Chapter-34

Isolation of Alkaloids from Medicinal Plants and Its Antidiabetic Activities

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Abstract

Recent epidemiological data suggest that diabetes mellitus is the most prevalent endocrine disorder. This metabolic condition affects a significant proportion of the global population and is currently ranked as the fifth leading cause of death worldwide. The prevalence of diabetes mellitus is increasing. In the United States, over 10% of the population is affected by this condition. Traditional medicine holds promise in the treatment of diabetes mellitus, with phytochemicals being considered a safer alternative to synthetic drugs due to their lack of side effects. Alkaloids, a major class of natural products, and their derivatives have been extensively utilized as sources of pharmacological agents for various medical conditions. Numerous studies have emphasized the effectiveness of alkaloids in managing diabetes, with several alkaloids isolated from medicinal plants exhibiting activity against the disease. A comprehensive

analysis of alkaloids with antidiabetic properties and their target enzymes has been conducted to further explore the potential of alkaloids as antidiabetic agents. Future research endeavors should focus on conducting robust clinical trials on alkaloids, their formulation, and relevant drug targets.

Keywords: Epidemiological Data, Alkaloids. Diabetes, Antidiabetic Agents.

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1. INTRODUCTION

Diabetes mellitus encompasses a range of conditions characterized by disrupted glucose regulation leading to high blood sugar levels. The manifestations of this condition vary, with some individuals showing no symptoms of glucose intolerance, while others experience sudden diabetic ketoacidosis, and some develop long-term complications like nephropathy, neuropathy, retinopathy, or accelerated atherosclerosis [1]. It is a prevalent chronic ailment, affecting 5-10% of adults in the Western world. The global prevalence of diabetes differs across populations, with certain groups such as some American Indian tribes, Micronesians, and Polynesians having notably high rates of the disease [2]. The incidence of diabetes is on the rise, with projections indicating a more than 50% increase in global prevalence between 2000 and 2030 [3].

Diabetes mellitus is not a singular disease but rather a genetically diverse group of disorders that all involve glucose intolerance. Understanding genetic heterogeneity, where different genetic or environmental factors can lead to similar outcomes, has significantly influenced the genetic study of this common condition [4,5]. Unlike specific diagnostic terms, diabetes, and glucose intolerance generally describe symptoms and laboratory findings that can stem from various causes.

Types of Diabetes Mellitus

Two primary types of diabetes mellitus are recognized, known as type I and II (Holt, 2004). Type I diabetes is characterized by the autoimmune destruction of pancreatic insulin-producing β-cells, resulting in reduced insulin levels in the body for proper metabolism. Individuals with type I diabetes are at a higher risk of developing ketoacidosis [6]. This type of diabetes typically manifests at an early age, usually before the age of 40, although it can occur at any stage of life. Patients with type I diabetes rely on hypoglycemic medications for their survival [7]. Type I diabetes accounts for approximately 5-10% of all diabetes cases and its prevalence is on the rise globally. On the other

hand, type II diabetes is the most common form of diabetes, caused by impaired insulin secretion by the pancreatic β-cells. The inheritance of type II diabetes is associated with the human leukocyte antigen (HLA) complex [8].

Compared to synthetic drugs, phytochemicals are often considered to be safer with fewer side effects. Despite the availability of various oral hypoglycemic drugs and insulin, there is a growing interest in herbal medicine due to its cost-effectiveness and lower toxicity compared to synthetic medications [9]. According to reports from the World Health Organization (WHO), approximately 80% of the global population uses herbal medicines for treating various ailments. Out of an estimated 400,000 plant species, only 6% have been studied, and 15% have been analyzed for phytochemical properties. A systematic approach is required to evaluate the phytopharmacology of herbal medicines [10]. The Plant Kingdom serves as a vast source of bioactive compounds that can be beneficial in treating various challenging disorders. Several natural compounds such as alkaloids, terpenoids, flavonoids, glycosides, polysaccharides, and saponins derived from medicinal plants have shown promising effects against diabetes [11]. In 2016, the US Food and Drug Administration (FDA) approved 39 new drugs, including 33 organic molecules and 6 biological drugs [12]. Among the 33 small organic molecules, at least 16 were alkaloids or structurally related compounds, highlighting the significance of alkaloids in drug development.

Alkaloids with Antidiabetic Activities

Alkaloids are a group of low-molecular-weight chemical compounds containing nitrogen in the form of primary, secondary, or tertiary amines. They are found in bacteria, fungi, plants, and animals, but their distribution within each kingdom is limited [13]. Alkaloids can exist as monomers, dimers, trimers, or tetramers, which can be either homo-oligomers or hetero-oligomers. They are categorized based on their chemical structure (heterocyclic/nonheterocyclic) and their biological or natural origin (specific sources). Approximately 20% of plant species are known to produce these secondary metabolites, which have significant bioactivities and serve as a valuable resource for drug discovery [14]. Over 12,000 alkaloids have been identified from plants, each with varying pharmaceutical importance [15].

Antidiabetic Mechanism of Action of Alkaloids

Antidiabetic alkaloids play a crucial role in combating hyperglycemia by enhancing glucose consumption and glycogen synthesis [16]. Phyto-drugs regulate metabolism by either inhibiting or inducing various molecules such as AMP-activated protein kinase (AMPK), Glucose transporter 4 (GLUT4),

glycogen synthase kinase-3 (GSK3), sterol regulatory element-binding proteins 1 (SREBP1), glucokinase (GK), glucose-6-phosphatase (G6Pase), acetyl-CoA carboxylase (ACC), peroxisome proliferator-activated receptor (PPAR), and protein tyrosine phosphatase 1B (PTP1B) expression to stimulate insulin [17]. Limited studies have explored the structure-activity relationship of alkaloids with antidiabetic properties. Derivatives of tetrahydropalmatine with nitrogen and various hydroxyl groups were synthesized and their inhibitory activity against the maltase-glucoamylase (MGAM) enzyme was investigated [18]. The study indicated that the permanent positive charge and hydroxyl groups are key features of alkaloids with MGAM inhibitory activity. Additionally, research has shown that the presence of a dioxymethylene group in protoberberine-type alkaloids is associated with rat lens aldose reductase (RLAR) and human recombinant aldose reductase (HRAR) inhibitory activities. Notably, the dioxymethylene group in the D ring appears to play a more significant role in aldose reductase inhibitory activity [19]. Furthermore, an alkaloid-rich extract from Capparis decidua led to a notable alteration in the activity of hepatic hexokinase, specifically glucokinase, and glucose-6-phosphatase, in treated animals compared to the control group. This effect corresponded with changes in hepatic hexokinase type IV expression levels, glucose-6-phosphatase, and phosphoenol pyruvate carboxykinase, enzymes crucial for glucose regulation and glycogen synthesis [20].

2. CONCLUSION

Different alkaloids have been extensively studied and are widely found in various plants. They are considered secondary metabolites and have gained significant attention due to their pharmacological properties. Among these properties, some alkaloids have been discovered to possess antidiabetic activities. However, further research is required to fully explore and utilize their potential in the treatment of diabetes. In this review, we have compiled information on various alkaloids that have been reported in the literature for their anti-diabetic effects. This comprehensive analysis aims to contribute to the advancement of research in addressing this crucial metabolic disorder.

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