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Original article

The effect of using synbiotic on weight loss, body fat percentage and anthropometric measures in obese women

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Summary. *Objective:* This is a randomly controlled, synchronously done, single-blind study which aims to investigate the effects of synbiotic use on anthropometric measurements and energy intake. *Materials and Methods:* Sixty-one not compliant with diet and exercise recommendations, sedentary obese women (BMI: 30-39.9 kg/m^2) who fulfilled inclusion criteria, aged between 18 and 48 randomly categorized into synbiotic(n=30) or control(n=31) group. The synbiotic and control groups consumed 1 synbiotic capsule/day or 1 placebo capsule/day during 6 weeks, respectively, without changing the ongoing diet. Anthropometric measurements (body weight, body mass index, waist circumference, hip circumference, waist / hip ratio and body fat ratio) are done at the beginning, at 3th week and at 6th week. Also, 24 hours of their food consumption are recorded at the beginning of the study and once a week during the study. *Results:* Repeated measurements of body weight, body fat ratio, waist circumference, hip circumference, and the calculations of body mass index and waist/hip ratio are analyzed with mixed effect linear model and therefore, the interaction terms with group and time effects are not found significantly ($p> 0.05$). No difference (increase or decrease) are observed in energy intake of participants in two groups at the beginning and during the study ($p> 0.05$). *Conclusion:* Synbiotic supplement did not change antropometric measures, body composition and daily energy intake in not compliant with diet and exercise recommendations obese women. Further studies are needed to indicate the effects of Synbiotic use in obesity treatment.

Key words: Obesity, Synbiotic, weight loss, nutrition, anthropometry.

Introduction

Obesity is an epidemic, which rapidly increases all over the world and has become a major public health problem in recent years, depends on the multifactorial causes such as genetic, environmental, cultural, socioeconomic, metabolic, behavioral, physiological and endocrine (1,2). Obesity affects several systems such as circulatory system, digestive system, musculoskeletal system, respiratory system, reproductive system and causes emotional tension and psychological problems. Obesity also increases the risk of some cancers (3). Probiotics are defined as " live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" (4). Being human-origin, harmless and reliable for human health, forming colonies in the intestines at least for a short, being adaptable to natural microflora, including a high live microorganisms, being viable in gastrointestinal tract and maintaining its metabolic activity, stimulating the immune system, and producing antimicrobial agents are needed for a microorganism to be accepted as a probiotic (5). Experimental animal studies and observational human studies have indicated that intestinal

microbiota is different in obese and underweight people, diabetic and non-diabetic people or in diseases related to obesity and malnutrition such as NASH and cardiovascular diseases (6). Several researchers suggest that the weight gain caused by microbiota may be modulated by probiotics. There are animal studies demonstrating that probiotic use reduces adipose tissue and adiposity (7,8). It has also been shown that the consumption of probiotic milk and milk products, defined as functional nutrients, reduces abdominal adiposity, BMI, waist and hip circumference (9-11). It has been suggested that dysbiosis may change energy homeostasis by harvest more energy from the diet, affecting the inflammatory markers and fatty acid composition in the tissues, altering intestinal permeability, increasing the triglyceride content in the liver and decreasing the free fat acid oxidation in the liver and muscle tissues (12). There are studies have shown that using probiotic and synbiotic may help weight loss and control, prevent weight loss resistance in the late phase by delaying the plateau phase in weight loss (13-15). While many studies have suggested that there is a close connection between probiotic use and weight control, a certain mechanism for explaining this connection has not been indicated yet (16). The aim of the present study was to investigate the effects of synbiotic use on anthropometric measurements, body composition and energy intake in not compliant with diet and exercise recommendations obese women.

Materials and Methods

Participant Selection and Settings: The study was carried out with 70 obese women (35 control group, 35 working group) who applied to be examined under follow-up for at least 3 months in İzmir Tepecik Training and Research Hospital Obesity Clinic of Health Sciences University met the conditions and agreed to participate in the study. *Inclusion Criteria:* To be a woman, to lose weight less than 10% of her initial weight with hypocaloric diet + physical activity recommendations for at least 3 months of obesity policlinic follow-up, to be between the ages of 18 and 50 years, have BMI between 30 and 39.9 kg / m^2, do not take any treatment other than medical nutrition therapy, to be a volunteer, to be approved by the doctor to participate in the study. *Non-inclusion Criteria:* To have a chronic disease, to use probiotic-prebiotic preparations or products containing probiotic-prebiotic within the last 15 days, to take antibiotics within the last 8 weeks, to get any nutritional supplements, to be a vegetarian, to be pregnant, to smoke, not to be approved by the doctor to participate in the study, to go through the menopause. *Exclusion Criteria:* To meet one of the conditions stated in non-inclusion criteria during the study period, taking less than 2/3 of the synbiotic/placebo capsules, not to obey the planned regular visits during the study (± 7 days missing from the appointment day), to lose study materials, to quit with her own request, to take antibiotics during the study.

General Plan of the Study: The trial is randomized, **placebo-controlled** and single-blind. The total time for each participant to complete the study was 6 weeks. In this period, the participants in the study were asked to consume one capsule per day with a glass of water before breakfast. Synbiotic capsules content probiotic microorganism($3x10^9$ cfu Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum, Bifidobacterium bifidum), Stabilizer (Hydroxypropylmethylcellulose), Prebiotic (159.45 mg Fructooligosaccharide), Coloring agent (Titanium Dioxide), anti-caking agent (Magnesium salts of fatty acids), placebo capsules content 1735 mg maltodextrin and 7.0 mg antioxidant (ascorbic acid). The placebo and synbiotic groups were randomized with the permutation method (17). At the first interview with the participants, a questionnaire including their general information and dietary habits, International Physical Activity Questionnaire (IPAQ), 24-hour food consumption and anthropometric measurement forms were filled by researchers with face-to-face interview, and each participant signed the consent forms. Participants were called with telephone every week to examine their capsule taking and food consumption records, and if any, their questions were answered. Participants filled the Participant Notebooks including the product use log and food consumption forms given by the researchers. Necessary guidance and instructions were made for those who quit, and those who completed the study in order to continue their treatment and follow-up at the Obesity and Diet Clinics. The study flow diagram

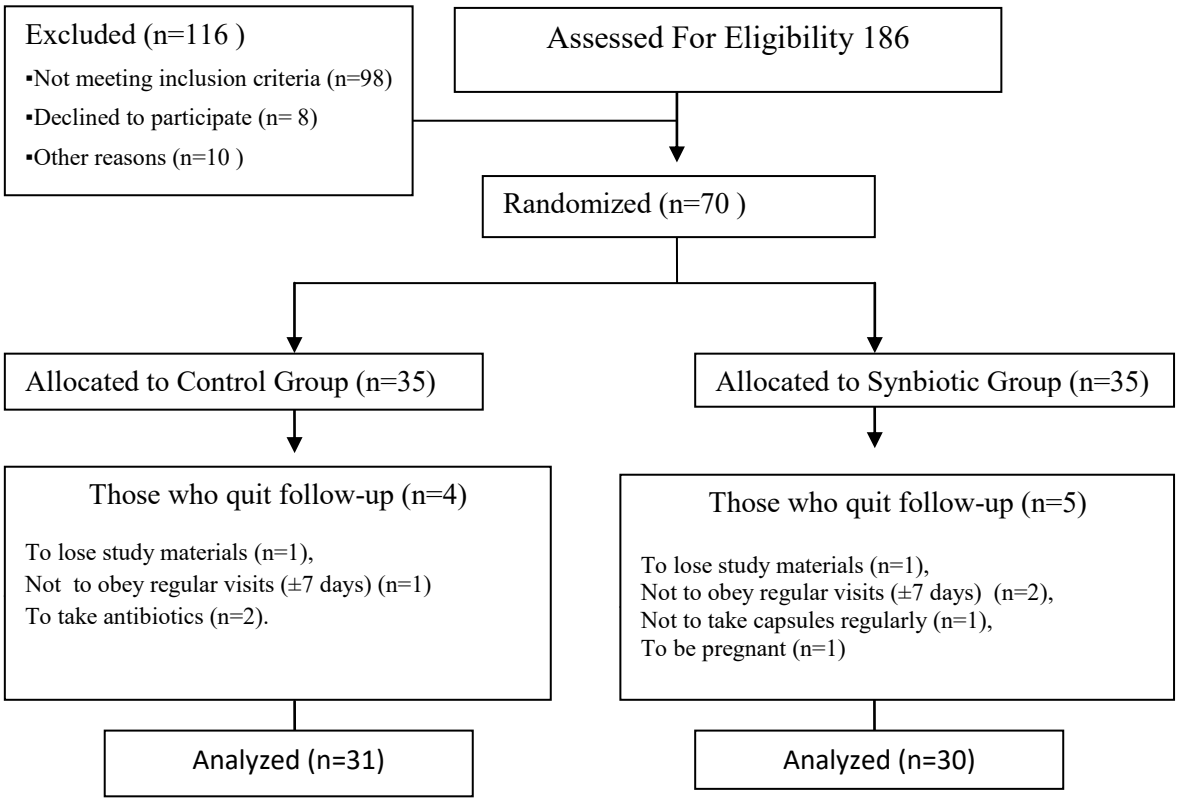

Figure 1. Study flow diagram

was given in Figure 1. The capsules with synbiotics and placebo were only known by the researchers during the study. The products are given to the participants in the same packages provided by the manufacturer.

Anthropometric Measurements: Anthropometric measurements and body composition were done in the beginning, at 3th week, and at the end of the study. Waist measurements was made at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Hip measurements was made at the widest portion of the hip and the circumference was measured in parallel to the floor. Each measurement was repeated twice and a non-stretchable and 150 cm long tape was used(with a sensitivity of 0.1 cm) (18). Height Measurement was made with the Charder Boy Scale HM-200P without shoes on Frankford plane (19). BMI was determined by dividing body weight by height squared (kg/m^2). Body Fat Ratio (%) was measured in the fasting state by using the Tanita SC 330, which conducted a body analysis with a 50 kHz electric current sent to the body with the principle of Bioimpedance Analysis (BIA). Before 24 hours of the measurement, the participants were asked to avoid heavy physical activity, not to drink alcohol, and not to consume tea and coffee four hours ago. It was confirmed on every measurement that participants did not use metal objects, cardiac pills (medical electronic devices) and portable electronic medical devices such as artificial heart/lung (20).

Energy Intake: At the beginning and during the study, food consumption records of 24 hours were taken once a week (every week, same weekday). Energy and nutrients intakes were calculated from food consumption records using BEBIS computer program.

Statistical Analysis: SPSS 22.0 version and R 3.2.5 were used in the evaluation of the data. In the evaluation of the data, Saphiro-Wilk test, Student-T test, Mann-Whitney U test, chi-square test were used, and mixed effect linear model was used for the analyses

Table 1. Daily energy intakes (kcal/kg)

		Beginning		3rd Week		6th Week	
		Average	SD	Average	SD	Average	SD
Energy (kkal/kg)	**Control Group(n=31)**	17.72	5.89	18.82	5.21	19.32	3.82
	Synbiotic Group(n=30)	19.73	6.33	18.86	4.23	19.84	4.14

*time p=0.291 and interaction (group*time) p=0.353*

Table 2. Energy intakes during the study period (kcal/day)

	Control Group(n=31)			Synbiotic Group (n=30)		
Kcal/day	**Average**	**Min-Max**	**SD**	**Average**	**Min-Max**	**SD**
Begining	1530.19	742.5-2718.9	512.67	1653.0	884.8-2743.4	498.90
2ndWeek	1561.24	874.2-2287.0	340.40	1563.4	982.0-2208.3	316.86
3rdWeek	1597.69	512.7 – 2162.7	428.42	1570.5	920.0 - 2263.9	315.29
4thWeek	1646.34	1156.9 – 2242.5	233.70	1483.7	785.5 – 1988.9	289.48
5thWeek	1688.38	1186.1 – 2321.5	237.89	1717.8	125.,8 – 2170.6	222.30
6thWeek	1636.79	990.3 – 2131.1	321.59	1652.7	983.3 – 2290.7	324.10

Group p=0.496. Time p=0.120; interaction (group*time) p=0.346.

Table 3. Energy contribution rates of macronutrients (%) and total fiber intake (g/day) are given in.

	Control Group				Synbiotic Group				p
	Min	**Max**	**Average**	**SD**	**Min**	**Max**	**Average**	**SD**	
Protein (%)	16.00	17.65	16.94	0.53	16.00	18.00	17.08	0.74	0.094
Fat (%)	37.65	39.97	39.11	0.84	40.23	42.03	40.91	0.70	0.085
Carbohydrate (%)	42.61	43.32	43.01	0.27	40.33	42.63	41.48	0.78	0.413
Fibre (g/day)	18.00	26.99	23.91	3.39	16.38	26.54	22.86	3.57	0.481

of repeated mesurements. Statistical significance was accepted as p <0.05.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and written informed consent was obtained from all subjects. Ethical compliance of the practises to be conducted in the study was evaluated and approved by the Local Ethics Committee of İzmir Tepecik Training and Research Hospital Obesity Clinic of Health Sciences University (T.No:26, K.No:24).

Results

The literature was searched to determine the study period. Based on studies showing that six weeks of synbiotic / probiotic use can change the intestinal flora (21-23) and affect metabolic status (24-27) the study period was determined as six weeks.

The average age of the participants in the control group was 35.42 ± 9.07, and the average age of the synbiotic group was 36.73 ± 6.34. None of the participants in the study used dietary supplements before and during the study period. According to the results of the IPAQ-short form on the first day of the study, daily sitting times were determined as 472.8 minutes/day in the synbiotic group and 439.4 minutes/day in the control group. The mean MET Score = 407 MET-min/week in the study group and the mean MET Score = 415 MET-min/week in the control group. While 20 participants (64.5%) were inactive and 11 participants (35.5%) were minimum active in the control group, 21 participants

Table 4. Anthropometric meausements and body composition before, during and at the end of the study

		Control Group (n=31)			Synbiotic Group (n=30)			
		Average	SD	Min-Max	Average	SD	Min-Max	P
Height (m)		1,59	0.07	1.45-1.75	1.59	0.04	1.52-1.68	0.378¶
Body Weight (kg)	Beginning	86.63	9.74	73.20-103.0	84.33	7.62	72.20-100.0	0.432¶
	3rd Week	85.75	9.845	72.20-102.00	84.02	7.75	72.00-99.60	0.545¶
	6th Week	85.36	10.18	72.20-101.80	83.92	7.59	70.50-98.30	0.676¶
BMI (kg/m2)	Beginning	34.25	3.06	30.08-39.90	33.10	2.42	30.12- 39.06	0.358¶
	3rd Week	33.86	2.98	30.14-39.78	32.97	2.71	29.41-39.54	0.789¶
	6th Week	33.69	2.98	29.83-39.70	32.96	2.65	28.91-39.13	0.480¶
Waist Circumference (cm)	Beginning	101.09	10.50	83.0-129.0	98.93	7.75	86.0-118.0	0.363†
	3rd Week	100.45	10.64	83.0-129.0	97.70	8.21	82.0-118.0	0.262†
	6th Week	98.66	10.29	80.0-129.0	96.03	7.88	82.0-117.0	0.267†
Hip Circumference (cm)	Beginning	116.77	8.92	103.0-138.0	113.37	8.36	98.0-134.0	0.129†
	3rd Week	115.35	9.29	102.0-138.0	111.33	7.72	98.0-127.0	0.071†
	6th Week	115.23	8.56	103.0-137.0	110.23	7.71	97.0-127.0	0.020*†
Waist/hip Ratio	Beginning	0.87	0.06	0.73-0.96	0.88	0.08	0.73- 1.12	0.902¶
	3rd Week	0.87	0.060	0.76-1.0	0.88	0.08	0.77-1.12	0.322¶
	6th Week	0.86	0.05	0.76-0.98	0.87	0.07	0.73-1.12	0.402¶
Body Fat Ratio (%)	Beginning	40.42	4.06	31.90-47.20	40.09	3.23	33.10-45.80	0.727†
	3rd Week	39.83	4.23	31.60-47.10	39.96	3.18	33.10-45.30	0.891†
	6th Week	39.93	4.55	31.20-47.00	39.31	3.19	32.80-44.40	0.541†

(†) t test, (¶) Mann Whitney U Test, *p<0.05

Table 5. Statistical analysis of repeated anthropometric measurements and body fat ratio (mixed effect linear model)

	Group (p)	Time (p)	Interaction (group*time) (p)
Weight	0.258	0.079	0.258
BMI	0.683	0.405	0.430
Waist Circumference	0.394	0.129	0.712
Hip Circumference	0.266	0.079	0.065
Waist/Hip Ratio	0.859	0.096	0.204
Body Fat Ratio (%)	0.915	0.398	0.722

(70.0%) were inactive and 9 participants (30.0%) were minimum active in the synbiotic group. All of the individuals participating in the study are sedentary. Before the study the average length of follow-up was 5.00 months (synbiotic group: 4.87 months/control: 5.13 months) and the weight loss of participants was 2.52 kg (synbiotic group: 1.93 kg/control: 3.06 kg).

Energy Intake: In two groups at the beginning and during the study, the energy additive ratios of the macronutrients did not comply with the recommended diet. The quantities of daily energy intake (kcal/kg) were indicated in Table 1. Two-way ANOVA was conducted in the analysis of repeated calculations of kcal/kg values in the control and working groups, but no significant difference was statistically found between the groups (p = 0.38).

A mixed effect linear model was used in the statistical analysis of daily total energy intakes (kcal/day). Interaction with the group and time main effect in the model was not found significant (see Table 2). No change (increase or decrease) was eventually found in the amount of energy between the groups.

The average of the food consumption records taken during the study were examined. Energy contribution rates of macronutrients (%) and total fiber intake (g/day) are given in Table 3. Contribution

rates of macronutrient elements to energy in both groups at the beginning and during the study did not comply with the recommended diet plan. According to the six-week food consumption records, 89.26% of the control group, 87.77% of the synbiotic group, the rate of saturated fatty acids to energy during the study is over 10%. There was no statistically significant difference between the two groups in terms of energy, micronutrients, macronutrients and fiber intake ($p > 0.05$).

Anthropometric Measurements: The mean±SD of anthropometric measurements and body fat ratio (%) of the volunteers before, during and at the end of the study was summerized in Table 4. At sixth week hip circumference is lower in synbiotic group ($p<0.05$). There was not diffirence in all other measurements in two groups ($p>0.05$).

The mixed effect linear model was used for the statistical analysis of the repeated measurements during the study (Table 5). Interaction terms with group and time main effects were not found significant ($p>0.05$).

Discussion

Compliance and maintenance of adequate and balanced nutrition is in an important relationship with weight loss (28). Along with diet, physical activity is accepted as one of the most important factors in the treatment of obesity (29). It is known that overweight and obesity are associated with a sedentary lifestyle and increased physical activity levels are an important part of obesity treatment (30). In this study all the paticipants are sedentary and they do not compliant with diet recommendations. Using synbiotics alone, without following dietary and physical activity recommendations, did not reduce anthropometric measurements.

Prebiotics are defined by FAO as: "a prebiotic is a non-viable food component that confers a health benefit to the host associated with the modulation of the microbiota" (31). There is evidence to suggest that the gut flora may affect nutrient utilization and energy balance (32). There are studies showing that prebiotics and probiotics can have positive effects on prevention and treatment of obesity (32,33). Fructooligosaccharide is one of the most studied prebiotic (34). It has been demonstrated in many in vivo and in vitro studies that fructooligosaccharide selectively contributes to the growth of bifidobacteria species in the intestine (35). Although sufficient fructooligosaccharide intake improves the growth and development of bifidobacteria in the intestinal flora, the number of bifidobacteria in the host intestine is important for fructooligosaccharide activity. (36). There are studies showing the positive effects of the use of fructooligosaccharides with probiotic bacterias on obesity (14, 36, 37). Based on all these, fructooligosaccharide was used with probiotic bacterias in this trial.

Bifidobacterium lactis is one of the most widely used bifidobacterium species. The benefits of this probiotic bacterium such as increasing resistance of the host to pathogens (38) and improving glycemia control have been reported (39). Stenman et al. (40) showed that bifidobacterium lactis controls body fat mass, decreases food intake and waist circumference. Uusitupa et al. (40) determined to be associated with management of body weight and metabolic health. However, the signaling pathway is not yet fully understood (41).

Animal studies are reporting that *Bifidobacterium longum* can improve metabolic syndrome (42) and prevent obesity and diabetes by reducing body weight and fat mass (43, 44). Schellekens et al. (45) have associated *Bifidobacterium longum* supplementation with decreased body weight and increased glucose tolerance in HFD-fed mice.

Bifidobacterium bifidum is one of the first colonies in the human intestine (46). Although its levels decrease in adulthood, it is a member of the healthy adult gut population (47). It has been revealed that daily use of *bifidobacterium bifidum* increases the number of healthy days in individuals under acute stress and decreases the prevalence of colds and flu (48). There are also studies reporting it reduces gastrointestinal complaints (49, 50), reduces inflammation (51,52), improves hyperglycemia, dyslipidemia, and oxidative stress (52, 53).

It has been determined that various Lactobacillus species may have therapeutic effects in conditions such as inflammatory bowel disease, rheumatoid arthritis, atopic dermatitis (54). It has been shown that *Lactobacillus acidophilus* can prevent osteoporosis (55) and be a suitable probiotic for the treatment of diseases

such as IBD in which immune response changes (56). Halawa et al.(57) concluded that the number of *Lactobacillus acidophilus* is lower in the stools of type 2 diabetic patients (57) and use of *Lactobacillus acidophilus* preserved insulin sensitivity (58).

In addition to reduce inflammation, improve antioxidant defense, increase insulin sensitivity, probiotic use has been suggested to improve beta-cell functions, balance blood fats and control body weight (59), and animal and human studies, which the effects of probiotic use on energy intake and anthropometric measurements are examined, have been carried out in recent years (8, 10, 11, 13, 15, 60).

Although the use of probiotics and/or prebiotic has been reported to reduce food intake, there are also studies showing that it does not (60-64). In the present study, the quantities of the energy intakes of participants were determined with the food consumption records at the beginning and during the study period, and it was seen that probiotic use did not change any of the energy intake.

It is reported that short-term probiotic use decreased body weight, BMI and body fat ratio (%) on overweight and obese adult participants were examined (65).

Rabiei et al. (14) revealed that the use of synbiotic which contains seven probiotics (two of them are *Lactobacillus acidophilus* and *Bifidobacterium longum*) and fructooligosaccharide decreased BMI, waist circumference, fat mass furthermore that symbiotic use could delay the plateau phase in weight loss. After six weeks of *Lactobacillus acidophilus* and *Bifidobacterium lactis* use, it has been shown that body weight, BMI (66, 67) and waist / hip ratio (62) were not different from the control groups. The use of probiotics in combination with a hypocaloric diet is reported to reduce body weight and BMI (11, 60, 68).

Product containing probiotics (Lactobacillus acidophilus, Bifidobacterium lactis, and Lactobacillus casei) in a randomized controlled study, Zarrati et al.(69) concluded that its use is not effective alone, and its combined use with a low-calorie diet has a synergistic effect and reduces BMI and body fat percentage.

In the evaluation of repeated measurements in our study, no significant difference was statistically determined in body weight, BMI, waist circumference, hip circumference, waist/hip ratio and body fat ratio (%) of obese women using probiotics for six weeks in comparison to the control group. Six-week use may not be adequate to observe the effects of probiotic and/or prebiotic use on obesity (70). Longer interventions with the same strain may be more effective on anthropometric measurements. In addition to that, the sample group consisted of sedentary participants who were followed for at least three months and lost less than 10% of their body weight. Probiotics and/or prebiotic used with a well-performed weight-loss diet and exercise program may reduce anthropometric measurements. The trial can be repeat with higher dose and larger sample. The effects of probiotics on general health are specific to the strain (71). Repeating the same study with different types can change the results of the study.

Conclusion

In our study synbiotic supplementation for six weeks (one capsule per day: $3x10^9$ cfu *Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum, Bifidobacterium bifidum,* 159.45 mg Fructooligosaccharide) for women who did not comply with diet and exercise recommendations did not change anthropometric measurements, body composition and daily energy intake. Further studies that can be conducted for a longer period, higher dose, or at different intervals to show the effect of synbiotic use on the treatment of obesity in adult women may reveal new results.

Conflict of interest

The current manuscript is a part of PhD thesis called The Effect of Using Probiotic on Weight Loss, Body Fat Percentage and Anthropometric Measures in Obese Women, written by Zehra Batu, Hacettepe University, Health Sciences Institute, Nutrition and Dietetics Programme. "No potential conflict of interest relevant to this article was reported by the authors".

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