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Costus Igneus: a review of biological potential

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Abstract: *Costus igneus*, commonly known as the Spiral flag, is a member of the Costaceae family and is primarily cultivated as an ornamental plant in India, it has gained recognition as the "insulin plant" due to its claimed ability to stimulate insulin production with the increasing demand for herbal remedies to address diabetes mellitus and the side effects associated with oral hypoglycemic agents, there is growing interest in exploring plant-based solutions. This review article explores the biological properties of *Costus igneus*, its potential as an antidiabetic agent, antibacterial activities, etc. Additionally, cytotoxic assays are discussed as part of the preliminary investigation into the plant's medicinal properties.

Keywords: Costaceae, diabetes, hypoglycemic, mellitus.

Introduction

The botanical name *Costus igneus*, known as "katar kata" in Sanskrit, is commonly referred to as "Fiery Costus" or "Spiral Flag". This plant species is a member of the Costaceae family and can be found in tropical regions of Africa, Asia, and Australia[1]and also in the coastal regions of India, such as the Uttar Kannada district in the state of Karnataka, *Costus igneus* is cultivated. Local tradition involves consuming 2-3 leaves of this plant twice daily as a means to manage diabetes. Initial analysis of the plant extract has detected the presence of various compounds, including

carbohydrates, proteins, steroids, alkaloids, tannins, glycosides, saponins, fixed oils, and flavonoids (as reported by Nandhakumar et al. in 2007). Research has also indicated that the flavonoids in the plant exhibit antioxidant properties[2-3]. Recent research on *Costus igneus* has shed light on the antimicrobial properties as well, which can be attributed to the secondary metabolites they produce[4]. These phytochemicals, with potent antibacterial effects, are crucial in combatting bacterial infections, especially in light of antibiotic resistance, and the entire *Costus igneus* plant and has traditionally been utilized for its anti-diabetic properties, and its potential to protect the body from diseases, historically the rhizome of this plant has been used to treat a variety of conditions, such as fever, rash, asthma, bronchitis, intestinal worm infestations, eye ailments, stomach issues, discomfort in the neck and jaw, as well as tongue and mouth disorders, diabetes mellitus and the associated side effects of oral hypoglycemic agents[1]. Moreover, it has been employed to address specific health concerns, including fever, edema, dyspnoea (wheezing), hemorrhoids, and spermaturia. In the Siddha medicine system, the root of *C. igneus* has been employed in various forms, including as a powder (chooranam), a decoction (kudineer), and an oil (thylam) andChemical analysis has confirmed the presence of resinoids, essential oils, the alkaloid saussurine, inulin, and resin in *C. igneus*[6,7]. There is a growing interest in exploring plant-based preparations from traditional medicinal systems. This insulin plant, originally native to Southeast Asia but now cultivated in India, it is gaining global recognition as an Ayurvedic medicinal herb. While primarily utilized as an ornamental plant, its leaves are also consumed as a dietary supplement in the treatment of diabetes. Phytochemicals, bioactive compounds derived from plants, hold great significance in traditional herbal medicine, playing a pivotal role in defining mechanisms and provides protection against various diseases [8,9]. This research serves as an initial investigation, with the potential for further support through more targets.

Plant Description

It's a perennial plant with an upright growth habit, spreading and extending itself along the ground. Its leaves are simple, alternate, oblong, and evergreen, measuring approximately 4-8 inches in length and displaying parallel veins. This tropical evergreen plant boasts smooth, large leaves arranged spirally, with dark green topsides and attractive light purple undersides. These features contribute to its appealing look as it forms clusters with arching growth from its subterranean rootstocks. In the warmer months, it graces us with pretty 1.5-inch orange flowers that appear in cone-like clusters at the branch tips. This plant is a rhizomatous shrub that propagates through underground tuberous rhizomes. The rhizome of this plant exhibits a soft, cylindrical form with a fleshy consistency and a smooth, pale brown surface that thrives within the temperature range of

approximately 30 to 40 °C. Its scent is notably pleasing indigenous to eastern Brazil, specifically in the states of Bahia and Espiritu Santo, this plant is also distributed across Tropical Africa, North America, Asia, and Australia. It found its way to India from the Americas, where it was introduced as an herbal remedy for diabetes within India, *Costus* predominantly flourishes in the regions of Kashmir and South India. The spiral flag plant is adaptable to various light conditions, thriving equally well in both full sunlight and partial shade. It flourishes when planted in nutrient-rich soil with ample moisture, typically near a readily accessible water source. For propagation, it can be multiplied through techniques like splitting clumps, taking cuttings, or separating the offsets or miniature plantlets that emerge beneath the flower heads. Potential threats include pests such as mites and nematodes, particularly in sandy soil with low density. Encouragingly, as of now, there are no major diseases known to significantly hinder the growth of this plant[10].

Figure-1. Insulin Plant

Figure-2: Stem of *Costus igneus*

Figure-3: Leaf of *Costus igneus*

Figure-4: Rhizomes of *Costus igneus*

Phytochemical Constituents:

Costus igneus contains a range of phytochemicals, including flavonoids, terpenoids, and alkaloids, which are found in various parts of the plant, including the leaves, stems, and rhizomes[11-13].

Leaves

The leaf contains a variety of compounds, including carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, and flavonoids, among others. Additionally, the leaves contain carbohydrates such as rhamnose, steroids, and fatty acids like oleic acid, tetradecanoic acid, hexadecanoic acid, 9,12-octadecanoic acid, ethyl oleate, and squalene[3].

Traditional Uses

Leaves: In Ayurveda, diabetic individuals were advised to include Insulin plant leaves in their daily routine for a month. Initially, they were instructed to chew four leaves daily (two in the morning and two in the evening) during the first week, ensuring thorough mastication before ingestion. Following that, the dosage was reduced to two leaves per day, one in the morning and one in the evening, maintaining this regimen for a total of 30 days. This method proved effective in managing blood sugar levels. Moreover, these leaves had traditional uses, including enhancing overall health and longevity, treating skin ailments, addressing respiratory conditions like asthma and bronchitis, reducing fever, and expelling intestinal parasites[14.]

Rhizome: The rhizome of the insulin plant possesses diverse properties and uses, acting as an agent with astringent, acrid, bitter, cooling, aphrodisiac, anthelmintic, purgative, febrifuge, depurative, and expectorant qualities. It proves advantageous in the treatment of conditions including burning sensations, constipation, leprosy, worm infections, skin ailments, fevers, asthma, bronchitis, inflammations, and anaemia [14].

Pharmacological Activities:

The *C. igneus* plant exhibits a range of activities, with some awaiting confirmation. The different parts of the plant, such as leaves, stem, roots, rhizome, and the entire plant, have demonstrated various beneficial effects. Specifically, the leaves display significant hypoglycemic potential, the stem exhibits anti-urolithic activity, and both the stem and root show substantial antioxidant activity

Observed physiological impacts of *Costus igneus* plants

Plant Part	Biological activity	Result
	Antioxidant	Indicated increased levels of Super dismutase (SOD), Catalase (CAT), and Glutathione (GSH)[15]
	Antibacterial	The methanolic extract demonstrated noteworthy

Root		effectiveness against both gram-positive and gram-negative bacteria[7].
Stem	Antimicrobial	The methanolic extract exhibited substantial antimicrobial efficacy**[7].**
	Antiurolithiatic	A reduction of 98.25% in the weight of CHPD crystal was noted[16]
	Antioxidative	Demonstrated notable antioxidative properties**[17].**
Leaf	Mitigate cognitive impairment and memory deficits.	Diabetic rats with *costus igneus* retained their natural behavior, displayed enhanced learning abilities, demonstrated improved entrance latency, and spent less time in the dark room[18]
	Antiurolithiatic	The aqueous leaf extract exhibited a 1.00% reduction in the nucleation rate and growth of CHPD crystal at most. However, the root and stem extracts displayed even greater effectiveness in this regard[16.]
	Hypolipidemic	A noteworthy decrease was observed in the levels of total cholesterol, LDL, VLDL, phospholipids, and triglycerides, while there was an increase in HDL levels[19].
	Antiproliferative	The methanolic extract demonstrated a remarkable reduction in tumor size and exhibited an impressive 97.46% cytotoxicity effect**[20]**.
	Antioxidant	A significant imcrease in enzyme levels, including SOD, CAT, and GSH, was observed. Complete restoration of enzyme levels was achieved at the highest dosage of 600mg/kg. Furthermore, there was a notable reduction in MDA levels[3].
	Anti-inflammatory	The isolated compound β-amyrin exhibited remarkable 97% inhibition of paw edema when applied at a dose of 100 µg **[21]**.
	Hypoglycemic	A decrease of 75.72% in blood glucose levels**[18].**
Rhizome	Antioxidant	Demonstrated increased levels of SOD, CAT, and GSH**[17].**
	Hypolipidemic	A notable decrease in total

		cholesterol (TC), LDL, VLDL, and a mitigation of serum HDL level [15].
	Hypoglycemic	A decrease of 68.26% in blood glucose levels[15.]
	Antiurolithiatic	A weight reduction of 97.12% for CHPD crystals was achieved [16].
Whole Plant	Hypoglycemic	A decrease of 50.46% in blood glucose levels[22.]

Anti-inflammatory activity

Kripa Krishnan and colleagues conducted a study in 2014 to investigate the anti-inflammatory potential of β-amyrin, which was extracted from the leaves of *Costus igneus* (C. igneus). They employed a combination of a rat model with carrageenan-induced inflammation and an in vitro model using human peripheral blood mononuclear cells (hPBMCs) stimulated with lipopolysaccharide (LPS). In their research, they utilized a method of differential fractionation to extract the active compounds from *Costus igneus* leaves. The methanolic extract (MEC) of these leaves demonstrated the highest percentage inhibition of paw edema when administered at a dose of 100 mg/kg body weight. The researchers fractionated the MEC using various solvents, including chloroform, hexane, ethyl acetate, and butanol. Among these fractions, the chloroform extract (CEC) of MEC exhibited the most significant beneficial effects when administered at a dose of 50 mg/kg body weight, treating carrageenan-induced rats with CEC, there was a notable reduction in the activities of enzymes such as cyclooxygenase (COX), lipoxygenase (LOX), myeloperoxidase (MPO), and nitric oxide synthase (NOS) compared to rats with carrageenan-induced inflammation. β-amyrin, which was isolated from CEC, displayed a dose-dependent decrease in paw edema. At a dose of 100 µg, it produced a remarkable 97% reduction in carrageenan-induced paw edema in rats [12].

Effect of *Costus igneus* on Learning and Memory:

In a study conducted by Shalini Adiga *et al.* in 2014, the impact of *Costus igneus* on learning and memory in both normal and diabetic-induced rats was investigated. They administered ethanolic extracts of *Costus igneus* at doses of 250mg/kg and 500mg/kg to rats with streptozotocin-induced diabetes (35mg/kg). After a 30-day study period, blood glucose levels were measured, and the rats underwent a passive avoidance test. The results revealed that the treatment with *Costus igneus* extract significantly lowered blood glucose levels in a dose-dependent manner, with a remarkable 75.70% reduction observed at the 500mg/kg dose in the diabetic-treated groups compared to the diabetic control group. Importantly, there was no notable impact on non-diabetic rats, as their blood

glucose levels remained within the normal range. During the passive avoidance test, the *Costus igneus*-treated diabetic rats exhibited a shorter time taken to enter the dark compartment, indicating that their innate behavior remained intact and that they showed improvements in learning. Conversely, the diabetic rats not treated with *Costus igneus* demonstrated impaired performance in the passive avoidance test. Furthermore, in post-shock retention testing conducted after 24 and 48 hours, the *Costus igneus*-treated rats displayed a significant increase in their movement toward the entrance of the darkroom and a decrease in the time spent in the darkroom[13,23]

Anti-Proliferative Potential:

In a study conducted by Prof. S. Dhanasekaran and colleagues in 2014, they explored the potential anti-proliferative and anticancer effects of a methanolic extract derived from powdered leaves of *Costus igneus* (MECiL) on the MCF7 breast cancer cell line in vitro. Their findings indicated that MECiL exhibited notable cell toxicity specifically against the MCF-7 cell line, particularly at a dosage of 2000 µg/ml, where it demonstrated significant anticancer activity with a cytotoxicity rate of 97.46±0.74 percent. This demonstrated that MECiL's cytotoxic effects were dose-dependent on MCF-7 cells. Furthermore, the researchers evaluated the impact of MECiL (at concentrations ranging from 15 to 2000 µg/ml) on the L6 cell line, a rat skeletal muscle cell line, using the MTT assay. Interestingly, MECiL did not display any cytotoxicity on the normal L6 cell line. While it did exhibit an IC50 value at the highest concentration (2000 µg/ml), it is worth noting that at elevated doses, MECiL also induced some cytotoxicity in normal cell lines, although this effect was not harmful[24].

Antimicrobial Activity

Arun Nagarajan and colleagues (2011) explored the antimicrobial potential of *Costus igneus* by utilizing 100mg of its root powder. Their study focused on assessing the antibacterial activity of in vitro cultivated root extracts against Gram-negative bacterial cultures, including Pseudomonas aeruginosa, Klebsiella pneumonia, Salmonella sp, and Proteus vulgaris. To extract the bioactive compounds, approximately 10 grams of root material, obtained from the application of two growth regulators, IAA and IBA, was subjected to Soxhlet extraction with acetone, chloroform, and methanol as solvents. In their research, the combination of IAA and IBA was introduced into the MS (Murashige and Skoog) medium to induce direct root growth. Interestingly, Klebsiella pneumonia exhibited significant susceptibility to root extracts derived from both IBA and IAA when acetone was used as the solvent, showing an impressive zone of clearance measuring 25 mm, which was comparable to the effectiveness of the commercially available antibiotic Gentamycin[25].

Antioxidant

Bioactive screening revealed that all three extracts are good sources of phytochemicals, including alkaloids, flavonoids, carbohydrates, glycosides, saponins, tannins, phytosterols, and phenolics. In *in vitro* antioxidant assays, the acetone extract of *C. igneus* exhibited higher FRAP activity, superoxide radical scavenging activity, and DPPH scavenging activity. The hexane extract of *C. igneus* demonstrated the highest potential in ABTS scavenging activity, antioxidant capacity in the phosphomolybdenum assay, and recorded significant maximum reducing power with the highest optical density. Meanwhile, the hot water extract exhibited the highest metal ion-chelating ability. The acetone extract of *C. igneus* displayed the highest cytotoxic activity against the cancer cell line (MCF-7) when compared to the positive control, doxorubicin. This study, therefore, highlights the efficient antioxidant activity and cytotoxic potential of *C. igneus*, suggesting its potential for safe and cost-effective biological applications[2].

Antiurolithiatic Property

Yuvrani and her team conducted a 2017 study investigating the antiurolithiatic properties of the insulin plant. They used aqueous extracts from the stem and rhizome of this plant and discovered that these extracts promoted the formation of hydroxyapatite (HAP) crystals while reducing the nucleation rate of CHPD crystals, a major component of calcium urinary stones. The growth of Calcium hydrogen phosphate dihydrate (CHPD) crystals was observed using the single diffusion gel growth technique, and the inhibitory effects of the aqueous extracts from the leaves, stems, and rhizome of *Costus igneus* on the growth of CHPD crystals were analyzed. To validate the effects of these extracts on CHPD crystal growth, five different concentrations (0.15%, 0.25%, 0.50%, 0.75%, and 1.00%) were tested. The plant extracts demonstrated inhibitory effects compared to the control group (pure calcium chloride), resulting in the minimal apparent growth of crystals. As the concentration of the aqueous extracts from *Costus igneus* increased from 0.15% to 1.00% (w/v), the weight of the formed crystals gradually decreased from 2.03 g to 0.06 g for leaves, 0.05 g for rhizomes, and 0.03 g for stems. This inhibitory activity was attributed to the presence of natural substances, including protein (18%), iron (40 mg), and antioxidants such as ascorbic acid, β-carotene, α-tocopherol, glutathione, phenols, flavonoids (like diosgenin and quercetin), steroids, alkaloids, and terpenoids[16].

Hypolipidemic Activity

Pazhanichamy Kalailingam and colleagues, in their 2011 study, explored the antihyperglycemic and hypolipidemic effects of the methanol extract of *Costus igneus* rhizome (MECiR) in diabetic albino rats induced with streptozotocin (STZ). They administered MECiR at doses of 100 and 200 mg/kg orally as a single daily dose to the diabetic rats over 30 days. The results revealed significant reductions ($p<0.05$) in fasting blood glucose levels, as well as in serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels in the diabetic rats. Conversely, there was a notable increase ($p<0.05$) in the serum high-density lipoprotein (HDL) levels, particularly with the 200 mg/kg dose. The antidiabetic and hypolipidemic effects observed in the STZ-induced diabetic albino rats were comparable to those of the standard reference drug, glibenclamide (5 mg/kg body weight)[15].

Toxicity study

Various studies have assessed the acute toxicity of different extracts from C. *pictus* and C. *igneus*. In the case of *C. pictus,* no mortality or behavioural issues were observed when aqueous extract doses ranging from 5 to 40 g/kg of body weight were administered[26]. Furthermore, a 30-day treatment with an aqueous extract at 1 g/kg body weight showed no adverse effects on general behavior, and all animals survived the test period. For *C. igneus,* the ethanolic extract exhibited no significant signs of toxicity when administered at doses from 50 mg/kg up to 5000 mg/kg of body weight[27]. There were no deaths reported during the study, indicating the safety of the extract at the highest tested dose of 5000 mg/kg[28]. However, a different study focusing on the methanolic extract of *C. igneus* found toxicity at a dose of 250 mg/kg body weight[29] Additionally, it's worth noting that palmitic acid, a major component found in the oils of C. pictus, has been associated with adverse effects such as myofibril degeneration in adult rat cardiomyocytes and an increased LDL to HDL cholesterol ratio, which is linked to coronary heart disease. This suggests that prolonged use of C. pictus leaves for diabetes treatment may pose a risk of serious cardiac diseases, making it an undesirable option for treatment.

Conclusion

The existing research on *Costus igneus* has demonstrated its significance as a medicinal herb, showcasing a range of pharmacological benefits. Investigations into this plant have revealed the presence of essential phytoconstituents such as conjugated flavonoids, flavones, flavonols, catechin and its derivatives, chlorophylls a and b, resinoids, essential oil, saussurine (an alkaloid), inulin, and resin, among others. These compounds have been identified as responsible for a variety of therapeutic properties, including its effectiveness in managing diabetes, inhibiting cell proliferation, displaying antimicrobial activity, preventing urolithiasis, reducing inflammation, enhancing cognitive function, acting as an antioxidant, offering neuroprotection, and lowering lipid levels.

Further research is essential to delve deeper into the medicinal properties and various phytoconstituents responsible for these pharmacological effects, aiming to develop more reliable and safer treatments for the well-being of humanity in the future.

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