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Effect of Prebiotic Inulin Supplementation on Glucose Metabolism and Lipid Profile in Type 2 Diabetic Women

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Abstract

This study determines the effect of inulin administration on fasting blood glucose (FBG), lipid profile "serum triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol), insulin and insulin resistance in women with Type 2 Diabetes (T2DM). T2DM is a multifactorial disease promoted by genetic and environmental factors, and there is a tight association between T2DM and dyslipidemia. Inulin is prebiotic that has been shown to improve insulin concentrations and ameliorate the lipid profile in people with diabetes. 100 T2DM females with predetermined criteria took four grams of inulin-type prebiotic daily for three weeks, with their FBG, Insulin, Insulin resistance (IR), and lipid profile measured before and after. This clinical study demonstrated that the inulin supplementation significantly decreased FBG, serum TG, TC, LDL, insulin, and IR levels and significantly increased HDL compared to the measurements before supplementation. This means that inulin may play a role in correcting the metabolic disorders caused by high fructose diets by improving carbohydrate and lipid metabolism.

Keywords: T2DM, Lipid profile, Inulin, Insulin Resistance, Blood Glucose.

1. Introduction

T2DM is considered a multifactorial disease, promoted by genetic and environmental factors [1], characterized by chronic hyperglycemia, IR, and dyslipidemia [2,3]. T2DM progresses because pancreatic β-cells cannot ultimately produce enough insulin to supplement the ongoing insulin resistance. There is a close relationship between T2DM and dyslipidemia. The latter is characterized by small elevated high-density LDL levels, elevated TG levels, and decreased HDL levels[4].

The global prevalence of diabetes is estimated by the International Diabetes Federation (IDF), with 436 million diabetics worldwide in 2019, of which T2DM accounts for about 90%. IDF ranked Egypt in the top 10 countries regarding the number of people with diabetes. In Egypt, the IDF estimates the prevalence of diabetes in adults aged 20-79 years at about 15.2%, with 8.9 million people suffering from diabetes and about 2.2 million people suffering from pre-diabetes. In addition, Egypt reports that 54.4% of diabetics and most pre-diabetes are unlikely to be diagnosed [5].

An essential activity of the human gut flora is to ferment dietary fiber into short-chain fatty acids (SCFAs), primarily acetates, propionates, and butyrates. Recent evidence suggests that increased SCFA levels in the colon and plasma can be used as a strategy for improving glucose and lipid metabolism[6].

Inulin is a type of fiber that has been shown to improve insulin levels in persons with diabetes[7]. Inulin-type (ITF) fructans are carbohydrates, but human intestinal enzymes do not digest their unique β2 → 1-binding glycosidic bonds. These glycosidic bonds reduce the caloric and fibrous effects of ITF[8]. Inulin is prebiotic that aims at the gut microbiota, affecting microbial composition and activity. Studies have shown that the human gut microbiota can ferment inulin into acetate, propionate, and a considerable amount of butyrate [9]. Additionally, several human studies have revealed that inulin supplementation daily increases fecal bifidobacteria, indicating a modification in gut microbial composition[10]. Many

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researchers showed that inulin supplementation caused significant reductions in plasma lipid concentrations and lowered FBG and insulin concentrations [11–13].

2. Subjects and Methods

Subjects:

One hundred T2DM women aged 40-65 years. Selected from a governorate hospital clinic. These formed the subject of this study, and their selection was based on the following criteria:

Inclusion criteria: Women with T2DM, overweight or obese, and who are or are not hypertensive. Patients were selected with similar socioeconomic status.

Exclusion Criteria: The patient did not have any acute or chronic sickness or condition that could impair his or her metabolic status, as an example:

- Acute or chronic bacterial infections include skin infections, ulcers, carbuncles, infected feet, and gangrene.
- Cancer lesion in any organ.
- Any endocrine gland malfunction, such as thyroid or suprarenal dysfunction.
- Take hormonal therapy or contraceptive pills.
- Decompensation of an organ such as the heart, lungs, liver, or kidney

Ethics committee approval: This work has been approved by the Egyptian National Research Center (NRC) under Ethics Certification Approval No. 15011.

Methods

Every day, each patient took four grams of an inulin-type prebiotic. Take two grams in the morning and two grams at night for three weeks.

Patients who took inulin as a supplement to their regular diabetic medication received it daily. Their diet was being followed up by nutrition specialists.

Inulin specifications: Inulin A.R ($C_6H_{10}O_5$) N ALPHA CHEMIKA Mumbai. 400002 (India) A company that has acquired ISO: 9001: 2000 certification.

Each patient underwent the following tests before and three weeks after taking inulin: At the end of the inulin intake period.

1. Fasting serum TG determination: quantitative estimation of serum TG was carried out spectrophotometrically as previously estimated by Fossati [14] using the kit from Centronic company in Germany.
2. Following Matthews et al., protocol, IR was measured using the homeostasis model assessment (HOMA) from FBG and fasting serum insulin level [15].
   The equation: insulin resistance (HOMA-IR) = FBG (mg/dl) x fasting insulin (I.U./ml)/405.
3. According to the National Committee for Clinical Laboratory Standards, fasting serum insulin was determined quantitatively using an enzyme immunoassay technique [16].
4. Estimation of FBG: This was done using an enzymatic colorimetric technique. According to Tietz, the primary mechanism is the enzymatic oxidation of glucose by the glucose oxidase enzyme[17].
5. Serum TC determination: quantitative assessment of serum cholesterol was done by spectrophotometric methods according to Allain [18] using the kit from Stanbio Laboratory USA.
6. HDL cholesterol determination: spectrophotometric methods were used to determine serum HDL cholesterol quantitatively, as Warnick and Wood [19] described using the kit from Interchim France.
7. LDL cholesterol determination: the quantitative estimation of serum LDL was done by spectrophotometric methods according to Bachorik[20] using the kit from ATLAS Medical, Germany.

3. Statistical Methods

The data were coded, tabulated, and statistically analyzed using IBM SPSS Statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp. Chicago, Illinois, USA, 2013. Descriptive statistics such as the minimum and maximum of the range and mean ± SD (standard deviation) were used for quantitative parametric data. In cases of two dependent groups with parametric data, inferential analysis was performed using paired t-tests for quantitative variables. If the P-value is < 0.050, the significance level is significant; otherwise, it is non-significant.

4. Results

4.1. Effect of inulin supplementation on patients' serum glucose level:

Table (1) and Fig. (1) demonstrate the mean of FBG in mg/dl before and after the inulin intake period by T2DM female patients enrolled in the study. They show a significant reduction in FBG means after the inulin intake period from 303.0 ± 61.0 to 239.1 ± 49.4.

Table 1: the values of fasting glucose before and after inulin intake.

Parameter	Before		After		#P
	Mean ± SD	Range	Mean ± SD	Range	
Fasting insulin (µI.U/ml)	16.7 ± 8.1	4.0 – 29.4	13.6 ± 7.2	2.9 – 26.1	<0.001*
IR	12.2 ± 7.7	2.5 – 32.1	7.9 ± 4.5	2.1 – 18.7	<0.001*

N=100, #P-value of paired t-test, *Significant

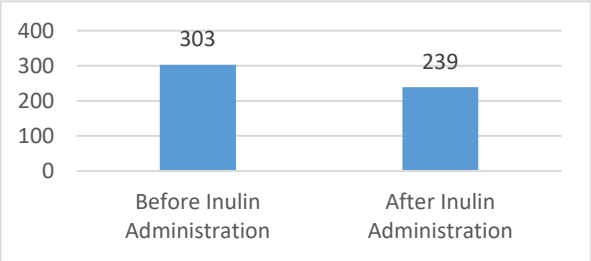

Fig. (1): Mean serum glucose in mg/dl before and after inulin intake period.

4.2. Effect of inulin supplementation on patients' fasting insulin level:

Table (2) and Fig. (2) reveal the mean fasting insulin in µI.U/ml before and after inulin intake period by T2DM female patients registered in the study, they show a significant reduction in fasting insulin mean after inulin intake period from 16.7 ± 8.1 to 13.6 ± 7.2.

Table 2: the values of fasting insulin and IR before and after inulin intake

Parameter (mg/dl)	**Before**		**After**		**#P**
	Mean ± SD	Range	Mean ± SD	Range	<0.001*
FBG	303.0 ± 61.0	210 - 450	239.1 ± 49.4	129 - 303	<0.001*

N=100, #P-value of paired t-test, *Significant

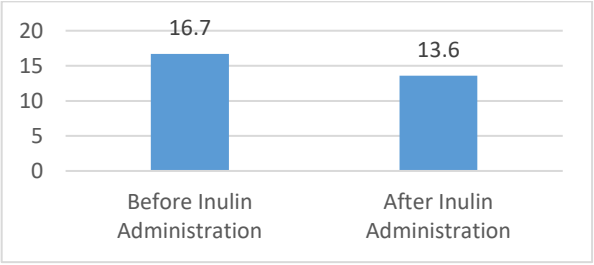

Fig. (2): Mean fasting insulin in µI.U/ml before and after the inulin intake period.

4.3. Effect of inulin supplementation on patients' IR level:

Table (2) and Fig. (3) demonstrate the mean of IR before and after inulin intake period by T2DM female patients enrolled in the study, they show a significant reduction in fasting IR mean after inulin intake period from 12.2 ± 7.7 to 7.9 ± 4.5.

4.3. Effect of inulin supplementation on patients' lipid profile:

Table (3) and Fig. (4) reveal the mean of the lipid profile parameters (TC, TG, LDL, and HDL) in mg/dl before and after the inulin intake period by T2DM female patients registered in the study. They show a significant reduction in the means of TC, TG, LDL from 256.9 ± 93.9, 236.6 ± 48.5, 170.8 ± 71.1 to 210.8 ± 84.8, 182.2 ± 37.0, 131.6 ± 37.9, respectively and the significant increase in HDL mean from 75.3 ± 25.7 to 89.7 ± 25.8.

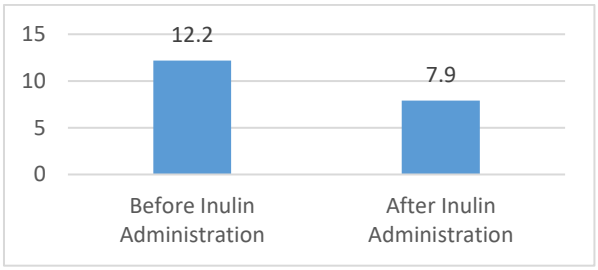

Fig. (3): Mean IR before and after inulin intake period.

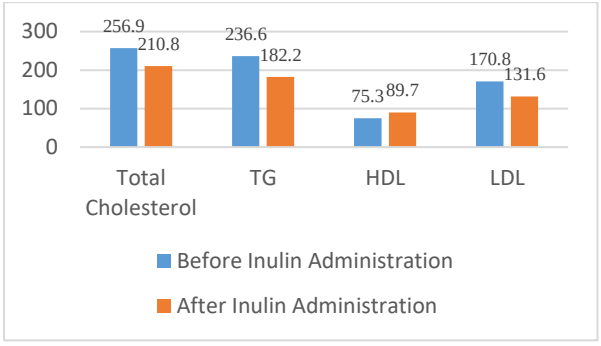

Fig. (4): Mean of lipid profile parameters in mg/dl before and after inulin intake period.

5. Discussion

The effects of three weeks of inulin supplementation on blood glycemic indices and lipidemic profiles in women with T2DM were investigated in this study. The lipid profile is affected by FBG and insulin, and high amounts are usually associated with reducing the poor lipid profile. The presence of insulin is known to boost the effect of glucose on gene transcription of lipogenesis-related enzymes[21]. Inulin, a dietary fiber, cannot be digested and absorbed in the human intestine but can be fermented in the gut microbiota, producing a wide variety of metabolites [22]. Inulin supplementation for three weeks in female diabetes patients dramatically reduced FBG, serum TG, TC, LDL-c, insulin, and IR, and elevated HDL-c compared to estimations taken before supplementation.

Table 3: laboratory findings for lipid profile among studied cases before and after inulin intake.

Parameter (mg/dl)	**Before**		**After**		**#P**
	Mean ± SD	Range	Mean ± SD	Range	
TC	256.9 ± 93.9	91 - 434	210.8 ± 84.8	80 – 392	<0.001*
TG	236.6 ± 48.5	174 - 355	182.2 ± 37.0	113 – 245	<0.001*
HDL Cholesterol	75.3 ± 25.7	41 - 193	89.7 ± 25.8	44 – 210	<0.001*
LDL Cholesterol	170.8 ± 71.1	40.8 – 355.0	131.6 ± 37.9	33.0 – 185.0	<0.001*

The experimental results are consistent with Nassar et al., 2013 who stated that supplementation with inulin resulted in a significant lowering of serum glucose, insulin, IR, TC, TG, LDL-c, and a significant rise in HDL-c [11].

Samal and group reported that 12 weeks of supplementation with inulin resulted in a significant decrease in LDL-c [23]. Bonsu and Johnson did not find a significant effect of inulin on serum lipid and serum glucose concentrations [24]. It has been reported that inulin can improve lipid profile [25] . Li and his colleagues demonstrated that the serum TG and TC levels were effectively decreased compared with those of the control group with inulin treatment for three stages of T2DM[26]. Studies by Rust and team found that fermentable fiber such as inulin improved insulin sensitivity due to FBG reductions [27].

The present work results follow previous researchers who observed that dietary inulin lowered serum glucose levels and significantly reduced insulin concentration [13]. Also, it has been demonstrated that inulin could improve insulin sensitivity and secretion, lowering the risk of diabetes[28]. However, Rozan and the group observed that supplementing rats of both sexes with inulin did not affect FBG levels in male and female rats [29]. In terms of lipid metabolism, the current findings are comparable to those of Li et al., 2021, who found that inulin induced a significant decrease in blood TC, TG, and LDL-cholesterol levels and a significant increase in HDL-cholesterol levels [30]. Also, Byung-Sung , proved that ingestion of inulin increased serum levels of HDL-cholesterol[31]. Inulin enhances blood lipid profiles in people, according to Liu and group [32]. However, inulin supplementation did not result in statistically significant changes in lipid profile in another tria [33]. The large bowel bacteria digesting inulin in the colon may be responsible for inulin's hypolipidemic action. This fermentation includes the anaerobic degradation of organic molecules to provide energy for microbial development and the synthesis of SCFAs such as acetate, propionate, and butyrate, which are quickly absorbed into the portal blood [34]. After inulin consumption, serum acetate, propionate, and butyrate levels were significantly elevated [9].

Because acetate is a lipogenic SCFA and lower acetate levels result in decreased lipogenesis, the rise in propionate generated by inulin could be the origin of cholesterol inhibition, as propionate has been found to diminish acetate incorporation into cholesterol [35]. Pingitore and colleagues stated that long-term colonic propionate delivery reduced non-esterified fatty acid levels, a recognized contributor to β-cell dysfunction and peripheral insulin resistance[36].

AMP-activated protein kinase (AMPK), a fundamental regulator of metabolic homeostasis and a primary cellular fuel, may benefit from an increase in SCFA products. Studies have suggested that AMPK can be activated by SCFA propionate either directly or indirectly, suggesting propionate's potential efficacy in the preventive and therapeutic management of diabetes [37] .

Because cholesterol produces bile acids, the body's principal method of removing cholesterol is through the bile. Because fewer bile acids are returned to the liver via the enterohepatic circulation due to increased bile acid excretion, hepatic absorption of serum cholesterol for de novo bile salt synthesis in this organ increases. ITF does not appear to bind to bile acids in the intestinal lumen. The fermentation of ITF in the intestinal mucosa, on the other hand, produces organic acids, which lowers the pH in the intestinal lumen. As a result, the bile acids become less soluble and are more likely to be excreted with the feces, reducing their intestinal absorption [38]. Also, due to the fermentation process, butyrate production increases the thickness of the intestinal wall, which hinders the absorption of cholesterol molecules[39]. This could have increased cholesterol catabolism in the liver, resulting in a hypocholesterolemic effect. Many prebiotics has been proposed to protect or treat animals with metabolic syndrome[40].

Bifidobacterium is an anaerobic bacteria found in the gut microbiome. These bacteria are well-known for providing numerous advantages to the host. The usage of inulin can increase the number of these bacteria in the intestine, resulting in increased production of SCFA [13] as a result of fermentation, which is necessary for optimizing the lipid profile. According to human and animal studies, consumption of ITF increases the number of Bifidobacterium in the gut microbiota [41].

Ramos and group discovered that feeding rats fermentable fibers and fructans stimulate certain intestinal microbial species (i.e., Bacteroides and Fusobacteria) to produce large amounts of polyamines in the large intestine, where spermidine or spermine administration improves glucose homeostasis and insulin sensitivity while also reducing adiposity and hepatic fat accumulation [42].

6. Conclusion

Finally, this research found that inulin seems to be a valuable compound, where the supplementation of four grams of inulin-type prebiotic daily for three weeks was sufficient to help rectifying metabolic disruptions in T2DM patients by enhancing gut microbiome, which is probably the main mechanism responsible for ameliorating glucose and lipid metabolism. It tackles numerous critical sites in the chain of carbohydrate metabolism disorders; most notably insulin resistance, which is the disease's core problem. Meanwhile, large sample sized trials of inulin supplementation for T2DM patients are needed in the future to assure the result of the work.

7. Conflicts of interest

The authors declare that there is no conflict of interest.

8. Acknowledgments

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