A Review of Recent Investigations on Medicinal Herbs Possessing Anti-Diabetic Properties

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Abstract

Globally, the pervasiveness of chronic, non-communicable disease diabetes mellitus is growing by leaps and bounds. It is one of the major causes of premature morbidity and mortality worldwide. Almost 3.2 million people die of diabetes across the world every year. The worldwide prevalence of diabetes is 6.4% (corresponding to 285 million people); this varies from 10.2% in the Western Pacific to 3.8% in the African region and expected to grow up to 7.4% (439 million) of the adult population by 2030. In the last 20 years there has been a threefold increase in the prevalence of diabetes. It is estimated that there are 30 to 33 million diabetics in India now, and every fourth diabetic in the world today is an Indian. Indians are genetically more susceptible to diabetes and the WHO predicts the number of diabetics in India would go up to 80 million by 2030. WHO has also issued a warning that India is going to be the diabetes capital of the world with Chennai emerging as the diabetic capital of India. Many plants possessing hypoglycemic principles/properties are known to exist in nature. Also a large number of polyherbal formulations (PHF’s) derived from these plants are presently being prescribed as medicinal/dietary supplements for diabetes mellitus. Even the WHO (World Health Organization) approves the use of plant drugs for different diseases, including diabetes mellitus. However, these formulations lack proper standardization of the active constituents. There is an urgent need to address the issues of scientific authenticity about their efficacy, safety and their interaction with modern allopathic drugs. The paper reviews composition, active principles and pharmacological effects of some important plants which are widely used in commercially available herbal and polyherbal formulations and provides a detailed list of plants reported to possess potential anti-diabetic activity.

Keywords: Diabetes mellitus; diabetes management; polyherbal formulations; alternative medicine; anti-diabetic activity

Introduction

Diabetes mellitus is a major endocrine disorder affecting more than 10% population in the contemporary world [1]. India has the dubious distinction of having the largest number of people with diabetes. Its occurrence in more affluent societies is spectacular and of general concern [2]. It is a debilitating metabolic disorder and robs persons of their energy and vitality. Population-based surveys of 75 communities in 32 countries illustrate that diabetes is rare in communities developing countries where a traditional lifestyle has been preserved. By contrast, some Arab, migrant Asian Indian, Chinese, and U.S. Hispanic communities that have undergone westernization and urbanization are at higher risk; in these populations, the prevalence of diabetes ranges from 14 to 20% (Table 1). Therefore, as considered previously it is no more a disease restricted to developed nations rather it is becoming the major health concern in developing nations (Figure 1 a & b). In spite of the introduction of the hypoglycemic agents, diabetes and related complications continue to be a major medical problem. Treatment of this disease with insulin and its derivatives is an invasive process and make the patients more susceptible to hypoglycemic episodes, premature atherosclerosis due to hyperinsulinemia, lipodystrophy [3]. Treatment with sulfonylureas may be associated with hypoglycemia, flatulence, weight gain, hyperinsulinemia, paresthesias, transient leukopenia, agranulocytosis, dementia and it is contraindicated in nursing mothers [4]. Biguanides may induce lactic acidosis, metallic taste, anorexia, vitamin B₁₂ deficiency and are contraindicated in patients suffering from cardiovascular, respiratory [5], hepatic and renal diseases [6]. Meglitinide analogues given preprandially have been found to arouse dyspepsia, arthralgia in some patients and cautioned in hepatic disease [7]. Thiazolidinediones may cause plasma volume expansion, mild anemia, myalgia, hepatic dysfunction, may fail contraception therapy and is contraindicated in liver and congestive heart failure [8]. α-Glucosidase inhibitors, the mild option to overcome insulin resistance may lead to gastric discomfort mainly due to flatulence and diarrhea particularly after a high carbohydrate meal and may also interfere with iron absorption [9]. Moreover, literature reports quote gain in body weight, cataracts and macular degeneration during oral anti-diabetic treatment in some patients. Therefore, the need of the hour is to look for a treatment which not only checks the glucose levels in circulation system, but at the same time avoids the adverse effects associated with the currently available

| Country/Region               | People suffering from diabetes (in millions) | 2000   | 2030   |
|------------------------------|---------------------------------------------|--------|--------|
| India                        |                                             | 31.7   | 79.4   |
| South East Asia              |                                             | 22.3   | 58.1   |
| Middle East Asia             |                                             | 20.0   | 52.8   |
| China                        |                                             | 20.8   | 42.3   |
| Europe                       |                                             | 28.3   | 37.4   |
| United States and Canada     |                                             | 19.7   | 33.9   |
| Latin America and The Caribbean |                                       | 13.3   | 33.0   |
| Sub-Saharan Africa           |                                             | 7.1    | 18.6   |
| Australia                    |                                             | 0.9    | 1.7    |

Table 1: Prevalence of diabetes: Estimated number of people region wise for the year 2000 and 2030.

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Received August 27, 2011; Accepted October 24, 2011; Published October 26, 2011

Citation: Aggarwal N, Shishu (2011) A Review of Recent Investigations on Medicinal Herbs Possessing Anti-Diabetic Properties. J Nutr Disorders Ther 1:102. doi:10.4172/2161-0509.1000102

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Gymnema sylvestre® plant derived bioactive products. The current review focuses on the botanicals as well as the acceptance of synergistic combinations of more importantly also provide guarantees of market exclusivity for barriers for botanicals and related products. These new guidelines botanical drugs. This keen interest has provided a significant fillip to (European Medicines Agency) have shown keen interest in reviewing for diabetes mellitus also suggest that it acts by regeneration of residual β-cells in insulin levels provided by repair/regeneration of endocrine pancreas. Investigations in streptozotocin treated rats indicate that this plant brings about blood glucose homeostasis through increased serum insulin levels provided by repair/regeneration of endocrine pancreas. Further clinical trials in patients with insulin dependent diabetes mellitus also suggest that it acts by regeneration of residual β-cells in insulin dependent diabetes mellitus and is insulinotropic. It is also one of the chief ingredients of ayurvedic preparations being sold as a remedy to treat diabetes mellitus available as Madhumehari Yog (Shree Baidyanath Ayurved Bhawan Private Limited, Jhansi, India), Diabecon® (Himalaya Herbal Healthcare®, Makali, Bangalore, India) and Amree plus (Aimil Pharmaceuticals (India) Limited).

Bitter melon also known as karela, bitter gourd, bitter apple, commercially available herbal and PHFs and provides an exhaustive list of plants with potential anti-diabetic activity.

Plants possessing hypoglycemic activity

The judicious and liberal use of medicinal plants in treatment of various human diseases has led to discovery and establishment of biological activity of many potent phytochemicals possessing hypoglycemic activity (e.g. glycosides, flavonoides, terpenes, steroidoid saponins, alkaloids, polysaccharides). The use of fresh fruit juice of karela (momordica), seeds of methi (fenugreek), jamun (black plum) seed powder, leaves of gurmar (gymnema) are some examples of the home remedies for diabetes which are being practiced since ages. More recently these natural remedies are being formulated as PHFs and prescribed in conjunction with the allopathic drugs. Table 2 (Shown as supplementary) enlists some polyherbal and herbal anti-diabetic formulations currently available in the Indian and international market. More than 400 plants have been incorporated in approximately 700 recipes which are used to treat diabetes mellitus in almost two thirds of the world population [12]. Extensive literature survey suggests that in the past ten years a large number of plants have been investigated for their hypoglycaemic potential. Table 3 (Shown as supplementary) enlists some of the important plants with potential anti-diabetic activity. Botanical source, active principles and pharmacological activities and mechanism of action of some of the important plants (Figure 2) which are widely used in commercially available polyherbal formulations are described below:

Gymnema is a woody plant found in tropical forests of India and Africa, biologically known as Gymnema sylvestre from family Asclepiadaceae, commonly called the milkweed family. It is commonly known as “gurmar”. The major bioactive constituents of gymnema are a group of oleanane type triterpenoid saponins known as gymnemic acids (gymnemosides) [178]. The active principles (gymnemic acids) show selective anesthetic effect on the sweet taste buds [179]. It has been reported to be an effective anti-diabetic agent in lowering blood sugar in both type I and type II diabetes. It also acts as a hepatoprotective, hypolipidemic, antiatherosclerotic, stomachic, diuretic, refrigerant, astringent and tonic. Experimental studies on rats showed comparable anti-hyperglycemic effect to that of tolbutamide. Gymnema’s antidiabetic activity appears to be due to a combination of mechanisms. It increases the activity of enzymes responsible for glucose uptake and utilization, and inhibits peripheral utilization of glucose by somatotrophin and corticotrophin [180]. Plant extracts have also been found to inhibit epinephrine-induced and corticosteroid-induced hyperglycemia [102]. The drug influences the disturbed carbohydrate metabolism in hyperglycemic animals by limiting the carbohydrate turnover and thus inhibiting the vicious cycle of hyperglycemia. It is known as a hepatoprotective, hypolipidemic, antiatherosclerotic, stomachic, diuretic, refrigerant, astringent and tonic. Experimental studies on rats showed comparable anti-hyperglycemic effect to that of tolbutamide. Gymnema’s antidiabetic activity appears to be due to a combination of mechanisms. It increases the activity of enzymes responsible for glucose uptake and utilization, and inhibits peripheral utilization of glucose by somatotrophin and corticotrophin [180]. Plant extracts have also been found to inhibit epinephrine-induced and corticosteroid-induced hyperglycemia [102]. The drug influences the disturbed carbohydrate metabolism in hyperglycemic animals by limiting the carbohydrate turnover and thus inhibiting the vicious cycle of hyperglycemia. Investigations in streptozotocin treated rats indicate that this plant brings about blood glucose homeostasis through increased serum insulin levels provided by repair/regeneration of endocrine pancreas [181]. Further clinical trials in patients with insulin dependent diabetes mellitus also suggest that it acts by regeneration of residual β-cells in insulin dependent diabetes mellitus and is insulinotropic [182]. It is also one of the chief ingredients of ayurvedic preparations being sold as a remedy to treat diabetes mellitus available as Madhumehari Yog (Shree Baidyanath Ayurved Bhawan Private Limited, Jhansi, India), Diabecon® (Himalaya Herbal Healthcare®, Makali, Bangalore, India) and Amree plus (Aimil Pharmaceuticals (India) Limited).

Bitter melon also known as karela, bitter gourd, bitter apple,
bitter cucumber and karolla, is a vegetable cultivated in tropical areas. Botanically it is known as *Momordica charantia* and belongs to family Cucurbitaceae. The fruits and seeds of this plant are been reported to exert hypoglycemic effect in animals and human subjects [183]. It has been taken for centuries as a part of diet. It contains several chemical constituents, including the glycosides (mormordin and charantin) and alkaloid (mormoridine). It also contains an insulin-like polypeptide called Polypeptide-P [184]. Polypeptide-P has been designated as the ‘plant insulin which lowers blood sugar levels when injected subcutaneously gerbils, langurs and diabetic patients [185]. Another hypoglycemic principle charantin a steroidal saponin found in the fruit of the plant is reported to be more potent than the drug tolbutamide [186]. It probably acts through an extrapancreatic mechanism such as improving glucose tolerance, promoting peripheral glucose utilization, decrease blood glucose synthesis through depression of the enzymes glucose-6-phosphatase, fructose-1, and 6 bisphosphatase and enhance glucose oxidation by enzyme glucose-6-phosphate dehydrogenase pathway [187]. Experimental studies in streptozotocin induced diabetic rats indicate that fruit juice of this plant may help in renewal/repair of partially destroyed β-cells [188]. Other reports demonstrate that fruit juice of bitter melon helps in prevention of diabetic cataract [189] and renal damage [190]. It is available in pure powder form (Himalaya Herbal Healthcare®, Makali, Bangalore, India) and is one of the components of Diason (Danish Medicine and Chemical Company) and Divya Madhu Nashini Vati & Divya Madhukalp Vati (Swami Ramdev’s Divya Pharmacy, Haridwar, India).

*Azadirachta indica* (neem) belongs to family Meliaceae. In common language it is also known as margosa, nim, nimba, nimbatikam, arishtha, praneem. The active ingredients are concentrated in seed oil, bark and leaves of this plant. Mainly leaf extracts and seeds are used to treat diabetes. The chief components present in neem oil extracted from seed are nimbin, nimbinin, and nimbidin respectively [191]. The seeds also contain a complex secondary metabolite azadirachtin. The leaves contain nimbin, nimbinine, 6-desacetylnimbinene, nimbandiol, nimbolide and quercetin. Leaves are also reported to contain β-sitosterol, n-hexacosanol and nonacosane [192]. Neem leaf extract and seed improve the blood circulation by diluting the blood vessels [193] and also help in reducing the requirement for insulin by 60-70%, however, the glucose levels remain intact [194]. Oral doses of neem leaf extracts significantly reduce insulin requirements for insulin dependent diabetes and have also been scientifically proved to be effective in treating and preventing diabetes [195]. The possible mechanism of anti-hyperglycemic effect of azadirachta leaf extract was found to be reduction in peripheral utilization of glucose and suppression of glycogenolysis effect due to epinephrine action [196]. The water soluble portion of the alcoholic extract of the leaves was found to possess a significant blood sugar lowering effect in glucose-fed and adrenaline-induced hyperglycemic rats. Treatment with ethanolic extract of leaves of neem is reported to ameliorate pancreatic islet lesions in streptozotocin induced diabetes [197]. According to a research report the blood sugar lowering capacity of extract of *Azadirachta* was more pronounced as compared to other antidiabetic plants like *Catharanthus*, *Gymnema* and *Ocimum* [198]. It is currently marketed by Himalaya Herbal Healthcare®, Makali, Bangalore, India as Neem capsules, Neem Guard™ (Goodcare Pharma Private Limited, Calcutta, India), Pancreatic tonic-glycoprin (US Botanicals, California, US) and Diabet Guard™ Granules and Capsules (Goodcare Pharma Private Limited, Calcutta, India).

*Vinca rosea*, commonly known as sadabahar, baramaasi, Madagaskar periwinkle; botanically is *Catharanthus roseus* and belongs to family Apocynaceae. The plant is reported to contain over 70 alkaloids of the indole type. The aqueous extracts of flower and leaves produce blood glucose homeostasis reversed changes in carbohydrate, protein, and lipid metabolism, metabolic and pathologic changes. The leaf juice or hot water decoction of the flowers and leaves of the plant are used as a folk medicine for the treatment of diabetes [199]. A significant antihyperglycemic activity of the leaf alcoholic extract [59], aqueous extract [200] and the dichloromethane-methanol extract of leaves and twigs [201] is also reported in laboratory animals. Fresh leaf juice of *C. roseus* has been reported to reduce blood glucose in normal and alloxan diabetic rabbits [202]. Literature survey reports hypoglycemic activity of vinca comparable to that of tolbutamide [201] and glibenclamide [202]. Another study shows that *Catharanthus* acts synergistically with fenugreek in reducing blood glucose levels [203]. The fresh leaf juice or leaf powder significantly reduced blood glucose levels to and also the levels of total cholesterol, triglycerides, low density lipoproteins (LDL) and very low density lipoproteins (VLDL) cholesterol and at the same time increased high density lipids (HDL) [204]. The antihyperglycemic action of *C. roseus* may be ascribed to increased plasma insulin concentration and insulin sensitivity due to the regeneration of pancreatic β-cells, which is probably due to the fact that the pancreas contains stable (quiescent) cells that have the capacity to regenerate [204,205]. Therefore, the surviving cells can proliferate to replace the lost cells. Phytochemicals such as flavonoids and alkaloids present in the *C. roseus* leaf powder may have protected the intact functional β-cells from further deterioration through oxidative stress [206]. The reduction in the levels of the LDL and VLDL could have resulted from the antioxidant effect of the fresh leaf juice whose phytochemical components include flavonoids [207]. Therefore, it can be said that *Vinca rosea* manifests its beneficial activity probably through enhanced insulin secretion, extrapancreatic mechanism, β-cell rejuvenation, regeneration and stimulation [208,209]. It is one of the components of Diabeta™ and Dyboss™ (Morpheme Remedies Private Limited, Panchkula, Haryana, India).

*Pterocarpus marsupium* (Indian Kino Tree) is a deciduous tree of the family Leguminosae. It is known as Vijaysar, Bijaka, Pitasa and Pitashalaka. Several polyphenolic compounds/flavonoids and their derivatives have been isolated from various parts of the plant [210]. The key chemical constituents include a diaryl propane derivative: propterol, a stilbene: pterostilbene, a hydrochalcone: pterosiprin, a benzofuranone: marsuparin, a flavonoid: liquiritigenin and a catechin: (-)-epicatechin. The first four are the main components of the heartwood, while (-)-epicatechin is found in the bark of the tree [211]. The phenolics, marsuparin, pterosiprin, and, pterostilbene have been identified as the blood sugar lowering [212] and antihyperlipidemic components [213]. The heartwood of the tree is used to make tumblers/goblets/beakers which are filled with water and allowed to stand overnight to give ‘Bijaka’, a brown tincture, which has shown good results against diabetes has been confirmed [170]. (-)-Epicatechin, its active principle, has been found to be insulinogenic, enhancing insulin release and conversion of proinsulin to insulin in vitro [214]. It restores the normal insulin production of the pancreas and stabilizes the normal sugar levels [215]. The extract of the bark of plant is found to prevent hyperglycemia, hypertyglycemia and insulin resistance [216]. It may also lower blood sugar through an unrelated pathway of that of insulin making it useful in the treatment of both types of diabetics [217]. It is also reported to help regenerate, reverse the damage and repopulate the β-cells in the pancreas. Experimental studies in diabetic rats show that the plant extract also exhibited anti-cataract effect [218]. It is one of the main ingredients of Dialbecon® (Himalaya Herbal Healthcare®, Makali, Bangalore, India), Pancreatic tonic-glycoprin
Fenugreek is a plant in the family Fabaceae botanically known as *Trigonella foenum graecum*. Fenugreek, more often called 'methi' is used both as a herb and as a spice. Fenugreek, a common curry ingredient in Indian and Middle Eastern cuisines, has been shown to regulate blood sugar levels and increase good cholesterol while lowering total cholesterol. The main chemical components of fenugreek seeds include galactomannans, 4-hydroxyisoleucine [226], a pseudo alkaloid trigonelline, steroids like sitosterol, steroidal saponins like trigogenin and gitogenin. Besides these linoleic and linolenic acid; g-lactone, sotolone (responsible for characteristic odor); diosgenin, trigocoumarin, trigomethylcoumarin, fibre and mucilage is also present [227]. Fenugreek seed in powder or germinated form exhibits anti-diabetic properties [228], hypcholesterolaemic effect [229] and effect on thymoxine-induced hyperglycaemia [230]. Fenugreek seeds have been used as an oral insulin substitute, and seed extracts have been reported to lower blood glucose levels [231]. The anti-diabetic and the blood cholesterol lowering activity are linked to the fibre and galactomannan rich fraction present in the seed [227]. The insulinotropic and anti-diabetic properties of the drug are associated with amino acid 4-hydroxyisoleucine [231], which causes direct β-cell stimulation, delayed gastric emptying and inhibition of glucose transport [232]. Various animal studies demonstrate the glucose lowering effects of fenugreek [233]. Another study showed that defatted fraction of the seeds lowered blood glucose levels, plasma triglycerides, somatostatin levels; carbohydrate-induced hyperglycaemia [234]. Also, reduction in cataract incidence has been reported in diabetic mice after treatment with extracts of seeds and leaves of the plant [218]. Galactomannans and saponins also contribute towards hypocholesterolemic activity [235]. Galactomannans decrease the uptake of bile acids, lower the blood and liver concentration of cholesterol and decrease hepatic cholesterol synthesis. It is commercially available as Fenuro™ (Fenfurô™, Panchkula, Haryana, India), Syndrex (Plethico Laboratories, Indore, India), Diabetan™ (Hamida™ Pharma, Lake Forest, California, US) and Fenugreek Plus (Metagenics, Gig Harbor, Washington, US).

Aloe vera a perennial, rosette forming plant belongs to family Liliaceae. It is also known as Indian aloe, Gularcumaria and Gwarpatha. It is rich in anthraquinones, saccharides, enzymes, vitamins, minerals, cholesterol etc. The principal constituents present in the leaves are barbaloin, chrysophanol glycoside and the aglycone, aloe-emodin [236]. The phytosterols present in the aloe vera gel have been reported to possess anti-hyperglycemic activity which may have a long term blood glucose level control effect and would be useful for treatment of Type I and Type II diabetes mellitus [237]. Another study reports the presence of inorganic trace elements (vanadium, zinc, copper; manganese and traces of chromium) in aloe leaf gel possessing hypoglycemic property, probably through improvement in impaired glucose tolerance thereby indirectly contributing to management of diabetes [238]. An experimental report states hypoglycemic activity on insulin dependent and non-insulin dependent rats with the effectiveness being enhanced for non-insulin dependent rats in comparison to glibenclamide [239]. In another study it was observed that *Aloe vera* successfully reduced the blood sugar as well as the blood triglyceride levels [237]. In a group of patients who were not responding to glibenclamide were given to *Aloe vera* and a 48% reduction in blood sugar levels and a 52% reduction in triglycerides was observed [239]. It is present in the anti diabetic polyherbal formulations namely GlucoCare® and Deacon® (Himalaya Herbal Healthcare®, Makali, Bangalore, India).

Stevia *rebaudiana*, commonly known as sweet leaf, sugarleaf, or simply stevia, belongs to the family Asteraceae and is widely grown for its sweet leaves. One of the main constituents of the extract is a diterpene glycoside, stevioside, which is known for its intense sweetness and has been applied as non-caloric sweetener in several countries [240]. The leaf extract of plant has been used for many years in the treatment of diabetes in South America [241]. Recently it has been established that both intravenous as well oral administration of stevioside exerts antihyperglycemic, insulinotropic and glucagonostatic actions [242]. Stevioside and its aglucone steviodol directly potentiate the glucose-stimulated insulin secretion, insulin utilization decreased protein levels of phosphoenol pyruvate carboxykinase by slowing down gluconeogenesis [243]. Stevioside also possess blood pressure lowering properties [244] which can be used as an effective means of preventing diabetic macrovascular complications [242]. Therefore, a multifactorial approach combining blood glucose, blood pressure and lipid lowering would be most effective in treating diabetes and preventing diabetic complications [245]. Stevioside also results in reduction in postprandial blood glucose levels in Type II diabetic patients, indicating improvement in the glucose metabolism [240]. It is marketed as Stevia sweetner and Stevia Plus® by Nutricare Group, Bangladesh.

Turmeric, haldi, arishia, pasupu, haridra, kurkum are the common names for ‘The Indian Solid Gold’ curcumin. Botanically it is *Curcuma longa* belonging to the family Zingiberaceae. The dried powdered rhizomes of *Curcuma*, have extensively been used for centuries as a spice, food preservative, and a yellow colourant for food, drugs, and cosmetics [246]. Curcumin along with its mono- and bisdemethoxy derivatives, collectively called curcuminoids, constitute the major orange-yellow colouring matter and the biologically active constituents of turmeric. Besides curcuminoinds, minor amounts of oils and resins are also present in curcumin. These include α-turmeron, β-turmeron, curlon, zingiberen. It is an important herb in most Ayurvedic treatments of diabetes as it lowers blood sugar, increases glucose metabolism and potentiates insulin activity more than three-folds.
The rhizome extract of the plant is shown to lower blood glucose in experimental, induced- diabetic rats [247]. It has also been observed that in type II diabetes, administration of curcumin reduced the blood sugar, hemoglobin, and glycosylated hemoglobin levels significantly in an alloxan-induced diabetic rat model [248]. Diabetic rats maintained on a curcumin diet for 8 weeks excreted less albumin, urea, creatinine and inorganic phosphorous. Dietary curcumin also partially reversed the abnormalities in plasma albumin, urea, creatinine and inorganic phosphorous in diabetic animals [249]. Several animal studies have demonstrated that curcumin can overcome insulin resistance and can delay cataract incidence in diabetic patients [250]. It is present in many polyherbal formulations viz. Diabecon® (Himalaya Herbal Healthcare®, Makali, Bangalore, India), Diabet Guard™ Granules and Capsules (Goodcare Pharma Private Limited, Calcutta, India) and Diabetes™ (Morpheme Remedies Private Limited, Panchkula, Haryana, India).

Summary

It is estimated that by the year 2030 India will have nearly 22% of the world’s diabetic population. If not adequately managed, diabetes would result in a wide range of complications that have clinical, social and economic complications. Many plants are known to possess anti-diabetic properties. If the active plant constituents of these potential plants are isolated and quantified suitably formulated it would definitely be a positive contribution towards the management of diabetes. Natural phytochemicals can be relevant today only if these are tested within the framework of modern sciences and subjected to the rigorous criteria for quality, safety and efficacy. Further the commercialization of such delivery systems possessing safe phytochemicals will save the patients from the undue side effects caused by present allopathic anti-diabetics. The anti-diabetic therapy with the natural phytochemicals together with a balanced diet rich in carbohydrates and having lesser fat content and regular exercise would help in increasing insulin sensitivity and improve the life quality of a diabetic patient. The study of such medicines may offer a natural key to unlock a diabetologist’s pharmacy for the future.

References

1. Burke JP, Williams K, Narayan KVM, Leibson C, Haftner SM, et al. (2003) A population perspective on diabetes prevention: whom should we target for preventing weight gain? Diabetes Care 26: 1999-2004.

2. Patel PM (2006) Development of quality control parameters of some polyherbal formulations used in diabetes mellitus. Ind J Pharm Educ Res 40: 287-288.

3. Khan A, Anderson RA (2003) Insulin potentiating factor (IPF) present in foods, species and natural products. Pak J Nutr 2: 254-257.

4. Hsu CC, Wahligvst ML, Lee MS, Tsai HN (2011) Incidence of dementia is increased in Type II diabetes and reduced by the use of sulfonylureas and metformin. J Alzheimers Dis 11: 2057-2062.

5. Euriach DT, Tsusyuki RT, Majumdar SR, McAlister FA, Lewanczuk R, et al. (2009) Metformin treatment in diabetes and heart failure: when academic equipoise meets clinical reality. Trials 9: 10-12.

6. Pongwecharak J, Tengmesiri N, Malanusorn N, Paniculata A, Phan D, et al. (2006) Anti-diabetic potentials of Momordica charantia and Andrographis paniculata and their effects on estrous cyclicity of alloxan-induced diabetic rats. Global J Pharmacol 1: 1-5.

7. Black C, Donnelly P, McIntyre L, Royle PL, Shepherd JP, et al. (2007) Hypoglycemic effect of Anacardium occidentale L. methanol extract and α-glucosidase by Adhatoda vasica Nees. Food Chemistry 108: 965-972.

8. Hsu CC, Wahligvst ML, Lee MS, Tsai HN (2011) Incidence of dementia is increased in Type II diabetes and reduced by the use of sulfonylureas and metformin. J Alzheimers Dis 11: 2057-2062.

9. Euriach DT, Tsusyuki RT, Majumdar SR, McAlister FA, Lewanczuk R, et al. (2009) Metformin treatment in diabetes and heart failure: when academic equipoise meets clinical reality. Trials 9: 10-12.

10. Pongwecharak J, Tengmesiri N, Malanusorn N, Panthong M, Pawangkapin N (2009) Prescribing metformin in Type II diabetes with a contraindication: Prevalence and outcome. Pharm World Sci 4: 481-486.

11. Black C, Donnelly P, McIntyre L, Royle PL, Shepherd JP, et al. (2007) Meglitinide analogues for Type II diabetes mellitus. Cochrane Database Syst Rev 2: CD004654.

12. Tolgan KM, Chandramouli J (2003) Hepatoxicity of the thiazolidinediones. Clin Liver Dis 7: 369-379.

13. Aoki K, Muraoka T, Ito Y, Togashi Y, Terauchi Y (2010) Comparison of adverse effects of Metformin, Sulfonylureas and Thiazolidinediones. J Nutr Disorders Ther 1:102. doi: 10.4172/2161-0509.1000102.

14. Chutwadee K, Seong-Ho L, Penchom P, Rungravi T, Seung JB (2011) Antidiabetic activities of Abutilon indicum (L.) sweet are mediated by enhancement of adipoocyte differentiation and activation of the GLUT1 Promoter. Evid Based Complement Alternat Med Article ID 167684.

15. Yasir M, Jain P, Debajoyti, Kharya MD (2010) Hypoglycemic and antihyperglycemic effect of different extracts of Acacia arabica lamk bark in normal and alloxan induced diabetic rats. Int J Phytomedicine 2: 133-138.

16. Edwin J, Siddheshwar BJ, Dharam CJ (2009) Biochemical study on the hypoglycaemic effects of extract and fraction of Acantha catechu wild in alloxan- induced diabetic rats. Int J Diabetes Metab 17: 63-69.

17. Akhtar MS, Iqbal J (1991) Evaluation of the hypoglycaemic effect of Acharyachus aspera in normal and alloxan-diabetic rabbits. J Ethnopharmacol 30: 49-57.

18. Padma V, Subrahmanya KK, Venugopalan SNN (2010) Cypersus rotundus, a substitute for Aconitum heterophyllum: Studies on ayurvedic concept of Abhava Pratidinhi Dravya (drug substitution). J Ayurveda Integ Med 1: 33-39.

19. Bhargav B, Rupal AV, Reddy AS, Narasimhacharya AVRL (2009) Antihyperglycemic and hypolipidemic effects of Adansonia digitata L. on alloxan induced diabetic rats. J Cell Tissue Res 9: 1879-1882.

20. Hong G, Yi-Na H, Bo G, Li P, Inagaki C et al. (2008) Inhibitory effect on α-glucosidase by Adhatoda vasica Nees. Food Chemistry 108: 955-967.

21. Fatima N, Maqsood ZT, Khan B (2005) Study of some micronutrients in selected medicinal plants. Scientia Iranica 12: 269-273.

22. Pillab M, Dhananjayy H, Bandypadayyya U, Mishra DK (2009) Biological activities of crude extracts and chemical constituents of Bael (Aegle marmelos). Ind J Exp Biol 47: 849-861.

23. Momo KEN, Ngwa AF, Dongmo GI, Ouen BE (2009) Antioxidant properties and antinociceptive inhibition of Terminalia superba, Albizia sp., Cola nitida, Cola odorata and Harungana madagascarnensis used in the management of diabetes in Cameroon. J Nutr Sci 55: 732-738.

24. Küçükjurt I, Ince S, Kegel H, Akkol EK, Avci G, et al. (2010) Beneficial effects of Aesculus hippocastanum L. seed extract on the body’s own antioxidant defense system on subacute administration. J Ethnopharmacol 129: 18-22.

25. Campos KE, Diniz YS, Cataneo AC, Faine LA, Alves MJ, et al. (2003) Hypoglycaemic and antioxidant effects of onion, Allium cepa: Dietary onion addition, antioxidant activity and hypoglycaemic effects on diabetic rats. Int J Food Sci Nutr 54: 241-246.

26. Al-Amin ZY, Al-Qattan KA, Shaban LH, Al-M (2007) Anti-diabetic and hypolipidaemic properties of garlic (Allium sativum) in streptozotocin-induced diabetic rats. Int J Diabetes Metab 15: 108-115.

27. Rajasekaran S, Sivagnanam R, Ravi K, Subramanian S (2004) Hypoglycemic effect of Aloe vera gel on streptozotocin-induced diabetes in experimental rats. J Med Food 7: 61-66.

28. Rani S, Khan SA, Ali M (2010) Phytochemical investigation of the seeds of Allthea officinalis L. Nat Prod Res 24: 1358-1364.

29. Girija K, Lakshman K, Chandrika U, Ghosh SS (2011) Anti-diabetic and anti-cholesterolemic activity of methanol extracts of three species of Amaranthus. Asian Pac J Trop Biomed 4: 133-138.

30. Sokeng SD, Lontsi D, Moundipa PF, Jasta HB, Watcho P, et al. (2007) Hypoglycemic effect of Anacardium occidentale L. methanol extract and fractions on streptozotocin-induced diabetic rats. Global J Pharmacol 1: 1-5.

31. Reyes BAS, Bautista ND, Tanquilut NC, anunciado RV, Leung AB, et al. (2006) Anti-diabetic potentials of Momordica charantia and Andrographis paniculata and their effects on estrous cyclicity of alloxan-induced diabetic rats. J Ethnopharmacol 105: 196-210.

32. Hua NK, Phan DV, Thuan ND, oterson CG (2004) Insulin secretion is stimulated by ethanol extract of Anemarrhena asphodeloides in isolated islet of healthy Wistar and diabetic Goto-Kakizaki rats. Exp Clin Endocrinol Diab 112: 520-525.

33. Kaleem M, Medha P, Ahmed QU, Asif M, Bano B (2008) Beneficial effects of Annona squamosa extract in streptozotocin-induced diabetic rats. Singapore Med J 49: 800-804.

34. Xi S, Zhou G, Zhang X, Zhang W, Cai L, et al. (2009) Protective effect of...
of total aralosides of Aralia elata (Miq) Seem (TASAES) against diabetic cardiomyopathy in rats during the early stage, and possible mechanisms. Exp Mol Med 41: 538-547.

35. Subramoniam A, Pushpangadan P, Rajasekaran S, Evans DA, Latha PG, et al. (1996) Effects of Artemisia pannonia wall on blood glucose levels in normal and alloxan-induced diabetic rats. J Ethnopharmacol 50: 13-17.

36. Hannan JM, Marean L, Ali L, Rokeya B, Flatt PR, et al. (2007) Insulin secretory actions of extracts of Asparagus racemosus root in perfused pancreas, isolated islets and clonal pancreatic beta-cells. J Endocrinol 192: 159-168.

37. Muthulingam M (2010) Antidiabetic efficacy of leaf extracts of Asteracantha longifolia (Linn.). Nees. on alloxan induced diabetics in male albino Wistar rats. Int J Pharm Biomed Res 1: 28-34.

38. Loizou NC, US Pat 20,090,110,674, (to William G S, Virginia US), 30 April 2009.

39. Chattopadhyay RR, Bandyopadhyaya M (2005) Effect of Azadirachta indica leaf extract on serum lipid profile changes in normal and streptozotocin induced diabetic rats. Afr J Biomed Res 8: 101-104.

40. Bapat SK, Ansari KU, Candna V (1969) Hypoglycemic effects of Bambusa dendrocalamus. Ind J Physiol Pharmacol 13: 189-190.

41. Serniaw S, Sharma RK (2011) Antibacterial activity of quillerepine lactone glucoside from seed pods of Bacthaii retusa. J Asian Nat Prod Res 13: 75-79.

42. Upwar NK, Patel R, Waseem N, Mahobia NK (2011) Hypoglycemic effect of methanolic extract of Berberis aristata DC stem on normal and streptozotocin induced diabetic rats. Int J Pharm Pharm Sci 3: 222-224.

43. Ozsoy-Sacan O, Karabulut-Bulan O, Bolkent S, Yanardag R, Ozgey Y (2004) Effects of chord (Beta vulgaris L. var Cica) on the liver of the diabetic rats: a morphological and biochemical study. Biosci Biotech Biochem 68: 1640-1648.

44. Chang SL, Chang CL, Chiang Y, Hsieh R, Tzeng C, et al. (2004) Polyacetylenic compounds and butanol fraction from Bidens pilosa can modulate the differentiation of helper t cells and prevent autoimmune diabetes in non-obese diabetic mice. Planta Med 70: 1045-1051.

45. Mushagq A (2005) Ethnophytopathological approaches for the treatment of diabetes by the local inhabitants of district Attock (Pakistan). Ethnobotanical Leaflets 1: Article 24.

46. Rao KN, Krishna MB, Srinivas N (2004) Effect of chronic administration of Boerhaavia diffusa Linn. leaf extract on experimental diabetes in rats. Trop J Pharm Res 3: 306-309.

47. Ponnusamy S, Ravindran R, Zinjarde S, Bhargava S, Kumar AK (2011) Evaluation of traditional Indian antidiabetic medicinal plants for human pancreatic amylase inhibitory activity in vitro. Evid Based Complement Alternat Med Article ID 515647.

48. Yadav SP, Vats V, Ammini AC, Grover JK (2004) Brassica juncea (Rai) significantly prevented the development of insulin resistance in rats fed fructose-enriched diet. J Ethnopharmacol 93: 113-116.

49. Andrade-Cetto A, Heinrich M (2005) Mexican plants with hypoglycemic effect used in the treatment of diabetes. J Ethnopharmacol 99: 325-348.

50. Vartanian GS, Karagezian KG (1981) Normalizing effect of Bryonia alba L. on alloxan-induced diabetes by the local inhabitants of district Attock (Pakistan). Ethnobotanical Leaflets 1:102. doi:10.4172/2161-0509.1000102
Citation: Aggarwal N, Shishu (2011) A Review of Recent Investigations on Medicinal Herbs Possessing Anti-Diabetic Properties. J Nutr Disorders Ther 1:102. doi:10.4172/2161-0509.1000102

77. Jain JB, Kumane SC, Bhattacharya S (2006) Medicinal flora of Madhya Pradesh and Chattisgarh – A review. Ind J Traditional Knowledge 5: 237-241.
78. Garg C, Khan SA, Ansari SH, Garg M (2009) Evaluation of standardisation and toxicological parameters for efficacy and safety of Cyamopsis tetragonolobus. Int J Pharma Recent Res 1: 27-30.
79. Singh SK, Kesari AN, Gupta RK, Jaiswal D, Watal G (2007) Assessment of antidiabetic potential of memecylon dactylon extract in streptozotocin diabetic rats. J Ethnopharmacol 114: 174-179.
80. Surles RL, Weng N, Simon PW, Tanumihardjo SA (2004) Carotenoid profiles and consumer sensory evaluation of specialty carrots (Daucus carota, L.) of various colors. J Agric Food Chem 52: 3417-3421.
81. Shin KO, Jeon JR, Lee JS, Kim YJ, Lee CH, et al. (2006) Lactic acid fermentation of Chinese yam (Dioscorea batatas Decne) flour and its pharmacological effect on gastrointestinal function in rat model. Biotechnol Bioproc E 11: 240-244.
82. Oyaama K, Minami I, Ishizaki K, Fuse M, Miki T (2006) Spontaneous recovery from hyperglycemia by regeneration of pancreatic β-cells in Kir6.2G132S transgenic mice. Diabetes 55: 1930-1938.
83. Niu HS, Liu IM, Cheng JT Lin CL, Hsu FL (2008) Hypoglycemic effect of syringin from Eulexoechochroes senticosus in streptozotocin-induced diabetic rats. Plant Sci 74: 109-113.
84. Suryanarayana P, Saraswat M, Petrasch JM, Reddy GB (2007) Emblica officinalis and its enriched tannoids delay streptozotocin-induced diabetic cataract in rats. Mol Vis 24: 1291-1297.
85. Maro J, Vasu VT, Aalinkeel R, Gupta S (2002) Glucose lowering effect of aqueous extract of Eichornia crassipes Blume in diabetes: a possible mechanism of action. J Ethnopharmacol 81: 317-320.
86. Kumar VS, Jaishanker R, Annamalai A, Iyer SP (2010) Ensete superbum (Roxb.) Cheesman: a rare medicinal plant in urgent need of conservation. J Curr Sci 86: 602-603.
87. Jouad H, Maghrani M, El Hassani RA, Eddouks M (2004) Hypoglycemic activity of aqueous extract of Eucalyptus globulus in normal and streptozotocin-induced diabetic rats. Planta Med 74: 279-288.
88. Gohil T, Pathak N, Jivani N, Devmurari V, Patel J (2010) Treatment with extracts of Eugenia jambolana seed and Aegle marmelos leaf extracts prevents hyperglycemia and hyperlipidemia in alloxan induced diabetic rats. Afr J Pharm Pharmacol 4: 270-275.
89. Birdane FM, Cemeke M, Birdane YO, Göğür TM, Büyükokuroğlu ME (2007) Beneficial effects of Foeniculum vulgare on ethanol-induced acute gastric mucosal injury in rats. World J Gastroenterol 26: 607-611.
90. Semalty M, Semalty A (2008) Hypoglycemic activity of ficus bengalensis in alloxan induced diabetic rats. The Indian Pharmaceutical 71: 61-64.
91. Sophia D, Manoharan S (2007) Hypolipidemic activities of Ficus Racemosa Linn. bark in alloxan induced diabetic rats. Afr J Tradit Complement Altern Med 4: 275-286.
92. Akhtar MS, Khan QM, Khalil T (1984) Effects of Euphorbia prostrata and Fumaria sylvestre leaf extracts in the regulation of corticosteroid induced diabetes mellitus: involvement of thyroid hormones. Pharmacazie 58: 413-415.
93. Patil P, Patel MM, Bhavsar CJ (2011) Preliminary phytochemical and hypoglycemic activity of leaves of Grewia asiatica L. Res J Pharm, Biol Chem Sci 2: 516-520.
94. Ghosal S, Kar A (2003) Effects of Inula racemosa root and Gymnema sylvestre leaf extracts in the regulation of corticosteroid induced diabetes mellitus: involvement of thyroid hormones. Pharmazie 58: 413-415.
95. Patil P, Patel MM, Bhavsar CJ (2011) Preliminary phytochemical and hypoglycemic activity of leaves of Grewia asiatica L. Res J Pharm, Biol Chem Sci 2: 516-520.
96. Ghosal S, Kar A (2003) Effects of Inula racemosa root and Gymnema sylvestre leaf extracts in the regulation of corticosteroid induced diabetes mellitus: involvement of thyroid hormones. Pharmazie 58: 413-415.
97. Satyavati GV, Tandon N, Sharma M (1989) Indigenous plant drugs for diabetes mellitus. ICMR 1-32.
98. Kumar G, Banu GS, Murugesan AG (2009) Anti-diabetic activity of Helicteres isora L. bark extracts on streptozotocin-induced diabetic rats. Int J Pharm Sci Nanotechnol 1: 379-382.
99. Hanif A, Hossan MS, Mia MMK, Islam MJ, Jahan R et al. (2009) Ethnobotanical survey of the rhakhin tribe inhabiting the Chittagong Hill tracts region of Bangladesh. Am.-Eurasian J Sustain Agric 3: 172-180.
100. Ali KM, Chatterjee K, De D, Bera TK, Ghosh D (2009) Efficacy of aqueous extract of seed of Holarrhena antidysenterica for the management of diabetes in experimental model rat: A correlative study with anti-hyperglycemic activity Int J Applied Res Nat Prod 2: 13-21.
101. Nozawa H (2005) Xanthohumol, the chalcone from beer hops (Humulus lupulus L.), is the ligand for farnesoid X receptor and ameliorates lipid and glucose metabolism in KK-A(y) mice. Biochem Biophys Res Commun 336: 754-761.
102. Selya AR, Patel NK (2009) Ethnomedicinal uses of climbers from Sarawasti River Region of Patan District, North Gujarat. Ethnobotanical Leaflets 7: Article 5.
103. Committee on Herbal Medicinal Products (HMPC)(2009) DRAFT Juniperi fructus, Juniperus communis L., fructus (juniper berry). European Medicines Agency Evaluation of Medicines for Human Use, EMEA/HMPC/424295/2008, London.14.
104. Choi J, Lee KT, Jung HJ, Park HS, Park HJ (2002) Anti-rheumatoid arthritis effects of the Kochia scoparia fruits and activity comparison of momordin ic, its prosapogenin and sapogenin. Arch Pharm Res 25: 336-342.
105. Fang L, Jee-kyung K, Yunsung L, Xue-qing L, Jing L, et al. (2001) An extract of Lagerstroemia speciosa L. has insulin-like glucose uptake-stimulatory and adipocyte differentiation–inhibitory activities in 3T3-L1 cells. J Nutr 131: 2242-2247.
106. Thakkar NV, Patel JA (2010) Pharmacological evaluation of "Glyoberb": A polyherbal formulation on streptozotocin-induced diabetic rats. Int J Diabetess Dev Ctries 30: 1-7.
107. Jofack T, Fokunang C, Guedje N, Karinecu F, Fongnanzossie E et al. (2010) Ethnobotanical uses of medicinal plants of two ethnoregional communities of Cameroon. Int J Medicinal J Med Sci 2: 60-79.
108. Syamsudin D, Sinemannark T (2006) The effects of Leucaena leucocephala (imik) De Witt seeds on blood sugar levels: an experimental study. Int J Sci Res 2: 49-52.
109. Park JH, Kim SY, Kang TH, Hwang EJ, Kang CH (2010) US Pat 20,100,093,852 (to Olson & Cepuritis Ltd. Chicago, US) 15 April.
110. Knecht KT, Nguyen H, Auker AD, Kindler DH (2006) Effects of extracts of lupine seed on blood glucose levels in glucose resistant mice: antihyperglycemic effects of Lupinus albus (white lupine, Egypt) and Lupinus caudatus (tallup lupine, Mesa Verde National Park). J Herb Pharmacolother 6: 89-104.
111. Lamela M, Cadavid I, Calleja JM (1986) Effects of Lythrum salicaria extracts on hyperglycemic rats and mice. J Ethnopharmacol 15: 153-160.
112. Yogisha S, Raveesha KA (2010) Dipeptidyl peptidase IV inhibitory activity of Mangifera indica. J Nat Prod 3: 76-79.
121. Baxi DB, Singh PK, Doshi AA, Arya S, Mukherjee R et al. (2010) Medicagostiva leaf extract supplementation corrects diabetes induced dyslipidemia, oxidative stress and hepatic renal functions and exerts antihyperglycaemic action as effective as Metformin. Ann Biol Res 1: 107-119.

122. Ooi CP, Yassin Z, Hamid TA (2010) Mor Dominic acharlita for Type II diabetes mellitus. Cochrane Database Syst Rev 17: CD007845.

123. Singab AN, El-Beshbishi HA, Yonekawa M, Nomura T, Fukai T (2005) Hypoglycemic effect of Egyptian Morus alba root bark extract: effect on diabetes and lipid peroxidation of streptozotocin-induced diabetic rats. J Ethnopharmacol 100: 333-338.

124. Bhaskar A, Vidyha VG, Ramya M (2008) Hypoglycemic effect of Mucuna pruriens seed extract on normal and streptozotocin-diabetic rats. Fitoterapia 79: 539-543.

125. Arulselvan P, Senthilkumar GP, Kumar SD (2006) Anti-diabetic effect of Murraya koenigii leaves on streptozotocin induced diabetic rats. Pharmacize 61: 874-877.

126. Mallick C, De D, Ghosh D (2009) Correction of protein metabolic disorders by composite extract of Musa paradisiaca and Cocinica indica in streptozotocin-induced diabetic albino rat: an approach through the pancreas. Pancreases 38: 322-329.

127. Huang CF, Chen YW, Yang CY, Lin HY, Way TD et al. (2011) Extract of lotus leaf (Nelumbo nucifera) and its active constituent catechin with insulin secretagogue activity. J Agric Food Chem 59: 1097-1094.

128. Bamosa AO, Kaatab H, Lebda FM, Abab AA, Al-Sultnab A (2010) Effect of Nigella sativa seeds on the glycemic control of patients with Type II diabetes mellitus. Int J Physiol Pharmacol 54: 344-354.

129. Rajagopal K, SaiSakila K (2008) Antiphanthycemic and antihyperlipidemic effects of Nymphaea stellata in alloxan-induced diabetic rats. Singapore Med J 49: 137-141.

130. Kapoor S (2008) Ocimum sanctum: A therapeutic role in diabetes and the metabolic syndrome. Horm Metab Res 40: 296-300.

131. Eidi A, Eidi M, Darzi R (2009) Antidiabetic effect of Olea europaea L. in normal and diabetic rats. Phytother Res 33: 347-350.

132. Yeh GY, Eisenberg DM, Kapchuk TM, Phillips RS (2003) Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care 26: 1927-1294.

133. Al-Masslem MQ, Hampton SM, Frost GS, Brown JE (2011) A study of Hassawi rice (Oryza sativa L.) in terms of its carbohydrate hydrolysis (in vitro) and glycaemic and insulinaemic indices (in vivo). Eur J Clin Nutr 65: 627-634.

134. Cho WCS, Chung W, Lee SKW, Leung AVN, Cheng CHK, et al. (2006) Ginsenoside Re of Panax ginseng possesses significant antioxidant and antihyperlipidemic efficacies in streptozotocin-induced diabetic rats. Eur J Pharmacol 550: 173-179.

135. Shded MG, Pulford IF, Hamed AI (2006) Presence of many and trace elements in seven medicinal plants growing in the South-Eastern Desert, Egypt. J Afr Environ 66: 210-217.

136. Ali H, Houghton PJ, Soumayananth A (2006) α-Amylase inhibitory activity of common constituents from traditional Chinese medicine used for diabetes-induced hyperlipidemic condition. J Complement Integr Med 6: Article 28.

137. Ali H, Houghton PJ, Soumayananth A (2006) α-Amylase inhibitory activity of common constituents from traditional Chinese medicine used for diabetes-induced hyperlipidemic condition. J Complement Integr Med 6: Article 28.

138. Al-Masslem MQ, Hampton SM, Frost GS, Brown JE (2011) A study of Hassawi rice (Oryza sativa L.) in terms of its carbohydrate hydrolysis (in vitro) and glycaemic and insulinaemic indices (in vivo). Eur J Clin Nutr 65: 627-634.

139. Cho WCS, Chung W, Lee SKW, Leung AVN, Cheng CHK, et al. (2006) Ginsenoside Re of Panax ginseng possesses significant antioxidant and antihyperlipidemic efficacies in streptozotocin-induced diabetic rats. Eur J Pharmacol 550: 173-179.

135. Shded MG, Pulford IF, Hamed AI (2006) Presence of many and trace elements in seven medicinal plants growing in the South-Eastern Desert, Egypt. J Afr Environ 66: 210-217.

136. Ali H, Houghton PJ, Soumayananth A (2006) α-Amylase inhibitory activity of common constituents from traditional Chinese medicine used for diabetes-induced hyperlipidemic condition. J Complement Integr Med 6: Article 28.

137. Ali H, Houghton PJ, Soumayananth A (2006) α-Amylase inhibitory activity of common constituents from traditional Chinese medicine used for diabetes-induced hyperlipidemic condition. J Complement Integr Med 6: Article 28.
al. (2011) In vitro antioxidant and inhibitory potential of Terminalia belerica and Emblica officinalis fruits against LDL oxidation and key enzymes linked to Type II diabetes. Food Chem Toxicol 49: 125-131.

167. Rao NK, Nammi S (2006) Antidiabetic and renoprotective effects of the chloroform extract of Terminalia chebula Retz. seeds in streptozotocin-induced diabetic rats. BMC Complement Altern Med 6: 17-22.

168. Grover JK, Vats R, Rathii SS (2000) Anti-hyperglycemic effect of Eugenia jambolana and Tinospora cordifolia in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. J Ethnopharmacol 73: 461-470.

169. Amin A, Lotfy M, Shaffullah M, Adeghate E (2006) The protective effect of Tribulus terrestris in diabetes. Annals of the New York Academy of Sciences, 1084: 391-401.

170. Adiga S, Bailey KL, Mehbaran A, Punita IS (2010) Hypoglycemic effect of aqueous extract of Trichosanthos dioica in normal and diabetic rats. Int J Diabetes Dev Ctries 30: 38-42.

171. Amer M, El-Habibi E, El-Gendy A (2004) Effects of Trifolium alexandrinum extracts on streptozotocin-induced diabetes in male rats. Ann Nutr Metab 48: 343-347.

172. Grover JK, Vats R, Rathii SS (2002) Evaluation of anti-hyperglycemic and hypoglycemic effect of Trigonella foenum-graecum Linn, Ocimum sanctum Linn and Pterocarpus marsupium Linn in normal and alloxanized diabetic rats. J Ethnopharmacol 79: 95-100.

173. Brounah M, Merhfour F, Zyiat A, Mehfti H, Aziz M, et al. (2003) Anthyperglycemic activity of the aqueous extract of Urta dioica. Fitoterapia 74: 677-681.

174. Ghosh D, Konishi T (2007) Anthocyanins and anthocyanin-rich extracts: role in diabetes and eye function. Asia Pac J Clin Nutr 16: 200-208.

175. Villaseforand IM, Lamadrid MRA (2006) Comparative anti-hyperglycemic potentials of medicinal plants. J Ethnopharmacol 104: 129-131.

176. Udayakumar R, Kasthuriengan S, Mariashsi TS, Rajesh M, Anbhasganan VR, et al. (2009) Hypoglycaemic and hypolipidemic effects of Withania somnifera root and leaf extracts on alloxan-induced diabetic rats. Int J Mol Sci 10: 2367-2382.

177. Hsu F, ChenY, Cheng JT (2000) Caffeic acid as active principle from the fruit of Xanthium strumarium to lower plasma glucose in diabetic rats. Planta Med 66: 228-230.

178. Islam MS, Choi H (2008) Comparative effects of dietary ginger (Zingiber officinale) and garlic (Allium sativum) investigated in a Type II diabetes model. J Med Food 11: 152-159.

179. Avizeh R, Najafzadeh H, Pourmahdi M, Mirzaee M (2010) Effect of Gymnema sylvestre on streptozotocin-induced diabetes mellitus in rat. Mol Cell Biochem 261: 63-70.

180. Singh N, Gupta M (2007) Regeneration of beta cells in islets of langerhans of pancreas of alloxan diabetic rats by acetone extract of Momordica charantia (Linn.) (bitter gourd) fruits. Ind J Exp Biol 45: 1055-1062.

181. Rathii SS, Grover JK, Vats R, Biswas NR (2002) Prevention of diabetic cataract by Indian Ayurvedic plant extract. Phytother Res 17: 74-77.

182. Kumar GS, Shetty AK, Salimath PV (2008) Modulatory effect of bitter gourd (Momordica charantia Linn.) on alterations in kidney heparan sulfate in streptozotocin-induced diabetic rats. J Ethnopharmacol 115: 276-283.

183. Ganguli S (2002) Neem: A therapeutic for all seasons. Curr Sci 82: 1304.

184. http://www.ayushveda.com/herbs/azadirachta-indica.htm

185. http://www.productosdeenem.com/neem-diabetes2.htm

186. Effect of Neem Leaves in controlling Diabetes (2009).

187. Grover JK, Vats R, Rathii SS, Biswas NR (2001) Traditional Indian anti-diabetic plants attenuate progression of renal damage in streptozotocin induced diabetic mice. J Ethnopharmacol 76: 233-238.

188. Chattopadhyay RR (1996) Possible mechanism of antihyperglycemic effect of Azadirachta indica leaf extract-Part IV. Gen Pharmacol 27: 431-434.

189. Akinola OB, Caxton-Martins EA, Dini L (2010) Chronic treatment with ethanolic extract of the leaves of Azadirachta indica ameliorates lesions of pancreatic islets in streptozotocin diabetes. Int J Morphol 28: 291-302.

190. Chattopadhyay RR (1999) A comparative evaluation of some blood sugar lowering agents of plant origin. J Ethnopharmacol 67: 367-372.

191. Don G (1999) Catharanthus roseus, in: Medicinal Plants of the World, edited by Ross I A, (Human Press, Totowa) 109.

192. Islam A, Akhtar AM, Khan MR, Hossain MS, Alam MK (2011) Antidiabetic and hypolipidemic effects of different fractions of Catharanthus roseus (Linn.) on normal and streptozotocin-induced diabetic rats. J Sci Res 1: 331-338.

193. Somananth MM, Praveen V, Shoba S, Radhey S, Kumari MM (2001) Effect of an antidiabetic extract of a Catharanthus roseus on enzymatic activities in streptozotocin induced diabetic rats. J Ethnopharmacol 76: 269-277.

194. Nammi S, Booni MK, Lodagala SD, Behara RBS (2003) The juice of fresh leaves of Catharanthus roseus reduces blood glucose in normal and alloxan diabetic rabbits. BMC Complement Altern Med 3: 1-4.

195. Satyanarayana S, Sharma GS, Ramesh A, Sushruta K, Srinivas N (2003) Evaluation of herbal preparations for hypoglycemic activity in normal and diabetic rabbits. Pharm Biol 41: 466-472.

196. Banerjee M, Kanitkar M, Bhonde RR (2005) Approaches towards endogenous pancreatic regeneration. Rev Diabet Stud 2: 165-176.

197. Cano DA, Rulfison IC, Heiser PW, Swigart LB, Pelengaris S et al. (2008) Antidiabetic effect through islet cell protection in streptozotocin diabetes: A preliminary assessment of two thiazolidin-4-ones in Swiss albino mice. Chem Biol Interact 177: 242-246.

198. Mustafa NR, Verpoorte R (2007) Phenolic compounds in Catharanthus roseus. Phytochem Rev 6: 243-258.

199. Rasineni K, Bellamkonda R, Singareddy SR, Desiddy S (2010) Anthihyperglycaemic activity of Catharanthus roseus leaves powder in streptozotocin-induced diabetic rats. Pharmacog Res 2: 195-201.

200. Kishore A, Nampurath GK, Mathew SP, Zachariah RT, Potu BK, et al. (2009) Effect of D-400, a herbomineral preparation on lipid profile, glycated haemoglobin and glucose tolerance on streptozotocin induced diabetes in rats. Indian J Exp Biol 33: 798-800.

201. Ahmad I, Adegheate E, Cummings E, Sharma AK, Singh J (2004) Beneficial effects and mechanism of action of Momordica charantia juice in the treatment of streptozotocin-induced diabetes mellitus in rat. Mol Cell Biochem 261: 63-70.
213. Sheehan EW, Zemaitis ZA, Slatkin DJ, Schiff PL (1983) A constituent of Pterocarpus marsupium, (-)-Epicatechin, as a potential anti-diabetic agent. J Nat Prod 46: 232-234.

214. Dhanabal SP, Kokate CK, Ramanathan M, Kumar EP, Suresh B (2006) Hypoglycaemic activity of Pterocarpus marsupium roxb. Phytother Res 20: 4-8.

215. Gupta R, Gupta RS (2009) Protective role of Pterocarpus marsupium in diabetes-induced hyperlipidemic condition. J Complement Integr Med 6: Article 28.

216. Rizvi SI, Zaid AM, Suhail M (1995) Insulin-mimetic effect of (-)-epicatechin on osmotic fragility of human erythrocytes. Ind J Exp Biol 33: 791-792.

217. Grover JK, Vats V, Yadav SP (2005) Pterocarpus marsupium extract (Vijayarass) prevented the alteration in the metabolic patterns induced in the normal rat by feeding an adequate diet containing fructose as a sole carbohydrate. Diab Obes Metab 7: 414-420.

218. Grover JK, Vats V, Yadav SP (2002) Effect of feeding aqueous extract of Pterocarpus marsupium on glycogen content of tissues and the key enzymes of carbohydrate metabolism. Mol Cell Biochem 241: 53-59.

219. Haritharan RS, Venkataraman S, Sunita P, Rajalakshmi S, Samal KC et al. (2005) Efficacy of Vijayarass (Pterocarpus marsupium) in the treatment of newly diagnosed patients with Type II diabetes mellitus: A flexible dose double-blind multicenter randomized controlled trial. Diabetologia Croatica 34: 13-20.

220. Vats V, Yadav SP, Biswas NR, Grover JK (2004) Anti-cataract activity of Pterocarpus marsupium bark and Trigonella foenum graecum seeds extract in alloxan diabetic rats. J Ethnopharmacol 93: 289-294.

221. Stanely P, Prince M, Menon VP (2003) Hypoglycaemic and hypolipidaemic action of alcohol extract of Tinospora cordifolia roots in chemical induced diabetes in rats. Phytother Res 17: 410-413.

222. Singh SS, Pandey SC, Srivastava S, Gupta VS, Patra B, et al. (2003) Chemistry and medicinal properties of Tinospora cordifolia (Guduchi). Ind J Pharmacol 35: 83-91.

223. Nagaraja PK, Kammar NF, Devi S (2007) Modulation of morphology and some gluconeogenic enzymes activity by Tinospora cordifolia (Wild.) in diabetic rat kidney. Biomed Res 18: 179-183.

224. Rajalakshmi M, Eliza J, Priya CE, Nirmala A, Daisy P (2009) Anti-diabetic properties of Tinospora cordifolia stem extracts on streptozotocin-induced diabetic rats. Ind J Clin Biochem 17: 33-43.

225. Nagaraja PK, Kammar NF, Devi S (2008) Efficacy of Tinospora cordifolia (Wild.) extracts on blood lipid profile in streptozotocin diabetic rats. Is it beneficial to the heart? Biomed Res 19: 5-8.

226. Stanely P, Prince M, Menon VP (2001) Antioxidant action of Tinospora cordifolia root extract in alloxan diabetic rats. Phytother Res 15: 213-218.

227. Grover JK, Rathi SS, Vats V (2002) Amelioration of experimental diabetic neuropathy and gastropathy in rats following oral administration of plant ( Eugenia jambolana, Mucuna pruriens and Tinospora cordifolia) extracts. Ind J Exp Biol 40: 273-276.

228. Broca C, Breil V, Cruciani-Guglielmacci C, Manteghetti M, Rouault C et al. (2004) The insulinotrophic agent 1D10114-(4-hydroxyisoleucine) activates insulin signaling in rat. Am J Physiol Endocrinol Metab 287: E463.

229. Hannan JM, Rokeya B, Faruque O, Nahar N, Mosihuzzaman M et al. (2003) Effect of soluble dietary fibre fraction of Trigonella foenum-graecum on glycemic, insulinemic, lipemic and platelet aggregation status of Type II diabetic model rats. J Ethnopharmacol 88: 73-77.

230. Devi BA, Kamakalakkannan N, Prince PS (2003) Supplementation of fenugreek leaves to diabetic rats-Effect on carbohydrate metabolizing enzymes in diabetic liver and kidney. Phytother Res 17: 1231-1233.

231. Coon JST, Ernst E (2003) Herbs for serum cholesterol reduction: a systematic view. J Fam Pract 52: 468-476.

232. Tahilliani P, Kar A (2003) Mitigation of thyroxine induced hyperglycaemia by two plant extracts. Phytother Res 17: 294-296.

233. Wang O, Ouazzani J, Sasaki NA, Potier P (2002) A practical synthesis of (2S,3R,4S)-4-hydroxyisoleucine, a potent insulinotropic α-amino acid from fenugreek. Eur J Org Chem 5: 834-839.

234. Vats V, Yadav SP, Grover JK (2003) Effect of Trigonella foenum-graecum on glycogen content of tissues and the key enzymes of carbohydrate metabolism. J Ethnopharmacol 85: 237-242.

235. Thakaran S, Salmundt M, Baquer NZ (2003) Oral administration of orthovandate and Trigonella foenum-graecum seed powder restore the activities of mitochondrial enzymes in tissues of alloxan-induced diabetic rats. Mol Cell Biochem 247: 45-53.

236. Venkatesan N, Devraj SN, Devraj H (2003) Increased binding of LDL and VLDL to Apo B, E receptors of hepatic plasma membrane of rats treated with Fibranat. Eur J Nutr 42: 262-271.

237. Anwar S, Desai S, Mandlik R (2009) Exploring anti-diabetic mechanisms of action of gallocatechin: a carbohydrate isolated from fenugreek seeds. J Complement Integr Med 6: Article 6.

238. Tanaka M, Misawa E, Habara N, Nomaguchi K, Yamada M, et al. (2006) Identification of five phytosterols from Aloe vera gel as anti-diabetic compounds. Biopol Pharm Bull 29: 1418-1422.

239. Oyar A, Can A, Akev N, Bakir G, Sultipinar N (2001) Effect of Aloe vera leaves on blood glucose level in Type I and Type II diabetic rat models. Phytother Res 15: 157-161.

240. Rajasekaran S, Sivagnanam K, Subramanian S (2006) Mineral contents of Aloe vera leaf gel and pulp extracts on the liver in Type-II diabetic rat models. Biol Pharm Bull 27: 694-698.

241. Can A, Akev N, Ozsoy N, Bolkent S, Arda BP et al. (2004) Effect of Aloe vera leaf gel and pulp extracts on the liver in Type-II diabetic rat models. Biol Pharm Bull 27: 694-698.

242. Mogra R, Dashora V (2009) Exploring the use of Stevia rebaudiana as a sweetener in comparison with other sweeteners. J Hum Ecol 25: 117-120.

243. Gregersen S, Jeppesen PB, Holst JJ, Hermansen K (2004) Antihyperglycemic effects of stevioside in Type II diabetic subjects. Metabolism 53: 73-76.

244. Jeppesen PB, Gregersen S, Alstrup KK (2002) Stevioside induces antihyperglycemic, insulinotropic and glucagonostatic effects in vivo: Studies in the diabetic Goto-Kakizuki (GK) rats. Phytomedicine 9: 9-14.

245. Chen TH, Chen SC, Chan P, Chu YL, Yang HY, et al. (2005) Mechanism of the hypoglycemic effect of stevioside, a glycoside of Stevia rebaudiana. Planta Med 71: 108-113.

246. Chan P, Tomlinson B, Chen YJ (2000) A double-blind placebo-controlled study of the effectiveness and tolerability of oral stevioside in human hypertension. Br J Clin Pharmacol 50: 215-220.

247. Ferreira EB, Neves FEA, da Costa MED, do Prado WA, Ferri LA et al. (2006) Comparative effects of Stevia rebaudiana leaves and stevioside on glycaemia and hepatic glycogenesis. Planta Med 72: 691-696.

248. Aggarwal BB, Kumar A, Aggarwal MS (2005) Curcumin derived from turmeric (Curcuma longa): a spice for all seasons, in Phytochemicals in Cancer Chemoprevention, edited by P D Debases Bagchi & H G Preuss, (CRC Press, New York) 349-387.

249. Eshral H, Hussain MA (2002) Hypoglycemic, hypolipidemic and antioxidant properties of combination of curcumin from Curcuma longa Linn. and partially purified product from Abroma augusta Linn. in streptozotocin induced diabetes. Ind J Clin Biochem 17: 33-43.

250. Nishizono S, Hayami T, Ikeda I, Imaiuzumi K (2000) Protection against diabeticogenic effect of feeding tert-butyldihydroxyquinone to rats prior to the administration of streptozotocin. Biosci Biotechnol Biochem 64: 1153-1158.

251. Majithiya JB, Balaraman R (2005) Time-dependent changes in antioxidant enzymes and vascular reactivity of aorta in streptozotocin-induced diabetic rats treated with curcumin. J Cardiovasc Pharmacol 46: 697-705.

252. Suryanarayana P, Sarawat M, Mudula T, Krishna TP, Krishnaswamy K (2005) Curcumin and turmeric delay streptozotocin-induced diabetic cataract in rats. Invest Ophthalmol Vis Sci 46: 2092-2099.