

## A critical review on Antidiabetic Potential of Herbal plants and its their bioactive components

T. Sivakumar<sup>1\*</sup> B. Deepa<sup>2</sup>,

*1\*Department of Botany, Annamalai University, Annamalai Nagar, Tamil Nadu, India-608 002. Department of Botany, Thiru A. Govindsamy Government Arts College, Tindivanam,*

*Tamil Nadu, India 604 307.*

*2. Department of Biochemistry and Biotechnology, Annamalai University, Annamalai Nagar-608 002. Dharmapuram Gnanmbigai Govt. Arts College for Women, Mayiladuthurai, Tamil Nadu (609 001), India*

1E-mail: [drtsiva\\_19@rediffmail.com](mailto:drtsiva_19@rediffmail.com); [drtsivanano@gmail.com](mailto:drtsivanano@gmail.com)

2\*E-mail: [bdeepa.sap@gmail.com](mailto:bdeepa.sap@gmail.com)

### Abstract

The aim of the recent critical review was to investigate the bioactive components, and antidiabetic activity of ten herbal plants extracts. Herbal plant-derived secondary metabolites of qualitative phytochemicals such as alkaloid, terpenoids, flavonoids, steroid, phenol, anthraquinones, saponin, tannin and glycoside. Herbal plants contain a diversity of biological properties beneficial to humans, like as their antioxidant, antimicrobial, antiallergic, anticancer, anti-inflammatory, and antidiabetic activities. Diabetes mellitus is a chronic disease of metabolic disorders in the  $\beta$ -cells of the pancreas with hyperglycemia. Hyperglycemia can be caused by a lack of insulin production by the pancreas (type 1 diabetes) or by insulin resistance (type 2 diabetes). Present diabetes medications focus on controlling blood glucose levels in the vessel and bringing them down to normal levels. Moreover, most modern drugs have many side effects that cause some important medical problems during treatment. Therefore, herbal plants have been used for a long time and play a vital role as alternative medicines. Also, in the last few years, some new bioactive ingredients isolated from herbal plants have indicated the antidiabetic activity better than the oral hypoglycemic agents used in clinical treatment. Herbal medicine has made a good medical practice and shows a bright future in the treatment of diabetes. Hence, this article modern reviews the bioactive compounds and medicinal effects of ten important herbal plants widely used in the treatment of diabetes.

**Key words:** Antidiabetics, herbal plants, Alkaloids, Phenols, Alpha amylase, B-glucosidase

### Introduction

Diabetes mellitus (DM) is defined by abnormally higher glucose levels due to abnormalities in insulin production or insulin resistance, and some individuals may have both causes [1]. Diabetes mellitus is divided into three main types [2–4]. Type 1 diabetes (insulin-dependent diabetes) is an autoimmune disorder that occurs when the body's insulin-producing cells in the pancreas are destroyed and the pancreas produces little or no insulin. A person with type 1 DM must take insulin daily to survive. It mostly develops in children and young adults. Type 2 diabetes is another term also known as “insulin-independent diabetes mellitus” which accounts for more than 90% of adults diagnosed with DM. This is when the pancreas produces enough insulin, but the body cannot use the insulin effectively, which is called insulin resistance. Gestational diabetes mellitus (GDM) is the degree of glucose intolerance with onset or first recognition in the second or third trimester of pregnancy. GDM is caused by pregnancy hormone or insulin deficiency. GDM is one of the most common metabolic disorders during pregnancy.

Symptoms shown by diabetic's patients include thirst, polyuria, blurred eyesight and weight loss. Ketoacidosis or non-ketotic hyperosmolarity can cause dehydration in a person and can lead to death without adequate treatment [5]. Along with physical activity, a healthy diet is important for diabetes management [6]. All types of oral hypoglycemic drugs and insulin are safe in elderly patients if treatment is properly administered, although each drug has certain limitations associated with

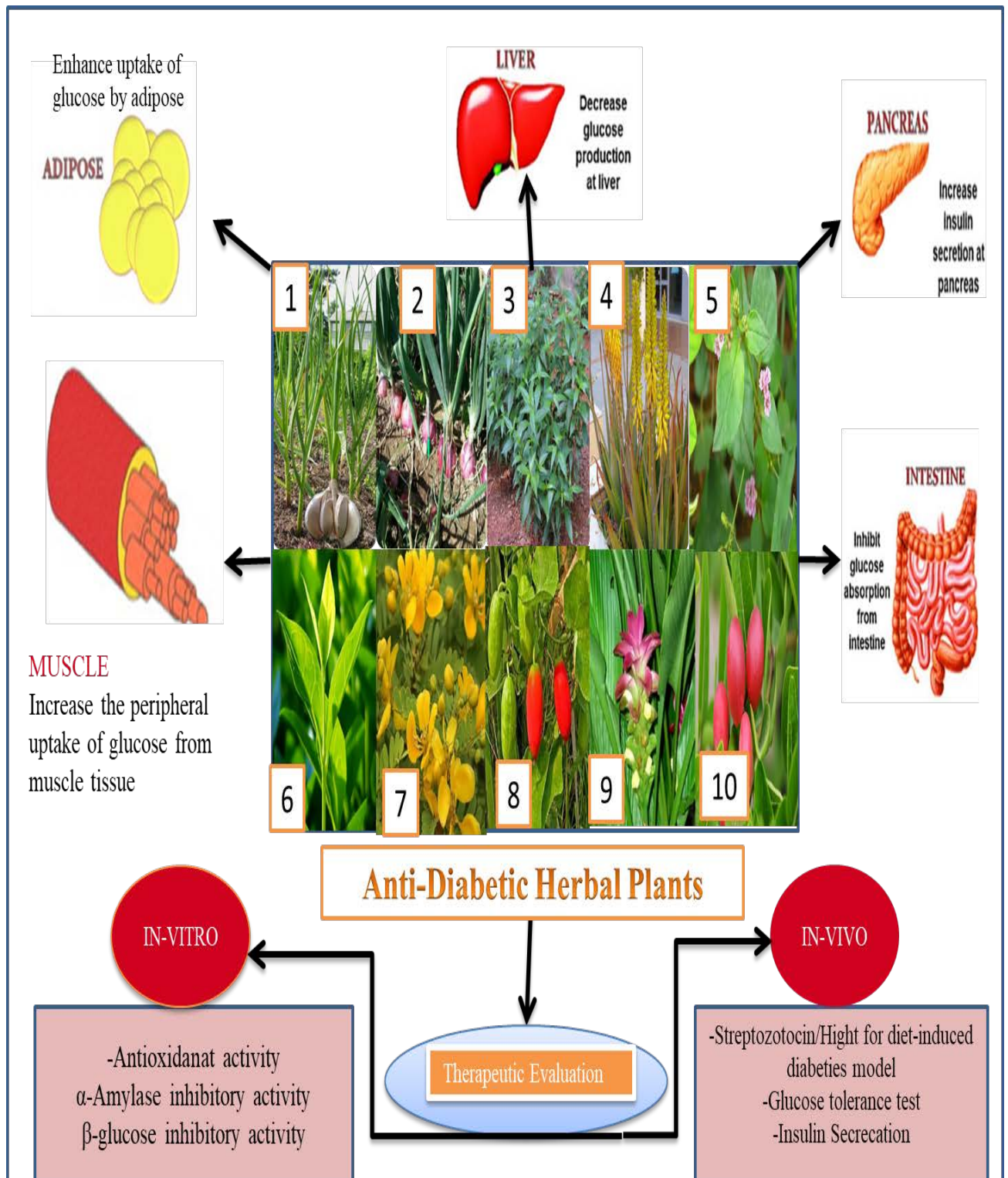
hypoglycemia risk or comorbidities [7]. According to Curtis (2007), despite many effective oral hypoglycemic agents, 5–10% of cases develop secondary failure. Secondary failure occurs when beta-cell function deteriorates, medication adherence is poor, weight gain, lack of exercise, dietary changes, or disease occur [8]. In underdeveloped countries (especially rural areas), pharmaceutical drugs and insulin used to treat diabetes are rare, expensive, and have significant side effects. Treatment costs are expensive and unaffordable in developing countries, which is a major underlying barrier to DM. In light of this, phototherapy and the use of natural products with antidiabetic properties are often the first lines of treatment and care [9].

Conventional medicines are normally the first choice for primary health care of patients in developing nations because of better cultural acceptance, better compatibility with the human body and fewer side effects than modern treatments. Currently, some medicinal plants have been reported to be effective in diabetes worldwide and have been used empirically as antidiabetic and antihyperlipidemic drugs. More than 400 medicinal plants having hypoglycemic activity are available in the literature [10-15], however, the study of new antidiabetic drugs from natural plants is still attracting because they contain phytoconstituents that prove alternative and safe effects in the treatment of diabetes mellitus. Most plants contain biochemical constituents such as phenolics, glycosides, alkaloids, terpenoids, flavonoids, carotenoids, Steroids, phenols which have been developed as anti-diabetic activities [16-21].

The plant is always been considered as one of the most reliable sources of cure for diseases and many synthetic drugs are directly or indirectly derived from them. Plants and plant products can exert promising antidiabetic efficacy based on recent studies. Plant sources of antidiabetic drugs have been popular since ancient times because they are relatively safer and more affordable alternatives than synthetic drugs and are also mentioned in many folk medicines including Indian, Korean and Chinese culture. Folk herbal medicines and functional foods are believed to improve diabetes syndrome through six significant mechanisms, including insulin secretion and sensitivity, glucose uptake by muscle cells and adipose tissue, inhibition of glucose uptake from the intestine, and inhibition of glucose production from hepatocytes, Anti-inflammatory properties [22]. As a result, functional foods and phytotherapies are becoming increasingly popular worldwide [23]. In this review, we have compiled the most significant herbal and food plants along with their isolated antidiabetic phytochemicals to provide unique insights for establishing novel functional foods and drug blocks against diabetes.

### **Herbal plants and antidiabetic activity**

Most common, easily available and effective antidiabetic herbal plants like as 1.Garlic (*Allium sativum*), 2.onion (*Allium cepa*), 3.kalomegh (*Andrographis paniculata*), 4.ghrita kumara (*Aloe vera*), 5.erect spiderling (*Boerhavia diffusa*), 6.Tea (*Camellia sinensis*), 7.Avaarai (*Cassia auriculata*), 8.ivy gourd (*Coccinia indica*), 9.Turmeric (*Curcuma longa*), 10. gurmar (*Gymnema sylvestre*) are shown in the (Fig.1: Table 1). These ten plants are a rich source of phytochemicals and antidiabetic activity.



**Figure.1. Schematic overview of effect of the antidiabetic activity of ten herb can be inhibit hyperglycemia, Diabetes mellitus, alpha amylase, beta glucosidase activity and stimulate pancreatic cell activity, insulin secretion activity.**

**Table 1. Antidiabetic activity, mechanism of well known herbal plants and its their bioactive components**

S. No.	Botanical Name	Family	used parts	Active Ingredients	Mechanism of Action	Activity	Types of Study
1	Allium sativum L.	Amaryllidaceae	Bulb	Allicin	Anti-hyperglycemic	Antidiabetic activity	Invivo
2	Allium cepa	Amaryllidaceae	Bulb	S-methyl cysteine sulfoxide, S-allyl cysteine sulfoxide	Stimulates pancreatic $\beta$ -cells	Hypoglycemic effect Antidiabetic activity	Invivo
3	Andrographis paniculata	Acanthaceae	Whole plant	Andrographolide,	Regeneration of pancreatic $\beta$ cells, insulin secretion	Antidiabetic & hepatoprotective	Invivo
4	Aloe barbadensis	Asphodelaceae	leaves	Aloin, barbaloin, isobarbaloin, aloetic acid	Insulin secretion and synthesis	Antidiabetic activity	Invivo
5	Boerhavia diffusa	Nyctaginaceae	Leaves	Punarnavine, Boeravinone A-F	Increase in hexokinase activity, increase plasma insulin level, antioxidant	Antidiabetic activity	Invivo
6	Camellia sinensis	Theaceae	Leaves	Epigallocatechin-gallate, gallic acid, epicatechin, (+) catechin, (-) epicatechin	Free radical scavenging activity, insulinonemetic activity	Antidiabetic activity Antihyperglycemic activity	Invivo
7	Cassia auriculata	Fabaceae	Leaf, flower, root	Bis (2-ethyl hexyl) phthalate	$\alpha$ -Glucosidase-inhibiting activity	Antidiabetic activity	invitro
8	Coccinia indica	Cucurbitaceae	Areal parts	- $\beta$ - Amyrin Acetate, Lupeol, Cucurbitacin B, Taraxerone, Taraxerol, $\beta$ -carotene, Lycopene	Initiate insulin secretion, carbohydrate digestion and absorption.	Antidiabetic activity	Invivo
9	Curcuma longa	Zingiberaceae	rhizomes	Curcumin, termerone, germacrone, zingiberene	Inhibition of $\alpha$ -glucosidase, inhibition of GSK-3 $\beta$	Antidiabetic activity	Invivo
10	Gymnema sylvestris	Asclepidaceae	leaf	Gymnemic acid, Stigmasterol, Gurmarin, betaine, gymnemosides	Regeneration of pancreatic $\beta$ cells, $\alpha$ -glucosidase inhibitor, insulin secretion	Antidiabetic agent	Invivo

### **Allium sativum L.**

*Allium sativum L.* commonly known as garlic is an herb that belongs to the Liliaceae family and also it can be found in Asia, Africa and Europe. Garlic originally from Asia and is now becoming widely used popular as a spices and condiment, especially in Asian cuisine [24]. Their activities prove that garlic has been a potent medicinal plant to treating various ailments for over a thousand years. According to many scientific research studies, garlic has been found to have a broad range of biological activities such as antitumor activity, antibiotic and antimicrobial activity, especially antihyperglycemic activity [16,25]. Green garlic contains many active phytochemicals such as alkaloids, flavonoids, cardiac glycosides, terpenes and steroids, resin. It also contains some sulfur compounds such as alliin, allicin, ajoene diallyl sulfide, enzymes, B-vitamins, proteins, minerals, saponins, flavonoids, which are not sulfur containing compounds[26].

Based on these scientific studies, it has been demonstrated that the biological activity of garlic against anti-diabetics is to control insulin excretion from  $\beta$ -cells, improve glucose tolerance and glycogen synthesis [27]. For example, allyl propyl disulfide and S-methylcysteine sulfoxide, two biochemical compounds extracted from garlic, can lower blood glucose levels. In addition, ethanol extract from garlic had antidiabetic activity by restoring the delayed insulin response [28].

### **Allium cepa**

*Allium cepa L.* Commonly known as onion, it belongs to Liliaceae family. It is a useful ingredient in cooking in many countries, especially India, Vietnam, China and Egypt. *A. cepa* can survive harsh conditions, e.g., winter or dryness, and thus can be stored for a long time without any change in phytonutrients. Onions contain a large number of biologically active compounds. These phytoconstituents including phenolics, flavonoids, thiosulfonates, amino acids, essential oils and vitamins, etc. have been successfully isolated and identified. Onion extracts exhibit different biological activities like antioxidant activity, anti-inflammatory activity, and anti-diabetic activity. The important bioactive ingredients of onion extraction were identified as quercetin, alliin (S-allyl L-cysteine S-oxide), allicin (S-oxodiallyl disulfide), diallyl disulfide (allyl disulfide), S-methyl L-cysteine S-oxide (3-(methyl sulfinyl alanine), propanethal S-oxide (thiopropional S-oxide) and 3-mercapto-2-methylpentan-1-ol [29]. Hypoglycemic activity of *Allium cepa L.* extracts have been reported. The bulb part contains S-methyl cysteine sulfoxide, S-allyl cysteine sulfoxide has been demonstrated anti-diabetic activity. S-methylcysteine sulfoxide exerts antidiabetic action in Three various ways: i) stimulate the production of insulin in the body and enhance the secretion of the pancreas ii) interfere with dietary glucose absorption iii) use insulin effectively [30].

### **Andrographis paniculata**

*Andrographis paniculata* (Burm. F.) belongs to the family Accanthaceae and is an annual herb growing wild in wastelands worldwide and occasionally planted in gardens. Traditionally, this plant has been used as an antioxidant, antidiabetic, hepatoprotective, anti-inflammatory, antispasmodic. *Andrographis paniculata* (Burm. f.) Nees contains major constituents like flavonoids, diterpenoids and polyphenols. The diterpenoids are andrographolide, 19-O-acetylanhydroandrographolide, neoandrographolide, 14-deoxy-dihydroandrographolide, deoxyandrographolide, and homoandrographolide [31]. Among them, andrographolide is a principle compound and is found abundantly in the plant.

Besides antidiabetic agent, *Andrographis paniculata* has been broadly studied as analgetic, antioxidants, antimalarial, antibacterial and hepatoprotector. Andrographolide is a diterpene lactone compound that predominates at approximately 4% of the whole plant. This andrographolide is an active ingredient as antidiabetes. Different studies on the pharmacological activity of *Andrographis paniculata* (especially andrographolide, compounds with pharmacological activity as an anti-diabetic agent) were carried out in in-vivo and in vitro study. *Andrographis paniculata* extract that can be used as an anti-diabetic agent is an extract containing not less than 15% andrographolide [32-34].

During the study of anti-diabetic activity of *Andrographis paniculata*, rats were used as experimental animals. In different studies on the anti-diabetic activity of a drug in an in-vivo study, most researchers have used streptozotocin (STZ) [35] or alloxan to stimulate insulin resistance. Alloxan is commonly used to induce type 1 diabetes mellitus (IDDM) but later revealed that alloxan is not selective for rat pancreatic beta cells. STZ can be used to induce both types of diabetes (IDDM; Insulin dependent diabetes mellitus and NIDDM; Non-insulin dependent diabetes mellitus) with a toxic effect on the beta cell [36]. Insulin resistance was caused by impaired fatty acid metabolism (intracellular) in the cells and the resulting accumulation of fatty acid CoA, diacylglycerol and ceramides. The results of this metabolism decrease the capacity of insulin receptors and activate the PI 3-kinase protein, which can reduce the function of GLUT-4 as a glucose transporter [37].

### **Aloe barbadensis**

*Aloe vera L.* belongs to the Liliaceae family is a popular medicinal plant used specifically in the cosmetic industry, and Pharmacology. It is native to Africa and the Mediterranean. It is widely distributed in the islands of Cyprus, Malta, Sicily, Cape Verde and India [38]. Aloe vera extract was evaluated in streptozotocin-induced diabetic mice and mouse embryonic NIH/3T3 cells. Administration of an extract at 130 mg/kg per day for four weeks resulted in significant reductions in blood glucose, TG, LDL, and TC, comparable to metformin. Furthermore, this study showed that a lyophilized aqueous aloe extract (1 mg/mL) increased GLUT-4 mRNA synthesis in NIH/3T3 cells. Aloe vera extract (300 mg/kg) exerted antidiabetic effects by improving insulin secretion and pancreatic  $\beta$ -cell function, restoring pancreatic islet mass in streptozotocin-induced diabetic rats [39].

Diabetes studies have shown that Aloe vera significantly reduces FBG alone or in integration with *Cnidioscolus chayamansa* extract. In 72 T2DM patients (49 men and 23 women, aged 35–70 years, with high FBG levels and a typical diabetic curve on glucose tolerance analysis) studied with glibenclamide, aloe vera extract (80%) did not respond to glibenclamide alone. Aloe vera extract significantly reduced FBG levels within two weeks and was protective in both kidney and liver. The treatment is safe on kidney and liver function and has been suggested to relieve vascular complications by activating the immune system. Aloe vera (AG) gel complex (Aloe QDM complex) evaluated in a randomized controlled trial showed borderline significant reductions in body weight, body fat mass, FBG, fasting serum insulin and homeostasis model of evaluated-insulin resistance (HOMA-IR) after eight weeks of treatment [40,41].

### **Boerhavia diffusa**

Punarnava is *Boerhavia diffusa L.* (Family: Nyctaginaceae) is a well-known herbal plant (common names: erect spiderling, tar vine and erect boerhavia) and potent important therapeutic applications. *B. diffusa* and *B. erecta* are similar species which are used as Punarnava in India. These two species of *Boerhavia* have similar phytochemical ingredients and may therefore exhibit similar pharmacological properties. It is an erect, perennial herb distributed in tropical and subtropical regions. It contains alkaloids, flavonoids, saponins, steroids, glycosides and polar compounds such as sugar, proteins, minerals and vitamins [42-46]. The root of the plant is diuretic, stomachic, cardiogenic, laxative, expectorant, anthelmintic, hepatoprotective, febrifuge, used to treat gonorrhoea, enlarged spleen, jaundice and other internal inflammations. In moderate doses, it is used to treat asthma [42]. Among the *Boerhavia* species, preliminary evaluation of antidiabetic and anti-hyperlipidemic activity was reported only for *B. diffusa* [47]. Three rotenoids, namely boravinone A, B and C and 3-O-(6'-palmitoyl- $\beta$ -D-glucopyranosyl) sitosterol, were isolated and their structure determined. The results showed that boravinone B in the extract of *B. diffusa* was 0.041% w/w and 0.011% in the polyherbal formulation.

### **Camellia sinensis**

Tea (*Camellia sinensis L.*) belongs to the family; Thiaceae and is a common beverage consumed daily in many parts of the world. It is classified as unfermented tea (green tea, white tea), semi-fermented tea (oolong tea) and fully fermented tea (black tea). The main chemical components

in unfermented tea are catechins and caffeine, stretch in semi-fermented and fully fermented tea, theaflavins, thearubigins and caffeine edominate.

The number of hydroxyl groups in bioactive ingredients is important for  $\alpha$ -glucosidase inhibition. The structure of the esterified gallate group at the 3-position of the C-ring of catechins is important, so catechins such as catechin gallate (CG), gallic catechin gallate (GCG), ECG and EGCG showed stronger inhibitory activity than their corresponding ungalated phytochemicals catechin (C), gallic catechin (GC), epicatechin (EC) and epigallocatechin (EGC), respectively [48]. Black tea theaflavins constitute a group of pigments formed from the condensation of catechins during the fermentation of black tea, and they can strongly inhibit  $\alpha$ -glucosidase activity. The  $\alpha$ -glucosidase reduce effects of theaflavins decreased in the order of potency of theaflavin-3-O-gallate, theaflavin-3,30-di-O-gallate, theaflavin-30-O-gallate and theaflavin. Catechins, caffeine and theaflavins have been confirmed to have a wide range of biological activities [49]. Tea has been shown to lower blood glucose levels and protect pancreatic  $\beta$  cells in diabetic rats. The hypoglycemic activity of crude tea leaves of *Camellia sinensis* was examined in streptozotocin-induced diabetic rats [50]. Tea (0.5 ml/day) was administered for 15 and 30 days and exerted antihyperglycemic and hypolipidemic (TG and DC) activities in diabetic rats. Also, protective effects such as recovery of some altered hematobiochemical parameters like creatinine, urea, uric acid, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and body weight reduced were observed.

### **Cassia auriculata**

Aavaramboo (*Cassia auriculata L.*) belongs to the family Fabaceae, and is widely distributed in India and Sri Lanka. A plant used in traditional medicine is *C. auriculata L.* Herbal tea prepared from five parts of the plant namely roots, leaves, flowers, bark and unripe fruits were used in the preparation of herbal tea, as Kalpa Herbal Tea (Aavari Panchaka Suranam). This tea is consumed mainly by people in Asian countries to lower blood sugar levels and control the symptoms of diabetes. Various parts of *C. auriculata L.* such as leaves [13,17] and flowers have been reported for their antidiabetic activity. However, the bud part of the plant is traditional consumed by people for the management of diabetes. Alpha Amylase Inhibitory Activity Polyphenols from plants are reported to have antidiabetic activity.

Preliminary in vitro antioxidant and in vitro antidiabetic activity of *C. auriculata*. The leaves bud and flower ethanol extract are reported to have antidiabetic activity [13]. This activity was evaluated by in vivo antidiabetic activity using high-fat diet and (streptozotocin) STZ-induced diabetic rat models. This model is ideal for studying human diabetes with metabolic aspects of diabetes [51].

Analytical results revealed the existence of compounds like quercetin, cyanidin, spermidine and N8 acetylspermidine in the bud extract and hesperidin and vitexin-2-O-rhamnoside in the flower extract. These compounds are reported to include antidiabetic properties. Quercetin is an active natural flavonoid group found in plants and has been reported to have many medicinal properties including antioxidant and antidiabetic property[13].

### **Coccinia indica**

*Coccinia indica L.* commonly an ivy gourd or small gourd comes under the Cucurbitaceae family. It is native to Africa and Asia (India). It is widely distributed as a weed throughout India and cultivated over a large area[52]. It shows the presence of various chemical constituents such as alkaloids, carbohydrates, glycosides, phenolic compounds, gums, mucilages, triterpenoids, flavonoids, anthraquinones and polysaccharides. Ayurveda and Unani systems propose to *C. indica* as antidiabetic agent and other traditional uses are anti-inflammatory, antipyretic, analgesic, antimicrobial, antibacterial, antidepressant and expectorant[53]. Scattered pharmacological studies have supported folklore claims of *C. indica* in treating diabetes.

Oral glucose tolerance test (OGTT) is used as the primary test for finding of diabetes amelioration and glucose intolerance in patients. Quercetin (5 mg/kg) and metformin (150 mg/kg) did not significantly lower blood glucose levels in normal rats, but only metformin significantly reduced blood glucose levels in diabetic rats after a 60-min glucose load. These observations confirmed that quercetin and metformin have no hypoglycemic effect in normal rats, but metformin exhibits hypoglycemic effect in diabetic rats. Our results are consistent with literature reports showing no hypoglycemic effects of quercetin and metformin in normoglycemic animals [54]. Flavonoids act as glucosidase inhibitors and exert their effect only on disaccharidases normalize glucose homeostasis through  $\alpha$ -glucosidase activity[55]. Quercetin induces  $\alpha$ -glucosidase inhibition and attenuates maltose-loaded postprandial hyperglycemia in T2DM patients and shows no effect on glucose load[56].

### **Curcuma longa**

*Curcuma longa* L. commonly known as Turmeric belongs to Gingeberaceae family, widely used in herbal medicine since they contain curcuminoids as one of the active compounds [57-62]. Composition and function has been reported to be based on curcuminoids where the plant is harvested. Consider potential activity of curcuminoids as antidiabetic agents, and various applications Curcuma species containing curcuminoids in Antidiabetic therapeutic, antidiabetic potentials based on curcuma species from various research are discussed [63].  $\alpha$ -glucosidase is an important enzyme in carbohydrate digestion. Inhibition of  $\alpha$ -glucosidase can delay intestinal carbohydrate absorption and slow the recovery of blood glucose levels.

The  $\alpha$ -glucosidase activity results of CLE, bisdemethoxycurcumin and curcumin showed  $\alpha$ -glucosidase inhibitory activity in a concentration-dependent manner. At higher concentration (37.50  $\mu$ M), the  $\alpha$ -glucosidase inhibitory activity of curcumin was comparable to that of bisdemethoxycurcumin, with a value of 70.74 $\pm$ 0.92% and 69.33 $\pm$ 4.60%, while a CLE value of 64.63%. Although, bistemethoxycurcumin has higher  $\alpha$ -glucosidase inhibitory activity[57,61]. These were supported by the results of IC50 value, bisdemethoxycurcumin had the lowest IC50 value (3.76 $\pm$ 0.33  $\mu$ g/ml) compared to curcumin (5.33 $\pm$ 0.16  $\mu$ g/ml), while CLE had the highest IC50 value (17.18 $\pm$ 0.56  $\mu$ g/ml). This is indicated that bisdemethoxycurcumin has higher  $\alpha$ -glucosidase inhibitory activity compared to CLE and curcumin.

### **Gymnema sylvestre**

*Gymnema sylvestre* is a native herb belonging to the Asclepiadaceae family. Popularly known as “gurmar” for its unique property of destroying sugar, it is a renowned herb in Ayurvedic system of medicine. The plant is native to western and central India, Australia and tropical Africa [64]. Phytochemistry of *G. sylvestre* is a good source of a large number of bioactive substances. The leaves contain Triterpene saponins such as gymnemic acids, gymnimasaponins, and gymnimasides and also other phytoconstituents include anthraquinones, flavones, hendry-acontane, pentadriacontane,  $\alpha$  and  $\beta$ chlorophylls, phytin, stigmaterol, dquercitol, resins, etc. Major secondary metabolites in gymnema include: Gymnemic acids consist of several members known as gymnemic acids I-VII, gymnimazaponins, and gymnimosides A-F. Gurmarin is one more essential phytoconstituent isolated from *G. sylvestre* [65].

The antidiabetic activity of gymnemic acids appears to be owing to a integration of mechanisms. It works by induced the secretion of insulin from the pancreas. It shows a similar effect by delaying the absorption of glucose into the blood. In the intestine it binds to a receptor present in the outer layer of the intestine, thereby preventing the absorption of sugar molecules by the intestine, resulting in a decrease in blood glucose levels [65]. The extract of the plant showed its efficacy in regenerating pancreatic  $\beta$  cells in a study [66]. Gymnemic acid is a major phytocompound present in the plant that has been reported to interact with glyceraldehyde-3-phosphate dehydrogenase (GAPDH), a key enzyme in the glycolysis pathway [66]. Furthermore, *G. sylvestre* has been reported to exhibit significant inhibitory activity against  $\alpha$ -glucosidase. Compared with glibenclamide,



gymnemic acid IV reduced blood glucose levels by 13.5 - 60.0% within 6 hours, and gymnemic acid increased plasma insulin levels in STZ-diabetic rats at a concentration of 13.4 mg/kg. IV [67].

## Conclusion

Diabetes is considered an important cause of patients, their families and the economy of society. Moreover, uncontrolled diabetes leads to severe chronic complications such as blindness, kidney failure and heart failure. Research into new antidiabetic agents to alleviate this problem is concerned. Due to the adverse effects of modern treatment methods, ten herbal medicines have been observed. Also, herbal extracts can now be used alongside standard medications for combination therapies. 1. Garlic (*Allium sativum*), 2. onion (*Allium cepa*), 3. kalomegh (*Andrographis paniculata*), 4. ghrita kumara (*Aloe vera*), 5. erect spiderling (*Boerhavia diffusa*), 6. Tea (*Camellia sinensis*), 7. Aaarai (*Cassia auriculata*), 8. ivy gourd (*Coccinia indica*), 9. Turmeric (*Curcuma longa*), 10. gurmar (*Gymnema sylvestre*). Each herb has its own active ingredients that can lower blood sugar levels and control the complications of diabetes. Future research will prove on the isolation, purification, identification, mechanism and applications of biological agents in plants. This review hopes to provide information needed for diabetes management. In our critical review, we have recorded a ten herbal plants list of anti-diabetic activities taken from the Google, Google scholars, Sciendirect, Springer and Traditional knowledge of village vaidyas. Isolation and identification of bioactive phytochemicals from these plants play a key role in improving insights into anti-diabetic functional food and drug development.

## References

1. Kharroubi, AT., Darwish, HM. (2015). Diabetes mellitus: the epidemic of the century. *World Journal of Diabetes*. 6,850,
2. World Health Organization. (1999). *Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications*; Department of Noncommunicable Disease Surveillance: Geneva, Switzerland.
3. American Diabetes Association. (2019). Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes–2019. *Diabetes Care*.42,1, S13-S28.
4. Faselis, C., Katsimardou, A., Imprialos, K., Deligkaris, P., Kallistratios, M., Dimitriadis, K. (2020). Microvascular Complications of Type 2 Diabetes Mellitus. *Current Vascular Pharmacology*.18, 117-124.
5. Adler, A., Bennett, P., Colagiuri Chair, S., Gregg, E., Venkat Narayan, K., Ines Schmidt, M., Sobngwi, E., Tajima, N., Tandon, N., Unwin, N., Wild, S., Yudkin, J., Levitt, N., Mohan, V., Montgomery, S., Nyirenda, MJ., Tuomilehto, J., Den Boon, S., Hocking, S. (2021). Reprint of: classification of diabetes mellitus, *Diabetes Research and Clinical Practice*. 108972,
6. Tao, Z., Shi, A., Zhao, J. (2015). Epidemiological perspectives of diabetes. *Cell Biochemistry and Biophysics*. 73,181-185.
7. Chentli, F., Azzoug, S., Mahgoun, S.(2015). Diabetes mellitus in elderly, *Indian Journal of Endocrinology and Metabolites*. 19,744.
8. Piero, MN., Nzaro, GM., Njagi, JM. (2015).Code for Mobile users Diabetes mellitusa devastating metabolic disorder. *Asian Journal of Biomedical and Pharmaceutical Science*. 2014, 1-7.
9. Chinsebu, KC.(2019). Diabetes mellitus and nature's pharmacy of putative antidiabetic plants, *Journal of Herbal Medicine*. 15,100230.
10. Patel, DK., Prasad, SK., Kumar, R., Hemalatha, S.(2012). An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pacific Journal of Tropical Biomedicine*.2, 320-330.
11. Angelin, JJ., Jothi, U., Thiyagarajan G., Subramanian, VK., Sivakumar T.(2020). Estimation of qualitative and quantitative analysis of antioxidant activity of different parts of *Catharanthus roseus* (L). *Plant Archives*.20,2,4187-4192.
12. Deepa, B., Sivakumar, T. (2020). Phytochemical Analysis and Antibacterial Efficacy of Ethanolic Extract of *Musa paradisiaca*. *Research Biotica International Journal*.2,3,126-130.
13. Sivakumar, T.(2021). Synthesis of silver nanoparticles using *Cassia auriculata* leaf extracts and their potential antidiabetic activity. *International Journal of Botany Studies*. 6,3,35-38.

14. Sivakumar, T. (2019). Phytochemical screening and GC- MS analysis of bioactive compounds and biosynthesis of silver nanoparticles using sprout extracts of *Vigna radiate* L. and their antioxidant and antibacterial activity. *Asian journal of Pharmaceutical and clinical research.*12,2, 80-184.
15. Thiyagarajan, G., Sivakumar, T.(2020). A review on Pepper and their common phytochemicals. *Research Biotica International Journal.* 2,4,149-153.
- 16 . Deepa, B., Sivakumar, T.(2023). Screening of Phytochemicals and in vitro studies of Garlic: An Updated review. *International Journal of Engineering Technology and Management Sciences.*7,1-2,6-11.
17. Sivakumar, T. (2021). Invitro antioxidant, total phenolic, total flavonoid content and biosynthesis of silver nanoparticles by *Cassia auriculata* leaves extracts. *International Journal of Botany Studies.*6,3,476-480.
18. Sivakumar, T., Deepa, B.(2020). A review on some folk medicinal plants and their common uses. *Research Biotica International Journal.*3,4,131-134.
19. Senthil Kumar, SR., Sivakumar, T., Arulmozhi, KT., Mythili, N.(2016). Antimicrobial Activity of Indian Commercial Green Teas (*Camellia Sinensis*). *International Journal of Biosciences and Nanosciences.* 3,7,108-112.
20. Senthilkumar, SR., Sivakumar, T., Arulmozhi, KT., Mythili, N.(2017). FT-IR analysis and correlation studies on the antioxidant activity, total phenolics and total flavonoids of Indian commercial teas (*Camellia sinensis* L.) - A novel approach. *International Research Journal of Biological Sciences.*6,3, 1-7.
21. Kayarohanam, S., Kavimani, S.(2015). Current Trends of Plants Having Antidiabetic Activity: A Review. *Journal of Bioanalysis and Biomedical.* 7, 55-65.
22. Sashikanth, YV., Aravindkumar, P., Swarupa, C.(2012). Two way relation of diabetes mellitus and periodontitis—a review. *Annals and Essences of Dentistry.*4, 1.
23. World Health Organization.(2002). Traditional medicine-growing needs and potential. WHO Policy Perspective on Medicines.2,1-6.
24. Singh, V., Kumar, R.(2017). Study of Phytochemical Analysis and Antioxidant Activity of *Allium sativum* of Bundelkhand Region. *International Journal of Life Science and Scientific Research.* 3, 1451-1458.
25. El-Saber Batiha, G., Beshbishy, AM., Wasef, LG., Elewa, YH., Al-Sagan, AA., El-Hack, MEA., Taha, AE., Abd-Elhakim, YM., Devkota, HP.(2020). Chemical Constituents and Pharmacological Activities of Garlic (*Allium sativum* L.): A Review. *Nutrients.*12, 872.
26. Nasir, A., Fatma, G., Neshat, N., Ahmad, MA. (2020). Pharmacological and therapeutic attributes of garlic (*Allium sativum* Linn.) with special reference to Unani medicine—A review. *Journal of Medicinal Plants Studies.* 8, 6-9.
27. Eidi, AL., Eidi, M., Esmaeili, E.(2006). Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin-induced diabetic rats. *Phytomedicine.* 13, 624-629.
28. Adinortey, MB., Agbeko, R., Boison, D., Ekloh, W., Kuatsienu, LE., Biney, EE., Kwarteng, J., Nyarko, AK.(2019). Phytomedicines Used for Diabetes Mellitus in Ghana: A Systematic Search and Review of Preclinical and Clinical Evidence. *Evid. Based Complement. Alternation of Medicine.* 6021209.
29. Kumari, K., Mathew, BC., Augusti, KT. (1995).Antidiabetic and hypolipidemic effects of S-methyl cysteine sulfoxide isolated from *Allium cepa* Linn. *Indian Journal of Biochemistry and Biophysics.*32, 49-54.
30. Kumari, K., Augusti, KT.(2002). Antidiabetic and antioxidant effects of S-methyl cysteine sulfoxide isolated from onions (*Allium cepa* Linn) as compared to standard drugs in alloxan diabetic rats. *Indian Journal Experimental Biology.*40, 1005-1009.
31. Sivakumar, T., Panneerselvam, R. (2011). Triadimefon Mediated Changes in Antioxidant and Indole Alkaloid Content in Two Species of *Datura*. *American Journal of Plant Physiology.*6, 252-260.
31. Aryani, T. (2005). Pengujian validasi analisis kadar andrografolid secara kromatografi cair kinerja tinggi (KCKT) dengan eluasi gradien terhadap ekstrak herba sambiloto (*Andrographis paniculata* Nees), Berk. Panel. Hayati. 11, 73-76,
32. Zhang, XF., Tan, BK. (2000). Anti-diabetic property of ethanolic extract of *Andrographis paniculata* in streptozotocin-induced diabetic rats. *Acta Pharmacologia Sinica.* 21,12, 1157-1164.

33. Sivakumar, T. (2022). A systematic review on traditional medicinal plants used for traditional control of insects. *International Journal of Botany Studies*.7, 12,32-36.
34. Sivakumar, T. (2022). A recent review on phytochemicals commonly found in herbal plants. *International Journal of Botany Studies*.7,12, 54-57.
35. Gayathri, V., Lekshmi, P., Padmanabhan, RN. (2011). Anti-diabetes activity of ethanol extract of *Centella asiatica* (L.) Urban (whole plant) in Streptozotocin-induced diabetic rats, isolation of an active fraction and toxicity evaluation of the extract. *International Journal of Medicinal Aromatic Plants*. 1,3,278-286.
36. Adriawan, IR., Andrie, M., Susilowati, R., Pramono, S., Nugroho, AE. (2014). Evaluasi efek anti-diabetes mellitus ekstrak terpurifikasi *Andrographis paniculata* (Burm. f.) Ness dan andrographolide dengan parameter indeks HOMA-IR. *Traditional Medicinal Journal*.19,1,19-23.
37. Shulman, GI. (2000). Cellular mechanism of insulin resistance. *Journal of Clinical Investigation*. 106, 2,171-3.
38. Ali, AM.(1990). Effect of aloes on blood glucose levels in normal and alloxan diabetic mice. *Journal of Ethnopharmacology*. 28, 215-220.
39. Noor, A., Gunasekaran, S., Vijayalakshmi, MA. (2017). Improvement of insulin secretion and pancreatic  $\beta$ -cell function in streptozotocin-induced diabetic rats treated with. *Pharmacognosy*.9, S99-S104.
40. Yagi, A., Hegazy, S., Kabbash, A., Wahab, EAE. (2009). Possible hypoglycemic effect of *Aloe vera* L. High molecular weight fractions on type 2 diabetic patients. *Saudi Pharmaceutical Journal*.17, 209-215.
41. Cardenas-Ibarra, L. Villarreal-Perez, JZ., Lira-Castillo, JC., Nava-Aleman, A. (2017). Randomized double blind crossover trial of aloe vera, *cnidoscolus chayamansa* and placebo for reducing hyperglycemia in women with early metabolic syndrome. *Clinical Nutrition Experiment*.14, 1-12.
42. Suriyavathana, M., Paraeswari, G. (2012). Penislus Shiyan, Biochemical and antimicrobial study of *Boerhavia erecta* and *Chromolaena odorata* (L.). *International Journal Pharmaceutical Science and Research*. 3, 2, 465e468.
43. Sivakumar, T. (2021). A modern review of silver nanoparticles mediated plant extracts and its potential bioapplications. *International Journal of Botany Studies*.6,3,170-175.
44. Senthilkumar, SR., Sivakumar, T. (2014). Studies on the Greengram (*Vigna radiata* L.) Sprout Assisted Synthesis of Silver Nanoparticles and their Antimicrobial Activities. *International Journal of Nanomaterial and Biostructure*.4,3, 52-57.
45. Sivakumar, T. (2021). A review on biosynthesis of Zinc Oxide Nanoparticles using plant extracts and its potential Bio Applications. *International Journal of Botany Studies*. 6,3,644-648.
46. Jothi, U., Angelin JJ., Sivakumar, T. (2019). *Study on Estimation and Antioxidant activity of Gloriosa superba* L. Whole Plant Extract. *International Journal of Scientific Research in Biological Sciences*.6,3,55-58.
47. Alam, P., Shahzad, N., Gupta, AK., Mahfoz, AM., Bamagous, GA., AlGhamdi, SS. (2018). Anti-diabetic Effect of *Boerhavia diffusa* L. root extract via free radical scavenging and antioxidant mechanism. *Toxicology and Environment Health Science*.10,220-227.
48. Wang, H., Shi, S., Bao, B., Li, X., Wang, S. (2015). Structure characterization of an arabinogalactan from green tea and its anti-diabetic effect. *Carbohydrate Polymers*. 124,98-108.
49. Pereira, CG., Barreira, L., Bijttebier, S., Pieters, L., Neves, V., Rodrigues, MJ., Rivas, R., Varela, J., Custódio, L. (2017). Chemical profiling of infusions and decoctions of *helichrysum italicum* subsp. *Picardii* by uhplc-pda-ms and in vitro biological activities comparatively with green tea (*Camellia sinensis*) and rooibos tisane (*Aspalathus linearis*). *Journal of Pharmacology and Biomedical Analysis*.145, 593–603.
50. Al-Attar, AM., Zari, TA. (2010). Influences of crude extract of tea leaves, *Camellia sinensis*, on streptozotocin diabetic male albino mice. *Saudi Journal of Biological Science*.17, 295–301.
51. Benalla, W., Bellahcen, S., Bnouham, M. (2010). Antidiabetic medicinal plants as a source of alpha glucosidase inhibitors. *Current Diabetes Review*. 6,4,247-54
52. Deokate, UA., Khadabadi, SS. (2019). Pharmacology and phytochemistry of *Coccinia indica*. *Pharmacophore*.3,11,179-85.

53. Abdelmoaty, MA., Ibrahim, MA., Ahmed, NS., Abdelaziz, MA.(2010). Confirmatory studies on the antioxidant and antidiabetic effect of quercetin in rats. *Indian Journal of Clinical Biochemistry.* 25,2,188-92.
54. Jadhav, R., Puchchakayala, G. (2012) Hypoglycemic and antidiabetic activity of flavonoids: boswellic acid, ellagic acid, quercetin, rutin on streptozotocinnicotinamide induced type 2 diabetic rats. *International Journal of Pharmaceutical Science.*4,251-6.
55. Pereira, DF., Cazarolli, LH., Lavado C., Mengatto, V., Figueiredo, MSRB., Guedes, A. (2011). Effects of flavonoids on  $\alpha$ -glucosidase activity: Potential targets for glucose homeostasis. *Nutrition.*27,11-12,1161-1167.
56. Hussain, SA., Ahmed, ZA., Mahwi, TO., Aziz, TA. (2012). Quercetin dampens postprandial hyperglycemia in type 2 diabetic patients challenged with carbohydrates load. *International Journal of Diabetes Research.*1,3,32-35.
57. Rohman A., Widodo H., Lukitaningsih E. (2019). Review on in vitro antioxidant activities of Curcuma species commonly used as herbal components in Indonesia. *Food Research.*4,286-293.
58. Sivakumar, T., Panneerselvam, R.(2011). Salinity induced changes in photosynthetic pigment and antioxidant responses in *Sesuvium portulacastrum*. *Pakistan Journal of Biological sciences.*14,21, 967-975.
59. Angelin JJ, Jothi U, Thiyagarajan G., Sivakumar T. (2019). Evaluation of antimicrobial activity and phytochemicals analysis of whole plant extract of *Vinca rosea*. *Asian journal of Pharmaceutical and clinical research.* 12, 8, 132-136.
60. Anburaj, R., Nabeel, MA., Sivakumar, T., Kathiresan K. (2012). Role of rhizobacteria on biochemical constituents of the mangrove associate halophyte *sesuvium portulacastrum* L., in response to salinity. *Russian Journal of Plant Physiology.*59,1, 115-119.
61. Nihayati, E., Wardiyati, T., Retnowati, R. (2013). The Curcumin content of temulawak (*Curcuma xanthorrhiza* Roxb.) rhizome as affected by N, K and micronutrients B, Fe,Zn. *Agrivita Journal of Agriculture Science.* 35,218-226.
62. Senthilkumar, SR., Sivakumar, T., Arulmozhi, KT., Mythili, N. (2015). Gas chromatography Mass spectroscopy evaluation of bioactive phytochemicals of commercial green teas (*Camellia sinensis*) of India. 2015. *Asian Journal of Pharmaceutical and Clinical Research.* 8,3, 278-282.
63. Kusumawati, I., Kurniawan, KQ., Rullyansyah, S. (2018). Anti-aging properties of *Curcuma heyneana* Valetton & Zipj: A scientific approach to its use in Javanese tradition. *Journal of Ethnopharmacology.*225,64-40.
64. Khare, CP.(2008). *Indian Medicinal Plants An Illustrated Dictionary*. Berlin: Springer.
65. Ishijima, S., Takashima, T., Ikemura, T., Izutani, Y. (2008). Gymnemic acid interacts with mammalian glycerol-3-phosphate dehydrogenase. *Molecular and Cell Biochemistry.*310,203-8.
66. Ahmed, A., Rao, AS., Rao, M. (2010).In vitro callus and in vivo leaf extract of *Gymnema sylvestre* stimulate  $\beta$ -cells regeneration and antidiabetic activity in Wistar rats. *Phytomedicine.* 17,13, 1033-1039.
67. Sugihara, Y., Nojima, H., Matsuda, H., Murakami, T., Yoshikawa, M., Kimura, I. (2000). Antihyperglycemic Effects of Gymnemic Acid IV, a Compound Derived from *Gymnema sylvestre* Leaves in Streptozotocin-Diabetic Mice. *Journal of Asian Natural Product Research.* 2, 321-327.