Comparing the effect of ultra-filtered feta cheese and yoghurt as probiotic carriers on lipid profile: A double blinded randomized controlled trial¹

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Abstract.

BACKGROUND: There have been studies investigating the effect of probiotic yoghurt on blood lipids. However the results are conflicting. Also, there have been few studies involving probiotic cheese.

PURPOSE: The goal of this trial was to compare the consumption effect of probiotic yoghurt with probiotic cheese on blood lipids.

METHODS: 180 subjects aged 18–65, with <6 mmol/l total cholesterol were participated in a 2-month trial. Subjects were assigned into three 60-person groups; probiotic cheese group (30 g/d), probiotic yoghurt group (100 g/d) and control.

RESULTS: A significant reduction in cholesterol was observed at the end within both groups; Cheese (-0.42 mmol/L; 95% CI, -0.47, -0.37; P < 0.0001), Yoghurt (-0.15 mmol/L; 95% CI, -0.25, -0.05; P = 0.007). HDL, LDL and Triglyceride also showed significant improvements during 2-month period. Cholesterol comparison with control also revealed a significant reduction in both groups; cheese (-0.51 mmol/L; 95% CI, -0.63, -0.39; P < 0.0001), yoghurt (-0.27 mmol/L; 95% CI, -0.39, -0.15; P < 0.0001). **CONCLUSION:** Probiotic cheese showed greater improvement effects on blood lipids compared to probiotic yoghurt. This trial was registered in the Australian New Zealand Clinical Trials Registry (ANZCTR) at http://www.anzctr.org.au as ACTRN12612000623897

Keywords: Probiotic cheese, probiotic yoghurt, blood lipids, Lactobacillus acidophilus LA5, Bifidobacterium lactis BB12

Clinical trial registry code: ACTRN12612000623897

1. Introduction

Cardiovascular diseases (CVD) are among the most common causes of morbidity and premature death worldwide [1]. Based on WHO reports, it has been noted that by 2030, CVD will be the leading causes of death with an impact on more than 23 million people globally [2]. Also, WHO delineated that 82% of CVD incidences will take place in low and middle-income countries [2]. Although CVD have multiple well known risk factors, dyslipidemia is thought to be a major determinant of these anomalies [3]. A mountain of evidence support the fact that higher levels

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of total cholesterol (TC), triglyceride (TG) and low density lipoproteins (LDL) are tenaciously associated with future incidence of cardiovascular complications [1, 3, 4]. Thereupon, alleviating hyperlipidemia seems to lower CVD risks [1, 5].

Although there are available drugs (such as statins) for management of hyperlipidemia, the financial burden of medicines (especially in low and middle-income countries) seems to be a limitation for pharmaceutical adhesion. As a result, alternative methods for controlling lipid profile such as diet therapy and using therapeutic bioactive food compounds are gaining more attention among the scientific society [6].

The attribution of probiotics (the live microorganisms with beneficial effects on the host) or probiotic containing food to modulate blood lipids received attention in recent years [3, 6, 7]. Lactic acid bacteria (LAB), (such as *Lactobacillus* and *Bifidobacterium*) have been the primary probiotic bacteria for modulation of blood lipid levels, however, certain *Bacillus* and *Enterococcus* have been reported to produce such effects as well [8, 9]. Moreover, probiotic fermented dairy products have been a major player in human health for millennia and are consumed in large scale nowadays [6, 7]. Role of probiotic yoghurt and fermented milk in human health has been investigated in different animal and human studies [7, 9–17], however, the data about role of probiotic cheese in human health is scarce [6, 18–20]. Cheese as probiotic carrier is a valuable alternative to yoghurt and fermented milk due to its dense matrix, higher pH, high quality protein and high fat content [18, 21, 22]. Due to the fact that results of studies investigated the effect of probiotic yoghurt on blood lipids are conflicting and considering the fact that less is known about the effect of probiotic cheese on human blood lipids, the current study was conducted.

The goal of this study was to compare the effect of commercial ultra-filtered feta cheese and yoghurt on lipid profile, as probiotic (*Lactobacillus acidophilus* LA5 and *Bifidobacterium* lactis BB12) carriers during a two-month period.

2. Subjects and methods

2.1. Subjects

Three cohorts of male and female participants (n = 180) with total cholesterol of, <6.0 mmol/l were recruited from the population (students and staff) of Science and Research Branch of Islamic Azad University (SRBIAU), Tehran, Iran through an online advertisement published by Omega Research Team (ORT). Recruitment was carried out during April of 2012. Subjects were 18–65 y with <30 kg/m² body mass index (BMI) and had no recent history of probiotic consumption. In order to make sure of the latter, a diet history was taken from participants by a dietitian. Also, a list of all available probiotic products in the country was generated, so individuals could point out any possible consumption, inflammatory intestinal diseases, thyroid disorders, liver or immunodeficiency diseases, diabetes and hypertension. Subjects were also excluded from the study if they were professional athletes or they were taking any supplements/drugs. Lactating or pregnant females were also considered not eligible for the study. The consistency of all subjects with the inclusion and exclusion criteria was screened by a trained researcher based on medical records, face to face interviews and personal examinations.

2.2. Trail design

A double blinded, parallel, randomized controlled trial was carried out during two months. After a week of pre-adjustment when participants were asked to consume low fat milk, they were randomly assigned into three 60-person balanced groups; control group (CG), probiotic cheese group (PC) and probiotic yoghurt group (PY). A 1:1:1 allocation ratio was considered. Moreover, subjects were asked not to either change their physical activity or their regular diet. They were also told to refrain any consumption of cheese and yoghurt other than the one provided by the research team during the trial. Full verbal and written instructions/guidelines were given to the participants in personal interviews.

The commercial ultra-filtered feta probiotic cheese was enriched with *Lactobacillus acidophilus* LA5 and *Bifi-dobacterium lactis* BB12 (Chr Hansen, Denmark) by using direct vat set (DVS) cultures. Microbial analysis of the probiotic cheese (final product) showed that it contained 5×10^6 CFU/g of both mentioned strains. Characteristics of probiotic cheese were as follows: fat content = 15%, protein = 17%, pH = 4.8 and lactose = 3–4%.

The probiotic yoghurt was also enriched with the same strains (same dosage in the final product). Furthermore, *Lactobacillus bulgaricus* and *Streptococcus thermophilus* were used as the starters (10^6 CFU/g) in the final product). Characteristics of probiotic yoghurt were as follows: fat content = 2.5%, protein = 3.8–4%, pH = 4–4.5 and lactose = 3–4%. Certain arrangements were made so that each participant would receive fresh yoghurt at the first day of each week (PY group) and fresh cheese at the start of 1st, 3rd and 5th week of the trial (PC group) direct from the producing factory.

2.3. Interventions and study procedure

Subjects of PC group received 5 probiotic cheese packets (packet net weight = 400 g). Participants of this group were told to consume 30 g of probiotic cheese in a daily basis. To make sure they consumed exactly the designated amount, certain visual scales (small match boxes or 1 inch slice) [23] were given to each individual. All subjects were instructed to consume probiotic cheese between main meals replacing snacks. Participants were also prohibited to consume cheese 1 hour before or after main meals and they were instructed to preserve cheese in refrigerator after opening the package.

Subjects of PY group received 24 probiotic yoghurts (package net weight = 300 g). At the start of each week three fresh probiotic yoghurts were delivered to each subject. Daily amount of yoghurt consumption was 100 g for this group. Other arrangements including visual scales and how to preserve the products were same as PC group. Likewise, control group individuals maintained their regular diet and did not receive any products.

Blood samples were taken from all participants at baseline and the end of 8th week. Fasting blood samples were collected by trained nurses following high quality control standards at Pathobiology Laboratory Center (Tehran, Iran). Anthropometric measurements were also conducted at baseline and final week following a standard protocol [24] at the office of ORT (Tehran, Iran).

In order to screen individuals' diets during each week of trial, three diet records were collected from each subject via E-mails, text messages or phone interviews. Consumption of products was also monitored 3 times a week by phone follow ups. In spite of the aforementioned follow ups, a nutritionist assessed the compliance of subjects to trial guidelines, once per week through weekly visits or phone interviews. Individuals would be excluded from the trial if they missed their probiotic products consumption.

2.4. Ethics

The study procedures were carried out according the Declaration of Helsinki and were approved by the ethics committee of Islamic Azad University. Written informed consent was also obtained from the participants.

2.5. Endpoints

A change in total serum cholesterol (mmol/l) during 2 months was of primary interest. Blood samples were taken by trained nurses from the antecubital vein in the arm. All participants were 12-hour fast and the sampling was conducted in the morning. Blood sera were used to measure the cholesterol level in the same day with sampling. Measurements were carried out by enzymatic method with Parsazmun kits (Diasys, Germany) using cholesterol oxidase-p-aminophenazone (CHOD-PAP) and glycerol phosphate oxidase-p-aminophenazone (GPO-PAP) [25, 26].

Secondary outcomes of interest were the changes in HDL, LDL, TG and BMI. All the sampling procedures were the same as cholesterol except the HDL which the measurement was conducted by direct clearance method (Randox, UK).

All the anthropometric measurements were operated following a standard protocol [24]. Heights were measured by Seca mechanical measuring tape (Model 206, Hamburg, Germany) with 0.1 cm accuracy. In the time of weight

measurement, participants were required to be without shoes (same as height measurements), with minimum clothing, in the fasting state. They were also asked to empty their bladder before weighing procedure. Seca electronic flat scale (Model 813, Hamburg, Germany) was used to measure the body weight (in kg) with 0.1 kg accuracy. Two measurements were taken for both height and weight and if the difference between first and second results was more than 1 cm for height or more than 1 Kg for weight, a third measurement was taken and the mean of all measurements were reported as the final result.

A self-reported diet record was also taken from each participant. The participants were asked to report the type and the amount of food they consumed through 3 non-sequent days in each week. Food intake amounts were estimated using household measures and portion sizes photographs [27].

2.6. Sample size

In order to ascertain a 17%–18% reduction in total serum cholesterol during the intervention period, which supports those of Khedkar et al. [28], a target sample of 180 persons (60 per group) was calculated. This estimation also provided a study power of 80% with SD of 28.0, a 2-sided 5% significance level and allowance of 20% loss in the follow ups.

2.7. Randomization and blinding

A 1:1:1 allocation ratio was considered to assign qualified participants into each group. Moreover, stratified blocked randomization was used by considering age, sex and BMI as stratification factors. Operational randomization software was SAS version 9.2 (SAS Institute Inc, Cary, NC, USA). Besides the participants and researchers, outcome assessors were also blinded to the grouping and the interventions each subject received. By using sequentially numbered, opaque, sealed envelopes (SNOSE), allocation concealment was maintained till the end of trial. The allocation sequence was generated by ShMM, JK assigned subjects into groups, AJ and MHG enrolled the subjects and assessed the eligibility of subjects for inclusion.

2.8. Statistical methods

Food Processor II (ESHA, Salem, OR, USA) was used to perform nutritional calculations of diet records. National Iranian food composition was considered to modify the software database.

All the statistical analyses were conducted with a 5% level of significance. Repeated measures ANOVA (rANOVA) was performed to assess the changes among three groups after the study period for both primary and secondary endpoints, considering time as repeated measure, and sex and interventions as fixed factors. Bonferroni *post hoc* test was also used to conduct multiple comparisons. PASW statistics version 18.0.1 (SPSS Inc, Chicago, IL, USA) software was used to perform all statistical analyses.

3. Results

As shown in Fig. 1, 323 individuals were assessed for eligibility to be included in the trial. The 180 included participants were randomly assigned into three 60-person groups. All participants lived in Tehran, Iran and their nationality was Iranian. The participant's total cholesterol was between <6.0 mmol/L and characteristics were not different between the three groups at baseline (Table 1). It should be also noted that 17 participants dropped out of the study during the intervention period.

3.1. Primary outcome

Comparing final week results of probiotic cheese group with control revealed a significant reduction in TC (-0.51 mmol/L; 95% CI, -0.63, -0.39; P < 0.0001). Probiotic yoghurt group also demonstrated a significant TC reduction (-0.27 mmol/L; 95% CI, -0.39, -0.15; P < 0.0001) when compared to control. Furthermore, comparisons within each group (final week with baseline) illustrated a significant TC reduction in both probiotic cheese



Fig. 1. Flow of study population through the trial.

group (-0.42 mmol/L; 95% CI, -0.47, -0.37; P < 0.0001) (Table 2) and probiotic yoghurt group (-0.15 mmol/L; 95% CI, -0.25, -0.05; P = 0.007) (Table 3). Also, comparing final week results of PC group with PY group showed a statistically significant difference in the primary outcome (-0.24 mmol/L; 95% CI, -0.36, -0.12; P = 0.0001) (Table 4).

3.2. Secondary outcomes

Comparison of probiotic cheese final week results with control revealed a statistical significant change in HDL (0.25 mmol/L; 95% CI, 0.02, 0.47; P = 0.031), LDL (-0.39 mmol/L; 95% CI, -0.52, -0.25; P = 000) and TG (-0.13 mmol/L; 95% CI, -0.20, -0.06; P = 000) but no significant difference was shown for BMI (-0.77 Kg/m2; 95 % CI, -2.40, 0.86; P = 480). However, no significant differences were found in secondary endpoints of probiotic yoghurt group comparing final week results to control; HDL (0.15 mmol/L; 95% CI, -0.21, 0.24; P = 0.985), LDL (-0.08 mmol/L; 95% CI, -0.21, 0.06; P = 0.353), TG (-0.03 mmol/L; 95% CI, -0.10, 0.04; P = 0.544) and BMI (-0.48 Kg/m2; 95 % CI, -2.11, 1.15; P = 748). All the secondary outcomes (HDL, LDL, TG and BMI) were significantly influenced by the consumption period in probiotic cheese group (Table 2). Moreover, comparing baseline to final week results of probiotic yoghurt group also showed significant changes in all secondary outcomes (Table 3).

		Baseline $(n = 180)$		End (<i>n</i> = 163)			
Charectristic	Cheese	Yoghurt	Control	Cheese	Yoghurt	Control	
Age (y)	40.4 ± 14.94^2	36.0 ± 13.78	38.4 ± 16.79	_	_	_	
Sex (n [%])							
Male	30 (50%)	30 (50%)	30 (50%)	_	_	_	
Female	30 (50%)	30 (50%)	30 (50%)	_	_	_	
Weight (kg)	59.73 ± 4.96	59.96 ± 6.99	60.33 ± 4.63	57.90 ± 5.29	58.80 ± 6.78	60.40 ± 4.51	
BMI(Kg/m ²)	22.05 ± 1.71	22.07 ± 1.69	22.14 ± 0.97	21.34 ± 1.75	21.63 ± 1.62	22.11 ± 0.89	
TC (mmol/l)	4.92 ± 0.08	4.90 ± 0.11	4.99 ± 0.13	4.50 ± 0.11	4.75 ± 0.11	5.01 ± 0.10	
MUFA (% energy)	34.1 ± 4.9	35.3 ± 5.2	35.0 ± 5.1	34.8 ± 5.3	34.3 ± 5.4	35.9 ± 5.9	
PUFA (% energy)	11.3 ± 2.9	11.1 ± 3.2	11.5 ± 3.5	10.6 ± 3.1	10.2 ± 3.3	11.4 ± 3.4	
SFA (% energy)	10.9 ± 2.1	11.1 ± 2.1	11.3 ± 1.9	11.2 ± 1.9	11.3 ± 2.2	10.8 ± 2.0	
Total fat (% energy)	34.1 ± 4.9	35.3 ± 5.2	35.0 ± 5.1	34.8 ± 5.3	34.3 ± 5.4	35.9 ± 5.9	
Total energy (kJ)	9383.66 ± 224.87	9599.52 ± 234.47	9599.68 ± 369.22	10126.75 ± 391.53	9574.76 ± 285.34	9710.39 ± 404.63	

 Table 1

 Base line and follow up charactristics of the study population¹

1: TC, Total cholesterol; BMI, body mass index. 2: Mean \pm SD (all such values).

 Table 2

 Treatment effects on primary and secondary endpoints (comparing final week with baseline)¹

Probiotic cheese group							Control group $(n=60)$	
Variables	Change (%)	Mean	SD	Lower 95% CI	Upper 95% CI	P value	Mean	SD
TC (mmol/l)	-8.54	-0.42	0.08	-0.47	-0.37	< 0.0001	0.016	0.03
TG (mmol/l)	-5.74	-0.12	0.01	-0.13	-0.11	< 0.0001	0.006	0.01
HDL (mmol/l)	16.77	0.26	0.06	0.22	0.30	< 0.0001	-0.011	0.02
LDL (mmol/l)	-8.46	-0.34	0.04	-0.37	-0.32	< 0.0001	0.003	0.01
BMI (kg/m ²)	-3.22	-0.71	0.32	-0.94	-0.48	< 0.0001	-0.03	0.22

1: TC, total cholesterol; TG, triglyceride; BMI, body mass index.

 Table 3

 Treatment effects on primary and secondary endpoints (comparing final week with baseline)¹

	Probiotic yoghurt group						Control group	
			(n = 51)			(<i>n</i> =	60)
Variables	Change (%)	Mean	SD	Lower 95% CI	Upper 95% CI	P value	Mean	SD
TC (mmol/l)	-3.06	-0.15	0.14	-0.25	-0.05	0.007	0.016	0.03
TG (mmol/l)	-0.96	-0.02	0.01	-0.03	-0.01	0.002	0.006	0.01
HDL (mmol/l)	2.61	0.04	0.04	0.01	0.07	0.011	-0.011	0.02
LDL (mmol/l)	-1.24	-0.05	0.02	-0.06	-0.04	< 0.0001	0.003	0.01
BMI (kg/m ²)	-1.99	-0.44	0.21	-0.59	-0.29	< 0.0001	-0.03	0.22

1: TC, total cholesterol; TG, triglyceride; BMI, body mass index.

i mai week results comparing encose and yoghart						
Variables	Mean	P value	Lower	Upper		
(mmol/l)			95% CI	95% CI		
TC	-0.24	< 0.0001	-0.36	-0.12		
TG	-0.10	0.003	-0.17	-0.03		
HDL	0.23	0.05	0.01	0.46		
LDL	-0.31	< 0.0001	-0.45	-0.17		
BMI	-0.29	0.89	-1.92	1.34		

Table 4 Final week results comparing cheese and yoghurt¹

1: TC, total cholesterol; TG, triglyceride; BMI, body mass index.

Significant improvements were also observed comparing final week results of probiotic cheese group with probiotic yoghurt except for BMI (Table 4).

4. Discussion

The present study was designed to compare the consumption effect of ultra-filtered feta probiotic cheese and probiotic yoghurt on blood lipids and to find out which dairy product is more effective on study outcomes. As far as we know, there has been no study comparing the effect of probiotic cheese and probiotic yoghurt (both enriched with *Lactobacillus acidophilus* LA5 and *Bifidobacterium lactis* BB12 strains) on blood lipids.

The main finding of this study demonstrated that probiotic cheese consumption was more effective on blood lipids as compared to both control and probiotic yoghurt group. According to the results, both treatment groups also showed a significant reduction in serum cholesterol compared to control. Likewise, probiotic cheese group showed a reduction in serum LDL and TG comparing to control and probiotic yoghurt group. Studies suggest different mechanisms which results in cholesterol lowering effects of probiotics. It has been reported that enzymatic deconjugation of bile acids is among the possible mechanisms. Probiotics have the potential to produce bile salt hydrolase (BSH) which catalyzes the hydrolysis of conjugated bile salt into free bile acids [29]. In an in vitro 2004 study by Jones and his colleagues, role of BSH in cholesterol reduction was investigated using Lactobacillus plantarum 80 (pCBH1). It was reported that activity of BSH was able to hydrolyze conjugated glycodeoxycholic acid and taurodeoxycholic acid, resulting in the deconjugation of glyco- and tauro-bile acids [30]. Moreover, studies suggest that once probiotics reach the gut, they ferment indigestible carbohydrate from food, resulting in the increase of short chain fatty acids (SCFA). SCFA has the potential to lower blood lipids by blocking the synthesis of hepatic cholesterol or through redirecting the plasma cholesterol toward the liver [3, 7]. It has been also suggested that the hypocholesterolemic effect of the probiotics may be attributed to their cholesterol binding ability in the gut. In an in vitro study by Usman and Hosono [31], strains of Lactobacillus gasseri removed cholesterol from laboratory media via binding to the cellular surface. In 2002, Kimoto et al. [32] also observed the cholesterol binding ability of probiotics. Authors investigated the role of probiotics in removal of cholesterol during different growth conditions. It was illustrated that growing probiotics removed more cholesterol in comparison with heat-killed cells, showing that killed cells could still remove cholesterol from media.

Results of current study also indicated a significant increase in the HDL level of probiotic cheese group. The HDL improving effect of probiotic cheese may be due to the presence of sphingolipids in cheese. Previous studies reported that sphingolipids not only improve HDL-cholesterol level but also reduce LDL-cholesterol [33, 34]. Probiotic cheese used in this trial contained 15% fat. Hence, sphingolipids content was higher than probiotic yoghurt (2.5% fat). Also, cell membranes of bacteria are another potential source of sphingolipids. A more dense texture in probiotic cheese which let more probiotics survive in the gastrointestinal tract (GIT) [18], could have led to a higher sphingolipids content and as a consequence significant improvement in HDL and LDL.

Improvement effects of probiotics observed in this study are in agreement with those of Ataie-Jafari et al. [17]. In their randomized crossover trial, they included 14 healthy subjects with serum total cholesterol 5.17–7.76 mmol/l. Authors reported that probiotic yoghurt consumption (Including *Lactobacillus acidophilus* and *Bifidobacterium lactis* –300 g/d) after 6 weeks caused a significant decrease in serum total cholesterol. Fabian and Elmadfa [9] also reported

positive effects of probiotics on blood lipids. In their 2006 parallel randomized controlled trial, authors investigated the effect of probiotic and conventional yoghurt consumption (100 g/d) in 34 young healthy women for 2 weeks. Authors reported a significant increase in the mean HDL cholesterol level and a significant reduction in plasma LDL after intervention period.

In contrast to positive results of probiotics on LDL and TG observed in current trial, Sadrzadeh-Yeganeh and her colleagues [7] found no significant improvement in LDL and TG after 6 week of probiotic consumption in their intervention group. In their parallel randomized trial, they investigated the effect of probiotic and conventional yoghurt consumption in a total of 90 women aged between 19 and 49 years, with cholesterol levels less than $6\cdot2 \text{ mmol/l}$. Although they reported a decrease in cholesterol level, no significant difference in TG and LDL was observed. Simons et al. [14] also reported no significant changes of blood lipids in their study. In their 2006 double blind, placebo-controlled, parallel design trial, 46 subjects with total cholesterol >or = 4 mmol/L received either *Lactobacillus fermentum* (2 capsules/d - each capsule containing 2×10^9 CFU) or placebo for a period of 10 weeks. Although a downward trend in TC, TG and LDL was reported, no significant improvement was reached.

The controversy between reported results may be due to differences in length of studies, amount of consumption, various bacterial strains and difference research designs. Inadequate sample size, failure in conducting follow ups and diet controls along with variations in level of blood lipids at baseline are the other factors which can be addressed for controvert results.

The current study had several strengthens. The randomized controlled allowed for an objective assessment of probiotic cheese/yoghurt effects on blood lipids. Study guideline compliance and follow up rates were high. Besides, the large number of participants resulted in a more in depth investigation of endpoints. As far as we know, this was the first study compared the efficacy of probiotic cheese and probiotic yoghurt on lipid profile. Several limitations also deserve comment. Current trial was carried out only for two months and the endpoint of study was not the long-term effect of probiotic consumption. Furthermore, no feces analysis was conducted to evaluate the presence of probiotics in feces. Last but not least, this study was carried out on healthy subjects rather than individuals with dyslipidemia.

Most of available data regarding the positive effects of probiotics on blood lipids are based on *in vitro* experiments and the number of well-designed clinical trials is scarce. Furthermore, few attempts have been made to investigate the mechanisms involved in regulating blood lipids based on clinical trials. In other words, most of current papers thus far have focused on clarifying the hypocholesterolemic effects of probiotics, rather than the possible involving mechanisms. Hence future studies should draw attention to evaluate possible hypocholesterolemic mechanisms *in vivo*. In addition, Wide range of studies is heavily focused on dairy based probiotic products whereas future studies can benefit from probiotic carriers other than dairy based ones. Finally, data on accurate dosage of probiotic administration has yet to be reported. Lack of dosage-response studies does not allow us to determine the minimal effective dosage of probiotics (when used in food products) for improving lipid profile.

5. Conclusions

To sum up, the results of this study allow us to draw the conclusion that consuming probiotic cheese is more effective than probiotic yoghurt in improving blood lipids. Although in light of study results, both treatment groups illustrated an improving trend on blood lipids, probiotic cheese showed the significant potential to be classified as a cholesterol-lowering product, ensuring passage of more sufficient number of probiotic bacteria to the target organ.

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