Research on the influence of diverse tea varieties on disease and exercise regulation

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Abstract. Tea and tea beverages are popular around the world due to their unique flavors, and tea is rich in a variety of bioactive compounds such as catechins, alkaloids, and polysaccharides, which are the main contributors to its health benefits. In recent years, an increasing body of research has indicated that incorporating tea consumption into daily life exerts positive effects in combating oxidation, cardiovascular diseases, inflammation, aiding in exercise recovery, and potentially mitigating cancer risks. The relevant mechanisms of the signaling pathways involved have been extensively studied. Clinical trials have also demonstrated the potential of tea products as dietary supplements and natural medicines. In this paper, we review the health effects of tea, the steroid metabolic diseases modulated by different teas and the effects of related substances on health campaigns.

Keywords: Tea; Tea polyphenols; Steroid metabolism; Sports; Exercise recovery.

1. Introduction

Tea is a traditional beverage in China with a long history. In recent decades, it has become increasingly popular around the world due to its unique flavors. According to the latest data, the main tea-producing countries in the world are China, southern India, and Sri Lanka, with increasing production levels, indicating its popularity[1]. Modern complex production and processing techniques have led to the categorization of tea into six main types: green tea, black tea, white tea, dark tea, yellow tea and oolong tea. Among them, green tea is lightly fermented, black tea is fully fermented, and dark tea is post-fermented. During fermentation or storage, the content of substances in the tea also changes. For example, in a low-temperature and high-humidity environment, the β-glucosidase activity level is highest in Longjing tea, resulting in the best quality and aroma.

Tea contains various active ingredients such as tea polyphenols, polysaccharides, alkaloids, flavonoids, and free amino acids, among others[2-3]. The content of these compounds varies in different types of tea, with phenolic compounds being the most prominent. These bioactive compounds are the main contributors to the health benefits of tea, including antioxidant, anti-inflammatory, anticancer, cardiovascular protection, liver protection, antidiabetic, anti-obesity, and neuroprotective properties[4-5]. This review mainly summarizes and discusses the health effects of tea, the regulation of steroid metabolism-related diseases by different types of tea, and the influence of related substances on health.

2. Tea and Health

2.1 Tea and Cardiovascular Diseases

The tea flavonoids in tea have a good cardiovascular protective effect. In a meta-analysis of 39 prospective cohort studies, linear regression showed that increasing the fixed amount of tea consumption per day can reduce the average cardiovascular disease mortality rate by 4% and the risk of cardiovascular peripheral diseases by 2%[6]. Atherosclerosis is one of the risk factors for
cardiovascular disease, and studies have shown that drinking Pu'er tea can significantly reduce the early formation of fat stripes and fibrous fatty plaques in ApoE-deficient mice, and by down-regulating the nuclear factor NF-κB (nuclear factor kappa-B, NF-κB) pathway to activate and accelerate apoptosis of macrophages in atherosclerotic plaques to reduce chronic inflammation and improve symptoms. According to the oxidative hypothesis of atherosclerosis, oxidative stress and inflammation are the two main factors in its development. When antioxidant activity is insufficient to reduce reactive oxygen species (ROS), an excess of the latter jeopardizes endothelial function and threatens plaque stability. The mechanism is mainly through the activation of nuclear transcription factor activator protein-1 (AP-1), nuclear transcription factor NF-κB and other major signaling pathways to inhibit phosphorylation to regulate the activity of nuclear transcription factors[7]; on the other hand, mainly through the regulation of mitogen-activated protein kinase (MAPK), which is the most important signaling pathway to inhibit the oxidation of LDLs.protein kinase (MAPK)-nuclear factor -erythroid 2 related factor 2 (Nrf2)-antioxidant response element (ARE)-antioxidant response element (ARE) signaling pathway to influence the expression of apoptosis-related genes and proteins[8].

2.2 Tea and anti-inflammatory effects

Anti-inflammation is related to the occurrence and development of many diseases. Studies have shown that EGCG has strong anti-inflammatory effects and therapeutic potential, affecting the expression of inflammation-related genes and proteins, such as TNF-α, IL-1 and MMPs[9], a brief description of its mechanism is shown in Figure 1. In a mouse model of colorectal cancer, epigallocatechin (EGC) administration reduced the levels of several inflammatory cytokines, including TNF, in the colorectal epithelium and inhibited inflammation-associated carcinogenesis, corroborating the anticancer effects described below. Gout is a common and complex arthritic inflammation caused by the deposition of urate in the joints, with sudden onset of pain, swelling, and inflammation at the joint site. LEE's study showed that EGCG inhibits the activation of NLRP3 inflammasomes in primary mouse macrophages by blocking mitochondrial DNA synthesis, thereby helping to prevent gout-related inflammation[10]. This means that for NLRP3-dependent diseases such as gout, EGCG may be a better treatment option. Furthermore, catechins are characteristic polyphenols produced during the fermentation of green tea into black tea, and can improve the expression of colonic epithelial cell inflammatory factors IL-6, IL-1β, tumor necrosis factor-α (TNF-α), and inhibit apoptosis by regulating miR-190 expression[11], thereby reducing lipopolysaccharide-induced inflammatory damage to colonic epithelial cells. In another study, EGCG can protect skin cells from inflammation damage by directly (clearing inflammasomes and inflammatory markers) and indirectly (inhibiting NF-κB, TNF-α and other inflammatory signaling pathways)[12].

![Figure 1 Anti-inflammation action of EGCG](image1)

![Figure 2 The possible mechanism of tea anti-tumor](image2)
2.3 Tea and anticancer effects

Cancer has become a global health issue, and a comprehensive review and meta-analysis of existing research results (including 64 observational studies corresponding to 25 types of cancer) indicate that drinking tea reduces the risk of cholangiocarcinoma, breast cancer, endometrial cancer, and liver cancer, with particularly significant effects on oral cancer[13], its possible impact pathways are shown in Figure 2. The possible mechanisms are as follows:(1) Induction of apoptosis and cell cycle arrest: apoptosis can be used as a protective mechanism against the development of malignant tumors[14]; (2) Inhibition of NK-κB and AP-1: These two transcription factors are very closely related to apoptosis, NF-κB activation is translocated to the nucleus, which leads to the expression of a variety of genes associated with carcinogenesis and tumor progression[15]. Other studies have shown that lower doses of 5-fluorouracil combined with EGCG therapy reduced the cell viability and migration distance of oral squamous cell carcinoma, while increasing the number of cells in the G2/M phase[16]. In addition, scientific evidence suggests that EGCG has a good effect on inhibiting tumor cell metastasis and may become a new direction for research on drug synergistic effects.

3. Tea and Steroid Metabolism Diseases

Steroid hormones are a class of hormones secreted by the human body, also known as steroidal hormones, divided into sex hormones (estrogens, androgens) and corticosteroids (glucocorticoids, mineralocorticoids). Steroid hormones play a wide and important role in maintaining life, regulating immunity, secondary sexual characteristics, nerve function, and skin disease treatment[17-20]. Currently, research on the effects of tea mainly focuses on cholesterol and estrogens.

3.1 Effects of Different Types of Tea on Cholesterol Content

In recent years, a large number of reviews and research results have indicated that tea intake can affect serum total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) cholesterol.

A comprehensive meta-analysis of 31 experiments showed that consuming green tea significantly lowers the levels of TC and LDL cholesterol, but has little impact on HDL cholesterol, and also slightly lowers triglyceride (TG) levels[21]. A 2016 study showed that tea dietary fiber significantly reduced the average daily weight gain of mice, lowered serum and hepatic TC, TG, and LDL cholesterol, increased the ratio of serum and hepatic HDL cholesterol to TC, and also promoted lipid fecal excretion due to their lipid binding capacity and inhibition of lipid peroxidation, thus improving the distribution of serum and hepatic lipids in high cholesterol-fed mice[22]. These findings indicate that tea dietary fiber may be used as a functional ingredient to control cardiovascular diseases. In Imran's experiment[23], red tea polyphenols and theaflavins could lower TC, LDL cholesterol, and TG levels in high-fat model-fed rats, while significantly increasing HDL cholesterol. Based on current reports from human cell studies, in a high cholesterol environment, catechins could reduce free cholesterol in umbilical vein endothelial cells after 24 hours by inhibiting the binding protein 2 of cholesterol regulatory elements (sterol regulatory element binding protein 2, SREBP-2)[24]. This may provide a valuable alternative treatment for atherosclerosis, reducing the side effects and toxicity of drugs, etc.

Table 1 Effects of various kinds of tea on serum related substances in rats

<table>
<thead>
<tr>
<th>Tea</th>
<th>Province</th>
<th>Group</th>
<th>TC (mmol·L⁻¹)</th>
<th>TG (mmol·L⁻¹)</th>
<th>LDL-c (mmol·L⁻¹)</th>
<th>HDL-c (mmol·L⁻¹)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>green tea</td>
<td>Luzhou</td>
<td>Model group</td>
<td>10.58±0.71</td>
<td>0.43±0.04</td>
<td>2.08±0.11</td>
<td>0.41±0.12</td>
<td>[44]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Experimental</td>
<td>6.44±0.47</td>
<td>0.43±0.04</td>
<td>1.35±0.11</td>
<td>0.88±0.11</td>
<td></td>
</tr>
</tbody>
</table>
Currently, research on the effects of various teas on cholesterol metabolism is based on the successful establishment of a high-fat model group of rats. From the table 1 above, it can be seen that various teas can reduce the levels of total cholesterol, TG, and LDL-c to varying degrees, with green tea and oolong tea having almost no effect on TG. In addition to oolong tea, the concentration of HDL-c increased significantly. This indicates that teas can lower the blood lipid levels of rats with hyperlipidemia, promote fat digestion, and prevent fatty liver and atherosclerosis. Combining foreign literature, it can be seen that, comparatively, white tea has the best anti-obesity effect[25-29]. White tea, yellow tea, and oolong tea may inhibit obesity by increasing energy consumption and fatty acid oxidation, while green and raw pu-erh tea play a role in inhibiting fatty acid synthesis[30].

3.2 Influence of EGCG on estrogen content

In modern society, there are many factors leading to female infertility, among which the occurrence and maturation of oocytes are the key factors. Currently, research in this area mainly focuses on animal experiments, using water buffalo oocytes for research. It was found that adding EGCG increased the maturation rate of oocytes, significantly increased the content of glutathione (GSH) in M II stage oocytes, and significantly reduced the level of reactive oxygen species (ROS), with the most effective concentration of EGCG being 10 μmol·L-1[31]. The tea polyphenols in green tea are the main active substances, of which flavonoids account for 80%. The main component is catechins, among which EGCG has the highest activity and the highest content.[32].

The essential substance for the growth and development of follicles is steroid hormones. The disorder of follicular development caused by the generation of steroids is the main problem for infertile women[33]. In addition, when cells are exposed to dexamethasone (DEX), EGCG pretreatment significantly increases the activity of osteoblasts and can reduce the mitochondrial and cellular levels of DEX-induced reactive oxygen species through related pathways. It also protects osteoblasts from apoptosis and regulates the formation of corticosteroids through 11β-hydroxysteroid dehydrogenase activity[34].

4. Tea Polyphenols and Exercise

4.1 The impact of tea polyphenols on doping-control

UGT2B17 is a member of the UDP-glucuronosyltransferase (UGT) family, which can catalyze the combination of glucuronic acid and non-polar small molecules. The hydrophilicity and polarity of the metabolite increase, making it easier to be excreted from the body through urine or feces bile, while the substance activity is reduced. Jenkinson et al.[35] conducted in vitro experiments, reacting tea extracts with human UGT2B17 microbodies, and using HPLC to detect residual testosterone levels after the reaction. The results showed that tea extracts inhibited the glucuronidation reaction
promoted by UGT2B17 enzyme. The main active tea extracts are: epigallocatechin (EGC), EGCG, and epicatechingallate (ECG). Since UGT2B17 is also involved in the metabolism of other androgens[36], scholars have studied the effects of tea drinking on the entire steroid profile (SP) [37-38] (Table 2).

In the study of Coll in 2018[39], quantitative analysis of EGCG in green tea was first conducted using LC-MS-MS. Then, SPE (Solid Phase Extraction) and UHPLC were used to analyze EGCG in plasma[40], GC-MS was used to analyze SP in urine[41], and the SP data was analyzed and organized using the ABP software provided by WADA. The results showed that the catechins extracted from green tea did not affect other UGT2B isoenzymes in the body and did not lead to changes in the excretion rate of T and other SP metabolites. After drinking a large amount of green tea, the concentration of EGCG in plasma was not high enough to inhibit UGT2B17 in the body. Therefore, green tea cannot be considered a confounding factor in the ABP steroid module.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Group</th>
<th>Concentration</th>
<th>Deseases</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone</td>
<td>Green tea and black tea</td>
<td>High-fat group</td>
<td>4.60±1.07 ng ⋅ mL-1</td>
<td>Male infertility in obese models, black tea is more effective than green tea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-fat+green tea</td>
<td>6.56±0.41 ng ⋅ mL-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-fat+black tea</td>
<td>8.00±0.29 ng ⋅ mL-1</td>
<td></td>
</tr>
<tr>
<td>Progesterone</td>
<td>EGCG</td>
<td>ELISA assay shows that the progesterone level significantly increases after EGCG intervention</td>
<td>EGCG affects ovarian steroidogenesis</td>
<td>[38]</td>
</tr>
</tbody>
</table>

4.2 The Impact of Tea Polyphenols on Exercise Recovery

Athletes often have to undergo overload training and exercise, especially during intense exercise, which systematically increases the oxygen consumption of various tissues. Multiple studies have shown that oxidative stress can lead to various complications in athletes, such as fatigue, inflammation, and muscle damage[42]. Tea leaves are rich in polyphenols, natural antioxidants that can increase the activity of superoxide dismutase and the expression of catalase, enzymes that protect cells from oxidative stress damage and promote fatigue recovery[43]. This is crucial for athletes to adjust their training programs and competitive status.

Currently, the use of doping is prohibited in sports competitions, so athletes pay particular attention to using natural substances to improve their physical function. Research has shown that drinking green tea can improve physical function with almost no side effects[44]. Green tea polyphenols can affect silent mating type information regulator 2 homolog 1 (SIRT1), which increases the activity of peroxisome proliferator-activated receptor gamma coactivator-1a (PGC-1a) after deacetylation, inducing the formation of skeletal muscle mitochondria[45].

5. Conclusion

In summary, tea is rich in bioactive substances with health effects that should not be ignored, of which tea polyphenols may become a key factor, dominated by the tea polyphenol EGCG in green tea, which has been proved to have great potential in cardiovascular protection, anti-inflammatory, anticancer and other functions. Notably, tea may be involved in the regulation of steroid metabolism, and related studies provide new ideas for clinical treatment. Accordingly, for doping control purposes, tea may improve athletes' physical performance, but not enough to confound the parameters of the ABP steroid module, a hypothesis that needs to be further explored. In addition, more studies have been conducted on green tea, whereas fewer studies have been conducted on other teas, and more comprehensive studies are needed.
In recent years, with the accelerated aging process and the elevated consumption level of the people, the pursuit of disease prevention and health concepts has been growing. In view of the positive significance of tea consumption on antioxidant, cardiovascular disease, anti-inflammatory, and cancer, the labelling of tea is shifting towards functional beverages, which are enriched with a variety of bioactive compounds to provide a new way of choice for clinical trials and health promotion. The mechanism of action and application scenarios of tea in the future will also be the direction of continuous research attention.

Acknowledgements

We are grateful to the Postdoctoral Research Foundation of China (CN) (2020M681357).

References


