Review article **Bimonthly published scientific journal**

INTERNATIONAL JOURNAL of Indigenous Herbs and Drugs

Medications of diabetes mellitus and antidiabetic medicinal plants: A review

Rakhee Raj[1]*, Sanjay Sahay[2], Jagriti Tripathi[3]

[1]Department of Botany, Barkatullah University Bhopal, Madhya Pradesh 462021 (India)

[2]Government Science and Commerce College, Benazir, Bhopal, Madhya Pradesh 462008 (India)

[3]Department of Botany, Unique College, Bhopal, Madhya Pradesh 462003 (India)

Abstract

Diabetes mellitus is a metabolic disorder characterized by resistance to the action of insulin, insufficient insulin secretion or both. It is becoming one of the most common diseases of the world. Type II diabetes in young has increased 30 fold over the last 20 years concomitant with an increase in obesity. In diabetes mellitus, besides hyperglycemia, cardiovascular disease (CVD) is a major cause of death in the world and is mainly due to atherosclerosis (hardening of the arteries). The treatment for diabetes mellitus would be a drug that not only controls the glycemic level but also prevents the development of atherosclerosis and other complications of diabetics. New drugs and new drug delivery systems for insulin have also been introduced. The Indian indigenous drugs have great importance both from the professional and economic point of view. A large number of plants have been reported to possess anti-diabetic activity e.g., *Aconitum napeilus, Aloe vera, Carum carvi, Cichorium intybus, Allium cepa, Aralia cachemirica, Allium sativum, Momordia charantia*, etc. Different model systems like alloxan, streptozotocins etc. are available to screen the anti-diabetic activity. Therefore, this review summarizes the current different antidiabetic drugs and also provides an overview of several medicinal plants used traditionally in the treatment of diabetes mellitus.

Keywords: Diabetes mellitus, Type II diabetes, Hyperglycemia, Medicinal plants, Antidiabetic drugs

Introduction

The human population has always been plagued by the diseases that have adversely affected health and well-being. Whilst for hundred years these ailments were caused by infectious agents. Non-communicable diseases have become the main public health concern in the 21st century [1]. Since ages, man has been exploring, experimenting, analyzing and utilizing the unexhaustive bounties of nature-relentlessly. It is through these experiments many human and animal ailments have been treated and cured successfully such as hepatitis, malaria, jaundice, inflammation, skin disorders and depression. There are many diseases like, diabetes, hepatitis, cancer etc on which extensive research is still going on to find a 'cure' which is not only effective in complete irradiation of disease but also safe and economical. On the eve of globalization and liberalization, the cost of drugs and treatment measures are increasing day by day, hampering the health care budgets of not only third world countries but also of individuals. According to World Health Organization projection, the diabetes population is likely to increase to 300 million or more by the year 2025 [2]. The current studies in India indicate that there is an alarming rise in prevalence of diabetes which has gone beyond epidemic form to a pandemic one [3]. Considering the patient compliance, many investigations have been undertaken to opt the possibilities of using plants, available at a hand stretch to treat human ailments. To overcome these issues, the synthetic drugs which are used concomitantly in some individuals may lead to side effects or drug interactions when used to treat such ailments e.g., sulfonamides inhibit metabolism or excretion of antidiabetic drug sulfonylureas thereby producing hypoglycemia, while rifampicin increases their metabolism to reduce their hypoglycemic effect. Hence, taking synthetic-drug interactions and side effects into account there is a new hope to look in for plants and herbal preparations for their therapeutic values.

The word 'diabetes' is derived from the Greek word "Diab" (meaning to pass through, referring to the cycle of heavy thirst and frequent urination); 'mellitus' is the Latin word for "sweetened with honey" (refers to the presence of sugar in the urine). Greeks had knowledge of a disease accompanied by polyurea and wasting of body, whereas Aretaeus of Cappadocia mentioned a disease characterized by thirst and polyurea. Subsequently the knowledge spreaded to Chinese Iranians and Arabians. From the Middle East, the knowledge of diabetes mellitus had spread to Spain as a disease characterized by polyurea, polydipsia with sugary flavoured urine. With the discovery of sugar in urine and its detection by laboratory test, the knowledge permeated into the 18th century. According to ancient Hindu physicians, 'Madhumeha'

Raj R, Sahay S, Tripathi J. Medications of diabetes mellitus and antidiabetic medicinal plants: A review. Int J Ind Herbs Drugs 2016; 1(1): 19-28.

is a disease in which a patient passes sweet urine and exhibits sweetness all over the body. They had recorded in their observations that 'if too many ants swarm around a spot of urine, then the person have symptoms of diabetes mellitus. The Greek physician Aretaeus noted that affected individuals passed increasing amounts of urine as if there was "liquefaction of flesh and bones into urine." The complete term "diabetes mellitus" was coined in 1674 by Thomas Willis. Mellitus is Latin for honey, which is how Willis described the urine of diabetics.

A young boy, Leonard Thompson, was the first patient to receive insulin treatment in the year 1922 and lived for thirteen years. Over the next 70 years, insulin was further refined and purified. A revolution came with the production of recombinant human DNA insulin in 1978. Instead of collecting insulin from animals, new human insulin could be synthesized. In 1923, Banting and Macloed were awarded the Nobel Prize for the discovery of insulin. In his Nobel Lecture, Banting concluded the following about their discovery: "Insulin is not a cure for diabetes; it is a treatment."

Epidemiology

Diabetes mellitus is a major public health problem in the developed as well as developing countries. It is a silent killer that kills 1 person every 8 seconds in the world and 4 million persons a year. Globally, diabetes mellitus presents enormous and increasingly important public health issues. The occurrence and consequences associated with diabetes are found to be high in countries like India (31.7%), China (20.8%) and United State of America (17.7%) [4]. It is predicted that by 2030, India, China and the United States will have the largest number of people with diabetes [5]. In most western countries, type 1 diabetes accounts for over 90% of childhood and adolescent diabetes although less than half of individuals with type 1 diabetes are diagnosed before the age of 15 years. Type 2 diabetes is becoming more common in youth onset diabetes in certain at risk populations. In addition, there is a distinct slowly progressive form of type 1 diabetes in Japan, which represents approximately one third of cases of type 1 diabetes. Type 1 diabetes is more common in the offspring of diabetic men compared with diabetic women [6].

The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetesis projected to rise from 171 million in 2000 to 366 million in 2030. Its prevalence is higher in men than women, but there are more women suffering from diabetes than men. The urban population in developing countries is projected to double during this period [7]. The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people > 65 years of age [8].

Hyperglycaemia is one of the common manifestations of diabetes. Chronic hyperglycaemia causes damage to the eyes, kidneys, nerves, heart and blood vessels [9].The etiology and pathophysiology leading to hyperglycaemia, however, show marked differences among patients with diabetes mellitus, warranting different preventive strategic, diagnostic techniques and treatment methods [10]. Large-vessel atherosclerosis is the most common cause of death in diabetics.

Present status projects that incidence of diabetes is on rise. Diabetes is predicted to become one of the most common diseases in the world within a couple of decades, affecting at least half a billion people. Only in year 2001, about 441,004 deaths were registered and 49,855 of them provoked by diabetes, representing 11.2% of the total population [11]. In United States, diabetes is the sixth leading cause of death [12].

Available therapy for diabetes mellitus

The treatment of diabetes mellitus is considered as the main global problem and successful treatment has yet to be discovered. Eventhough insulin therapy and oral hypoglycemic agents are the first line of treatment for the diabetes mellitus they have some side effects and fail to significantly alter the course of diabetic complications [13].

Human insulin

Human insulin is a polypeptide, having a molecular weight of about 6000 Da, consisted of two amino acid chains A and B , which are linked by two disulphide (-S- S-) linkages. Normal human pancreas contains about 8-10 mg of insulin. Insulin is not suitable for oral administration due to inactivation by digestive enzymes. 80% of exerted insulin is normally degraded in the liver and kidneys. The amount of insulin secreted per day in a normal human is about 40 units. The dose of insulin required to control the diabetes varies from patient to patient and from time to time in the same patient [14].

Oral hypoglycemic drugs

Currently available oral therapies for treatment of diabetes mellitus are sulfonylureas, biguanides, α-glucosidase inhibitors, and glinides, which can be used alone or combined with other drugs to achieve better effect. Many of these oral antidiabetic agents have a number of serious adverse effects, thus, the management of diabetes without any side effects is still a challenge [2, 3]. Sulphonylureas are useful in the treatment of diabetes which cannot be controlled by diet or other available therapy. Sulphonylureas are absorbed rapidly from the intestine, some important drugs of this group are tolbutamide, chlorpropamide, glibenclamide, tolazamide etc. Biguanides is the other class of oral anti-diabetic agents which control all types of diabetes mellitus. It reduces glucose absorption from the intestine and can also be used to treat

Rakhee Raj, E-mail:- srpharma@rediffmail.com

mild diabetes during pregnancy [14]. If the diet of the diabetic patients is not properly controlled, insulin or oral hypoglycemic drugs will not act properly. A diabetic person should take more care about his body weight and food habit, regular exercise can also improve the utilization of the blood glucose through different tissue in the body which can reduces the symptoms of diabetes [14].

Table 1: Synthetic drug and their side effects

Agent	Mechanism	Site of action	Advantages	Side effects
Sulphonylureas	Stimulating insulin production by inhibiting the K-ATP channel	Pancreatic beta cells	Effective and inexpensive	Hypoglycemia and weight gain.
Metformin	Decreases insulin resistance	Liver	Weight loss Does not cause hypoglycemia	Nausea and diarrhea. Hypoglycemia occurs when combined with sulfonylurea or insulin.
Thiazolidi-nediones	Reduce insulin resistance by activating PPAR-γ	GI tract	Low risk	Increased liver enzymes, weight gain, edema, mild anemia.
α-glucosidase inhibitors	Reduces intestinal glucose absorption	Fat, muscle	Decreases postprandial plasma triglyceride levels	Diarrhea, Serum levels of transaminases increases at doses.

Herbal remedies for diabetes mellitus

Herbal medications have been used for the treatment of variety of ailments, a huge number of population in the world is entirely dependent on traditional medicines [15]. A number of medicinal plants and their formulations are used for treating diabetes in Ayurvedic medicine system as well as in ethnomedicinal practices [3]. In India, indigenous remedies have been used in the treatment of diabetes mellitus since the time of Charaka and Shusrutha. From the ethnobotanical information, about 800 plants which may possess anti-diabetic potential have been found [13, 14, 16]. Several plants have been used as dietary adjuvant and in treating the number of diseases even without any knowledge on their proper functions and constituents. This practice may be due to its fewer side effects compare to the synthetic hypoglycemic agents and because of their safety, effectiveness, and availability [17]. Although various synthetic drugs were developed to treat diabetes but still very less number of drugs is available for the treatment of diabetes [17]. There are about 200 pure compounds from plant sources reported to show blood glucose lowering effect. The compounds may be alkaloids, carbohydrates, glycosides, flavonoids, steroids, terpenoids, peptides and amino acids, lipids, phenolics, glycopeptides and iridoids. Many anti-diabetic products of herbal origin are now available in the market. More than 1200 species of plants have been screened for activity on the basis of ethnomedicinal uses [14].

Table 2: Medicinal plants with antidiabetic and their reported effect on experimental models

Botanical Name	Family	Antidiabetic and other beneficial effects	References
Achiliea santolina L.	Asteraceae	Hypoglycemic, antioxidant	18
Artemisia patterns	Asteraceae	Hypoglycemic, increases peripheral glucose utilization	19
Areca catechu L.	Arecaceae	Hypoglycemic	20
Beta vulgaris L.	Chenopodiaceae	Increases glucose tolerance in OGTT	21
Boerhaavia diffusa L.	Nyctaginaceae	Decreases blood glucose level and increases plasma insulin levels	22
Bombax ceiba L.	Malvaceae	Hypoglycemic	23
Butea manosperma (Lam)	Caesalpinaceae	Anti-hyperglycemic	24
Carum carvi L.	Apiaceae	Potent anti-hyperglycemic	25
Cogniauxia podoleana Baillon Bail Ion	Cucurbitaceae	Hypoglycemic and anti-hyperglycemic	26
Commelina communis L.	Conimelinaceae	Anti-hyperglycemic, management of non-insulin-dependent	27

Rakhee Raj, E-mail:- srpharma@rediffmail.com

		diabetes.	
Croton cajucara Benth	Euphorbiaceae	Anti-hyperglycemic	28, 29
Curcuma longa L.	Zingiberaceae	Hypoglycemic, plays a role in PPAR-gamma activation	30
Cynodon dactylon Pers	Poaceae	Anti-hyperglycemic	31
Enicostemma littorale Blume	Gentianaceae	Decreases plasma glucose level, glycosylated haemoglobin and glucose-6-phosphatase activity in liver	32
Eriobotrya japonica Lindl.	Rosaceae	Hypoglycemic	33
Gentiana olivieri L.	Gentianaceae	Hypoglycemic, anti-hyperlipidemic	34
Ginkgo biloba L.	Ginkgoaceae	Hypoglycemic, increases pancreatic beta-cell in NIDDM	35, 36
Globularia alypum L.	Globulariaceae	Hypoglycemic, increases plasma insulin levels	37
Glycyrrhiza uralensis Fish.	Papilionaceae	PPAR-gamma ligand-binding activity, decreases the blood glucose levels	38
Gymnema nwntanum Hook	Asclepiadaceae	Anti-peroxidative, antioxidant, may prevent the cholinergic neural and retinal complications of hyperglycemia in diabetes	39
Gymnema sylvestre R. Br.	Asclepiadaceae	Hypoglycemic. Hypolipidemic	40
Hintonia standleyana	Rubiaceae	Anti-hyperglycemic	41
Ibervillea sonorae S.	Cucurbitaceae	Acute and chronic hypoglycemic	42
Ipomoea aquatic Forsk.	Convolvulaceae	Decreases serum glucose concentration by 29.4% in Type II diabetic patients. hypoglycemic	43
Kalopanax pictus Thumb.	Araliaceae	Anti-diabetic activity, hypocholesterolmic and hypolipidemic	44
Lagerstroemia speciosa L.	Lythraceae	Insulin-like actions, glucose uptake, anti-adipogenesis	45, 46
Medicago saliva L.	Fabaceae	Anti-hyperglycemic, insulin-releasing and insulin-like activity	47
Morus alba L.	Moraceae	Protects pancreatic beta cells from degeneration anddiminishes lipid peroxidation	48
Morus indica. L.	Moraceae	Hypoglycemic	49, 50
Morus inignis L.	Moraceae	Hypoglycemic	51
Murraya koenigii L.	Rutaceae	Hypoglycemic, increases glycogenesis,decreases gluconeogenesis and glycogenolysis	52
Nelumbo nucifera L.	Neluntbonaceae	Improves glucose tolerance and potentiates the action of exogenouslyinjected insulin	53
Nigella saliva Gaertn.	Ranunculaceae	Decreases oxidative stress and preserves pancreatic beta-cell integrity.	54
Ocimum gratissinuim L. Var.	Lamiaceae	Hypoglycemic	55
Pandanus odorus Ridl.	Pandanaceae	Hypoglycemic, increases serum insulin levels and liver glycogen	56
Parmentieru edulis A.DC	Bignoniaceae	Hypoglycemic	57
Phyllanthus sellowianus Mull.Arg	Euphorbiaceae	Hypoglycemic	58
Psacalium decompositum (Gray) H.	Asteraceae	Hypoglycemic	59
Psacalium peltatum (Kunth)	Asteraceae	Anti-hyperglycemic	60
Punica granatum L.	Punicaceae	Improves postprandial hyperglycemia in type 2 diabetes and obesity by inhibiting intestinal alpha-glucosidase activity	61
Solaria oblonga	Celastraceae	Hypoglycemic and possess anti-oxidant activity	62
Sambucus nigra L.	Adoxaceae	Insulin-releasing and insulin-like activity	63
Sanguis draxonis	Apocynaceae	Increase insulin sensitivity and improve the development of insulin resistance in rats	64
Sclerocarya birea (A.Rich)	Anacardiaceae	Hypoglycemic	65
Scoparia dulcis L.	Scrophariaceae	Hypoglycemic, antihyperlipidemic, antidiabetic	66, 67
Swertia chirayita (Roxb)	Gentianaceae	Stimulates insulin release from islets	68

Rakhee Raj, E-mail:- srpharma@rediffmail.com

Syzygium alternifolium (Wt) Walp.	Myrtaceae	Hypoglycemic, antihyperglycemic and antihyperlipidemic	69, 70
Terminalia bellirica (Gaertn)	*Combretaceae*	Stimulates insulin secretion. Enhances insulin action andinhibits both protein glycation and starch digestion	71
Terminalia chebula Retz.	Combretaceae	Dose-dependent glucose lowering effect, antidiabetic and renoprotective,decreases hepatic and skeletal muscle glycogen content, increases insulin release from the pancreatic islets	72-74
Teucriumpolium	Lamiaceae	Increases insulin release, antioxidant and hypoglycemic	75
Tinospora cordifolia Miers..	Menispermaceae	Hypoglycemic	76
Tinospora crispa (L) Hook.	Menispermaceae	Anti-hyperglycemic, stimulates insulin release from islets	77
Urtica dioica L.	Urticaceae	Anti-hyperglycemic	78
Urtica pilulifera L.	Urticaceae	Hypoglycemic	79
Vinca rosea L.	Apocynaceae	Anti-hyperglycemic	80
Withania soimifera (L) Dunal	Solanaceae	Hypoglycemic, antioxidant, diuretic and hypocholesterolemic	81, 82
Withania coagulans Dunal	Solanaceae	Anti-hyperglycemic, anti-hyperlipidemic and hypoglycemic	83, 84
Zizyphus sativa Gaertn	Rhamnaceae	Hypoglycemic	85
Zizyphus spina-christi L.	Rhamnaceae	Insulinotropic, hypoglycemic anddepressant effect on the central nervous system	86
Zygophyllum gaetulum Emb	Zygophyllaceae	Hypoglycemic, increases plasma insulin levels	87

Marketed products

Today, up to 600 traditional plant medicines has been reported in India for diabetes. Numerous medicinal preparations in varied forms have been tried out and are used in Ayurvedic system of medicines for diabetes. These medicines are prescribed in different forms; most commonly used are - choorna, vati, arka, quath, etc. These preparations may contain the aqueous extracts or powders of the different parts of the plants which are used in the treatment of diabetes. All the antidiabetic formulations available in the market contain 3 to 25 herbs and mainly, used herbs are *Coccinia indica, Tragia involucrata, G. sylvestre, Pterocarpus marsu-pium, T. foenum-graecum, Moringa oleifera, Eugenia jambolana, Tinospora cordifolia, Swertia chirayita, Momordica charantia, Ficus glomerata, Ficus benghalensis, Vinca rosea, Mucuna prurita, Terminalia bellirica, Azadirachta indica, Zingiber officinale, Aegle marmelos, Cinnamomum tamala, Ocimum sanctum, Salacia oblonga, Cassia auriculata, Curcuma longa, An-drograpis paniculata, Emblica officinalis,* etc. Following are few preparations available in the market for the treatment of diabetes that contains drug in powder form or as extracts. Only the names of the herbs added in the preparations are reported, along with these herbs some preparations may contain animal-derived products and minerals.

Hyponidd tablets, *Momordica charantia*, *Swertia chirata*, *Melia azadiracta*, *Tinospora cordifolia*, *Gymnema sylvestre*, *Enicostemma litterole*, *Emblica officinalis*, *Eugenia jambolana*, *Cassia auriculata*, *Curcuma longa*.

Mersina capsules, *Gymnema sylvestre*, *Mo-mordica charantia*, *Cassia auriculata*, *Syzigium cumini*, *Phyllanthus emblica*, *Melia azadiracta*, *Trigonella foe-num graecum*, *Coccinia indica*, *Tinospora cardifolia*, *Potassi carbonas*.

Herbovedics mahantak churna**,** Nai, Kadu, Kariyatu, Kalijeeri, Methi, Kalumbo, Kakach, Indrajav, Karela, Haldi, Jeshthimadha.

Madhuhari powder, Gudmar, Karela beej, Jamun, Babul ki chhal, Amba haldi, Gudwel, Bilva patra, Neem patra, Shilajeet, Trivang bhasm.

Dianex, *Gymnema sylvestre*, *Eugenia jambolana*, *Momordica charantia*, *Azadirachta indica*, *Cassia auri-culata*, *Aegle marmelos*, *Withania somnifera* and *Cur-cuma longa*.

Diamed**,** *Azadirachta indica*, *Cassia auriculata* and *Momordica charantia*.

Aavirai kudineer, *Cassia auriculata*, *Cassia fis-tula*, *Salacia prinoides*, *Cyperus rotundus*, *Saussurrea lappa*, *Eugenia jambolana* and *Terminalia arjuna*.

Madhumeha churna**,** *Azadirachta indica*, *Cassia auriculata*, *Cassia auriculata*, *Gymnema sylvestre*, *Eugenia jambolana*, *Eugenia jambolana*, *Zizyphus mau-ritiana*, *Curculigo orchioides*, *Melochia corchorifolia*, *Michelia champaca*, *Cynodon dactylon*, *Murraya koenegii*, *Acacia catechu*, *Cassia fistula*, *Salacia ob-longa* and *Momordica charantia*.

Diagon tablets, *Eugenia jambolana*, *Andrograpis paniculata*, *Tinospora cordifolia*, *Curcuma longa*, *Ber-beris aristata*, *Vetiveria zizanoides*, *Strychnos potato-rum*, *Mimosa pudica*, *Gymnema sylvestre*.

Glucolev capsule**,** Amalaki powder, Sudha shila-jeet, Jasad bhasma, Methika beej, Jambu beej, Mad-hunasini, Ashwagandha

Rakhee Raj, E-mail:- srpharma@rediffmail.com

Gluco-essentials capsules, *Vaccinium myrtil-lus*, *Gymnema sylvestris*, *Momordica charantia*, *Cinna-momum zeylanicum*, *Trigonella foenum graecum*, *Panax quinque*, *Panax ginseng*, *Viscum alba*, *Amorphophallus konjac*, *Hydrastis cadensis*, *Ocimum basilicum*, *Cynara scolymus*, *Plantago ovata*, *Pfaffia paniculata*, *Arc-tostaphylos uva ursi*.

Diasulin, *Casssia auriculata*, *Coccinia indica*, *Curcuma longa*, *Momordica charantia*, *Scoparia dulcis*, *Gymnema sylvestre*, *Emblica officinalis*, *Syzgium cumini*, *Tinospora cordifolia*, *Trigonella foenum graecum*.

Glucolib, *Eugenia jambolana*, *Gymnema sylvestris*, *Aegle marmelos*, *Melia azadiracta*, *Momordica charan-tia*, *Enicostema littorale*, *Trigonella foenum graecum*.

Diaveda capsule, *Trigonella foenum graecum*, *Emblica officinalis*, *Curcuma longa*, *Melia azadiracta*, *Gymnema sylvestris* , *Tribulus terrestris*, *Tinospora cordifolia*, *Syzygium cumuni*, *Azadirachta indica*, *Ter-minalia belerica*, *Terminalia chebula*, *Piper nigrum*, *Piper longum*, *Zingiber offcinalis*.

GlucoCare, *Glycyrrhiza glabra*, *Asparagus ra-cemosus*, *Pterocarpus marsupium*, *Gymnema sylvestris*, *Momordica charantia*, *Commiphora mukul*.

Glucomap tablets, *Enicostema littorale*, *Phyllan-thus niruri*, *Eugenia jambolana*, *Melia azadiracta* , *Ter-minalia arjuna*, *Asphaltum*, *Aegle mermelos*, *Mo-mordica charantia*.

Glucova, *Pterocarpus marsupium*, *Enicostema lit-torale*, *Eugenia jambolana*, *Tinospora cordifolia*.

Pancreas tonic, *Tinospora cordifolia*, *Sygigium cumini*, *Melia azadiracta*, *Momordica charantia*, *Gymnema sylvestra*, *Pterocarpus marsupium*, *Aegle mermelos*, *Cinnamomum zeylanicum*.

Tincture of Panchparna, *Coccinia indica*, *Coc-culus villosus*, *Catharanthus roseus*, *Gymnema sylvestre* and *Momordica charantia*.

DWN-12, *Strychnos potatorum*, *Terminalia che-bula*, *Emblica officinalis*, *Terminalia belerica*, *Salacia reticulata*, *Pterocarpus marsupium*, *Piper longum*, *Coscinium fenestratum*, *Tribulus terrestris*, *Syzigium cumini*, *Rhabdia lyuoides*, *Elettaria cardamomum*.

Conclusion

Regardless of the type of diabetes, patients are required to control their blood glucose with medications and/or by adhering to an exercise program and a dietary plan. Insulin therapy by injection is given to those with type 1 DM and also to some patients with type 2 DM when oral hypoglycaemic drugs fail to lower blood glucose. Due to modernization of lifestyle, non-insulin dependent diabetes mellitus is becoming a major health problem in developing countries. Patients with type 2 DM are usually placed on a restricted diet and are instructed to exercise, the purpose of which primarily is weight control. If diet and exercise fail to control blood glucose at the desired level, oral antidiabetic medication is prescribed.

Oral antidiabetic agents exert their effects by various mechanisms: (1) stimulation of beta cells in the pancreas to produce more insulin (sulfonylureas and meglitinides), (2) increasing the sensitivity of muscles and other tissues to insulin (thiazolidinediones), (3) decreasing gluconeogenesis by the liver (biguanides), and (4) delaying the absorption of carbohydrates from the gas-trointestinal tract (alpha-glucosidase inhibitors). These treatments have their own drawbacks, ranging from the developing of resistance and adverse effects to lack of responsiveness in large segment of patients population. Sulfonylureas lose effectiveness for 44% of patients within six years. Also, these treatments are associated with side effects or even toxic effects (e.g., thiazolidinediones may cause liver toxicity; sulphonylureas might worsen heart disease, lower the glucose below the normal range and increase the body weight gain; bloating, flatulence, diarrhea and abdominal discomfort and pain are the major complaints with glucosidase inhibitors). According to literature, two -thirds of medications prescribed for use in children have not been proven safe or effective for this patient population. Moreover, none of these glucose-lowering agents adequately controls the hyperlipidemia that frequently met with the disease.

Herbal drugs or their extracts are prescribed widely, even when their biological active compounds are unknown. Therefore studies with plant extracts are useful to know their efficacy and mechanism of action and safety. Medicinal plants useful in diabetes were reviewed recently. The hypoglycemic effect of some herbal extracts has been confirmed in animal and human models of Type 2 diabetes. There are reports of using herbal extracts for the treatment of diabetes mellitus in humans. Adverse effects are indeed a cause of concern, however, available evidence suggests that herbal medicines are relatively safe.

The potential role of the medicinal plants as hypoglycemic agents has been reviewed by several authors. Many Indian medicinal plants are reported to be useful in diabetes.

Although there are no definitive preventive measures that can be taken against diabetes at this time, except for identifying persons at high risk and encouraging appropriate management. Research into the causes and control of this disease continues to provide the possibility of new cures. The therapy of diabetes will surely be altered dramatically over the next few decades.

Research continues on the islet cell transplantation techniques, including research that uses stem cells derived from pancreatic ducts.

There has been laboratory success with transplantation of islet cells derived from stem cells in mice, but not yet in humans.

Looking further into the future, researchers are studying the

Rakhee Raj, E-mail:- srpharma@rediffmail.com

use of gene therapies to correct the genetic defects that are the original cause of diabetes. As successful gene therapy will affect a true cure of the disease, it seems likely that researchers will continue to pursue its development, despite many hurdles. At this point, however, gene therapy for treatment of diabetes appears far away in the future.

Medicinal plants have been used for diabetes safely and with reasonable success. Despite the great strides that have been made in understanding and management of diabetes mellitus, serious complications continue to confront patients and physicians. The graph of diabetes related mortality is raising unabated. Therefore, search for new anti-diabetic drugs continue.

References

1. Zimmet P, Alberti KGMM, Shaw J. Global and societal implication of the diabetes epidemic. Nature 2001; 414: 782-787.
2. Meenakshi P, Bhuvaneshwari R, Rathi MA, Thirumoorthi L, Guravaiah DC, J iji MJ, *et al*. Antidiabetic activity of ethanolic extract of *Zaleya decandra* in alloxan-induced diabetic rats. Appl Biochem Biotechnol 2010; 162: 1153-1159.
3. Pareek H, Sharma S, Khajja BS, Jain K, Jain GC. Evaluation of hypoglycemic and anti hyperglycemic potential of *Tridax procumbens* (Linn.). BMC Complement Altern Med 2009; 9: 48
4. Balaraman AK, Singh J, Dash S, Maity TK. Antihyperglycemic and hypolipidemic effects of *Melothria maderaspatana* and *Coccinia indica* in Streptozotocin induced diabetes in rats. Saudi Pharm J 2010; 18: 173-178.
5. Frode TS, Medeiros YS. Animal models to test drugs with potential antidiabetic activity. J Ethnopharmacol 2008; 115: 173-183.
6. Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. Pediatr Diabetes 2009; 10: 3-12.
7. King H. Diabetes mellitus: a growing international health care problem. Int Diab Monitor 1997; 9: 1-6.
8. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27 (5): 1047-1053.
9. Davidson MB, Peters AL, Schriger DL. An alternative approach to the diagnosis of diabetes with a review of the literature. Diabetes Care 1995; 8: 1065-1071.
10. Susman JL, Helseth LD. Reducing the complications of type II diabetes: a patient centered approach. Am Fam Physician 1997; 56: 471-80.
11. INEGI/Secretaria de Slaud. Direction general de informacion en salud. CONAPO, Proyecciones de la poblacion de Mexico, 2002: 2000-2050.
12. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Diabetes Statistics. Bethesda, MD: NIH publication no. 96-392, 1995.
13. Venkatesh S, Madhava Reddy B, Dayanand Reddy G, Mullangi R, Lakshman M. Antihyperglycemic and hypolipidemic effects of *Helicteres isora* roots in alloxan-induced diabetic rats: A possible mechanism of action. J Nat Med 2010; 64: 295-304.
14. Warjeet Singh L. Traditional medicinal plants of Manipur as anti-diabetics. J Med Plants Res 2011; 5: 677-687.
15. 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 2011; 133: 67-74.
16. Patel DK, Kumar R, Laloo D, Hemalatha S. Evaluation of phytochemical and antioxidant activities of the different fractions of Hybanthus enneaspermus (Linn.) F. Muell. (Violaceae). Asian Pac J Trop Med 2011; 4: 391-396.
17. Dewanjee S, Das AK, Sahu R, Gangopadhyay M. Antidiabetic activity of *Diospyros peregrina* fruit: effect on hyperglycemia, hyperlipidemia and augmented oxidative stress in experimental type 2 diabetes. Food Chem Toxicol 2009; 47: 2679-2685.
18. Yazdanparast R, Ardestani A, Jamshidi S. Experimental diabetes treated with *Achillea santolina*: effect on pancreatic oxidative parameters, J Ethnopharmacol 2007; 112:, 13-8
19. Subramoniam A, Pushpangadan P, Rajasekharan S, Evans DA, Latha PG, Valsaraj R. Effects of *Artemisia pollens* Wall. On blood glucose levels in normal andalloxan-induced diabetic rats. J Ethnopharmacol 1996; 50: 13-17.
20. Chempakam, B. Hypogiycemic activity of arecoline in betel nut *Areca catechu* L. Ind J Exp Biol 1993; 31: 474-475.
21. Yoshikawa M, Murakami T, Kadoya M, Matsuda H, Muraoka O, Yamahara J, Murakami N. Medicinal foodstuff. III. Sugar beet. Hypoglycemic oleanotic acid oligoglycosides, betavulgarosides 1, II, III and IV, from the root of *Beta vulgaris* L. Chemical and Pharmaceutical Bulletin 1996; 44: 1212-1217.
22. Pari L, Amarnath Satheesh M. Anlidiabetic activity of *Boerhaavia diffusa* L. effect on hepatickeyenzymes in experimental diabetes. J Ethnopharmacol 2004; 91: 109-13
23. Saleem R, Ahmad M, Hussain SA, Qazi AM, Ahmad SI, Qazi MH, Ali M, Faizi S, Akhtar S, Husnain SN. Hypotensive, hypoglycemic and toxicological studies on the flavonol C-glycosideshamimin from *Bombax ceiba*.

Rakhee Raj, E-mail:- srpharma@rediffmail.com

Planta Medica 1999; 5: 331-334.

24. Somani R, Kasture S, Singhai AK. Antidiabetic potential of *Butea monospenna* in rats. Fitoterapia 2006: 77: 86-90.
25. Eddouks M, Lemhadri A, Michel JB.Caraway and caper: potential anti-hyperglycaemie plants in diabetic rats. J Ethnopharmacol 2004; 94: 143-148.
26. Diatewa M, Samba CB, Assah TC, Abena AA.Hypoglycemic and antihyperglycemic effects of diethyl ether fraction isolated from theaqueous extract of the leaves of *Cogniauxia podoleana* Baillon in normal and alloxan-induced diabetic rats. J Ethnopharmacol 2004; 92: 229-232.
27. Youn JY, Park HY, Cho KH. Anti-hyperglycemic activity of *Commeuna communis* L.: inhibition of alpha-glucosidase. Diabetes Res CHn Pract 2004;, 66:, S149-S155.
28. Farias RA, Rao VS, Viana GS, Silveira ER, Maciel MA, Pinto AC. Hypoglycemic effect of trans-dehydrocrotonin, a nor-clerodanc diterpene from *Croton cajucara*. Planta Med 1997; 63: 558-560.
29. Rodrigues G, Marcolin E, Bona S, Porawski M, Lehmann M, Marroni NP. Hepatics alterations and genotoxic effects of *Croton cajucara* Benth (SACACA) indiabetic rats. Arq Gastroenterol 2010; 47: 301-305.
30. Kuroda M, Mimaki Y, Nishiyama T, Mae T, Kishida H, Tsukagawa M, Takahashi K, Kawada T, Nakagawa K, Kitahara M. Hypoglycemic effects of turmeric (*Curcuma longa* L. rhizomes) on genetically diabeticKK-Ay mice. Biol Pharm Bull 2005; 28: 937-939.
31. Jarald EE, Joshi SB, Jain DC. Antidiabetic activity of aqueous extract and non-polysaccharide fraction of *Cynodondactylon Pers*. Indian J Exp Biol 2008; 46: 660-667.
32. Vijayvargia R, Kumar M, Gupta S. Hypoglycemic effect of aqueous extract of *Enicostemma littorale* Blume (chhota chirayata) on alfoxan induced diabetes mellitus in rats. Indian J Exp Bioi 2000; 38: 781-784.
33. Tanaka K, Nishizono S, Makino N, Tamaru S, Terai O, Ikeda I. Hypoglycemic activity of *Eriobotrya japonica* seeds in type 2 diabetic rats and mice. Biosci Biotechnol Biochem 2008; 72: 686-693.
34. Sezik E, Aslan M, Yesilada E, Ito S. Hypoglycaemic activity of *Gentiana olivieri* and isolation of the active constituent through bioassay-directed fractionation techniques. Life Sci 2005; 76: 1223-1238.
35. Sugiyama T, Kubota Y, Shinozuka K, Yamada S, Wu J, Umegaki K. *Ginkgo biloba* extract modifies hypoglycemic action of tolbutainide via hepatic cytochrome P450 mediated mechanism in aged rats. Life Sci 2004; 75: 1113-1122.
36. Kudolo GB. The effect of 3-month ingestion of *Ginkgo biloba* extract (EGb 761) on pancreatic beta-cell functionin response to glucose loading in individuals with non-insulin-dependent diabetes mellitus. J Clin Pharmacol 2001; 41: 600-611.
37. Skim F, Lazrek HB, Kaaya A, el Amri H, Jana M. Pharmacological studies of two antidiabetic plants: *Globularia alypum* and *Zygophyllum gaetulum*. Therapie 1999; 54: 711-715.
38. Kuroda M, Mimaki Y, Sashida Y, Mae T, Kishida H, Nishiyama T, Tsukagawa M, Konishi E, Takahashi K, Kawada T, Nakagawa K, Kitahara M. Phenolics with PPAR-gamma ligand-binding activity obtained from licorice (*Glycyrrhiza uralensis* roots) and ameliorative effects of glycyrin on genetically diabetic KK-A(y) mice. Bioorg Med Chem Lett 2003; 13: 4267-4272.
39. Ramkumar KM, Latha M, Ashokkumar N, Pari L, Ananthan R. Modulation of impaired cholinesterase activity in experimental diabetes: effect of *Gymnema montanum* leaf extract. J Basic Clin Physiol Pharmacol 2005; 16: 17-35.
40. Daisy P, Eliza J, Mohamed Farook KA. A novel dihydroxy gymnemic triacetate isolated from *Gymnema sylvestre* possessing normoglycemic and hypolipidemic activity on STZ-induced diabetic rats. J Ethnopharmacol 2009; 126: 339-344.
41. Guerrero-Analco JA, Hersch-Martínez P, Pedraza-Chaverri J, Navarrete A, Mata R. Antihyperglycemic effect-of constituents from *Hintonia standleyana* in streptozotocin-induced diabetic rats. Planta Med 2005, 71, 1099-1105.
42. Alarcon-Aguilar FJ, Calzada-Bermejo F, Hernandez-Galicia E, Ruiz-Angeles C, Roman-Ramos R. Acute and chronic hypoglycemic effect of *Ibervillea sonorae* root extracts-11. J Ethnopharmacol 2005; 97: 447-452.
43. Malalavidhane TS, Wickramasinghe SM, Perera MS, Jansz ER. Oral hypoglycaemic activity of *Ipomoea aquatica* in streptozotocin-induced, diabetic wistar rats and Type II diabetics. Phytother Res 2003; 17: 1098-1100.
44. Park HJ, Kim DH, Choi JW, Park JH, Han YN. A potent anti-diabetic agent from *Kalopan axpictus*.Arch Pharm Res 1998; 21: 24-29.
45. Hattori K, Sukenobu N, Sasaki T, Takasuga S, Hayashi T, Kasai R, Yamasaki K, Hazeki O. Activation of insulin receptors by lagerstroemin J Pharmacol Sci 2003; 93: 69-73.
46. Klein G, Kim J, Himmeldirk K, Cao Y, Chen X. Antidiabetes and Anti-obesity Activity of *Lagerstroemia speciosa*. Evid Based Complement Alternat Med 2007; 4: 401-407.

Rakhee Raj, E-mail:- srpharma@rediffmail.com

47. Gray AM, Flatt PR. Pancreatic and extra-pancreatic effects of the traditional anti-diabetic plant, *Medicago saliva* (lucerne). Br J Nutr 1997; 78: 325-334.
48. Singab AN, El-Beshbishy HA, Yonekawa M, Nomura T, Fukai T. Hypoglycemic effect of Egyptian *Moms albaroot* bark extract: effect on diabetes and lipid peroxidation of streptozotocin-induced diabetic rats. J T-Etnnopharmacol 2005; 100: 333-338.
49. Devi VD, Urooj A. Hypoglycemic potential of *Moms indica.* L and *Costus igneus*. Nak.—a preliminary study. Indian J Exp Biol 2008; 46: 614-616.
50. Andallu B, Suryakantham V, Lakshmi Srikanthi B, Reddy GK. Effect of mulberry (*Morus indica* L.) therapy on plasma and erythrocyte membrane lipids in patients with type 2 diabetes. Clin Chim Acta 2001; 314: 47-53.
51. Basnet P, Kadota S, Terashima S, ShimizuM, Namba T. Two new 2-arylbenzofuran derivatives from hypoglycemic activity-bearing fractions of *Morus insignis*. Chem Pharm Bull (Tokyo) 1993; 41: 1238-1243.
52. Khan BA, Abraham A, Leelamma S.Hypoglycemic action of *Murraya koenigii* (curry leaf) and *Brassica juncea* (mustard) mechanism of action. Ind J Biochem Biophys 1995; 32: 106-108.
53. Mukherjee PK, Saha K, Pal M, Saha BP.Effect of *Nelumbo nucifera* rhizome extract on blood sugar level in rats. J Ethnopharmacol 1997; 58: 207-213.
54. Kanter M, Coskun O, Korkmaz A, Oter S. Effects of *Nigella sativa* on oxidative stress and beta-cell damage in streptozotocin-induced diabetic rats. Anat Rec A Discov Mol Cell Evol Biol 2004; 279: 685-691.
55. Aguiyi JC, Obi CI, Gang SS, Igweh AC. Hypoglycaemic activity of *Ocimum gratissimum* in rats. Fitoterapia 2000; 71: 444-446.
56. Peungvicha P, Temsiririrkkul R, Prasain JK, Tezuka Y, Kadota S, Thirawarapan SS, Watanabe H.4-Hydroxybenzoic acid: a hypoglycemic constituent of aqueous extract of *Pandanus odorus* root. J Ethnopharmacol 1998; 62: 79-84.
57. Perez RM, Perez C, Zavala MA, Perez S, Hernandez H, Lagunes F. Hypoglycemic effects of lactucin-8-O-melhyl aery late of *Parmentiera edulis* fruit. J Ethnopharmacol 2000; 71: 391-394.
58. Hnatyszyn O, Miño J, Ferraro G, Acevedo C. The hypoglycemic effect of *Phyllanthus sellowiamts* fractions in streptozotocin-induced diabetic mice. Phytomedicine 2002;, 9: 556-559.
59. Alarcon-Aguilar FJ, Jimenez-Estrada M, Reyes-Chilpa R, Roman-Ramos R. Hypoglyceraic effect of extracts and fractions from *Psacalium decompositum* in healthy and alloxan-diabetic mice. J Ethnopharmacol 2000; 72: 21-27.
60. Contreras-Weber C, Perez-Gutierrez S, Alarcon-Aguilar F, Roman-Ramos R. Anti-hyperglycemic effect of *Psacalium peltatum*. ProcWest Pharmacol Soc 2002; 45: 134-136.
61. Li Y, Wen S, Kota BP, Peng G, Li GQ, Yamahara J, Roufogalis BD. *Punica granatum* flower extract, a potent alpha-glucosidase inhibitor, improves postprandial hyperglycemia in Zucker diabetic fatty rats. J Ethnopharmacol 2005; 99: 239-244.
62. Krishnakumar K, Augusti KT, Vijayammal PL. Hypoglycaemic and anti-oxidant activity of *Salacia oblonga* Wall, extract instreptozotocin-induced diabetic rats. Indian J Physiol Pharmacol 1999; 43: 510-514.
63. Gray AM, Abdel-Wahab YH, Flatt PR. The traditional plant treatment, *Sambucus nigra* (elder), exhibits insulin-like and insulin-releasing actions *in vitro*. J Nutr 2000; 130: 15-20.
64. Hou Z, Zhang Z, Wu H. Effect of *Sanguis draxonis* (a Chinese traditional herb) on the formation of insulin resistancein rats. Diabetes Res Clin Pract 2005; 68: 3-11.
65. Ojewole JA. Hypoglycemic effect of *Sclerocarya birrea* [(A. Rich.)Hochst.Anacardiaceae] stem-bark aqueous extract in rats. Phytomedicine 2003; 10:, 675-681.
66. Beh JE, Latip J, Abdullah MP, Ismail A, Hamid M. Scoparia dulcis (SDF7) endowed with glucose uptake properties on L6 myotubes compared insulin. J Ethnopharmacol 2010; 129: 23-33.
67. Pari L, Latha M. Antihyperlipidemic effect of *Scoparia dulcis* (sweet broomweed) in streptozotocin diabetic rats. J Med Food 2006; 9: 102-107.
68. Saxena AM, Bajpai MB, Murthy PS, Mukherjee SK. Mechanism of blood sugar lowering by a Swerchirin containing hexane fraction (SWI) of *Swertia chirayita*. Ind J Exp Biol 1993; 31: 178-181.
69. Rao BK, Rao CH. Hypoglycemic and antihyperglycemic activity of *Syzygium alternifblium* (Wt.) Walp. Seed extracts in normal and diabetic rats. Phytomedicine 2001; 8: 88-93.
70. Kasetti RB, Rajasekhar MD, Kondeti VK, Fatima SS, Kumar EG, Swapna S, Ramesh B, Rao CA. Antihyperglycemic and antihyperlipidemic activities of methanol:water (4:1) fraction isolated from aqueous extract of *Syzygium alternifolium* seeds in streptozotocin induced diabetic rats. Food Chem Toxicol 2010; 48: 1078-1084.
71. Kasabri V, Flatt PR, Abdel-Wahab YH. *Terminalia bellirica* stimulates the secretion and action of insulin and inhibits starch digestion and protein glycation *in vitro*. Br J Nutr 2010; 103: 212-217.

Rakhee Raj, E-mail:- srpharma@rediffmail.com

72. Singh I, Singh PK, Bhansali S, Shafiq N, Malhotra S, Pandhi P, Pal Singh A. Effects of three different doses of a fruit extract of *Terminalia chebula* on metabolic components of metabolic syndrome, in a rat model. Phytother Res 2010; 24: 107-112.
73. Rao NK, Nammi S. Antidiabetic and renoprotective effects of the chloroform extract of *Terminalia chebula* Retz.seeds in streptozotocin-induced diabetic rats. BMC Complement Altern Med 2006; 6: 17.
74. Murali YK, Anand P, Tandon V, Singh R, Chandra R, Murthy PS. Long-term effects of *Terminalia chebula* Retz.on hyperglycemia and associated hyperlipidemia, tissue glycogen content and *in vitro* release of insulin in streptozotocin induced diabetic rats. Exp Clin Endocrinol Diabetes 2007; 115: 641-646.
75. Esmaeili MA, Zohari F, Sadeghi H. Antioxidant and protective effects of major flavonoids from *Teucrium polium* on beta-cell destruction in a model of streptozotocin-induced diabetes. Planta Med 2009; 75: 1418-1420.
76. Sengupta S, Mukherjee A, Goswami R, Basu S. Hypoglycemic activity of the antioxidant saponarin, characterized as alpha-glucosidase inhibitor present in *Tinospora cordifolia*. J Enzyme Inhib Med Chem 2009; 24: 684-690.
77. Noor H, Ashcroft SJ. Pharmacological characterization of the anti-hyperglycemic properties of *Tinospora crispa* extract. J Ethnopharmacol 1998; 62: 7-13.
78. Bnouham M, Merhfour FZ, Ziyyat A, Mekhfi H, Aziz M, Legssyer A. Antihyperglycemic activity of the aqueous extract of *Urtica dioica*. Fitoterapia 2003; 74: 677-681.
79. Kavalali G, Tuncel H, Göksel S, Hatemi HH. Hypoglycemic activity of *Urtica p'dulifera* in streptozotocin-diabetic rats. J Ethnopharmacol 2003; 84: 241-245.
80. Chattopadhyay RR, Sarkar SK, Ganguly S, Banerjee RN, Basu TK. Hypoglycemic and anti-hyperglycemic effect of *Vinca rosea* Linn. Ind. J Physiof Pharmacol 1991; 35: 145-151.
81. Adallu B, Radhika B. Hypoglycemic, diuretic and hypocholesterolemic effect of winter cherry (*Withania somnifera*, Dunal) root. Indian J Exp Biol 2000; 38: 607-609.
82. Udayakumar R, Kasthurirengan S, Vasudevan A, Mariashibu TS, Rayan JJ, Choi CW, Ganapathi A, Kim SC. Antioxidant effect of dietary supplement *Withania somnifera* L. reduce blood glucose levels in alloxan-induced diabetic rats. Plant Foods Hum Nutr 2010; 65: 91-98.
83. Hoda Q, Ahmad S, Akhtar M, Najmi AK, Pillai KK, Ahmad SJ. Antihyperglycaemic and antihyperlipidaemic effect of poly-constituents in aqueous and chloroform extracts, of *Withania coagulans* Dunal in experimental type 2 diabetes mellitus in rats. Hum Exp Toxicol 2010; 29: 653-658.
84. Hemalatha S, Wahi AK, Singh PN, Chansouria JP. Hypoglycemic activity of Dunal in streptozotocin induced diabetic rats. J Ethnopharmacol 2004; 93: 261-264.
85. Anand KK, Singh B, Chand D, Chandan BK, Gupta VN. Effect of *Zizyphus saliva* leaves on blood glucose levels in normal and alloxan-diabeticrats. J Ethnopharmacol 1989; 27: 121-127.
86. Abdel-Zaher AO, Salim SY, Assaf MH, Abdel-Hady RH. Antidiabetic activity and toxicity of *Zizyphus spinachnsti* leaves. J Ethnopharmacol 2005; 101: 129-138.
87. Skim F, Lazrek HB, Kaaya A, el Amri H, Jana M. Pharmacological studies of two antidiabetic plants: Globuiaria *alypum* and *Zygophy Uumgaetulum*. Therapie 1999; 54: 711-715.

Conflict of Interest: None declared,
Received: 22 November 2016, Revised: 28 November 2016, Accepted: 02 December 2016

Rakhee Raj, E-mail:- srpharma@rediffmail.com