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A Brief Review on The Therapeutic Uses of Insulin Plant, *Costus igneus*

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ABSTRACT
According to WHO about 21,000 plant species have the medicinal potential and estimated that 80% of people worldwide rely on herbal medicine. Insulin plant is better anti-diabetic potential plant and worldwide used. It included in the family Costaceae consists of 4 genera and 200 species. The genus Costus is the largest in the family having about 150 species. Insulin plant is a perennial, upright, spreading plant with spirally arranged leaves and attractive flowers. In South-India, the plant grows as an ornamental and its leaves are used as in the treatment of diabetes mellitus. Costus showed potential use in the medical field as, antidiabetic, anti-proliferation, antimicrobial, antiurolithiatic, antiinflammation, antioxidant, anticancer, putative, diuretic, hypolipidemic, neuroprotective and ameliorative. It also constitutes phytochemical, biochemical, bioactive compounds including the presence of carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, flavonoids, steroid, and trace elements as K, Ca, Cr, Mn, Cu, and Zn. This work is an attempt to compile and explore the different pharmacological and phytochemical studies reported till date.
Keywords: *Insulin plant, Costus igneus, medicine, phytochemical, biochemical, bioactive compounds.*

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INTRODUCTION

The medicinal plant includes various types of plants used in practice of the medicinal and therapeutic use. These plants are used for the medicinal as a form of alternative medicine. These plants are also used as food, flavonoid, medicine, perfumes, aesthetic values and spiritual activities in India. These plants have been used from prehistorical period as a medicine. It has been used in Unani, Indian Ayurveda, European and Mediterranean culture since long over 4000 years as medicine. The various cultures such as Rome, Egypt, Iran, Africa, and America used plants in their healing rituals also developed traditional medicinal systems such as Unani, Ayurveda and Chinese Medicine with respect to the therapeutic use systemically [1]. Indian ancient civilization has been known to be rich storage of medicinal plants. Indian forests are rich sources of medicinal and aromatic plants. These plants collected and used for manufacturing of drugs and perfume products. There are about 8,000 herbal remedies has been identified and coded in Ayush system in India. Ayurveda, Unani, Siddha and Tribal medicine are the major threptic system in Indigenous medicines. In which Ayurveda and Unani are widely developed in India. Recently World Health Organization (WHO) estimated that 80% of people worldwide rely on herbal medicine. According to WHO about 21,000 plant species have the medicinal potential. As per the data three-quarters of world population depend on herbal medicine. More than 30% plant species at one time or more were used for medicinal purpose [1,2]. It has been noticed that 25% of the total drugs were used in United States, while 80% of the total drugs were used in India and China. The treatment of medicinal plant is considered to be safe and no or minimal side effects. The herbal treatment is independent of any age group and the sexes. The ancient treatment believed that the herbs are the better solution to cure many health-related problems and diseases[1,2]. Diabetes is a group of metabolic diseases that cause high blood sugar levels. This may happen due to inadequate production of insulin by the pancreas or when the cells of the body do not respond to the insulin produced. Type-1 diabetes is a situation where chronic condition in which pancreas produces little or no insulin and usually develops in childhood or adolescence, or at any age. The other is a chronic condition with type-2 diabetes, the body either doesn't produces enough insulin or it resists insulin. The type-2 diabetes reported about 90% of all cases of diabetes worldwide. Other than these two types, there is also a third kind, gestational diabetes, which affects females during pregnancy. Diabetes mellites has been

rising more rapidly in low- and middle-income countries than in high-income countries. Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. The global diabetes in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. The prevalence is higher in urban (10.8%) than rural (7.2%) areas, and in high-income (10.4%) than low-income countries (4.0%). Which lead to the economic and social problems of world. Hence there is need to control diabetic. The most efficient way to maintain the blood sugar level close to normal as possible. Nowadays Insulin plant is widely used to control the diabetic. It is also called anti-diabetic plant and common name is fiery Costus or spiral flag. It is a herbaceous plant in the Costaceae family native to eastern Brazil [3]. In India, it is known as insulin plant for its purported anti-diabetic properties [4]. In India insulin plant called by various vernacular names.

Table 1: Vernacular names.

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	Kempuhonne
Malayalam	Honne, Karintakara, Vengai, Venna-maram
Sanskrit	Asana, Bandhukapushpa Tamil Neyccarikamaram, Venkai-c-ciray, Kostam
Gujarati	Pakarmula
Marathi	Honi ,Pushkarmula

Table 2: Taxonomic position.

Botanical name	Costus igneus
Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Viridaeplantae
Phylum	Tracheophyta
Subphylum	Euphylophitina
Infraphylum	Radiotopses
Class	Liliopsida
Subclass	Commelinidae
Superorder	Zingiberane
Order	Zingiberales
Family	Costaceae
Subfamily	Asteroideae
Tribe	Coriopsidae
Genus	Costus
Species	igneus

Insulinplant, *Costus igneus* (Nak)[syn. (Costus pictus (D. Don), Costus mexicanus (Liebm ex Petersen) or Costus congenitus (Rowle)], commonly known as Fiery costus, Step ladder or Spiral flag or Insulin plant. It is native to South and Central America. This is a recently introduction in India from America. It is an herbal cure for diabetes and hence commonly called as insulin plant. It is commonly grown in gardens as ornamental plant in South India and also run wild in many places. It is used in India to control diabetes, and it is known that diabetic people eat one leaf daily to keep their blood glucose low. Leaves of C. igneus were one among the plants known to be effectively used for treating diabetes by the tribal people of Kolli hills of Namakkal district, Tamilnadu. In Mexican folk medicine, the aerial part of *C. pictus* (D. Don) is used as an infusion in the treatment of renal disorders [5].

The plant belongs to the family Costaceae. The Costaceae was first raised to the rank of family by Nakai on the basis of spirally arranged leaves and rhizomes being free from aromatic essential oils. Before the elevation to family status, Engler and Prantlin 1886 recognized Costoideal as a subfamily under Zingiberaceae. Several anatomical and morphological features support this isolated position including well

developed aerial shoot with distinct, rigid, and commonly branched stems. The leaves are inserted in a low spiral with divergences. The family Costaceae consists of 4 genera and approximately 200 species. The genus Costus is the largest in the family with about 150 species that are mainly tropical in distribution [5]. In Siddha medicine, it is called as kostum. It is being cultivated in Kashmir and the Himalayan regions for its root purpose. It is related to the gingers and was originally part of the Zingiberaceae family. But now the *Costus* species and their kin have been reclassified into their own family, Costaceae[6]. The species reproduces vegetative by rhizome and birds disperse seeds. *Costus* products are sometimes called *Costus comosus* and are edible in nature. The flower petals are quite sweet and nutritious. It's a lower grower and makes a great ground cover. The long red flower spikes of *Costus pulverulentus* are unique to the family and they are sure to create interest in the garden. The plant grows very quickly and the propagation is by stem cutting. It needs sunshine but it also grows in slightly shady areas. It is cultivated in India for its use in traditional medicine and as an ornamental [6].

Its leaves help to build up insulin in the human body[7]. It is an oral hypoglycemic agent. 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 of such traditional plant which is getting global acceptance nowadays and is now widely used as an ayurvedic medicinal herb. 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 [7].

Plant description

Costus igneus (N.E.Br.) is a perennial, upright, tropical evergreen plant. The evergreen leaves which are simple, alternate, entire and oblong, having 4 to 8 inches length with parallel venation. The large, smooth, dark greens leave 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. Beautiful orange flowers are produced in the warm months having a 2.5 to 12.5cm diameter, appears on cone-like heads at the tips of branches. The propagation of insulin plant is by stem cutting[7,8].

Phytoconstituents

Phytochemicals are important metabolites that are produced using different parts of plants via their primary or secondary metabolism, have essential functions in the plant for general growth and defense against animals, insects and microorganisms [9,10]. Primary metabolites such as carbohydrates, lipids, and proteins have a direct relationship to the growth and metabolism of the plant. Secondary metabolites are derived from primary metabolites, which are not necessary for survival, but are involved in significant functions in the plant, such as protection, competition, and species interactions[11,12]. Phytochemical screening of insulin plant noticed 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. The sequential screening for phytochemicals of insulin leaves also revealed that it is rich in protein, iron, and antioxidant components such as ascorbic acid, α-tocopherol, β-carotene, terpenoids, steroids, and flavonoids [8, 13,14,15,16].

It was revealed in another study that methanolic extract was found to contain the highest number of phytochemicals such as carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, and flavonoids [17]. Preliminary phytochemical evaluation of Insulin plant revealed that the leaves contain 21.2% fibers. Successive extracts gave 5.2% extractives in petroleum ether, 1.06% in cyclohexane, 1.33% in acetone, and 2.95% in ethanol. Analysis of successive extracts showed presence of steroids in all extracts. The ethanol extract contained alkaloid also. The major component of the ether fraction was bis (2'-ethylhexyl)-1,2-benzenedicarboxylate (59.04%) apart from α-tocopherol and a steroid, ergosterol (George et al, 2007). Stem showed the presence of a terpenoid compound lupeol and a steroid compound stigmasterol [18]. Bioactive compounds quercetin and diosgenin, a steroidal sapogenin, were isolated from C. igneus rhizome [19]. Trace elemental analysis showed that the leaves and rhizomes of C. pictus contains appreciable amounts of the elements K, Ca, Cr, Mn, Cu, and Zn [20]. Steam distillation of stems, leaves, and rhizomes of C. pictus yielded clear and yellowish essential oils[21].

Medicinal use

Medicinal plants are the richest bio-resource of drugs of traditional system of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediaries and chemical entities for synthetic drugs [1].

Leaves

The diabetes patients have to chew the Insulin plants leaves for a month. The patient has to chew two leaves per day in the morning and must be chewed well before swallowing evening for one week. Then after one week, the patient should chew 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. Chew insulin plant a leaf a day keeps diabetes away [7].

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 [8].

Pharmacological Activities

The pharmacological benefits of medicinally important plants are primarily due to bioactive phytochemicals produced in the plant tissues as primary and secondary metabolites. These constituents have been identified as alkaloids [22], glycosides [23], flavonoids [22]. phenolics[24], saponins [25], tannins [22], and essential oils [26],and steroids.

Several pharmacological studies have confirmed that medicinal plants exhibit a broad range of biological activities and that plant species can containa diverse range of bioactive molecules responsible fora collection of pharmacological properties [27]. The insulin plant has been reported with many activities and some are yet to be validated. The various plant parts are shown various activities such as leaf, stem, root, rhizome and whole plant also. Leaves are contributed to prominent hypoglycemic activity. The stem is majorly reported with antiurolithiatic activity. Both stem and root have been shown significant antioxidant activity. The whole plant *C. igneus* were used for its antidiabetic property and prevents the body from hyperglycemia, protects mind and which prolongs the life longevity. The rhizome has been used to treat fever, rash, asthma, bronchitis, intestinal worms, ailments of eyes, stomach, neck, jaws, tongue, mouth and also be used for curing fever, edema, wheezing (dyspnoea), haemorrhoids, spermaturia. In siddha medicine system *C. igneus* root has been used as in the form of powder (chooranam), decoction(kudineer) and oil (thylam). Until now, *C. igneus* has been reported to contain resinoids, essential oil, and alkaloid named saussurine, inulin and resin [28].

Antidiabetic

The chronic disease of diabetes mellitus afflicts a large proportion of people all over the world.It is a serious chronic condition that is a major source of ill health worldwide. It is metabolic disorder and characterized by hyperglycemia and disturbance of carbohydrate, protein and fat metabolism, secondary to an absolute or relative lack of the hormone insulin. It also includes dislipidemia or hyperlipidemia are involved in the development of micro and macrovascular complication of diabetes, which are the causes of morbidity and death. Evaluation of plant products to treat diabetes mellitus is of growing interest as they contain many bioactive substances with therapeutic potential. In recent years several researchers evaluated and identified antidiabetic potential of traditionally used Indian medicinal plants creating experimental on test animals. Earlier studies confirmed the efficacy of several medicinal plants on disease diabetes mellitus. However, many medicinal plants have been tested for their antidiabetic effects, these effects remain to be investigated in several other Indian medicinal plants.

Insulin plant is a traditionally used medicinal plant and 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. It should be molecular activities and should be studied details. The molecular mechanism should be indeed to investigate. The 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 [1,4,5].

Howsoever, an *in vitro* study of ethanolic extract of *C. pictus* leaf was analyzed to study GLUT4 translocation and glucose uptake activity, which showed no direct peripheral action at 300 µg/ml dose comparable with insulin and metformin[29]. A study evaluated the ability of a tea made from the leaves of *C. spicatus* to alter glucose homeostasis in C57BLKS/J (KS) *db*/*db* mice, a model of obesity-induced hyperglycemia, with progressive beta-cell depletion. Intraperitoneal (IP) insulin tolerance testing after the 70 days study period showed that *C. spicatus* tea consumption did not alter insulin sensitivity, which suggested that at the dose given, tea made from *C. spicatus* leaves had no efficacy in the treatment of obesity-induced hyperglycemia[30].

Antiproliferative

These are of or relating to a substance used to prevent or retard the spread of cells, especially malignant cells, into surrounding tissues. There are several plants showed this activity.

Dhanasekaran[31] evaluated the antiproliferative 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.

A study was carried out to comparatively evaluate the methanolic and aqueous extracts of C. igneus in diabetes-induced hyperlipidemia in rats. The study revealed that methanolic and aqueous extracts at a dose of 200 mg/kg body weight reversed the diabetes-induced hyperlipidemia [32]. Alcoholic extract of C. igneus at the dose of 400 mg/kg (p.o) had significantly decreased the levels of serum cholesterol, triglycerides, LDL in Triton-induced hyperlipidemic rats[33].

Diuretic

A diuretic is any substance that promotes diuresis, the increased production of urine. This includes forced diuresis. There are several categories of diuretics. Diuretics, also called water pills, are a common treatment for high blood pressure. Find out how they work and when you might need them. Diuretics, sometimes called water pills, help rid your body of salt (sodium) and water. Most of them help your kidneys release more sodium into your urine.

A study was carried out to measure the diuretic effect of an aqueous extract of C. pictus at doses of 100 and 200 mg/kg body weight and to compare it with the one induced by furosemide at 4 mg/kg. The results revealed that C. pictus induced a natriuretic effect similar to furosemide. The aqueous extract induced an increment in sodium and potassium clearance like the one obtained with furosemide, suggesting that it represents significant dieresis [34].

Antimicrobial

An antimicrobial is an agent that kills microorganisms or stops their growth. Antimicrobial medicines can be grouped according to the microorganisms they act primarily against. For example, antibiotics are used against bacteria, and antifungals are used against fungi.

Nagarajan [35] investigated the antimicrobial activity of *Costus igneus* using its 100mg of root powder. Gram-negative Bacteria cultures like Pseudomonas aeruginosa, Klebsiella pneumonia, Salmonella sp., Proteus 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) 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.

Methanolic extract of C. igneus showed maximum anti-bacterial activity against gram-positive *Bacillus cerus, Bacillus megaterium, Micrococcus leuteus, Staphylococcusn aureus, Streptococcus lactis*, and gram-negative strains *Pseudomonas aeruginosa*, *Escherichia coli*, *Enterobacter aerogenes*, Klebsiella pneumoniae, and Salmonella typhimurium[36].The isolated compound from the ethanolic extract of Costus igneus showed moderate anti-bacterial and anti-fungal activity against Staphylococcus aureus, Eschericia coli, and Candida albicans[37]. Among the extracts of various parts of C. pictus, methanolic extracts of stem and flower exhibited maximum inhibitory activity on the growth of tested microbes, viz., Shigella flexneri, Klebsiella pneumonia, Bacillus subtilis, Escherichia coli at the concentration of 150 µg/ml[38].

Antiurolithiatic

Urolithiasis defined as the urinary stone originating anywhere in the urinary tract. Medicinal plants are established as renewable sources with antiurolithiatic effects. There are many marketed formulations which are having antiurolithiatic activity, some of them are Cystone, Calcuri and Chandraprabhabati. These formulations have been widely used clinically to dissolve urinary calculi in the kidney and urinary bladder. Apart from these, there are series of other traditional plants available and have been scientifically assessed for their antiurolithiatic activity. So, the present review article explains the potential of medicinal plants in the treatment of urinary stone.

Yuvarani [39] 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.

Anti-inflammatory

Anti-inflammatory (or anti-inflammatory) is the property of a substance or treatment that reduces inflammation or swelling. There are several plant species noticed this activity.

Krishnan [40] studied the anti-inflammatory potential of β-amyrin isolated from the leaves of Costus 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 body weight. 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.

Learning and Memory

Learning and memory are closely related concepts. Learning is the acquisition of skill or knowledge, while memory is the expression of what you've acquired. If you acquire the new skill or knowledge slowly and laboriously, that's learning. If acquisition occurs instantly, that's making a memory.

Adiga[41] 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 and 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.

Antioxidant

Antioxidants are substances that can prevent or slow damage to cells caused by free radicals, unstable molecules that the body produces as a reaction to environmental and other pressures. They are sometimes called free-radical scavengers. The sources of antioxidants can be natural or artificial.

Ramya and Chauhan[42] studied the effect of Methanol extract on antioxidant activity against Klebsiella oxytoca, Pseudomonas fragi, *Enterobacter aerogens* using various concentrations ranging from 100 µg/mL to 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 level 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.

An in vitro study of alcoholic extract of leaves of C. mexicanus showed moderate antioxidant activity[43]. The antioxidant activities of leaves and rhizomes in methanol, aqueous, ethanol, and ethyl acetate extracts were assessed using different models like DPPH, β-carotene, Deoxyribose, superoxide anion, reducing power, and metal chelating assay at different concentrations. Leaves and rhizomes of C. pictus showed good antioxidant activity of about 89.5% and 90.0% when compared with standard BHT (Butylated Hydroxy Toulene) (85%) at a concentration of 400 µg/ml. Results obtained revealed that methanolic extracts of both

leaves and rhizomes of C. pictus possess higher antioxidant activity when compared with other extracts[44]. In another study, methanolic leaf extract of C. pictus caused significant increase in superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, vitamin-A, vitamin-C, vitamin-E and reduced glutathione, and thus, could be effective in reducing oxidative stress and free radical-mediated diseases. The antioxidant property of this plant may be due to the presence of phenolic substances[45]. Methanolic extracts of flower and stem of C. pictus possess in vitro antioxidant activity against oxidative protein damage [46].Among the extracts tested for, chloroform extract of C. pictus D. Don bark possessed high antioxidant activity [47]. Oral administration of ethanolic extract of C. igneus rhizome at 200 mg/kg body weight to diabetic rats for 30 days induced a significant antioxidant effect. The bioactive compound quercetin and diosgenin present in the plant exhibited antioxidant activity, which was sufficient to reverse oxidative stress in liver, pancreas, and kidney of diabetic rats as well as to stimulate glycolytic enzymes and control gluconeogenesis in diabetic animals[19].

Ameliorative effect

Ameliorate is often wrongly used where alleviate is meant. Ameliorate is properly used to mean `improve', not `make easier to bear', so one should talk about alleviating pain or hardship, not ameliorating it.

A study was conducted to evaluate the ameliorative effect of ethanolic extract (50 mg/kg body weight, orally) of rhizome on mitochondrial enzymes in alcohol-induced free radical toxicity in male albino rats. After 21 days of treatment, mitochondrial enzymes were restored to normal levels, which showed that C. pictus improved mitochondrial activities during alcohol-induced free radical stress [48].

Anticancer

Anticancer drugs are also called antineoplastic drug, any drug that is effective in the treatment of malignant, or cancerous, disease. There are several major classes of anticancer drugs; these include alkylating agents, antimetabolites, natural products, and hormones. In addition, there are a number of drugs that do not fall within those classes but that demonstrate anticancer activity and thus are used in the treatment of malignant disease.

A lot of studies report the significance antitumor effects of different extract of the plant and isolated. The ethanolic extract of leaves of C. pictus was found to have anti-proliferative and anti-cancer potential in in-vitro mammalian fibrosarcoma (HT-1080) cells[49]. All the extracts of bark had potent anti-cancer properties against HT 29 and A549 cells[47].

Putative

The term is commonly used to describe an entity or a concept that is based on what is generally accepted or inferred even without direct proof of it, meaning it denotes something, like an inference or a supposition, that is accepted because it is deemed to be the case or what has been commonly believed even without solid evidence to back it up.

Aqueous extract of Costus stem and isolated compounds lupeol, and stigmasterol had an inhibitory effect on calcium oxalate urolithiasis, and its putative activity was confirmed by the promotion of formation of calcium oxalate dehydrate (COD) crystals and may possibly treat urinary stones by inhibiting the formation of calcium oxalate monohydrate (COM) crystals [50].

Neuroprotective

Neuroprotection refers to the relative preservation of neuronal structure and/or function. In the case of an ongoing insult (a neurodegenerative insult) the relative preservation of neuronal integrity implies a reduction in the rate of neuronal loss over time, which can be expressed as a differential equation.

Gupta [51] 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.

Hypolipidemic

Hypolipidemic drugs are a class of drugs that lower the concentrations of lipoproteins, the agents that transport cholesterol and triglycerides in blood. The lipid-lowering drugs include statins, fibrates, bile-acid sequestrants, and nicotinic acid and acipimox and producing or resulting from a decrease in the level of lipids in the blood a hypolipidemic drug hypolipidemic effects.

Kalailingam[19] investigated the antihyperglycemic and hypolipidemic (Mani et al, 2014) 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).

Toxicity

Plants by virtue of their chemical constituents are potentially toxic; thus, some plants used in traditional medicine are intrinsically toxic. Some plants well known in traditional medicine to be toxic or poisonous. Which are used in the traditional medicine in India.

Acute toxicity studies were carried out with different doses of aqueous extract of C. pictus from 5, 10, 20, and 40 g/kg body weight. None of the doses of this extract produced mortality or any behavioral disorders (Melendez et al, 2006). Acute toxicity studies revealed that the administration of aqueous extract 1 g/kg body weight/day for 30 days produced no effect on the general behavior and all the animals survived the test period[52]. Administration of ethanolic extract of C. igneus leaves from 50 mg/kg body weight up to the dose of 5000 mg/kg body wight did not show significant toxicity signs during the first four hours and followed by daily observations for 14 days, and no mortality was also observed; the drug was found to be safe at the tested dose level of 5000 mg/kg body weight [53]. However, in a study carried out on the methanolic extract of C. igneus, findings indicated toxicity at 250 mg/kg body weight[54]. Further, in another investigation, palmitic acid was found to be the major component in the stem, leaf, and rhizome oils of C. pictus. Palmitic acid is found to induce degeneration of myofibrils in healthy adult rat cardiomyocytes, enhance LDL to HDL cholesterol ratio, and it was found to be the important precursor for the development of coronary heart diseases. So, the constant use of C. pictus leaves for diabetic treatment may cause serious cardiac diseases, and it is not recommended for the treatment[21].

Bioactive compound

Bioactive compounds such as amides, alkaloids, flavonoids, tannins, saponins, glycosides, terpenoids and phenolic compounds have been widely reported to be present in the seeds, leaves, and stem bark of plant species. Some of these are discussed below.

Tri-terpenoids

Tri-terpenoids acts mainly by inhibiting alpha-glucosidase and alpha-amylase activity that delay the absorbance of carbohydrates in intestine leading to a decrease in the postprandial insulin level [33]. It causes insulin resistance, normalization of plasma glucose and insulin level and glucose metabolism. The known triterpenes, oleanolic and ursolic acid show activity against diabetic complications might be due to its effect on expression of aldose reductase and SDH.

The suppression is caused by aldose reductase, and SDH decreases endogenous AGE generation and carbonyl stress involved in the progression of diabetic complications. Ursolic acid reduces expression of DGAT in protein which might also be involved in the hepatic triglyceride deposition and also helps in enhancing insulin receptor [55]. Corosolic acid helps in glucose uptake [56]. But the amount of corosolic acid present in Costus igneus is very less, obtained from different literature.

Steroids

Steroids are a man-made version of chemicals, known as hormones, that are made naturally in the human body. Steroids are designed to act like these hormones to reduce inflammation. They're also known as corticosteroids, and are different **to** anabolic steroids used by bodybuilders and athletes**.** Steroids like diosgenin decreases the activities of diabetes associated enzymes (such as ATP-cytrate lyase, pyruvate kinase and glucose-6-phosphate dehydrogenase) in the liver of diabetic rats[57]. Diosgenin is effective against reducing plasma glucose levels in diabetic rats. It can be useful in the treatment of diabetes by promoting adipocyte differentiation and by inhibiting inflammation in adipose tissues. Therefore, it may be useful to improve the patients' condition in the glucose metabolic disorder associated with obesity. In this context, in another experimental model, it was observed that diosgenin led to a reduction of plasma and hepatic triglyceride in obese diabetic mice and may be useful for the management of diabetes-related hepatic dyslipidemias. In diosgenin treated diabetic rats, a reduction of hyperglycemia, hypercholesterolemia, and hyperglyceridemia was observed. In another report, it was demonstrated that after administration of diosgenin to diabetic rats, the activity of glucokinase decreased, while the activities of glucose-6-phosphatase and fructose-1, 6-biphosphatase in the liver have increased.

In the other work, among other positive changes in several parameters linked with diabetes, the supplementation with diosgenin decreased blood glucose levels in diabetic rats when compared to the group of rats fed with normal diet. It stimulates the renewal of β-cells in the pancreas or helps in recovery of partially destroyed β-cells and helps in pancreatic insulin secretion as a result plasma insulin level increased and blood glucose is controlled. All of these reports stating that diosgenin has hypoglycemic properties. It is highly present in *Costus igneus***[58].** Another steroid, stigmasterol increases cholesterol efflux and decreases LDL-induced pro-inflammatory cytokine secretion and to prevent beta-cell

dysfunction induced by glucolipotoxicity. Glucolipotoxicity reduces insulin secretion by inducing cholesterol accumulation because excess cholesterol is a possible contributing factor to beta cell failure.
The direct effect of stigmasterol on beta cells is not clearly known. Stigmasterol protects pancreatic beta cells from glucolipids-toxicity by preventing accumulation of free cholesterol and ROS improving insulin secretion, increasing insulin context. Stigmasterol is present in *Costus igneus* **[50].** But the mode of action is not obtained from various literatures. Beta-sitosterol, another antidiabetic component is obtained from *Costus igneus* [59]. It increases the fasting plasma insulin levels. It improves the oral glucose tolerance test with an increase in glucose-induced insulin secretion. It also increases glucose uptake in adipocytes and stimulates adipogenesis in differentiating preadipocytes. Like insulin it down regulates GLUT4 but no clinical study has yet progressed.

Alkaloids

Alkaloids, a class of nitrogen-containing organic compounds, are widely distributed in nature with more than 18,000 alkaloids having been discovered. These compounds have a lot of structural diversity and, in some instances, having the presence of one or more nitrogen atoms seems to be the only common feature among molecules of different chemical structures and of different sources. Alkaloids can be of microbial, plant and animal origin [60]. No remarkable anti-diabetic alkaloids are found in *Costus igneus*.

Flavonoid

Flavonoids, a group of plant secondary metabolites in which the molecular framework is characterized by variable phenolic structures, are widely distributed in plants [61]. Many flavonoids are known to possess anticancer activity [62]. Flavonoid like quercetin increases the activity of glycogen synthesis, the rate-limiting enzyme of glycogen synthesis[63]. It also increases anti-oxidant enzymes like SOD, GPX, CAT, **etc**. and reduces intestinal glucose absorption by inhibiting GLUT2. By blocking tyrosine kinase, quercetin is reported to have effects against diabetes [64]. Some other functions of flavonoids are enhancing insulin secretion via pancreatic β-cell regeneration, enhancement of insulin-mediated glucose uptake by target cells, inhibition of aldose reductase, calcium uptake increase etc. it is highly present in *Costus igneus* **[65].**
Catechin, epicatechin showed strong radical scavenging activity due to the presence of hydroxyl group[66]. They are alpha-glucosidase inhibitors because they act to decelerate the breakdown of complex sugars into glucose resulting in a delay in glucose absorption which lowers the postprandial blood sugar level. Epigallocatechin gallate (EGCG), a component of catechin reduce the blood glucose level by alpha-glucosidase inhibition and retard the postprandial rise in blood glucose with sucrose loading but not glucose loading.

CONCLUSION

The medicinal value of insulin plants lies in some chemical substances that produce a definite physiological action on the human body. Different phytochemicals have been found to possess a wide range of activities, which may help in protection against chronic diseases. The qualitative analysis of the five different leaf extract of *Costus igneus* reveals the presence of medicinally valued bio active components like, flavonoids, tannins, alkaloids, saponin, reducing sugar, phenolic compounds and glycosides. Quantitative estimation *Costus igneus* leaf contained higher content of saponins and total flavonoids, with lesser number of phenols and alkaloids. *Costus igneus* are used for discovering and screening of the phytochemical constituents which are very helpful for the manufacturing of new drugs for treatment of various diseases. The research is in progress to discover its biological activity and enhance the pharmacological profile of it in the area of traditional medicine.

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