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Mini Review

Antidiabetic Agents

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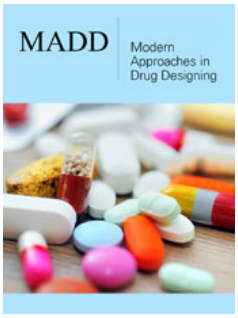

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Abstract

Diabetes mellitus is a chronic metabolic disorder that is of worldwide concern. It results in several complications such as high blood pressure, neuropathy, glaucoma, kidney damage and feet ulcers. There are principally two types of diabetes that affect humans: Type 1 and Type 2. Several drugs have developed over the years to combat or controlled diabetes. However, the side effects that they produced, along with the cost of synthesis and environmental issues, there is a need to resort to plant based anti-diabetic agents. Research have been increasing in this direction. Plant based anti-diabetic agents are superior because they are cheaper and environmentally safe. However, if they are to replace synthetic analogues, their anti-diabetic potency must be comparable to synthetic analogue such as metformin and glibenclamide.

Introduction

Diabetes mellitus is a chronic metabolic disorder of the endocrine system [1]. It's referred to as the sweetness like honey (mellitus) of the urine of diabetic people [2]. It's characterized by the presence of glucose in the urine and is caused by a deficiency in the production of insulin or the inability of insulin to act or by insulin resistance [3]. Insulin resistance arises as a consequence of obesity, a sedentary life and aging, resulting in hyperglycemia and diabetes. Insulin is produced by the β-cells of the pancreas and is necessary to transport glucose to the cells where it can be used or it stimulate receptors on the cells, so that each cell can assimilate glucose. Glucose is necessary for the normal functioning of cells. It provides us with energy. It's known in many parts of the world and is on the increase because of the change in the lifestyle of the people [4]. Diabetes is the source of many complications such as high blood pressure, neuropathy, glaucoma, kidney damage, feet ulcers etc. There are two main types of diabetes mellitus: Type 1 and Type 2. Type 1 diabetes results when the body produce little or no insulin. This results from an auto-immune disorder, whereby the immune system considers the pancreas as foreign and so destroy it. In Type 2 DM, the body produces insulin. However, it's not produced in sufficient amount to transport glucose molecules to the receptor of cells i.e there is impaired secretion of insulin. It can also result from both peripheral insulin resistance and impaired insulin secretion. Antidiabetic agents are those that produce a hypoglycemic effect and restore the blood glucose level to its normal level. However, such agents must be carefully administered to prevent overdosage that can result in coma etc. These agents include Insulin Lispro, sulfonylureas, biguanides, α-glucosidase inhibitors, aldose reductase inhibitors, glinides [1] etc. Aldose reductase is a key enzyme in the polyol pathway that catalyse the reduction of glucose to sorbitol. The latter doesn't diffuse readily across cell membranes. Intracellular accumulation of Sorbitol has been implicated in the chronic complications of diabetes, such as peripheral neuropathy, retinopathy and cataracts [5]. Synthetic antidiabetic agents have side effects which are usually non-reversible [1]. Thus, there is a need to use safer anti-diabetic agents. There must be a paradigm shift in the class of anti-diabetic agents used. One such class is plant-based antidiabetic agents or green

antidiabetic agents or Complementary Alternative Medicine (CAM). These are found in sustainable abundance and are environmentally safe. It's the Natural Products in the plants, acting singly or in combination that is responsible for the anti-diabetic effect.

Mechanism of action

The mechanism of several classes of anti-diabetic agents are known, whereas those of medicinal plants have been investigated. For example, the Thiazolidinediones, such as Troglitazone, the first thiazolidinedione introduced increase target tissue sensitivity to insulin. They increase glucose uptake in muscle and adipose tissue and inhibits hepatic gluconeogenesis. a-Glucosidase inhibitors such as Acarbose and Miglitol are carbohydrates in nature that act within the intestine to inhibit the enzyme, a-glucosidase to prevent the conversion of complex starches, oligosaccharides and disaccharides to the monosaccharides that can be transported in the bloodstream. Biguanides, such as Metformin act via reduced hepatic gluconeogenesis, stimulation of glycolysis in peripheral tissues, reduction of glucose absorption from the GI tract and reduction of plasma glucagon levels [6]. Figure 1 shows a list of synthetic anti-diabetic drugs.

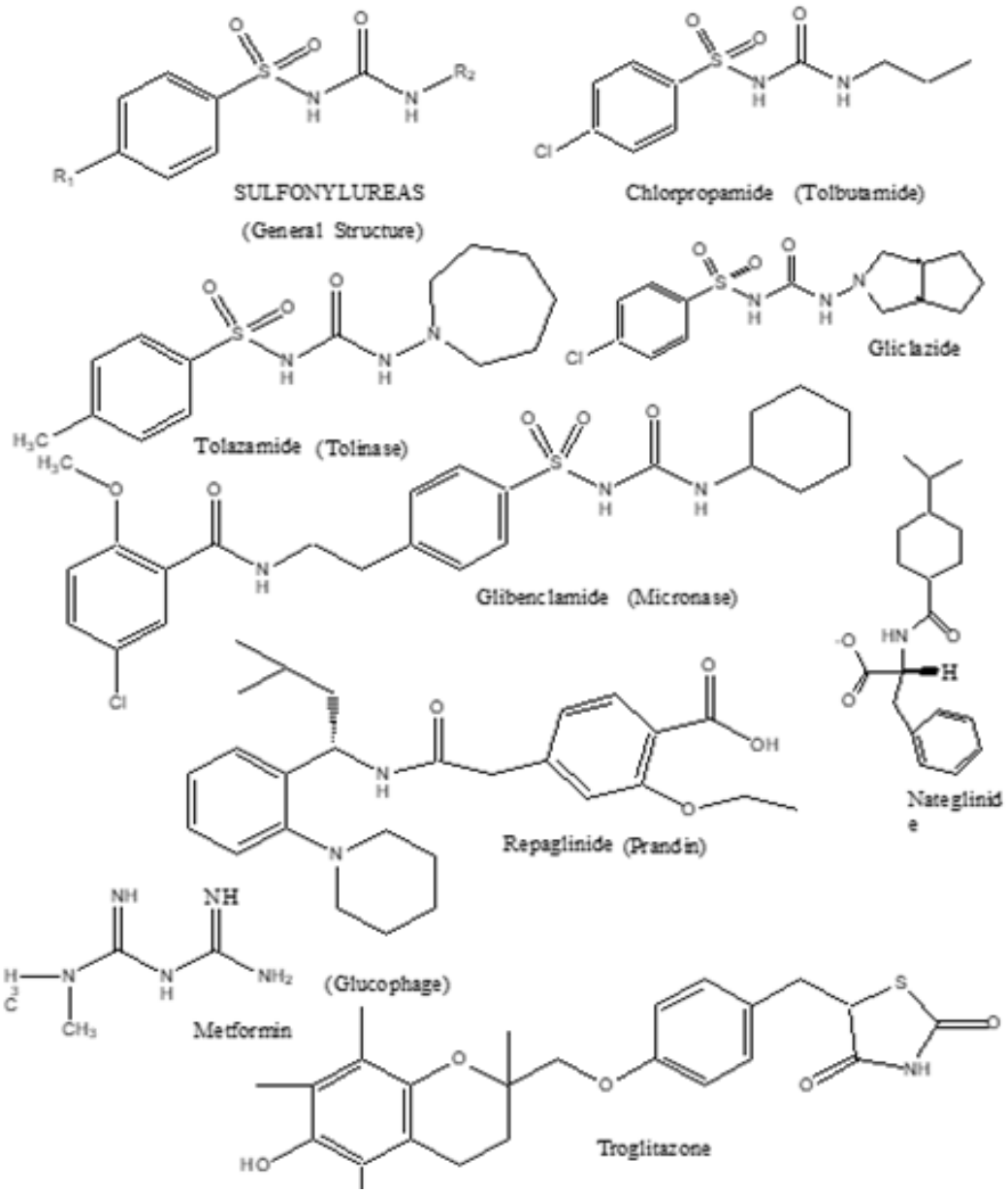

Figure 1: List of synthetic anti-diabetic drugs.

Literature Review

There has been an increasing number of articles on the study of plant extracts as anti-diabetic agents. An article reviewing medicinal plants that have shown experimental or clinical antidiabetic activity has been reported [1]. Other reviews on the chemistry of medicinal plants with anti-diabetic potential have been noted [7].

Anti-diabetic activity of the aqueous extract of Emblica officinalis seeds in animal models' study has been reported [4]. The animals were made anti-diabetic via the use of Streptozotocin (STZ) induced type 2 diabetes. STZ selectively destroys the b-cells of the pancreas, resulting in hyperglycemia in animal models. Standardized doses of 100, 200, 300 and 400mgkg-1 body weight of the extract were administered orally to normal and diabetic rats to assess their hypoglycemic effect. It was found that a dose of 300mgkg-1 of the aqueous extract produced a maximum fall of 41.6% ($p<0.01$) in the blood glucose level as compared with 27.3% ($p<0.01$) in the blood glucose level of normal rats. The anti-diabetic potential of the petroleum ether, methanol and aqueous extracts of Terminalia catappa Linn (Combretaceae) fruit on fasting blood sugar levels of alloxan-induced diabetic rats was investigated. All three extracts produced a hypoglycemic effect at dose levels 1/5 of their lethal doses. Histological studies revealed regeneration of the pancreas by the methanolic and aqueous extracts [3]. It was noted that the ethanolic extract of Nymphaea stellata induced a hypoglycemic state in alloxan induced diabetic rats. The ethanolic extract was given as a dose of 100 and 200mg/kg/day. A corresponding reduction in blood glucose sugar by 31.6 and 42.6% was noticeable [8]. Another article reports the antidiabetic activities of aqueous leaves extract of Leontes leonurus in Streptozotocin induced diabetic rats for a period of 15 days. The induced diabetic rats exhibited high blood glucose level, cholesterol, High Density Lipoprotein (HDL) and triglycerides. The continuous oral administration of the extract at a dose of 125, 250 and 500mg/kg over the 15 days period lowered the blood glucose level, HDL feed and water intake, whilst that of LDL increased. Thus, the aqueous extract of L. leonurus possesses antihyperglycemic and anti-lipidemic potential [9].

Plants as antidiabetic agents

Table 1 shows the list of some plants being used as anti-diabetic agents.

Table 1: List of Plants used as anti-diabetic agents.

Plants	Common Name
Gentiana olivieri griseb	Chinese: xie wan que qin jiao
Bauhinia forficate koeingii (*Leguminosae*)	Purple Camel's foot
Eugenia jambolana L. (*Myrtaceae*)	Java plum
Lactuca indica L	Indian lettuce
Mucuna pruriens	Velvet bean
Tinospora cordifolia W	heart-leaved moonseed
Momordica charantia L. (*Cucurbitaceae*)	Bitter melon, bitter gourd
Aporosa lindleyana Baill (*Euphorbiaceae*)	Salle Mara
Terminalia pallida (*Combretaceae*)	Button wood

Conclusion

Diabetes mellitus is a chronic metabolic disorder that is increasing worldwide. It's the source of several complications and thus there is a need to use anti-diabetic agents such as glibenclamide and metformin. However, due to the side effects of the synthetic analogues and environmental safety, there is a need to use a Complementary Alternative Medicine (CAM) in plant based anti-diabetic agents. The potency of these plant based anti-diabetic agents should be comparable with that of the synthetic analogues.

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