v. 4, n. 81, 2024

International Journal of Health Science

THE INFLUENCE OF PROBIOTIC USE IN THE TREATMENT OF OBESITY

Carolina Mendes dos Santos da Costa
Student of medicine course at:
``UniVassouras``, Vassouras, RJ, Brazil
https://orcid.org/0000-0001-5990-2381

Jonas César Moreira Corrêa
Student of medicine course at
``UniVassouras``, Vassouras, RJ, Brazil
https://orcid.org/0000-0001-6562-527X

Nardo da Silva Ouriques
Professor of medicine course at
``UniVassouras``, Vassouras, RJ, Brazil
https://orcid.org/0009-0009-7810-7952

Abstract: Goal: This study aimed to analyze the influence of changes in the intestinal microbiota on these changes' secondary to obesity, as well as the possible role of probiotics in its treatment. **Methods:** The Virtual Health Library (BVS) and National Library of Medicine (Pubmed) databases were used, in a time frame from 2013 onwards, using the descriptors "influence of probiotics", "microbiota" and "obesity", using the Boolean operator "AND", resulting in a total of 506 articles, which were read and selected based on the inclusion and exclusion criteria. For inclusion of the articles, original works, free and paid access, clinical trials, randomized clinical trials and observational studies were chosen, and articles outside the theme and duplicates were excluded. **Results:** It was observed that the use of probiotics is a treatment that has demonstrated beneficial results both when used in association with already known treatments, and has also demonstrated benefits to its exclusive use when compared to placebo. **Conclusion:** as it is still very recent, new studies are still necessary since they have not yet demonstrated a patient profile that is most suited to treatment and the ideal time to start use and what would be the best concomitant use.
Keywords: influence of probiotics; microbiota; obesity.

INTRODUCTION

According to the World Health Organization, obesity is a chronic disease defined by the abnormal or excessive accumulation of fat in the body resulting from a caloric intake that is higher than what is expended by the body to maintain its basal metabolic rates and perform daily activities.1 Obesity and overweight are considered a major risk factor for chronic diseases, including cardiovascular diseases, including heart disease and coronary syndromes, which are associated with causes of death worldwide. Another association between obesity and overweight is with diabetes mellitus and its associated conditions such as blindness, limb amputation and the need for hemodialysis. Obesity has also been associated with some types of cancer such as endometrial, breast, ovarian, prostate, liver, gallbladder, kidney and colon cancer. (World Health Organization).

As described by the National Health Survey (PNS, 2020), more than half of the 60.3% of adults are overweight, which represents 96 million people, and obesity affects 25.9% of the population, reaching 41.2 million adults. This metric tends to continue increasing, as eating habits consisting of ultra-processed and hyperpalatable foods that are harmful to health and increasingly encourage their consumption have been normalized.[2]

Obesity is a dysfunction with multifactorial origins, including environmental, genetic and endocrinological. It occurs as a response to environmental, genetic stimuli, predispositions and abnormalities or a combination of these (CONWAY; RENE, 2004). Regarding genetic dysfunction and predisposition, obesity has a polygenic etiology containing more than 200 genes and chromosomal markers implicated in its pathophysiology (GARDNER D, 2022).

Studies have shown that some of the following genes are associated with body fat or BMI, such as: Uncoupling Protein (UCP), Tumor Necrosis Factor alpha (TNF-α), Lipoprotein Lipase (LPL) and Dopamine D2 Receptor (DRD2) (LOCKE et al., 2015). Approximately 4% of severely obese patients have a mutation in the melacortin-4 receptor gene, the gene most widely associated with common obesity (DAS, 2001). This increased expression of tumor necrosis factor (TNF-α) by adipocytes in obesity is related to an increased response to infection as well as stimulating a higher inflammatory response and apoptosis (BENN, 1970).

In addition to storing lipids, adipocytes also act as endocrine cells releasing hormones such as leptin, resistins, adipsin, adiponectin, and other substances and substrates. Leptin acts by up-regulating the immune inflammatory response (WALLACE et al., 2001). This data, in addition to implying another topic in the pathophysiology of obesity, also correlates with the complications of obesity, since it is involved in the pathogenesis of atherosclerosis (ABENAVOLI et al., 2019) and also stimulates platelet aggregation (CHEN D; GARG A, 2021).

The human intestine is composed of ten trillion diverse symbionts and approximately 100 bacterial species collectively known as microbiota. This is ten times more abundant than human germ cells. In an individual, 150 to 170 bacterial species predominate and benefit from the warm, nutrient-rich environment of the intestine and perform protective, metabolic, and structural functions (ADAK; KHAN, 2018).

The bacteria that make up the intestinal microbiota are related to metabolism in several ways, helping to convert complex nutrients in a way that contributes to their absorption, in addition to stimulating effective intestinal digestion and epithelial proliferation, since the microbiota is one of the main components in the formation of the intestinal defense barrier that makes up the human immune system (TREMBLAY; DOUCET, 2000).

With regard to obesity, the phyla that stand out the most are Firmicutes and Bacteroidetes, their relationship is of great importance in maintaining intestinal homeostasis and when there is any imbalance in this relationship, it is considered dysbiosis and is found in obesity with an increase in Firmicutes and a decrease in Bacteroidetes. The increase in Firmicutes is believed to be due to their ability to ferment and metabolize carbohydrates and lipids, increasing their stock and facilitating the propensity for obesity (STOJANOV; BERLEC; ŠTRUKELJ, 2020). This relationship is greatly influenced by the individual's lifestyle, but mainly by diet, which is a major modulator of the intestinal microbiota (DAVID et al., 2013).

Recent studies have demonstrated a relationship between the intestinal microbiota and obesity, with the latter being capable of altering the intestinal microbiota and having a close relationship with its pathogenesis, since it affects human immunity and metabolism (STEPHENS; ARHIRE; COVASA, 2018).

The use of probiotics, which is nothing more than the oral consumption of microorganisms, aiming to improve health, especially intestinal health, is something known and is not recent. A study carried out in 2019 demonstrated a relationship with the treatment and prevention of other diseases such as *Clostridium difficile* infection, irritable bowel syndrome, reduced risk of neonatal infection and sepsis by enterococci. However, these studies are questioned regarding the method and their quality. However, the use of probiotics has been increasingly studied in recent years (SUEZ et al., 2019).

As one of the consequences of the pathophysiology of obesity is the decline in human immunity, the use of probiotics in the treatment of this pathology is questionable, since they influence obese patients, since they act mainly on immunity (FUJISAKA; WATANABE; TOBE, 2022).

According to the National Health Surveillance Agency, probiotics are live microorganisms that, when administered in certain quantities, promote a benefit to the individual's health by favoring gastrointestinal functions, reducing the risk of constipation and colon cancer. These microorganisms are composed of several genera and species, and can be consumed as fermented milk, yogurts and other fermented dairy products (ALVES, 2008).

Therefore, since there is a relationship between the mechanism of action of the Probiotic and the pathophysiology of obesity, the objective of this study was to evaluate whether the use of probiotics is effective in the treatment of this pathology.

METHODOLOGY

This is an integrative literature review, in which references were taken from the Virtual Health Library (BVS) and National Library of Medicine (PubMed) databases. The search was performed using the descriptors "influence of probiotics", "microbiota" and "obesity", using the Boolean operator "AND". The literature review was carried out following the following steps: establishing the theme; defining the eligibility parameters; defining the inclusion and exclusion criteria; checking the publications in the databases; analyzing the studies found and presenting the results. Articles published in the last 10 years (2013– 2023) and articles of the clinical trial, randomized clinical trial and observational study type were included. Articles that were outside the theme addressed and duplicates were excluded.

RESULTS

The search resulted in a total of 506 articles, of which 331 were selected from the PubMed database and 195 from the BVS database. After applying the exclusion and inclusion criteria, 15 articles remained in the BVS database and 10 articles in the PubMed database, of which 7 were duplicates, leaving 10 articles in the PubMed database and 8 in the BVS database, as shown in figure 1. Of the 18 articles analyzed shown in table 1, six were controlled clinical trials, six were randomized controlled clinical trials, one was randomized clinical trial and five were observational studies. Only three did not demonstrate a correlation between the use of probiotics and their influence on the intestinal microbiota and obesity. In the others, either by reducing the percentage of fat and total body mass, or by modeling the microbiota, influencing which microorganisms make it up and thereby increasing the host's immunity, thus acting on one of the pathophysiological mechanisms of obesity. The influence of probiotic use could be observed in the study in which its use was exclusive, not associated with any other type of intervention, and thus, it obtained positive results regarding weight loss and modulation of the microbiota.

As well as its use associated with other interventions such as the Mediterranean diet, it had a potentiated effect when compared to the diet alone.

However, some authors have reported a need for further studies so that the mechanism of action of probiotics can be further elucidated for a better understanding of their greater effectiveness.

DISCUSSION

The clinical trial divided the participants into two groups, group A and group B. Both maintained a diet with the same caloric value, being hypocaloric, but composed of different foods. Group A received a larger amount of probiotic in its various forms per daily intake, while group B ingested a smaller amount of probiotic only once a week. After three months, both groups demonstrated a reduction in body weight, fat percentage, abdominal circumference and BMI, but group B had a greater loss in abdominal circumference than group A. Regarding the bacterial count, the women in group B showed a significant reduction, while group A showed no change. According to the author of the study, since the study lasted 3 months, there was too little time to obtain any information about the influence of the probiotic and its mechanism of action in both groups with regard to weight loss in these patients.

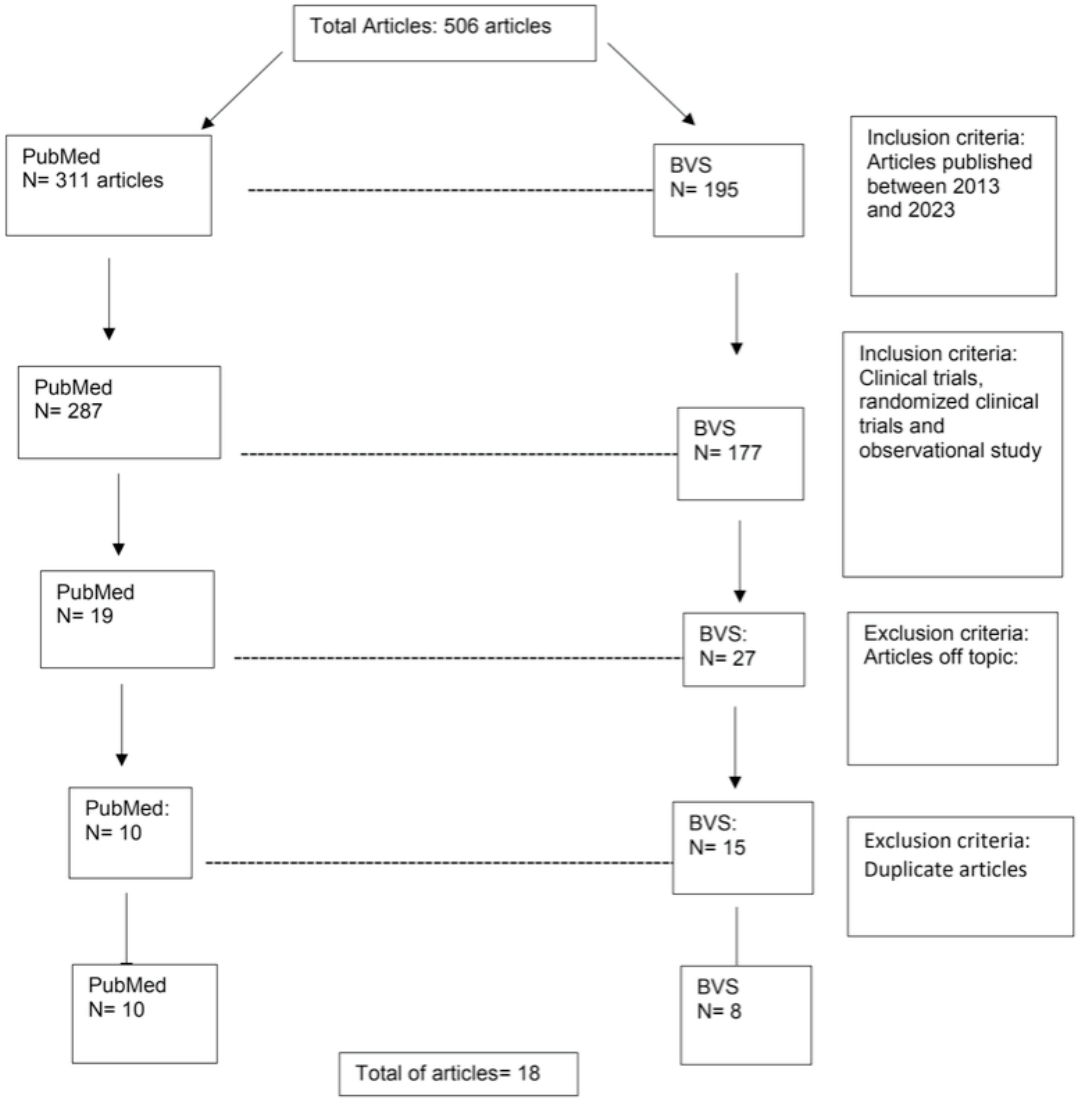

Figure 1: Flowchart of identification and selection of articles in the PubMed databases and BVS

Source: Author (2024)

Author	Year	Title	Type of study	Main conclusions
JAGIELSKI et al., (2023)	2023	Effect of diet containing sources of Prebiotics and Probiotics and Modification of The Gut Microbiota on the Reduction of body fat	Controlled clinical trial	A study demonstrated significant weight loss through a calorie-restricted diet enriched with pre- and probiotics. In addition, the group that received the pre- and probiotics showed changes in the intestinal microbiota, but this had both positive and negative aspects in relation to the reduction of certain microorganisms.
KACZMARCZYK M, et al., (2022)	2022	Treatment with Multi-Species Probiotics Changes the Functions, Not the Composition of Gut Microbiota in Postmenopausal Women With Obesity: A Randomized, Double-Blind, Placebo-Controlled Study	Randomized controlled clinical trial	This study demonstrated that in addition to the change in the composition of the microbiota, its physiology and biochemistry also underwent modifications after the use of probiotics. In addition to the weight loss related to the decrease in certain bacteria in the intestinal microbiota.

RAHAYU ES, et al., (2021)	2021	Effect of probiotic Lactobacillus plantarum Dad-13 powder consumption on the gut microbiota and intestinal health of overweight adults	Randomized controlled clinical trial	Probiotic consumption demonstrated weight reduction while the placebo group did not demonstrate any change in weight, body mass or microbiota composition.
SOLITO A, et al., (2021)	2021	Supplementation with Bifidobacterium breve BR03 and B632 strains improved insulin sensitivity in children and adolescents with obesity in a cross-over, randomized double-blind placebo-controlled trial	Randomized controlled clinical trial	The trial demonstrated a decrease in weight loss and E. coli count, in addition to improving metabolic parameters and sensitivity to insulin resistance.
ALIPOUR H, et al., (2021)	2021	Effect of Probiotic Lactobacillus rhamnosus PB01 on Mechanical Sensitivity in a Female Diet-Induced Obesity Model	Controlled trial	The use of Lactobacillus rhamnosus as a supplement induced weight loss and promoted a change in pain sensitivity.
PETRAROLI M, et al., (2021)	2021	Gut Microbiota and Obesity in Adults and Children: The State of the Art.	Controlled Clinical Trial	The study did not demonstrate any change in the use of probiotics in pediatric patients, since they suffer external influences related to their immunity and modulation, such as breastfeeding, food introduction, pregnancy, among others.
GOMES HOFFMANN, MOTA. (2020)	2020	Gut microbiota is associated with adiposity markers and probiotics may impact specific genera	Randomized controlled clinical trial	The study considers the use of probiotics as promising for the treatment of obesity but still requires further studies and evidence for its application.
PELLEGRINI M, et al. (2020)	2020	Gut Microbiota composition after diet and probiotics in overweight breast cancer survivors: a randomized open-label pilot intervention trial	Clinical trial	The use of probiotics together with the Mediterranean diet has been shown to have a positive influence on the intestinal microbiota, a benefit that has been shown to be superior to the use of both alone. And it may possibly have a protective effect.
JANCZY A, et al (2020)	2020	Impact of diet and synbiotics on selected gut bacteria and intestinal permeability in individuals with excess body weight – A Prospective, Randomized Study	Controlled Clinical Trial randomized	The use of synbiotics demonstrated a change in the composition of the intestinal microbiota but did not result in any change in weight loss or changes in body composition.
EDWARDS PT, KASHYAP PC, PREIDIS GA (2020)	2020	Microbiota on biotics: probiotics, prebiotics, and synbiotics to optimize growth and metabolism	Observational study	Study did not demonstrate any significant results, requiring further experiments.
ARNORIAGA-RODRÍGUEZ M, FERNÁNDEZ-REAL JM (2019)	2019	Microbiota impacts on chronic inflammation and metabolic syndrome - related cognitive dysfunction	Observational study	Study demonstrates relationship between microbiota composition and its changes with the pathophysiology of diseases that cause an inflammatory reaction in the body, such as obesity.
HEALEY GR, et al., (2017)	2017	Interindividual variability in gut microbiota and host response to dietary interventions	Observational study	Dietary consumption has a regulatory function on the composition of the intestinal microbiota, which influences the host's immunity and metabolism, serving as a predisposition to other diseases such as obesity.
HALKJAER SI, et al (2016)	2016	Effects of probiotics (Vivomixx®) in obese pregnant women and their newborn: study protocol for a randomized controlled trial	Clinical trial Randomized	The use of probiotics in pregnant women has shown benefits in reducing the risk of pre-eclampsia, infections and has demonstrated maintenance of insulin levels.
STENMAN LK, BURCELIN R, LAHTINEN S (2016)	2016	Establishing a causal link between gut microbes, body weight gain and glucose metabolism in humans - towards treatment with probiotics	Observational study	Diet has a great influence on the intestinal microbiota, but more studies are still needed to demonstrate how it influences metabolism.

KIM SM (2015)	2015	Obesity and Dysbiosis	Observational study	There is still no evidence regarding the use of probiotics and how to use them in treatment, and further studies are needed.
UCHIYAMA-TANAKA Y (2014)	2014	A 10-patient case study on the influence of two different probiotics on individual intestinal microbiota.	Observational study	Each probiotic exerts an influence on the intestinal microbiota, therefore when selecting it for use, compatibility with each intestinal bacterial flora must be taken into consideration.
LEE SJ, et al., (2014)	2014	The effects of co-administration of probiotics with herbal medicine on obesity, metabolic endotoxemia and dysbiosis: A randomized double-blind controlled clinical trial	Controlled Clinical Trial	Studies have shown a relationship between intestinal microbiota and changes in body composition, indicating that the use of probiotics can influence obesity metabolism.
KELISHADI R, et al (2014)	2014	A randomized triple-masked controlled trial on the effects of synbiotics on inflammation markers in overweight children	Controlled Clinical Trial	The use of synbiotics in children demonstrated a positive influence on supplementation and on the alteration of inflammatory markers that are related to weight loss.

Table 1: Analysis of results

Source: Author (2024)

Further studies are needed to clarify this topic. Although weight loss is very important for the treatment of obesity, in this study this result is more linked to diet than to the use of probiotics (JAGIELSKI et al., 2023).

On the other hand, a new study demonstrated that dietary intake plays a regulatory role in the composition of the intestinal microbiota, so it is questionable whether this regulation is influenced in any way when probiotics are also used concomitantly and whether the regulatory function is enhanced when this association is present (HEALEY et al., 2017). The same was observed in an observational study carried out by Stenman LK, 2018 (*). However, another analysis demonstrated that the association of probiotic use concomitantly with the Mediterranean diet demonstrated superior results to patients who were restricted to the Mediterranean diet. These results implied a change in the composition of the intestinal microbiota, weight reduction, BMI, abdominal circumference, among others, thus being used and obtaining beneficial results as a treatment for obesity (PELLEGRINI et al., 2020).

Another study carried out with a total of 56 postmenopausal women participants received probiotics in a low dose, high dose and placebo. Changes were observed in both the group that received the low dose and the group that received a higher dose of probiotic. In addition, it was also observed that the use of probiotics can modify the effect that the microbiota has on the biochemical and physiological patterns of the individual, regardless of the change in the composition of the microbiota and its metabolic function over time. The increase in certain species (such as the Alcaligenaceae family) culminated in increased weight loss in addition to the reduction in BMI. Regarding dosage, there was no change in the result when using high and low dosages. Thus, through the results demonstrated in this study and because the experiment was based only on the use of the probiotic, without any external interference, it can be said that the probiotic influenced the microbiota and the reduction of anthropometric parameters (KACZMARCZYK et al., 2022).

The clinical trial carried out with 60 people with BMI > 25 consumed indigenous probiotics (L. plantarum Dad-13) for 90 days, with no specific diet or physical activity recommended.

The result demonstrated was that patients who used it achieved a reduction in body weight and BMI, as well as a change in the

composition of the microbiota, in which the number of Bacteroidetes increased while the quantity of Firmicutes decreased significantly. On the other hand, the group that received placebo did not demonstrate any change in either weight or microbiota composition, demonstrating an influence of the use of probiotics both in terms of weight loss and changes in the intestinal microbiota, acting on one of the pathophysiological pillars of obesity (RAHAYU et al., 2021).

CONCLUSION

Obesity is now considered a public health problem due to the continuous increase in the number of patients. Therefore, it is necessary to study all forms of action to better control this pathology, since it can cause serious consequences for the patient.

After analyzing the results and discussing them, it can be said that the use of probiotics has an influence on the treatment of obesity. However, this is still a subject that needs to be addressed more, since it is a more recent topic in the field of study and its results have only begun to show benefits in the last five years. The associations of the use of probiotics with other treatments different from those demonstrated in this study are also necessary to better elucidate which combinations have proven to be most beneficial, enhancing the action of the probiotic and the best time to start as a concomitant treatment with those already known.

On the other hand, it was not clear whether there are any restrictions or contraindications for any population group, so a more in-depth approach is needed so that the profile of the most suitable patient can be outlined and treatment can be started as soon as possible.

Therefore, it is essential that studies on the use of probiotics continue, since the greater the possibility of approach, the better it will be for the patient who will be able to have individualized treatment with great potential to improve both obesity and their quality of life.

REFERENCES

ABENAVOLI, L. et al. **Gut Microbiota and Obesity: A Role for Probiotics. Nutrients**, v. 11, n. 11, 7 nov. 2019.

ADAK, A.; KHAN, M. R. **An insight into gut microbiota and its functionalities**. Cellular and Molecular Life Sciences, v. 76, n. 3, p. 473–493, 13 out. 2018.

ALIPOUR, H. et al. **Modulatory Effect of Probiotic Lactobacillus rhamnosus PB01 on Mechanical Sensitivity in a Female Diet-Induced Obesity Model**. **Pain Research and Management**, v. 2021, p. 1–8, 29 jun. 2021.

ALVES, B. / O. / O.-M. **Alimentos funcionais | Biblioteca Virtual em Saúde MS**. 5 jun, 2008

ARNORIAGA-RODRÍGUEZ, M.; FERNÁNDEZ-REAL, J. M. **Microbiota impacts on chronic inflammation and metabolic syndrome - related cognitive dysfunction**. Reviews in Endocrine and Metabolic Disorders, v. 20, n. 4, p. 473–480, dez. 2019.

BENN, R. T. **Indices of height and weight as measures of obesity**. British Journal of Preventive & Social Medicine, v. 24, n. 1, p. 64, 1 fev. 1970.

CHEN D;GARG A. **Monogenic disorders of obesity and body fat distribution**. Journal of lipid research, v. 40, n. 10, 2021.

CONWAY, B.; RENE, A. **Obesity as a disease: no lightweight matter**. Obesity Reviews: An Official Journal of the International Association for the Study of Obesity, v. 5, n. 3, p. 145–151, 1 ago. 2004.

DAS, U. N. **Is obesity an inflammatory condition?** Nutrition, v. 17, n. 11-12, p. 953–966, nov. 2001.

DAVID, L. A. et al. **Diet rapidly and reproducibly alters the human gut microbiome**. Nature, v. 505, n. 7484, p. 559–563, 11 dez. 2013.

EDWARDS, P. T.; KASHYAP, P. C.; PREIDIS, G. A. **Microbiota on biotics: probiotics, prebiotics, and synbiotics to optimize growth and metabolism**. American Journal of Physiology. Gastrointestinal and Liver Physiology, v. 319, n. 3, p. G382–G390, 1 set. 2020.

Excesso de peso e obesidade. Disponível em: <https://www.gov.br/saude/pt-br/composicao/saps/promocao-da-saude/excesso-de-peso-e-obesidade>. 07 jun, 2021

FUJISAKA, S.; WATANABE, Y.; TOBE, K. **The gut microbiome: a core regulator of metabolism**. Journal of Endocrinology, v. 256, n. 3, dez. 2022.

GARDNER D. **The etiology of obesity**. Missouri medicine, v. 100, n. 3, 2022.

GOMES, A. C.; HOFFMANN, C.; MOTA, J. F. **Gut microbiota is associated with adiposity markers and probiotics may impact specific genera**. European Journal of Nutrition, v. 59, n. 4, p. 1751–1762, 1 jun. 2020.

HALKJAER, S. I. et al**. Effects of probiotics (Vivomixx®) in obese pregnant women and their newborn: study protocol for a randomized controlled trial**. Trials, v. 17, n. 1, 11 out. 2016.

HEALEY, G. R. et al. **Interindividual variability in gut microbiota and host response to dietary interventions**. Nutrition Reviews, v. 75, n. 12, p. 1059–1080, 28 nov. 2017.

JAGIELSKI, P. et al. **Effects of a Diet Containing Sources of Prebiotics and Probiotics and Modification of the Gut Microbiota on the Reduction of Body Fat**. International Journal of Environmental Research and Public Health, v. 20, n. 2, p. 1348, 11 jan. 2023.

JANCZY, A. et al. **Impact of diet and synbiotics on selected gut bacteria and intestinal permeability in individuals with excess body weight – A Prospective, Randomized Study**. Acta Biochimica Polonica, 16 dez. 2020.

KACZMARCZYK, M. et al. **Treatment With Multi-Species Probiotics Changes the Functions, Not the Composition of Gut Microbiota in Postmenopausal Women With Obesity: A Randomized, Double-Blind, Placebo-Controlled Study**. Frontiers in Cellular and Infection Microbiology, v. 12, 11 mar. 2022.

KELISHADI, R. et al. **A randomized triple-masked controlled trial on the effects of synbiotics on inflammation markers in overweight children**. Jornal de Pediatria, v. 90, n. 2, p. 161–168, mar. 2014.

KIM, S. M. **Obesity and Dysbiosis**. The Korean Journal of Obesity, v. 24, n. 3, p. 121–125, 30 set. 2015.

LEE, S. J. et al. **The effects of co-administration of probiotics with herbal medicine on obesity, metabolic endotoxemia and dysbiosis: A randomized double-blind controlled clinical trial.** Clinical Nutrition, v. 33, n. 6, p. 973–981, dez. 2014.

LOCKE, A. E. et al. **Genetic studies of body mass index yield new insights for obesity biology.** Nature, v. 518, n. 7538, p. 197–206, fev. 2015.

PELLEGRINI, M. et al. **Gut Microbiota composition after diet and probiotics in overweight breast cancer survivors: a randomized open-label pilot intervention trial.** Nutrition, p. 110749, 29 jan. 2020.

PETRAROLI, M. et al. **Gut Microbiota and Obesity in Adults and Children: The State of the Art.** Frontiers in Pediatrics, v. 9, 19 mar. 2021.

RAHAYU, E. S. et al. **Effect of probiotic Lactobacillus plantarum Dad-13 powder consumption on the gut microbiota and intestinal health of overweight adults**. World Journal of Gastroenterology, v. 27, n. 1, p. 107–128, 7 jan. 2021.

SOLITO, A. et al. **Supplementation with Bifidobacterium breve BR03 and B632 strains improved insulin sensitivity in children and adolescents with obesity in a cross-over, randomized double-blind placebo-controlled trial**. Clinical Nutrition, v. 40, n. 7, p. 4585–4594, jul. 2021.

STENMAN, L. K.; BURCELIN, R.; LAHTINEN, S. **Establishing a causal link between gut microbes, body weight gain and glucose metabolism in humans – towards treatment with probiotics.** Beneficial Microbes, v. 7, n. 1, p. 11–22, fev. 2016.

STEPHENS, R. W.; ARHIRE, L.; COVASA, M. **Gut Microbiota: From Microorganisms to Metabolic Organ Influencing Obesity.** Obesity, v. 26, n. 5, p. 801–809, 23 abr. 2018.

STOJANOV, S.; BERLEC, A.; ŠTRUKELJ, B. **The Influence of Probiotics on the Firmicutes/Bacteroidetes Ratio in the Treatment of Obesity and Inflammatory Bowel disease.** Microorganisms, v. 8, n. 11, p. 1715, 1 nov. 2020.

SUEZ, J. et al. **The pros, cons, and many unknowns of probiotics**. Nature Medicine, v. 25, p. 716–729, 6 maio 2019.

TREMBLAY, A.; DOUCET, E. **Obesity: a disease or a biological adaptation?** Obesity Reviews, v. 1, n. 1, p. 27–35, maio 2000.

UCHIYAMA-TANAKA, Y. **A 10-Patient Case Study on the Influence of Two Different Probiotics on Individual Intestinal Microbiota**. The Journal of Alternative and Complementary Medicine, v. 20, n. 10, p. 800–803, out. 2014.

WALLACE, A. M. et al. **Plasma Leptin and the Risk of Cardiovascular Disease in the West of Scotland Coronary Prevention Study (WOSCOPS)**. Circulation, v. 104, n. 25, p. 3052–3056, 17 dez. 2001.