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EFFECT of GREEN TEA and *Lactobacillus gasseri* AGAINST OBESITY*

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YEŞİL ÇAY ve *Lactobacillus gasseri*'nin OBEZİTEYE KARŞI ETKİSİ

ÖZET

Obezite ülkemizde ve dünyada en önemli sağlık sorunlarından biridir. Aşırı kilo ve obezite, dünya çapında fazla sayıda ölümle ilişkilidir ve birçok kronik hastalığa neden olur. Yapılan araştırmaların çoğu obezite tedavisinin temel amacının kilo kaybı olduğunu göstermektedir. Bu nedenle obeziteyi önlemeyi hedefleyen gıdaların üretimi günümüzde önemli bir konu haline gelmiştir. Probiyotikler sağlıklı insan bağırsağında bulunan ve GRAS (genelde güvenli olarak kabul edilen) listesinde yer alan mikroorganizmalardır. İnsan sağlığına faydalı etkisi nedeniyle birçok gıda ürününde yaygın olarak kullanılmaktadır. Probiyotik bir mikroorganizma olan *Lactobacillus gasseri*'nin obeziteye karşı etkili olduğu yapılan çalışmalarla belirlenmiştir. Ayrıca insan sağlığına faydalı olan ve yaygın olarak tüketilen yeşil çayın (*Camelia sinensis*) kilo vermede de etkili olduğu gözlemlenmiştir. Bu çalışmada yapılan araştırma sonucunda insan sağlığına faydalı etkileri olan *Lactobacillus gasseri* ve yeşil çayın obeziteye karşı olumlu etkileri olduğu konusunda kapsamlı bilgiler verilmiştir.

Anahtar Kelimeler: Obezite, Probiyotikler, *Lactobacillus gasseri*, Yeşil Çay

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ABSTRACT

Obesity is one of the most important health problems in our country and in the world. Overweight and obesity are associated with large numbers of deaths worldwide and cause many chronic diseases. Most of the researchs conducted show that weight loss is the main goal of obesity treatment. Therefore, the production of foods that aims prevention of obesity has become an important issue today. Probiotics are microorganisms that reside in the healthy human gut and are on the GRAS (generally recognized as safe) list. It is widely used in many food products due to its beneficial effect on human health. *Lactobacillus gasseri*, a probiotic microorganism, has been determined to be effective against obesity by studies. In addition, it has been observed that green tea (*Camelia sinensis*), which is beneficial for human health and widely consumed, is also effective in loss weight. In this study, as a result of the research conducted, comprehensive information was given that *Lactobacillus gasseri* and green tea, which have beneficial effects for human health, have positive effects against obesity.

Keywords: Obesity, Probiotics, *Lactobacillus gasseri*, Green Tea

INTRODUCTION

Obesity is an important health problem that negatively affects the quality of life, causes many chronic diseases and shortens the life span, and concerns all individuals of all ages (1). The most important reasons why obesity is a health problem in our country and in the world can be demoted to main three groups. These groups are the calories taken as a result of consuming more food than the suggested daily consumption amount, the widespread consumption of foods containing high amounts of sugar, fat and salt, and the decrease in people's physical activity (2; 3). In addition to these, age, gender, education level and genetics are among the most important factors. In the treatment of obesity, drugs are used in cases where exercise and low-calorie diets are insufficient (4).

The intense interest in food and drugs that can be used in weight control and healthy nutrition started with the spread of obesity as a result of industrialization in the 19th century (5) The variety of strategies to combat obesity makes it possible to develop a variety of food products that can meet individual needs. However, prior to market release, metabolic effects should be extensively compared. In addition, the concrete profile of people who can benefit from the consumption of formulated functional foods should be defined (6).

Probiotic bacteria are microorganisms that have positive effects on human health and are widely used in the production of many food products (7). Commercially, *Lactobacillus* and *Bifidobacterium* bacterial species are widely used in probiotic foods. The biggest reason for the

use of these bacteria is that they have been used for years because they are safe, they are dominant in the human intestine and they are on the GRAS (generally accepted as safe) list (8; 9).

Probiotics have specific features and targets in the human intestinal tract and gut microbiota. Each probiotic strain is unique, regardless of its genus and species, and therefore, the characteristics of each strain and its effects on human health need to be evaluated on a case-by-case basis (10).

Probiotics mainly provide many health benefits such as preservation of normal intestinal microflora, protection against gastrointestinal pathogens, strengthening of the immune system, lowering of serum cholesterol level and blood pressure, anti-carcinogenic activity, better utilization of nutrients and improving the nutritional value of foods (11).

In order for probiotic microorganisms to have a beneficial effect, they must be present in the products at a level of at least 10^6 - 10^7 cfu/g (12). The demand for functional foods containing probiotics is increasing rapidly due to the increasing awareness of consumers about the positive impact of these foods on health (11).

Studies have shown that consumption of *L. gasseri*, which is considered a probiotic, is effective against obesity as it reduces body weight, BMI, waist and hip circumferences, and body mass (13). Due to these beneficial effects on health, *L. gasseri* is widely used in various fermented food products and dietary supplements (14).

Apart from probiotics, various natural products are also used in the treatment of obesity and related diseases (15). Several randomized controlled intervention studies and epidemiological evidence have shown an inverse relationship between particularly green tea consumption and person's body fat levels and waist circumference (16).

Obesity

Obesity is defined as the accumulation of more than normal amount of fat in the body when the energy taken is more than the energy spent (17). The normal range of adipose tissue in men is between 15-20% of body weight, and between 25-30% in women. Obesity is mentioned as a result of these rates exceeding 25% for men and 30% for women (1).

The prevalence of obesity is increasing day by day in many parts of the world (1). WHO defines obesity as a chronic disease prevalent in both developed and developing countries (18).

Overweight and obesity are linked to more deaths worldwide than underweight. While only less than 1% of children and adolescents aged 5-19 were obese in 1975, 124 million children and adolescents (6% of girls and 8% of boys) were obese in 2016. Worldwide, obesity nearly tripled between 1975 and 2016. According to the data of the World Health Organization in 2016, more than 1.9 billion adults aged 18 and over were overweight and more than 650 million were obese. It was also reported that over 340 million children and adolescents aged 5-19 years were overweight and obese in 2016. According to 2019 data, it has been determined that 38.2 million children under the age of 5 are overweight and obese. Finally, according to 2020 data, it has been determined that 39 million children under the age of 5 are overweight or obese (19).

According to studies, 1/3 of obese children and 80% of obese adolescents continue to be obese when they become adults. Therefore, it has been stated that it is important to start the prevention of obesity and the fight against obesity from childhood (17).

Obesity and Intestinal Microbiota

It has been determined that the intestinal microbiota, which affects nutrient absorption and energy distribution, plays a role in the pathogenesis of obesity and metabolic syndromes (17). Consuming foods high in fat and energy changes the number and composition of intestinal bacteria (20). As a result, an unhealthy flora called dysbiosis occurs (21). Caloric intake, intestinal permeability, increase in the levels of pro-inflammatory cytokines and endotoxemia occur in the intestine whose microbial balance is disturbed (22).

Microbiota takes part in weight control by acting on different mechanisms. The first of these mechanisms is the microbiota-gut-brain axis, which helps to determine the places that the major metabolites will take in metabolism, together with the substances secreted from the vagus nerve and brain, adipose tissues. Microbiota elements control the satiety hormones glucagon-like peptide-1 (GLP1) and Peptide YY (PYY) by converting them to short-chain fatty acids, while some subgroups of *Lactobacillus* and *Bifidobacterium* groups regulate food intake by producing γ-aminobutyric acid (GABA) (23; 24;25).

With obesity, the rate of *Firmicutes* increases in the intestines of people, and the rate of *Bacteroides* and *Bifidobacteria* decreases (17;20). *Firmicutes* bacteria are known to cause fat accumulation by hydrolyzing indigestible polysaccharides, providing more energy gain (22). Although Bifidobacteria are not a dominant bacterial population in the intestinal microbiota, it has been stated that the decrease in the amount of Bifidobacteria is a very important change in

the intestinal microflora of obese individuals. Therefore, it has been determined that the bacterial population that should be targeted primarily in treatment is Bifidobacteria (20). In addition, it has been determined that *Lactobacillus* species are more concentrated in obese and overweight people than thin people and have a positive relationship with body mass index (BMI) (22).

The increase number of gram-negative bacteria in the intestinal microbiota of people who eat high-fat diet increases lipopolysaccharide (LPS) levels and causes chronic systemic inflammation. This also plays a role in the development of obesity (17; 21).

Obesity-Related Diseases

Obesity negatively affects all aspects of human life and is associated with many diseases (26). Obesity, is an important risk factor for non-communicable diseases such as cardiovascular diseases (especially heart disease and stroke), diabetes, metabolic syndrome, musculoskeletal disorders (especially osteoarthritis- a degenerative disease that debilitates the joints), many types of cancer (endometrial, breast, ovarian, prostate, liver, gall bladder, kidney and colon), respiratory system disorders, hypertension, sleep apnea and psychological disorders (1;2;18; 19). Excess body fat increases the health risks of individuals (18). However, 5-10% weight loss greatly reduces the risk of these diseases (1).

Treatment of Obesity

The treatment to be used to combat obesity is a long and continuous process. Therefore, the individual's determination and active participation are required (17).

The aim of obesity treatment is to provide an individual negative energy balance (27). Lifestyle changes, behavioral changes, medication or surgical treatment are used in the treatment of overweight and obesity (28). Lifestyle change should be applied first in treatment (1). Dietary changes combined with increased physical activity are defined as first-line therapy in adults and children (27).

In cases where obesity cannot be prevented by lifestyle changes, medication or surgical treatment should be used (1). Although drugs aid weight loss and prevent relapse, they have many side effects and the patient still needs to follow a certain diet and exercise (26). Because of this benefit-risk balance, drug and surgical treatments are considered as second and third line treatments (27).

Lactobacillus gasseri and Its Effect Against Obesity

L. gasseri, within the genus *Lactobacillus acidophilus*, which is widely used as a probiotic, is an important species of human microflora (29). *L. gasseri* is naturally found in human milk, gastrointestinal and vaginal systems (30). These microorganisms are generally accepted as safe (GRAS) and are used in various commercial probiotic products (30;31).

L. gasseri is a gram-positive, rod-shaped lactic acid bacteria species (32). This bacterium is acid-resistant, bile-tolerant, and adheres to the host epithelium (33; 34). In addition, it was determined that it showed antibacterial activity against foodborne pathogenic bacteria (*Staphylococcus aureus, Escherichia coli* O157:H7, *Listeria monocytogenes, Salmonella, Typhimurium* and *Bacillus cereus*) and produced bacteriocins and antibacterial substances (35). *L. gasseri* has beneficial effects on health such as maintaining intestinal homeostasis, regulating the immune system, preventing bacterial and viral infections, reducing allergic symptoms, alleviating infectious disease symptoms, alleviating *Helicobacter pylori* infection, curing diarrhea, and lowering serum cholesterol concentrations (14; 29; 33). In addition, consumption of this bacterium is effective against obesity as it reduces body weight, BMI, waist and hip circumferences and body mass. The anti-obesity effect of *L. gasseri* is associated with its ability to settle in the human gut and improve the intestinal environment. Such properties of *L. gasseri*, together with its ability to reduce lipid absorption, result in a reduction of abdominal fat and other body dimensions (13). Due to these beneficial effects on health, *L. gasseri* is widely used in various fermented food products and dietary supplements (14).

In some studies, it has been observed that the use of prebiotics and probiotics changes the intestinal flora and provides weight loss. It has been determined as a result of studies that prebiotics, probiotics and their combinations can be used in the treatment and prevention of obesity problem, and it has been concluded that more studies should be done on this subject (20).

Green Tea and Its Effect Against Obesity

Green tea (*Camellia sinensis*) is one of the widely consumed beverages in the world (36). Green tea from the *Theaceae* family is brewed from the unfermented dried leaves of the *Camellia sinensis* plant (16;37).

As a chemical structure, green tea contains alkaloids, lignin, flavanol glycosides, carbohydrates, amino acids, minerals and vitamins, and it also consists of high amounts of polyphenols

(catechins) (38). The many benefits of green tea, making it a valuable functional food, are associated with polyphenol compounds with high antioxidant properties. Catechins are the primary polyphenol in tea, accounting for 30-42% of the dry weight in green tea leaves (39). The main polyphenolic components found in green tea are epicatechins (EC), epigallocatechin (EGC), epicatechin-3-gallate (ECG), and epigallocatechin-3-gallate (EGCG) and gallocatechin (GC) (37). Representing 50-80% of the total catechin content, epigallocatechin-3-gallate (EGCG) is the most abundant catechin in green tea. In addition, this catechin is considered to be the most bioactive component of green tea (16). These catechins, which are found in high amounts in green tea, give green tea a bitter and bitter taste (38). Additionally, green tea contains caffeine, theaflavins, theanine, quercetin, thearubigins, myricetin, chemferol, and other phenolics such as gallic acid and chlorogenic acid (16; 36). The structure of the major catechins in green tea extract is shown in Figure 1.

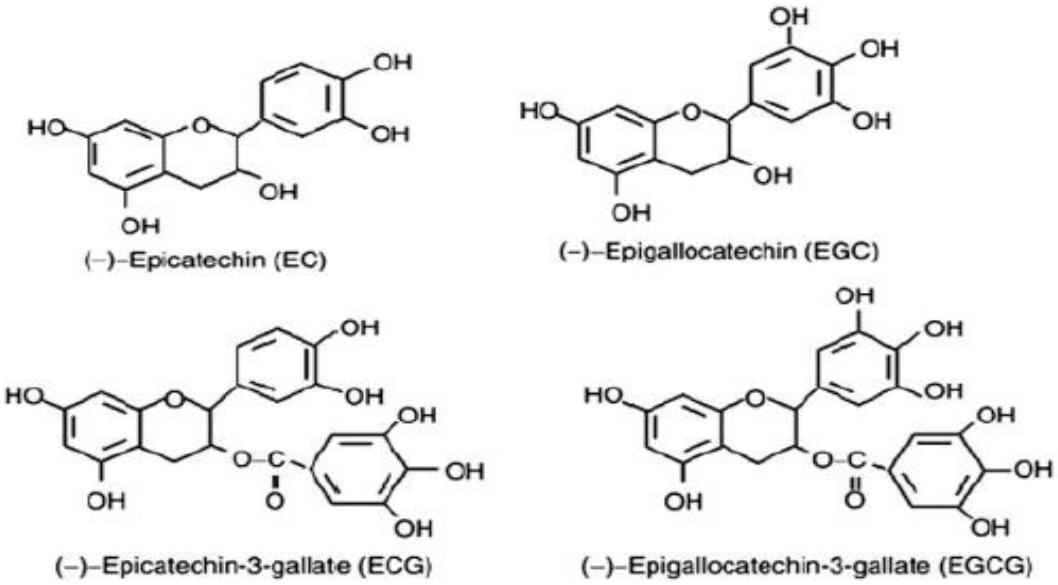

Figure 1. Structure of major catechins in green tea extract (40).

It is known that green tea and its components provide many benefits to human health. Since green tea is in the least processed form, it keeps all healthy ingredients in their natural form (41). Green tea catechins and derivatives provide many health benefits, including protection against cardiovascular disease, lowering cholesterol, preventing atherosclerosis, protection against kidney and liver diseases, and anticarcinogenic and anti-obesity effects (42; 43; 44). In addition, it has been reported that green tea catechins have anticancer, anti-atherosclerotic, antidiabetic, antiviral, antibacterial, antimetabolic syndrome, anti-infectious and neuroprotective effects (15;42). It is known that tea polyphenolics such as catechins have

antimicrobial effects against many microorganisms, including pathogens, but these compounds do not inhibit lactic acid bacteria (LAB) (41). Caffeine in green tea, on the other hand, provides the expansion of capillaries, increases the blood flow rate, thus providing the body's sense of fatigue and refreshing effects (38). In addition, consumption of green tea is effective against anxiety and stress (45).

The anti-obesity effect of green tea is related to caffeine and catechins, (-)- epigallocatechin-3-gallate contents (36). In addition, according to the results obtained from the laboratory studies have determined that green tea has important roles in fat metabolism by reducing food intake, interrupting lipid emulsification and absorption, suppressing adipogenesis and lipid synthesis, and increasing energy expenditure through thermogenesis, fat oxidation and fecal lipid excretion (46). Green tea helps to control weight and increase fat metabolism due to the epigallocatechin gallate and caffeine it contains (5).

Due to its positive effects on human health, green tea is widely used as a natural food additive. In addition, by adding green tea extract to foods, the flavor and shelf life of the food can be increased and consumers can be offered foods with a healthier appearance (42). Due to these positive effects, green tea has been used in milk, yogurt, fruit flavored milk drinks, fermented milk, probiotic dairy products and ice cream mixes (44, 47).

The Anti-Obesity Effect of *Lactobacillus gasseri* and Green Tea

In a study in which green tea and green coffee extracts were added to yoghurt samples, the chemical composition of yoghurts, their sensory evaluation and their effect on reducing complications in rats were investigated. It was determined that samples containing green tea and green coffee contained high levels of antioxidant activity. Yoghurts containing green tea and green coffee had higher sensory scores than control yoghurt. Green tea and green coffee extracts added to yoghurts increase the viscosity of yoghurts. It was determined that feeding obese rats with green tea and yoghurt supplemented with green coffee was effective in losing weight compared to the control group. In addition, in this study, it was determined that green tea and green coffee have beneficial effects on health (48).

The anti-obesity character of green tea is due to its effect on many mechanisms associated with fat synthesis, inflammatory cytokine production, and insulin sensitivity, as well as reducing oxidative stress (49).

An epidemiological study conducted in South Korea with 10,030 participants aged 40-69 years showed that the risk of abdominal obesity was lower (odds ratio 44%) in those who drank 4 or more cups of green tea a day compared to those who did not, and that the protective effect against obesity was increased, especially in middle-aged women (50).

A study of rats fed a high-fat diet for 15 weeks examined the relationship between green tea consumption and the rates of non-alcoholic fatty liver disease and obesity, which are related diseases. It has been observed that Chaoqing Green Tea enriched with selenium is more effective than other green tea derivatives in reducing liver weight and oxidative stress. The active ingredients that create this effect were determined as gallate gallocathechin and epigallocatechin (51).

In a study on mice without leptin receptors, it was observed that inflammatory gene expression in adipose tissue and the dipeptidyl peptidase 4 (DPP4) enzyme, which binds and activates an inflammatory cytokine, Nuclear Factor kappa B (NF-kB), decreased in the green tea-consuming group. In addition, insulin sensitivity and glucose tolerance increased in mice by increasing the GLP1 enzyme. With these mechanisms, it would be correct to say that green tea ingredients prevent the increase of adipose tissue and reduce the risk of diabetes (52).

In the study of Macêdo et al. (53), although the lipid profile (cholesterol, triglyceride, LDL) improved in animals, green tea was already found to be insufficient to control lipid profiles in obese individuals, and as a result of this study, it is mentioned that green tea has a protective effect rather than a cure.

Another anti-obesity mechanism of green tea is the increase of carnitine acyl transferase enzyme due to protein kinase phosphorylation activated by AMP and the decrease in metabolic and inflammatory contents such as glycogen synthase, kinase 3 beta, Interleukin 6, tumor necrosis factor alpha with fatty acid synthesis. With the mentioned mechanism, lipid biosynthesis and inflammation are reduced (54).

When the effect of green tea on microbiota is investigated, it is seen that polyphenols reduce the growth of pathogenic bacteria while helping to increase probiotic bacteria. Probiotic bacteria also increase the effect by providing selective fermentation of polyphenols. Based on this information, the symbiotic relationship between them can be benefited by consuming green tea derivatives containing high amounts of polyphenols together with products containing *L. Gasseri* (55).

In the study of Lima, Monteiro and Pasquali (56), it was determined that the concentration of *L. gasseri* in passion fruit juice with 15% green tea added increased above 9 log cfu/ml. This result is instructive that the combination of green tea and probiotic bacteria will be functional.

In another study, mice were fed a normal diet, a high sucrose diet, or a high sucrose diet containing *L. gasseri* BNR17 (10^9 or 10^{10} cfu) for 10 weeks. *L. gasseri* BNR17 significantly reduced body weight and white adipose tissue weight of administered mice regardless of dose. It was determined that the mRNA levels of genes related to fatty acid oxidation were significantly higher in groups fed *L. gasseri* BNR17 and the levels of genes related to fatty acid synthesis were lower compared to the high-sucrose diet group. Expression of the glucose transporter-4, GLUT4, was increased in groups fed L gasseri BNR17. *L. gasseri* BNR17 also reduced serum leptin and insulin levels. This result suggests that the anti-obesity effects of *L. gasseri* BNR17 can be attributed to high expression of fatty acid oxidation-related genes and low leptin levels. It has also been reported that the anti-diabetes activity of *L. gasseri* BNR17 may be due to high GLUT4 and low insulin levels (57).

It has been reported that the intake of *L. gasseri* provides a significant decrease in body weight and the amount of fat mass, while also lowering the triglyceride level in the liver, but this effect is achieved not only by inhibiting lipogenic gene up-regulation, but also by inhibiting pro-inflammatory gene expression (58). In addition, *L. gasseri* numbers were found to be decreased in samples taken from the saliva of obese kindergarten children, and based on this result, it was thought that *L. gasseri* might have a protective effect against obesity (RR: 0.49–$p < 0.05$) (59).

Conclusion

Disruption of the balance of intestinal microbiota plays an important role in the development of obesity. It has been determined that the anti-obesity effect of *L. gasseri*, a probiotic microorganism, is associated with improving the intestinal environment and providing loss weight. It has been concluded that *L. gasseri*, when taken it sufficient amount to the body, reduces lipid absorption, as well as it reduces abdominal fat and other body measurements. The effect of green tea, which is a natural product, against obesity is related to the caffeine and catechin in its contents. It has been determined that the consumption of this food product has important effects in fat metabolism by reducing person's food intake, interrupting lipid emulsification and absorption, suppressing adipogenesis and lipid synthesis, and increasing energy consumption through thermogenesis, fat oxidation and fecal lipid excretion. As a result of the researches, it has been determined that *L. gasseri* and green tea have positive effects for

improving the intestinal microbiota and preventing obesity. Due to these positive effects, more comprehensive research should be conducted to produce food products containing *L. gasseri* and green tea, and to produce new products that are both effective against obesity and beneficial for human health.

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