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Exploring the effectiveness of lactobacillus probiotics in weight management: A literature review

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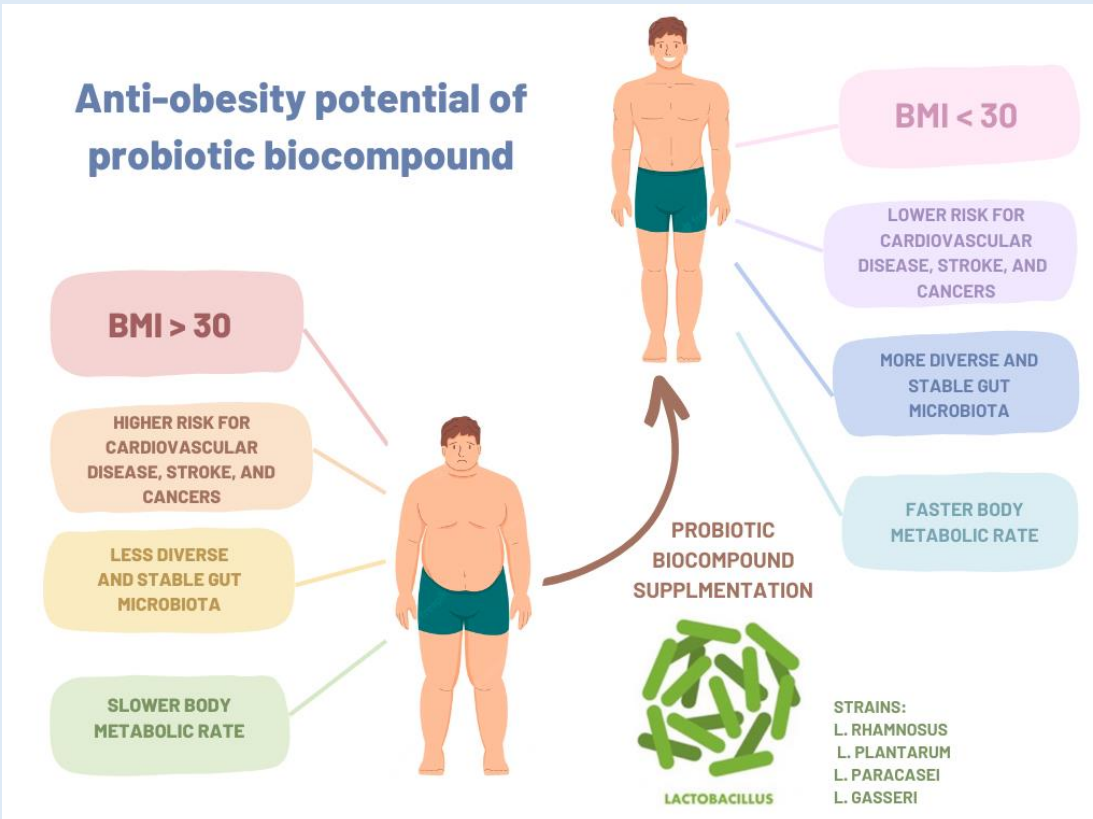
ABSTRACT

The objective of this literature review was to evaluate the effectiveness of the exploring the effectiveness of lactobacillus probiotics in weight management: a literature review in weight management. Obesity is defined as the accumulation of excessive fat, which may result in many potential health risks. A body mass index over 30 is considered obese, and obesity rates have increased by over 400% since 1975. Obesity is one of the leading underlying causes of health issues in developed nations, causing problems such as cardiovascular disease, stroke, and certain cancers. Additionally, obesity is also known to be heavily associated with type ii diabetes, high blood pressure (hypertension), and musculoskeletal disorders. To combat the issues connected with obesity, diet, and exercise are essential. In this article, we recommend the use of probiotics' biocompound from the genus *lactobacillus* in addition to diet and exercise as an intervention for obese individuals. Probiotics may facilitate weight loss by increasing microbiome quantity and variety, regulating immune responses, and improving metabolic rates. An online search was conducted in the following databases: pubmed® and the functional food center's journal database. Studies published between January 1, 2010, and april 1, 2023, were included. More rcts are needed to increase the certainty of the evidence and to verify our conclusions, especially in those who have conditions that are comorbid with obesity, such as type 2 diabetes.

Another major objective of this research will be reviewing accumulated data from the perspective of functional food definition and steps on how to create ideal functional food products. Functional foods, products that contain bioactive compounds, such as vitamins, minerals, antioxidants, and other beneficial substances, are crucial in promoting health and preventing diseases. Functional food science involves isolating and combining bioactive compounds to create functional ingredients that provide targeted health benefits. The development of functional food incorporates a multidisciplinary approach to food science, nutrition, biotechnology, and other related fields. Hence, by accumulating data on functional food science and by using quantum end tempus theories about bioactive compounds, researchers can provide valuable insights for creating ideal and innovative functional food products that meet consumer demands for healthier food options.

Keywords: Obesity, probiotics, *Lactobacillus,* quantum theory of functional foods, type 2 diabetes



INTRODUCTION

Obesity is a growing health concern worldwide, affecting millions of people and contributing to numerous health complications. With 1 billion people now considered obese [1], obesity has become a serious concern that causes severe health issues such as cardiovascular disease, stroke, and certain cancers [2-3]. Furthermore, obesity is comorbid with type 2 diabetes mellitus [4], which may cause blindness, kidney failure, and amputations [5, 6, 7, 8]. Obesity and its health consequences have become so ubiquitous and serious that it is now considered a global pandemic [9].

Obesity, according to the definition of World Health Organization, is a condition where an individual possesses an accumulation of body fat that has negative effects on the individual's health [10]. Obesity can be diagnosed by calculating an individual's body mass index

(BMI), which can be found by dividing the weight (kg) of the individual by the height (m) squared.

$$BMI = \frac{weight\ (kg)}{height\ (m)^2}$$

A BMI of 30 or higher is a sign of obesity. However, BMI alone may not be an accurate indication of body fat contribution or overall health condition, so other measures such as waist circumference, body fat percentage, and metabolic health markers can be considered as well.

Since obesity is a multifactorial issue, many different approaches must be considered when creating an effective solution. While diet and exercise are essential methods of combatting obesity, recent studies have revealed that incorporating probiotic supplementation could be a potential approach. The human gut microbiota is composed of trillions of microorganisms, which play an important role in regulating the digestive system. The microbiota affects the likelihood of developing obesity. Probiotic supplements contain living microorganisms that can provide health benefits when consumed in an adequate amount, and these microorganisms also regulate the gut microbiota and potentially aid in weight management.

One potential mechanism of how probiotics may impact obesity is through their ability to alter the composition of the gut microbiota. Research has revealed that obese individuals exhibit a less diverse gut microbiota than lean individuals, and obese individuals have a lower abundance of beneficial bacteria such as Bifidobacterium and Lactobacillus. Probiotic supplements containing these beneficial bacterial strains have been shown to improve gut microbiota composition, leading to improvements in metabolic health markers such as glucose and lipid metabolism [27].

Another mechanism by which probiotics impact obesity is their ability to regulate inflammation and the immune response. Obesity is often co-morbid with a chronic low-grade inflammatory state, and probiotics have shown promising results in effectively reducing inflammation and improving immune health in animal and human studies [11].

Recently, there has been a rise of interest in studying the potential benefits of probiotics in improving metabolic health and weight management. Many studies further reveal the significance of gut microbiota diversity on obesity intervention. While many studies suggested that probiotic supplementation possesses a positive impact on reducing obesity, the results are still limited and inconclusive. Hence, this literature review paper aims to provide an overview of the current studies of probiotic supplementation as well as an overarching analysis of the implication of probiotics supplementation for future research and clinical practices.

METHODOLOGY

A literature review of published studies concerning the effects of probiotics on human weight management was conducted electronically utilizing PubMed® and the Functional Food Center's journal database. Studies published between January 1, 2010, and April 1, 2023, were included. Both review and research papers were included. Eligible articles provided reasonable, scientific evidence on the effects of bioactive compounds on the weight management of humans, and animal studies were also included. Articles unavailable in English were excluded. Keywords for the search included: probiotics, Lactobacillus, L. Paracasei, L. Gasseri, L. Rhamnosus, L. Plantarum, obesity, overweight, weight management, diabetes, diabetes mellitus, and type 2 diabetes.

THE EFFECTS OF BIOACTIVE COMPOUNDS ON WEIGHT MANAGEMENT IN HUMANS

Probiotic supplementation of Lactobacillus: The human digestive system is a complex ecosystem that consists of a vast array of microorganisms, collectively known as the gut microbiota, which are necessary for humans' well-being [12]. Among the many varieties of microorganisms, Lactobacillus is a genus of bacteria that has been studied extensively for its implication on providing specific health benefits. Probiotics contain beneficial microorganisms which naturally occur in the human digestive tract [13]. The genus *Lactobacillus* contains 261 species of bacteria [14]. *Lactobacilli* occur in foods such as choratan, yogurt, Kefir, injera, sauerkraut, and kimchi [15, 16, 17, 18, 19]. Probiotics may also be taken as a supplement. Probiotic quality may vary according to multiple factors, such as additives and spices mixed into the product [17]. Probiotic knowledge and usage appear to be higher among American Millennials, those born between 1982 and 2000, when compared to previous years [20]

Table 1. Major bacteria phyla and genera predominating in human gut microbiota [21]

Phyla	Percentage of gut microbiome composition
Firmicutes (phyla containing lactobacillus genus)	60-80%
Bacteroidetes	20-30%
Actinobacteria	<10%
Proteobacteria	<1%

The table above depicts the percentage of gut microbiome composition of each major bacteria phyla and genera. Firmicutes, a phylum that contains the Lactobacillus genus, make up 80% of the gut microbiome composition. An increase in the diversity and number of *Lactobacillus* may lead to benefits such as increased regulation of both proinflammatory and anti-inflammatory cytokines, alleviation of the severity of allergic rhinitis symptoms, mild alleviation of depressive symptoms, and the prevention of bacteria-caused diarrhea. Studies have shown that certain strains of Lactobacillus can regulate cytokine production, which results in the reduction of inflammation and immune response [22, 23, 24, 25].

There is also growing evidence that *Lactobacillus* may play a role in weight management. Perna et al. conducted a systematic review and meta-analysis of 20 randomized control trials with a total of 1411 subjects published between 2009 and 2019 [27]. The purpose of their review was to evaluate the effectiveness of probiotics on body weight loss in subjects who are overweight or obese, especially those with related metabolic diseases. The anthropometric parameters used in this study were weight, BMI, WC, and hip circumference (HC). The probiotics in the study were all from the genus *Lactobacillus*, although the species varied between studies. The meta-analysis showed no significant decrease in body weight. However, the meta-analyzed mean differences for random effects revealed decreased WC and HC. Likewise, BMI also showed a significant decrease. Perna et al. concluded that certain strains of *Lactobacillus* (L. Paracasei, L. Gasseri, L. Rhamnosus, L. Plantarum) showed the most promising anti-obesity effects [26].

Abenavoli et al. conducted a systematic literature review for a relationship between gut microbiota and obesity [28]. They concluded that probiotics may regulate obesity through species-specific mechanisms such as increasing satiety and increasing insulin sensitivity. In addition, probiotics may regulate weight through their antimicrobial activity, increased intestinal barrier function, and immunomodulation within the digestive system. Like Perna et al., this review also found that certain strains of Lactobacillus, such as L. Paracasei, L. Gasseri, L. Rhamnosus, and L. Plantarum were associated with obesity and weight management [27].

In a 2020 randomized controlled study of 86 obese patients with type 2 diabetes, researchers randomly assigned subjects to either a control group or a probiotic supplement group for 24 weeks [29]. The probiotic supplement was taken twice a day, and the supplement contained 3 × 108 living L. Paracasei YIT 9029 (strain Shirota: LcS) organisms, 3 × 108 living Bifidobacterium breve YIT 12272 (BbrY) organisms. During the 24-week study period, the BMI levels did not significantly change between the two groups. However, other benefits did occur in the probiotic group, such as a significant positive change in HbA1c at 12 weeks [28]

Table 2. Studies published since 2020 regarding the relationship between L. Plantarum and weight loss

Study	Supplement	N	Patients	Duration	Outcome
randomized, double-blind, placebo-controlled study [29]	1 g of skimmed milk powder containing the probiotic L. plantarum Dad-13 of 2 × 109 CFU in sachet packing	60 total	Overweight yet healthy adults	90 days	Significant decrease in body weight and BMI ($P < 0.05$) in the probiotic group, especially in the female subjects.
randomized, double-blind, placebo-controlled, clinical trial [30]	2 daily allocations of 2 × 109 CFU of Lactobacillus plantarum K50 (total 4 × 109 CFU/day)	81 initials; 71 final	Overweight yet healthy adults	12 weeks	No significant differences in subjects' body weight, fat mass, or abdominal adipose tissue area. The total cholesterol level decreased in the probiotic group.
Randomized, double-blinded, placebo-controlled clinical trial [31]	1 capsule daily. containing 250 mg of L. curvatus HY7601 and L. plantarum KY1032 (5 × 109 colony-forming units (cfu) each).	72 initials; 64 final	Overweight yet healthy adults	12 weeks	The probiotic group had a statistically significant decrease in body weight ($p < 0.001$), BMI, visceral fat mass ($p < 0.025$), and WC ($p < 0.007$).
randomized, double-blind, placebo-controlled clinical trial [32]	2 capsules daily containing LMT1-48	107 initials; 100 final	Overweight yet healthy adults	12 weeks	LMT1-48 decreased body weight, abdominal visceral fat, insulin resistance, and leptin levels.

Recent randomized controlled trial studies regarding L. Plantarum often focus on obese adults to investigate its possible relationship to weight management. As shown in Table 2, these trials usually run 3 months or less, therefore decreasing the ability to observe the long-term effects of *L. Plantarum* supplementation.

Table 3. Studies published since 2014 regarding the relationship between L. Rhamnosus and weight loss

Study	Supplement	N	Patients	Duration	Outcome
randomized, double-blind, placebo-controlled study [33]	Two capsules per day of a LPR formulation (1.6 x 10^8 colony-forming units of LPR/capsule with oligofructose and inulin	125 total (48 males and 77 females)	Age 18 - 55 Overweight yet healthy adults	24 weeks	No significant difference in weight loss between LPR group and placebo group; however, mean weight loss in women in LPR group was significantly higher than women in placebo group (p = 0.02) after the first 12 weeks.
Nonrandomized, prospective, double blind, placebo-controlled study [34]	Vials with 90ml of probiotic (a strain of Lactobacillus Rhamnosus IAL 1883)	44 total	Age 8 - 17 Pubertal children and adolescent with obesity	6 months	Probiotic group did not exhibit significant benefits; and reduction in DMI SD in both groups may be due to improvement of diet.
Randomized, double blind, placebo-controlled study [35]	fish oil: 1.9 g docosahexaenoic acid and 0.22 g eicosapentaenoic acid, probiotics: Lactobacillus Rhamnosus HN001 and Bifidobacterium animalis ssp.	439 total	Pregnant women with obesity	Intervention lasted from early pregnancy to 6 months postpartum	Probiotics solely in combination with fish oil during pregnancy to women with obesity lowered the overweight odds of their 24-month-old children.
2×2 factorial design randomized, parallel-groups placebo-controlled; double-blinded for probiotic, single-blinded for cereal [36]	Capsules containing Lactobacillus Rhamnosus (HN001) (6×109 colony-forming units/day)	153 total	Community dwelling adults aged 18-80 years with pre-diabetes	6 months	No evidence of clinical benefit from the supplementation with either HN001 and/or cereal containing 4 g OBG on HbA1c
Randomized controlled trial [37]	12 × 109 CFU/day of Lactobacillus Rhamnosus supplement	40 total	Overweight and obese women with PCOS	20 weeks	Twenty weeks of probiotic supplementation has no additional beneficial effects on selected gut bacteria abundance, SCFA levels, or lipid profile
single-center 2x2 factorial randomized controlled, double blind, placebo-controlled study [38]	capsules of Lactobacillus Rhamnosus GG and Bifidobacterium lactis BB12, at a minimum dose of 6.5 × 109 colony forming units (CFU) per day.	230 total	Obese women with singleton pregnancy	36 weeks (approx.)	No significant beneficial effects of probiotics on mental health outcomes were observed

Recent randomized controlled trial studies regarding L. Rhamnosus often focus on obese adults to investigate its possible relationship to weight management. As shown in Table 3, the intervention length of these trials ranges from 24 weeks to 6 months, therefore inhibiting the ability to observe long-term effects of *L.* Rhamnosus supplementation. The trials studies regarding L. Rhamnosus, unlike those of L. Plantarum, revealed no significant effects of L. Rhamnosus probiotics on weight loss, except for the third trial with the result of probiotics solely in combination with fish oil during pregnancy for women with obesity lowered the overweight odds of their 24-month-old children.

Table 4. Studies published since 2022 regarding the relationship between L. Paracasei and weight loss

Study	Supplement	N	Patients	Duration	Outcome
randomized, placebo-controlled study [39]	L. Paracasei K56 powder	40 total	6 weeks old male C57BL/6J mice	8 weeks	Significant lower body weight, weight gain, perirenal and epididymal fat mass of the L. Paracasei K56 fed mice than those of control group.
randomized, single-blind, placebo-controlled, pilot study [40]	L. Paracasei K56 capsule (dosage ranged from 10^7 CFU to 10^{11} CFU/day) 2 capsules per day	74 total	Overweight yet healthy adult humans between the ages of 18 and 60.	60 days	Significant decreased in the mean value of percent body fat in low-K56 group and high-K56 group. Total body fat mass was significantly reduced in the low-K56 group.
randomized, placebo-controlled study [41]	L. Paracasei LC-N1115 oral supplement	40 total	4 weeks old male C57BL/6J mice	24 weeks	The mice in the treatment groups that were given different dosage of LC-N115 (NH, NM, NL) had significantly lower body weight than those in the control group.

There are also many recent randomized, placebo-controlled clinical studies regarding the relationship between L. Paracasei strain (K56 and LC-N1115) and weight management. The mentioned studies incorporated both human test subjects as well as lab mice (C57BL/6J) to conduct their clinical experiments. As shown in Table 4, the intervention ranges from 8 weeks to 24 weeks, therefore inhibiting the ability to observe the long-term effects of L. Paracasei supplementations [40-43]. Unlike the trial studies regarding L. Rhamnosus supplementation, all three of the mentioned L. Paracasei showed significant results.

For instance, in 2022, a randomized, placebo-controlled pilot study of 74 obese yet healthy adult individuals were recruited and assigned to one of the five different treatment groups that received different dosages of the L. Paracasei K56 capsule [41]. The results of the study revealed that the low dosage group (L_K56) exhibiteda significant decrease in percent body fat ($p = 0.004$), visceral fat area ($p = 0.0007$), total body fat mass ($p = 0.018$), and waist circumference ($p = 0.003$) [41].

Table 5. Studies published since (2013) regarding the relationship between L. Gasseri and weight loss

Study	Supplement	N	Patients	Duration	Outcome
randomized, double-blinded, placebo-controlled clinical trial [42]	L. Gasseri BNR17 capsule (1010 cfu) 6 capsules per day	62 total	Obese individuals aged 19 to 60	12 weeks	No significant changes in fat percentage or muscle amount. Notable decrease of waist and hip circumference in the BNR17 group compared to the placebo group.
randomized, double-blinded, placebo-controlled trial [43]	L. Gasseri BNR17 capsule (low-dose group received 109 CFU/day, and the high-dose group received 1010 CFU/day) 4 capsules per day	90 total	Obese individuals aged 20 to 75	12 weeks	Mean body weight and waist circumference were significantly different among the treatment and the control group. BMI, hip circumference, and waist-to-hip ratio were not significantly different.

CONCLUSION

The gut microbiota and its diverse microorganism play an important role in human health. The genus Lactobacillus contains 261 species of bacteria, and many studies have investigated the species-specific effects of each strain. However, further in-depth studies of individual species strains' effects on weight management are warranted. Certain strains of Lactobacillus, such as L. Rhamnosus, L. Plantarum, L. Paracasei, and L. Gasseri, have shown some promising anti-obesity effects. For instance, in the study of the effect of probiotic lactobacillus plantarum Dad-13 powder consumption on gut microbiota, a significant decrease in body weight and BMI is seen in the experimental probiotic group [30]. Moreover, the treatment of L. Rhamnosus in combination with fish oil for pregnant women lowered the overweight odds of their 24-month-old children [36]. While there is abundant evidence of the effect of supplementation of probiotics treatments, it is also important to acknowledge that not all mentioned studies have shown significant outcomes. This implies that studies with larger sample sizes and longer observation periods are necessary, and more extensive investigation of probiotics supplementation is needed to gain more knowledge. For future investigations, researchers should primarily focus on examining the impact of optimal dosage, specific probiotic bacteria strain, age, sex, diet, exercise, and medical history on the effectiveness of probiotic supplement interventions. Probiotic supplements include a broad range of bacterial strains, where each strain might exhibit a different impact on human health; hence, it's crucial to understand the corresponding health benefits of each bacterial strain and to be able to incorporate different dosages of each strain to enhance the potential benefits of the supplement. Moreover, individuals of different ages, sex, diet, and exercise routines might exhibit different responses and reactions towards probiotic supplementation; therefore, examining the interaction between dietary patterns and exercise routine on gut microbiota composition can provide insight into personalized supplementation to maximize probiotic efficacy. In addition, long-term studies require funding to observe possible benefits or side effects of prolonged supplementation.

For future implications in the functional food science field, researchers can explore various formulation methods that incorporate probiotics into day-to-day food matrices, such as dairy products, fermented food, and dietary drinks, while ensuring the vitality and functionality of the probiotic supplements. To further implement probiotic supplements into food, many other factors, such as the processing environment, storage condition, and interaction with other food compounds, need to be studied to guarantee the safe consumption of probiotic supplements in food. Investigating the potential benefits of combining probiotic supplements with another bioactive compound to maximize health benefit yield could also be a potential field for food scientists to explore in the near future.

The strains L. Rhamnosus, L. Plantarum, L. Paracasei, and L. Gasseri have robust randomized control trials supporting their effects on body weight and BMI. Even though two of the three trials studying the impact of L. Paracasei involved lab mice as the subject, all three trials showed significant results. Therefore, we propose that these 4 Lactobacillus strains should be considered as potential functional food components. Functional Foods are defined by the Functional Food Center as "natural or processed foods that contain biologically active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms" [45].

The Functional Food Center's 17-step process, shown in Table 6, explains how to develop functional food products for the consumer market [45-46]. For steps 1 and 2, the goals of the functional food products and the identification of the bioactive compounds will occur. As both L. Rhamnosus and L. Plantarum aid weight management, this is a potential goal. Step 3 establishes the appropriate dosage of the bioactive compounds [45-46]. In this review, we discovered that dosage varied from study to study [27, 28, 30-39, 45-46]. Therefore, researchers will need to refine the proper dosage for maximum benefits and minimal harm. Step 4 establishes the appropriate time of consumption [45]. In the previously cited studies, supplement administration times varied in frequency and time of day. Further studies investigating the optimal times and frequency could be helpful. As for step 5, specific pathways and mechanisms of action are to be established [45-46]. A baseline of the microbiota's interaction with the immune system has been established, but further exploration of the weight management aspects is necessary [12]. Step 6 requires that relevant biomarkers ought to be established [45]. Throughout the previous research, common biomarkers were body weight, BMI, WC, and HC [27, 28, 30-39]. While these were common measures, additional measurements may also be helpful. As for step 7, an appropriate food vehicle will be chosen for the bioactive compound. Lactobacillus naturally occurs in many foods; therefore, certain foods are already promising candidates for further supplementation [16-20]. Step 8 requires preclinical studies on efficacy and safety, and step 9 requires clinical trials for dosage, time of consumption, efficacy, and safety [45]. Step 10 is the development of a label for consumers so that they know the most effective consumption methods. This label would contain the benefits of the product and the proper dosage.

Next, step 11 requires research regarding the functional food to be published in peer-reviewed journals, preferably in open access [45]. This step ensures transparency for consumers, as well as an educational tool for the general public. As it is important for the general public to be well-informed regarding the functional food product, step 12 is educating the general public [45]. For step 13, information will be sent to the appropriate governmental agencies for approval. Additional requirements for scientific support may vary from country to country. Finally, step 14 establishes the creation of a functional food product. When the product finally reaches the market for consumption (step 15), it is considered a level C functional food. As further epidemiological studies and after-market research becomes available, the food may be re-classified as a level B or level A functional food.

Table 6. Steps to develop Functional Food Products and bring them to the market as proposed by the Functional Food Center. This table is from reference 45.

Step Number	Description of Steps to create FF Products
1	Establishes a goal of the functional food product
2	Determines relevant bioactive compound(s)
3	Establishes the appropriate dosage of bioactive compound(s)
4	Establishes the appropriate time of consumption of bioactive compound(s)
5	Determines the specific pathway and mechanism of action
6	Establishes relevant biomarker(s)
7	Chooses an appropriate food vehicle for bioactive compound(s)
8	Provides preclinical studies on efficacy and safety
9	Provides clinical trials for dosage, time of consumption, efficacy, and safety
10	Creates a special label that informs the consumers of the most effective way to consume the product
11	Publications are submitted to peer-reviewed journals, preferably in open access
12	Educates the general public
13	Sends information to credible governmental agencies, such as the FDA, for approval
14	Official establishment of the accredited functional food product
15	Release the functional food product to the market. (Receive the basic category (level C)
16	Provides epidemiological studies. (Reapply for the approval for a new category (level B)
17	Provides after market research. (Reapply for the approval for a new category (level A)

Overall, probiotics containing Lactobacillus exhibit the potential to provide certain health benefits, including weight management, and future research may reveal more detailed applications of these microorganisms. However, while these studied bioactive compounds may hold benefits, they are not a replacement for physical activity and proper nutrition.

The Novelty of this work: We explored the positive effects of lactobacillus probiotics on weight management and critically analyzed data using Quantum and Tempus theories regarding bioactive compounds within functional food science. Notably, by assessing Lactobacillus probiotic activity, we discovered how to create the ideal functional food product and determined the steps needed to be taken to market it as an "A" level functional food.

Author's Contribution: DM conceived the idea of analyzing the implication of bioactive compounds (Lactobacillus probiotics) on combating obesity and discussed it with KW and THO. THO conducted research data gathering and organized information into tables. THO and KW worked together on writing the manuscript. DM advised and participated in reviewing articles and editing the manuscript.

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Abbreviations: BMI- Body Mass Index, WC- waist circumference, HC- hip circumference, HbA1c- Hemoglobin A1c

Conflict of Interest: There are no conflicts of interest associated with this review.

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