdem yesiladaa and Shigeru lto: Hypoglycemic activity of *Gentiana olivieri* & isolation of active constituent through bioassay directed fractionation techniques. Life Sciences 2005; 76:1223-1238
60. Swanston-flatt SK, Day C, Bailey CJ and Flatt PR: Traditional plant treatment for diabetes studies in normal and streptozotocin diabetic mice. Diabetologia 1990; 33(8):462-464
61. Akowuah GA, Sadikun A and Mariam A: Flavonoid identification and hypoglycemic studies of butanol fraction from *Gynura procumbens.* Pharmaceutical Biology 2002; 40(6):405-410
62. Sachdewa A and Khernani LD: A preliminary investigation of possible hypoglycemic activity of *Hibiscus rosa sinensis*. Biomedical & environmental sciences 1999; 12: 222-226
63. Chakrabarti R, Vikramaditya RK and Mullangi R: Hypoglycemic and hypolipidemic activity of Helicteres isora in animal models. Journal of Ethnopharmacology 2002;81(3): 343-349
64. Naismith DJ, Mahdi GS and Shakir NN: Therapeutic value of barley in the management of diabetes. Annals of Nutrition and Metabolism 1991; 35(2)61-64
65. Ji Y,chen S, Zhang K and Wang W: Effects of *Hovenia dulcis* Thunb on blood sugar and hepatic glycogen in diabetic mice. Zhong Yao Cai 2002; 25(3):190-191
66. Malalavidhane TS, Wickramasinghe SMDN, Perera MSA, Jansz ER: Oral hypoglycemic activity of *Ipomoea aquatica* in streptozotocin induced diabetic wistar rats and type II diabetes. Phytotherapy Research 2003; 17(9): 1098-1100
67. Kusano S and Abe H: Hypoglycemic activity of white skinned potato (*Ipomoea batata*) in obese zucker fatty rats. Biological and Pharmaceutical Bulletin 2000, 23:23-26

68. Sanchez de Medina F, Gamez MJ, Jimenez I, Osuna JI and Zarzuelo A: Hypoglycemic activity of *Juniper berries*. Planta Medica 1994; 60(3): 197-200
69. Tsiodras S, Shin RK, Chritian M, Shaw LM, and Sass DA: Anticholinergic toxicity associated with lupine seed as a home remedy for diabetes mellitus. Annals of Emergency Medicine 1999; 33(6): 715-717
70. EI-Fiky FK, Abou-Karam MA and Afify EA: Effect of *Luffa aegyptiaca* (seeds) & *Cariss edulis* (leaves) extract on blood glucose level of normal and streptozotocin diabetic rats. Journal of Ethanopharmacology 1996; 50(1): 43-47
71. Kakali Saha, Pulok K. Mukherjee, Das J, Subhash C. Mandal, Pal M and Saha BP: Hypoglycemic activity of *Leucas lavandulaefolia* Rees. in streptozotocin induced diabetic rats. Phytotherapy Research 1998; 11(6): 463-466
72. Kakuda T, Sakane I,Takihara T, Ozaki Y, Takeuchi H and Kuroyanagi M: Hypoglycemic effect of extract from lagerstroemia speciosa L. leaves in genetically diabetic KK-AY-mice. Biosci Biotechnol Biochem 1996; 60(2): 204-208
73. Eddouks M, Maghrani M, Zeggwagh NA, Michel JB: Study of the hypoglycemic activity of *Lepidium sativum* L aqueous extract in normal and diabetes rats. Journal of Ethnopharmacology 2005; 97 (2): 391-395
74. Aderibigbe AO, Emudianughe TS, Lawal BA: Anti hyperglycemic effect of *Mangifera indica* in rats. Phytotherapy Research 1999; 13(6): 504-507
75. Aylin Sepici, llhan Gurbuz, Cemal Cevik and Erdem Yesilada: Hypoglycemic effect of myrtle oil in normal and alloxan induced diabetic rats. Journal of Ethnopharmacology 2004; 93:311-318
76. Amdraj T and Ignacinuthu S: Evaluation of the hypoglycemic effect of *Memecylon umbellatum* in normal and alloxan induced diabetic mice. Journal of Ethnopharmacology 1998, 62: 247-250
77. Rao BK, Kesavulu MM, Giri R and Apparao C: Hypoglycemic and hypolipidemic effect of momordica cymbalania Hook.fruit powder in alloxan diabetic rats. Journal of Ethnopharmacology 1999; 67: 103-109
78. Akhtar MS, Qureshi AQ and Iqbal J: Hypoglycemic evaluation of *Mucuna pruriense* Linn seed. Journal of Pakistan Medical Association 1990; 40 :147-150
79. Pari L and Umamaheswari J: Antihyperglycemic activity of *Musa sapientum* flower: effect on lipid peroxidation in alloxan induced diabetic rats. Phytotherapy Research 2000; 14 :136-138
80. Chaturvedi P, Geoge S, Milinganyo M and Tripathi YB: Effect of *Momordica Charantia* on lipid profile and oral glucose tolerance in diabetic rats. Phytotherapy Research 2004; 18(11) : 954-956
81. Andallu B and Varadacharyulu NC: Control of hyperglycemia and retardation of cataract by mulberry (*Morus indica* L.) leaves in streptozotocin diabetic rats. Indian Journal of Experimental Biology 2002; 40(7) :791-795
82. Khan BA, Abraham A and Leelamma S: Hypoglycemic action of *Murraya*

koeingii (curry leaf) & *Brassica juncea* (mustard): mechanism of action. Indian Journal of Biochemistry & Biophysics 1995; 32:106-108

83. Mukherjee PK, Saha K, Pal M and Saha BP: Effect of *Nelumbo neucifera* rhizome extract on blood sugar level in rats. Journal of Ethnopharmacology 1997; 58(3): 207-213
84. Chatopadhyay RR: Hypoglycemic effect of *Ocimum sanctum* leaf extract in normal & streptozotocin diabetic rats. Indian Journal of Experimental Biology 1993; 31(11): 891-893
85. Gonzalez M, Zarzuelo A, Gamez MJ, Utrilla MP, Jimenez J and Osuna I: Hypoglycemic activity of olive leaf. Planta Medica 1992; 58(6): 513-515
86. Frati-munari AC, De Leon C, Aliza andraca R, Banales-Ham MB, Lopez-Ledesma R and Lozoya X: Effect of a dehydrated extract of nopal (*Opuntia ficus indica* Mill) on blood glucose. Arch Invest Med (Mex) 1989; 20(3): 211-216
87. Peungvicha P, Thirawarapan SS and Watanabe H: Hypoglycemic effect of water extract of the root of *Pandanus odorus*. Biological Pharmaceutical Bulletin 1996; 19(3): 364-366
88. Oshima Y, Konno C and Hikino H. Isolation and hypoglycemic activity of Panaxans glycans of *Panax ginseng* root. Journal of Ethanopharmacology 1985; 14(2-3): 255-259
89. Ashish K.Das, Subhash C. Mandal, Sanjay K. Baberjee,Sanghamitra Sinha, B.P.Saha and M.Pal: Studies on the hypoglycemic activities of *Punica granatum* seed in streptozotocin induced diabetic rats. Phytotherapy Research 2001; 15(7): 628-629
90. Joy KL and Kuttan R: Antidiabetic activity of *Picrorrhiza kurroa* extract. Journal of Ethnopharmacology 1999; 67:143-148
91. Srividya N and Periwal S: Diuretic, hypotensive, and hypoglycemic effect of *Phyllanthus amarus.* Indian Journal Experimental Biology 1995; 33(11): 861-864
92. Pari L and Subramanian Venkateswaran: Protective role of *Phaseolus vulgaris* on changes in fatty acids composition in experimental diabetes. Journal of Medicinal food 2004; 7(2): 204-209
93. Matsuda H, Murakami T, Yashiro K, Yamahara J and Yoshikawa M: Hypoglycemic principles of natural medicine IV aldose- reductase & alpha glucosidase inhibitors from the root of *Salacia oblonga* Wall. (Celastraceae) structure of a new friedelane type triterpene kotalagenin-16-acetate. Chemical and Pharmaceutical Bulletin(Tokyo) 1999; 47: 1725-1729
94. Yoshikawa M, Murakami T, Yashiro K and Matsuda H: Kotalanol-a potent α glucosidase inhibitor with thio sugar sulfonium sulfate structure from hypoglycemic ayurvedic medicine *Salacia reticulate*. Chemical and Pharmaceutical Bulletin(Tokyo) 1998; 46: 1339-1340
95. Saxena AM, Mukherjee SK and Murthy PS: Mode of action of three structurally different hypoglycemic agents: a comparative study. Indian Journal of Experimental Biology 1996; 34(4): 351-355
96. Pandey M and Khan A: Hypoglycemic effect of defatted seeds and water soluble fibre from

the seeds of *Syzygium cumini* Linn. Skeels in alloxan diabetic rat. Indian Journal of Experimental Biology 2002, 40(10): 1178-1182

97. Pari L and Venkateswaran S: Hypoglycemic activity of *Scoparia dulcis* L. extract in alloxan induced hyperglycemic rats. Phytotherapy Research 2002; 16: 662-664
98. Ajabnoor MA and Tilmisany AK: Effect of *Trigonella foenum graceum* on blood glucose level in normal and alloxan diabetic mice. Journal of Ethnopharmacology 1988; 22(1): 45-49
99. Li M, Qu W, Wang Y, Wan H and Tian C: Hypoglycemic effect of saponin from *Tribulus terrestris*. Zhong Yao Cai 2002; 25(6): 420-422
100. Noor H and Ashcroft SJ: Antidiabetic effects of *Tinospora crispa* in rat. Journal of Ethnopharmacology 1989; 27(1-2): 149-161
101. Stanely P, Prince M and Menon VP: Hypoglycemic and other related action of *Tinospora cardifolia* roots in alloxan induced diabetic rats. Journal of Ethnopharmacology 2000; 70(1): 9-15
102. Maiti R, Jana D, Das UK and Ghash D: Antidiabetic effects of aqueous extract of seed of *Tamarindus indica* in streptozotocin induced diabetic rats. Journal of Ethnopharmacology 2004; 92: 85-91
103. Fort DM, Rao K, Jolad SD, Luo J, Carlson TJ and King SR: Antihyperglycemic activity of *Teramnus labialis* (Fabaceae). Phytomedicine 2000; 6(6):465-467
104. Bigan Farzami, Ahmadvand D, Vardosbi S, Majin FJ and Khaghani S: Induction of insulin secretion by a component of *Urtica dioica* leaf extract in perifused inlets of langerhans and its in vivo effects in normal and streptozotocin diabetic rat. Journal of Ethnopharmacology 2003; 89: 47-57
105. Onal S, Timur S, Okutucu B and Zihnioglu F: Inhibition of α glucosidase by aqueous extract of some potent antidiabetic medicinal herbs. Prep Biochem Biotechnol 2005; 35(1) : 29-36
106. Ghosh S and Suryawanshi SA: Effect of *Vinca rosea* extract in treatment of alloxan diabetes in male albino rats. Indian Journal of Experimental Biology 2001; 39(8): 748-759
107. Andallu B and Radhika B: Hypoglycemic, diuretic and hypocholesterolemic effect of winter cherry (*Withania somnifera* Dunal) root. Indian Journal of Experimental Biology 2000; 38(6): 607-609
108. Hsu FL, Chen YC and Cheng JT: Caffeic acid as active principle from the fruit of *Xanthium strumarium* to lower plasma glucose in diabetic rats. Planta Medica 2000; 66(3): 228-230
109. Akhani SP, Vishwakarma SL and Goyal RK: Antidiabetic activity of *Zingiber officinale* in streptozotocin induced type I diabetic rats. Journal of pharmacy and Pharmacology 2004; 56: 101-105
110. Anand KK, Singh B, Chand D, Chandan BK and Gupta VN: Effect of *Zizyphus sativa* leaves on blood glucose level in normal and alloxan diabetic rats. Journal of Ethnopharmacology 1989; 27: 121-127
111. Mukhrjee PK: Evaluation of Indian traditional medicine. Drug information Journal 2001; 35: 623-631

112. Mukhrjee PK: Quality control of herbal drugs, Business horizons, New Delhi 2002:543-545
113. Pan, GY, Huang ZJ, Wang GJ, Fawcett JP, Liu XD, Zhao XC, Sun,JG and Xie YY, The antihyperglycaemic activity of berberine arisesfrom a decrease of glucose absorption. Planta Medica 2003; 69: 632–636.
114. Kirtikar, KR and Basu, BD: Indian Medicinal Plants, vols. 1–4. Periodical Experts, Delhi.1993
115. Uanhong, L, Caili F, Yukui R, Guanghui H and Tongyi C: Effects of protein-bound polysaccharide isolated from pumpkin on insulin in diabetic rats. Plant Foods for Human Nutrition 2005; 60, 13–16.
116. Vessal M, Hemmati M and Vasei M: Hypoglycemic effects of quercetin in streptozocin-induced diabetic rats. Comparative Biochemistry and Physiology C: Toxicology and Pharmacology 2003; 135: 357–364.
117. Chau CF, Huang YL and Lee MH: *In vitro* hypoglycemic effects of different insoluble fiber-rich fractions prepared from the peel of *Citrus sinensis* L. cv. Liucheng. Journal of Agricultural and Food Chemistry 2003; 51, 6623–6626
118. Ng TB, Wong CM, Li WW and Yeung HW: Insulin-like molecules in *Momordica charantia* seeds. Journal of Ethnopharmacology 1986; 15, 107
119. Nomura E, Kashiwada A, Hosoda A, Nakamura K, Morishita H, Tsuno T and Taniguchi H: Synthesis of amide compounds of ferulic acid, and their stimulatory effects on insulin secretion *in vitro*. Bioorganic and Medicinal Chemistry 2003; 11, 3807–3813.
120. Tormo MA, Gil-Exojo I, Romero de Tejada A, and Campillo JE: Hypoglycemic and anorexigenic activities of an alpha amylase inhibitor from white kidney beans (*Phaseolus vulgaris*) in wistar rats. British Journal of Nutrition 2004; 92: 785-790