Proceedings of the 2nd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/15/20240380

Mechanisms of action of tea polyphenols in the modulation of obesity through gut microbiota

Jiahao Tang

Department of food, South China Agricultural University, No. 483, Wushan Street, Tianhe District, Guangzhou, Guangdong, 510642, China

tjh85602375@163.com

Abstract. Obesity has become an increasingly serious global issue in recent years, leading to a myriad of health concerns for a growing population. Consequently, the quest for rational and safe methods to combat excess body fat has emerged as a mainstream demand among consumers. This paper focuses on tea polyphenols as the primary subject of investigation, employing gut microbiota as a mediator to explore and summarize existing research regarding the anti-obesity effects of tea polyphenols. Current reports suggest that the mechanisms by which tea polyphenols exhibit anti-obesity effects primarily encompass two aspects. Firstly, tea polyphenols can regulate the composition of the gut microbiota, primarily targeting the Firmicutes and Bacteroidetes phyla. This regulation occurs both in their digested state and undigested form, with a greater emphasis on their undigested state. Tea polyphenols primarily function by reducing the abundance of Firmicutes while increasing that of Bacteroidetes, thereby enhancing gut microbiota diversity to exert anti-obesity effects. Secondly, the metabolites of tea polyphenols also play a role in modulating gut microbiota, with phenolic acid compounds being the key metabolites responsible for anti-obesity effects. Compared to the parent tea polyphenols, phenolic acid compounds exhibit higher bioavailability and biological activity.

Keywords: Anti-Obesity, Tea Polyphenols, Gut Microbiota, Mechanisms.

1. Introduction

In recent years, obesity has emerged as a chronic metabolic disease that significantly impacts human health on a global scale. The 2023 edition of the "World Obesity Map," published on the official website of the World Obesity Federation, predicts that by 2035, over 4 billion people worldwide will be categorized as obese or overweight, constituting 51% of the global population. Among these, the Pacific island nation of Kiribati is projected to have the highest adult obesity rate at 67%. In the "World Obesity Map," overweight is defined as having a BMI (Body Mass Index) of ≥25 kg/m2, while obesity is defined as having a BMI of ≥30 kg/m2. Data indicates that in the global population aged >5 years, the "overweight/obesity rate" is expected to rapidly increase from 38% in 2020 to 51% in 2035, with the number of affected individuals rising from 2.6 billion in 2020 to over 4 billion in 2035. The "obesity rate" is projected to increase from 14% in 2020 to 24% in 2035, affecting nearly 2 billion individuals [1]. Currently, dietary habits characterized by high-fat consumption have become a significant factor adversely affecting human health. Such habits are closely associated with obesity and related metabolic disorders, leading to inflammation and changes in the structure and behavior of the gut microbiota.

DOI: 10.54254/2753-8818/15/20240380

Research suggests a close relationship between the control of obesity symptoms and the intake of bioactive substances, the quantity of skeletal muscle, and dietary patterns [2]. Current research on the treatment and prevention of obesity predominantly focuses on elucidating the mechanisms of action of bioactive substances, such as polyphenols and polysaccharides of plant origin. Both of these substances share similarities in their mechanisms for weight management, involving the regulation of the body's enzymes, hormone secretion, and the composition of the gut microbiota. From a chemical perspective, polyphenols offer a more distinct and suitable option for dietary incorporation compared to polysaccharides [3, 4]. Plant-derived polyphenols, primarily sourced from tea, are well-known in current research. This paper will investigate the mechanisms by which tea polyphenols, through the modulation of the gut microbiota, exert their anti-obesity effects, focusing on this current research hotspot.

2. Literature review

Tea polyphenols are a core class of bioactive compounds found in tea, and they make up around 18% to 36% of the total dry weight of tea leaves. Tea polyphenols have been linked to a variety of health benefits. Catechins, which are classified as polyphenols, are the most abundant type of tea polyphenol and are responsible for around 70–80 percentage points of the total inventory of tea polyphenols. Catechins, on the other hand, are comprised of four primary forms, which are as follows: epigallocatechin gallate (EGCG), epicatechin gallate (ECG), epigallocatechin (EGC), and epicatechin (EC), with EGCG emerging as the most important component of the group. The multifaceted mechanisms that are responsible for the anti-obesity properties of tea polyphenols encompass a spectrum of actions, including the inhibition of specific digestive enzymes, the modulation of gut microbiota, the facilitation of the synthesis of beneficial fatty acids, and the direct orchestration of lipid metabolism [5, 6]. Tea polyphenols have been shown to have anti-obesity properties.

The human gastrointestinal microbiota is an ecosystem that is constantly changing within the human body. It is distinguished by a microbe count that is 10 to 100 times higher than that of human cells. This ecosystem is known as the human microbiome. This intricate microbial environment that exists within the gut is susceptible to influence from a wide variety of factors, including dietary patterns, seasonal variations, lifestyle choices, stress levels, antibiotic utilization, and the presence of underlying medical problems. It is now possible, through the manipulation of these parameters, to modify the species composition and abundance levels of the gut microbiota, and in doing so, to elicit indirect implications on human health that can either be beneficial or harmful. The interaction between tea polyphenols and the microbiota in the gut has quickly risen to the forefront of research enquiries in the fields of food science, nutritional science, and biology in recent years [5, 7].

The active substances produced by the metabolism of tea polyphenols by gut microbiota have antioxidant, lipid-lowering, and anti-inflammatory properties, thereby impacting human health. Among these, the lipid-lowering and anti-obesity effects of tea polyphenols have garnered particular attention from researchers. However, there are multiple theoretical hypotheses concerning the mechanisms of tea polyphenol-induced fat reduction. These include the inhibition of carbohydrate-hydrolyzing enzymes, pancreatic lipase, regulation of short-chain fatty acid production, modulation of lipid metabolism, and regulation of gut microbiota composition, among others [2]. Considering the complexity of the mechanisms by which tea polyphenols exert anti-obesity effects through the gut microbiota, this paper aims to summarize and review the relevant literature in order to serve as a reference for future researchers. The main body of this paper will be divided into three sections: the regulatory effects of tea polyphenols on gut microbiota, the metabolic processes of tea polyphenols in the gut, and the influence of tea polyphenols on specific microbial species and metabolite generation within the gut [8].

3. Mechanisms of anti-obesity action of tea polyphenols

3.1. Regulation of gut microbiota by tea polyphenols for anti-obesity effects

In recent years, a rising amount of academic investigation has dug into the complex relationship that exists between obesity and the composition of the microbiota in the gut. The composition of the

DOI: 10.54254/2753-8818/15/20240380

microbiota in the gut has been shown to have a strong correlation with not only obesity but also the disorders that frequently accompany it, such as diabetes. This correlation has been established through empirical research. The ability of gut microbiota to exert control over fat storage, glycemic homeostasis, and the modulation of hormones that drive appetite and fullness has been established by research that has been peer-reviewed and found to be credible. Firmicutes and Bacteroidetes are the two taxonomic groups that make up the majority of the human gut microbiota, each accounting for approximately 40% to 60% of the total. Bacteroidetes account for approximately 20% to 40% of the total. These phyla play crucial roles in the complex machinery that is responsible for the metabolism and storage of fat. According to the findings of scholarly studies, tea polyphenols are able to exert an influence on the composition of the gut microbiota by increasing the proportionate abundance of Firmicutes while decreasing the proportional abundance of Bacteroidetes. Correcting the ratio of Firmicutes to Bacteroidetes and increasing the overall variety of the gut microbiota are both necessary steps in the process of mitigating the negative effects of a diet high in fat. This corrective strategy shows promise in terms of host benefit and stands as a realistic strategy in the field of obesity prevention; in this quest, tea polyphenols have emerged as a promising therapeutic agent.

Roughly 2% to 20% of ingested tea polyphenols find absorption within the small intestine, with the extent of absorption contingent upon their chemical makeup. Consequently, a substantial portion of tea polyphenols remains unmetabolized until they reach the expansive environs of the large intestine, where they wield influence over the gut microbiota. The modulatory mechanisms exercised by tea polyphenols on the gut microbiota have been substantiated through an amalgamation of in vitro fermentation studies, animal models, and investigations involving human subjects. Notably, diverse varieties of tea, including green tea, oolong tea, and black tea, have been subjected to scrutiny. The empirical outcomes collectively reveal that these tea variants hold the capacity to significantly augment the populations of Bifidobacterium, Lactobacillus, and Enterococcus, concurrently repressing the proliferation of Prevotella and Bacteroides. Probiotic strains such as Bifidobacterium, as substantiated by empirical sources (insert reference), have demonstrated their ability to hinder the accrual of adipose tissue. Wang et al. conducted a protracted intervention study with tea polyphenols to scrutinize the longitudinal changes in the gut microbiota of female Sprague-Dawley rats. Their findings elucidated an augmentation in the prevalence of Bacteroides and Oscillospira, both of which have previously been linked to a lean phenotype in human and animal research. Furthermore, investigations have disclosed that the consumption of darker tea varieties, exemplified by Pu'er tea, can also impart a favorable transformation in the proportions of beneficial bacterial species within the gut milieu. This, in turn, leads to an alteration in the composition of the gut microbiota, culminating in beneficial consequences for the human organism. Such effects encompass the mitigation of weight gain through the augmentation of Bifidobacterium proportions. Collectively, the compendium of research underscored herein underscores the indirect ability of tea polyphenols to attenuate adipose accumulation and foster a lean phenotype. This regulatory phenomenon entails the amplification of beneficial bacterial cohorts while concurrently curtailing the expansion of deleterious bacterial populations [9].

3.2. Anti-obesity effects of metabolites of tea polyphenols in the gut

There has been a lot of research done on the metabolism of phenolic compounds by the microbiota in the gut, and a lot of the benefits of these phenolic compounds come from the breakdown of polyphenols into metabolites. The majority of the tea polyphenols that are taken by a human body eventually make their way to the colon, where they are metabolized by the microbes living there, resulting in the development of more manageable chemicals. Before they are broken down, the various forms of catechin share similar structural characteristics. As shown in Figure 1, the process of microbial degradation begins with the cleavage of the C-ring, which is then followed by hydroxylation at certain sites within the B-ring. After that, the A-ring, which is also referred to as the catechol ring, is cleaved, which results in the production of matching hydroxyphenyl-valeric acids and phenyl-gamma-valerolactones. These molecules are capable of undergoing additional dehydroxylation, which will result in the production of equivalent valeric acids. In the end, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid,

DOI: 10.54254/2753-8818/15/20240380

3-hydroxyphenylpropionic acid, and 4-hydroxyphenylpropionic acid are formed as a result of either or oxidation of phenolic acid. Other minor phenolic acid derivatives are also created. Catechol is another potential end product of this process. The bacteria in the stomach are responsible for converting tea polyphenols into simpler phenolic acid molecules, which not only increases the bioavailability of these polyphenols but also amplifies the bioactivity of their metabolites. According to the findings of several studies, the absorbability and usefulness of metabolites that are produced through the process of gut microbial breakdown are significantly increased. For example, the bioavailability of quercetin-3-ol increases to 62% after it has been degraded by the microbes in the colon. One of these tea polyphenol metabolites, known as phenyl-gamma-valerolactone, has been shown to have the ability to protect brown adipocytes from the damaging effects of oxidative stress. These adipocytes have the ability to jumpstart the thermogenic process, which leads to weight loss.

It is known that undigested carbohydrates can stimulate gut microbiota to produce short-chain fatty acids, which can activate AMP protein kinase, promoting weight loss. In fermented teas like Pu'er tea, there is a more abundant presence of tea polyphenol metabolites and inhibitory effects on carbohydrate absorption compared to regular teas. Therefore, fermented teas can induce higher levels of short-chain fatty acids and are more effective in reducing body weight.

Additionally, the therapeutic potential of short-chain fatty acids, namely butyric acid, acetic acid, and propionic acid, in mitigating obesity-linked metabolic disorders has been empirically validated. Significantly, these organic acids and small molecular salts constitute some of the breakdown byproducts of tea polyphenols within the colonic environment. Notably, research has documented that the supplementation of oligofructose with quercetin and catechins leads to an augmentation in the production of butyric acid and propionic acid, respectively. Moreover, anthocyanins, a subgroup of dietary polyphenols, exhibit the capacity to stimulate the generation of short-chain fatty acids when they interact with the gut microbiota. This offers an intriguing avenue for synergistic exploration when contemplating the therapeutic benefits of tea polyphenols [10].

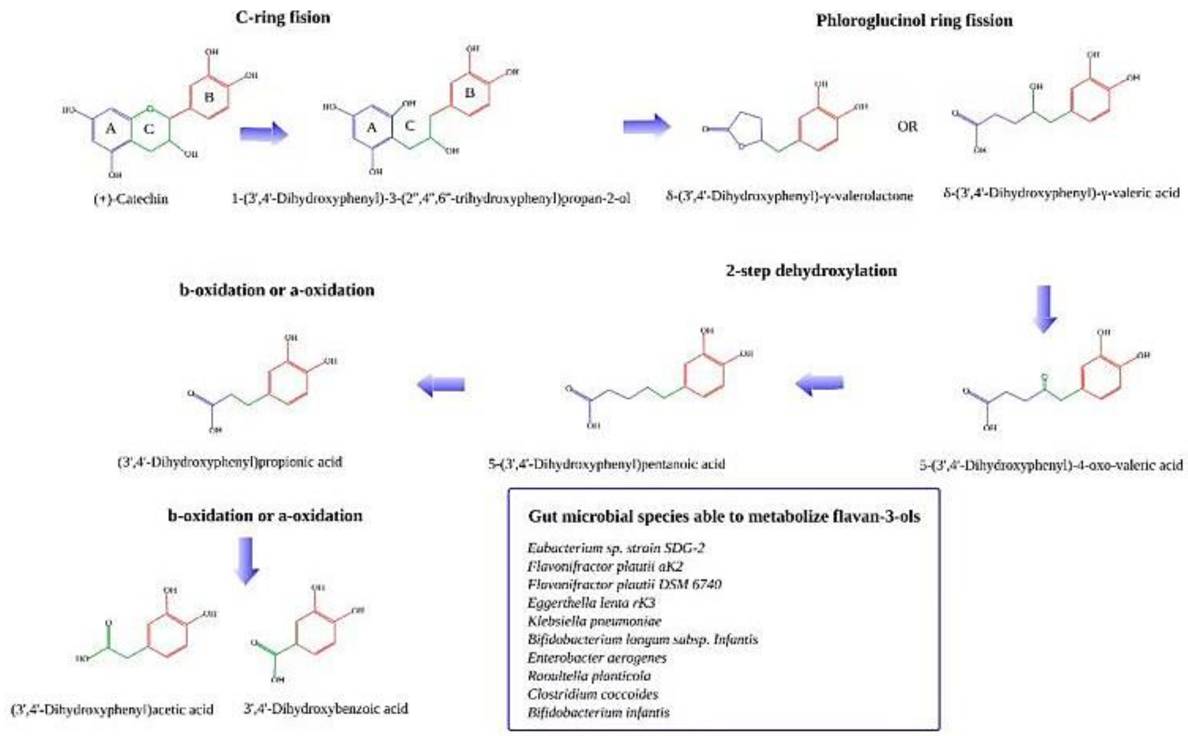

Figure 1. Process of tea polyphenol degradation by gut microbiota [11].

DOI: 10.54254/2753-8818/15/20240380

3.3. Anti-obesity effects of specific gut microbial species induced by tea polyphenols

Tea polyphenols can inhibit fat generation, promote fat oxidation, regulate host energy metabolism, and reduce fat accumulation by altering the composition of specific gut microbial species and the expression of related genes. This leads to an improvement in obesity and its complications. Reports indicate that treatment with red tea polyphenols can induce a reduction in the Firmicutes phylum and an increase in the Bacteroidetes phylum in the cecum. This elevation is associated with increased phosphorylation of AMP-activated protein kinase (AMPK). Leptin can stimulate fatty acid oxidation through phosphorylation of AMPK (AMP-activated protein kinase) and ACC (acetyl-CoA carboxylase), achieving the goal of weight loss [12]. Tea polyphenols can also regulate the expression of genes related to lipid metabolism, stimulate fat oxidation and decomposition, and inhibit fat accumulation in fat cells, thereby exerting anti-obesity effects. In another experiment, researchers fed gerbils with extracts from green tea that had been fermented with Bacillus spores. These fermented tea extracts reduced the abundance of Firmicutes and decreased energy absorption from constant nutrients in the body, thus exerting anti-obesity effects. In a separate investigation, Remely et al. administered a high-fat diet to obese mice, devoid of supplementary tea polyphenols, resulting in an elevation of the Firmicutes/Bacteroidetes ratio among the obese cohort. This perturbation was notably rectified, leading to a diminished propensity for obesity, upon the introduction of tea polyphenols into the dietary regimen. Concurrently, Gou et al. undertook a parallel experimental approach, where obese mice were subjected to a three-week dietary supplementation of green tea polyphenols. In harmony with prior research findings, their study observed an augmentation in the Bacteroidetes phylum and a concomitant reduction in the Firmicutes phylum within the gut microbiota. Furthermore, these alterations were accompanied by a reduction in obesity-associated markers among the obese murine subjects. Tea polyphenols can improve symptoms related to obesity by altering the quantity of specific microbial species in the gut microbiota and the expression of related genes [11].

4. Conclusion and discussion

This paper discusses the growing issue of obesity in the population and proposes the intake of tea polyphenols as a means to alleviate this problem. Focusing on the mechanisms behind the anti-obesity effects of tea polyphenols, this paper presents arguments from three aspects:

1. Regulation of Gut Microbiota Composition by Tea Polyphenols: Tea polyphenols can regulate the composition of gut microbiota in both digested and undigested states, with a primary emphasis on the undigested state. The main targets of regulation are the Firmicutes phylum and the Bacteroidetes phylum. Research has shown that the ratio of these two populations is critically related to fat storage and metabolism. A higher proportion of the Firmicutes phylum is associated with a lean phenotype and is more favorable for lipid reduction.

2. Regulatory Effects of Tea Polyphenol Metabolites on Gut Microbiota: Studies indicate that many of the positive effects of tea polyphenols on the human body stem from their metabolites after being broken down by gut microbiota, which primarily consist of phenolic acids. Compared to the parent tea polyphenols, phenolic acid substances have higher bioavailability and bioactivity. Their functions are closely related to anti-obesity effects, such as inhibiting carbohydrate absorption in the human body and promoting the production of short-chain fatty acids. Short-chain fatty acids have been proven to prevent obesity-related metabolic diseases and reduce body weight.

3. Tea Polyphenols' Role in Regulating Specific Gut Microbial Species in Obesity: Tea polyphenols primarily regulate certain specific microbial species in the gut, such as the Firmicutes and Bacteroidetes phyla. An increase in the proportion of the Firmicutes phylum is often associated with obesity, and tea polyphenol intake can reverse this process.

The aim of this paper is to summarize theories and mechanisms related to weight reduction by focusing on tea polyphenols and gut microbiota. It serves as a reference for future researchers in this field.

References

[1] World Obesity Atlas 2023 Report. Retrieved August 9, 2023, from https://www.worldobesityday.org/assets/downloads/World_Obesity_Atlas_2023_Report.pdf

[2] Zhang, Z., et al. (2023). Research progress on the lipid-lowering and weight loss effects of tea and the mechanism of its functional components. Journal of Nutritional Biochemistry, 112, 109210. DOI: 10.1016/j.jnutbio.2022.109210.

[3] Ma, G., & Chen, Y. (2020). Polyphenol supplementation benefits human health via gut microbiota: A systematic review via meta-analysis. Journal of Functional Foods, 66, 103829. doi: 10.1016/j.jff.2020.103829.

[4] Pathak, S., et al. (2018). Chapter 25 - Metabolism of Dietary Polyphenols by Human Gut Microbiota and Their Health Benefits. In R. R. Watson, V. R. Preedy, & S. Zibadi (Eds.), Polyphenols: Mechanisms of Action in Human Health and Disease (Second Edition) (pp. 347–359). Academic Press. doi: 10.1016/B978-0-12-813006-3.00025-8.

[5] Ma, H., Hu, Y., Zhang, B., Shao, Z., Roura, E., & Wang, S. (2022). Tea polyphenol – gut microbiota interactions: hints on improving the metabolic syndrome in a multi-element and multi-target manner. Food Science & Human Wellness, 11(1), 11–21. doi: 10.1016/j.fshw.2021.07.002.

[6] Effect of tea polyphenols on the prevention of neurodegenerative diseases through gut microbiota - ScienceDirect. Retrieved August 11, 2023, from https://www.sciencedirect.com/science/article/pii/S1756464623002694

[7] Islam, M. R., Arthur, S., Haynes, J., Butts, M. R., Nepal, N., & Sundaram, U. (2022). The Role of Gut Microbiota and Metabolites in Obesity-Associated Chronic Gastrointestinal Disorders. Nutrients, 14(3), 624. doi: 10.3390/nu14030624.

[8] Rothenberg, D. O., Zhou, C., & Zhang, L. (2018). A Review on the Weight-Loss Effects of Oxidized Tea Polyphenols. Molecules, 23(5), 1176. doi: 10.3390/molecules23051176.

[9] Tea Polyphenols and Their Interaction with Intestinal Microbiota and Their Impact on Human Health. Retrieved from http://hnxbl.cnjournals.net/hznydxzr/article/abstract/202205006 (Accessed on August 11, 2023).

[10] Gogga, P., Szałajda, M., & Janczy, A. (2021). Green tea and obesity: Effects of catechins on the energetic metabolism. Postępy Higieny i Medycyny Doświadczalnej. Retrieved August 10, 2023, from https://www.semanticscholar.org/paper/Green-tea-and-obesity%3A-Effects-of-catechins-on-the-Gogga-Sza%C5%82ajda/63a1112932ae76e477930ab11232017da5651667

[11] Pérez-Burillo, S., Navajas-Porras, B., López-Maldonado, A., Hinojosa-Nogueira, D., Pastoriza, S., & Rufián-Henares, J. Á. (2021). Green Tea and Its Relation to Human Gut Microbiome. Molecules, 26(13), 3907. doi: 10.3390/molecules26133907.

[12] Janovská, A., Hatzinikolas, G., Staikopoulos, V., McInerney, J., Mano, M., & Wittert, G. A. (2008). AMPK and ACC phosphorylation: effect of leptin, muscle fibre type and obesity. Molecular and Cellular Endocrinology, 284(1–2), 1–10. doi: 10.1016/j.mce.2007.12.013.