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Formulation Strategies for Bioactive Compounds of *Kyllinga Triceps* in The Management of Diabetes Mellitus: A Comprehensive Review

Ankur Srivastava*, Navneet Verma

Department Of Pharmacy, IFTM University, Moradabad

ABSTRACT

Diabetes mellitus is a chronic metabolic disorder defined by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The increasing global burden of diabetes and the limitations of current therapies have intensified research into plant-derived bioactive compounds as alternative or complementary hypoglycemic agents. Traditional medicinal systems in India have long used *Kyllinga triceps* (Cyperaceae) for managing symptoms associated with diabetes, supporting ethnobotanical claims of its therapeutic potential. Phytochemical investigations reveal that *K. triceps* contains significant levels of flavonoids, sterols, phenolics, and other secondary metabolites, many of which are linked to antidiabetic mechanisms such as carbohydrate-digesting enzyme inhibition, antioxidant activity, and insulin sensitization. Experimental studies in diabetic animal models indicate that extracts of *K. triceps* and its fractions produce meaningful reductions in blood glucose levels, validating aspects of its traditional use and suggesting possible pharmacological relevance. Despite promising pharmacodynamic data, therapeutic translation requires addressing challenges related to the stability, solubility, bioavailability, and targeted delivery of its bioactive constituents. This review synthesizes current evidence on the phytochemistry, and antidiabetic pharmacology of *K. triceps*, and outlines formulation strategies that enhance the clinical potential of its bioactive compounds. Approaches such as extract standardization, solubility enhancement, nano- and microencapsulation, controlled release systems, and synergistic herbal combinations are evaluated for their ability to improve systemic exposure and therapeutic efficacy. Mechanistic insights are discussed in the context of known bioactive classes, including their roles in modulating key diabetes-related pathways such as carbohydrate digestion, oxidative stress, insulin signaling, and glucose uptake. Finally, gaps in current research are identified, and future directions are proposed to guide comprehensive preclinical and clinical evaluation. This evidence-based framework aims to support the development of safe, effective, and scalable antidiabetic formulations derived from *Kyllinga triceps* bioactives, aligning traditional knowledge with modern pharmaceutical science.

Keywords: *Kyllinga triceps*, diabetes mellitus, phytochemicals, flavonoids, antidiabetic mechanisms, formulation strategies, bioavailability, herbal drug development

INTRODUCTION

Diabetes mellitus (DM) represents one of the most serious global public health challenges of the twenty-first century. It is a complex, chronic metabolic disorder characterized by persistent hyperglycemia arising from defects in insulin secretion, insulin action, or a combination of both. According to the World Health Organization, the global prevalence of diabetes has increased steadily over the past few decades, driven by urbanization, sedentary lifestyles, dietary changes, and population aging. If not adequately managed, prolonged hyperglycemia leads to severe microvascular complications such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications including cardiovascular disease and stroke, significantly increasing morbidity and mortality (American Diabetes Association, 2023; IDF, 2021).

Conventional management of diabetes primarily relies on insulin therapy and various classes of oral hypoglycemic agents, including sulfonylureas, biguanides, thiazolidinediones, sodium–glucose

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cotransporter-2 (SGLT2) inhibitors, and dipeptidyl peptidase-4 (DPP-4) inhibitors. While these drugs are effective in controlling blood glucose levels, their long-term use is often associated with adverse effects such as hypoglycemia, gastrointestinal disturbances, weight gain, cardiovascular risks, and declining efficacy over time. In addition, high treatment costs and limited accessibility pose challenges, particularly in low- and middle-income countries where the burden of diabetes is rapidly increasing (Forouhi & Wareham, 2019; DeFronzo et al., 2021).

In this context, there has been growing scientific interest in herbal medicines and plant-derived bioactive compounds as complementary or alternative approaches for diabetes management. Medicinal plants are rich sources of secondary metabolites such as flavonoids, phenolic acids, alkaloids, sterols, and terpenoids, many of which exhibit antidiabetic, antioxidant, anti-inflammatory, and insulin-sensitizing properties. Unlike single-target synthetic drugs, phytochemicals often act through multiple biochemical pathways, including enhancement of insulin secretion, improvement of insulin sensitivity, inhibition of carbohydrate-digesting enzymes, and reduction of oxidative stress, which plays a key role in diabetes progression and complications (Ghorbani, 2017; Marín-Peñalver et al., 2016).

Kyllinga triceps Rottb., a small perennial tufted grass belonging to the family Cyperaceae, is widely distributed across tropical and subtropical regions of India. In traditional Indian ethnomedicine, the plant has been used for the treatment of fever, excessive thirst, urinary disorders, inflammation, and diabetes. Rural and indigenous practitioners commonly employ decoctions or extracts of the roots, rhizomes, or whole plant to manage hyperglycemia and associated symptoms. Ethnobotanical surveys have documented its regular use in folk remedies for metabolic disorders, highlighting its therapeutic relevance (Khare, 2007; Nadkarni, 2009).

Phytochemical investigations of Kyllinga triceps have revealed the presence of bioactive constituents such as flavonoids, phenolics, sterols, and other secondary metabolites known for their antidiabetic and antioxidant potential. Experimental studies have reported hypoglycemic, antioxidant, anti-inflammatory, and antimicrobial activities of different extracts of the plant, suggesting its possible role in glycemic control and protection against diabetes-induced oxidative stress. However, despite promising preliminary findings, systematic evaluation of its bioactive compounds, mechanisms of action, and formulation approaches remains limited and fragmented across the literature (Verma et al., 2016; Aneela et al., 2014).

The present review aims to critically analyze and synthesize existing ethnobotanical, phytochemical, and pharmacological evidence related to the antidiabetic potential of Kyllinga triceps. Particular emphasis is placed on identifying key bioactive compounds, understanding their possible mechanisms of action, and exploring formulation strategies that may enhance bioavailability and therapeutic efficacy. By consolidating current knowledge, this review seeks to highlight research gaps and provide a scientific basis for the future development of plant-based antidiabetic formulations derived from Kyllinga triceps.

2. Ethnobotany and Traditional Uses of *Kyllinga triceps* Rottb

Kyllinga triceps Rottb (family Cyperaceae) is a perennial herb widely distributed across the tropical and subtropical regions of India. It is known by several vernacular names including **Nirvishaa** and **Mustaa**, and has been integrated into diverse traditional healing practices across tribal and rural communities.

2.1 Traditional and Folk Medicine Practices

Ethnobotanical surveys and classical medicinal texts describe *K. triceps* as a multipurpose medicinal plant. Traditional systems prescribe decoctions of the root and aerial parts for a range of metabolic and systemic disorders. Among tribal communities in regions such as Madhya Pradesh, Manipur, and Chhattisgarh, decoctions are specifically used to manage **symptoms related to diabetes mellitus** and to relieve **excessive thirst** associated with metabolic imbalance.

Beyond its use in glycemic control, the plant is cited as having demulcent, diuretic, tonic, and febrifuge properties. It has been used to address gastrointestinal

disturbances, fever, polyuria, and liver disorders in folk practice. Decoctions and infusions are commonly prepared and administered orally in these contexts.

In Ayurvedic tradition, *K. triceps* features as a supportive herb in formulations targeting **vitiated pitta and vata doshas**, hyperdipsia (excessive thirst), dermatoses, and cough. Its rhizomes are employed as refrigerant and demulcent agents, reflecting its perceived cooling and soothing action in traditional texts.

2.2 Use in Tribal and Regional Systems

Ethnobotanical field data confirm the plant's role in local medical systems across India's ethnolinguistic landscape. In the Thoubal district of Manipur, tribal healers administer boiled extracts of *K. triceps* to treat diabetes. Similar traditional prescriptions have been documented among Irula tribes in the Nilgiris, where the plant's juice is used for glycemic management.

Reports from Madhya Pradesh and Chhattisgarh also note its use among tribal healers for diabetes and associated disorders, indicating a consistent pattern of antidiabetic application across culturally distinct regions.

2.3 Broader Traditional Applications

Across India and in some Southeast Asian traditional practices, *K. triceps* has been used beyond metabolic conditions. Its pharmacological profile in folk medicine includes applications as an **anthelmintic, stomachic, and febrifuge** agent. The leaves and root parts have been brewed into teas or applied externally in poultices for skin ailments and inflammatory conditions.

Traditional practitioners have also employed *K. triceps* as a diuretic to manage fluid retention and as a tonic to support general health and digestion. These broad uses underscore the plant's integration into local healthcare systems long before modern pharmacological investigation.

2.4 Connection to Pharmacological Research

The ethnomedicinal claims surrounding *K. triceps* have motivated scientific studies. Experimental research using streptozotocin-induced diabetic rat models has demonstrated significant **hypoglycemic activity**, supporting the traditional use of *K. triceps* extracts in glycemic control. Extract doses-maintained body weight and significantly lowered blood glucose levels compared with untreated controls, aligning with ethnobotanical claims of antidiabetic efficacy.

3. Phytochemical Profile of *Kyllinga triceps*

Phytochemical studies of *Kyllinga triceps* (family Cyperaceae) demonstrate a rich and varied secondary metabolite composition, identified through a combination of preliminary screening, chromatographic separation, and spectroscopic characterization. These metabolites include major classes such as flavonoids, sterols, phenolic compounds, tannins, saponins, alkaloids, and terpenoids. This profile is consistent with other Cyperaceae species that exhibit a broad repertoire of bioactive constituents with potential health effects.

Preliminary phytochemical screening of methanolic extracts of *K. triceps* confirmed the presence of multiple secondary metabolite classes. Alkaloids, phenolic compounds, flavonoids, tannins, saponins, steroids, and sugars were detected using standard qualitative assays, suggesting a complex phytochemical makeup that could underpin traditional uses of the plant in ethnomedicine (Aneela, Dey & De, 2014).

Column chromatographic isolation coupled with FT-IR, HR-EIMS, and NMR spectroscopy enabled the identification and structural elucidation of key bioactive molecules from the plant. Four principal compounds isolated from *K. triceps* were quercetin dihydrate, rutin, β-sitosterol, and stigmasterol. Quercetin dihydrate and rutin represent flavonoid compounds widely studied for antioxidative and metabolic regulatory effects, while β-sitosterol and stigmasterol are plant sterols associated with cholesterol modulation and anti-inflammatory properties (Verma et al., 2017).

Flavonoids and Phenolic Compounds. The identification of quercetin and rutin highlights *K. triceps* as a source of flavonoid glycosides. Flavonoids are phenolic structures with established

free radical scavenging capacity, attributed to their ability to donate hydrogen atoms or electrons to reactive oxygen species, thereby modulating oxidative stress. These molecules also influence key metabolic enzymes involved in glucose homeostasis and have been linked to antidiabetic effects, including inhibition of α-amylase and α-glucosidase activities and enhancement of insulin sensitivity in cellular models (Citations in related species suggest similar functional mechanisms).

Sterols. β-Sitosterol and stigmasterol isolated from *K. triceps* belong to the phytosterol class. These compounds share structural similarity with cholesterol and have been implicated in lipid-lowering effects, modulation of inflammation, and potential antidiabetic activity via improvements in insulin responsiveness and metabolic regulation pathways. Stigmasterol, in particular, has been shown in other plant studies to exert antioxidant, antidiabetic, and lipid-modulating activities in vitro and in vivo.

Other Secondary Metabolites. Alongside major constituents, preliminary analyses indicate the presence of additional bioactive classes such as terpenoids, tannins, and saponins. These contribute both to traditional therapeutic claims and to a diverse biochemical profile that supports multiple biological activities. For example, tannins and phenolic compounds have documented antioxidant activities, while saponins may influence membrane stability and immune responses. Although comprehensive GC-MS profiling of these minor constituents in *K. triceps* is limited, related studies using GC-MS have detected a variety of phytochemicals, adding to the evidence of the plant's chemical complexity (Aneela, Dey & De, 2014).

The prominent presence of flavonoids and phenolics in *K. triceps* aligns with the growing body of evidence supporting the antioxidant and antidiabetic potential of plant extracts rich in these compounds. Their structural diversity enables interaction with multiple biological targets, including oxidative pathways and glucose metabolic enzymes, justifying further pharmacological investigations.

4. Pharmacological Evidence of Antidiabetic Activity

4.1 Hypoglycemic Activity in Animal Models

Experimental pharmacological studies provide growing evidence supporting the antidiabetic potential of *Kyllinga triceps*, particularly through in vivo animal models of chemically induced diabetes. Streptozotocin (STZ)-induced diabetic rat models, widely accepted for evaluating hypoglycemic agents due to their selective pancreatic β-cell toxicity, have been extensively used to assess the efficacy of *K. triceps* extracts.

In one notable study, oral administration of crude *Kyllinga triceps* extract at doses of 100 and 200 mg/kg body weight produced a significant reduction in fasting blood glucose levels in STZ-induced diabetic rats. Both acute and sub-acute treatment regimens showed sustained hypoglycemic effects when compared with untreated diabetic controls. Importantly, treated animals demonstrated prevention of diabetes-associated body weight loss, suggesting an overall improvement in metabolic status. The glucose-lowering effect observed at higher doses was found to be comparable to that of the standard sulfonylurea drug glibenclamide, indicating a potential insulin-modulatory or insulin-sensitizing mechanism (Verma et al., 2016).

Further pharmacological fractionation studies have provided insights into the bioactive components responsible for this activity. Root extracts of *K. triceps* were fractionated using solvents of increasing polarity, including toluene, ethyl acetate, and 1-butanol. Among these, the ethyl acetate fraction exhibited the most pronounced antihyperglycemic activity in neonatal streptozotocin-induced diabetic rats. Sub-acute administration of this fraction resulted in a significant decrease in blood glucose levels and effectively restored altered serum biochemical parameters such as total cholesterol, triglycerides, and liver enzyme markers. These findings suggest a protective role against diabetes-associated dyslipidemia and hepatic dysfunction (Aneela et al., 2014).

The observed hypoglycemic effects may be attributed to the presence of flavonoids, phenolic compounds, and sterols identified in *K. triceps*. These phytoconstituents are known to enhance peripheral glucose uptake, inhibit intestinal glucose absorption,

and protect pancreatic β-cells from oxidative stress. Additionally, antioxidant activity reported for *K. triceps* may contribute indirectly to glycemic control by reducing oxidative damage associated with chronic hyperglycemia (Lal et al., 2012; Khare, 2007).

The available animal studies strongly validate the traditional use of *Kyllinga triceps* in diabetes management. However, despite promising preclinical evidence, detailed mechanistic studies, standardized extract development, toxicity profiling, and clinical validation remain limited. Future research should focus on elucidating molecular pathways involved in glucose homeostasis and exploring formulation strategies to enhance bioavailability and therapeutic efficacy.

4.2 Mechanisms of Action

Direct mechanistic studies on *Kyllinga triceps* are limited, but available phytochemical investigations show that the plant contains a range of bioactive compounds including flavonoids (e.g., quercetin, rutin), phytosterols (e.g., β-sitosterol), phenolics, glycosides, and terpenoids. These constituents have been linked with antidiabetic properties through multiple biochemical pathways in preclinical models and in related plant systems.

4.2.1 Enzyme Inhibition

One of the primary mechanisms through which *Kyllinga triceps* phytochemicals may exert glucose-lowering effects is by inhibiting key carbohydrate-digesting enzymes. Flavonoids such as quercetin and rutin have been shown to inhibit α-amylase and α-glucosidase activity, delaying the breakdown and absorption of complex carbohydrates in the gut and thereby attenuating postprandial glucose excursions. Molecular docking and in vitro studies suggest that rutin, in particular, binds to and inhibits enzymes involved in carbohydrate hydrolysis and the polyol pathway, which may contribute to its antihyperglycemic action . In addition, isolated phytochemicals including β-sitosterol exhibit moderate inhibitory activity against α-amylase and α-glucosidase in model systems, supporting the hypothesis that enzyme inhibition contributes to glycemic control .

This mechanism parallels the action of clinically used agents such as acarbose, and suggests that the enzyme-modulating effects of *Kyllinga triceps* extracts could blunt rapid glucose absorption following meals.

4.2.2 Antioxidant Activity

Oxidative stress is a well-recognized contributor to β-cell dysfunction and insulin resistance in diabetes. Phenolic compounds and flavonoids present in *Kyllinga triceps* possess significant antioxidant capacity, scavenging reactive oxygen species and upregulating endogenous antioxidant defense systems. Quercetin, a major flavonoid isolated from the plant, enhances the activity of superoxide dismutase, catalase, and glutathione peroxidase and reduces lipid peroxidation in experimental diabetes models, thereby protecting pancreatic β-cells from oxidative damage and preserving insulin secretion potential . Rutin also exhibits antioxidative actions by reducing the formation of reactive oxygen species, advanced glycation end products, and pro-inflammatory cytokines, all of which are implicated in the progression of diabetic complications.

Phenolic antioxidants may further influence redox-sensitive signaling pathways, including Nrf2/ARE, which regulate cellular responses to oxidative stress and maintain metabolic homeostasis.

4.2.3 Modulation of Insulin Sensitivity

Improved insulin sensitivity is another mechanism ascribed to *Kyllinga triceps* phytochemicals. Sterols like β-sitosterol have been shown in other plant systems to ameliorate lipid profiles and reduce inflammatory mediators, which are key drivers of insulin resistance. By modulating lipid metabolism and inflammatory pathways, β-sitosterol may enhance peripheral insulin responsiveness, though direct studies on *Kyllinga triceps* remain sparse.

Quercetin itself has been extensively studied for its insulin sensitizing effects. It promotes glucose uptake in insulin-sensitive tissues by facilitating GLUT4 translocation to the cell membrane via activation of AMP-activated protein kinase (AMPK) and PI3K/Akt pathways. These actions increase glucose utilization in skeletal muscle and adipose tissue, while

simultaneously reducing hepatic gluconeogenesis through downregulation of enzymes such as glucose-6-phosphatase. Quercetin also suppresses pro-inflammatory cytokines like TNF-α and IL-6, which are known to impair insulin signaling, thereby contributing to improved insulin sensitivity and metabolic control in type 2 diabetes models. Taken together, these enzyme-modulating, antioxidant, and insulin-sensitizing actions suggest that *Kyllinga triceps* exerts its reported hypoglycemic effects through a network of complementary mechanisms. While preclinical evidence supports these pathways, further targeted molecular studies and clinical trials are needed to fully characterize the mechanisms and therapeutic potential of *Kyllinga triceps* compounds in diabetes management.

5. Formulation Strategies for Bioactives

The successful translation of traditional herbal extracts into clinically acceptable antidiabetic formulations depends largely on overcoming challenges related to poor stability, low aqueous solubility, limited bioavailability, and lack of site-specific delivery. Bioactive compounds present in *Kyllinga triceps*, particularly flavonoids and phenolic constituents, show promising antidiabetic potential but require suitable formulation strategies to achieve consistent therapeutic outcomes. Recent advances in pharmaceutical and nutraceutical formulation science provide several approaches to enhance the efficacy, safety, and reproducibility of such plant-derived bioactives.

5.1 Standardization of Extracts

Standardization is a critical prerequisite for the development of herbal formulations intended for clinical use. Variability in phytochemical composition due to differences in geographical origin, harvesting time, extraction methods, and storage conditions can significantly affect pharmacological activity. For *Kyllinga triceps*, standardization involves the identification and quantification of key marker compounds such as quercetin, rutin, and other phenolic constituents associated with antidiabetic and antioxidant effects. Analytical techniques such as high-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC–MS), and gas chromatography–mass spectrometry (GC–MS) are commonly employed to ensure batch-to-batch consistency. These methods allow precise quantification of active constituents and help establish quality control parameters. Standardized extracts not only improve reproducibility in experimental and clinical studies but also facilitate regulatory acceptance and commercialization of herbal formulations (Patel et al., 2018; Kunle et al., 2012).

5.2 Solubility Enhancement

Poor aqueous solubility is a major limitation for many plant-derived bioactives, leading to inadequate dissolution in gastrointestinal fluids and reduced oral bioavailability. Several phytochemicals identified in *Kyllinga triceps*, including flavonoids and sterols, exhibit low water solubility, which restricts their therapeutic effectiveness. Advanced formulation techniques such as nanoemulsions, solid lipid nanoparticles (SLNs), and cyclodextrin inclusion complexes have been widely explored to address this issue. Nanoemulsions improve solubility by reducing particle size and increasing surface area, thereby enhancing intestinal absorption. SLNs offer additional advantages such as protection from chemical degradation and controlled drug release. Cyclodextrins, through host–guest complexation, can significantly increase the apparent solubility and stability of hydrophobic bioactives (Jain & Jain, 2015; Loftsson & Brewster, 2012). These approaches are particularly suitable for oral antidiabetic formulations, where improved dissolution translates directly into enhanced pharmacological response.

5.3 Encapsulation and Controlled Release

Encapsulation strategies play a vital role in protecting sensitive bioactive compounds from degradation due to gastric acidity, enzymatic activity, and oxidative stress. Natural biopolymers such as alginate and chitosan have gained attention for encapsulating herbal extracts due to their biocompatibility, biodegradability, and mucoadhesive properties. Encapsulation within polymeric matrices can provide sustained and controlled release of bioactives, maintaining therapeutic plasma concentrations over extended periods.

Liposomes and polymeric nanoparticles further enhance bioavailability by facilitating transcellular

transport across intestinal epithelial barriers. These delivery systems can also reduce dosing frequency and minimize potential side effects by preventing rapid systemic exposure. Controlled-release formulations are particularly advantageous in chronic conditions such as diabetes mellitus, where long-term glycemic control is required (Bilia et al., 2014; Kumari et al., 2010).

5.4 Targeted Delivery

Targeted delivery systems represent an advanced approach to improve therapeutic efficacy while reducing off-target effects. Polymeric nanoparticles and ligand-conjugated carriers can be engineered to preferentially accumulate in specific metabolic organs, including the pancreas, liver, and adipose tissue. Such targeting may enhance insulin secretion, improve glucose uptake, and modulate key metabolic pathways involved in diabetes. Surface modification of nanoparticles with ligands such as peptides, sugars, or antibodies enables receptor-mediated uptake by target cells. Although targeted delivery of herbal bioactives is still an emerging area, preliminary studies with other plant-derived antidiabetic compounds suggest that such systems can significantly enhance pharmacodynamic outcomes at lower doses (Sahoo et al., 2011; Zhang et al., 2020). Applying these strategies to *Kyllinga triceps* bioactives could open new avenues for precision-based herbal therapeutics.

5.5 Synergistic Herbal Combinations

Polyherbal formulations are a hallmark of traditional medicine systems and are increasingly supported by modern pharmacological evidence. Combining *Kyllinga triceps* extracts with other well-established antidiabetic herbs such as *Gymnema sylvestre* and *Cinnamomum* species may result in synergistic effects through complementary mechanisms of action. These may include inhibition of carbohydrate-digesting enzymes, enhancement of insulin secretion, improvement of insulin sensitivity, and reduction of oxidative stress.

Synergistic formulations can allow dose reduction of individual components, potentially minimize adverse effects while maximize therapeutic benefits. However, rational design of such combinations requires careful pharmacokinetic and pharmacodynamic evaluation to avoid antagonistic interactions. Standardization and formulation optimization are essential to ensure consistency and reproducibility of polyherbal antidiabetic products (Wagner, 2011; Parasuraman et al., 2014).

6. Safety and Toxicity Considerations

Herbal products require thorough evaluation of safety profiles before clinical use, even when traditional use suggests general tolerability. For *Kyllinga* species, existing toxicology data are limited, and most evidence comes from acute toxicity models or preliminary bioassays rather than formal subchronic or chronic evaluations. These findings underscore both the need for systematic toxicity assessment and the early indications of low inherent toxicity in certain species.

6.1 Acute and Subacute Toxicity Studies

A key study on *Kyllinga brevifolia* investigated the acute toxicity and central nervous system effects of rhizome extracts in mice. Intraperitoneal administration yielded an LD₅₀ of 575 mg/kg, while oral doses up to 3000 mg/kg produced no overt toxic symptoms, such as mortality or severe behavioral changes. These results suggest a relatively broad margin of safety for oral intake in rodents, though central nervous effects (e.g., decreased locomotion and enhanced hypnotic response) were observed at pharmacologically active doses, indicating potential for dose-dependent neurobehavioral effects (Basualdo et al., as cited in *Journal of Ethnopharmacology*).

For *Kyllinga polyphylla*, acute toxicity testing extended to high oral doses in mice. No mortality or significant alterations in biochemical, hematological, or histological parameters were reported at doses as high as 5000 mg/kg, and LD₅₀ could not be established below this threshold. Histopathology of the major organs showed normal tissue architecture compared to controls, further supporting an absence of gross toxicity in acute exposure models (Nguyen et al., 2024).

Additional brine shrimp lethality tests on the aqueous extracts of *K. brevifolia* indicated no significant

toxicity across a range of concentrations, suggesting low cytotoxicity in this model system. However, the brine shrimp test is a preliminary screening tool and should not substitute for mammalian toxicity testing (Kamal et al., 2023).

6.2 Subchronic and Chronic Toxicity Data Gaps

Despite the indications of low acute toxicity, subchronic and chronic toxicity assessments are largely missing for *Kyllinga* species. Standard chronic exposure studies following OECD guidelines are necessary to evaluate effects on organ systems over prolonged use, potential for carcinogenicity, reproductive toxicity, and cumulative toxic effects. Without such data, safety profiles remain incomplete, particularly if extracts are considered for long-term therapeutic use.

6.3 Species-Specific and Exposure Route Considerations

Toxic responses can vary considerably between species, extract types, and administration routes. For example, central nervous system effects observed in *K. brevifolia* at pharmacologically active doses highlight the need to distinguish between therapeutic actions and systemic toxicities. Oral dosing in rodents often mimics potential human use more closely than intraperitoneal routes, but differences in metabolism, absorption, and elimination still limit direct extrapolation to human safety profiles.

6.4 Importance of Standardized Extracts and Phytochemical Characterization

Plant extracts vary in composition depending on species, plant part, harvest conditions, and extraction methods. Phytochemical profiling and standardization are essential to identify compounds that may contribute both to efficacy and to toxicity. For instance, flavonoids and other phenolics detected in *Kyllinga* extracts may confer antioxidant activity but also influence metabolism of coadministered drugs. Consistent characterization of active constituents will strengthen safety assessments and support reproducibility across studies.

6.5 Regulatory and Clinical Considerations

Regulatory agencies require comprehensive toxicological data before herbal products are approved for clinical use. This includes acute, subchronic, chronic, genotoxicity, and reproductive toxicity studies conducted under Good Laboratory Practice (GLP) conditions. For *Kyllinga* species, current evidence is insufficient to meet these criteria. Careful dose selection, identification of potential target organs, and well-designed toxicity trials are critical next steps. Clinical monitoring for adverse effects should accompany early human use, especially given the limited toxicology database.

CONCLUSION

Kyllinga *triceps* has a growing body of pharmacological evidence supporting its traditional use in diabetes management. Several experimental studies using streptozotocin (STZ)-induced diabetic rodent models have demonstrated significant hypoglycemic activity following administration of *Kyllinga triceps* extracts. In both acute and chronic treatment protocols, ethanolic and methanolic extracts at doses between 100 and 200 mg/kg produced statistically significant reductions in fasting blood glucose compared to diabetic controls, confirming a glucose-lowering effect that parallels the standard antidiabetic agent glibenclamide (Lal, Gupta, & Awanish, 2012; Vanapatla, Mohan, & Kumar, 2011). These effects were accompanied by attenuation of diabetes-related weight loss, suggesting not only glycemic control but also modulation of systemic metabolic stress in diabetic animals.

Phytochemical investigations have identified several classes of bioactive constituents in *Kyllinga triceps* that may underlie its antidiabetic effects. Flavonoids such as quercetin and rutin, along with phytosterols like β-sitosterol and stigmasterol, have been isolated from this species; these compounds are well documented in the wider phytomedicine literature for their antioxidant, anti-inflammatory, and glucose-modulating properties, including enhancement of cellular glucose uptake and insulin signaling pathways. Although the specific mechanisms in *Kyllinga triceps* remain to be fully elucidated, the presence of these compounds supports hypotheses that multiple molecular pathways may be involved, including inhibition of carbohydrate-digesting

enzymes and mitigation of oxidative stress, both of which are relevant to type 2 diabetes pathophysiology.

From a formulation standpoint, advancing *Kyllinga triceps* toward clinical application will require overcoming challenges related to bioavailability and targeted delivery. Many plant-derived bioactives, particularly flavonoids and sterols, exhibit poor aqueous solubility and variable absorption profiles in vivo. Approaches such as nanoparticle encapsulation, solid lipid carriers, and controlled-release matrices should be explored to enhance systemic exposure and sustain therapeutic plasma concentrations. Standardization of raw extract to defined marker compounds, supported by validated analytical methods, will be essential to ensure reproducibility and regulatory compliance for eventual human studies. Finally, translating these promising preclinical results into therapeutic options demands an integrated research strategy. Well-designed pharmacokinetic and toxicology studies are needed to characterize safety profiles and dosing parameters. Controlled clinical trials will be critical to determine efficacy and tolerability in human subjects. Continued interdisciplinary research linking pharmacology, formulation science, and clinical investigation will clarify the therapeutic potential of *Kyllinga triceps* and help realize its role as an evidence-based antidiabetic agent.

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