Chapter 6
Medicinal Plants for the Treatment of Type 2 Diabetes

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ABSTRACT

Type 2 diabetes (T2D) is a metabolic disorder related to persistent hyperglycemia. It is characterized by lack of secretion and activity of insulin, which causes chronic complications including cardiovascular and renal diseases, high blood pressure, and infections. Medicinal plants offer many therapeutic agents to improve the symptoms and prevent the progression of T2D. Treatment with present synthetic drugs leading to several adverse effects stimulates further search into natural products in order to find effective anti-diabetic candidates. This chapter reviews molecular targets of T2D treatment as well as medicinal plants and their bioactive compounds that were searched from Medline, Google Scholar, PubMed database, or other bibliographic reviews of relevant articles. The authors hope that this review will contribute to develop further investigations into potential alternatives against T2D.

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INTRODUCTION

Diabetes mellitus, a chronic state of metabolic diseases, is caused by deficiency of insulin secretion and insulin activity. There are three principal types of the disease: type 1, type 2 and gestational, among them, type 2 diabetes or non-insulin dependent diabetes is the most prevalent form in the population of the world (Jin et al., 2019). The prevalence of this pathology has significantly increased from 285 million (9.3%) in 2019 to 578 million (10.2%) in 2030 and 700 million (10.9%) in 2045 (Federation, 2019). Although the main risk factors for T2D are obesity, age, family history, hypercaloric diets and inactive lifestyle, the influence of this disease on non-obese and physically active people is important in further researches concentrated on the onset mechanism (Ferhati et al., 2019). The stable levels of glucose are maintained by a complicated mechanism containing hepatic glycogenlysis and gluconeogenesis. After a meal, pancreatic β-cells secrete insulin preventing hepatic glucose output and stimulating the glucose absorption into peripheral tissues (Alvim et al., 2015). The World Health Organization has suggested that the oral glucose tolerance test (OGTT) is designed for the diagnostic criteria of diabetes with fasting glucose 7.0 mmol/L or more. In addition, the expert committee of the American Diabetes Association recommended a cut-point for the diagnostic criteria at 6.5% or more of HbA1c level (Forouhi & Wareham, 2010). The aim of therapeutic options is to maintain blood glucose levels of patients close to physiological range and to prevent serious symptoms as well as late complications in long term. Antidiabetic therapy currently contains oral drugs reducing hyperglycaemia and exogenous insulin injection as a last method (Ferhati et al., 2019). This review article will focus on the mechanism of T2D with some potential therapeutic targets. We also summarize natural products as antidiabetic agents and their mechanisms of action for the treatment of T2D.

Molecular Mechanisms of the Type 2 Diabetes Treatment

AMP-Activated Protein Kinase (AMPK)

The AMPK heterotrimeric complex contains an α-catalytic subunit with β and γ-regulatory subunits. Twelve different AMPK molecules are composed by four isoforms of α and β subunits (α_1, α_2, β_1,β_2) and three isoforms of γ subunit (γ_1, γ_2, γ_3) (Alvim et al., 2015). Recent studies showed an important role of AMPK in glucose uptake with non-depend insulin in muscle cells. After the skeletal muscles contract, the glucose uptake is prompted by increasing AMP/ATP ratio and decreasing creatine/phosphocreatine ratio. The levels of AMP increase significantly leading to AMPK activation via residual threonine phosphorylation (Thr^{172}) in the α-subunit by LKBI