# Probiotic foods as functional foods for modulating obesity

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#### **ABSTRACT**

**Introduction:** Obesity is a multifactorial chronic disease that involves many internal and external factors, causing the death of at least 2.8 million people each year, according to the World Health Organization. Therefore, there is a need for nobler treatments to lose weight. Probiotic foods are classified as functional foods due to their nutritional contribution. **Objective:** To describe the impact of probiotic foods in the treatment of obesity. **Methods:** A review of 61 studies from different databases was carried out. **Results:** It is known that probiotics have several action mechanisms that beneficially affect the gut microbiota to maintain homoeostasis in the whole organism. The relationship between these microorganisms and the control and modulation of a person's body weight has been observed. **Conclusion:** The beneficial effects of probiotics are strain-specific and may impact obesity through different action mechanisms, such as abdominal fat decrease, changes in inflammatory biomarkers, microbiota restoration, and reduction in triglycerides serum levels.

**Key words:** obesity; functional foods; probiotic foods; gut microbiota; gut brain axis.

## **RESUMEN**

Introducción: La obesidad es una enfermedad crónica multifactorial que involucra muchos factores internos y externos que causan la muerte de al menos 2.8 millones de personas cada año de acuerdo con la Oganización Mundial de la Salud. Por tanto, surge la necesidad de encontrar tratamientos más nobles. Los alimentos probióticos se clasifican como alimentos funcionales por su aporte nutricional. Objetivo: Describir el impacto de los alimentos probióticos en el tratamiento de la obesidad. Metodología: Se llevó a cabo una revisión de 61 estudios de diferentes bases de datos. Resultados: Se sabe que los probióticos tienen varios mecanismos de acción que afectan de manera beneficiosa a la microbiota intestinal para mantener la homoeostasis en todo el organismo. Se conoce la relación entre estos microorganismos y el control y modulación del peso corporal de una persona. Conclusión: Los efectos benéficos de los probióticos son específicos de la cepa y pueden impactar a la obesidad a través de diferentes mecanismos de acción como disminución de la grasa abdominal, cambios en biomarcadores inflamatorios, restauración de la microbiota y reducción de los niveles de triglicéridos séricos .

Palabras clave: obesidad; alimentos funcionales; alimentos probióticos; microbiota intestinal; eje intestino-cerebro.

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#### INTRODUCTION

Obesity is characterized by being a multifactorial chronic disease that involves many environmental, genetic, and metabolic factors. It refers to an abnormal increase in body fat. The body mass index (BMI) is usually used as a diagnostic measure; this value is derived from the relationship between weight and height (kg/m²), classifying an individual as underweight < 18.5 kg/m<sup>2</sup>, normal weight 18.5–24.9 kg/m<sup>2</sup>, overweight 25–29.9  $kg/m^2$ , and obese > 30  $kg/m^2$ . In early 2020, the World Health Organization (WHO) warned that obesity and overweight had reached global epidemic figures, affecting approximately 40% of the population (children, teenagers, and adults), and caused the death of at least 2.8 million people each year. It also pointed out that those who show greater susceptibility are men under 50 years old.<sup>2</sup> The pathophysiology of obesity may seem very simple: Calorie consumption exceeds energy expenditure. However, it is not only the result of bad habits, such as a diet high in sugar, alcohol, and fat, or a sedentary lifestyle. There is evidence that the pathogenesis involves processes much more complex than just calorie accumulation.3 There are multiple etiological factors that have been identified, among them are: absence of leptin (an adipokine that increases satiety),<sup>4</sup> genetic mutations,5 and hypothyroidism, characterized by a low concentration of thyroid hormones triiodothyronine (T3) and thyroxine (T4), associated with a decrease in metabolic activity. Obesity is also a risk factor associated with other chronic ailments as diabetes, cardiovascular diseases, cancer, arterial hypertension, coronary heart disease, cerebrovascular accidents, lung diseases, liver diseases, and osteoarthritis.6

If dietary approaches and physical activity are not sufficient to achieve goals, health professionals may consider implementing drug and supplement therapies (like appetite suppressants). In severe cases, options like bariatric surgery (stomach portion removal) may be considered. These strategies can have unfavorable side effects;<sup>7</sup> therefore, new approaches are necessary for weight loss improvement. Consumers nowadays believe that food may directly impact their health. There is a general perception on the benefits of different food therapies that may be more effective than medical treatments. So, many food products not only satisfy hunger and provide different necessary nutrients but also contribute with essential components for the prevention of different diseases and improve physical and mental health. They are known as functional foods.<sup>8</sup>

The Science of Functional Foods in Europe (FUFOSE) defines functional foods as those "that satisfactorily demonstrate in adequate concentrations beneficially affect one or more functions in the human body beyond nourishing it in such a way as to improve its state of health and/or prevent diseases. They are still food and part of a normal diet." They can be used as weight management tools to fight obesity and enhance

weight loss by regulating appetite, satiety, energy output, thermogenesis, and adipogenesis. <sup>10</sup> Carbohydrate-based food (brown rice), protein-based food (legumes), fruits and vegetables, and specific beverages (tea) are selected foods due to the potential effects on weight loss. <sup>10</sup>

Probiotic foods are well known and widely used because they possess various nutritional and therapeutic properties to the host when administered in adequate amounts. They are considered functional foods that may be used strategically as weight management tools against obesity, specifically restoring balance by acting directly upon the gut microbiota. The gut microbiota are all the living microorganisms mainly in the colon. The microbiota has digestive properties and is also involved in nutrition and immunity as well as other homeostatic aspects. 11 In recent years, much attention has been drawn to the contribution of gut microbiota to the development of obesity. Research has shown that the microbiota of obese individuals is structurally and functionally different from healthier individuals. Most obesity studies evaluating overweight and obese patients show an imbalance characterized by a lower diversity and alterations in action mechanisms (immune dysregulation, energy, and gut hormone regulation, and proinflammatory mechanisms), which can lead to uncontrolled weight. 12,13 The objective of this review is to describe the impact of probiotic foods in the treatment of obesity, the microorganisms involved, and their action mechanisms.

## **METHODS**

A literature search was conducted using Google Scholar as the main search engine. On the other hand, the scientific databases used were National Center of Biotechnology (NCBI), PubMed Central (PMC), ResearchGate, MDPI SciELO, Wiley Online Library, Frontiers, Science Direct, and MDPI Karger. The following keywords were used: obesity AND probiotics, obesity AND functional foods, functional food AND probiotic foods, gut microbiota AND obesity, gut microbiota AND probiotics, gut microbiota AND gut-brain axis. The articles were selected based on the following criteria: open accessibility, publication year (2015–2021; but some older articles were selected due to their methodology and results), studies in English and Spanish, and clinical trials and animal obesity model studies using probiotic foods.

## **RESULTS**

#### **Gut microbiota and obesity**

Gut microbiota refers to the all the microorganisms found in an environment whereas microbiome refers to all the microorganisms and their genes, a collection of their genomes.



Sometimes these terms are used as synonyms but differ from one another.<sup>14</sup> Gut microbiota consists of three main phyla: Bacteroidetes (Porphyromonas, Prevotella, Bacteroides), Firmicutes (Ruminococcus, Clostridium, Lactobacillus and Eubacteria) and Actinobacteria (Bifidobacteria), along with Proteobacteria, Fusobacteria, and Verrumicrobia. 15 The gut microbiota comprises all commensal and pathogenic bacteria residing in the gastrointestinal tract (GIT). It plays a key role in the maintenance of health, metabolism modulation, and disease pathogenesis.16 To do so, in the host's organism, it executes various action mechanisms of nutritional and immune nature.<sup>17,18</sup> It enhances nutrient and mineral absorption, enzyme synthesis, water-soluble B and K vitamins, amino acids, folic acid, and biotin. It also favors the production of short-chain fatty acids (SCFAs) through the fermentation of non-digestible substrates of dietary fibers. In addition, the gut microbiota and the innate immune system are in extensive communication. This means gut microbiota stimulates the development of nonspecific or innate (physical and chemical barriers, epithelial surfaces) and specific or adaptive (lymphocytes and their antibodies) immune system components as well as the maturation of immune cells, just after birth and during the host's entire life. The gut represents a stable ecological niche for its inhabiting bacteria that rely on the host's physiology to maintain their basic biological processes. Then, it establishes an interaction, called symbiosis, with the host. 19 It contributes to all the physiology from digestion to fertility, and it affects the brain function for the regulation of the host's appetite.<sup>20</sup>

# Appetite regulation and host metabolism

The hypothalamus is the main center of homeostatic control of energy balance through the neural and humoral pathways.<sup>21</sup> This center involves a homeostatic regulation of food intake by energy inflow and expenditure or outflow, and it communicates directly with the gut; this circuit is called gut-brain-axis.<sup>22</sup> It is an enteroendocrine system and is the largest endocrine organ in the human body. Its enteroendocrine cells (EEC) are distributed throughout the intestinal tract and secrete several peptides that act like hormones (hunger hormones) and neurotransmitters: gastrin, ghrelin, somatostatin, serotonin, cholecystokinin (CCK), glucose-dependent insulinotropic peptide (GIP), glucagon-like peptide 1 (GLP-1), and peptide YY (PYY). They act as a response to the presence of food (nutrient and mechanical stimuli). These hormones and neurotransmitters mediate effects on the secretion of other gastrointestinal substances (insulin, bile acids, and gastric acids), gut motility, and food intake by the activation of the vagus nerve (VN).23,24 The latter innervates all the digestive system, and its fibers are all distributed across all the layers of the digestive system. VN sends a signal to the hypothalamus to control satiation and the host energy balance and metabolism. Evidence indicates that the gut microbiota plays an important role in a bidirectional communication between the brain and the gut. The bacteria greatly influence the host energy metabolism, produce several proteins that activate satiety pathways, and subsequently, affect food intake and energy homoeostasis.<sup>24</sup>

## Gut microbiota in gut-brain axis

The VN does not cross the epithelial layer, so it is not in direct contact with the microbiota. The nerve fiber only senses microbiota signals through the diffusion of bacterial compounds, metabolites, and enterochromaffin cells. These cells detect signals coming from the gut microbiota through toll-like receptors (TLR), which recognize bacterial lipopolysaccharides (LPS) and others in order to express peptide hormones for modulating appetite.<sup>25</sup> Gut microbiota-derived metabolites can modify the release of these hormones and neurotransmitters. Some dietary nutrients are converted into plasma metabolites by the gut microbiota, including SCFAs (lactate, butyrate, and acetate), dopamine, and serotonin. SCFAs play a special role in satiety and inflammation and can suppress VN activity during food intake and in the blood brain barrier. They also mediate the G protein-coupled receptors (GPR41 and GPR43) that inhibit fat accumulation in adipose tissue and promote glucose metabolism in the liver and muscle.26

#### Dysbiosis in obesity

Several studies have found an association between microbial dysbiosis in obesity and VN signaling. In obese subjects, there is an imbalance of the hunger hormones and neurotransmitters as well as changes in gut microbiota composition and proportions and derived metabolites. Such imbalance causes diverse pathophysiologies related to weight imbalance and improper energy homoeostasis. 27 The gut microbiota of healthy individuals changes in time due to aging and environmental factors such as dietary habits, type of food, lifestyle, and antibiotics, among others. Between individuals there are large differences in microbiome attributed to age, ethnicity, lifestyle, and diet. 28 These factors could modify its composition, leading to a dysbiosis in which opportunistic microorganisms take advantage to cause diseases. Dysbiosis is defined as a reduction in microbial diversity, a combination of the loss of beneficial bacteria and an increase in pathogenic ones. This imbalance likely promotes diet-induced obesity and metabolic complications. It is also associated with diarrhea, irritable bowel syndrome, allergies, multiple sclerosis, type 1 and type 2 diabetes, rheumatoid arthritis, Alzheimer's and Parkinson's diseases, autism, and atherosclerosis.29 Accordingly to the scientific literature Firmicutes and Bacteroidetes ratio (F/B) has been associated with host homoeostasis and is frequently cited as a hallmark of obesity.30



## Firmicutes/Bacteroidetes ratio (F/B)

The Firmicutes/Bacteroidetes ratio is an eventual biomarker or hallmark of obesity. Alterations affecting these phyla were first described in obese animals and subjects that exhibited increased abundance of Firmicutes at the expense of Bacteroidetes. When the subjects were submitted to a calorie-restricted diet for one year, Bacteroidetes increased as compared to Firmicutes. In fact, higher proportions of Bacteroidetes are found in people whose diet is rich in fiber. On the other hand, Firmicutes are found in people who consume large amounts of protein, sugar, starch, and calories. Firmicutes are more capable of extracting energy from foods than Bacteroidetes, promoting a more efficient calorie absorption and weight gain.31 So, restoring the balance of the gut microbiota through the use of probiotics is clinically an important target to treat obesity and other diseases related to the imbalance in gut microbiota. One method is reversing microbial dysbiosis by the consumption of probiotics.31

#### **Probiotics**

The term probiotic means for life in Greek. Through the years, different definitions have been proposed, and in 2001 the United Nations Food and Agriculture Organization (FAO) adopted the current formal definition: "Live microorganisms that, when administered in adequate doses, confer benefits for the health of the organism."32 Probiotics can be naturally found within or added to food products (probiotic foods), as fermented milk or dairy products (yogurt, cheese, and kefir) and fruit juice. It has been demonstrated that these products transport the bacteria to the intestine. Once in the gut, they colonize the colon, avoiding the adhesion of pathogens. They act directly on the microbiota and affect its composition and function. 33 Probiotics that potentially reduce the F/B ratio, and subsequently obesity, are mostly bacteria from the genera Lactobacillus (L. rhamnosus, L. paracasei, and L. salivarius) and Bacillus (B. amyloliquefaciens) and yeasts from the genus Saccharomyces (S. boulardii).34 It is well known that probiotics have multiple effects on the host. These mechanisms affect the development of gut microbiota and inhabit the host to ensure a proper balance between the microorganisms necessary for the optimal functions of the organism.35

# **Action mechanisms of probiotics**

Major probiotic action mechanisms of the gut microbiota include enhancement of epithelial barrier, which is not clearly understood yet. Several studies indicate that some bacteria, specifically the genera Lactobacillus, modulate the regulation and transcription of several genes encoding adherence junction proteins, as E-cadherin and B-catenin, their phosphorylation,

and protein kinase C (PKC).<sup>36</sup> Probiotics execute other types of action mechanisms:<sup>37, 38</sup>

Increased adhesion to intestinal mucosa and concomitant inhibition of pathogen adhesion (manipulation of intestinal microbial communities). Several Lactobacillus proteins have been shown to promote mucous adhesion and interaction with intestinal epithelial cells, as surface adhesins that mediate the attachments. Probiotics also cause alterations in intestinal mucins that prevent pathogen binding; and induce the release of small peptides/proteins from epithelial cells against pathogens.<sup>37</sup>

*Production of antimicroorganism substances.* Probiotics are able to produce low-molecular-weight (LMW) peptides, such as organic acids (acetic acid and lactic acid) and antibacterial peptides bacteriocins that inhibit pathogenic bacteria.<sup>37</sup>

Modulation of immune system. Probiotic bacteria are well known for interacting with epithelial, dendritic cells (DCs), monocytes, macrophages, and lymphocytes that can exert an immunomodulatory effect.<sup>38</sup>

#### Effects on gut microbiota

The possibility that the diet affects the gut microbiota has been discussed within the scientific community for a long time. Indeed, human diets may have direct effects on the microbiota, which results in changes in its composition. Experiments using animal models and subjects have demonstrated that some foods may contribute to the restoration of the F/B ratio and gut balance in general (vitamins, minerals, amino acids and dietary fiber) while others might affect the intestinal microbiota (fat and sugar-enriched diet).<sup>39</sup> Due to their potential action mechanisms in the host, probiotics are considered a functional food for weight management.<sup>40</sup> In this review, several clinical trials were found to describe the potentially beneficial effect of probiotic foods in the gut microbiota of obese experimental models (Table 1).

## **DISCUSSION**

Probiotics confer health benefits to the host when administered in adequate amounts. They are commonly used as food supplements that improve the host's intestinal balance. It is known that the metabolic activity of gut microorganisms affects host homoeostasis, and variations in its composition are associated with obesity pathogenesis and some other complications. Among the probiotics included in many functional foods and dietary supplements for human and animal consumption are Bifidobacterium and Lactobacillus spp., these are the predominant and subdominant groups of



TABLE 1. Clinical trials using probiotics for weight management in animal and human obesity models.

PROBIOTIC (BACTERIA STRAIN)	PROBIOTIC FOOD	CHARACTERISTICS	DOSE/ DURATION	RESULTS
Clostridium butyricum <sup>53</sup>	Cottage cheese and Greek- style yogurt made from pasteurized cow's, goat's or camel's milk The final products were inoculated with Clostridium butyricum (CFUs not specified) after manufacture	Model: 30 female C57BL/6 mice, 6–8 weeks old, weighing 14–16 g Induced rodent diet 5001 (mix of sugars, fat, proteins, vitamins, and minerals)	1 mL/day/ 5 weeks	Significant gut microbiota enrichment was observed in mice supplemented with cow milk cheese and camel milk, manifesting an increase in Clostridiales, Ruminococcaceae, Lachnospiraceae, and Anaerostipes spp), producing butyrate (one of the main short-strain fatty acids, SCFAs, linked to protective effects against metabolic syndrome)
Bifidobacterium spp. and Lactobacillus spp. <sup>54</sup>	Cheese The final product was inoculated with Bifidobacterium spp. and Lactobacillus spp. (CFUs not specified) after manufacture	Model: SD albino rats and C57BL/6J mice Induced High-fat diet (HD), mix of sugars, proteins, vitamins and minerals, to increase weight	Not specified	Lactobacillus strains were more effective in reducing weight gain, fatty acid synthesis, and live intake due to the enhanced adiponectin production and AMPK activation related with the expression of lipid oxidative genes in adipose tissue, liver, and skeletal muscle
Lactobacillus gasseri SBT2055 <sup>55</sup>	Yogurt The final product was inoculated with <i>Lactobacillus</i> gasseri SBT2055 (5 x 10 <sup>10</sup> CFU/100g) after manufacture	53 obese people (29 men and 14 women) aged 33–63; BMI 24.2–30.7 kg/m <sup>2</sup>	200 g/ day/12 weeks	Decrease in abdominal and subcutaneous fat (4.6%), BMI, and waist and hip circumference.
Lactobacillus plantarum <sup>56</sup>	Cheese The final product was inoculated with <i>Lactobacillus plantarum</i> (5 x 10 <sup>11</sup> CFU/100 g) after manufacture	40 obese people (20 men and 20 women) aged 30–69 Diagnosis of metabolic syndrome characterized by obesity	50 g/day/ 3 weeks	Reduced serum triglycerides, arterial blood pressure, and BMI
Lactobacillus fermentum and Lactobacillus amylovorus <sup>57</sup>	Yogurt Two yogurt treatments: Yogurts inoculated with 1.08x10° CFUs of <i>Lactobacillus</i> fermentum (LB) or 1.30 x 10° CFUs of <i>Lactobacillus</i> amylovorus (LA)	28 obese people (10 men and 18 women) aged 18–60 years BMI 25–32 kg/m²; induced HD (mix of sugars, proteins, vitamins, and minerals) to increase weight	Not specified	Participants lost 4% (LA group), 3% (LB group), and 1% (control group) of total fat mass , respectively, but body weight and composition did not differ significantly between treatments LA treatment resulted in the largest fat reduction and the largest decrease in prevalence of some bacteria clusters in gut, as <i>Clep</i> , related to a greater loss of body adiposity
Lactobacillus fermentum TSI2 and Lactobacillus fermentum S2 <sup>59</sup>	Yogurt The final product was inoculated with 8 log CFU/mL of Lactobacillus fermentum TSI2 and Lactobacillus fermentum S2 after manufacture	Model: Male SD rats, 6 weeks old, weighing 200 g Induced HD (mix of sugars, proteins, vitamins, and minerals) to increase weight	1 mL/200 g body weight/ 8 weeks	TSI and MIX groups presented significantly smaller adipocytes than HF group in abdominal fat tissue Adiponectin increased in TSI and epididymal fat was lower in S2 than in HF



TABLE 1. Clinical trials using probiotics for weight management in animal and human obesity models (continuation).

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PROBIOTIC (BACTERIA STRAIN)	PROBIOTIC FOOD	CHARACTERISTICS	DOSE/ DURATION	RESULTS				
Lactobacillus plantarum DK211 <sup>60</sup>	FWB The product was manufactured with Lactobacillus plantarum DK211 (109 CFU/mL)	Model: Male SD rats, 4 weeks old, weighing 156.04 ± 11.74 g Induced HD (mix of sugars, proteins, vitamins, and minerals) to increase weight	3000 mg/ day Over 4 weeks	HDFWB showed significantly lower organ weights, abdominal and epididymal fat pads, LDL-cholesterol levels, blood glucose, serum insulin, and serum appetite-related hormones (leptin and ghrelin) vs HD				
Lactobacillus delbrueckii subsp. bulgaricus, Streptococcus thermophilus, and Bifidobacterium animalis <sup>61</sup>	Yogurt Conventional yogurt containing starter cultures Lactobacillus delbrueckii subsp. bulgaricus (CFU: 108/mL) and Streptococcus thermophilus (CFU: 108/mL) Probiotic yogurt containing starter cultures and additional Bifidobacterium animalis (CFU: 108/mL)	Model: 30 male mice, 5 weeks old Induced HD (mix of sugars, proteins, vitamins, and minerals) to increase weight	2–3 mL/ day/60 days	Intestinal microbiota improved in conventional yogurt group with increased <i>Lactobacillus spp.</i> population Both yogurts improved histology of small intestine; normalized glucose, LDL, HDL, and cholesterol in serum; and promoted cytokine production (IL-6, IL-10 and INF-y), that reinforce epithelial barrier to prevent inflammatory response				
Streptococcus thermophilus, Lactobacillus acidophilus, Enterococcus faecium, and Lactobacillus rhamnosus <sup>58</sup>	Yogurt  3 yogurt treatments: Test yogurt StLa fermented with two strains of Streptococcus thermophilus (CFU: 10x10 <sup>7</sup> /mL each) and two strains of Lactobacillus acidophilus (CFU: 2x10 <sup>7</sup> /mL each) Test yogurt StLr: was fermented with two strains of Streptococcus thermophilus (CFU: 8x10 <sup>8</sup> /mL each) and one strain of Lactobacillus rhamnosus (CFU: 2x10 <sup>8</sup> /mL each) Test yogurt GAIO® (G): fermented using the Ukrainian bacterial culture CAUSIDO® This culture contained one strain of Enterococcus faecium (CFU: 6 x 10 <sup>7</sup> /mL each) and two strains of Streptococcus thermophilus (CFU: 1 x 10 <sup>9</sup> / mL each) GAIO® (G): fermented milk product	70 obese adults (20 men and 50 women) aged 18–55, BMI 25–37 kg/m <sup>2</sup>	450 mL/ day/8 weeks	There was a decrease in LDL-cholesterol after the consumption of GAIO® due to a possible cholesterol reabsorption in the small intestine				

Abbreviations: CFU= colony forming units/mL, SCFA= short chain fatty acids, SD= Sprague Dawley rats, HD: induced high fat diet, BMI= body mass index, GAIO® (G): fermented milk product, LA= *Lactobacillus amylovorus* group, LB= *Lactobacillus fermentum* group, *Clep*= Clostridium cluster, TSI= HD-fed rats orally administered yogurt fermented by *L. fermentum* TSI (n=8), HF= High-fat diet, MIX= HD-fed rats orally administered yogurt fermented by a mixture of *L. fermentum* TSI and S2 (n=8), FWB= fermented whey beverage, HDFWB= high fat diet plus fermented whey beverage, LDL= low density lipoprotein, HDL= high density lipoprotein.



the gastrointestinal microbiota.<sup>42</sup> Both strains are lactic acid bacteria (LAB) and have been reported to improve the inhibition of pathogenic microorganisms and protection against gastrointestinal diseases through the maintenance of the intestinal barrier and the enhancement of immune response.<sup>43</sup>

Those LAB considered commercial probiotics belong mostly to the Lactobacillus genus, with over one hundred species recognized. Among them are those shown in Table 1: L. acidophilus, L. casei, L. gasseri, L. fermentum, L. plantarum, and L. rhamnosus. They are generally recognized as safe (GRAS). The Bifidobacterium genus (B. infantis, B. animalis, B. longum, and B. Breve B3) is also found in probiotic products but not as frequently.44 For decades, Lactobacilli have been used as an effective therapy to treat gastrointestinal conditions and other pathologies, displaying an overall positive safety profile.45 Lactobacillus strains are the most widely reported in the articles here mentioned (see Table 1). The changes observed after probiotic intake in experimental groups compared to control include SCFA production and an increase in gut bacteria count. There is also a reduction in abdominal fat, hip circumference, and proinflammatory cytokines (IL-1, IL-6, IL-10, and INF-γ) as well as lower levels of sugar, cholesterol, and triglycerides. It is worth mentioning that these effects are considered biomarkers associated with weight loss control and could influence weight management strategies. Nevertheless, the efficacy and action mechanisms are strain-dependent or strain-specific. Then, they cannot be ascribed indistinctly or extended to all probiotics of the same genus or species. Some strains may equally play a significant role against obesity in their own way or have a greater positive impact.46 For example, a meta-analysis conducted by Million, Angelakis, Paul, Armougom, Leibovici and Raoult (2012) reported that L. casei strain Shirota (LAB 13), L. gasseri, L. rhamnosus, and L. plantarum have a more positive effect on weight loss.<sup>47</sup> In fact, they appear to be protective against obesity. Results reported in table 1 show some antiobesity effects, such as a decrease in abdominal and subcutaneous fat (*L. gasseri SBT2055*) and a reduction in serum triglycerides and LDL cholesterol (L. rhamnosus). Clinical and experimental studies suggest that L. plantarum shows the most promising effects against several pathological conditions, including obesity. This strain is able to inhibit weight gain and fat accumulation.48 Furthermore, lowers serum cholesterol, glucose and triglycerides levels in blood.49 Changes observed in Table 1, after L. plantarum intake also include the reduction of serum appetite related hormones (leptin and ghrelin) On the other hand, L. fermentum and L. acidophilus are associated with weight gain. These bacteria are widely present in many products intended for increasing energy efficiency, as freezedried foods (fruits, vegetables, cereals, meat, and poultry). Finally, Clostridium butyricum, Lactobacillus amylovorus, Enterococcus faecium, and Lactobacillus delbrueckii subsp.

bulgaricus are not commonly consumed by humans. In fact, they are still under experimentation. Still, the results after intake (Table 1) demonstrate that these bacteria strains could be applied as future probiotics for weight control purposes.

Probiotics are classified as modified functional ingredients added to the food that owe their special properties to bioactive compounds. Those a considered as primary and secondary metabolites of nutritious and non-nutritive natural components found in small proportions. Despite this, they can trigger mechanisms that improve human health as they have antioxidant, anti-inflammatory, antifungal, and antibacterial properties.<sup>50</sup> In Table 1, all authors mention that probiotics were added to the food, and that all the food matrixes were fermented dairy products. They are commonly found in this type of food; products such as yogurt and cheese are excellent probiotic vectors due to their nutritional composition, acidity, and shelf life. Cheese is also a suitable transport for bacteria given its high buffering capacity, a result of its high fat content and dense structure, that may protect them during gastric transit.51

#### CONCLUSION

Several works suggest that some probiotic strains may have a greater positive impact in the treatment of obesity while others exert a beneficial effect on weight loss. Some of the changes observed in Table 1 after probiotic intake include reduction in abdominal fat, but also reduction of triglycerides serum levels and proinflammatory cytokines (IL-1 IL-6, IL-10, INF-γ). Available data suggest significant therapeutic effects of probiotics in weight management, and some strains have been approved for consumption. Still, some sanitary regulators, as the Food and Drug Administration, have not approved any probiotics related to overweight/obesity treatment.52 Studies and clinical trials support the therapeutic effects of probiotics. However, older studies (before 2010) fail to understand or associate the action mechanisms involved, and little or no continuity has been reported. Further work is necessary to meet all quality standards for medical applications. Probiotics may provide an advanced understanding of obesity etiology and metabolic consequences. Even these markers can be a direct target for future obesity perspectives and new and innovative techniques for weight management.

#### **CONFLICT OF INTEREST**

The authors declare they have no conflict of interest.



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