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REVIEW ARTICLE

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# The role of gut microbiota in the obesity: a literature review

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## Abstract

**Introduction:** Obesity is a multifactorial and polygenic condition that, according to the World Obesity Federation, will affect over 1 billion people by 2030. In this regard, research is being conducted regarding gut microbiota influence on the pathogenesis of this disease, such as inflammation and insulin resistance. Therefore, understanding the gut microbiota and the mechanism by which its modulation through diet and/or the use of probiotics can impact the host and contribute to the treatment of obesity is essential. **Methods:** A systematic review was conducted on the PubMed, Scielo, and ScienceDirect databases, following the PRISMA protocol, from January 2018 to September 2022. **Results and Conclusion:** 415 articles were found. 36 studies were evaluated, and 20 were included in this review. The use of calorierestricting diets, along with the consumption of grains and cereals, was found to be useful in reducing strains that promote inflammation and insulin resistance, factors that are associated with obesity pathogenesis, leading to weight reduction. Other studies examined probiotics use, which led to lipopolysaccharides and insulin resistance reduction, as well as a decrease in the quantity of pro-inflammatory cytokines associated with obesity and type 2 diabetes mellitus. Therefore, combining diets with probiotic therapies may be a strategy for microbiota modulation, aiming to reduce inflammatory markers and insulin resistance.

**Keywords:** Obesity. Gut microbiota. Nutrological therapy.

## Introduction

Obesity is a multifactorial and polygenic condition that, according to the World Obesity Federation, will affect more than 1 billion people by 2030 **[1]**. There has been evidence since the 1990s that obesity results in chronic inflammation related to Toll-like TNF-γ receptor signaling and the production of pro-inflammatory cytokines and chemokines, promoting resistance to the action of insulin **[2]**.

The gastrointestinal tract (GIT) is densely populated by microorganisms, approximately 100 trillion microbes, constituting the gut microbiota, which is considered an endocrine organ involved in the maintenance of energy homeostasis, eating behavior, and the central nervous system (CNS) **[3,4]**.

Diets rich in fats, with a positive energy balance, favor GIT inflammation **[5]**, since they lead to an

imbalance between the main phyla of bacteria in the body, dysbiosis. This, in turn, can alter the functioning of the intestinal barrier and gut-associated lymphoid tissues (GALT) by allowing the passage of structural components of bacteria, such as lipopolysaccharides (LPS), which activate inflammatory pathways that can contribute to the development of insulin resistance [6].

In this inflammatory context, it is known that certain populations of bacteria produce enzymes that increase the efficiency of nutrient digestion, and therefore, the supply of nutrients to the host, thus contributing to increased energy storage in adipose tissue. In addition, the intestinal microbiome can modulate genes involved in energy storage and expenditure. Such findings indicate that modulation of the gut microbiota may have potential therapeutic implications [7].

Thus, probiotics have been increasingly studied for their modulation of the gut microbiota. It is believed that "probiotic supplementation appears to reduce concentrations of low-density lipoproteins (LDL) and total cholesterol; improve atherogenic indices; improve glycemic control; reduce body weight, waist circumference, BMI and abdominal visceral adipose tissue; to improve body composition; and reduce concentrations of pro-inflammatory markers, such as interleukin 6 (IL-6) and TNF-α [8].

Considering the influence of the microbiota on the genesis and progression of obesity, as well as its consequences, knowledge about the gut microbiota and the mechanism by which its modulation through diet and/or use of probiotics can act on the host and contribute to the treatment of obesity is essential.

## Methods

A search was conducted in the PubMed, Scielo, and Science Direct databases adhering to the PRISMA protocol. The search for publications used the following descriptors: "obesity" AND "gut microbiota" AND "inflammation" AND "treatment", according to the database algorithm. The search covered all available texts in English and Portuguese, published between January 2018 and September 2022. The inclusion criteria were: clinical trials, original articles, treatment descriptions, and studies in humans and patients with obesity. The following characteristics were used to eliminate publications: literature reviews, animal studies, letters, articles not available in full, incomplete trials, articles dealing with surgical approaches, the use of vitamins, and physical exercise. Titles and abstracts were analyzed to screen those with positive exclusion criteria. The data were removed from the eligible ones, which include: 1) Probiotic therapy and microbiota change after intervention. 2) Role of these microorganisms in systemic inflammation. 3) Microbiota diversity and its influence on satiety. 4) Influence of microbiota modulation on glucose absorption and insulin resistance. 5) Therapeutic use of intervention with diet and/or live microorganisms such as probiotics in the treatment of obesity.

## Results

The search resulted in 415 articles. The titles and abstracts were evaluated and, based on the exclusion criteria, 288 publications were eliminated. After this initial screening, 127 studies were considered for eligibility, of which 91 were excluded because they met the exclusion criteria. Duplicate publications and those whose content was not within the context of the study were excluded. Thus, 36 studies were considered eligible for analysis. During the full reading of the studies, 16 were disregarded because they met exclusion criteria such as studies in rats, in vitro studies, surgery, use of vitamins, physical exercise as an intervention, and review articles. Consequently, 20 articles were analyzed and included in this review (Table 1), separating those that deal exclusively with probiotics in Table 2.

Table 1. General data of the studies.

| References | Microbiota Modulating Therapy | Microbiota After Therapy | Inflamation | Satiety | Insulin and Glucose |
|---|---|---|---|---|---|
| [9] | Whole Grain | No significant changes | Reduction of IL6 | No change in leptin, GLP-1 and GLP-2 | No significant changes in glucose absorption |
| [10] | Synbiotic supplementation (*Lacticaseibacillus paracasei* strain Shirota; *Bifidobacterium breve*; galactooligosaccharides) | ↑Bifidobacterium, ↑Lactobacillus. ↓*Akkermansia muciniphila* | No significant changes in IL-6 levels | Criterion not assessed | Partially improved the intestinal environment, but without significant changes in glucose absorption. |
| [11] | Pasteurized Akkermansia muciniphila | No significant changes in the gut microbiota | Reduces plasma LPS | No significant changes | Improved insulin sensitivity; reduced insulinemia and total cholesterol |

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|---|---|---|---|---|---|
| [12] | Mediterranean diet versus Control | ↑*Faecalibacterium prausnitzii*; ↓*Ruminococcus gnavus* (pro-inflammatory) | Reduction of inflammation by modulation of microbiota | No significant changes | No significant changes in glycemia. The reduction in insulin resistance was dependent on increased levels of Bacteroides and reduced levels of *Prevotella sp.* and *P. copri*. |
| [13] | Low-Calorie Ketogenic Diet Associated with Synbiotic Supplementation | Diet: Increased microbiota diversity; reduced Proteobacterium; increased Firmicutes.<br><br>Symbiotic supplementation: no significant changes. | Reduction of inflammation by modulation of the microbiota | Criterion not evaluated | Criterion not evaluated |
| [14] | Probiotic Group: Diet + Bifidobacterium lactis.<br><br>Symbiotic Group: Diet + Bifidobacterium lactis and fructooligosaccharides<br><br>Control Group: Diet | Probiotics and Synbiotics: Change in Bacteroidetes, Firmicutes and Verrucomicrobia | All groups showed a reduction in inflammation, so diet alone was sufficient | Criterion not evaluated | The Symbiotic Group obtained an increase in serum glutamine and arginine, which may be related to increased insulin sensitivity and reduced inflammation. |
| [15] | High-fiber diet | ↑Lachnospira ↓Actinomycetaceae | High concentration of acetate, inhibiting the production of proinflammatory cytokines | Increased Short Chain Fatty Acids, which can increase leptin and PYY levels | Attenuation of isovalerate production, reducing insulin resistance |
| [16] | Weight loss through lifestyle changes | No significant changes. Slight increase in families Desulfovibrionaceae, Leptospiraceae, Syntrophomonadacea and , Thermotogaceae and Verrucomicrobiaceae. | Reduction of proteins related to inflammation | Criterion not evaluated | Improved insulin sensitivity |
| [17] | Mediterranean diet versus high-protein diet | Mediterranean Diet: Reduction of Ruminococcaceae, Acidaminococcaceae, Coriobacteriaceae. Increase in Clostridiaceae and Desulfovibrionaceae. | Criteria not evaluated | Criterion not evaluated | High-protein diet more effectively reduced insulin resistance and improved glycemic variability |
| [18] | Whole Grains and Fruits+Vegetables | Increased diversity in the Fruits+Vegetables group | Whole Grains and Fruits+Vegetables: Reduced LBP<br><br>Fruits+Vegetable s: Reduced IL-6.<br><br>Whole Grains: Reduced TNF-α | Criterion not evaluated | Criterion not evaluated |
| [19] | Rye vs Wheat | Rye-based diet increased Agathobacter numbers and reduced Ruminococcus group abundance | Microbiota alteration in ryebased diet may have reduced inflammation | Butyrate, related to reduced appetite, had an increased amount in the Rye group. | No changes |

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| [20] | High-Protein, High-Fat Diet (Low Carbohydrate HighFat/LCHF) | Increase in Alistipes, Odoribacter splanchnicus, Ruminococcus bicirculans, Butyricimonas, and Enterobacteriaceae<br><br>Reduction in Collinsella and Dorea, often associated with inflammation | Reduced inflammation due to microbiota change | Criterion not evaluated | Criterion not evaluated |
| [21] | Probiotic Group (Bifidobacterium pseudocatenulatum CECT 7765) versus Control Group | Probiotic administration significantly increased the proportion of members of the family Rikenellaceae and the genus Alistipes | Reduced inflammation with increased groups of bacteria associated with lean phenotype. Increased levels of omentin-1 (antiinflammatory) | Criterion not evaluated | Criterion not evaluated |
| [22] | Very Low Calorie Diet (VLCD) | Reduction of the genus Roseburia. Increase of Christensenellaceae; | Criterion not assessed | Pronounced drop in serum leptin levels. | Increased insulin sensitivity |
| [23] | Pomegranate Extract versus Control | Pomegranate Extract Group: Increase in Bacteroides, Faecalibacterium, Butyricicoccus, Odoribacter and Butyricimonas. Reduction in Parvimonas, Methanobrevibacter and Methanosphaera, associated with inflammation. | Pomegranate Extract Group obtained a reduction in PCR. | Criterion not evaluated | Criterion not evaluated |
| [24] | Prebiotic (inulin) versus Placebo (maltodextrin) | Inulin Group: increase in Bifidobacterium, at the level of the Bifidobacteriaceae phylum | Inulin Group: reduction of fecal calprotectin, an inflammatory marker, suggesting reduced inflammation | Increase in Short Chain Fatty Acids | Criterion not evaluated |
| [25] | Western Diet Rice-Based Diet Korean Diet | Western diet: Bacteroides predominant. Rice-based diet: Prevotella predominant. Korean diet: Ruminococcaceae predominant | Participants on the Korean Diet had lower PCR results, indicating less inflammation. | Rice-based diet with Prevotella dominance increased production of Short-Chain Fatty Acids | Criterion not evaluated |
| [26] | Multifunctional Diet (potential antiinflammatory) versus Control | Multifunctional Diet Group: Increased Prevotella copri | Reduction of cardiovascular inflammatory markers | Criterion not evaluated | Criterion not evaluated |
| [27] | Oleoylethanolamide (OEA) versus Placebo | Increase in Akkermansia muciniphila. | Reduction of proinflammatory cytokines. | OEA stimulates the release of GLP-1, controlling appetite. | Criterion not evaluated |

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|---|---|---|---|---|---|
| [28] | Probiotic (*Lactobacillus reuteri* V3401) versus Placebo | Increase in the phylum Verrucomicrobia. | Reduction of IL6 | Criterion not evaluated | No significant effects |

Table 2. Probiotics.

| References | Probiotics | Dose | Usage Time |
|---|---|---|---|
| [8] | Mixed: *Lactobacillus acidophilus and casei; Lactococcus lactis; Bifidobacterium bifidum* and *lactis* | 2x$10^{10}$ Colony forming units/day | 8 weeks |
| [10] | *Lacticaseibacillus paracasei strain Shirota* e *Bifidobacterium breve strain Yakult*, e *galactooligosaccharides* | 3.0 g powder containing at least 3 ×$10^{8}$ living *Lacticaseibacillus paracasei*, 3×$10^{8}$ Bifidobacterium, and 7.5 g galactooligosaccharides per day. Patients were instructed to ingest the mixture twice daily (2.0g powder and 5.0g galactooligosaccharides at breakfast and 1.0g powder and 2.5 g at dinner). | 24 weeks |
| [11] | *Akkermansia muciniphila* | $10^{10}$ per day | 3 weeks |
| [14] | Probiotic Group: Diet + *Bifidobacterium lactis*.<br><br>Symbiotic Group: Diet + *Bifidobacterium lactis* and fructooligosaccharides.<br><br>Control Group: Diet | Probiotic Group: $10^{9}$ colony-forming units of *B. lactis* and one sachet containing 5g of maltodextrin.<br><br>Symbiotic Group: $10^{9}$ colony-forming units of *B. lactis* and one sachet containing 5g of fructooligosaccharides. | 8 weeks |
| [28] | *L. reuteri* V3401 | 5 x $10^{9}$ colony forming units per day | 12 weeks |

## Development

### Influence of Diet on Microbiota Variety

The mechanisms that relate diet, microbiota, and obesity are linked to increased endotoxemia, intestinal permeability [29], and inflammation, mediated by the imbalance of the gut microbiota. Given this, therapies that alter the caloric intake of obese patients, to modulate the intestinal population and reduce the inflammatory status, are the new line of study in the treatment of the disease.

### Diets

This study found data that favor the hypothesis that some dietary interventions can modulate the microbiota. Among them, studies that used a diet rich in whole grains did not obtain significant changes in the microbiota, despite proving a reduction in inflammatory cytokines, TNF-alpha (18) and IL-6 [9], restoring intestinal permeability. Given this, the use of a diet rich in grains can be considered a strong ally in the fight against obesity, both in terms of weight loss and in reducing inflammation, despite not significantly modulating the population of intestinal microorganisms.

Other widely studied cereals are wheat and rye. A recent study [19] compared diets based on these two grains, finding an increase in Agathobacter and a reduction in Ruminococcus in the rye-based diet, suggesting that this change in the microbiota may have reduced systemic inflammation. Among other diets, the Mediterranean diet was studied by Meslier et al. [12], who found a reduction in inflammation resulting from the modulation of the microbiota by changing eating habits, which increased the amount of *Faecalibacterium prausnitzii* and reduced *Ruminococcus gnavus* (pro-inflammatory). The study also found a reduction in insulin resistance, which was dependent on the increase in Bacteroidetes, which is in line with what is found in the current literature.

Still, in the context of the Mediterranean diet, another study [17] compared the effects of this diet with the High Protein Diet. The results favor the Mediterranean diet, as there was a reduction in Ruminococcaceae, Acidaminococcaceae, and Coriobacteriaceae and an increase in Clostridiaceae and Desulfovibrionaceae. Despite this, the high protein diet was more effective in reducing insulin resistance, thus combating the pathogenesis of obesity. Therefore, further studies comparing the two diets are needed to elucidate the mechanisms of each one in the body and the gut microbiota.

Diets rich in fiber facilitate healthy intestinal flow, so studies have been conducted to evaluate the influence of a fiber-based diet on the microbiota [15].

There was an increase in Lachnospira and a reduction in Actinomycetaceae, contributing to the high concentration of acetate, consequently inhibiting the synthesis of pro-inflammatory cytokines, and combating the systemic inflammation common in obesity. In addition, there was the production of isovalerate, a molecule that contributes to the reduction of insulin resistance.

Low-calorie and low-carbohydrate diets have become famous in the media over the last decade due to their use by influential figures in society. Some studies have been conducted on diets that use the term "low carb", that is, low in carbohydrates. One of them **[20]** analyzed a diet rich in protein and fat, but low in carbohydrates, finding a reduction in the BMI of volunteers who underwent this intervention. In addition, there was a parallel reduction in the BMI of bacteria commonly associated with inflammatory processes, such as Collinsella and Dorea. Thus, the study found a strong relationship between the reduction in systemic inflammation and the modulation of intestinal microorganisms via dietary changes based on lower carbohydrate intake, which also aids in weight loss by reducing BMI.

In addition to this study, Alemán and colleagues studied the physiological consequences of a low-calorie diet (Very Low-Calorie Diet/VLCD) **[22]**, finding an increase in insulin sensitivity. Other studies have focused on dietary differences between populations. Wu and colleagues compared three different types of diets found in South Korea: a Western diet, a rice-based diet, and the Korean diet **[25]**. The results found a predominance of different bacteria in each type of diet. In the Korean diet, the predominant group was Ruminococcaceae, which may have contributed to the lower amounts of C-reactive protein, suggesting lower inflammation in those who followed these foods. In this sense, it is essential to conduct studies that delve deeper into the theme of the predominance of different microorganisms depending on the food culture of different countries and socioeconomic segments of society.

Finally, researchers evaluated some foods with potential anti-inflammatory effects in the diet **[26]**. Patients who underwent this intervention had an increase in *Prevotella copri* in their gut microbiota with a reduction in cardiovascular inflammatory markers.

## Prebiotics, Probiotics and Symbiotics

The findings regarding the use of probiotics are extremely favorable in terms of modulating microorganisms. Symbiotic supplementation with the use of *L. paracasei shirota* **[10]** increased the number of individuals of the Lactobacillus genus, despite reducing the number of the bacterium *Akkermansia muciniphila,* known for its anti-inflammatory characteristics. Depommier and colleagues **[11]** used pasteurized *Akkermansia muciniphila* supplementation in their study, significantly reducing the concentration of LPS in plasma, a factor that contributed to combating systemic inflammation. Furthermore, the study found good results in improving insulin sensitivity, a factor that contributes immensely to the pathophysiology of obesity associated with type 2 DM.

A study administered *Lactobacillus reuteri* V3401, managing to alter the microbiota at the phylum level, increasing the amount of Verrucomicrobia. This change was associated with a reduction in IL-6, an inflammatory cytokine **[28]**. Another way to use synbiotic supplementation was to combine it with already-known diets, such as the Low-Calorie Ketogenic Diet **[13]**. The administration of synbiotics did not affect the diversity of the microbiota but showed an increase in the population of Odoribacter and Lachnospira, producers of anti-inflammatory mediators.

Crovesy et al. **[14]** demonstrated that the use of probiotics and symbiotics is capable of altering the Firmicutes/Bacteroidetes ratio, in addition to altering the quantity of Verrucomicrobia. In the study, the group in which only symbiotics were administered had a significant increase in serum glutamine levels, which was associated with increased insulin sensitivity and combating the systemic inflammatory process. The use of Bifidobacterium pseudocatenulatum CECT 7756 as a probiotic obtained good results in modulating the microbiota **[21]**. It significantly increased the proportion of members of the Rikenellaceae family and the Alistipes genus, reducing inflammation due to the increase in bacteria commonly associated with the lean phenotype, in addition to increasing the level of omentin-1, an antiinflammatory cytokine. Another study **[24]** used prebiotics (inulin) to manipulate the intestinal microbial population, achieving an increase in Bifidobacterium, in addition to reducing fecal calprotectin, an important intestinal inflammatory marker, a fact that can be associated with changes in the microbiota.

The use of substances that stimulate the growth of specific species of microbiota is also studied, to select the predominant type of microorganism in the intestine and modulate tissue inflammation. In this context, Yahoo et al. studied oleoyl ethanolamide and its effect on the species *Akkermansia muciniphila* **[27]**. The results were significant regarding the increase in the desired species through the use of the compound, in addition to reducing the production of pro-inflammatory cytokines.

Also in this perspective, another study evaluated the influence of vitamin D supplementation on the microbiota **[30]**, evidencing an increase in the genus Lachnospira and a reduction in the genus Blautia. Despite the changes in the microbiota, no significant reduction in inflammation or insulin sensitivity was detected. A study that evaluated pomegranate extract as an intervention obtained better results regarding the modulation of microbiota and inflammation **[23]**. The increase in Bacteroides and the reduction in Parvimonas, Methanobrevibacter, and Methanosphaera, bacteria associated with inflammation, contributed positively to the reduction of the systemic inflammatory process.

### Does Microbiota Therapy Have Any Influence on Blood Glucose and Insulin Resistance?

Insulin resistance is usually present in patients with Metabolic Syndrome, presenting Type 2 Diabetes Mellitus together with obesity. In this view, the attempt to increase insulin sensitivity in patients is a promising path in the biotherapeutic alternatives for the treatment of obesity.

In this sense, the modulation of Bacteroidetes was positively associated with the reduction of insulin resistance and was dependent on Bacteroides **[12]**. Another result in this sense was the increase in *Akkermansia muciniphila* causing an increase in insulin sensitivity, reducing insulinemia, and pasteurized *A. muciniphila* markedly and significantly improved the insulin sensitivity index by approximately 30% compared to the Placebo group **[11]**. Furthermore, probiotics from the Bifidobacterium group were related to increased insulin sensitivity **[14]**.

Obesity has a complex and multifactorial etiology, and limited progress in the treatment of obesity can largely be attributed to the failure to apply a systems biology-based approach to understand its pathophysiology and develop individualized strategies to achieve sustained weight loss and prevention. It has been identified how the gut microbiota can regulate metabolism, adiposity, homeostasis, and energy balance, as well as central appetite and food reward signaling, which together play crucial roles in obesity. Therefore, it is now another strategy to be added to anti-obesity therapy.

High-fat diets appear to be more relevant in modulating dysbiosis, with most studies showing an increase in the Firmicutes and Bacteroidetes ratio, with several other changes in other taxa, thus leading to inflammatory processes that alter permeability, which can lead to obesity. Further studies are essential to clarify how the various interventional diets can alter the microbiota, preventing inflammatory processes. Furthermore, it is necessary to address the mechanisms of changes in satiety and appetite after modulation of the gut microbiota, to better treat patients with new therapies.

Finally, probiotic therapy may be a strategy in conjunction with dietary changes to improve the composition of the microbiota, among which the following stand out: *L. paracasei Shirota, Akkermansia muciniphila*, and *Lactobacillus reuteri* V3401, responsible for the reduction of inflammatory markers. In most of the studies evaluated, it was clear that modulation of the microbiota through physical exercise, diet, use of prebiotics, and/or probiotics have a positive effect in reducing inflammatory markers and stimulating satiety. Regarding the regulation of glucose homeostasis and its relationship with insulin, further studies are needed to evaluate this criterion.

## Conclusion

It was concluded that the gut microbiota is becoming a target for new anti-obesity therapies. Further research is needed to elucidate the intricate gut-microbiota-host relationship and the potential of gut microbiota-targeted strategies, such as dietary interventions and fecal microbiota transplantation, as promising metabolic therapies that help patients maintain a healthy weight throughout life. This is achieved by combining several mechanisms that have been proven in this regard, including increased insulin sensitivity, reduced systemic inflammation, and control of satiety.

## CRediT

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No additional data are available.

## Conflict of Interest

The authors declare no conflict of interest.

## Similarity Check

It was applied by Ithenticate[@].

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It was performed.



## References

1. World Obesity Atlas 2022. One Billion People Globally Estimated to be Living with Obesity by 2030. Httpswwwworldobesityorgresourcesresource-Libr-Obes-Atlas-2022. 2022 Mar;
2. Rogero M, Calder P. Obesity, Inflammation, Toll-Like Receptor 4 and Fatty Acids. Nutrients. 2018 Mar 30;10(4):432.
3. Duranti S, Ferrario C, van Sinderen D, Ventura M, Turroni F. Obesity and microbiota: an example of an intricate relationship. Genes Nutr. 2017 Dec;12(1):18.
4. Rosenbaum M, Knight R, Leibel RL. The gut microbiota in human energy homeostasis and obesity. Trends Endocrinol Metab. 2015 Sep;26(9):493–501.
5. Shen W, Gaskins HR, McIntosh MK. Influence of dietary fat on intestinal microbes, inflammation, barrier function and metabolic outcomes. J Nutr Biochem. 2014 Mar;25(3):270–80.
6. Barazzoni R, Cappellari GG, Ragni M, Nisoli E. Insulin resistance in obesity: an overview of fundamental alterations. Eat Weight Disord - Stud Anorex Bulim Obes. 2018 Apr;23(2):149–57.
7. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Human gut microbes associated with obesity. Nature. 2006 Dec;444(7122):1022–3.
8. Gomes AC, de Sousa RGM, Botelho PB, Gomes TLN, Prada PO, Mota JF. The additional effects of a probiotic mix on abdominal adiposity and antioxidant Status: A double-blind, randomized trial: Probiotic Mix and Abdominal Adiposity. Obesity. 2017 Jan;25(1):30–8.
9. Roager HM, Vogt JK, Kristensen M, Hansen LBS, Ibrügger S, Mærkedahl RB, et al. Whole grain-rich diet reduces body weight and systemic low-grade inflammation without inducing major changes of the gut microbiome: a randomised cross-over trial. Gut. 2019 Jan;68(1):83–93.
10. Kanazawa A, Aida M, Yoshida Y, Kaga H, Katahira T, Suzuki L, et al. Effects of Synbiotic Supplementation on Chronic Inflammation and the Gut Microbiota in Obese Patients with Type 2 Diabetes Mellitus: A Randomized Controlled Study. Nutrients. 2021 Feb;13(2):558. 11.
11. Depommier C, Everard A, Druart C, Plovier H, Hul MV, Vieira-Silva S, et al. Supplementation with Akkermansia muciniphila in overweight and obese human volunteers: a proof-of-concept exploratory study. Nat Med. 2019 Jul;25(7):1096–103.
12. Meslier V, Laiola M, Roager HM, Filippis FD, Roume H, Quinquis B, et al. Mediterranean diet intervention in overweight and obese subjects lowers plasma cholesterol and causes changes

in the gut microbiome and metabolome independently of energy intake. Gut. 2020 Jul;69(7):1258–68.

13. Gutiérrez‐Repiso C, Hernández‐García C, García‐Almeida JM, Bellido D, Martín‐Núñez GM, Sánchez‐Alcoholado L, et al. Effect of Synbiotic Supplementation in a Very-Low-Calorie Ketogenic Diet on Weight Loss Achievement and Gut Microbiota: A Randomized Controlled Pilot Study. Mol Nutr Food Res. 2019 Oct;63(19):1900167.
14. Crovesy L, El-Bacha T, Rosado EL. Modulation of the gut microbiota by probiotics and symbiotics is associated with changes in serum metabolite profile related to a decrease in inflammation and overall benefits to metabolic health: a double-blind randomized controlled clinical trial in women with obesity. Food Funct. 2021;12(5):2161–70.
15. Mayengbam S, Lambert JE, Parnell JA, Tunnicliffe JM, Nicolucci AC, Han J, et al. Impact of dietary fiber supplementation on modulating microbiota–host–metabolic axes in obesity. J Nutr Biochem. 2019 Feb;64:228–36.
16. Biemann R, Buß E, Benndorf D, Lehmann T, Schallert K, Püttker S, et al. Fecal Metaproteomics Reveals Reduced Gut Inflammation and Changed Microbial Metabolism Following Lifestyle-Induced Weight Loss. Biomolecules. 2021 May;11(5):726.
17. Tettamanzi F, Bagnardi V, Louca P, Nogal A, Monti GS, Mambrini SP, et al. A High Protein Diet Is More Effective in Improving Insulin Resistance and Glycemic Variability Compared to a Mediterranean Diet—A Cross-Over Controlled Inpatient Dietary Study. Nutrients. 2021 Dec;13(12):4380.
18. Kopf JC, Suhr MJ, Clarke J, Eyun S il, Riethoven JJM, Ramer-Tait AE, et al. Role of whole grains versus fruits and vegetables in reducing subclinical inflammation and promoting gastrointestinal health in individuals affected by overweight and obesity: a randomized controlled trial. Nutr J. 2018 Dec;17(1):72.
19. Iversen KN, Dicksved J, Zoki C, Fristedt R, Pelve EA, Langton M, et al. The Effects of High Fiber Rye, Compared to Refined Wheat, on Gut Microbiota Composition, Plasma Short Chain Fatty Acids, and Implications for Weight Loss and Metabolic Risk Factors (the RyeWeight Study). Nutrients. 2022 Apr;14(8):1669.
20. Jaagura M, Viiard E, Karu‐Lavits K, Adamberg K. Low‐carbohydrate high‐fat weight reduction diet induces changes in human gut microbiota. MicrobiologyOpen. 2021 Jun;10(3).
21. Sanchis-Chordà J, Pulgar EMG del, Carrasco-Luna J, Benítez-Páez A, Sanz Y, Codoñer-Franch P. Bifidobacterium pseudocatenulatum CECT 7765 supplementation improves inflammatory status in insulin-resistant obese children. Eur J Nutr. 2018 Sep;
22. Alemán JO, Bokulich NA, Swann JR, Walker JM, Rosa JCD, Battaglia T, et al. Fecal microbiota and bile acid interactions with systemic and adipose tissue metabolism in diet-induced weight loss of obese postmenopausal women. J Transl Med. 2018 Dec;16(1):244.
23. González-Sarrías A, Romo-Vaquero M, García-Villalba R, Cortés-Martín A, Selma MV, Espín JC. The Endotoxemia Marker Lipopolysaccharide-Binding Protein is Reduced in Overweight-Obese Subjects Consuming Pomegranate Extract by Modulating the Gut Microbiota: A Randomized Clinical Trial. Mol Nutr Food Res. 2018 Jun;62(11):1800160.
24. Neyrinck AM, Rodriguez J, Zhang Z, Seethaler B, Sánchez CR, Roumain M, et al. Prebiotic dietary fibre intervention improves fecal markers related to inflammation in obese patients: results from the Food4Gut randomized placebo-controlled trial. Eur J Nutr. 2021 Sep;60(6):3159–70.
25. Wu X, Unno T, Kang S, Park S. A Korean-Style Balanced Diet Has a Potential Connection with Ruminococcaceae Enterotype and Reduction of Metabolic Syndrome Incidence in Korean Adults. Nutrients. 2021 Feb;13(2):495.
26. Marungruang N, Tovar J, Björck I, Hållenius FF. Improvement in cardiometabolic risk markers following a multifunctional diet is associated with gut microbial taxa in healthy overweight and obese subjects. Eur J Nutr. 2018 Dec;57(8):2927–36.
27. Payahoo L, Khajebishak Y, Alivand MR, Soleimanzade H, Alipour S, Barzegari A, et al. Investigation the effect of oleoylethanolamide supplementation on the abundance of Akkermansia muciniphila bacterium and the dietary intakes in people with obesity: A randomized clinical trial. Appetite. 2019 Oct;141:104301.
28. Tenorio-Jiménez C, Martínez-Ramírez MJ, Castillo-Codes ID, Arraiza-Irigoyen C, Tercero-Lozano M, Camacho J, et al. Lactobacillus reuteri V3401 Reduces Inflammatory

Biomarkers and Modifies the Gastrointestinal Microbiome in Adults with Metabolic Syndrome: The PROSIR Study. Nutrients. 2019 Jul;11(8):1761.

29. Ghosh SS, Wang J, Yannie PJ, Ghosh S. Intestinal Barrier Dysfunction, LPS Translocation, and Disease Development. J Endocr Soc. 2020 Feb 1;4(2):bvz039.
30. Naderpoor N, Mousa A, Arango LFG, Barrett HL, Nitert MD, Courten B de. Effect of Vitamin D Supplementation on Faecal Microbiota: A Randomised Clinical Trial. Nutrients. 2019 Nov;11(12):2888.