

The Potential Role of apigenin in Diabetes Mellitus

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Abstract:

Diabetes mellitus is a serious disease with a high incidence of occurrence all over the world. The number of diabetic patient will jump to 439 million by 2030. Diabetes cause a lot of complication as it can affect the entire organ in the body as liver, kidney, retina and heart. Apigenin is a potent antioxidant, it can stimulate the metabolism of glucose and transportation of it in the peripheral tissues; also enhance secretion of insulin from pancreas. It has the ability to overcome dyslipidemia which result as a non-control of diabetes. Apigenin can enhance the metabolism of glucose via suppression the activities of gluconeogenic enzymes and aldose reductase enzyme and so prevent diabetic complication as cataracts, retinopathy, and neuropathy that may result if sorbitol diffuses out cell membrane.

Keywords: diabetes; medicinal plants; apigenin;

Introduction

Diabetes mellitus is a critical disease [1]. World Health Organization stated that, there will be about 346 million have a diabetes by the year 2025, and 10 % increase to become 439 million by 2030 [2].

Celery is a much consumed vegetable contain flavonoid as apigenin which considers a potent antioxidant ingredient [3]. Many plants have numerous activities and can have a marked role in forbidding many diseases [4]. Diabetes raises the concentration of blood glucose, and hence causes the activity of aldose reductase increases, hence, the sorbitol accumulates intracellularly and leads to diabetic complications as neuropathy, retinopathy, and cataract, celery apigenin can suppress the activity of this enzyme and hence decrease the complication of diabetes [5].

Apigenin has been found in abundant in several fruits, vegetables, and medicinal plants [6]. This compound assumed to have an antioxidant effect, decrease inflammatory, fight cancer and minimize diabetes complication [7]. It has the ability to encourage insulin secretion and glycogen storage [8]. So, the present article review is mention the biological activity and mechanism action of flavonoid apigenin on diabetes.

Glucose and insulin

Apigenin stimulate the metabolism of glucose and transportation of it in peripheral tissues; also enhance secretion of insulin from pancreas [7]. In a study by [9] they confirmed the ability of apigenin to prevent destruction of β -cell and cause insulin release. Moreover, Apigenin extract can interact by classical cellular insulin metabolic signaling [10]. Apigenin can raise the GLUT-4 protein concentration and ease GLUT4 translocation in the skeletal muscles of diabetic rats [11]. It also said that it can enhance glucose tolerance via prevent microRNA maturation in

miRNA103 transgenic mice model group [8]. Furthermore, a type of apigenin known as apigenin-6-C- β -fucopyranoside said to have the ability to raise glucose uptake in muscle via insulin signaling pathways as insulin receptor tyrosine kinase activity, phosphoinositide 3-kinase, atypical protein kinase - C and mitogen activated protein kinase [12]. In an astudy by [13] they confirmed the ability of apigenin to mend and control hyperglycemia state and improve antioxidant levels.

Lipid profile

Apigenin extract could improve disturbance of lipid profile of diabetic rats, hence the risk of cardiovascular disease decrease that can occur as result of reducing blood glucose level [14]. Also, it can decrease free fatty acid, cholesterol, plasma apoB and the apoB/apoA1 ratio which confirmed it is ability to overcome dyslipidemia [15]. It can decrease cholesterol via encouraging hepatic LDL-C bad cholesterol absorption and enhance conversation to bile acid and thus apigenin can mend disorder in lipid profile [16].

α -amylase:

Apigenin can suppress the activity of alpha-amylase depending on its action on carbohydrate binding regions of α -amylase enzymes that decrease the absorption of starch in to the body, and hence catalyze hydrolysis of α - 1,4 glucosidic linkages in the starch and polysaccharides and hence prevent hyperglycemia after meal [17]. Inhibition of the α -amylase may occur via direct blockage of the active center at various sub-sites of the enzyme as a mention for another inhibitor. So, apigenin extract act as α -amylase inhibitor.

Liver and kidneys

Both liver and kidney structure and function altered by diabetes as a result of decrease insulin level that cause hyperglycemia and thus inhibit glucose uptake by tissue and the storage in liver as in the form of glycogen

[18]. Apigenin can enhance the metabolism of glucose via suppression the activities of gluconeogenic enzymes [19]. It also mends glucose tolerance [15]. Apigenin fucopyranoside can encourage insulin secretion from pancreas and glycogen creation [8]. So, apigenin is capable of repairing pancreatic cells which cause insulin secretion.

Oxidative stress

Apigenin can hinders ROS that result from diabetes, the reduction of L-MDA levels can be attributed the existence of OH group in their structure that can raise their antioxidant activity [20], apigenin depend on their structure in fighting free radicals and activation antioxidant enzymes [20] In a study by [21] they stated that small concentration of apigenin (1.5mg/kg. B.Wt) can mend necrosis, fibrotic alteration and decrease the injuries of pancreas and also it can keep pancreatic β -cells.

The mechanism action of apigenin in diabetes

Apigenin said to be anti-diabetic agent as it can suppress the activity of α -glucosidase, stimulate insulin secretion [22], and manage reactive oxygen species [23], which can manage diabetic complications [24]. Apigenin can provide the endothelial cells by nitric oxide, and hence, prevent or decrees damage of endothelial cell that result from increase glucose level in blood [24]. Apigenin thought to have cardio-protective effects, as it improve cardiac disorder, fibrosis, increases of 4-hydroxynonenal which resulted through down regulation of B-cell lymphoma 2, Glutathione peroxidase, and Superoxide dismutase, upregulation L-malondialdehyde, cleaved caspase3 antibodies, pro-apoptotic protein Bax gene, and finally translocation of NF- κ B in mice [25]. Small dose of Apigenin can mend renal problems, oxidative stress, and fibrosis in rats [26].

Aldose reductase enzyme which is the main enzyme in the polyol pathway [27], can be controlled with Apigenin extract [5, 27, 28], apigenin prevent the diffuse out of the cell membranes, as increased level of sorbitol in diabetes cause many problems as cataracts, retinopathy, and neuropathy [27]. Thus, celery apigenin consider an anti-diabetic agent and can inhibit complications of uncontrolled diabetes [29].

Both seeds and leaves of celery contain phenolic compounds like those of apigenin which characteristic by their ability to manage diabetes, and enhance insulin secretion from pancreas and diminished gluconeogenesis process [29, 30]. Moreover, histopathology of pancreatic tissue treated with celery apigenin confirmed the ability of this compound to keep the architecture of the islets of langerhans and also immunohistochemical confirmed the secretion of insulin by pancreatic cell [3, 30]. Flavonoids as apigenin can manage free radicals which result as a result of diabetes and stopping injury of pancreas [31]. Flavonoids as apigenin can regulate, absorption of glucose, carbohydrate ingestion, and control the cell-signaling AMP-activated protein kinase pathways, also improve glucose in the skeletal muscle cells [32]. Both of apigenin and luteolin act as sodium-glucose cotransporter-2 inhibitors in neuro-diabetic patients [33]. Flavonoids like apigenin up-regulate glucose Transporter-1 expression and can manage patient with type II diabetes [34]. Phenolics can enhance glucose uptake and glucose transporter-4 expression [34]. So, apigenin consider anti-hyperglycemic agent [33].

Conclusion

This article review has abbreviated the fundamental role of apigenin as an antidiabetic agent. apigenin from various plants have been reported to have a hypoglycemic activity. The activity of apigenin can controls blood glucose level and prevents diabetic complications due to their antioxidant activity. Dyslipidemia which is attributed to diabetes may be managed with apigenin, it can diminution the risk of atherosclerosis and cardiovascular disease in patients suffering from diabetes.

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