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Review Article

Mechanisms of Anti-Obesity Effects of Catechins: A Review

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ABSTRACT

Overweight and obesity is a public health problem worldwide. Green tea catechins are a group of plant flavonoids from flavanol subgroup. The beneficial effects of catechins on weight loss and prevention of obesity has been previously acknowledged. A great number of animal and human studies have investigated the possible mechanisms of catechins action in prevention of obesity, but this area of research is still under investigation. What has been known for now is that the mechanisms of anti-obesity effects of catechins are very diverse. These mechanisms include increased fat oxidation, stimulation of sympathetic nervous system activity, upregulation of mRNA level of fat β-oxidation genes, downregulating expression of enzymes involved in fat synthesis, and increased expression of adipose tissue uncoupling proteins. Many of these effects are exerted through induction of genes or inhibition of transcription factors. Catechins can also inhibit fat absorption through suppression of pancreatic lipase. By correction of colonic microbiota, catechins improve production of small absorbable metabolites in the colon, which can display anti-obesity effects after absorption.

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Introduction

Overweight and obesity is a public health problem around the world (1). In recent decades, the prevalence of obesity has sharply increased (2). Overweight and obesity is the cause of extensive morbidity and mortality, imposing high economic burden on nations (3). Investigations have recognized the relationship between obesity and a number of diseases, such as heart diseases (4), insulin resistance and type 2 diabetes (5), non-alcoholic fatty liver disease (6), gallstones and pancreatitis (7), esophageal reflux (8), inflammatory bowel syndrome (9), chronic kidney disease (10), polycystic ovary syndrome (11), neurological diseases (12), and several types of cancer (13).

Green tea catechins belong to flavanol subgroup of plant flavonoids, while flavonoids are a widespread group of plant phytochemicals with astonishing biological properties for prevention of diseases (14). These properties include antioxidant, anti-inflammatory, vasorelaxant, anticoagulant, cardio-protective (14, 15), anti-obesity and anti-diabetic (16), chemoprotective (17), neuroprotective (18), and antidepressant (19) activities.

The anti-obesity potential of catechins has been acknowledged in the last decade. Animal studies have documented beneficial effects of catechins on weight loss and prevention of obesity (20). A number of randomized controlled clinical trials have also shown that consumption of green tea catechins may

reduce body weight and fat tissue (21). Several meta-analyses have also demonstrated the anti-obesity of catechins (22-24). In this work, we present molecular and cellular mechanisms that have been proposed for the anti-obesity effect of catechins.

Green Tea Catechins

Catechins, including catechin, epicatechin, epicatechingallate, gallocatechin, epigallocatechin, and epigallocate chingallat, are the major flavonoids of green tea (Figure 1) (25). These constitute about 60% of total phenolics of green tea. Other phenolic compounds of green tea include flavonols such as quercetin and kaempferol, gallic acid derivatives, hydroxycinammatequinic esters, and purine alkaloids.

Increased Energy Expenditure

Green tea and its components have shown thermogenic effect through increasing fat oxidation and sympathetic nervous system activity (26-28). There are two modes of action for catechins in stimulating fat oxidation: first, non-tissue specific thermogenesis and fat oxidation, which is induced by stimulating sympathetic nervous system, instigating reduction of whole body fat; and second, hepatic fat β-oxidation which is exerted by direct impact of catechins on the liver due to their accumulation in hepatocytes, suppressing specifically hepatic and visceral fat deposition (29). In addition to stimulation of sympathetic nerves, catechins increase fat oxidation by inhibition of catechol-O-methyltransferase, the enzyme responsible for degrading norepinephrine (30).

However, green tea catechins exert their effect on fat oxidation in postprandial energy expenditure but do not elevate resting energy expenditure (31). Also, they increase energy expenditure in a 24-h period during which three meals were consumed but no energy expenditure increase was found during sleep (26). On the other hand, catechins upregulate the mRNA level of fat β-oxidation genes, including carnitinepalmitoyl transferase-1 (CPT-1), acyl-CoA oxidase (ACO), acyl-CoA dehydrogenase (MCAD), and PPARα (32). This catechin-induced fat oxidation is increased during exercise (33, 34), one of the strategies that are commonly used for prevention or treatment of obesity.

Downregulation of Fat Synthesis

Green tea and its catechins have shown to downregulate expression of enzymes involved in fat synthesis, such as malic enzyme, glucose-6-phosphate dehydrogenase, acetyl CoA carboxylase-1 (ACC), stearoyl-CoA desaturase-1 (SCD1), and fatty acid synthase (FAS) (35, 36); as well as other genes involved in adipogenesis, including the fatty acid-carrier protein adipocyte fatty acid-binding protein (aP2), the nuclear receptor peroxisome proliferator-activated receptor-γ (PPAR-γ), and the transcription factors CCAAT-enhancer binding protein-α (C/EBP-α) and regulatory element-binding protein-1c (SREBP-1c) (37, 38).

A part of gene-regulatory effects of catechins are exerted through inhibition of nuclear factor κ-B, which following activation, prevents the transcription factor PPARα and its downstream genes (39). Suppressive effect of tea catechins on body fat accumulation is also associated with increased expression of adipose tissue

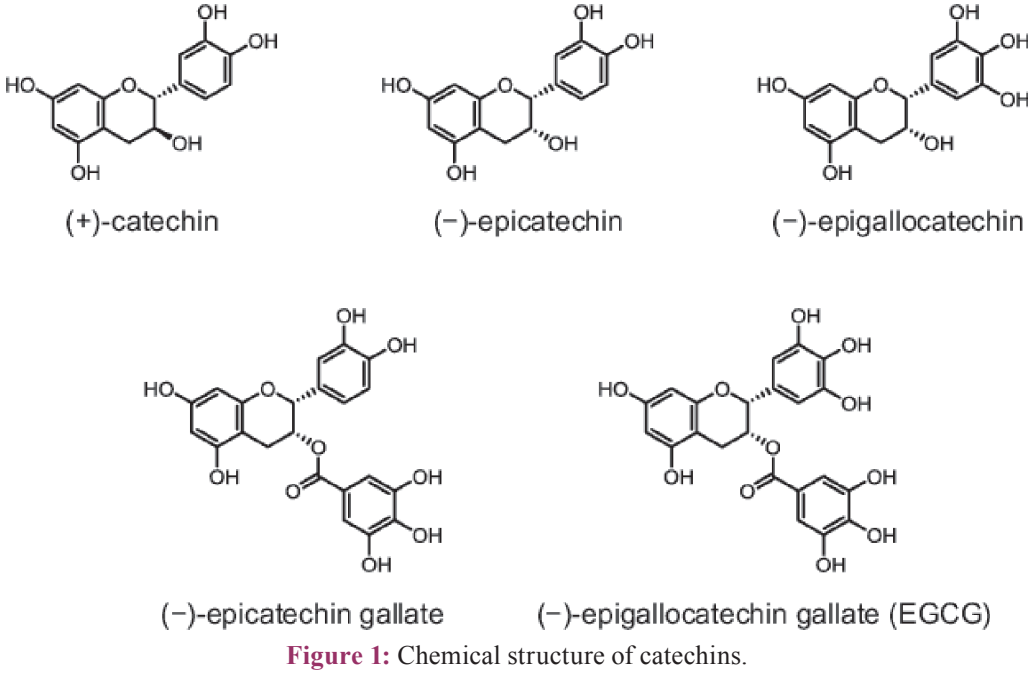

Figure 1: Chemical structure of catechins.

uncoupling proteins (UCPs), proteins involved in mitochondrial proton leak and heat production (40, 41). Concomitant with gene- and protein-regulatory effects which prevent lipogenesis and stimulate fatty acid β-oxidation, catechins inhibit lipoprotein lipase (41) and upregulate enzymes involved in fatty acid mobilization from adipose tissue: adipose triglyceride lipase and hormone sensitive lipase (38, 42).

Antioxidant and Pro-Oxidant Effects

Due to their antioxidant effect, catechins have the ability to demonstrate pro-oxidant activity in high concentrations. These high concentrations of catechins are unlikely to occur in usual dietary consumptions, but more possibly in the form of supplements or extracts. Evidence suggests that catechins have potential to affect fat metabolism by their pro-oxidant activity. Epigallocatechingallate (EGCG) as the most biologically active catechin with possible pro-oxidant activity has demonstrated anti-adipogenic capacity by oxidation and activation of adenosine monophosphate-activated protein kinase (AMPK), an upstream molecule for the aforementioned lipogenesis and lipolysis genes (38, 43).

Inhibition of Lipid Absorption

In addition to metabolic effects, catechins can exhibit anti-obesity effect by inhibition of pancreatic lipase (44) and phospholipase A_2 (45), thus reducing lipid absorption (46). Green tea catechins may also prevent dietary fat absorption by interfering with emulsification, digestion, and micellarsolubilization of lipids (47). A part of anti-obesity effect of flavonoids may also be exerted through decreased carbohydrate absorption as an inhibitory effect of flavonoids, including flavanols, on pancreatic α-amylase has been detected (48). Furthermore, an inhibitory effect of green tea catechins on intestinal sodium-dependent glucose transporter 1 (SGLT 1) was seen as a mechanism for preventing intestinal glucose uptake and absorption (49).

Green tea also decreases translocation of glucose transporter 4 (GLUT4) and thus reduces glucose uptake by adipose tissue, but inversely increases translocation of GLUT4 and glucose uptake by skeletal muscle (50). Moreover, in cell lines, high concentrations of catechins especially EGCG have demonstrated the ability to induce adipocyte apoptosis and to inhibit adipogenesis (49). Inhibition of adipocyte differentiation by upregulation of insulin-like growth factor binding protein (IGFBP)-1 has also been stated as a mechanism of anti-obesity effect of green tea (51). EGCG also has the ability to regulate appetite and decrease food intake by inhibition of ghrelin secretion or affecting genes involved in the control of appetite in the hypothalamus (52, 53).

Appetite Control

A crossover trial showed that epicatechin in doses >1.6 mg/kg is helpful in control of food intake (54). The regulation of appetite is proposed to be through inhibition of ghrelin although this mechanism has not been indicated yet.

Intestinal Bacteria

Recently the effect of intestinal microbiota in prevention of obesity has attracted many attentions. Because of low availability, flavonoids including catechins mostly pass through the small intestine and reach the colon unchanged (55, 56). The unabsorbed compounds are metabolized by intestinal microflora in the colon, producing smaller more bioavailable components which have potent anti-obesity effects (20). Following consumption of catechins, the total number of colonic bacteria increases but also species of bacteria are changed and in addition production of short-chain fatty acids increases (57). Fermented tea are reported to be more effective.

Ethnic-Dependent Effects

It seems that the anti-obesity effect of catechins is stronger in Asian populations compared to populations from other parts of the world (22, 24). The ethnic difference in the response to the anti-obesity effects of flavanols may have occurred due to high intake of coffee in Western nations. The caffeine component of coffee has anti-obesity effect. It is likely that habitual caffeine intake of participants in Western countries has prevented the appearance of anti-obesity potential of flavanols (58).

Conclusion

The mechanisms of anti-obesity effects of catechins are very diverse, ranging from decreased intestinal fat absorption, to increased fat oxidation, prevention of fat synthesis, and stimulation of energy wasting. As most of these mechanisms have been reported in animal studies. Future studies are needed to explore these and other possible mechanisms in human.

Conflict of Interest

None declared.

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