



Effects of insulin plant (*costus igneus*) leave on diabetes mellitus: A review

Dr.Ananta Shrivastava* , Priyanka Raj**

*Corresponding author_ Professor, Galgotias University, Greater Noida

** Student_ M.Sc. Clinical Nutrition and Dietetics, Galgotias University, Greater Noida

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ABSTRACT -

Diabetes mellitus is a disease of high blood sugar levels and this condition is known as hyperglycemia. In this the blood glucose level increases due to insulin resistance or any underlying condition. this disease can damage many organs like the kidney by microvascular complications by decreasing glomerular filtration rate, and eyes by causing damage to the eye blood vessels that are present on the back of the eyes. Arteries, by causing inflammation produce inflammasomes that cause atherosclerosis. and the nervous system by changes in the volume of the grey matter of the brain that can cause Alzheimer's disease and Parkinson's disease. nowadays about 70 to 80% of the population in the world suffers from Diabetes Miletus. Globally in 2017, it is determined that approximately 462 million people were affected by type 2 diabetes mellitus worldwide. In total, it was almost 6.28 % of the world and 4.4% of the people were aged 15 to 49 years. 15% of them are between 50 -69 years and 22% of them were 70+ age group, and the prevalence was 6095 per 100,000. Diabetes is the 9th leading cause of death in the year 2017 (Abdul et al., 2020). This review, paper discusses the insulin plant *Costus igneus*. There are more than 200 varieties of insulin plant which is known to lower blood sugar levels with its many properties which help to lower the blood glucose level are tannis, saponins, flavonoids, terpenoids, and cardiac glycoside. These bioactive compounds of *Costus igneus* are different mechanisms of action on receptor cells or by changing the action of insulin which is reviewed in this paper. Insulin plants take almost 15 days to lower the blood sugar level. Albino rats were used in these studies. The insulin plant also helps reduce hyperglycemia symptoms like polyuria, polydipsia, and polyphagia. The compounds in the insulin plant act on the disease in many ways by restoring the Beta cells and increasing the number of liver-protecting enzymes inhibiting intestinal glucose absorption. In this review, we also discuss the tolerance and toxicity of *Costus igneus*. With the help of this

review, we can understand the mechanism of insulin plant action, mechanism, role in the body, and affliction of insulin in diabetes mellitus, some case studies, how the capacity of insulin plants to reduce the blood sugar level in different extracts like ethanol and methanol and which is working better. From the future perspective, it shows how *costus igneus* can replace oral hypoglycaemic drugs and protection from destroying beta cells and reversing diabetes mellitus with the consumption of insulin plants and a balanced diet.

Keywords: *costus igneus*, insulin plant, hyperglycemia, diabetes mellitus, antioxidants,

INTRODUCTION

DIABETES MELLITUS TYPE 2

Type 2 diabetes mellitus is a type of metabolic disorder spread worldwide and it leads to slow and progressive damage to the beta cells of the pancreas, it can be caused by the reduction in the number of beta cells in the pancreas or can be due to the smaller number of receptors present to bind and leads to insulin resistance, the loss of beta cells can be inflammation (Galicia-garcia et al., 2020; Pasquali, 2020). Recent research in 2022 reveals that the widespread presence of diabetes mellitus is getting bigger, especially in the growing countries, countries filled with 80% of the diabetic population. India and China occupy 40% of the list of developing countries. An estimation accounts that 74 million people in the population suffer from diabetes mellitus. And it is reported that about 70-80% of the population in India comes up under the middle middle-income group that cannot afford the price of insulin that they need to survive daily (Fralick et al., 2022).

If not treated or managed well, the type of disease leads to severe complications and death. The starting phase of diabetes mellitus does not get easily identifiable it starts with some common symptoms like polyurea, polydipsia, polyphagia, and glycosuria, and after that, there are some clinical symptoms also seen in type 2 diabetes mellitus are neuropathy, retinopathy, nephropathy, and CVD cardiovascular disease, late wound healing, progressively organ failure. According to WHO diabetes mellitus is mainly a disease of middle-class income group countries. This disease is mainly affected by social and economic change through the consumption of high carbohydrates and processed foods. aging also contributes to type 2 diabetes mellitus.

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15% of them are between 50-69 years and 22% of them were 70+ age group, and the prevalence was 6095 per 100,000. Diabetes is the 9th leading cause of death in the year 2017 (Abdul et al., 2020).

EFFECTS OF DIABETES MELLITUS ON BODY FUNCTIONS

There are many complications associated with type 2 diabetes mellitus like central nervous system and its related complications. It is seen that a patient who is suffering from type 2 diabetes mellitus complains about memory loss and attention. It is also observed that many cognitive diseases such as Alzheimer's disease dementia, and vascular dementia. When an individual suffers from diabetes mellitus for more than 20 years it is recorded that the volume of grey matter.

In a report it is recorded that the microvascular complications of diabetes initiate renal damage, mainly micro-albuminuria, which is the early sign of kidney damage, it is also known as diabetic nephropathy. In which glomerular filtration rate decreased day by day with elevation of blood pressure and lastly resulting in end-stage renal failure(Thipsawat, 2021)(Mahler & Adler, 1999).

In many researches, it is suggested that diabetes mellitus can raise inflammation which is significantly proven that the main factor of increase in atherosclerotic cardiovascular disease. It is characterized by an increase in the level of proinflammatory cytokines by raising the activity of inflammasomes(Di Pietrantonio et al., 2023).

Diabetes also hinders eye function it is known as diabetic retinopathy. It is a very common complication in diabetes and it is preventable blindness at any age in developed countries. It is primarily due to high blood sugar levels and high blood pressure due to diabetes mellitus(Simó-Servat et al., 2019).

MANY THERAPIES AND TREATMENTS FOR DIABETES MELLITUS.

In the line of treatment by pharmacotherapy metformin comes first in the name of drug and in herbal therapies many herbal therapies. An individual is marked as having diabetes if their hbA1c is more than 7.0% and the normal level is below 5.6% this indicates the history of fluctuations of the past 3 months.

But while treatment with drugs there are many side-effects like it reduces the blood glucose level very fast and long-term use can also reduce blood glucose level very low suddenly.

Some multitarget compounds select their target selectively.

Incretin therapy – Incretin-based therapies utilize activities of the glucose that depends on the insulinotropic peptide hormone GIP. This controls the postprandial blood glucose level, but when there is a disturbance in metabolism it shows a lack of their action.

SOME OTHER THERAPIES – Some other targeting therapies are SGLT-1 and SGLT-2 inhibitors. SGLT-1 Sodium-glucose co-transporter-1 is responsible for the reabsorption of the glucose in the renal tubule (70-90%). This mechanism reduces the amount of glucose in the gastrointestinal tract. SGLT-2 increases the glucagon peptide-1 and peptide-YY levels in the body that protect against hyperglycemia.

HERBAL THERAPIES- As with multi-target drugs the herbal treatments work on signal targets. They are derived from the plants and its part, algae, and lichens. Herbal treatment includes bitter melon, fenugreek, cinnamon, and garlic, these are phytotherapy treatments for type 2 diabetes mellitus. The extract of bitter melon inhibits the action of glucose absorption in the intestine, fenugreek is commonly used as the treatment of type 2 diabetes mellitus. It carries some bioactive compounds called diosgenin (3 β hydroxy- 5 Spiro Stene) 4 hydroxy isoleucine and soluble dietary fiber, it helps to regenerate beta cells and also stimulates insulin secretion. Cinnamon has its own 250 species. The compound called procyanidin oligomers present in this shows antidiabetic activity. Garlic antidiabetic activity includes hyperinsulinaemia, hypoglycemia, hypocholesterolaemia, and anti-lipid actions (Artasensi A et al., 2020; Ota & Ulrih, 2017; Zarezadeh et al., 2017).

Costus igneus (costus Nak) is a plant that is crop up in India, it has many varieties that are ground in our nature and it is also known as the insulin plant and has a step ladder and fiery costus due to its curl shape, this is the territorial plant of south India and Central America (Prakash et al., 2014; Shetty et al., 2010). It undergoes the family of costaceae, this family has almost along with 200 varieties and four subdivision families (Shetty et al., 2010), The plant of *Costus igneus* was investigated and named the fiery Costus or spiral flag. This plant is about two feet long and found with a mostly trouble-free dark green color, this plant comes from the ornamental family that can be grown in full sunlight or partially shaded sunlight (Shetty et al., 2010). Firstly, the community of hill tribes or kinship groups from the Koli hills of Namakkal district which is situated in Tamil Nadu, India. At that time, they were used to treat diabetes with this leaf. This plant's other families also help treat many diseases like nephrological disorders.

It is investigated in the phytochemical study of the *Costus igneus* plant which is also rich in many nutrients like iron, protein, and many antioxidation nutrients like vitamin C (Ascorbic acid), an active component of vitamin

E (alpha-tocopherol), beta carotene, steroids, terpenoids, and flavonoids. It is explored that ingestion of *Costus igneus* leaf reduces the pre-prandial and postprandial glucose levels in the blood of albino rats. In humans, it is practiced by an Ayurvedic doctor Dr. Bhandarkar from Mangalore situated in Karnataka, India. It is reported that the ingestion of *costus igneus* leaves two times a day morning and evening can lower the blood glucose level both pre and post-prandial (Shetty et al., 2010). A report suggests that chewing this leaf, grinding it with teeth, and safely swallowing it reduces blood glucose levels (Mathew & Varghese, 2019; Prakash et al., 2014).

As reported this leaf is beneficial in diabetes mellitus, Diabetes mellitus is a disease of high blood sugar levels in the blood it is also known as the condition of hyperglycemia, (hyper means high and glycemia means the existence of glucose in the blood. In this condition, there is a level of glucose is high in the blood both in-prandial (before eating, the level of glucose in the blood) and post-prandial (two hours after eating the level of glucose in the blood) glucose level. This disease comes with many complications and can results in organ-damaging diseases like retinopathy (damage to the retina of the eye), nephropathy (damage to the nephrons of the kidney), and neuropathy (damage to the neurons), it can also lead to the damage of the heart functions. The classification of diabetes mellitus depends on the patient's clinical, diagnostic, and symptomatic evaluation (Malik & Andag-silva, 2014).

Recent research in 2022 reveals that the widespread presence of diabetes mellitus is getting bigger, especially in the growing countries, filled with 80% of the diabetic population. India and China occupy 40% of the list of developing countries. An estimation accounts that 74 million people in the population suffer from diabetes mellitus. And it is reported that about 70-80% of the population in India comes up under the middle middle-income group that cannot afford the price of insulin that they need to survive daily (Fralick et al., 2022).

The ethanolic extract of *C. igneus* has shown a potent antidiabetic effect in alloxan-induced diabetic rats (Joshi et al., 2013).

MECHANISM OF INSULIN FUNCTION

Insulin is mainly an anabolic endocrine hormone secreted from the beta cells of the pancreas and helps maintain the body's glucose level, tissue development, and growth (Pessin & Saltiel, 2000). Insulin is secreted by the Langerhans of beta cells of the pancreas in response to the food we eat, and the number of carbohydrates ingested, Insulin is made up of two peptides chain that contain 51 amino acids, these peptides chains are divided into two

groups of insulin peptides A and B (A group chain contains 21 amino acids and B group chain contain 30 amino acids)(Horvath A, Szabadki G, Varnai P, n.d.; Pessin & Saltiel, 2000; Santosh, 2015).. these insulin chains are attached by the bridges at the Acys⁷/ B-cys⁷ and A-cys²⁰ -B-cys¹⁹ and also in the bridge Acys⁶/Acys¹¹ there is no intercorrelation.

Insulin helps us in many ways like

- By reducing gluconeogenesis and glycogenolysis.
- By increasing the absorption of glucose.

Beta cells of the pancreas have a glucose sensing mechanism used that is known as glucose transporter GLT4, in this the mechanism of the insulin also depends on a pathway called the singling pathway(Pessin & Saltiel, 2000), for the function of growth and cell development insulin-like growth factor, IGF is utilized and for the metabolic fluxes' insulin works as the primary source, insulin also does affect skeletal muscles, fat cells, and the liver.

The target cell of the plasma membrane that lies on the insulin receptor INSR gets attached to the receptor called the binding receptor. Insulin receptors are a two-way pathway that is also called heterotetrameric receptor tyrosine mainly formed from the extracellular alpha-subunits, which bind insulin. Insulin tyrosine kinase regulates insulin receptors and behaves like an allosteric enzyme(Kahn & White, 1988). There are two beta subunits in it one and all. Some evidence suggested that the biological concentration of one insulin particle of insulin binds and activates INSR and there is seen that induced conformity change in the beta-subunit replaces through auto reticence in the kinase activation loop and permits autophosphorylation. these signals are further divided into mutagenic and metabolic signals.

Mutagenic signals are responsible for the activation of the mutagenic activated protein kinase (MAPK) pathway that is common for the various receptor tyrosine kinase the concentration of the stimulation of metabolic responses that are lower than the responses needed for the mutagenic pathway(Petersen & Shulman, 2018; White, 2016).

GLYCOLYTIC AND MITOCHONDRIAL PATHWAY

In this the beta cells use glucose transporter 2 (GLUT2), glucokinase, and glycosidic and mitochondrial pathway that reacts to glucose to transform ADP Adenosinediphosphate or ATP Adenosine triphosphate, beta cells use messenger that sends a message to operate ATP-sensitive K^+ ion or potassium ion channel that is in the beta cells, plasma membrane these channels opens when the extracellular concentration of the glucose is low. And the potassium ion is transported to the intracellular compartment and then the voltage-gated L-type calcium channel opens these enter the beta-cells and increase cytosolic calcium ion concentration and stimulates the gesticulation and secretion of insulin(Horvath A, Szabadki G, Varnai P, n.d.).

INSULIN RESISTANCE IN TYPE 2 DIABETES MELLITUS:

Insulin resistance is recognized as an impaired organic response to insulin stimulation of goal tissues, more often than not the liver, muscles, and adipose tissue. Insulin resistance impairs glucose disposal, resulting in a compensatory boom in beta-mobile insulin production and hyperinsulinemia. The metabolic effects of insulin resistance can result in hyperglycemia, high blood pressure, dyslipidemia, visceral adiposity, hyperuricemia, increase inflammatory marks, endothelial dysfunction, and a prothrombic kingdom. In addition to type 2 diabetes mellitus, the spectrum of sicknesses related to insulin resistance includes weight problems, cardiovascular disorders, non-alcoholic fatty liver diseases, metabolic syndrome, and polycystic ovarian syndrome (PCOS)(Nanayakkara et al., 2021; Petersen & Shulman, 2018).

INSULIN PLANT

Costus igneus plant is perennial herb habitat, large smooth dark green with violet underside leaves and orange- or yellow-colored flowers they have large greenly brackels, minutes with black and white fleshy pool seeds, there are different parts of the plant to treat different diseases(Santosh, 2015). In India insulin plant is known by different names in different regions in English it is knowns as spiral ginger or painted spiral ginger, in Hindi it is known as banda, big-sal, keukand, etc(Mathew & Varghese, 2019). This plant is about two feet long and found with a mostly trouble-free dark green color, this plant comes from the ornamental family that can be grown in full sunlight or partially shaded sunlight(Shetty et al., 2010). The taste of the *Costus igneus* leaf is a type of sour taste like amla, after drying and grinding it shows a smooth brown powdery texture(Deogade et al., 2017).

It is shown in the phytochemical study of the insulin plant *Costus igneus* extracted compound with the reaction of ethanol and methanol is terpenoids, phlabtannis, tannins, flavonoids, steroidsstigmastero some steroids are also present like cardiac glycosides, phenols, alkaloids, fatty acid, proteins, carbohydrates, saponins, there are two ways of extraction of phytochemicals from the insulin plant methanol and ethanol extraction and methanol extraction there is found a high amount of saponins found from ethanol extraction(Deogade et al., 2017; Priya, 2019; Santosh, 2015). leaves contain carbohydrates like rose oxide, fatty acids like hexadecenoic acid, 9, 12-octadecanoic acid, tetra decanoic acid, ethyl oleate, oleic acid, and squalene in leaves of this plant(Shinde, 2022). *Costus igneus* plant has antibacterial effects and it helps to prevent E. Coli bacteria that most diabetic patients suffer from it has also had a good effect on streptomycin(Joseph et al., 2017; Kennard & Jacob, 2022; Shinde, 2022). The insulin plant *Costus igneus* have the potential benefits of antioxidant activity. There is also 75.43% more reducing power than ascorbic acid, and it also helps prevent oxidation activity in the body(Chacko et al., 2019).

Table. 1 **COSTUS IGNEUS INSULIN PLANT CASE STUDY ON DIABETIC RATS: -**

Plant	Plant part	Method of extraction	Dose	Reduction in blood glucose %	References
<i>Costus igneus</i>	Leaves	Crushing fresh leaves	500 mg	170-150 mg/dl	(Isaac & Alphonse, 2011)
	Leaves	Crude extract	100mg	115.0 ±1.7	(Shetty et al., 2010)
			250 mg	91.0 ±1.4	
			500 mg	89.0 ±1.5	
			100 mg	170 ± 1.4	
			250 mg	127 ±1.7	
			500 mg	120 ±1.6	
	Leaves	Crude extract	150 mg	218 ±11.73	(Fauni-guirre & Ching, 2022)

	Leaves	Cold extract	500 mg	263 ±86	(Devi & Urooj, 2008)
	Leaves	Aqueous extract	100 mg	112.29 ±2.07	(Vijayalakshmi et al., 2011)
	Leaves	Ethanol extract	25µg 50µg 100µg	180± 6 120 ±6 90 ± 6	(Joshi et al., 2013)
		Crude extract	200mg	100±6	
	Leaves	Ethanolic extract and aqueous extract	8.0 mg per kg of body weight	250 ±4	(Hardikar et al., 2016)

Table.2 PRESENCE OF BIOACTIVE COMPOUDS IN INSULIN PLANT *COSTUS IGNEUS*: -

Extract of leaves	Tannis	Phlobatannis	Saponin	Flavonoids	Steroids	Terpenoids	Cardiac glycosides	Alkaloids
Methanol	+	+	-	+	-	+	+	-
Ethanol	+	+	+	+	+	+	+	+

(Joseph et al., 2017; Kennard & Jacob, 2022; Shinde, 2022).

Table.3 MECHANISM OF INSULIN PLANTS BY THEIR BIOACTIVE COMPOUNDS

CHEMICAL COMPOUND	MECHANISM
Terpenoids	• The corosolic acid present in it enhances the stimulation of insulin beta phosphorylation and secondary it also blocks some non-protein receptors.

	• This also may increase the GLUT4 transporters by taking up the glucose from the muscle cell. • The transportation of GLUT4 transporters also increases by the replacement of fructose 2-6 biphosphate by the corosolic acid and increases glycolysis.
Steroids (diosgenin)	• The bioactive compound found in <i>Costus igneus</i> helps restore the beta cells of the pancreas and also helps the bad effect of an enzyme related to the liver. It also decreases the regulation of enzymes related to gluconeogenesis and the export of glucose and increases the amount of liver protective and antioxidant enzymes.
Flavonoids (quercetin)	• This is the group of C-3 OH position and acts as inhibitory action towards the center cell and the replacement of c-3 and c-4 OH group enhances this activity. When there is an absence of c-4 and double bonds
Phenol (catechin)	• It has an antioxidant activity that helps to fight free radicles through hydrogen donating activity in vivo and in vitro tests. • Catechin control over the generation of oxygen radicals because of an increase in hyperglycemia.

Insulin identical protein	It works through the signaling pathway that can be used as an oral hypoglycaemic drug.
flavonoids and steroids	It increases the production of insulin from beta cells of the pancreas and also stimulates the secretion of insulin
Steroids (diosgenin), Flavonoids (quercetin)	By increasing the uptake of glucose and utilization by the tissues. Gluconeogenesis and decreasing the absorption of glucose from the intestine

(Fauni-guirre & Ching, 2022; Horvath A, Szabadki G, Varnai P, n.d.; Shinde, 2022).

CONCLUSION

Insulin plant act as a hypoglycaemic drug instead of metformin and sulfonylureas by their action of mechanical work on the beta cells of the pancreas and intestine, *costus igneus* work like it inhibits the absorption of glucose in the intestine and controls the GLUT4 transporters or by the action of gluconeogenesis and it is better than the oral hypoglycaemic drugs because it has no side effects and it does not decrease too much of glucose level in the blood as the oral hypoglycaemic drugs do. The stability of reducing blood sugar levels over some time is better than oral drugs and compare to other homemade remedies it can be comparatively better because it includes all the function and garlic have some similarities. *Costus igneus* also helps to repair the liver by producing liver protecting enzyme it not only reduces the blood sugar level it also reduces the symptoms of diabetes mellitus like polyphagia, polydipsia, and polyurea over some time, the consumption of *costus igneus* leaves also helps to prevent us from the infection like mostly occur in DMT2 ex the infection of E. coli and the infection of streptomycin. The consumption of two leaves every day can lower blood glucose levels in diabetic patients. Chewing this leaf directly or making any type of dish with this ex-leaf mixed with curd can also be effective. The ethanolic extract of the insulin plant is more effective than the methanolic extract. There is also some toxicity of this plant like some serum exhibitions getting higher and GPT value was also shown to be decreased and GOT activity reported increased. The level of alkaline phosphatase and acid phosphatase also increased, some study report that the safe dose of insulin plant is 100mg/kg body weight. Some studies show that a dose of 250mg/kg

body weight can cause toxicity and some shows that this is a safe level, some more studies reported some toxicity like the excitement of the tissues of the heart, liver, pancreas, kidney, and heart arteries and the asphyxiation of the organs and some side effects like acidity, GI disorders, and abdominal cramps, some people experience no change in random blood sugar level. Whereas some studies have shown no side effects, some show both side effects and toxicity. **REFERENCES**

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