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Awesome Insulin Plant (*Costus igneus*): An Ecstasy of Natural Remedy for Diabetes Mellitus

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Abstract

Insulin plant (*Cogtus Igneus*) is a medicinal plant and capable of having Magic Cure for Diabetes. Leaf of this herbal plant helps to build up insulin by strengthening β-cells of pancreas in the human body thus popularly known as "Insulin plant" in India. In view of the above aspect the present review provides profiles of this plant with hypoglycemic properties, available through literature source from various databases with proper categorization according to the parts used, mode of reduction in blood glucose (insulin mimetic or insulin secretagogues activity) and active phytoconstituents having insulin mimetics activity. The review describes some new bioactive drugs and isolated compounds from plants. Thus, from the review majorly, the antidiabetic activity of studied medicinal plant is attributed to the presence of polyphenols, flavonoids, terpenoids, coumarins and other constituents which show reduction in blood glucose levels. The review also delineates the management aspect of diabetes mellitus using this plant and its
principles.
Keywords: Phytoconstituents, Blood glucose, Insulin, β-cell, Antidiabetic activity, Metabolic disorder, Herbal medicine, Hypoglycaemic activity, Trace elements

Contents

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1. Introduction

This so-called "Insulin plant" is indigenous to Southeast Asia, particularly on the Greater Sunda Islands situated in Indonesia. It has become increasingly popular in Indonesia, we show appreciations to its amazing medicinal properties that make it a wonderful cure for diabetes. This plant has large and ample leaves which are spirally disposed around the stem. The plant can grow about 2 feet tall and it requires a lot of sun[1-4]. However, it can also sprout quickly in shady areas. Costus igneus (Figure 1. a,b,c) has attractive orange flowers that are about 1.5 inch in diameter. These flowers have a sweet aroma and are considered to be highly nutritious. Moreover, they seem to look like cone heads at the extremities of the branches and flowering takes place during the warm season. In southern

India, it usually grows as an ornamental plant and its leaves are used as a dietary supplement in the treatment of diabetes mellitus. Recently, a number of researches have been carried out to evaluate the anti-diabetic potential of this plant. Besides, it has been proven to possess various pharmacological activities like hypolipidemic, diuretic, antioxidant, anti-microbial, anti-cancerous. Further, various phytochemical investigations reveal the presence of carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, flavonoids, steroid, and appreciable amounts of trace elements [5-11].

Figure 1. Insuin plant & its fowers [a, b, c]

This work is an attempt to compile and explore the different pharmacological and phytochemical studies reported till date. *Costus Igneus*, commonly known as insulin plant in India, belongs to the family Costaceae. Consumption of the leaves are believed to lower blood glucose levels, and diabetics who consumed the leaves of this plant did report a fall in their blood glucose level12. In this review, natural products classified into terpenoids, alkaloids, flavonoids, phenolics, and some other categories have shown antidiabetic potential through the insulinomimetic activity of the plant extract. Roseoside, epigallocatechin gallate, beta-pyrazol-1-ylalanine, cinchonain Ib, leucocyandin 3-O-beta-d-galactosyl cellobioside, leucopelargonidin-3-O-alpha-L rhamnoside, glycyrrhetinic acid, dehydrotrametenolic acid, strictinin, isostrictinin and pedunculagin, epicatechin and christinin-A isolated from the plant material have shown significant insulinomimetic activity along with significant antidiabetic potential. Additionally, some flavonoids and polyphenols, as well as sugar derivatives, are found to be effective due to some other extrapancreatic mechanisms[13-19].

Figure 2. Insulin plant leaves [a, b, c]

This plant is cultivated in India mostly for its medicinal properties, whereas in other parts of the world it is cultivated for ornamental reasons. It is basically given as a remedy due to its anti-diabetic qualities. For instance, one Ayurvedic treatment requires patients with diabetes to chew *Costus Igneus* leaves (Figure 2. a, b, c) for a month. Patients need to use 2 leaves, one in the morning and the other one in the evening. They are carefully advised to chew them prior to swallowing. Remember to chew the first leaf before breakfast and don't worry about its sour taste. You'll get used to it [20-27]. This treatment is also prescribed by allopathic medical practitioners who claim that it is significantly effective in reducing high blood sugar level and maintaining it under control. It's highlighted that this dosage of 2 leaves per day shouldn't be modified and for the cure to work its miracles, it needs to be continued for 30 days. If you decide to take up such a treatment, you must consult a health-care provider, who is well-informed about your past and current health conditions [28-31].This plant is frequently used in the Siddha medical system, one of the oldest systems that have been around for more than twelve thousand years. According to

it, medicine should not only treat illnesses and prevent them, but also protect the mind. This way, the patient will be able to have a healthy and longevous life. Numerous Ayurvedic cures include the use of Costus igneus, particularly the rhizome so as to treat various ailments like intestinal worms, rash, asthma, fever and bronchitis. It is also used in Kama Sutra as an ingredient in a cosmetic product. This is applied on eyelashes to arouse sexual magnetism [32-39].

Epidemiological studies over the last three decades have shown a fivefold increase in the prevalence of diabetes in India. Primary prevention studies have shown a significant reduction in the relative risk of the development of diabetes using lifestyle modifications as well as drugs like metformin, acarbose and rosiglitazone, among others40-44. The use of such strategies which are adapted to suit the local culture along with the use of traditional approaches like yoga and ayurveda, would go a long way in responding to the challenges. When compared to non-diabetics, patients with diabetes have an increased risk of morbidities involving multiple organ systems. There is a 25 fold increased risk of renal failure, 20-fold risk of blindness, 40-fold risk of amputation, threefold risk of stroke and fivefold risk of myocardial infarction. The expected lifespan is reduced by an average of 15 years. In the developed world, diabetes is the leading cause of blindness, end-stage renal disease and amputation. Besides morbidity and mortality, these disorders impact the socio-economic status of individuals as well as the state [3].

Costus igneus leaves–have been claimed to have antidiabetic effects in the ayurvedic system of medicine, as a treatment for diabetes. This review supports the therapeutic potential of the leaves in diabetes. However, these results have to be further evaluated and revalidated by clinical trials. The anti-diabetic effect of its leaves is currently been tested in diabetic patients [48-55]. Studies reveal its role in various diseases, which opens up new clinical research areas. Furthermore, it paves new avenues to explore the compounds responsible for these therapeutic effects, and study the mechanism of– their action. The aim of this review is to collect the data available on plants material having hypoglycemic activity through either increased secretion of the insulin from pancreas or similar action to the insulin reported in different source of literature. According to the search insulin plant has been described as hypoglycaemic.

2. Diabetes at a Glance

Diabetes is a disorder of carbohydrate, fat and protein metabolism caused due to insufficient production of insulin or due to its inhibitory action, which can be considered as a major cause of high economic loss which can in turn impede the development of nations. Before there were drugs from drug companies, natural cures were used and they can still be used today. There are many herbs with strong anti-diabetic properties. Herbal treatments for diabetes have been used in patients with insulin dependent and non-insulin dependent diabetes, diabetic retinopathy, diabetic neuropathy, etc. In the experiments, oral glucose tolerance test, streptozotocin and alloxan-induced diabetic mouse or rat were most commonly used model for the screening of antidiabetic drugs. Numerous mechanisms of actions have been proposed for plant extracts. Some hypothesis relates to their effects on the activity of pancreatic β-cells, increase in the inhibitory effect against insulinase enzyme, increase of the insulin sensitivity or the insulin-like activity of the plant extracts. Other mechanisms may also be involved such as increase of peripheral utilization of glucose, increase of synthesis of hepatic glycogen or decrease of glycogenolysis, inhibition of intestinal glucose absorption, reduction of glycaemic index of carbohydrates and reduction of the effect of glutathione.

The complications of Diabetes mellitus are related to glycaemic control. Normoglycaemia or near normoglycaemia is the desired, but often elusive, goal. Regardless of the level of hyperglycaemia, improvement in glycaemic control will lower the risk of diabetes complications. Consumption of the leaves of the insulin plant has been claimed to achieve glycaemic control. The review describes some new bioactive drugs and isolated compounds from plants. such as roseoside, epigallocatechin gallate, beta-pyrazol-1-ylalanine, cinchonain Ib, leucocyandin 3-O-β-d-galactosyl cellobioside, leucopelargonidin-3- O-α-L rhamnoside, glycyrrhetinic acid, dehydrotrametenolic acid, strictinin, isostrictinin, pedunculagin, epicatechin and christinin-A showing significant insulinomimetic and antidiabetic activity with more efficacy than conventional hypoglycaemic agents. According to International Journal of Ayurveda Research a new study on Insulin plant (Costus igneus) was published recently. The leaves of insulin plant (Costus igneus) reduced the fasting and postprandial blood sugar levels, bringing them down towards normal, in dexamethasone-induced hyperglycemia in rats. Reduction in the fasting and the postprandial blood sugar levels with leaves of insulin plant was comparable with that obtained with Glibenclamide 500 µg/kg at 250 mg/kg/day and 500 mg/kg/day of powdered leaves of the insulin plant.

Veggies and Type 2 Diabetes

Based on what is known of the components of plant-based diets and their effects from cohort studies, there is reason to believe that vegetarian diets would have advantages in the treatment of type 2 diabetes. At present there are few data on vegetarian diets in diabetes that do not in addition have weight loss or exercise components. Nevertheless,

the use of whole-grain or traditionally processed cereals and legumes has been associated with improved glycemic control in both diabetic and insulin-resistant individuals. Long-term cohort studies have indicated that whole-grain consumption reduces the risk of both type 2 diabetes and CHD. In addition, nuts (eg, almonds), viscous fibers (eg, fibers from oats and barley), soy proteins, and plant sterols, which may be part of the vegetarian diet, reduce serum lipids. In combination, these plant food components may have a very significant impact on CHD, one of the major complications of diabetes. Furthermore, substituting soy or other vegetable proteins for animal protein may also decrease renal hyperfiltration, proteinuria, and renal acid load and in the long term reduce the risk of developing renal disease in type 2 diabetes. The vegetarian diet, therefore, contains a portfolio of natural products and food forms of benefit for both the carbohydrate and lipid abnormalities in diabetes. It is anticipated that their combined use in vegetarian diets will produce very significant metabolic advantages for the prevention and treatment of diabetes and its complications[12-17].

Growth of interest in dietary fiber and its possible metabolic benefits in the prevention and treatment of chronic diseases, including diabetes, has been put forward as one of the reasons to include more plant foods in the diet. There is therefore an urgent need for further assessments of the effects of plant-based diets in diabetes, especially in view of the benefits of such diets in nondiabetic subjects and the increasing recognition of the potential benefits of components of plant-based diets in both hyperlipidemia and diabetes. These components include dietary fiber, vegetable proteins, plant sterols, unsaturated vegetable oils, and slow-release carbohydrates (especially of cereal and legume origin). Increased intake of fruits and vegetables has been endorsed as public health policy for a number of reasons. Displacement of saturated fat and increased intake of fiber have been seen as general reasons for increasing fruit and vegetable consumption. Increased fiber intake may improve glycemic control in diabetes. Perhaps one of the major benefits that a vegetarian diet may have in the treatment of diabetes is its effect in increasing satiety, possibly related to amino acid composition or the sheer bulk of the diet. Evidence for this is the “confounding” effect of weight loss in interpreting the results of vegetarian diets on diabetic patients in the previous section. The weight loss, far from being “confounding,” may be one of the advantages of vegetarian diets. The paramount importance of body weight has been illustrated in recent studies where diet and lifestyle changes have prevented the development of diabetes in susceptible individuals.There have been no major studies in the absence of weight loss that have attempted to determine the potential advantages of a vegetarian or vegan diet in the treatment of diabetes. However, there are many facets or components of a plant-based diet that might confer benefits on glycemia and, more specifically, on blood lipids..There is therefore good reason to expect a dietary portfolio in the treatment of diabetes will have significant metabolic benefits [19-21].

Diabetes mellitus is one of the common metabolic disorders acquiring around 2.8% of the world's population and is anticipated to cross 5.4% by the year 2025. Diabetes mellitus, in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced[202-231]. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). There are three main types of diabetes: Type 1 diabetes: results from the body's failure to produce insulin, and presently requires the person to inject insulin. (Also referred to as insulin-dependent diabetes mellitus, IDDM for short, and juvenile diabetes.)Type 2diabetes: results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. (Formerly referred to as non-insulin-dependent diabetes mellitus, NIDDM for short, and adult-onset diabetes.) Gestational diabetes: is when pregnant women, who have never had diabetes before, have a high blood glucose level during pregnancy. It may precede development of type 2DM. Insulin is a hormone central to regulating carbohydrate and fat metabolism in the body. Insulin causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle. Insulin stops the use of fat as an energy source by inhibiting the release of glucagon[232-251]. With the exception of the metabolic disorder diabetes mellitus and Metabolic syndrome, insulin is provided within the body in a constant proportion to remove excess glucose from the blood, which otherwise would be toxic. When blood glucose levels fall below a certain level, the body begins to use fat as an energy source through glycogenolysis, for example, by transfer of lipids from adipose tissue to the liver for mobilization as an energy source. As its level is a central metabolic control mechanism, its status is also used as a control signal to other body systems (such as amino acid uptake by body cells). In addition, it has several other anabolic effects throughout the body[25-29].

Cram of Phytochemcal Therapeuticability

Sequential screening for phytochemicals of *C. Igneus* leaves revealed that it is rich in protein, iron, and antioxidant components such as ascorbic acid, α-tocopherol, β-carotene, terpinoids, steroids, and flavonoids [40-42]. 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.[260-267] 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, ergastanol. Stem showed the presence of a terpenoid compound lupeol and a steroid compound stigmasterol. Bioactive compounds quercetin and diosgenin, a steroidal sapogenin, were isolated from *insulin plant* rhizome. Trace elemental analysis showed that the leaves and rhizomes of *insulin plant* contains appreciable amounts of the elements K, Ca, Cr, Mn, Cu, and Zn. Steam distillation of stems, leaves, and rhizomes yielded clear and yellowish essential oils.

3. Antioxidant activity

An *in vitro* study of alcoholic extract of leaves of insulin plant showed moderate antioxidant activity. 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 *insulin plant* 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 insulin plant possess higher antioxidant activity when compared with other extracts. In another study, methanolic leaf extract of *insulin plant.* Don 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. Methanolic extracts of flower and stem of insulin plant possess *in vitro* antioxidant activity against oxidative protein damage. Oral administration of ethanolic extract of *insulin plant* 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.

4. Conclusion

Diabetes mellitus is the most common metabolic disorder. Severe condition of diabetic can leads to micro and macro vascular diseases. Plant products have been used in folk medicine and traditional healing systems and are being evaluated for their hypoglycemic effects. The study was planned to evaluate the insulin-sensitizing effects of the insulin plant (*Costus igneus*). The available clinical data suggesting anti-diabetic activity of plants identified in this survey is limited. Most of the clinical studies lacked sufficient sample size, randomized controlled study design or revealed only low anti-diabetic efficacy following the treatment with *Costus igneus* plant. In this context, it is also questionable to what extent the numerous anti-diabetic effects of plants and their extracts found in experimental animal and *in vitro* studies can be extrapolated to human settings. We henceforth propose to focus future research on the conduction of high-quality clinical studies while concentrating on this plant which shows the most promising anti-diabetic efficacy in already performed clinical studies. It's also of particular interest to include safety issues and to study dose-dependent relationships. But this has to be further investigated by clinical trials meeting the requirements of evidence-based medicine. Such studies are of enormous public health interest as they may offer an evidence-based and safe use of non-expensive plant-derived medications against the growing epidemic of diabetes, particularly for low-income countries.

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