SEVEN
publicações acadêmicas

Action of probiotics, prebiotics and symbiotics on the gut microbiota of obese individuals

Crossref doi
https://doi.org/10.56238/Connexpemultidisdevolpfut-167

Lorena Pinto Andrade
Professor of the Nutrition course - Centro Universitário de Barra Mansa (UBM)
Rituaali Clinic and Spa

Franciele Florêncio de Oliveira
Rituaali Clinic and Spa

Gisele Gonçalves Rosa
Rituaali Clinic and Spa

Flávia Almeida
Rituaali Clinic and Spa

Aline Maíra Santos Trindade
Rituaali Clinic and Spa

Cassio Lucas Dias do Prado
Rituaali Clinic and Spa

Luciana Vedia Ost
Rituaali Clinic and Spa

Vinícius Andrade Jordan
Medical student – Universidade Federal Fronteira Sul (UFRRS)

ABSTRACT
Obesity is a chronic disease that corresponds to excess accumulated fat, has a multifactorial etiology, and is a risk factor for other chronic pathologies. Changes in the diversity and composition of the gut microbiota are increasingly associated with various disease states, including obesity and behavioral disorders. Evidence shows that in obese individuals there are more bacteria of the phylum Firmicutes, than in a person with eutrophic weight, there is more imbalance of the microbiota influenced by the increase in the energetic extraction of the components of the diet, lipogenesis, and intestinal permeability. Thus, studies have shown therapeutic action through intestinal modulation with functional foods, using probiotics, prebiotics and symbiotics, since it is necessary to reduce the public costs assigned to obesity. This work aims to describe the action of probiotics, prebiotics and symbiotics along with a balanced diet for obese adults. This is a systematic review of the literature conducted with publication in the period from 2011 to 2021, which used as database the Medical Literature Analysis and Retrieval System Online (Pubmed), Scientific Electronic Library Online (Scielo) and Virtual Health Library (VHL). In the studies evaluated, the most used strains and concentrations were Bifidobacterium and Lactobacills at 1010 CFU/g. With the results of decreased body composition such as body fat mass, waist circumference, energy intake and body weight and that the use of these supplements can modulate the human gut microbiota, increasing potentially beneficial microbial species.

Keywords: Obesity, Gut Microbiota, Probiotics, Prebiotics, Symbiotics.

1 INTRODUCTION

Obesity is a growing health problem in children and adults, impairing physical and mental status and impacting health system costs in developed and developing countries. Individuals with excessive weight gain often develop obesity-related complications, which are primarily known as Chronic Noncommunicable Diseases (NCDs), including cardiovascular disease, type 2 diabetes *mellitus*, metabolic syndrome, nonalcoholic fatty liver disease, hypertension, hyperlipidemia, and many other risk factors proven to be associated with chronic inflammation, causing disability and reduced life expectancy. (ENGIN, 2017).

Obesity is a pathology with multifactorial etiology, called as the accumulation of adipose tissue that is responsible for numerous functions, such as regulator of body temperature, energy storage, secretion of proteins and bioactive peptides and autocrine and paracrine mechanisms, which secretes multiple bioactive peptides, called adipokines (proteins synthesized and secreted by adipose tissue). And it also causes changes in glycemic homeostasis and lipid profile, changes in these metabolic pathways by obesity may be related to the intestinal microbiota. (BESSERA, 2014; SIPPEL et al., 2014; CANI, 2016).

The gut microbiota has become an extremely important source of study for the knowledge and treatment of certain pathologies. The gastrointestinal tract is a stereo organ at birth, acquiring microorganisms soon after childbirth, hosts a vast microbiota, in which microorganisms participate in several interrelated activities for the maintenance of intestinal homeostasis. (PAIXÃO and CASTRO, 2016). As an aid in the digestion and absorption of nutrients, in addition to decreasing the proliferation of pathogens, regulate the homeostasis of energy, lipid and glucose through various mechanisms. (FERREIRA, 2014).

Changes in microbial diversity and composition are increasingly associated with various disease states, including obesity and behavioral disorders. The obesity-associated microbiota alters the individual's basal metabolic rate, insulin resistance, inflammation, and fat deposition. In addition, the gut microbiota can regulate metabolism, adiposity, homeostasis, and energy balance, as well as central appetite and food reward signaling, which together have crucial roles in obesity. In addition, some strains of bacteria and their metabolites can reach the brain directly through vagal stimulation or indirectly through immuno-neuroendocrine mechanisms. (TORRES-FUENTES, 2017).

Restrictive diets decreased microbiota abundance, correlated with nutrient deficiency rather than weight loss, and generally reduced butyrate producers *Firmicutes, Lactobacillus* sp., and *Bifidobacterium* sp. promote changes in microbial composition that can have detrimental long-term effects on the colon. Probiotics differ in tension and duration with diverse effects on the microbiota and tend to reduce body fat. Prebiotics had a bifidogenic effect and increased butyrate producers, likely due to cross-feeding interactions, contributing to the intestinal barrier and improving metabolic outcomes. (SEGANFREDO, et al., 2017).

In contrast, prebiotics can restore a healthy microbiome and reduce body fat by reducing energy intake that would lead to weight loss with consequent improvement in metabolic and inflammatory parameters and exert their effects by modulating adipogenesis. In addition, the combination of a probiotic with a prebiotic was termed symbiotic. Symbiotics have the potential to induce more substantial effects on gut microbiota and host health than isolated intake of pre- or probiotics, since they provide the probiotic bacteria in combination with a prebiotic component that stimulates the survival and growth of probiotic bacteria in the gastrointestinal tract. The use of these functional foods has been increased through diet therapy with the intention of improving health status. (SEGANFREDO, et al., 2017; DAVIS, 2016; FROTA, et al., 2015; FLESCH; POZIOMYCK; DAMIN, 2014).

Therefore, ensuring a healthy and balanced microbiota is one of the focuses of obesity treatment. Proper diet for the treatment of dysbiosis in conjunction with supplementation of probiotics, prebiotics and symbiotics could aid in weight loss and avoid the complications commonly associated with obesity. (SCHMIDT et al., 2017).

2 THEORETICAL FRAMEWORK

2.1 OBESITY: CONCEPTS, FORMS OF EVALUATION AND THEIR EPIDEMIOLOGY

Obesity can be defined as a chronic disease characterized by excessive accumulation of body fat, which can be localized or generalized (LUMENA, 2014; FIRMINO, SALOMON, 2018). The World Health Organization (WHO, 2020) defines it as "(...) an abnormal accumulation, an excess of fat that can be harmful to health." It is a disease that is part of the group of Chronic Non-Communicable Diseases (NCDs) and these diseases are characterized as follows:

> (...) diseases with a prolonged, multifactorial natural history, unknown etiological factors, long latency period, long asymptomatic course, generally slow, prolonged and permanent clinical course, clinical manifestations with periods of remission and exacerbation, cell lesions often irreversible and evolution to different degrees of disability or death. (FILHO *et al*., 2011, p. 5).

Obesity is considered a disease with multiple etiologies, interaction between genetic, social, and environmental factors and a problem for the public health system. For Araújo et al. (2019), "obesity has become one of the most relevant public health problems due to its high prevalence worldwide and its contribution to high morbidity and mortality rates."

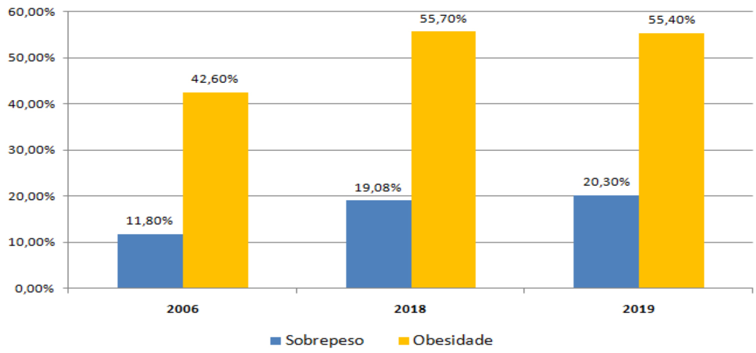
With excess body fat we can identify the predisposition to cardiovascular diseases, such as hypertension and stroke, diabetes, and others. The study done by Nilson et al. (2020), says that: "the total costs of hypertension, diabetes and obesity in the SUS reach 3.45 billion reais (R$) in which 11% were related to the treatment of obesity about 379 million."

According to the WHO (World Health Organization):

> Obesity worldwide has nearly tripled since 1975. In 2016, more than 1.9 billion adults, aged 18 and over, were overweight. Of these, more than 650 million were obese, 39% of adults aged 18 and over were overweight in 2016, and 13% were obese, most of the the world's population lives in countries where overweight and obesity kill more people than underweight, and 38 million children under 5 were overweight or obese in 2019. (WHO, 2020).

In Brazil, the 2018 Surveillance Survey of Risk and Protective Factors for Chronic Diseases by Telephone Survey (VIGITEL), conducted by the Ministry of Health, identified that "the prevalence of obesity has increased from 67.8% in the last thirteen years, from 11.8% in 2006 to 19.8% in 2018." The same research also points out "a considerable growth of overweight among the Brazilian population, more than half of the population, 55.7% is overweight. An increase of 30.8% when compared to 42.6% in 2006." In the VIGITEL survey conducted in 2019, it shows a decrease of 0.3% in overweight and an increase of 0.5% in obesity compared to 2018 (Graph 1).

Chart 1 – Research on overweight and obesity in 2018 and 2019



Source: VIGITEL (2018); VIGITEL (2019). Adapted by the authors.

The analysis of body composition is essential for the diagnosis and nutritional management. The quantification and differentiation of adipose tissue and free tissues minimizes errors, where the choice of method for evaluation should consider the advantages and limitations of each of the methodologies and the population studied. (SOUZA et al., 2014).

One of the methods used to diagnose obesity in adults and the elderly, both at the population and individual level, is the Body Mass Index (BMI), the [1]WHO is based on this standard to classify obesity and the risk of associated diseases, the calculation is made using the following formula:

$$IMC = \frac{Weight\ (Kg)}{Height^2\ (m)}$$

For Souza et al. (2015, p. 53) the calculation of BMI aims to "(...) assess whether the person is at their ideal weight and identify the association between BMI and chronic disease or mortality." Thus, the WHO (2000, p. 8-9) defines the "overweight with BMI equal to or greater than 25 Kg/m² and obesity with BMI equal to or greater than 30 Kg/m²", in Table 1 below, we can observe the classification of BMI for adults according to the nutritional status and risk of comorbidities of adult individuals aged 20 to 60 years:

[1] BMI, also known as the Quételet index, was developed by Lambert Quételet at the end of the nineteenth century, becoming an international predictor of obesity adopted by the WHO. See in: SOUZA, Luciana Lopes de; GUEDES, Erika Paniago; BENCHIMOL, Alexander Koglin. Anthropometric Definitions of Obesity. In: MANCINI, Marcio C. et al. Obesity treatise. 2. ed. Rio de Janeiro: Guanabara Koogan, 2015. p. 52.

Table 1 – Classification of adults according to BMI (Body Mass Index)

Classification	BMI (Kg/m²)	Risk of Comorbidities
Underweight	<18.50	Low *(but may be at risk for other types of clinical complications)*
Normal Interval	18,50 – 24.99	Medium
Overweight	≥ 25.00	
Pre-obese	25,00 – 29,99	Increased
Obese – Class I	30,00 – 34,99	Moderate
Obese – Class II	35,00 – 39,99	Serious
Obese – Class III	≥ 40.00	Very Serious

Source: WHO, 2000, p. 9. Available in: <https://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/>. Accessed: 07 Apr. 2020. Adapted by the authors.

The BMI despite being a globally used index, it does not exactly define the body content of fat or lean mass, that is, the high BMI can be assumed as an excess of fat mass and an acceptable obesity index, but it does not characterize the distribution of body adiposity.

Adiposity concentrated in the abdominal region is associated with a higher risk of cardiovascular and metabolic diseases, Bray (1989) highlights the existence of "(...) relationship between overweight and abdominal fat deposition, and between this and several chronic diseases, such as coronary heart disease, cardiovascular diseases, hypertension, hyperlipidemias, cancer, type II diabetes and gallstones, among others."

Therefore, waist circumference (WC) and waist/hip ratio (WHR) are used as indicators to measure the centralized distribution of adipose tissue (WHO, 2000, p. 10), which is obtained by dividing the measurements of waist and hip perimeters, as highlighted by Kamimura et al. (2014, p. 119) with the equation described below:

$$RCQ = \frac{Waist\ circumference}{Hip\ Circumference}$$

For the calculation of waist circumference, Monteiro (1998, p. 37) describes that: "Some authors suggest that waist measurement be considered at the level of the navel". But Monteiro also states that the smallest circumference between the last rib and the anterosuperior iliac spine can be considered as a waist. The author also defines that the hip be measured in the region of greatest perimeter at the level of the gluteal region.

According to the WHO (2000, p. 10) it has become accepted that a high WHR is characterized when the result is: "WHR > 1.0 in men and > 0.85 in women". The WHO (2000, p. 10) suggests only the measurement of waist circumference to calculate the distribution of abdominal fat and diseases associated with health:

> Waist circumference is a convenient and simple measurement that is independent of height, correlates closely with BMI and WHR, and is an approximate index of intra-abdominal fat mass and total body fat. In addition, changes in waist circumference reflect changes in risk factors for cardiovascular disease and other forms of chronic disease (...). (WHO, 2000, p. 10).

Thus, WHR may remain useful research, but individuals can be identified as having a higher risk of obesity-related diseases, using only waist circumference as a screening tool. In Table 2 below, according to the WHO (2000, p.11) the borderline values of waist circumference associated with the development of obesity-related complications:

Table 2 – Sex-specific waist circumference and risk of metabolic complications associated with obesity

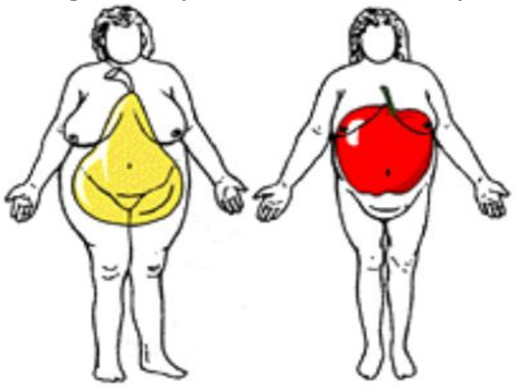
Risk of metabolic complications	**Waist circumference (cm)**	
	Men	**Women**
High	≥ 94	≥ 80
Very high	≥ 102	≥ 88

Source: WHO, 2000, p. 11. Available in: <https://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/>. Accessed: 07 Apr. 2020. Adapted by the authors.

With anthropometric evaluation, we can evaluate the fat that is stored in the adipose (subcutaneous) tissue mainly in the intraperitoneal cavity, in the liver and in other organs. It presents in two forms, central or android and peripheral or gynecoid. The central or android fat is characterized by the accumulation of fat in the abdominal region, mainly in the viscera compartment and is directly related to NCDs.

According to Matos and Oliveira (2008, p.11), "the central deposition of fat is associated with the increase of metabolic disorders, especially in the visceral deposits, due to the intense lipolysis that these tissues suffer (...)". The peripheral or gynecoid fat deposit is located in the gluteofemoral region. According to Matos and Oliveira (2008, p. 11) this is due to the fact that "there is less intense lipolysis in this region, it has less metabolic repercussion (...)". Figure 2 below illustrates the form of distribution of central or android and peripheral or gynecoid body fat:

Figure 1 – Gynoid and Android Obesity



Source: AMER; SANCHES; MORAES, 2001, p. 99. Available in: <http://periodicos.uem.br/ojs/index.php/RevEducFis/article/view/3752/2584>. Access on: 25 mai. 2020.

Adipose tissue is an organ that performs many significant physiological functions, its excess in the body results in pathological states in many of its organs and systems. It is not only a tissue that stores fat and plays a protective role, it is an important endocrine organ where signals sent from different tissues are generated and integrated, it is also morphologically and physiologically differentiated. (MURAWSKA-CIAŁOWICZ, 2017).

However, due to their plasticity, adipocytes can undergo a transformation and change their structure and metabolism, depending on the physiological state of the organism and the conditions to which it is exposed. It contains countless adipokines and lymphocytes secreted by adipose tissues, as well as peptides and lipids with biological activity have been discovered so far. Both white adipose tissue and brown and beige adipose tissue are known to contribute to energy homeostasis and metabolic regulation. (FRIGORET; GUTIÉRREZ- AGUIALAR, 2020).

The finding that obesity and metabolic disorder are accompanied by chronic low-grade inflammation has fundamentally changed the view of the underlying causes and progression of obesity and metabolic syndrome. It is known that the inflammatory program is activated at the beginning of adipose expansion and during chronic obesity, permanently distorting the immune system to a pro-inflammatory phenotype, and thus beginning to delineate the reciprocal influence of obesity and inflammation. (DABKE, et al., 2019).

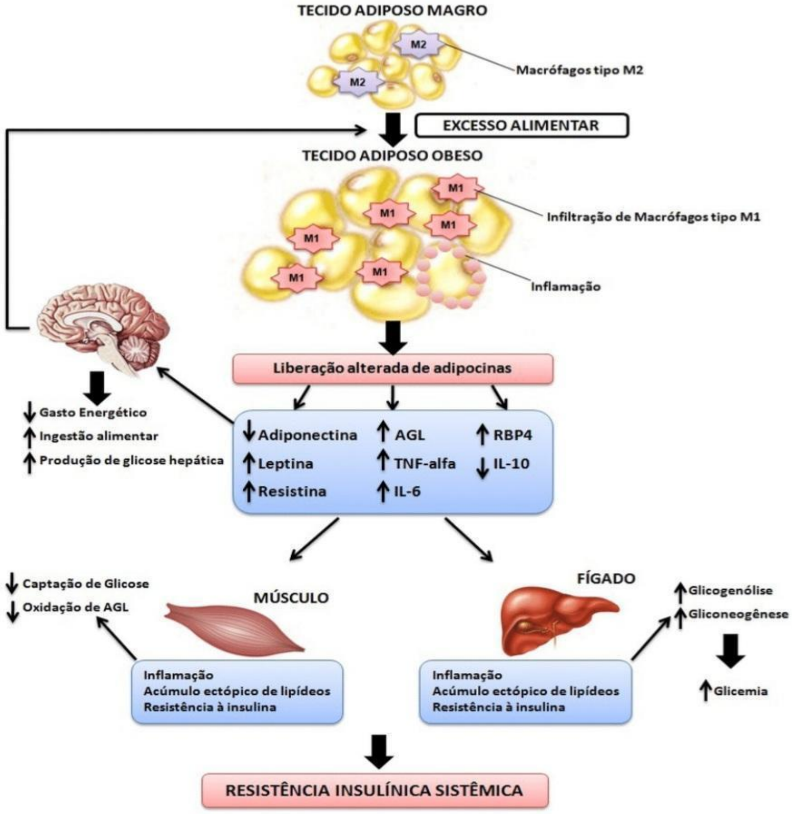
It secretes several substances, collectively called adipocytokines, which are inflammatory markers: interleukin 6 (IL-6), leptin, tumor necrosis factor (TNF), resistin, adiponectin, PAI-1 (plasminogen activator inhibitor 1), angiotensinogen, visfatin, interleukin 1 (IL-1). Inflammation of adipose tissue occurs because of obesity, characterized by the infiltration and activation of cells of the immune system, increasing the synthesis of cytokines and chemokines, with higher expression of pro-inflammatory adipocytokines and lower expression of anti-inflammatory. (SIPPEL et al., 2014).

This chronic inflammation contributes to the mechanisms of induction of insulin resistance and, consequently, to the development of type 2 diabetes. In this tissue their leptin informs the brain of the presence of excess adipose tissue, inducing blockade of neuropeptide Y (NPY), a potent orexigenic and suppressing appetite. When fat stores are low, decreased leptin stimulates NPY production with increased appetite and reduced leptin secretion reduces energy expenditure and increases cortisol secretion. (BORGES et al., 2014).

There are three primary components in the neuroendocrine system involved with obesity. The afferent system, which involves leptin and other signals of satiety and short-term appetite, the processing unit of the central nervous system related to neurotransmitters such as neurons expressing orexigenic neuropeptides, NPY (neuropeptide Y) and AgRP (agouti-related peptide) that interfere with peripheral signals such as leptin, ghrelin and insulin to act on food control and energy expenditure and the efferent system, a complex of appetite satiety autonomic, thermogenic effectors that leads to energy storage. (BORGES et al., 2014; DAMARINI; DAMARINI, 2011).

Figure 2 below shows a picture of adipose tissue hypertrophy, inducing the infiltration and proliferation of macrophages and the alteration in adipokine secretion, which leads to chronic inflammation of low intensity. This condition, associated with the increase of circulating free fatty acids, causes increased food intake, decreased energy expenditure, and changes in the homeostasis of peripheral tissues, such as muscle and liver, promoting ectopic accumulation of fat, inflammation, and insulin resistance. (GALIC and STEINBERG, 2010 apud SPERETTA et al., 2014).

Figure 2 – Hypertrophy of adipose tissue



Source: GALIC and STEINBERG, 2010 apud SPERETTA et al., 2014. p. 64. Available at: <https://www.e-publicacoes.uerj.br/index.php/revistahupe/article/download/9807/8769>. Accessed: 01 Apr. 2021

The brain interprets and integrates neuronal and hormonal signals to promote a coordinated regulatory response of energy homeostasis, this system is centered on the hypothalamus and brainstem, which have reciprocal neuronal connections, the control station for nutritional interpretation is in the caudal portion of the brainstem, which receives information from the taste buds, of the olfactory apparatus and the gastrointestinal tract, the arcuate nucleus (ARCA) receiving information that originates in peripheral organs and mediated by circulating hormones and metabolites, as well as by neural pathways from the brainstem. (PARREIRA, 2017).

According to Lee, Yacyshyn and Yacyshyn (2019, p. 479) "despite the growing understanding of the factors driving the obesity epidemic, therapeutic interventions to prevent or reverse obesity are limited in their impact." Manipulation of the human gut microbiome provides a potential new therapeutic approach in the fight against obesity, specific gut bacteria and their metabolites are known to affect host metabolism and feeding behavior, and dysbiosis of this biosystem may lead to metabolic syndrome, which will be addressed next.

2.2 GUT MICROBIOTA AND DEVELOPMENTAL IMPLICATION IN OBESITY

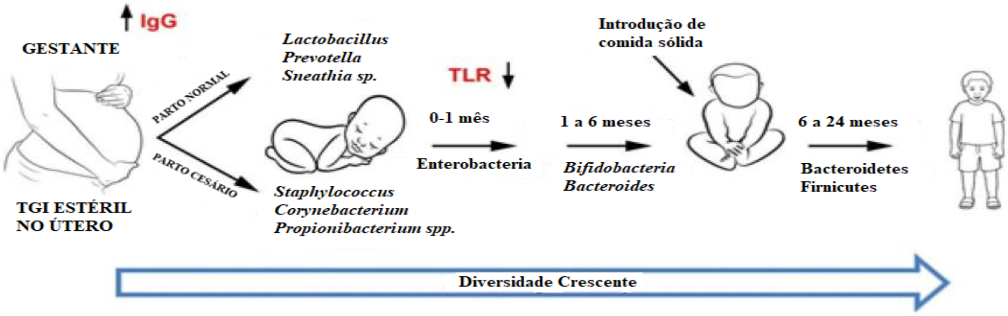
According to Gérard (2016), "the human gut harbors a complex bacterial community called the gut microbiota and this microbiota is specific to each individual, despite the existence of several bacterial species shared by most adults." They are composed of microorganisms such as bacteria, viruses and fungi that are present throughout the human body, and this bacterial community is acquired in the postnatal period. (OLIVEIRA et al., 2020).

The formation of the gut microbiota is a process influenced by internal factors, intrinsic to the host, and external ones. External ones include the composition of the maternal microbiota, the form of birth (cesarean section or normal delivery), contamination, feeding and the use of medicines. The internals are related to the anatomy of the gastrointestinal tract (GIT), peristalsis, bile acids, intestinal hydrogen potential (pH) and immune response. (NEVES, 2017, p. 88).

The process of colonization begins from the intrauterine period. This fact was observed in studies in healthy full-term pregnancies, even those who had elective cesarean sections, without rupture of the placental membrane. They showed that there is already the presence of bacteria in the placenta, aminiotic fluid and meconium that resemble the bacteria found in the intestine of newborns (MOREIRA, 2019).

During the first years of life, the microbiota is largely influenced by external factors (Figure 3), such as the form of delivery and the type of feeding (breast milk or artificial formula). Subsequently, the intake of solid foods, as well as the gradual maturation of the immune system, modulates the intestinal microbiota. By 2–3 years of age, the microbiota resembles that of an adult with Bacteroidetes and Firmicutes as the main phyla. (LAZAR et al., 2019).

Figure 3 – Development of the gut microbiota



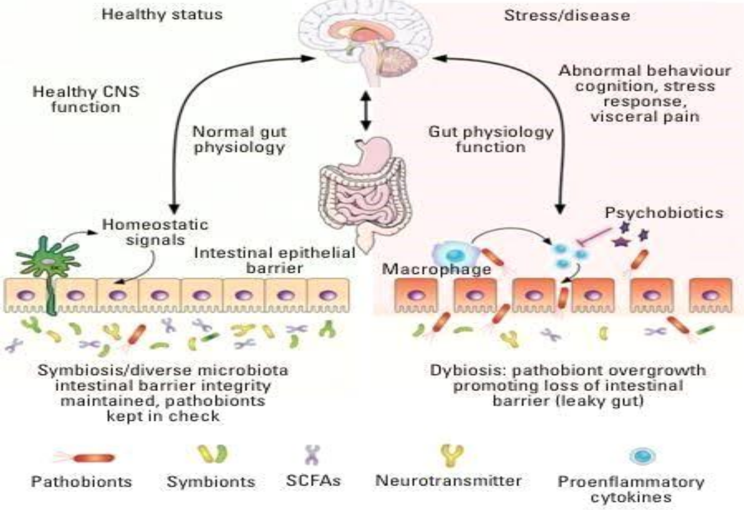
Source: LAZAR et al., 2019, p. 3. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6424913/>. Accessed: 01 Apr. 2021.

In most individuals, about 90% of the phyla are *Firmicutes and* Bacteroidetes*, with the remainder being composed* of Actinobacteria (family *Bifidobacteriaceae*) and *Proteobacteria (family Enterobacteriaceae*). Then, in order of frequency, the phyla *Synergistetes*, *Verrucomicrobia, Fusobacteria* and *Euryarchaeota* appear, representing a small percentage of our microbiota. Of the main members of the microbiota the *Firmicutes* are the classes *Bacilli, Clostridia and Molicutes*, and the Bacteroidetes the *Bacteroides*, Flavobacteria *and* Sphingobacterias *(MORAES et al., 2014).*

The gut microbiota is involved in functions crucial to host homeostasis, such as digestion and synthesis of nutrients, development of the host's immune system and digestive tract, and production of pharmacologically active molecules. In addition, it can act as a barrier against pathogens and seems to have an influence on the development of the nervous system and cognitive functions. (GOMES, 2017).

Some factors can cause changes in the composition of the microbiota by both external and internal factors such as environment, medicine, food, immune system, genetics, probiotics and prebiotics. Maintaining a beneficial microbiota requires a homeostatic balance within microbial communities, and between the microorganisms and the host. The non-realization or maintenance of this complex homeostasis from childhood to adulthood, called eubiosis, leads to negative health consequences, causing diseases and/or intestinal disorders, due to a picture of intestinal dysbiosis (Figure 4). (REDDEL, PUTIGNANI and CHIERICO, 2019).

Figure 4 – Alteration of the microbiota (dysbiosis)



Source: CARABOTTI; SCIROCCO; MASELLI; SEVERI, 2015, p. 204. Available at: <https://pubmed.ncbi.nlm.nih.gov/25830558/>. Access in: 25 set. 2020.

Intestinal dysbiosis can be characterized as an imbalance of pathogenic and beneficial bacteria existing in the gastrointestinal tract, this alteration in the intestinal microbiota can be a result of external and internal factors, which may result in damage to health and trigger various diseases, numerous factors are responsible for this imbalance. (FLORES, 2017).

Santos and Ricci highlight how the process of intestinal dysbiosis occurs, as well as the relationship of the intestinal microbiota with obesity:

> Dysbiosis occurs due to the use of antibiotics, excess laxatives, and the consumption in large quantities of industrialized foods, red meat, animal fat and the low consumption of vegetables and fruits. It leads to imbalance in nutrient absorption, altering body metabolism. Obesity is also being linked to the alteration of the gut microbiota. In obese individuals, 50% more bacteria of the phylum *Firmicutes* were found than in people of normal weight. Research with germ-free mice showed that after receiving microbiota from obese mice, they increased their body fat by 60 percent, even with a 29 percent reduction in food intake. Thus, it is understood that one type of microbiota can extract more calories from one diet than another. With the increase of *Firmicutes*, the intestine changes its surface layer, absorbing more bacteria, both beneficial and pathogenic. This entry of pathogenic bacteria causes a process of inflammation to begin causing insulin resistance. With this inflammation installed, the breakdown of fatty acids into energy is inhibited, there is increased breakdown of triglycerides into fatty acids, which get accumulated in the blood and adipose tissue. Fatty acids are ligands of enzymes that inhibit lipolysis, not taking energy from body fat, and thus, the body understands that it needs to take more energy from food. (SANTOS and RICCI, 2016, p. 81).

The dysbiosis of the intestinal microbiota (Figure 5) is the most relevant point for obesity where it interferes with intestinal integrity, because it alters the intestinal barrier and increases the content of gram-negative bacteria, rich in lipopolysaccharides, which are absorbed generating metabolic endotoxemia and secretion of pro-inflammatory cytokines, such as TNF-a, IL-6, IL-2 and INF-g, secreted by both adipocytes and monocytes that infiltrate this tissue. (SCHMIDT et al., 2017).

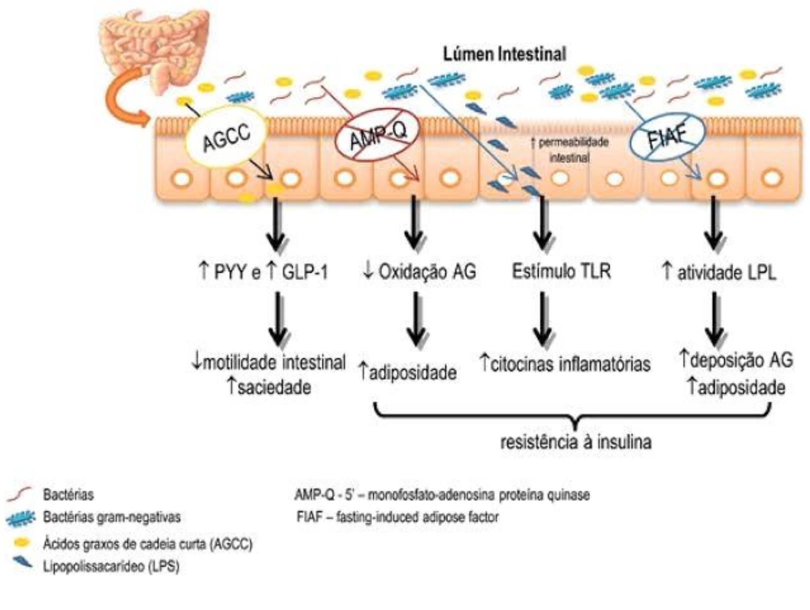
A study conducted on mice found that the endocannabinoid system controls permeability and adipogenesis and also shows that LPS acts as a master switch to control adipose tissue metabolism by blocking cannabinoid-powered adipogenesis. These data indicate that the gut microbiota determines adipose tissue physiology through regulatory loops of the LPS-endocannabinoid system and may have critical functions in adipose tissue plasticity during obesity. (MUCCIOLI, et al., 2010).

Food intake and energy expenditure are controlled by complex and redundant neural systems, true integrative systems, receiving afferent signals from the digestive system, through the adipose tissue and reaching the central structures (DAMIANI; DAMIANI, 2011).

Thus, the consumption of a high-fat diet leads to obesity and chronic systemic inflammation and the intestinal microbiota is an environmental factor capable of increasing energy yield from the diet, and of regulating peripheral metabolism, which may result in weight gain. Ensuring a healthy microbiota is critical in modulating energy metabolism, and that modifications of the composition of the gut microbiota may be associated with increases or decreases in body weight and body mass index. (BRUSAFERRO et al., 2018).

Potential therapies to alter the gut microbiota to treat obesity include dietary changes, dietary supplementation with probiotic organisms and prebiotic compounds that influence bacterial growth, and the use of fecal microbiota transplantation, in which gut microbiota from healthy individuals are introduced into the gut. (LEE, YACYSHYN and YACYSHYN, 2019).

Figure 5 – Relationship between microbiota and metabolic diseases



Source: MORAES; SILVA; PITITTO; FERREIRA, 2014, p. 320.
Available at: <https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302014000400317>. Access on: 20 ago. 2020.

2.3 INTESTINAL MODULATION: THERAPEUTIC ALTERNATIVE FOR THE TREATMENT OF OBESITY

2.3.1 Food, Probiotics, Prebiotics and Symbiotics

A healthy diet occurs when habitual eating patterns include adequate nutrient intake and sufficient, but not excessive, energy intake to meet the individual's energy needs (HAINES, et al., 2019). Maintaining a healthy diet throughout life prevents not only malnutrition in all its forms, but also a range of NCDs and other health conditions. However, increased production of processed foods, rapid urbanization, and changing lifestyles have given way to a shift in dietary patterns. People now consume more foods high in calories, fats, free sugars, and salt/sodium—and many don't eat enough fruits, vegetables, and other dietary fiber. (PAHO, 2019).

Diet is a determining factor of the characteristics of intestinal colonization. Hippocrates said: "Let your medicine be your food and your food be your medicine", therefore, functional foods have the ability to develop additional benefits to the diet, for example, probiotics and prebiotics, have acquired great prominence in relation to the restructuring and maintenance of the intestinal microflora and in the prevention of diseases, contributing to the functioning and development of an adequate body physiology. Currently, in Brazil, there are already several functional foods present in the food industries, and the application of probiotics in food is an example of great relevance. (OLIVEIRA; ALMEIDA; BOMFIM, 2017).

According to Oliveira et al. (2020, p. 3-4):

> Chronic inflammation, characteristic of obesity, results from the release of pro-inflammatory adipokines by adipocytes, which attract macrophages to the affected area, triggering the inflammatory process and oxidative stress. Thus, foods with functional properties that act in the modulation of inflammation and oxidative stress stand out. The insertion of these foods that present, in their composition, bioactive compounds, such as polyphenols, catechins and flavonoids, contributes to homeostasis and the normal functioning of the organism. Among the foods, turmeric, green tea, pomegranate, oats and olive oil stand out as important foods in the prevention and treatment of obesity, given the potential of foods to modulate inflammation in obesity. (Oliveira et al., 2020, p. 3-4).

The intake of foods with high levels of saturated fats, the high intake of animal proteins, sugar and salt provide a favorable environment for the selection of bacteria of the phylum *Firmicutes to the* detriment of beneficial bacteria, leading to possible alterations of the intestinal barrier, by inducing an inflammatory state of the organism generated by the activation and production of pro-inflammatory mediators. On the other hand, the consumption of complex polysaccharides and plant protein may be associated with an increase in the amount of beneficial bacteria, stimulating the production of short-chain fatty acids that are produced by the fermentation of soluble dietary fibers by the healthy microbiota, such as the genera *Bifidobacterium* and *Bacteroides* exert modulatory effects on inflammatory responses. (VIEIRA, 2011; RINNINELLA et al., 2019).

In addition, omega-3s, polyphenols, and micronutrients appear to have the potential to confer health benefits through modulation of the gut microbiota and westernization of the diet, including additives, may reduce gut microbial diversity in terms of phylum and gender leading to dysbiosis, altered barrier function and permeability, and abnormal activation of immune cells, leading to high incidences of chronic diseases. To date, the Mediterranean diet (Figure 6) remains the evergreen solution for modulating the diversity and stability of the microbiota, as well as the regular permeability and activity of the human host's immune functions. (RINNINELLA et al., 2019).

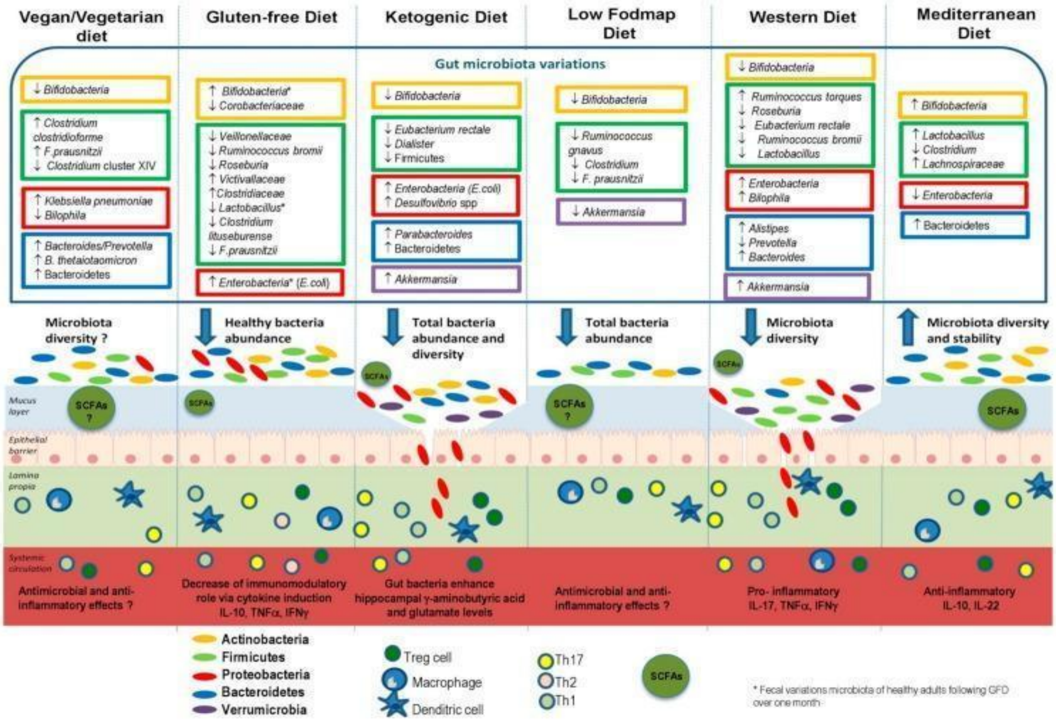
However, the intake of fiber, fruits and vegetables provides an increase in the production of derivatives of the fermentation of carbohydrates resulting in an unfavorable environment for them. In this way, the gut microbiota can quickly adapt to the availability of a specific nutrient, producing different metabolic responses in the individual. (BOAS, 2017).

Studies have shown that the use of probiotics, prebiotics and symbiotics along with a healthy diet represent a preventive or therapeutic measure, by favoring a healthy composition and greater functionality of the microbiota, reducing circulating LPS, endotoxemia and chronic subclinical inflammation. (SCHMIDT et al., 2017).

Probiotics and prebiotics are live bacteria and ingredients that promote the growth and development of these microorganisms, respectively, such as fiber, yogurt, and fermented milk that are beneficial to the gut microbiota:

> Probiotics are defined as living microorganisms, which when administered in satisfactory and adequate amounts check great benefits to the host, noting a significant improvement in the modulation of the intestinal microbiota (Figure 7). Prebiotics are termed fermented substances that cause changes in the formation and activity of the gastrointestinal microbiota, resulting in benefits to the health and well-being of the host. (SANTANA et al., 2018, p.1).

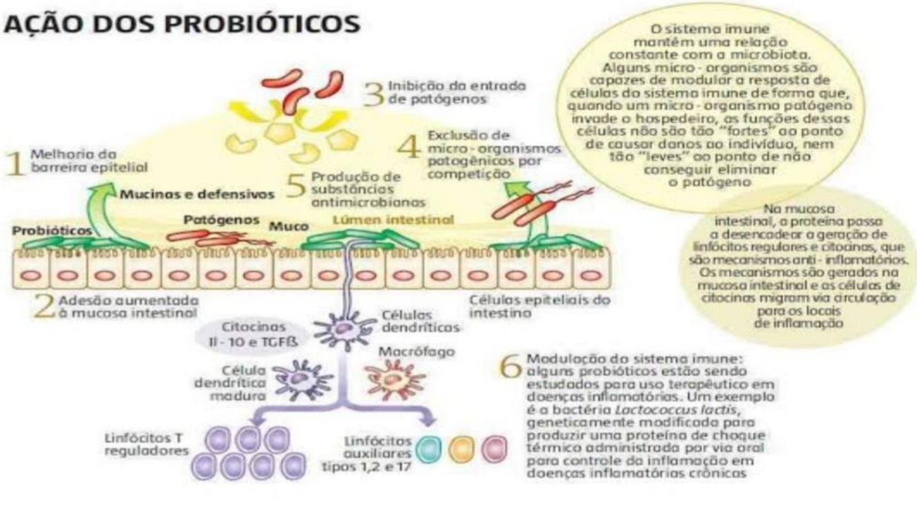
Figure 6 – Action of different diets on the gut microbiota



Source: RINNINELLA et al., 2019, p. 10. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6835969/>. Access in: 25 set. 2020.

Probiotics can contribute not only to the regularization of the intestine, but can also play an important role in the digestion and absorption of nutrients, in protecting the structure and function of the intestine, and in strengthening the body's defenses against substances and microorganisms harmful to health. In Figure 7, we can observe the action of probiotics in the intestine:

Figure 7 – Probiotic action on the gut microbiota



Source: COTA, 2014. Available at: <https://www.uai.com.br/app/noticia/saude/2014/12/03/noticias-saude,191089/amp.html>. Accessed: 20 Apr. 2021.

Because of this some key findings are the ability of some strains to reduce body weight and anthropometric measurements of waist and hip circumference, as well as body composition measures of lean mass, abdominal visceral fat, and abdominal subcutaneous fat. The probiotic effect on body weight and metabolism is specific to tension and that only some of the species included in the genera *Lactobacillus* and *Bifidobacterium* are effective, while the use of other strains can be deleterious, capable of changing the population of microorganisms in the intestinal microbiota and controlling the functioning of the gut microbiota ecosystem acting in the prevention of human and animal diseases, But nevertheless, the doses, duration of administration, and long-term effects of administering probiotics to prevent overweight and obesity are not known. (RODRIGUES, 2016; BRUSAFERRO et al., 2018).

Several species and strains of *Lactobacililli*, including *Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus rhamnosus, and* Lactobacillus *helveticus,* have been extensively studied in the prevention of human and animal diseases. These probiotic species are able to change the population of microorganisms in the gut microbiota and control the functioning of the microbiota ecosystem, there is considerable evidence from clinical trials of probiotics in animal and human models have reported suitability for the treatment of a variety of diseases, and this number continues to grow. (AZAD, et al., 2018).

The concentrations to obtain the desired effects, probiotic bacteria must be present in adequate amounts in the products, but this number is not yet well established. In general, a consumption of probiotic bacteria between 108 and 1011 CFU (colony-forming unit) is recommended. A recommended daily dose is twice daily of 1010 *Lactobacillus* GG and each dose corresponds to approximately 80 mL of fermented milk. (ALVES, 2020). Some concentrations of the most commonly used probiotics as examples are *Lactobacillus casei with 1010 cfu/g -2x/day, Lactobacillus acidophilus* 109- 1010 cfu/g–1 at 3x/day and Bifidobacterium lactis 1010 cfu/ *g -2x/* day. (NUNES; GARRIDO, 2018).

According to the World Gastroenterology Organization (WGO) Global Guidelines (2017): "(...) One of the main aspects of the prebiotic is that it is not digestible by the host and that it benefits the health of the individual thanks to its positive effect on indigenous beneficial microbes."

Prebiotic fibers are non-digestible carbohydrates that promote the growth of beneficial bacteria in the gut, animal studies have evaluated the response to a prebiotic diet in the gut microbiota, body composition, and risk factors associated with obesity. They highlight the prebiotic function of dietary fiber in the metabolic alterations of obesity by functioning as a fermentable substrate that, through the production of SCFA, act in the regulation and intestinal hormones, in the control of appetite and in the reduction of the inflammatory process. Cashew fiber has been highlighted for its positive effects on health, and can be used as a functional ingredient in both normal metabolism and obesity due to compounds, for example, low molecular weight (FcSM) promotes satiety in animals, improving glucose and lipid metabolism and that the positive effects of obesity prevention may be associated with the production of SFCA. (CARVALHO; GALLÃO; BRITO, 2020).

Some absorbable or non-absorbable sugars, fiber, sugar alcohols and oligosaccharides are within this concept of prebiotics. Of these, oligosaccharides, short chains of polysaccharides composed of 3 to 10 simple sugars linked together have received the most attention for the numerous prebiotic properties attributed to them. Fructooligosaccharides are polysaccharides that have shown good prebiotic effects, can be obtained in natural form in seeds and roots of some vegetables such as chicory, onion, garlic, artichoke, asparagus, barley, rye, in legumes such as: soybeans, chickpeas, beans, lentils, peas. (NUNES; GARRIDO, 2018).

The consumption of foods rich in bioactive compounds such as carotenoids, ascorbic acid and phenolic compounds, flavonoids and anthocyanin, also present chemical composition of the cashew stalk, these components is related to beneficial health effects in the prevention of chronic non-communicable diseases through their antioxidant properties, avoiding the initiation or propagation of chain oxidation reactions. (CARVALHO; GALLÃO BRITO, 2020).

Finally, symbiotics are composed of living microorganisms that, when administered in appropriate doses, can bring benefits to the health of the host, formed by the association of one or more probiotics with one or more prebiotics. Its use optimizes the intestinal immune system and favors the control of the flora, decreasing the incidence of infections, due to probiotics increase circulating lymphocytes and cytokines, which stimulate phagocytosis and can promote the increase in the number of bifidobacteria, glycemic control, reduction of the rate of blood cholesterol, balancing of the healthy intestinal microbiota that helps in reducing constipation and / or diarrhea, Improvement of intestinal permeability and stimulation of the symbiotic immune system, therefore, provide the joint action of probiotics and prebiotics. (FLESCH; POZIOMYCK; DAMIN, 2014).

The symbiotics, commonly, are of dairy origin, such as yogurts, containing prebiotic and probiotic, there is also consumption in capsules and sachets with the daily recommendation of a symbiotic should contain minimum viable probiotic portion around 10^8 to 109 CFU and at least 4g per day of the prebiotic portion. Most studies investigate the effect of prebiotic and probiotic separately and not in synergism, there are few studies investigating the action of symbiotics on obesity and its comorbidities in which they show to improve blood glucose concentrations, increase the intestinal content of bifidobacteria and improve inflammatory parameters with reduction of pro-inflammatory cytokines. (OSTROWSKI, 2016).

Thus, the aforementioned lifestyle, which includes eating large portions, rich in saturated fats and refined sugars, and sedentary habits are strongly associated with obesity and related metabolic diseases, promoting inflammation and structural and behavioral changes in the gut microbiota. Increased knowledge about the interactions between the gut microbiota and the host can certainly reveal, in the not too distant future, new therapeutic perspectives for obesity and its related diseases and although data on prebiotics and probiotics in weight reduction are still limited, the effect on obesity prevention is very promising. (SILVA-JUNIOR et al., 2017).

3 METHODOLOGY

This is an integrative review of the literature, based on the research problem "How to modulate the gut microbiota of obese patients with intestinal dysbiosis in order to help reduce obesity?". To perform the search, the following descriptors were used in English, from the Health Sciences Descriptors (DeCS) in the Virtual Health Library (VHL), and the Boolean operator AND: *obesity* AND gastrointestinal microbiome AND probiotics AND *prebiotcs* AND *synbiotics*.

The strategy of identification and selection of articles will follow the following inclusion criteria for better delimitation of studies: full-text articles available in Portuguese and English, which address the theme of the research and with publication in the period from 2010 to 2020. In addition, they are indexed in the Medical Literature Analysis and Retrieval System Online (Pubmed), Scientific Electronic Library Online (Scielo) and Virtual Health Library (VHL) databases.

The analysis of the articles was carried out in three stages: 1) reading the titles of the articles that will be found in the research; 2) selective reading of abstracts and exclusion of duplicate articles or articles that do not have affinity with the theme; and 3) reading the articles in full for the elaboration of an interpretative synthesis, relating the findings to the question raised by this work.

In addition, to carry out the research, theses and dissertations available in the Theses Bank of the Coordination of Personal Improvement of Higher Education (BTC/CAPES) and in the Brazilian Digital Library of Theses and Dissertations of the Brazilian Institute of Information in Science and Technology (BDTD/IBICT) were consulted, as well as books that address the researched theme.

4 RESULTS AND DISCUSSION

As a result of this research there are three practical studies, in this context, Stenman et al., in 2016 used *Bifidobacterium animalis ssp. lactis* 420 (B420) and the dietary fiber Litesse® Ultra polydextrose (LU) approximately 10 x 10 10 CFU/d and 12g/d, respectively, in obese volunteers who were divided into four groups in which one was administered placebo, another LU, the third B420 and the last LU along with B420 for six months, soon found that probiotics with or without fiber compared to placebo determined reduction in body fat mass, waist circumference, energy intake and body weight, B420 and LU seem to have synergistic effects on increasing lean body mass and polydextrose Litesse Ultra alone had no effect on the parameters tested.

The prebiotic employed, Litesse® Ultra polydextrose (LU), is a randomly interceded glucose polymer, which remains indigestible by the host and can increase the number of *Bifidobacteria* in a colonial continuous culture system. Its administration was to induce satiety and to soften the glycemic response to a glucose load, indicating potential benefits for weight maintenance and metabolic health. (STENMAN et. al, 2016).

Krumbeck et al., 2018 using prebiotic galactooligosaccharides (GOS) and the probiotic strains Bifidobacterium adolescentis IVS-1 and *Bifidobacterium lactis BB-12, for three weeks in obese men and women, in the amount* of probiotic treatments at a daily dose of 1 × 109 CFU and 6.9 g of lactose as carrier/control. The symbiotics contained 6.9 g of Vivinal and 0.1 g of probiotic (or *B. Adolescentis* IVS-1 or *B . Animalis* BB-12), for a total dose of 7.0 g and placebo samples contained 7.0 g lactose. The results indicated that the probiotic strains and the GOS prebiotic improved barrier function, a combination of the two did not result in apparent synergism. It's unclear how competition for the prebiotic can be avoided, but it's possible that higher doses are needed.

Finally, according to Sergeev et al., 2020 obese volunteers were induced at the beginning to an eating plan with low carbohydrate consumption, high protein content and low energy intake, sequentially, used symbiotics that contained in the probiotic component 69 mg or 15 × 109 CFU of proprietary strains of *Lactobacillus acidophilus* DDS-1*, Bifidobacterium lactis* UABla-12, *Bifidobacterium longum* UABl-14 and Bifidobacterium bifidum *UABb-10 and 5.5g/day of galacto-oligosaccharide mixture of the prebiotic component for 3 months, verified that no significant changes in body composition in symbiotic supplementation increased the abundance of intestinal bacteria associated with positive health effects, especially* Bifidobacterium *and Lactobacillus*, over time decrease over time in blood glucose and an increase in the abundance of *Lactobacillus* particularly in the symbiotic group and the decrease in body components was associated with a decrease in the abundance of *Bifidobacterium.*

Galacto-oligosaccharides (GOS) have a positive effect on the composition of the intestinal microbiota, contributing to the increase of the population of *Bifidobacterium* and *Lactobacillus* with the consequent reduction of the concentration of putrefactive bacteria. They are produced through the reaction of transgalactosylation of lactose, by the enzyme β-galactosidase, extracted from various sources, the microbial being the most common are resistant to the action of digestive enzymes and, therefore, non-digestible have low caloric value; Because they are not metabolized by microorganisms of the oral cavity, they are not cariogenic. The beneficial effects to the gastrointestinal tract range from the modulation of the immune system to digestive advantages such as regulation in intestinal transit and achieve nutritional gains. (CAMARGO, 2018; LISBOA et.al, 2012).

Table 3 – Relationship between probiotics, prebiotics and symbiotics in the reduction of obesity

Author	Material used	Number and Gender of participants	Groups/Intervention	Search Duration	Findings
Stenman et al., 2016	*Bifidobacterium animalis ssp. lactis* 420 (B420) e a dietary fiber Litesse Ultra polidextrose® (LU).	225 healthy volunteers (healthy, BMI 28-34.9) were randomized into four groups (1:1:1:1).	1) Placebo, microcrystalline cellulose, 12g/d; 2) LU, 12g/d; 3) B420, 1010CFU/d in microcrystalline cellulose, 12 g/d; 4) LU + B420, 12g + 1010 CFU/d.	6 months of treatment	It presents preliminary clinical evidence that the probiotic B420 with or without polydextrose Litesse Ultra may reduce body fat mass, waist circumference, energy intake, and body weight compared to placebo. In addition, B420 and LU appear to have synergistic effects on increasing lean body mass. LU alone had no effect on the parameters tested. Mechanistically, the reduction in body fat mass may be related to circulating zonulin, a potential marker of intestinal barrier function, and attenuated low-grade inflammation, which support previous findings of experimental animals.
Krumbeck et al., 2018	Galactooligossacarídeos prebióticos (GOS) e as cepas probióticas *Bifidobacterium adolescentis* IVS-1 e *Bifidobacterium lactis* BB-12.	114 volunteers, women and men between 18 and 65 years with BMI of 30.0-40.0 kg/m2.	The GOS prebiotic contained 72.5% GOS, 22.8% lactose and 4.7% monosaccharides (galactose and glucose). The probiotic treatments were divided into sachets, each containing 0.1 g of probiotic powder (1010 CFU/g), resulting in a daily dose of 1 × 109 CFU and 6.9 g of lactose as carrier/control. The symbiotics contained 6.9 g of Vivinal and 0.1 g of probiotic (or *B. Adolescentis* IVS-1 or *B . Animalis* BB-12), for a total dose of 7.0 g. The placebo samples contained 7.0 g of lactose.	3 weeks of treatment	They showed that the autochthony of a bacterial strain is more important than the supply of prebiotic substrate at a dose of 5 g for the establishment of a probiotic in the human intestine. In addition, although the probiotic strains and the GOS prebiotic improved barrier function, a combination of the two did not result in apparent synergism. It's unclear how competition for the prebiotic can be avoided, but it's possible that higher doses are needed. Although the symbiotic approach tested in this study does not provide measurable synergism, our findings clearly show that both

					probiotic and prebiotic strains improved markers of intestinal permeability. Therefore, this report provides a basis for the use of these treatments (or combinations thereof) in pathologies with an underlying intestinal secretion.
Sergeev et al., 2020	*Lactobacillus acidophilus, Bifidobacterium lactis* , *Bifidobacterium* longum and *Bifidobacterium bifidum* and the prebiotic component was a mixture of galacto-oligosaccharide.	20 volunteers were recruited in the study (10 in the placebo group (control) and 10 in the symbiotic group (treatment)). The average BMI of the study participants was 33.5 kg/m2 and the mean age was 47.4 years. Most participants were female (80% in the placebo group and 70% in the symbiotic group).	Participants were enrolled in the weight loss program at the start of the study and followed a low-carb, high-protein, low-energy eating plan. The probiotic component of the symbiotic used in the study contained a mixture (one capsule contained 69 mg or 15 × 109 CFU) of proprietary strains of *Lactobacillus acidophilus* DDS-1, Bifidobacterium lactis UABla-12, Bifidobacterium longum UABl-14, and *Bifidobacterium bifidum UABb-10* . The prebiotic component was a mixture *of trans-galactooligosaccharide (*GOS) at a dose of 5.5 g/d (2.75 g of GOS and the remaining simple sugars).	3 months of treatment	The results showed no statistically significant differences in body composition (body mass, BMI, body fat mass, body fat percentage, lean body mass, and bone mineral content) between the placebo and symbiotic groups at the end of the clinical trial. Symbiotic supplementation increased the abundance of gut bacteria associated with positive health effects, especially *Bifidobacterium* and *Lactobacills*, and also appeared to increase the richness of the gut microbiota. A decreasing trend in gut microbiota diversity in the placebo and symbiotic groups was observed at the end of the trial, which may imply the effect of the high-protein, low-carbohydrate diet used in the weight loss program. Regression analysis performed to correlate species abundance after supplementation with body composition parameters and obesity biomarkers found an association between a decrease over time in blood glucose and an increase in *Lactobacillus* abundance , particularly in the symbiotic group. However, the

					decrease over time in body mass, BMI, waist circumstance and body fat mass was associated with a decrease in *Bifidobacterium* abundance. The results obtained support the conclusion that the symbiotic supplement used in this clinical trial modulates the human gut microbiota, increasing the abundance of potentially beneficial microbial species.

Cast out: STENMAN et al. (2016); KRUMBECK et al. (2018); SERGEEV et al. (2020).

5 CONCLUSION

Currently there is talk of the interference of the intestinal microbiota in the various pathophysiology, therefore, the research of the last 10 years shows us that there is evidence of intestinal modulation through the intake of a balanced diet, along with the use of probiotics, and prebiotics and symbiotics in humans. With changes in to reduce body fat mass, waist circumference, energy intake and body weight even reaching in the increased abundance of gut bacteria associated with positive health effects, especially *Bifidobacterium* and *Lactobacills*.

However, some doubts persist, such as which combination of probiotic and prebiotic to use, the right dose to have results, since most of the concentration is used higher than recommended, how long of treatment to see significant evolution. Finally, they are questions that need to be defined to confirm the potential effectiveness and efficiency for obesity and improve people's quality of life and the costs imposed on it.

Therefore, it is important to highlight that more nutritional studies are still needed, since through a balanced diet and the administration of probiotics, and prebiotics and symbiotics can induce potential beneficial effects for weight maintenance and metabolic health, as well as the maintenance of the health of the gastrointestinal tract.

REFERENCES

ALVES, C. D. Efeito da suplementação de prebiótico ou simbiótico na atividade de enzimas antioxidantes em indivíduos com obesidade mórbida: um ensaio clínico, randomizado, placebo controlado e triplo cego. 2020, 143p. Dissertação de mestrado em Nutrição, Universidade Federal de Santa Catarina. Disponível em: <repositorio.ufsc.br/bitstream/handle/123456789/219298/PNTR0272-D.pdf?sequence=-1&isAllowed=y>. Acesso em: 20 mar. de 2021.

AMER, N. M.; SANCHES, D.; MORAES, S. M. F. Índice de massa corporal e razão cintura/quadril de Praticantes de atividade aeróbica moderada. Revista da Educação Física/UEM, Maringá, v. 12, n. 2, p. 97-103, 2. sem. 2001. Disponível em: <http://periodicos.uem.br/ojs/index.php/RevEducFis/article/view/3752/2584>. Acesso em: 25 mai. 2020.

ARAÚJO, D. G. S. et al. Alteração da microbiota intestinal e patologias associadas: importância do uso de prebióticos e probióticos no seu equilíbrio. Temas em Saúde, João Pessoa, v. 19, n. 6, nov. 2019. Disponível em: <http://temasemsaude.com/wp-content/uploads/2020/01/196.pdf>. Acesso em: 25 abr. 2020.

AZAD, M. D. A. K; SARKER, M.; LI, T.; YIN, J. Espécies probióticas na modulação da microbiota intestinal: uma visão geral. Biomed Res Int. 2018. Disponível em: <www.ncbi.nlm.nih.gov/pmc/articles/PMC5964481/#B43 >. Acesso em 10 de janeiro de 2021.

BLAUT, M. Gut microbiota and energy balance: role in obesity. Proc Nutr Soc, v.74, n. 3, p. 227-234, Aug. 2015. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/25518735/>. Acesso em: 25 set.2020.

BESSERA B. T. S. Avaliação da Microbiota Intestinal e sua relação com parâmetros metabólicos em mulheres com obesidade mórbida. 2014. 109p. Dissertação (Mestrado em Nutrição) - Universidade Federal de Santa Catarina. Disponível em: <https://repositorio.ufsc.br/xmlui/bitstream/handle/123456789/129567/329288.pdf?sequence=1&isAllowed=y>. Acesso em: 26 set. 2020.

BOAS, F. B. R. V. Obesidade e sua possível relação com a microbiota intestinal. 2017. 19f. Trabalho de Conclusão de Curso (Bacharelado em Biomedicina). Curso de Biomedicina. Centro Universitário de Brasília (UNICEUB), Brasília, DF, 2017. Disponível em: <https://repositorio.uniceub.br/jspui/bitstream/235/11720/1/21485287.pdf>. Acesso em: 25 set. 2020.

BORGES, F. M.; PAULA, T. O.; GAMEIRO, J.; SILVA, V. L.; DINIZ, C. G. O papel da microbiota na modulação da homeostase dos hospedeiros: correlação entre microbioma intestinal e obesidade. HU Revista, Juiz de Fora, v. 40, n. 1 e 2, p. 107-116, jan./jun. 2014. Disponível em: <https://periodicos.ufjf.br/index.php/hurevista/article/view/2452/932>. Acesso em: 25 set. 2020.

BRASIL. Ministério da Saúde. Diabetes, hipertensão e obesidade avançam entre os brasileiros. Brasília, 2020. Disponível em: <https://www.gov.br/saude/pt-br/assuntos/noticias/diabetes-hipertensao-e-obesidade-avancam-entre-os-brasileiros-2>. Acesso em: 20 set. 2020.

BRASIL. Ministério da Saúde. Vigitel Brasil 2018. Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico: estimativas sobre frequência e distribuição sociodemográfica de fatores de risco e proteção para doenças crônicas nas capitais dos 26 estados brasileiros e no distrito federal em 2013. Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Análise em Saúde e Vigilância de Doenças não Transmissíveis. Brasília: Ministério da Saúde, 2019. Disponível em: <https://portalarquivos2.saude.gov.br/images/pdf/2019/julho/25/vigitel-brasil-2018.pdf>. Acesso em:

25 set. 2020.

BRASIL. Ministério da Saúde. Vigitel Brasil 2019. Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico: estimativas sobre frequência e distribuição sociodemográfica de fatores de risco e proteção para doenças crônicas nas capitais dos 26 estados brasileiros e no distrito federal em 2019. Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Análise em Saúde e Vigilância de Doenças não Transmissíveis. Brasília: Ministério da Saúde, 2020. Disponível em: <https://portalarquivos.saude.gov.br/images/pdf/2020/April/27/vigitel-brasil-2019-vigilancia-fatores-risco.pdf >. Acesso em: 25 set. 2020.

BRAY, G. A. Classification and evaluation of the obesities. Medical Clinics North America, Philadelphia, v.73, n.1, p.161-184, 1989.

BRUSAFERRO, A.; COZZALI, R.; ORABONA, C.; BISCARINI, A.; FARINELLI, E.; CAVALLI, E.; GRONHANN, U.; PRICIPI, N.; ESPOSITO, S. Is It Time to Use Probiotics to Prevent or Treat Obesity? Nutrients. V. 10, p. 1613, nov. 2018. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266556/>. Acesso em: 29 ago. 2020.

CAMARGO, V. E. Produção de galacto-oligossacarídeos (gos) a partir da transgalactosilação da lactose com β-galactosidases de leveduras isoladas de grãos de kefir de leite. 84p., 2018. Dissertação de mestrado em Biotecnologia, Universidade Federal de São Paulo (UNIFESP. Disponível em: <repositorio.unifesp.br/handle/11600/52787>. Acesso em: 20 de abr. 2021.

CANI, P. D. Interactions between gut microbes and host cells control gut barrier and metabolism. International Journal of Obesity Suplementes, v. 6, p. 28-30, 2016. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5485881/>. Acesso em: 25 set. 2020.

CARABOTTI, M.; SCIROCCO, A.; MASELLI, M. A.; SEVERI, C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Annals Gastroenterologia. V. 28, n. 2, p. 203–209. 2015. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/25830558/>. Acesso em: 25 set. 2020.

CARVALHO, D. V.; GALLÂO, M. I.; BRITO, E. S. Obesidade e fibra dietética: destaque para a fibra de caju. Braz. J. of Develop.,v. 6, n. 7, p.43474-43488, Curitiba, 2020. Acesso em: 20 mar. de 2021.

COTTA, C. Micro-organismos 'do bem' podem contribuir não só com o intestino, mas beneficiar até pacientes com câncer. Portal Uai (Jornal Estado de Minas), 03 dez. 2014. Disponível em: <https://www.uai.com.br/app/noticia/saude/2014/12/03/noticias-saude,191089/amp.html.> Acesso em: 20 abr. 2021.

DABKE, K.; HENDRIK, G.; DEVKOTA, S. O microbioma intestinal e a síndrome metabólica. J Clin Invest, v1.1, n° 10, p. 4050-4057, 2019. Disponível em: <www.ncbi.nlm.nih.gov/pmc/articles/PMC6763239/ >. Acesso em 10 de janeiro de 2021.

DAMIANI, D.; DAMIANI, D. Sinalização cerebral do apetite. Revista Brasileira de Clínica Médica, São Paulo, v. 9, n. 2, p. 138-145, mar./abr. 2011. Disponível em: <http://files.bvs.br/upload/S/1679-1010/2011/v9n2/a1828.pdf>. Acesso em: 25 set. 2020.

DAVIS, C. D. The Gut Microbiome and Its Role in Obesity. Nutrition today, n.º 51, p. 167-174, 2017. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5082693/>. Acesso em: 01 abr. 2021.

DING, X.; YANG, X.; WANG, H. Metodologia, eficácia e segurança do transplante de microbiota fecal no tratamento de doença inflamatória intestinal. Medicina e microecologia. Disponível em: <www.sciencedirect.com/science/article/pii/S2590097820300252#bib51>. Acesso em: 01 de abr. 2021.

ENGIN, A. The Pathogenesis of Obesity-Associated Adipose Tissue Inflammation. Adv Exp Med Biol. p-221-245, 2017. Disponível em: <pubmed.ncbi.nlm.nih.gov/28585201/>. Acesso em: 10 jan. de 2021.

FERREIRA, G. S. Disbiose intestinal: aplicabilidade dos prebióticos e dos probióticos na recuperação e manutenção da microbiota intestinal. 2014. 33p. Monografia (Ciências Farmacêuticas). Curso de Farmácia. Centro Universitário Luterano de Palmas (ULBRA). Palmas, TO. Disponível em: <https://ulbra-to.br/bibliotecadigital/uploads/document55e9f4b59e0bd.pdf>. Acesso em: 24 set. 2020.

FILHO, M. A. C. Obesidade e Diabetes: da origem ao caos. In: CINTRA, Dennys Esper; ROPELLE, Eduardo Rochete; PAULI, José Rodrigo. Obesidade e diabetes: fisiopatologia e sinalização celular. São Paulo: Savier, 2011. p. 3-35.

FIRMINO, P. L.; SALOMON, A. L. R. Influência do processo inflamatório ligado à obesidade no metabolismo de nutrientes. Centro Universitário de Brasília – (UNICEUB). Faculdade de Ciências da Educação e Saúde. Curso de Nutrição. Disponível em: <repositorio.uniceub.br/jspui/bitstream/prefix/13289/1/21508968.pdf>. Acesso em: 20 mar. de 2021.

FLESCH, A.G.T.; POZIOMYCK, A.K.; DAMIN, D.C. O uso terapêutico dos simbióticos. Arq Bras Cir Dig, v.27, n° 3, p.206-209, 2014. Disponível em:<www.scielo.br/pdf/abcd/v27n3/pt_0102-6720-abcd-27-03-00206.pdf>. Acesso em 01 abr. 2021.

FLOR, A. R. Disbiose e obesidade: Uma revisão de literatura. Trabalho de Conclusão de Curso a obtenção do título de Bacharel em Nutrição com linha específica em Nutrição Clínica, Universidade Federal da Paraíba. Disponível em:<repositorio.ufpb.br/jspui/bitstream/123456789/11171/1/ARF05072018.pdf>. Acesso em: 20 mar. de 2021.

FRIGORET, M. E.; GUTIÉRREZ- AGUIALAR, R. The colors of adipose tissue, Gac Med Mex, v.156, n. 2, p. 142-149, 2020. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32285854/>. Acesso em: 24 set. 2020.

FROTA, K.M.G.; SOARES, M.R.M.; MUNIZ, V.R.C.; FONTINELLE, R.C.; CARVALHO, C.M.R.G. Efeito de prebióticos e probióticos na microbiota intestinal e nas alterações metabólicas de indivíduos obesos. Nutrire, v.40, n°2, p.173-187, 2015. Acesso em 01 abr. 2021

GÉRARD, P. Gut microbiota and obesity. Cellular and molecular life sciences: CMLS, v. 73, n. 1, p. 147-162, jan. 2016. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/26459447/>. Acesso em: 25 set. 2020.

GOMES, A. P. P. A microbiota intestinal e os desenvolvimentos recentes sobre o seu impacto na saúde e na doença. 2017. 50p. Monografia de Mestrado (Mestrado Integrado em Ciências Farmacêuticas). Faculdade de Farmácia. - Universidade de Lisboa. Portugal. Disponível em: <https://repositorio.ul.pt/bitstream/10451/36100/1/MICF_Ana_Patricia_Gomes.pdf>. Acesso em: 26 set. 2020.

HAINES, J.; HAYCRAFT, E.; LYTLE, L.; NICKLAUS, S.; KOK, F. J.; MERDJI, M.; FISBERG, M.; MORENO, L. A.; GOULET; HUGHES, S. O. Nutrindo a alimentação saudável das crianças:

declaração de posição. Apetite. v. 1, n. 37, p. 124-133, 2019. Disponível em: < pubmed.ncbi.nlm.nih.gov/30797837/>. Acesso em: 07 de jan. de 2021.

KAMIMURA, M. A.; BAXMANN, A. C.; RAMOS, L. B.; CUPPARI; L. Avaliação nutricional. In: CUPPARI; L.. Guia de nutrição: clínica no adulto. 3. ed. Barueri/SP: Manole, 2014. p. 111-149.

KRUMBECK, J.A.; RASMUSSEN, H.E.; HUTKINS, R.W.; CLARKE, J.; SHAWRON, K.; KESHAVARZIAN, A., WALTER, J. Probiotic Bifidobacterium cepas e galactooligossacarídeos melhoram a função de barreira intestinal em adultos obesos, mas não mostram sinergismo quando usados juntos como simbióticos. Microbiome, v. 6, n. 1, p. 1-16, jun. 2018. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6022452/>. Acesso: 15 mar. 2020.

LAZAR, V.; DITU, L. M.; PIRCALABIORU, G.G.; PICU, A.; PETCU, L.; CUCU, N.; CHIFIRIUC, M.C. Gut Microbiota, Host Organism, and Diet Trialogue in Diabetes and Obesity. Front Nutr., n.º 6, p. 21, 2019. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6424913/>. Acesso em: 01 abr. 2021.

LEE, P.; YACYSHYN, B. R.; YACYSHYN, M.B. Gut microbiota and obesity: An opportunity to alter obesity through faecal microbiota transplant (FMT). Diabetes Obes Metab, v. 3, n. 21, p. 479-490, mar. 2019. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/30328245/>. Acesso em: 26 set. 2020.

LISBOA, C.R.; COSTA, F.A.A.; BURKERT, J.F.M.;BURKERT, C.A.V. Síntese de galacto-oligossacarídeos a partir de lactose usando β-galactosidase comercial de Kluyveromyces lactis. Braz. J. Food Technol., Campinas, v. 15, n. 1, p. 30-40, jan./mar. 2012. Disponível em:<www.scielo.br/pdf/bjft/v15n1/04.pdf>. Acesso em: 20 de abr. de 2021.

MATOS, A. F. G.; OLIVEIRA, J. Diagnóstico e Classificação da Obesidade e da Síndrome Metabólica. In: HALPERN, Alfredo; MANCINI, Márcio C. Obesidade e Síndrome Metabólica para o Clínico. São Paulo: Roca, 2008. p. 3-19.

MOREIRA, L. N. (2019). Evolução da colonização da microbiota fecal de recém-nascidos prematuros submetidos à colostroterapia, 2019. Dissertação (Mestrado em Fisiopatologia) –UNIVERSIDADE DE SÃO PAULO. São Paulo, Programa de Pós-graduação em Farmácia, 68 f.

MURAWSKA-CIALOWICZ, E. Adipose tissue - morphological and biochemical characteristic of different depots. Postepy Hig Med Dosw (Online), v.7, n.0, p.:466-484, JUN/2017. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/28665277/>. Acesso em: 26 set. 2020.

NILSON, E. A. F.; ANDRANDE, R. C. S.; BRITO, D. A.; OLIVEIRA, M. L. Custos atribuíveis a obesidade, hipertensão e diabetes no Sistema Único de Saúde, Brasil. Revista Panamericana Salud Publica, v. 43, p. 1-5, 2020. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7147115/pdf/rpsp-44-e32.pdf>. Acesso em: 29 ago. 2020.

NEVES, C. T. C. O microbioma da infância à idade adulta. In: FAINTUCH, Joel. Microbioma, disbiose, probióticos e bacterioterapia. Baruei: Manole, 2017. P. 88-103.

NUNES, M. L.; GARRIDO, M. P. A obesidade e a ação dos prebióticos, probióticos e simbióticos na microbiota intestinal. Nutrição Brasil, v.17, n°3, p.189-196, 2018. Disponível em: <portalatlanticaeditora.com.br/index.php/nutricaobrasil/article/view/907/4470>. Acesso em: 20 mar. de 2021.

OLIVEIRA, A. M.; HAMMES, T. O. Microbiota e barreira intestinal: implicações para obesidade. Clinical and biomedical research. Porto Alegre, v. 36, n. 4, p. 222-229. 2016. Disponível em: <https://www.lume.ufrgs.br/handle/10183/158718>. Acesso em: 19 ago. 2020.

OLIVEIRA, J. L.; ALMEIDA, C.; BOMFIM, N. S. A importância do uso de probiótico na saúde humana. Unoesc & Ciência - ACBS, Joaçaba, v. 8, n. 1, p. 7-12, jan./jun. 2017. Disponível em: <https://pdfs.semanticscholar.org/d21f/47781563268023981b780007f060ae19509e.pdf>. Acesso em: 19 ago. 2020.

OLIVEIRA, J. M. S.; SANTOS, G. M.; SALDANHA, N. M. V. P; SOUSA, P. V. L; CARVALHO, A. C. S. Efeitos de probióticos no tratamento da obesidade. C&D-Revista Eletrônica da FAINOR, Vitória da Conquista, v.10, n.2, p.154-165, jun./ago. 2017. Disponível em: <http://srv02.fainor.com.br/revista/index.php/memorias/article/viewFile/656/33>. Acesso em: 20 ago. 2020.

OMS. Organização Mundial de Saúde. Obesidade. Genebra: OMS, 2020. Disponível em: <https://www.who.int/topics/obesity/es/>. Acesso em: 29 ago. 2020.

OMS. Organização Mundial de Saúde. Obesidade e excesso de peso. Genebra: OMS, 2020. Disponível em: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Acesso em: 29 ago. 2020.

OLIVEIRA, L. O. Efeito de probiótico (Bifidobacterium lactis) e simbiótico (Bifidobacterium lactis e frutooligossacarídeo) sobre a microbiota intestinal, perda de peso corporal e parâmetros metabólicos de mulheres com obesidade. 2020, 159f. Tese (Doutorado em Ciências Nutricionais). Programa de Pós-Graduação em Nutrição (PPGN) - Universidade Federal do Rio de Janeiro (UFRJ). Rio de Janeiro, RJ. Disponível em: <http://www.ppgn.ufrj.br/wp-content/uploads/2020/07/Louise-Crovesy-de-Oliveira-tese.pdf>. Acesso em: 22 ago. 2020.

OPAS. Organização Pan-Americana da Saúde. Folha informativa – Alimentação saudável, 2019. Disponível em: <www.paho.org/bra/index.php?option=com_content&view=article&id=5964:folha-informativa-alimentacao-saudavel&Itemid=839>. Acesso em: 07 jan. de 2021.

OSTROWSKI, M. Efeito do consumo de simbiótico por mulheres obesas: avaliação do impacto sobre peso corporal e variáveis associadas à obesidade. 126p, 2016. Dissertação obtenção do título de mestre em Nutrição Humana. Universidade Federal do Rio de Janeiro, Rio de Janeiro. Disponível em: <www.ppgn.ufrj.br/wp-content/uploads/2017/11/DISSERTACAO-Marjorie-Ostrowski.pdf>. Acesso em: 01 abr. 2021.

PAIXÃO, L. A.; CASTRO, F. F. S. A colonização da microbiota intestinal e sua influência na saúde do hospedeiro. Universitas: Ciências da Saúde, Brasília, v. 14, n. 1, p. 85-96, jan./jun. 2016. Disponível em: <https://www.publicacoesacademicas.uniceub.br/cienciasaude/article/viewFile/3629/3073>. Acesso em: 25 set. 2020.

PARREIRA, K. E. L. F. Um estudo dos mecanismos hormonais, comportamento alimentar e impacto psíquico e emocional. 2017. 18p. Trabalho de Conclusão de Curso (Bacharelado em Biomedicina). Graduação em Biomedicina. Centro Universitário de Brasília, Brasília, DF, 2017. Disponível em: <https://repositorio.uniceub.br/jspui/bitstream/235/11675/1/21450269.pdf>. Acesso em: 25 set. 2020.

REDDEL, S.; PUTIGNAN, L.; CHIERICO, F. D. The Impact of Low-FODMAPs, Gluten-Free, and Ketogenic Diets on Gut Microbiota Modulation in Pathological Conditions. Nutrients, v. 11, n. 373, p.1-12, 2019. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6413021/>. Acesso em: 26 set. 2020.

RINNINELLA, E.; CINTONI, M.; RAOUL, P.; LOPETUSO, L. R.; SCALDAFERRI, F.; PULCINI, G.; MIGGIANO, G. A. D.; GASBARRINI, A.; MELE, M. C. Food Components and Dietary Habits: Keys for a Healthy Gut Microbiota Composition . Nutrientes, v. 11, n. 2393, p. 1-14, out. 2019. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6835969/>. Acesso em: 25 set. 2020.

RODRIGUES, L. S. V. Relação entre microbiota intestinal e obesidade: terapêutica nutricional através do uso de probióticos. Centro Universitário de Brasília (UNICEUB). Brasília, DF, 2016. Disponível em: <https://repositorio.uniceub.br/jspui/bitstream/235/9243/1/21358420.pdf>. Acesso em: 25 set. 2020.

SANTANA, R. S.; BARBOSA, B. S. D.; NASCIMENTO, E. S.; SOUZA, P. C.; CAVALCANTI, N.; QUIÑONES, E. M. Disbiose intestinal e o uso de prebióticos e probióticos como promotores da saúde humana. Revista cientifica das faculdades de medicina, Enfermagem, Odontologia, Veterinária e Educação Física, Santos, v.2, n.3, 2018. Disponível em: <https://periodicosunimes.unimesvirtual.com.br/index.php/higeia/article/view/955/797>. Acesso em: 22 ago. 2020.

SANTOS, K. E. R.; RICCI, G. C. L. Microbiota intestinal e a obesidade. Revista UNINGÁ Review, v. 26, n. 1, p. 74-82, abr. 2016. Disponível em: <http://revista.uninga.br/index.php/uningareviews/article/view/1794/1400>. Acesso em: 26 set. 2020.

SCHMIDT, L.; SODER, T. F.; DEON, R. G.; BENETTI, F. Obesidade e sua Relação com a Microbiota Intestinal. Revista Interdisciplinar de Estudos em Saúde (RIES), Caçador, v. 6, n. 2, p. 29-43, 2017. Disponível em: <https://periodicos.uniarp.edu.br/index.php/ries/article/view/1089/686>. Acesso em: 19 ago. 2020.

SEGANFREDO, F. B.; BLUME, C. A.; MOEHLECKE, M.; GIONGO, U. M.; CASAGRANDE, D. S.; SPOLIDORO, J. V. N.; PADOIN, U. M. V.; SCHAAN, B. D.; MOTTIN, C. C. Intervenções de perda de peso e alterações na microbiota intestinal em pacientes com sobrepeso e obesidade: uma revisão sistemática. Reverendo obeso, v.18, n. 8, p. 832-851, 2017. Disponível em: <pubmed.ncbi.nlm.nih.gov/28524627/>. Acesso em: 10 jan. 2021.

SERGEEV, I. N.; ALJUTAILY T.; WALTON G.; HUARTE E. Effects of Synbiotic Supplement on Human Gut Microbiota, Body Composition and Weight Loss in Obesity. Nutrients, v. 12, n. 1, p. 1-18, jan. 2020. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/31952249/>. Acesso: 15 mar. 2020.

SPERETTA, G. F. F.; LEITE, R. D.; Duarte, A. C. G. Obesidade, inflamação e exercício: foco sobre o TNF-alfa e IL-10. Revista HUPE, Rio de Janeiro, 2014; n.º 13, p. 61-69 Disponível em: <https://www.e-publicacoes.uerj.br/index.php/revistahupe/article/download/9807/8769>. Acesso em: 01 abr. 2021.

SIPPEL, C.; BASTIAN, R. M. A; GIOVANELLAC, J.; FACCIND, C.; CONTINIE, V.; BOSCO, S. M. D. Processos inflamatórios da obesidade. Revista de Atenção à Saúde, São Caetano do Sul/SP, v. 12, n. 42, p. 48-56, out./dez. 2014. Disponível em: <https://seer.uscs.edu.br/index.php/revista_ciencias_saude/article/download/2310/1656/9765>. Acesso em: 24 set. 2020.

SILVA-JUNIOR, V. L.; LOPES F. A. M.; ALBANO, R. M.; SOUZA, M. G. C.; BARBOSA, C. M. L.; MARANHÃO, P. A.; BOUSKELA, E.; KRAEMER-AGUIAR, L. G. Obesity and gut microbiota - what do we know so far?. Medical Express (São Paulo, online), v.4, n. 4, São Paulo, July/Aug. 2017. Disponível em: <https://www.scielo.br/scielo.php?script=sci_arttext&pid=S2358-042920170004000

01>. Acesso em: 24 set. 2020.

SOUZA, L. L.; GUEDES, E. P.; BENCHIMOL, A. K. Definições Antropométricas da Obesidade. In: MANCINI, M. C. et al. Tratado de obesidade. 2. ed. Rio de Janeiro: Guanabara Koogan, 2015. p. 51-69.

SOUZA, R. G. M.; GOMES, A.C.; PRADO, C. M. M.; MOTA, J. F. Métodos de análise da composição corporal em adultos obesos. Revista de Nutrição, Campinas-SP, vol.27, n. 5, p.569-583, Sept./Oct. 2014. Disponível em: <https://www.scielo.br/scielo.php?script=sci_arttext&pid=S1415-52732014000500
569>. Acesso em: 25 set. 2020.

STENMAN, L. K. et al. Probiotic With or Without Fiber Controls Body Fat Mass, Associated With Serum Zonulin, in Overweight and Obese Adults-Randomized Controlled Trial. EBioMedicine, v. 13, p. 190-200, Oct. 2016. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/27810310/>. Acesso em: 18 abr. 2021

TORRES-FUENTES, C.; SCHELLEKENS, H.; DINAN, G. T.; CRYAN, J. F. O eixo microbiota-intestino-cérebro na obesidade. Lancet Gastroenterol Hepatol, n. 2, p. 747-756, Out. 2017. Disponível em: <pubmed.ncbi.nlm.nih.gov/28844808/>. Acesso em: 10 jan. de 2021.

WGO. World Gastroenterology Organization. Diretrizes Mundiais da Organização Mundial de Gastroenterologia: Probióticos e prebióticos. Estados Unidos: WGO, 2017. Disponível em: <https://www.worldgastroenterology.org/guidelines/global-guidelines/probiotics-and-prebiotics/probiotics-and-prebiotics-portuguese>. Acesso em: 01 abr. 2021.