

A Combination of Prebiotic Inulin and Oligofructose Improve Some of Cardiovascular Disease Risk Factors in Women with Type 2 Diabetes: A Randomized Controlled Clinical Trial

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Abstract

Purpose: This trial was conducted to evaluate the effects of oligofructose-enriched inulin on some of cardiovascular disease risk factors in women with type 2 diabetes.

Methods: 52 females (25<BMI<35 kg/m²) with type 2 diabetes were randomly assigned to two groups. Participants received 10g/d oligofructose-enriched inulin (n=27) or 10g/d placebo (n=25) for 8 weeks. Fasting blood samples were taken to measure metabolic profiles, malondialdehyd and antioxidant enzymes at baseline and after the 8 weeks intervention. Paired, unpaired sample t-test and analysis of covariance were used to comparison of quantitative variables.

Results: After 8 weeks, in the oligofructose-enriched inulin group there was a significant increase in total antioxidant capacity (0.2 mmol/l, 20.0%) and a significant decrease in fasting plasma glucose (19.2 mg/dL, 9.4%) HbA1c (0.5%, 8.4%), total cholesterol (TC) (28.0 mg/dL, 14.1%), low-density lipoprotein cholesterol (LDL-c) (22.0 mg/dL, 21.7%), TC/HDL-c ratio (0.73, 20.7%), LDL-c/HDL-c ratio (0.55, 27.5%) and malondialdehyd (1.7 nmol/ml, 39.7%) compared to the placebo group. Changes in concentrations of triglycerides, high-density lipoprotein cholesterol (HDLc), superoxide dismutase, catalase and glutathione peroxidase were not significant in oligofructose-enriched inulin group compared to the placebo group.

Conclusion: Oligofructose-enriched inulin may improve glycemic indices, lipid profile, antioxidant status and malondialdehyd in women with type 2 diabetes.

Introduction

Diabetes mellitus (DM) is a common health problem in developing and developed countries. The prevalence of DM in the world is estimated to be 8.3% in US.¹ In Iran, the prevalence of DM and its health expenditure were 8% and 600 million US dollars in 2010, respectively.² DM is a metabolic disease that is characterized by hyperglycemia together with biochemical alterations of lipid profile, insulin resistance and oxidative stress.³ Increased oxidative stress plays a key role in the initiation, propagation and development of diabetes complications such as retinopathy, neuropathy and nephropathy.⁴ Improvement of serum lipids and oxidative stress are associated with better glycemic control. Dietary intervention can alter the potential consequence of oxidative stress and lipid abnormalities.

Inulin-type fructan belong to indigestible carbohydrates which its chain contains a variable number of fructose units, linked by β -(1 \rightarrow 2) D-fructosyl-fructose bonds, usually terminates with only one glucose. It is a substitute for sugar or fat having a very low caloric value, arranged as nonviscous, soluble and fermentable fibers. Oligofructose-enriched inulin is a mixture of oligofructose and inulin. Oligofructoses and inulin are metabolised in the proximal colon and distal colon, respectively. Oligofructose-enriched inulin is fermented in the colon throughout; hence it can produce different effects than inulin and oligofructose alone.⁵ Oligofructose-enriched inulin can change composition of the gut microflora toward bifidobacteria and lactobacilli.⁶

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Some animal studies had shown the specific effects of inulin-type fructans on lipid profile⁷ and oxidative stress.^{8,9} The results of reviews have shown beneficial effect of inulin-type fructans on the blood glucose¹⁰ and lipid profiles¹¹ in human, limited data are available assessing the effects of inulin-type fructans on metabolic profiles and oxidative stress biomarkers in diabetic patients. Review of the related literature in this area shows a need for further research of the inulin-type fructans effects in diabetic patients. Animal studies have shown that degree of polymerization of inulin-type fructans differentially affects metabolic status.^{12,13} A randomized clinical trial to compare inulin and oligofructose-enriched inulin effect on glycemic indices and blood pressure in women with type 2 diabetes showed that inulin is effective than oligofructose-enriched inulin on food intake, glycemic indices and blood pressure in type 2 diabetes patients.¹⁴ Recently, we have reported that supplementation of diabetic patients with inulin (10g/d for 2 months) improves glycemic status and oxidative stress biomarkers.¹⁵ The present study is a part of recent clinical trial that was designed to assess the efficacy of oligofructose-enriched inulin on some of cardiovascular disease risk factors including glycemic indices, lipid profile and oxidative stress biomarkers in women with type 2 diabetes.

Materials and Methods

Study design

In this randomized, triple-blind, placebo-controlled trial, conducted from December 2011 to February 2012, 70 diabetic female volunteers from Iran Diabetes Society and Endocrinology and Metabolism Clinics of Tabriz University of Medical Sciences participated. This study is part of a large clinical trial that was approved by the Ethics Committee of the Tabriz University of Medical Sciences and it was registered on the Iranian Registry of Clinical Trials website (www.irct.ir/IRCT201110293253N4).

Participant

In this trial, seventy females with type 2 diabetes who were between 20 and 65 y old were participated. Inclusion criteria were as follows: having type 2 diabetic for >6 months; taking oral anti-diabetic drugs and maintaining them throughout the trial; normal diet; and Body Mass Index (BMI) >25 kg/m² for the past 3 months. Type 2 diabetic was defined as having a fasting glucose level of ≥ 126 mg/dl.¹⁶ Subjects recorded their daily physical activity on a calendar. These recordings were reviewed to ensure subjects maintained a consistent level of physical activity throughout the study. Patients were excluded if they had a history of gastrointestinal, cardiovascular diseases; if they had renal, thyroid, liver, or pancreatic diseases; if they were smoker, pregnant, lactating; if they are currently taking prebiotics, probiotics, antibiotics, antacids, alcohol, anti-diarrheal, anti-inflammatory, laxatives drugs; if they had taken lipid-lowering medications within 2 weeks before the

intervention or during the intervention; if they had a daily fiber intake of >30g; or if they changed their oral antidiabetic medication during the intervention. The diagram of study is shown in Figure 1.

Intervention

Before the intervention, an appointment was made for each patient to provide trial information, to fill a questionnaire, and to provide written informed consent. Participants were randomly assigned to either an intervention group, in which participants received 10 g/d oligofructose-enriched inulin (Frutafit, Sensus, Borchweg 3, 4704 RG Roosendaal the Netherlands), or to a control group, in which participants received similar amounts of maltodextrin as the placebo (JiujiangHuirong Trade CO., LTD, China) for 8 weeks. Daily supplements were divided into two packages of 5 g each to be eaten during breakfast and dinner with a cup of water. Both the maltodextrin and the oligofructose-enriched inulin had a similar taste and appearance, and they were given to the volunteers in similar opaque packages. Supplements divided between participants in accordance with the allocation code after randomization. Participants received half of packages at the beginning and the remainder in the middle of the trial. In order to minimize dropout, assurance of supplements consumption and monitor of supplements compliance, the participants received a phone call once per week. Subjects were recommended to return all packets (full and empty) to assess consumption status.

Measurements

At baseline, information including age, menopausal status, diabetes duration (years) and drugs was collected using a general questionnaire. Measurement of anthropometric indices, food intake and serological tests were performed at baseline and after 8 weeks. Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. BMI was calculated as weight in kilograms divided by the square of height in meters. Dietary intakes were evaluated using a 3-day food diary (two usual and one weekend). Dietary intakes were analyzed using the nutritionist 4 software (First Databank Inc., Hearst Corp., San Bruno, CA) containing the database from tables of content and nutritional value.

At baseline and at the end of trial, 10 ml venous blood samples were collected between 7-9 a.m. after an overnight fasting. Fasting plasma glucose (FPG) concentration was measured by the enzymatic method using an Abbot Model Alcyon 300, USA autoanalyzer with Pars-Azmone kit (Tehran, Iran). HbA1c in whole blood was determined using an automated high performance liquid chromatography analyzer with commercially Bio-Rad D-10 Laboratories, Schiltigheim, France kit. The concentrations of TC, TG and HDL-c were measured by enzymatic colorimetric method (Cholesterol CHOD-PAP and Triglycerides GPO-PAP, Pars-Azmone, IRI) on an automatic analyzer (Abbott, model Alcyon300, USA). Serum LDL-c was calculated

according to the Friedewald equation.¹⁷ Since the TC/HDL-c and LDL-c/HDL-c ratios determine the relative risk of coronary artery disease, they were also calculated. The levels of glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) and total antioxidant capacity (TAC) were measured by colorimetric method (TAS: RANDOX kits, SOD: RANSOD kits and GSH-Px: RANSEL kits; RANDOX Laboratory, UK), on an automatic analyzer (Abbott model Alcyon 300, USA). Malondialdehyde (MDA), as a marker of lipid peroxidation and oxidative stress was measured through reaction with thiobarbituric acid

(TBA) as a TBARS to produce a pink colored complex. Then, its fluorescence intensity was measured at 547 nm with excitation at 525 nm by a spectrofluorimeter (Kontron, model SFM 25A, Italy).¹⁸ The levels of catalase were estimated by the method of Aebi.¹⁹ Catalase degrades hydrogen peroxide which can be measured directly by the decrease in the absorbance at 240 nm. One unit of catalase activity was defined as the amount of catalase which absorbed in 30 seconds at 25°C. The catalase was expressed as units per milliliter and TAC was expressed as mmol/l.

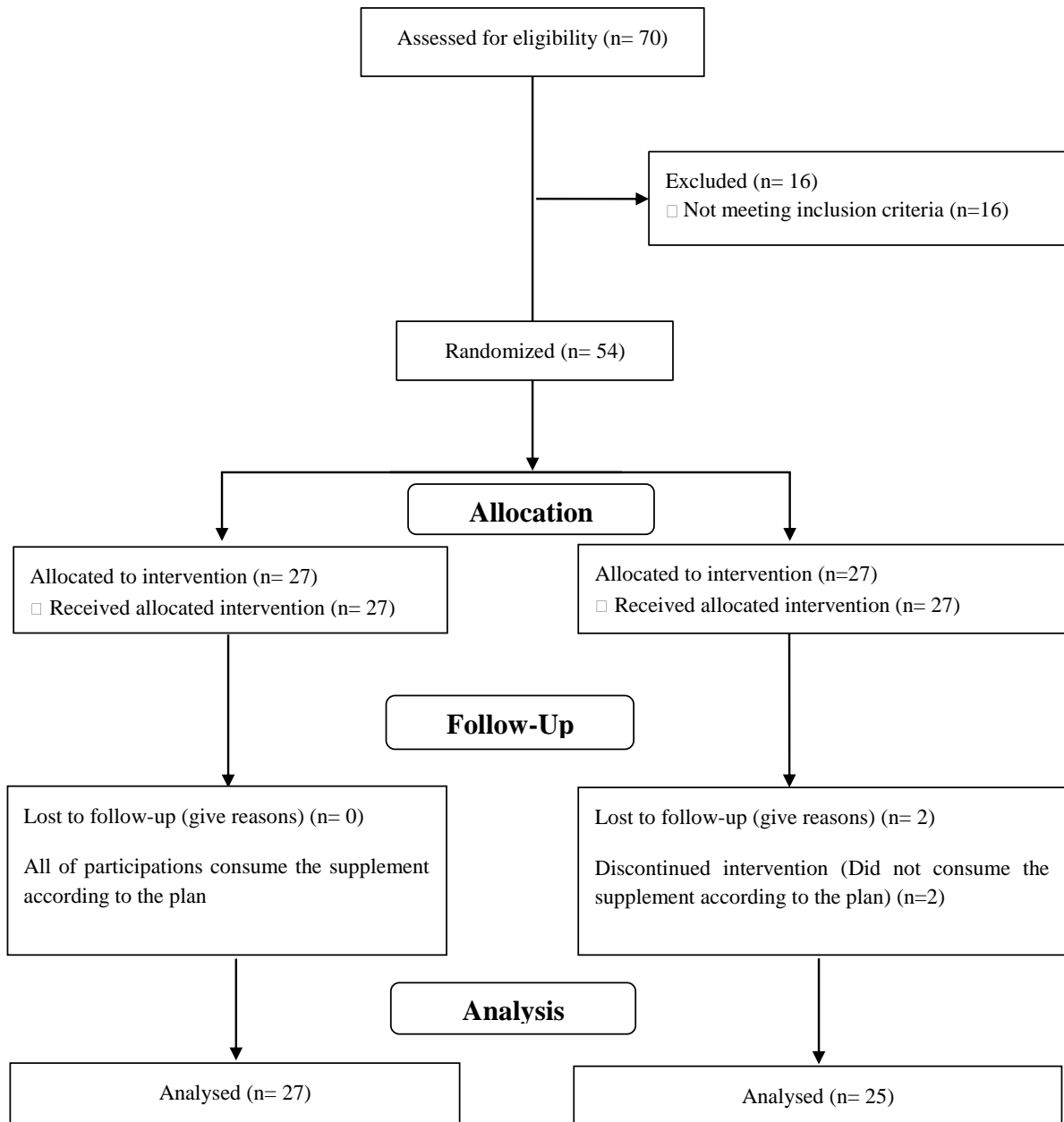


Figure 1. Flow diagram.

Statistical analyses

Data were analyzed using SPSS software (version 13). All statistical analyses were performed based on

intention to treat analysis. The Sample size was determined based on information obtained from the study by Sheu and colleagues²⁰ for LDL-c. For an

anticipated change of 28.3mg/dL between experimental and control groups with a confidence level of 95% and, a power of 90%. The sample size was estimated at least 19 per group. To cover an anticipated dropout of 25%, the sample size was increased to 27 in each group. In this trial, participants were randomly assigned in to one of two groups by using a block randomization procedure, which matched subjects to each block based on BMI and age. In every block of participants, five subjects allocated to each arm of the trial. The allocation sequence was randomly generated by random allocation software (RAS). To maintain blinding, the allocation was performed by an investigator with no clinical involvement in the study, whereas main investigator and statistician remained blind until the end of analysis. All data were kept according to code until the end of study. The results were expressed as mean (SD). The normality of the distributions was evaluated by the one-sample Kolmogorov-Smirnov test. Paired and unpaired sample t-tests were used to compare comparison of quantitative variables. Medications used in two groups were compared using the Mann-Whitney U test. ANCOVA was used to identify any differences between the two groups after intervention, adjusting for baseline values and covariates including diabetes duration, weight and energy intake changes. Mean changes of markers between groups were calculated by [(intervention

values-control values)/control values)]. $P < 0.05$ were considered to be statistically significant.

The primary outcomes of the study were FPG, HbA1c, TC, TG, LDL-c, HDL-c, TC/ HDL-c ratio, LDL-c/HDL-c ratio, MDA, TAC, SOD, GSH-Px, catalase while the secondary outcomes were weight and energy changes. In addition, diabetes duration, energy intake and weight changes for glycemic parameters, lipid profile, MDA and related antioxidant enzymes were considered as covariates variables in this study.

Results

Participants flow

Out of 70 participants assigned to the trial, 52 participants completed the study (intervention group, 27; placebo group, 25; Figure 1). Participants had good compliance with oligofructose-enriched inulin and no adverse effects or symptoms were reported following supplementation.

Baseline characteristics

Table 1 shows the baseline characteristics of participants in the two groups. The two groups were similar in initial characteristics expecting diabetes duration. To take this difference into consideration, duration of diabetes was included as covariate in analyses of efficacy outcomes.

Table 1. Baseline characteristics of the study participants

Characteristics	Placebo group (n=25)	Intervention group (n=27)
Age (year) (range)	48.40 (9.70) (40-65)	48.45(8.40) (40-60)
Pre / Postmenopause n (%)	5(20.00) / 20 (80.00)	4 (14.80)/ 23 (85.20)
Weight (kg)	70.50(11.00)	76.00 (12.20)
Height (cm)	153.50 (6.50)	154.10 (5.30)
Body mass index (kg/m ²)	29.90 (4.10)	31.90(4.00)
Diabetes duration (y)	5.30 (4.60)	8.50 (5.00) ^a
Metformin, 500mg (tablets/d)	2.70 (0.90)	2.70 (0.92)
Glibenclamide, 5mg (tablets/d)	1.90 (1.20)	2.40(1.10)

Data are presented as mean (SD) excepting menopause status that is presented n (%). ^a $P < 0.05$, unpaired *t* test.

Dietary intake of energy and macronutrients was reported previously.²¹ There were no significant differences between the baseline dietary intakes of the two groups in energy, carbohydrate, protein, fat, saturated fat, monounsaturated fat, polyunsaturated fat, cholesterol and dietary fiber. Participants' dietary composition -with the exception of energy and total fat, which significantly decreased in the intervention group-did not significantly change during the study period. In the intervention group, energy and total fat intake decreased significantly, while in the placebo group they remained unchanged.

Efficacy results

Anthropometric indices, glycemic control and lipid profile

The comparison between two groups showed that there were no significant differences at baseline anthropometric indices; FPG, HbA1c and lipid profile. Change in glycemic status including fasting blood glucose and serum HbA1c has been reported elsewhere.²¹ After 8 weeks supplementation, body weight, BMI, FPG and HbA1c remained unchanged in the placebo group, while body weight and BMI were significantly decreased in the intervention group (76.0 ± 12.4 to 72.9 ± 12.4 kg, 31.9 ± 4.5 to 30.6 ± 4.6 kg/m², respectively; $P < 0.05$).

Significant reductions were observed in FPG (19.2 mg/dL; 9.5%) and HbA1c (1.0%; 8.4%) in the intervention group as compared with the placebo group. These changes were significant compared to the placebo group ($P < 0.05$, ANCOVA adjusted for diabetes duration, weight and energy intake changes and baseline values).

Oligofructose-enriched inulin decreased significantly, serum TC (28.0 mg/dL, 14.1%), LDL-c (22.0 mg/dL, 21.7%), TC/HDL-c ratio (0.7, 20.7%), LDL-c/HDL-c ratio (0.5, 27.5%). We observed a nonsignificant decrease in TG (38.8 mg/dL, 16.2 %) and a nonsignificant increase in HDL-c (1.9 mg/dL, 8.9%) compared with the placebo group after adjusting for diabetes duration, weight and energy intake changes and baseline values. In the placebo group changes for TC, TG, LDL-c, HDL-c, TC/HDL-c ratio and LDL-c /HDL-c ratio were not significant (Table 2).

Table 2. Changes in lipid profile of patients at baseline and at the end of the study

Variables	Period	Placebo group (n=25)	Intervention group(n=27)
TC (mg/dL)	Initial	197.9 (37.7)	198.6 (38.7)
	End	203.1 (45.6)	175.0 (36.3) ^{a, b}
TG (mg/dL)	Initial	213.0 (68.0)	211.2 (80.0)
	End	216.8 (59.8)	176.9 (61.2) ^a
HDL-c (mg/dL)	Initial	40.6 (5.6)	38.8 (5.9)
	End	43.4 (4.2)	45.4 (6.5) ^a
LDL-c (mg/dL)	Initial	114.6 (35.3)	117.4 (36.7)
	End	116.3 (42.9)	94.3 (34.3) ^{a, b}
TC /HDL-c	Initial	4.9 (0.8)	5.2 (1.3)
	End	4.7 (0.9)	3.9 (0.9) ^{a, b}
LDL-c /HDL-c	Initial	2.8 (0.7)	3.1 (1.0)
	End	2.7 (0.9)	2.1 (0.8) ^{a, b}

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein. Values are presented as the mean (SD). ^a $P < 0.05$, paired *t* test. ^b $P < 0.05$, ANCOVA adjusted for diabetes duration, weight and energy intake changes and baseline values.

MDA and antioxidant markers

Comparison between the two groups showed that there were no significant differences with regard to baseline TAC, SOD, GSH-Px, catalase and MDA (Table 3). After 8 weeks, no statistically significant difference existed in TAC, MDA, SOD, GSH-Px and catalase in the placebo group. Significant increase in the levels of TAC (0.2 mmol/l, 20.0%) and significant decrease in the levels of MDA (1.7 nmol/ml, 39.7%) were observed in the intervention group compared to the placebo group ($P < 0.05$, ANCOVA adjusted for diabetes duration, weight and energy intake changes and baseline values). No significant increase was observed in the levels of SOD, GSH-Px and catalase in the intervention group compared to the placebo group ($P > 0.05$, ANCOVA adjusted for diabetes duration, weight and energy intake

changes and baseline values). The levels of SOD and catalase increased in the intervention group ($P < 0.05$, paired *t* test) but glutathione peroxidase was not changed significantly ($P > 0.05$, paired *t* test). In the placebo group changes for TAC, MDA, SOD, GSH-Px and catalase were not significant.

Table 3. Changes in oxidative stress biomarkers of patients at baseline and at the end of the study

Variables	Period	Placebo group (n=25)	Intervention group(n=27)
TAC (mmol/L)	Initial	0.9 (0.1)	0.9 (0.1)
	End	0.8 (0.2)	1.0 (0.2) ^{a, b}
SOD (U/mg Hb)	Initial	1599.6 (138.1)	1633.9 (237.3)
	End	1580.0 (144.5)	1684.7 (254.2) ^a
GSH-Px (U/g Hb)	Initial	33.4 (2.6)	33.7 (5.1)
	End	33.3 (2.8)	34.4 (5.4)
Catalase (U/g Hb)	Initial	66.5 (17.7)	57.2 (16.0)
	End	65.0 (18.4)	69.5 (20.2) ^a
MDA (nmol/ml)	Initial	3.8 (1.2)	3.4 (1.0)
	End	4.3 (1.9)	2.6 (1.2) ^{a, b}

TAC, total antioxidant capacity; SOD, superoxide dismutase; GSH-Px, glutathione peroxidase; MDA, malondialdehyde. Data are presented as the mean (SD).

^a $P < 0.05$, paired *t* test.

^b $P < 0.05$, ANCOVA adjusted for diabetes duration, weight and energy intake changes and baseline values

Discussion

This clinical trial, showed that the oligofructose-enriched inulin supplementation for 8 weeks in diabetic patients decreased significantly body weight, BMI, the levels of FPG, HbA1c, TC, LDL-c, TC/ HDL-c ratio, LDL-c/HDL-c ratio and MDA, however, we could not find any significant effect on TG, SOD, GSH-Px and catalase compared to the placebo group.

Increased body weight and BMI are associated with diabetes. We demonstrated that supplementation with oligofructose-enriched inulin resulted in a significant decrease in body weight and BMI. Similar results have been reported with oligofructose supplementation in a systematic review.²²

In our study, energy intake of the oligofructose-enriched inulin group was significantly decreased. The exact mechanism(s) of weight reduction by oligofructose-enriched inulin remains unclear. Some gut satiety hormones that is released as response to diet composition, including glucagon-like peptide-1 (GLP-1), Peptide YY (PYY), and ghrelin, are proposed for weight reduction.²²

In this study, we showed that oligofructose-enriched inulin supplementation for 8 weeks reduced FPG, HbA1c, TC, LDL-c, TC/ HDL-c ratio and LDL-c/ HDL-c ratio, but could not significantly affect TG and HDL-c levels compared to maltodextrin group. Nassar and colleagues⁷ reported that inulin resulted in significant decrease in serum glucose, insulin, insulin resistance,

TC, TG, LDL-c and significant increase in HDL-c. Garcia and colleagues²³ reported that 5 weeks supplementation with inulin was resulted in 8% decrease in LDL-c. Bonsu and colleagues²⁴ did not find significant effect of inulin on serum lipid and serum glucose concentrations. We have already reported that inulin can improve lipid profile.²⁵ Beneficial effects of oligofructose-enriched inulin on lipid profile mainly mediated by short chain fatty acid (SCFA). Butyrate inhibits liver cholesterol synthesis and provides a source of energy for human colon epithelial cells. Acetate may act as a precursor for cholesterol synthesis, while propionate could inhibit hepatic cholesterol synthesis by decreasing the use of acetate as a precursor of cholesterol.²⁶ Also, inulin-type fructans may contribute to cholesterol reduction by increasing fecal bile acid excretion, reducing intestinal cholesterol absorption, as well as increasing of the expression of 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase).²⁷ Their impact on TLR4 signaling and proinflammatory cytokines might be explaining the role of their lipid lowering.²⁸ Prebiotics might also improve glycemic status via increasing insulin sensitivity with their impact on gene expression which involved in reduction of inflammatory activity and adiposity.²⁹

The current study showed that oligofructose-enriched inulin (10 g/day for 8 weeks) in diabetic patients significantly increased plasma TAC levels and significantly decreased plasma MDA levels, but did not significantly affect SOD, catalase and GSH-Px activities. Because antioxidant micronutrients and kind of fat remained unchanged in throughout study, it suggests oligofructose-enriched inulin supplementation might be the main factor affecting the oxidative stress in this study. In a study by Wang and colleagues²⁹ increased activity of catalase, SOD and GSH-Px enzymes and decreased levels of MDA were observed by the use of 5% wheat bran xylooligosaccharides in rats. Similar results had been shown in treated mice with *Lactobacillus acidophilus* in conjunction with inulin.³⁰ In a study by Nikniaz and colleagues,³¹ supplementation of lactating mothers with symbiotic (*Lactobacillus* + *Bifidobacterium* + fructooligosaccharide for 30 days) resulted in a significant increase in plasma TAC levels and a nonsignificant decrease in levels of MDA. We have already reported that supplementation of diabetic patients with inulin (10g/day for 2 months) improves oxidative stress and antioxidants (TAC, SOD).¹⁵ These results are in agreement with our results. Despite these, some studies reported conflicting findings. In rat model, supplementation with inulin and FOS did not affect serum TAC, GSH-Px and SOD activities, while the concentration of TBARS was decreased.⁸ In another study, dietary supplementation with dextrin or oligofructose led to a 20% decrease in total and reduced glutathione. The activities of glutathione dependent antioxidant enzymes, SOD, catalase, and MDA remained unchanged in dextrin or oligofructose groups.⁹ Asemi and colleagues³² reported that symbiotic food

(*Lactobacillus* + inulin for 6 weeks) consumption in diabetic patients led to a significant increase in plasma total GSH and serum uric acid levels. No significant change was observed in plasma TAC levels.

These discrepancies may be due to differences between species, different study designs, the dosage and kind of supplementation used, variation in diet, basal antioxidant and glycemic status, duration of supplementation, basal gut microflora as well as the patients under investigation. The underlying mechanism(s) of the modulation of oxidative stress by inulin-type fructans have remained obscure. Inulin-type fructans exerts antioxidant effects in biological systems through direct and indirect pathways. The fructans may act as antioxidant themselves; they could act directly as reactive oxygen species (ROS) scavenger and indirectly through modulation of SCFA production,³³ cytokine³⁴ as well as gene expression.³⁵ Butyrate as SCFA, leads to reduction in colonic myeloperoxidase activity, restoration of glutathione concentration and reduction in ROS-mediated p 42/44 mitogen-activated protein kinase (MAPK) phosphorylation.³³ We have already reported that Oligofructose-enriched inulin and resistant dextrin, as prebiotic, improve some inflammatory markers and metabolic endotoxemia in women with type 2 diabetes mellitus.^{21,36} Furthermore, the inulin-type fructans may improve oxidative stress status through modulation of cytokine-induced oxidative stress, down-regulation of genes involved in oxidative stress and TLR pathways,³⁴ modification of antioxidant enzymes gene expression.³⁵ Moreover, modification of microflora toward *Lactobacilli* containing antioxidants in the gastrointestinal tract and releasing their intracellular antioxidants upon lyses of *Lactobacilli* resident³⁰ might be other mechanism.

Some aspects need to be considered in the interpretation of our results, including short interventional time, lack of assessment serum fatty acids, glucose clamp, lack of define gut microflora changes and other oxidative stress indices, such as F (2)-isoprostanes. Also, the sample size was determined on the basis of changes in LDL-c, in the case of this particular variable, the power obtained was sufficient to produce significant results. However, for some other variables, it seems that a larger sample size and a higher power are needed to attain statistical significance. Despite these limitations, this is the first triple blind study to investigate the effect of oligofructose-enriched inulin on lipid profile and oxidative stress in diabetic patients.

Conclusion

Based on the results of this trial, oligofructose-enriched inulin supplementation may improve glycemic indices, lipid profile, antioxidant status and decrease MDA concentrations in type 2 diabetic patients. These finding propose a safe and effective therapy in diabetes management and its complications. Obviously, more investigations are needed for confirmation of positive effects of oligofructose-enriched inulin on metabolic

status, antioxidant indices in diabetic patients and clarify its underlying mechanism(s).

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Ethical Issues

Not applicable.

Conflict of Interest

The authors declare that they have no conflict of interest.

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