

ROLE OF HERBAL PLANTS IN THE DIABETES MELLITUS THERAPY: AN OVERVIEW**MANI RUPESHKUMAR¹, KUNCHU KAVITHA¹, PALLAB KANTI HALDAR^{2,*}**¹East Point College of Pharmacy, Bidarahalli, Bangalore-49, Karnataka, India, ²Department of Pharmaceutical Technology, Jadavpur University, Kolkata-32, West Bengal, India. Email: pallab_haldar@rediffmail.com*Received: 19 Feb 2014, Revised and Accepted: 29 April 2014***ABSTRACT**

Diabetes mellitus has been recognized as a growing worldwide epidemic by any health's advocacy group. The World Health Organization (WHO) has estimated that diabetes will be one of the world leading causes of death and disability with the next quarter century. There is a unit Associate in nursing calculable 143 million folks within the world with diabetes and this variety will most likely double by the year 2030. Oral hypoglycaemic agents like sulphonylureas and biguanides are still the major players in the management of the disease, but there is growing interest in herbal remedies due to the side effects associated with the oral hypoglycemic agents. Herbal medicines have been highly esteemed source of medicine throughout the human history. They are widely used today indicating that herbs are a growing part of modern high-tech medicine. In recent times, there has been a revived interest within the plant remedies. In this review article an attempt has been made to focus on hypoglycaemic plants and may be useful to the health professionals, scientists and scholars working in the field of pharmacology & therapeutics to develop evidence based alternative medicine to cure different kinds of diabetes in man and animals.

Keywords: Diabetes Mellitus, Insulin, Hypoglycaemic agents, Herbal treatment.**INTRODUCTION**

Medicinal plants constitute an important natural wealth of a country. They play a significant role in providing primary health care services to the rural population. They serve as therapeutic agents as well as important raw materials for the manufacture of traditional medicines. Ethnopharmacology is the study of plants used in traditional medicine and is therefore heavily reliant on interactions between researchers and indigenous communities who passed on the traditional knowledge over generations. Whilst in the main, ethnopharmacology focuses on the presence or absence of evidence for specific therapeutic responses through the use of herbal remedies, the field also extends into phytochemistry where the aim is to identify the chemical constituent of the plant or plant extract that is responsible for the pharmacological activities inherent to a specific plant [1].

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter [2]. WHO has listed 21,000 plants, which are used for medicinal purposes around the world [3]. Therefore, with the rising number of diseases lately, many researchers have evaluated the medicinal plants as alternative therapeutic agents. The effectiveness and safety of drugs derived from medicinal plants require scientific evaluation to establish the profiles of therapeutic effectiveness and toxicity of plant products. One example of such products is antihyperglycemic agents for use in the treatment of diabetes mellitus.

Importance of medicinal plants and traditional medicines

Medicinal plants, since time immemorial, have been used in virtually all cultures as a source of medicine. It has been estimated that about 80-85% of population both in developed and developing countries rely on traditional medicine for their primarily health care needs and it is assumed that a major part of traditional therapy involves the use of plant extracts or their active principles [4-6]. Due to lack of organized health care systems in developing countries like Ethiopia, people with chronic diseases like diabetes are among the worst sufferers in their communities today. Hence, most of the populations still have limited access or no access, especially those in remote areas, to modern medicines. Instead they use traditional medicines for a range of diabetic complications [7-8].

Diabetes mellitus

Diabetes mellitus is described as metabolic disorder which resulting from defects in insulin secretion or insulin action or both diabetes mellitus could cause long-term damage, dysfunction and failure in many organs. Patients with diabetes can develop heart disease, kidney disease, blindness, vascular or neurological problems that can lead to amputation and can suffer increased rates of mortality. Moreover, the death rate in patients with diabetes is much higher than in persons without the disease. According to the estimation of the International Diabetes Federation (IDF) [9], one among ten adults would have diabetes by 2030. There were 366 million people having diabetes in 2011; this will increase to 552 million people by 2030.

The number of people got type 2 diabetes is increasing every year and many people remain un-diagnostic. In the demand of preventing and treating Diabetes Mellitus, there are many synthetic drugs have been researched and developed such as Sulphonylureas, thiazolidinediones, Glinide, Metformin.... However, they are not optimum solution especially for developing country like Vietnam. They retain many side effects and relatively expensive. There is a need to investigate herbal drug based medicine, which has available resources, easy to use, cheap and less side effects.

Classification of diabetes mellitus [10, 11]

Type I diabetes: Insulin-dependent or childhood-onset, is characterized by a lack of insulin production.

Type II diabetes: Non-insulin-dependent or maturity/adult-onset diabetes.

Type III or Gestational diabetes: This type of diabetes first occurs during pregnancy.

Secondary diabetes: Diabetes may develop as a consequence of other diseases or medication.

Prevalence and incidence of diabetes mellitus

Globally, the prevalence of diabetes, without type distinction, was estimated to be 4% in 1995. According to WHO, it is estimated that 3% of the world's population have diabetes and the prevalence is expected to double by the year 2025 to 6.3% [12-13]. There will be a 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to 228 million, in the developing countries. Thus, by the year 2025, over 75% of all people with diabetes will be in the developing countries, as compared to 62% in 1995 [14].

Diabetes mellitus and Phytotherapy

Natural products and their derivatives have been a successful source of bioactive molecules in medicines much before the advancement of other modern therapeutics in the post-genomic era. Medicinal plants have been used virtually in all cultures as a source of medicine [15]. The use of medicinal plants for treatment of diabetes mellitus dates back from the Ebres papyrus about 1550 B. C [16-19]. Traditional medicines derived mainly from plants play a major role in the management of diabetes mellitus. World Health Organization (WHO) has recommended the evaluation of traditional plant treatments for diabetes as they are effective, non-toxic, with less or no side effects and considered to be excellent candidates for oral therapy [20-25]. To date, over 400 traditional plant for diabetes has been reported, although only a small number of these have received a scientific and medical evaluation to assess their efficacy [26].

The importance of phytotherapy in treatment of type 2 diabetes mellitus seems to gradually increase in coming years. Phytotherapy can be effective in prevention of diabetes and its complications as well as optimization of the treatment and life standards. As in case of many chronic metabolic diseases, the mechanism is closely related, particularly in diabetes, to oxidative stress and inflammation in the body. Therefore, due to the antioxidant properties herbs should be considered for both prevention and treatment of diabetes [27]. The use of medicinal plants has flourished as an alternative for the treatment of diabetes because modern medicines are tagged with several side effects and are also expensive. A multitude of herbs and medicinal plants and some compounds purified from them has been studied for the treatment of diabetes throughout the world as they might provide a basis of new synthetic antidiabetic analogues with potent activity. Indeed, the widely prescribed insulin-sensitizer metformin was derived from guanidine, a molecule isolated from *Galega officinalis* L. (French lilac) [28-30].

Table 1: List of pharmacologically tested anti-diabetic plant materials in streptozotocin induced diabetic animal model

Plant Name	Family
<i>Azelia africana</i>	Fabaceae
<i>Amaranthus caudatus</i>	Amaranthaceae
<i>Andrographis lineata</i>	Acanthaceae
<i>Annona squamosa</i>	Annonaceae
<i>Artocarpus heterophyllus</i>	Moraceae
<i>Boerhaavia diffusa</i>	Nyctaginaceae
<i>Berberis vulgaris</i>	Berberidaceae
<i>Brassica juncea</i>	Brassicaceae
<i>Caesalpinia bonduc</i>	Fabaceae
<i>Caesalpinia digyna</i>	Caesalpiniaceae
<i>Cassia glauca</i>	Fabaceae
<i>Cassia siamea</i>	Fabaceae
<i>Cleome aspera</i>	Capparaceae
<i>Clitoria ternatea</i>	Fabaceae
<i>Coccinia indica</i>	Cucurbitaceae
<i>Decalepis root</i>	Asclepiadaceae
<i>Diospyros peregrina</i>	Ebenaceae
<i>Dodonaea viscosa</i>	Sapindaceae
<i>Enicostemma littorale</i>	Gentianaceae
<i>Eucalyptus globules</i>	Myrtaceae
<i>Holarrhena antidysenterica</i>	Apocynaceae
<i>Hybanthus enneaspermus</i>	Violaceae
<i>Hypericum perforatum</i>	Hypericaceae
<i>Lawsonia inermis</i>	Lythraceae
<i>Leonotis leonurus</i>	Lamiaceae
<i>Litsea coreana</i>	Lauraceae
<i>Madhuca longifolia</i>	Sapotaceae
<i>Morus rubra</i>	Moraceae
<i>Nyctanthes arbor-tristis</i>	Oleaceae
<i>Olea europaea</i>	Oleaceae
<i>Otostegia persica</i>	Lamiaceae
<i>Phlomis persica</i>	Lamiaceae
<i>Punica granatum</i>	Lythraceae
<i>Rhus coriaria</i>	Anacardiaceae
<i>Rosa canina</i>	Rosaceae
<i>Salmalia malabarica</i>	Bombacaceae
<i>Sansevieria roxburghiana</i>	Ruscaceae
<i>Swietenia macrophylla</i>	Meliaceae
<i>Symplocos cochinchinensis</i>	Symplocaceae
<i>Syzygium cumini</i>	Myrtaceae
<i>Tapinanthus bangwensis</i>	Loranthaceae
<i>Terminalia bellerica</i>	Combretaceae
<i>Terminalia superba</i>	Combretaceae
<i>Thespesia populnea</i>	Malvaceae
<i>Tinospora cordifolia</i>	Menispermaceae

Ethanopharmacological surveys indicate that more than 1200 plants are used in traditional medicine for their allied hypoglycemic activity. In diabetes, some herbal alternatives are proven to provide symptomatic relief and assist in the prevention of the secondary complication of the

disease. As per ancient literature, more than 800 plants are reported to have antidiabetic properties, although only a small number of these have received scientific and medicinal evaluation to assess their efficacy [31-32]. Some of the pharmacologically tested anti-diabetic plant materials in

streptozotocin induced diabetic animal model are listed in the Table 1 [33].

CONCLUSION

In conclusion, this paper has presented a list of anti-diabetic plants used in the treatment of diabetes mellitus. Many new bioactive drugs isolated from plants having hypoglycaemic effects showed anti-diabetic activity equal and sometimes even more potent than known oral hypoglycaemic agents. However, many other active agents obtained from plants have not been well characterized. More investigations must be conducted to evaluate the mechanism of action of medicinal plants with anti-diabetic effect. Consequently, it is necessary to perform toxicological investigation of all plants empirically used in order to avoid the risk of side effects related to phytotherapy. This review has been presented in a very interactive manner showing geographical region of availability, parts of plant used, mechanism of action and phytoconstituents responsible for particular action; thereby, it will be of great importance to interested readers to easily identify and go for further research on the plant of their interest.

REFERENCES

- Mulholland DA, Chukwujekwu JC, Smith P, Coombes PH, Van-Standen J. Antispasmodial diterpenoid from leaves of *Hyptis suaveoleus*. *J Ethnopharmacol* 2005;102:295-7.
- Sangeeta R, Sudhir C, Pradeep S, Garima M, Jha KK, Khosa RL. *Cressa Cretica* Linn: an important medicinal plant-A review on its traditional uses, phytochemical and pharmacological properties. *J Nat Prod Plant Resour* 2011;1:91-100.
- Maurya U, Srivastava S. Traditional Indian Herbal medicine used as antipyretic, antiulcer, antidiabetic and anticancer: a review. *IJRPC* 2011;1:1152-9.
- Ignacimuthu S, Ayyanar M, Sivaraman SK. Ethnobotanical investigations among tribes in Madurai district of Tamil Nadu (India). *J Ethnobiol Ethnomed* 2006;2:1-7.
- Elujoba AA, Odeleye OM, Ogunyemi CM. Traditional medicine development for medical and dental primary health care delivery system in Africa. *Afr J Tradit Complementary Altern Med* 2005;2:46-61.
- Tomlinson TR, Akerele O. Medicinal plants: their role in health and biodiversity. University of Pennsylvania Press, Philadelphia; 1998. p. 11-41.
- Kochhar A, Nagi M. Effect of supplementation of traditional medicinal plants on blood glucose in non-insulin-dependent diabetics: a pilot study. *J Med Food* 2005;8:545-9.
- Zibula SMX, Ojewole JAO. Hypoglycemic effects of *Hypoxis hemerocallidea* corm 'African potato' methanolic extract in rats. *Med J Islamic Academy Sci* 2000;13:75-8.
- International Diabetes Federation. Brussels, Belgium: International Diabetes Federation. *IDF Diabetes Atlas*, 5th edn; 2011.
- WHO-World Health Organization. *Diabetes Fact Sheet* Number 312; 2006.
- Davidson MB. *Diabetes mellitus: Diagnosis and treatment*. Churchill Livingstone Incorporated. USA; 1991.
- Andrade-Cetto A, Heinrich M. Mexican plants with hypoglycemic effect used in the treatment of diabetes. *J Ethnopharmacol* 2005;99:325-48.
- Attele AS, Zhou Y, Xie J, Wu JA, Zhang L, Dey L, et al. Antidiabetic effects of *Panax ginseng* Berry extract and the identification of an effective component. *Diabetes* 2002;51:1851-8.
- Ramachandran A, Snehalatha C, Viswanathan V. Burden of type 2 diabetes and its complications-The Indian scenario. *Curr Sci* 2002;83:1471-6.
- Sofowora A. Research on medicinal plants and traditional medicine in Africa. *JCAM* 1996;2:365-72.
- Kesari AN, Gupta RK, Watal G. Hypoglycemic effect of *Murraya koenigii* on normal and alloxan diabetic rabbits. *J Ethnopharmacol* 2005;97:247-51.
- Gupta RK, Kesari AN, Murthy PS, Chandra R, Tandon V, Watal G. Hypoglycemic and antidiabetic effect of ethanolic extract of leaves of *Annona squamosa* L. in experimental animals. *J Ethnopharmacol* 2005;99:75-81.
- Kako M, Miura T, Nishiyama Y, Ichimaru M, Moriyasu M, Kato A. Hypoglycemic activity of some triterpenoid glycosides. *J Nat Prod* 1991;60:604-5.
- Shruthi A, Latha KP, Vagdevi HM, Pushpa B, Shwetha C. Antidiabetic activity of the leaves extracts of *Wrightia Tinctoria* on alloxan induced diabetic rats. *J Chem Pharm Res* 2012;4:3125-8.
- Sunil Kumar, Smita Narwal, Dinesh Kumar, Gurvirender Singh, Sumit Narwal, Renu Arya. Evaluation of antihyperglycemic and antioxidant activities of *Saraca asoca* (Roxb.) De. Wild leaves in streptozotocin induced diabetic mice. *Asian Pac J Trop Dis* 2012;170-6.
- Khan MRI, Islam MA, Hossain MS, Asadujjaman M, Wahed MII, Rahman BM, et al. Antidiabetic effects of the different fractions of ethanolic extracts of *ocimum sanctum* in normal and alloxan induced diabetic rats. *J Sci Res* 2010;2:158-68.
- Virendra Singh, Mohan Lal Kori. Antidiabetic effect of hydroalcoholic combined plant extract of *portulaca oleracea* and *caralluma attenuata* in streptozotocin induced diabetic rats. *Indo Am J Pharm Res* 2014;4:1391-6.
- Ahmed I, Adeghate E, Cummings E, Sharma AK, Singh J. Beneficial effects and mechanism of action of *Momordica charantia* juice in the treatment of streptozotocin-induced diabetes mellitus in rat. *Mol Cell Biochem* 2004;261:63-70.
- Platel K, Srinivasan K. Plant foods in the management of diabetes mellitus: vegetables as potential hypoglycaemic agents. *Nahrung* 1997;41:68-74.
- Day C. Traditional plant treatments for diabetes mellitus: pharmaceutical foods. *Br J Nutr* 1998;80:203-8.
- Ajithadas Aruna, Ramraj Nandhini, Venkatachalam Karthikeyan, Pandi Bose, Kannappan Vijayalakshmi. Comparative anti-diabetic effect of methanolic extract of insulin plant (*costus pictus*) leaves and its silver nanoparticle. *Indo Am J Pharm Res* 2014;4:3217-30.
- Kato A, Miura T, Fukunaga T. Effects of steroidal Glycosides on blood glucose in normal and diabetic mice. *Biol Pharm Bull* 1995;18:167-8.
- Witters LA. Understanding the benefit of metformin use in cancer treatment. *J Clin Invest* 2001;108:1105-7.
- Bailey C, Day C. Metformin: its botanical background. *Pract Diabetes Int* 2004;21:115-7.
- Eddouks M, Jouad H, Maghrani M, Lemhadri A, Burcelin R. Inhibition of endogenous glucose production accounts for hypoglycemic effect of *Spergularia purpurea* in streptozotocin mice. *Phytomed Int J Phytother Phytopharmacol* 2003;10:594-9.
- Kesari AN, Kesari S, Santosh KS, Rajesh KG, Geeta W. Studies on the glycemic and lipidemic effect of *Murraya koenigii* in experimental animals. *J Ethnopharmacol* 2007;112:305-11.
- Sabu MC, Subburaju T. Effect of *Cassia auriculata* Linn. on serum glucose level, glucose utilization by isolated rat hemidiaphragm. *J Ethnopharmacol* 2002;80:203-6.
- Wadkar KA, Magdum CS, Patil SS, Naikwade NS. Anti-diabetic potential and Indian medicinal plants. *J Herb Med Toxicol* 2008;2:45-50.