Institute of Experimental Morphology, Pathology and Anthropology with Museum
Bulgarian Anatomical Society

Acta Morphologica et Anthropologica, 33 (1-2)
Sofia ● 2026

Green tea‘s Potential Benefits for Metabolic Syndrome

Sabri Sabri[1], Nicole Kirchev[2] Nadya Penkova[1], Petar Hrischev[3]*

[1] *Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University – Plovdiv, Bulgaria*
[2] *Student, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria*
[3] *Department of Physiology, Faculty of Medicine, Medical University – Plovdiv, Bulgaria*

*Corresponding author e-mail: Sabri.Sabri@mu-plovdiv.bg

Metabolic syndrome is a combination of related disorders, such as insulin resistance, hyperglycemia, dyslipidemia, high blood pressure and abdominal obesity, which significantly increase the risk of cardiovascular disease and type 2 diabetes. The development of this syndrome involves the interaction of genetic factors, diet and environment. Physical activity and nutrition are no less important than pharmacological therapy. Green tea is prepared from leaves which are subjected to minimal oxidation during processing. It contains bioactive compounds such as polyphenols, the amino acid L-theanine, caffeine, alkaloids, B vitamins. In the present study, we summarize the literature data on the role of different components of green tea in the low-grade chronic inflammation of the intestinal tract, found in metabolic syndrome. The inclusion of appropriate foods and nutritional supplements, such as green tea and its extract, in the dietary regimen would inhibit endotoxin-mediated inflammatory reactions, which are the basis of the metabolic syndrome symptoms.

Key words: Green tea, metabolic syndrome, low-grade chronic inflammation, intestines, intestinal microbiota

Introduction

Metabolic syndrome is a growing problem in modern healthcare, which also carries a huge economic burden. It represents a complex of physiological, biochemical, clinical, and metabolic factors that increase the risk of cardiovascular disease, type 2 diabetes mellitus, etc. It includes a combination of central obesity (abdominal fat accumulation), hyperglycemia, reduced glucose tolerance, insulin resistance, hypertension, dyslipidemia (high triglyceride levels, low HDL cholesterol levels) [16]. The development of this syndrome is determined by the interaction between genetic factors, diet, and the environment. Although effective clinical, surgical, and

pharmacological methods have been developed to treat symptoms associated with metabolic syndrome, these treatments can be expensive and have potential adverse effects [6, 7, 24]. The development of dietary agents for the prevention or treatment of one or more of the symptoms of metabolic syndrome, alone or in combination with lifestyle changes and pharmaceutical agents, could represent a cost-effective and safe approach to the problem [25].

Green tea is made from the leaves of Camellia sinensis, which undergo minimal oxidation during processing. It contains bioactive compounds such as polyphenols, the amino acid L-theanine, caffeine, alkaloids (such as theobromine and theophylline), and B vitamins. The preventive effects of green tea and its ingredients on metabolic syndrome are being studied in both animal models and humans.

Effects of green tea on risk factors for metabolic syndrome

With regard to the various risk factors for metabolic syndrome, the ingredients of green tea have both an independent effect as dietary supplements and a synergistic effect when green tea is consumed (as a beverage or dietary supplement).

• Intestinal microbiota

Metabolic syndrome is a combination of related disorders, such as insulin resistance, hyperglycemia, dyslipidemia, high blood pressure, and abdominal obesity, which significantly increase the risk of cardiovascular disease and type 2 diabetes [16]. The development of this syndrome involves an interaction between genetic factors, diet, and the environment.

One of the key factors in the pathogenesis of metabolic syndrome is low-grade chronic inflammation induced by the intestinal microbiota.

By altering the composition of the gut microbiota, including an increase in Akkermansia, green tea reduces inflammatory markers and improves metabolic parameters [22]. The Firmicutes/Bacteroidetes (F/B) ratio is a measure of the balance between two dominant types of bacteria in the human gut microbiome. A high ratio (more Firmicutes) is associated with obesity [29]. L-theanine modulates the gut microbiota by reducing the Firmicutes/Bacteroidetes ratio, which is associated with obesity, and increases the concentration of short-chain fatty acids (SCFA), which support energy metabolism and regulate inflammatory processes in the intestine, as well as improve insulin sensitivity [13] (**Fig. 1**).

Changes in bacterial composition and intestinal lumen can induce metabolic disorders, regardless of caloric intake and body weight [2]. The transfer of microbiota from obese humans to germ-free mice shows that gut bacteria alone can cause glucose intolerance, insulin resistance, and vascular dysfunction without changing the body weight of the animals [33].

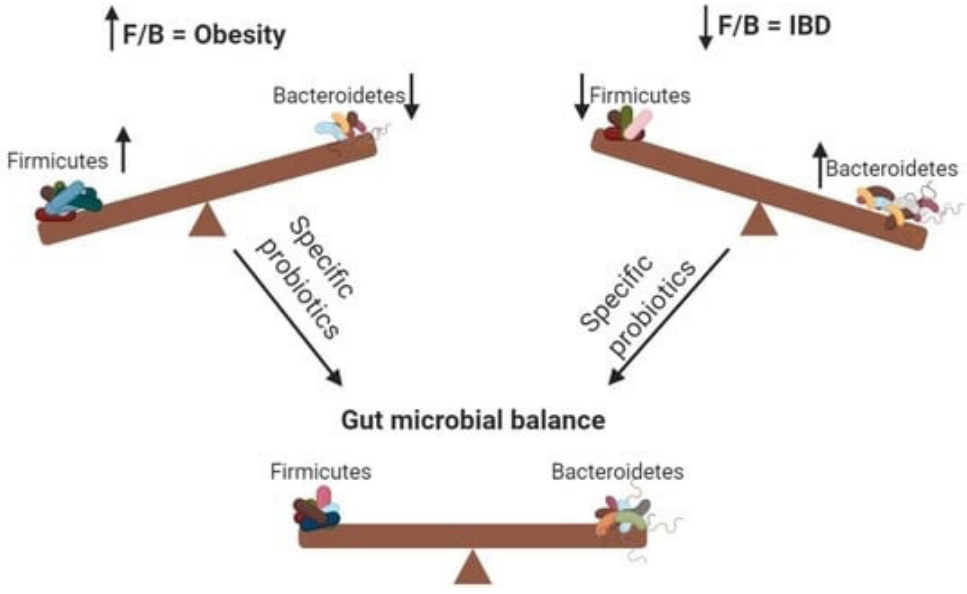

Fig. 1. Changes in the Firmicutes/Bacteroidetes (F/B) ratio

Stojanov, S., Berlec, A., & Štrukelj, B. (2020). https://doi.org/10.3390/microorganisms8111715

• Diet, obesity, and metabolic syndrome

The type of diet, composition, and proportions of the main components of food: proteins, carbohydrates, and lipids are of great importance for the pathogenesis of metabolic syndrome.

Green tea has a beneficial effect on metabolic syndrome induced by a high-calorie diet in mice, as the addition of 2% and 4% significantly reduces weight gain and lipid mass, as well as reducing inflammatory changes compared to the group fed only with high-fat diet (HFD). By altering the composition of the gut microbiota, including an increase in Akkermansia, green tea reduces inflammatory markers and improves metabolic parameters [22]. The HFD complicates the picture of metabolic syndrome by activating TLR4-dependent inflammatory pathways and leading to systemic inflammation, which is associated with visceral hypersensitivity and changes in metabolism [32]. HFD causes intestinal inflammation, which precedes and correlates with the development of obesity and insulin resistance, showing that the interaction between diet and bacteria plays a critical role in metabolic syndrome. Changes in bacterial composition lead to the activation of inflammatory signals and changes in the local immune response, which promotes the disruption of glucose and lipid metabolism [5]. Even short-term exposure to HFD affects immune function by disrupting macrophage activity, maintaining local inflammation, and enhancing systemic metabolic effects. Acute dietary changes and associated dysbiosis can rapidly induce metabolic disturbances and inflammatory responses that undermine normal

glucose and vascular homeostasis [14]. Dysbiosis in a high-fat diet is also characterized by reduced bacterial diversity, an increased Firmicutes/Bacteroidetes ratio, and an increase in LPS-producing taxa [5] (**Fig. 2**).

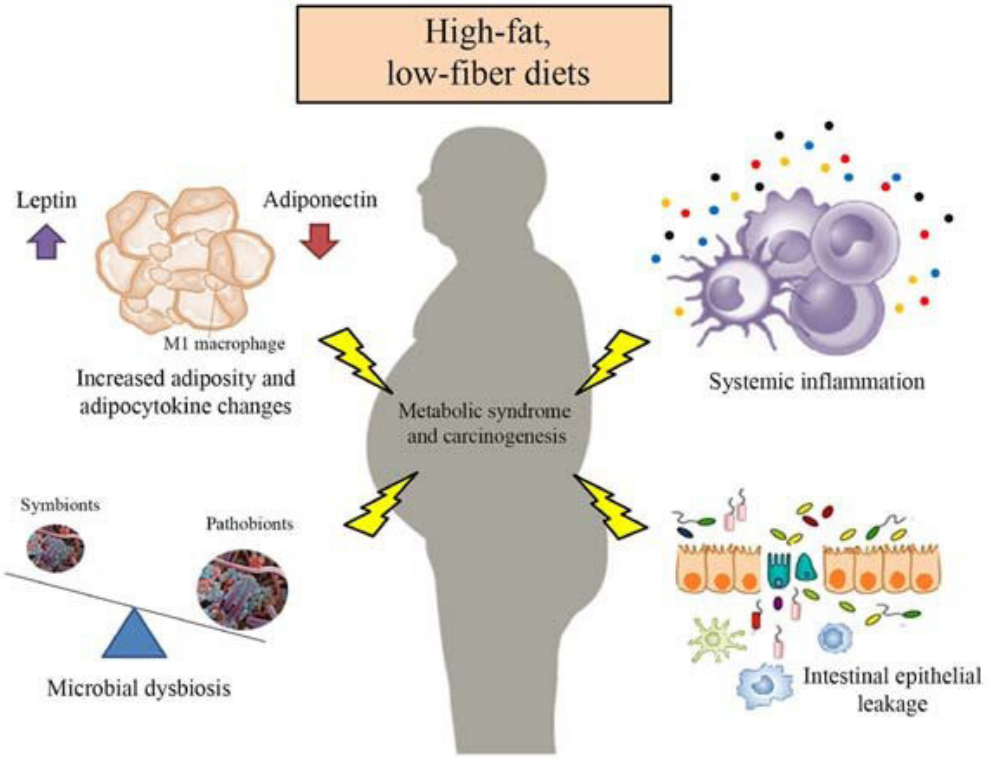

Fig. 2. Obesity and metabolic syndrome.

Saetang, J., & Sangkhathat, S. (2017). https://doi.org/10.3892/or.2017.5385

• Catechins and metabolic syndrome

Catechins are monomeric polyphenols characteristic of green tea. They constitute 25–40% of its dry weight [4, 11]. The most common catechin in green tea is epigallocatechin-3-gallate (EGCG), which has been found to perform various biological functions, including antioxidant and anti-inflammatory effects [12]. EGCG is one of the most potent polyphenolic compounds in green tea due to its effects on glucose and lipid metabolism and insulin resistance [35]. Li et al. showed that EGCG alleviates peripheral insulin resistance caused by free fatty acids (FFA) through insulin signaling and AMPK activation [19]. Many studies have focused on the effects of purified tea catechin preparations or pure EGCG. It has been found that supplements of high-fat-fed C57BL/6J mice fed 0.2 and 0.5% tea catechin reduce body weight gain, visceral fat mass (44–87% reduction), and liver triglycerides (53–75% reduction) [23, 31]. Treatment with tea catechin also reduced total plasma cholesterol and plasma

glucose under fasting conditions [23]. Treatment of C57BL/6J mice fed a high-fat diet with 0.32% EGCG for 16 weeks reduced body weight gain by 33–41% compared to control groups fed a high-fat diet [3] (**Fig. 3**).

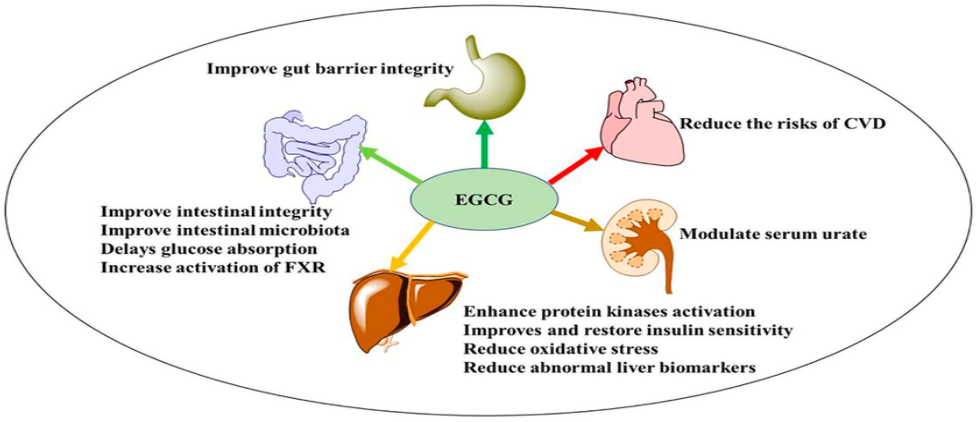

Fig. 3. EGCG and metabolic syndrome.

James, A., Wang, K., & Wang, Y. (2023). https://doi.org/10.3390/nu15133022

- **Caffeine and metabolic syndrome**

The best-known molecule in the fruit of coffee plant is alkaloid methylxanthine caffeine (1,3,7 trimethylxantin) which is a toxin protecting the plant from herbivores [28]. Caffeine is also found in the leaves of Camellia sinensis, with an average content of 3.8%, but this can vary depending on the time of harvest, storage, fermentation, and method of preparation [8].

Caffeine acts as an adenosine antagonist, thereby reducing norepinephrine levels. At the same time, it inhibits phosphodiesterase and increases protein kinase activity. The mixture of catechins and caffeine in green tea activates a signaling cascade that stimulates the sympathetic nervous system, along with hormone-sensitive lipase and upregulation of uncoupling protein, leading to increased energy expenditure and fat oxidation [15]. It was shown that caffeine decreased food intake and increased thermogenesis and this thermogenic effect leads to weight loss. Furthermore, it has been found that caffeine-induced thermogenesis is synergistically enhanced by catechins in the adipose tissue of rats [38].

- **L-Theanine and metabolic syndrome**

L-theanine is an amino acid found in green tea. L-theanine (L-gamma-glutamyl ethyl amide or N5-ethyl-L-glutamine) is a non-proteinogenic amino acid similar to L-glutamate and L-glutamine. It is produced by certain plants, such as Camellia sinensis (the tea plant), as well as by some fungi. As an important component of green tea, L-theanine has attracted the attention of scientists due to its positive role in metabolic syndrome.

L-theanine also modulates the gut microbiota by reducing the Firmicutes/ Bacteroidetes ratio, which is associated with obesity, and increases the concentration of short-chain fatty acids (SCFAs), which support energy metabolism, regulate inflammatory processes in the gut, and improve insulin sensitivity [13].

L-theanine exhibits antioxidant and anti-inflammatory properties that can counteract the low-grade inflammation observed in metabolic syndrome, as well as in functional bowel disorders [20]. In the gastrointestinal tract, L-theanine enhances the antioxidant capacity of the intestine via the Nrf2 signaling pathway, which plays a crucial role in cellular antioxidant defenses. As a regulator of antioxidant genes, activation of the Nrf2 signaling pathway reduces oxidative stress in intestinal epithelial cells exposed to the cytotoxic effects of hydrogen peroxide. [20, 26]. In a cellular model of porcine intestinal enterocytes from the jejunum (IPEC-J2 cells) exposed to hydrogen peroxide, L-theanine increases the expression of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, thereby reducing oxidative stress.

Green tea and its components, including L-theanine, have a direct antibacterial effect on the gut microbiota by destroying the exopolysaccharides and membranes of a number of pathogenic anaerobic and Gram-negative gut bacteria: Staphylococcus sp., Clostridium botulinum, Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, and Salmonella. [1, 36] Exosome-like nanoparticles derived from tea leaves (TELN), which contain L-theanine, significantly improve the barrier function of the intestinal epithelium. [10]. In an in vitro experiment, TELN protect the rat intestinal epithelium from damage caused by lipopolysaccharides. In an in vivo experiment on stressed rats, oral administration of TELN improved the barrier function of the intestinal epithelium by preventing the translocation of bacteria from the intestinal lumen into the submucosa of the intestinal mucosa. TELN improve the function of the intestinal immune barrier through the mediation of interleukin-22 and increased secretion of the antimicrobial peptide Reg3g [9]. (**Fig. 4.**).

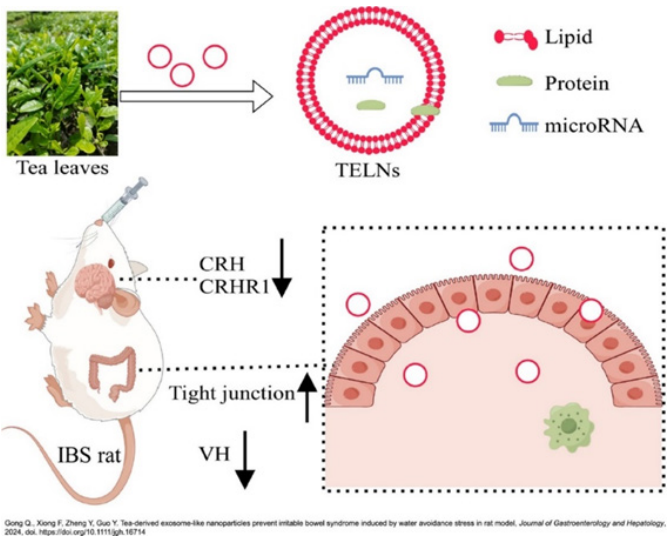

Fig. 4. L-theanine in the form of TELN exosomes—nanoparticles in green tea with a protective effect on intestinal permeability. (Gong et al., 2024). https://doi.org/10.1111/jgh.16714.

L-theanine affects not only intestinal permeability but also has a positive effect on resorptive processes in the small intestine. An improved balance of ingested nutrients is of great importance for metabolic syndrome.

Studies in a mouse model with L-theanine administration at doses of 300 and 400 mg/kg show that L-theanine is also involved in absorptive processes in the small intestine. Through intercellular signaling mechanisms, it influences the synthesis of transport proteins in the duodenum and jejunum. By activating the mTOR (mechanistic target of rapamycin) signaling pathway and the phosphorylation of the mTOR downstream proteins S6 and S6K1, L-theanine participates in the synthesis and modulation of a large number of transporters for various amino acids. In this way, L-theanine improves protein uptake and promotes protein metabolism by increasing intestinal absorption of amino acids and nitrogen utilization. [21]. An experimental rat model administered L-theanine at doses of 0, 50, 200, and 400 mg/kg per day for two weeks also demonstrated its modulatory role in nutrient absorption in the small intestine. In this experiment, the authors observed inhibition of the expression of SGLT3 and GLUT5 carbohydrate transporters, as well as GPR120 and FABP2 fatty acid transporters, while the expression of SLC7a1 and SLC7a9 essential amino acid transporters was increased. Serum glucose and high-density lipoprotein levels were also reduced [34]. Fat accumulation in mice is suppressed by the administration of green tea powder [27], and it is specifically L-theanine that is responsible for this suppressive effect [38].

Metabolic syndrome is also associated with high levels of stress. Chronic stress triggers persistent activation of the hypothalamic-pituitary-adrenocortical axis and the sympathetic nervous system, leading to elevated cortisol levels. In this way, the key components of metabolic syndrome—central obesity, insulin resistance, hypertension, and low-grade chronic inflammation—can be triggered. Stress is also a cause of unhealthy behaviors such as comfort eating and reduced physical activity [37, 38].

L-theanine has a proven calming effect on the nervous system, reducing stress and anxiety while improving cognitive function and memory. As a dietary supplement, this amino acid acts as a natural relaxant [18]. Experiments with oral administration of L-theanine to rats demonstrate its good absorption in the small intestine, and 15 to 30 minutes after administration, between 0.23% and 0.39% of its blood level is detected in the brain [30]. It has been found that in mice, L-theanine increases serotonin levels and decreases levels of dopamine, norepinephrine, and corticotropin in the cerebral cortex, striatum, and hippocampus [17].

Conclusion

Metabolic syndrome, as a borderline condition with various subclinical complications, is largely influenced by lifestyle. Physical activity and nutrition are no less important than pharmacological therapy. The inclusion of green tea in the diet would have a positive effect on the prevention and development of metabolic syndrome due to the various pathogenetic pathways of action of its components.

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