American Journal of Essential Oils and Natural Products

Available online at www.essencejournal.com

AkiNik

AJEONP

American Journal of Essential Oils and Natural Products

ISSN: 2321 9114
AJEONP 2015; 2(4): 22-28

Received: 30-03-2015
Accepted: 02-05-2015

Rakesh K. Joshi
Department of Education, Government of Uttrakhand, India.

William N. Setzer
Department of Chemistry, University of Alabama in Huntsville, Huntsville, AL 35899, USA

Valdir F. da Veiga Junior
Department of Chemistry, Exact Sciences Institute, Amazonas Federal University Manaus, Brazil

Correspondence:
Rakesh K. Joshi
Department of Education, Government of Uttrakhand, India.

Aromatic and medicinal plants with anti-diabetic potential from India: A review

Rakesh K. Joshi, William N. Setzer, Valdir F. da Veiga Junior

Abstract
Uttarakhand is characterized by a rich diversity of ethno-medicinal plants as well as a rich heritage of traditional medicine. Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian literature have mentioned the use of plants in treatment of various human ailments. Medicinal plants play an important role in the management of diabetes mellitus especially in developing countries where resources are meager. Diabetes is a growing health concern worldwide and is now emerging as an epidemic. The management of diabetes is still a major challenge. According to the World Health Organization (WHO), up to 90% of the population in developing countries uses plants and their products as traditional medicine for primary health care. There are about 800 plants that have been reported to show anti-diabetic potential. Thus there is great opportunity for research on natural products with anti-diabetic properties. Numerous studies have confirmed the benefits of medicinal plants with anti-hyper-glycemic effects in the management of diabetes mellitus. This literature based review provides a starting point for future studies of bioactive anti-diabetic compounds present in plants from Uttrakhand.

Keywords: Diabetes, Medicinal plants, Essential oil

1. Introduction
Plants have been used in traditional medicine for several thousand years [1]. Herbal medicines occupy a distinct place in our life that provides information on the use of plants or plant parts as traditional medicine. However, healing properties of plants in different diseases had been mentioned in Rigveda and subsequently in Atharva Veda (1200 B.C.). Since the time of Charaka and Susruta (400 B.C.) the medicinal plants were regrouped and Nagarjuna while editing Susruta Samhita described the presence of active pharmacological materials in bark, leaf, flower, fruit, rhizome etc. The knowledge of medicinal plants has been accumulated in the course of many centuries based on different medicinal systems such as Ayurveda, Unani & Siddha. In India, it is reported that traditional healers use 2500 plant species and 100 species of plants serve as regular sources of medicine [2]. During the last few decades there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world [3-7]. India holds a credibility of diverse social, cultural and medical heritage with an unbroken tradition coming down across millennia. Although medical heritage is centuries old, millions people in rural area still depend on traditional medicine to congregate their healthcare needs [8]. Collection of information and documentation of traditional knowledge plays an important role in scientific research on drug development [9]. A study by the World Health Organization (WHO) depicts that over 80% of world's population depends on natural biological resources for their primary healthcare demands [10]. Documenting the indigenous knowledge through ethno-botanical studies is important for the conservation and utilization of biological resources. Diabetes mellitus has become a common disease of the world. It is a disease in which the body is unable to produce or unable to properly use and store glucose (a form of sugar). Glucose backs up in the bloodstream-causing one's blood glucose or "sugar" to rise too high. It is a metabolic syndrome of multiple etiologies characterized by chronic hyperglycemia with abnormalities in carbohydrate, fat and protein metabolism due to defect in insulin secretions. India is facing a diabetic explosion and the exact cause of which is unknown but both genetic and life style factors can be blamed. The country has the world's largest diabetic population, about 25 million, and the number is predicted to rise to 35 million by 2010 and to 57 million by 2025 [11]. The rapid growth of this disease is due to heredity, endocrine imbalance, dietary imprudence, after effects of infection, obesity, severe and continued mental stress, reduction in physical labor large differences in social structure etc,.

which provide a productive atmosphere for diabetes [12]. Diabetes mellitus is a growing problem worldwide entailing enormous financial burden and medical care policy issues [13]. According to the International Diabetes Federation (IDF), the number of individuals with diabetes in 2011 crossed 366 million, with an estimated 4.6 million deaths each year [14]. The Indian subcontinent has emerged as the capital of this diabetes epidemic. The reported prevalence of diabetes in adults between the ages of 20 and 79 is as follows: India 8.31%, Bangladesh 9.85%, Nepal 3.03%, Sri Lanka 7.77%, and Pakistan 6.72% [15].

2. Diabetes mellitus

According to WHO, the term diabetes mellitus is defined as a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs. Diabetes mellitus may present with characteristic symptoms such as thirst, polyuria, blurring of vision and weight loss [16].

2.1 Types of diabetes mellitus

2.1.1 Insulin Dependent Diabetes Mellitus (IDDM, Type 1): It is probably an autoimmune disorder. Antibodies that destroy β cells of islets of Langerhans in the pancreas and are often detectable in blood. Insulin in circulation is low or absent, more prone to ketosis. This type is less common and has a low degree of genetic predisposition. The disease is usually found before the age of 40 [17].

2.1.2 Non-Insulin Dependent Diabetes Mellitus (NIDDM Type 2): There is no loss in β cell mass, insulin in circulation is low, normal or even high degree of genetic predisposition, generally has a late onset past middle age, often found after the age of 40. The main cause of the disease is abnormality in gluco-receptor of β cells so that they respond at higher glucose concentration, reduced sensitivity of peripheral tissues to insulin in insulin receptors. Many hypertensives are hyperinsulinemic but normoglycemic exhibit insulin resistances, and excess of hyperglycemic hormones (glucagons) causes obesity due to relative insulin deficiency. Insulin is a hormone discovered in 1921 by Banting and Best. It is synthesized in the β cells of pancreas islets. Diabetes mellitus is a common metabolic disease, caused by lack of insulin. One of the chief functions of insulin is to act on the cell membrane rendering it more permeable to the transport of glucose. Thus a deficiency of insulin results in buildup of glucose in the blood and a deficiency of the necessary glucose in the cell [17].

2.1.3 Gestational diabetes (Type 3): It refers to initial recognition of glucose in tolerance during pregnancy, usually in the second or third trimester. It occurs in about 4% of all pregnancies. Patients with GD have a 30% to 50% chance of developing DM, usually type 2 DM [17].

3. Indian aromatic and medicinal plants with anti-diabetic potential: Traditional anti-diabetic plants might provide new oral anti-diabetic compounds, which can counter the high cost and poor availability of the current medicines for many rural populations in developing countries [17, 18]. In India, indigenous remedies have been used in the treatment of diabetes mellitus since the time of Charaka and Sushruta (6th century BC) [19]. The World Health Organization (WHO) has listed 21,000 plants which are used for medicinal purposes around the world. Among these, 2500 species are in India. There are about 800 plants that have been reported to show anti-diabetic potential. India is the largest producer of medicinal herbs endowed with a wide diversity of agro-climatic conditions and is known as the botanical garden of the world [20]. Pharmacological and clinical trials of medicinal plants have shown anti- diabetic effects and repair of β-cells of islets of Langerhans [21] The most common and effective anti-diabetic medicinal plants of Indian origin are babul (*Acacia arabica*), bael (*Aegle marmelos*), 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 globulus*), banyan tree (*Ficus benghalenesis*), gurmar (*Gymnema sylvestre*), urhal (*Hibiscus rosa-sinesis*), sweet potato (*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*) *Abelmoschus moschatus* [22].

***Abelmoschus moschatus* Medik. (Malvaceae):** *A. moschatus* is an aromatic medicinal plant. It improves insulin sensitivity through increased post-receptor insulin signaling mediated by enhancements in IRS-1-associated PI3-kinase and GLUT 4 activity in muscles of obese Zucker rats [23].

***Acacia arabica* (Lam.) Willd. (Fabaceae):** It is cosmopolitan in distribution. Throughout India it is cultivated and found wild also. Significant hypoglycemic effect versus controls was found in rats. However, the same diet failed to show any hypoglycemic effect in alloxanized rats (175 mg/kg SC) indicating that plant acts through release of insulin. Powdered seeds of *A. arabica* administered in doses of 2, 3 and 4 g/kg body weight exerted a significant ($p<0.05$) hypoglycemic effect in normal rabbits by initiating the release of insulin from pancreatic beta cells. No acute toxicity or behavioral changes were observed at those doses [24].

***Achyranthes aspera* L. (Amaranthaceae):** Oral administration of *A. aspera* powder produced a significant dose-related hypoglycemic effect in normal as well as in diabetic rabbits. The water and methanol extracts also decreased blood glucose levels in normal and alloxan diabetic rabbits. The acute toxicity study in rabbits does not reveal any adverse or side effects of this folk medicine at dosages up to 8 g/kg orally [25].

***Aegle marmelos* (L.) Correea (Rutaceae)**: The leaf extract has significantly effect to decrease in liver glycogen of diabetic rats and brought them near normal levels and also decreased the blood urea and serum cholesterol concentrations. Oral administration of aqueous decoctions of *Aegle marmelos* root bark (1 mL/100 g) showed hypoglycemic effects which were maximum (44%) at 3 h in normal fasted rats. In addition, the same extract completely prevented peak rise of blood sugar at 1 h in the Oral Glucose Tolerance Test (OGTT). The hypoglycemic activity was reduced upon storage of extract [11]. Aqueous extract of the leaves (1 g/kg for 30 days) significantly

controlled blood glucose, urea, body weight, liver glycogen and serum cholesterol of alloxanized (60 mg/kg IV) rats as compared to controls and this effect was similar to insulin treatment. When fed as an aqueous leaf extract (1 g/kg/day) to streptozotocin (STZ 45 mg/kg IV) diabetic rats for 2 weeks, maltase dehydrogenase (an enzyme known to increase in diabetes) levels were decreased in comparison to diabetic controls [26].

***Agrimonia eupatoria* L. (Rosaceae):** About 62.5 g/kg of agrimony, used as a diet (and drinking water (2.5 g/L) was shown to counter the weight loss, polydipsia, hyperphagia and hyperglycemia of STZ-diabetic mice. Aqueous extract (1mg/mL) stimulated insulin secretion from the BRIN-BDII pancreatic β-cell line, 2-deoxyglucose transport, glucose oxidation and incorporation of glucose into glycogen in mouse abdominal muscle comparable with 0.1μM-insulin. These results demonstrate the presence of anti-hyperglycemic, insulin-releasing and insulin-like activity in *A. eupatoria* [27].

***Allium cepa* L. (Amaryllidaceae):** *A. cepa* (onion) is very common and cultivated in many states of India. Various ether-soluble fractions as well as insoluble fractions of dried onion powder have shown anti-hyperglycemic activity in diabetic rabbits. *A.cepa* is also known to have anti-oxidant and hypo-lipidemic activity. Administration of a sulfur-containing amino acid, *S*-methyl cysteine sulfoxide (SMCS) (200 mg/kg for 45 days) to alloxan-induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues. When diabetic patients were given a single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels. Petroleum ether-insoluble fraction of the ether extract of dried onion powder (100 mg/kg) given orally for 7 days to alloxanized (180 mg/kg) diabetic rabbits caused a significant anti-hyperglycemic effect. Oral administration of 250 mg/kg of ethanol, chloroform, or acetone extracts of pulverized dried onion showed maximal reduction of 18.57, 8.35 and 3.20% in fasting blood glucose of alloxanized (150 mg/kg IP) diabetic rabbit. In a preliminary study of seven different fractions obtained from onion bulb, only petroleum ether and chloroform extracts significantly lowered blood sugar in OGTT (2 gm/kg) in rabbits [28, 29].

***Allium sativum* L. (Amaryllidaceae):** It is cultivated throughout India and is commonly used as a food ingredient. Oral administration of 0.25 g/kg of ethanol, petroleum ether or diethyl ether extracts of *A. sativum* caused 18.9, 17.9 or 26.2% reduction in blood sugar, respectively, in alloxan-diabetic rabbits (150 mg/kg). Oral administration of 0.25 g/kg allicin (isolated from *A. sativum*) produced hypoglycemia comparable to tolbutamide in mildly diabetic rabbits (glucose levels ranging from 180 to 300 mg %), while it showed no such effect in severely diabetic animals (blood sugar >350 mg %). Aqueous homogenate of garlic (10 mL/kg/day) administered orally to sucrose-fed rabbits (10 g/kg/day in water for 2 months) significantly increased hepatic glycogen and free amino acid contents, decreased fasting blood sugar, triglyceride levels in serum, liver and aorta and protein levels in serum and liver in comparison to sucrose controls [30, 31].

***Aloe vera* (L.) Burm f. (Xanthorrhoeaceae):** It grows in arid climates and is widely distributed in Africa, India and other arid areas. *Aloevera* gel at 200 mg/kg had significant anti-diabetic and cardio-protective activity and reduced the increased TBARS and maintained the superoxide dismutase and catalase activity up to the normal level and increased reduced glutathione by four times in diabetic rats [18]. The leaf pulp extract showed hypoglycemic activity on IDDM and NIDDM rats, the effectiveness being enhanced for type II diabetes in comparison with glibenclamide [20]. Both *Aloe vera* and *A. vera* gibberellins (over a dose range of 2-100 mg/kg) inhibited inflammation in a dose-dependent manner and improved wound healing in STZ diabetic mice. The dried sap of the plant (half a teaspoonful daily for 4-14 weeks) has shown significant hypoglycemic effect in diabetic mice, both clinically as well as experimentally [18, 32].

***Artemisia pallens* Wall. Ex-DC. Besser (Asteraceae):** It is a shrub endemic to southern India especially in Mysore state and is used in folk medicine in parts of southern India. Oral administration of the methanol extract of aerial parts of *A. pallens* showed a dose-dependent (100, 500 and 1000 mg/kg) anti-hyperglycemic effect in glucose-fed hyperglycemic and alloxanized rats (60 mg/kg). The effect was moderate in fasted normal rats but greater in diabetic rats [33].

***Azadirachta indica* A.Juss. (Meliaceae):** This is commonly known as neem and is a tree native to India, Burma, Bangladesh, Sri Lanka, Malaysia and Pakistan and is growing in tropical and semi-tropical regions. Low (0.5g) and high (2g) doses of powdered part, aqueous extract or alcoholic extract of *A. indica* was successfully combined with oral hypoglycemic agents to show significant hypoglycemic activity in high-dose agents in type-2 diabetic patients whose diabetes was not controlled by these agents [34].

Boerhavia diffusa L (Nyctaginaceae): It is distributed widely all over India. The root and the whole plant are used as an Ayurvedic medicine in India and Unani medicine for the treatment of diabetes, stress, dyspepsia, abdominal pain, inflammation, jaundice, enlargement of spleen, congestive heart failure and bacterial infections. The aqueous leaf extract of the plant has been studied for its anti-diabetic effect in alloxan-induced diabetic rats. The anti-diabetic activity of the chloroform leaf extract on streptozotocin-induced NIDDM (non-insulin dependent diabetes mellitus) model diabetic rats was evaluated and the herb possesses anti-diabetic activity. The herb mainly acts by reducing blood glucose level and increasing insulin sensitivity [35].

***Bombax ceiba* L. (Malvaceae):** Shamimin a C-flavonol glucoside isolated from *B. ceiba* leaves has been shown to exert significant hypoglycemic activity at a dose of 500 mg/kg in rats [36].

***Brassica juncea* (L.) Czern. (Brassicaceae):** It is commonly used spice in various food items in India. Oral feeding of *B. juncea* diet (10% w/w) for 60 days to normal rats led to significant hypoglycemic effect. This effect was attributed to stimulation of glycogen synthesis (leading to increase in hepatic glycogen content) and suppression of glycogen phosphorylase and other gluconeogenic enzymes. Anti-oxidant and hypolipidemic activity is also described in literature [37].

***Capparis decidua* (Forssk.) Edgew. (Capparaceae):** It is found throughout India. Oral feeding of diet containing (30%) *C. decidua* fruit powder for 3 weeks to alloxanized (80 mg/kg IP) diabetic rats (blood glucose, 450 mg %) showed significant

hypoglycemia (blood glucose, 120-130 mg %). In addition, anti-oxidant and hypolipidemic activity has been described in literature [38].

***Casearia esculenta* Roxb. (Salicaceae):** *C. esculenta* root is widely used in traditional system of medicine to treat diabetes in India. Aqueous root extract (300 mg/kg body weight) for 45 days resulted in a significant reduction in blood glucose and in the activities of glucose-6-phosphatase and fructose-1, 6-bisphosphatase and an increase in the activity of liver hexokinase. However, in the case of 200 mg/kg body weight of extract, it showed less activity. The study clearly shows that the root extract of *C. esculenta* possesses potent anti-hyperglycemic activity but weaker than that of glibenclamide [39].

***Cocculus hirsutus* (L.) W.Theob. (Menispermaceae):** Roots of *C. hirsutus* are bitter, acrid, laxative, demulcent and anti-periodic in fever, tonic and diuretic. The aqueous leaf extract of *C. hirsutus* has shown anti-hyperglycemic activity in alloxan-induced diabetic mice. The anti-hyperglycemic potential of *C. hirsutus* aqueous extract of may be due to lowering serum glucose levels in diabetic mice and increased glucose tolerance [40].

***Citrullus colocynthis* (L.) Schrad. (Cucurbitaceae):** It is cosmopolitan in distribution and found wild as well as cultivated throughout India in the warm areas. The fruit of this plant is traditionally used as anti-diabetic in Mediterranean part of the World. Aqueous extract of its fruit showed dose-dependent increase in insulin release from isolated islets. Aqueous extract of *C. colocynthis* (300 mg/kg) in normal rabbits significantly reduced plasma glucose after 1 h and highly significant reduction after 2, 3 and 6 h. The glycosidic extract (50 mg/kg) was more effective in lowering fasting glucose as compared to the alkaloid extract. Graded doses (10, 15 and 20 mg/kg) of saponin also reduced plasma glucose concentrations in alloxanized rabbits. Thus, saponins and glycosidic components levels of the rind of *C. colocynthis* are apparently responsible for its hypoglycemic effect [41].

***Ficus benghalensis* L. (Moraceae):** A very large tree distributed throughout India from sea level to 1200 m. Bengalenoside aglucoside isolated from the bark of *F. benghalensis* showed more potent hypoglycemic action as compared to crude ethanolic extract. Oral dose of bark extract showed significant anti-hyperglycemic effect in STZ diabetic rats by raising serum insulin levels both the in liver and the kidney. Oral administration of a leucopelargonidin derivative (100 mg/kg) isolated from bark of *F. benghalensis* exerted significant hypoglycemic activity in normal and moderately alloxanized diabetic dogs (60 mg/kg IV injection). A leucocyanidin derivative (100 mg/kg) isolated from the bark of *F. benghalensis* was hypoglycemic in normal rats. Combination of single dose of this chemical and low dose insulin controlled diabetes in alloxanized rats as effectively as that of high dose of insulin [42].

***Helicteres isora* L. (Malvaceae):** *H. isora* is distributed widely in forests throughout India. The hot water extract of fruit of *H. isora* exhibited significant antioxidant activity and moderate anti-diabetic activity at 200 mg/mL doses. It showed glucose-up take activity and was found to have activity comparable to insulin and met formin. The ethanolic extract had insulin-sensitizing and hypolipidemic activity and therefore has the potential for use in the treatment of type-2 diabetes [43].

***Hibiscus rosa-sinensis* L (Malvaceae).:** *H. rosa-sinensis* is cultivated as an ornamental plant throughout India and has been mentioned in Ayurveda for its medicinal value. Single oral administration of 250- mg/kg ethanol extract of *H. rosa-sinensis* showed mild but significant hypoglycemia at 120 min in glucose loaded rat. Repeated administration over several days showed significant hypoglycemic effect at 30, 90 and 120 min similar to tolbutamide and possibly due to insulin release by stimulation of pancreatic β cells or an increase of the glycogen deposition in liver [44].

***Inula racemosa* Hook.f. (Asteraceae):** It grows in the temperate and alpine western Himalayas. The petroleum ether extract of roots lowered plasma insulin and glucose levels within 75 min of oral administration to albino rats and it significantly counteracted adrenaline-induced hyperglycemia in rats. The extract further showed negative inotropic and negative chronotropic effects on frog heart. All these findings indicate that one of the constituents of *I. racemosa* may have adrenergic beta-blocking activity [45].

***Lantana camara* L. (Verbenaceae):** A large aromatic shrub found throughout India. It is mentioned in Ayurveda for treatment of various vitiated body conditions. Once daily administration of *L. camara* leaf juice (1500 mg/kg/day for 14 days) showed significant hypoglycemic effect in rats. However, the plant is hepatotoxic in nature [46].

***Mangifera indica*L. (Anacardiaceae):** The tree is found throughout India and traditionally its seeds and fruits are used for treatment of various ailments. Oral administration of aqueous extract of the leaves (1 gm/kg) failed to alter the blood glucose levels in normoglycemic or STZ-induced diabetic rats. However, the extract showed anti-diabetic activity when given 60min before or concurrently with glucose and this action could be due to reduction in intestinal absorption of glucose. However, the possibility of other mechanism can notbe excluded. *M. indica* has also been shown to exert powerful anti-oxidant activity *in vitro* [47].

***Murraya koenigii* (L.) Spreng. :** It is commonly known as curry patta and is widely used condiment and spice in India. In normal and alloxan diabetes the aqueous extract of the leaves of *M. koenigii* produced hypoglycemic effect. Oral feeding of this plant for 60 days to normal rats showed an increase in the concentration of hepatic glycogen due to hypoglycemic activity. It has been reported that feeding different doses of *M. koenigii* leaves to diabetic rats plays a role in control of mild diabetic rats to moderate, severe and type I diabetes [48].

***Ocimum sanctum* L. (Lamiaceae):** It is commonly known as tulsi. This plant is known for its significant reduction in blood sugar level in both normal and alloxan-induced diabetic rats. Significant reduction in fasting blood glucose, uronic acids, total amino acids, total cholesterol, triglycerides and total lipids indicate the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats. Oral administration of plant extracts (200 mg/kg) for 30 days led to decreases in the plasma glucose levels. Renal glycogen content increased 10 fold while skeletal muscle and hepatic glycogen levels decreased by 68 and 75%,

respectively, in diabetic rats as compared to control [49].

***Picro rhizakurrooa* Royle ex Benth. (Plantaginaceae):** It is small herb found in the Himalayan region from Kashmir to Sikkim. Alcoholic extracts of *P. kurrooa* showed anti-hyperglycemic effect in alloxanized diabetic rats. Serum glucose decreased by 43 and 60% with 75 and 150 mg/kg of the extracts, respectively [50].

***Punica granatum* L. (Lythraceae):** A shrub or small tree grows wild in the warm valleys and outer hills of the Himalayas and also cultivated throughout India. The flowers of *P. granatum* are used as anti-diabetic in Unani medicine called Gulnar farsi. Oral dose of aqueous ethanolic extract (50% v/v) led to significant blood glucose lowering effect in glucose-fed hyperglycemic and alloxanized diabetic rats with the maximum effect at the dose of 400-mg/kg body weight. Anti-oxidant activity has been described in the literature [51].

***Swertiachirayita* H. Karst. (Gentianaceae)** Chirata (Hindi) it is mainly found in temperate Himalayas between the height of 1200 and 1300 m. Various crude extracts and its isolated fractions have shown hypoglycemic activity in various animal models. Oral administration of ethanolic extracts (95%) and hexane fraction of *S. chirayita* (10, 50 and 100 mg/kg) to normal, glucose-fed and STZ-induced diabetic rats significantly lowered blood glucose in all groups of animals [52].

***Terminalia chebula* Retz. (Combretaceae):** It has been widely used in diabetes in Ayurveda and is widely distributed in India. An herbal formulation containing *T. chebula* named "triphala" is traditional medicine for the treatment of diabetes. Anti-diabetic and reno-protective effects of the chloroform extract of *T.chebula* seeds in streptozotocin-induced diabetic rats were demonstrated. It also showed potent reno-protective action [53].

***Tinospora cordifolia* (Willd.) Miersex Hook. f. & Thomson (Menispermaceae):** Commonly known as "guduchi" an herbaceous vine indigenous to the tropical areas of India, Myanmar and Sri Lanka. Oral administration of an aqueous *T. cordifolia* root extract to alloxan diabetic rats caused a significant reduction in blood glucose and brain lipids. Although the aqueous extract at a dose of 400 mg/kg could elicit significant antihyperglycemic effects in different animal models, its effect was equivalent to only one unit of insulin /kg of body mass [54].

4. Conclusion

Presently many countries face large increases in the number of people suffering from diabetes. In spite of the presence of known anti-diabetic medicines in the pharmaceutical market, remedies from medicinal plants are used with success to treat this disease. Many traditional plant treatments for diabetes are used throughout the world. In India, Uttrakhand has diversity of aromatic and medicinal plants. These plants may be used as a huge amount of raw material for pharmaceutical industries for manufacturing anti-diabetic medicines.

5. References

1. Abu-Rabia A. Urinary diseases and ethno-botany among pastoral nomads in the Middle East. Journal of Ethnobiology and Ethnomedicine 2005; 1:4-14.
2. Pei SJ. Ethno-botanical approaches of traditional medicine studies: Some experiences from Asia. Pharmaceutical Biology 2001; 39:74-79.
3. Lev E. Ethno-diversity within current ethno-pharmacology as part of Israeli traditional medicine – A review. Journal of Ethnobiology and Ethnomedicine 2006; 2:4.
4. Al-Qura'n S. Ethnobotanical survey of folk toxic plants in southern part of Jordan. Toxicon 2005; 46:119-126.
5. Gazzaneo LR, Paiva de Lucena RF, Paulino de Albuquerque U. Knowledge and use of medicinal plants by local specialists in a region of Atlantic Forest in the state of Pernambuco (Northeastern Brazil). Journal of Ethnobiology and Ethnomedicine 2005; 1:9.
6. Hanazaki N, Tamashiro JY, Leitao-Filho H, Gegossi A. Diversity of plant uses in two Caicaras communities from the Atlantic forest coast, Brazil. Biodiversity and Conservation 20009; 597-615.
7. Rossato SC, Leitao-Filho H, Gegossi A. Ethnobotany of Caicaras of the Atlantic forest coast (Brazil). Economic Botany 1999; 53:387-395.
8. Ved DK, Goray GS. Demand and Supply of Medicinal Plants in India, Bishen Singh, Mahendra Pal Singh, Dehra Dun and FRLHT, Bangalore, India, 2008.
9. Ragupathy S, Newmaster SG, Maruthakkutti M, Velusamy B, Ul-Huda MM. Consensus of the 'Malasars' traditional aboriginal knowledge of medicinal plants in the Velliangiri holy hills, India. Journal of Ethnobiology and Ethnomedicine 2008; 27(4):8-15.
10. WHO. General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine Geneva, Switzerland WHO/EDM/TRM 2000; 1:1-80.
11. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance. In Diabetes Atlas. International Diabetes Federation.Third Edition. Gan D, Ed, International Diabetes Federation, Belgium 2006; 15-103.
12. Raghuram TC, Swaran Pasricha, Sharma RD. Diet and Diabetes, Nation Institute of Nutrition, India council of Medical Research, Hyderabad 2003; 1-6.
13. Keter LK, Mutiso PC. Ethno-botanical studies of medicinal plants used by traditional health ractitioners in the management of diabetes in Lower Eastern Province, Kenya. Journal of Ethnopharmacology 2012; 139(1):74-80.
14. Dong H, Wang N, Zhao L, Lu F. Berberine in the treatment of type 2 diabetes mellitus: a systemic review and meta-analysis. Evidence-Based Complementary and Alternative Medicine, 2012, 12.
15. Unwin N, Whiting D, Guariguata L, Ghyoot G, Gan D. IDF. Diabetes Atlas, International Diabetes Federation, Brussels, Belgium, 5th Edition, 2011.
16. WHO Expert Committee on Diabetes Mellitus. Second Report. Geneva: WHO, 1980. Technical Report Series 2000; 15:646.
17. Bastaki S. Review of Diabetes mellitus and its treatment. International Journal of Diabetes and Metabolism 2005; 13:111-134.
18. Noor A, Gunasekaran S, Manickam AS, Vijayalakshmi MA. Anti-diabetic activity of *Aloe vera* and histology of organs in streptozotocin–induced diabetic rats. Curr. Sci 2008; 94:1070-1076.
19. Grover JK, Vats V. Shifting paradigm from conventional to alternate medicine. An introduction on traditional Indian medicine. Asia Pacific. Biotech News 2001; 5:28-

32.
20. Seth SD, Sharma B. Medicinal plants of India. Indian Journal of Medical Research 2004; 120:9-115.
21. Patil R, Ahirwar B, Ahirwar D. Current status of Indian medicinal plants with anti-diabetic potential: a review. Asian Pacific Journal of Tropical Biomedicine 2011; 1(2):S291–S298.
22. Rizvi SI, Mishra N. Traditional Indian medicines used for the management of diabetes mellitus. Journal Diabetes Research, 2013. doi: 10.1155/2013/712092.
23. Liu IM, Tzeng TF, Liou SS, Lan TW. Improvement of insulin sensitivity in obese Zucker rats by myricetin extracted from *Abelmoschus moschatus*. Planta Medica 2007; 73:1054-60.
24. Wadood A, Wadood N Shah SA. Effects of *Acacia arabica* and *Caralluma edulis* on blood glucose levels of normal and alloxan diabetic rabbits. JPMA. The Journal of Pakistan Medical Association 1989; 39(8):208-12.
25. Akhtar MS, Iqbal J. Evaluation of the hypoglycaemic effect of *Achyranthes aspera* in normal and alloxan-diabetic rabbits Journal of Ethnobiology and Ethnomedicine 1991; 31:49-57.
26. Das AV, Padayatti PS Paulose CS. Effect of leaf extract of *Aegle marmelose* (L.) *Correa* ex Roxb. on histological and ultrastructural changes in tissues of streptozotocin induced diabetic rats. Indian Journal of Experimental Biology 1996; 34(4):341-45.
27. Gray AM, Flatt PR. Actions of traditional anti-diabetic plant, *Agrimony eupatoria* (agrimony): effects on hyperglycaemia, cellular glucose metabolism and insulin secretion. British. Journal of Nutrition 1998; 80(l):109-14.
28. Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycemic effect of some edible plants. Journal of Ethnobiology and Ethnomedicine 1995; 48:25-32.
29. Kumari K, Mathew BC, Augusti KT. Anti-diabetic effects of S-methyl cysteinesulfoxide, isolated from *Allium cepa* Linn. Indian Journal of Biochemistry Biophysics 1995; 32:49-54.
30. Zacharias NT, Sebastian KL, Philip B, Augusti KT. Hypoglycemic and hypolipidemic effects of garlic in sucrose fed rabbits. Indian Journal of Physiology and Pharmacology 1980; 24:151-54.
31. Swanston-Flatt SK, Day C, Bailey CJ, Flatt PR. Traditional plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetologia 1990; 33(8):462-64.
32. Ghannam N, Kingston M, Al-Meshaal IA, Tariq M, Parman NS, Woodhouse N. The anti-diabetic activity of aloes: preliminary clinical and experimental observations. Hormone Research 1986; 24:288-94.
33. Subramoniam A, Pushpangadan P, Rajasekharan S. Effect of *Artemisia pallen* Wall. on blood glucose levels in normal and alloxan induced diabetic rats. Journal of Ethnopharmacology 1996; 50:13-17.
34. Waheed A, Miana GA Ahmad SI. Clinical investigation of hypoglycemic effect of seeds of *Azadirachta inidca* in type-2(NIDDM) diabetes mellitus. Pakistan Journal of Pharmaceutical Sciences 2006; 19:322-25.
35. Rao KN, Krishna MB, Srinivas N. Effect of chronic administration of *Boerhaavia diffusa* Linn. leaf extract on experimental diabetes in rats. Tropical Journal of Pharmaceutical Research 2004; 3:305.
36. Saleem R, Ahmad M, Hussain SA, Qazi AM, Ahmad SI, Qazi MH *et al*. Hypotensive, hypoglycemic and toxicological studies on the flavonol C-glycoside shamimin from *Bombax ceiba*. Planta Medica 1999; 65(4):331-34.
37. Anand P, Murali KY, Tandon V, Chandra R, Murthy PS. Preliminary studies on antihyperglycemic effect of aqueous extract of *Brassica nigra* (L.) Koch in streptozotocin induced diabetic rats. Journal of Experimental Biology 2007; 45:696-701.
38. Agarwal V, Chauhan BM. A study on composition and hypolipidemic effect of dietary fiber from some plant foods. Plant Foods and Human Nutrition 1988; 38(2):189-97.
39. Prakasam A, Sethupathy S, Pugalendi KV. Antihyperglycaemic effect of *Casearia esculenta* root extracts in streptozotocin-induceddiabetic rats. Pharmazie, 2002; 57:758-60.
40. Badole S, Patel N, Badhankar S. Antihyperglycemic activity of aqueous extract of leaves of *Cocculus hirsutus* (L.) Diels in alloxan-induced diabetic mice. Journal of Pharmacology 2006; 38:49.
41. Abdel-Hassan IA, Abdel-Barry, Tariq JA, Mohammeda S. The hypoglycemic and anti-hyperglycemic effect of *Citrullus colocynthis* fruit aqueous extract in normal and alloxan diabetic rabbits. Journal of Ethnopharmacology 20007; 1(1-2):325-330.
42. Augusti KT, Daniel RS, Cherian S, Sheela CG, Nair CR. Effect of leucopelargonin derivative from *Ficus bengalenesis* Linn. on diabetic dogs. Indian Journal of Medical Research 1994; 99:82-86.
43. Chakrabarti R, Vikramadithyan RK, Mullangi R, Sharma VM, Jagadheshan H, Rao YN *et al.* Antidiabetic and hypolipidemic activity of *Helicteres isora* in animal models. Journal of Ethnopharmacology 2002; 81:343-49.
44. Sachdeva A, Khemani LD. A preliminary investigation of the possible hypoglycemic activity of *Hibiscus rosasinensis*. Biomedicine and Environmental Science 1999; 12(3):222-26.
45. Tripathi YB, Tripathi P, Upadhyay BN. Assessment of the adrenergicbeta-blocking activity of *Inula racemosa*. Journal of Ethnopharmacology 1988; 23:3-9.
46. Sharma OP, Vaid J, Pattabhi V, Bhutani KK. Biological action of lantadene C, a new hepatotoxicant from *Lantana camara* var. *aculeata*. Journal of Biochemistry and Toxicology 1992; 7(2):73-79.
47. Martinez G, Delgado R, Perez G, Garrido G, Nunez AJ, Selles, Leon OS. Evaluation of the *in vitro* antioxidant activity of *Mangifera indica* L. extract. Phytotherapy Research 2000; 14(6):424-27.
48. Khan BA, Abraham A, Leelamma S. Role of *Murraya koeingii* (curry leaf) and *Brassica juncea* (Mustard) in lipid peroxidation. Indian Journal of Physiology and Pharmacology 1996; 40(2):155-58.
49. Vats V, Yadav SP Grover JK. Ethanolic extract of *Ocimum sanctum* leaves partially attenuates streptozotocin-induced alteration in glycogen content and carbohydrate metabolism in rats. Journal of Ethnopharmacology 2004; 90:155-60.
50. Joy KL, Kuttan R. Anti-diabetic activity of *Picrorrhiza kurroa* extract. Journal of Ethnopharmacology 1999; 67(2):143-48.
51. Schubert SY, Lansky EP, Neeman I. Antioxidant and enzyme inhibition properties of pomegranate seed oil and fermented juice flavonoids. Journal of Ethnopharmacology 1999; 66(1):11-17.

52. Sekar BC, Mukherjee B, Chakravarti RB, Mukherjee SK. Effect of different fractions of Swertia chirayita on the blood sugar level of albino rats. Journal of Ethnopharmacology 1987; 21(2):175-81.
53. Rao NK, Nammi S. Antidiabetic and renoprotective effects of the chloroform extract of *Terminalia* chebula Retz. seeds in streptozotocin-induced diabetic rats. BMC Complement. Ary & Alternative Medicine, 2006, (6)17. http:www.biomedcentral.com/ 1472-6882/6/17.
54. Dhaliwal KS. Method and composition for treatment of diabetes, US Patent, 1999, 5886029.