Herbal Drugs for Diabetic Treatment: An Updated Review of Patents

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Abstract: Diabetes mellitus is the most common endocrine disorder, affecting 16 million individuals in the United States and 200 million worldwide. Despite the use of advanced synthetic drugs for the treatment, use of herbal remedies is gaining higher importance because of synthetic drugs have drawbacks and limitations. The herbal drugs with antidiabetic activity are extensively formulated commercially because of easy availability, affordability and less side effects as compared to the synthetic antidiabetic drugs. Antidiabetic herbal formulations (AHF) are considered to be more effective for the management of diabetes. There are around 600 herbal drug manufacturers in India of which almost all manufacturers are developing AHF in addition to others. Till date, no article is published to give detailed information of the patents on AHF. Thus, this review article undertake the attempt for providing updated information on the type of diabetes and patented AHF which will enhance the existing knowledge of the researchers.

Keywords: Anti-diabetic herals, diabetes, neutraceuticals, Phytopharmaceutical agents.

INTRODUCTION

WHO defined Diabetes mellitus as “a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both” [1]. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs including kidney, nerves, heart and gastrointestinal tract. It is the most common endocrine disorder worldwide with an incidence varying between 1 to 8% [2]. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025 [3]. Diabetes is classified into two major categories i.e., insulin dependent diabetes (Type-1) and non-insulin dependent diabetes (Type-2 diabetes). Despite the advancement in the synthetic anti-diabetic drugs in the recent past, diabetes is still remarkably not cured successfully. Treatment of diabetes is complicated due to the lack of drugs with safety and efficacy, and are incapable of sustained clinical, biochemical, and histological cure. On the contrary the herbal drugs have gained wider importance worldwide, mostly due to higher safety, lesser number of adverse effects and consistent blood glucose lowering capacity. In the developed countries, the use of herbal medicine for the sufferers of diabetes is encouraged by the concern about the adverse effects and cost associated with chronic use of synthetic drug. There are wide range of phytoconstituents useful in the treatment of diabetes. These include alkaloids, glycosides, peptidoglycan, hypoglycan, steroids, guanidine, glycopeptides, terpenoids, amino acids and inorganic ions. According to ethno botanical survey, there are about 800 plants which possesses antidiabetic potential [4]. Among the type-2 diabetic patients, 25% uses herbal drugs, while 75% still rely on synthetic modern drugs. However, 10% of type-1 diabetic patients frequently use medicinal plants, in addition to insulin treatment [5].

Antidiabetic herbal formulations (AHF) are considered to be more effective for the management of diabetes [6] as compared to single herbs. There are around 6000 herbal drug manufacturers in India. Till date, no article is published to give detailed information on the patented AHF. The present review gives an exhaustive account to update on the several types of diabetes and patented AHF to upgrade the existing knowledge on the prior art.

DIABETES AND ITS TYPES

Classification of diabetes into type-1 or 2 based on the clinical presentation may be difficult [7]. Diagnosis of the main forms of diabetes depends on clinical judgment based mainly on the age of the subject and the severity of insulin deficiency at presentation, as well as the presence or absence of features of the metabolic syndrome [8]. As per WHO classification in 1998, an etiological classification was chosen to subgroup diabetes mellitus into different types. [9]

TYPE-1 DIABETES MELLITUS

Insulin-dependent diabetes (IDDM; Type I diabetes) is one of the most serious metabolic disorders, affecting approximately 1 person in 300 in the U.S., while epidemiological studies in Europe suggested that the incidence are in-
creasing [10, 11]. Type-1 diabetes occurs due to permanent (95%) destructions of β-cells of islets of Langerhans present in the pancreas, by an autoimmune process, or other unknown causes leading to absolute insulin deficiency. An individual with Type-1 process may be metabolically normal before the disease is clinically manifest, but the process of β-cell destruction can be detected. On the basis of etiology it is further classified as Immune Mediated and Idiopathic one.

**IMMUNE MEDIATED DIABETES**

This form of diabetes is the results of a cell-mediated autoimmune destruction of the β-cells in the pancreas. It is characterized by the presence of Anti-glutamic acid decarboxylase (Anti-GAD) antibodies, islet cell or insulin antibodies without processes that lead to β-cell destruction [12]. Thus, this category of type-1 diabetes can be identified if appropriate antibody determinations are performed [13]. Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others have modest fasting hyperglycemia that can rapidly change to severe hyperglycemia or ketoacidosis in the presence of infection or other stress. Still others, particularly adults may retain residual β-cell functions sufficient to prevent ketoacidosis for many years. Many such individuals with this form of type-1 diabetes eventually require insulin for survival.

**IDIOPATHIC DIABETES**

In some subjects with type-1 diabetes, particularly non-Caucasians, no evidence of an autoimmune disorder is demonstrable and these are classified as idiopathic type-1. Only a minority of patients with type-1 diabetes fall into this category and showed clinical symptom of episodic ketoacidosis with varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited and it is not associated with HLA.

**TYPE-2 DIABETES MELLITUS**

The most common type of diabetes mellitus constituting about 90% of diabetic population and often associated with a family history of diabetes, older age, obesity and lack of exercise [14]. It is characterized by disorders of insulin action and insulin secretion, either of the two which may be the predominant feature. Both are usually present at the time when this form of diabetes is clinically manifested. The specific reasons for the development of these abnormalities are not yet known [13]. Ketoacidosis is very rare in type 2 diabetes and does not require insulin therapy. The insulin resistance occurs in this type is partly explained by the obesity that often coexists with the disease.

**GESTATIONAL DIABETES MELLITUS (GDM)**

Gestational diabetes is a state of carbohydrate intolerance resulting in hyperglycaemia of variable severity, with onset or first recognition during pregnancy. It does not exclude the possibility that the glucose intolerance may leads to pregnancy but has previously gone unrecognized. The definition applies irrespective of whether or not insulin is used for treatment or whether the condition persists after pregnancy.

**OTHER SPECIFIC TYPE OF DIABETES**

Many other form of diabetes are associated with mono- genetic defects in β-cell function and characterized by onset of hyperglycaemia at an early age called as maturity-onset diabetes of the young (MODY) further, it also showed impaired insulin secretion with minimal or no defects in insulin action. [15-17]

Other specific types are currently less common causes of diabetes mellitus, but the conditions in which the underlying defect or disease process can be identified in a relatively specific manner, this include

- Genetic defects in insulin action, such as leprechaunism
- Diseases of the exocrine pancreas, such as cancer of the pancreas, cystic fibrosis and fibrocalculous pancreatopathy (a form of diabetes, which was formerly classified as one type of malnutrition-related diabetes mellitus)
- Endocrinopathies, such as cushing syndrome, acromegaly and phaeochromocytoma
- Drugs or chemicals, such as steroids and thiazides
- Infections, such as rubella
- Uncommon forms of immune-related diabetes, such as the type associated with as Klinefelter
- Other rare genetic syndromes associated with diabetes, such as Down syndrome.

**PHYTOCONSTITUENTS IN THE TREATMENT OF DIABETES MELLITUS**

Many phytoconstituents isolated from plants including the compounds belongs to the class of alkaloids, glycosides, terpenoids, flavonoids are constituted as vital elements to combat diabetes mellitus. However, the use of single phytoconstituents in the treatment of diabetes is quite ineffective. Examples of some of the important phytoconstituents are described in the prior art of patent literatures. These includes traditional Indian medicinal plants and modern herbs like Gymnema sylvestre, Momordica charantia, Syzygium cumini, Pterocarpus marsupium, Trigonella foenum-graceum, Cinnamomum tamala, Withania somnifera, Coccinia indica, Pueraria tuberosa, Asparagus racemosus, Boerhaavia diffusa, Aegel marmelos, Piper longum, Chlorophytum tuberosum, Curcuma longa, Lagerstroemia speciosa and Elettaria.
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cardamomum have been satisfactorily explored for their anti-diabetic activity. Several mechanisms are proposed for explaining the anti-diabetic activity of these phytoconstituents including GLP-4 inhibitor, DPP-4 inhibitors, stimulation of glucose metabolism through peripheral gluconeogenesis, and sequestration of Ca\(^{2+}\) ions from the membrane of the \(\beta\)-cells [18, 19]. An account on several patented literature instances on various types of anti-diabetic herbal formulations are depicted in the Table 1 [18-69].

**ANTI-DIABETIC HERBAL FORMULATIONS (AHF) WITH MULTIPLE PHYTOCONSTITUENTS**

Instead of using single phytoconstituents for the treatment of diabetes, the herbal formulations containing multiple phytoconstituents are found to be more effective under several clinical studies for reducing blood glucose level. The several compositions of AHF are mentioned provides variable pharmacological action for treatment of diabetes [70]. The multiple combinations of phytoconstituents provide synergistic action. In a US patent 7014872, Pushpangadan and Prakash described AHF containing *Piper longum* fruit powder, *Curcuma longa* rhizome powder, *Chlorophyllum tuberosum* and *Elettaria cardamomum* [71].

**ANTI-DIABETIC NUTRACEUTICAL FORMULATIONS (ANF)**

These include formulations containing a mixture of herbal extracts, constituents from animal and mineral origin to provide synergistic anti-diabetic action. In a US Patent 7153528, Malleshi *et al.* (2006) described nutraceutical formulation containing soy, fenugreek seed powder, cereals, milk, edible oil, mineral premix, Spice mix, *Garcinia cambogia* etc with enhanced blood glucose lowering action against Type-2 diabetes [72]. Similarly, Massoud described in a European patent about the anti-diabetic herbal formulation containing *Centaurii herba*, *Teraxaci radix*, *Urticae herba*, *Cichorii radix*, *Morus nigra* [73].

**MARKETED ANTI-DIABETIC HERBAL PREPARATIONS**

Several anti-herbal formulations are currently being marketed in India and Internationally are represented in Table 2.

**CONCLUSION**

At present the prevalence of Diabetes mellitus has reached 16 million individuals in the United States and 200 million worldwide. Despite of the advancement in drug discovery to synthesize drug, use of herbal remedies are continue because of the existing synthetic drugs have several limitations and side effects. The easy availability, affordability and fewer side effects of herbal drugs with anti-diabetic activity are extensively formulated commercially compared to the synthetic drugs. The researches for the herbal drugs are still in the infancy. One can look at the future of integrated medicine and hope that research in alternative medi-
cine will help identify what is safe and effective rather than marginalizing, unorthodox medical claims and findings. The use of traditional/lay remedies in the sample, far from indicating fatalism or non-compliance with modern medicine. Illustrates an effort on the part of the patient to co-opt therapies that are considered efficacious in maintaining good health. Hence, the use of local therapies and their effectiveness warrants further examination.

CURRENT & FUTURE DEVELOPMENTS

Despite of the several anti-diabetic herbal and nutraceuticals formulations for diabetes treatment, the research has taken a drag towards preparing anti-diabetic herbal formulations using novel drug delivery systems for effective treatment of diabetes mellitus. Looking into the score of patent and literature it has been conceived that the area of anti-diabetic treatment by herbal drugs is exploring successfully at a greater pace. This leads to many of the herbal formulation being marketed domestically as well as internationally.

CONFLICT OF INTEREST

Authors have no conflict of interest.

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Herbal Drugs for Diabetic Cure


