

Antidiabetic Properties of Natural Products of *Cyperus* Species Plants: A Review

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ABSTRACT

Natural products are reported to have a vital role in the treatment of various diseases and drug design. In recent developments, natural drug molecules of plant origin have been reported exclusively for diabetic management. Type-2 diabetes or hyperglycemia is one such disease which is particularly studied for plant-based therapy in the last few decades. Though various plant extracts and metabolites have been reported for potential hyperglycemic activities, the *Cyperus* species plants have acquired a unique place in the phytochemical study as they are endowed with various health-beneficial bioactive metabolites and have proven biological properties. The present report is focused on the *Cyperus* species plants that are studied for antidiabetic properties *in vitro* as well as *in vivo* and the potential metabolites identified for such activities. The antidiabetic studies of metabolites or crude products from plants such as *Cyperus articulatus*, *Cyperus esculentus*, *Cyperus kyllingia*, *Cyperus laevigatus*, *Cyperus pangorei*, *Cyperus rotundus*, *Cyperus scariosus* and *Cyperus tegetum* were reviewed. The metabolites, responsible for such activities were listed from the literature survey wherever purification and identification works were reported. The review focused on the importance of natural products in managing diabetes mellitus and the pharmaceutical importance of *Cyperus* plants in managing diabetes, their pharmaceutical importance, drug safety and effectiveness. The secondary metabolites listed in this review may be helpful for further molecular and clinical-level research and drug design.

Keywords: Antidiabetic, α -Glucosidase inhibition, *Cyperus articulatus*, *Cyperus esculentus*, *Cyperus rotundus*, Secondary metabolites.

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INTRODUCTION

Human civilization has a long history of herbal or traditional medicine therapy for treating several diseases and disorders. In recent times, research on traditional medicine and screening of different plant species have been actively pursued due to the lack of effectiveness in synthetic and available drugs or their adverse effects on health.¹ Diabetes mellitus (DM) or hyperglycemia, in particular, continues to be a chronic disorder that is most challenging to manage and has been declared an epidemic by the World Health Organization.² There have been extensive studies in the making of antidiabetic drugs in the past decades. Poor regulation of blood sugar leads to a high glycemic index. One of the effective ways to control diabetes is managing the excess postprandial hypoglycemia.³ Proper diet and different classes of oral hypoglycemic drugs (such as thiazolidinediones, sulfonylureas, α -glucosidase inhibitors

and biguanides) control blood glucose level (BGL). It is also reported that commercially procured drugs (such as Acarbose, Miglitol, Metformin, and Sulfonyl urea) adversely affect human health⁴⁻⁶. Medicinal plants or herbs possessing antidiabetic properties include many phytochemicals such as saponins, flavonoids, alkaloids, anthraquinones, terpenes, coumarins, phenolics and polysaccharides. Natural products are reported to have a vital role in the treatment of various diseases and drug research and design, and preclinical/clinical studies. The affordability with fewer side-effects compared to synthetic drugs has made pharmaceutical research lean towards discovering new natural antidiabetic drugs targeting the mechanism associated with DM or type 2 diabetes.⁷ In addition to lowering blood glucose in experimental models and clinical trials, the stimulation of β -cell proliferation is also being studied as a thrust area.⁸ The anti-hyperglycemic effects of plant-based medicine are aimed at α -glucosidase inhibition, reducing intestinal glucose absorption, enhancing insulin secretions, and improving the performance of pancreatic tissue.^{9,10}

It is evident that inhibitors of α -amylase and α -glucosidase delay the sugar hydrolysis in the small intestine and control postprandial hyperglycemia.^{11,12} Many natural products proved to have a direct or indirect effect on diabetes pathways through inhibition of aldose reductase, α -glucosidase and



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alpha-amylase, oxidative stress protection and lowering plasma glucose levels. Over the last few decades, α -glucosidase and α -amylase inhibition studies have been in the prime area of pharmaceutical research.¹³ Among the enzyme inhibitors, the compound, which resembles a non-hydrolyzable sugar moiety, inhibits pancreatic α -amylase significantly. The intestinal α -glucosidase activity is not suppressed by such compounds, causing fermentation of starch by intestinal bacteria leading to many side effects. Hence pharmacological studies have been exploring various α -glucosidase inhibitory metabolites of natural origin.^{14,15} Under such circumstances, natural products such as polyphenols/flavonoids, which are of non-sugar derivatives and have high natural abundance are of prime focus in antidiabetic study.

Biological activities of *Cyperus* species plants

Plants belonging to the Cyperaceae family are widely distributed in the tropical and subtropical regions of the world as perennial plants. There are around 699 accepted species names of the genus *Cyperus* recorded in the plant list (<http://www.theplantlist.org>) so far. The rhizome of *Cyperus* plants like *Cyperus rotundus*, *Cyperus distans*, *Cyperus articulatus*, *Cyperus esculentus* and *Cyperus papyrus* from various geographical regions have been reported as traditional or folk medicine. Many *Cyperus* species are traditionally used to treat analgesic, diuretic and carminative. The pharmacological studies on *Cyperus* species plants suggested various biological activities such as antioxidant, anticonvulsant, anti-inflammatory, antimicrobial, hepatoprotective, gastroprotective, anti-malarial and antidiabetic activities.¹⁶⁻¹⁹ Several works of literature reported the presence of phenolics, flavonoids, alkaloids, terpenoids and their essential oils. Solvent extracts of the rhizome of various *Cyperus* plants were studied to evaluate their biological activities and have reported their potential medicinal properties.^{3,20-23} Several research groups reported the chemical composition and antimicrobial activities of the rhizome essential oil, indicating the plant as a pharmaceutically important source.²⁴ Until now, some of the *Cyperus* plants have been extensively studied for their antidiabetic properties in both *in vitro* and *in vivo*. Many research groups have isolated, identified and reported the lead molecules responsible for such activities. The use of herbal antidiabetic medication has been in practice as the evidence about their effectiveness and drug safety has been proved in the past few decades through several works of literature in the field of phytochemistry, pharmacognosy and ethnopharmacology. In the present report, the *Cyperus* plants that are studied for the potential α -glucosidase inhibitory compounds or antidiabetic properties are reviewed

Cyperus articulatus L.

Cyperus articulatus is widely distributed in India and the Asian subcontinent. The plants appear long grass-like and are usually

grown in aquatic habitats or marshy soil.³ The plant rhizome has been used in folk medicine to treat ailments like epilepsy, malaria and dysentery in different parts of the world.¹⁶ Many researchers worked on the essential oil of these species to identify monoterpenes and sesquiterpenes.²² The essential oil of *Cyperus articulatus* was reported in various works of literature to have antimicrobial, anticancer, anticonvulsant and anti-malaria properties whereas the rhizome solvent extracts shown to have high antioxidant activities.²⁴⁻²⁷ Potential α -glucosidase inhibition activity of the rhizome extract of *Cyperus articulatus* was studied by Swain and Hariprasad.³ The dried rhizome was powdered and subjected to soxhlet extraction through a series of solvents in polarity order. The acetone extract was highly rich in phenolic (207.5 μ g GAE/mg of extract) and flavonoid (105.6 μ g QCTE/mg of extract) metabolites and showed high enzyme inhibition activity against α -glucosidase (yeast extracted). The acetone extract showed up to 95% inhibition at a maximum concentration of 62.5 μ g/mL. The IC_{50} value was measured as 9.1 μ g/mL crude extract. When subjected to various chromatographic separations, the extract yielded two fractions with significant α -glucosidase inhibitory activities. Those bioactive fractions were analyzed using HPLC-MS/MS to get phenolic and non-phenolic compounds. The non-phenolic compounds were N-(2-hydroxyethyl) palmitamide, 7,8-dihydroxystearic acid, phloionolic acid, c-16 sphinganine, phytosphingosine and lagochilin. The phenolic compounds detected in the study were quercetin, dihydroquercetin, embelin, mycophenolic acid and koparin-2-methylether. The compounds were not purified in that study to check their respective bioactivities. The phenolic-rich fraction showed competitive inhibition and the non-phenolic fraction showed non-competitive type inhibition in the α -glucosidase inhibition kinetics study. The phenolic inhibitors are of great importance because they are non-sugar type and could have potential inhibitory activity against intestinal α -glucosidase.

The detected compounds were studied for molecular docking with the yeast α -glucosidase (RCSB PDB: 3A4A). Significant interactions at the active site were responsible for the high binding energy for embelin, mycophenolic acid, quercetin and dihydroquercetin. These compounds formed H-bonding with one or more active site amino acid residues (Asp349, Asp212, Arg439, His277, Glu274 and Asp66) and the catalytic residues (Glu274, Asp349, and Asp212) of the enzyme. The flavonoid compounds were earlier reported to have high binding affinity with α -glucosidase active site amino acid residues.²⁸ The non-phenolic class of compounds is of hydroxyl fatty acid type of molecules. Such compounds (liposoluble fatty acids) were also earlier studied to have potential α -glucosidase inhibitory activities.^{29,30} Among the non-phenolics, 7,8-dihydroxystearic acid and N-(2-Hydroxyethyl)-palmitamide strongly interacted with the amino acid residues other than the catalytic ones but those interactions lead to significantly high binding energy.

Cyperus esculentus L.

Cyperus esculentus L. commonly known as Tigernut is a grass-like perennial plant that has an underutilized rhizome (tubers).³¹ This species has high biomass in tropical and Mediterranean regions.³² Southern European inhabitants use the tuber as a valuable food.³³ The tuber is rich in useful phytochemicals that effectively treat diseases such as obesity, diabetes, coronary heart diseases and gastrointestinal diseases.³⁴ The plant tuber was reported to have antioxidant, anti-inflammatory and anti-apoptotic properties and thus have a protective effect against lead acetate-induced testicular dysfunction in Wistar rats.³⁵

Oluwajuyitan and Ijarotimi studied the effect of tuber flour in different food compositions and measured the blood glucose concentration in streptozotocin (STZ)-induced diabetic rats.³⁶ Through physiological saline, the Wistar albino rats were induced by streptozotocin (150 mg/kg body weight (b.w.)). The rats were given 5% glucose solution to avoid the hypoglycemic effects of the drug. The BGLs were measured up to 72 h. It was observed that the blood glucose concentration, glycemic index (%) and glycemic load of Albino rats were significantly reduced when the rats fed on two formulated meals containing tuber flour and tuber flour proportionally mixed with defatted soybean.

Ijarotimi *et al.*³⁷ studied *Cyperus esculentus* flour for possible utilization in food formulation. The rhizome contains an appreciable amount of dietary fiber, carbohydrates, essential amino acids, and fatty acids. The study also reported the glycemic index of rhizome flour samples varied from 83.3%–95.9% revealing it as oral antidiabetic food.

Sabiu *et al.*³⁴ also studied the inhibition potential of aqueous extract of *Cyperus esculentus* rhizome on α -amylase and α -glucosidase taking PNPG as substrate. The inhibitory activities (IC_{50}) values were 5.19 and 0.78 mg/mL, respectively for α -amylase and α -glucosidase enzymes. The kinetic study showed the competitive and non-competitive modes of inhibition respectively for the two enzymes. In all these works the secondary metabolite analysis was not done.

Vega-Morales *et al.*,³⁸ studied the chemical composition of industrially processed *Cyperus esculentus* rhizome ethanolic extract where the compounds such as quercetin, stigmaterol, glycerol esters of linoleic acid and oleic acid, 4-chlorobutyl oleate, oleamide, myricetin, tyramine and *N*-feruloyltyramine, were detected. These compounds are expected to have antidiabetic properties as the other works of literature reported in their study.

Cyperus kyllingia Endl.

Cyperus kyllingia Endl. (Nut grass) is reported to have traditional use in treating malarial chills, pruritus of the skin, fever and diabetes.³⁹ It was reported in different studies that the methanol extract of the leaves has potential analgesic activities and the

ethanolic extract of the rhizome demonstrated depression of the central nervous system (CNS) activities.^{39,40} It is also used as an anti-venom product.⁴¹

Sudipta *et al.*,⁴² studied the antidiabetic effect of methanolic extract of *Cyperus kyllingia* root in alloxan-induced (A-I) diabetic rats. The Swiss adult Albino mice were injected with 180 mg/kg b.w alloxan monohydrate. Then they were administered with glucose solution after 6 h. The BGL was measured at regular intervals up to 48 h. As Alloxan (a β -cytotoxin), destroys the β -cells of the islets and thus reduces synthesis and release of insulin, it results in a rise in BGL. In the experiment, methanol extract of the rhizome was treated as a drug in the diabetic rat group. The LD_{50} value of methanolic extract was found to be 1758.28 mg/kg b.w. The dosage of methanol extract showed a significant decrease in the BGL. It was observed that initially (on the 0th day) the BGL of normal rat, diabetic controlled rat and treated rat were 116.34, 118.34 and 120 mg/dL, respectively, which changed to 116, 203 and 202 mg/dL respectively on the 1st day. On the 7th day, the BGL was measured as 117.5, 206, and 118.67 mg/dL, respectively. So the methanol extract of the rhizome was capable of reducing glucose level (glycemic index) *in vivo*. Histological study of the pancreas of the normal mice and different treated and untreated rats also supported the anti-hyperglycemic activity of the extract. The body weight of the treated rat also did not change much compared to the normal rat, unlike the diabetic-controlled rat.

Cyperus laevigatus L

Elshamy *et al.*¹⁹ studied the Antioxidant, anti-inflammatory and antidiabetic potential of the areal part solvent extract of *Cyperus laevigatus*. STZ adult albino rats (200-210 g) were divided into 4 groups (15 rats in each): control group, intra-gastric *Cyperus laevigatus* methanolic fraction treated group and diabetic group. The diabetes was induced by STZ (50 mg/kg b.w.). The rats having fasting glucose levels of 200 mg/dL after 48 hours of the injection were taken for the experiment. There were no toxic symptoms or mortality in rats up to 5000 mg/kg b.w. after 14 days. The diabetic group of rats treated with *Cyperus laevigatus* extract (50 mg /kg b.w. day) showed a decrease in the glucose, glucagon, and NO serum levels and promoted serum insulin and paraoxonase levels. In the histological study, there was a decrease in pancreatic islet size, atrophy, vacuolation, and connective tissue invasion in diabetic rats. The pancreatic β -cell numbers were reduced compared to the control group. A total of 8 flavonoid compounds of apigenin, luteolin chrysoeriol and tricetin-based structure, and their glycoside compounds were isolated and identified from the active fractions of hydro-methanolic extract (Table 1). The isolated compounds were characterized and established using various analytical methods, including UV, 1D, 2D-NMR and HR-ESI-MS.

Table 1: List of *Cyperus* plants and their detected ingredients studied for antidiabetic properties.

Plant	Part	Major bioactive constituent(s) detected	Activity of constituents/ extracts	References
<i>Cyperus articulatus</i> L.	Rhizome (Solvent extract)	Quercetrin, Dihydroquercetin, Embelin, Mycophenolic acid, Koparin-2-methyl ether, N-(2-Hydroxyethyl)palmitamide, 7,8-dihydroxy stearic acid, C16-sphinganine, Phytosphingosine, Rabilol and Lagochilin.	α -Glucosidase inhibition (p). IC ₅₀ 9.1 μ g/ml.for crude acetone extract.	3
<i>Cyperus esculentus</i> L.	Rhizome (Solvent extract)	NA	α -Amylase and α -glucosidase inhibition (p) by aqueous extract. IC ₅₀ values were 5.19 and 0.78 mg/ml respectively.	34
	Rhizome (flour)	NA	Reduced blood glucose concentration in STZ-induced diabetic rats.	36
<i>Cyperus kyllingia</i> Endl.	Rhizome (Solvent extract)	NA	Methanol extract reduced blood glucose concentration in the alloxanized mice.	42
<i>Cyperus laevigatus</i> L.	Aerial parts (Solvent extract)	Chrysoeriol 7-O- β -(6'''-O-acetyl- β -Dgluco pyranosyl)- glucopyranoside, Apigenin, Apigenin 7-O- β -glucopyranoside, Luteolin, Luteolin 7-O- β -glucopyranoside, Chrysoeriol, Chrysoeriol 7-O- β -glucopyranoside, and Tricin.	70% methanol extract reduced Mean serum glucose, glucagon and NO levels in STZ-induced diabetic rats. Serum insulin and serum paraoxonase activity level were increased.	19
<i>Cyperus pangorei</i> Rottb.	Rhizome (Solvent extract)	NA	Ethyl acetate sub fractions from ethanolic extract were treated with STZ induced diabeticrats. There was reduction in the level of serum TG, TC, LDL and VLDL and increase in seruminsulin and HDL level.	18

Plant	Part	Major bioactive constituent(s) detected	Activity of constituents/ extracts	References
<i>Cyperus rotundus</i> L.	Rhizome (Solvent extract)	(1) (2RS,3SR)-3,4,5,6,7,8-hexahydroxyflavane, (2) Cassigarol E, (3) Scirpusin A (4) Scirpusin B.	IC ₅₀ values (in μ M) for isolated individual compounds from methanol extract against α -Amylase and α -glucosidase (p) respectively: (1): 24.2 and 0 (2): 21.7 and 210.5 (3): 0 and 168.1 (4): 0 and 94.3.	44
	Rhizome (Solvent extract)	NA	Ethanollic extract exhibited significant anti-hyperglycemic activity (reduction in BGL) and also showed improvement in body weight, SGPT, SGOT, and lipid profile.	49
	Rhizome (Solvent extract)	(1) Stigmasterol (2) β -Sitosterol (3) 4-Hydroxyl cinnamic acid, (4) Caffeic acid (5) Kaempferol.	α -Amylase inhibition (%) at 40 μ g/ml and α -glucosidase (p) inhibition (%) at 20 μ g/ml respectively: (1) 12.3 and 4.0 (2) 10.2 and 0.0 (3) 23.5 and 6.3 (4) 9.7 and 4.8 (5) 5.4 and 0.0.	50
	Rhizome (Water extract)	NA	Inhibition of intestinal glucose absorption and promoting glucose consumption in type-1 and type-2 diabetic rat.	51
<i>Cyperus scariosus</i> R.Br	Rhizome (Solvent extract)	(1) Stigmasterol (2) β -Sitosterol (3) Lupeol (4) Gallic acid (5) Quercetin.	α -Amylase inhibition (%) at 40 μ g/ml and α -glucosidase (p) inhibition (%) at 20 μ g/ml respectively: (1) 12.3 and 4.0 (2) 10.2 and 0.0 (3) 7.3 and 13.1 (4) 31.2 and 2.7 (5) 5.6 and 24.7.	50
<i>Cyperus tegetum</i> Roxb	Rhizome (Solvent extract)	NA	Methanolic extract significantly reduced the BGL in alloxan-induced diabetic rats.	52

NA: Not analyzed, (p): PNPG as substrate (starch was taken as substrate in α -amylase inhibition assay).

***Cyperus pangorei* Rottb.**

Jain *et al.*,¹⁸ studied the *Cyperus pangorei* plant rhizome extract to measure the elevated levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) and decrease the level of high-density lipoprotein (HDL) and serum insulin level in STZ-induced diabetic rats. There were significant differences observed in serum insulin levels and serum lipid profiles in subfractions treated diabetic rats, diabetic

control and normal rats. Two ethyl acetate subfractions were found to minimize serum TG, TC, LDL and VLDL levels and increase serum insulin and HDL level. These subfractions showed significant anti-hyperglycemic activities in STZ-induced diabetic rats. It was observed that these ethyl acetate subfractions reduced the fasting plasma glucose concentrations from the initial day (197.7 and 188.86 mg/dL) to the 15th day (145.25 and 106.62 mg/dL) systematically. Histopathological studies supported the result as, after treatment with ethyl acetate subfractions, there was a

significant change in the beta cells of the pancreas, reduction in adipose tissue and intact cells of islets of Langerhans. The ethyl acetate extract is envisaged to be of good therapeutic value in preventing diabetes. Sub fractions also showed improvement in lipid profile as well as regeneration of β -cell of the pancreas and thus can be a source in the treatment of diabetes. The isolation and characterization of active compounds in the extract were not done in the study.

Cyperus rotundus L.

Cyperus rotundus has high distribution worldwide and has been extensively studied by many research groups for various biological activities. The plant has been used to treat menstrual disorders, dysmenorrhea, stomachache and inflammation.^{43,44} The strong antioxidant properties of the rhizome extract and its rich polyphenol profile have been reported by many research groups.^{20,45,46} It has also been reported that the rhizome metabolites showed cytotoxic effects against various tumor cells and anti-allergic activity *in vitro* and *in vivo*.^{46,47} The rhizome was earlier investigated for the phenolic/flavonoid compounds and the metabolites such as 3-hydroxy-4-methoxy-benzoic acid, galloyl quinic acid, ferulic acid, quercetin, luteolin, afzelechin, catechin were detected.⁴⁷

Hemanth Kumar *et al.*,²⁰ studied the rhizome for various biological assays. The 70% ethanolic extract of the rhizome has shown high antioxidant activities in radical scavenging, metal chelation, DNA protection and protein oxidation prevention. The same extract was shown to have anticholinesterase inhibitory properties in a dose-dependent manner up to a maximum concentration of 500 $\mu\text{g/mL}$. The LC-ESI-MS/MS analysis revealed a total of 22 metabolites of various classes in the extract. Raut and Gaikwad have studied the antidiabetic activities of rhizome extract in A-I hyperglycemic rats.⁴⁸ Oral administration of 70% ethanol extract (200 and 500 mg/kg) significantly controlled BGLs.

Tran *et al.*⁴⁴ have isolated four compounds namely (2RS,3SR)-3,4,5,6,7,8-hexahydroxyflavane, cassigarol E, scirpusin A and scirpusin B from the methanol extract of *Cyperus rotundus* rhizomes using chromatographic and spectroscopic methods (IR, NMR, HR-ESI-MS). The methanol extract was shown to have high inhibitory activity against α -glucosidase and α -amylase. The compounds in the extract responsible for the inhibition were also separately studied. The compound cassigarol E inhibited both α -glucosidase and α -amylase while the flavane compound acted only on α -amylase. The compounds scirpusin A and scirpusin B showed the best result on α -glucosidase (Table 1). In this study, the stilbene dimers were proposed as potential α -glucosidase inhibitors and, thus as promising anti-hyperglycemic agents.

Singh *et al.*⁴⁹ worked on the bioactivity of ethanolic extract of *Cyperus rotundus* rhizome to perform *in vivo* antidiabetic activity experiments in STZ-induced diabetic mice. The STZ-induced

diabetic mice were administered ethanol extract in a dose of 250 and 500 mg/kg b.w. Normal and diabetic control mice were also kept along with standard glibenclamide (10 mg/kg b.w.) treated mice. The fasting BGL in normal mice, STZ-induced diabetic mice and 500mg/kg b.w. Extract-treated mice were 77.66, 317.5 and 318.66 mg/dL, respectively on the day 1. The values changed to 78.16, 364.5 and 170.54 mg/dL, respectively on the 21st day. The extract exhibited significant anti-hyperglycemic activity and showed improvement in body weight, serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), and lipid profile during the experiment.

Kakarla *et al.*,⁵⁰ studied *in vivo* antioxidant, anti-inflammatory and antidiabetic activities of metabolites from *Cyperus scariosus* R.Br and *Cyperus rotundus* L. The solvent extracts (hexane, chloroform and methanol) were subjected to exhaustive chromatographic separation to isolate nine compounds. Stigmasterol, β -sitosterol, β -amyrin, Oleanolic acid, β -amyrin acetate were isolated from hexane extract. The compounds 4-hydroxyl butyl cinnamate and 4-hydroxyl cinnamic acid were isolated from chloroform extract. Caffeic acid and Kaempferol were isolated from the methanol extract. The compound concentration was increased up to 40 and 20 $\mu\text{g/mL}$ respectively for the α -amylase and α -glucosidase inhibition study. Among these compounds and 4-hydroxyl cinnamic acid showed the highest antidiabetic activities (Table 1).

Krisanapun *et al.*, reported the hypoglycemic or antidiabetic activities of water extract of *Cyperus rotundus* L. in type 1 or type 2 diabetic rats.⁵¹ The oral glucose tolerance test on type 1 or type 2 diabetic rats revealed that the water extract 0.5 g/kg could significantly reduce the plasma glucose levels and the toxicity of the water extract with a single oral LD₅₀ was more than 5 g/kg. The results of the experiments showed that the extract at a dose of 5 mg/mL could inhibit intestinal glucose absorption significantly and the extract at 1 mg/mL could enhance the glucose utilization of muscle like the function of insulin.

Cyperus scariosus R.Br

The antioxidant, anti-inflammatory and antidiabetic potential of the plant *Cyperus scariosus* were studied by Kakarla *et al.*⁵⁰ Five compounds were isolated from different solvent fractions through an extensive chromatographic method. Stigmasterol and β -sitosterol were isolated from hexane extract. Lupeol was isolated along with stigmasterol and β -sitosterol from the chloroform extract. Gallic acid and quercetin were isolated from methanol extract. These compounds were tested for α -amylase and α -glucosidase inhibition using the standard protocol. The compound concentration was increased up to 40 and 20 $\mu\text{g/mL}$ respectively for the α -amylase and α -glucosidase inhibition study. Among these five compounds, gallic acid and quercetin showed significant inhibitory activities (Table 1), while others showed mild and very little inhibition.

Cyperus tegetum Roxb.

Chaulya *et al*⁵² have studied the antidiabetic activity of methanol extract of rhizomes of *Cyperus tegetum* on alloxan-induced diabetic rats. Hyperglycemia was initially induced in fasted Wistar strain rats by i.p. injection of alloxan monohydrate (150 mg/kg b.w). The BGLs of the samples were tested on the 15th day. The rats having 200 mg/dL or above BGL were taken for an antidiabetic study. The BGLs were evaluated at regular time intervals. The glycemic index was lowered by administering methanol extract in a dose of 250 and 500 mg/kg b.w. after 4 h of treatment. It was observed that the fasting BGL in a normal rat, an alloxanized rat and 500mg/kg b.w. an extract-treated rat was 81.62, 215.21 and 304.36 mg/100 mL respectively on the initial day which changed to 78.06, 213.73 and 124.52 mg/100 mL respectively on the 7th day. The phytochemical screening of methanol extract was done to detect the presence of flavonoids, phenolic compounds, alkaloids, tannins, saponins and reducing sugars. In this study, the isolation and characterization of individual compounds were not performed.

CONCLUSION

Cyperus species plants having high distribution in different continents may be envisaged as a valuable source of economical, potent, and safer drug ingredients for diabetic management. The species *Cyperus articulatus* and *Cyperus rotundus* have been studied by many research groups to validate a range of biological activities including antidiabetic activities. The secondary metabolite profiles of these two plants were also exclusively studied to support their drug properties. Further preclinical and clinical studies may support the efficacy and drug safety of individual phytomolecules. The bioactive metabolites from *Cyperus esculentus*, *Cyperus kyllingia*, *Cyperus pangorei* and *Cyperus tegetum* have not been analyzed or isolated so far even though the crude products have shown significant antidiabetic activities. Some metabolites of *Cyperus* plants were reported to be good α -glucosidase inhibitors whereas other rhizome extracts and metabolites were shown to control the BGL, LDL and other parameters in different *in vivo* model experiments. The review advocates the need for further molecular and clinical-level research on the isolated metabolites from the studied *Cyperus* species plants and emphasized the importance of natural products in formulating antidiabetic or anti-hyperglycemic drugs. More phytochemical and biological studies are needed to explore the medicinal values of other underutilized *Cyperus* plants and the vast array of natural products for the benefit of humankind.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

ABBREVIATIONS

BGL: Blood Glucose Levels; **GAE:** Gallic Acid Equivalent; **HDL:** High-density Lipoprotein; **LDL:** Low-density Lipoprotein; **PNPG:** 4-Nitrophenyl β -D-glucopyranoside; **QCTE:** Quercetin Equivalent; **STZ:** Streptozotocin; **SGOT:** Serum Glutamic Oxaloacetic Transaminase; **SGPT:** Serum Glutamic Pyruvic Transaminase; **TC:** total cholesterol; **TG:** triglycerides; **VLDL:** Very Low-density Lipoprotein.

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