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# Literature Review: Alkaloid Compounds in Medicinal Plants: Mechanisms and Anti-Diabetic Potential

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**Abstract**

Alkaloids are a group of chemical compounds found in nature with the most basic nitrogen atoms. As many as 20% of plant species contain alkaloid compounds, one of which is flowering plants. Plants that contain alkaloid compounds have the potential to be antidiabetic agents. This literature review research uses the narrative literature review method. Using keywords from the range of 2014-2024, a total of 25 articles were obtained. Diabetes is a common metabolic disease caused by insulin deficiency. The plants that contain bioactive alkaloid compounds are Catharanthus roseus, Portulaca oleracea L. (PO), Momordica charantia (Bitter Melon), Uncaria Nervosa Elmer (Bajakah), Peperomia Pelucida (Water Pepper), Mulberry, Ageratum conyzoides L (Ageratum), Syzygium sp (Red Pakoba Fruit), Sansevieria trifasciata (Mother-in-law's Tongue), Triumfetta cordifolia, Phrynium Capitatum (Rice Leaf), and Annona Muricata L. (Soursop Leaf), which have been proven to contain alkaloid activity compounds that can be used as anti-diabetic agents. Alkaloid compounds play an essential role in diabetes management through various mechanisms that regulate blood glucose levels.

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## INTRODUCTION

Diabetes mellitus is one of the most prevalent and serious chronic endocrine disorders globally. It is characterized by hyperglycemia resulting from insufficient insulin production or impaired insulin function (Santhiya, 2016). This metabolic imbalance affects the regulation of carbohydrates, proteins, lipids, electrolytes, and water, leading to a wide range of complications, including cardiovascular disease, nephropathy, and neuropathy. Southeast Asia has witnessed a steep rise in diabetes-related deaths, with Indonesia ranking sixth in global diabetes prevalence after India, China, Russia, Japan, and Brazil. According to WHO, an estimated 1.5 million people died from diabetes in 2012, and in 2014, approximately 422 million adults were living with the disease (Ubrusun et al., 2021; Obet et al., 2020).

Conventional diabetes treatments rely heavily on synthetic drugs such as metformin, insulin, and sulfonylureas. However, long-term use of these drugs often results in serious side effects, including abrupt hypoglycemia, altered lipid profiles, and increased obesity. These limitations have triggered a global search for safer and more sustainable treatment alternatives, with particular interest in plant-derived therapeutic compounds (Hasan et al., 2022).

Among the most promising natural compounds are alkaloids—a broad class of nitrogen-containing chemical compounds that are primarily basic in nature, though some exhibit neutral or weakly acidic properties. It is estimated that about 20% of plant species, especially flowering plants (Angiospermae), contain alkaloid compounds (Roy, 2017). Recent pharmacological studies have shown that alkaloids possess significant hypoglycemic activity, including

enhancing glucose uptake, regenerating damaged pancreatic β-cells, and stimulating the sympathetic nervous system to promote insulin secretion (Hasan et al., 2022).

While previous studies have explored individual plant species or isolated alkaloids for their antidiabetic effects, there remains a lack of comprehensive reviews that consolidate this growing body of knowledge into a unified framework. Many existing works are fragmented and fail to map the broader pharmacological mechanisms and comparative efficacy of different alkaloid-containing plants. This underscores the urgent need for a systematic review that provides an integrative understanding of how plant-derived alkaloids can serve as antidiabetic agents. Therefore, the objective of this article is to present a comprehensive review of plants containing alkaloid compounds and to evaluate their potential as antidiabetic agents. This work aims to bridge gaps in the existing literature and to offer a foundation for further research in the field of herbal-based diabetes management and natural drug development.

## METHOD

The narrative literature review method is used in this literature study. Selecting the research topic to be examined to provide general information on alkaloid compounds in medicinal plants that have anti-diabetic properties is the first stage. The second step was to use Google Scholar to look for works published between 2014 and 2024. In this review of the literature. Following data analysis, papers discussing alkaloid chemicals found in medicinal plants and those with potential anti-diabetic effects are grouped into multiple categories. The A table of article metadata, including journal name, article title, year of publication, author name, and research findings, is used to display this grouping.

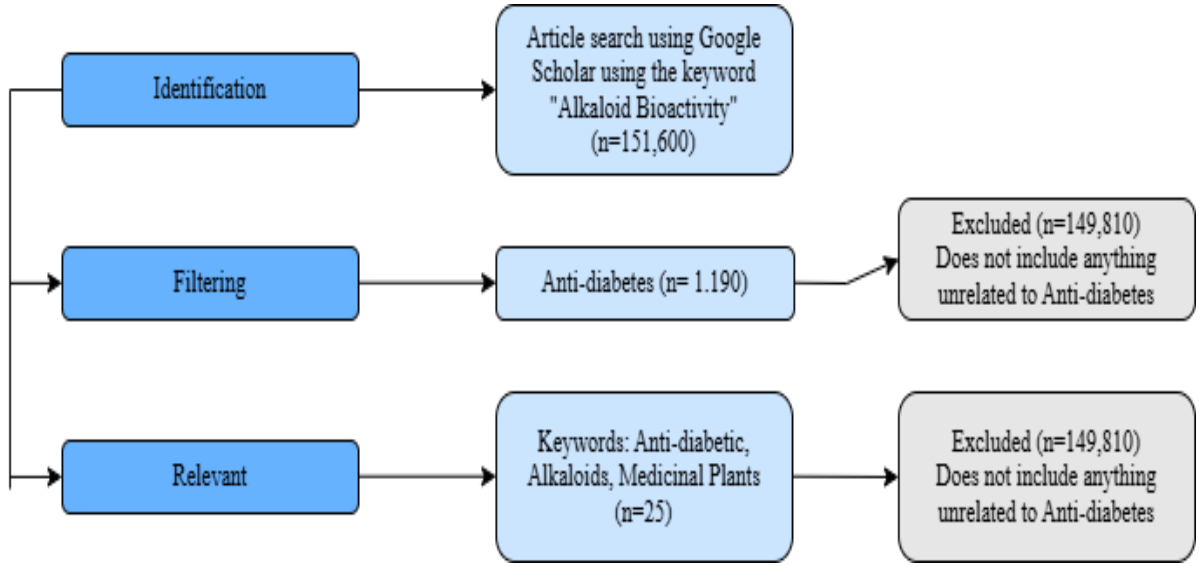


Figure 1. Data retrieval strategy flowchart

A search for research literature relevant to the topic of this study was conducted with the keyword "alkaloid bioactivity," and 151,600 articles were found. The articles obtained then were filtered using the keyword "anti-diabetes" as many in 1,190 articles, so 149,810 articles were not included because they were not related to anti-diabetes. Then filtered again using the keyword "medicinal plants", so that 1,165 articles were not included because the articles were not in accordance with the bioactivity of alkaloids as anti-diabetes. In the end, the number of articles selected after sorting according to the subject of discussion was 25 articles. The criteria for the articles included: (1) Articles on the bioactivity approach of alkaloids as antidiabetics. (2) Limitation year between 2014 and 2024. (3) Articles in reputable publications with open access.

## RESULTS AND DISCUSSION

### Definition of Alkaloids and Antidiabetic Bioactivity

Alkaloid compounds are natural active substances that possess hypoglycemic activity. Both flavonoids and alkaloids function as hypoglycemic agents through two main mechanisms: intrapancreatic and extrapancreatic pathways. In the intrapancreatic mechanism, alkaloids and flavonoids work by regenerating damaged pancreatic β-cells, protecting β-cells from further damage, and stimulating insulin secretion. Alkaloids have been proven to possess regenerative capabilities, as alkaloid extracts have shown a significant ability to regenerate damaged pancreatic β-cells. In addition, alkaloids can stimulate the sympathetic nerves (sympathomimetic effect), which leads to increased insulin secretion (Larantukan et al., 2014).

Diabetes Mellitus (DM) is a condition characterized by hyperglycemia due to either the absence of insulin or insulin resistance. Generally, DM is classified into two types: type 1 DM and type 2 DM. In type 1 DM, hyperglycemia is caused by the absence of insulin due to genetically inherited pancreatic beta-cell damage. In type 2 DM, hyperglycemia results from insulin's inability to mobilize blood glucose into cells due to insulin resistance at its receptor. Type 2 DM is not directly inherited genetically. Instead, it is usually triggered by factors such as age, race, family history, diet, lifestyle, and other metabolic disorders. Type 2 DM accounts for approximately 90% of all DM cases. It typically appears around the age of 40 and peaks at around 60 years old. Nearly 50% of type 2 DM cases remain undiagnosed for a long time due to the often unrecognized symptoms. Currently, the global prevalence of type 2 DM is estimated at around 3–6%, while in Indonesia it ranges from 1.4–1.6% (Sinulingga et al., 2020).

According to the International Diabetes Federation (IDF), the number of people with DM in 2017 had reached 425 million and is projected to increase to 629 million by 2045. Indonesia ranks seventh in terms of the number of diabetics, after India, China, the United States, Mexico, Brazil, and Russia. One of the main causes of diabetes is the presence of oxidants (free radicals) produced from the formation of Reactive Oxygen Species (ROS), which is why diabetes patients require a high intake of antioxidants to counteract these radicals (Wulandari et al., 2021)..

A combination of antioxidants and α-amylase enzyme inhibitors is expected to provide synergistic pharmacological effects. The α-amylase enzyme plays a crucial role in breaking down oligosaccharides and disaccharides into monosaccharides, making them ready for absorption. Inhibiting this enzyme can delay and prolong carbohydrate digestion time, thereby reducing glucose absorption rate and preventing spikes in postprandial blood glucose due to insulin resistance and beta-cell damage. Matoa (*Pometia pinnata* J.R. Forst. & G. Forst.), a plant from the Sapindaceae family, has long been used as traditional medicine by certain ethnic groups for its antibacterial (against *S. aureus*), antiviral (against HIV-1N), and antioxidant properties. Organic compounds isolated from matoa leaves belong to the flavone (aurone) group (Sinulingga et al., 2020.

In Indonesia, people widely utilize traditional herbal medicines sourced from local plants as alternative treatments. One such plant is benalu kersen (Dendroptera petandra (L.) Miq), which is a traditional herbal remedy in countries like China, Japan, Indonesia, Malaysia, and Taiwan. It has been studied and shown to possess various biological activities, including antidiabetic effects. Extracts and active fractions of *D. petandra* leaves are believed to have antidiabetic potential due to their content of flavonoids, alkaloids, terpenoids, tannins, and saponins. These metabolites are suspected to inhibit the activity of the α-glucosidase enzyme in the small intestinal wall, and have been proven to exhibit antidiabetic bioactivity (Sinulingga et al., 2020 & Wulandari et al., 2021).

Blood glucose levels increase due to digestive enzymes that hydrolyze dietary polysaccharides. α-glukosidase and α -amylase, enzymes that belong to the hydrolase class, catalyze the hydrolytic breakdown of starch, glycogen, and various oligosaccharides, leading to hyperglycemia. Inhibition of these digestive enzymes by secondary metabolites from plants is a common technique to lower postprandial blood glucose levels. To prevent the formation of enzyme-substrate complexes, which in turn reduces enzyme activity, alkaloids can bind to the enzymes involved in digestion at both competitive and non-competitive sites (Alamzeb, 2024).

**Plants as a Source of Antidiabetic Alkaloids**

Indonesia is rich in natural resources, particularly medicinal plants, including those containing active compounds that can help lower blood sugar levels or serve as antidiabetic agents. These plants are commonly found in tropical and subtropical regions (Alfani et al.,2021). Therefore, the following are examples of plants that contain alkaloid compounds used in the treatment of diabetes.

Table 1. Plants as Sources of Antidiabetic Alkaloids

| Plant Name | Part Used | Bioactive Compounds | Bioactivity | Health Benefits | Reference |
|---|---|---|---|---|---|
| *Catharanthus roseus* | Flowers and leaves | Alkaloids (Catharanthine, Vindoline, Vinblastine, Vincristine, Leurosine, Lochnerine, Tricin (Flavone), Vingramine, Mitraphylline) | Antimicrobial, Antidiabetic, Antifungal, Antioxidant, Antidiarrheal | Treats menorrhagia, rheumatism, diabetes, skin tightening, urinary disorders, menstrual issues, and hypertension | (Chaturvedi et al.,2022) |
| *Portulaca oleracea* (PO) | Stem | Flavonoids, alkaloids, monoterpene glycosides, phenolics, fatty acids, α-linolenic acid (Omega-3), vitamins, minerals | Analgesic, Antibacterial, Muscle relaxant, Wound healing, Anti-inflammatory, Antispasmodic, Antidiabetic | Antidiabetic by regulating blood lipids and glucose levels | (Arfan & Habibi., 2024) |
| *Momordica charantia* (Bitter Melon) | Fruit and seeds | Steroids, Momordicosides (A–L), acyl glycosyl sterols, fatty acids, amino acids, alkaloids, phenolics, steroidal saponins, vitamins, carbohydrates, minerals | Anti-inflammatory, Antioxidant, Antiviral, Anticancer, Antibacterial, Antidiabetic | Enhances glucose tolerance in diabetic and normal rats as well as in humans | (Tran et al., 2020) |
| *Uncaria nervosa* Elmer (Bajakah) | Stem | Rhynchophylline, Isorhynchophylline, Flavanol, Flavonol | Antidiabetic, Anticancer | Treats wounds, headaches, ulcers, digestive disorders, microbial infections, neural diseases, hypertension, asthma, stroke, rheumatism | (Ridho, 2023) |

| Plant Name | Part Used | Bioactive Compounds | Bioactivity | Health Benefits | Reference |
|---|---|---|---|---|---|
| *Peperomia pellucida* (Shiny Bush) | Whole plant | Alkaloids, flavonoids, saponins, terpenoids, steroids, glycosides | Antidiabetic | Used traditionally to treat diabetes and gout | (Hidayati, 2021) |
| Mulberry | Leaves | Steroids, alkaloids, flavonoids, amino acids, triterpenes, various organic compounds | Antidiabetic | Improves glucose levels and inhibits sucrase, maltase, and α-glucosidase enzymes | (Hussain & Munir., 2022) |
| *Ageratum conyzoides* L (Goat Weed) | Leaves | Alkaloids, saponins, flavonoids | Antidiabetic | Antioxidant that protects pancreatic β-cells from free radicals, increases insulin production, and lowers blood glucose | (Pay et al.,2022) |
| *Syzygium* sp. (Red Pakoba Fruit) | Fruit | Alkaloids, terpenoids, steroids, flavonoids, saponins, tannins | Antidiabetic | Reduces blood glucose levels | (Sangkal, 2022) |
| *Sansevieria trifasciata* (Snake Plant) | Leaves | Flavonoids, glycosides, alkaloids, steroids | Analgesic, Antipyretic, Antibacterial, Antioxidant, Antidiabetic | Treats diabetes, earache, sore throat, and skin itching; acts as a pain reliever and fever reducer | (Yumma et al., 2018) |
| *Triumfetta cordifolia* | Leaves | Alkaloids, glycosides, tannins, steroids, flavonoids, terpenoids | Antidiabetic | Used for digestive disorders, dysentery, diarrhea, diabetes, rhinitis, mental disorders, and fever | (Ebele & Estella., 2022) |
| *Phrynium capitatum* (Nasi Leaf) | Leaves | Alkaloids, phenolics, flavonoids, saponins, steroids, triterpenoids | Antidiabetic | Reduces blood glucose levels | (Obet et al., 2020) |
| *Annona muricata* L. (Soursop) | Leaves | Flavonoids, alkaloids, saponins, tannins | Antidiabetic | Lowers blood sugar via multiple mechanisms | (Fadel & Besan., 2020) |

## Comparison of Study Findings

The diagram shows how four medicinal plants, *Catharanthus roseus*, *Momordica charantia*, *Peperomia pellucida*, and *Mulberry*, contribute to antidiabetic activity through their bioactive compounds. Each plant contains alkaloids, with some also containing flavonoids or other secondary metabolites. These compounds act through multiple mechanisms: inhibiting digestive enzymes like α-glucosidase and α-amylase, stimulating insulin secretion, and

suppressing sucrase and maltase activity. These actions work together to reduce postprandial blood glucose spikes, highlighting the therapeutic potential of plant-derived alkaloids in diabetes management. The comparison of the findings is showed below.

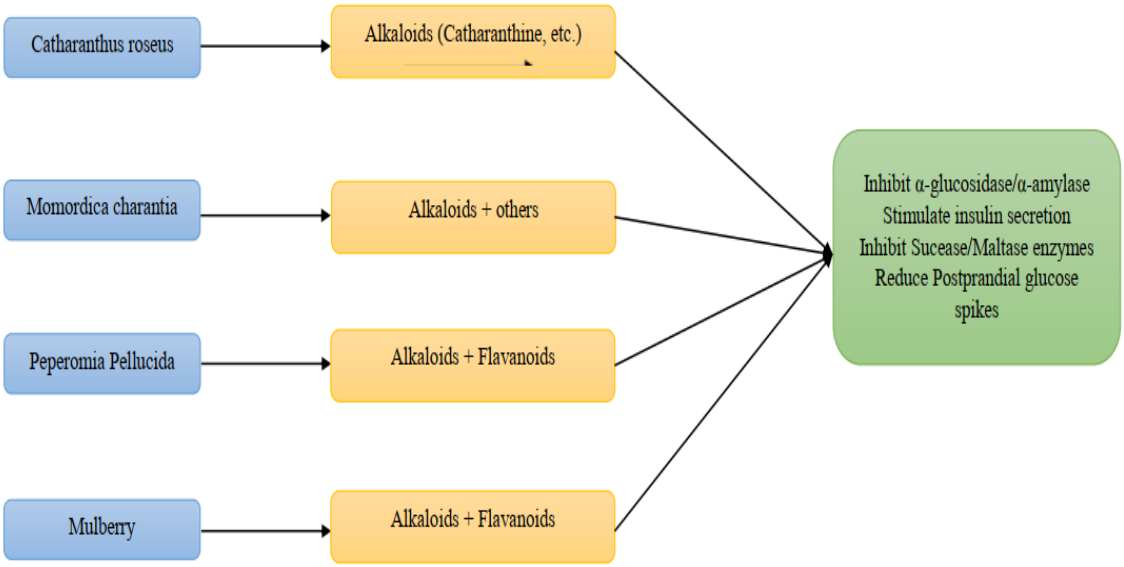


Figure 2. Comparison of study results from several plants

**Mechanism of Alkaloid Compounds as Antidiabetic Agents**

Diabetes is a common metabolic disease caused by insulin deficiency. One of the primary functions of insulin is to act on the cell membrane to increase its permeability for glucose transport. Therefore, a lack of insulin leads to glucose accumulation in the blood and a deficiency of glucose within the cells where it is needed (Semwal et al.,2017). Diabetes mellitus (DM) is a metabolic disorder caused by various factors and is characterized by chronic hyperglycemia along with disturbances in the metabolism of carbohydrates, lipids, and proteins due to abnormalities in insulin secretion, insulin action, or both. The impact of diabetes includes long-term damage, dysfunction, and failure of various organs. Diabetes is marked by insulin resistance and β-cell dysfunction, thus requiring treatment strategies that aim to improve insulin resistance, enhance glucose uptake, reduce blood glucose concentrations, and protect or regenerate existing pancreatic islet β-cells (Tran et al., 2020).

Type 2 diabetes mellitus (T2DM) is a global health problem whose prevalence continues to increase along with changes in people's lifestyles and diets. Data from the International Diabetes Federation (IDF) in 2021 noted that more than 537 million people in the world live with diabetes, and is estimated to increase to 643 million in 2030, and reach 783 million in 2045 if no effective intervention is carried out. Indonesia itself is ranked fifth highest globally, with an estimated more than 19.5 million diabetes sufferers in the same year, the majority of whom are type 2. This condition is not only a burden on individual health, but also has a significant impact on the health care system and the national economy (Anggraini et al., 2025).

Alkaloids are secondary metabolites found in plants, as well as in bacteria, fungi, and other animals. They are classified as true alkaloids, such as nicotine, atropine, and morphine, and protoalkaloids. Alkaloids have been proven to be active compounds in several medicinal plants used for antidiabetic purposes (Aba & Asuzu, 2018). Alkaloids are a group of phytochemicals with potential as antidiabetic agents. Research has shown that alkaloids can actively contribute to lowering blood glucose levels through various mechanisms. Several plants are known to contain bioactive alkaloid compounds, including *Catharanthus roseus*, *Portulaca oleracea* (PO), *Momordica charantia* (Bitter Melon), *Uncaria nervosa* Elmer (Bajakah), *Peperomia*

*pellucida* (Shiny Bush), Mulberry, *Ageratum conyzoides* L (Goat Weed), *Syzygium* sp. (Red Pakoba Fruit), *Sansevieria trifasciata* (Snake Plant), *Triumfetta cordifolia*, *Phrynium capitatum* (Nasi Leaf), and *Annona muricata* L. (Soursop Leaf). These plants have been proven to contain alkaloid compounds with antidiabetic activity.

Alkaloids are a group of phytochemical compounds proven to have antidiabetic effects through various mechanisms. One of the main mechanisms by which alkaloids exert their function is by inhibiting digestive enzymes, particularly α-glucosidase and α-amylase. These enzymes play a critical role in the digestion of carbohydrates into glucose. By inhibiting their activity, alkaloids can slow the absorption of glucose into the bloodstream, thereby preventing spikes in blood glucose levels after meals. For example, annonaine, a compound found in soursop (*Annona muricata*), has demonstrated α-glucosidase inhibitory activity with a low $IC_{50}$ value, making it a promising candidate for diabetes therapy (Ubrusun et al., 2021; Puspanelli et al., 2023; Akuba et al., 2022).

On a molecular level, alkaloids can bind to the active site of α-glucosidase, thereby blocking its enzymatic activity. In vitro studies have supported this mechanism, showing that alkaloids such as nummularine-R and vindoline are capable of inhibiting α-glucosidase. Alkaloids may also stimulate insulin secretion from pancreatic β-cells. Insulin is a key hormone that regulates blood glucose levels by facilitating glucose transport into the body's cells. These compounds are basic in nature, typically contain one or more nitrogen atoms, are often heterocyclic, and are derived from amino acids. Alkaloids may influence glucose uptake in the intestines or activate insulin-dependent molecular pathways (Behl et al.,2022).

For instance, berberine**,** an alkaloid found in *Berberis vulgaris*, has been shown to enhance insulin secretion and improve β-cell function, contributing to lowered blood glucose levels in patients with type 2 diabetes (Hasan et al., 2024). Damage to pancreatic β-cells is one of the main causes of diabetes. Certain alkaloids possess the ability to stimulate the regeneration of these cells, thereby increasing the body's capacity to produce insulin. Research has shown that Moringa oleifera leaf extract, which is rich in alkaloids, can repair damage to pancreatic β-cells and enhance insulin production (Anugrahini & Wahyuni, 2021). Additionally, alkaloids may improve insulin sensitivity in peripheral tissues such as muscle and liver. Insulin resistance**,** a hallmark of type 2 diabetes, occurs when the body fails to respond properly to insulin. Piperine, an alkaloid from black pepper (*Piper nigrum*), has demonstrated the ability to enhance insulin sensitivity and improve glucose metabolism (Rohdiana et al., 2022).

In summary, alkaloid compounds offer a wide range of mechanisms that make them valuable in diabetes treatment. From inhibiting digestive enzymes to stimulating insulin secretion and improving insulin sensitivity, these compounds show great potential. Further research is required to fully understand their benefits and clinical applications, but current findings offer promising prospects for the development of more effective and safer treatments for diabetes.

## Advantages and Challenges

Alkaloids are a group of chemical compounds commonly found in plants and have demonstrated significant potential as antidiabetic agents. Generally, diabetes treatment involves insulin injections, oral antidiabetic drugs, and blood glucose control to prevent further complications. However, insulin therapy and oral antidiabetic medications are often costly, making them inaccessible to lower-income populations. Moreover, long-term use of some of these medications may lead to side effects such as weight gain and hypoglycemia. Therefore, research into the use of herbal medicine as an alternative treatment for diabetes is crucial (Sadik & Anwar, 2022).

The use of natural ingredients as traditional medicine is gaining increasing attention. This trend is driven by the fact that traditional medicines, especially those derived from plants, tend to be

more affordable, widely available, and generally safer, with fewer side effects, compared to synthetic drugs. Currently, there are approximately 800 species of plants worldwide that have been identified as having potential antidiabetic properties (Hasan et al., 2022).

The mechanism by which alkaloids reduce blood glucose levels involves several extra-pancreatic processes, including enhancing glucose transport in the blood, inhibiting glucose absorption in the intestines, stimulating glycogen synthesis, and suppressing glucose production through the inhibition of key gluconeogenic enzymes such as glucose-6-phosphatase and fructose-1,6-bisphosphatase. These enzymes play essential roles in the gluconeogenesis pathway. Furthermore, alkaloids enhance glucose oxidation by activating glucose-6-phosphate dehydrogenase. Inhibiting glucose-6-phosphatase and fructose-1,6-bisphosphatase contributes to reduced glucose formation from non-carbohydrate sources (Larantukan et al., 2014).

Alkaloid compounds offer several advantages in diabetes management, including the ability to repair and protect damaged pancreatic β-cells, as well as stimulate glucose uptake and glycogen synthesis**.** Alkaloids are a class of basic secondary metabolites that contain one or more nitrogen atoms. These compounds can be found in various parts of plants, such as flowers, seeds, leaves, twigs, roots, and bark 9Ningrum et al., 2016). Alkaloids are chemical compounds commonly found in various types of plants and exhibit a wide range of biological effects, including potential as antidiabetic agents. Although alkaloids are capable of reducing blood glucose levels, there are several limitations and challenges that must be considered in their use. Alkaloids exert antidiabetic activity primarily by inhibiting enzymes involved in carbohydrate metabolism, such as α-amylase and α-glucosidase (Santhiya et al., 2016).

However, many alkaloids are derived from plants that are difficult to access or possess chemically unstable compositions. This situation presents a major obstacle in achieving consistent standardization of dosage and formulation, which remains a significant challenge in both research and clinical application (Hasan et al., 2022).

## CONCLUSION

Alkaloid compounds play a crucial role in diabetes management through various mechanisms that help regulate blood glucose levels. These compounds are distributed in various plant parts, including flowers, seeds, leaves, twigs, roots, and bark—found in species such as *Catharanthus roseus, Portulaca oleracea* (PO), *Momordica charantia* (bitter melon), and Mulberry. As a key finding, the ability of alkaloids to modulate glucose metabolism through enzyme inhibition and insulin stimulation highlights their therapeutic potential as natural antidiabetic agents. Specifically, by inhibiting digestive enzymes like α-glucosidase and α-amylase, alkaloids reduce carbohydrate absorption and blunt postprandial glucose spikes. Furthermore, their role in enhancing insulin secretion supports glycemic control in diabetic conditions. These multifaceted actions position alkaloids as promising candidates in the development of alternative or complementary therapies. The exploration of plant-derived alkaloids thus offers a valuable contribution to future diabetes research, particularly in the search for safer, affordable, and sustainable treatment options.

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