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Review Article

Phytochemical Profiling and In-Vitro Antidiabetic Evaluation of Costus Igneus and Vernonia Amygdalina Leaf Extracts: A Comprehensive Review

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ABSTRACT

Diabetes mellitus is one of the most prevalent chronic metabolic disorders worldwide and is characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. The increasing global burden of diabetes, coupled with the limitations and adverse effects associated with conventional antidiabetic drugs, has accelerated the search for safer and more effective plant-derived therapeutic alternatives. Medicinal plants rich in bioactive phytochemicals have emerged as promising candidates owing to their multitarget mechanisms, antioxidant potential, and comparatively lower toxicity. Among these, Costus igneus (Insulin Plant) and Vernonia amygdalina (Bitter Leaf) have attracted considerable scientific attention because of their traditional use in the management of diabetes and their diverse pharmacological properties. This review comprehensively summarizes the phytochemical composition, extraction techniques, phytochemical profiling approaches, and in-vitro antidiabetic activities of Costus igneus and Vernonia amygdalina. Major phytoconstituents identified in these plants include flavonoids, phenolic acids, alkaloids, tannins, terpenoids, saponins, glycosides, phytosterols, and various antioxidant compounds. Advanced analytical techniques have significantly enhanced the identification and characterization of these bioactive molecules. The review further discusses the antidiabetic mechanisms demonstrated through various in-vitro experimental models, including α-amylase inhibition, α-glucosidase inhibition, glucose uptake assays, glucose diffusion retardation, protein glycation inhibition, pancreatic β-cell protection, antioxidant assays, and insulin-mimetic activities. Overall, the available evidence suggests that Costus igneus and Vernonia amygdalina represent valuable natural reservoirs of bioactive compounds with substantial potential for the development of novel plant-based antidiabetic therapeutics. Their multifunctional pharmacological properties support their continued investigation as complementary and alternative strategies for diabetes management. This review provides an updated scientific perspective that may facilitate future translational research and pharmaceutical development in herbal antidiabetic therapy.

Introduction

Diabetes mellitus (DM) represents one of the fastest-growing non-communicable diseases worldwide and poses a significant challenge to global healthcare systems. The disease is characterized by chronic hyperglycemia resulting from impaired insulin secretion, defective insulin action, or a combination of both, leading to disturbances in carbohydrate, lipid, and protein metabolism. Persistent hyperglycemia is associated with progressive damage to multiple organ systems, including the kidneys, eyes, nervous system, cardiovascular system, and peripheral vasculature. Consequently, diabetes contributes substantially to morbidity, premature mortality, and escalating healthcare expenditures across both developed and developing nations [1].

According to the International Diabetes Federation (IDF), more than 537 million adults were living with diabetes in 2021, and this number is projected to exceed 783 million by 2045 if current trends continue. Type 2 diabetes mellitus (T2DM) accounts for approximately 90–95% of all diagnosed cases and is strongly associated with obesity, sedentary lifestyle, aging, unhealthy dietary habits, chronic inflammation, oxidative stress, and genetic predisposition. The rapidly increasing prevalence of diabetes in low- and middle-income countries has further complicated disease management because of limited healthcare resources and inadequate access to modern pharmacotherapy.

Current pharmacological management of diabetes primarily includes biguanides, sulfonylureas, meglitinides, thiazolidinediones, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, α-glucosidase inhibitors, and exogenous insulin therapy. Although these therapeutic agents have substantially improved glycemic control, their long-term clinical application is often associated with adverse effects such as hypoglycemia, gastrointestinal disturbances, hepatotoxicity, nephrotoxicity, weight gain, cardiovascular risks, reduced patient compliance, and progressive decline in therapeutic effectiveness. These limitations have prompted extensive research into safer, affordable, and multitarget therapeutic alternatives derived from natural products [2,3].

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Medicinal plants have served as the foundation of traditional healthcare systems for thousands of years and continue to contribute significantly to modern drug discovery. Approximately 80% of the world's population relies partially on herbal medicines for primary healthcare, particularly in developing countries. Plant-derived secondary metabolites possess remarkable structural diversity and exhibit multiple pharmacological activities including antioxidant, anti-inflammatory, antihyperglycemic, antihyperlipidemic, immunomodulatory, antimicrobial, hepatoprotective, nephroprotective, and cardioprotective properties. Unlike synthetic drugs that frequently target a single molecular pathway, phytochemicals often modulate several interconnected biochemical pathways simultaneously, making them particularly attractive for managing complex metabolic disorders such as diabetes [4].

Among numerous medicinal plants investigated for antidiabetic activity, Costus igneus (Insulin Plant) and Vernonia amygdalina (Bitter Leaf) have emerged as highly promising botanical candidates. Costus igneus, belonging to the family Costaceae, has gained widespread recognition in India because diabetic patients traditionally consume its fresh leaves to reduce blood glucose levels. Experimental investigations have demonstrated that the plant possesses antihyperglycemic, antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, nephroprotective, hypolipidemic, and insulin-sensitizing activities. These biological effects are primarily attributed to flavonoids, terpenoids, alkaloids, phenolic compounds, glycosides, phytosterols, and other bioactive constituents present in its leaves.

Similarly, Vernonia amygdalina, commonly known as Bitter Leaf, is extensively used throughout Africa as both a medicinal herb and a functional food. The leaves contain abundant quantities of sesquiterpene lactones, flavonoids, saponins, steroidal glycosides, phenolic acids, tannins, alkaloids, and dietary antioxidants. Numerous experimental studies have demonstrated its ability to improve insulin sensitivity, suppress oxidative stress, inhibit carbohydrate-hydrolyzing enzymes, reduce inflammatory mediators, protect pancreatic β-cells, and regulate glucose metabolism. Furthermore, its long history of dietary consumption supports its potential safety for long-term therapeutic applications [5].

Recent advances in analytical chemistry have enabled comprehensive phytochemical profiling of medicinal plants through sophisticated analytical platforms such as HPLC, UHPLC, LC-MS/MS, GC-MS, FTIR spectroscopy, HPTLC, and metabolomics-based

approaches. These technologies have facilitated accurate identification, quantification, and structural elucidation of biologically active compounds responsible for antidiabetic activity. Simultaneously, various in-vitro screening models—including α-amylase inhibition, α-glucosidase inhibition, glucose uptake assays, glucose diffusion studies, advanced glycation end-product inhibition assays, pancreatic β-cell protection models, and antioxidant assays—have become indispensable tools for evaluating the pharmacological potential of herbal extracts before in-vivo and clinical investigations [6].

This review aims to provide a comprehensive and updated overview of the phytochemical composition, extraction methodologies, analytical profiling techniques, and in-vitro antidiabetic potential of Costus igneus and Vernonia amygdalina. The review further discusses their molecular mechanisms of action, comparative pharmacological efficacy, therapeutic prospects, existing limitations, and future research directions. By integrating traditional knowledge with recent scientific evidence, this review seeks to highlight the potential of these medicinal plants as valuable sources for developing novel plant-based antidiabetic therapeutics.

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Global Burden of Diabetes Mellitus

Diabetes mellitus (DM) has emerged as one of the most significant public health challenges of the twenty-first century. It is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Persistent elevation of blood glucose levels leads to progressive damage of multiple organs, including the pancreas, kidneys, retina, peripheral nerves, cardiovascular system, and liver. Consequently, diabetes is associated with increased morbidity, premature mortality, reduced quality of life, and substantial socioeconomic burden.

The global prevalence of diabetes has risen dramatically over the past three decades due to rapid urbanization, sedentary lifestyles, unhealthy dietary habits, obesity, population aging, and genetic susceptibility. Unlike infectious diseases, diabetes requires lifelong management, making it one of the most expensive chronic diseases worldwide. The growing incidence of diabetes in developing countries has further intensified healthcare challenges because of inadequate access to diagnostic facilities, medications, and preventive healthcare services [16-19].

Epidemiology of Diabetes

According to the International Diabetes Federation (IDF), approximately 537 million adults aged 20–79 years were living with diabetes in 2021. This number is projected to increase to 643 million by 2030 and 783 million by 2045, representing one of the fastest-growing global epidemics. More than three-quarters of diabetic patients reside in low- and middle-income countries, where healthcare resources are often inadequate to manage the disease effectively.

Type 2 diabetes mellitus (T2DM) accounts for approximately 90–95% of all diabetes cases and is primarily associated with obesity, insulin resistance, genetic predisposition, physical inactivity, and unhealthy dietary practices. Type 1 diabetes mellitus (T1DM), although less prevalent, results from autoimmune destruction of pancreatic β-cells leading to absolute insulin deficiency. Gestational diabetes mellitus (GDM) also contributes significantly to maternal and neonatal morbidity, increasing the future risk of T2DM in both mother and offspring.

India is recognized as one of the countries with the largest diabetic populations worldwide. Rapid socioeconomic development, urban migration, westernized diets, decreased physical activity, and increasing obesity have substantially contributed to the rising prevalence of diabetes across both urban and rural populations. The coexistence of diabetes with hypertension, dyslipidemia, and cardiovascular diseases further complicates disease management and increases healthcare expenditure [20,21].

Limitations of Conventional Antidiabetic Drugs

The management of diabetes mellitus has evolved considerably over the last century, with the introduction of numerous pharmacological agents that effectively

lower blood glucose levels and reduce the risk of diabetes-related complications. Current therapeutic options include insulin preparations, biguanides, sulfonylureas, meglitinides, thiazolidinediones, α-glucosidase inhibitors, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, dual incretin agonists, and several emerging biological therapies. Although these medications have significantly improved glycemic control and patient survival, none provides a permanent cure for diabetes. Instead, most therapies focus on symptom management by controlling hyperglycemia while the underlying metabolic dysfunction continues to progress.

Long-term pharmacotherapy is frequently associated with adverse drug reactions, declining therapeutic efficacy, poor patient compliance, high treatment costs, and increased risk of drug interactions. Furthermore, conventional antidiabetic agents generally target one or two specific metabolic pathways, whereas diabetes is a multifactorial disease involving insulin resistance, oxidative stress, chronic inflammation, mitochondrial dysfunction, lipid abnormalities, endothelial impairment, and pancreatic β-cell failure. These shortcomings have prompted growing interest in identifying safer and multitarget therapeutic agents from medicinal plants [23,24].

Current Classes of Antidiabetic Drugs

Modern pharmacological treatment of diabetes consists of several therapeutic classes, each targeting a specific aspect of glucose metabolism.

Major Classes of Antidiabetic Drugs

Table 1: Major Classes of Antidiabetic Drugs

Drug Class	Examples	Primary Mechanism
Biguanides	Metformin	Decreases hepatic glucose production
Sulfonylureas	Glibenclamide, Glipizide	Stimulate insulin secretion
Meglitinides	Repaglinide, Nateglinide	Rapid insulin release
Thiazolidinediones	Pioglitazone	Improve insulin sensitivity
α-Glucosidase inhibitors	Acarbose, Miglitol	Delay carbohydrate digestion
DPP-4 inhibitors	Sitagliptin, Linagliptin	Increase endogenous incretin activity
GLP-1 receptor agonists	Semaglutide, Liraglutide	Enhance insulin secretion and suppress appetite
SGLT2 inhibitors	Empagliflozin, Dapagliflozin	Increase urinary glucose excretion
Insulin	Rapid-, intermediate-, and long-acting insulin	Replace endogenous insulin

Despite their diverse mechanisms, these medications present several limitations that restrict long-term therapeutic success.

Limitations of Biguanides

Metformin remains the first-line treatment for Type 2 diabetes because of its effectiveness, relatively low cost, and cardiovascular benefits. It primarily suppresses hepatic gluconeogenesis while improving peripheral insulin sensitivity [25].

However, prolonged therapy may result in several complications.

Major limitations

- Gastrointestinal intolerance
- Nausea
- Diarrhea
- Metallic taste
- Vitamin B12 deficiency
- Reduced patient compliance

Metformin is contraindicated in patients with severe renal impairment because of the potential risk of lactic acidosis, a rare but life-threatening complication.

Although metformin effectively lowers blood glucose levels, it cannot reverse pancreatic β-cell degeneration or completely eliminate insulin resistance.

Limitations of Sulfonylureas

Sulfonylureas stimulate pancreatic β-cells to release insulin irrespective of circulating blood glucose concentration [26].

Common drugs include:

- Glibenclamide
- Glimepiride
- Gliclazide
- Glipizide

Major drawbacks

- Severe hypoglycemia
- Weight gain
- Progressive β-cell exhaustion
- Reduced long-term efficacy
- Limited effectiveness in advanced diabetes

Continuous stimulation of pancreatic β-cells accelerates β-cell dysfunction, ultimately necessitating insulin therapy in many patients.

Limitations of Thiazolidinediones

Thiazolidinediones improve insulin sensitivity through activation of peroxisome proliferator-activated receptor gamma (PPAR-γ) [27].

Representative drugs include:

- Pioglitazone
- Rosiglitazone

Although effective in improving insulin resistance, their clinical application has declined because of several safety concerns.

Major adverse effects

- Fluid retention
- Peripheral edema
- Weight gain
- Increased fracture risk
- Congestive heart failure
- Possible bladder cancer risk

These adverse effects substantially restrict their long-term use, particularly in elderly patients with cardiovascular disease.

Limitations of α-Glucosidase Inhibitors

α-Glucosidase inhibitors delay carbohydrate digestion within the small intestine, thereby reducing postprandial hyperglycemia [28].

Examples include:

- Acarbose
- Miglitol
- Voglibose

However, poor gastrointestinal tolerability frequently limits patient acceptance.

Common adverse reactions include:

- Flatulence
- Abdominal discomfort
- Diarrhea
- Bloating

Because these drugs mainly control postprandial glucose excursions, they are often insufficient as monotherapy in advanced diabetes.

Limitations of DPP-4 Inhibitors

DPP-4 inhibitors prolong incretin activity, thereby increasing glucose-dependent insulin secretion [29].

Examples include:

- Sitagliptin
- Saxagliptin
- Linagliptin
- Vildagliptin

Although generally well tolerated, several limitations remain.

Limitations

- Moderate glucose-lowering efficacy
- High treatment cost
- Possible pancreatitis
- Joint pain
- Requirement for lifelong therapy

They also exhibit limited efficacy in patients with severe β-cell dysfunction.

Limitations of SGLT2 Inhibitors

SGLT2 inhibitors reduce blood glucose by increasing urinary glucose excretion [30].

Common agents include:

- Empagliflozin
- Dapagliflozin
- Canagliflozin

These drugs provide significant cardiovascular and renal protection; however, several concerns persist.

Major limitations

- Urinary tract infections
- Genital fungal infections
- Polyuria
- Dehydration
- Hypotension
- Euglycemic diabetic ketoacidosis

Their effectiveness also declines with progressive renal impairment.

Limitations of GLP-1 Receptor Agonists

GLP-1 receptor agonists have transformed diabetes treatment because of their combined antihyperglycemic and weight-loss effects [31].

Examples include:

- Semaglutide
- Liraglutide
- Dulaglutide
- Exenatide

Despite their clinical advantages, these agents possess several disadvantages.

Limitations

- Injectable administration
- Gastrointestinal adverse effects
- High treatment cost
- Poor accessibility in developing countries
- Long-term adherence issues

Nausea and vomiting remain the most frequently reported side effects during initiation of therapy.

Limitations of Insulin Therapy

Insulin remains the cornerstone treatment for Type 1 diabetes and advanced Type 2 diabetes.

Although lifesaving, insulin therapy presents multiple practical limitations.

Clinical challenges

- Frequent injections
- Pain and discomfort
- Risk of severe hypoglycemia
- Weight gain
- Lipodystrophy
- Dose adjustment complexity
- Continuous glucose monitoring requirement

Furthermore, insulin replacement cannot completely restore physiological pancreatic function or prevent disease progression.

Drug Resistance and Progressive Disease

Type 2 diabetes is characterized by progressive β-cell dysfunction.

Initially, patients respond well to oral hypoglycemic agents; however,

- insulin secretion gradually declines,
- insulin resistance worsens,
- combination therapy becomes necessary,
- insulin replacement eventually becomes unavoidable.

This progressive nature limits the long-term effectiveness of conventional pharmacotherapy.

Economic Burden of Pharmacotherapy

Diabetes management imposes a substantial financial burden on patients and healthcare systems.

Major contributors include:

- lifelong medication
- regular physician consultations
- laboratory monitoring
- insulin supplies
- glucose monitoring devices
- management of complications

In low- and middle-income countries, many patients discontinue therapy because of financial constraints, leading to poor glycemic control and increased complications.

Need for Plant-Based Therapeutics

The limitations of conventional drugs have renewed scientific interest in medicinal plants possessing antihyperglycemic activity.

Plant-derived phytochemicals offer several potential advantages.

Advantages of medicinal plants

- Multitarget mechanism of action
- Lower incidence of adverse effects
- Natural antioxidant properties
- Anti-inflammatory activity
- Improvement of insulin sensitivity
- Protection of pancreatic β-cells
- Cost-effectiveness
- Better patient acceptability
- Potential synergistic effects among multiple phytochemicals

Unlike synthetic drugs, medicinal plants contain numerous bioactive constituents—including flavonoids, alkaloids, terpenoids, tannins, phenolic acids, glycosides, saponins, and phytosterols—that act simultaneously on multiple biochemical pathways involved in diabetes. Such multitarget pharmacological activity may help overcome several limitations associated with single-target synthetic drugs.

Rationale for Investigating Costus igneus and Vernonia amygdalina

Among the numerous medicinal plants investigated for diabetes management, Costus igneus and Vernonia amygdalina have gained considerable scientific

attention because of their rich phytochemical composition and documented antidiabetic activity.

Experimental studies indicate that extracts of these plants can:

- inhibit α-amylase and α-glucosidase enzymes,
- enhance glucose uptake,
- improve insulin sensitivity,
- reduce oxidative stress,
- suppress inflammatory mediators,
- protect pancreatic β-cells,
- improve lipid metabolism,
- reduce advanced glycation end-product formation.

Their diverse phytochemical profile suggests that these medicinal plants may provide complementary or alternative therapeutic strategies for diabetes management while minimizing adverse effects commonly associated with conventional pharmacotherapy [33].

Role of Medicinal Plants in Diabetes Management

Medicinal plants have served as the foundation of healthcare systems for thousands of years and continue to play an indispensable role in the prevention and treatment of numerous chronic diseases. Among these, diabetes mellitus has emerged as one of the primary targets of herbal therapeutics because of its multifactorial pathogenesis and the limitations associated with conventional pharmacotherapy. The increasing prevalence of diabetes, coupled with the adverse effects, high costs, and declining long-term efficacy of synthetic antidiabetic drugs, has renewed scientific interest in plant-derived bioactive compounds as alternative or complementary therapeutic agents.

According to the World Health Organization (WHO), approximately 80% of the global population relies partly on herbal medicines for primary healthcare, particularly in developing countries where medicinal plants are affordable, accessible, and culturally accepted. Traditional systems of medicine such as Ayurveda, Siddha, Unani, Traditional Chinese Medicine (TCM), and African ethnomedicine have documented hundreds of medicinal plants possessing antihyperglycemic activity. Scientific investigations over the past three decades have validated many of these traditional claims by identifying bioactive phytochemicals capable of regulating glucose metabolism through multiple molecular pathways [34].

Historical Perspective of Herbal Medicine in Diabetes

The medicinal use of plants for diabetes predates modern pharmacology by several centuries. Ancient civilizations recognized the symptoms of excessive urination and sweetness of urine and employed herbal remedies to alleviate these conditions.

In the Ayurvedic system of medicine, diabetes is referred to as Madhumeha, meaning "honey urine," and is described as a metabolic disorder involving impaired digestion and altered tissue metabolism. Classical Ayurvedic texts recommend numerous medicinal plants, including Gymnema sylvestre, Momordica charantia, Azadirachta indica, Tinospora cordifolia, Trigonella foenum-graecum, and Costus igneus, for glycemic control.

Similarly, Traditional Chinese Medicine utilizes herbs such as Panax ginseng, Coptis chinensis, and Astragalus membranaceus to restore metabolic balance and improve insulin sensitivity. African traditional medicine extensively employs Vernonia amygdalina (bitter leaf), Moringa oleifera, and Ocimum gratissimum in the management of diabetes and associated metabolic disorders [35].

The continued use of these medicinal plants across different cultures has encouraged scientific investigations into their phytochemical composition and pharmacological mechanisms.

Importance of Plant-Derived Phytochemicals

Plants synthesize a vast array of secondary metabolites that contribute to their defense against environmental stress and pathogens. Many of these secondary metabolites exhibit significant pharmacological activities in humans. Unlike synthetic drugs that usually target a single receptor or enzyme, phytochemicals simultaneously regulate multiple biochemical pathways involved in diabetes progression.

The principal classes of antidiabetic phytochemicals include:

- Flavonoids
- Phenolic acids
- Alkaloids
- Terpenoids
- Tannins
- Saponins
- Glycosides
- Phytosterols
- Coumarins
- Lignans
- Anthraquinones
- Carotenoids

Mechanisms of Antidiabetic Action of Medicinal Plants

Medicinal plants regulate blood glucose through multiple interconnected mechanisms rather than a single biochemical pathway.

Table 2: Major Phytochemicals and Their Antidiabetic Activities

Phytochemical Class	Major Compounds	Antidiabetic Activity
Flavonoids	Quercetin, Kaempferol	Improve insulin sensitivity, antioxidant
Phenolic acids	Gallic acid, Chlorogenic acid	Reduce oxidative stress
Alkaloids	Berberine-like alkaloids	Improve glucose metabolism
Terpenoids	Corosolic acid	Enhance glucose uptake
Tannins	Gallotannins	α-Amylase inhibition
Saponins	Steroidal saponins	Improve insulin secretion
Phytosterols	β-Sitosterol	Improve lipid metabolism
Glycosides	Various glycosides	Insulin-mimetic activity

Botanical and Ethnomedicinal Profile of Costus igneus

Costus igneus Nak. (family: Costaceae), commonly known as the "Insulin Plant," is an important medicinal herb widely recognized for its traditional application in the management of diabetes mellitus and other metabolic disorders. It is a perennial, rhizomatous plant native to tropical regions and is extensively cultivated in India and other tropical countries due to its ornamental value and therapeutic importance. The plant belongs to the order Zingiberales and is closely related to the ginger family (Zingiberaceae), although it is taxonomically placed under Costaceae. The increasing interest in Costus igneus has emerged from its ethnomedicinal reputation, particularly among diabetic patients who traditionally consume its leaves to maintain blood glucose levels. The plant represents an important link between indigenous knowledge and modern pharmacological research, providing opportunities for the discovery of bioactive compounds with therapeutic potential [36].

Botanically, Costus igneus is an evergreen, herbaceous perennial plant that generally grows up to 1–2 meters in height under favorable environmental conditions. It possesses underground rhizomes that serve as storage organs and play an important role in vegetative propagation. The rhizomes are branched, fleshy, and rich in bioactive constituents responsible for several pharmacological activities. The aerial stem is erect, cylindrical, succulent, and often spirally arranged, giving the plant a distinctive appearance. Unlike many conventional plants, the leaves of Costus igneus are arranged in a spiral pattern around the stem, forming a dense foliage structure. The leaves are simple, broad, lanceolate to oblong in shape, with a smooth surface, prominent midrib, and parallel venation characteristic of monocotyledonous plants. The upper surface of the leaves is dark green, while the lower surface is comparatively lighter.

The flowers of Costus igneus are attractive and arranged in terminal or axillary cone-like inflorescences. The flowers are generally orange to reddish in color and emerge from compact, overlapping bracts, contributing to the ornamental importance of the plant. The fruit is a capsule containing small seeds; however, propagation is mainly achieved through rhizome division due to better survival and faster growth. The plant thrives well in warm and humid tropical climates with adequate sunlight and well-drained soil. It can grow effectively in organic-rich soils and requires moderate watering for optimal biomass production. Due to its adaptability and low maintenance requirements, Costus igneus is commonly cultivated in home gardens and medicinal plant gardens [37].

The ethnomedicinal importance of Costus igneus is primarily associated with its traditional use as an antidiabetic plant. In several regions of India, local communities consume fresh leaves of the plant either directly or in powdered form as a natural remedy for controlling elevated blood glucose levels. Traditionally, one or two fresh leaves are chewed daily by diabetic individuals based on the belief that the plant improves insulin activity and helps regulate blood sugar metabolism. This traditional practice has led to the popular name "Insulin Plant," although the plant does not contain insulin itself but may influence glucose metabolism through various phytochemical mechanisms.

Apart from its antidiabetic application, Costus igneus has been traditionally used for the treatment of several health conditions. Folk medicine systems utilize different parts of the plant, especially leaves and rhizomes, for managing inflammation, digestive

disorders, infections, and oxidative stress-related conditions. The leaves are traditionally considered beneficial for improving digestion and relieving stomach discomfort. In some indigenous practices, plant extracts are used for treating respiratory problems, fever, and general weakness. The antimicrobial properties of the plant have also contributed to its traditional use in wound management and prevention of infections.

The ethnopharmacological significance of Costus igneus is supported by the presence of diverse phytoconstituents, including flavonoids, alkaloids, terpenoids, steroids, tannins, saponins, phenolic compounds, and essential oils. These secondary metabolites are considered responsible for its various biological activities. Flavonoids and phenolic compounds contribute significantly to antioxidant activity by scavenging reactive oxygen species and reducing oxidative stress. Since oxidative stress plays an important role in the progression of diabetes and its complications, the antioxidant properties of Costus igneus may contribute to its protective effects. Similarly, terpenoids and steroidal compounds have been associated with anti-inflammatory and metabolic regulatory activities [38].

Several experimental studies have investigated the antidiabetic potential of Costus igneus. Extracts prepared from the leaves have demonstrated hypoglycemic activity in experimental diabetic models, showing reductions in blood glucose levels and improvements in glucose tolerance. The proposed mechanisms include enhancement of insulin secretion, stimulation of glucose uptake by peripheral tissues, inhibition of carbohydrate-digesting enzymes such as α-amylase and α-glucosidase, and protection of pancreatic β-cells from oxidative damage. These findings provide scientific support for its traditional use in diabetes management. However, further clinical investigations are required to establish standardized dosage, long-term safety, and therapeutic efficacy in humans.

The plant also exhibits promising antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, and antihyperlipidemic activities. The antioxidant activity helps protect cellular components from free radical-mediated damage, while anti-inflammatory effects may involve inhibition of inflammatory mediators. Preliminary antimicrobial investigations suggest that extracts of Costus igneus possess inhibitory effects against certain bacterial and fungal strains, supporting its traditional application in infection-related disorders.

Botanical and Ethnomedicinal Profile of Vernonia amygdalina

Vernonia amygdalina Delile, commonly known as "bitter leaf," is an important medicinal plant belonging to the family Asteraceae. It is widely distributed throughout tropical and subtropical regions of Africa and has gained global attention due to its nutritional, ethnomedicinal, and pharmacological significance. The plant has been traditionally used for centuries in African traditional medicine for the management of several ailments, including diabetes, hypertension, gastrointestinal disorders, fever, malaria, inflammation, and infections. The characteristic bitter taste of the leaves, attributed to the presence of bioactive phytochemicals such as sesquiterpene lactones and flavonoids, has made it a highly valued medicinal and dietary plant. Due to its extensive traditional applications and experimentally demonstrated biological activities, Vernonia amygdalina has become an important subject of research in ethnopharmacology and natural product-based drug discovery [39].

Botanically, Vernonia amygdalina is a perennial shrub or small tree that generally grows between 2–10 meters in height under favorable environmental conditions. It possesses a woody stem with numerous branches and a dense arrangement of foliage. The plant is commonly found in tropical forests, cultivated fields, home gardens, and rural landscapes. The leaves are the most widely utilized medicinal part of the plant and are characterized by their simple, opposite arrangement, elliptical to lanceolate shape, pointed apex, and serrated margins. The leaves are dark green, slightly rough in texture, and possess a strong bitter flavor due to the accumulation of secondary metabolites. The leaf surface contains glandular structures responsible for the production and storage of various phytoconstituents contributing to its therapeutic properties.

The root system of Vernonia amygdalina consists of a well-developed taproot with lateral branches that provide stability and facilitate absorption of nutrients and water. The stem is erect, cylindrical, and branched, with a bark surface that becomes woody with maturity. The plant produces small flowers arranged in compact clusters known as capitula, which are typical characteristics of the Asteraceae family. The flowers are usually white to cream-colored and occur in terminal or axillary inflorescences. The fruits are small, dry achenes containing seeds that aid in propagation. Although sexual propagation through seeds is possible, vegetative propagation using stem cuttings is commonly practiced due to faster establishment and better maintenance of desirable characteristics.

Vernonia amygdalina grows effectively in warm tropical climates with adequate rainfall and sunlight. It prefers fertile, well-drained soils and can tolerate a wide

range of environmental conditions. Due to its adaptability, the plant is cultivated as both a medicinal herb and a vegetable crop in many African countries. The leaves are frequently harvested throughout the year and consumed as part of traditional diets after processing to reduce excessive bitterness. Various preparation methods, including boiling, squeezing, infusion, and extraction, are used depending on the intended medicinal application [40].

The ethnomedicinal importance of Vernonia amygdalina is deeply rooted in African traditional healthcare systems. It is commonly referred to as "bitter leaf" because of its characteristic taste and is traditionally used as a remedy for numerous diseases. The leaves are consumed as fresh juice, decoctions, or cooked vegetables for improving general health and treating metabolic disorders. One of the most significant traditional applications of Vernonia amygdalina is its use in diabetes management. Traditional healers recommend leaf preparations to reduce excessive blood glucose levels and improve symptoms associated with diabetes. This traditional claim has encouraged scientific investigations into its hypoglycemic potential.

Apart from diabetes, Vernonia amygdalina has been traditionally employed for treating hypertension and cardiovascular disorders. Leaf extracts are believed to assist in maintaining normal blood pressure and improving circulation. The plant is also used in traditional medicine for gastrointestinal problems, including stomach pain, constipation, intestinal worms, and loss of appetite. The bitter principles present in the leaves are considered beneficial for stimulating digestion and improving gastrointestinal function. In several African communities, leaf decoctions are used for treating fever, malaria, and infectious diseases due to their perceived antipyretic and antimicrobial properties.

The plant has also been traditionally used in the management of inflammatory conditions, arthritis, and wound-related disorders. Extracts prepared from leaves and roots are applied externally for wound healing and skin infections. The anti-inflammatory properties of Vernonia amygdalina are associated with its ability to reduce inflammatory mediators and oxidative stress. Additionally, traditional practices utilize the plant for improving immune function and relieving symptoms associated with respiratory disorders.

The medicinal potential of Vernonia amygdalina is attributed to its rich phytochemical composition. Major bioactive constituents reported from the plant include flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, steroids, glycosides, and sesquiterpene lactones. The sesquiterpene lactones, particularly vernodalin, vernolide, and related compounds, are considered characteristic chemical markers of the plant and contribute significantly to its pharmacological effects. Flavonoids and phenolic compounds exhibit strong antioxidant properties by neutralizing free radicals and protecting cells from oxidative damage. Alkaloids, saponins, and terpenoids contribute to antimicrobial, anti-inflammatory, and metabolic regulatory activities.

Several experimental studies have demonstrated the pharmacological activities of Vernonia amygdalina. The antidiabetic activity of the plant has been extensively investigated, with studies suggesting that leaf extracts may reduce blood glucose levels through mechanisms such as enhancement of insulin secretion, improvement of glucose utilization, inhibition of carbohydrate-digesting enzymes, and protection of pancreatic β-cells. The antioxidant activity of the plant further supports its protective role against diabetes-associated oxidative stress and complications.

The antimicrobial activity of Vernonia amygdalina has been reported against various bacterial and fungal pathogens, supporting its traditional use in infectious diseases. Its anti-inflammatory activity is linked to modulation of inflammatory pathways and reduction of pro-inflammatory mediators. Studies have also suggested hepatoprotective, nephroprotective, anticancer, and lipid-lowering effects, although further investigations are required to establish clinical relevance. The anticancer potential has been associated with the ability of certain phytochemicals to induce apoptosis and inhibit abnormal cell proliferation [33].

Phytochemical Constituents of Costus igneus and Vernonia amygdalina

The therapeutic potential of Costus igneus and Vernonia amygdalina is primarily attributed to the presence of a diverse range of bioactive phytochemical constituents, including phenolic compounds, flavonoids, alkaloids, terpenoids, steroids, saponins, tannins, glycosides, and other secondary metabolites. These phytoconstituents contribute significantly to the pharmacological activities of both plants, including antidiabetic, antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, and metabolic regulatory effects. The qualitative and quantitative distribution of these compounds varies depending on plant part, geographical origin, maturity stage, extraction method, and environmental conditions.

Costus igneus is reported to contain a wide spectrum of phytochemicals, particularly in its leaves and rhizomes,

which are the most commonly investigated medicinal parts. The leaves are rich sources of polyphenolic compounds, flavonoids, alkaloids, terpenoids, steroids, saponins, tannins, and reducing sugars. Flavonoids such as quercetin and related flavonoid derivatives contribute significantly to the antioxidant and antidiabetic potential of the plant by scavenging reactive oxygen species and protecting pancreatic β-cells from oxidative damage. Phenolic compounds present in Costus igneus exhibit strong free radical neutralizing ability and are associated with protection against oxidative stress-mediated complications of diabetes. The presence of alkaloids and terpenoids has been linked with glucose-lowering effects through possible modulation of insulin secretion and carbohydrate metabolism. Steroidal constituents and phytosterols may contribute to lipid regulation and improvement of metabolic abnormalities associated with diabetes [29].

The leaves of Costus igneus also contain important bioactive compounds such as saponins and tannins, which have demonstrated antioxidant, antimicrobial, and enzyme-inhibitory properties. Saponins are believed to contribute to hypoglycemic activity by influencing glucose absorption and improving insulin sensitivity. Tannins and other polyphenolic molecules may inhibit carbohydrate-digesting enzymes, including α-amylase and α-glucosidase, thereby reducing postprandial blood glucose elevation. Essential oils and volatile components identified in the plant further contribute to its biological activities. Advanced analytical investigations using techniques such as high-performance liquid chromatography (HPLC), gas chromatography–mass spectrometry (GC-MS), and liquid chromatography–mass spectrometry (LC-MS) have revealed the presence of several bioactive molecules responsible for its pharmacological effects. The combined action of these phytochemicals supports the traditional use of Costus igneus as a natural antidiabetic and antioxidant medicinal plant.

Similarly, Vernonia amygdalina possesses a complex phytochemical profile that accounts for its extensive ethnomedicinal applications. The leaves, which are the most widely used medicinal part, contain high levels of phenolic compounds, flavonoids, alkaloids, tannins, saponins, terpenoids, steroids, glycosides, and characteristic sesquiterpene lactones. Among these, sesquiterpene lactones such as vernodalin, vernolide, hydroxyvernolide, and related compounds are considered important chemical markers responsible for many biological activities of the plant. These compounds contribute to the bitter taste of the leaves and possess significant antimicrobial, anti-inflammatory, antioxidant, and cytotoxic properties. Flavonoids and phenolic acids present in Vernonia amygdalina play a major role in antioxidant defense by scavenging free radicals and preventing oxidative cellular damage.

The alkaloids present in Vernonia amygdalina contribute to its diverse pharmacological activities, including antimicrobial and metabolic effects. Saponins and tannins exhibit membrane-stabilizing, antioxidant, and enzyme-modulating properties, while terpenoids and steroids contribute to anti-inflammatory and lipid-lowering effects. The plant is also reported to contain vitamins, minerals, and other nutritional components that enhance its value as both a medicinal and dietary plant. Phenolic compounds and flavonoids are particularly associated with its antidiabetic activity by improving glucose metabolism, enhancing antioxidant capacity, and reducing inflammatory responses associated with metabolic disorders. Furthermore, the presence of bioactive compounds such as vernodalin and related lactones has been investigated for their potential anticancer activity through mechanisms involving apoptosis induction and inhibition of tumor cell proliferation.

Comparatively, both Costus igneus and Vernonia amygdalina exhibit overlapping phytochemical profiles, particularly with respect to flavonoids, phenolics, alkaloids, terpenoids, steroids, tannins, and saponins. These common phytoconstituents contribute to their antioxidant, anti-inflammatory, and antidiabetic properties. However, Costus igneus is particularly characterized by flavonoid-rich and polyphenolic compounds associated with glucose regulation and pancreatic protection, whereas Vernonia amygdalina is distinguished by the presence of sesquiterpene lactones, which contribute to its bitter taste and broad pharmacological activities. The synergistic interaction among these phytochemicals enhances the therapeutic potential of both plants and supports their traditional applications in the management of chronic diseases. Further phytochemical isolation, structural characterization, and bioactivity-guided investigations are necessary to identify specific active molecules and develop standardized herbal formulations with proven efficacy and safety [36].

Extraction and Phytochemical Profiling Techniques

The extraction of bioactive constituents from Costus igneus and Vernonia amygdalina plays a crucial role in determining their pharmacological potential and therapeutic efficacy. Selection of appropriate extraction methods depends on the nature of phytochemicals, plant part used, polarity of compounds, and intended biological application. Traditionally, extraction has

been performed using maceration, infusion, decoction, and Soxhlet extraction methods with solvents such as water, ethanol, methanol, acetone, and hydroalcoholic mixtures. Aqueous extracts are commonly prepared due to their similarity with traditional consumption methods, whereas ethanol and methanol extracts are frequently preferred for obtaining a broader range of phenolic compounds, flavonoids, terpenoids, and other secondary metabolites. Advanced extraction approaches, including ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and supercritical fluid extraction (SFE), have been increasingly explored to improve extraction efficiency, reduce solvent consumption, and preserve thermolabile phytoconstituents.

Phytochemical profiling of Costus igneus has revealed the presence of flavonoids, phenolic compounds, alkaloids, terpenoids, steroids, saponins, tannins, glycosides, and other bioactive molecules. Similarly, Vernonia amygdalina contains characteristic phytochemicals such as sesquiterpene lactones (vernodalin, vernolide), flavonoids, phenolic acids, alkaloids, tannins, saponins, and terpenoids. Preliminary phytochemical screening involves qualitative chemical tests for detection of major classes of secondary metabolites, whereas quantitative estimation includes determination of total phenolic content (TPC), total flavonoid content (TFC), and antioxidant capacity. Modern analytical techniques such as high-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC-MS), gas chromatography–mass spectrometry (GC-MS), Fourier-transform infrared spectroscopy (FTIR), and nuclear magnetic resonance (NMR) spectroscopy are widely employed for identification, characterization, and quantification of individual phytoconstituents. These techniques provide valuable information regarding chemical composition and help establish quality control parameters for herbal preparations [22,38].

In-vitro Antidiabetic Screening Methods

In-vitro antidiabetic evaluation provides preliminary evidence regarding the glucose-lowering potential of medicinal plants before proceeding to animal and clinical investigations. Several enzyme-based assays are commonly used to evaluate the antidiabetic activity of Costus igneus and Vernonia amygdalina. One of the most widely used approaches is the α-amylase inhibition assay, which evaluates the ability of plant extracts to inhibit the breakdown of complex carbohydrates into simple sugars. Inhibition of α-amylase delays carbohydrate digestion and reduces rapid postprandial glucose elevation. Another important screening method is the α-glucosidase inhibition assay, where extracts are evaluated for their ability to inhibit intestinal carbohydrate-digesting enzymes responsible for glucose release.

The glucose uptake assay using yeast cells, adipocytes, or muscle cell models is another important in-vitro method used to assess glucose utilization potential. Plant extracts that enhance glucose uptake may improve peripheral glucose metabolism and mimic insulin-like activity. Additionally, advanced cellular models involving insulin-sensitive cell lines are used to investigate molecular pathways associated with glucose transport and insulin signaling. Protein glycation inhibition assays are also performed to evaluate the ability of plant extracts to prevent the formation of advanced glycation end products (AGEs), which contribute to diabetic complications.

Studies on Costus igneus have demonstrated significant α-amylase and α-glucosidase inhibitory activities, supporting its traditional use in diabetes management. Similarly, Vernonia amygdalina extracts have shown promising enzyme inhibitory activity, glucose uptake enhancement, and protective effects against oxidative damage associated with hyperglycemia. These in-vitro findings provide scientific validation for their traditional antidiabetic applications.

Mechanisms of Antidiabetic Action

The antidiabetic effects of Costus igneus and Vernonia amygdalina are mediated through multiple complementary mechanisms involving glucose metabolism, insulin regulation, oxidative stress reduction, and protection of pancreatic tissues. One major mechanism involves inhibition of carbohydrate-digesting enzymes such as α-amylase and α-glucosidase, resulting in delayed glucose absorption and reduced postprandial hyperglycemia. Phenolic compounds and flavonoids present in both plants contribute significantly to enzyme inhibition [21].

Costus igneus is believed to exert antidiabetic effects through enhancement of insulin secretion, regeneration or protection of pancreatic β-cells, and improvement of peripheral glucose utilization. Bioactive flavonoids and polyphenolic compounds may stimulate insulin release and enhance insulin sensitivity by influencing intracellular signaling pathways. The antioxidant activity of the plant protects pancreatic β-cells from oxidative stress-induced damage, which is an important factor in diabetes progression.

Vernonia amygdalina exhibits antidiabetic activity through mechanisms including stimulation of insulin secretion, inhibition of hepatic glucose production,

enhancement of glucose uptake, and improvement of lipid metabolism. Sesquiterpene lactones and flavonoids present in the plant may regulate inflammatory pathways and oxidative stress associated with insulin resistance. The plant may also improve pancreatic function by reducing free radical-mediated cellular injury [17].

Both plants demonstrate a multi-target approach toward diabetes management, which is particularly relevant because diabetes involves complex disturbances in glucose regulation, inflammation, oxidative stress, and metabolic imbalance.

Antioxidant–Antidiabetic Relationship

Oxidative stress plays a central role in the development and progression of diabetes mellitus. Persistent hyperglycemia increases the generation of reactive oxygen species (ROS), leading to oxidative damage of pancreatic β-cells, impaired insulin secretion, inflammation, and development of diabetic complications. Therefore, antioxidant activity is considered an important mechanism contributing to the antidiabetic effects of medicinal plants.

Costus igneus and Vernonia amygdalina possess strong antioxidant potential due to their high content of flavonoids, phenolic compounds, tannins, and other reducing agents. These compounds neutralize free radicals, enhance endogenous antioxidant defense systems, and protect cellular structures from oxidative damage. In diabetic conditions, antioxidant phytochemicals may preserve pancreatic β-cell integrity, improve insulin sensitivity, and reduce inflammation.

The antioxidant–antidiabetic relationship suggests that plant-derived compounds do not merely reduce blood glucose levels but also prevent long-term complications associated with oxidative damage. This dual activity enhances the therapeutic importance of both plants in diabetes management.

Comparative Evaluation of Costus igneus and Vernonia amygdalina

Both Costus igneus and Vernonia amygdalina are traditionally recognized as antidiabetic medicinal plants; however, they differ in botanical characteristics, phytochemical composition, and pharmacological profiles. Costus igneus is primarily associated with diabetes control through its flavonoid-rich leaves, antioxidant activity, and potential insulin-modulating effects. Its traditional use involves direct consumption of fresh leaves, particularly among diabetic populations [7].

In contrast, Vernonia amygdalina possesses a broader ethnomedicinal profile and is widely used as both food and medicine. The presence of unique sesquiterpene lactones distinguishes it from Costus igneus and contributes to additional antimicrobial, anti-inflammatory, and anticancer activities. While both plants demonstrate glucose-lowering potential, Vernonia amygdalina exhibits broader systemic effects due to its diverse phytochemical composition.

Comparative studies suggest that both plants may serve as valuable sources of natural antidiabetic agents, although differences in chemical composition, mechanism of action, and safety profiles must be considered for therapeutic application.

Toxicological and Safety Considerations

Although Costus igneus and Vernonia amygdalina have extensive traditional usage, systematic toxicological evaluation is essential before their incorporation into standardized therapeutic products. Acute and sub-chronic toxicity studies of Costus igneus extracts have generally indicated a favorable safety profile at therapeutic doses; however, excessive consumption may potentially cause metabolic disturbances or interactions with antidiabetic medications.

Vernonia amygdalina is widely consumed as a vegetable, suggesting relative safety; however, concentrated extracts may exhibit dose-dependent effects. High doses may influence liver enzymes, electrolyte balance, or interact with conventional drugs. Variations in phytochemical composition due to extraction methods and geographical factors can also affect safety outcomes [22].

Important safety assessments include acute toxicity testing, repeated-dose toxicity studies, cytotoxicity evaluation, genotoxicity assessment, and investigation of herb–drug interactions. Particular attention should be given to diabetic patients using conventional antidiabetic medicines, as combined use may increase the risk of hypoglycemia. Therefore, future studies should focus on establishing standardized extracts, therapeutic dosage ranges, long-term safety profiles, and clinical efficacy to ensure the safe utilization of Costus igneus and Vernonia amygdalina as complementary antidiabetic agents.

Conclusion

Costus igneus and Vernonia amygdalina represent two important medicinal plants with significant ethnomedicinal relevance and promising antidiabetic potential. Both plants have been traditionally utilized for the management of diabetes and related metabolic

disorders, and modern scientific investigations have provided substantial evidence supporting their therapeutic properties. Their pharmacological activities are primarily attributed to diverse phytochemical constituents, including flavonoids, phenolic compounds, alkaloids, terpenoids, steroids, saponins, tannins, and other bioactive molecules.

The antidiabetic effects of these plants involve multiple mechanisms, including inhibition of carbohydrate-digesting enzymes, enhancement of glucose utilization, improvement of insulin sensitivity, protection of pancreatic β-cells, and reduction of oxidative stress. The strong antioxidant capacity of both plants plays a crucial role in preventing diabetes-associated cellular damage and complications. While Costus igneus is particularly recognized for its insulin-like activity and glucose-regulating effects, Vernonia amygdalina exhibits a broader pharmacological profile due to the presence of unique compounds such as sesquiterpene lactones, which contribute to its antioxidant, anti-inflammatory, antimicrobial, and metabolic effects.

Comparative evaluation indicates that both plants possess considerable potential as natural sources of antidiabetic agents; however, differences in phytochemical composition, mechanisms of action, and therapeutic applications highlight their complementary roles. Costus igneus may offer advantages in glucose regulation and pancreatic protection, whereas Vernonia amygdalina provides broader systemic benefits associated with inflammation control and oxidative stress reduction.

Despite encouraging findings, significant challenges remain, including phytochemical variability, limited clinical evidence, uncertain pharmacokinetics, and inadequate long-term safety data. Future research should prioritize standardization of extracts, identification of active compounds, advanced formulation development, molecular mechanism studies, and well-controlled clinical trials. Establishing evidence-based therapeutic protocols will be essential for transforming these traditionally used plants into scientifically validated herbal medicines.

Overall, Costus igneus and Vernonia amygdalina represent valuable candidates in the search for safer and more effective natural approaches for diabetes management. Their rich phytochemical diversity and multifunctional biological activities provide a strong foundation for future drug discovery and development. With systematic research, quality standardization, and clinical validation, these medicinal plants may contribute significantly to integrative approaches for controlling diabetes and improving metabolic health.

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Conflict of Interest

None.

Author Contributions

All the authors contributed to the study.

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