Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

REVIEWARTICLE
Volume:3 Issue:4 Year:2025
https://doi.org/10.5281/zenodo.17960178

Obesity and Cardiometabolic Diseases: A Gut Microbiota Centered Perspective

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ABSTRACT

The escalating trajectory of obesity worldwide constitutes a severe public health crisis, intimately linked to elevated rates of death and chronic disease burden. Contemporary medical understanding has shifted from viewing obesity solely as a caloric equilibrium issue to recognizing it as a complex, multifactorial pathology driven by neurohormonal disruptions, metabolic dysregulation, and inflammatory cascades. Adipose tissue is no longer regarded merely as an energy depot; it is an active endocrine organ where cellular expansion and hypoxia precipitate chronic low-grade inflammation, a precursor to insulin insensitivity and metabolic breakdown. Recently, the intestinal ecosystem has been identified as a central architect in the development of metabolic syndrome and cardiovascular impairments. Individuals with obesity typically exhibit a distinct microbial signature characterized by diminished diversity and dysbiosis. Mechanistically, the gut flora dictates host metabolic health by modulating lipid profiles, energy harvesting, and immune responses via several pathways, including the fermentation of fibers into short-chain fatty acids, the regulation of bile acid signaling, the modulation of metabolic endotoxemia, and the inhibition of FIAF. Of particular concern is the synthesis of trimethylamine-N-oxide (TMAO) by gut bacteria, which directly exacerbates atherosclerotic plaque progression and heightens platelet reactivity. Furthermore, the bidirectional communication via the gut-brain axis plays a pivotal role in regulating satiety and dietary choices. In light of these associations, therapeutic strategies that reshape the microbial landscape—ranging from probiotic and prebiotic administration to fecal microbiota transplantation and novel pharmacological modulators—hold significant promise for mitigating the cardiometabolic risks associated with obesity.

Keywords: Obesity, Cardiometabolic Diseases, Gut Microbiota, Dysbiosis.

INTRODUCTION

Obesity, which is witnessing a continuous rise in prevalence both in our country and worldwide, represents a critical public health issue that has escalated to epidemic levels. While traditionally viewed merely as an imbalance in energy, this condition is now acknowledged as a sophisticated neurohormonal and metabolic disease (1). Data from the World Health Organization (WHO) indicates that in 2022, 43% of the adult population aged 18 and older fell into the overweight category, while the prevalence of obesity surpassed 890 million (2). Nevertheless, recent research underscores the increasing severity of this condition. The "World Obesity Atlas 2024," released by the World Obesity Federation, projects that if current trajectories persist, over half of the global population (54%) will be classified as overweight or obese by the year 2035. The same report highlights that the acceleration of childhood obesity rates surpasses that of adults and estimates that the economic burden of obesity on the global economy will escalate to $4 trillion annually (3).

Pathophysiology of Obesity: Adipose Tissue Dysfunction and Inflammation

Obesity is defined as a complex, multifactorial disease characterized by excess fat accumulation coupled with low-grade inflammation. The primary drivers of fat deposition include the disruption of energy homeostasis stemming from an excess of caloric intake relative to energy expenditure and a lack of physical activity (4, 5). Beyond dietary habits, factors such as environmental influences, behavioral patterns, and genetics also play a role in fat accumulation. However, this process involves more than just an increase in the number of fat cells (adipocytes). Adipose tissue acts not only as a reservoir for

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Received: 16.11.2025, Accepted: 15.12.2025, Published Online: 20.12.2025
Cited: Bektaş I, et al. Obesity and Cardiometabolic Diseases: A Gut Microbiota Centered Perspective. Acta Medica Ruha. 2025;3(4):199-207. https://doi.org/10.5281/zenodo.17960178

energy but also functions as an active endocrine organ, thereby contributing to the pathogenesis of obesity. Numerous molecular components and systems (including glucose, insulin, fatty acids, adipocytes, and the gut microbiota (GM)) are involved in obesity's pathogenesis; specifically, the expansion of adipocyte volume (hypertrophy) and number (hyperplasia) linked to fat storage compromises tissue oxygenation, resulting in hypoxia. This hypoxic state modifies the profile of immune cells residing within the adipose tissue. In particular, the phenotypic switch of M2 macrophages, which possess anti-inflammatory traits, to pro-inflammatory M1 macrophages constitutes the foundation of chronic inflammation observed in obesity (6, 7). This state of low-grade inflammation hastens the progression of obesity by fostering insulin resistance and metabolic complications. Moreover, gastrointestinal hormones and the nervous system, which govern appetite through the gut-brain axis, combined with alterations in adipose tissue, precipitate life-threatening obesity and its associated comorbidities (8-10).

Obesity-Related Comorbidities and Metabolic Syndrome

Excess body weight acts as a central pivot for a spectrum of chronic pathologies, most notably type 2 diabetes (T2D), metabolic syndrome (MetS), and cardiovascular disorders (CVD) (11-13). Data indicates that, relative to their normal-weight counterparts, individuals with obesity face a greater than 60% surge in the likelihood of developing CVD. Furthermore, increased adiposity is a direct precipitant of specific cardiac events, including the progression of atherosclerosis, coronary artery complications, and heart failure (11, 14, 15). Concurrently, the clustering of T2D which frequently manifests alongside obesity with hypertension, lipid abnormalities, and microbial imbalance (dysbiosis) is widely acknowledged to synergistically amplify the susceptibility to both MetS and CVD (12, 16, 17).

The core components of MetS (Metabolic Syndrome) are characterized by the presence of insulin resistance alongside any two of the following: hypertension, dyslipidemia, and abdominal obesity (indicated by elevated waist circumference or body mass index). Secondary components encompass coronary artery disease, non-alcoholic fatty liver disease, polycystic ovary syndrome, inflammation, endothelial dysfunction, and a hypercoagulable state (18). Currently, the cluster of MetS risk factors diabetes, hypertension, hyperlipidemia, and coronary artery disease is collectively referred to as cardiometabolic diseases.

In individuals with obesity, metabolic dysfunction typically initiates with insulin resistance and advances toward MetS. Numerous cardiometabolites are involved in this progression. It is also established that increased adiposity promotes the development of MetS and cardiovascular disease by modulating the levels of specific hormones and cytokines (19). For instance, various cytokines and chemokines secreted by adipocytes, including tumor necrosis factor-α (TNF-α), interleukin (IL)-6, resistin, and monocyte chemoattractant protein-1 (MCP-1), have been reported to foster atherosclerosis by inducing insulin resistance, endothelial dysfunction, thrombosis, and systemic inflammation (20). Additionally, the interplay between monocytes/macrophages and T-lymphocytes with endothelial and smooth muscle cells has been demonstrated to contribute to the formation of atherosclerotic lesions (21).

Gut Microbiota: The "Forgotten Organ" and Dysbiosis

The GM resembles a fingerprint, possessing a distinct composition, diversity, and set of functional traits. Within the human host, a remarkable 90% of the total microbial population is attributed to several major taxonomic phyla (22). This ecosystem, hosting approximately 100 trillion microorganisms in an adult, contains genetic material that exceeds the human genome by 150-fold (23).

Healthy individuals exhibit high microbial diversity. Conversely, in conditions like obesity, T2D, and MetS, this diversity diminishes, and alterations occur at the phylum level. Generally, it has been reported that in obese subjects, there is an increase in the Firmicutes phylum and a decrease in the Bacteroidetes phylum (leading to an elevated F/B ratio) (24).

Research indicates that dysbiosis also plays a role in obesity and diseases related to obesity (16, 25-27). Modifications in the microbiota can arise from factors such as diet, toxins, pharmaceutical agents, genetics, and pathogens. Factors in early life are particularly crucial in shaping the future composition of the microbiota. Delivery via cesarean section, the use of formula instead of breast milk, and antibiotic exposure during infancy are among the factors that adversely impact microbial diversity and heighten the risk of obesity in later life. Consequently, the symbiotic relationship between the host and the microorganisms may be compromised. Alterations in microbiota composition and the ensuing imbalance (dysbiosis) can contribute to the pathogenesis of metabolic diseases (25, 28). Therefore, the mechanisms by which microbiota contributes to the pathogenesis of obesity are detailed below.

Gut Microbiota-Related Mechanisms

When evaluating the potential mechanisms linking microbiota to these diseases, it is hypothesized that it acts as a risk factor through two primary pathways. The first pathway involves dysbiosis, which modifies host metabolism, disrupts energy homeostasis, and leads to metabolic disorders; the second pathway involves metabolic byproducts generated by the microbiota, which induce systemic inflammation and result in disease (25, 29).

Gut Metabolites: SCFA and Energy Homeostasis

The gut microbiota (GM) is integral to the maintenance of metabolic, systemic, and immune homeostasis, primarily through bioactive byproducts generated during the breakdown of nutrients. Complex carbohydrates that escape digestion in the upper gastrointestinal tract enter the colon, where bacterial fermentation converts them into monosaccharides and short-chain fatty acids (SCFAs). These microbial metabolites are potent stimulators that induce adipose tissue to release leptin, while simultaneously prompting enteroendocrine cells to secrete glucagon-like peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2), and peptide YY (30). Functionally, leptin drives satiety mechanisms by blocking the activity of neuropeptide Y (NPY) within the hypothalamus (31). Specifically, leptin stimulates anorexigenic (appetite-suppressing) neurons in the arcuate nucleus while inhibiting orexigenic (appetite-stimulating) neurons. It also influences T cells, exerting a regulatory effect on the immune system. Thus, leptin signals the presence of adequate fat stores, activating mechanisms that limit food consumption and enhance energy expenditure. It suppresses appetite, promotes satiety, and boosts sympathetic nervous system activity, thereby elevating blood pressure, heart rate, and thermogenesis (32). GLP-1 modulates the host's satiety levels by reducing appetite (33), whereas GLP-2 mitigates metabolic endotoxemia by fostering the proliferation of intestinal epithelial cells and preserving barrier integrity (34). Peptide YY, conversely, demonstrates an anorexigenic effect by retarding intestinal motility and diminishing gastric and pancreatic secretions (35).

Fat Accumulation and FIAF inhibition.

A pivotal pathway connecting dysbiosis to increased adiposity is the suppression of fasting-induced adipose factor (FIAF), alternatively known as angiopoietin-like protein 4. Current literature suggests that a balanced and healthy microbiome profile is essential for the upregulation of FIAF expression (36). Notably, research highlights propionate as a key modulator in FIAF synthesis (37). Physiologically, FIAF serves as a systemic inhibitor of lipoprotein lipase (LPL). Synthesized across various tissues—including white and brown adipose depots, the liver, and the gut—FIAF restrains LPL activity, which is the enzyme responsible for regulating fatty acid oxidation in muscle and fat tissues. Since LPL drives the extraction of fatty acids from circulating VLDL and chylomicrons for storage as triglycerides, the FIAF-mediated blockade of LPL effectively curtails the accumulation of lipid deposits (38).

Bile Acids and Metabolic Signaling

Bile acids, traditionally known for their role in fat digestion, have recently been shown to exhibit hormone-like properties (39, 40). Bile acids secreted into bile undergo deconjugation and

dehydroxylation by the GM to generate secondary bile acids, namely lithocholic acid and deoxycholic acid. This conversion illustrates that the microbiota metabolizes not only dietary nutrients but also endogenous host molecules, producing systemic effects. Secondary bile acids serve as ligands for the Farnesoid X receptor (FXR), which regulates the host's lipid homeostasis, causing an upregulation of this receptor. Evidence suggests that this process enhances liver triglyceride accumulation in obesity induced by high-fat diets (41). Secondary bile acids also bind to receptors other than FXR. Among these, the receptor exhibiting the highest affinity is the G-protein coupled bile acid receptor-1 (GPBAR-1 or TGR5). Activation of the TGR5 receptor by bile acids has been demonstrated to boost GLP-1 release. In turn, GLP-1 stimulates insulin secretion from the pancreas, thereby regulating glucose homeostasis (40). Beyond these effects, it has been proposed that activated FXR suppresses gluconeogenesis and improves insulin sensitivity in adipose tissue, while TGR5 contributes to enhanced insulin sensitivity and energy expenditure in adipose tissue (38).

Metabolic Endotoxemia and Leaky Gut

Diets high in fat and emulsifiers present in processed foods compromise mucosal integrity and elevate plasma levels of lipopolysaccharide (LPS), a primary constituent of the cell wall of gram-negative bacteria. LPS possesses endotoxin properties due to its lipid A component and can translocate from the gastrointestinal mucosa into the circulation via a mechanism involving Toll-Like Receptor-4 (TLR-4) through increased intestinal permeability (leaky gut) junctions or chylomicrons (42). "Metabolic Endotoxemia" as characterized by Cani et al., denotes a chronic, persistent elevation in LPS levels that remains lower than those seen in sepsis (34).

Inflammation resulting from endotoxemia also triggers the breakdown of the intestinal barrier. Compromised intestinal permeability incites systemic inflammation accompanied by high fat deposition in the liver. The binding of LPS to its receptor, CD14, initiates inflammation. TLR-4, the co-receptor for this binding, activates nuclear factor κβ (NF-κβ) within the inflammatory pathway (43). This leads to increased blood concentrations of pro-inflammatory cytokines such as IL-1, IL-6, plasminogen activator inhibitor-1 (PAI-1), and TNF-α. AMP-activated protein kinase (AMPK), which is activated by SCFAs, suppresses FIAF expression, leading to enhanced LPS activity and the inhibition of peroxisome proliferator-activated receptor (PPAR) co-activator 1α (Pgc-1α), a key player in beta-oxidation. The suppression of PGC-1α, which governs transcription factors involved in glucose, lipid, and cholesterol metabolism such as PPAR-α, PPAR-γ, PPAR-δ, and FXR, accelerates the onset of metabolic diseases like obesity and diabetes (29, 44).

Gut Microbiota and TMAO in the Pathogenesis of Atherosclerosis

Atherosclerosis represents another key pathology heavily influenced by microbial activity. Through the metabolic processing of dietary substrates—specifically choline, phosphatidylcholine, lecithin, and L-carnitine—intestinal bacteria synthesize trimethylamine (TMA). Once absorbed into the portal bloodstream, this metabolite travels to the liver, where the enzyme flavin monooxygenase 3 (FMO3) oxidizes it into trimethylamine N-oxide (TMAO) (45). The accumulation of TMAO in plasma is strongly correlated with a spectrum of adverse outcomes, including cardiovascular disorders, intensified platelet reactivity, and systemic inflammation (46). Current meta-analytic data suggest that TMAO serves as an independent risk factor driving not only the development of atherosclerotic lesions but also chronic kidney disease and heart failure. Mechanistically, TMAO creates a pro-inflammatory environment by upregulating cytokines like IL-1β and TNF-α, while simultaneously suppressing the release of anti-inflammatory mediators such as IL-10 (47). Beyond TMAO synthesis, FMO3 exerts a broader regulatory impact on lipid homeostasis. Experimental models using mice with suppressed FMO3 activity revealed that, even under a high-cholesterol dietary regimen, these animals exhibited reduced hepatic cholesterol synthesis and intestinal lipid uptake, alongside an enhancement in reverse cholesterol transportFurthermore, research exploring the diet-microbiota-thrombosis axis has established that the microbiota modulates hemostasis. Specifically, via the generation of TMAO, gut

bacteria have been shown to potentiate platelet hyperresponsiveness, aggregation, and collagen adhesion—ultimately accelerating clot formation through pathways dependent on thrombin and ADP (49).

Gut-Brain Axis

The influence exerted by the microbial community is not limited to the local intestinal environment; it extends centrally to the nervous system through a critical communication channel termed the "Gut-Brain Axis." Intestinal bacteria possess the inherent capacity to synthesize various neurotransmitters such as serotonin, gamma-aminobutyric acid (GABA), and dopamine or alternatively, to modulate the metabolic precursors required for their production (50). This intricate, bidirectional signaling is fundamentally mediated by the vagus nerve, which functions as the primary anatomical conduit linking the brain and the gut. When microbial balance is compromised, leading to dysbiosis, the resulting disruption in vagal transmission can lead to a desensitization of the body's satiety centers, thereby driving an increase in hedonic and uncontrolled eating patterns (51).

Therapeutic Targets and Future Perspectives

Given these effects, microbiota has become a focal point for treating obesity and its comorbidities. It is believed that medical nutrition therapy can preserve a healthy microbiota or correct dysbiosis. Recent research suggests that this can be accomplished using probiotics and/or prebiotics (13, 48). Studies have shown that prebiotics, such as fructooligosaccharides or galactooligosaccharides, can ameliorate obesity and MetS by manipulating the GM (52-54). The consumption of fructooligosaccharides and galactooligosaccharides enhances the abundance of Bifidobacterium and Lactobacillus strains, which yield positive metabolic outcomes (55). In patients who are obese or overweight, a twelve-week course of fructooligosaccharides led to weight loss, reduced caloric intake, and improved glucose tolerance; these improvements were ascribed to a reduction in postprandial ghrelin and an elevation in peptide YY levels (56).

Prebiotics exert their molecular effects by regulating insulin secretion, fat storage, energy homeostasis, plasma cholesterol levels, and normalizing adipogenesis. Currently, it is proposed that these molecular shifts are mediated through mechanisms involving SCFAs, bacterial bile salt hydrolase activity, metabolic endotoxemia, and the endocannabinoid system (13, 57). Additionally, several studies have indicated that prebiotics also influence risk factors for atherosclerotic cardiovascular disease, including blood pressure and endothelial function (58, 59).

Next Generation Probiotics and Postbiotics

Beyond traditional probiotics (Lactobacillus and Bifidobacterium), the concept of "Next-Generation Probiotics" has emerged in the literatüre (60). The most prominent bacterium in this category is Akkermansia muciniphila. While this bacterium is plentiful in the intestinal mucus layer of healthy individuals, its levels are observed to decline in those with obesity and diabetes (61). Supplementation with Akkermansia has been demonstrated to fortify the intestinal barrier, lower metabolic endotoxemia, and enhance insulin sensitivity. Moreover, in scenarios where live bacteria might pose a risk, "postbiotics" which contain bacterial components or metabolites (e.g., pasteurized Akkermansia) offer a safe alternative (60).

Fecal Microbiota Transplantation (FMT)

FMT involves the transfer of a fecal suspension from a healthy donor to a patient. Animal models have demonstrated that transferring microbiota from obese mice to lean mice results in the lean mice gaining fat. In human trials, it has been reported that FMT from lean donors temporarily boosts insulin sensitivity in patients with MetS, although its impact on long-term weight loss remains inconclusive (62-64).

Pharmacological Agents and Gut Microbiota

It is hypothesized that some of the weight-loss benefits of GLP-1 receptor agonists, which have recently risen in popularity, are mediated through microbiota modulation. While these medications delay gastric emptying and induce satiety, there is also evidence suggesting they can shift the GM composition toward a healthier profile (such as increasing Akkermansia abundance) (65, 66).

CONCLUSION

Obesity and metabolic diseases are recognized to be linked with GM diversity. Moreover, GM contributes to the pathogenesis of these conditions through alterations in the intestinal barrier. Identifying potential opportunities to reverse the pathogenic mechanisms of obesity and related diseases is of paramount importance. Although studies exist demonstrating the relationship between obesity and various genera and species within the Firmicutes phylum, research elucidating mechanisms related to other phyla remains insufficient. Based on this information, modulation of GM stands out as a promising, innovative, and holistic strategy not only for weight management but also for the prevention and treatment of diabetes, CVD, and MetS.

DESCRIPTIONS

No financial support.

No conflict of interest.

REFERENCES

1. Karunarathna I, Gunathilake S, Kap De Alvis P, et al. Obesity: A Multifactorial Disease of Energy Imbalance, Chronic Inflammation, and Systemic Consequences.

2. Organization WH. WHO European regional obesity report 2022. WHO European Regional Obesity Report 20222022.

3. World Obesity Atlas 2024. London: World Obesity Federation.

4. Johansen VBI, Petersen J, Lund J, Mathiesen CV, Fenselau H, Clemmensen C. Brain control of energy homeostasis: Implications for anti-obesity pharmacotherapy. Cell. 2025;188(16):4178-212.

5. Duan F, Wu J, Chang J, et al. Deciphering endocrine function of adipose tissue and its significant influences in obesity-related diseases caused by its dysfunction. Differentiation. 2025;141:100832.

6. Reyes-Farias M, Fernández-García P, Corrales P, et al. Lipid-associated macrophages are more abundant in subcutaneous than visceral adipose tissue in patients with obesity. Obesity. 2025;33(8):1543-54.

7. Azar S, Rehermann B. The role of immune responses and microbiota in adipose tissue homeostasis. The Journal of Physiology. 2025.

8. Cercato C, Fonseca F. Cardiovascular risk and obesity. Diabetology & metabolic syndrome. 2019;11(1):74.

9. Khanna D, Welch BS, Rehman A. Pathophysiology of obesity. 2021.

10. Lin X, Li H. Obesity: epidemiology, pathophysiology, and therapeutics. Frontiers in Endo-crinology, 12, 706978. 2021.

11. Carbone S, Canada JM, Billingsley HE, Siddiqui MS, Elagizi A, Lavie CJ. Obesity paradox in cardiovascular disease: where do we stand? Vascular health and risk management. 2019:89-100.

12. Lampignano L, Zupo R, Donghia R, et al. Cross-sectional relationship among different anthropometric parameters and cardio-metabolic risk factors in a cohort of patients with overweight or obesity. PLoS One. 2020;15(11):e0241841.

13. Kim B, Choi H-N, Yim J-E. Effect of diet on the gut microbiota associated with obesity. Journal of obesity & metabolic syndrome. 2019;28(4):216.

14. Ghanim H, Monte S, Caruana J, Green K, Abuaysheh S, Dandona P. Decreases in neprilysin and vasoconstrictors and increases in vasodilators following bariatric surgery. Diabetes, Obesity and Metabolism. 2018;20(8):2029-33.

15. La Sala L, Pontiroli AE. Prevention of diabetes and cardiovascular disease in obesity. International journal of molecular sciences. 2020;21(21):8178.

16. Stols-Gonçalves D, Tristão LS, Henneman P, Nieuwdorp M. Epigenetic markers and microbiota/metabolite-induced epigenetic modifications in the pathogenesis of obesity, metabolic syndrome, type 2 diabetes, and non-alcoholic fatty liver disease. Current diabetes reports. 2019;19(6):31.

17. Zeng C, Tan H. Gut microbiota and heart, vascular injury. Gut Microbiota and Pathogenesis of Organ Injury. 2020:107-41.

18. Neeland IJ, Lim S, Tchernof A, Gastaldelli A, Rangaswami J, Ndumele CE, et al. Metabolic syndrome. Nature Reviews Disease Primers. 2024;10(1):77.

19. Mili N, Paschou SA, Goulis DG, Dimopoulos M-A, Lambrinoudaki I, Psaltopoulou T. Obesity, metabolic syndrome, and cancer: pathophysiological and therapeutic associations. Endocrine. 2021;74(3):478-97.

20. Su X, Peng D. Emerging functions of adipokines in linking the development of obesity and cardiovascular diseases. Molecular Biology Reports. 2020;47(10):7991-8006.

21. Moore KJ, Tabas I. Macrophages in the pathogenesis of atherosclerosis. Cell. 2011;145(3):341-55.

22. Gomaa EZ. Human gut microbiota/microbiome in health and diseases: a review. Antonie Van Leeuwenhoek. 2020;113(12):2019-40.

23. Dabuo B, Abubakari A, Sankah FE, Aryee HA. Antibiotics and Antimicrobial Resistance Genes in a Gut Microbiota as a Reservoir—A Review. Advanced Gut & Microbiome Research. 2025;2025(1):6574751.

24. Tsai Y-C, Tai W-C, Liang C-M, et al. Alternations of the gut microbiota and the Firmicutes/Bacteroidetes ratio after biologic treatment in inflammatory bowel disease. Journal of Microbiology, Immunology and Infection. 2025;58(1):62-9.

25. Liu H, Zhuang J, Tang P, Li J, Xiong X, Deng H. The role of the gut microbiota in coronary heart disease. Current Atherosclerosis Reports. 2020;22(12):77.

26. Sonnenburg JL, Bäckhed F. Diet–microbiota interactions as moderators of human metabolism. Nature. 2016;535(7610):56-64.

27. Gomes AC, Hoffmann C, Mota JF. The human gut microbiota: Metabolism and perspective in obesity. Gut microbes. 2018;9(4):308-25.

28. Carding S, Verbeke K, Vipond DT, Corfe BM, Owen LJ. Dysbiosis of the gut microbiota in disease. Microbial ecology in health and disease. 2015;26(1):26191.

29. Ilhan N. Gut microbiota and metabolism. Int J Med Biochem. 2018;1(3):115-28.

30. Ahmad S, Assaf M, Thomas B, et al. Fecal Short-Chain Fatty Acids (SCFAs) and Their Role in Metabolic Disorders: A Systematic Review. Cureus. 2025;17(9):e91579.

31. Cunningham A, Stephens J, Harris D. A review on gut microbiota: a central factor in the pathophysiology of obesity. Lipids in health and disease. 2021;20(1):65.

32. Durak M, Akbıyık F, Demirpençe E. Obezite patogenezi. Hacettepe Tıp Dergisi. 2007;38(4):6.

33. Christiansen CB, Gabe MBN, Svendsen B, Dragsted LO, Rosenkilde MM, Holst JJ. The impact of short-chain fatty acids on GLP-1 and PYY secretion from the isolated perfused rat colon. American Journal of Physiology-Gastrointestinal and Liver Physiology. 2018;315(1):G53-G65.

34. Cani PD. Crosstalk between the gut microbiota and the endocannabinoid system: impact on the gut barrier function and the adipose tissue. Clinical Microbiology and Infection. 2012;18:50-3.

35. Merlino DJ, Blomain ES, Aing AS, Waldman SA. Gut-brain endocrine axes in weight regulation and obesity pharmacotherapy. Journal of clinical medicine. 2014;3(3):763-94.

36. Kallus SJ, Brandt LJ. The intestinal microbiota and obesity. Journal of clinical gastroenterology. 2012;46(1):16-24.

37. Lukovac S, Belzer C, Pellis L, et al. Differential modulation by Akkermansia muciniphila and Faecalibacterium prausnitzii of host peripheral lipid metabolism and histone acetylation in mouse gut organoids. MBio. 2014;5(4):10.1128/mbio. 01438-14.

38. Conterno L, Fava F, Viola R, Tuohy KM. Obesity and the gut microbiota: does up-regulating colonic fermentation protect against obesity and metabolic disease? Genes & nutrition. 2011;6(3):241-60.

39. Boulangé CL, Neves AL, Chilloux J, Nicholson JK, Dumas M-E. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. Genome medicine. 2016;8(1):42.

40. Thomas C, Gioiello A, Noriega L, et al. TGR5-mediated bile acid sensing controls glucose homeostasis. Cell metabolism. 2009;10(3):167-77.

41. Parséus A, Sommer N, Sommer F, Caesar R, Molinaro A, Ståhlman M, et al. Microbiota-induced obesity requires farnesoid X receptor. Gut. 2017;66(3):429-37.

42. Xie H, Yu S, Tang M, Xun Y, Shen Q, Wu G. Gut microbiota dysbiosis in inflammatory bowel disease: interaction with intestinal barriers and microbiota-targeted treatment options. Frontiers in Cellular and Infection Microbiology. 2025;15:1608025.

43. Jumpertz R, Le DS, Turnbaugh PJ, et al. Energy-balance studies reveal associations between gut microbes, caloric load, and nutrient absorption in humans. The American journal of clinical nutrition. 2011;94(1):58-65.

44. Fluitman KS, De Clercq NC, Keijser BJ, Visser M, Nieuwdorp M, IJzerman RG. The intestinal microbiota, energy balance, and malnutrition: emphasis on the role of short-chain fatty acids. Expert Review of Endocrinology & Metabolism. 2017;12(3):215-26.

45. Wang X, Chen L, Teng Y, et al. Effect of three oral pathogens on the TMA-TMAO metabolic pathway. Frontiers in Cellular and Infection Microbiology. 2024;14:1413787.

46. Verhaar BJ, Prodan A, Nieuwdorp M, Muller M. Gut microbiota in hypertension and atherosclerosis: a review. Nutrients. 2020;12(10):2982.

47. Chen K, Zheng X, Feng M, Li D, Zhang H. Gut microbiota-dependent metabolite trimethylamine N-oxide contributes to cardiac dysfunction in western diet-induced obese mice. Frontiers in physiology. 2017;8:139.

48. Warrier M, Shih DM, Burrows AC, et al. The TMAO-generating enzyme flavin monooxygenase 3 is a central regulator of cholesterol balance. Cell reports. 2015;10(3):326-38.

49. Zhu W, Gregory JC, Org E, et al. Gut microbial metabolite TMAO enhances platelet hyperreactivity and thrombosis risk. Cell. 2016;165(1):111-24.

50. Strandwitz P. Neurotransmitter modulation by the gut microbiota. Brain Res. 2018;1693(Pt B):128-33.

51. Wang Y, Duan C, Du X, et al. Vagus Nerve and Gut-Brain Communication. The Neuroscientist. 2025;31(3):262-78.

52. Mallappa RH, Rokana N, Duary RK, Panwar H, Batish VK, Grover S. Management of metabolic syndrome through probiotic and prebiotic interventions. Indian journal of endocrinology and metabolism. 2012;16(1):20-7.

53. Nihei N, Okamoto H, Furune T, et al. Dietary α-cyclodextrin modifies gut microbiota and reduces fat accumulation in high-fat-diet-fed obese mice. Biofactors. 2018;44(4):336-47.

54. Cluny NL, Eller LK, Keenan CM, Reimer RA, Sharkey KA. Interactive effects of oligofructose and obesity predisposition on gut hormones and microbiota in diet-induced obese rats. Obesity. 2015;23(4):769-78.

55. Guarner F, Hernández M, García-Peris P, et al. Effect of a mixture of inulin and fructo-oligosaccharide on lactobacillus and bifidobacterium intestinal microbiota of patients receiving radiotherapy; a randomised, double-blind, placebo-controlled trial. Nutricion hospitalaria. 2012;27(6):1908-15.

56. Parnell JA, Reimer RA. Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. The American journal of clinical nutrition. 2009;89(6):1751-9.

57. Green M, Arora K, Prakash S. Microbial medicine: prebiotic and probiotic functional foods to target obesity and metabolic syndrome. International journal of molecular sciences. 2020;21(8):2890.

58. Yeo S-K, Ooi L-G, Lim T-J, Liong M-T. Antihypertensive properties of plant-based prebiotics. International journal of molecular sciences. 2009;10(8):3517-30.

59. O'Connor S, Chouinard-Castonguay S, Gagnon C, Rudkowska I. Prebiotics in the management of components of the metabolic syndrome. Maturitas. 2017;104:11-8.

60. Abraham L, Raise A, Beney L, Lapaquette P, Rieu A. Membrane vesicles produced by next-generation probiotics from the gut as innovative tools for human health. Gut Microbes. 2025;17(1):2552344.

61. Ding Y, Hou Y, Lao X. The Role of Akkermansia muciniphila in Disease Regulation. Probiotics and Antimicrobial Proteins. 2025;17(4):2027-38.

62. Hemachandra S, Rathnayake SN, Jayamaha AA, et al. Fecal Microbiota Transplantation as an Alternative Method in the Treatment of Obesity. Cureus. 2025;17(1).

63. Li X, Sun B, Qin Y, Yue F, Lü X. Amelioration of Obesity-Related Disorders in High-Fat Diet-Fed C57BL/6 Mice Following Fecal Microbiota Transplantation From DL-Norvaline-Dosed Mice. Molecular Nutrition & Food Research. 2025;69(3):e202400577.

64. Zhang Y, Cao J, Wang Y, Fan X, Deng R, Mi J. Effects of Fecal Microbiota Transplantation on Glycemic and Lipid Profiles in Overweight or Obese Patients with Metabolic Disorders: A Systematic Review and Meta-Analysis. Frontiers in Endocrinology.16:1737543.

65. Feng J, Teng Z, Yang Y, Liu J, Chen S. Effects of semaglutide on gut microbiota, cognitive function and inflammation in obese mice. PeerJ. 2024;12:e17891.

66. Gofron KK, Wasilewski A, Małgorzewicz S. Effects of GLP-1 Analogues and Agonists on the Gut Microbiota: A Systematic Review. Nutrients. 2025;17(8):1303.