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Recent advances of anti-hyperglycemia and anti-diabetes actions of tea in animal studies

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A growing body of evidence showed that tea has anti-hyperglycemia and anti-diabetes effects during recent years. Tea may exert beneficial effects on decreasing blood glucose and ameliorating insulin resistance by first, suppressing carbohydrates absorption; second, stimulating glucose metabolism; and third, alleviating the oxidative stress. Furthermore, it was also reported that tea consumption could ameliorate the complications of diabetes mellitus. However, being a key factor in the occurrence and development of diabetes mellitus, oxidative stress should be paid more attention. The relationship between the anti-oxidative efficacy and anti-diabetes actions of tea, and the underlying molecular mechanisms of this relevance need further meticulous research. In order to understand the research trends of this field, this review highlights the latest advances in the anti-hyperglycemia and anti-diabetes actions of tea in animal studies since 2012.

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Introduction

Diabetes mellitus (DM) is a serious and chronic metabolic disease. Based on data from 130 countries, Guariguata *et al.* estimated that 382 million people had diabetes in 2013 and this number was expected to rise to 592 million by 2035 [1]. Diabetes is a characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both [2]. There are two major classifications of diabetes: Type 1 and 2 diabetes. Type 1 diabetes mellitus (T1DM), which accounts for only 5–10% of those with diabetes [2], is associated with complete or near-total insulin deficiency related to autoimmune-mediated destruction of pancreatic β-cells [3]. And type 2 diabetes mellitus (T2DM), accounting for 90–95% of the diabetic population, is associated with variable degrees of insulin resistance, impaired insulin secretion, moderate to severe β-cell apoptosis and increased hepatic glucose production [3].

Tea is the second most popular beverage in the world. Recently, the health-promoting functions of tea and its bioactive ingredients have been intensively investigated. Aside from the cancer prevention and weight control effects of tea, its anti-hyperglycemic and anti-diabetes efficacies have become another hot topic for molecular nutrition and food research. Therefore, in order to better understand the research trends in this field, the latest advances in the anti-diabetes actions of tea from animal studies since 2012 were briefly reviewed in this paper. The databases, 'Web of science' and 'Medline', were employed for literature retrieval in this paper, and the key words were 'tea', 'catechins', 'EGCG', 'hyperglycemia', 'diabetes', 'mice' and 'rat'.

Main categories of teas

Tea is made of the buds and/or leaves of the plant *Camellia sinensis*, *Theaceae*. Based on the processing technology, tea is classified into three major types: green tea, black tea, and oolong tea. Green tea is an unfermented tea. Owing to its enzyme-inactivated procedure under high temperature during the manufacturing process, green tea retains most of the contents of fresh leaves. Green tea possesses characteristic polyphenolic compounds known as catechins, which are mainly comprised of (−)-epicatechin (EC), (−)-epigallocatechin (EGC), (−)-epicatechin gallate (ECG), (−)-epigallocatechin gallate (EGCG), (+)-catechin (C), and (+)-gallocatechin (GC), plus a small amount of (−)-catechin gallate (CG) and (−)-gallocatechin gallate (GCG). Black tea is a fermented tea and exquisitely made through the wilting, rolling, fermentation and drying processes. During this process, most of the catechins are oxidized, dimerized, and polymerized to form theaflavins and thearubigins. And oolong tea is a semi-fermented tea, which is manufactured by crushing only the rims of the leaves and limiting fermentation to a short period of time to produce a specific flavor and taste. Generally, oolong tea contains catechins, theaflavins, and thearubigins as well as some characteristic components such as epigallocatechin esters,

theasinensins, dimeric catechins, and dimeric proanthocyanidins [4].

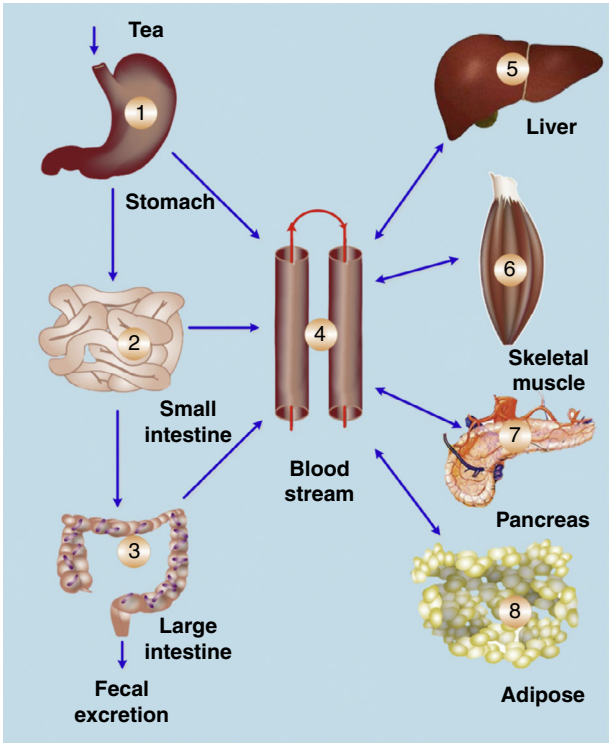
In addition, there are several other types of tea in Asia countries, especially in China, such as white tea, yellow tea and dark tea. The technical process of white tea is the simplest, just composed of wilting and drying. And yellow tea is briefly manufactured by inactivation, yellowing, rolling and drying. Due to the slight oxidation of tea catechins during the characteristic processes of rolling and yellow in white and yellow tea production, respectively, the fermented degrees of these two kinds of tea are between green and oolong tea. Moreover, dark tea in china is a type of postfermented tea, such as Pu-erh tea and brick tea. Specifically, deactivated leaves of *C. sinensis* and *Camellia assamica* are post-fermented by natural microorganism under controlled conditions to make dark teas. Their qualities are highly dependent on local environmental and climatic features [5].

Anti-hyperglycemia and anti-diabetes actions of teas in animal studies

Glucose homeostasis is extremely important for human health, and being strictly controlled by a series of hormones. Among them, insulin and glucagon are the principal hormones that control blood glucose concentrations by maintaining the homeostasis of glycolysis and gluconeogenesis *in vivo*. After being digested in the gastrointestinal tract to monosaccharides, dietary carbohydrates are absorbed into the circulation. Then, the elevated blood glucose promotes secretion of insulin from the β-cells of the islets of Langerhans in the pancreas, and insulin mediates the uptake of glucose in peripheral tissues including muscle, adipose tissue and kidney, promotes storage of glucose in liver as glycogen, and inhibits lipolysis in adipose tissue [6]. On other hand, glucagon is secreted from the pancreatic α-cells once the blood glucose level begins to fall below normal, which promotes liver glucose production by inducing glycogenolysis and gluconeogenesis to ensure adequate circulating glucose to fuel the body functions [6], and thus increases lipolysis and release of free fatty acids (FFAs) from adipose tissue [7]. Evidently, the utmost issue in manipulating diabetes mellitus (DM) is to control the blood glucose concentration and to improve the glucose tolerance, which is tightly related to the regulation of glucose absorption in gastrointestinal tract, the glucose metabolism, or the amelioration of insulin resistance (Figure 1).

In the past two years, the anti-hyperglycemia effects of a variety of teas were intensively investigated in diabetic rodent models. Wein *et al.* demonstrated that 14 days supplementation of green tea extract at nonpharmacological doses (1 g/kg) notably decreased the fasting glycemia of the female db/db-mice compared with control female mice [8]. Various fractions of aqueous extract from Pu-erh tea (50 mg/kg BW) significantly decreased

Figure 1



The underlying anti-hyperglycemia and anti-diabetes mechanisms of tea. After intake, tea or its bioactive ingredients could interfere with the processes as followed: (1, 2, 3) to inhibit the energy absorption in digestive tract, (4) to alleviate oxidative damage and improve endothelial function, (5, 6) to stimulate glucose metabolism, (7) to enhance pancreatic islet function and improve insulin secretion, (8) to improve insulin resistance in adipose tissue.

postprandial hyperglycemia in alloxan induced diabetic mice compared with a model group. And the 95% ethanol precipitate fraction showed the better suppressive effect, which is nearly equivalent to that of acarbose at the same dosage [9]. Awa-ban tea, a uniquely flavored, pickled and anaerobically fermented tea, made only in the Tokushima prefecture of the Shikoku region of Japan, was also shown to suppress the blood glucose increase after oral administration of maltose, sucrose, or glucose in male C57BL/6J mice [10].

Suppressing carbohydrates absorption

Several studies showed that tea has regulating roles in carbohydrates absorption in gastrointestinal tract and glucose metabolism *in vivo*. EGCG was proved to significantly inhibit pancreatic amylase activity and reduced the postprandial blood glucose levels after administration of common corn starch to fasted CF1 mice; while no significant changes were induced in the expression of two small intestinal glucose transporters (GLUT2 and SGLT1)