Research Article

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Effects of the use of prebiotics in the treatment of obesity

Abstract

Obesity is growing public health problem and is associated with the risk of developing chronic non-communicable diseases. Changes in the intestinal microbiota of the obese, such as dysbiosis, are responsible for metabolic dysregulation, and the use of prebiotics is used as a way to improve these conditions. In this article which is a systematic review, the effects of prebiotics as a therapeutic approach to overweight were highlighted. Among the results, it was shown to improve inflammatory conditions, systemic endotoxemia, microbiota composition, in addition to favoring SCFA production.

Keywords: no-communicable chronic diseases, intestinal microbiota, obese, dysbiosis

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Introduction

The projections of the world population profile, according to the World Obesity Federation,[1] are that, by 2025, one in five adults will be affected by obesity, and a third of these will have the Body Mass Index (BMI). above 35 kg/m² and at high risk of developing chronic non-communicable diseases (NCDs). In Brazil, the obesity scenario is worrying, according to the 2019 National Health Survey, 21.8% of men and 29.5% of women in the adult population are obese, and this prevalence of obese increases with age.[2]

Obesity is represented by excess body fat resulting from a positive energy balance, demonstrating a food consumption greater than the individual's energy expenditure.[3] In addition, it is considered a condition of chronic inflammation and presented as a common risk factor of several metabolic alterations, such as dyslipidemias, diabetes mellitus, cholesterolemia and cancers.[4]

Studies show that obese individuals can present changes in the intestinal microbiota and these changes are responsible for metabolic deregulations and a low-grade inflammation that would culminate in the emergence of chronic diseases. The intestinal microbiota and its physiological and compositional changes are related to the individual's health and disease condition, mainly to the development of metabolic disorders.[5]

The diversity of the intestinal microbiota was inversely related to adiposity, that is, the lower the diversity of microorganisms present in this environment, the greater the adiposity. In addition, it demonstrated a relationship between low diversity and the presence of insulin resistance and dyslipidemia.[6] Studies reinforce that conditions of dysbiosis, imbalance of the microbiota, can activate the immune system and provide a metabolic deregulation predisposing to CNCDs.[7]

Prebiotics, which are substrates used selectively by microorganisms of individuals, bringing improvement to their health, presenting benefits such as reduction of blood lipids, effects on insulin resistance, improvement of immunity, among others.[8] The fermentation of these prebiotics generate short-chain fatty acids (SCFA) that have metabolic and anti-inflammatory functions.[9]

Butyrate and acetate, which are the most abundant SCFAs, reduce intestinal permeability, increase tight junction expression. They are responsible for inhibiting the expression of inflammatory mediators, such as nuclear factor kappa b (NF-kB), tumor necrosis factor alpha (TNF-alpha), interleukin-6 and interleukin-12 and increasing the expression of interleukin-10[9].

Inulin-type prebiotics have demonstrated changes in the gut microbiota, increasing the growth of Bifidobacterium and Faecalibacterium prausnitzii that are beneficial and correlated with the decrease in serum lipopolysaccharides, in addition to increasing the postprandial glucagon-like peptide-1 (GLP-1) response. and peptide YY (PYY) with a decrease in ghrelin and, consequently, affecting food consumption.[10] In view of this scenario of a worldwide epidemic of obesity and observing the relationship between the microbiota conditions of the obese individual and the development of metabolic alterations, the present study sought to investigate the effect of prebiotics in the treatment of obesity.

Methods

The work is a systematic review based on research on the effects of prebiotics in improving the conditions of the intestinal microbiota of obese individuals, answering the following question: What are the possible effects of prebiotics in the treatment of obesity? The achievement of the review followed the following steps: identification of the theme and elaboration of the guiding question; search for studies using eligibility criteria; identification of previously selected studies; data extraction; analysis and interpretation of the results and, finally, elaboration of the review.

For data collection, the acronym PICOT (Population of interest, Intervention, Comparator, Outcomes, Type of Study) was used, in which individuals with obesity were defined as population, intervention the use of prebiotics, comparison group as those who did not was exposed to sources of prebiotics and outcomes such as improved obesity treatment. The research was carried out between February and November 2021 in the following Pubmed, Scielo and Lilacs databases, using the following descriptors: "prebiotics" and a combination of "obesity and prebiotics" and "obesity and gastrointestinal microbiome".

In the second step, a search for articles in the databases was carried out, considering eligibility, following the inclusion criteria: original articles published in the last 5 years with availability in full, whether they were randomized or non-randomized clinical trials in individuals in the age from 18 to 65 years. Articles that were carried out in children and pregnant women, in animals or "in vitro" and review studies were excluded.

For the achievement of the third stage, initially, the studies were selected by reading the title, later, the abstracts were analyzed in order to identify the articles that addressed the use of inulin in obese individuals. It is important to point out that there were duplicate articles in the researched databases that were excluded, and those that remained were selected by reading titles and abstracts until they were read in full in order to identify whether the research, in fact, addressed the effects of prebiotics in improving the intestinal microbiota of obese and overweight individuals. After finishing the reading of the previously selected articles, in the fourth step, a standardized table was prepared to assist in the extraction of data referring to the studies, with information about the authors, year of publication, title, objective, study variables, methodology, main authors' results and conclusions.

It is important to highlight that both the reading and the extraction of the data were carried out by two reviewers independently, who, at the end of the process, compared the results found.

Results

The initial search on search platforms was carried out with the descriptors and their combinations, identifying 5081 publications. Among them, duplicate articles were first removed from 326 publications. Subsequently, the publication time selection criterion was applied, and the titles of articles were evaluated, finding 27 publications to analyze abstract. At this stage of selection, 15 publications were excluded, as they were studies that did not match the object of the research. In this way, 12 articles adapted to the parameters of demand, being carried out the complete reading of the publication and 11 articles were included in the review (Figure 1), were analyzed regarding the effects of the use of prebiotics in individuals with obesity and overweight described the findings represented in Table 1.

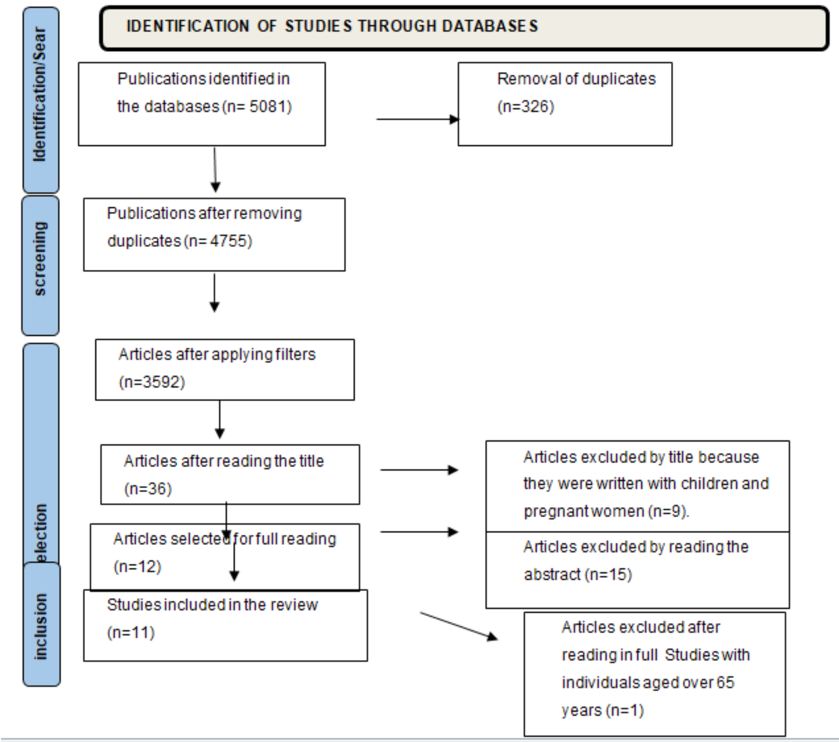

Figure 1 Flowchart of articl selection.

Table 1 Characteristics of the studies analyzed in the systematic review

Authors/Year/ Type of study	Sample characterization and intervention time (n)*	Study objective	Variables of study interest	Main outcomes
Hibberd AA, et al.[11] Randomized and controlled clinical trial	134 participants BMI between 28 to 34.9 kg/m² Age between 48 to 58 years. Intervention time: 6 months.	To investigate whether changes in the gut microbiota may be associated with the observed clinical benefits.	faecal samples Plasma samples (glucose, insulin, glycated hemoglobin, lipid profile, cortisol, liver markers). Anthropometric measurements (fat mass, fat-free mass, BMI, waist and hip circumference).	It demonstrated that the consumption of probiotics with or without prebiotics resulted in changes in the intestinal microbiota and the metabolism of overweight or obese individuals. Modification of the gut microbiota to a favorable composition improves gut barrier and obesity-related markers.

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Table Continued...

Authors/Year/ Type of study	Sample characterization and intervention time (n)*	Study objective	Variables of study interest	Main outcomes
Leyrolle Q, et al.[12] Randomized, single-blind, multicenter, controlled trial.	106 participants BMI > 30 kg/m² Age between 18 to 65 years. Intervention time: 3 months.	To analyze the use of prebiotic inulin and the link between changes in the intestinal microbiota and the effects on psychological parameters.	biochemical tests stool samples Questionnaires and cognitive tests – mood and emotion regulation ability	Potential effect of prebiotic inulin in obese individuals improving their mood. Changes in microbial, metabolic and inflammatory characteristics were also observed.
Hiel S, et al.[13] Randomized, single-blind, multicenter trial.	150 participants BMI > 30 kg/m², Age between 18 to 65 years. Intervention time: 3 months	To evaluate the impact of native inulin on gut microbiota-related outcomes in obese patients.	Stool sample. Food questionnaires. Anthropometric measurements behavioral assessment biochemical tests	The inulin-enriched diet is able to promote weight loss in obese patients in a healthy lifestyle context. Supplementation with inulin is an approach to consider before introducing treatments that target metabolic disorders.
Pol K, et al.[15] Triple-blind, parallel, randomized, controlled intervention study.	56 participants BMI between 25 to 35 kg/m² Age between 20 to 60 years. Intervention time: 3 months.	To investigate the effectiveness of 16g of oligofructose supplementation on weight management, including satiety, body weight and body composition.	Body weight Body composition food questionnaires Questionnaire on hunger and satiety	The use of oligofructose does not affect energy intake, body weight and body composition. There was an indication that appetite decreased after consumption of the oligofructose bar.
Chambers ES. et al.[24] Randomized, double-blind, placebo-controlled crossover trial.	12 participants BMI between 25 to 40 kg/m² Age between 18 to 65 years Intervention time: 42 days.	To investigate the underlying mechanisms behind changes in glucose homeostasis with propionate delivery to the human colon through a comprehensive and coordinated analysis of gut bacterial composition, plasma metabolome, and immune responses.	stool samples biochemical tests	Intervention with inulin and esterified propionate brought positive results in measures of insulin resistance in obese and overweight individuals.
Hess AL. et al.[18] Randomized, placebo-controlled, double-blind parallel intervention trial.	116 participants BMI between 18 to 45 kg/m² Age between 18 to 60 years Intervention time: 12 weeks.	To investigate the additive effects of combining restriction with dietary fiber on change in body weight and gut microbiota composition.	Anthropometric assessment stool sample Biochemical exams Blood pressure Physical activity level Dietary records and appetite	Inulin and resistant maltodextrin supplementation did not provide additional weight loss during a restrictive diet, but did have a blood pressure lowering effect. The intervention stimulated the growth of bacteria of the genus Parabacteroides and Bifidobacteria that have a beneficial potential, contributing to the production of SCFAs, thus modulating metabolic health.
Neyrinck AM. et al.[19] Multicenter, double-blind, placebo-controlled clinical trial.	56 participants BMI > 30kg/m² Age between 18 to 65 years Intervention time: 3 months.	To study the link between prebiotic intake, intestinal microbial signature in terms of bacterial composition, the profile of gut-derived metabolites and fecal biomarkers related to intestinal barrier function and intestinal inflammation, such as fecal zonulin and fecal calpronectin.	Stool sample. Assessment of energy and nutrient intake.	Intake of prebiotics decreases fecal calpronectin indicating an approach to combat inflammatory bowel disorders that occur in obesity.

Table Continued...

Authors/Year/ Type of study	Sample characterization and intervention time (n)*	Study objective	Variables of study interest	Main outcomes
Padilla-Camberos, EE, *et al.*[21] Randomized and controlled trial.	28 participants BMI > 30kg/m² Age between 20 to 55 years. Intervention time: 12 weeks	To evaluate the effects of agave fructans on weight control, lipid profile and physical tolerability.	Anthropometric measurements Biochemical tests (glucose, insulin, total cholesterol, HDL, LDL and triglycerides)	It demonstrated that the use of agave fructans provides a decrease in body mass index, total fat percentage and triglyceride levels in people with obesity grades I and II. Intake of agave fructans is well tolerated and safe.
Parnell JÁ[25] Randomized, double-blind, controlled clinical trial.	37 participants Intervention time: 12 weeks	To determine the effect of prebiotic supplementation on metabolic endotoxemia and systemic inflammation.	Anthropometry Eating behavior questionnaire faecal microbiome	Regular supplementation with 21g of oligofructose reduces endotoxemia and PAI-1, in addition to reducing weight and body fat mass. The use of this prebiotic may decrease some markers of inflammation associated with obesity, reducing the risk of developing associated complications.
Jamar G, et al.[29] Double-blind, randomized controlled trial.	35 participants BMI Ages between 31 and 59 years. Intervention time: 6 weeks.	To investigate the ability of the juçara berry to modulate some commensal bacteria and the production of SCFA.	Anthropometric measurements faecal samples	Supplementation with 5g of lyophilized juçara for 6 weeks promoted the growth of probiotic and commensal bacteria, suggesting the potential prebiotic effect of juçara on the intestinal microbiota.
Van Der Beek CM, et al.[14] Double-blind randomized controlled study.	14 men BMI between 25 to 35 kg/m² Age between 20 to 50 years. Intervention time: 2 to 5 days.	To investigate the acute metabolic effects of inulin ingestion compared to digestible carbohydrates and to track inulin-derived SCFAs using stable isotope tracer methodology.	plasma sample Breathing Feces appetite and satiety	Ingestion of prebiotic inulin improves fat oxidation and promotes fermentation in SCFAs. favoring metabolism.

Discussion

The beneficial effects related to prebiotics in the treatment of overweight and obese individuals observed in the studies were related to the improvement of the intestinal microbiota and consequently improvement of systemic endotoxemia and inflammation, the reduction of weight and percentage of fat and the increase of SCFAs. One of the studies included in the review analyzed the intervention of prebiotics, probiotics and synbiotics, this study demonstrated that the use of probiotics with or without prebiotics brought improvements to the intestinal microbiota of individuals.[11]

Researches[12] observed in their studies that the administration of 16g of inulin during 3 months of intervention in obese individuals favored a decrease in negative emotions, improving the mood of these individuals, and that individuals who had a higher level of Coprococcus obtained positive responses in relation to the intervention. There were also changes in microbial characteristics favoring the prevention of metabolic consequences resulting from obesity.

Another study[13] evaluated the intervention of 16g of inulin in obese individuals during a 3-month intervention, resulting in beneficial changes in the bacterial communities present in these obese individuals. Prebiotic use increased in Actinobacteria phylum and Bifidobacteriaceae family, increased B. bifidum, Bididobacterium longum, B. adolescents, and decreased Desulfobibrio and Roseburia. In addition to these changes in the intestinal microbiota, it provided bodily changes, such as weight reduction.

A recente survey[14] demonstrate that the use of 24g of inulin did not change the GLP-1 and PYY hormones, nor the satiety and appetite scores. Others researches[15] investigated the intervention of 16g of oligofructose inserted in a granola bar for 3 months, the results expressed that there were no changes in body composition, nor did it affect energy intake, and in the last weeks of studies a decrease of hungry. In contrast, a study[16] observed that the 10g inulin intervention in overweight and obese subjects suppressed appetite, despite not altering hunger and satiety-related hormones.

A study,[17] with 35 overweight and obese individuals with type 2 diabetes mellitus, with the intervention of 16g of oligofructose and inulin in one group and in the control group the use of 16g of maltodextrin, during a period of 6 weeks, resulted in no change in the perception of satiety, nor did they reduce energy intake.

Changes in anthropometric measurements, such as waist-hip ratio, were found after the intervention of prebiotic supplementation indicating that there is a decreased risk of developing NCDs with the use of prebiotics.[11]

In study[18] with 86 participants, with the intake of 20 g of dietary fiber by one group and another placebo group and both groups were in caloric restriction, observed that the use of fiber had no effect on plasma glucose and that fiber intake resulted in an increase in Parabacteroides and Bifidobacteria inducing beneficial changes in the gut microbiota and an increase in SCFAs contributing to the prevention of metabolic outcomes resulting from obesity.

A recent survey,[19] observed that the use of 16g of inulin in obese subjects during a 3-month intervention reduced fecal calpronectin, which is a marker of intestinal inflammation, increased the amount of AGGs, in addition to increasing the number of Bifidobacteria. It was also found in studies with obese insulin-resistant animals that the use of butyrate reduced lipid accumulation, body weight and increased energy expenditure. Mice treated with butyrate had an improved ability to oxidize lipids, a reduction in inflammatory markers was also demonstrated, reinforcing the anti-inflammatory potential of this metabolite.[20]

Prebiotics have the ability to modulate the lipid profile of individuals, in their study,[21] found that 96mg of agave fructans for 12 weeks was able to decrease triglyceride levels, in addition to favoring weight loss and fat percentage. According to the study, this amount was well tolerated by the research participants. Inulin and oligofructose are used by the industry to replace sucrose and preserve sweetness and texture. In a study with 39 participants, the use of a yogurt drink with oligofructose was analyzed and it was observed that glucose was significantly lower after consumption of the drink with oligofructose compared to whole sugar. The insulin response was also lower with the oligofructose-containing beverage. In parallel, the use of inulin in fruit jelly was studied compared to the use of whole sugar, similar results with lower glucose and insulin levels with the inulin intervention. Both products added with prebiotics were well tolerated, and may be a proposal to be used by the food industry for the purpose of glycemic controls.[22]

With regard to insulin and plasma glucose, researchers[14] observed that the consumption of 24g of inulin by overweight and obese men had positive responses in these markers, demonstrating lower values with this intervention. There was an increase in fat oxidation and an increase in SCFAs, promoting an improvement in the individual's metabolism. Corroborating this study, another study[23] resulted from the intervention of 20g of inulin and esterified propionate, improvements in insulin sensitivity.

Researchers[24] observed that the use of 21g of oligofructose for 12 weeks reduced plasma concentrations of LPS and PAI-1, but did not affect inflammatory markers such as IL-6, TNF-alpha, adiponectin and resistin.

Changes in the intestinal microbiota in obesity can produce systemic endotoxemia and be a risk factor for the development of NCDs. A study[25] analyzed obese mice that had intestinal barrier dysfunction induced by the Western standard diet. They fed one group of mice a Western standard diet and the other group a Western standard diet with inulin and butyrate supplementation for 12 weeks. The results showed positive effects of the use of inulin and butyrate even with the Western standard diet. They attenuated hepatosteatitis, reduced body weight, liver weight and hepatic triglyceride level. An improvement in the intestinal barrier, a decrease in TNF-alpha and IL-6, and, consequently, a decrease in systemic endotoxemia were also demonstrated.

The intervention[26] of 16g of inulin in individuals who have a diet rich in fiber and in individuals who have a diet low in fiber was performed to assess the influence of this prebiotic on different habitual fiber intakes. The 34 participants who were used in the analysis and the study found that inulin led to an increase in Bifidobacterium, a decrease in Coprococcus, Dorea, Ruminococcis and relative abundance of Faecalibacterium. In the same sense of improvement in bacterial composition, researchers[27] investigated the effectiveness of using fructooligosaccharides and their doses. The 80 participants were divided into four groups, receiving 3 levels of doses 2.5 g, 5 g, 10 g and the placebo group, the results showed that the consumption of fructooligosaccharides increased Bifidobacterium and Lactobacillus. Butyrate-producing bacteria also had their levels increased, such as Faecalibacterium, Ruminococcus, and Oscillospina promoting benefits to the host. Finally, a study[28] showed that supplementation with 5g of lyophilized juçara for 6 weeks in adults promoted the growth of probiotic and commensal bacteria, suggesting the potential prebiotic effect of juçara on the intestinal microbiota.

The use of prebiotics can bring improvements in the intestinal microbiota, from changes in microbial composition to changes related to structural integrity, reflecting in the prevention of metabolic outcomes resulting from overweight and in the improvement of obesity conditions. These benefits demonstrate the relevance of further studies on the topic of using prebiotics as a therapeutic approach to obesity.

Conclusion

Studies indicate that the use of prebiotics promotes an improvement in the health of overweight or obese individuals, reducing the risk of developing NCDs and the endotoxemia present, improving the conditions of the intestinal microbiota and decreasing body weight. The use of prebiotics promotes fermentation in SCFAs that demonstrate positive effects on intestinal mucosal integrity, reducing intestinal permeability and preventing harmful metabolic outcomes. In addition to improving the microbial diversity of the intestinal microbiota, promoting the increase of beneficial bacteria to the health of the individual.

The present study indicates the use of prebiotics as an aid in the treatment of obesity. It is suggested that further studies be carried out in order to clarify the dosage of the types of prebiotics and duration of use to achieve effective results in the treatment of obesity and the resulting metabolic complications.

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Conflict of interest

The authors declare that they have no competing interests.

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