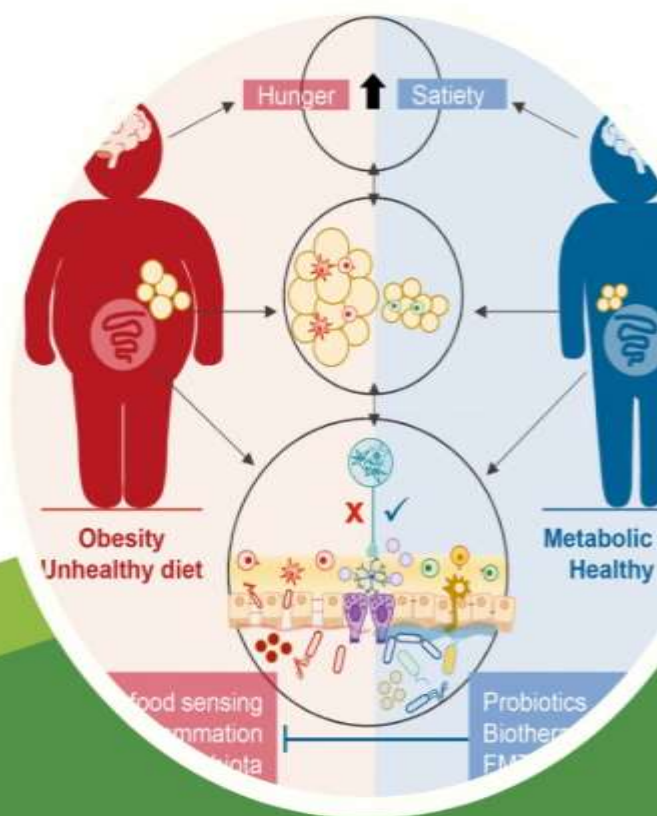


Gut Microbiota and Obesity: The Probiotics Solution

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Gut Microbiota and Obesity: The Probiotics Solution

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ABSTRACT

Obesity is a complex metabolic disorder characterized by extreme fat assemble, increasing the risk of various chronic diseases, and affect many diseases such as cardiovascular diseases and metabolic syndrome. The gut microbiota plays acute role in obesity development and management. Probiotics, which are live beneficial microorganisms, have been proposed as a potential intermediation to adjust gut microbiota composition and improve metabolic health studies. Any probiotic strains, usually from the Lactobacillus and streptococcus thermophilus, have been shown to change gut microbiota number and enhance gut barrier function. Clinical and animal studies show that probiotic may help reduce body weight. Probiotics have physical functions that provide to the health of gut microbiota, act as food supplements, decrease body weight and regulate metabolic functions among gastrointestinal pathways and gut bacterial colony. There is a clue for the relation between gut bacteria and obesity both in infants and in adults. There are different genetic, metabolic, and provocative pathophysiological pathways involved in the interplay between gut microbes and obesity. Microbial difference in the human gut can be measured as a factor involved in obesity development in humans. The different strains of the bacterial growth in the digestive tract can help to adapt the metabolic profile in the obese host as shown by different data from animal and human studies. Hence, a vast revision of the use of probiotics, prebiotics and antibiotics in obese sick person and their effects is conceivable.

Keywords: Probiotic bacteria, Obesity, Lactobacillus, gastrointestinal pathways.

INTRODUCTION

Probiotics are "live microorganisms which when administered in adequate amounts" according to the World Health Organization and the Food and Agricultural Organization of the United Nations. quantities promote the host's health [1]. Numerous studies have demonstrated the positive effects of probiotic consumption on improving intestinal flora balance. It goes without saying, however, that probiotic side effects vary by community and should be carefully evaluated as a health concern. Obesity is characterized as having excessive levels of body fat. It results from an imbalance between energy intake and expenditure (grams divided by height in meters squared). Numerous studies have shown the J shape diagram of BMI and morbidity/mortality risk [2]. A higher BMI increases the risk of gallstones, cardiovascular disease (CVD), dyslipidaemia, hypertension, atherosclerosis, inflammatory skin conditions such as psoriasis and atopic dermatitis, and some forms of cancer [3, 4] Over the past few decades, the prevalence of obesity has been steadily increasing globally, to the point where it is now regarded as a pandemic. The World Health Organization (WHO) predicts that 39% of individuals in today's society will suffer from obesity by 2035 [4]. For this reason, new public policies in primary health care and prevention are now more important than ever. Unusual or excessive fat accumulation that could be detrimental to one's health is called obesity [5]. Its aetiology has been linked to an energy imbalance between calories expended and calories consumed, primarily due to inadequate physical activity and poor food, but it is actually a combination of factors that includes interactions between hormones, the environment, and heredity [6]. Accordingly, recent research on humans and animals has demonstrated how the gut microbiota population regulates host metabolic processes and contributes to the development of obesity [6,7]. Additionally, a number of bacterial strains have been demonstrated in animal settings to suppress or reduce immune responses linked to chronic inflammation [7]. Microorganisms that are present in the epidermis, oral, vaginal, and nasal cavities as well as the colon are part of the human natural flora. There are many bacteria in the intestine that have an impact on human health. Microorganisms that are found in the colon, on the skin, and in the oral, vaginal, and nasal cavities are all part of the typical human flora. The intestine is home to more bacteria that are vital to metabolism, particularly the

fermentation of carbohydrates. Diet, antibiotics, surgeries, probiotics, and prebiotics can all change the gut microbiota, which in turn affects the prevalence of obesity and metabolic disorders [8].

An imbalance in energy intake and expenditure is the cause of the rising prevalence of obesity, which is defined as excessive body fat, primarily visceral fat, as determined by body mass index (BMI: weight in kilograms divided by height in meters squared). Numerous studies have shown the J shape diagram of BMI and morbidity/mortality risk. [9] The global obesity epidemic and associated conditions including type 2 diabetes, fatty liver disease, and cardiovascular diseases are mostly caused by high calorie intake and a sedentary lifestyle. It has recently been suggested that the gut microbiota contributes to the development of obesity [10]. This recommendation was supported by multiple observations. Compared to normal-weight people, overweight subjects had a lower proportion of Bacteroidetes and a higher number of Firmicutes [11]. Ninety percent of all bacterial cells in the human gut belong to these two groups. In obese individuals, losing weight results in a drop in Firmicutes and a corresponding decrease in decline in the Bacteroidetes. Mice have shown essentially the same observation. It's interesting to note that by transferring their gut flora, obese mice may be able to obtain energy from their diet more effectively than lean mice probiotics [11].

Live, non-pathogenic microorganisms known as probiotics are given to enhance microbial balance, especially in the gastrointestinal system. They are controlled as foods and supplements and are made up of lactic acid bacteria, including *Lactobacillus* and *Bifidobacterium* species, or *Saccharomyces bouvardia* yeast. Probiotics work by reducing intestinal pH, preventing pathogenic organisms from colonizing and invading the gut, and altering the host immune response, among other ways. the advantages of probiotics linked to one species or strain may not apply to another. Probiotics' therapeutic efficacy has been most strongly demonstrated in the treatment of paucities and acute diarrhoea, which are most frequently caused by rotavirus. The role of probiotics in avoiding vulvovaginal candidiasis, irritable bowel syndrome, ulcerative colitis, Crohn's disease, travellers' diarrhoea, antibiotic-associated diarrhoea, and *Clostridium difficile* infection requires further investigation. The idea that the gut microbiota offers defence against a number of illnesses is the foundation for the probiotic approach's positive effects. This is supported by indisputable evidence from multiple sources. First, it can be demonstrated that animals without germs are more prone to illness than their traditional counterparts, who have a full spectrum of gut flora. This distinction has been demonstrated for illnesses brought on by *Clostridium botulinum* and *Salmonella enteritidis*^{3,4}. This kind of comparison cannot be conducted in human subjects for obvious reasons, but it is logical to believe that at least some of these findings would hold true for humans as well [12].

EFFECT OF PROBIOTICS



Fig.1 Effect of Probiotics

Probiotic Bacteria

According to earlier evaluations, probiotics may reduce the incidence and length of diarrhoea, boost cellular and humoral immunity, prevent cancer, and reduce harmful metabolites such ammonium and pro cancerogenic enzymes in the colour. Furthermore, the effects of gut microbiota on a person's health have been the subject of numerous research in recent years. By altering intestinal microbes, probiotics that can colonize the intestinal tract have been shown to benefit metabolic disorders like diabetes and obesity [13]. In addition to the advantages already discussed, numerous discoveries in the last few decades have added to our knowledge of probiotics' antioxidant potential.[14] It was discovered that Bifidobacterium animals 01's culture supernatant, intact cells, and intracellular cell-free extracts scavenge superoxide anion and hydroxyl radicals in vitro while boosting mice's anti oxidase activities in vivo. Additionally, multispecies probiotics can reduce oxidative stress in people with type 2 diabetes. [15]. Probiotics are mostly represented by lactic acid bacteria (LAB) strains in the food and pharmaceutical industries [16]. Treatment and maintenance of ulcerative colitis (UC) have been found to benefit from LAB. Additionally; they were linked to improvements in metabolic illnesses. Furthermore, in fish, Lactobacillus rhamnoses or Lactobacillus lactis improved the oxidative status, growth, and immune system of sea bream, Pagris major. Another popular probiotic bacterium is Probiotic Bifidobacterium. It helped women with irritable bowel syndrome and boost antitumor immunity [17]. The feed industry favours Bacillus species because to their capacity to manufacture a wide range of enzymes and their stability as spore-forming bacteria.[18] Numerous probiotic organism strains have been employed in therapeutic settings to treat gastrointestinal diseases in both adults and children. These include acute diarrhoea caused by bacteria or viruses, conditions where medications or radiation therapy compromise mucosal integrity, and conditions that prevent pathogens from colonizing the gut. These studies found no indication of probiotic-induced opportunistic infection.[19]

Mechanism of action of probiotics bacteria

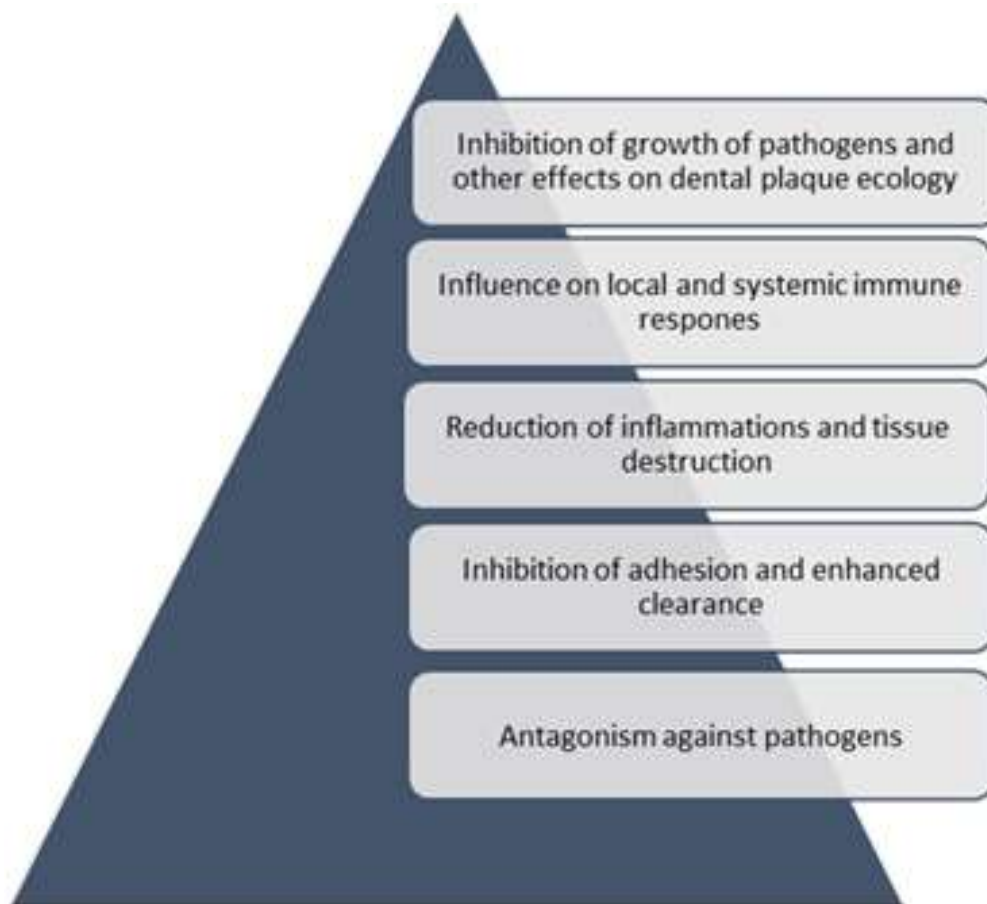


Fig.2 Mechanism of action of probiotics bacteria

CLASSIFICATION OF PROBIOTIC BACTERIA

Table 1. Classification of Probiotic Bacteria

Organism	Infection potential
Lactobacillus	Mainly non pathogen, some opportunistic infections usually in immunocompromised patients.
Lactococcus	Mainly non pathogen
Leucistic	Mainly non pathogen, some isolated cases of infection.
Streptococcus	Oral streptococci mainly non- pathogens (including streptococcus thermophilus); some may cause opportunistic infections.
Enterococcus	Some strains are opportunistic pathogens with haemolytic activity and antibodies resistance.
Bifidobacterium	Mainly non- pathogen, some isolated cases of human infection
Saccharomyces	Mainly non-pathogen, some isolated cases of human infection.

ADVANTAGES OF PROBIOTICS BACTERIA

Improved Digestion: Probiotics bacteria can help improve digestion, reduce symptoms of irritable bowel syndrome, and alleviate lactose intolerance.[20]

Boosted Immune System: Probiotics bacteria can help boost the immune system by increasing the production of antibodies and activating immune cells.[21]

Reduced inflammation: Probiotics bacteria can help reduce inflammation in the body, which can reduce the risk of chronic diseases such as heart diseases, diabetes, and cancer.[22]

Improved Mental Health: Probiotics bacteria can help improve mental health by reducing symptoms of anxiety and depression.[23]

Weight Management: Probiotics bacteria can help with weight management by regulating appetite, improving metabolism, and reducing inflammation.[24]

Improved Skin Health: Probiotics bacteria can help improve skin health by reducing inflammation, improving skin elasticity, and reducing symptoms of acne.[25]

Reduced Allergy Symptoms: Probiotics bacteria can help reduce allergy symptoms by regulating the immune system and reducing inflammation.[26]

Improved Oral Health: Probiotics bacteria can help improve oral health by reducing the risk of dental caries, gum diseases, and bad breath.[27]

Reduced Symptoms of Menopause: Probiotics bacteria can help reduce symptoms of menopause such as hot flashes, night sweats, and vaginal dryness.[28]

Improved Gut Barrier Function: Probiotics bacteria can help improve gut barrier function, which can reduce the risk of leaky gut syndrome and other gastrointestinal disorders. [29]

OBESITY

Serious public health concerns have been raised by the sharp increase in childhood and teenage overweight and obesity rates over the previous three decades. However, in the early 1970s, 15% of children between the ages of 2 and 19 were thought to be at danger of being overweight or by 2003-2006, the prevalence of overweight risk and overweight in children and adolescents rose to about 32% [30]. Overweight is defined as being at or above the 85th percentile of the sex-specific body mass index [BMI] on age growth charts [31]. High childhood obesity rates have serious negative effects on health, such as an increased risk of type 2 diabetes, cardiovascular issues, and other mental and physical issues [32]. Additionally, children who are overweight have a significantly higher chance of becoming overweight adults than children of normal weight [33]. Public health initiatives to reverse these trends must first better understand the causes and consequences of childhood obesity. Numerous theories

have been put up to explain the rising issue of childhood obesity in the United States. Although obesity susceptibility is believed to be influenced by hereditary variables [34], a significant shift in the gene pool is unlikely to account for the increase in obesity during the previous few decades [35]. Rather, a large portion of the obesity issue is thought to be caused by a decline in physical activity. Neighbourhood and community surroundings that encourage passive modes of recreation and commuting have been linked to these behavioural tendencies [36–37,38,39]. The relationship between environmental factors and children's and adolescents' physical activity has been the subject of an increasing amount of research in recent years. According to a review by Davison and Lawson [40] elements like Youth physical activity was linked to sidewalks and regulated intersections, access to schools and recreational facilities, and public transportation and destination accessibility. According to a second research paper, children's activity levels were linked to their home and school surroundings, whereas adolescents' physical activity was linked to a low frequency of neighbourhood crime [41].

Causes of Obesity

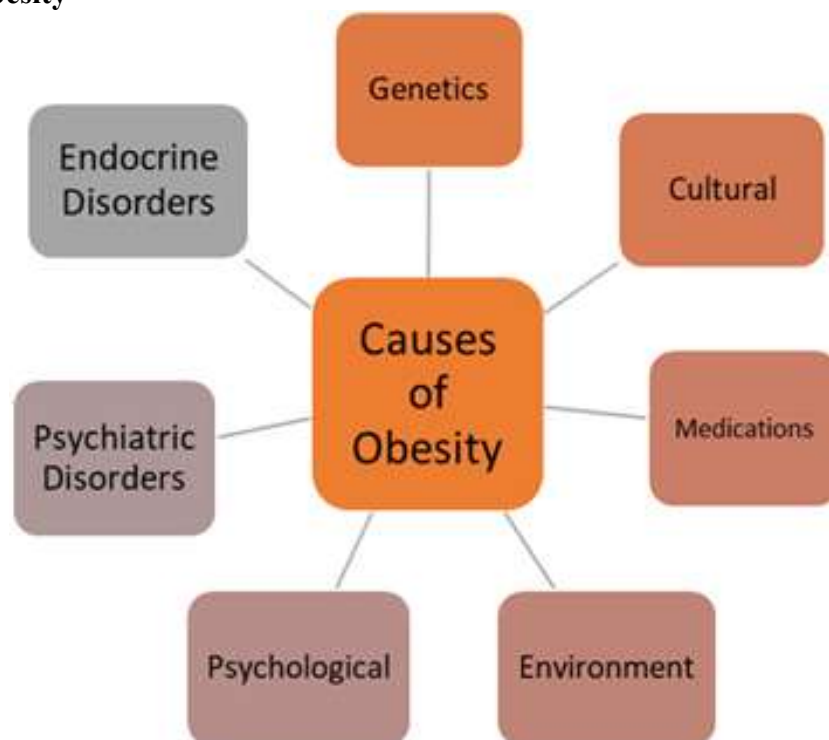
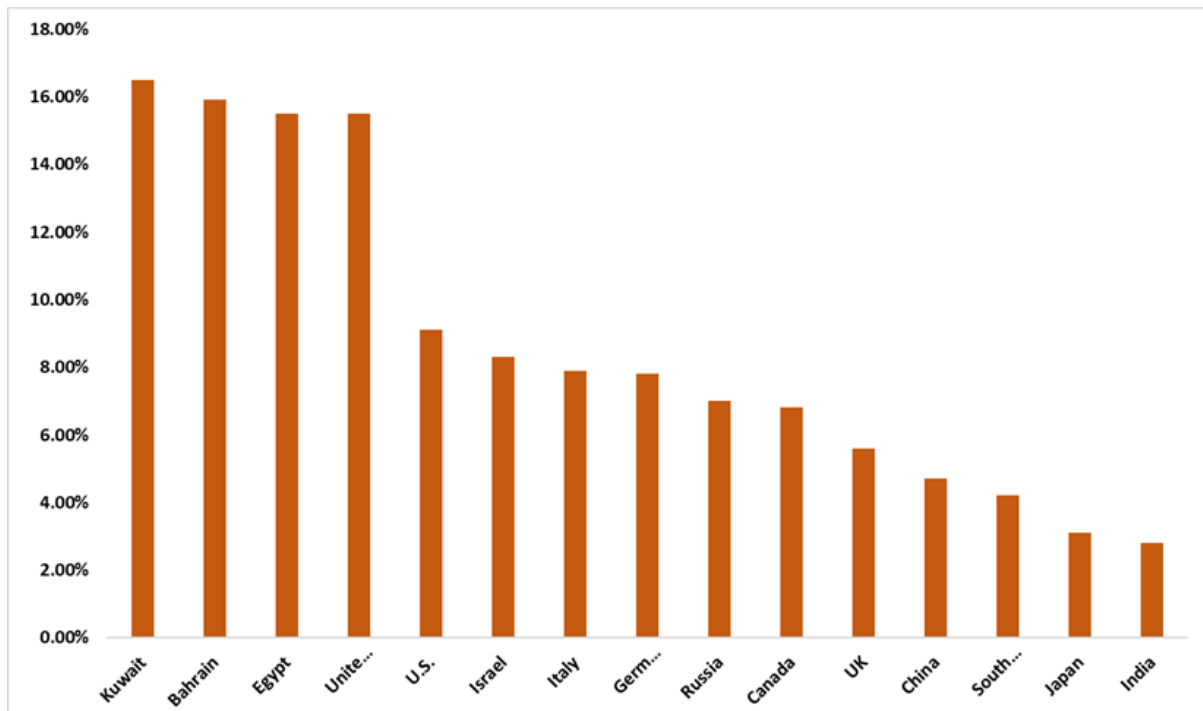


Fig.3 Cause of Obesity

Death Ratio

Late in 2019, a new coronavirus known as SARSCoV-2, which causes COVID-19, surfaced and has since become a global menace with terrible outcomes. [42, 43] The illness is still spreading today, with new variations appearing and breakthrough infections becoming seen, and the medical system is overburdened.[44]. As of September 14, 2021, 4 657 736 people had died globally as a result of 226 418 035 infected cases.[45].

Older age, male sex, and concomitant conditions such diabetes, hypertension, chronic kidney disease, chronic lung disease, and cardiovascular disease have all been shown to negatively impact the prognosis of COVID-19[46]. These comorbidities predispose individuals with obesity because they are linked to both obesity and malfunctioning adipose tissue. a higher chance of developing severe COVID-19. According to studies, ACE2 receptors, which serve as a gateway for SARS-CoV-2 to enter human cells, are abundant in adipose tissues.[47]. Furthermore, it has been demonstrated that obesity changes immune function and makes a person more vulnerable to infection by many pathogens.6. More recently, a number of meta-analyses revealed a link between obesity and a bad prognosis for COVID-19. [48,49] These meta-analyses, however, were constrained by the quantity of included research, which ranged from three to sixty, and primarily employed body mass index (BMI) as a metric.



Graph 1. Death ratio graph of Obesity

Controlling Methods

The main causes of the prevalence of obesity worldwide include bad diets, sedentary work, and technological advancements. The prevalence of obesity is sharply rising worldwide. This issue has grown to be a public health concern. global economies and systems [50].

The primary cause of obesity and overweight is an energy imbalance between calories expended and consumed due to the modern lifestyle, where long workdays and increasingly computer-dependent jobs are making people more sedentary and decreasing their physical activity (PA). Additionally, this circumstance promotes the consumption of fast food and foods high in calories. The composition of a healthy body for both men and women are depicted in Figure 1 as an example [51]. Generally speaking, environmental and societal changes related to social growth and the absence of supportive legislation in areas like health are what cause changes in eating habits and PA. the fields of education, transportation, urban planning, agriculture, food processing, distribution, and marketing.

Obesity and overweight are regarded as significant risk factors for noncommunicable diseases, including cardiovascular diseases, which were the primary cause of mortality, diabetes, musculoskeletal conditions, and some types of cancer [52]. As the body mass index (BMI) rises, so does the risk for certain noncommunicable diseases. Additionally, juvenile obesity is linked to a higher risk of obesity, early mortality, and impairment as an adult. In addition to these potential hazards, children who are fat have early indicators of cardiovascular disease, insulin resistance, psychological consequences, respiratory problems and an increased risk of fractures and hypertension. Obesity, overweight, and noncommunicable diseases associated with obesity can all be avoided. In this way, people can decide to consume less energy from total fat and sweets, eat more fruits, vegetables, legumes, and grains, and engage in frequent physical activity. The full effectiveness of individual responsibility requires that people have access to a healthy way of living. Furthermore, it is crucial to support individuals in adhering to such suggestions at the societal level by implementing demographic policies that are supported by scientific data and would enable regular PA and healthier food options that are accessible and reasonably priced for everyone, especially the most impoverished. Countries should work hard to address this issue, emphasising the adoption of a physically active lifestyle and a culture of good food. By creating new, popular, lightweight, user-friendly, and reasonably priced consumer-based fitness wearable trackers and food intake systems, modern technology has helped to alleviate the problem of obesity, which causes numerous health issues [53]. These useful resources offer an unbiased assessment of a user's long-term eating history, PA, and daily energy expenditure (EE). Additionally, users can monitor their data over time using websites or mobile applications [54]. However, in order to provide an accurate

measurement and improve health outcomes, the data gathered by these systems must be pertinent, intelligible, and widespread.

CONTROLLING METHOD

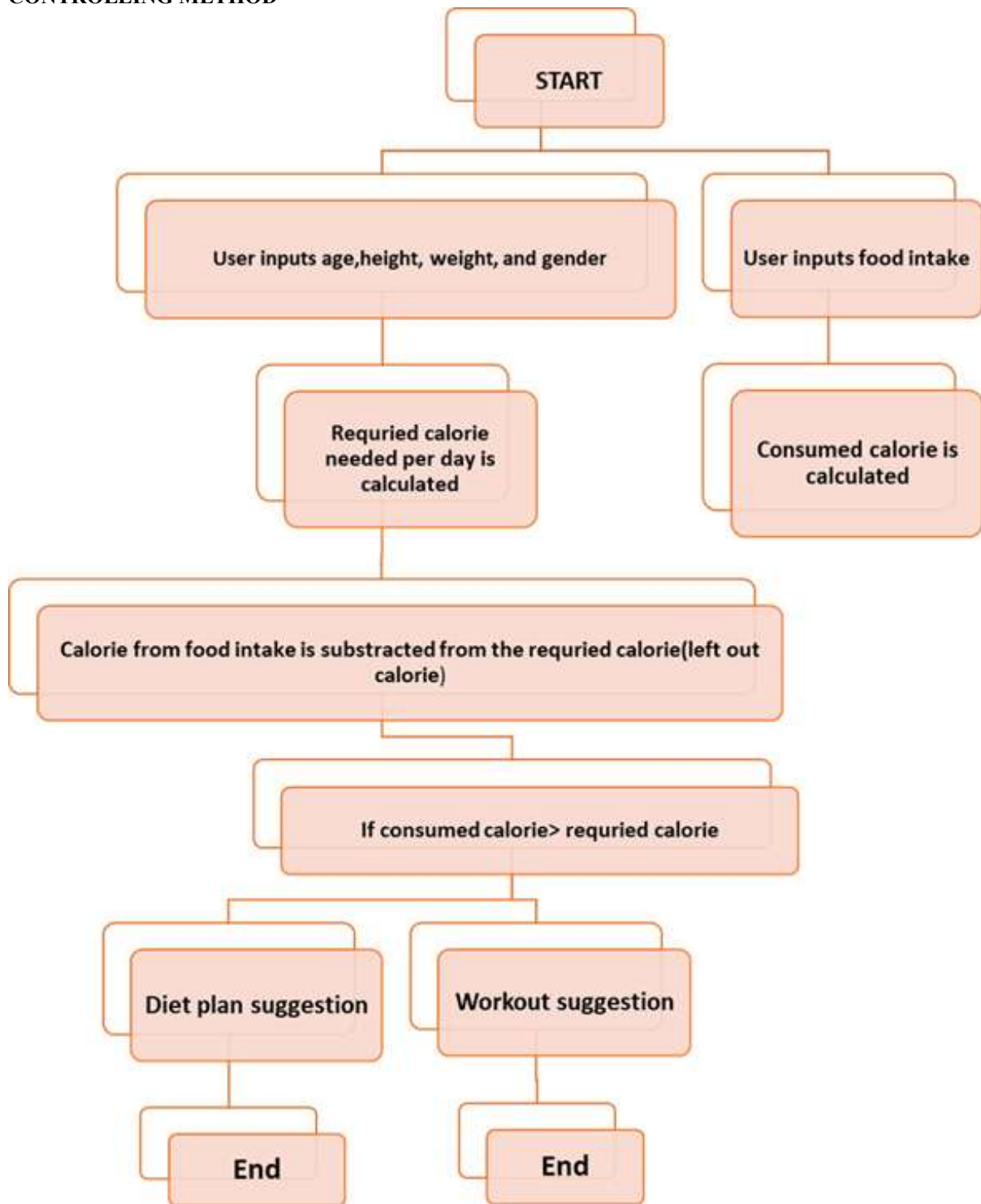


Fig.4. Controlling Method of Obesity

Probiotic and obesity correlation

Factors that contribute to obesity is a common public health issue with a complicated etiologic. According to several studies, obesity is brought on by energy intake that is greater than energy utilization and is influenced by both acquired environmental factors and congenital genetic factors [55]. Many conditions, such as fat buildup, insulin resistance, persistent inflammation, and an imbalance in the gut flora, are brought on by this imbalance [56]. Obesity is also characterized by these symptoms.

Accumulation of lipids

Energy is transformed into fat and stored in adipose tissues because the body cannot use all of its energy at once. This causes the body to gain weight, particularly in the white adipose tissue of the abdomen [57]. Triglycerides are the primary constituents of white adipose tissue. Disorders of lipid metabolism can arise from lipid accumulation or excessive body transformation, which can alter blood lipid levels, raise triglyceride and low-density lipoprotein levels, and lower the amount of high-density lipoprotein [58]. Chronic inflammation, insulin resistance, and other symptoms are brought on by lipid accumulation

Resistance to insulin

Insulin resistance, a condition in which different bodily tissues are not sensitive to insulin, frequently coexists with obesity. Long-term exposure of liver cells, adipose tissues, and other tissues to high-energy compounds in obese individuals decreases insulin's ability to absorb and use glucose, raising blood glucose levels while the body secretes too much insulin to maintain blood glucose levels, leading to insulin resistance. Obesity can occur in people with type 2 diabetes as a result of aberrant glucose metabolism brought on by excessive energy intake and insulin resistance brought on by excessive carbohydrate synthesis. According to studies, adipocyte-secreted adipokines (leptin, adiponectin, and resistin) play significant roles in the development of insulin resistance, and the primary cause of insulin resistance is obesity brought on by lipid accumulation [59].

Chronic inflammation

Chronic inflammation is a long-lasting, low-level inflammatory response that has negative effects on the body. According to studies, obesity involves long-term inflammation of adipose tissues, whereas chronic inflammation is linked to the release of endotoxins and adipocytokines, which triggers an immunological reaction. In addition to being endocrine organs that can release hormones and cytokines such as leptin, adiponectin, resistin, and inflammatory agents, adipose cells also store energy. Many adipocytokines and inflammatory factors are generated when there is an excess of adipose tissue, which triggers an inflammatory response and opens an inflammatory signalling pathway in tissues. Obese patients' adipose tissues overexpress pro-inflammatory factors, significantly raising their risk of diabetes, heart disease, and cancer [60].

Unbalanced intestinal flora

About 150 times as many genes as human genes are carried by the 100 trillion distinct microbes that make up the human intestine, which is more than ten times the number of human cells. A complex micro-ecosystem, the intestinal flora is made up of six to ten different types of bacteria, with Firmicutes and Bacteroidetes making up the majority (around 90%) of the total. An increase in Firmicutes' abundance leads to obesity, increases the body's energy intake, and facilitates the intestine absorption of nutrients. Obesity thus arises when the ratios of Bacteroidetes and Firmicutes are changed. Metabolites of gut flora are also essential for host health. The most prevalent substances in these metabolites are short chain fatty acids (SCFAs), which control energy metabolism. Examples of these include propionic acid and butyric acid. Butyric acid can decrease intestinal permeability, improve the function of the intestinal epithelial cell barrier, and stop endotoxins such lipopolysaccharides from getting into the bloodstream. Additionally, butyric acid can increase energy consumption and encourage the conversion of white adipose tissue to brown adipose tissue [60]. Propionic acid, on the other hand, can bind to intestinal L cells' free fatty acid receptors to decrease energy intake and encourage the release of intestinal anorexic hormones such glucagon-like peptide-1 and peptide YY. Bacteria that produce SCFAs, including butyric acid and propionic acid, are decreased and the risk of obesity is raised when the intestinal flora is out of balance [60].

The composition and function of the gut microbiota

An intricate organ system that is vital to the host's health is the intestinal gut microbiota. In order to ascertain which bacteria, live in the gut and how they operate, the gut microbiome—which includes the genes of microbial cells—has been closely examined in recent years using genetic and molecular identification techniques, such as 16S ribosomal RNA gene sequencing. The proximal small intestine has roughly 101–103 cfu/mL of bacteria, the distal small intestine contains 104–107 cfu/mL, and the colon contains 104–1011 cfu/mL of bacteria. Three major phyla make up the gut microbiome: Firmicutes (Ruminococcin, Clostridium, Lactobacillus, and Eubacteria), Bacteroidetes (Porphyromonas, Prevotella, and Bacteroides), and Antibacterial (Bifidobacteria) [61]. Bifidobacterium and Bacteroides make up the majority of the intestinal flora. These microbes perform crucial metabolic, structural, and defensive roles. The gut microbiome's commensal bacteria, for instance, defend the host by dislodging infections, battling them for nutrition, and generating antimicrobial substances. These bacteria also give the host structural roles, including immune system development, immunoglobulin A (IgA) induction, and mucosal barrier reinforcement. Additionally, by producing vitamin K, folate, and biotin, among other things, and helping the host absorb iron, calcium, and magnesium ions, the commensal bacteria perform metabolic tasks that are advantageous to the host. Short-chain fatty acids (SCFAs) are produced as a result of the fermentation of indigestible food items and the metabolism of dietary components by these bacteria [61].

Insulin Resistance and Obesity

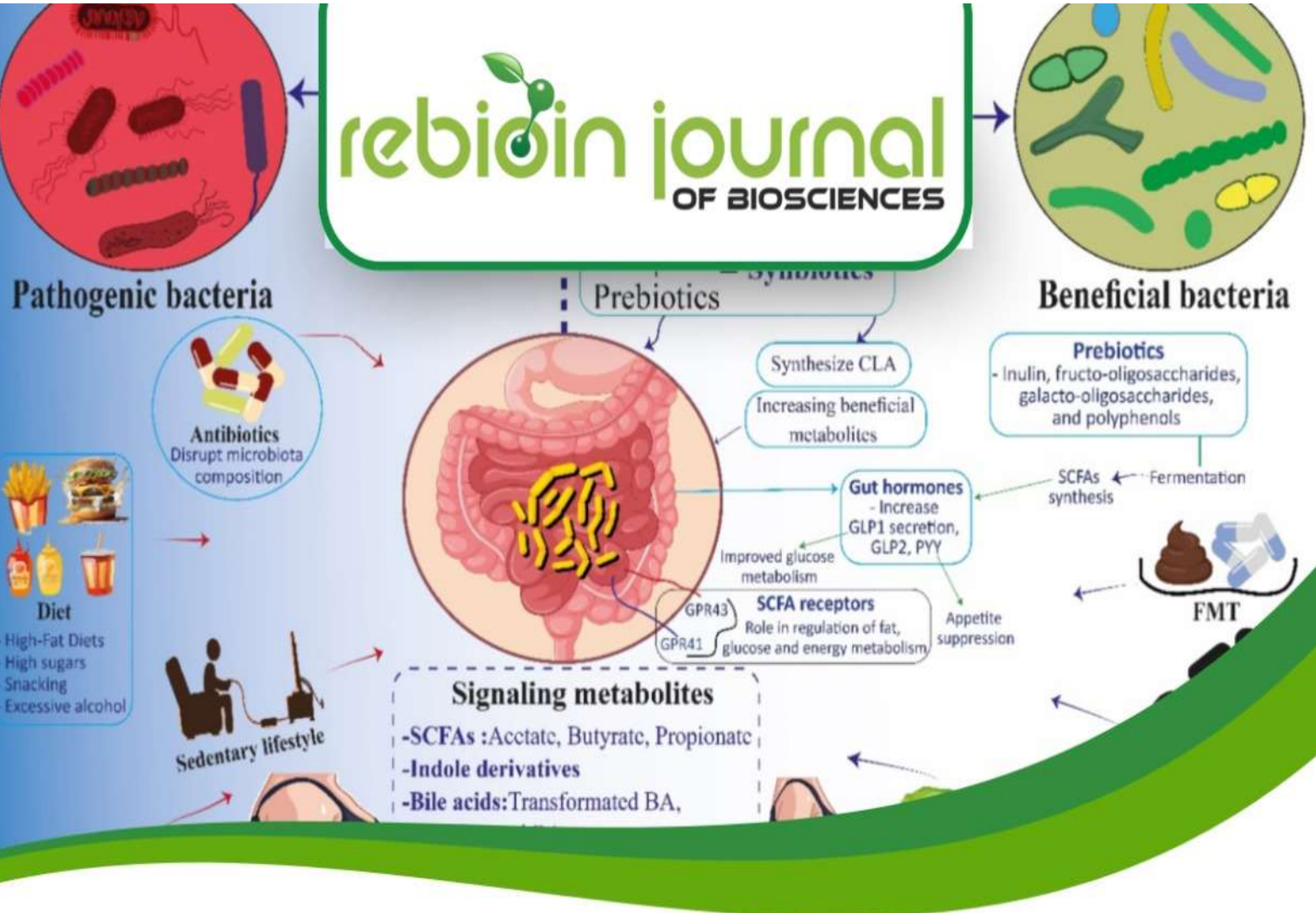
The early pioneering investigations that shown that adult mice lacking gut microbiota (i.e., germ free) developed a 60% rise in body fat content after being recolonized with a healthy cercal microbiota have established a connection between gut microbiota and obesity. The capacity of bacteria to extract energy from meal components and control the host's energy balance was formerly assumed to be the mechanism causing such a rise in body fat. SCFAs including propionate, acetate, and butyrate are produced when Bacteroides and Firmicutes break down dietary polysaccharides and fibre in the stomach. Through the liver's de novo synthesis of lipids and glucose, propionate serves as a vital source of energy for the host [61]. While butyrate serves as a significant source of energy for the colon's lining epithelial cells, acetate is utilized in peripheral tissues as a substrate for the synthesis of cholesterol. Additionally, through gut peptide signalling, blood hormone effects, or direct neural system modulation, microbiota plays a role in the regulation of energy balance, food intake, and satiety. As demonstrated by germ-free mice's higher amounts of pro-obesity peptides such neuropeptide-Y and lower levels of anti-obesity peptides, the proper balance of these regulatory peptides may be upset if the microbiota makeup is changed [61]

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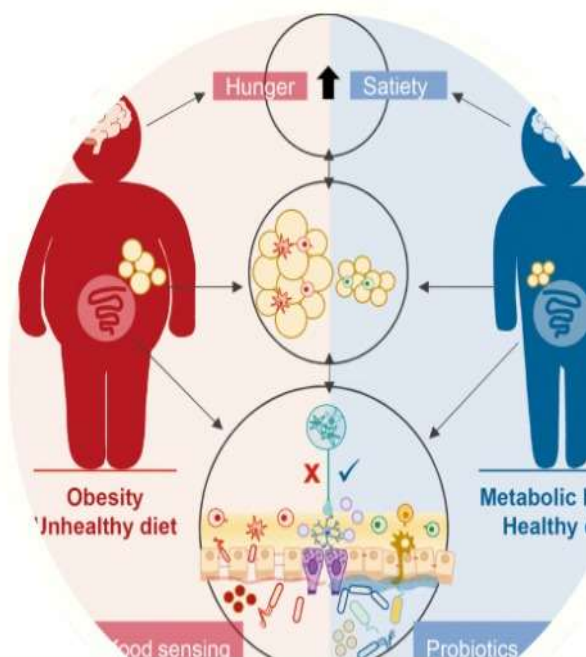
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