ROLE OF CATECHINS IN DIABETES MELLITUS

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ABSTRACT: Diabetes mellitus is a disease that affects many metabolic pathways. It is associated with insulin resistance, impaired insulin signaling, β-cell dysfunction, abnormal glucose levels, altered lipid metabolism, sub-clinical inflammation, and increased oxidative stress. The present study aimed to explore the role of catechin in the treatment of Diabetes mellitus. Catechins are polyphenolic compounds or flavanols of the flavonoid family found in a variety of plants. Catechins and their antioxidant activity, and the mechanisms of action involved in the prevention of oxidative stress-caused diseases such as cancer, cardiovascular diseases, and neurodegenerative diseases. Insulin resistance in patients with diabetes mellitus causes complications such as cardiovascular and renal diseases. Studies have shown that catechins can be effective in controlling hyperglycemia and preventing the complications of diabetes by improving insulin sensitivity and reducing the risk factors for Type 2 Diabetes Mellitus such as oxidative stress, dyslipidemia, and obesity. Nowadays, diabetes and diabetes-mediated dysfunctions are overwhelming at every corner of the world which has been a sober concern to the current health care professionals. The benefit of catechin consumption still requires confirmation. So, in the present study, an attempt was made to review the use of catechin in diabetes mellitus.

KEYWORDS: Catechin, Polyphenols, Diabetes, Hyperglycaemia,

INTRODUCTION

Diabetes mellitus is a metabolic disorder resulting from abnormality or deficiency of insulin function and it is characterized by hyperglycemia. According to WHO report 2011, 9% of the total population above 18 years are suffering from Diabetes Mellitus (DM). If this scenario continues, the projected number of diabetic patients would be approximately 552 million in 2030.¹ Evidence also documented that around one-third of diabetic subjects suffer from diabetic nephropathy (DN) resulting in the overall cost of the treatment beyond reach.² Type 1 DM is also known as insulin-dependent DM, resulted from the cell-mediated autoimmune destruction of the β cell of the pancreas. Type 2 DM is known as non-insulin dependent DM results from insulin resistance or insulin deficiency. This form of diabetes accounts for near about 90-95% of those with diabetes.³ Type 2 diabetes is characterized by two main features: peripheral insulin resistance and beta-cell dysfunction. Both hereditary and environmental factors, such as obesity and prolonged hyperglycemia, may trigger or exaggerate human type 2 diabetes. It is associated with insulin resistance (IR), impaired insulin signaling, β-cell dysfunction, abnormal glucose levels, and altered lipid metabolism. It is also linked to sub-clinical inflammation and increased oxidative stress. These metabolic disorders lead to long-term pathogenic illnesses including micro-and macro-vascular complications, neuropathy, retinopathy, nephropathy, and, consequently, decreased quality of life and increased rate of mortality.⁴,⁵ Linked to their biological properties, polyphenols may be useful nutraceuticals and supplementary treatments for various aspects of diabetes mellitus. Based on several in
vitro animal models and some human studies, polyphenols may play a role in many metabolic processes. They can modulate carbohydrate and lipid metabolism, attenuate hyperglycemia, dyslipidemia, and insulin resistance, improve adipose tissue metabolism, and alleviate oxidative stress and stress-sensitive signaling pathways and inflammatory processes.

Catechin, the name of which is derived from catechu, is 3,3',4',5,7-pentahydroxyflavan with two steric forms of (+)-catechin and its enantiomer. Also, in a broad sense, catechin represents the chemical family name of the compounds derived from catechin. Catechins are distributed in a variety of foods and herbs including tea, apples, persimmons, cacaos, grapes, and berries. In a broad sense, catechin represents the chemical family name of the compounds derived from catechin. Catechins are distributed in a variety of foods and herbs including tea, apples, persimmons, cacaos, grapes, and berries. 

Tea, a product obtained from the leaves and buds of the plant *Camellia sinensis*, is one of the richest catechin sources and contains, as the major catechin, (−)-epigallocatechin-3-gallate (EGCG). Green tea is used as one of the most popular traditional tea, dietary supplement, and beverage in worldwide. Green tea contains various amounts of catechins (CTNs), and several investigations have indicated that the antioxidant properties of green tea come from the flavonoids. So, in the present study, an attempt was made to review the use of catechin in diabetes mellitus.

**Catechins in diabetes mellitus**

Catechin chemically consists of two benzene rings (A- and B-rings) and a dihydropyran heterocycle (the C-ring) with a hydroxyl group on carbon 3. There are two chiral centers on the molecule on carbons 2 and 3. Catechin stereoisomers in cis ((−)-epicatechin) or trans ((+)-catechin) configuration, with respect to carbons 2 and 3, are flavan-3-ol compounds. Catechin adjusts oxygen radical generation, which may be responsible at least in part for the improved hyperglycemia, hyperlipidemia, and oxidative stress.

![Chemical structure of catechin](image)

**Fig No. 1- Chemical structure of catechin**

Catechins' effect on hyperglycemia In-vivo studies has shown that green tea can improve insulin sensitivity. Green tea extract is a rich source of catechins that have reported the hypoglycaemic effect in animal studies. Epidemiological studies have reported that green tea consumption may reduce the risk of type 2 diabetes. Fukino et al reported clinical that supplementation with green tea extract reduces the glycated hemoglobin in people with abnormal blood sugar. It is reported that EGCG causes an increase in insulin sensitivity and facilitates the entry of glucose into cells.

There are some clinical studies carried out in diabetic patients and reported that tea polyphenols are capable to lower the hyperglycemic condition and also can be effective against diabetes mellitus. A prospective cross-sectional study was carried out on women 45 years old and free from cardiovascular disease, cancer, and diabetes. It was observed that the risk of occurrence of type 2 DM was decreased by 30% by taking 4 cups of green tea per day. Liu et al.’s study showed the EGCG supplementation for 12 weeks in mice can reduce the levels of FBS and fasting insulin by a change in the expression of GLUT4 gene. Hsu et al. showed that 1500 mg of green tea extract supplementation (856 mg EGCG) for 16 weeks on obese people with type 2 diabetes can cause a significant reduction in fasting insulin, insulin resistance, and glycated hemoglobin.
Another randomized controlled clinical study was carried out using 300 pre-diabetic Mauritians aging between 35 to 65 years. They were allowed to drink 1 cup of green tea thrice a day for 14 weeks. At the end of the study, it was found that there was a significant increase in serum antioxidant capacity, decreased mean arterial pressure\(^1\). Nagao et al. showed that the 12-week intervention of a catechin-rich drink, including green tea containing 528.8 mg of catechins than a green tea drink containing catechins can significantly 96 mg of the reduced insulin levels in type 2 diabetic patients, although no significant difference was observed in fasting glucose levels and glycosylated hemoglobin\(^2\). Saeed et al reported that the IP injection of CTN significantly recovered the adverse metabolic effects in the serum of animals treated with STZ in a dose-dependent manner. Catechin injection after STZ treatment caused lower serum glucose levels and ameliorated lipid profile. The present investigation proposes that CTN may ameliorate diabetes and its complications by modification of oxidative stress\(^3\).

A study by Josic et al. showed that an intervention of 300 mg of green tea compared to placebo (drinking water) can increase glucose levels after meals (Postprandial), although the increase in the levels of fasting insulin and area under the curve the blood glucose was observed\(^4\). A meta-analysis of randomized controlled trials reported that the administration of green tea catechins with or without caffeine resulted in a significant reduction in fasting blood glucose.\(^5\)

Wenjun et al reported in a study that HSP27 levels increased in STZ-induced DR rats, and became further upregulated after catechin treatment. Furthermore, IL-1β, IL-6, and TNF-α levels were upregulated in the retinas of STZ-induced DR rats, but these changes were partially inhibited after treatment with catechin. Moreover, the application of catechin inhibited the activation of NF-κB, which was upregulated in STZ-induced DR. A negative correlation was observed between the concentrations of catechin and the expression of inflammatory factors. Catechin can weaken DR induced by STZ by increasing HSP27 levels and decreasing the production of associated inflammatory factors\(^6\).

Baer et al. showed that a five-day intervention using tea along with catechins, on healthy people cannot change a significant change in the levels of FBS, fasting insulin, the area under the oral glucose tolerance curve, and area under the insulin level curve\(^7\). Toolsee et al. reported that the intervention of 200 ml of green tea for 14 days in patients with pre-diabetes cannot have significant changes in fasting blood glucose and glycosylated hemoglobin\(^8\). Another randomized clinical trial by Mozaffari-Khosravi et al was carried out on 100 individuals, aging between 20-60 years with a 5 years history of diabetes. They were instructed to drink green tea for 4 weeks, thrice a day, each after 2 hours of the meal. At the end of the study, it was found that there is a significant decrease in their systolic and diastolic blood pressure but there were no significant changes in their blood glucose level\(^9\).

A study by Parki JH reveals that the glucose intolerance was ameliorated by gallate catechin-deficient GTE or GTE mixed with polyethylene glycol, which was used as an inhibitor of intestinal absorption of gallate catechins. These findings may suggest that the gallate catechin when it is in the circulation elevates blood glucose level by blocking normal glucose uptake into the tissues, resulting in secondary hyperinsulinemia, whereas it decreases glucose entry into the circulation when they are inside the intestinal lumen. These findings encourage the development of non-absorbable derivatives of gallate catechins for preventative treatment of type 2 diabetes and obesity, which would specifically induce only the positive luminal effect\(^10\). A randomized, double-blinded, placebo-control clinical trial was carried out in 68 individuals aging between 20-65 years having type 2 diabetes. They were given 856 mg of EGCG for 16 weeks and at the end of the study, blood parameters were evaluated. It was found that EGCG potentially decreases the fasting blood insulin and glucose level, creatinine, uric acid but potentially increases the ghrelin level\(^11\).
Animal model studies suggested that green tea bioactive components might protect against the development of coronary heart disease by reducing blood glucose levels and body weight. Green tea flavonoids had insulin-like activities as well as insulin-enhancing activity. Epigallocatechin gallate inhibited intestinal glucose uptake by the sodium-dependent glucose transporter (SGLT1), indicating its increase in controlling blood sugar.

CONCLUSION
As the complications of diabetes are increasing enormously, a safe and alternative treatment must be approached. Numerous investigations have already proved that catechins are capable of ameliorating the conditions associated with diabetes mellitus. Catechins act as an antidiabetic agent mainly by reducing oxidative stress, inhibiting α-amylase and α-glucosidase enzymes, ameliorating the insulin resistance, and having a protective effect on β-cells of the pancreas. We can therefore affirm that animal and cellular studies, and some in vivo studies, provide mounting evidence that the catechins may have beneficial actions to fight diabetic complication. The molecular and cellular mechanisms, although not fully elucidated, involve a large number of biochemical pathways and are under active investigation. Further studies are needed to clarify the mechanisms underlying the action of catechins in diabetes.

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