

The Effects of Flaxseed on Weight Loss in Women with Polycystic Ovarian Syndrome: a Randomized Controlled Trial

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Abstract

Objective: The aim of this study was to evaluate the effectiveness of flaxseed consumption in improving weight loss and altering anthropometric indices in overweight and obese women with polycystic ovary syndrome (PCOS). Our hypothesis was that the high fiber and α -linolenic (ALA) contents of flaxseed would decrease weight, body mass index (BMI), waist circumference and fat mass, so it would improve PCOS.

Materials and Methods: Sixty eight patients between the ages of 20 and 40 years participated in this double-blinded, randomized placebo-controlled study. Subjects were randomly assigned to flaxseed and placebo groups to use 15 grams of flaxseed or placebo daily for 12 weeks. Sixty two participants completed anthropometric measurements before and after study.

Results: The results showed that weight, BMI, waist circumference, visceral fat percentage and body fat percentage were significantly decreased and body muscle percentage was significantly increased in both groups. In addition consumption of 15 gr/days flaxseed for 12 weeks by overweight or obese women with PCOS significantly decreased the mean change of BMI (P -value= 0.04) and in regards of weight, the reduction was marginally significant (P -value= 0.05). However, there was no significant difference in the mean change of waist circumference (P -value= 0.46), percentage of body fat (P -value= 0.78), muscle (P -value= 0.18) and visceral fat (P -value= 0.43) between flaxseed and control groups.

Conclusion: These findings represented that flaxseed supplementation could reduce BMI and weight but other factors did not change significantly. Further studies are needed to show that flaxseed can be used as a supplement for weight loss in PCOS.

Keywords: Polycystic ovarian syndrome, Body mass index, flaxseed

Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder in women of reproductive age and its prevalence

varies from 5 to 21% (1). PCOS is the most common cause of infertility in women, (2) and characterized by acne, high levels of androgen

hormones, menstrual disorders, infertility and hirsutism (3). Studies showed that PCOS is strongly associated with insulin resistance, metabolic syndrome, abdominal obesity, type 2 diabetes, heart disease and dyslipidemia (3-7). Furthermore, PCOS increases the risk of mental disorders such as depression and anxiety (8).

Approximately 50% of women with PCOS are obese (9). Obesity may also play a role in the etiology of PCOS and affects fertility through various mechanisms such as hyperandrogenism, increase in Luteinizing Hormone (LH) and insulin resistance (9). Obese women with PCOS show a higher level of insulin resistance and hyperinsulinemia which contributes to androgen excess and lack of ovulation (9). Additionally, the substances produced by the adipose tissue, including adiponectin, resistin and visfatin may also play a role in the pathophysiology of PCOS(10).

Studies showed that weight loss improves some of the clinical aspects of PCOS, including menstruation and fertility (11) and also it could improve many cardiovascular risk factors associated with PCOS such as insulin resistance and dyslipidemia(12).

Flaxseed (*Linum usitatissimum L.*) is a functional food(13), and it contains several biological active substances such as alpha linolenic acid (ALA), lignin (Secoisolariciresinol- diglycoside (SDG)), and mucilage soluble fiber (d-Xylose, L-Galactose, LRhamnose, dgalacturonic acid), which have significant health effects (14). Further, it is a rich food source of lignan, which is one of the groups of phytoestrogens (15). Flaxseed and its components have beneficial effects on decreasing risk of cardiovascular diseases, diabetes, blood pressure and hyperlipidemia (16-18). Some studies showed an inverse relationship between flaxseed consumption and body composition indices (19,20), while other studies demonstrated little or no effect on body composition compared to control group (21-23).

As obesity is an important contributory factor for PCOS, the purpose of this study was to

assess the efficacy of supplementation with flaxseed on a weight reduction, change of the body mass index (BMI), waist circumference, body fat, and muscle in overweight and obese PCOS patients.

Materials and Methods

All researchers were blind to the treatment allocation until the completion of the study. Randomization was performed by using computer-generated random numbers, and the packing of supplement was undertaken by a third person who was not involved in patient contact or the sample collection and analysis. Random assignment was only decoded when all data had been collected and computed. The random assignment was conducted in 2 blocks to enable a balance between the groups.

This trial was carried out among 68 women with PCOS, diagnosed based on the Rotterdam criteria (24) who referred to Shahid Beheshti hospital in Isfahan. The inclusion criteria was being overweight or obese ($BMI \geq 25$), age between 20 to 40 and willingness to collaborate in the study. We excluded subjects who were pregnant or lactating, using steroids, hormones or antiplatelet drugs, positive history of gastrointestinal obstruction or inflammatory bowel disease and people with allergy to flaxseed. Patients provided informed written consent before starting the study.

Participants were randomly assigned to take either flaxseed or placebo for 12 weeks. The shapes of placebo and flaxseed package were completely similar, and each package consists of 15 grams of flaxseed or placebo, that their calories were also nearly equal. Participants should use one package of flaxseed or placebo every day with their lunch or dinner. Compliance was monitored by asking participants to return any unused package to the researchers at the end of each visit and if they use less than 80% of supplements, they will be excluded from the analysis.

We ask the participants not to change their physical activity, and they were on a weight loss diet during the intervention. The weight

loss diet was designed based on body composition of participants. First, the basic energy expenditure of person was calculated, Then the physical activity level and thermic effect of food were added to it, finally to achieve a weight reduction, the total energy was reduced by 500 Kcal.

To assess the dietary intake and physical activity of subjects we ask them to complete 3-day food records (A weekend and 2 day of the week) and physical activity records as metabolic equivalents at the beginning and in the end of intervention. Daily calorie intake was calculated by nutritionist IV software (First Databank, San Bruno, CA).

The weight of participants was measured with the minimum dress using the Omron Digital Scales Model BF511 with a precision of 100 grams. The fat mass and muscle mass were also measured using the same device. Height was measured in standing position, without shoes with leg heels sticking to the wall by measuring tape with a precision of 0.1 cm. Waist circumference (WC) of individuals was also measured at each visit using a tape meter measuring 0.1 cm in the smallest space between the last rib and the iliac bone.

The normality of data distribution was assessed by using the Kolmogorov–Smirnov test. To compare variables between groups Paired T-test and independent T-test were used. All statistical analyses were conducted by SPSS software, version 22, and P -value > 0.05 was considered to be statistically significant.

Ethical considerations

This study was approved by Committee of Ethics in Research of Shahid Sadoughi University of Medical Sciences, Yazd, Iran with number of IR.SSU.SPH.REC. 1395.140, and it was registered in the Iranian Clinical Trial Registration Center (www.irct.ir) with IRCT2017021110826N22 code. In addition at the beginning of the study, all patients completed written consent.

Results

Initially 83 participants were screened for inclusion criteria. Fifteen subjects were excluded due to lack of our inclusion criteria. Participants were randomly assigned to intervention (n=34) and control (n=34) groups, during the intervention period 6 subjects were dropped out for pregnancy (n=3) and personal reasons (n=3). Finally our analysis was conducted on 62 participants (Figure 1). The initial characteristics of the participants at baseline in both groups were summarized in Table 1. There were no significant differences in age, height, weight, BMI, waist circumference, percent of body fat and muscle, visceral fat, physical activity level and total energy intake between groups. According to 3 day food record and physical activity questionnaire that collected at baseline and end of the study there were significant reduction in energy intake in each group because of weight loss diet, (P -value ≤ 0.001) (Table2), while no significant difference was reported for levels of physical activity after 12 weeks of intervention.

Table 1. Baseline characteristics of study participants

Variable	Intervention group (n=32)	Control group (n=30)	P -value
Age (years)	29.59 (± 5.75)	30.33 (± 6.93)	0.64 ^a
Height (cm)	159.95 (± 6.74)	159.66 (± 5.62)	0.85 ^a
Weight (kg)	80.49 (± 11.74)	82.71 (± 14.6)	0.51 ^a
BMI (kg/m ²)	31.55 (± 5.06)	32.40 (± 5.08)	0.51 ^a
Waist circumference (cm)	102.78 (± 11.05)	105.26 (± 10.30)	0.37 ^a
Percent of fat	45.94 (± 5.09)	46.90 (± 4.25)	0.42 ^a
Percent of muscle	23.04 (± 2.30)	22.96 (± 1.81)	0.87 ^a
Percent of visceral fat	7.06 (± 1.36)	7.63 (± 1.58)	0.12 ^b
energy intake (kcal/day)	1931.25 (± 225.31)	1880 (± 238.38)	0.38 ^a
Physical activity level (met-minute/week)	2089.40 (± 47.26)	2093.73 (± 47.75)	0.72 ^a

a: independent T-test

b: Mann-Whitney U

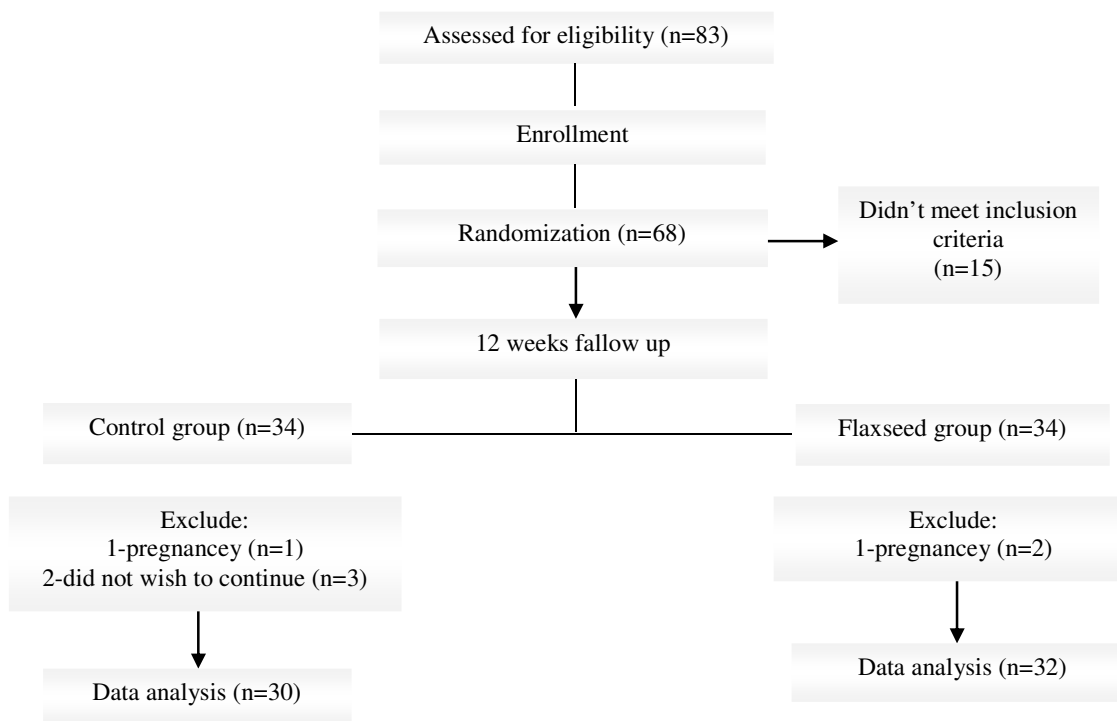


Figure 1. The CONSORT follo diagram of sampling

There was no meaningful difference regarding energy intake and physical activity between groups at the end of trial. The mean changes of anthropometric indices were depicted in Table 3. Our analysis showed that mean decrease in BMI was different between two groups (P -value= 0.04) and in regards of weight reduction was marginally significant after 12 weeks (P -value= 0.05). While the rest of variables such as waist circumference, percentage of body fat, muscle and visceral fat did not significantly change.

Discussion

This randomized, double blinded, controlled clinical trial showed that co-administration of flaxseed with weight loss diet can reduce BMI and weights of patients with PCOS more remarkable than weight loss diet with placebo. To our knowledge, this study is the first research of flaxseed supplementation on anthropometric indices among women with PCOS.

The results of one study (25) that investigated the effects of flaxseed supplementation in metabolic syndrome management illustrated that body weight, WC and BMI reduced significantly greater in flaxseed group rather than control group. In addition, the results of another study reported that the change in body weight and BMI during the treatment period was significantly different between the control group and flaxseed groups in type 2 diabetes patients (19).

Regarding to BMI and waist circumference, the results of Mandasescu et al. (26), that assessed the effect of supplementation with 20 grams of flaxseed with a hypolipidic diet in hyperlipidaemic individuals for 60 days showed no significant differences in BMI change. Also, the results of Machado et al (27).

Study that evaluated the effects of brown and golden flaxseed in overweight adolescents showed no significant differences in the groups for anthropometric parameters and body composition.

Table 2. Nutritional composition of diet according to 3 days food records in both groups and times assessed

Variable	Time	Intervention group (n=32)	Control group (n=30)	P-value*
Energy (kcal/day)	Initial	225.31 (±1931.25)	238.38 (±1880)	0.38
	Final	221.38 (±1479.68)	171.07 (±1446)	0.50
	P-value**	<0.001	<0.001	
Carbohydrate (g/d)	Initial	18.42 (±81.64)	27.23 (±81.21)	0.94
	Final	19.35 (±80.84)	1.46 (±73.1)	0.08
	P-value**	0.86	0.15	
Protein (g/d)	Initial	51.84 (±274.15)	58.31 (±256.83)	0.21
	Final	62.04 (±171.38)	52.60 (±196.44)	0.09
	P-value**	<0.001	<0.001	
Fat (g/d)	Initial	14.83 (±66.73)	20 (±66.56)	0.97
	Final	1.72 (±57.02)	9.61 (±56.07)	0.79
	P-value**	0.03	0.01	
SFA (g/d)	Initial	3.05 (±18.89)	7.44 (±21.64)	0.06
	Final	4.84 (±21.15)	3.97 (±19.88)	0.26
	P-value**	<0.001	0.29	
MUFA (g/d)	Initial	5.13 (±19.86)	7.66 (±2029)	0.79
	Final	5.09 (±15.12)	3.96 (±15.43)	0.79
	P-value**	0.001	0.002	
PUFA (g/d)	Initial	2.27 (±14.24)	7.22 (±15.41)	0.38
	Final	8.57 (±13.41)	8.53 (±13.39)	0.99
	P-value**	0.60	0.28	
Dietary cholesterol (mg/d)	Initial	136.48 (±306.03)	4.73 (±261.67)	0.09
	Final	98.90 (±186.62)	103.09 (±234.85)	0.06
	P-value**	0.001<	0.17	
Total fiber (g/d)	Initial	2.82 (±12.97)	3.04 (±12.66)	0.67
	Final	1.74 (±16.57)	5.13 (±16.46)	0.76
	P-value**	0.001<	0.001<	

*independent T-test

**paired T-test

Table 3. Anthropometric data, according to study group and time of assessment

Variable	Intervention group (n=32)				Control group (n=30)				P-value**		P-value (change)**
	0 week	12 week	P-value*	Change (%)	0 week	12 week	P-value*	Change (%)	0 week	12 week	
Weight (kg)	80.49 (±11.74)	75.85 (±11.13)	<0.001	-5.73	82.71 (±14.62)	79.36 (±14.02)	<0.001	-4	0.51	0.27	0.05
BMI (kg/m ²)	31.55 (±5.06)	29.66 (±4.70)	<0.001	-5.89	32.40 (±5.08)	31.09 (±5.05)	<0.001		0.51	0.25	0.04
Waist circumference (cm)	105.26 (±10.5)	98.95 (±19.78)	<0.001	-6.12	102.78 (±11.5)	98.64 (±11.06)	0.004	-4	0.37	0.93	0.48
Percent of fat	45.94 (±5.09)	42.73 (±5.69)	<0.001	-7.03	46.90 (±4.25)	43.32 (±8.71)	0.009	-7.85	0.42	0.75	0.78
Percent of muscle	23.04 (±2.3)	24.54 (±2.15)	<0.001	6.90	22.96 (±1.89)	23.90 (±2.58)	0.002	4.04	0.78	0.29	0.14
Percent of visceral fat	7.06 (±1.36)	6.56 (±1.41)	<0.001	-7.19	7.63 (±1.58)	7.23 (±1.52)	<0.001	-5	0.13	0.07	0.22

* paired T-test

** Independent sample T-test

In another randomized research that evaluated the effects of daily flaxseed consumption in obese men and women with pre-diabetes showed that body weight, BMI, or percent of fat mass were not significantly different during treatment periods (18). These contrasts in the results of studies may be attributed to the

difference health status of participants(18,26), age, gender and low adherence of participants (27). This decrease in BMI may be due to the high fiber content of flaxseed. Dietary fiber, particularly soluble one, has anti-obesity effects that have been shown to decrease body weight (28). Dietary fiber can prevent weight

gain or improve weight loss by several mechanisms. It can delay gastric emptying, creates a feeling of satiety through absorbing a lot of water (29) and enhances the production of short chain fatty acids that can increase satiety by a variety of mechanisms (30). In addition, dietary fiber can increase viscosity and reduce biliary acid reabsorption, consequently reducing micelle formation and lipid uptake (31). Another mechanism can be attributed to α -linolenic acid (ALA) in flaxseed. As we know, ALA is converted to eicosapentaenoic acid and docosahexaenoic acid in the human body. The mechanisms by which these fatty acids can help improve body composition are suppressing appetite and promoting apoptosis of adipocytes (32). Furthermore, they can alter the expression of genes involved in the regulation of fat metabolism in a number of tissues such as liver, intestine, cardiac muscle and skeletal muscle, and reduce the expression of genes involved in lipogenesis in adipose tissue (32). This study had several strengths, it has controlled clinical trial design, the moderate drop-out rate, in addition we use whole-grain flaxseed instead of flaxseed oil or lignin. The limitation of this study is that, we did not measure the ALA content of erythrocyte membranes, which used as a marker of adherence to flaxseed supplementation. However, we tried to control this problem by follow-up participants and asking them to bring the unused supplements in each visit,

and it was shown that compliance of participants was 88%. There were also some limitations in present study including use of a single dose of flaxseed for intervention; also we could not measure the other PCOS-related factors, such as inflammatory factors, and insulin resistance due to financial constraints. We suggest that double-blinded studies with larger sample size and longer intervention time are needed to clarify the efficacy of flaxseed in weight loss of PCOS patients.

Conclusions

This randomized controlled clinical trial shows that dietary supplementation with flaxseed in PCOS patients can reduce BMI and weight but had no effect on other anthropometric indices.

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Conflict of interest

The authors declare no conflict of interest regarding this study.

References

1. Teede HJ, Misso ML, Deeks AA, Moran LJ, Stuckey BG, Wong JL, et al. Assessment and management of
2. polycystic ovary syndrome: summary of an evidence-based guideline. *Medical Journal of Australia*. 2011;195:S65-112.
3. Amooee S, Parsanezhad ME, Shirazi MR, Alborzi S, Samsami A. Metformin versus chromium picolinate in clomiphene citrate-resistant patients with PCOs: A double-blind randomized clinical trial. *Iranian Journal of Reproductive Medicine*. 2013;11(8):611.
4. Liepa GU, Sengupta A, Karsies D. Polycystic Ovary Syndrome (PCOS) and Other Androgen Excess-Related Conditions: Can Changes in Dietary Intake Make a Difference?. *Nutrition in clinical practice*. 2008;23(1):63-71.
5. McGowan MP. Polycystic ovary syndrome: a common endocrine disorder and risk factor for vascular disease. *Current treatment options in cardiovascular medicine*. 2011;13(4):289-301.
6. O'Connor A, Gibney J, Roche HM. Metabolic and hormonal aspects of polycystic ovary syndrome: the impact of diet. *Proceedings of the Nutrition Society*. 2010;69(4):628-35.
7. Sartor BM, Dickey RP. Polycystic ovarian syndrome and the metabolic syndrome. *The American Journal of The Medical Sciences*. 2005;330(6):336-342.

8. Wild RA. Dyslipidemia in PCOS. *Steroids*. 2012;77(4):295-9.
9. Jamilian M, Samimi M, Mirhosseini N, Ebrahimi FA, Aghadavod E, Talaei R, et al. The influences of vitamin D and omega-3 co-supplementation on clinical, metabolic and genetic parameters in women with polycystic ovary syndrome. *Journal of Affective Disorders*. 2018;238:32-8.
10. Messinis IE, Messini CI, Anifandis G, Dafopoulos K. Polycystic ovaries and obesity. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2015;29(4):479-88.
11. Lim SS, Norman RJ, Davies MJ, Moran LJ. The effect of obesity on polycystic ovary syndrome: a systematic review and meta-analysis. *Obesity Reviews*. 2013;14(2):95-109.
12. Crosignani PG, Colombo M, Vegetti W, Somigliana E, Gessati A, Ragni G. Overweight and obese anovulatory patients with polycystic ovaries: parallel improvements in anthropometric indices, ovarian physiology and fertility rate induced by diet. *Human reproduction*. 2003;18(9):1928-32.
13. Thomson RL, Brinkworth GD, Noakes M, Clifton PM, Norman RJ, Buckley JD. The effect of diet and exercise on markers of endothelial function in overweight and obese women with polycystic ovary syndrome. *Human Reproduction*. 2012;27(7):2169-76.
14. Pilar BC, da Costa Güllich AA, Ströher DJ, Zuravski L, Mezzomo J, Coelho RP, et al. 28-days dietary supplementation with golden flaxseed improves biochemical and oxidative parameters in patients with metabolic syndrome. *Journal of Functional Foods*. 2014;10:232-42.
15. Shim YY, Gui B, Arnison PG, Wang Y, Reaney MJ. Flaxseed (*Linum usitatissimum* L.) bioactive compounds and peptide nomenclature: A review. *Trends in food science & technology*. 2014;38(1):5-20.
16. Mohammadi-Sartang M, Mazloom Z, Raeisi-Dehkordi H, Barati-Boldaji R, Bellissimo N, Totosty de Zepetnek JO. The effect of flaxseed supplementation on body weight and body composition: a systematic review and meta-analysis of 45 randomized placebo-controlled trials. *Obesity Reviews*. 2017;18(9):1096-107.
17. Bassett CM, Rodriguez-Leyva D, Pierce GN. Experimental and clinical research findings on the cardiovascular benefits of consuming flaxseed. *Applied physiology, nutrition, and metabolism*. 2009;34(5):965-74.
18. Ursoniu S, Sahebkar A, Andrica F, Serban C, Banach M, Lipid and Blood Pressure Meta-analysis Collaboration. Effects of flaxseed supplements on blood pressure: A systematic review and meta-analysis of controlled clinical trial. *Clinical nutrition*. 2016;35(3):615-25.
19. Hutchins AM, Brown BD, Cunnane SC, Domitrovich SG, Adams ER, Bobowiec CE. Daily flaxseed consumption improves glycemic control in obese men and women with pre-diabetes: a randomized study. *Nutrition research*. 2013;33(5):367-75.
20. Taylor CG, Noto AD, Stringer DM, Froese S, Malcolmson L. Dietary milled flaxseed and flaxseed oil improve N-3 fatty acid status and do not affect glycemic control in individuals with well-controlled type 2 diabetes. *Journal of the American College of Nutrition*. 2010;29(1):72-80.
21. Yari Z, Rahimlou M, Eslamparast T, Ebrahimi-Daryani N, Poustchi H, Hekmatdoost A. Flaxseed supplementation in non-alcoholic fatty liver disease: a pilot randomized, open labeled, controlled study. *International Journal of Food Sciences and Nutrition*. 2016;67(4):461-9.
22. Barceló-Coblijn G, Murphy EJ, Othman R, Moghadasian MH, Kashour T, Friel JK. Flaxseed oil and fish-oil capsule consumption alters human red blood cell n-3 fatty acid composition: a multiple-dosing trial comparing 2 sources of n-3 fatty acid. *The American Journal of Clinical Nutrition*. 2008;88(3):801-9.
23. Faintuch J, Bortolotto LA, Marques PC, Faintuch JJ, França JI, Ceconello I. Systemic inflammation and carotid diameter in obese patients: pilot comparative study with flaxseed powder and cassava powder. *Nutricion hospitalaria*. 2011;26(1):208-13.
24. Khalatbari Soltani S, Jamaluddin R, Tabibi H, Mohd Yusof BN, Atabak S, Loh SP, Rahmani L. Effects of flaxseed consumption on systemic inflammation and serum lipid profile in hemodialysis patients with lipid abnormalities. *Hemodialysis International*. 2013;17(2):275-81.
25. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Human reproduction*. 2004;19(1):41-7.
26. Yari Z, Rahimlou M, Poustchi H, Hekmatdoost A. Flaxseed supplementation in metabolic syndrome management: a pilot randomized, open-labeled, controlled study. *Phytotherapy Research*. 2016;30(8):1339-44.
27. Mandaşescu S, Mocanu V, Dăscaliţa AM, Haliga R, Nestian I, Stitt PA, et al. Flaxseed supplementation in hyperlipidemic patients. *Revista medico-chirurgicala a societăţii de Medici si naturalisti din Iasi*. 2005;109(3):502-6.
28. Machado AM, de Paula H, Cardoso LD, Costa NM. Effects of brown and golden flaxseed on the lipid profile, glycemia, inflammatory biomarkers, blood pressure and body composition in overweight adolescents. *Nutrition*. 2015;31(1):90-6.

29. Howarth NC, Saltzman E, Roberts SB. Dietary fiber and weight regulation. *Nutrition reviews*. 2001 May 1;59(5):129-39.
30. Kristensen M, Jensen MG. Dietary fibres in the regulation of appetite and food intake. Importance of viscosity. *Appetite*. 2011;56(1):65-70.
31. Sleeth ML, Thompson EL, Ford HE, Zac-Varghese SE, Frost G. Free fatty acid receptor 2 and nutrient sensing: a proposed role for fibre, fermentable carbohydrates and short-chain fatty acids in appetite regulation. *Nutrition research reviews*. 2010;23(1):135-45.
32. Kristensen M, Jensen MG, Aarestrup J, Petersen KE, Søndergaard L, Mikkelsen MS, et al. Flaxseed dietary fibers lower cholesterol and increase fecal fat excretion, but magnitude of effect depend on food type. *Nutrition & metabolism*. 2012;9(1):8.
33. Buckley JD, Howe PR. Anti-obesity effects of long-chain omega-3 polyunsaturated fatty acids. *Obesity reviews*. 2009;10(6):648-59.