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The antidiabetic activity of bioactive compounds of Indian medicinal plants: A meta data review

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ABSTRACT

Diabetes, one of the most common chronic metabolic disorders affecting a large proportion of nearly all countries is characterized by the deficiency in insulin production and resistance against insulin action. The disease ultimately leads to inappropriate and prolonged hyperglycemia which in turn affects the every system and mechanism of the body. The disorder is treated with several synthetic drugs but due to several limitations and side effects of the synthetic drugs the attention is drawn towards the employment of plant and plant product in development of herbal drugs. The ease of access, affordability and the ability of herbals to produce minimum side effects on administration have convinced a major portion of population globally to switch to this alternative approach of medicine. The plants are always been the source of immense products for the human welfare from the time immemorial. This study has mainly focused on the variety of bioactive constituents, carried out by plants, having potent medicinal properties. The article has also listed some of the famous medicinal plants of India having the potential to be used as an effective source for the herbal drug development because these plants are reservoir of many phyto-constituents for human welfare. The study concludes that if explored and studies well these plants could act the unlimited source of bioactive compounds to be used in herbal medicine development.

INTRODUCTION

Diabetes, a chronic metabolic disorder possessing a major health challenge worldwide and is very common and most prevalent diseases that affects the citizens of both developed and developing countries. Estimation gives the proportion that about 25% of the world population is affected by the disease. The current status of India revealed that there are around 40.9 million diabetic patients and the expectation are still high up to

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69.9 million by 2025 (Mohan *et al*., 2007). Due to this high rate of the diabetic patients India has been tagged as the diabetic capital of the world (Joshi and Parikh, 2007). Lack of an urgent preventive measure could lead it to become the major health issue among the Indian population. Number of deaths due to diabetes estimated by the Indian Diabetes Federation (IDF) is around 3.9 million that represents 6.8% of the total global mortality count (IDF, 2009). The abnormality of the carbohydrate metabolism that is due to the disturbance in the optimum level of the insulin in blood leads to the onset of the disease Diabetes (Maiti *et al*., 2004). Diabetes is also caused due to the deficiency of the insulin function or due to the insensitivity of the organ to insulin. This abnormality leads to a prolonged hyperglycemia which in turn disturbs other metabolic pathways of the human body as well (Bastaki, 2005). When left untreated this could lead to some severe damages of tissue and vascular damages that can lead to serious compilation such as retinopathy (Bearse *et al*., 2004), neuropathy (Seki *et al*., 2004), nephropathy (Looker *et al*., 2003), ulceration (Wallace *et al*., 2002) and the cardiovascular complications (Svensson *et al*., 2004). Being the most common endocrine disorder Diabetes has indirect relationship with many other diseases.

Both of the pancreatic endocrine hormones, insulin and glucagon work simultaneously to control the blood glucose level in the body to an adequate level on the basis of the body's requirement. In normal conditions insulin is secreted by the β-cells of the islets of Langerhans when there is high blood sugar level in the blood. This enzyme increases the potential ability of muscles, red blood cells, and fat cells to absorb the excess sugar out of the blood and use it for other metabolic pathways that could help to restore the optimum level of sugar in blood (Gupta, 2012). Contrast to this acts glucagon enzyme which is secreted by the β-cells of the pancreas in response to the low blood sugar level. This enzyme act to initiate the liver and other muscles cells to release the stored glucose into the blood stream for consumption by the working cells. Retention of high blood glucose level for long duration can ultimately lead to the long term damage to the organs like kidney, eyes, liver, nerves, heart and blood vessels. This type of complication in such organs may cause the death of the individual (Pari and Saravanan, 2004). The dysregulated metabolism caused due to diabetes causes certain pathophysiological changes in some organs that cause a tremendous burden on the individual. Diabetes mellitus act as the cause for several diseases like end stage renal disease, adult blind, non-traumatic lower extremity amputation, (Gupta, 2012).

The two main widely accepted types of the diabetes mellitus are type 1 and type 2 (Zimmet *et al*., 2004). The type 1 diabetes occurs in the patients with very little or no insulin secretory capacity. These types of patients are in the need for the replacement therapy in order to stay alive. The type 1 is also of two type that is type 1a conferring almost 90% of the type 1and type 1b conferring 10% of it. It is also referred as the juvenile diabetes. The type 1a results from the destruction of the pancreatic cells caused due to immunological damages and are associated with certain diseases like Addison's disease, Grave's disease and Hashimoto's thyroiditis (Atkinson and Maclaren, 1994). While type 1b is idiopathic without any etiological basis. The patients suffering from this type of diabetes possess the predominant deficiency of insulin and are susceptible to keto-acids but there is no evidence of any autoimmune disease development (MacLarty *et al*., 1990). The type 2 diabetes is the most common form of diabetes. This type is characterized by the abnormality in the insulin produced and its resistance (DeFronzo *et al*., 1992). This type is dominating in the elderly people, over 40 years. It may occur in the obese person, person with decreased body activity and this type may also be inherited from parents to offsprings (Zimmet *et al*., 1990). This type is also associated with individuals suffering from hypertension and dyslipidemia. Dietary supplements, physical activity and the oral hypoglycemic agents are responsible to enhance the disease (Zimmet *et al*., 2001, Wang *et al*., 2018; Al-Attar *et al*., 2019).

Several factors contribute to the on-set and development of diabetes in any individual. These factors are termed as the predisposing or the risk factors. Some environmental factors like diet, obesity and sedentary life style increases the risk of diabetes. Some other factors are also responsible including insulin resistance, high family aggregation, age, lifestyle, nutritional status (Deepashree and Prakash, 2007). Common symptoms of diabetes include frequent urination, excessive thirst, increased appetite, fatigue, blurred vision, slow wound healing, weight loss regardless of increased appetite (type 1), tingling, pain, or numbness of hands/feet (type 2) (Ramchandran, 2014). Diabetes mellitus is attributed to insulin inactivity or resistance as a direct result of the destruction or dysfunction of the pancreatic cells (Rezaei *et al*., 2016). The global study report states that Diabetes Mellitus is one of the non-communicable diseases based on the number of cases and its prevalence has continued to increase over the last few decades (WHO, 2016).It is evident that Diabetes mellitus leads to hyperglycemia and to many other complications such as hyperlipidemia, hypertension, atherosclerosis, retinopathy, neuropathy, and nephropathy (Wang *et al*., 2018; Al-Attar *et al*., 2019).

Importance and role of medicinal plants

The therapies available currently for the treatment of diabetes include various oral hypoglycemic agents along

with insulin like sulfonyl ureas, metformin, glucosidase inhibitors, troglitazone etc. But these agents are reported to produce several side effects on the body organs causing liver problems, lactic acidosis, and severe diarrhea (Rajalakshmi *et al*., 2009). These adverse side effects are currently affecting approx. 143 million peoples (Mentreddy *et al*., 2005) and this count down is thought to increase several folds in coming years up to 366 million (Ponnusamy *et al*., 2011). The recent encouragement is on the use of medicinal plants as alternative remedies attributed to the elevation of medication cost, synthetic medicine side influences, and lack of full recovery of diabetic patients treated with chemical hypoglycemic agents. The recently developed traditional therapies originated from medicinal plants have shown a vital role in the control of Diabetes Mellitus (Cheng *et al*., 2013).

Many plant species have been used for the prevention and management of diabetes by the leading nations like America, China, South America and Asia (Mentreddy *et al*., 2005). There are several indigenous Indian medicinal plants that have been found capable of successfully managing diabetes. The most important advantage carried out by these medicinal plants is that they are readily available and have very low or no side effects. The pharmacologically active compounds or the bioactive compounds of plants show there hypoglycemic effect by decreasing effect on α-amylase and various direct and indirect effects of the different parameters of blood that re responsible for developing diabetes (Murali, 2006).

They have an extraordinary source of drug and many of the today's generation drugs are directly or indirectly derived from the medicinal plants. The report from the ethnobotanical information covers about 800 plants that possess the antidiabetic potential in one or more of their parts (Alarcon-Aguilara *et al*., 1998). Research studies have come across several herbs with the antidiabetic property proven by the modern experimental techniques (Jafri *et al*., 2000). The study have revealed that Asian and African continents constitute up to 56% and 17% of the worldwide distribution of the therapeutic plants respectively (Chung-Hung *et al*., 2012). The plants confer the biological action due to the presence of various bioactive compounds in them like phenolics, alkaloids, flavonoids, terpenoids, coumarins and glycosides. The presence of these active lead compounds in the plant kingdom has made them as the target search by the multinational drug companies. These medicinal plants are also part of our diet as spices, vegetables, and fruits. The confer one of the most potential source for the medicine in modern society for instance, quinine, atropine, opium alkaloid and the popular hypoglycemic drug Glucophage are derived from Galega officinalis (Grover *et al*., 2002). These plants depict their effect by delaying the development of diabetic complication and also correct the metabolic abnormalities.

Virtually in all the culture the medicinal plants are used as the source of medicine (Sofowora, 1996). Treatment of diabetes mellitus using medicinal plants backs from the Ebres papyrus around 1550 BC (Kesari *et al*., 2005; Shruthi *et al*., 2012). The World Health Organization recommends the treatment of diabetes by the traditional medicines as they are effective, non-toxic, with less or no side effects and they are considered as the excellent oral therapy candidate (Khan *et al*., 2010; Singh and Koiri, 2014). Out of the 400 traditional plants discovered, only small proportion of it has received the evaluation of its efficacy by the scientists (Aruna *et al*., 2014). The report of World Health organization reveals that 90% of the populations of developed countries use plant and its products as the primary health care medicine (WHO 2002). The organization has listed around 21000 plants being used for the medicinal purpose across the world and among them 2500 plants are from India (Modak *et al*., 2007). The anti-hyperglycemic activity of these plants is due to their ability to restore the lost functions of pancreatic tissue by causing an increased output of insulin production or increases the glucose absorption and may also facilitate the metabolites in an insulin dependent process.

The most common and effective antidiabetic medicinal plants of Indian origin are Babul (*Acacia arabica*), bael (*Aegle marmelose*), church steeples (*Agrimonia eupatoria*), onion (*Allium cepa*), garlic (*Allium sativum*), ghrita kumara (*Aloe vera*), neem (*Azadirachta indica*), ash gourd (*Benincasa hispida*), Beetroot (*Beta vulgaris*), fever nut (*Caesalpinia bonducella*), bitter apple (*Citrullus colocynthis*), ivy gourd (*Coccinia indica*), eucalyptus (*Eucalyptus globules*), banyan tree (*Ficus benghalenesis*), gurmar (*Gymnema sylvestre*), gurhal (*Hibiscus rosa-sinesis*), sweetpotato (*Ipomoea batatas*), purging Nut (*Jatropha curcas*), mango (*Mangifera indica*), karela (*Momordica charantia*), mulberry (*Morus alba*), kiwach (*Mucuna pruriens*), tulsi (*Ocimum sanctum*), bisasar (*Pterocarpus marsupium*), anar (*Punica granatum*), jamun (*Syzygium cumini*), giloy (*Tinospora cordifolia*), and methi (*Trigonella foenum-graecum*); all these plants are a rich source of phytochemical compounds (Rizvi and Mishra, 2013).

Bioactive agents of the plants with hypoglycemic activity:

The Mother Nature has blessed us with the variety of plants with the medicinal properties. Survey carried out by several national and international organizations reported a diversity of the plants with the antidiabetic activity. These plants possess the ability of this activity due to the presence of the several bioactive agents

that includes alkaloids, phenols, flavonoids, steroids, glycolipid, terpenoids, saponins, amino acids, glycolpeptides etc. different plant possess these bioactive compounds in different proportion in them hence carry out some of the specific function. They carry out these effects by either increasing the level of insulin in the blood serum or they increase the production of the insulin by the β-cells of the pancreas, they can also inhibit the absorption of glucose in the gut or can increase the glucose uptake by the body for different activities (Saxena *et al*., 2004; Gupta *et al*., 2008). These bioactive compounds are reported to carry out a potent and effective hypoglycemic, anti-hyperglycemic and glucose suppressive activities (Saxena *et al*., 2006). Some of the important bioactive agents carry out the antioxidant, anti-cataract and hypolipidemic properties along with the enzymatic function restoration and repair and regeneration properties as well (Mukherjee *et al*., 2006).

Allium sativum contains sulfur amino acid called as S-allyl cysteine (Rabinkov *et al*., 1998) that could act as an alternate for insulin because the short term and long term treatment of the diabetic models with it corrects hyperglycemia (Nasim *et al*., 2009). The naturally occurring compounds with hypoglycemic and antioxidant properties are flavonoids. Flavonoids are responsible for improving the altered glucose and oxidative metabolism of the diabetic stage (Song *et al*., 2005). The phytosterols of *Aloe vera* including lophenol, 24-methyl-lophenol, 24-ethyl-lophenol, cycloartanol and 24-methylene-cycloartanol carried out the antidiabetic function in type 2 diabetic mice (Tanaka *et al*., 2006). Steroids like β-Sitosterol found in *A. indica* (Prabhakar and Doble, 2008) and gymnemic acid IV from Gymnema sylvestre possess the potent hypoglycemic activity found in the animal models (Kimura, 2006). The plants like *Allium cepa* (Kumari and Augusti, 2007; Islam et al., 2007) and *Allium sativum* (Saravanan and Ponmurugan, 2010) are good source of sulphur containing amino acids like S-methyl cysteine sulfoxide and Diallyl thio-sulfinate. These amino acids activate the enzyme hexokinase, glucose-6-phosphatase and hence help in rapid consumption of glucose. The polysaccharides of *Aloe vera* are found to increase the level of insulin in blood and also show hypoglycemic properties (Yagi *et al*., 2009). Flavonoid rich extract from the seeds of *Eugenia jambolana* possess hypoglycemic properties and is experimentally reported in the rat models (Bhavana *et al*., 2008).

These many findings related with the antidiabetic role of bioactive compounds from plants have demonstrated the importance of medicinal plants and their potential use for the human welfare. The data available on the antidiabetic effects of the phytochemical compounds suggests that the plants also possess some other compounds in there different parts which acts through different pathway and have role in curing several other disease than diabetes. They may be regarded as a new type of chemotype that will help the phytochemist to offer the potential cost effective management of diabetes through cost-effective manners (Mentreddy *et al*., 2005). The antidiabetic effects of these bioactive agents have been studied in various models of animals like mice, rats and rabbits with different dosage of the plant extract and the period of incubation varied from 24 hours to 45 days. Ferulic acid and Cuminosides from the ethanolic and methanolic extracts respectively of *S. cumini* seeds have shown a significant hypoglycemic and antioxidant potential (Mandal *et al*., 2008; Farswan *et al*., 2009).

Some plants with potent antidiabetic properties:

Aegle marmelos

It is a member of family Rutaceae and is commonly called as Holy Fruit tree. The aqueous leaf extract of *Aegle marmelos* was found to be as potent as insulin in controlling the blood glucose level in STZ diabetic rats when administered orally (Grover *et al*., 2002). Alcoholic extract the plant also show effective role as the methanolic extract of the plant decreases blood glucose level in alloxan diabetic rats and also lowers the oxidative stress by reducing the peroxidation of serum and liver lipid, elevates the level of enzymes including catalase, glutathione peroxidase and superoxide dismutase (Sabu and Kuttan, 2004). Reduction in the FBG level was shown when aqueous seed extract was administered orally. This was accompanied by the decrease in total cholesterol level and triglycerides and caused a concomitant elevation in level of HDL (Keasri *et al*., 2006).

The mode of action includes the stimulation of glucose uptake or enhances the insulin secretion or both in some cases. In addition to this it helps in improving the function of beta cells and regenerates the damaged pancreatic parts (Maity *et al*., 2009). Fruit of the plant also carry out the antidiabetic function as the oral and intraperitoneal administration of aqueous fruit extract showed significant antidiabetic activity in STZ induced rats. The fruit extract caused significant reduction in blood glucose level, also glycosylated the hemoglobin and elevated the level of blood insulin and liver glycogen. A specific dose of 250 mg/kg of the fruit extract is found to be more potent than glibenclamide (Maity *et al*., 2009). The effective and relevant hypoglycemic effect shown by the plant extract is mainly due to its coumarins that are responsible for stimulation of insulin secretion from pancreatic beta cells (Maity *et al*., 2009).

Allium cepa and Allium sativum

They are member of the Liliaceae family and are one of the important dietary supplements and are mainly

involved in eastern kitchen. Ethanol extract of garlic, shown by study, regulates the blood sugar level by normalizing the activity of both liver hexokinase and glucose-6-phosphatase. The active component of *Allium cepa* is the secondary metabolite present in the form of cysteine derivative as S-alkyl cysteine sulfoxides that decompose in the presence of Allinase upon extraction into polysulfides and thio-sulfinates. The antidiabetic activity of both the plants can be conferred to the presence of these volatile decomposed products that are dominant in their oils in addition to the other non-volatile sulfur containing peptides and proteins (Augusti, 1996).Ether fractions of onion bulb are found to show hypoglycemic effect by decreasing the glucose peak in subcutaneous glucose tolerance test (Grover *et al*., 2002).

Allium cepa is responsible in increasing the fasting serum high density lipoprotein value and also exhibits the alleviation of hyperglycemia in diabetic rats. This hypoglycemic and hypolipidemic effects of onion is usually associated with its antioxidant property. The major active components present in there extracts include sulfur-containing compounds like diallyl disulfide (allicin) in garlic and allyl propyl disulfide (APDS) in onions (Dey *et al*., 2003). The ethanol extract of garlic was found to be more potent in its antidiabetic activity than the commonly known drug Glibenclamide (Eidi *et al*., 2006). The extract was found to be responsible for elevating the level of liver glycogen, serum insulin and free amino acids that causes the significant reduction in level of FBG, serum triglycerides, cholesterol, urea, creatinine, AST and ALT level (Goel *et al*., 2012).

Cinnamomum zeylanicum

Commonly known as cinnamon and is widely used in East Asia and Europe. It belongs to the family Lauraceae. It is extensively under use in the folk medicine preparation used for the treatment of diabetes. Major component of cinnamon includes the volatile oil cinnamaldehyde. It also marks the increase in the level of serum insulin, hepatic glycogen and high density lipoprotein in a dose dependent manner (Subash *et al*., 2007).

The ingestion of cinnamon decreases the total sugar level in plasma and improves the insulin sensitivity. The oral administration of the chief component cinnamaldehyde results in the significant reduction in serum glucose level, total cholesterol and triglycerides level. The aqueous extract of cinnamon is revealed to be a potent antidiabetic agent by up regulating the uncoupling protein-1 (UCP-1) and by enhancing the translocation of GLUT4 in the muscles and adipose tissues (Shen *et al*., 2010). It helps in reducing the gastric emptying and decreases the postprandial glycemic responses (Goel *et al*., 2012).

Azadirachta indica

It is the member of family Meliaceae. *A. indica* has been employed for long time in the traditional medicine for treatment of several ailments along with diabetes. Presence of characteristic high fiber content in its leaves is potent for the management of diabetes and for controlling the post-prandial hyperglycemia via delaying the gastric emptying and increasing the viscosity of the gastro-intestinal tract content. This phenomenon leads to the suppression of digestion and absorption of carbohydrate with no risk of hypoglycemia and unexpected weight gain (Atangwho *et al*., 2009). The leaves, stem, bark and seeds all are medicinally very important and all possess hypoglycemic activity by increasing the insulin secretion from the pancreatic beta cells (Tripathi *et al*., 2011).

Eugenia jambolana

It is commonly called as black plum or jamun. It is member of the family Myrtaceae. Another name for this plant is *Syzygium cumini* and this plant has been widely used over centuries for the treatment of diabetes in the traditional medicine practices. Enhancement of insulinemia, was observed resulting from the oral administration of the fruit pulp extract, through stimulating the insulin secretion and suppression of insulinase activity in liver and kidney (Grover *et al*., 2002). The seed extract of this plantwhich is flavonoid rich has shown a potent antidiabetic activity manifested by the reduction in fasting and peak blood glucose level. The mechanism of action deduced is by the upregulation of both PPARα and PPARγ and also by its ability to differentiate 3T3-L1 preadiopocytes (Sharma *et al*., 2008).

The extract of seed kernel was effective by inhibiting the function of α-glucosidase (Shinde *et al*., 2008).When alcohol extract of dried seeds was administered orally then it led to hypoglycemia and decreased glycosuria and partially restored the glycogen content as wells as hexokinase and glucose-6-phosphatse, phosphofructokinase and glucokinase enzyme of altered hepatic and skeletal muscle (Kumar *et al*., 2011).

Momordica charantia

It is a very well-known member of the family Cucurbitaceae which is commonly called as bitter melon. It is one of widely used plant in the folk medicine therapies for treatment of diabetes. The oral administration of the fruit juice or the seed powder is found to cause potent decline in the level of FBG and cause amelioration of glucose tolerance that exerts both insulin secretagogue and insulinomimetic activities (Raman, 1996). The potent antidiabetic activity of this plant is due to the presence of polypeptide similar to insulin called as pol-

ypeptide-P, and it is similar in structure to bovine insulin that reduces plasma sugar levels, into type I diabetic patients, when injected subcutaneously. Other hypoglycemic agents in the plant include sterol glucoside mixture charantin isolated from the fruit and the pyrimifine nucleoside vicine also abundant in the seeds (Raman, 1996). The polypeptide-P appears to inhibit the gluconeogenesis process. In addition to this it also improves the tolerance of glucose in type II diabetic patients (Grover *et al*., 2002; Goel *et al*., 2012).

Psidium guajava

This plant belongs to the family Myrtaceae and is commonly called as Guava. It is a reservoir of vitamins including B1, B2, B6, C, free sugars like glucose, fructose and sucrose and carotene. The aqueous extract of leaf, when administered orally as well as intraperitoneally, showed a beneficial effect on the blood glucose level in the hyperglycemic rat induced by alloxan. Beside this it also carried out potent effect on the body weight, glucose and ketone level of urine and pancreatic tissue which indicated its effect on inhibiting the tyrosine phosphatase 1B protein (Oh, *et al*., 2005). Ethanol extract of the bark of the plant have shown hypoglycemic effect by stimulating the insulin release from the pancreatic β-cells (Mukhtar *et al*., 2006). The potent constituents of this plant, includes the flavonoid glycoside exemplified by pedunculagin, isostrictinin and strictinin, widely used for the clinical treatment of diabetes to improve the insulin sensitivity (Goel *et al*., 2012).

Ocium sanctum

A member of family Labiateae is commonly known as Holy basil or Tulsi. The plant is administered as a potent medicinal agent for traditional treatment of several diseases and due to its lots of medicinal properties it is considered sacred in India. Alcohol extract of *O. sanctum* reduces glycemia and enhances the action of insulin exogenously. The presence of eugenol, the chief active constituent, is considered to be the potential reason behind its antidiabetic activity. It helps in reducing elevated serum sugar, cholesterol triglycerides levels along with lactate dehydrogenase, alanine transaminase, aspartate transaminase and alkaline phosphatase enzyme (Prakash and Gupta, 2005). Reduction in the level of FBG after 1 month administration of leaf powder was found in the diabetic rats (Tripathi *et al*., 2011).

Trigonella foenumgraecum

It is member of family Fabaceae and is commonly called as fenugreek seeds. The deflated seeds administration caused decreased fasting and posprandial blood levels of glucagon, glucose, insulin, somatostatin, total cholesterol and caused increment in the level of HDL-cholesterol levels. The chemical analysis of the seed fiber led to the conclusion that the major constituent called as galactomannan attributes to the antidiabetic activity of the seeds (Basch *et al*., 2003). The mechanism of action of the fenugreek seeds may include the enhancing of insulin synthesis and its release from the pancreatic cells. Intake of the seeds decreases absorption rate of sugar delays the gastric emptying and inhibits the blood glucose levels after meals. It also causes the stimulation of insulin receptors to burn the glucose at high-fiber diet. In case of type 1diabetes the mode of action included the reversion of lipid and glucose metabolizing enzyme activity to normal levels, and thus stabilizes the glucose homeostasis in liver and kidney (Dey *et al*., 2003). The seeds are have prominent importance due to the presence of mucilage, proteins, proteinase inhibitors, steroids saponins and saponins-peptide esters, steorls, flavonoids, nicotinic acid, coumarin, trigonelline and volatile oils (Bnouham *et al*., 2006).

Hibiscus rosa-sinesis

It is a flowering tree distributed throughout the India and is commonly known as Gudhal. Evaluation of the plant extract was carried out on both acute and subacute animal models. For the study ethanolic extract of the flower was administered to the rats at 250mg/kg and 500mg/kg doses. The administration showed a significant reduction in the blood glucose level in the animal models. The duration of reduction varied from 1, 3, 5, hours to 1, 3, 5, 7 days in acute and subacute models respectively. The result evaluated the effective applicability of the ethanol extract of the flower for the treatment of both acute and chronic diabetes (Venkatesh *et al*., 2008).

Holarrhena antidysenterica

An indigenous plant distributed throughout the Indian subcontinent and commonly called as kurchi. The seeds of the plant were evaluated for the hypoglycemic activity in the albino rat models. The study work comprises the normal and diabetic rats both treated with 1.5ml/kg normal saline and 350mg seed extract/kg. After 7 days of the extract administration the glucose level was found to be reduced and it was significant in both preprandial and postprandial level of glucose. Level of glucose also reduced in case of the normal rats. The glucose level decrement was 142.5±1.82 and 182.5±5.88 in case of fasting and feeding state respectively. Along with the hypoglycemic effect the extract treatment also improved the lipid profile of the diabetic rats while no anti-hyperlipidemic effect was observed in the normal rats. Long duration treatment with the extract also revealed some anti-hypercholesterolemic activity around 14 days of treatment, followed by effective reduction in the level of

urea nitrogen in blood after 28 days of treatment (Pankaj *et al*., 2006).

Argemone Mexicana L.

It is a member of family Papaveraceae and is commonly called as prickly poppy or Pili or Kateli and this herb is indigenously being used for medicinal purpose in several parts of Rajasthan. The plant is rich in several bioactive agent that is alkaloids including berberine, protopine, sarguinarine, optisine, chelerythrine etc. this plant is genuily very important for the primary health care as it is good source of both traditional and modern medicines. The ethanolic and aqueous extract of the whole plant have been administered on the diabetic rats induced by alloxan, and the extract have shown a good hypoglycemic effect by the single dose and multi dose treatment (Nayak *et al*., 2011).

Catharanthus roseus

A member of the family Apocynaceae and locally termed as Rose periwinkle is a plant with several medicinal activity. It is widely used in the herbal preparation of the diabetes. A major phyto-constituent of the plant is Catharanthine that shows the antidiabetic activity. This plant is a good reservoir of the phytochemical like alkaloids (Jean *et al*., 1999), flavonoids (Gilles *et al*., 1999), and steroids (Akirai, 1999). This plant is also reported to acquire many properties like anti-cancerous activity (Jean *et al*., 1999), antioxidant activity (Jaleel *et al*., 2000), beside its antidiabetic properties (Sumana *et al*., 2001), it possess hypolipidemic activity (Antia and Okokon, 2005) also.

Ficus religiosa

A member of Moraceae and coomonly known as Peepal and is considered sacred in India. This plant has been reported to be used in the traditional medicine preparation for diabetis treatment for long time (Simmonds and Howes, 2006). The bark of the tree is used to prepare the decoction which is used for treatment of diabetes. This plant contains several bioactive agents due to which carries out several active function. The major bioactive agents include tannins, polyphenolic compounds, flavonoids, saponins, and sterols. The bioactive agents that impart the hypoglycemic activity are leucocyandin 3-O-beta-d-galactosyl cellobioside, leucopelargonidin-3-O-alpha-L rhamnoside (Bonuham *et al*., 2006; Avodhya *et al*., 2010). The leaves of the plant are used in the anti-hyperglycemic activity study (Deshmukh *et al*., 2007). This plant has shown to provide a wide spectrum in vitro and in vivo activity. These activities includes antidiabetic, antitumor, antiulcer, antianxiety, hypolipidemic, anti-inflammatory, estrogenic, anti-asthmatic, apoptosis inducer, analgesic, cognitive enhancer and anti-hypertensive (Singh *et al*., 2011). Aqueous extract of the plant when administered orally showed significant result by lowering blood glucose level and elevated the level of insulin. *F. religiosa* is found to modulate the enzymes of the antioxidant defense system hence helps to combat the problem of oxidative stress.

Morus alba

It is a short lived plant belonging to the family Moraceae and locally known as white mulberry. The constituent of the plant with hypoglycemic effects are Moracin M, steppogenin-4'-O-β-D-glucoside and mulberroside A and they were isolated form the root bark plant (Zhang *et al*., 2009). The ethanol extract of leaves when administered has shown the antihyperglycemic, antioxidant and antiglycation effect in the rats suffering from chronic diabetes (Naowaboot *et al*., 2009). Freeze dried powder of the mulberry was also analyzed for the hypolipidemic activity as well (Yang *et al*., 2010). Mulberroside A is a glycosylated stilbenoid and it is found to be useful in treatment of the hyperuricemia and gout disease (Kim *et al*., 2010; Wang *et al*., 2011).

The disease Diabetes is spreading at an alarming rate throughout the world and a large population of world is affected which in tur is considered as a major cause of the high economic loss which can in turn impede the development of the nation. The uncontrolled diabetes leads to many other complications as well. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Therefore the treatment of the disease with the plant derived materials which are easily accessible to most people and which do not require the laborious pharmaceuticals synthesis seems more approaching and highly attractive method.

The current study has focused on several common plants and herbs, which are easily available, for their potent antidiabetic properties along with their mode of action and some other accessory effects too. The study has revealed the importance of such common plants and herbs in effectively controlling the disease through several practical analyses. These plants have been used for many other purposes as well hence provide many other useful applications other than being antidiabetic agents. Due to their potential properties there is needed to look forward for the conservation and guidance for the effective use of these plants in daily life. According to Ayurveda there are a lot more plants and herbs available contributing to the huge collection of antidiabetic plants in the world. Not only is this there are several plants with many other important properties, nature full of potent plants with many medicinal properties against

many more disease. These plants also contribute in overcoming the complications of diabetes.

The future studies could focus on isolation, purification, characterization and analysis of such important phytochemical compounds from the plants and to study their potential in other disease treatments as well. The future studies could focus on exploring some other easily available plant and herbs with potential of treating diabetes in order to enhance the usage of plant products among world populations which indirectly will confer to conserve these important natural gifts. The further studies could focus on analyzing the individual importance and role of each phytochemical compound present such medicinal plants.

CONCLUSION

Since the time immemorial the medicinal plants are utilized widely for maintenance of the human well beings. As per Ayurveda the Mother Nature has blessed us with a huge collection of the medicinal plants with potent activities. The natural resources are still considered as the best source for the drug development programs. The medicinal plants provide us with the mine of bioactive agents that play crucial role in maintaining the human health in various aspects. The nature has provided us with lots of medicinal plants carrying out the antidiabetic activity. With the proper understanding and proper use these plants can be used as an effective resource for the treatment of this world wide disease, Diabetes. In today's generation the data on the study of the biological activity and bioactive compounds of plant is tremendously increasing. There is a need to grab the information and exploit it in a right way to obtain a better solution of the health issue. The outcome of these studies and research will help to provide the starting point for the development of the herbal drugs. The herbal drugs have gain popularity in modern time due to their effectiveness without any side effects. The plants are a rich source of variety of phytochemical that confers the disease management properties in them. The major effort should to be kept in minimizing the time for screening the plant for its antidiabetic properties and as wells as for isolation of bioactive compounds for natural drug development. If the direction of exploration is kept appropriate then these plants can act as the infinite source of the active components that can cure the disease and disorders.

REFERENCES

Akirai S. (1999). Brassinosteroid biosynthesis, Plant Physiol Biochemistry; 37:351-61.

Alarcon-Aguilara FJ, Roman-Ramos R, Perez-Gutierrez S, Aguilar-Contreras A, Contreras-Weber CC, Flores-Saenz JL. (1998), Study of the anti-hyperglycemic effect of plants used as antidiabetics, J. Ethnopharmacology; 61: 101-110.

Al-Attar A. M. and Alsalmi F. A., Effect of *Olea europaea* leaves extract on streptozotocin induced diabetes in male albino rats, Saudi Journal of Biological Sciences, vol. 26, no. 1, pp. 118–128, 2019.

Ambike S. and Rao M. (1967), Studies on a phytosterolin from the bark of *Ficus religiosa*, The Indian Journal of Pharmacy; 29:91–94.

Antia BS, Okokon JE. (2005). Effect of leaf juice of *Catharanthus roseus* Linn. On cholesterol, triglyceride and lipoproteins levels in normal rats. Indian J Pharm.; 37: 401-2.

Aruna A., Nandhini R., Karthikeyan V., Bose P., Vijayalakshmi K. (2014). Comparative anti-diabetic effect of methanolic extract of insulin plant (*Costus pictus*) leaves and its silver nanoparticle. Indo Am J Pharm Research; 4:3217-30.

Atangwho IJ, Ebong PE, Eyong EU, Williams IO, Eteng MU. (2009). Comparative chemical composition of leaves of some antidiabetic medicinal plants: *Azadirachta indica, Vernonia amygdalina and Gongronema latifolium*, African J Biotech; 8: 4685-4689.

Atkinson MA, Maclaren NK (1994). The pathogenesis of insulin-dependent diabetes mellitus. New Eng. J Med; 331: 1428-1436.

Augusti K (1996). Therapeutic values of onion (*Allium cepa L.)* and garlic (*Allium sativum L.*). Indian J Exper. Biology; 34: 634-640.

Ayodhya S., Kusum S., and Anjali S. (2010). Hypoglycemic activity of different extracts of various herbal plants Singh, International Journal of Ayurveda and Research in Pharmacy; 1(1):212–224.

Basch E, Ulbricht C, Kuo G, Szapary P, Smith M (2003). Therapeutic applications of fenugreek. Alter Med Rev; 8: 20-27.

Bastaki A (2005). Diabetes mellitus and its treatment. International Journal Diabetes Metabolism; 13: 111-134.

Bearse MA, Han Y, Schneck ME, Barez S, Jacobsen C. (2004). Local multifocal oscillatory potential abnormalities in diabetes and early diabetic retinopathy. Inv Ophthalmol Visual Science; 45: 3259-3265.

Bhavna, S., Chandrajeet, B. and Partha, R., (2008). Hypoglycemic and hypolipidemic effects of flavonoid rich extract from *Eugenia jambolana* seeds on streptozotocin induced diabetic rats. Food Chem. Toxicology; 46, 2376–2383.

Bnouham M, Ziyyat A, Mekhfi H, Tahri A, Legssyer A (2006). Medicinal plants with potential antidiabetic activity-A review of ten years of herbal medicine research (1990-2000). Int Diabetes Metabo; 14: 1-25.

Bnouham M., Ziyyat A.,Mekhfi H. , Tahri A., and Legssyer A. (2006). Medicinal plants with potential antidiabetic activity—a review of ten years of herbal medicine research (1990–2000), International Journal of Diabetes and Metabolism; 14(1):1–25.

Cheng D., Liang B., and Li Y., Antihyperglycemic effect of *Ginkgo biloba* extract in streptozotocin-induced diabetes in

rats, BioMed Research International, vol. 2013, Article ID 162724, 7 pages, 2013.

Chung-Hung C, Gek-Cheng N, Yusoff R. (2012). A brief review on anti-diabetic plants: Global distribution, active ingredients, extraction techniques and acting mechanisms. Pharmacogn Rev; 6(11):22-28.

Deepashree BN, Prakash JA. (2007). Study on nutritional status of diabetics and associated risk factors. J Human Ecol.; 21:269-274.

DeFronzo RA, Bonadonna RC, Ferrannini E (1992). Pathogenesis of NIDDM: a balanced overview. Diabetes Care; 15: 318-368.

Deshmukh T.A., Yadav B. V., Badole S. L., Bodhankar S. L., and Dhaneshwar S. R. (2007). Antihyperglycaemic activity of petroleum ether extract of *Ficus racemosa* fruits in alloxan induced diabetic mice, Pharmacology online; 2:504–515.

Dey L, Attele AS, Yuan C-S (2003). Alternative therapies for type 2 diabetes. Textbook of Complementary and Alternative Medicine.Taylor & Francis, Boca Raton, USA.

Eidi A, Eidi M, Esmaeili E (2006). Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin-induced diabetic rats. Phytomed 13: 624-629.

Farswan, M., Mazumder, P. M., Parcha, V. and Upaganlawar, V. (2009). Modulatory effect of *Syzygium cumini* seeds and its isolated compound on biochemical parameters in diabetic rats. Int. J. Green Pharm., 5, 127–133.

Gilles B, Marie GD, Bruno D, Anne MM. (1999). A new flavonol glycoside from *Catharanthus roseus*. Phytochemistry; 50:167-9.

Goel R, Bhatia D, Gilani SJ, Katiyar D (2012). Medicinal plants as antidiabetics: A review. Int Bull Drug Res 1: 100-107.

Grover J, Yadav S, Vats V (2002). Medicinal plants of India with anti-diabetic potential. J Ethnopharmacology; 81: 81-100.

Gupta PD, De A (2012). Diabetes Mellitus and its herbal treatment. International Journal Res. Pharmaceutical Biomedical science; 3: 706-721.

Gupta, R., Bajpai, K. G., Johri, S. and Saxena, A. M. (2008). An overview of Indian novel traditional medicinal plants with antidiabetic potentials. Afr. J. Tradit. Complement. Altern. Med., 5, 1–17.

International Diabetes Federation, IDF Diabetes Atlas, IDF, Brussels, Belgium, 2009, 4th edn, pp. 21–27.

Islam, M. S., Choi, H. and Loots, D. T. L. (2008). Effects of dietary onion *Allium cepa* L. in a high-fat diet streptozotocin-induced diabetes rodent model. Ann. Nutr. Metab.; 53, 6 12.

Jafri MA, Aslam M, Javed K, Singh S. (2000). Effect of *Punica granatum* Linn (flowers) on blood glucose level in normal and alloxan-induced diabetic rats. J. Ethnopharmacology; 70: 309-314.

Jaleel CA, Gopi R, Manivannan P, Sankar B, Kishorekumar A, Panneerselvam R. (2007). Antioxidant potentials and ajmalicine accumulation in *Catharanthus roseus* after treatment with giberellic acid. Colloids Surf B Biointerfaces; 60:195-200.

Jean HR, Jean MN, Gaelle LC, Philippe T, Monique ZH, Louisette LM, (1999). Isolation of indole alkaloids from *Catharanthus roseus* by centrifugal partition chromatography in the pH-zone refining mode. J Chromatogr A; 849:421-31.

Joshi, S. R. and Parikh, R. M. (2007). India – diabetes capital of the world: now heading towards hypertension. J. Assoc. Physicians India; 55, 323–324.

Kesari AN, Gupta RK, Singh SK, Diwalar S, Watal G (2006). Hypoglycemic and anti-hyperglycemic activity of *Aegle marmelos* seed extract in normal and diabetic rats. J Ethnopharmacology; 107: 374-379.

Kesari AN, Gupta RK, Watal G. (2005). Hypoglycemic effect of *Murraya koenigii* on normal and alloxan diabetic rabbits. J Ethnopharmacology; 97:247-51.

Khan MRI, Islam MA, Hossain MS, Asadujjaman M, Wahed MII, Rahman BM, (2010). Antidiabetic effects of the different fractions of ethanolic extracts of *Ocimum sanctum* in normal and alloxan induced diabetic rats. J Sci Research; 2:158-68.

Kim JK, Kim M, Cho SG, Kim MK, Kim SW, Lim YH. (2010). Biotransformation of mulberroside a from *Morus alba* results in enhancement of tyrosinase inhibition. J Ind Microbiol Biotechnology; 37:631-7.

Kimura, I. (2006). Medical benefits of using natural compounds and their derivatives having multiple pharmacological actions. Yakugaku Zasshi; 126, 133–143.

Kumar AS, Kavimani S, Jayaveera K (2011). A review on medicinal Plants with potential antidiabetic activity. International J Phytopharmacology 2: 53-60.

Kumari, K. and Augusti, K. T. (2007). Lipid lowering effect of *S*-methyl cysteine sulfoxide from *Allium cepa* Linn in high cholesterol diet fed rats. J. Ethnopharmacology; 109, 367–371.

Looker HC, Campagna AF, Gunter EW, Pfeiffer CM, Venkat Narayan KM. (2003) Homocysteine as a risk factor for nephropathy and retinopathy in Type 2 diabetes. Diabetologia; 46: 766-772.

Maiti R, Jana D, Das UK, Ghosh D. (2004). Antidiabetic effect of aqueous extract of seed of *Tamarindus indica* in streptozotocin induced diabetic rats. J Ethnopharmacology; 92: 85-91.

Maity P, Hansda D, Bandyopadhyay U, Mishra DK (2009) Biological activities of crude extracts and chemical constituents of Bael, *Aegle marmelos* (L.) *Corr. Indian J Exper Biology*; 47: 849-861.

Mandal, S., Barik, B., Mallick, C., De, D. and Ghosh, D. (2008). Therapeutic effect of ferulic acid, an ethereal fraction of ethanolic extract of seed of *Syzygium cumini* against streptozotocin-induced diabetes in male rat. Methods Find. Exp. Clin. Pharmacology; 30, 121–128.

McLarty DG, Athaide I, Bottazzo GF, Swai AMB, Alberti KGMM (1990). Islet cell antibodies are not specifically associated with insulin-dependent diabetes in Tanzanian Africans. Diabetes Res clinical Prac 9: 219-224.

Mentreddy, S. R., Mohamed, A. I. and Rimando, A. M., Medicinal plants with hypoglycemic/anti-hyperglycemic properties: a review. Proc. Assoc. Adv. Ind. Crop Conf., 2005, **20**, 341–353.

Modak M., Dixit P., Londhe J. , Ghaskadbi S., and Devasagayam T. P. A.(2007). Indian herbs and herbal drugs used for the treatment of diabetes, Journal of Clinical Biochemistry and Nutrition; 40(3):163–173.

Mohan, V., Sandeep, S., Deepa, R., Shah, B. and Varghese, C. (2007). Epidemiology of type-2 diabetes: Indian scenario. Indian J. Med. Research; **125**, 217–230.

Mukherjee, P. K., Maiti, K., Mukherjee, K. and Houghton, P. J., (2006). Leads from Indian medicinal plants with hypoglycemic potentials. J. Ethnopharmacology; **106**, 1–28.

Mukhtar HM, Ansari SH, Bhat ZA, Naved T, Singh P (2006). Antidiabetic activity of an ethanol extract obtained from the stem bark of *Psidium guajava* (Myrtaceae). Die Pharmazie - An Int J Pharmaceu Science; 61: 725-727.

Murali Mohan N. (2006).Thesis entitled Biochemical studies on α-amylase inhibitors derived from Indian medicinal herbs as potential anti-diabetic agent submitted to Andhra University, Visakhapatnam: 25-30.

Naowaboot J, Pannangpetch P, Kukongviriyapan V, Kongyingyoes B, Kukongviriyapan U. (2009). Antihyperglycemic, antioxidant and antiglycation activities of mulberry leaf extract in streptozotocin-induced chronic diabetic rats. Plant Foods Hum Nutr; 64:116-21.

Nasim, S. A., Dhir, B., Samar, F., Rashmi, K. and Mahmooduzzafar, M. A. (2009). Sulphur treatment alters the therapeutic potency of allin obtained from garlic leaf extract. Food Chem. Toxicology; 47, 888–892.

Nayak P, Kar DM, Maharana L. (2011). Antidiabetic activity of aerial parts of *Argemone mexicana* L. In alloxan induced hyperglycaemic rats. Pharmacology Online; 1:889-903.

Oh WK, Lee CH, Lee MS, Bae EY, Sohn CB. (2005). Antidiabetic effects of extracts from *Psidium guajava*. J Ethnopharmacology; 96: 411-415.

Pankaj NK, Alam M, Roy BK, (2006), Antidiabetic activity of seed powder of *Holarrhena antidysenterica* in rabbits. Journal of Research, Birsa Agricultural University.

Pari L., Saravanan R. (2004). Antibiabetic effect of diasulin, a herbal drug, on blood glucose, plasma insulin and hepatic enzymes of glucose metabolism in hyperglycaemic rats. Diabetes, obesity and metabolism; 6:286-292.

Ponnusamy S, Ravindran R, Zinjarde S, Bhargava S, Kumar AR. (2011). Evaluation of traditional Indian antidiabetic medicinal plants for human pancreatic amylase inhibitory effect *in vitro*. Evid Based Complementary Altern Med; 1-10.

Prabhakar, P. K. and Doble, M. A. (2008). Target based therapeutic approach towards diabetes mellitus using medicinal plants. Curr.Diabetes Rev.; **4**, 291–308.

Prakash P, Gupta N (2005). Therapeutic uses of *Ocimum sanctum* Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review. Indian J Phys Pharmacology; 49: 125.

Rabinkov, A., Miron, T., Konstantinovski, L., Wilchek, M., Mirelman, D. and Weiner, L. (1998). The mode of action of allicin: trapping of radicals and interaction with thiol containing proteins. Biochim. Biophys. Acta; **1379**, 233–244.

Rajalakshmi M, Eliza J, Priya CE, Nirmala A, Daisy P. (2009). Antidiabetic properties of *Tinospora cordifolia* stem extracts on streptozotocin-induced diabetic rats. African J Pharm Pharmacology; 3(5):171-180.

Raman ALau C (1996). Anti-diabetic properties and phytochemistry of *Momordica charantia* L. (Cucurbitaceae). Phytomed; 2: 349-362.

Ramchandran A., Know the signs and symptoms of diabetes. Indian J Med Res. 2014; 140(5):579-81.

Rezaei S, Asgari Mobarake K, Saberi A, Keshavarz P, Leili EK. Brain-derived neurotrophic factor (BDNF) Val66Met polymorphism and post-stroke dementia: a hospital-based study from northern Iran. Neurol Sci. 2016; 37(6):935- 42.

Rizvi S I and Mishra N, Traditional Indian Medicines Used for the Management of Diabetes Mellitus, Journal of Diabetes Research, Volume 2013, Article ID 712092, 11 pages.

Sabu M, Kuttan R (2004). Antidiabetic activity of Aegle marmelos and its relationship with its antioxidant properties. Indian J Physiol Pharmacology; 48: 81-88.

Saravanan, G. and Ponmurugan, P. (2010). Beneficial effects of S-allylcysteine (SAC) on blood glucose and pancreatic antioxidant system in streptozotocin diabetic rats. Plant Foods Hum. Nutrition; **65**, 374–378.

Saxena, A. and Vikram, N. K. (2004). Role of selected Indian plants in management of type 2 diabetes: a review. J. Altern. Complement. Med.; **10**, 369–378.

Saxena, A. M., Mukherjee, S. K. and Shukla, G. (2006). Progress of diabetes research in India during 20th century. National Institute of Science and Communication (CSIR), New Delhi: 1–104.

Seki M, Tanaka T, Nawa H, Usui T,Fukuchi T, (2004). Involvement of brain-derived neurotrophic factor in early retinal neuropathy of streptozotoc ininduced diabetes in rats therapeutic potential of brain-derived neurotrophic factor for dopaminergic amacrine cells. Diabetes; 53: 2412-2419.

Sharma B, Balomajumder C, Roy P (2008). Hypoglycemic and hypolipidemic effects of flavonoid rich extract from *Eugenia jambolana* seeds on streptozotocin induced diabetic rats. Food Chem Toxicology 46: 2376-2383.

Shen Y, Fukushims M, Ito Y, Muraki E, Hosono T. (2010). Verification of the antidiabetic effects of cinnamon (*Cinnamomum zeylanicum*) using insulinun controlled type 1 diabetic rats and cultured adipocytes. Biosci Biotechnol Biochem 74: 2418-2425.

Shinde J, Taldone T, Barletta M, Kunaparaju N, Hu B. (2008) α-Glucosidase inhibitory activity of *Syzygium cumini* (Linn.) Skeels seed kernel in vitro and in Goto–Kakizaki (GK) rats. Carbohydrate Research; 343: 1278-1281.

Shruthi A, Latha KP, Vagdevi HM, Pushpa B, Shwetha C. (2012). Antidiabetic activity of the leaves extracts of *Wrightia tinctoria* on alloxan induced diabetic rats. J Chem Pharm Res; 4:3125-8.

Simmonds M. and Howes M. (2006). Plants used in the treatment of diabetes, in Traditional Medicines for Modern Time–

Antidiabetic Plants, A. Soumyanath, Ed., vol. 6th, pp. 19–82, CRC Press/Taylor and Francis Group.

Singh D., Singh B. and Goel R. K. (2011). Traditional uses, phytochemistry and pharmacology of *Ficus religiosa*: a review, Journal of Ethnopharmacology; 134 (3) 565–583.

Singh V., Kori M. L. (2014). Antidiabetic effect of hydroalcoholic combined plant extract of *Portulaca oleracea* and *Caralluma attenuata* in streptozotocin induced diabetic rats. Indo Am J Pharm Research; 4:1391-6.

Sofowora A. (1996). Research on medicinal plants and traditional medicine in Africa. JCAM; 2:365-72.

Song, Y., Manson, J. E., Buring, J. E., Howard, D. and Simin Liu, S. (2005). Associations of dietary flavonoids with risk of type 2 diabetes and markers of insulin resistance and systemic inflammation in women: a prospective study and cross-sectional analysis. J. Am. Coll. Nutrition; **24**, 376–384.

Subash Babu P, Prabuseenivasan S, Ignacimuthu S. (2007). Cinnamaldehyde-A potential antidiabetic agent. Phytomed 14: 15-22.

Sumana G, Suryawanshi SA. (2010). Effect of *Vinca rosea* extracts in treatment of alloxan diabetes in male albino rat. Indian J Exp Biology; 39:74859.

Sunil Kumar, Smita Narwal, Dinesh Kumar, Gurvirender Singh, Sumit Narwal, Renu Arya. (2012). Evaluation of antihyperglycemic and antioxidant activities of *Saraca asoca* (Roxb.) De. Wild leaves in streptozotocin induced diabetic mice. Asian Pac J Trop Dis; 170-6.

Svensson M, Eriksson JW, Dahlquist G (2004). Early glycemic control, age at onset, and development of microvascular complications in childhood-onset type 1Diabetes a population-based study in Northern Sweden. Diabetes Care; 27: 955-962.

Tanaka, M. (2006). Identification of five phytosterols from *Aloe vera* gel as antidiabetic compounds. Biol. Pharm. Bull; **29**, 1418–1422.

Tripathi Ak, Bhoyar PK, Baheti JR, Biyani DM, Khalique M. (2011) Herbal antidiabetics: A review. Int J Res Pharm Science; 2: 30-37.

Venkatesh S, Thilagavathi J, ShyamSundar D. (2008). Antidiabetic activity of flowers of *Hibiscus rosasinensis*, Fitoterapia; 79(2):79-81.

Wallace C, Reiber GE, LeMaster J, Smith DG, Sullivan K. (2002) Incidence of falls, risk factors for falls, and fall-related fractures in individuals with diabetes and a prior foot ulcer. Diabetes Care; 25: 1983-1986.

Wang CP, Wang Y, Wang X, Zhang X, Ye JF, Hu LS, (2011). Mulberroside a possesses potent uricosuric and nephroprotective effects in hyperuricemic mice. Planta Med; 77:786-94.

Wang X., Gao L., Lin H. et al., Mangiferin prevents diabetic nephropathy progression and protects podocyte function via autophagy in diabetic rat glomeruli, European Journal of Pharmacology, vol. 824, pp. 170–178, 2018.

World Health Organization (2002). Traditional medicine-growing needs and potential; *WHO* Policy Perspective on Medicines; 2:1–6.

World Health Organization. Global Report on Diabetes. WHO Library Cataloguing in Publication Data. Geneve. 2016; 978.

Yagi, A., Hegazy, S., Kabbash, A. and Abd-El Wahab, E. (2009). Possible hypoglycemic effect of *Aloe vera* L. High molecular weight fractions on type 2 diabetic patients. Saudi Pharma. Journal; **17**, 209–215.

Yang X, Yang L, Zheng H. (2010). Hypolipidemic and antioxidant effects of mulberry (*Morus alba* L.) fruit in hyperlipidaemia rats. Food Chem Toxicology; 48:2374-9.

Zhang M, Chen M, Zhang HQ, Sun S, Xia B, Wu FH. (2009). In *vivo* hypoglycemic effects of phenolics from the root bark of *Morus alba*. Fitoterapia; 80:475-7.

Zimmet P, Alberti K, Shaw J (2001). Global and societal implications of the diabetes epidemic. Nature 414: 782-787.

Zimmet P, Cowie C, Ekoe JM, Jonathan S (2004). Classification of diabetes mellitus and other categories of glucose intolerance. Int Text book Diabetes Mellitus. John Wiley & Sons, Ltd, New York, USA.

Zimmet P, Dowse G, Finch C, Serjeantson S, King H (1990). The epidemiology and natural history of NIDDM–lessons from the South Pacific. Diabetes/ metabolism Rev; 6: 91-124.