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AN OVERVIEW ON ITS REPORTED SYNTHETIC DRUGS AND MEDICINAL PLANTS HAVING ANTIDIABETIC POTENCY

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a global pandemic, as evident from the global cartographic picture of diabetes by the International Diabetes Federation. Insulin resistance or reduced insulin sensitivity and in some cases relatively reduced insulin secretion are characteristic of the type 2 diabetes mellitus. The body tissue is defective responsiveness to insulin resistance encompasses the insulin receptor in cell membranes. The specific defects are not known but diabetes mellitus is classified separately on the basis of various defects. Worldwide, approximately 200 million people are affected by type 2 diabetes mellitus, covering especially elderly people living in developed countries. First line treatment includes diet management and exercise with oral hypoglycaemic agents that helps in prevention of macrovascular and microvascular impedance.

INTRODUCTION

Unusually increased level of sugar in the blood is a characteristic feature of diabetic mellitus. The etiology of the disease comprises of insufficient insulin production or produced in low quantity. The two major types of diabetes with their respective prevalence rates are type 1 with 5% and type 2 with 95%. Type 1 diabetes is an autoimmune problem while type 2, is often accompanied by obesity. Some times during pregnancy, gestational diabetes is observed, which is caused by a single gene mutation.[1] Hyperglycemia is allied with a high possibility of occurrence of dementia, cancer, and heart diseases, which is responsible for significant impairment of quality of patient life ultimately significant increase in the financial burden of health.[2]

Epidemiology

World status

The whole world, there are more people of 20-79 years with the diabetic patient in urban versus rural (279.2 million V/S 145.7 million) surroundings, and the frequency is higher in urban 10.2% versus rural 6.9% in 2017. The number of diabetic patients in urban areas is supposed to elevation to 472, 6 million in 2045 due to mostly global urbanization. Age-adjusted similar preponderance compares diabetes incidence is between countries and regions. The North America and Caribbean region (NAC) have the maximum age-adjusted relative prevalence 20-79 years in 2017 and 2045 (11.0% and 11.1%). The Africa region has the lowermost prevalence in 2017 and 2045 (4.2% and 4.1%), likely due to lower levels of urbanization, under-nutrition, lower stages of obesity and a large number of infectious diseases (Flu, HIV/AIDS, and Hantavirus.). The enormous numbers of diabetic patients from age 20-79 years are in China, India, and the United States in 2017.[3]

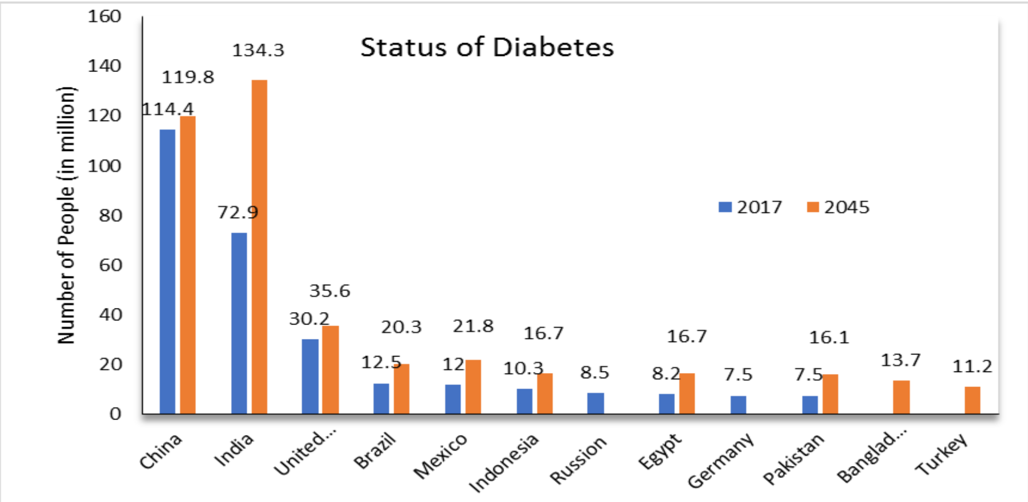


Figure 1.1: Estimated number of diabetic people in Global.

National status

India is one of the epicenters of the global DM pandemic.[2] There was over 72946400 number of diabetic people in India in 2017.[3] Indian Council of Medical Research India Diabetes Study (ICMR-INDIAB) showed the most significant number of a diabetic patient in north India among all studied districts. These numbers are projected to rise to 101.2 million by 2030. This emphasizes the sheer magnitude of the diabetes epidemic in India.[4] The diabetic population in the country is close to striking the alarming mark of 69.9 million by

2025 and 80 million by 2030. This denotes that the developing country is expected to observe a rise of 266%. The statistics recently accumulated showcase that culture of diabetes is more prevalent in the urban areas as 28% of the population stand in cities are affected, whereas 5% of the rural population are positive with hyperglycaemic. Diabetes has become the 5th leading cause of blindness across the globe. Diabetic retinopathy is one of the significant reasons for visual impairment and blindness among diabetic patients across the globe. The overall population affected by this hyperglycaemic-related disease is reported to be 382 million as per the statistics of 2013, and it is expected to cross the number of 592 million by 2025.[5] Hyperglycaemic is fast the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. In 2000, India (31.7 million) topped position in global with the most significant number of the diabetic patient followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively.[6] There were an estimated 37.76 million diabetic people in India by 2004; 21.4 million in the urban zone and 16.36 million in rural zones.[7]

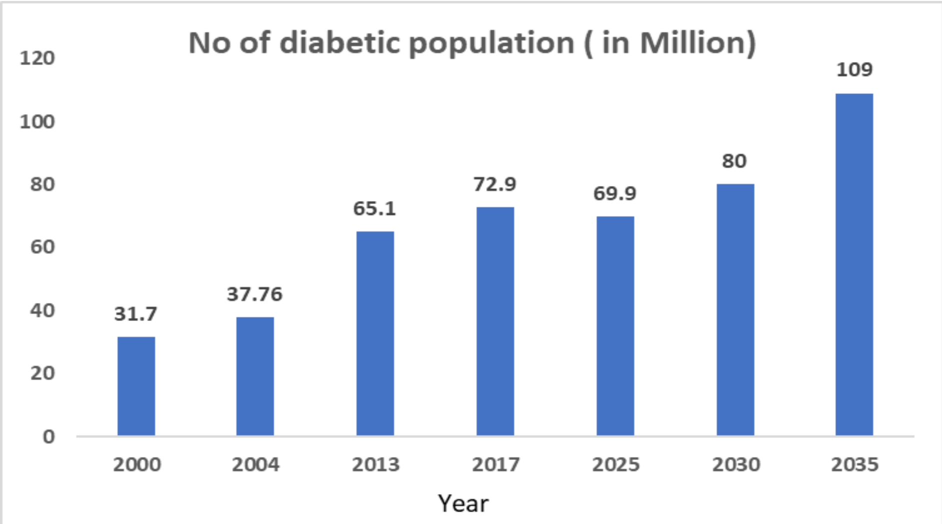


Figure 1.2: Estimated number in the diabetic subject in India.

Diabetes mellitus is degenerative endocrine disease which occurs either reduced insulin secretion, sensitivity and activity due to damage to pancreatic β-cells affecting ultimately fat, protein and carbohydrate metabolism.[18] Type 2 diabetes is the most common disease which occurred by β-cell destruction. Treatments include the following-

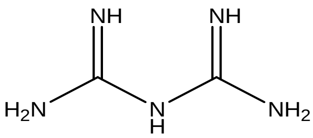
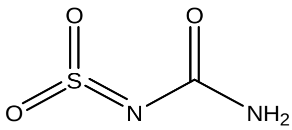
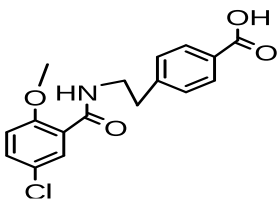
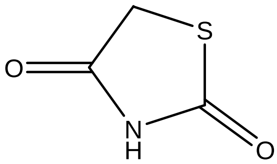
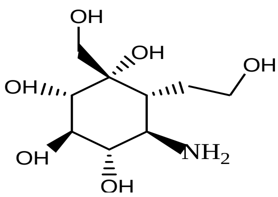
- Increase insulin secreted by pancreas with agents.
- Increase the sensitivity of target organs to insulin with agents.
- Decrease the rate at which the glucose is absorbed from GIT with agent and mostly drug administration by orally, which are effective in type 2 diabetes mellitus.[19]

Treatment of diabetes mellitus

Treatment modalities in modern medicine

Type 2 diabetes mellitus is caused by the destruction of pancreatic beta cells, and thus insulin is no longer produced in these cells, leading to hyperglycaemia, ketoacidosis and potentially death if not treated with insulin. Summarises the list of available allopathic medication for diabetes management.[10]

Allopathic medication available for diabetes management.[11]

Classification	Structure	Active ingredients	Mode of action
Biguanides	 Biguanide	Metformin, Phenformin, Buformin	The liver is Inhibit of glucose production
Sulfonylureas (2nd-generation)	 Sulfonylurea	Glimepiride, Glipizide, Glyburide	Islet of Langerhans pancreas (β-cell) Increase of insulin secretion
Meglitinides		Repaglinide, Nateglinide	Islet of Langerhans pancreas (β-cell) Increase of insulin secretion
Thiazolidinediones (TZDs)	 Thiazolidinedione	Pioglitazone, Rosiglitazone	Skeletal muscle is an increase in glucose uptake
Alpha-glucosidase inhibitors		Acarbose, Miglitol	Decreased absorption of carbohydrate in the small intestine

Treatment modalities in ayurveda

Diabetes mellitus (Madhumeha) was known to ancient Indian physicians and an elaborate description of its clinical features and management appears in *Ayurvedic* texts. *Ayurvedic* practitioners treat diabetes with a multi-pronged approach, using diet modification, Panchkarma to cleanse the system, herbal preparations, yoga and breathing exercises. The herbs which are used to treat diabetes include shilajit, turmeric, neem, coccinea indica, amalaki, triphala, bitter gourd, rose apple, leaves of bilva, cinnamon, gymnema, fenugreek, bay leaf and aloe vera. Decoctions of triphala, fenugreek and Shilajit are commonly used. Powders (Churana) used include Amalaki Churna, Haldi powder (Turmeric powder) and Naag Bhasma. The *Ayurvedic* preparations 'Vasanta Kusumakar Ras' and 'Chandraprabhavati' are believed to lower sugar levels. Proprietary *Ayurvedic* medications are also used to treat diabetes.[12]

List of medicinal plant used in traditional medicine for the treatment of diabetes.

S. no	Plants Name	Part of Plant	Extract	Model	Chemical constituents	REF No.
1	*Stevia rebaudiana*	leaves	ethanolic	alloxan-induced diabetic rats	proteins, sterols, alkaloids, tannins, glycosides, flavonoids, and saponins	[13]
2	Hybanthus enneaspermus	Whole plant	alcohalic	streptozotocin-induced diabetic rats	Phenol, flavonoid, flavonol	
3	*Glycosmis pentaphylla*	stem bark	Ethanolic	Streptozotocin – Nicotinamide Induced Diabetic Wistar Rats	carbohydrates, sterols, alkaloids, tannins, glycosides, flavonoids, phenolic compounds, and saponins	[14]
4	*Tridax procumbens*	whole plant	Ethanolic	Streptozotocin – Nicotinamide Induced Diabetic Wistar Rats	carbohydrates, proteins, sterols, alkaloids, tannins, glycosides, flavonoids, phenolic compounds, and saponins	[14]
5	*Mangifera indica*	leaves	Ethanolic	Streptozotocin – Nicotinamide Induced Diabetic Wistar	carbohydrates, proteins, sterols, flavonoids, phenolic	[14]

				Rats	compounds, and saponins	
6	*Terminalia paniculata*	Bark	Aqueous	streptozotocin-nicotinamide	tannins, glycosides, flavonoids	[15]
7	*Melia azadarach*	Twigs	Ethanol	Streptozotocin (STZ)-induced diabetic Sprague-Dawley albino rats	tannins, glycosides, flavonoids, phenolic compounds, and saponins	[16]
8	*Zanthoxylum alatum*	Leaves	Ethanol	Streptozotocin (STZ)-induced diabetic Sprague-Dawley albino rats	alkaloids, tannins, glycosides, flavonoids, and saponins	[16]
9	*Tanacetum nubigenum*	Leaves	Ethanol	Streptozotocin (STZ)-induced diabetic Sprague-Dawley albino rats	carbohydrates, proteins, sterols, alkaloids, tannins, glycosides, flavonoids, phenolic compounds, and saponins	[16]
10	*Datura stramonium* L	root	Hydromethanolic	streptozotocin (STZ)-induced diabetic mice models	phenols, flavonoids, tannins, saponins, anthraquinones, terpenoids.	[17]
11	*Sorbus decora* C.K.Schneid	bark	Ethanolic	streptozotocin	carbohydrates, proteins, sterols, alkaloids, tannins, and saponins	[18]
12	*Ocimum canum*	leaves	methanolic	streptozotocin	Alkaloids, anthraquinones, terpenoids, glycosides, and steroids.	[19]
13	*Stephani hernandifolia*	Whole plant	ethanolic and aqueous extracts	Streptozotocin-Induced-Diabetic Rats	carbohydrates, proteins, sterols, alkaloids, flavonoids, phenolic	[20]
14	*Ducrosia anethifolia* Boiss	leaves and stems	Ethanolic	Male Wister albino rats	carbohydrates, proteins, sterols, alkaloids, tannins, glycosides, flavonoids,	[21]
15	*Ajuga remota* Benth	leaves	ethanol, Aqueous	alloxan-induced diabetic mice	Alkaloids, Anthraquinones,	[22]

					Flavonoids, Saponins, Steroidal, Tannins	
16	*Momordica charantia* Linn	fruit	Aqueous	streptozotocin-induced in rats	glycosides, flavonoids, phenolic compounds,	[23]
17	Picris japonica Thunb	whole herbal plants	Aqueous	Diabetic KK-Ay Mice	phenolics, flavonoids, saponins	[23]
18	Cayratia trifolia (L.) Domin	root	ethyl acetate and ethanol	streptozotocin induced in rats	glycosides, flavonoids, phenolic compounds,	[25]
19	Mongolian Oak Cups		Ethanol	alloxan-induced rats	alkaloids, tannins, glycosides, flavonoids, phenolic compounds, and saponins	[26]
20	*Cissampelo spareira*	leaf	aqueous extract	Streptozotocine nicotinamide induced diabetic male mice	sterols, alkaloids, glycosides, flavonoids,	[27]
21	*Merremia emarginata*	Whole plant	methanol	streptozotocin induced diabetic rats	alkaloids, flavonoids,	[28]
22	Murraya koenigii (Linn.)	leaf	aqueous	Alloxan-Induced Diabetic Rats	phenolic compounds, and saponins	[29]
23	Artemisia afra	leaf	Aqueous	streptozotocin-induced diabetic rats	glycosides, flavonoids, phenolic compounds,	[30]
24	Nigella sativa and propolis	seeds	methanol	streptozotocin induced diabetic male rats	flavonoid	[31]
25	Capparis spinosa	root	hydro-alcoholic	STZ induced diabetes in Wistar rats	glycosides, flavonoids	[32]

Review of literature

Goyal kumar A. *et al.* 2017

To investigated the toxicity, anti-diabetic activity along with in vitro antioxidant activity of the leaf of *Bambusa balcooa Roxb* (*B. balcooa*) in alloxan-induced diabetic rats. A dose of *B. balcooa* aqueous extract (BAQE) at one hundred and two hundred milli gram per killo gram body weight. and compared to the standard drug glibenclamide administration orally in alloxan-induced diabetic rats. significant reduction in fasting blood glucose and glycated haemoglobin while plasma insulin level. The BAQE treated diabetic rats showed significant increase in the endogenous antioxidant enzymes superoxide dismutase, glutathione peroxidase and decrease in malondialdehyde levels. HPLC analysis of BAQE showed the presence of rut in, Gallic acid and b sitosterol. Thus, it can be inferred from this study that BAQE possess antidiabetic and in vivo antioxidant activity. The overall activity might be possibly due to the presence of potential antioxidants.[33]

Kumar M, *et. al.*, 2014

Investigated the mechanism involved behind antidiabetic activity of standardized *Houttuynia cordata* Thunb. extract in streptozotocin-induced diabetic rats. A dose of two hundred and four hundred milli gram per killo gram body weight when given orally for twenty-one days was found to significantly decrease fasting plasma glucose level and elevated levels of insulin. Moreover, the altered levels of biochemical parameters viz, blood urea, creatinine, total lipid profile, Also, the extract significantly reversed the expression patterns of various glucose homeostatic enzyme genes like GLUT-2, GLUT-4, and caspase-3 levels while regulating the mitochondrial membrane potential and the activity of succinate dehydrogenase enzyme. Therefore, extract of *H. cordata* exhibited its anti-diabetic action by upregulation of GLUT-4 and potential antioxidant activity.[34]

Ghazanfar K. *et al.*, 2014

Investigated the antidiabetic and antihyperlipidemic effects of petroleum ether, ethyl acetate, methanol, and hydroethanolic extracts of *Artemisia amygdalina*. in diabetic rats. A dose of two hundred fifty and five hundred milli gram per killo gram body weight of the hydroethanolic and methanolic extracts, significantly reduced blood glucose levels. The elevated level of the biochemical parameter like cholesterol, triglycerides, low density lipoproteins (LDL), serum creatinine, serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), and alkaline phosphatise (ALP) were found to be reduced. Moreover, histopathological study revealed the regenerative/protective effect on β-cells of pancreas.[35]

Doan H.V. *et al.*, 2018

Reported the antidiabetic activity of *Chrysophyllum cainito* L. investigated by the induction of extract (five hundred milli gram per killo gram b.w.) orally given in alloxan-induced diabetic mice and comparison was done with glibenclamide showed a significant reduced in blood glucose level. Phytochemistry and extract antioxidant capacity was investigated in in-vitro in normal and diabetic mice induced by alloxan. The hypoglycemic activity was examined in the jejunum and abdominal muscles (isolated from mice), which were used to carry out the effect of *C. cainito* extract on glucose absorption and glucose uptake assay respectively. Finally, the activity of α-glucosidase was evaluated in the in-vitro method. Strong antioxidant activity was possessed by extract of *C. cainito* comparable to the butylated hydroxytoluene and ascorbic acid. Significantly, the area under the curve of blood glucose level was reduced by extract at five hundred milli gram per killo gram body weight. by OGTT in normal mice after six hours of administration. A single dose of the extract was responsible for a decrease in fasting blood glucose level in alloxan-induced diabetic mice model. The extract did not inhibit glucose absorption during isolated jejunum. In the presence of insulin at a dose of fifty micro gram per milli liter, the amount of glucose uptake increased significantly by abdominal muscles. The activity of α-glucosidase (IC50 = 1.20 ± 0.09 micro gram per milli liter) was inhibited than acarbose (IC50 = 198.17 ± 4.74 micro gram per milli liter). The α-glucosidase inhibitory effect, glucose uptake stimulation and possible modes of action of *C. cainito* stem bark together with direct evidence the antidiabetic activity were reported for the first time herein.[36]

Pandhare B. R. *et al.*, 2011

Evaluated the antidiabetic activity of the aqueous leaves extract *of Sesbania sesban* (L) Merr in streptozotocin-induced diabetic rats. A dose (two hundred fifty milli gram per killo gram and five hundred milli gram per killo gram body weight) of aqueous leaves extract administered orally in streptozotocin-induced diabetic rats for thirty days. A reduction in fasting blood glucose level and serum insulin level was found. Moreover, biochemical parameters were evaluated and compared with glibenclamide (anti-diabetic drug). Significantly, serum insulin, HDL levels, liver glycogen and body weight increase and reduced in level of blood glucose, serum triglycerides, glycosylated hemoglobin and total cholesterol.[37]

Nabeel MA. *et al.*, 2010

Reported the antidiabetic activity of the *mangrove species Ceriops decandra* by orally administered dose (thirty, sixty, one hundred twenty milli gram per killo gram body weight) in alloxan-induced diabetic rats for thirty days. Blood glucose level, Hb, HbA1c, liver glycogen, and some carbohydrate metabolic enzymes significantly evaluated.[38]

Sabitha V. *et al.*, 2011

Evaluated the antidiabetic and hypolipidemic activity of *Abelmoschus esculentus* peel and seed powder in streptozotocin-induced (sixty milli gram per killo gram)- diabetic rats. Administration of AEPP and AESP at one hundred and two hundred milli gram per killo gram dose in diabetic rats for time period 28 day. significant increase in body weight, and reduction in blood glucose level (p<0.001) than diabetic control rats. A significant (p<0.001) increased level of Hb, TP, and decreased level of HbA1c, SGPT were observed after the treatment of both doses of AEPP and AESP. Also, elevated lipid profile levels returned to near normal in diabetic rats.[39]

CONCLUSION

After the study many review article and research paper we found that there are many plants and synthetic hypoglycaemic drugs. which have a medicinal value in the antidiabetic activity in their different pharmaceutical preparation.

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