Review

Weight loss probiotic supplementation effect in overweight and obesity subjects: A review

Camila Guazzelli Marques a, *, Aline de Piano Ganen a, Andrea Zaccaro de Barros b, Ronaldo Vagner Thomatieli dos Santos c, d, Marcus Vinicius Lucio dos Santos Quaresma a, d, e

a Curso de Nutrição do Centro Universitário São Camilo, São Paulo, SP, Brazil
b Brazilian Association of Sport Nutrition, São Paulo, SP, Brazil
c Universidade Federal de São Paulo, Departamento de Psicobiologia, São Paulo, SP, Brazil
d Universidade Federal de São Paulo, Departamento de Biociências, São Paulo, SP, Brazil
e Universidade de São Paulo, Programa de Pós-graduação em Nutrição e Saúde Pública, São Paulo, SP, Brazil

Summary

Background: Composition and the minor diversity of intestinal microbiota (IM) were evidenced in obese individuals, therefore it is suggested that the intestinal dysbiosis can be, at least in part, a contributor for the development of obesity, once the IM influences the host metabolism affecting not only the energetic balance, but also the inflammation and functions of the intestinal barrier. Soon, the probiotics supplementation can be an important nutritional tool in treatment and prevention of this metabolic disorder and other associated diseases, since its action is based on IM modulation.

Purpose: Verify the effect of probiotic supplementation in the weight loss process in individual with overweight and obesity.

Materials and methods: It was done a bibliographic narrative/systematic search from periodicals in England, only in PubMed database.

Results: It was reviewed 14 studies and found ones pointed that some bacterial strains can reduce body mass and the adiposity in individuals, even suggested possible mechanisms such as decrease gut microbiota permeability, inflammatory status, and improve satiety.

Conclusion: In summary, few studies have found that probiotics alone help to reduce body fat and the mechanism of action is unclear. The small sample, control of the total calorie intake, as well as the type of nutrients that ingested, are significant limitations. Finally, many doubts still surround the effect of different probiotic strains to understand their impact on the weight loss process.

© 2019 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

1. Introduction

The global prevalence of overweight and obesity has been increasing in populations and age groups in recent years [1]. A recent data analysis of 195 countries has shown that obesity prevalence has doubled in more than 70 countries since 1980 [2], and prospects are not promising in this scenario. According to the World Health Organization (WHO), over 2.1 billion adults were considered overweight or obese in 2014, representing 39% of the world's population [1]. Even more alarming, estimates predict a substantial increase for 3.3 billion people with a Body Mass Index (BMI) greater than or equal to 25.0 kg/m², corresponding to 57.8% of the world's adult population by the year 2030 [3].

Therefore, obesity is a significant and growing public health problem in the world. Globally, at least 2.8 million people die each year as a result of being overweight or obese, and an estimated 35.8 million (2.3%) of Disability Adjusted Life Years (DALYs) are caused by obesity or obesity. The DALYs for a disease or health condition are calculated based on the sum of the years of life lost due to premature mortality in the population and the years lost due to disability for people living with the health condition or its consequences, in short, a DALYs can be considered as a lost year of "healthy" life [4].

* Corresponding author. Nutrition Department, Centro Universitário São Camilo, Avenida Nazaré, 1501 - Ipiranga, São Paulo, CEP: 04261-200, SP, Brazil.

E-mail address: marcus.santos.nutri@gmail.com (C.G. Marques).

https://doi.org/10.1016/j.clnu.2019.03.034

0261-5614/© 2019 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.
Obesity is defined by body mass disproportionate to height with excessive accumulation of adipose tissue (AT), usually accompanied by a low-grade chronic systemic inflammation [1]. In recent years, it has been recognized as a chronic disease that, in turn, is commonly associated with the development of other clinical conditions such as type 2 diabetes mellitus, cardiovascular diseases, some types of cancer, musculoskeletal disorders, among others [2].

Body mass and, therefore, obesity, are determined by a matrix of genetic, epigenetic and lifestyle factors that interact with one another and also act within a broad physical-sociocultural environment that act on various physiological mediators of food intake and energy expenditure, culminating in the deposition of body fat [1]. In summary, the pathophysiology of obesity is complex, multifactorial and not yet completely elucidated. However, the cause attributed to its genesis is the permanent and prolonged imbalance between caloric intake and energy expenditure, resulting in a chronic positive energy balance [3].

In this context, recent evidence also adds that gut microbiota (GM) is also a contributing factor for the development of obesity, since the GM is able to modulate host metabolism affecting not only energy balance but also low-grade chronic systemic inflammation and intestinal barrier function [4,5].

GM can be defined as a diverse and dense community of commensal microorganisms, those that do not seem to harm or benefit the host, which inhabit the human intestine [8]. The composition of human GM is defined primarily by two bacterial phyla, such as Bacteroidetes (for example, Bacteroides spp.) and Firmicutes (for example, Clostridium and Bacillus spp.), but there are still some other phyla such as Actinobacteria, Bifidobacterium spp. [9,10]. GM resident is increasingly recognized for performing essential functions not only in the intestinal mucosa but also in host metabolism and thus reflecting on health and disease [10]. However, there is a substantial variation among individuals in response to the environment, genetics, eating habits, use of antibiotics, lifestyle influences, and body composition [11].

In this context, it has been evidenced that the GM composition is altered in obese people [12]. Studies that investigated the relationship between GM composition and obesity found that the number of bacteria in the Firmicutes phylum was increased, while the amount of Bacteroidetes was reduced in obese mice and humans compared to eutrophic [13–15]. According to Angelakis et al. [12] this relationship Firmicutes/Bacteroidetes seemed to facilitate the extraction of energy from ingested foods and increase energy storage in the host adipose tissue. In addition, it is also suggested that obesity seems to be associated with a lower diversity of GM bacteria [6].

Therefore, for some authors, the Firmicutes/Bacteroidetes ratio, as well as specific characteristics of resident bacteria of the intestinal microbiota, contributes, at least in part, to the development of obesity [6,16]. In this perspective, Komaroff [17] further proposes that the microbiome can be both, a reflection of this metabolic disorder as well as a cause. Several mechanisms by which GM can affect body mass has been proposed [7], is mentioned as follows: According to Cox et al. [15], regardless of the underlying mechanisms, changes in intestinal permeability, mainly due to alterations in the structure of junction proteins, known as tight junctions that are present in the intestinal epithelial cells or enterocytes [18] have potential to trigger a process called metabolic endotoxemia [10]. Metabolic endotoxemia is represented by high concentrations of lipopolysaccharides (LPS), a component of the cell wall of gram-negative bacterial species that are circulating in response to non-infectious stimuli, and the presence of LPS in the circulation is proposed as a result of its passive diffusion through the intestinal barrier, where the integrity of these junction proteins, especially claudins and occludins, were compromised, leading to an increase in intestinal permeability [10] (Table 1).

This LPS-LBP binding allows the activation of several classical immunological pathways, including nuclear-kB factor activation (NF-kB) and subsequent inflammatory responses how interleukin-6 and tumor necrosis factor alpha (TNF-alpha), that can lead insulin resistance in several tissues [10]. These local and systemic inflammatory changes in response to LPS are mainly justified by the expression of Toll-like receptor 4 (TLR4) in immunological cells, such as monocytes, macrophages, neutrophils and non-immunological cells including adipocytes, myocytes and cells endothelial cells [10].

Another proposed mechanism by which GM can modulate energy intake and host metabolism is by the production of short chain fatty acids (SCFA) of indigestible polysaccharides [7]. The SCFA, such as acetate, butyrate and propionate produced by bacterial fermentation act as energetic substrates, as well as regulators of satiety and food intake, since when they activate receptors such as GPR41 and GPR43 coupled to G protein in intestinal epithelial cells, they stimulate the YY peptide (YY) and glucagon-like peptide (GLP-1) secretion, capable of suppressing intestinal mobility and slowing intestinal transit, allowing a higher uptake of nutrients [7].

Considering the role of GM in the regulation of host metabolism, energy homeostasis and central control of appetite, GM has been gaining more prominence in the last decade in the scientific field, becoming a target in the context of health and disease. This interest can also be justified by the rapid technological development that made possible a better understanding of the microorganisms that inhabit the human intestine, its functionality, and its roles [9].

Thus, it is suggested that strategies able to change GM may be relevant in the prevention and treatment of obesity and associated metabolic disorders [19]. Among the strategies studied, diet appears to be a determining factor for GM composition and activity, dietary changes could account for 57% of the structural variations of total GM [19]. In addition to nutrients and dietary patterns, probiotics are also being studied with enthusiasm in the obesity scenario by able to modulate the GM composition positively and to act on intestinal barrier integrity [19]. Probiotics are defined as live microorganisms which, when administered in appropriate amounts, confer beneficial health effects on the host [20]. In this scenario, studies have highlighted the potential role of probiotics in the context of obesity [19]. Studies with different bacterial strains have demonstrated positive effects on obesity in several aspects, such as reduction of adipose tissue inflammation, endotoxemia, adiposity, body mass, lepton levels, and energy consumption, with the probiotic species Bifidobacterium and Lactobacillus spp. are the most evidenced [19]. In addition, Akkermansia muciniphila is one of the main intestinal bacteria with the ability to reverse the metabolic effects induced by a high-fat diet, which seems to positively influence host metabolism [19].

Although some studies have recognized that probiotics could be of value in this setting, it is believed that the effects of these bacteria are dependent on the strain and dose [21,22]. In this perspective, Brusaferro et al. [23] add that the effect of probiotic on body mass and metabolism is specific to the strain and that only some of the species included in the genera Lactobacillus and Bifidobacterium are effective in this scenario, while the use of other strains may be deleterious, so the interest in researching them. Studies that evaluated the effects on body weight and fat mass in overweight individuals are still scarce and controversial [24].

Therefore, the main objective of this narrative review is to carry out a bibliographic survey to discuss whether probiotics, in different amounts, strains, and combinations, can contribute to the
Table 1
Chronology of the studies on the effects of probiotics in the weight loss process in humans.

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Sample</th>
<th>Study Design</th>
<th>Name of investigated probiotic strain(s)</th>
<th>Probiotic type and dose (per day)</th>
<th>Dietary/exercise intervention associated</th>
<th>Groups</th>
<th>Duration of intervention</th>
<th>Main results</th>
<th>Parameters without significant changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kadooka et al., 2013 [29]</td>
<td>Healthy adults, with the visceral fat area between 80.2 and 187.7 cm², aged (35–60) years. (n = 210, participants, women = 105, men = 105).</td>
<td>Randomized, double-blind, parallel-group, multicenter clinical trial.</td>
<td>Lactobacillus gasseri SBT2055 (LG2055).</td>
<td>200 g/day of fermented milk (2 servings of 100 g), containing 1 × 10⁷ or 1 × 10⁸ CFU 100 g LG2055.</td>
<td>Not applicable: individuals were instructed to maintain their usual lifestyle, including diet and physical exercise.</td>
<td>Group 10⁷ fermented milk containing LG2055 (n = 69)</td>
<td>12 weeks</td>
<td>† of the visceral fat area in groups 10⁷ and 10⁸ at weeks 8 and 12 compared to baseline (p &lt; 0.01)</td>
<td>No significant differences observed in the abdominal subcutaneous fat area between groups 10⁷ and 10⁶ compared to control at weeks 8 and 12 (p &gt; 0.05)</td>
</tr>
<tr>
<td>Omar et al., 2013 [30]</td>
<td>Healthy overweight and obese adults, BMI (25.0–32.0) kg/m², aged (18–60) years. (n = 28, women = 18, men = 10).</td>
<td>Placebo-controlled, randomized, double-blind, cross-over.</td>
<td>Lactobacillus acidophilus; Lactobacillus fermentum</td>
<td>100 g/day yogurt containing 10 g of Lactobacillus acidophilus and 10 g of Lactobacillus fermentum (1.39 × 10⁷ CFU) and (1.08 × 10⁵ CFU)</td>
<td>During each treatment period, participants received diets containing 35% of fat (SFA = 7.7%, PUFA = 8.8% and MUFA = 14.1%), 50% carbohydrates and 15% protein.</td>
<td>LF group (n = 14) – yogurt containing Lactobacillus fermentum</td>
<td>8 weeks</td>
<td>† of 3% of the fat mass in the LF group (p &lt; 0.05) at the beginning of treatment</td>
<td>No significant differences in body weight observed at the beginning or the end of the three treatments. The total fat mass did not differ significantly between the groups at the end of the intervention</td>
</tr>
<tr>
<td>Zarrati et al., 2013 [31]</td>
<td>Healthy overweight and obese adults, BMI (25–35.0) kg/m², aged (20–50) years. (n = 75, women = 51, men = 24)</td>
<td>Randomized, double-blind, controlled clinical trial.</td>
<td>Lactobacillus casei DN001, Bifidobacterium lactis Bb12</td>
<td>200 g/day of probiotic yogurt, containing 1 × 10⁷ CFU/g.</td>
<td>Hypocaloric diet (not described)</td>
<td>RICD group (n = 25) – regular yogurt + low-calorie diet</td>
<td>8 weeks</td>
<td>† of 1% of the fat mass in the control group (p &lt; 0.05) at baseline</td>
<td>There was no difference between waist/hip ratio values between the three groups</td>
</tr>
<tr>
<td>Sanchez et al., 2013 [32]</td>
<td>Healthy overweight and obese adults, BMI (29–41.0) kg/m², aged (18)</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>Lactobacillus rhamnosus CGMCC1.3724 (LPR)</td>
<td>2 capsules/day (30 min before breakfast and 30 min before dinner). Each capsule contained 10 mg of LPR powder,</td>
<td>Each participant received a caloric restriction diet plan of 500 kcal/day for the first 12 weeks (phase 1). In LPR group (n = 62) – probiotic capsule Placebo group (n = 63) – placebo capsule</td>
<td>LPR group (n = 62) – probiotic capsule Placebo group (n = 63) – placebo capsule</td>
<td>24 weeks/two-phase intervention. Phase 1 (weight loss period): Dietary restriction with or without probiotic therapy. Phase 2 (weight maintenance period): No dietary changes.</td>
<td>† body mass of women in the LPR group compared to placebo (p &lt; 0.02) in phase 1 and phase 2 and † body mass of women</td>
<td>There was no significant change in body mass loss during the caloric restriction period (week 12, phase 1)</td>
</tr>
</tbody>
</table>

(continued on next page)
There was no difference in body mass loss between groups after 3 weeks (p = 0.083). There was no difference in muscle mass (p = 0.677), fat mass (p = 0.169) and waist hip ratio (p = 0.788) in the probiotic group after 3 weeks. There was no difference in muscle mass (p = 0.967), fat mass (0.211) and waist hip ratio (0.590) in the control group after 3 weeks.

Table 1 (continued)

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Sample</th>
<th>Study Design</th>
<th>Name of investigated probiotic strain(s)</th>
<th>Probiotic type and dose (per day)</th>
<th>Dietary/exercise intervention associated</th>
<th>Groups</th>
<th>Duration of intervention</th>
<th>Main results</th>
<th>Parameters without significant changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharafedtinov et al., 2013</td>
<td>Obese adults, diagnosed with metabolic syndrome, BMI (36.3–37.7) kg/m², aged (30–69) years. (n = 40, women = 27, men = 13)</td>
<td>A parallel, randomized, double-blind, placebo-controlled pilot study</td>
<td>Lactobacillus plantarum TENSIA</td>
<td>Hypocaloric diet (1512.0 kcal/day)</td>
<td>Probiotic cheese group (n = 25) – cheese containing probiotic + hypocaloric diet</td>
<td>Control group/regular cheese (n = 15) – regular cheese without probiotic added + hypocaloric diet</td>
<td>3 weeks</td>
<td>treated with LPR compared to women treated with placebo in phase 2 (p &lt; 0.02)</td>
<td>BMI in the probiotic cheese group and control group after 3 weeks (p &lt; 0.001)</td>
</tr>
<tr>
<td>Jung et al., 2015</td>
<td>Healthy adults, with (BMI 25.0)</td>
<td>Randomize, double-blind,</td>
<td>2 g of powder of the two probiotic strains</td>
<td>Subjects instructed to maintain their eating</td>
<td>Probiotic group (n = 49) – sachets</td>
<td>12 weeks</td>
<td>Body weight (p = 0.008); BMI</td>
<td>Total lean body mass did not differ</td>
<td></td>
</tr>
</tbody>
</table>
placebo-controlled study.

**Madjd et al., 2016** [35]
Healthy overweight and obesity women, BMI (27.0–40.0) kg/m², aged (18–50) years. (n = 89)

**Gomes et al., 2016** [36]
Women BMI (24.9–40.0) kg/m², aged (20–59) years. (n = 43)

**De Lorenzo et al., 2017** [37]
Women BMI (≥25) kg/m², % body fat <30, aged (20–65)

**Lactobacillus curvatus** HY7601 or Lactobacillus plantarum KY1032) each at 2.5 × 10⁸ CFU, 2x/day, immediately after breakfast and dinner.

**Lactobacillus acidophilus** LAC e Bifidobacterium lactis BB12 containing probiotics

Placebo group (n = 46) – placebo sachets containing crystalline cellulose, blueberry flavoring lactose

**400 g/day of probiotic yogurt, being 2x/day of 200 g before the main meals, containing 1 × 10⁷ CFU**

**The proposed diet based on an energy deficit of 500–1000 kcal based on the estimated energy needs at the beginning of the study for each participant. Physical activity stimulated, the objective was to gradually increase activity levels to reach 60 min of moderate exercise 5 d/week.**

**LF group** (n = 45) – hypocaloric diet + conventional low-fat, non-probiotic yogurt

**PY group** (n = 44) – hypocaloric diet + low-fat yogurt with probiotic

**Isocaloric diet (25–30 kcal/kg) and guidelines for healthy eating. It consisted of six meals, and with the same amount of protein, lipids and carbohydrates between groups. They were also instructed to maintain their usual program of exercise and physical activity.**

**Group DI** (n = 22) – isocaloric dietary intervention + sachets

**Group DI + P** (n = 21) – isocaloric dietary intervention + probiotic sachets

**Normocaloric diet** (25–30 kcal/kg) and guidelines for healthy eating. It consisted of six meals, and with the same amount of protein, lipids and carbohydrates between groups. They were also instructed to maintain their usual program of exercise and physical activity.

**One sachet/day of 3 g containing 1.5 × 10¹⁰ CFU of each species: Streptococcus thermophilus, Bifidobacterium animalis subsp. Lactis, Termofilos de Cuir**

**Not reported**

**WNL group – women with 3 weeks BMI <25 kg/m² and % fat <30; NWO group – women with BMI <25 kg/m² and % fat ≥30;**

(continued on next page)
<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Sample</th>
<th>Study Design</th>
<th>Name of investigated probiotic strain(s)</th>
<th>Probiotic type and dose (per day)</th>
<th>Dietary/exercise intervention associated</th>
<th>Groups</th>
<th>Duration of intervention</th>
<th>Main results</th>
<th>Parameters without significant changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al., 2017 [38]</td>
<td>Healthy adults, categorized by overweight (BMI not reported) (n = 66, sex not reported)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Lactobacillus curvatus (L. curvatus HY7601) and Lactobacillus plantarum (L. plantarum KY1032)</td>
<td>Two sachets per day (After breakfast and dinner) containing 2.5 × 10⁸ CFU of L. curvatus HY7601 and L. plantarum KY1032</td>
<td>Probiotic group (n = 32) – sachet consumption with probiotic strains; Placebo group (n = 34) – placebo sachet consumption</td>
<td>12 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mobini et al., 2017 [39]</td>
<td>Adults with type 2 diabetes mellitus, with BMI (25–45) kg/m², aged 50–75 years, (n = 46, 11 women, 35 men)</td>
<td>A double-blind, randomized, placebo-controlled study with three parallel groups</td>
<td>Lactobacillus reuteri DSM 17938</td>
<td>One sachet/serving per day before breakfast containing 10⁸ or 10¹⁰ CFU of L. reuteri DSM 17938</td>
<td>Not applicable: Patients were instructed not to change their lifestyle throughout the study.</td>
<td>Group L. reuteri low (n = 15) – sachet with 10⁸ CFU; Group L. reuteri high (n = 14) – sachet with 10¹⁰ CFU; Placebo group (n = 15) – placebo sachet</td>
<td>12 weeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 (continued)

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Sample</th>
<th>Study Design</th>
<th>Name of investigated probiotic strain(s)</th>
<th>Probiotic type and dose (per day)</th>
<th>Dietary/exercise intervention associated</th>
<th>Groups</th>
<th>Duration of intervention</th>
<th>Main results</th>
<th>Parameters without significant changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Streptococcus, Bifidobacterium bifidum, Lactobacillus delbrueckii spp., Bulgaricus, Lactococcus lactis subsp. Lactis, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus reuteri</td>
<td>thermophilus SGS01, Bifidobacterium animalis subsp. Lactis SGB06, Streptococcus thermophiles, Bifidobacterium bifidum SGB02, Lactobacillus delbrueckii spp., Bulgaricus DSM 2008, Lactococcus lactis subsp. Lactis SGLc01, Lactobacillus acidophilus SGL11, Lactobacillus plantarum SGL07, Lactobacillus reuteri SGL01.</td>
<td></td>
<td>PreOB/OB group – women with BMI ≥ 25 kg/m² and % fat ≥ 30</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kim et al., 2017 [38]

Healthy adults, categorized by overweight (BMI not reported) (n = 66, sex not reported)

Randomized, double-blind, placebo-controlled.

Lactobacillus curvatus (L. curvatus HY7601) and Lactobacillus plantarum (L. plantarum KY1032).

- Two sachets per day (After breakfast and dinner) containing 2.5 × 10⁸ CFU of L. curvatus HY7601 and L. plantarum KY1032.

Probiotic group (n = 32) – sachet consumption with probiotic strains; Placebo group (n = 34) – placebo sachet consumption.

12 weeks

- There was no significant decrease in the area of subcutaneous fat in the L1 region of the probiotic group, but there was a tendency to decrease after 12 weeks (p < 0.05).
- There was no significant change in body mass, BMI waist circumference, body fat after 12 weeks in the probiotic group.
- There was a significant decrease in BMI (p < 0.05), fat mass (p < 0.01), and fat percentage (p < 0.05) after 12 weeks in the probiotic group.
- There was no significant decrease in the total fat area (cm²) and subcutaneous fat area (cm²) in the placebo group.
- When compared baseline changes between control and probiotic groups, there were significant differences in body mass (p = 0.008), BMI (p = 0.008), fat percentage (p = 0.02), and subcutaneous fat area (cm²) (p = 0.016) in the placebo group. However, it observed that the probiotic group showed a reduction in these parameters, whereas the control group increased after the treatment of 12 weeks.

Mobini et al., 2017 [39]

Adults with type 2 diabetes mellitus, with BMI (25–45) kg/m², aged 50–75 years, (n = 46, 11 women, 35 men).

A double-blind, randomized, placebo-controlled study with three parallel groups.

Lactobacillus reuteri DSM 17938

- One sachet/serving per day before breakfast containing 10⁸ or 10¹⁰ CFU of L. reuteri DSM 17938.

- Probiotic group low (n = 15) – sachet with 10⁸ CFU; Probiotic group high (n = 14) – sachet with 10¹⁰ CFU; Placebo group (n = 15) – placebo sachet.

12 weeks

- There were no significant changes in body mass, BMI waist circumference, body fat after 12 weeks in the placebo group.
- There were no significant changes in body mass, BMI waist circumference, body fat after 12 weeks in the probiotic group.
Please cite this article as: Marques CG et al., Weight loss probiotic supplementation effect in overweight and obesity subjects: A review, Clinical Nutrition xxx (xxxx) xxx

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Study Design</th>
<th>Probiotic</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al., 2018 [40]</td>
<td>Randomized, double-blind, placebo-controlled study</td>
<td>Lactobacillus gasseri BNR17 (BNR-H)</td>
<td>Two capsules (400 mg/capsule) of low dose (10^6 CFU) or high dose (10^10 CFU) of L. gasseri BNR17 twice daily, preferably after breakfast and dinner.</td>
<td>The subjects were instructed to reduce 200 kcal per day of their energy intake and increase the expenditure of 100 kcal per day in their physical activity during the intervention period.</td>
<td>No significant changes in waist circumference and body fat after 12 weeks in the group supplemented with the lowest dose of L. reuteri.</td>
</tr>
<tr>
<td>Szulinska et al., 2018 [41]</td>
<td>Randomized, double-blind, placebo-controlled clinical trial</td>
<td>Bifidobacterium bifidum W23, Bifidobacterium lactis W51, Bifidobacterium lactis W52, Lactobacillus acidophilus W37, Lactobacillus brevis W63, Lactobacillus casei W56, Lactobacillus salivarius W24, Lactococcus lactis W19, and Lactococcus lactis W85.</td>
<td>Two sachets per day of lyophilized powder from the Ecologic® Barrier probiotic mixture containing 1 x 10^10 UFC or 2.5 x 10^9 CFU One sachet should intaked before breakfast and the other before going to sleep.</td>
<td>Not applicable: Participants were instructed not to change their physical activity routine and dietary habits and consumption.</td>
<td>There was no difference between the groups for CC after 12 weeks, but the high dose group reduced in greater magnitude.</td>
</tr>
</tbody>
</table>

BMI = body mass index; n = number of participants; CFU = colony forming units; ↓ = decrease; ↑ = increase; kg = kilograms; m² = meters (height) squared; cm² = square centimeters.
reduction of body mass, body fat and/or other parameters of adiposity in individuals with excess of as well as discuss the mechanisms linked to the results.

2. Literature research

The PICO criteria were used to carry out the research. P (obesity/adiposity/overweight); I (probiotics/Lactobacillus/bifidobacterium); C (not applied); O (weight loss/body weight/body weights/weight, body/weights, body/body composition/body compositions/composition, body/compositions, body/abdominal fat/abdominal adipose tissue/body fat distribution. Publications referenced in PubMed were analyzed with the following terms in combination: [obesity OR adiposity OR overweight] OR probiotics OR lactobacillus OR Bifidobacterium] OR [body weight OR body weights OR weight, body/weights, body/body composition OR body compositions OR composition, body/weights, body/body composition OR body compositions, body OR abdominal fat OR abdominal adipose tissue OR body fat distribution OR weight loss OR weight reduction].

We considered as inclusion criteria: adults ≥18 years), overweight individuals (BMI = mean 25.00 – 29.99 kg/h²), individuals with obesity (BMI = mean 30.00 – 40.00 kg/h² or more) and evaluate or have as primary or secondary endpoint body composition parameters. Studies with probiotics, lactobacillus and bifidobacterium. Exclusion criteria were: studies with children or adolescents, pregnant women, athletes, post-bariatric individuals, prebiotic or symbiotic interventions, and probiotics associated with food (yogurt, egg, cheese, etc.).

We found 817 articles, considering as a filter: clinical trials, last ten years, only studies with humans. After reading the titles and abstracts, 82 studies were selected for reading in full and 14 included in this review (Fig. 1).

3. Results and discussion

Until the present moment, in the light of our knowledge, there are few published human intervention studies that verify probiotic effect on weight loss.

In 2015, Park and Bae [25] published a systematic review and meta-analysis containing nine randomized controlled trials. Only four studies included in the meta-analysis, and there was no difference in weight reduction (p = 0.26) compared to the control group, and the same result shown in the BMI analysis (p = 0.14). The Lactobacillus strain, consumed by dairy foods (yogurt, cheese, and milk) or supplemented form was the most used (6 studies).

Authors emphasize that limitations such as quantity and time of intervention make it difficult to interpret the results. The control of energy intake is not accurate, and it is not possible to state that weight loss occurs due to the effect of probiotics or caloric restriction (even if not adequately controlled). Moreover, the authors considered weight loss and BMI such main outcomes, two anthropometric parameters that are limiting the body fat decrease comprehension.

In a more recent systematic review and meta-analysis, published by Borgeraas et al. [26], the authors verified the effect of probiotics in the weight loss process (weighted mean difference), considering body weight, BMI and fat mass (kg and %) as parameters of analysis. The authors included 15 studies with a total of 957 subjects (63% women). With a mean BMI of 27.6 kg/h² and age between 18 and 75 years. Two-thirds of the published studies were done with healthy people, while the others were published with people with chronic diseases, being hypertension (n = 1); non-alcoholic fatty liver disease (n = 1); diabetes mellitus type 2 (n = 1); and fasting hyperglycemia (n = 1). Of these, eight studies contained only those who were overweight or obese, while the others did not describe the exclusion of eutrophic persons; however, the mean BMI was above to 25 kg/h².

In relation to body mass, analyzing 13 studies, the authors verified that the supplemented individuals showed weight loss (WMD [95% CI]: -60 [-1.19 - 0.01] kg, p = 0.02) and BMI (WMD [95% CI]: -0.27 [0.45, 0.08] kg m⁻²). However, when authors analyzed only those overweight and obese individuals, the weight loss and BMI magnitude, reduced (WMD [95% CI]: -0.14 [0.45, 0.18] kg m⁻², respectively).

However, in this review, the authors note that in excluding one of the studies [27], that verified greater weight loss in the control group compared to the intervention group, the results modify, with a body weight and BMI reduction of (WMD [95% CI]: - 1.46 [- 0.01] kg) and (WMD [95% CI]: - 0.25 [- 0.06, 0.09] kg m²⁻). Respectively, considering only those who were overweight or obese. In addition, when the amount of fat (kg and %) was analyzed, there was a reduction in fat mass (WMD [95% CI]: 0.42 [1.08, 0.23] kg).

Authors emphasized that limitations such as quantity and time of intervention make it difficult to interpret the results. The control of energy intake is not accurate, and it is not possible to state that weight loss occurs due to the effect of probiotics or caloric restriction (even if not adequately controlled). Moreover, the authors considered weight loss and BMI such main outcomes, two anthropometric parameters that are limiting the body fat decrease comprehension.

Please cite this article as: Marques CG et al., Weight loss probiotic supplementation effect in overweight and obesity subjects: A review, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.03.034
[27,28], the magnitude of fat loss (WMD [95% CI]; 0.97 [1.28, 0.66] kg) increased. Nine studies used only one probiotic strain, while 4 used multiple strains. Seven studies had time to intervention for over eight weeks. However, the discussion about the effect of caloric restriction not is made.

*Lactobacillus acidophilus* is the main strain used in the different studies. In addition, the control group is heterogeneous (e.g. low-fat yogurt, yogurt, cheese, capsules), which makes it difficult to understand the findings. Moreover, the authors point out that the 12 industry-funded studies presented in the review, and the results should be analyzed with caution.

In the present study we discussed the effect of caloric restriction and the amount and type of strains capable of influencing the body fat. Moreover, we evaluated in detail the components of the total body mass that reduced, not only weight and BMI.

Kadooka et al. (2013) [29] showed that the *Lactobacillus gasseri* SBT2055 (LG2055) intake at concentrations 1 × 10⁶ and 1 × 10⁷ CFU in the fermented milk decreases 8.6 cm² (p < 0.01) and 9.6 cm² (p < 0.01) visceral fat area, respectively, after 12 weeks. However, only the 1 × 10⁷ group demonstrated a subcutaneous fat reduction (6.8 cm²) in the same period (p < 0.05). Anthropometric parameters such as BMI, waist and hip circumference also reduced over time in the suprastructure only 1%. Interestingly, after four weeks of protocol end, positive results were attenuated, suggesting that constant intake may be necessary for the maintenance of the effects.

The authors suppose that the findings are due to the recognition of enterocytes by the enteroviruses, leading to a transient colonisation, and also the specific characteristics of these bacteria could contribute to the maintenance of the integrity of the intestinal barrier, reducing the intestinal permeability, relation to the low-inflammatory state, commonly associated with obesity and other metabolic disorders.

Kim et al. (2018) [40] investigated the effect same strain (*Lactobacillus gasseri* BNR17) at 10⁹ and 10¹⁰ CFU, which they consider as low and high dose, respectively. The authors verified a reduction in visceral fat mass after protocol (p = 0.038) in both dosages. Subcutaneous fat mass area, total fat area, % fat, and body fat mass were not significantly different between the three groups. However, it can be observed that the reductions in the visceral fat area for the dose 10⁸ (−1.8 cm²) and 10¹⁰ (−1.4 cm²) it’s smaller when compared to those observed in the Kadooka study. However, it is important to consider that in both studies the strain used collaborated to reduce visceral fat mass. And despite the higher amounts consumed in the study by Kim et al. lower amounts generated more expressive results.

Moreover, authors controlled the energy intake with hypocaloric diet of −200 kcal per day and despite caloric restriction, the authors do not call attention to this factor, although the literature shows that energy restriction is the main factor that influences weight loss.

Omar et al. (2013) [30] investigated the consumption of two other strains, *Lactobacillus amylovorus* (LA) and *Lactobacillus Fermentum* (LF), added in yoghurt at concentrations of 1.39 × 10⁸ UFC and 1.08 × 10⁹ UFC for 3 phases of 43 days, separated by a 6-week interval. The authors did not find significant changes in total body mass and body composition (fat mass and lean mass) after the treatment period between the different groups. However, the groups treated with probiotics had more robust reductions compared to the start of the placebo group treatment, with LF reducing about 3% of the fat mass, whereas LA about 4% and the control group, only 1%. In addition, it observed that the total amount of *Lactobacillus* increased significantly in response to LA and LF treatments compared to the control group, and in addition, LA ingestion also appeared to exert an inhibitory effect on the *Clostridial IV* group (Clep) in the gut of the participants who received the treatment when compared to the control. *Clostridial IV* (Clep) is known to be commensal, however it belongs to the microbial phylum Firmicutes, which seems to facilitate the energy extraction of ingested foods and increase energy storage in the adipose tissue of the host [16]. According to the study’s authors, the findings indicate that increasing levels of lactic acid bacteria create a microbial environment that inhibits the growth of pathogenic bacteria and promotes the proliferation of beneficial bacteria.

Zarrati et al. (2013) [31] investigated the effects of probiotics by ingestion of yogurt with the combination of *Lactobacillus acidophilus* LA5, *Lactobacillus casei* DN001 and *Bifidobacterium lactis* BB12 at the dose of 10⁷ UFC/g for 8 weeks. In summary, the probiotic groups with diet and the group with diet without probiotic reduced body mass, BMI and CC after 8 weeks (p < 0.001), with no difference between the groups. Therefore, only the groups with a low-calorie diet reduced body mass, and no additional effect of probiotics was observed, demonstrating that caloric restriction was determinant for weight loss.

Sanchez et al. (2013) [32], as well as Zarrati et al. (2013) [31] investigated the impact of probiotic supplementation associated with a calorie restriction. However, Sanchez et al. evaluated the supplementation of *Lactobacillus rhamnosus* CGMCC1.3724 (LPR) alone at a dose of 1.6 × 10¹⁰ CFU per day for 24 weeks. The results showed that after the first 12 weeks and after 24 weeks the mean body mass was not significantly different between the LPR and placebo groups when all subjects were considered, results corroborating those of Zarrati et al. (2013) [31]. However, when women treated with LPR were observed to have a significantly greater mean body mass loss than women in the placebo group after the first 12 weeks. In addition, women in the LPR group not only continued to lose body mass over time but still reduced fat mass significantly (<0.05) after 24 weeks compared to the placebo group.

Jung et al. (2015) [34] investigated the effects of supplementation of the association of two probiotic strains, *Lactobacillus curvatus* HV7601 to 2.5 × 10¹⁰ CFU and *Lactobacillus plantarum* KY1032 also to 2.5 × 10⁹ CFU in body adiposity in overweight subjects. After 12 weeks of intervention, the probiotic group had a significant reduction in body mass (p < 0.01), BMI (p < 0.01), WC (p < 0.05) and subcutaneous fat area (p < 0.05) in relation to the beginning of treatment, however, no significant decreases in the visceral fat mass area observed in this group.

The study by Gomes et al. (2017) [36] evaluated in overweight and obese women the consumption of 4 sachets containing 5 different strains of *Bifidobacterium* and *Lactobacillus* (*Lactobacillus acidophilus* LA-14, *Lactobacillus casei* LC-11, *Lactococcus lactis* LL-23, *Bifidobacterium bifidum* BB-06, *Bifidobacterium lactis* BL-4), totaling 2 × 10¹⁰ CFU/day, before breakfast for 8 weeks.

The results showed that only the group diet + probiotic (DI + P) significantly reduced fat mass and presented a better decrease in waist circumference, waist-height ratio and conicity index than the diet-only group. However, at the end of the intervention, there was no difference between the groups in the cytokines IL-6, IL-10 and LPS concentration, which may suggest that this combination was not able to improve intestinal barrier function and inflammation, although contribute to body composition more effectively than intervention based on diet alone.

In addition to the few strains used in this study, it is possible that the short intervention time will be determinant in some changes that not observed. Furthermore, this data shows that the relationship between LPS and obesity is still not well understood, considering that, even without LPS reduction, the individuals analyzed reduced body fat.

Interestingly, De Lorenzo et al. (2017) [37] observed that supplementation of 1 sachet/day containing 1.5 × 10¹⁰ CFU of each
Several mechanisms are proposed to elucidate the relationship between microbiota and obesity [7]. It believed that obesity microbiota is more efficient in extracting energy from food, increasing the stock of substrates in the adipocyte [6]. Furthermore, it suggested that the microbiota regulates food intake from short-chain fatty acid (SCFA)-mediated mechanisms [7,42]. SCFAs such as acetate, propionate, and butyrate activate G-protein-coupled receptors GPR41 and GPR43 in intestinal epithelial cells, as well as stimulate peptide YY (PYY) and glucagon-like-peptide 1 (GLP1), slowing gastric motility, improving the absorption of nutrients and, finally, increasing satiety [7]. In addition to the reduction in food intake generated by SCFAs, these seem to reduce insulin resistance, creating a more favorable environment for the mobilization and use of fat as an energy source [7].

Finally, it suggested that probiotics could decrease low-grade systemic inflammation present in obesity [19]. Thus, obesity and disturbances in the microbiota appear to directly affect gut permeability, leading to a higher translocation of compounds, especially lipopolysaccharide (LPS), a fragment of gram-negative bacteria. This LPS binds to lipopolysaccharide binding protein (LBP), improving its sensitivity to peripheral receptors, especially toll-like-receptor 4 (TLR-4) [10]. This mechanism increases the activity of nuclear factor kappa B (NF-kB) which increases the expression of proinflammatory cytokines (IL-6 and TNF-α). These cytokines contribute to insulin resistance, oxidative stress, and increased visceral fat deposition [10]. Thus, probiotic supplementation, through the regulation of the microbiota, could contribute to attenuation of these diverse mechanisms, given that the deregulation of the microbiota seems to be the genesis of several changes related to obesity [19].

However, the studies have several limitations such as, small sample, inadequate control of caloric intake as well as no control over the type of nutrient that consumed, since it known that different nutrients influence the intestinal microbiota. Still, the age of the participants was very heterogeneous, making it difficult to understand the results, since age per se changes the gut microbiota.

In order to correctly understand the effect of probiotics in the slimming process, new studies are needed, especially studies that control the amount of kilocalories, the type of nutrients consumed, the age of the participants, the level of insulin sensitivity and body composition, as well as the analysis metabolic and immunological parameters such as LPS and interleukins, so as to better elucidate the mechanism of action by which probiotics can collaborate to reduce body fat.

In this review, we verified that two studies [29,40] that used Lactobacillus gasseri varying between $1 \times 10^6$ and $1 \times 10^{10}$ promoted a body fat reduction. Besides, although not included in the review due to the exclusion criteria, Kadooka et al. (2010) [46] also verified the reduction of body fat after the intervention using the same strain.

4. Conclusion

In summary, few studies have found that probiotics alone help to reduce body fat and the mechanism of action is unclear. The small sample, control of the total calorie intake, as well as the type of nutrients that ingested, are significant limitations. Thus, studies that can control these variables, as well as analyze specific parameters for understanding the process of weight loss are necessary.

Finally, many doubts still surround the effect of different probiotic strains to understand their impact on the weight loss process.
Conflict of interest

None declared.

References


