

Polyherbal formulations based on Indian medicinal plants as antidiabetic phytotherapeutics

Shikha Srivastava^{1,*}, Vijay Kumar Lal², Kamlesh Kumar Pant³

¹Department of Pharmacy, Sagar institute of technology and Management Barabanki, India

²Director, Department of Pharmacy, Sagar Institute of Technology and Management Barabanki, India.

³Head Department of Pharmacology, Chatrapati Sahuji Maharaj Medical University, Lucknow, India

*Corresponding Author: Email: Shkh.srivastava@gmail.com

Received: 7 September 2011, **Revised:** 26 September 2011, **Accepted:** 13 October 2011

Abstract

In spite of all the advances in therapeutics, diabetes still remains a major cause of morbidity and mortality in the world. Herbal formulations are becoming popular now days particularly in the treatment of Type 2 diabetes. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal formulations are preferred due to lesser side effect and low cost. This review focuses on the potential of different polyherbal formulation in the treatment of diabetes and also reviews their pharmacological investigations.

Key words: Polyherbal, formulation, antidiabetic activity, medicinal plants, Type 2 diabetes, ayurvedic

Introduction

Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid, and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both (Joseph, 2011; Mutalik 2003). It is one of the refractory diseases identified by Indian Council of Medical Research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a growing problem in the contemporary world (Piyush *et al* 2006). India has today become the diabetic capital of the world with over 20 million diabetes and this number is likely to increase to 57 million by 2025 (Cook *et al*,2008). This astronomic increase in the prevalence of diabetes has made diabetes a major public health challenge for India and is become important human ailment afflicting many from various walks of life in different countries and once again the whole world being looked upon Ayurvedic the oldest healing system of medicine for the treatment of diabetes (Joseph, 2011). Although there are many synthetic medicines developed for patients, but it is the fact that it has never been reported that someone had recovered totally from diabetes (Zhengh *et al*, 2004). The modern oral hypoglycemic agents produce undesirable and side effects. Thus in the recent years considerable attention has been directed towards the antidiabetic potential

of medicinal plants and their herbal formulation in the management of disease. Here we enlisting (table 1) some of the medicinal plants with potential antidiabetic activities reported with their possible mode of action

Table 2. Medicinal plants used for the treatment of diabetes.

Plant name	Part Used	Possible mechanism of action	References
<i>Aegle marmelos</i>	Leaf	Increases utilization of glucose; either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion and has potent antioxidant activity, which may account for the hypoglycemic potential	Sachdewa et al, 2001
<i>Allium cepa</i>	Bulb	Lowers blood glucose level and has potent antioxidant activity, which may account for the hypoglycemic potential	Augusti,1973
<i>Allium sativum</i>	Whole plant	Increased the insulin like activity of plasma	Jain et al,1975
<i>Aloe vera</i>	Whole plant	Maintains glucose homeostasis by controlling the carbohydrate metabolizing enzymes	Rajasekaran et al,2004; Okyar et al,2001
<i>Artemisia pallens</i>	Aerial part	Inhibits glucose re-absorption or increase in peripheral glucose utilization	Subramoniam et al,1996
<i>Annona squamosa</i>	Leaf	Lowers blood glucose level	Gupta et al,2005
<i>Andrographis paniculata</i>	Whole Plant	Prevents glucose absorption from gut	Yu BC et al,2003
<i>Azadirachta india</i>	Leaf	Reduce blood glucose level by regeneration of β cells	Chatopadhyay et al,1996
<i>Biophytum sensitivum</i>	Whole plant leaf	Stimulates pancreatic beta cells to release insulin.	Puri et al,1998
<i>Beta vulgaris</i>	Root	Lowers blood glucose level	Yoshikawa et al,1996
<i>Brassica juncea</i>	Whole plant	Increases the concentration of hepatic glycogen and glycogenesis and suppressed the activity of glycogen phosphorylase and gluconeogenic enzymes, lead to reduction in glycogenolysis and gluconeogenesis	Khan et al,1995
<i>Boerhavia diffusa</i>	Leaf	Increases plasma insulin levels and improves glucose tolerance, produced significant antioxidant activity	Satheesh et al, 2004

<i>Cassia auriculata</i>	Flower	Increased utilization of glucose through increased glycolysis	Abesundara <i>et al</i> ,2004; Latha <i>et al</i> ,2003
<i>Caesalpinia bonducella</i>	Seed	Increases the release of insulin from pancreatic cells	Sharma <i>et al</i> ,1997
<i>Catharanthus roseus</i>	Leaf	Increases metabolism of glucose	Singh <i>et al</i> ,2001
<i>Cajanus cajan</i>	Leaf and stem twigs	It lowers plasma glucose level	Esposito <i>et al</i> ,1991
<i>Citrullus colocynthis</i>	Seed	The oral administration of plant extract reduced the plasma level of AST and LDH significantly.	Al-Ghaithi <i>et al</i> ,1995
<i>Coccinia indica</i>	Leaves	Suppresses glucose synthesis, through depression of the key gluconeogenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and enhances glucose oxidation by shunt pathway through activation of its principal enzyme glucose-6-phosphate dehydrogenase	Kamble <i>et al</i> ,1994; Shibib <i>et al</i> ,1993
<i>Casearia esculenta</i>	Root	Exhibits significant reduction in blood glucose level, a decrease in the activities of glucose-6-phosphatase and fructose-1,6-bisphosphatase and an increase in the activity of liver hexokinase, resulting in potent hypoglycemic activity	Prakasam <i>et al</i> ,2002
<i>Camellia sinensis</i>	Leaves	Epigallocatechin gallate, present in tea increases insulin activity and prevent oxidative damages, responsible for the hypoglycemic activity	Gomes <i>et al</i> ,1994
<i>Enicostemma littorale</i>	Leaves	Decrease glycosylated Hb & glucose 6 phosphatase	Srinivasan <i>et al</i> ,2005; Maroo <i>et al</i> 2002
<i>Eugenia jambolana</i>	Seed powder	It exhibits normoglycemia and better glucose tolerance.	Ravi <i>et al</i> ,2004
<i>Eucalyptus globulus</i>	Leaves	Increase insulin secretion from clonal pancreatic beta line (BRIN-BD 11)	Gray <i>et al</i> ,1998
<i>Ficus bengalensis</i>	Bark	Inhibits insulin degradative processes	Kumar <i>et al</i> ,1989

<i>Gymnema sylvestre</i>	Leaves	Lowers plasma glucose level	Ghalap et al,1998
<i>Hibiscus rosa sinensis</i>	Whole Plant Leaf and Flower	Stimulates insulin secretion from pancreatic beta cells and increases utilization of glucose, either by direct stimulation of glucose uptake.	Sachdewa et al, 2001b.
<i>Mangifera indica L</i>	Leaf	Possibly act through the intestinal reduction of glucose as well as pancreatic and extra pancreatic mechanism	Aderibigbe et al,1999
<i>Morus indica L</i>	Leaf	Acts by increasing glucose uptake	Andallu et al,2002
<i>Murraya koeingii</i>	Leaf	Increases glycogenesis and decreases glycogenolysis and gluconeogenesis	Khan et al,1995
<i>Momordica charantia</i>	Fruit	Reduce blood glucose level	Chen F et al,1995
<i>Ocimum sanctum</i>	Leaf	Its powdered leaf has produced potent hypoglycaemic and hypolipidemic effect in normal and diabetic rats	Vats et al,2004a
<i>Salacia reticulata</i>	Whole plant	Inhibits alpha-glucosidase activity	Jayawardena et al,2005
<i>Swertia chirayita</i>	Whole plant	Stimulates insulin release from islets of Langerhans by depleting aldehyde-fuchsin stained beta-granules and immunostained insulin	Saxena et al,1993;Saxena et al,1991
<i>Syzygium cumini</i>	Seed	Decrease blood glucose level and also inhibit alpha glucosidase enzyme.	Pandey et al,2002
<i>Scoparia dulcis</i>	Leaves	Decrease glycosylated Hb & Inc. total Hb, Insulin-secretagogue activity	Pari et al,2002
<i>Trigonella foenum graceum</i>	Seed	Decrease blood glucose concentration	Ajabnoor et al,1998; Onal et al,2005
<i>Vinca rosea</i>	Whole plant	Alpha glucosidase inhibitors	Ghosh et al, 2001
<i>Withania somnifera</i>	Leaves	Beta cell rejuvenation, regeneration, stimulation	Andallu et al,2000
<i>Zingiber officinale</i>	Leaves	Decrease blood glucose level.	Akhani et al,2004

Major formulations used in Ayurveda are based on herbs used as decoctions, infusion, tinctures and powders. Drug formulation in Ayurveda (As mention in Ayurvedic treatise like Charaka Samhita, Sushruta Samhita) is based on two principles: (a). Use as single drug, and (b). Use of more than two drugs. When two or more herbs are used in formulation they are known as polyherbal formulation. Sometimes herbs are combined with mineral preparation.

The concept of polyherbalism is peculiar to Ayurveda although it is difficult to explain in term of modern parameter. Sarandghar Samhita highlights the concept of synergism behind polyherbal formulations. Ayurveda has fundamental aspects for drug formulation. The herbs are selected according to disease other herbs are used to prevent side effect arising from chief herb. It is evident that there are many herbal formulations of varying potency since these preparation act by different mechanism, it is theoretically possible that different combination of these extract will do better job in reducing blood glucose. In the traditional system of plant medicine it is usual to use plant formulation and combined extract of plant are used as a drug of choice rather than individual ones (Kumar, 2010)], to get the benefit of synergism and to find suitable antidiabetic and antioxidant combination therapy. Here we focuses on potential of different polyherbal formulation that have been confirmed by scientific investigation, which appear to be most effective relatively nontoxic and have substantial documentation of efficacy.

Dihar

A polyherbal formulation containing eight different herbs *Syzygium cumini*, *Momordica charantia*, *Embllica officinalis*, *Gymnema sylvestre*, *Enicostemm*, *Azadirachta indica*, *Tinospora cordifolia* and *Curcuma longa* (Patel *et al*2009). Literatures revealed that combination of these eight herbs shows effective Anti-hyperglycemic activity in Strptozotocin (STZ,45 mg/kg iv single dose) induced type 1 diabetic rats. Treatment with Dihar (100 mg/kg) for 6 weeks produced decrease in STZ induced serum glucose and lipid levels and increases insulin levels as compared to control. Dihar produced significant decrease in serum creatinine urea level and lipid peroxidation in diabetic rats. Administration of Dihar to diabetic rats significantly increased the activity of antioxidant enzyme (Patel *et al* 2009).

Diabet

A polyherbal formulation containing *Curcuma longa*, *Coscinium fenestratum*, *Strychnos potatorum*, *Phyllanthus reticulatus*, *Tamarindus indica*, *Tribulus terrestris* and containing marketed for diabetes was investigated for its glucose tolerance and antidiabetic activity in alloxan induced diabetic rats. The glucose tolerance test and hypoglycemic studies carried out in normal rats at a dose of 500mg/kg. The product showed its effectiveness at a dose of 500 mg/kg but does not hypoglycemic effect (Patel *et al*, 2009).

Diasol

A polyherbal antidiabetic formulation containing plant extracts of *Eugenia jambolana*, *Foenum graceum*, *Terminalia chebula*, *Quercus, infectoria*, *Cuminum cyminum*, *Taraxacum officinale*, *Embllica officinalis*, *Gymnea sylvestre*, *Phyllanthus nerui* and *Enicostemma littorale* (www.ssbherbs.com; Babuji.*et al*. 2010) Previous investigation showed Diasol prod-

uced 63.4 % reduction of blood glucose level in a dose of 125 and 250 mg/kg b.w i.p and proved to be effective antidiabetic polyherbal formulation(Babuji. *et al*2010).

Dianex

A polyherbal formulation was screened for antidiabetic activity in rats and it has been reported in literatures that Dianex produce significant hypoglycemic activity in both normal and diabetic mice. It was administered orally in different doses of 100, 250 and 500 mg/kg bw up to 6 weeks. Research concluded that the continuous administration of Dianex up to 6 weeks showed it to be effective in long term treatment (Mutalik. *et al.* 2010).

DRF/AY/5001

An indigenous polyherbal formulation (containing *Gymnema sylvestre*, *Syzygium cumini*, *Pterocarpus marsupium*, *Momordica charantia*, *Embllica officinalis*, *Terminalia belirica*, *Terminalia chebula* and *Shudh shilajit*) developed by Dabur Research foundation Gaziaabad, elicit hypoglycemic/antidiabetic effect in both normal and experimentally induced hyperglycemic rats.DRF/AY/5001 inhibited significantly the hyperglycemia induced by epinephrine. It showed significant reduction in blood glucose level at 1-3 hr with single dose treatment in alloxan induced diabetes rats and 15 days treatment of rats with 600 mg/kg of Drf/Ay/5001 was similar to that of Glibenclamide.DRF/AY/5001 gave nearly comaparable result with that of synthetic drug Glibenclamide (Mandlik *et al*, 2008).

Diashis

A study was conducted on polyherbal formulation composed of eight medicinal plants for the management of streptozotocin (STZ)-induced diabetes in rats. As oxidative stress is one of the consequences of diabetes,(Wright and Bacon ,2006) the activities of hepatic antioxidant enzymes and metabolic enzymes were evaluated. The study revealed that treatment with 'Diashis' in STZ-induced diabetic rats resulted in a significant recovery in the activities of hepatic hexokinase, glucose-6-phosphate dehydrogenase, and glucose-6-phosphatase along with correction in the levels of fasting blood glucose, glycated hemoglobin, and liver and skeletal muscle glycogen. The oxidative stress status in the liver was corrected by 'Diashis' which was highlighted by the recovery in the activities of catalase, peroxidase, and glutathione-S-transferase along with the correction in the quantity of thiobarbituric acid-reactive substances and conjugated diene. 'Diashis' was not found to have any metabolic toxicity (Bera *et al*, 2010).

Diabrid

A herbal based antidiabetic formulation for maturity onset diabetic patients was clinically evaluated in 60 diabetic patients for six months. The clinical studies revealed that Diabrid was well tolerated in high doses and was found to be a potential antidiabetic drug in mild and moderate diabetic cases (180-280 mg/dl). The blood sugar level was controlled within 2-8 week depending upon initial blood sugar level. No side effect was observed. The hypoglycemic activity was dose dependent and gradual. The drug also maintained the body weight and blood pressure of diabetic patients. No deleterious effect was observed on kidney and liver (Quadri *et al*, 2006).

Diakyur

A polyherbal formulation (composed of *Cassia javanica*, *Cassia auriculata*, *Salacia reticulata*, *Gymnema sylvestre*, *Mucuna pruriens*, *Syzygium jambolaum*, *Terminalia arjuna*), scientifically proved to be a potential antidiabetic formulation in previous studies. Report indicated that Diakyur has shown significant hypoglycemic activity as well as antilipid peroxidative activity so that it can be used as an adjuvant along with allopathic treatment of medicine to treat diabetes as well as to delay the late complications of diabetes (Joshi *et al*, 2007). Literature studies concluded that Diakyur at a dose of 1600 mg/kg p.o is safe for long term treatment in diabetic condition (Chandra *et al* 2007).

Diasulin

A polyherbal formulation containing *Cassia auriculata*, *Coccinia indica*, *Curcuma longa*, *Embllica officinalis*, *Gymnema sylvestre*, *Momordica charantia*, *Scoparia dulcis*, *Syzygium cumini*, *Tinospora cordifolia*, *Trigonella foenum graecum* Previous Investigation suggest that controls the blood glucose level by increasing glycolysis and decreasing gluconeogenesis with a lower demand of pancreatic insulin than in untreated rats. This is possible, because it regulates the activities of hepatic glucose metabolic enzymes (Pari and Saravanan, 2004). Diasulin also resulted in significant decrease in tissue lipids and lipid peroxide formation (Ramalingam and Pari, 2005).

Diabecon

A polyherbal formulation containing *Gymnema sylvestre*, *Pterocarpus marsupium*, *Glycyrrhiza glabra*, *Casearia esculenta*, *Syzygium cumini*, *Asparagus racemosus*, *Boerhavia diffusa*, *Sphaeranthus indicus*, *Tinospora cordifolia*, *Swertia chirata*, *Tribulus terrestris*, *Phyllanthus amarus*, *Gmelina arborea*, *Gossypium herbaceum*, *Berberis aristata*, *Aloe vera*, *Triphala*, *Commiphora wightii*, shilajeet, *Momordica charantia*, *Piper nigrum*, *Ocimum sanctum*, *Abutilon indicum*, *Curcuma longa*, *Rumex maritimus* is reported to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells repair and regeneration and increase c peptide level. It has antioxidant properties and protects B cells from oxidative stress. It exerts insulin like action by reducing the glycated haemoglobin levels, normalizing the microalbuminuria and modulating the lipid profile. It minimizes long term diabetic complications (www.himalayahealthcare.com, www.diabecon.com), Previous Studies also revealed that Diabecon is a safe drug to prevent complications such as retinopathy in diabetic patients. Diabecon resolved retinal and vitreal haemorrhages and its subsequent prevention. It also enhanced the absorption of hard and soft exudates by anti-inflammatory properties Studies concluded that Diabecon can be used as an adjuvant with conventional treatment in NIDDM and IDDM patients.

Dia-Care:

A herbal formulation containing Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal is claimed to be effective for both Type 1, Type 2 diabetes within 90 days of treatment and cures within 18 months. Persons taking insulin will eventually be liberated from the dependence on it. The whole treatment completes in 6 phases, each phase

being of 90 days. Approx. 5 grams (1 tea spoon) powder is mixed with 1/2 glass of water, stirred properly, kept overnight and filtered. The filtrate is taken in the morning on empty stomach. To the remaining medicine fresh water is added and kept for the whole day and is consumed half an hour before dinner. The taste of the drug is very bitter. It is a pure herbal formula without any side effects (Kant *et al.*2002).

Diabetes-Daily Care

Diabetes-Daily Care containing Alpha Lipoic Acid, Cinnamon 4% Extract, Chromax, Vanadium, Fenugreek 50% extract, *Gymnema sylvestre* 25% extract, Momordica 7% extract, Licorice Root 20% extract is a Unique, Natural Formula, which effectively and safely Improves Sugar Metabolism (Modak et al ,2007; www.yourhealthsupply.com/diabetes-daily-care.com/medbroadcast.com/sanofi-aventisca.com).

Diabecure

A formulation containing *Juglans regia*, *Berberis vulgaris*, *Erythrea centaurium*, Millefolium, Taraxacum effective in lowering the blood sugar level (Modak *et al*, 2007).

Diabeta

A formulation containing *Gymnema sylvestre*, *Vinca rosea* (Periwinkle), *Curcuma longa* (Turmeric), *Azadirachta indica* (Neem), *Pterocarpus marsupium* (Kino Tree), *Momordica charantia* (Bitter Gourd), *Syzygiumcumini* (Black Plum), *Acacia arabica* (Black Babhul), *Tinospora cordifolia* , *Zingiber officinale* (Ginger) available in the capsule form is an anti-diabetic with combination of proven anti-diabetic fortified with potent immunomodulators, antihyperlipidemics, anti-stress and hepatoprotective of plant origin. The formulation of Diabeta is based on ancient ayurvedic references, further corroborated through modern research and clinical trials. Diabeta acts on different sites in differing ways to effectively control factors and pathways leading to diabetes mellitus. It attacks the various factors, which precipitate the diabetic condition, and corrects the degenerative complications, which result because of diabetes. Diabeta is safe and effective in managing Diabetes Mellitus as a single agent supplement to synthetic anti-diabetic drugs. Diabeta helps overcome resistance to oral hypoglycemic drugs when used as adjuvant to cases of uncontrolled diabetes. Diabeta confers a sense of well-being in patients and promotes symptomatic relief of complaints like weakness giddiness, pain in legs, body ache, polyuria and pruritis (Modak et al ,2007; www.diabetes-daily-care.com/medbroadcast.com).

ESF/AY/500

A polyherbal formulation intended to be used for diabetic patients has been screened for antioxidant activity and composed of eight medicinal plants, namely *Aerva lanata*, *Aegle marmelos*, *Ficus benghalensis*, *Catharanthus roseus*, *Bambusa arundinaceae*, *Salacia reticulata* and *Szygium cumini* and ‘*Eruca sativa*’ the ethanolic extract of ESF/AY/500 exhibited significant antioxidant activity showing increased levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and reduced glutathione(GSH) and decreased level of lipid peroxidation (Sajeeth *et al* ,2010).

EFPTT/09

A polyherbal formulation containing five ingredients of herbal origin that is used in medicine to treat diabetes. Literature revealed that EFPTT/09 elicits hypoglycemic and antidiabetic effect in both normal and alloxan induced diabetes rats. It also elicited a significant antioxidant effect in diabetic rats by its ability to inhibit lipid peroxidation and elevate the enzymatic antioxidant in pancreatic tissue. It has been found that at a dose of 600 mg/kg the hypoglycemic effect of EFPTT/09 nearly comparable to that of glibenclamide (5 mg/kg.). (Yoganandam and Bimlendu, 2010).

5EPHF

Lanjhiyana et al developed new polyherbal formulation (5EPHF) consisting of five medicinal plant extracts viz., *Aegle marmelos*, *Murraya koenigii*, *Aloe vera*, *Pongamia pinnata* and *Elaeodendron glaucum*. Research showed that treatment with 5EPHF at dose 200 mg/kg to diabetic rats resulted in significant reduction of serum glucose, glycosylated haemoglobin, total cholesterol, triglyceride, low density lipoprotein, creatinine and urea whereas significant increased level of insulin and high density lipoprotein was observed. The formulation treatment significantly inhibited lipid peroxidation and elevates the level of antioxidant enzymes in alloxanized rats (.Lanjhiyana *et al* 2007).

Glyoherb

A polyherbal formulation was evaluated for its antihyperglycemic, antihyperlipidemic and antioxidant effects against normal and streptozotocin-induced diabetic rats. 'Glyoherb' sugar control granules possess potential antidiabetic activity as it lowers serum glucose levels and increases glucose tolerance in STZ-induced type 1 diabetic rats. This polyherbal formulation also possess significant antihyperlipidemic activity as it lowers serum cholesterol and triglyceride levels. 'Glyoherb' did not exert any toxic effects in STZ-induced impaired kidney and liver functions. It was rather found to be improving kidney and liver functions. In addition, 'Glyoherb' possesses potential antioxidant activity as it decreases lipid peroxidation and enhances antioxidant status in diabetic rats. The antidiabetic activity of 'Glyoherb' may be attributed to its antioxidant properties also. Thus previous research concluded that 'Glyoherb' may be regarded as a promising natural and safe remedy for the prevention or delay of diabetic complications (Thakkar and Patel, 2007).

Karmin Plus

An indigenous polyherbal formulation containing *Momordica charantia*, *Azadirachta indica*, *Picrorrhiza kurroa*, *Ocimum sanctum* and *Zinziber officinale* was evaluated for antidiabetic activity by Banger et al and it was found that product showed effectiveness at two dose levels at 200 mg/kg and 400 mg/kg b.w for antidiabetic activity(Om Prakash *et al* 2009).

Okudiabet

Studies on formulation containing *stachytarpheta angustifolia*, *Alstonia congensis* bark and *Xylopia acthiopica* fruits extract showed that polyherbal formulation was effective in decreasing plasma glucose levels in the diabetic rats and proved to have a better plasma

glucose lowering effect that glibenclamide and also having good reducing effect on Cardiovascular system. The high LD 50 value (16.5g/kg) indicates that formulation could be safe for use (Ogbonnia *et al.*, 2010).

SMK001

Literatures revealed that SMK001 is a potential antidiabetic polyherbal formulation. Kim Jong Dae *et al.* investigated the therapeutic anti-diabetic effect of SMK001, a poly herbal formula was evaluated in the streptozotocin (STZ; 60 mg/kg, single intraperitoneal injection) induced diabetic rats. Result showed that SMK001 significantly reduces the blood and urine glucose level and it shows more favourable effect at a dose of 100mg/kg compared to that of Glibenclamide 5mg/kg (Kim Jong Dae *et al.*, 2006).

PM021:

Herbal formula consists of two herbal components, Mori Folium and Aurantii Fructus, is routinely used to treat diabetes in Korea. Jong Hoon Kim investigated the antidiabetic effect of PM021 on the type II diabetic Otsuka Long–Evans Tokushima Fatty (OLETF) rats. The results showed that PM021 significantly prevented increases in body weight, blood glucose, and urine and food intake that resulted from the induction of obesity and diabetes. PM021 also improved glucose tolerance in OLETO rats. However, PM021 had no effect on LETO rats, a control group of OLETF rats. Taken together, these findings indicate that PM021 has distinct anti-diabetic effects without any adverse effects or toxicities (Jong-Hoon Kim,).

An indigenous herbal formulation containing Methi, Black sesame seed, Katha safeed, Neem leaves, Karela were evaluated for hypoglycemic activity on adult wistar albino rats using normo glycemic, glucose loaded and alloxan induced hyperglycemic rats. Research proved that this formulation showed promising results that is comparable to that of reference standard glibemclamide. However the exact biological active constituent responsible for hypoglycemic effect has not been reported (Khan *et al.*, 2011).

In the recent years there is a great interest towards Ayurvedic forms of medication not only for diabetes but also for other disease like arthritis and cancer as the danger and shortcoming of modern medicine have started getting more apparent, majority of Ayurvedic formulation are prepared from herb and many herbal formulation are in market and are immensely used by diabetic patients on the advice of physicians.

Conclusion

The above-mentioned formulations have been considered for their possible hypoglycemic actions and the researchers have carried out some preliminary investigations. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level Thus many different plants have been used individually or in formulations for treatment of diabetes and its complications. One of the major problems with this herbal formulation is that the active ingredients are not well defined. It is important to know the active component and their molecular interaction, which will help to analyze therapeutic

efficacy of the product and also to standardize the product. Efforts are now being made to investigate mechanism of action of some of these plants using model systems.

References

- Abesundara KJ, Matsui T, Matsumoto K. (2004). Alpha-glucosidase inhibitory activity of some Sri Lanka plant extracts, one of which, *Cassia auriculata*, exerts a strong antihyperglycemic effect in rats comparable to the therapeutic drug acarbose. *Journal of Agricultural & Food Chemistry*, 52, 2541–2545.
- Aderibigbe AO, Emudianughe TS, Lawal BA (1999). Antihyperglycaemic effect of *Mangifera indica* in rat. *Phytotherapy Research*, 13, 504–507.
- Ajabnoor MA and Tilmisany AK (1988). Effect of *Trigonella foenum graecum* on blood glucose level in normal and alloxan diabetic mice. *Journal of Ethnopharmacology*, 22, 45-49
- Akhani SP, Vishwakarma SL and Goyal RK (2004). Antidiabetic activity of *Zingiber officinale* in streptozotocin induced type I diabetic rats. *Journal of pharmacy & Pharmacology*, 56, 101-105.
- Al-Ghathith F, El-Ridi, MR, Adeghat E, Amiri MH. (1995). Biochemical effects of *Citrullus colocynthis* in normal and diabetic rats. *Molecular and Cellular Biochemistry*, 261, 143–149.
- Andallu B and Radhika B (2000). Hypoglycemic, diuretic and hypocholesterolemic effect of winter cherry (*Withania somnifera* Dunal) root. *Indian Journal of Experimental Biology*. 38, 607-609
- Andallu B and Varadacharyulu NC. (2002). Control of hyperglycemia and retardation of cataract by mulberry (*Morus indica* L.) leaves in streptozotocin diabetic rats. *Indian Journal of Experimental Biology*, 40, 791-795.
- Augusti KT (1973) Studies on the effects of a hypoglycemic principle from *Allium Cepa* Linn. *Indian Journal of Medical Research*, 61, 1066–1071.
- Joseph B, Jini D (2011). An insight in hypoglycemic effect of traditional indian herbs used in the treatment of diabetes. *Research Journal of Medicinal plant*; 5, 352-376.
- Hamid BSS, Debasish S, Vethambur B, Tajudeen K (2010). Evaluation on safety and efficacy of a polyherbal antidiabetic formulation-DIASOL *Asia Pacific Journal of Molecular Biology & Biotechnology* 18, 59-61.
- Bera TK, De D, Chatterjee K, Ali KM, Ghosh D (2010). Effect of *Diashis*, a polyherbal formulation, in streptozotocin-induced diabetic male albino rats. *International Journal of Ayurveda Research*. 1, 18-24.
- Chandra shekhar Joshi, Ekabaram Sanmuga Priya, Subramanian (2007). Acute and Sub acute toxicity of polyherbal antidiabetic formulation Diakyur in experimental animal models. *Journal of Health Sciences*, 53, 245-249.
- Chatopadhyay RR (1996). Possible mechanisms of antihyperglycemic effect of *Azadirachta indica* leaf extract part. *General Pharmacology*, 27, 3:431-434.
- Chen F, Nakashima N, Kimura I, Kimura M. (1995) Hypoglycemic activity and mechanisms of extracts from mulberry leaves (*Folium mori*) and cortex mori radice in streptozotocin-induced diabetic mice. *Yakugaku Zasshi*, 115, 476–482.
- Cooke DW and Plotnick L (2008). Type 1 diabetes mellitus in pediatrics. *Pediatrics in Review*, 29, 374-385.

- Esposito AM, Diaz A, de GI, DTR, Gupta MP. (1991). Evaluation of traditional medicine: effects of *Cajanus cajan* L. and of *Cassia fistula* L. on carbohydrate metabolism in mice. *Revista Medica de Panama*, 16, 39–45.
- Ghalap S and Kar A. Gymnemic acid from *Gymnema sylvestre* potentially regulates dexamethasone induced hyperglycemia in mice. *Pharmaceutical Biology*, 43, 192-195
- Ghosh S and Suryawanshi SA(2001) Effect of *Vinca rosea* extract in treatment of alloxan diabetes in male albino rats. *Indian Journal of Experimental Biology*, 39, 748-759.
- Gomes A, Vedasiromoni JR, Das M, Sharma RM, Ganguly DK. (1995) Antihyperglycemic effect of black tea (*Camellia sinensis*) in rat. *Journal of Ethnopharmacology*, 45, 223–226.
- Gray AM and Flatt PR. (1998). Antihyperglycemic action of *Eucalyptus globules* (eucalyptus) is associated with Pancreatic & extra pancreatic effects in mice. *Journal of Nutrition*, 128, 2319-2323.
- Gupta RK, Kesari AN, Murth PS, Chandra R, Tandon V, Watal G. (2005). Hypoglycemic and hypoglycemic effect of ethanolic extract of leaves of *Annona squamosa* L. in experimental animals. *Journal of Ethnopharmacology*, 99, 75–81.
- Jain RC, Vyas CR (1975). Garlic in alloxan-induced diabetic rabbits: *American Journal of Clinical Nutrition*, 28; 684–685.
- Jayawardena MH, de Alwis, NM, Hettigoda V, Fernando, DJ. (2005). A double blind randomised placebo controlled cross over study of a herbal preparation containing *Salacia reticulata* in the treatment of type 2 diabetes. *Journal of Ethnopharmacology*, 97; 215–218.
- Kim JH, Chung HS, Kang M, Kim Y, Kim B-S, Kim Y-S, Bae H (2011) Anti-diabetic effect of standardized herbal formula PM021 consisting of Mori Folium and Aurantii Fructus on type II diabetic Otsuka Long–Evans Tokushima Fatty (OLETF) rats. *Diabetes Research & Clinical practice*. 93, 198-204.
- Joshi CS, Priya ES, Venkataraman S (2007). Hypoglycemic and antilipidperoxidation of polyherbal formulation Diakyur in experimentally induced diabetes. *Journal of Health Sciences*, 53, 734-739.
- Kamble SM, Kamlakar PL, Vaidya S, Bambole VD (1998). Influence of *Coccinia indica* on certain enzymes in lycolytic and lipolytic pathway in human diabetes. *Indian Journal of Medical Sciences*, 52, 143–146.
- Shri K, Sahu M, Sanjeev S (2002). Effect of Diabecon (D-400), an Ayurvedic Herbomineral Formulation on Diabetic Retinopathy. *Indian Journal of Clinical Practice*, 12, 49-56.
- Khan A, Ali S, Ahmad J (2011). Antidiabetic activity of traditional herbal formulation. *International Journal of Drug Formulation & Research*, 2, 96-104.
- Khan BA, Abraham A, Leelamma S(1995). Hypoglycemic action of *Murraya koeingii* (curry leaf) and *Brassica juncea* (mustard): mechanism of action. *Indian Journal of Biochemistry & Biophysics*, 32, 106–108.
- Kim JD, Kang SM, Seo BI, Choi HY, Choi HS, Ku SK (2006). Anti-diabetic activity of SMK001, a poly herbal formula in streptozotocin induced diabetic rats: Therapeutic study. *Biological & Pharmaceutical Bulletin*, 29, 477-482.
- Kumar RV, Augusti KT. (1989). Hypoglycemic effect of a leucocyanidin derivative isolated from the bark of *Ficus bengalensis* Linn. *Indian J Biochem & Biophysics*, 26, 400–404.
- Kumar Jaya (2010). Herbal medicine for Type 2 diabetes. *International Journal of Diabetes Developing Countries*, 30; 111-112.

- Lanjhiyana Sweety, Garabadu Debapriya, Ahirwar Dheeraj, Rana Avtar Chand, Ahirwar Bharti, Lanjhiyana Kumar Sanjay (2011). Pharmacognostic Standardization and Hypoglycemic Evaluations of Novel Polyherbal Formulations *Der Pharmacia Lettre* 3, 319-333.
- Latha M, Pari L (2003) Preventive effects of *Cassia auriculata L.* flowers on brain lipid peroxidation in rats treated with streptozotocin. *Molecular & Cellular Biochemistry*, 243, 23–28.
- Li W.L. Zheng H.C, Bukuru J(2004). Natural medicines used in the traditional Chinese medical system for therapy of diabetes mellitus. *Journal of Ethnopharmacology* 92, 1-21.
- Pari L and Saravanan L (2004). Antidiabetic effect of Diasulin, a herbal drug on blood glucose, plasma insulin, hepatic enzymes of glucose metabolism in hyperglycemic rats. *Diabetes. Obesity & Metabolism*, 6, 286–292.
- Maroo J, Vasu VT, Aalinkeel R, Gupta S (2002). Glucose lowering effect of aqueous extract of *Encostemma littorale Blume* in diabetes: a possible mechanism of action. *Journal of Ethnopharmacology*, 81, 317– 320.
- Mandlik RV, Desai SK, Naik SR, Sharma G, Kohli RK (2008). Antidiabetic activity of a polyherbal formulation (DRF/AY/5001). *Indian Journal of Experimental Biology*, 46, 599-606.
- Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TPA. (2007). Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes. *Journal of Cliical & Biochemical Nutrition*, 40, 163–173
- Mutalik S, Sulochana B, Chetana M, Udupa N Devi UP (2003). Preliminary studies on acute and subacute toxicity of an antidiabetic herbal preparation, dianex. *Indian Journal of Experimental. Biology*, 4, 316-320.
- Ogbonnia SO, Mbaka GO, Adekunle A, Anyika EN, Gbolade OE, Nwakakwa N (2010). Effect of a poly-herbal formulation, *Okudiabet*, on alloxan-induced diabetic rats. *Agriculture and Biology Journal of North America*, 1, 139-145.
- Okyar A, Can A, Akev N, Baktir G, Sutlupinar N. (2001). Effect of *Aloe vera* leaves on blood glucose level in type I and type II diabetic rat models. *Phytotherapy Research*, 1, 157–161.
- Onal S, Timur S, Okutucu B (2005). Inhibition of glucosidase by aqueous extract of some potent antidiabetic medicinal herbs. *Preparative Biochemistry & Biotechnology*, 35, 29-36.
- Om PB, EEdwin J, Asghar S, Ahmad S. (2009). Antidiabetic activity of polyherbal formulation (Karmin Plus). *International Journal of Green Pharmacy*, 3, 211-214.
- Pandey M and Khan A (2002). 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*, 40, 1178-1182
- Pari L and Venkateswaran S (2002). Hypoglycemic activity of *Scoparia dulcis L.* in alloxan induced hyperglycemic rats. *Phytotherapy Research*, 16, 662-664.
- Patel SS, Shah RS, Goyal RK (2009). Antihyperglycemic, Antihyperlipidemic, Antioxidant effect of Dihar, a polyherbal Ayurvedic formulation in Streptozotocin induced diabetes rats. *Indian Journal of Experimental Biology*, 47;564-570
- Piyush MP, Natvarlal MP, Ramesh KG (2006). Holistic classification of herbal antidiabetics: A review. *Pharma Times*, 38, 19-25.

- Prakasam A, Sethupathy S, Pugalendi KV (2002). Antihyperglycaemic effect of *Casearia esculenta* root extracts in streptozotocin-induced diabetic rats. *Pharmazie*, 57, 758–760.
- Puri D and Baral N (1998). Hypoglycaemic effect of *Biophytum sensitivum* in the alloxan diabetic rabbits. *Indian Journal of Physiology & Pharmacology*, 42, 401–406.
- Quadri NM, Rehman ZU, Shireen K (2006). Evaluation of Antidiabetic activity of Diabrid, a Herbal Formulation, in Type-II Diabetic Patients. *Journal of The Chemical Society of Pakistan*, 28, 281–283.
- Rajasekaran S, Sivagnanam K, Ravi K, Subramanian S (2004). Hypoglycemic effect of *Aloe vera* gel on streptozotocin-induced diabetes in experimental rats. *Journal of Medicinal Food*, 7, 61–66.
- Sraravanan R and Pari LV (2005) Antihyperlipidemic and Antiperoxiadtative effect of Diasulin,a polyherbal polyherbal formulation in alloxan-induced hyperglycemic rats. *BMC Complimentary & Alternative Medicine*, 4; 5-14.
- Ravi K, Ramachandran B, Subramanian S. (2004) Protective effect of *Eugenia jambolana* seed kernel on tissue antioxidants in streptozotocin induced diabetic rats. *Biol Pharm Bulletin*, 27, 1212–1217.
- Sachdewa A, Nigam R, Khemani LD. (2001). Hypoglycemic effect of *Hibiscus rosa sinensis* L. leaf extract in glucose and streptozotocin induced hyperglycemic rats. *Indian Journal of Experimental Biology*, 39, 284–286.
- Sajeeth CI, Manna PK, Manavalan R, Jolly CI (2010), Phytochemical Investigation and Antioxidant Activity of a Polyherbal Formulation (ESF/AY/500) on Streptozotocin Induced Oxidative Stress in Rats *Der Pharma Chemica*, 2, 184-189.
- Satheesh MA, Pari L (2004). Antioxidant effect of *Boerhavia diffusa* L. in tissues of alloxan induced diabetic rats. *Indian Journal of Experimental Biology*, 42; 989–992.
- Saxena AM, Bajpai MB, Murthy PS, Mukherjee S (1993). Mechanism of blood sugar lowering by a Swerchirin-containing hexane fraction (SWI) of *Swertia chirayita*. *Indian Journal of Experimental Biology*, 31; 178–181.
- Saxena A M, Bajpai MB, Mukherjee SK.(1991) Swerchirin induced blood sugar lowering of streptozotocin treated hyperglycemic rats. *Indian Journal of Experimental Biology*, 29; 674–675.
- Sharma SR, Dwivedi SK, Swarup D. (1997). Hypoglycemic, antihyperglycemic and hypolipidemic activities of *Caesalpinia bonducella* seeds in rats. *Journal of Ethnopharmacology*, 58, 39–44.
- Shibib BA, Khan LA, Rahman R(1993) Hypoglycemic activity of *Coccinia indica* and *Momordica charantia* in diabetic rats: depression of the diabetic mice. *Journal of Asian Natural Product Research*, 2, 321– 327.
- Singh SN, Vats P, Suri S, Shyam R, Kumria MM, Ranganathan S, Sridharan K..(2001) Effect of an hypoglycemic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats. *Journal of Ethnopharmacology*, 76; 269–277.
- Srinivasan M, Padmanabhan M, Prince PS. (2005). Effect of aqueous *Encostemma littorale* Blume extract on key carbohydrate metabolic enzymes, lipid peroxides and antioxidants in alloxan-induced diabetic rats. *Journal of Pharmacy & Pharmacology*, 57; 497–503.
- Subramoniam A, Pushpangadan P, Rajasekharan S, Evans DA, Latha PG, Valsaraj R (1996). Effects of *Artemisia pallens* Wall on blood glucose levels in normal and alloxan-induced diabetic rats. *Jornal of Ethnopharmacology*, 50, 13–21.

- Thakkar NV, Jagruti AP (2010). Pharmacological evaluation of “Glyoherb”: A polyherbal formulation on streptozotocin-induced diabetic rats. *International journal of Diabetes in Developing Countries*, 30, 1–7.
- Umamaheswari S, Joseph LD, Srikanth J, Lavanya R, D. Chamundeeswari Reddy C. Uma Maheswara. (2009) Antidiabetic Activity of a Polyherbal Formulation (DIABET) *International Journal of Pharmaceutical Sciences*, 2, 18-22.
- Vats V, Yadav SP, Grover JK. (2004). Ethanolic extract of *Ocimum sanctum* leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. *Journal of Ethnopharmacology*, 90, 155–160.
- Wright E Jr, Scism-Bacon JL, Glass LC (2006). Glass .Oxidative stress in type 2 diabetes: the role of fasting and postprandial glycaemia *International Journal of Clinical Practice*, 60, 308–314.
- Yoganandam G Prakash, Jha Kumar Bimlendu Effect of EFPTT/09, a herbal formulation, on blood sugar of normal and alloxan induced diabetic rats *Res J Pharm Bio Curr Sci* 2010; 1(4):987.
- Yoshikawa M, Murakami T, Kadoya M, Matsuda H, Muraoka O, Yamahara J, Murakami N(1996) Medicinal foodstuff. III. Sugar beet. Hypoglycemic oleanolic acid oligoglycosides, beta vulgarosides I, II, III, and IV, from the root of *Beta vulgaris* L. (Chenopodiaceae). *Chemical and pharmaceutical Bulletin* (Tokyo),44;1212–1217.
- YuBC, Hung CR, Chen WC, Cheng JT (2003). Antihyperglycemic effect of andrographolide in streptozotocin-induced diabetic rats. *Planta Medica*, 69; 1075–1079.