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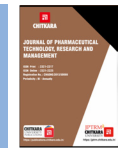

Review of Phytochemicals with Anti-Diabetic Potential: Plant Sources and Mechanism

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ABSTRACT

Background: Phytochemicals, the bioactive compounds found in plants, have garnered substantial attention for their potential health benefits. This review delves into the multifaceted therapeutic applications of phytochemicals, particularly in the management of diabetes and its associated complications.

Purpose: The review highlights the intricate tapestry of phytochemical interventions, exploring their diverse roles in addressing various aspects of diabetes care. This article delves into the potential side effects and risks associated with the use of phytochemicals, emphasizing the importance of a comprehensive assessment of their safety profile.

Methods: To accomplish these objectives, literature has been surveyed from PUBMED, MEDLINE, EMBASE, etc. like search engines, for detailed knowledge about phytochemicals in the management of diabetes and its complications.

Result: Various studies have meticulously examined the potential adverse effects and risks intertwined with phytochemicals, underscoring the need for careful consideration in their therapeutic applications.

Conclusion: The review explores the diverse therapeutic applications and uses of anti-diabetic phytochemicals, such as the clinical applications of berberine and the therapeutic potential of Stevia rebaudiana Bertoni extracts. The review highlights the importance of continued research and exploration in this burgeoning field to unlock the full potential of phytochemicals in the management of diabetes and its complications.

1. Introduction

Phytochemicals are incredible bioactive compounds that are entrenched in the botanical world and have received a lot of attention due to their inherent capability to enhance the health of a human. These are chemicals that are primarily present in various plant food products and have many health advantages. They possess a high potential to improve the nutritional value of suitable products and are a unique source for the consumers to achieve specific health benefits (Skendi *et al.*, 2019). Plant-based foods that are highly abundant in phytochemicals, such as fruits, vegetables, and numerous others, act in synergy and assist in postponing the development of cancer. This mutual co-operation allows carcinogen to be detoxified, detoxification enzymes to be regulated, and free radicals to be suppressed. These bioactive compounds improve the antioxidant reactions within the body, accelerate cells, proteins, and DNA repair, and control alterations in biological processes contributing to the development of cancer (Monica *et al.*, 2025).

The field of research of phytochemicals in terms of not only anti-inflammatory properties, but also gut health concerns and metabolic profile complications, has been drastically evolving recently. Though it is approximated that more than 5,000 phytochemicals have already been identified in the over 150,000 edible plants that are present on Earth, a large percentage of them remain unknown and have to be identified. The strategic change of direction is a dynamic and diversified development of related functions of these compounds, which has a significant role in preserving human health (Xiao *et al.*, 2022). Phytochemicals have become a vibrant and energetic one in terms of the prevention and treatment capabilities due to the emergence and growth of civilizations that were closely associated with the use and exploration of the healing properties of medicinal plants, in particular.

Their anti-inflammatory and antioxidant properties play a crucial role in alleviating pulmonary-induced damage by SARS-COVID (Majnooni *et al.*, 2020). Moreover, bioactive molecules such as curcumin have also been demonstrated to be strong anti-cancer agents by modulating the important signaling pathways and inhibition of tumor formation (Di Meo *et al.*, 2019). The analysis of the bioactive compounds as being universal to the enhancement of health, their transformative effectiveness on food and disease prevention, as well as the growing potential of further research and inquiry in the field, underscores the increasing possibilities of further studies and exploration in this field. Finally, it is necessary to carry out more rigorous research into this area because of the crucial importance of phytochemical in health improvement and the prospects of preventing diseases and revolutionizing nutrition.

2. The Use of Phytochemical in the Treatment of Diabetes

The research on phytochemicals into unraveling the potential anti-diabetic potential proceeds in a convoluted pathway by another series of bioactive composites, each with a distinct functional property. Among them are naringenin, naringin, hesperidin, and quercetin, which have been known to have the potential in the treatment of diabetes. By altering or controlling these pathways, including Glucose Transporter Type 4 (GLUT4) and Peroxisome Proliferator-Activated Receptor γ (PPARγ), these flavonoids are able to enhance insulin sensitivity and glucose absorption. They are exceptionally accurate whenever handling the complex matters regarding diabetes and its complications. They increase the levels of insulin secretion and activity of the pancreatic β-cells by decreasing inflammation and oxidative stress. The compounds are also useful in controlling the postprandial glucose levels by blocking the enzymes such as DPP-IV and α-glucosidase (Al-Ishaq *et al.*, 2019).

The possible potential of *Curcuma longa*, polyphenolic curcuminoid, has undergone comprehensive research to prevent and treat type 2 diabetes mellitus. It is shown to be a hypoglycemic agent and adds complexity to a complex network of phytochemicals that affect the work of diabetes (Pivari *et al.*, 2019). The anti-diabetic effects of *Curcuma longa* are mediated via one of the numerous molecular pathways, i.e., AMP-activated protein kinase (AMPK), which is essential in the cellular energy regulation. Curcuminoids have been found to increase insulin resistance, adiponectin production, reduce insulin and glucose levels, and decrease leptin, resistin, interleukin (IL)-6, IL-1β, and tumor necrosis factor-α (TNF-α) in patients with type 2 diabetes. Based on the findings, these substances can affect the diabetic complications, glucose homeostasis, and the vascular risk of type 2 diabetes patients. The use of curcumin in the form of supplements improves their lipid profiles and general antioxidant properties and improves glycemic control through lowering chronic inflammation (Marton *et al.*, 2021).

Combined, these studies point out the various and future possibilities of phytochemicals to play in the complicated environment of controlling diabetes and related complications. An interesting study of therapeutic operations reviews in detail the promising application of flavonoids to diabetic cardiomyopathy and examines the sphere of oxidative stress, inflammation, and apoptosis in the heart. This emphasizes the versatile nature of phytochemicals in managing different elements of diabetes issues, as well as proving their polychromatic therapeutic properties by being better than traditional therapies (Jubaidi *et al.*, 2021). The recent pre-clinical and clinical studies on the flavonoid products in the management of diabetic complications are discussed and offer information that could explain the therapeutic potential of these substances in management of diabetes, contributing to the understanding of how the substances ease the various challenges that come with the disease (Caro-Ordiere *et al.*, 2020). The research provides a new chapter to the growing body of research on the way phytochemicals operate in disease, as it shows a new potential in treating diabetes and obesity and raises awareness of phytochemicals in the metabolic disorders context (Hansen *et al.*, 2019).

In addition, another study examines the potential of *Morinda citrifolia* (Noni) as a hypoglycemic agent using a number of pathways in order to examine its anti-diabetic effects. Recent studies discover its effect primarily because of higher levels of insulin secretion and pancreatic β-cell activity modulation, which is expressed through the effect of escalation of the C-peptide levels (Algenstaedt *et al.*, 2018). Moreover, Noni also has powerful anti-inflammatory and antioxidant properties, which reduce the high-sensitivity C-reactive protein (hs-CRP) as an indicator, which is mainly high in diabetic patients. Its pharmacological effects can be explained by various phytochemicals, such as flavonoids, terpenoids, and anthraquinones, that lower the oxidative stress and stimulate glucose metabolism, which requires further clinical research to assert its safety and effectiveness (Algenstaedt *et al.*, 2018).

3. Phytochemicals of Anti-Diabetic Plants

In recent times, phytochemicals of various plant sources have received a lot of attention in regard to their potential application in the treatment of diverse problems that diabetes presents. The naringenin, naringin, hesperidin, and quercetin flavonoids have been some flavonoids that have reported a powerful antidiabetic effect in scientific literature by modulating cellular and molecular pathways in blood sugar disorders (Al-Ishaq *et al.*, 2019). These substances establish themselves as powerful antidiabetic agents with great potential since their 15-carbon backbones and aromatic rings generate a high-quality cascading effect of hypoglycaemia (Neveu *et al.*, 2010). This plot is slowly developed by flavonoids, which are plant lipophilic compounds that unveil a particular therapeutic facet that regenerates diabetic cardiomyopathy by regulating oxidative stress, inflammation, and apoptosis in the cardiac healing symphony (Panda *et al.*, 2025).

Luteolin is a flavone which is primarily found in medicinal plants, special in its outstanding antioxidant, anti-inflammatory, and anti-allergic properties, and thus can be used as a potential bioactive protector in combating diabetes. Luteolin attains its antidiabetic effect by enhancing pancreatic β-cell sensitivity, pancreatic β-cells protection, and regulated blood glucose levels because it acts as a modulator of major signaling pathways, including Akt2 and PPARγ (Chang and Yue, 2025). Brassica vegetables contain bioactive substances that are necessary in supplementing diets and maintaining human health, including glucosinolates, vitamins (especially vitamin C, folate, tocopherol, and phytomenadion), carotenoids, phenols, and minerals. They exhibit certain anti-diabetic activities, converting them into bioactive isothiocyanates and indoles, which provide them with a more sophisticated level of plant profile (Kolodziejski *et al.*, 2019).

Red blood glucose is controlled by this mechanism of actions as *Syzygium cumini* (Jamun), *Azadirachta indica* (Neem), *Gymnema sylvestre*, and *Coccinia cordifolia* (Ivy gourd) have strong anti-diabetic potential. They enhance insulin secretion, inhibit carbohydrate-degrading enzymes, mimic the insulin functions, and protect pancreatic β-cells against insulin-like oxidative damage. All these plants offer a complementary approach to the management of diabetes, combining the ancient knowledge base with the potential of modern treatment (Zanzabil *et al.*, 2023).

Ficus benghalensis leaves have exhibited a significant antioxidant and anti-diabetic effect by inhibiting α-glucosidase and α-amylase enzymes, which reduces post-meal glucose spikes by regulating the PI3K/Akt signaling pathway and enhances the secretion of insulin and glucose uptake. They are an up-and-coming and natural source of protection of metabolic health due to their rich phytochemical composition (Rauf *et al.*, 2024). *Persea americana* Mill also shows anti-diabetic effects. Ensuring which, (Avocado), *Annona muricata* (Graviola), and *Montrichardia arborescens* (Moco-Moco) have proven important in the current narcissistic struggle against diabetes mellitus.

Besides, the discovery of two xanthone anti-diabetic-potent compounds of *Swertia punicae*, methylswertianin and bellidifolin, and modes of action suggest promising therapeutic benefits, which contribute to the artistic relevance of a scientific publication (Boston *et al.*, 2020). Also, an extensive number of bioactive chemicals are found during the search of plant-based anti-diabetic medicines; most of them are flavonoids, curcumin, *Ficus benghalensis*, and Brassica vegetables, and all of these compounds possess strong therapeutic potential. Taken together, they are a thrilling approach to managing diabetes and imply a new avenue of studies into the particularities of the mechanisms of action, as well as their clinical implications.

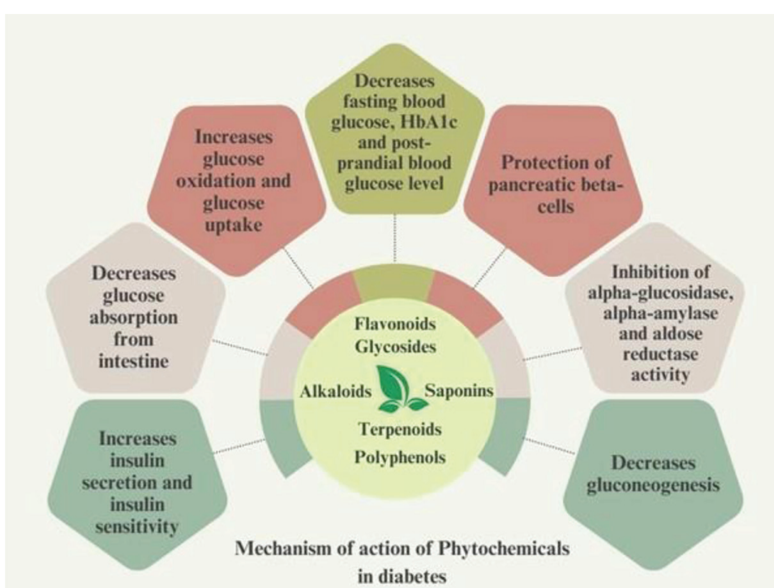


Figure 1: Bioactive Plant Compounds in the Management of Diabetes

The antidiabetic effects of phytochemicals are mainly due to their multifunctional actions on glucose metabolism and insulin regulation by preserving the structural and functional integrity of pancreatic β-cells and thereby enhancing endogenous insulin secretion. Additionally, these compounds also improve peripheral insulin sensitivity, stimulate glucose oxidation and uptake, decrease fasting blood glucose levels, while at the same time inhibiting intestinal absorption of glucose and gluconeogenesis in the liver. Many phytochemicals have inhibitory actions on key enzymes involved in carbohydrate breakdown and glucose synthesis, including α-glucosidase, α-amylase, and glucose-6-phosphatase.

4. Comparison Between Source of Different Plants

A high concentration of research has been done in many studies analyzing different plant sources and its phytochemicals, which have been noted to play a key role in the reduction of diabetes and complications, known to have promising therapeutic effects. The wide variation of bioactive compounds can be easily evaluated through a thorough comparison study, so it is easy to see the effectiveness of the bioactive compounds in reference to the biological pathways to successful intervention and with positive hypoglycemic effects. An example of an antidiabetic plant is *Bidens pilosa*, which, however, has scarce studies to demonstrate its botanical, phytochemical, pharmacological, or toxicological functions, but it identified the plant components capable of curing type 1 and type 2 diabetes, especially the polyenes (Yang, 2014).

Relative classification is concerned with evaluation of the phytochemical profile, including in a comprehensive study of *Vitex trifolia* L. (Viticis Fructus), which induces reduction of sugar levels by activation of adipogenesis akin to rosiglitazone (ROS) and intracellular lipid accumulation, which qualifies as a possible candidate in the management of diabetes. This indicates the crucial role of the comparisons of different botanical sources of an herbal drug to identify minor differences in clinical efficacy (Wu *et al.*, 2023). The place of origin of the source is important when considering the therapeutic efficacy of plant-derived materials.

The detailed analysis of *Stevia rebaudiana* Bertoli leaf extract shows that the study of pharmacological activity can also be better understood with the help of a detailed analysis. As per the research, postprandial blood glucose levels were reduced by 18 percent in comparison to controls 240 minutes following stevioside intake, and the index of insulinogenicity had risen by 40 percent (Shahid *et al.*, 2022). The enzymes with high binding affinity and stability with the specific compounds found in the leaf extract include enzymes like α-amylase, DPP-4, and PPARγ through molecular docking. The steviosides reduce the long-term blood glucose level through the increase in insulin secretion. Research has demonstrated that stevioside increases the level of HDL with a significant reduction in total cholesterol, triglycerides, LDL, and VLDL levels (Shahid *et al.*, 2022).

A comprehensive study indicates a broad spectrum of bioactive molecules with a potential of new pharmacologies, and through comparison studies, it improves the scientific knowledge of their anti-diabetic effects.

Table 1: Phytochemicals Plant Source and their Mechanism of Action (Uti *et al.*, 2025)

Plant	Plant Source	Major Phytochemicals	Mechanism of Action in Diabetes
Curcuma longa	Turmeric rhizome	Curcumin	Enhances insulin sensitivity, reduces oxidative stress, inhibits NF-κB and inflammatory cytokines
Berberis vulgaris	Barberry root and bark	Berberine	Activates AMPK, improves insulin sensitivity, reduces hepatic gluconeogenesis
Morinda citrifolia	Noni fruit and leaves	Scopoletin, damnacanthal	Antioxidant, improves insulin secretion, reduces lipid peroxidation
Syzygium cumini	Jamun seeds and bark	Jambosine, ellagic acid, glycosides	Inhibits starch-to-sugar conversion, enhances insulin activity
Azadirachta indica	Neem leaves and bark	Nimbin, nimbidin, azadirachtin	Stimulates insulin secretion, inhibits α-glucosidase, reduces oxidative stress
Gymnema sylvestre	Gymnema leaves	Gymnemic acids	Regenerates β-cells, inhibits glucose absorption, enhances insulin secretion
Annona muricata	Soursop fruit and leaves	Acetogenins, flavonoids	Inhibits α-amylase and α-glucosidase, reduces postprandial glucose
Persea americana	Avocado fruit and leaves	Oleic acid, flavonoids, lutein	Enhances insulin secretion, reduces β-cell apoptosis, activates PI3K/Akt pathway

Montrichardia arborescens	Moco-moco fruit and leaves	Flavonoids, tannins, alkaloids	Inhibits α-amylase, antioxidant and anti-inflammatory effects
Vitex trifolia	Simpleleaf chastetree leaves	Vitexilactone, luteolin, flavonoids	Activates PPARγ, improves insulin sensitivity, inhibits IRS-1 phosphorylation
Stevia rebaudiana	Stevia leaves	Stevioside, rebaudioside A	Stimulates insulin secretion, inhibits α-glucosidase, improves glucose tolerance
Mitragyna speciosa	Kratom leaves	Mitragynine, speciociliatine	Inhibits DPP-4, reduces blood glucose, antioxidant and anti-inflammatory effects
Costus spicatus	Spiked spiralflag ginger leaves	Diosgenin, saponins	Reduces blood glucose, improves lipid profile, restores pancreatic histology
Coccinia cordifolia	Ivy gourd leaves and fruit	Alkaloids, flavonoids, glycosides	Stimulates insulin secretion, regenerates β-cells, improves glucose tolerance
Trigonella foenum-graecum	Fenugreek seeds	4-Hydroxyisoleucine, trigonelline, diosgenin	Fenugreek seeds contain soluble fiber and other compounds that lower blood glucose levels and improve insulin sensitivity
Cinnamomum verum	Ceylon cinnamon bark	Cinnamaldehyde, cinnamic acid, cinnamate	Improves insulin sensitivity, lowers blood glucose levels, and has antioxidant properties
Allium sativum	Garlic bulb	Allicin, S-allyl cysteine, diallyl disulfide	Lowers blood glucose levels and improves insulin sensitivity

5. The Phytochemicals with the Management of Diabetes

The positive but demanding roles of phytochemicals in the management of diabetes have raised a lot of eyebrows. It is still debated and one of the literature states that phytochemicals are crucial in improving the translocation of GLUT4 proteins. It is concerned with the progressive mechanisms of insulin resistance in type 2 diabetes that has made a ripple effect among the researchers (Sayem *et al.*, 2018). The insulin signaling mechanism has an important role in the regulation of glucose uptake that mainly comprises the transportation of GLUT4 at the cell membrane. It begins with the insulin attaching with its receptor on the surface of adipose and muscular tissue, thus leading to the activation of intrinsic tyrosine kinase activity on the receptor. This also results in phosphorylation of IRS-1/2 (insulin receptor substrates), inducing and recruiting PI3K. PI3K facilitates the conversion of PIP2 to PIP3 that causes docking sites of Akt (or Protein Kinase B) (Sayem *et al.*, 2018). Upon activation, Akt phosphorylates AS160, one of the key regulators of GLUT4 vesicle, and proceeds on moving the vesicles carrying GLUT4 to the plasma membrane where GLUT4 is inserted in the cells and allows the entry of glucose. The phytochemicals such as quercetin, resveratrol, curcumin, and asiatic acid are better able to activate the above pathway (Sayem *et al.*, 2018).

The same way, with regards to the widespread distribution of flavonoids and their effect on diabetic retinopathy in comparison to its capacity to alleviate the oxidative stress which is associated with diabetes mellitus and the potential to become a therapeutic agent based on the effects. To a great extent, due to their antioxidant effect, plant metabolites, including flavonoids, have also been reported to be effective in the prevention of complications, including diabetic retinopathy, neuropathy, and nephropathy (Matos *et al.*, 2020). The sequence of the molecular interactions occurs when protocatechuic acid and cyanidin-3-O-β-glucoside are in the focus under discussion, which imitates insulin as a property and coordinates the amplification of the activity of PPARγ. The combination of their effect presupposes the most extensive anti-diabetic activity and their pharmacology impresses researchers (Jia *et al.*, 2020). Succinctly, the multifaceted research field on phytochemicals presents some of the paths of action in the treatment of diabetes such as insulin signals, glucose transportation, and diabetes retinopathy management. The scientific debate currently underway makes focus on research of medicinal properties of plants derived chemicals on-going research.

Naturally occurring compounds showed a major impact on the insulin signaling pathway by enhancing and initiating a cascade of molecular events. It involves the activation of Insulin Receptor Substrate 1 (IRS-1), which in turn recruits and activates Phosphoinositide 3-Kinase (PI3K). PI3K catalyzes the phosphorylation of Phosphatidylinositol Bisphosphate (PIP2) to Phosphatidylinositol Trisphosphate (PIP3), a key secondary messenger that enables the activation of Phosphoinositide-Dependent Kinase 1 (PDK1). PDK1 then phosphorylates and activates the central regulator of glucose metabolism, i.e., Protein Kinase B (Akt). Activated Akt promotes the translocation of Glucose Transporter Type 4 (GLUT4) to the plasma membrane, enabling efficient glucose uptake into muscle and adipose tissues. Additionally, Akt also inhibits Glycogen Synthase Kinase 3 (GSK3), thereby activating Glycogen Synthase (GS) and promoting glycogen synthesis. Phytochemicals modulate various nodes of this signaling cascade, either by enhancing receptor sensitivity, stabilizing IRS-1, or amplifying PI3K/Akt signaling. Their impact on GLUT4 translocation is particularly crucial, as it directly regulates cellular glucose uptake and utilization.

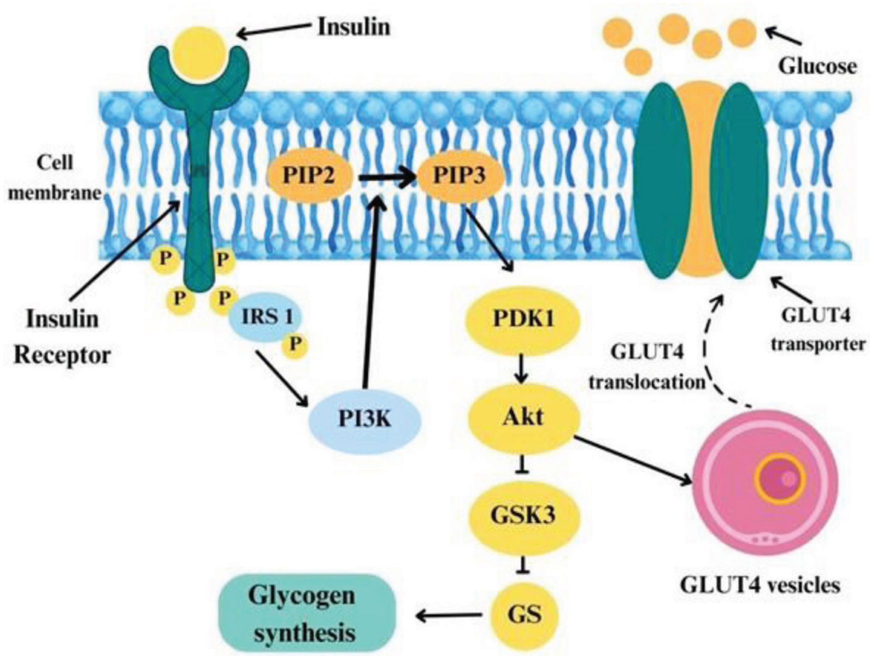


Figure 2: Effects on Key Molecular Target of Phytochemical Interactions in the Insulin Signals and Glycemic Regulation

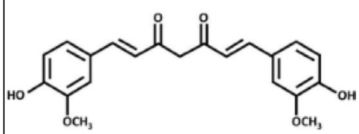
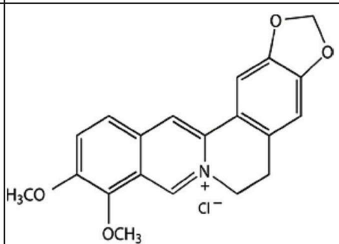
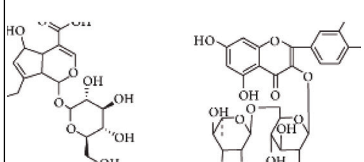
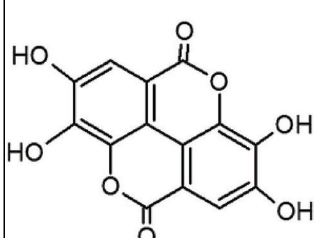
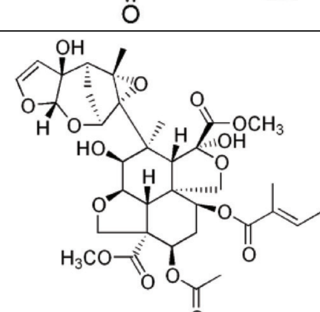
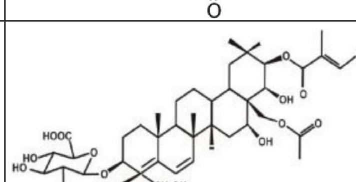
6. The Patient Side Effects and Potential Risks of Phytochemicals

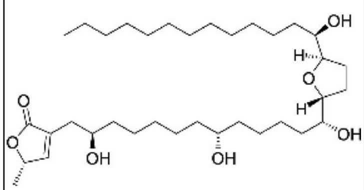
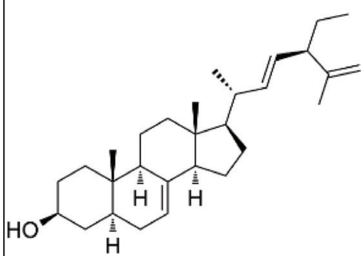
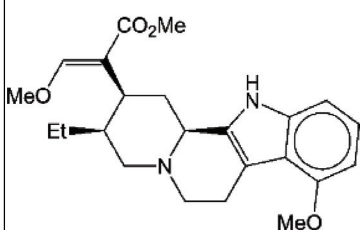
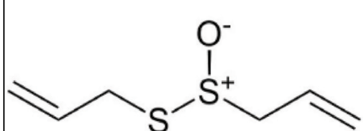
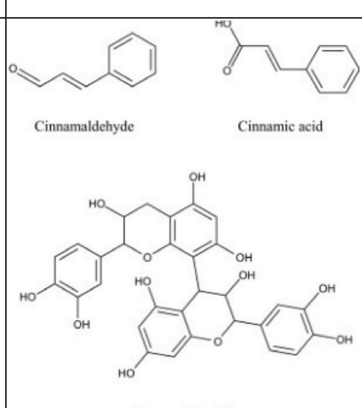
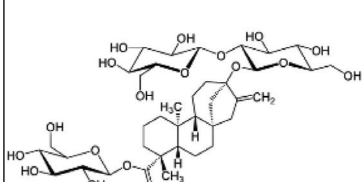
Numerous botanical ingredients must be researched thoroughly on their potential use in curing diabetes and its related dangers and adverse effects. The wide variety of research papers on phytochemicals is focused on this. Even though they can have curative worth in a number of the medicinal applications, a more balanced and informed perspective would involve the expertise of any side effects that could be experienced. Many studies have confirmed these threats and concerns, studies which have elevated the argument to the cautious scientific evaluation. A critical analysis refers to the negative consequences of herbs in the treatment of atherosclerosis, highlights the side effects that are inevitable when taking regular antidiabetic drugs, and highlights the importance of the safety assessment (Soltani *et al.*, 2021).

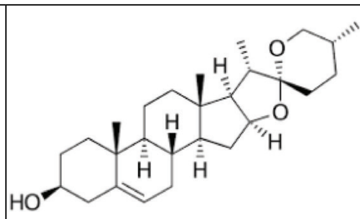
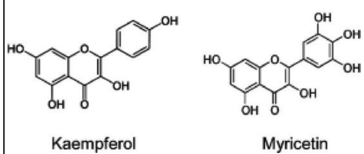
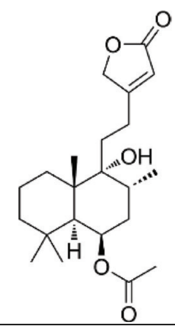
There are those substances that alter the activity of the enzymes that influence the vital metabolic pathways. The review of accretion of dangerous metabolites can be adverse, especially when the metabolite is consumed in their abundance. Other phytochemicals may lead to gastrointestinal upset, i.e., nausea and diarrhea, more especially when consumed in large doses. The alkaloids are neurotoxins and affect the nerve system, and the cardiac glycosides, which are not characteristic in addressing diabetes, but instead, it is the disorders in cardiac rhythms. The interactions to the traditional anti-diabetic medications can either increase the toxicity or reduce the activities.

The need to determine how safe they were in their use as a remedy of psoriasis, the delicate ratio between the effectiveness and the damage of derma treatment. These challenges highlight the necessity to review and observe how phytochemicals can be used in the treatment of diabetes (Tumusiime, 2025). The therapeutic possibilities of the chemicals are gigantic, which would have to be taken in close consideration with any side effects. The in-depth, careful, and descriptive examination of the safety profile of phytochemicals are pre-emptive precautions of the safe, prudent, and effective functioning of phytochemicals with the diversity of treatment therapies, and therefore makes it more challenging and riskier to discuss the possible medical applications of phytochemicals (Wanget *et al.*, 2022).

Table 2: Phytochemicals with Potentials Side Effects and Safety Considerations

Plant and their major Phytochemical	**Chemical Structure**	**Antidiabetic Effect**	**Potential Side Effects**	**Safety Considerations**	**References**
Curcuma Longa (Curcumin)		Suppresses oxidative stress, lowers blood glucose, improves insulin signaling	Nausea, diarrhea, kidney stone risk at high doses	Safe in moderate doses; poor bioavailability without enhancers like piperine	(Pivari *et al.*, 2019)
Berberis Vulgaris (Berberine)		Improves insulin sensitivity, reduces gluconeogenesis	GI discomfort, low blood pressure	Safe in moderate doses; caution with anticoagulants	(Imenshahidi & Hosseinzadeh, 2019)
Morinda Citrifolia (Scopoletin, damnacanthal)		Inhibits α-amylase/ α-glucosidase, enhances glucose uptake	Liver toxicity at high doses	Safe in traditional doses; monitor liver enzymes	(Algenstaedt *et al.*, 2018)
Syzygium cumini (Ellagic acid)		Inhibits starch conversion, lowers blood glucose	Hypo-glycemia, GI discomfort	Widely used in Ayurveda; safe in seed powder form	(Zanzabil *et al.*, 2023)
Azadirachta indica (Azadirachtin)		Lowers blood glucose, antioxidant, anti-inflammatory	Bitter taste, liver enzyme elevation	Safe in leaf extracts; caution with seed oil	(Zanzabil *et al.*, 2023)
Gymnema sylvestre (Gymnemic acids)		Inhibits glucose absorption, regenerates β-cells	Hypo-glycemia in combination with drugs	Safe in moderate doses; monitor blood sugar	(Zanzabil *et al.*, 2023)

Annona muricata (Acetogenins)		Inhibits α-amylase/ α-glucosidase, improves glucose tolerance	Neurotoxicity at high doses	Safe in leaf extracts; avoid prolonged use of seeds	(Boston *et al.*, 2020)
Cucurbita pepo (7,22,25-Stigmastatrienol)		Contains polysaccharides and antioxidants that help lower blood glucose and improve insulin tolerance	Generally well tolerated; excessive intake may cause mild gastrointestinal discomfort	Safe in dietary amounts; pumpkin seeds may interact with diuretics due to potassium content	(Gowtham *et al.*, 2022)
*Mitragyna speciosa (*Mitragynine)		May reduce blood glucose via alkaloid-mediated pathways; limited evidence.	Dependency risk, nausea, dizziness, liver toxicity, withdrawal symptoms.	Use with extreme caution; not recommended for routine antidiabetic therapy.	(Zailan *et al.*, 2022)
Allium sativum (Allicin S-allyl cysteine Diallyl disulfide)		Enhances insulin sensitivity, reduces fasting blood glucose, and improves lipid profile	GIT discomfort, bad breath, allergic reactions, bleeding risk at high doses	Generally safe in dietary amounts; caution with anticoagulants and surgery	(Uti *et al.*, 2025)
Cinnamomum verum (Cinnamaldehyde, Cinnamic acid)		Improves insulin receptor function, lowers blood glucose, and has antioxidant properties	Liver toxicity at high doses (especially with cassia cinnamon due to coumarin), allergic reactions	Safe in moderate dietary use; prefer C. verum over cassia to avoid coumarin toxicity	(Uti *et al.*, 2025)
Stevia rebaudiana (Steviol glycoside)		Inhibit α-amylase, DPP-4, and PPAR-γ; regulate blood glucose and reduce oxidative stress	Bloating, nausea, hypotension in sensitive individuals	Generally recognized as safe; monitor in hypotensive or pregnant individuals	(Shahid *et al.*, 2022)

Costus spicatus (Diosgenin)		Traditionally used to lower blood sugar; contains flavonoids and saponins with hypoglycemic potential	Limited data; possible diuretic effect, mild gastrointestinal upset	Insufficient clinical evidence; use cautiously and avoid in pregnancy until validated	(Azhagu Madhavan *et al.*, 2021)
Moringa oleifera (Kaempferol, Myricetin)		Reduces blood glucose, improves insulin secretion, and combats oxidative stress	Mild laxative effect, possible interactions with thyroid medications	Generally safe; monitor thyroid function	(Zainab *et al.*, 2020)
Vitex trifolia (Vitexilactone)		Exhibits significant α-amylase inhibitory activity, helping regulate postprandial blood glucose levels	May cause mild GI discomfort, dry mouth, headache, or allergic reactions	Generally considered safe in moderate doses. Avoid in cases of blood or stomach deficiency	(Wu *et al*, 2022)

7. Use and Therapeutical Implications of Phytochemical Anti-Diabetic Agents

Phytochemicals, being plant-based, have the potential to be efficiently utilized in the management of diabetes and its complications. Extensive studies on these bioactive compounds primarily reveal their wide-ranging uses and highlight the massive therapeutic potential they offer. A significant advancement in clinical research is the identification of berberine, the major constituent of *Berberis vulgaris* (barberry) roots, as a potent anti-diabetic agent. Berberine activates the AMPK pathway, which facilitates insulin sensitivity, enhances cellular glucose uptake, reduces hepatic glucose production, and modulates lipid metabolism, collectively contributing to glycemic control in diabetes (Imenshahidi and Hosseinzadeh, 2019).

Among the most promising anti-diabetic agents are the non-toxic extracts of *Stevia rebaudiana* Bertoli, which exhibit multiple biological activities (Ruiz-Ruiz *et al.*, 2017). Additionally, studies have identified new bioactive compounds in the genus *Cucurbita* (yellow and white pumpkin), which demonstrate anti-inflammatory and antimicrobial activity, contributing to diabetes management (Gowtham *et al.*, 2022). In-silico studies on *Moringa oleifera* phytochemicals propose their potential as diabetes mellitus therapeutics, opening doors to novel treatment approaches (Zainab *et al.*, 2020).

Molecular dynamics studies have assisted researchers in identifying specific phytochemicals as inhibitors of biological pathways implicated in diabetic nephropathy, thereby mitigating secondary complications associated with diabetes (Kausar *et al.*, 2022). The methanolic extract of *Mitragyna speciosa* has also been analyzed, confirming its significant potential in diabetes treatment alongside other vegetable-based interventions (Zailan *et al.*, 2022). Similarly, *Syzygium cumini* has been studied using integrative computational and pharmacological strategies, revealing its therapeutic potential due to its rich phytochemical composition (Rashid *et al.*, 2022). Research on *Costus spicatus* phytochemicals indicates their applicability in managing diabetes mellitus, suggesting a role as an adjuvant in treatment strategies (Rashid *et al.*, 2022).

In conclusion, anti-diabetic phytochemicals represent a highly promising field of therapeutic research. Their multiple mechanisms of action and intrinsic potency make them attractive for future investigation. As the number of plant-based interventions increases, the opportunities to develop innovative approaches to diabetes management also expand.

8. Phytochemicals: Recent Studies and Future Outlook in the Treatment of Diabetes

The study of phytochemicals from a wide variety of plants appears promising in the overall field of diabetes therapy.

Ongoing research aims to elucidate and develop the full therapeutic potential of these substances, fostering optimism for combined or complementary diabetes treatments in the future. Active bioactive compounds present in plants are expanding the scientific understanding of therapeutics, demonstrating significant effects in diabetes management (Shanak *et al.*, 2019).

Recent studies highlight the complexity of treating diabetic nephropathy and identify key advances in therapeutic strategies, marking steps toward more efficient disease management (Khazeei Tabari *et al.*, 2022). Phytochemicals have also been shown to modulate the insulin signaling pathway, particularly by promoting GLUT4 translocation, a crucial mechanism for enhanced glucose uptake in response to insulin (Khazeei Tabari *et al.*, 2022). Their epigenetic regulatory effects further support their potential as diabetes therapeutics, paving the way for the development of personalized treatment strategies (Shanak *et al.*, 2019).

Flavonoids, polyphenols, alkaloids, and terpenoids have demonstrated significant benefits in both in vitro and in vivo models. However, challenges such as poor bioavailability and lack of standardization currently limit their clinical application. Phytochemicals are increasingly being studied for their nutrigenomic and epigenetic properties in addition to their biochemical effects. They can modulate gut microbiota, alter gene expression, and contribute to the design of personalized treatment regimens for diabetes patients (Qin *et al.*, 2022).

Pigment-based phytochemicals, such as anthocyanins, carotenoids, and curcumin, are of particular interest for their ability to modulate inflammatory and metabolic signaling pathways relevant to type 2 diabetes (Qin *et al.*, 2022). The Nrf2-ARE pathway plays a critical role in antioxidant defenses, redox signaling, and gut microbiota balance, providing a mechanistic basis through which phytochemicals can confer protection against oxidative stress and metabolic dysregulation in diabetes (Root *et al.*, 2017).

Overall, phytochemicals demonstrate significant potential in the site-specific and natural treatment of diabetes. Their increasing research presence continues to inspire innovative therapeutic strategies, with future prospects including management of diabetic retinopathy and other diabetes-related complications.

9. Anti-Diabetic Phytochemicals Conjugated in Applications and Therapy

Phytochemicals, derived from numerous plant sources, can be effectively employed in the treatment of diabetes and its related complications. Extensive research on these bioactive compounds demonstrates their broad therapeutic potential. Substantive studies have sought to extend the boundaries of traditional treatments. A notable advancement in clinical research is the identification of *Berberis vulgaris* (berberine), a potent agent and the primary constituent of barberry roots. Berberine activates the AMPK pathway, enhancing insulin sensitivity, promoting cellular glucose uptake, reducing hepatic glucose production, and improving lipid metabolism, collectively resulting in glycemic control (Imenshahidi & Hosseinzadeh, 2019).

Focusing on promising anti-diabetic agents, *Stevia rebaudiana* Bertoli extracts have shown significant pharmacological potential due to their non-toxic nature and multiple biological activities (Ruiz-Ruiz *et al.*, 2017). Research on *Cucurbita* species (yellow and white pumpkin) has revealed bioactive compounds with anti-inflammatory and antimicrobial properties, which contribute to diabetes management (Gowtham *et al.*, 2022). In-silico studies on *Moringa oleifera* phytochemicals suggest their potential as therapeutic agents for diabetes mellitus, opening pathways for innovative treatment strategies (Zainab *et al.*, 2020).

Molecular dynamics simulations have facilitated the identification of specific phytochemicals as inhibitors of key biological pathways implicated in diabetic nephropathy, mitigating secondary complications associated with diabetes (Kausar *et al.*, 2022). The phytochemical composition, antioxidant activity, and anti-diabetic potential of *Mitragyna speciosa* methanolic extract demonstrate its significance as an adjunctive therapy in plant-based diabetes interventions (Zailan *et al.*, 2022). Similarly, computational and pharmacological analyses of *Syzygium cumini* have revealed its rich phytochemical profile and possible therapeutic outcomes, expanding the repertoire of natural therapies (Rashid *et al.*, 2022). Phytochemical screening of *Costus spicatus* also indicates its potential in diabetes management, further supporting its use as an alternative or complementary treatment (Rashid *et al.*, 2022).

In summary, anti-diabetic phytochemicals represent a promising frontier in contemporary therapeutic research. Their diverse mechanisms of action and intrinsic efficacy underscore the need for continued investigation. As the range of plant-based interventions expands, opportunities to develop novel approaches for diabetes care will continue to grow.

10. Recent Studies and Future Outlook of Phytochemicals in the Treatment of Diabetes

Phytochemicals are increasingly becoming a major focus of research in the multifaceted field of diabetes and its complications. Their diverse bioactive profiles possess therapeutic potential, positioning them as viable options for future diabetes management. Recent findings indicate that innovative solution processing methods can enhance the properties of bulk heterojunction films and conjugated polymers, potentially improving diabetes monitoring and treatment (Noguchi *et al.*, 2006). Non-invasive biosensors utilizing adjustable solid polymer electrolytes can now measure glucose levels in flexible and wearable formats, reducing the need for frequent finger-prick tests (Noguchi *et al.*, 2006).

Additionally, studies on M-Kyoto solutions demonstrate potential in promoting the generation of functional cellular "islands" post-isolation, aiding in diabetes treatment through the regulation of trypsin and collagenase activity (Chugh *et al.*, 2019). Recent agricultural research focuses on optimizing phytochemical profiles in crops, creating a paradigm shift toward functional foods rich in phytoceuticals and nutraceuticals, surpassing traditional agricultural methods (AlSabagh *et al.*, 2023).

Curcumin is emerging as a key therapeutic agent in diabetes research, showing the ability to prevent angiogenic reactions in diabetic rat models and contributing to nutrition-centered wellness systems (Janssens *et al.*, 2015). Intramyocellular lipids (IMCL) in lean and diabetic rats have also been identified as critical energy sources during exercise, emphasizing the synergy between physical activity and diabetes management (Zhang *et al.*, 2025).

Furthermore, extracts of *Blumea eriantha* have shown potential in inhibiting metastasis, opening new avenues for research in diabetes complications and overall disease management (Bora, 2021). The dynamic effects of phytochemicals, combined with exercise and dietary interventions, underscore their multifaceted role in diabetes care.

With the growing therapeutic applications of phytochemicals, a new era of innovation emerges, providing solutions for the challenges of diabetes management and offering a promising frontier in preventive and therapeutic strategies.

Table 3: Overview of Polyphenols (flavonoids) and their Sources

S.No.	Plant Parts/Extract Used	Phytochemical Responsible	Antidiabetic Potential	Antioxidative Potential	Reference
1	Leaves, fruits, seeds, peels	Polyphenols, carotenoids	Yes	Yes	Liang *et al.*, 2022
2	Fruits, vegetables, nuts, cocoa, tea, grain seeds, herbs	Flavonoids	Yes	Yes	Al-Ishaq *et al.*, 2019
3	Tea leaves, herbs, citrus fruits, Radix puerariae root	Flavonoids, flavonols, flavanols, isoflavones, flavanones, anthocyanidins	Yes	Yes	Jubaidi *et al.*, 2021
4	NA	Polyphenols	NA	NA	Panda *et al.*, 2025
5	Roots, bark, leaves, seeds	Alkaloids, flavonoids, sesquiterpene lactones, diterpenes, triterpenes, naphthoquinones	NA	NA	Panda *et al.*, 2025
6	Roots, stems, fruits, leaves	Polyphenols, 3β-taraxerol, Astragalus polysaccharide, cyanidin-3-O-β-glucoside, protocatechuic acid, daidzein, iridoid, catalpol, specioside, verminoside, gallic acid, berberine, vanillic acid, piperine, pipernonaline, dehydropipernonaline, ellagitannins, kotalanol, salacinol, mangiferin	Yes	Yes	Sayem *et al.*, 2018
7	Fruits, leaves, seeds, bark, stem bark, aerial plant parts, rhizome	Polyphenols, flavonoids, alkaloids, stilbenes, organosulfurs, sesquiterpenes, phytosterols	Yes (genistein, organosulfur, sesquiterpene, phytosterols)	Yes (polyphenols, flavonoids, resveratrol)	Matos *et al.*, 2020
8	Flower extract (Costus spicatus)	Alkaloids, carbohydrates, flavonoids, proteins, amino acids, phenols, tannins, glycosides, steroids	NA	Yes	Azhagu Madhavan *et al.*, 2021
9	Leaves of pear, soursop, and moco-moco	Alkaloids, flavonoids, saponins, tannins	Yes	Yes	Boston *et al.*, 2020

10	Momordica charantia, Pterocarpus marsupium Roxb., Trigonella foenum-graecum	Terpenoids, alkaloids, flavonoids, phenolics	Yes	NA	Bora, 2021
11	Roots and rhizomes	Flavonoids, phenolic compounds, alkaloids, phytosteroids, saponins, tannins, terpenoids, anthraquinones, cardiac glycosides	Yes	NA	Zanzabil *et al.*, 2023
12	Whole grains (rootlets)	Phenolic acids, flavonoids	NA	Yes	Salehi *et al.*, 2019
13	Leaves	Carotene, thiamine, austroinulin, riboflavin, diverse terpenes, flavonoids, steviol glycosides (stevioside, rebaudioside A, rebaudioside C, dulcoside)	Yes	Yes	Ruiz-Ruiz *et al.*, 2017
14	Peel, flesh, and seed of yellow and white pumpkin varieties	Tannins, flavonoids, steroids, saponins, carbohydrates, proteins, alkaloids, phenols	Yes	Yes	Gowtham *et al.*, 2022
15	Leaves, seeds, pods (Moringa oleifera)	Anthraquinones, 2-phenylchromenylium (anthocyanins), hemlock tannin, sitogluside (glycoside)	Yes	NA	Zainab *et al.*, 2020
16	Leaves (Mitragyna speciosa), Chelonanthus albus, Annona cherimola, Liriodendron tulipifera, Artabotrys hexapetalus	Flavonoids, polyphenols	Yes	Yes	Zailan *et al.*, 2022
17	Roots, stems, fruits, leaves	Polyphenols, 3β-taraxerol, Astragalus polysaccharide, cyanidin-3-O-β-glucoside, protocatechuic acid, daidzein, iridoid, catalpol, specioside, verminoside, vanillic acid, pipernonaline, dehydropipernonaline, ellagitannins, kotalanol, salacinol, mangiferin	Yes	Yes	Jia *et al.*, 2020
18	Roots, leaves, fruits	Flavonoids, polyphenols, lignans, pyranocoumarins, iridoid glycosides, xanthones, phytoestrogens, anthraquinones, naphthoquinones, sesquiterpenes, monoterpene glycosides, isothiocyanates, anthocyanins, isoquinolines	Yes	Yes	Tabari *et al.*, 2022

11. Conclusion

The massive potential of the phytochemicals—bioactive compounds of plants—in the management of diabetes, together with its complications, has recently been placed under the spotlight and proves immersive potential. Substantial compounds supplied are flavonoids, curcumin, luteolin, and all compounds produced out of Brassica vegetables that have demonstrated superior anti-diabetic effect. Their salient features include protection of pancreatic beta-cells, insulin secretion, insulin insensitivity, and regulated glucose metabolism. These phytochemicals have other health benefits besides glycemic control, and these include being anti-inflammatory, balancing gut microbiota, and preventing metabolic syndrome, which again supports the holistic impact of the chemicals on human health. The line of study of phytochemicals in the management of diabetes is growing and diversifying rapidly, with a curiosity in their pharmacodynamics and mechanism of action. It can also be applied in the study of new ways of treating the disease. Although it has massive potential, phytochemicals must be evaluated with regard to safety, bioavailability, and long-term impact to ensure that they can be useful in clinical practice. Finally, another dynamic and multidisciplinary strategy in the treatment of diabetes, combining traditional knowledge and biomedical science, is the use of phytochemicals. Their implementation into treatment programs can change the negative chronic metabolic processes strategies unless sustained research establishes and maximizes their application.

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Declaration

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Conflict of Interest

The authors declare that there is no conflict of interest.

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