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A DISCUSSION ABOUT INSULIN PLANT

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ABSTRACT: "*Costus igneus*," popularly known as the "insulin plant," is a herb that has been used for medicinal purposes in Southeast Asia since ancient times. It is just recently that the plant was imported to India, and in the southern region of the country, it is being grown as an appealing plant. In addition to other phytochemicals, the insulin plant contains elements such as steroids, alkaloids, flavonoids, triterpenes, glycosides, and saponins. Diabetes mellitus is being treated using the leaves of this plant by incorporating them into the diet of the patient. "A leaf a day keeps diabetes away" is the mantra that the plant has adopted. A wide variety of pharmacological effects can be observed, including those that are anti-inflammatory, anti-proliferative, antibacterial, anti-urolithiasis, and anti-diabetic, amongst others. Therefore, the purpose of this review study is to evaluate the many medicinal characteristics of the "insulin plant," also known as *Costus igneus*, to make it possible for it to be utilized in future research and to assist individuals.

INTRODUCTION: Consequences of insufficient insulin production include hyperglycemia and disturbances in carbohydrate, lipid, and protein metabolism and a host of other metabolic abnormalities are hallmarks of diabetes mellitus (DM), a disease or chronic metabolic disorder with numerous origins. Diabetes mellitus is a major issue throughout the globe due to anomalies in insulin production by β-Langerhans or in the capacity of cells to react to insulin properly [1–5]. The current prevalence is expected to be 8.3% (382 million), with a projected increase to 10% (592 million) by 2035. Around 5 million lives have been lost due to complications of diabetes mellitus [6–11].

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The goal of diabetes treatment is to restore insulin sensitivity to slow the progression of the disease and its associated consequences. This can be accomplished in part through the use of a sugar-lowering medication orally, such as "metformin, glyburide, chlorpropamide, *etc*.", and insulin. The World Health Organization has emphasized the importance of investigating plant-based alternatives to conventional diabetic agents in the management of this disease [12, 13].

Metformin, a common diabetic medicine, was initially developed from *Galega officinalis*, a European herb high in guanidine that was proven to lower the glucose level. This achievement prompted researchers to look for another potential plant as an antihyperglycemic agent, and they discovered the insulin plant, also known as yacon (*Smallanthus sonchifolius*), in Indonesia [14, 15]. It is imperative to comprehend the efficacy, security, and mechanism of insulin plants in the treatment of diabetes mellitus.

The leaves contain enhedryin and sesquiterpene lactone, both of which reduce postprandial glucose in diabetic animals at a minimal dose of 0.80 mg/kg5 [16–19]. This article aims to summarise current insulin plant research for diabetics.

"*Costus igneus* (Insulin plant)": The Costus plant's leaves, which are a member of the family "Costaceae", are used to increase insulin production in humans, earning it the name "insulin plant" in India. Herbal therapies for diabetes mellitus are in high demand due to the increasing awareness of the risks associated with oral hypoglycemic medications [20, 21]. Traditional and folk medical practices use a broad range of plant-based medications to treat and control diabetes mellitus. For future pharmaceutical entity development or as a dietary complement to existing therapies, Research on novel plant-derived oral hypoglycemic compounds will be used as a standard [22, 23]. The plant that produces insulin is one of these historical plants that is currently commonly used as an ayurvedic medicinal herb and is gaining favor on a global scale. It has been reported that diabetics whose treatment included the use of these leaves had a reduction in their blood glucose levels [24, 25]. The Greater Sunda Islands off the coast of Indonesia are where the insulin plant was first discovered. As a decorative plant, it has only recently been introduced to the Indian state of Kerala. Chewing the leaves of the plant for a month is the traditional Ayurveda treatment for diabetes. This results in a more stable blood glucose level [26, 27].

Taxonomical Plant Description: *Costus igneus* is a perennial, erect, evergreen tropical plant that pertains to the Costaceae genus. Simple, alternating, entire, oblong, 4–8-inch leaves with parallel venation [28, 29–33].

The huge, glossy, dark green leaves are arranged in a spiral around the stems and have light purple undersides; these plants grow from elegant, arching rootstocks in the ground. The tallest stems collapse and lie on the ground at a height of around 60cm [34–36]. In the warmer months, cone-shaped heads at the ends of the branches 2 are covered in stunning orange flowers with a diameter of 2.5-12.5 cm. Stem cutting is a method of plant propagation for insulin [37–40].

Common names: "Fiery Costus, Spiral flag, Insulin plant, Step ladder" [41].

TABLE 1: TAXONOMY [42]

Botanical Name	*Costus igneus*
Domain	eukaryote
Kingdom	Plantae
Subkingdom	Virdaeplantae
Phylum	Treacheophyta
Subphylum	Euphylophitina
Infra-Phylum	Radiotopses
Class	Liliosida
Subclass	Commelinidae
Super Order	Zingiberrance
Order	Zingiberales
Family	Costaceae
Subfamily	Asteroideae
Tribe	Coriopsidae
Genus	Costus
Specific Epithet	igneus

Phytoconstituents: "Steroids, triterpenoids, alkaloids, tannins, flavonoids, glycosides, saponins, carbohydrates, and proteins" were all detected using phytochemical analysis. The highest concentration of phytochemicals was discovered in the methanol extract [43–45]. During initial screening, methanolic extracts of wild plants and calluses (MS and LS media) contained high concentrations of phytochemicals such as phenols, alkaloids, flavonoids, and terpenoids. Protein, iron, and antioxidant components were all found in high concentrations in a sequential screening of the phytochemicals in Costus leaves [46, 47, 48–52].

Medicinal Uses in Ayurvedic System:

Leaves: For 30 days, diabetics must consume the leaves of the Insulin plant. The prescribed regimen entails the patient taking two intermittent pauses per diem, specifically in the morning and evening, over seven consecutive days [53, 54]. It's important to chew the leaves thoroughly before consuming. After a week, the patient can increase their dosage to one leaf taken twice daily [55, 56]. During the next 30 days, keep taking this dose. It's recommended by conventional medical professionals and proved to help achieve complete blood sugar control. "a leaf a day keeps diabetes away" is the insulin plant's tagline [57–61].

Rhizome: Used for treating a "burning feeling, constipation, leprosy, worm infection, skin illnesses, fever, asthma, bronchitis, inflammations, and anemia, the rhizome of the insulin plant is also astringent, acrid, cooling, aphrodisiac, purgative, anthelmintic, depurative, febrifuge, and expectorant” [62–65].

Insulin Plant Pharmacological Activities: “The insulin plant has been reported with many activities. Among them, some are yet to be validated. The various plant parts are shown such activities are leaf, stem, root, rhizome, and whole plant. Leaves contribute to prominent hypoglycemic potential. The stem is majorly reported with antiurolithiatic activity. Both stem and root have been shown significant antioxidant activity” [66–70].

Anti-Diabetic Effects: Diabetic rats produced with streptozotocin (D-STZ) are frequently used in research on the efficacy of insulin plants as an antidiabetic medication. Extracts of the insulin plant (either from the roots or the leaves) are given to diabetic rats [71, 72]. Klinsman (2018) evaluated the effect of insulin leaves extract and found that glycemia decreased by 63.9 percent, insulin concentration increased by 49.3 percent, Pancreatic islet cells improved, triacylglycerol and free fatty acid levels reduced, antioxidant enzyme activity rose, and cardiac tissue was repaired [73, 74]. Correspondingly, Genta (2010) evaluated five organic compounds and found that all five significantly improved dysmetabolism and cardiomyopathy associated with DM [75–77]. Extracts in 50, 10, and 20 mg/kg of methanol, butane, and chloroform are hypoglycemic. After taking the extract once a day for eight weeks, blood sugar levels and insulin production are under control. Caffeic acid, chlorogenic acid, and three dicaffeoylquinic acids were found to be the most abundant phytochemicals in the butanol extract, the most potent fraction. “Enhedrin, a major sesquiterpene lactone from insulin leaves, has been shown to reduce postprandial glucose and is useful in diabetes” [78, 79]. Explains how the effect works by suggesting that methanol extract from the insulin plant may affect the alpha-amylase alpha-glucosidase enzyme that lowers blood glucose and could help people with diabetes who have high blood sugar.

Gilberto (2013) compares four groups: a control (C), a group given Insulin plant extract (Y), Type 1 diabetes (DM-1) without treatment, and Type 1 diabetes treated with insulin plant extract (Y-DM1) [80, 81]. Water and food consumption are said to have dropped dramatically in Y-DM1. Diabetes-related metabolic abnormalities in rats were considerably improved by consuming YRAE. Habib (2011) reported that fasting plasma triacylglycerol and LDL were significantly reduced by insulin plant roots diet oral supplementation in D-STZ rats, indicating that YRAE has a hepatoprotective effect [82, 83]. Triacylglycerol postprandial plasma peak and pancreatic cells are both safeguarded by supplement use. Those who were given an insulin plant roots supplement also showed an increase in GLP-1, one of the two incretin hormones [84, 85].

Extracts from both roots and leaves have been studied for their effects on D-STZ rats. Both extracts are useful against hyperglycemia. Nevertheless, when it comes to lowering reactive oxygen species (ROS) and restoring antioxidant enzyme performance, root extract is superior to leaf extract [86–89]. It is suggested that root extract is superior to leaf extract. Using a plant extract to treat diabetic rats has a preventive effect against the complication of nephropathy, which is brought on by free radicals. The usefulness of insulin plants in the treatment of diabetes goes beyond the antihyperglycemic impact or increase in insulin production, as shown by the plant extract's potent anti-free radical effects when tested in vitro on the roots [90]. The insulin plant's high phenolic chemical content in its roots and leaves is responsible for its antioxidant properties. Much more phenolic acid can be found in the insulin plant's leaves than in its interior spaces [91, 92].

The active component on the insulin plant's leaves and roots is responsible for its ability to lower blood sugar levels [93]. For instance, improving insulin receptor sensitivity with a high phenol chemical content may help with the management of diabetic Mellitus. A phenolic extract from insulin plants has been shown to boost mRNA expression in the livers of rats, leading to lower blood sugar levels in those animals. Since it inhibits -glucosidase, caffeoylquinic may also play a role in lowering blood sugar [94].

Anti-Proliferative Potential: The “Methanolic extract of *Costus igneus* powdered leaves (MECiL)” was tested for its anti-proliferative and apoptotic activities on the “MCF 7 (Michigan Cancer Foundation-7)” breast cancer cell line *in-vitro* by [95] S. Dhanasekaran *et al.* in 2014. The extract (MECiL) shrank the tumor without harming the healthy cells. Additionally assessed were the supplied extract's cytotoxicity and cell viability on the “L6 Rat skeletal muscle cell line (15-2000 g/ml)” using the “MTT (3- (4, 5- dimethyl thiazol-2-yl)-2, 5-diphenyl tetrazolium bromide assay test)”. The insulin plant leaf extract found in this research has an IC50 value of 2000 g/ml. Only at very high doses did the extract exhibit cytotoxicity consistent with that of the common cell lines, but it did not cause apoptosis in the common cell lines. At a dosage of 2000 g/ml, the extract was shown to have a cytotoxicity of 96.45 0.75%, indicating potent anticancer activity. Additionally, the plant's extract exhibits dose-dependent cytotoxicity when applied to the MCF-7 cell line [96].

Antimicrobial Activity: Using its 100mg of powdered root, worked and researched the antibacterial properties of *Costus igneus* [97]. Testing for antibacterial activity was conducted using Gram-negative bacteria such as *Cholera vulgaris*, K. pneumonia, Salmonella sp., and *P. aeruginosa*, among others (*Costus igneus* root extracts cultured *in-vitro*). Approximately 10 grams of roots were extracted using the Soxhlet technique with 5 milliliters of acetone, chloroform, and methanol from “Indole 3-acetic acid (IBA)” and “Indole butyric acid (IAA)”. Direct root induction was investigated by adding the two growth regulators IAA and IBA to MS (Murashige and Skoog) media. Most susceptible to both of the aforesaid regulators generated from the roots of the insulin plant, *Klebsiella pneumonia* was shown to be a solvent utilizing acetone. Its zone of inhibition was discovered to be 25 mm2, almost identical to the antibiotic Gentamycin [98, 99].

Antiurolithiasis Property: The insulin plant's aqueous stem and rhizome extract have been studied for their antiurolithiatic qualities, and researchers have shown that it can stimulate the development of “Hydroxyapatite (HAP)” crystals and slow the nucleation rate of CHPD crystals, both of which are key components of urinary calcium stones [100]. The inhibitory effect of aqueous extracts of *Costus igneus* leaves stems, and rhizome on the formation of "calcium hydrogen phosphate dihydrate (CHPD)" crystals was investigated using the single diffusion gel growth technique [101]. Single diffusion gel growth produced CHPD crystals. Later, *Costus igneus* leaves, stem, and rhizome aqueous sex tracts were tested for CHPD crystal formation. Five plant extract concentrations (0.15%, 0.25%, 0.50%, 0.75%, and 1.00%) were chosen. Plant extracts inhibited with shorter crystals than controls. (Pure calcium chloride). The produced crystals weight decreased from 2.003g to 0.003g (stem), 0.005g (rhizome), and 0.006g (leaves) as the *Costus igneus* aqueous extract concentration increased from 0.15% to 1.00%.

Anti-Inflammatory Potential: The study conducted by Kripa Krishnan and colleagues in 2014 investigated the potential anti-inflammatory properties of β-amyrin derived from the leaves of *Costus igneus* [102]. The research was carried out using a rat model induced with carrageenan, as well as human peripheral blood mononuclear cells stimulated with LPS *in-vitro* (hPBMCs).

Paw edema was significantly reduced by the "Methanolic extract (MEC)" generated by an asymmetric fractionated *Costus igneus* leaves, with the greatest decrease shown at a dosage of 100 mg/kg. Chloroform, hexane, ethanol, and butanol were used to separate the methanolic extract. 500mg ME the most significant result was seen in the Cgivenata chloroform extract (CEC).

CEC dramatically reduced COX, LOX, MPO, and NOS activity in carrageenan-induced rats. Its β-amyrin reduced paw edema by 97% in carrageenan-induced pawed main rats at 100μg [103].

Antioxidant Activity: Ramya Urs S. K. *et al.* (2015) examined the impact of methanolic extraction antioxidant activity against “*Klebsiella oxytoca*”, “*Pseudomonas fragi*”, and “*Enterobacter aerogens*” at various doses ranging from 100 g/mL to 500 g/Ml [99]. Root and stem extracts of the plant *Costus igneus* were studied for their antioxidant and radical-scavenging abilities. Root extract had a much greater rate of inhibition than stem extract. The root extract has significant vitamin E concentrations. Furthermore, it was found that root extracts had a higher total phenolic content than stem extracts.

Hypolipidemic Activity: The effects of the methanol extract of the *Costus igneus* rhizome (MECiR) on blood sugar and cholesterol levels were examined by Pazhanichamy Kalailingam *et al.* (2011) in albino rats with streptozotocin (STZ)-induced diabetes [51]. Rats induced with diabetes were administered MECiR orally twice daily for 30 days, at doses of 100 and 200 mg/kg.

The results demonstrated that while serum levels of "High-Density lipoprotein (HDL)" were significantly elevated (p 0.05), "fasting blood glucose levels", "total serum cholesterol (TC)", "triglycerides (TG)", "low-density lipoprotein (LDL) levels", and "very-low-density lipoprotein (VLDL)"levels in diabetic rats were markedly reduced. With 200mg/kg, better outcomes were attained. The effects of glibenclamide (5 mg/kg/bw) as a standard reference drug were equivalent to those of anti-diabetic and hypolipidemic drugs in STZ-induced diabetic albino rats.

Hepatoprotective Activity: *Costus igneus* plant protected rats from paracetamol-induced liver injury, according to Nimmy Chacko *et al.* (2012) [49]. Oral paracetamol 300mg/kg caused liver damage in this trial. *Costus igneus* leaf alcoholic extract, Silymarin, and 100mg/kg ardina were used. High blood enzyme levels and histological evidence of zonal focal necrosis revealed liver injury. *Costus igneus* extracts before paracetamol protected harm ($P < 0.05$). Normal enzyme levels and no necrotic alterations in pathological investigations supported it.

400mg/kg *Costus igneus* had an effect similar to silymarin. Paracetamol-treated rats had significant inflammation with localized necrosis, but *Costus igneus*-treated rats had almost normal hepatocytes. Thus, *Costus igneus* alcoholic extract reversed paracetamol-induced hepatotoxicity.

Extraction of Insulin Plant: Fresh *Costus igneus* leaves were gathered, washed, and shade-dried before being mechanically processed into powder, processed through a 20-mesh filter to ensure uniform size, and weighed separately. The powdered materials (10 g) were split using a Soxhlet apparatus and extracted with methanol, as seen in **Fig. 1.** The extraction process took place for 8 hours at 30 °C in the room. The extracts were used for further examination after being concentrated and filtered at 70 °C in a rotary evaporator [104, 105].

FIG. 1: SOXHLET APPARATUS FOR METHANOLIC EXTRACTION OF PHYTOCHEMICALS FROM THE LEAVES OF *COSTUS IGNEUS*

CONCLUSION: A powerful herbal remedy that has been used for centuries is *Costus igneus*. The current review paper demonstrates the great medicinal value of the *Costus igneus* plant. The existence of significant phytochemical components including "diosgenin, corsolic acid, beta-sitosterol, beta-amyrin, quercetin", and others, as well as their pharmacological activity, demonstrated that the plant has the potential to become a major player in the future development of novel, effective medications.

This analysis will help researchers develop more effective insulin plant extract formulations for the treatment of diabetes mellitus and other conditions where it has shown promise, including as an anti-inflammatory, antioxidant, anti-proliferative, anti-urolithiasis, and hypolipidemic agent.

The *in-silico* method of study demonstrates the promising effects of insulin plant leaves and their phytochemical components, despite the fact that they have shown therapeutic potential when used as a dietary supplement or in conjunction with synthetic anti-diabetic medicines, more research is needed to fully understand their role in the management of diabetes mellitus. Future study is advised to improve the bioavailability, therapeutic impact, and drug delivery of insulin plants utilizing innovative formulations that use each separated ingredient.

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