

**HISTORY, ORAL HYPOGLYCEMIC DRUGS AND PLANT ALTERNATIVES RELATED TO DIABETES MELLITUS: A REVIEW**

Lekhana A. R. \*, Palaksha M. N, Mamatha B. S and Nandini K.N.

Dept.of Pharmacology, Bharathi College of Pharmacy, Bharathinagara 571422.

**\*Corresponding Author: Lekhana A. R.**

Dept.of Pharmacology, Bharathi College of Pharmacy, Bharathinagara 571422.

Article Received on 09/07/2019

Article Revised on 30/07/2019

Article Accepted on 20/08/2019

**ABSTRACT**

Diabetes mellitus is a metabolic disease which is characterized by hyperglycaemia, hyper aminoacidemia and hypoinsulinemia this leads to decrease in insulin secretion and insulin action. Diabetes mellitus were described 3000 years ago by the ancient Egyptians. Oral hypoglycemic agents are used to treat diabetes mellitus and also some of the traditional medicines are used as an alternative to treat diabetes mellitus. The modern era in the history of diabetes mellitus is rediscovered by Thomas Willis in 1675 of sweetness urine of the diabetic patients. In 1946, Loubatieres demonstrated experimentally that the sulphonamides group was responsible for the hypoglycemic action.

**KEYWORDS:** Diabetes, History.**History**

Diabetes mellitus is a chronic metabolic disorder occurs due to the presence of high concentration of glucose in the blood and also due to increase or decrease in the production of the insulin in the pancreas. Diabetes mellitus has been considered as one of the major health concerns all around the world.<sup>[1-2]</sup> Diabetes mellitus is characterized by hyperglycemia, hyper aminoacidemia and hypoinsulinemia. Diabetes is the dreadful disease and also one of the most leading disorder, it may increase the secondary applications which may affecting the eye, kidney and nerves.<sup>[3]</sup> Oral hypoglycemic agents are used to treat diabetes mellitus and these agents may cause undesirable side effects. Some of the traditional medicines are used as an alternative to treat diabetes mellitus. Clinical features similar to diabetes mellitus were described 3000 years ago by the ancient Egyptians. The term "diabetes" was first introduced by Aretus of Cappadocia (81-133AD). Later the word "mellitus" (honey sweet) was added by Thomas Willis in 1665.<sup>[5]</sup> Diabetes mellitus is a disease, for example a constellation of symptoms, but not its pathogenesis. It has been known by physicians for nearly 3,500 years in ancient Egypt.<sup>[6]</sup> The papyrus contains information of various diseases; among them is a polyuric syndrome, probably diabetes. The Egyptians proposed various remedies to this syndrome. The Indians identifies the relation of diabetes to heredity, obesity and diet. They suggested freshly harvested cereals and bituminous preparations containing benzoates and silica as a remedy for diabetes.<sup>[7]</sup> Aretus said "Diabetes is a wonderful affection being a melting down of the flesh and limbs into urine. The patient never stops drinking water but the

flow is incessant as if from the opening of aqueducts. The patient is short lived."<sup>[8]</sup>

**Diabetes in modern times**

The history of diabetes mellitus in the modern time is coincided with the establishment of experimental foundation of modern medicine. Two prominent measurements in the history of medicine paved the way towards understanding the pathogenesis of Diabetes. The first one was the application of chemistry as a diagnostic tool in the second half of the 18th century<sup>[9]</sup>. The other one was the emergence of endocrinology as a formal discipline with the works of Claude Bernard (1813-1878) and Brown-Sequard (1817-1894). Bernard established the concept of organs of internal secretions. The modern era in the history of diabetes mellitus is rediscovered by Thomas Willis in 1675 of sweetness urine of the diabetic patients.<sup>[10]</sup> Four years later, Frank classified the disease, on the basis of presence sugar like substance into diabetes insipidus (tasteless urine) and diabetes Vera (sweet urine). In 1776, Liverpool physician confirmed the presence of sugar in both urine and blood<sup>[10]</sup>. In 1798, John Rollo, a French physician, misguidedly concluded that diabetes was a disease of the stomach as a result of abnormal transformation of vegetable nutrients into sugar.<sup>[11]</sup>

**Oral hypoglycemic drugs**

Oral hypoglycemic drugs are the agents which are used to treat diabetes mellitus. In 1930, the hypoglycemic effect of sulphonamides was firstly detected.<sup>[12]</sup> Professor M. J. Janbon noticed that the substance testing on animals could cause severe hyperglycemia.<sup>[13]</sup> In 1946,

Loubatieres demonstrated experimentally that the sulphonamides group was responsible for the hypoglycemic action.<sup>[14]</sup> In 1950, Metformin and Phenformin were developed from the active ingredient of Galega officinalis. Phenformin was withdrawn from the market in the early 1970 as the high frequency of lactic acidosis resulted from its use.

## CLASSIFICATION

### 1. Sulfonyl ureas

- First generation drugs: Tolbutamide, Chlorpropamide
- Second generation drugs: Glipizide, Glibenclamide

### 2. Meglitinides

Repaglinide, Nateglinide

### 3. Biguanides

Metformin, Phenformin

### 4. Thiazolidinedione's

Rosiglitazone

### 5. $\alpha$ – glucosidase inhibitors

Acarbose, Miglitol

#### ➤ Mechanism action of Sulfonyl ureas

Sulfonylureas reduce the blood glucose level by:

- Stimulating the release of insulin from the pancreatic  $\beta$  cells.
- Increasing the sensitivity of peripheral tissues to insulin.
- Increasing the number of insulin receptors.
- Suppressing hepatic gluconeogenesis.

#### ➤ Mechanism action of Meglitinides

Meglitinides enhance the release of insulin by blocking the ATP-dependent  $K^+$  channels in the pancreatic  $\beta$  cells.

#### ➤ Mechanism action of Biguanides

- Suppress hepatic gluconeogenesis.
- Inhibit glucose absorption from the intestines.
- Stimulate glycolysis in the tissues.
- Reduce plasma glucagon levels.

#### ➤ Mechanism action of Thiazolidinedione's

TZDs activate the PPAR-gamma receptors and modulate the expression of insulin-sensitive genes, i.e. they induce the synthesis of genes which enhance insulin action.

#### ➤ Mechanism action of $\alpha$ -glucosidase inhibitors

$\alpha$  -glucosidase inhibitors inhibits  $\alpha$ - glucosidase in intestinal brush border this prevents the absorption and delay digestion of carbohydrates and reduce the postprandial blood sugar.

## Some of the Medicinal plants used for the treatment of diabetes mellitus

Sl.No	Botanical Name	Common Name	Family	Parts used	Activity	Reference
01	<i>Abrama augusta</i>	Devil's cotton	Sterculiaceae	Stem & Bark	Anti-diabetic	15
02	<i>Abrus precatorius L</i>	Kundumani	Fabaceae	Leaves	Anti-diabetic	16
03	<i>Albizia odoratissima</i>	Black siris	Mimosaceae	Bark	Anti-diabetic	17
04	<i>Bougainvillea Glabra</i>	Paper flower	Nyctanginaceae	Leaves	Anti-diabetic	18
05	<i>Bryonia alba</i>	White bryony	Curcubitaceae	Roots	Anti-diabetic	19
06	<i>Caesalpinia digyna</i>	Vakeri mool	Fabaceae	Root	Anti-diabetic	20
07	<i>Cajanus cajan</i>	Pigeon pea	Fabaceae	Leaves	Anti-diabetic	21
08	<i>Ceibapentandra</i>	Silk cotton tree	Bombcaceae	Roots & Bark	Anti-diabetic	22
09	<i>Prosopis glandulosa</i>	Honey mesquite	Fabaceae	Whole plant	Anti-diabetic	23
10	<i>Punica granatum</i>	Pomegranate Anar	Punicaceae	Flower	Anti-diabetic	24
11	<i>Tinospora cordifolia</i>	Guduchi, giloy	Menispermaceae	Root	Anti-diabetic	25
12	<i>Semecarpus anacardium</i>	Bhilawa	Anacardiaceae	Nut	Anti-diabetic	26
13	<i>Symplocos cochinchinensis</i>	Kambli-vetti	Symplocaceae	Leaves	Anti-diabetic	27
14	<i>Syzygium cumini</i>	Jamun , Jambul	Myrtaceae	Seeds	Anti-diabetic	28
15	<i>Vitis vinifera</i>	Woody vine	Vitaceae	Leaves	Anti-diabetic	29
16	<i>Aconitum Palmatum</i>	Aconite	Raunculaceae	Stem & Bark	Anti-diabetic	15
17	<i>Abutilon indicum</i>	Thuthi	Malvaceae	Stem & Bark	Anti-diabetic	15
18	<i>Trigonella foenum-graceum</i>	Fengugreek	Fabaceae	Seed	Anti-diabetic	25
19	<i>Wattakaka volubilis</i>	Perun – kurinjan	Asclepiadaceae	Leaves	Anti-diabetic	25
20	<i>Picrorhiza kurrooa</i>	Kutki	Scrophulariaceae	Rhizome	Anti-diabetic	15
21	<i>Potentilla fulgens</i>	Cinquefoils	Rosaceae	Root	Anti-diabetic	15
22	<i>Campylandra Aurantiaca</i>	Nakima	Liliaceae	Flower	Anti-diabetic	15

## CONCLUSION

Diabetes mellitus is a chronic metabolic disorder occurs due to the presence of high concentration of glucose in the blood. Diabetes is the dreadful disease and also one of the most leading disorders; it may increase the

secondary applications. The history of diabetes mellitus in the modern time is coincided with the establishment of experimental foundation of modern medicine. In 1776, Liverpool physician confirmed the presence of sugar in both urine and blood. The Indians identifies the relation

of diabetes to heredity, obesity and diet. They suggested freshly harvested cereals and bituminous preparations containing benzoates and silica as a remedy for diabetes. Oral hypoglycemic agents are used to treat diabetes mellitus. Sulfonylureas reduce the blood glucose level by stimulating the release of insulin from the pancreatic  $\beta$  cells. Meglitinides enhance the release of insulin by blocking the ATP-dependent  $K^+$  channels in the pancreatic  $\beta$  cells.

## REFERENCE

1. Stolar MW, Hoogwerf BJ, Boyle PJ, Gorshow SM, Wales DO. Managing type 2 diabetes: going beyond glycemic control. *Journal of Managed Care Pharmacy*, 2008; 14(5): 1-22.
2. Kruger DF, Lorenzi GM, Dokken BB, Sadler CE and Mann K, Valentine V. Managing diabetes with integrated teams: maximizing your efforts with limited time. *Postgraduate medicine*, 2012; 124(2): 64-76.
3. Lekhana AR, Palaksha MN, Gnanasekaran D, Senthilkumar GP, Tamizmani T. MEDICINAL PLANTS POTENTIAL TO TREAT DIABETES: A Review. *World Journal of Pharmaceutical Research*, 2018; 7(19): 492-503.
4. Satyanarayana T, Katyayani BM, Latha EH, Routhu KV, Prasad YD. Phytochemical studies on roots of *Gmelina asiatica* Linn. *Pharmacognosy Magazine*, 2007; 3(11): 156.
5. Ahmed AM. History of diabetes mellitus. *Saudi medical journal*, 2002; 23(4): 373-8.
6. Ebbell B. *The Papyrus Ebers*. Copenhagen and Oxford: Oxford University Press, 1937; 115.
7. Algaonker SS. Diabetes mellitus as seen in Ancient Ayurvedic Medicine. In: Bajaj AS, editor. *Insulin and Metabolism*. Bombay (India): Indian Press, 1972; 1-19.
8. Aretus C. On causes and symptoms of chronic diseases. Translated by Adam CF. London. (UK): London Sydenham Society, 1856; 138.
9. McGrew R. *ENCYCLOPEDIA OF MEDICAL HISTORY*. 1<sup>st</sup> ed. London. (United Kingdom): McMillan Press, 74-297.
10. Dobson M. Experiments and observation on the Urine in diabetes. *Medical Observations and Enquiries*, 1776; 5: 298-316.
11. Rollo J. An account of two cases of the diabetes mellitus, etc. Cases of the diabetes mellitus; with the results of the trials of certain acids, and other substances, in the cure of the lues venerea... with large additions. C. Dilly, 1798; 260.
12. Ruiz CL, Silva LL, Libenson L. Contribución al estudio sobre la composición química de la insulina. Estudio de algunos cuerpos sintéticas sulfurados con acción hipoglucemiante. *Revista Societa du Argentina biological*, 1930; 6: 134.
13. Pathak AK, Sinha PK, Sharma J. Diabetes – A Historical review. *Journal of Drug Delivery and Therapeutics*, 2013; 3(1).
14. Loubatieres A, Mariani MM, Alric R, Ribes G, De Malbosc H, Houareau MH. Etude expérimentale d'un nouveau sulfamide hypoglycémiant particulièrement actif, le HB 419 ou glibenclamide. *Diabetologia*, 1969; 5(4): 219-27.
15. Chhetri DR, Parajuli P, Subba GC. Antidiabetic plants used by Sikkim and Darjeeling Himalayan tribes, India. *Journal of Ethnopharmacology*, 2005; 99(2): 199-202.
16. Dwivedi C, Dasgaul S. Antidiabetic herbal drugs and polyherbal formulation used for diabetes: A review. *Journal of Phytopharmacology*, 2013; 2(3): 44-51.
17. Kumar D, Kumar S, Kohli S, Arya R, Gupta J. Antidiabetic activity of methanolic bark extract of *Albizia odoratissima* Benth. In alloxan induced diabetic albino mice. *Asian Pacific journal of tropical medicine*, 2011; 4(11): 900-3.
18. Adebayo GI, Alabi OT, Owoyele BV, Soladoye AO. Anti-diabetic properties of the aqueous leaf extract of *Bougainvillea Glabra* (Glory of the Garden) on alloxan-induced diabetic rats. *Records of Natural Products*, 2009; 3(4): 187.
19. Singh R, Rajasree PH, Sankar C. Screening for anti-diabetic activity of the ethanolic extract of *Bryonia Alba* roots. *International Journal of Pharmacy and Biological Sciences*, 2012; 2(3): 210-5.
20. Kumar R, Patel DK, Prasad SK, Lalloo D, Krishnamurthy S, Hemalatha S. Type 2 antidiabetic activity of bergenin from the roots of *Caesalpinia digyna* Rottler. *Fitoterapia*, 2012; 83: 395-401.
21. Ezike AC, Akah PA, Okoli CC, Okpala CB. Experimental evidence for the antidiabetic activity of *Cajanus Cajan* leaves in rats. *Journal of basic and clinical pharmacy*, 2010; 1(2): 81.
22. Djomeni PD, Tédong L, Asongalem EA, Dimo T, Sokeng SD, Kamtchouing P. Hypoglycaemic and antidiabetic effect of root extracts of *Ceiba pentandra* in normal and diabetic rats. *African Journal of Traditional, Complementary and Alternative Medicines*, 2006; 3(1): 129-36.
23. George C, Lochner A, Huisamen B. The efficacy of *Prosopis glandulosa* as antidiabetic treatment in rat models of diabetes and insulin resistance. *Journal of ethnopharmacology*, 2011; 137(1): 298-304.
24. Huang TH, Peng G, Kota BP, Li GQ, Yamahara J, Roufogalis BD, Li Y. Anti-diabetic action of *Punica granatum* flower extract: activation of PPAR- $\gamma$  and identification of an active component. *Toxicology and applied pharmacology*, 2005; 207(2): 160-9.
25. Ibeh BO, Ezeaja MI. Preliminary study of antidiabetic activity of the methanolic leaf extracts of *Axonopus compressus* (P. Beauv) in alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, 2011; 138(3): 713-6.
26. Khan HB, Vinayagam KS, Palanivelu S, Panchanatham S. Anti-diabetic effect of *Semecarpus anacardium* Linn nut milk extract in a high fat diet STZ-induced type 2 diabetic rat models.

- Comparative Clinical Pathology, 2012; 21(6): 1395-400.
27. Sunil C, Ignacimuthu S, Agastian P. Antidiabetic effect of *Symplocos cochinchinensis* (Lour.) S. Moore. In type 2 diabetic rats. *Journal of Ethnopharmacology*, 2011; 134(2): 298-304.
  28. Mishra R, Shuaib M, Shravan, Mishra PS. A review on herbal antidiabetic drugs. *Journal of Applied Pharmaceutical Science*, 2011; 1: 235-7.
  29. Şendoğdu N, Aslan M, Orhan DD, Ergun F, Yeşilada E. Antidiabetic and antioxidant effects of *Vitis vinifera* L. leaves in streptozotocin-diabetic rats. *Turkish Journal of Pharmaceutical Sciences*, 2006; 3(1): 7-18.