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Overview of Bioactive Compounds in Herbs and Their Anti-Diabetic Properties

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ABSTRACT

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia, resulting from defects in insulin secretion, action, or both. The global rise in diabetes prevalence has led to an increasing demand for alternative and complementary treatment options, as conventional therapies often have limitations, including side effects and long-term sustainability issues. Herbal medicine, with its rich history of usage across various traditional healing systems, has gained significant attention as a promising therapeutic approach for managing diabetes. Numerous herbs contain bioactive compounds that demonstrate anti-diabetic properties, offering a natural alternative to pharmaceutical interventions. These bioactive compounds function through various mechanisms, such as improving insulin sensitivity, promoting insulin secretion from pancreatic beta cells, and reducing hepatic glucose production. Additionally, certain herbs possess antioxidant and anti-inflammatory properties, which help protect against the oxidative stress and inflammation associated with diabetic complications, including neuropathy, nephropathy, and retinopathy. Moreover, some herbs regulate the absorption of glucose from the gastrointestinal tract, thereby reducing postprandial blood glucose spikes. This review aims to explore the diverse range of bioactive compounds found in herbs, highlight their anti-diabetic effects, and discuss their potential therapeutic value in diabetes management, providing a more comprehensive understanding of their role in modern diabetes care. Keywords: Diabetes mellitus, Bioactive compounds, Herbal medicine, Insulin sensitivity, Antioxidant, Hypoglycemic properties

INTRODUCTION

Diabetes mellitus, particularly type 2 diabetes (T2DM), is one of the most prevalent chronic diseases worldwide, posing a significant burden on public health, economics, and society $\lceil 1 \rceil$. The increasing global incidence of diabetes, particularly in low- and middle-income countries, is attributed to factors such as urbanization, poor dietary habits, sedentary lifestyles, and an aging population [2]. While conventional treatments, such as insulin therapy, oral hypoglycemic agents, and lifestyle modifications, remain the mainstay for managing T2DM, they often come with limitations, including side effects, longterm dependency, and insufficient effectiveness in preventing diabetes-related complications [3]. Consequently, there is growing interest in exploring alternative or adjunctive therapies to manage diabetes, with herbal medicine gaining widespread attention [4] Herbal remedies have been utilized for centuries in traditional medicine systems, including Ayurvedic, Traditional Chinese Medicine, and Native American healing practices, for the treatment of various ailments, including diabetes [5]. Over the years, scientific studies have begun to validate the anti-diabetic properties of many commonly used herbs, as they contain bioactive compounds with therapeutic effects [6]. These compounds exert their anti-diabetic effects through various mechanisms, such as enhancing insulin secretion from pancreatic beta cells, improving insulin sensitivity in peripheral tissues, and reducing the absorption of glucose from the intestines [7]. Additionally, many herbs possess potent antioxidant and anti-inflammatory effects, which help mitigate the oxidative stress and chronic inflammation that contribute to the development of diabetic complications, including nephropathy, neuropathy, and retinopathy [8].

The bioactive compounds found in herbs, such as alkaloids, flavonoids, terpenoids, and phenolic acids, have been shown to play a crucial role in regulating blood glucose levels, reducing insulin resistance, and improving overall metabolic health [9]. This review explores the bioactive compounds present in

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commonly used herbs and examines their potential therapeutic benefits in the management of diabetes, offering new insights into the growing role of herbal medicine in modern diabetes care.

Bioactive Compounds in Herbs and Their Anti-Diabetic Mechanisms

Bioactive compounds in herbs are natural substances that have a biological effect on the human body [10]. These compounds often have multiple pharmacological activities, making them potential candidates for the treatment of diabetes [6]. The primary classes of bioactive compounds that exhibit anti-diabetic properties include alkaloids, flavonoids, terpenoids, phenolic acids, and glycosides [9]. The following section highlights key bioactive compounds in herbs with proven anti-diabetic effects and their mechanisms of action.

Alkaloids

Alkaloids are nitrogen-containing compounds found in many plants, including Berberis vulgaris (barberry) and Glycyrrhiza glabra (licorice) [11]. These compounds have been shown to possess antihyperglycemic properties by improving insulin sensitivity and regulating glucose metabolism [12]. Berberine, an alkaloid found in Berberis species, has been extensively studied for its anti-diabetic effects. It acts by activating the AMP-activated protein kinase (AMPK) pathway, improving insulin sensitivity, reducing hepatic glucose production, and increasing glucose uptake in peripheral tissues. Berberine has been shown to lower blood glucose levels and improve lipid profiles in diabetic individuals [13].

Flavonoids

Flavonoids are a large group of plant secondary metabolites known for their antioxidant, antiinflammatory, and anti-diabetic properties [14]. Common flavonoids found in herbs such as Citrus sinensis (orange), Camellia sinensis (green tea), and Ginkgo biloba have demonstrated promising results in managing blood glucose levels [15]. Quercetin, a flavonoid present in Onion and Apple, has been shown to inhibit α -glucosidase, an enzyme responsible for breaking down carbohydrates into glucose $\lceil 16 \rceil$. This action slows down the absorption of glucose from the intestine, thereby preventing postprandial hyperglycemia [16]. Additionally, quercetin has been shown to improve insulin sensitivity and reduce inflammation, two key factors in the pathophysiology of diabetes [17].

Terpenoids

Terpenoids are a diverse group of bioactive compounds that are widely distributed in plants. They have shown promising anti-diabetic properties by improving insulin secretion, reducing blood glucose levels, and exhibiting antioxidant effects [18]. Herbs such as Ocimum sanctum (holy basil) and Cinnamomum verum (cinnamon) contain terpenoids with potential anti-diabetic benefits [19]. Cinnamaldehyde, the primary active compound in cinnamon, has been found to enhance insulin sensitivity by activating insulin signaling pathways and increasing glucose uptake in peripheral tissues [20]. Additionally, cinnamon has been shown to improve lipid profiles and reduce the risk of cardiovascular complications in diabetic patients $\lceil 21 \rceil$.

Phenolic Acids

Phenolic acids, including chlorogenic acid, ellagic acid, and caffeic acid, are abundant in herbs such as Coffea arabica (coffee) and Salvia officinalis (sage) [22]. These compounds possess potent antioxidant and anti-inflammatory properties that help reduce oxidative stress, a major factor in the development of diabetic complications. Chlorogenic acid, found in coffee, has been shown to inhibit glucose absorption from the digestive tract and improve insulin sensitivity [23]. This compound also reduces hepatic glucose output and helps in maintaining better blood sugar levels in diabetic patients [23].

Glycosides

Glycosides are compounds that consist of a sugar molecule bound to a non-sugar component (aglycone) $\lfloor 24 \rfloor$. These compounds have been reported to possess hypoglycemic effects through various mechanisms, including the inhibition of α -amylase and α -glucosidase enzymes $\lfloor 25 \rfloor$. Glycyrrhizin, the active glycoside in licorice, has been shown to reduce blood glucose levels by increasing insulin secretion from pancreatic β -cells $\lfloor 26 \rfloor$. It also exhibits antioxidant and anti-inflammatory effects, which may help mitigate diabetic complications $\lfloor 27 \rfloor$.

Clinical Evidence and Efficacy of Herbal Remedies in Diabetes Management

Over the past few decades, there has been growing interest in the use of herbal remedies for the management of diabetes mellitus, particularly type 2 diabetes [4]. This interest has been fueled by the rising global prevalence of the disease, the limitations and side effects of conventional therapies, and the historical use of medicinal plants in traditional healing systems [28]. Numerous clinical studies and trials have evaluated the efficacy of various herbal medicines in regulating blood glucose levels, improving insulin resistance, and mitigating complications associated with diabetes [29].

Among the most studied herbal remedies is Cinnamomum verum, commonly known as cinnamon.

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Clinical trials have consistently shown that cinnamon supplementation can lead to a significant reduction in fasting blood glucose levels and improvements in hemoglobin A1c (HbA1c), a key marker of long-term glucose control [30]. These effects are believed to be due to cinnamon's ability to mimic insulin activity, increase insulin receptor sensitivity, and enhance glucose uptake by cells [31]. In addition, cinnamon has antioxidant properties that may help reduce oxidative stress, a major contributor to the progression of diabetes and its complications $\lceil 32 \rceil$. Another well-researched herb is Gymnema sylvestre, traditionally used in Ayurvedic medicine as an antidiabetic agent [33]. Clinical studies have shown that this plant can lower blood glucose levels by stimulating the secretion of insulin from pancreatic beta cells and increasing the sensitivity of insulin receptors [34]. Some trials have reported that patients using Gymnema sylvestre were able to reduce or even discontinue their use of conventional diabetic medications under medical supervision $\lceil 35 \rceil$. The active compounds in this herb, known as gymnemic acids, are believed to be responsible for its glucose-lowering effects [36]. Allium sativum, more commonly known as garlic, has also demonstrated hypoglycemic effects in clinical settings [37]. Research indicates that garlic supplementation can help reduce fasting blood glucose and total cholesterol levels, as well as improve insulin sensitivity [38]. The sulfur-containing compounds in garlic, such as allicin, are thought to play a central role in modulating glucose metabolism and enhancing pancreatic function [39]. While these findings are promising, it is important to consider that the efficacy of herbal remedies can be influenced by several factors, including the method of preparation, the dosage, and the duration of treatment [28]. The pharmacokinetics and bioavailability of herbal compounds can also vary significantly between individuals, affecting therapeutic outcomes [40]. Moreover, many studies suffer from limitations such as small sample sizes, short follow-up periods, and variability in herbal product quality, making it difficult to draw definitive conclusions. Despite these challenges, the current body of evidence supports the use of certain herbal medicines as adjunctive therapies in the management of diabetes [41]. However, these treatments should not be viewed as replacements for conventional medications, especially in cases of poorly controlled or advanced diabetes. Instead, they should be integrated into a comprehensive treatment plan that includes lifestyle modifications, dietary changes, and pharmacologic interventions when necessary $\lceil 42 \rceil$.

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Ultimately, while the clinical efficacy of herbal remedies in diabetes management is supported by a growing number of studies, there remains a need for larger, high-quality, and long-term randomized controlled trials. These studies should aim to establish standardized dosages, assess long-term safety, and evaluate the potential of these herbs to prevent or delay the onset of diabetes-related complications. Until such evidence is available, healthcare providers and patients should approach the use of herbal therapies with informed caution and under professional guidance.

Safety Considerations and Potential Side Effects Although herbal medicines are often perceived as safe due to their natural origin, this perception can be misleading. Just like conventional pharmaceuticals, herbal remedies can exert powerful biological effects and may lead to adverse outcomes if not used properly [28]. In the context of diabetes management, it is particularly important to consider the potential for hypoglycemia, drug interactions, organ toxicity, and allergic reactions associated with certain herbal products [43]. One of the primary concerns with herbal anti-diabetic agents is their potential to cause hypoglycemia, especially when used alongside insulin or oral hypoglycemic drugs such as sulfonylureas or metformin [44]. For instance, Gymnema sylvestre, known for its blood glucose-lowering properties, can significantly amplify the effects of conventional medications, leading to dangerously low blood sugar levels [45]. Symptoms of hypoglycemia, such as dizziness, confusion, sweating, and even loss of consciousness, can pose serious risks if not promptly recognized and treated [46]. Another notable example is Berberis vulgaris, which contains berberine-a compound that has demonstrated efficacy in improving glucose and lipid metabolism [47]. However, berberine can also inhibit certain liver enzymes responsible for drug metabolism, potentially leading to increased blood levels of other medications [49]. This can alter the effectiveness or toxicity of those drugs, including commonly used anticoagulants, antibiotics, and cardiovascular medications [49].

Liver and kidney toxicity are additional concerns when using herbal remedies, particularly in individuals with pre-existing hepatic or renal conditions [50]. Certain herbs, if consumed in high doses or over prolonged periods, may cause hepatic enzyme elevation, nephrotoxicity, or other forms of organ damage. For example, excessive use of Momordica charantia (bitter melon) has been linked to gastrointestinal distress and hepatotoxicity in sensitive individuals [51]. These risks underline the

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necessity of routine monitoring of liver and kidney function during the use of herbal therapies, especially when they are used in conjunction with other medications. Contamination and adulteration of herbal products are further safety issues that cannot be ignored. Studies have revealed that some commercially available herbal supplements may contain undeclared pharmaceutical ingredients. heavy metals, or microbial contaminants 52]. This can result from poor manufacturing practices or lack of regulatory oversight, particularly in regions where herbal products are not subject to stringent quality controls [52]. Therefore, it is essential for consumers to purchase herbal supplements from reputable sources that adhere to good manufacturing practices and offer transparency in labeling. Furthermore, allergic reactions, ranging from mild skin rashes to severe anaphylactic responses, have been reported with the use of various herbal products $\lceil 54 \rceil$. These

Herbal medicines offer promising potential for managing diabetes and its complications. The bioactive compounds found in herbs, such as alkaloids, flavonoids, terpenoids, phenolic acids, and glycosides, exhibit a wide range of anti-diabetic effects through various mechanisms. While clinical evidence supports the efficacy of many herbs in lowering blood glucose and improving insulin

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reactions are often unpredictable and may be exacerbated by individual sensitivities or crossreactivity with other allergens. As with any therapeutic agent, a thorough medical history should be obtained before initiating herbal treatment, and any signs of adverse reactions should prompt immediate discontinuation and medical evaluation. Given these considerations, healthcare professionals play a critical role in guiding patients on the safe use of herbal medicines. Patients should be encouraged to disclose all herbal products they are using or intend to use, as this information is vital for identifying potential drug-herb interactions and managing treatment plans effectively. Ultimately, the safe integration of herbal remedies into diabetes care requires a balanced approach that combines scientific evidence, clinical judgment, and patient education [55].

CONCLUSION

sensitivity, further research, including long-term clinical trials, is necessary to fully understand their therapeutic potential and safety. Healthcare providers should carefully consider the appropriate use of herbal remedies, ensuring that they are used safely and in conjunction with conventional treatments to achieve optimal diabetes management.

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