Review Article

A Review on Medicinal Exploration of *Costus igneus*: The Insulin plant

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ABSTRACT

Costus igneus (or insulin plant) is a traditionally used medicinal herb which is native to Southeast Asia. The plant has been recently introduced into India and it is grown as an ornamental plant in south India. Insulin plant contains various phytochemical constituents like steroid, alkaloid, flavonoid, triterpene, glycoside, and saponins. Its leaves are being used as a dietary supplement in the treatment of diabetes mellitus. The catchphrase of the plant is: "a leaf a day keeps diabetes away". Various pharmacological activities include antidiabetic effect, antiproliferative potential, antimicrobial activity, antiurolithiatic property anti-inflammatory potential, its effect on learning and memory, antioxidant activity, neuroprotective role, hypolipidemic activity etc. The present review article attempts to explore various medicinal properties of *Costus igneus* (insulin plant) for research purposes and its suitable formulation development in the future for the welfare of mankind.

Keywords: *Costus igneus*, Insulin plant, Leaf, Phytoconstituents, Ayurvedic use, Pharmacological activities, Marketed products.

INTRODUCTION

Costus belongs to the family Costaceae, commonly known as insulin plant in India because its leaves help to build up insulin in the human body[1]. Since oral hypoglycemic agents possess various side effects, there is a growing demand for herbal remedies for the treatment of diabetes mellitus. Many plant preparations are used in folklore and traditional system of medicine to manage diabetes mellitus. Investigation on new oral hypoglycemic compounds from medicinal plants will set a milestone for the development of pharmaceutical entities or as a dietary adjunct to existing therapies in the future. Insulin plant is one such traditional plant which is getting global acceptance nowadays and is now widely used as an ayurvedic medicinal herb. Consumption of the leaves are believed to lower blood glucose levels, and diabetics who consumed the leaves of this plant said to have a fall in their blood glucose levels. Insulin plant is native to Southeast Asia, especially on the Greater Sunda Islands in Indonesia. It is relatively a new entrant to India and is being grown as an ornamental plant in Kerala. In the Ayurvedic system of medicine, diabetes is traditionally treated by chewing the plant leaves for a period of one month to get a controlled blood glucose level[1].

Plant Description

Figure 1: Insulin Plant

Costus igneus N.E. Br. is a perennial, upright, tropical evergreen plant belongs to the family Costaceae. Possesses evergreen leaves which are simple, alternate, entire and oblong, having 4-8 inches length with parallel venation. The large, smooth, dark greens leaves possess light purple undersides and are spirally arranged around stems, forming attractive, arching clumps arising from underground rootstocks. It reaches a height of about 60cm with the tallest stems falling over and lying on the ground. Beautiful orange flowers are produced in the warm months having a 2.5-12.5cm diameter, appears on cone-like heads at the tips of branches[2]. Propagation of insulin plant is by stem cutting[1].

Common names: Fiery Costus, Spiral flag, Insulin plant, Step ladder[3]

Table 1: Vernacular names[4]

Languages	Names
English	Spiral Ginger, Spotted Spiral Ginger, Painted Spiral Ginger
Telugu	Peddavesiga, Yeangesha
Urdu	Bijasar, Dam al akhwain
Bengali	Piasal
Hindi	Banda, Bija-sal, Peisar , jarul, Keukand
Kannada	Kempu honne
Malayalam	Honne, Karintakara, Vengai, Venna-maram
Marathi	Honi , Pushkarmula
Sanskrit	Asana, Bandhukapushpa
Tamil	Neyccarikamaram, Venkai-c-ciray , Kostam
Gujarati	Pakarmula

Table 2: Taxonomic position[5]

Botanical name	*Costus igneus*
Domain	Eukaryo ta
Kingdom	Plantae
Subking dom	Viridaeplantae
Phylum	Tracheophyta
Subphylum	Euphylophitina
Infraphylum	Radiotopses
Class	Liliopsida
Subclass	Commelinidae
Superorder	Zingiberane
Order	Zingiberales
Family	Costaceae
Subfamily	Asteroideae
Tribe	Coriopsidae
Genus	Costus
Specific epithet	igneus

Phytoconstituents

Phytochemical screening showed the presence of steroids, triterpenoids, alkaloids, tannins, flavonoids, glycosides, saponins, carbohydrates, and proteins. The methanol extract was found to contain the highest number of phytochemicals. Wild plant and callus (MS and LS medium) extracted with different solvents in preliminary screening indicated the presence of high content of phytochemicals like phenols, alkaloids, flavonoids, and terpenoids in methanolic extracts. And the sequential screening for phytochemicals of Costus leaves revealed that it is rich in protein, iron, and antioxidant components such as ascorbic acid, α-tocopherol, β-carotene, terpenoids, steroids, and flavonoids[2,6].

Table 3: Nutrient composition of the dehydrated sample[2]

Moisture	4.0%
Fat	2.8%
Total ash	6.3%
Protein	18%
Iron	40mg
Phosphorous	6.6mg
Calcium	5.1mg
Total phenols	4.4g
Total flavonoids	0.848mg/g
B-carotene	667µg
A-tocopherol	149mg
Ascorbic acid	81mg
Glutathione(GSH)	75mmol

Medicinal Use in Ayurvedic System

Leaves

The diabetes patients have to chew down the Insulin plants leaves for a month. That is the patient has to take two leaves per day in the morning and evening for one week. Care should be taken that the leaves must be chewed well before swallowing. Then after one week, the patient should take one leaf each in the morning and evening. This dosage should be continued for 30 days. Allopathic doctors also recommend this and are found to be effective in bringing blood sugar levels under completely under control. The catchphrase of insulin plant is "a leaf a day keeps diabetes away"[1].

Rhizome

The rhizome of insulin plant is considered as a bitter, astringent, acrid, cooling, aphrodisiac, purgative, anthelmintic, depurative, febrifuge, expectorant and useful in burning sensation, constipation, leprosy, worm infection, skin diseases, fever, asthma, bronchitis, inflammations, and anemia[2].

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 also. Leaves are contributed to prominent hypoglycemic potential. The stem is majorly reported with antiurolithiatic activity. Both stem and root have been shown significant antioxidant activity.

Anti-Diabetic Effects

Costus igneus is a traditionally used medicinal plant and a common member of ornamental plants in south Indian Gardens. Leaves are the important part which produces significant antidiabetic activity. It reduces fasting as well as postprandial blood glucose levels. But the exact mechanism of action behind the antidiabetic activity is not known yet. Along with the antidiabetic activity, insulin plant also reduces the diabetic associated complications; bring renal, hepatic parameters to a controlled level, decreases the amount of glycosylated haemoglobin, corrects the lipid profile, increases body weight as well as insulin level and shows marked improvement in the histopathological examination.

Anti-Proliferative Potential

Prof.S.Dhanasekaran et al., (2014) evaluated the anti-proliferative and apoptotic action of methanolic extract of *Costus igneus* powdered leaves (MECiL) on in vitro MCF 7 (Michigan Cancer Foundation-7) Breast cancer cell line. The extract (MECiL) was able to reduce the tumor size without affecting the Normal cells. Also evaluated the Cytotoxicity and Cell Viability for given extract (15-2000µg/ml) on L6 (Rat skeletal muscle cell line) using MTT (3- (4, 5-dimethyl thiazol-2-yl)-2, 5-diphenyl tetrazolium bromide) assay. It showed IC 50 Value of 2000 µg/ml extract. The extract showed cytotoxicity aligned with the

normal cell lines only at very high concentration, but it wasn't apoptotic to the normal cell lines. At the maximum dose of 2000 µg/ml the extract showed potent anticancer activity, that is 97.46±0.74 percentage Cytotoxicity. The extract possessed dose-dependent cytotoxicity against the MCF-7 cell line.[11]

Table 4: Reported Biological activities of *Costus igneus*

Plant part	Reported Biological activity	Result	Reference
Leaf	Hypoglycemic	75.70% reduction of blood glucose level	Shalini Adiga et al., 2014[7]
	Hypolipidemic	Significant reduction in total cholesterol, LDL, VLDL, phospholipids and triglyceride levels and rise in HDL level	P.Mani et al., 2014[8]
	Antioxidant	The marked rise in enzyme levels such as SOD, CAT, and GSH. Complete recovery of enzyme level shown at the highest dose, 600mg/kg. And a significant reduction in MDA level also has been indicated.	Shivaprakash et al., 2014[9]
	Antiurolithiatic	1.00% of aqueous extract of leaves could reduce the nucleation rate and growth of CHPD crystals at maximum. But the activity was more for root and stem extracts.	Kesavan Manjula et al., (2017)[10]
	Antiproliferative	The methanolic extract could reduce the tumor size and showed 97.46% cytotoxicity.	Prof.S.Dhanasekaran et al., (2014)[11]
	Anti-inflammatory	Isolated compound β-amyrin has shown 97% inhibition of paw edema at a given dose of 100 µg.	Kripa Krishnan et al., (2014)[12]
	Prevent learning and memory deficit	*Costus igneus* treated diabetic rats maintained their innate behavior and indicated an improvement in their learning tendency. Also shown a marked improvement in the entrance latency and decrease in the time spent in the dark room.	Shalini Adiga et al., 2014[7]
Stem	Antiurolithiatic	98.25% decrease in the weight of CHPD crystals has been observed	Kesavan Manjula et al., (2017)[10]
	Antioxidant	Showed significant antioxidant activity	Ramya Urs S.K et al.,(2015)[13]
	Antimicrobial	Methanolic extract showed significant antimicrobial activity	Kala et al., 2014[14]
Root	Antibacterial	Methanolic extract indicated significant activity against for both gram positive and gram negative bacteria	Kala et al., 2014[14]
	Antioxidant	Maximum activity due to the presence of highest phenol content	Ramya Urs S.K* et al.,(2015)[13]
Rhizome	Hypoglycemic	68.26% reduction of blood glucose level	Pazhanichamy Kalailingam et al., 2011[15]
	Antioxidant	Showed elevated levels of SOD, CAT, and GSH	Pazhanichamy Kalailingam et al., 2011[15]
	Hepatoprotective	Hepatoprotective potential is indicated by bringing AST, ALT to near normal levels	Pazhanichamy Kalailingam et al., 2011[15]
	Hypolipidemic	Significant reduction of TC, TG, LDL, VLDL, and attenuation of serum HDL levels	Pazhanichamy K et al., 2011[16]
	Antiurolithiatic	97.125% weight reduction of CHPD crystals has been obtained	Kesavan Manjula et al., (2017)[10]
Whole plant	Hypoglycemic	50.46% reduction of blood glucose level	V.Palanivel et al., 2013[17]

Table 5: Summary of Anti diabetic studies of *Costus igneus*

Plant	Plant part	Extraction method	Animal/ Induction	Dose	% Reduction in glucose	Reference
Costus igneus	Leaves	Alcohol extract	STZ induced Wistar rats	250mg	70.97%	SHALINI ADIGA et al., 2014[7]
				500mg	75.70%	
				DC	419.16±5.403	
	Leaves 100g	Ethanolic extract	STZ induced Wistar rats	200mg	61.40%	P.Mani et al., 2014[8]
				300mg	67.86%	
				DC	280.11±19.33	
	Glibenclamide			5mg/kg	69.93%	
	Leaves	powdered leaves of in distilled water orally	dexamethasone-induced (10 mg/kg/day) male Wistar rats	FBG		Akhila Shetty et al., 2010[18]
				250mg	24.35%	
				500mg	26.01%	
				DC	120.3±1.8	
				Drug	27.59%	
				PPBG		
				250mg	30.47%	
				500mg	33.91%	
	Glibenclamide 500µg/kg			DC	182.8±1.7	
				Drug	31.56%	
	Leaves	Ethanolic extract 500mg	Alloxan induced (150 mg/kg body wt i.p.)adult albino rats of Wistar strain (150-200 gms) of either sex	500mg	21.78%	Vishnu Bhat et al.,2010[19]
				DC	345.21±5.427	
	Glibenclamide 600µg/kg			Drug	61.90%	
	Leaves	Methanol extract	Alloxan induced (150 mg/kg body wt i.p.)Male Wistar albino rats (150-200 gms)	50 mg/kg	52.44%	R. Arun Kumar* et al.,2010[20]
				100mg/kg	64.81%	
				200mg/kg	69.08%	
		aqueous extract		50mg/kg	48.47%	
				100mg/kg	59.76%	
				200mg/kg	67.52%	
				DC	295.0± 3.3	
	glibenclamide (0.5 mg/kg)			Drug	71.79%	
	Leaves	crude extract	Alloxan induced (150 mg/kg body wt, i.p.)male albino rats (150-250 gms)	250 mg/kg	62.81%	Leena Chimurkar et al., 2018[21]
				500 mg/kg	55.84%	
				DC	349.17±1.01	
	Glibenclamide (5 mg/kg body wt)			Drug	58.03%	
	Rhizome	Ethanol extract	STZ induced (40mg/kg bw,i.p.) Albino Wistar rats(150-200g)	100mg	63.30%	Pazhanichamy Kalailingam et al., 2011[15]
				200mg	68.26%	
				DC	285.13±1.315	
	Glibenclamide (0.5mg/kg bw per day)			Drug	62.64%	
	Whole plant	ethanol extract	dexamethasone induced	250mg	50.46%	V.Palanivel et al., 2013[17]
				DC	283.00 ± 1.52	
	Glibenclamide			10mg/kg	55.33%	

DC – Diabetic control STZ – Streptozotocin

Antimicrobial Activity

Arun Nagarajan et al., (2011) investigated the antimicrobial activity of *Costus igneus* using its 100mg of root powder. Gram-negative Bacterial cultures like Pseudomonas aeruginosa (P. aeruginosa), Klebsiella pneumonia (K. pneumonia), Salmonella sp, Proteus vulgaris (P. vulgaris) were used in the study to determine the antibacterial activity (in vitro raised root extracts of *Costus igneus*). About 10 grams of the IBA (Indole 3-acetic acid) and IAA (Indole butyric acid) derived root materials subjected to Soxhlet extraction using 5ml of acetone, chloroform, and methanol. In the study, two growth regulators IAA and IBA in combinations were added to MS (Murashige and Skoog) medium for direct root induction. Klebsiella pneumonia was found to be most susceptible to both IBA and IAA derived roots using acetone as solvent. Its zone of clearance was found to be 25 mm, which was almost equal to that of commercially available antibiotic Gentamycin.[22]

Antiurolithiatic Property

Kesavan Manjula et al., (2017) studied the antiurolithiatic property of insulin plant using its aqueous extract of stem and rhizome and through the work found out that the plant extract was able to promote the formation of hydroxyapatite (HAP) crystals and reduce the nucleation rate of CHPD crystals, a major component of calcium urinary stone. The growth of Calcium hydrogen phosphate dihydrate (CHPD) crystals has done by the single diffusion gel growth technique and the inhibitory effect of aqueous extracts of leaves, stems, and rhizome of *Costus igneus* on the growth of CHPD crystals has been investigated. To validate the effect of the aqueous extract of leaves, stems, and rhizomes of *Costus igneus* on the growth of CHPD crystals, a series of five different concentrations of 0.15, 0.25, 0.50, 0.75 and 1.00% of these plant extracts were selected. The plant extract exhibited an inhibitive effect compared to control (pure calcium chloride), and a minimum apparent length of growing crystals. As the concentration of aqueous extracts of *Costus igneus* increased from 0.15% to 1.00% (w/v), the weight of the formed crystals gradually reduced from 2.03 g to 0.06 g (leaves), 0.05 g (rhizome), 0.03 g (stem) respectively. The inhibitory activity of plant extract was due to the presence of natural substances such as protein(18%), iron(40 mg) and antioxidant components such as ascorbic acid, β-carotene, α-Tocopherol, glutathione, phenols, flavonoids (diosgenin, quercetin), steroids, alkaloids, and terpenoids.[10]

Anti-Inflammatory Potential

Kripa Krishnan et al., (2014) studied the anti-inflammatory potential of β-amyrin isolated from the leaves of *Costus igneus* (C. igneus) using carrageenan-induced rat model along with LPS-induced human peripheral blood mononuclear cells (hPBMCs) in vitro model. The differential fractionation methanolic extract (MEC) of *Costus igneus* leaves indicated a maximum percentage inhibition of paw edema at a given dose of 100 mg/kg body weight. The fractionation of MEC had been performed using various solvents such as chloroform, hexane, ethyl acetate, and butanol. The maximum beneficial effect was shown by chloroform extract (CEC) of MEC at a dose of 50 mg/kg bw. Treatment of carrageenan-induced rats with CEC significantly decreased cyclooxygenase (COX), lipoxygenase (LOX), myeloperoxidase (MPO) and nitric oxide synthase (NOS) activities when compared to carrageenan-induced rats. β-amyrin isolated from it shown a dose-dependent decrease in paw edema and at a dose of 100 µg it produced a 97 % decrease in carrageenan-induced paw edema in rats.[12]

Effect of *Costus Igneus* on Learning and Memory

Shalini Adiga et al.,(2014) has evaluated the effect of *Costus igneus* on learning and memory in normal and diabetic-induced rats using passive avoidance test at doses of 250&500mg/kg ethanolic extract. For the induction of diabetes, a single dose of streptozotocin was injected (35 mg/kg) intraperitoneally. After a study period of 30 days, blood glucose level measured and rats were subjected to a passive avoidance test. The treatment with *Costus igneus* significantly reduced the blood glucose level in a dose-dependent manner (75.70% reduction for 500mg) in diabetic treated groups when compared to the diabetic control group. But no significant effect was obtained with nondiabetic rats and it was comparable to the normal control values. Rats were subjected to three acquisition trials. *Costus igneus* treated diabetic rats shown a decrease in the time taken to enter the dark compartment suggesting that they maintained their innate behavior and also showed improvement in learning tendency. Non-treated diabetic rats showed impairment in the passive avoidance test. During their post-shock retention testing at 24 and 48 hours, treatment with *Costus igneus* extract showed a significant increase in the entrance latency and decrease in the time spent in the dark room. As summarizing the ethanolic extract of *Costus igneus* was able to produce a significant effect on learning and memory in diabetic rats when treated with at a dose of 500mg.[7]

Antioxidant Activity

Ramya Urs S.K* et al.,(2015) studied the effect of Methanol extract on antioxidant activity against Klebsiella Oxytoca, Pseudomonas Fragi, Enterobacter aerogens using various concentrations ranging from 100 µg/mL - 500 µg /mL. The antioxidant and radical scavenging activities of *Costus igneus* were assessed both Stem extract and Root extract. Root extract showed a high inhibition rate than stem extract. And among the stem and root extracts of *Costus igneus*, the total phenolic contents were found to be greater for roots extracts rather than the stem. Root extract also possesses a high amount of vitamin E. Flavonoids with a certain structure and hydroxyl position in the molecule can act as proton donating and show radical scavenging activity. It was

evident from the study that the polyphenols and antioxidants not only scavenge off the free radicals but also inhibits the generation of the free radical.[13]

Neuroprotective Role

Gupta D, Rai S, Hajam YA et al.,(2018) investigated the neuroprotective role of exogenous melatonin and insulin plant (*Costus igneus* nak.) extract on the brain in streptozotocin-induced female diabetic rats. The extract showed a significant decrease of lipid peroxidation (TBARS) in brain tissue compared to the control group of rats. In addition, plant extract and melatonin produced a significant decrease in antioxidative enzyme viz. superoxide dismutase (SOD), catalase (CAT), reduced Glutathione (GSH) of the brain. Melatonin as well as plant extract showed significant recovery to restore the brain complication induced by hyperglycemic effect caused by the diabetic condition and rescued the brain tissue by restoring the number of astrocytes and glial cells.[23]

Hypolipidemic Activity

Pazhanichamy Kalailingam et al., (2011) investigated the antihyperglycemic and hypolipidemic activities of methanol extract of *Costus igneus* rhizome (MECiR) in streptozotocin (STZ) induced diabetic albino rats. MECiR has given at doses of 100, 200 mg/kg orally as a single dose per day to diabetes-induced rats for a period of 30 days. The results indicated that fasting blood glucose, serum total cholesterol(TC), triglycerides(TG), low-density lipoprotein(LDL), very low-density lipoprotein(VLDL), levels were significantly ($p<0.05$) decreased, whereas serum high-density lipoprotein(HDL level significantly ($p<0.05$) increased in the diabetic rats. Better result obtained with 200 mg/kg. The antidiabetic and hypolipidemic effects in STZ induced diabetic albino rats were comparable to standard reference drug glibenclamide (5mg/kg/bw).[16]

Marketed Products

Table 6: Various Marketed products of *Costus igneus*

PLANT NAME	PRODUCT NAME	CATEGORY	MANUFACTURER
Costus igneus	Insulin Plant Leaf powder 180g	Dietary supplement	TheInsulinPlant.com, USA[24]
	Kostam Keerai (*Costus igneus*) Capsule 500mg	-	Agroline Mori tantraa[25]
	Diabestop 500mg Capsule	Food supplement	Herbs & Nutri Pharma[26]
	Glucobeet plus Capsule 500mg	Blood sugar supportive Supplement	Orange organic pharma[27]
	Daun Insulin	20 Herbal tea bags	Tigadaun[28]

CONCLUSION

The research works that have been done yet showed that *Costus igneus* is an important medicinal herb presented with various pharmacological actions. The studies have done on this plant proved that it possesses many important phytoconstituents such as conjugated flavonoids, flavones, flavonols, catechin and catechin derivatives, chlorophylls a and b, resinoids, essential oil, and alkaloid named saussurine, inulin and resin etc.[29,30] And these compounds found to be responsible for various pharmacological properties such as antidiabetic effect, antiproliferative effect, antimicrobial activity, antiurolithiatic property, anti-inflammatory potential, the effect on learning and memory, antioxidant activity, neuroprotective Role, hypolipidemic activity etc. Further exploration of medicinal properties and various phytoconstituents responsible the pharmacological actions are required to be done to make the treatment more assuring, reliable, with fewer side effects for the welfare of mankind in the future.

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