



## **Effect of flaxseed consumption on central obesity, serum lipids, and adiponectin level in overweight or obese women: A randomised controlled**

Downloaded from: <https://research.chalmers.se>, 2026-04-20 07:36 UTC

Citation for the original published paper (version of record):

Motlagh, H., Aalipanah, E., Mazidi, M. et al (2021). Effect of flaxseed consumption on central obesity, serum lipids, and adiponectin level in overweight or obese women: A randomised controlled clinical trial. *International Journal of Clinical Practice*, 75(10). <http://dx.doi.org/10.1111/ijcp.14592>

N.B. When citing this work, cite the original published paper.

## ORIGINAL PAPER

## Metabolism &amp; Endocrinology

# Effect of flaxseed consumption on central obesity, serum lipids, and adiponectin level in overweight or obese women: A randomised controlled clinical trial

Hoda Ahmadniay motlagh<sup>1</sup> | Erfaneh Aalipanah<sup>1</sup> | Mohsen Mazidi<sup>2</sup> | Shiva Faghih<sup>1</sup> 

<sup>1</sup>Nutrition Research Center, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>2</sup>Department of Biology and Biological Engineering, Food and Nutrition Science, Chalmers University of Technology, Gothenburg, Sweden

## Correspondence

Shiva Faghih, Department of Community Nutrition, School of Nutrition and Food Sciences, Razi Boulevard, Shiraz, Iran.  
Email: shivafaghih@gmail.com

## Abstract

**Background:** Flaxseed may be beneficial for the management of obesity due to its high content of alpha-linolenic acid, fibre, and lignans.

**Objective:** We aim to evaluate the effect of flaxseed consumption on serum lipids, adiponectin, leptin, and anthropometric indices in overweight or obese women.

**Methods:** This randomised controlled clinical trial involved 60 overweight or obese women. Participants were randomly allocated into two groups: (a) a balanced diet plus 30 g/day milled flaxseed (as treatment group) and (b) a balanced diet plus 30 g/day milled rice (as control group). Anthropometric indices, serum lipids, leptin, and adiponectin level were measured at baseline and at the end of intervention after 12 weeks.

**Results:** After 12 weeks of intervention, there was significantly higher reduction rate in waist circumference (WC) and waist-to-hip ratio (WHR) (both  $P < .05$ ) in the flaxseed-consuming group compared with the control group. Moreover, adiponectin level was significantly increased from  $(12.11 \pm 7.1)$  to  $(17.15 \pm 6.1)$  in the flaxseed-consuming group compared with the control group from  $(12.48 \pm 4.7)$  to  $(12.01 \pm 5.8)$  ( $P = .002$ ). However, no significant difference was observed in serum lipid level in the study groups before and after the intervention (all  $P > .05$ ).

**Conclusion:** Flaxseed consumption may improve adiposity markers, such as adiponectin level. Thus, flaxseed consumption could be an adjunctive therapy to attenuate central obesity. Serum lipid profile has not changed meaningfully after flaxseed consumption.

## 1 | INTRODUCTION

Obesity is one of the most important inflammatory diseases, and its prevalence is increasing across the world.<sup>1</sup> Obesity and overweight are associated with increased risk of several chronic disorders and certain types of cancers.<sup>2</sup> Adipokines as bioactive mediators which stimulate the adipocyte function and regulate multiple metabolic reactions are secreted by adipose tissue which is an active endocrine organ. Adipose tissue also regulates fat mass.<sup>3,4</sup> There are numerous adipokines related to obesity, such as omentin-1, neuregulin 4, adiponectin, and leptin. Neuregulin 4 (Nrg4) has a main role in the

modulation of glucose and lipid metabolism and energy balance.<sup>5</sup> Previous findings are reporting meaningful lower serum omentin-1 level in morbidly obese women in comparison with normal weight women.<sup>6</sup> Also, other studies show that circulating serum adiponectin concentrations are positively correlated with plasma omentin-1. They speculate that an inverse relationship between obesity and both omentin-1 and adiponectin level may implement similar regulation.<sup>3</sup>

It is found that expression and secretion of adiponectin within the adipose tissue decrease in obese individuals.<sup>7</sup> Adiponectin is the most prevalent adipokine which has beneficial effects on

metabolism, fatty acids catabolism, low-density lipoprotein cholesterol (LDL-C) oxidation, insulin sensitivity, and suppression of inflammation.<sup>8,9</sup> Moreover, leptin as another adipokine has an energy balance regulation role, various hormonal function, and highly correlation with body fat mass.<sup>10</sup>

Flaxseed or linseed (*Linum usitatissimum* L. seed), known as a functional food, contains healthy components such as alpha-linolenic acid (ALA), lignans, dietary fibres, and a variety of antioxidants and phytoestrogens.<sup>11,12</sup>

Flaxseed lignans have numerous health benefits; for instance, they can regulate expression and secretion of adipokines such as adiponectin and leptin.<sup>13-16</sup> The other component, ALA, is known as anti-inflammatory, antithrombotic, and antiarrhythmic agent.<sup>15,17,18</sup> ALA can deposit into adipose tissue where it may affect adipose tissue function and adipokine secretion.<sup>7</sup> Besides, flaxseed is a rich source of phytoestrogens with potential benefits including cardioprotective and endocrine regulation effects.<sup>19,20</sup> It has been proposed that these components modify blood lipids level mainly through regulating the gene expression of enzymes involved in the fatty acids metabolism.<sup>21-23</sup> Previous studies in experimental models found an attenuating effect of flaxseed supplementation on serum lipids abnormalities and adiponectin and leptin secretion.<sup>24-27</sup> However, the findings from clinical trials are conflicting.<sup>28,29</sup>

Therefore, in order to find the beneficial effects of whole flaxseed supplementation as an adjunct therapy to balanced diet on serum adipokines, body weight, waist circumference (WC), and lipid level, we conducted the present trial on overweight or obese women.

## 2 | METHODS

### 2.1 | Study participants

The present study is a randomised, double-blind, placebo-controlled clinical trial in which 60 overweight or obese women aged from 25 to 50 years with a body mass index (BMI) of 25-35 kg/m<sup>2</sup> and regular menstrual cycles participated. Participants were excluded if they met one or more of the following criteria: (a) having any chronic disease such as cardiovascular, renal, liver, and infectious diseases as well as cancer, diabetes mellitus, and thyroid disorders; (b) have a history of allergy to flaxseed; (c) being pregnant or nursing; (d) taking any medications that could affect lipid metabolism such as steroids, antihyperglycaemic agents, and statins; (e) taking supplements including multivitamins, minerals, and also herbal preparations; and (f) history of smoking or alcohol and drug abuse. The minimum sample size estimated for each group was 25 at a power (1 -  $\beta$ ) of 80% and  $\alpha = 0.05$  for a two-arm parallel study with two-tailed testing to detect a difference of 4 ng/mL in serum adiponectin concentration with a standard deviation of 5 ng/mL, obtained from a previous study.<sup>30</sup> Assuming a 10% drop out, a total number of 60 participants were considered for this study. The study protocol, risks, and benefits

### What's known

- Findings from previous clinical trials are still controversial. Therefore, we aimed to supplement whole flaxseed among overweight or obese women to understand its effect on serum adipokines (adiponectin and leptin), anthropometric indices, and lipid profile.

### What's new

- Our findings show that flaxseed potentially can reduce visceral obesity and decrease the risk of obesity through increasing adiponectin concentration.

were clarified to the participants, and they signed a written informed consent at the time of enrolment. This study was approved by the ethics committee of Shiraz University of Medical Sciences, Shiraz, Iran (registration No. IR.SUMS.REC.1395.22), and was registered at Iranian Registry of Clinical Trials website (IRCT2016050327733N1).

### 2.2 | Study design

The participants were randomly assigned to consume a balanced diet containing 30 g/day brown milled flaxseed (flaxseed group: n = 30) or 30 g/day raw milled rice (control group: n = 30) for 12 weeks. Random allocation was performed using blocked randomisation method. The study participants, investigators, and outcome assessors were blinded to the type of interventions into which the individuals were allocated. The shape, colour, and texture of milled rice were similar to the flaxseed product. For this purpose, we added edible colours to milled rice at the laboratory of pharmacy in Shiraz University of Medical Sciences. Calorie requirement of each subject was estimated using the estimated energy requirement (EER) equation<sup>31</sup> All diets consist of 55% carbohydrates, 18% proteins, and 27% fats. Also, we provided a portion-size descriptive booklet of common foods for each participant. All the brown flaxseed products were purchased from registered herb provider Maleki Commercial Co. and stored in a cool, dark, and dry place. They were milled within a week before delivery to the patients. Participants were asked to mix the powder with their dessert or daily meals (eg, yogurt, salads, or soup) preferably for lunch. Moreover, participants were advised to maintain their usual physical activity during the intervention.

To assess the participants' adherence to the intervention, we asked them to bring back any unused flaxseed/placebo at each follow-up visit, so the investigators can estimate their adherence to supplementation during the study period. Participants were excluded if they consumed less than 90% of flaxseed/placebo. Follow-up assessments were done every 4 weeks (on 4th, 8th, and 12th weeks) in which participants were provided with enough supplement for the next four weeks. All measurements including anthropometric

indices, blood level of lipid profiles, leptin, adiponectin, and dietary intakes and physical activities were performed at the baseline and at the end of the study (Week 12).

### 2.3 | Assessment of anthropometric indices and blood lipid profile

Anthropometric indices (height, weight, and waist and hip circumferences) were measured for each participant at the baseline (Day 0) and at the end of the study (Week 12). Height was measured to the nearest 0.1 cm using a stadiometer (Seca 214 portable stadiometer) without shoes. Weight was recorded to the nearest 0.1 kg in light clothes, using a digital scale (Seca 881). BMI was calculated as body weight (kg)/height squared ( $m^2$ ). Waist circumference was measured to the nearest 0.1 cm by a nonstretch measuring tape in standing position, between the lower rib and iliac crest.<sup>32</sup> To assess the serum lipids, 5 cc of blood sample was collected from each participant after 12 hours of fasting between 7:00 and 8:00 AM. The whole blood was centrifuged, and the obtained serum was kept at  $-70^\circ\text{C}$  until the end of study for the further analysis. Serum concentration of lipid profile including triglyceride (TG), total cholesterol (TC), LDL-C, and high-density lipoprotein cholesterol (HDL-C) were measured by the colorimetric method using commercial kits (Pars Azmoon Co.). Serum leptin and adiponectin concentration were measured using enzyme-linked immunosorbent assay (ELISA) by IBL kit (Pars Azmoon Co.).

### 2.4 | Assessment of dietary intake and physical activity

Energy and nutrients intake were estimated using 24-hour dietary recalls for three nonconsecutive days (two weekdays and one weekend day) and then were analysed using Nutritionist IV (N-Squared Computing). Physical activity was evaluated using international physical activity questionnaire (IPAQ) for three days (two regular days and one weekend day). It was expressed as MET.h/day by multiplying the time of each physical activity by its relative Metabolic Equivalent Task (MET).

### 2.5 | Statistical methods

Normality of each variable was tested by Kolmogorov–Smirnov. Pre- and post-treatment values were compared within groups using paired *t* test. Between-groups comparison were made using independent sample *t* test. Effects of potential confounding factors were adjusted by the analysis of covariance. Also, the analysis of covariance (ANCOVA) was used to adjust the effect of confounding variables (BMI, WHR, physical activity, and energy intake).  $P < .05$  was considered as statistically significant. SPSS version 22 (SPSS, Inc) was used for the analysis.

## 3 | RESULTS

A total of 100 women enrolled, and after eligibility checking, 60 individuals entered the study. During the follow-ups, eight participants were excluded (one in the flaxseed-consuming group and seven in the control group) due to personal reasons. Finally, 52 subjects, 29 of flaxseed group and 23 of control group, completed the trial (Figure 1).

Baseline characteristics of participants are shown in Table 1. There were no significant differences in height, weight, BMI, and waist and hip circumferences of participants between flaxseed and control groups at the beginning of the study.

No significant differences were observed between the two groups in mean daily intake of energy, protein, carbohydrate, fat, saturated fatty acids (SFAs), polyunsaturated fatty acids (PUFAs), monounsaturated fatty acids (MUFAs), and omega-6 fatty acids at the beginning and the end of study. However, the amount of ALA and dietary fibre intake increased significantly in the flaxseed group ( $P < .001$  and  $P = .01$ , respectively). At the end of the study, ALA intake was significantly different between the two groups ( $P < .001$ ) (Table 2).

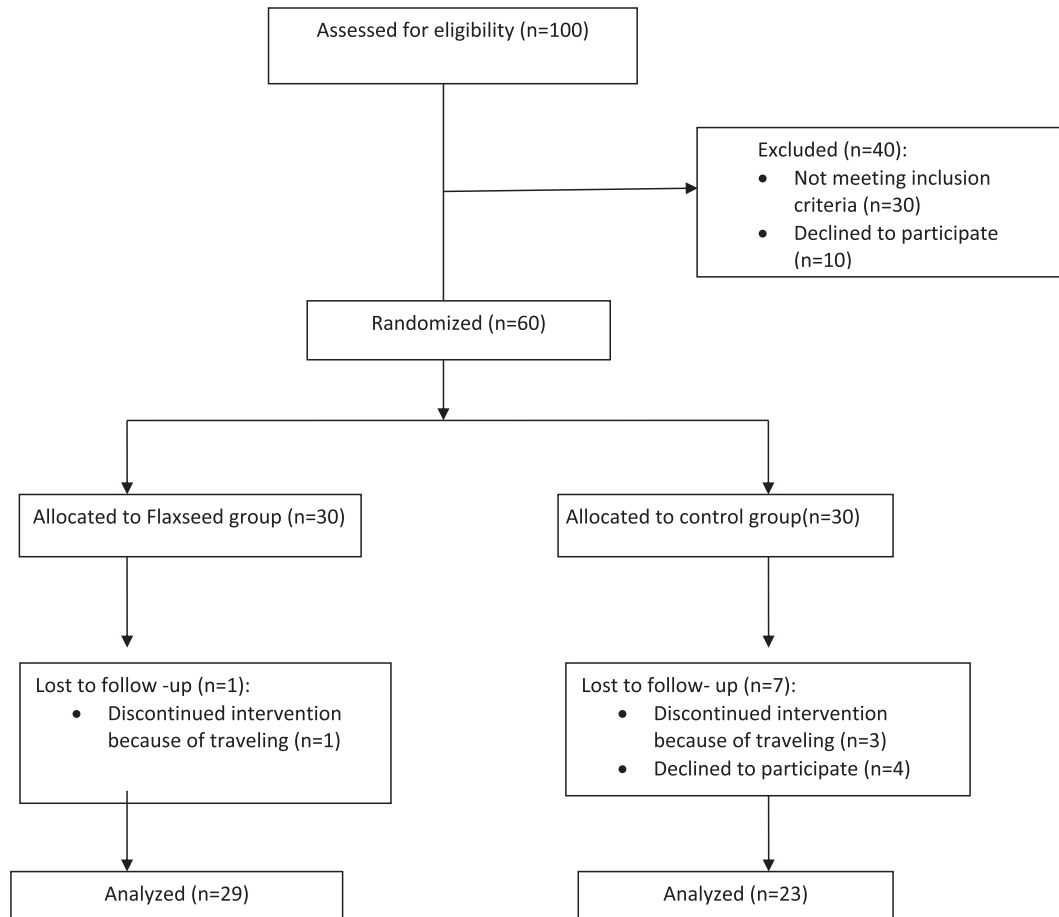
As shown in Table 3, there were significant reductions in serum TG and TC in the flaxseed group after 12 weeks of the intervention ( $P < .001$  for all), whereas no significant decrease was observed in the control group. In addition, no significant changes were observed in serum HDL-C and LDL-C within each group after 12 weeks. There was no significant difference in serum TC, TG, LDL-C, and HDL-C between the study groups at baseline and at the end of study.

Moreover, weight, BMI, waist and hip circumferences ( $P < .001$  for all), and WHR ( $P = .003$ ) decreased significantly in flaxseed group. Reductions of waist circumference ( $P = .001$ ) and WHR ( $P = .021$ ) were significantly more in flaxseed group compared with the control group. After the follow-up period, adiponectin concentration increased significantly in flaxseed group ( $P < .001$ ) which was statistically significant more than the control group ( $P = .002$ ). In addition, leptin concentration decreased significantly only in the flaxseed group; however, this reduction was not statistically significant compared with the control group ( $P = .291$ ).

## 4 | DISCUSSION

We examined the effects of flaxseed consumption on anthropometric indices, serum leptin, lipids, and adiponectin in overweight or obese women. Our findings indicate that the flaxseed group as treatment group has significant reduction in weight and anthropometric indices such as waist and hip circumferences and WHR. However, flaxseed consumption does not result in statistically significant effect on lipid profile compared with the placebo group as the control group.

Our data suggesting the benefits of flaxseed consumption on central adiposity compared with control group are in line with the previous studies.<sup>15</sup> Park et al<sup>33</sup> found that flaxseed lignan (primarily



**FIGURE 1** Flow chart of participants through the study

Variable	Flaxseed group (n = 29)	Control group (n = 23)	P
Age (y)	38.28 ± 7.46	41.74 ± 7.20	.097
Height (m)	1.58 ± 0.04	1.54 ± 0.05	.423
Weight (kg)	76.67 ± 7.40	74.19 ± 8.52	.268
BMI (kg/m <sup>2</sup> )	30.67 ± 2.83	30.92 ± 2.84	.757
WC (cm)	98.51 ± 8.11	100.21 ± 7.01	.430
WHR	0.87 ± 0.05	0.89 ± 0.07	.206
Physical activity (h/day)	27.79 ± 2.18	27.44 ± 2.22	.571
Energy (kcal/day)	1.594.16 ± 516.74	1.539.67 ± 528.63	.711
Total carbohydrates (g/day)	248.81 ± 81.58	249.60 ± 91.43	.974
Total fat (g/day)	45.84 ± 21.52	41.21 ± 16.16	.395
Total protein (g/day)	51.97 ± 18.89	48.65 ± 19.80	.543

Note: All values are mean ± SD.

Abbreviations: BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio.

<sup>a</sup>Independent sample *t* test.

secoisolariciresinol diglucoside [SDG]) might provide beneficial effects on obesity via reducing weight and fat accumulation. Wu et al<sup>34</sup> showed that flaxseed supplementation (30 g/day) for 12 weeks reduces central obesity, weight, and waist circumference when combined with healthy lifestyle counselling. Conversely, Pineda et al<sup>35</sup> reported no significant changes in weight, BMI, and waist circumference following

supplementation with 30 g/day flaxseed for 8 weeks. We assume that the duration of the study (less than 12 weeks) might be the reason why no significant anthropometric effects were observed.<sup>36</sup>

The exact mechanism by which flaxseed can decrease abdominal obesity remains unclear. Some studies have suggested that a diet rich in PUFAs may result in reduction of abdominal obesity,<sup>34</sup>

**TABLE 2** Dietary intake of participants at baseline and week 12

Variables	Flaxseed group			Control group			
	Baseline	Week 12	<i>p</i> <sup>b</sup>	Baseline	Week 12	<i>p</i> <sup>b</sup>	<i>p</i> <sup>a</sup>
Energy (kcal)	1.594.16 ± 516	1.554.85 ± 516	0.767	1.539.67 ± 528	1.495.03 ± 437	.780	.593
Total fat (g/day)	45.84 ± 21.52	42.06 ± 21.56	0.423	41.21 ± 16.16	42.07 ± 16.00	.876	.416
Total protein (g/day)	51.97 ± 18.89	52.33 ± 23.18	0.951	48.65 ± 19.80	48.53 ± 13.55	.983	.954
Total carbohydrates (g/day)	248.81 ± 81.58	247.65 ± 82.82	0.901	249.60 ± 91.43	247.17 ± 78.49	.990	.944
Dietary fibre (g/day)	13.16 ± 6.71	15.52 ± 5.91	0.011	13.82 ± 5.70	12.80 ± 5.41	.399	.121
SAFAs (g/day)	12.71 ± 7.02	12.51 ± 7.61	0.920	11.70 ± 5.60	13.28 ± 7.32	.479	.605
MUFAs (g/day)	13.55 ± 7.32	12.40 ± 7.38	0.466	12.23 ± 6.51	12.40 ± 6.30	.938	.722
PUFAs (g/day)	14.02 ± 8.86	12.04 ± 7.58	0.245	11.98 ± 6.38	11.83 ± 4.61	.930	.320
Alpha linolenic acid	0.191 ± 0.16	0.263 ± 0.17	0.001	0.190 ± 0.20	0.090 ± 0.10	.015	<.001

Note: All values are mean ± SD.

Abbreviations: MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; SAFAs, saturated fatty acids.

<sup>a</sup>Independent sample *t* test.

<sup>b</sup>Paired *t* test.

**TABLE 3** Comparison of anthropometric indices and biochemical factors between flaxseed and control groups

Variables	Flaxseed group			Control group			
	Baseline	Week 12	<i>p</i> <sup>b</sup>	Baseline	Week 12	<i>p</i> <sup>b</sup>	<i>p</i> <sup>a</sup>
Weight (kg)	76.67 ± 7.41	74.31 ± 7.5	<.001	74.19 ± 8.5	73.23 ± 8.6	.042	.039
BMI (kg/m <sup>2</sup> )	30.67 ± 2.8	29.72 ± 2.9	<.001	30.92 ± 2.8	30.52 ± 3.03	.043	.051
WC (cm)	98.51 ± 8.1	93.17 ± 5.9	<.001	100.21 ± 7.01	99.39 ± 7.01	.197	<.001
WHR	0.87 ± 0.05	0.84 ± 0.04	.003	0.89 ± 0.07	0.89 ± 0.06	.586	.021
Adiponectin (ng/mL)	12.11 ± 7.1	17.15 ± 6.1	.001	12.48 ± 4.7	12.01 ± 5.8	.641	.002
Leptin (ng/mL)	53.76 ± 17.2	45.84 ± 20.9	.012	51.48 ± 20.6	49.38 ± 18.8	.270	.291
TG (mg/dL)	160.55 ± 47.3	123.28 ± 30.4	<.001	150.86 ± 39.2	142.36 ± 42.7	.072	.561
TC (mg/dL)	192.07 ± 33.9	174.55 ± 30.7	<.001	185.61 ± 28.2	183.26 ± 31	.504	.322
LDL-C (mg/dL)	114.97 ± 25.3	112.17 ± 27.7	.387	114.77 ± 23.9	113.22 ± 26.4	.665	.795
HDL-C (mg/dL)	48.34 ± 7.2	47.72 ± 6.4	.567	52.48 ± 21.9	52.61 ± 21.3	.882	.602

Note: All values are mean ± SD.

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-to-hip ratio.

<sup>a</sup>Independent sample *t* test.

<sup>b</sup>Paired *t* test.

because increasing PUFAs in the diet might act as an important modulator for body fat deposition. Also, according to the previous studies, the high content of SDG can reduce or prevent obesity through increased fat oxidation.<sup>37,38</sup>

Very few randomised clinical trials have examined the effect of flaxseed supplementation on blood adiponectin and leptin concentration in people who are healthy.<sup>30,39,40</sup> Some of experimental studies reported remarkable effects of flaxseed on leptin and adiponectin<sup>7,37</sup> and also altered circulating level of these hormones following supplementation with flaxseed.<sup>7,22</sup>

In the present study, the serum concentration of adiponectin increased significantly in the flaxseed-consuming group compared with the control group. Cassani et al<sup>41</sup> also showed that

weight loss diet through 60 g/day flaxseed supplementation in men with cardiovascular risk factors could improve adiponectin levels. Contrary to our findings, Hutchins et al's<sup>42</sup> study on prediabetes men and women with flaxseed supplementation shows no significant change in adiponectin level. This contradictory finding might be due to the association of adiponectin with insulin resistance. According to other studies, response of adiponectin to an intervention might be quite different in insulin-resistant population than in insulin-sensitive individuals.<sup>43-45</sup> Furthermore, Nelson et al<sup>30</sup> found a decrease in adiponectin level of healthy overweight adults treated with flaxseed oil for 8 weeks which is consistent with our findings. The present study demonstrated that this effect might be attributed to a reduced demand for adiponectin's

anti-inflammatory actions in face of high omega-3 fatty acids. In fact, in the case of adiponectin, the dosage of flaxseed given in different studies is critical, because the insulin sensitising and anti-inflammatory effects of ALA (the main component of flaxseed products) might deactivate the effects of adiponectin and result in a decreased demand for adiponectin.<sup>46</sup> On the other hand, some researchers did not find significant correlation between PUFAs and circulating level of adiponectin.<sup>47</sup> Therefore, they suggested ALA as an activator of peroxysomal proliferator activated receptor gamma (PPAR $\gamma$ ) in adipocytes.

All in all, the adiponectin-inducing effect of flaxseed might be because of its rich content of ALA. It seems that ALA is involved in increasing adiponectin secretion through stimulating transcription receptor PPAR $\gamma$ .<sup>39</sup> PPAR $\gamma$  is one of the key transcription factors which regulates adipogenesis, and it can also control expression of adiponectin, leptin, and glucose transporter type 4 (GLUT4).<sup>48</sup> Moreover, SDG in flaxseeds could act as a PPAR $\gamma$  agonist and regulate adiponectin through an increase in PPAR $\gamma$  DNA binding activity in adipocytes.<sup>37</sup> Therefore, flaxseed could probably be an effective component which can alter the metabolic process in adipose tissues in favour of lower visceral fat accumulation.

It should be considered that different outcomes from flaxseed intervention may be related to interindividual differences involved in the metabolic processes, resulting in altered adiponectin level in circulation.

Previously high concentration of leptin in obese individuals has been reported in several studies.<sup>49</sup> We found reduction in serum leptin of both groups. However, this reduction was only significant in the flaxseed group. McCullough et al<sup>7</sup> have reported that leptin expression is positively correlated to ALA content of flaxseed; thus, its effects on obesity-related diseases might be due to a change in leptin expression; however, in a study by Taylor et al<sup>36</sup> which investigated the effect of dietary milled flaxseed and flaxseed oil on patients with type 2 diabetes, leptin concentration has not changed. Zhou et al<sup>50</sup> have suggested that insulin resistance might be correlated with depressed desaturase enzyme activity; thus, these patients are not able to transform ALA to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). This could be the reason Taylor et al study could not show beneficial effect of omega-3 PUFAs from flaxseed on leptin level.

Our finding that flaxseed consumption has not a significant effect on lipid profile is consistent with the report by Kaul et al<sup>51</sup>, which shows that among apparently healthy adults, intake of 2 g/day flaxseed oil for 12 weeks has no significant effect on the lipid parameters in blood. In contrast, several clinical trials that have been conducted in individuals with elevated level of blood lipids reported the beneficial effect of flaxseed supplementation on reduction of serum lipids.<sup>21,52-55</sup> Torkan et al<sup>54</sup> showed that consumption of 30 g/day of flaxseed powder in hyperlipidaemic patients for 40 days caused a significant decrease in TG, TC, and LDL-C compared with the placebo-consuming group. Moreover, another clinical trial conducted in postmenopausal women with hypercholesterolaemia shows a significant reduction in TC and

LDL-C compared with the placebo, following the flaxseed supplementation at the dosage of 30 g/day for 12 weeks.<sup>53</sup> In the present study, the mean serum concentrations of lipids in both study groups were within the normal ranges, which could be the reason for disagreement of our results with the previous studies. Not all of the clinical trials that were conducted on patients with hyperlipidaemia resulted in significant effects of flaxseed on blood lipids outcomes. Paschos et al<sup>56</sup>, for example, found that the intake of 15 mL of flaxseed oil for 12 weeks had no significant effect on lipid parameters in patients with dyslipidaemia. Also, in a study amongst 62 individuals with baseline values of LDL-C between 130 and 200 mg/dL, intake of 40 g/day of flaxseed-containing baked products for 10 weeks did not significantly change LDL-C, even caused a significant decrease in HDL-C in men, however, not in women.<sup>57</sup> Besides the initial serum lipids, it should be noted that some methodological differences such as small sample size, short duration of follow-up, type of the flaxseed product, the dosage of supplementation, and the degree of adherence to the intervention may be the possible reasons for the discrepancy between the studies.

Several mechanisms have been suggested for the beneficial effects of flaxseed on blood lipids. Flaxseed has a high content of ALA, a plant base omega-3 fatty acid, as well as its highest amount of lignin among the plant foods.<sup>58</sup> It has been shown that these compounds could reduce TC and LDL-C by reducing the gene expression of sterol regulatory element-binding protein 1-c (SREBP-1c), which is involved in synthesis of fatty acids, and increasing the mRNA expression of peroxisome proliferator-activated receptor- $\alpha$  (PPAR- $\alpha$ ), which stimulates  $\beta$ -oxidation of fatty acids.<sup>21,23</sup> In addition, flaxseed is a rich source of dietary fibres, both soluble and insoluble. Dietary fibre is proposed to reduce blood cholesterol mainly through increasing bile acid excretion, synthesis of short-chain fatty acids, and insulin sensitivity.<sup>59</sup>

This study has some noticeable strengths including the use of an appropriate placebo for flaxseed. In addition, we used whole grain flaxseed instead of flaxseed oil or lignan. Nonetheless, our findings should be considered in light of several limitations. In particular, our sample size was small. Also, the present study cannot distinguish if the effects are directly due to ALA or lignan in flaxseeds. Moreover, although some studies found significant effect of flaxseed on lipid profile, our study finds no such effect. The possible reasons for insignificant results following the whole flaxseed product consumption may be due to the differences in the quality of the test product, the amount of bioactive components, and their bioavailability in the presence of some compounds such as glycosides and phytic acid in the flaxseed products.<sup>57</sup>

## 5 | CONCLUSION

Overall, daily consumption of 30-g milled flaxseed for 12 weeks amongst overweight or obese women had no significant effect on blood lipid parameters. However, flaxseeds which contains PUFAs

and lignan could potentially reduce visceral obesity and is therefore a promising food to help decrease the risk of obesity through increasing the adiponectin concentration.

## ETHICS

All participants signed the written informed consent before initiating the study. The study was approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (registration no. IR.SUMS.REC.1395.22), and was registered at Iranian Registry of Clinical Trials website (IRCT2016050327733N1).

## ACKNOWLEDGEMENTS

We thank the participants for their involvement in this study. This manuscript funded by Shiraz University of Medical Sciences, Shiraz, Iran (grant no. IR.SUMS.REC.1395.22).

## DISCLOSURES

The authors declare no relevant conflict of interest.

## AUTHOR CONTRIBUTIONS

H. A. and S. F. contributed to study conception and data collection. H. A., S. F., E. A., and M. M. contributed to analysis and interpretations. H. A., S. F., and M. M. contributed to manuscript preparation and revision for intellectual content. All authors read and approved the final version prior to submission.

## ORCID

Shiva Faghih  <https://orcid.org/0000-0002-0554-538X>

## REFERENCES

- Woo JG, Guerrero ML, Ruiz-Palacios GM, et al. Specific infant feeding practices do not consistently explain variation in anthropometry at age 1 year in urban United States, Mexico, and China cohorts. *J Nutr*. 2013;143(2):166-174.
- Vriz O, Lu H, Visentin P, Nicolosi L, Mos L, Palatini P. Gender differences in the relationship between left ventricular size and ambulatory blood pressure in borderline hypertension: the HARVEST Study. *Eur Heart J*. 1997;18(4):664-670.
- Escoté X, Gómez-Zorita S, López-Yoldi M, et al. Role of omentin, vaspin, cardiotrophin-1, TWEAK and NOV/CCN3 in obesity and diabetes development. *Int J Mol Sci*. 2017;18(8):1770.
- Frühbeck G, Gómez-Ambrosi J. Adipose tissue structure function and metabolism. In: Caballero B, ed. *Encyclopedia of Human Nutrition*. Amsterdam, the Netherlands: Elsevier; 2013:1-13.
- Tutunchi H, Ostadrahimi A, Hosseinzadeh-Attar M-J, Miryan M, Mobasser M, Ebrahimi-Mameghani M. A systematic review of the association of neuregulin 4, a brown fat-enriched secreted factor, with obesity and related metabolic disturbances. *Obes Rev*. 2020;21:e12952.
- Auguet T, Quintero Y, Riesco D, et al. New adipokines vaspin and omentin. Circulating levels and gene expression in adipose tissue from morbidly obese women. *BMC Med Genet*. 2011;12:60.
- McCullough RS, Edel AL, Bassett CM, et al. The alpha linolenic acid content of flaxseed is associated with an induction of adipose leptin expression. *Lipids*. 2011;46(11):1043-1052.
- Haluzik M, Parizkova J, Haluzik M. Adiponectin and its role in the obesity-induced insulin resistance and related complications. *Physiol Res*. 2004;53(2):123-130.
- Iacobellis G, Pistilli D, Gucciardo M, et al. Adiponectin expression in human epicardial adipose tissue in vivo is lower in patients with coronary artery disease. *Cytokine*. 2005;29(6):251-255.
- Zhou Y, Rui L. Leptin signaling and leptin resistance. *Front Med*. 2013;7(2):207-222.
- Goyal A, Sharma V, Upadhyay N, Gill S, Sihag M. Flax and flaxseed oil: an ancient medicine & modern functional food. *J Food Sci Technol*. 2014;51(9):1633-1653.
- Yari Z, Rahimlou M, Poustchi H, Hekmatdoost A. Flaxseed supplementation in metabolic syndrome management: a pilot randomized, open-labeled, controlled study. *Phytother Res*. 2016;30(8):1339-1344.
- Daleprane JB, Batista A, Pacheco JT, et al. Dietary flaxseed supplementation improves endothelial function in the mesenteric arterial bed. *Food Res Int*. 2010;43(8):2052-2056.
- Yang WS, Lee WJ, Funahashi T, et al. Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. *J Clin Endocrinol Metab*. 2001;86(8):3815-3819.
- Barre D, Mizier-Barre K, Stelmach E, et al. Flaxseed lignan complex administration in older human type 2 diabetics manages central obesity and prothrombosis—an invitation to further investigation into polypharmacy reduction. *J Nutr Metab*. 2012;2012:1-7.
- Blüher S, Mantzoros CS. Leptin in humans: lessons from translational research. *Am J Clin Nutr*. 2009;89(3):991S-997S.
- 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):90-96.
- Khalatbari Soltani S, Jamaluddin R, Tabibi H, et al. Effects of flaxseed consumption on systemic inflammation and serum lipid profile in hemodialysis patients with lipid abnormalities. *Hemodial Int*. 2013;17(2):275-281.
- Bloedon LT, Szapary PO. Flaxseed and cardiovascular risk. *Nutr Rev*. 2004;62(1):18-27.
- Pan A, Yu D, Demark-Wahnefried W, Franco OH, Lin X. Meta-analysis of the effects of flaxseed interventions on blood lipids. *Am J Clin Nutr*. 2009;90(2):288-297.
- Fukumitsu S, Aida K, Shimizu H, Toyoda K. Flaxseed lignan lowers blood cholesterol and decreases liver disease risk factors in moderately hypercholesterolemic men. *Nutr Res*. 2010;30(7):441-446.
- Wang M, Zhang XJ, Feng K, et al. Dietary  $\alpha$ -linolenic acid-rich flaxseed oil prevents against alcoholic hepatic steatosis via ameliorating lipid homeostasis at adipose tissue-liver axis in mice. *Sci Rep*. 2016;6:26826.
- Jump DB, Botolin D, Wang Y, Xu J, Christian B, Demeure O. Fatty acid regulation of hepatic gene transcription. *J Nutr*. 2005;135(11):2503-2506.
- Felmlee MA, Woo G, Simko E, Krol ES, Muir AD, Alcorn J. Effects of the flaxseed lignans secoisolariciresinol diglucoside and its aglycone on serum and hepatic lipids in hyperlipidaemic rats. *Br J Nutr*. 2009;102(3):361-369.
- Park JB, Velasquez MT. Potential effects of lignan-enriched flaxseed powder on bodyweight, visceral fat, lipid profile, and blood pressure in rats. *Fitoterapia*. 2012;83(5):941-946.
- Pellizzon MA, Billheimer JT, Bloedon LT, Szapary PO, Rader DJ. Flaxseed reduces plasma cholesterol levels in hypercholesterolemic mouse models. *J Am Coll Nutr*. 2007;26(1):66-75.
- Prasad K, Mantha S, Muir A, Westcott N. Reduction of hypercholesterolemic atherosclerosis by CDC-flaxseed with very low alpha-linolenic acid. *Atherosclerosis*. 1998;136(2):367-375.
- Cornish SM, Chilibeck PD, Paus-Jennsen L, et al. A randomized controlled trial of the effects of flaxseed lignan complex on metabolic

- syndrome composite score and bone mineral in older adults. *Appl Physiol Nutr Metab*. 2009;34(2):89-98.
29. Lemay A, Dodin S, Kadri N, Jacques H, Forest J-C. Flaxseed dietary supplement versus hormone replacement therapy in hypercholesterolemic menopausal women. *Obstet Gynecol*. 2002;100(3):495-504.
  30. Nelson TL, Stevens JR, Hickey MS. Adiponectin levels are reduced, independent of polymorphisms in the adiponectin gene, after supplementation with  $\alpha$ -linolenic acid among healthy adults. *Metabolism*. 2007;56(9):1209-1215.
  31. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: a review. *Eur J Intern Med*. 2016;31:3-10.
  32. Mahan LK, Raymond JL. *Krause's Food & the Nutrition Care Process-E-Book*. Amsterdam, the Netherlands: Elsevier Health Sciences. 2016.
  33. Park JB, Velasquez MT. Potential effects of lignan-enriched flax seed powder on blood pressure, fat accumulation, and lipid profile in rats. *FASEB J*. 2011;25(S1):339-6.
  34. Wu H, Pan A, Yu Z, et al. Lifestyle counseling and supplementation with flaxseed or walnuts influence the management of metabolic syndrome. *J Nutr*. 2010;140(11):1937-1942.
  35. Pineda AMR, Gómez BLG, Alzate CMA, Castaño CFM, Marín BEL. Consumo de linaza molida para la reducción de peso corporal en personas con exceso de peso. *Perspect Nutr Humana*. 2011;13(1):56.
  36. 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. *J Am Coll Nutr*. 2010;29(1):72-80.
  37. Fukumitsu S, Aida K, Ueno N, Ozawa S, Takahashi Y, Kobori M. Flaxseed lignan attenuates high-fat diet-induced fat accumulation and induces adiponectin expression in mice. *Br J Nutr*. 2008;100(03):669-676.
  38. Prasad K. Reduction of serum cholesterol and hypercholesterolemic atherosclerosis in rabbits by secoisolariciresinol diglucoside isolated from flaxseed. *Circulation*. 1999;99(10):1355-1362.
  39. Kratz M, Swarbrick MM, Callahan HS, Matthys CC, Havel PJ, Weigle DS. Effect of dietary n-3 polyunsaturated fatty acids on plasma total and high-molecular-weight adiponectin concentrations in overweight to moderately obese men and women. *Am J Clin Nutr*. 2008;87(2):347-353.
  40. Hallund J, Ravn-Haren G, Bügel S, Tholstrup T, Tetens I. A lignan complex isolated from flaxseed does not affect plasma lipid concentrations or antioxidant capacity in healthy postmenopausal women. *J Nutr*. 2006;136(1):112-116.
  41. Cassani RSL, Fassini PG, Silvah JH, Lima CMM, Marchini JS. Impact of weight loss diet associated with flaxseed on inflammatory markers in men with cardiovascular risk factors: a clinical study. *Nutr J*. 2015;14(1):5.
  42. 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. *Nutr Res*. 2013;33(5):367-375.
  43. Patel JV, Lee KW, Tomson J, Dubb K, Hughes EA, Lip GY. Effects of omega-3 polyunsaturated fatty acids on metabolically active hormones in patients post-myocardial infarction. *Int J Cardiol*. 2007;115(1):42-45.
  44. Weyer C, Funahashi T, Tanaka S, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. *J Clin Endocrinol Metab*. 2001;86(5):1930-1935.
  45. Flachs P, Mohamed-Ali V, Horakova O, et al. Polyunsaturated fatty acids of marine origin induce adiponectin in mice fed a high-fat diet. *Diabetologia*. 2006;49(2):394-397.
  46. Babcock TA, Novak T, Ong E, Jho DH, Helton WS, Espot NJ. Modulation of lipopolysaccharide-stimulated macrophage tumor necrosis factor- $\alpha$  production by  $\omega$ -3 fatty acid is associated with differential cyclooxygenase-2 protein expression and is independent of interleukin-10. *J Surg Res*. 2002;107(1):135-139.
  47. Fernández-Real J-M, Vendrell J, Ricart W. Circulating adiponectin and plasma fatty acid profile. *Clin Chem*. 2005;51(3):603-609.
  48. Rosen ED, Walkey CJ, Puigserver P, Spiegelman BM. Transcriptional regulation of adipogenesis. *Genes Dev*. 2000;14(11):1293-1307.
  49. Hariri M, Ghiasvand R, Shiranian A, Askari G, Iraj B, Salehi-Abargouei A. Does omega-3 fatty acids supplementation affect circulating leptin levels? A systematic review and meta-analysis on randomized controlled clinical trials. *Clin Endocrinol*. 2015;82(2):221-228.
  50. Zhou YE, Kubow S, Dewailly E, Julien P, Egeland GM. Decreased activity of desaturase 5 in association with obesity and insulin resistance aggravates declining long-chain n-3 fatty acid status in Cree undergoing dietary transition. *Br J Nutr*. 2009;102(6):888-894.
  51. Kaul N, Kreml R, Austria JA, et al. A comparison of fish oil, flaxseed oil and hempseed oil supplementation on selected parameters of cardiovascular health in healthy volunteers. *J Am Coll Nutr*. 2008;27(1):51-58.
  52. Mandasescu S, Mocanu V, Dascalita AM, et al. Flaxseed supplementation in hyperlipidemic patients. *Rev Med Chir Soc Med Nat Iasi*. 2005;109(3):502-506.
  53. Patade A, Devareddy L, Lucas EA, Korlagunta K, Daggy BP, Arjmandi BH. Flaxseed reduces total and LDL cholesterol concentrations in native American postmenopausal women. *J Women's Health*. 2008;17(3):355-366.
  54. Torkan M, Hassan Entezari M, Siavash M. Effect of flaxseed on blood lipid level in hyperlipidemic patients. *Rev Recent Clin Trials*. 2015;10(1):61-67.
  55. Zhang W, Wang X, Liu Y, et al. Dietary flaxseed lignan extract lowers plasma cholesterol and glucose concentrations in hypercholesterolaemic subjects. *Br J Nutr*. 2008;99(6):1301-1309.
  56. Paschos GK, Zampelas A, Panagiotakos DB, et al. Effects of flaxseed oil supplementation on plasma adiponectin levels in dyslipidemic men. *Eur J Nutr*. 2007;46(6):315-320.
  57. Bloedon LT, Balikai S, Chittams J, et al. Flaxseed and cardiovascular risk factors: results from a double blind, randomized, controlled clinical trial. *J Am Coll Nutr*. 2008;27(1):65-74.
  58. Singh K, Mridula D, Rehal J, Barnwal P. Flaxseed: a potential source of food, feed and fiber. *Crit Rev Food Sci Nutr*. 2011;51(3):210-222.
  59. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr*. 1999;69(1):30-42.

**How to cite this article:** Ahmadniay motlagh H, Aalipanah E, Mazidi M, Faghieh S. Effect of flaxseed consumption on central obesity, serum lipids, and adiponectin level in overweight or obese women: A randomized controlled clinical trial. *Int J Clin Pract*. 2021;75:e14592. <https://doi.org/10.1111/ijcp.14592>