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Effectiveness of Insulin plant in Management of Diabetes Mellitus

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A B S T R A C T

Diabetes mellitus, to this day, is still one of the significant health problems and created significant morbidity and mortality among world populations. Current diabetic drugs still have unpleasant side effects and costly prices. Seeking new diabetic drugs from natural resources is one of the practical actions for alternative management of the disease. The insulin plant, which originated in the Andes, has been cultivated in Indonesia. The insulin plant is rich in caffeic acid, chlorogenic acid, flavonoid, phenolic compound, and sesquiterpenes lactone and has antihyperglycemic and antioxidant effects that possibly have a role in diabetes management. Several studies have reported the potential of the insulin plant as an antidiabetic agent. This review aims to summarize and organize current literature on the effectiveness and role of insulin plants on diabetes mellitus patients.

1. Introduction

Diabetes mellitus (DM) is defined as a disease or chronic metabolism abnormalities with multiple causes, characterized by high levels of blood sugar, carbohydrate, lipid, and protein metabolism problem as a result of insulin function deficiency. Insulin function deficiency is caused by abnormalities in the production of insulin by beta Langerhans or the inability of cells to respond adequately to insulin.[1,2] Diabetes mellitus is still a significant problem all over the world. It is estimated that 8,3% of the world population (382 million) has the disease is and projected to be 10% (592 million) in 2035. Diabetes mellitus has caused mortality in more than 5 million people.[3,4]

Diabetes management's aim is to correct insulin deficiency resistance to reduce complications related to the disease and prevent further decline of β-pancreatic cells. One way to achieve this is by using an oral hypoglycemic agent (e.g., metformin, glyburide, chlorpropamide, etc and insulin although some drugs still have unpleasant side effects and costly prices. World Health Organisation stated research on alternative diabetic agents originating from the plant is important for the management of this disease. Plant sources diabetic agents are also shown to have fewer side effects than conventional ones with reduced blood glucose.[5]

One of the conventional diabetic drugs, metformin, also originated from Europe traditional plant, Galega officinalis, which is rich in guanidine, and was later found able to decrease blood sugar. Metformin's success drove scientists to find another potential plant as an antihyperglycemic agent. One medicinal plant with this potential and also found in Indonesia is the

insulin plant or also called yacon (*Smallanthus sonchifolius*.) Rich in caffeic acid and chlorogenic acid, this plant is able to decrease blood sugar. Enhedryin and sesquiterpene lactone in the leaves is also effective in decreasing postprandial glucose in diabetic animal (minimal dose 0,8 mg/kg).[5,6] Therefore it is important to know the effectiveness, safety, and role of insulin plants in diabetes mellitus. This review aims to summarize and organize current literature on the effectiveness and role of insulin plants in patients with diabetes mellitus.

Insulin plant

The insulin plant, also called Yacon (*Smallanthus sonchifolius*) is a crop native to Peru, Ecuador, Colombia, and Argentina. The plant begins to be cultivated outside its native countries such as Japan, Europe, and the United States due to the potential harbored. In Indonesia, the plant has been cultivated since 2006 in Bandung and Yogyakarta.[7] The plant could also be found in Jambi, at Jabung Barat Regency. Generally, the crop could optimally grow at highland at 24-30^{o}C.[8]

The insulin plant has old and big green leaves that give rise to stems about 1,5-3 m high and have rooted for food storage. The plant comes from the Plantae kingdom, Magnoliophyta Division, Magnoliopsida Class, Asterales order, Asteraceae family, Smallanthus genus, and Smallanthus sonchifolius species.[7]

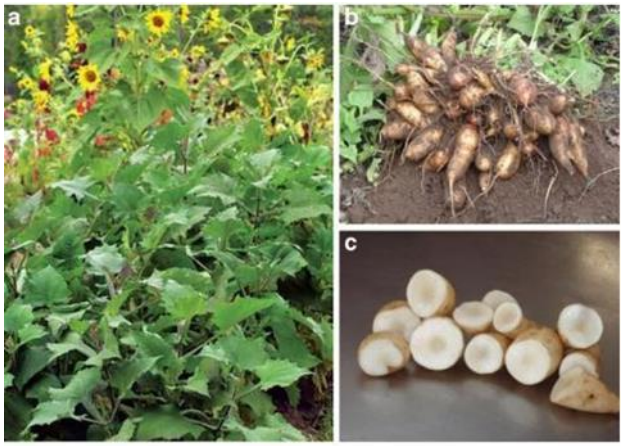

Figure 1. A) Insulin plant; B) Roots of insulin plant; C) Cross-section of insulin plant roots[5]

Insulin plant roots' water content is >70% and the rest is dry matter such as fructooligosaccharides. Fructooligosaccharids made up 6.4%-70% of the dry matter depending on the crop and location. The insulin plant, just like other plants, has high carbohydrate, lipid, protein, fiber, and water content. The insulin plant also has compounds such as oxalic acid, carotenoids, sesquiterpene lactones, flavonoids, and high content of phenolic compounds. Caffeic acid, gallic acid, rosmarinic acid, ferulic acid, chlorogenic acid, and quercetin were also shown to be high in this plant and these substances may cause antioxidant and antidiabetic activity. In addition, flavonoids and sesquiterpene lactones have also been associated with a hypoglycemic effect.[7–9]

Potential as an antidiabetic agent

Studies evaluating the potential of insulin plants as an antidiabetic agent commonly streptozotocin-induced ed diabetic rats (D-STZ) as the subject. Insulin plant is given he diabetic rats in form of extract, either from roots or leaves. One of the research evaluating the effect on insulin leaves extract is done by Klinsman (2018) who found improvement in dysmetabolism and cardiomyopathy related to DM in form of glycemia decreased by 63,9%, an increase in insulin concentration by 49,3%, a decrease of triacylglycerol and free fatty acid, amelioration of

pancreatic islet cells increase of antioxidant enzyme activity and repair of cardiac tissue.10In accordance with this, Genta (2010) evaluate five organic extracts and pure crystalline enhedryn from insulin plant leaves with normoglycemic, hyperglycemic, and D-STZ rats. Methanol, butanol, and chloroform extract has hypoglycemic activity in 50,10, and 20 mg/kg dosage. Daily administration of extract for 8 weeks causes controlled blood sugar and an increase in insulin. Phytochemical analysis from the most active fraction, butanol extract, show caffeic, chlorogenic, and three dicaffeoilquinic acids as the significant component. Furthermore, Enhedrin, a major sesquiterpene lactone from insulin leaves able to decrease postprandial glucose and found to be useful in diabetes.6Russo (2015) elucidates the mechanism of the effect by methanol extract from insulin plant may have an inhibitory activity to alpha-amylase alpha-glucosidasease enzyme, thereby able to decrease blood glucose and may be useful in hyperglycemia due to diabetes.[11]

Gilberto (2013) evaluates the aqueous extract of insulin plant roots (YRAE) in four groups, control (C), group that received aqueous extract of insulin plant (Y), DM-type 1 without intervention (DM-1), and DM-type 1 managed by with insulin plant extract (Y-DM1). It is reported there is a significant decrease in water and food consumption in Y-DM1. YRAE consumption decrease glycemia, total cholesterol, VLDL, LDL, and triacylglycerol significantly in diabetic rats. YRAE normalizes ALT levels on Y-DM1 which indicates its hepatoprotective effect.[12] Another study by Habib (2011) on D-STZ rats found a significant decrease in fasting plasma triacylglycerol and LDL with insulin plant roots diet oral supplement. Supplement consumption also has a protective effect on triacylglycerol postprandial plasma peak and pancreatic cells. Furthermore, there is an increase in GLP-1, one of the two incretin hormones, in groups given insulin plant roots supplement.[13]

There are also studies comparing the effectiveness between roots and leaf extract in D-STZ rats. Both extract is found effective in preventing hyperglycemia. However, root extract is more effective against the normalization of antioxidant enzyme function and decrease of reactive oxygen species (ROS) while leaf extract is ineffective.[5,14] Therefore due to better benefits, root extract is perhaps better than leaf extract.

The role of insulin plants in diabetes management isn't only from the antihyperglycemic effect or increase of insulin secretion but also by increasing lipid metabolism, oxidative status, and vascular endothelial function[6,12,15,16] Diabetic rats' management with the plant extract has a protective effect on against nephropathy, a complication caused by free radical.[17] Furthermore, the roots and plant extract show high activity against free radicals when measured in vitro. The antioxidant effect of the insulin plant is related to the high level of the phenolic compound on its roots and leaves. The leaves of the insulin plant even have a higher level of phenolic acid compared to its rooms.[18,19]

The mechanism underlying the insulin plant's effect on reducing glucose lies in the active compound on its leaves and roots. A high level of phenol compound, for example, can increase insulin receptor sensitivity and has an implication in treating diabetes Mellitus. Other research shows a phenolic extract from insulin plants could increase hepatic rats' mRNA expression and cause decreased blood glucose. Decreased blood glucose could also be mediated by caffeoylquinic which inhibits α-glucosidase in the body.[8]

Not only insulin-like effect, but the plant also has other benefits. Another compound such as phenolic and caffeoylquinic, chlorogenic acid, polyphenol, and tryptophan has antioxidant activity that prevents membrane cell damage and decreases reactive oxygen species which plays a role in DM complication such as nephropathy.[17,20]

There are few studies evaluating the consumption of insulin plants in human subjects. Only two studies have been done to the author's knowledge. Scheid (2014) evaluate the effect of daily consumption of freeze-dried powdered insulin plants for 9 weeks on

glucose, lipid, and bowel transit in geriatric patients and found a significant decrease in glucose.20 Insulin plant is reported not to cause side effects to bowel transit such as bloating, flatulence, and abdominal discomfort. The plant is concluded safe for daily consumption and practical to use.[20]

Genta (2010) reported a significant decrease in body weight, waist circumference, and body mass index in pre-menopause obese women who take insulin plant syrup for 120 days. Recommended syrup consumption not to cause unpleasant gastrointestinal side effect is 0,14 g fructooligosaccharides/kg. Meanwhile, other research found no significant effect on blood glucose (fasting blood sugar) and lipid serum, only showing a protective effect on LDL. The difference in the finding suggests a different forms of insulin plants can result in different effects. Rocio (2020) evaluates the toxicogenic effect of Smallanthus sonchifolius and found aqueous extract of the plant has cytotoxic, cytostatic, and genotoxic effects. However, the insulin plant is safe for consumption as a 2% tea infusion (one teabag/100 mL) maximum of 250 ml/day.[21]

Several studies compare insulin plant extract to traditional diabetic drugs. Otto (2020) research on Rattus norvegicus found that insulin plant extract is just as effective as metformin in decreasing glucose.[22] Supporting the findings, Dwitiyanti (2020) also found insulin extract from leaves is comparable to metformin in decreasing blood glucose and increasing glycogen synthesis in the liver on hamsters, thereby insulin plant has the potential to manage hyperglycemia with high fatty diets.[23]

2. Conclusion

Diabetes still causes significant morbidity and mortality in the world. The administration of antidiabetic agents derived from plants is an important alternative for the management of the disease. Insulin plants are the natural crop that can be found in Indonesia and current literature shows many phytoconstituents of the plants such as flavonoids, caffeic acid, chlorogenic acid, phenolic compounds, and sesquiterpene lactones are useful as antihyperglycemic and antioxidant. Further studies on the phytoconstituents responsible for the pharmacological activity of this plant still need to be done to make the treatment better and reliable with minimal side effects.

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