Nutrición Hospitalaria

SENPE

Efectos de la suplementación con probióticos sobre los lípidos sanguíneos en pacientes obesos hipercolesterolémicos: un ensayo piloto aleatorizado, doble ciego y controlado con placebo

Effects of probiotic supplementation on blood lipids in hypercholesterolemic obese patients: a randomized, double-blind, placebo-controlled pilot trial

10.20960/nh.05563

03/03/2025

OR 5563

Effects of probiotic supplementation on blood lipids ın hypercholesterolemic obese patients: a randomized, double-blind, placebo-controlled pilot trial

Efectos de la suplementación con probióticos sobre los lípidos sanguíneos en pacıentes obesos hıpercolesterolémicos: un ensayo pıloto aleatorızado, doble cıego y controlado con placebo

Sibel Bulut[1], Seray Kabaran[2]

[1]Department of Sports Coaching Education. Faculty of Sports Sciences. Selçuk Üniversitesi. Konya, Turkey. [2]Department of Nutrition and Dietetics. Faculty of Health Sciences. Eastern Mediterranean University. Famagusta, T.R. North Cyprus. Turkey

Received: 15/10/2024

Accepted: 28/12/2024

Correspondence: Sibel Bulut. Department of Sports Coaching Education. Faculty of Sports Sciences. Selçuk Üniversitesi. Konya. Turkey

e-mail: dytsibelblt@gmail.com

The design and conduct of the work was performed by the all authors. The manuscript has been written, read, and approved by all the author. The material has not been previously published, in whole or in part, and it also is not under consideration for publication elsewhere. There is no potential conflict of interest for the study.

Acknowledgment: We are grateful to the participants for their willingness to participate in this study.

Funding: This research did not receive any financial support and any other funding. However, the probiotic supplements and placebo supplements were obtained from NBL Company.

Conflict of interest: The authors declare no conflict of interest.

Artificial intelligence: The authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

ABSTRACT

Objective: this trial aimed to determine the effects of probiotic supplementation on weight loss and lipid profiles in hypercholesterolemic obese patients.

Methods: ın this pilot randomized, double-blind, placebo-controlled trial, hypercholesterolemic obese patients (BMI = 30.0-35.0 kg/m^2) were randomly divided into 2 groups to receive either probiotic capsules (n = 12) or a matching placebo (n = 12) groups. The patients in the probiotic group took capsules 2 times a day that contained *Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophiles, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum* (1.5 × 10^9 CFU/g) for 8 weeks. All patients adhered to a medical nutrition therapy that aimed for a weight loss of 0.5 to 1 kg per week. Anthropometric measurements and body composition were taken at baseline and were monitored every week throughout the study. Blood lipids were assessed at baseline and after the 8-week intervention.

Results: after the 8-week dietary intervention, both probiotic and placebo groups showed significant decreased in total cholesterol (-36.50 ± 19.27 vs -25.91 ± 19.25, mg/dl), LDL-C (-(31.75 ± 18.11 vs -31.91 ± 31.00 mg/dl) and TG (-31.83 ± 67.37 vs -28.25 ± 59.09), respectively ($p < 0.05$). Body weight, BMI, body fat ratio, and waist circumference also significantly decreased after the dietary intervention in

both groups ($p < 0.05$). Overall, no significant difference was found neither in the reductions of total cholesterol, LDL-C, TG concentrations nor the anthropometric indices between the probiotic and placebo groups ($p > 0.05$).

Conclusions: the results of our study demonstrated that the administration of probiotic supplements for 8 weeks in obese subjects with hypercholesterolemia had favorable effects on lipid profiles, although there was no beneficial effect compared to the control group. These results indicate that anthropometric indices significantly decreased in response to adherence to the low-calorie diet recommended by dietitians in both the groups. However, conducting more trails with large sample size and longer follow-up time is necessary.

Keywords: Probiotics. Obesity. Hypercholesterolemic. Blood lipids.

RESUMEN

Objetivo: este ensayo tuvo como objetivo determinar los efectos de la suplementación con probióticos en la pérdida de peso y los perfiles lipídicos en pacientes obesos con hipercolesterolemia.

Métodos: en este ensayo piloto aleatorizado, doble ciego, controlado con placebo, los pacientes obesos con hipercolesterolemia (IMC = 30,0-35,0 kg/m^2) se dividieron aleatoriamente en 2 grupos para recibir cápsulas probióticas ($n = 12$) o un grupo placebo equivalente ($n = 12$). Los pacientes del grupo probiótico tomaron cápsulas 2 veces al día que contenían *Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophiles, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum* (1,5 × 10^9 UFC/g) durante 8 semanas. Todos los pacientes adhirieron a una terapia nutricional médica que tenía como objetivo una pérdida de peso de 0,5 a 1 kg por semana. Se tomaron medidas antropométricas y de composición corporal al inicio del estudio y se controlaron todas las semanas durante todo el estudio. Se evaluaron los lípidos en sangre al inicio y después de la intervención de 8 semanas.

Resultados: después de la intervención dietética de 8 semanas, tanto el grupo probiótico como el grupo placebo mostraron una disminución significativa en el colesterol total (-36,50 ± 19,27 frente a -25,91 ± 19,25 mg/dl), LDL-C (-31,75 ± 18,11 frente a -31,91 ± 31,00 mg/dl) y TG (-31,83 ± 67,37 frente a -28,25 ± 59,09), respectivamente ($p < 0,05$). El peso corporal, el IMC, el índice de grasa corporal y la circunferencia de la cintura también disminuyeron significativamente después de la intervención dietética en ambos grupos ($p < 0,05$). En general, no se encontraron diferencias significativas ni en las reducciones de colesterol total, LDL-C, concentraciones de TG ni en los índices antropométricos entre los grupos probiótico y placebo ($p > 0,05$).

Conclusiones: los resultados de nuestro estudio demostraron que la administración de suplementos probióticos durante 8 semanas en pacientes obesos Los sujetos con hipercolesterolemia tuvieron efectos favorables en los perfiles lipídicos, aunque no hubo ningún efecto beneficioso en comparación con el grupo control. Estos resultados indican que los índices antropométricos disminuyeron significativamente en respuesta a la adherencia a la dieta baja en calorías recomendada por los dietistas en ambos grupos. Sin embargo, es necesario realizar más estudios con un tamaño de muestra grande y un tiempo de seguimiento prolongado.

Palabras clave: Probióticos. Obesidad. Hipercolesterolemia. Lípidos en sangre.

INTRODUCTION

Obesity is a pathological condition characterized by excessive body mass accumulation, particularly in the abdominal region resulting from an imbalance between energy intake and expenditure. Importantly, obesity is a risk factor for many fatal diseases, especially diabetes, cardiovascular diseases, non-alcoholic fatty liver disease, and several cancer types. Obesity is associated with abnormal blood lipid levels (total cholesterol

(TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG)) which are the major risk factors for cardiovascular diseases (1).

A recent meta-analysis observed a linear association between serum cholesterol levels and cardiovascular disease (CVD) mortality. One of the effective population-based strategies of cardiovascular disease prevention is associated with decreased cholesterol levels by improving the nutritional status of the population (2). Although dietary recommendations and exercise are the primary treatment for hypercholesterolemic patients, these methods can only modestly improve high blood cholesterol levels among patients (3). Owing to the known side effects of statin-like drugs that reduce serum cholesterol levels, there is a growing interest in non-drug therapies to improve the blood cholesterol profile. Probiotics, safe for human consumption and available as functional foods and nutritional supplements, have been shown to reduce serum cholesterol levels, offering a potential non-drug therapy for improving human blood cholesterol levels (4,5).

At present, the most widely accepted scientific definition of probiotic determined by WHO (World Health Organization) and FAO (Food and Agriculture Organization of the United Nations) is "*live microorganisms that support health conditions in the host when given in appropriate amounts*" (6). Several genera are used as probiotics, including *Lactobacillus, Bifidobacterium, Bacillus, Pediococcus*, and several yeasts (7). Probiotics are available in various forms, including food and dietary supplements in capsules, tablets, liquids, and powders. Many probiotic supplements contain 1-10 billion CFU per dose, in addition both specific strains and mixtures of specific strains in effective doses are important to make the connection between clinical benefits. Besides these live, active microorganisms can be found in fermented dairy products such as kefir, yoghurt, and cheese (5).

Different types of probiotics have different functions so that human health benefits have mainly been demonstrated for specific probiotic strains (7,8). The health benefits of fermented functional foods are expressed

either directly through the interactions of ingested live microorganisms with the host (probiotic effect) or indirectly by ingesting microbial metabolites synthesized during fermentation (biogenic effect) (9,10). Among them, dairy products (particularly fermented milk and yogurt) are by far the most efficient and widely used (11,12). The content and activity of a bioactive compound in dairy-fermented foodstuffs result from the type of food matrix, the individual bacterial strain properties, the processing conditions, and storage time. In this regard, it should be noted that the high bioactive biosynthetic rates observed in culture media might not always be extrapolated to dairy products. Therefore, factors such as optimal temperature for microbial growth and viability, food composition or bioactive stability, and shelf-life in the final foodstuff are paramount to reaching the final product's maximum concentration and activity of probiotics (9).

Probiotics have been shown to modulate intestinal flora, prevent the colonization of harmful bacteria in the intestine, strengthen the immune system, reduce and prevent symptoms related to diarrhea and constipation, and have beneficial effects on cancer and inflammatory bowel diseases. Thus, consuming probiotics is useful for maintaining health against pathogenic bacteria in the gut microbiota, and maintaining the normal balance of gut microbiota helps to improve digestive health as well as the immune system. Accordingly, the main evidence-based positive effects of probiotics have been shown to include antimicrobial and antimutagenic activities, also anticarcinogenic properties. The advantages of probiotics are associated with the increase in bioavailability of macro and micronutrients, mitigation of nutritional intolerances, beneficial effects on intestinal diseases and Crohn’s disease, alleviation of allergic incidences and decrease of LDL and total cholesterol levels (7,8).

Supplementation with probiotics significantly reduced TC, LDL-C, and TGs and increased HDL-C in hypercholesteremic patients. Also, probiotic supplementation improved the anthropometric measurements (11,13). Meta-analysis of randomized clinical trials revealed that probiotic supplementation could be useful in the primary prevention of

hypercholesterolemia and may lead to reductions in risk factors for cardiovascular disease (14,15). Similarly, a systematic review study suggests that probiotic supplementation should be indicated as adjunctive treatment for dyslipidemias (11).

Probiotics have been suggested to lowering plasma cholesterol levels through various mechanisms (5,16). Possible mechanisms than can be attributed to the hypocholesterolemic effect of probiotics *in vitro* and *in vivo* studies include; assimilation of dietary cholesterol into the cell surface, binding of cholesterol to the cellular surface, inhibition of *de-novo* synthesis of cholesterol, disruption of cholesterol micelles, and deconjugation of bile salt and bile salt hydrolase (BSH) activity (17-19).

The genera most often administered to groups treated with probiotics were *Lactobacillus* and *Bifidobacterium*. Less frequently than these other genera used were *Saccharomyces, Streptococcus,* and *Enterococcus* (11). Probiotic strains, particularly *Lactobacillus*, play a significant role in lowering cholesterol levels (4). In a randomized, double-blind placebo-controlled study results showed that both single *(Lactobacillus rhamnosus)* and combined strains *(Lactobacillus acidophilus* and *Bifidobacterium animalis)* of probiotics, which are used regularly for 8 weeks, could be effective in hypercholesterolemic patients to reducing serum lipids (20). No significant differences were observed for any probiotics for serum lipids in a 18-week, randomised, double-blind crossover study with healthy obese adults (21). Available evidence indicates that probiotics supplements can significantly reduce serum TC. Furthermore, higher baseline TC, longer intervention time, and probiotics in capsules form might contribute to a better curative effect. The present study was conducted to evaluate the effects of combined strains probiotic supplementation on weight loss and lipid profiles in obese hypercholesterolemic patients. This randomized, double-blind, placebo-controlled pilot trial were designed to evaluate the effects of probiotics on the lipid profile with *Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophiles, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum* strains.

MATERIAL AND METHODS

Study design

This 2-arm parallel randomized, double-blind, placebo-controlled trial was conducted in Nutrition and Diet Polyclinic in Özel Konya Hospital lasting 12 weeks, individuals with a total cholesterol level of > 240 mg/dl and a BMI value of 30.0-35.0 kg/m^2 who applied to the diet polyclinic for weight loss were included.

This study protocol was approved by the Ethics Committee of Eastern Mediterranean University (approval date: 21.06.2016, approval no: 2016/28-14). The present study was performed according to the principals of the Declaration of Helsinki. Written consent was obtained from each participant prior to the study. All the patients were considered for possible enrollment into the study, and they were screened by an expert cardiologist for eligibility.

Study population

The inclusion criteria for this study were: a) being hypercholesterolemic obese patient with total cholesterol > 240 mg/dl, and having a body mass index (BMI) 30.0-35.0 kg/m^2; b) men and women aged between 25 and 55 years; c) having no infections and no any other metabolic diseases (diabetes, hypertension, coronary heart disease, renal or liver failure, thyroid disease, severe gastrointestinal disease); d) not using of any regular medications; and e) not using omega-3, antioxidants, multivitamin, or polyphenols supplements for the last 3 months prior to the study. Individuals were excluded if they: a) taking statin-type drugs, bile acid sequestrants, cholesterol absorption inhibitors, or nicotinic acid and drug combination therapy due to hyperlipidemia; b) using alcohol or smoking cigarette; c) taking weight loss drugs or applying recent weight reduction program; and d) being pregnancy, and lactation.

Randomization

Each participant was randomly assigned into intervention or placebo group, according to 1:1 equal proportion rule. Randomization assignment was performed using computer-generated random numbers. The randomized allocation sequence, enrolling and allocating participants to interventions were conducted by an independent investigator not involved in the assessment of the participants or in the data collection and analysis. All participants were blinded to treatment allocation (Fig. 1).

Dietary intervention

In this randomized, double-blind, placebo-controlled trial, hypercholesterolemic obese patients were randomly divided into 2 groups to receive either probiotic capsules ($n = 13$) or a matching placebo ($n = 15$) groups. The patients in the probiotic group took capsules 2 times a day (morning and evening after meals) (8) that contained *Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophiles, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum* (1.5×10^9 cfu/g) for 8 weeks. Participants in the placebo group received a capsule that contained starch but no bacteria. The appearance of the placebo was indistinguishable in colour, shape, size and packaging, smell and taste from the probiotic capsule. All capsules were produced by NOBEL Company (Turkey), that was approved by Food and Drug Administration. The products were delivered to the dietitian by the company and were given to individuals by the dietitian according to their 2-week usage amounts.

All patients adhered to a medical nutrition therapy that aimed for a weight loss of 0.5 to 1 kg per week, checked weekly during the visits, by a dietitian. The subjects included in the probiotic and control groups adhered to a medical nutrition therapy (MNT) for 8 weeks. Each individual in the research group consisting of obese individuals was given a low-fat, low-cholesterol weight loss diet by a dietitian from the beginning of the study. All obese individuals continued a MNT including all food groups. Also, weekly 0.5-1 kg body weight loss was targeted in the applied MNT. Accordingly, the energy content of the applied diet was calculated to be

500 kcal/day less than the total energy requirements of the individuals. The content of the diet applied was consist of 50-55 % carbohydrate, 12-15 % protein, and 25-30 % fat. Macronutrients, micronutrients, the fiber content of the diet were calculated to be similar between groups, and also both groups take a low cholesterol diet. They were advised not to modify their physical activity habits.

Data collection

Dietary intake

At baseline, demographic data and general nutritional habits were obtained with a form. To control the confounding effects of dietary intake, 24-h food consumption records (1 regular day) were collected from all individuals, and data were analyzed by a dietitian to obtained macronutrients and micronutrients intake, with Nutrition Data Base Software (version 7.2, Mavi Elma Group, Turkey).

Anthropometric measurements

Anthropometric measurements of the subjects were obtained at the beginning of the study and were monitored every week throughout the study. Body weight and body composition were measured by standard protocols in a fasting status and, without shoes and heavy clothing to the nearest 0.1 kg by using Tanita BF-350 body composition analyzer. Height measurement was conducted without shoes to the nearest 0.5 cm with a stadiometer (Medicaplus) in the Frankfort plane position. BMI was calculated by dividing the weight in kilograms by the square of the height in meters.

Biochemical analysis

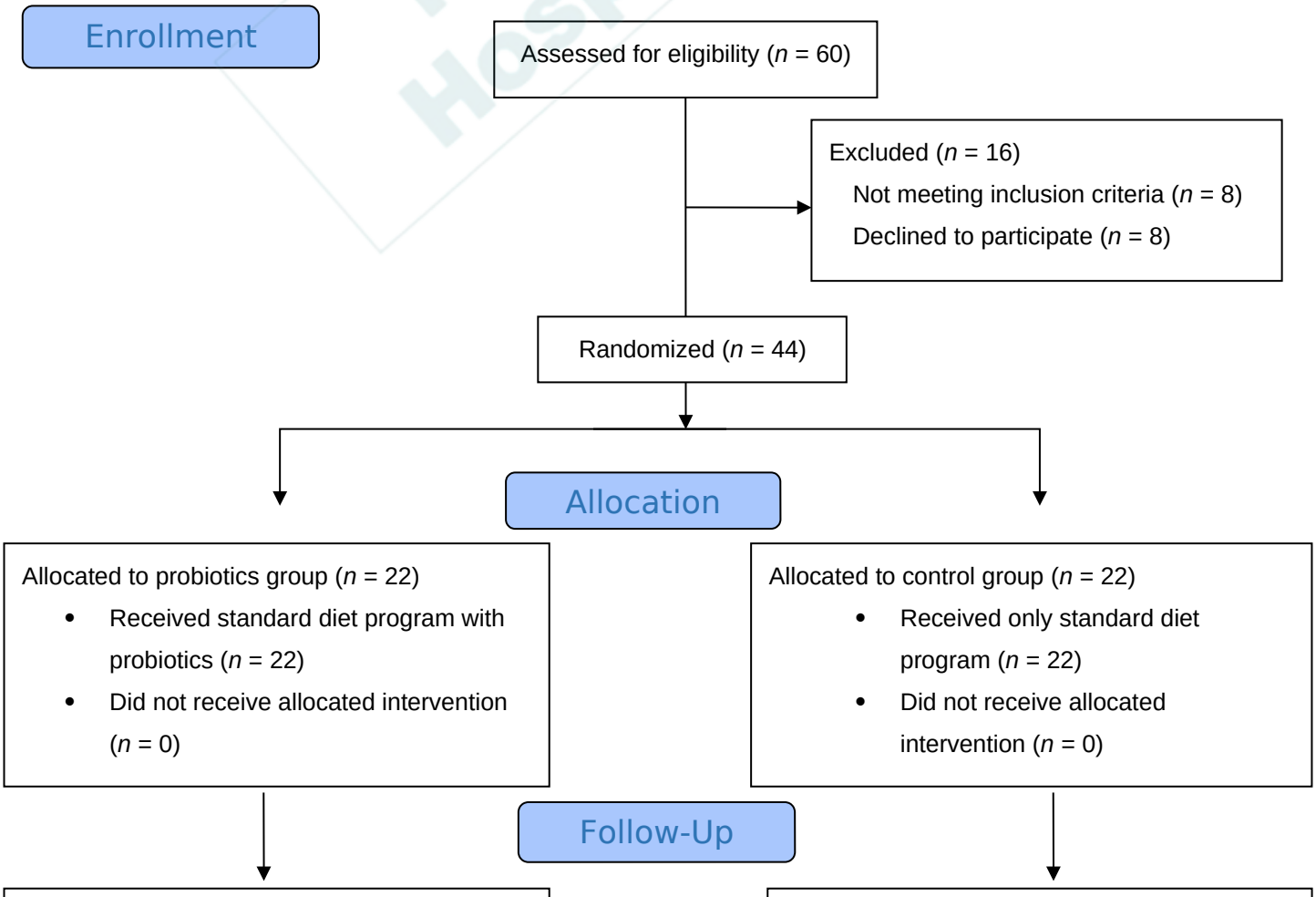
Blood samples (10 ml) were taken in 12-h overnight fasting state at the beginning and after 8 weeks of intervention. After separation of serum, blood parameters were measured. The levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL-C) and high-density lipoprotein (HDL-C) cholesterol were determined using a Dimension Xpand

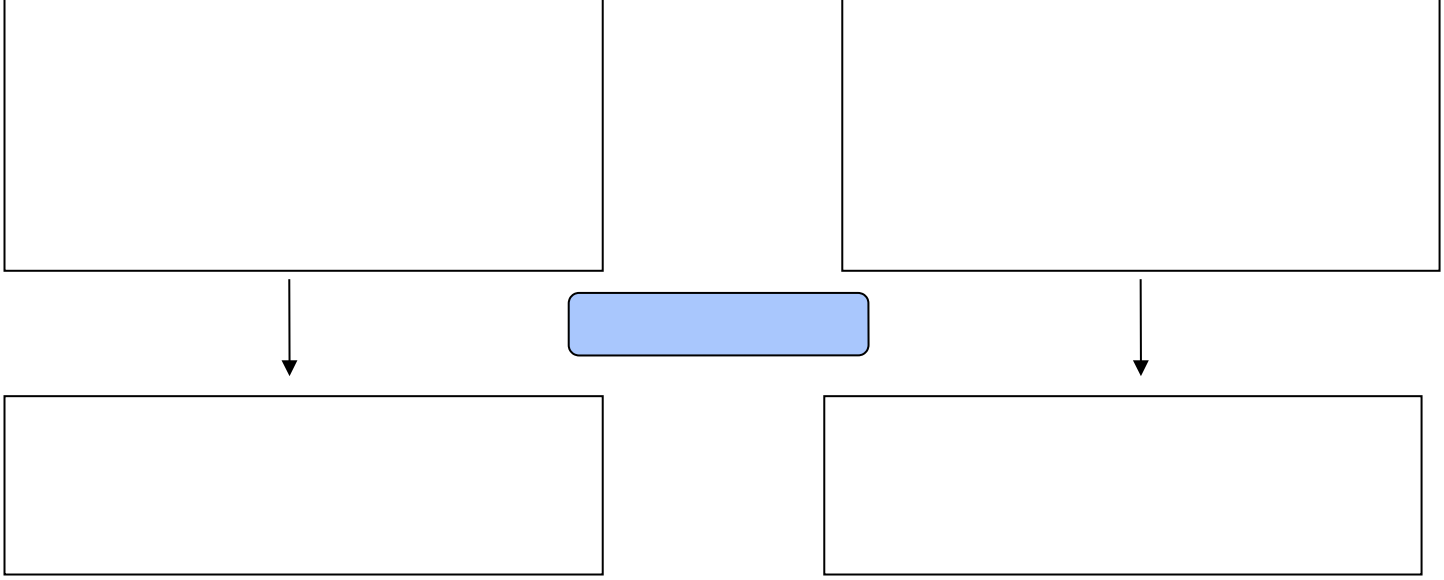
Plus integrated clinical chemistry autoanalyzer (Siemens Healthcare Diagnostics, Deerfield, IL, USA) in Özel Konya Hospital biochemistry laboratory.

Statistical analysis

Statistical analyses were performed using the software package of SPSS Statistics for Windows (version 20.0, Statistical Package for the Social Sciences). Non-parametric hypothesis tests were used in the study. Quantitative variables were compared between groups at baseline and at the end of the study using a Mann-Whitney U test. Quantitative variables before and after treatment within each group were compared using Wilcoxon test**.** All analyses were performed on participants who completed the study duration (15 in probiotics and 15 in the placebo group). All values are reported based on mean ± SD, p value < 0.05 was considered as the statistical significance level.

Figure 1. Flow diagram of the study.





RESULTS

Daily dietary intakes of the participants are presented in table I. There were no significant differences in daily total energy and intakes between the probiotics and placebo groups at the beginning of the intervention ($p > 0.05$). There was no difference in the average energy amount recommended from the dietitian between the groups during intervention ($p > 0.05$). Also, comparisons showed no significant differences in age, marital status, physical activity level and education status between the two groups at baseline ($p > 0.05$) (data not shown).

Table I. Age, daily dietary intakes and recommended energy of the participants at the beginning of the intervention

Dietary intakes, mean ± SD	**Probiotics (*n* = 12)**	***p****	
Women			

Age (year)	43,88 ± 12,75	43,77 ± 9,39	
Energy (kcal)	1906,88 ± 308, 10	1982,18 ± 315 ,07	
Protein (%)	15,49 ± 4,64	15,33 ± 4,74	
Fat (%)	35,50 ± 7,72	37,88 ± 6,67	
Carbohydrate (%)	49,01 ± 7,69	46,79 ± 7,14	
Cholesterol (mg)	246,04 ± 131,0 9	232,05 ± 144, 99	
Fiber (g)	27,80 ± 6,77	28,96 ± 6,29	
RE	1777.77 ± 156. 66	1733.33 ± 141 .42	
			< 0.05
Men			
Age (year)	44,66 ± 12,01	44,00 ± 10,60	
Energy (kcal)	2229,70 ± 339, 02	2191,33 ± 319 ,20	
Protein (%)	14,44 ± 6,02	14,96 ± 4,04	
Fat (%)	38,23 ± 8,21	36,75 ± 6,94	
Carbohydrate (%)	47,33 ± 7,21	48,295 ± 2,62	
Cholesterol (mg)	279.23 ± 143.1 0	262.83 ± 148. 06	
Fiber (g)	30.40 ± 7.00	29.20 ± 6.95	
RE	2113.33 ± 135. 50	2133.33 ± 157 .73	

Values are expressed as mean ± (SD). *Mann-Whitney test was used to calculate the *p* value. RE: recommended daily energy intake from dietitian during intervention.

Table II shows the effect of probiotic supplementation on lipid profiles of the participants after 8 weeks of intervention. There were no significant differences in lipid profiles between the probiotics and placebo groups at the beginning of the intervention ($p > 0.05$). After 8 weeks of probiotics or placebo supplementation, changes in total cholesterol and LDL-C were found to be significant within both groups, notedly in women. No significant change in other parameters (HDL-C, and TG) were observed within groups. Overall, a non-significant decrease in serum TC (-36.50 ± 19.27 vs -25.91 ± 19.25, mg/dl, $p = 0.193$), LDL-C concentrations (-31.75 ± 18.11 vs -31.91 ± 31.00 mg/dl, $p = 0.908$), TG (-31.83 ± 67.37 vs -28.25 ± 59.09, $p = 0.932$) were detected following the supplementation with probiotic, compared to the placebo. Thus, taking probiotics resulted in a non-significant decrease in lipid profiles in comparison with the placebo (Table II).

Table II. Effect of probiotics supplementation on lipid profile of the participants after 8 weeks of intervention

Variable	**Probiotic group (*n* = 12)**	**Placebo group (*n* = 12)**	***p* value****
TC (mg/dL)			
Men (n = 3)			
Before	266.33 ± 8.50	276.33 ± 20.79	0.513
After	210.66 ± 13.31	245.66 ± 44.09	0.275
MD, *p* value*	-55.66 ± 7.63, 0.109	-30.66 ± 28.00, 0.109	0.275
Women (n = 9)			
Before	266.22 ± 20.14	271.44 ± 27.12	0.860
After	236.11 ± 30.09	247.11 ± 25.23	0.539
MD, *p* value*	-30.11 ± 17.68,	-24.33 ± 17.39,	0.691

	0.008	*0.008*	
Total (n = 12)			
Before	266.25 ± 17.55	272.66 ± 24.86	0.665
After	229.75 ± 28.69	246.75 ± 28.58	0.184
MD, *p* value*	-36.50 ± 19.27, *0.002*	-25.91 ± 19.25, *0.002*	0.193
TG (mg/dL)			
Men (n = 3)			
Before	213.66 ± 77.39	269.66 ± 220.61	0.827
After	141.33 ± 15.50	278.00 ± 220.46	0.827
MD, *p* value*	-72.33 ± 64.50, 0.109	-91.66 ± 85.80, 0.109	0.513
Women (n = 9)			
Before	197.88 ± 93.3	165.55 ± 45.40	0.596
After	168.44 ± 61.42	158.44 ± 37.03	0.269
MD, *p* value*	-18.33 ± 66.19, 1.00	-7.11 ± 30.83, 0.779	0.965
Total (n = 12)			
Before	201.83 ± 86.49	216.58 ± 117.09	0.453
After	170.00 ± 56.69	188.33 ± 112.95	0.371
MD, *p* value*	-31.83 ± 67.37, 0.224	-28.25 ± 59.09, 0.130	0.932
LDL (mg/dL)			
Men (n = 3)			
Before	176.00 ± 4.00	174.00 ± 41.94	0.513
After	139.33 ± 8.08	144.66 ± 58.51	0.827
MD, *p* value*	-36.66 ± 10.26, 0.109	-29.33 ± 57.07, 0.593	0.513
Women (n = 9)			
Before	183.88 ± 18.38	190.66 ± 27.36	0.331
After	153.77 ± 21.91	157.88 ± 21.60	0.566

MD, *p* value*	-30.11 ± 20.31, *0.008*	-32.77 ± 22.45, *0.008*	0.791
Total (n = 12)			
Before	181.91 ± 16.17	186.50 ± 30.35	0.272
After	150.16 ± 20.09	154.58 ± 31.58	0.435
MD, *p* value*	-31.75 ± 18.11, *0.002*	-31.91 ± 31.00, *0.008*	0.908
HDL			
Men (n = 3)			
Before	45.00 ± 8.54	38.00 ± 18.68	0.513
After	51.66 ± 4.50	38.66 ± 15.50	0.127
MD, *p* value*	6.66 ± 4.16, 0.109	0.66 ± 9.01, 0.655	0.376
Women (n = 9)			
Before	51.88 ± 17.50	55.44 ± 11.19	0.424
After	49.94 ± 12.00	53.65 ± 14.36	0.965
MD, *p* value*	-1.94 ± 8.33, 0.677	-1.78 ± 9.81, 0.635	0.825
Total (n = 12)			
Before	50.16 ± 15.67	50.15 ± 15.67	0.506
After	50.37 ± 10.44	49.90 ± 15.48	0.686
MD, *p* value*	0.20 ± 8.29, 0.271	-1.17 ± 9.28, 0.689	0.590

MD: mean difference; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglyceride; TC: total cholesterol. Values are expressed as mean ± (SD). *Wilcoxon test. **Mann-Whitney test.

As shown in table III, BMI, weight, FM, and FM % decreased significantly by the end of study in both probiotics and placebo groups, although no statistically significant difference was observed between the groups at baseline and after intervention ($p > 0.05$). Within-group analyses indicated that anthropometric indices significantly decreased in response to adherence to low-calorie diet recommended by dietitian in both groups.

Table III. Effect of probiotic supplementation on anthropometric indices after 8 weeks of intervention

Variable	**Probiotic Group (*n* = 12)**	**Placebo Group (*n* = 12)**	***p* value****
	BMI (kg/m^2)		
Man (n = 3)			
Before	31.33 ± 1.71	30.40 ± 0.36	0.376
After	30.43 ± 1.32	28.83 ± 1.04	0.127
MD, *p* value*	-0.09 ± 0.65, 0.109	-1.56 ± 1.36, 0.180	0.513
Women (n = 9)			
Before	32.70 ± 2.36	32.50 ± 2.97	0.479
After	31.57 ± 3.21	31.32 ± 3.52	0.627
MD, *p* value*	-1.12 ± 1.28, *0.008*	-1.17 ± 1.13, *0.011*	0.625
Total (n = 12)			
Before	32.35 ± 2.16	31.97 ± 2.71	0.347

After	31.29 ± 2.84	30.70 ± 3.23	0.319
MD, *p* value*	-1.06 ± 1.13, *0.002*	-1.27 ± 1.14, *0.004*	0.630
BW (kg)			
Man (n = 3)			
Before	93.43 ± 11.47	95.66 ± 5.25	0.827
After	90.66 ± 11.15	90.20 ± 2.02	0.513
MD, *p* value*	-2.76 ± 2.00, 0.109	-5.46 ± 3.91, 0.109	0.275
Women (n = 9)			
Before	79.16 ± 5.00	86.73 ± 15.08	0.354
After	76.41 ± 7.00	83.06 ± 15.85	0.596
MD, *p* value*	-2.75 ± 2.88, *0.008*	-3.66 ± 2.56, *0.008*	0.340
Total (n = 12)			
Before	82.73 ± 9.15	88.96 ± 13.66	0.242
After	80.05 ± 9.98	84.85 ± 13.92	0.478
MD, *p* value*	-2.75 ± 2.60, *0.002*	-4.11 ± 2.87, *0.002*	0.266
FM (%)			
Man (n = 3)			
Before	31.13 ± 2.83	27.46 ± 0.55	0.052
After	28.56 ± 2.50	26.16 ± 2.15	0.275
MD, *p* value*	-2.56 ± 1.53, 0.109	-1.30 ± 2.17, 0.285	0.513
Women (n = 9)			
Before	40.01 ± 2.65	42.04 ± 5.44	0.331
After	38.22 ± 3.85	40.38 ± 4.75	0.566
MD, *p* value*	-1.78 ± 1.70, *0.008*	-1.65 ± 2.33, 0.068	0.691
Total (n = 12)			
Before	37.79 ± 4.76	38.40 ± 8.06	0.832
After	35.80 ± 5.56	36.83 ± 7.65	0.630
MD, *p* value*	-1.98 ± 1.63,	-1.56 ± 2.20,	0.443

	0.002	*0.029*	
FM (kg)			
Man (n = 3)			
Before	28.83 ± 1.61	26.20 ± 2.13	0.127
After	25.80 ± 1.65	23.60 ± 2.22	0.127
MD, *p* value*	-3.03 ± 2.30, 0.109	-5.46 ± 3.91, 0.285	0.827
Women (n = 9)			
Before	31.56 ± 3.25	36.91 ± 10.88	0.566
After	29.85 ± 5.21	34.18 ± 10.58	0.691
MD, *p* value*	-1.71 ± 2.32, *0.021*	-3.66 ± 2.56, *0.011*	0.170
Total (n = 12)			
Before	30.88 ± 3.11	34.23 ± 10.51	0.977
After	28.84 ± 4.85	31.54 ± 10.26	1.000
MD, *p* value*	-2.04 ± 2.29, *0.006*	-2.69 ± 2.34, *0.005*	0.347
FFM (kg)			
Man (n = 3)			
Before	65.50 ± 11.59	69.13 ± 3.69	0.827
After	65.10 ± 10.07	66.80 ± 1.85	0.513
MD, *p* value*	-0.40 ± 2.35, 1.00	-2.33 ± 2.01, 0.109	0.275
Women (n = 9)			
Before	47.41 ± 3.10	49.48 ± 4.88	0.200
After	46.97 ± 3.35	48.87 ± 5.50	0.965
MD, *p* value*	-0.43 ± 1.93, 0.407	-0.61 ± 2.70, 0.110	0.566
Total (n = 12)			
Before	51.93 ± 9.91	54.40 ± 9.94	0.378
After	51.50 ± 9.68	53.35 ± 9.40	0.954
MD, *p* value*	-0.42 ± 1.93, 0.455	-1.04 ± 2.58, *0.034*	0.266

MD: mean difference; BMI: body mass index; BW: boyd weight; FM: fat-mass; FFM: fat-free mass. Values are expressed as mean ± (SD). *Wilcoxon test. **Mann-Whitney test.

DISCUSSION

In the present study receiving 1.5 × 10^9 CFU/g combined strains probiotic capsules for 8 weeks along with individualized dietary intervention in hypercholesterolemic obese patients showed significant decreased in total cholesterol, LDL-C and TG concentrations. However, no intergroup statistical differences were determined in the reductions of total cholesterol, LDL-C, TG concentrations between the probiotic and placebo groups.

Daily dietary intakes of the participants are presented in table I. There were no significant differences in daily total energy and intakes between the probiotics and placebo groups at the beginning of the intervention ($p > 0.05$). There was no difference in the average energy amount recommended from the dietitian between the groups during intervention ($p > 0.05$). In this study, when the anthropometric values of male individuals in the probiotics and control groups were examined before and after the study, no significant statistical difference was found between the values at the beginning and end of the study within the groups ($p < 0.05$). However, when the pre and post-study values of the female participants in this study were examined, the values were found to be 79.16 ± 5.00 kg and 76.41 ± 7.00 kg, respectively, in the group receiving probiotics 86.73 ± 15.08 kg and 83.06 ± 15.85 kg, respectively, in the group receiving placebo. In addition, a significant decrease was observed between the pre and post-study values within the groups in some of the anthropometric measurements ($p < 0.05$) (Table III). This was attributed to the fact that there was no significant difference because the number of male individuals was lower than the number of female individuals, while

the significant decrease in body weight in women revealed the effectiveness of the low-fat, low-cholesterol weight loss diet given by the dietitian. Regularly monitoring the groups depending on the nutritional treatment by the dietitian led to weight loss in both the probiotics and control groups. The most crucial step in the treatment of obesity is medical nutrition therapy, and the treatment aims to reduce obesity, and all kinds of complications related to obesity (22). Meckling et al. examined 31 overweight and obese individuals to evaluate the effectiveness of a low-fat diet; the mean weight loss at the end of 10 weeks was 6.8 kg, and the mean decrease in BMI was 2.2 kg/m^2 (23). Hu et al. examined the effect of two different diet programs containing low carbohydrate (< 40 g/day) and low fat (< 30 % kcal/day and 7 % saturated fat) for 12 months. The mean weight loss in the low-carbohydrate diet group was 5.3 kg, whereas it was 1.5 kg in the low-fat diet group (24). In this study, weight loss in both the study and control groups due to the nutritional treatment created by the dietitian led to improved lipid levels. One of the reasons there was no significant difference in lipid levels between the group receiving probiotics and the group receiving placebo in both men and women was attributed to the improvement in lipid levels caused by the weight loss in the placebo group due to the diet recommended by the dietitian.

In this study, the mean weight loss in male participants was 2.46 kg in the probiotics group and 5.46 kg in the control group. The mean decrease in BMI was 0.90 kg/m^2 in the probiotics group and 1.56 kg/m^2 in the control group. Statistically, there was no significant difference between this weight loss and the decrease in BMI values ($p > 0.05$). Similarly, the mean weight loss in female participants was 2.75 kg in the probiotics group and 3.66 kg in the control group. The mean decrease in BMI was 1.12 kg/m^2 in the probiotics group and 1.17 kg/m^2 in the control group. Statistically, there was no significant difference between this weight loss and the decrease in BMI values ($p > 0.05$) (Table III). No statistically significant group differences were found in the anthropometric measurements taken at the beginning and end of the study, which was attributed to factors

such as the fact that the study was conducted on obese individuals, the study period was limited (8 weeks), and the small sample size.

One meta-analysis has highlighted the effects of consuming fermented foods and positive impacts on weight maintenance, while separate studies have demonstrated that consumption of fermented yogurts and dairy foods can attenuate the likelihood of developing CVD and type 2 diabetes *mellitus* (26). Milk hydrolysis generates peptides with satiety or anti-obesity effects. Consumption of fermented milk enriched with probiotics positively affects body weight reduction and serum lipids. In a study of 14 healthy individuals, it was observed that consumption of probiotic yoghurt (*Lactobacillus acidophilus* and *Bifidobacterium lacti*) caused a significant decrease in serum total cholesterol levels compared with normal yoghurt ($p < 0.05$) (12). In a study conducted by Larsen et al., 70 obese participants (20 men and 50 women) aged between 18 and 55 years were randomly assigned to five groups over an 8-week period. One group consumed the experimental yoghurt Gaio®, while the second and third groups were given two newly developed yoghurts fermented with different bacterial cultures. The yoghurt provided to one of these groups was fermented with two strains of *S. thermophilus* and two strains of *L. acidophilus*, while the yoghurt given to the other group was fermented with two strains of *S. thermophilus* and one strain of *L. rhamnosus*. The fourth group received a placebo yoghurt, and the final group was given two daily placebo tablets. When all five treatment groups were compared after adjusting for small changes in body weight, a significant reduction in LDL cholesterol levels (8.4 %, $p < 0.05$) was observed after 8 weeks in the group consuming only Gaio® product (27). However, in fermented milk or yogurt consumption, it is more difficult to achieve standardization due to factors such as optimum temperature for microbial growth and viability, food composition, or bioactive stability (9). In this trial, we considered these standardization difficulties as a limitation and preferred to use probiotic strains. Standardization of used products affects quality in research. However, it is thought that planning and conducting this study with a fermented milk product may support similar positive results in

obese individuals. We also preferred to use supplement forms to highlight the effects of probiotics on blood lipids in obese individuals. In addition to this, dietary supplements can differ in quality, purity, and consistency, leading to inconsistencies in dosing. To avoid this, all products are supplied from the same company in this research.

In this study, when the pre- and post-study values of male and female individuals in the probiotics group were compared, it was observed that total cholesterol and LDL cholesterol levels decreased significantly at the end of the study ($p < 0.05$) (Table II). In addition to this, when HDL levels and triglyceride levels of male and female individuals in the probiotics and control groups were compared before and after the study, no significant statistical difference was found ($p > 0.05$) (Table II). While no significant change was observed in HDL levels in 9 of the 11 meta-analyzed studies ($p = 0.59$), no significant change was observed in triglyceride levels in 8 ($p = 0.89$) (15). In the study conducted by Fuentes et al., no statistically significant differences were found in total cholesterol, triglycerides, LDL, and HDL cholesterol levels between individuals with cholesterol levels > 250 mg/dL who received either a placebo or *L. plantarum* at baseline and after 6 weeks. However, a significant decrease in LDL cholesterol and total cholesterol levels was observed after 12 weeks (4). In a meta-analysis of 11 randomized clinical trials that conducted to evaluate the effects of probiotics on blood lipids, a significant decrease in total cholesterol and LDL values was found ($p = 0.001$) (14). One of the reasons for these inconsistent results was that the study period was limited to 8 weeks, and another reason was that there was an insufficient number of people during randomization. Again, the same meta-analyse study demonstrated the duration of probiotic supplementation was positively associated with the LDL-C lowering effects of probiotics, also high-dose probiotics more effectively reduced LDL-C levels than low-dose probiotics (14). Based on these studies, it was thought that a significant decrease in blood lipid levels could be seen when the study period was increased above 8 weeks. Also, the effectiveness of each probiotic strain depended on the dosage.

In this study a non-significant decrease in serum TC, TG, and LDL-C concentrations were detected following the supplementation with probiotic, compared to the placebo. Thus, taking probiotics resulted in a non-significant decrease in lipid profiles in comparison with the placebo (Table II). If we discuss this information by emphasizing important studies in the literature; in a study conducted by Jones et al. on hypercholesterolemic adults by giving yoghurt containing BSH-active *Lactobacillus reuteri* NCIMB 30242, no statistically significant difference was observed when total cholesterol, LDL, HDL and triglyceride levels were compared between the two groups receiving placebo yoghurt and yoghurt containing *L. reuteri* after 3 weeks ($p > 0.05$). When the differences of the same values were compared after 6 weeks, significant decreases were observed in total cholesterol ($p = 0.031$) and LDL cholesterol ($p = 0.016$) levels, whereas no statistically significant difference was observed in HDL ($p = 0.808$) and triglyceride ($p = 0.230$) levels (28). In another study conducted by Jones et al. using a capsule containing *Lactobacillus reuteri* NCIMB 30242, when total cholesterol, LDL, HDL and triglyceride levels were compared after 9 weeks, significant decreases were observed in total cholesterol and LDL cholesterol levels ($p < 0.001$), while no statistically significant difference was observed in HDL and triglyceride levels (29). While several clinical trials have shown that probiotics have cholesterol-lowering activity (27,30), some studies have shown the opposite result (31). These negative results may be related to poor bacterial strain selection, the study method or the clinical design of the trial, and these studies did not specify BSH activity as a characteristic of the strain administered. In contrast, a BSH-active strain (*L. plantarum* and *L. reuteri)* has been shown to significantly reduce total cholesterol and LDL cholesterol when administered as a synbiotic in humans (32). Probiotics with BSH activity have often been found to have cholesterol-lowering effects *in vivo* studies (33,34). In a meta-analysis, it was determined that when yoghurt containing two strains of *S. thermophilus* and *E. faecium* was given, these strains showed a cholesterol-lowering effect (35). These results suggest that the use of

probiotics may improve lipid metabolism by decreasing total and LDL cholesterol concentrations. However, both the efficacy of probiotics for cholesterol lowering and safety should be investigated further in well-designed clinical trials. The findings of recent meta-analysis suggest that probiotics can enhance SCFA content in the body, improve oxidative stress and inflammation, and effectively alleviate hyperlipidemia. The primary lipid-lowering mechanisms of probiotics encompass: a) the production of BSH, which enhances cholesterol excretion; b) the promotion of cholesterol catabolism and the inhibition of cholesterol synthesis in the body via key intestinal metabolites, specifically SCFAs; and c) the modulation of immune regulation and the intestinal barrier through signaling molecules (36). In a recent study results demonstrated that regular and strain-specific use of probiotics (probiotics containing *Lactobacillus* or *Bifidobacterium*) could be effective to reducing plasma lipid level in hypercholesterolemic patients (20). In this study, a probiotic product supplement containing 1.5×10^9 CFU active probiotic microorganisms (*Lactobacillus acidophilus, Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophillus, Bifidohacterium lactis, Bifidobacteriurn longum*) was used. Also the other reason for inconsistent results may attributed to the different type of strains that have been used (11). Finally, the confusing and interconnected reasons for this study's results between groups may be attributed to the different types of probiotic strains used, doses of probiotics, delivery matrix, study duration, and study population. However, not all probiotic interventions are effective against dyslipidemia. The results are controversial and depend on several factors such as probiotic strain, dose, duration of the treatment, lifestyle changes, etc. Additional studies are highly recommended on the cholesterol-lowering property of probiotics, which could help to reduce the risk of CVD and other dyslipidemia-associated health issues.

CONCLUSION

In this randomized controlled clinical trial, dietary supplementation of probiotics for 8 weeks had no prominent favorable effect on serum total cholesterol, LDL-C, TG levels, and body weight loss in obese subjects with hyperlipidemia. However, further well-designed large sample size randomized controlled trials, with longer supplementation durations are needed for a stronger assessment of the lipid-modulating properties of probiotics on obese subjects. Thus, more specific data regarding the duration and dosage of probiotic use in obese individuals may reveal significant beneficial effects on health.

LIMITATIONS

Some limitations might explain the contradictory findings of the present trial. Firstly, the reduced number of patients is one of the major limitations of this study, this is probably the reason why there are no differences in most of the parameters evaluated. Secondly, the short follow-up time is another limitation of the study. Moreover, doses of probiotics and type of strains that have been used may attributed to the inadequate results. Additionally, it was emphasized that the efficacy of probiotics would be strengthened by increasing the treatment period to ≥ 8 weeks. Also, during the regulation of nutritional intake, the individual declaration is taken into consideration so that, unbalanced and higher consumption amounts may also affect the results.

REFERENCES

1. Lingvay I, Cohen RV, Rou X CW. Obesity in Adults. Lancet 2024;404(10456):972-87. DOI: 10.1016/S0140-6736(24)01210-8

2. Jung E, Kong SY, Ro YS, Ryu HH, Shin SD. Serum Cholesterol Levels and Risk of Cardiovascular Death: A Systematic Review and a Dose-Response Meta-Analysis of Prospective Cohort Studies. Int J Environ Res Public Health 2022;19(14):8272. DOI: 10.3390/ijerph19148272

3. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart

Association Task Force on Clinical Practice Guidelines. Circulation 2019;140(11):596-646. DOI: 10.1161/CIR.0000000000000678
4. Fuentes MC, Lajo T, Carrión JM, Cuñé J. Cholesterol-lowering efficacy of Lactobacillus plantarum CECT 7527,7528 and 7529 in hypercholesterolaemic adults. Br J Nutr 2013;109(10):1866-72. DOI: 10.1017/S000711451200373X
5. Maftei NM, Raileanu CR, Balta AA, Ambrose L, Boev M, Marin DB, et al. The Potential Impact of Probiotics on Human Health: An Update on Their Health-Promoting Properties. Microorganisms 2024;12(2):234. DOI: 10.3390/microorganisms12020234
6. Fao Food and Nutrition Paper 85, Word Health Organization Food and Agriculture Organization of the United Nations Rome. 2006. Health and Nutrition Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria. Argentina. Available from: http://www.fao.org/3/a-a0512e.pdf. (23.12.2023).
7. Das TK, Pradhan S, Chakrabarti S, Mondal KC, Ghosh K. Current status of probiotic and related health benefits. Applied Food Research 2022;2(2):100185. DOI: 10.1016/j.afres.2022.100185
8. Roobab U, Batool Z, Manzoor MF, Shabbir MA, Khan MR, Aadil RM. Sources, formulations, advanced delivery and health benefits of probiotics. Curr Opin Food Sci 2020;32:17-28.
9. Linares DM, Gómez C, Renes E, Fresno JM, Tornadijo ME, Ross RP, et al. Lactic Acid Bacteria and Bifidobacteria with Potential to Design Natural Biofunctional Health-Promoting Dairy Foods. Front Microbiol 2017;18(8):846. DOI: 10.3389/fmicb.2017.00846
10. Gobbetti M, Cagno R, Agnelis M. Functional microorganisms for functional food quality. Crit Rev Food Sci Nutr 2010;50(8):716-27. DOI: 10.1080/10408398.2010.499770
11. Gadelha CJMU, Bezerra AN. Effects of probiotics on the lipid profile: systematic review. J Vasc Bras 2019;9(18):e20180124. DOI: 10.1590/1677-5449.180124

12. Ataie-Jafari A, Larijani B, Alavi Majd H, Tahbaz F. Cholesterol-lowering effect of probiotic yogurt in comparison with ordinary yogurt in mildly to moderately hypercholesterolemic subjects. Ann Nutr Metab 2009;54(1):22-7. DOI: 10.1159/000203284
13.Sivamaruthi BS, Kesika P, Chaiyasut C. A Mini-Review of Human Studies on Cholesterol-Lowering Properties of Probiotics. Scientia Pharmaceutica 2019;87(4):26. DOI: 10.3390/scipharm87040026
14. Shimizu M, Hashiguchi M, Shiga T, Tamura HO, Mochizuki M. Meta-Analysis: Effects of Probiotic Supplementation on Lipid Profiles in Normal to Mildly Hypercholesterolemic Individuals. PLoS One 2015;10(10):e0139795. DOI: 10.1371/journal.pone.0139795
15. Jiang J, Wu C, Zhang C, Zhao J, Yu L, Zhang H, et al. Effects of probiotic supplementation on cardiovascular risk factors in hypercholesterolemia: A systematic review and meta-analysis of randomized clinical trial. J Funct Foods 2020;74:104177. DOI: 10.1016/j.jff.2020.104177
16. Ishimwe N, Daliri EB, Lee BH, Fang F, Du G. The perspective on cholesterol lowering mechanisms of probiotics. Mol Nutr Food Res 2015;59(1):94-105. DOI: 10.1002/mnfr.201400548
17. Degirolamo C, Rainaldi S, Bovenga F, Murzilli S, Moschetta A. Microbiota modification with probiotics induces hepatic bile acid synthesis via downregulation of the Fxr-Fgf15 axis in mice. Cell Rep 2014;7(1):12-8. DOI: 10.1016/j.celrep.2014.02.032
18. Liong MT, Shah NP. Acid and bile tolerance and cholesterol removal ability of lactobacilli strains. J Dairy Sci 2005;88 (1): 55-66. DOI: 10.3168/jds.S0022-0302(05)72662-X
19. El-Waseif AA, Gaber HS, Ewais EA. Hypocholesterolemic Operating Parameters of Novel Probiotics In vitro. Res J Pharm Technol 2021;14(10):5197-1. DOI: 10.52711/0974-360X.2021.00904
20. Okburan G, Baş M, Ogmen S. A randomized double-blind controlled clinical trial demonstrating efficacy of different probiotic strains on serum lipids and glycemic biomarker. Nutr Hosp 2024;41(4):793-803. DOI: 10.20960/nh.04724

21. Culpepper T, Rowe CC, Rusch CT, Burns AM, Federico AP, Girard SA, et al. Three probiotic strains exert different effects on plasma bile acid profiles in healthy obese adults: randomised, double-blind placebo-controlled crossover study. Beneficial Microbes 2019;10(5):497-509. DOI: 10.3920/BM2018.0151
22. Hassapidou M, Vlassopoulos A, Kalliostra M, Govers E, Mulrooney H, Ells L, et al. European Association for the Study of Obesity Position Statement on Medical Nutrition Therapy for the Management of Overweight and Obesity in Adults Developed in Collaboration with the European Federation of the Associations of Dietitians. Obes Facts 2023;16(1):11-28. DOI: 10.1159/000528083
23. Meckling A, O'Sullivan C, and Saar D. Comparison of a Low-Fat Diet to a Low-Carbohydrate Diet on Weight Loss, Body Composition, and Risk Factors for Diabetes and Cardiovascular Disease in Free-Living, Overweight Men and Women. J Clin Endocrinol Metabol 2004;89(6):2717-23. DOI: 10.1210/jc.2003-031606
24. Hu T, Yao L, Reynold K. The Effects of a Low-Carbohydrate Diet vs. A Low-Fat Diet on Novel Cardiovascular Risk Factors: A Randomize Controlled Trial. Nutrients 2015;7(9):7978-94.
25. Park S, Bae JH. Probiotics for weight loss: a systematic review and meta-analysis. Nutr Res 2015;35(7):566-75. DOI: 10.1016/j.nutres.2015.05.008
26. Mathur H, Beresford T, Cotter PD. Health Benefits of Lactic Asid Bacteria (LAB) Fermentates. Nutrients 2020;12(6):1679. DOI: 10.3390/nu12061679
27.Larsen LA, Raben A, Haulrik N, Hansen AS, Manders M and Astrop A. Effect of 8 week intake of probiotic milk products on risk factors for cardiovascular diseases. Eur J Clin Nutrit 2000;54(4):288-97.
28. Jones ML, Martoni CJ, Parent M, and Prakash S. Cholesterol-lowering efficacy of a microencapsulated bile salt hydrolase-active Lactobacillus reuteri NCIMB 30242 yoghurt formulation in hypercholesterolaemic adults. Br J Nutr 2012;107(10):1505-13. DOI: 10.1017/S0007114511004703

29. Jones ML. Martoni CJ. Prakash S. Cholesterol lowering and inhibition of sterol absorption by Lactobacillus reuteri NCIMB 30242: a randomized controlled trial. Eur J Clin Nutr 2012;66(11):1234-41. DOI: 10.1038/ejcn.2012.126
30. Schaafsma G, Meuling WJA, van Dokkum W, and Bouley C. Effects of a milk product, fermented by Lactobacillus acidophilus and with fructo-oligosaccharides added, on blood lipids in male volunteers. Eur J Clin Nutr 1998;52(6):436-40.
31. Lewis SJ, Burmeister S. A double-blind placebo-contralled study of the effects of Lactobacillus acidophilus on plasma lipids. Eur J Clin Nutr 2005;59(6):776-80. DOI: 10.1038/sj.ejcn.1602139
32. Ooi LG, Ahmad R, Yuen KH, Liong MT. Lactobacillus gasseri CHO-220 and inulin reduced plasma total cholesterol and low-density lipoprotein cholesterol via alteration of lipid transporters. J Dairy Sci 2010;93(11):5048-58. DOI: 10.3168/jds.2010-3311
33. Ha CG, Cho JK, Chai YG, Ha YA, Shin SH. Purification and characterization of bile salt hydrolase from Lactobacillus plantarum CK 102. J Microbiol Biotech 2006;16(7):1047-52.
34. Park YH, Jong GK, Young WS, Kim SH, Whang KY. Effect of dietary inclusion of Lactobacillus acidophilus ATCC 43121 on cholesterol metabolism in rats. J Microbiol Biotech 2007;17(4):655-62.
35. Agerholm-Larsen L, Bell ML, Grunwald GK, Astrup A. The effect of a probiotic milk product on plasma cholesterol: a meta-analysis of short-term intervention studies. Eur J Clin Nutr 54(11):856-60. DOI: 10.1038/sj.ejcn.1601104
36. Yao Y, Hong Q, Ding S, Cui J, Li W, Zhang J, et al. Meta-analysis of the effects of probiotics on hyperlipidemia. Curr Res Food Sci 2024;9:100885. DOI: 10.1016/j.crfs.2024.100885