RESEARCH ARTICLE AGROBIOLOGICAL RECORDS
ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

HYPOGLYCEMIC EFFECT OF FLAXSEED LIGNAN AND B GLUCAN IN POSTMENOPAUSAL DIABETIC PATIENTS

Faiqa Javed [1],*, Mian Kamran Sharif [1] and Naheed Abbas[2]

[1]National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan; [2]Institute of Home Sciences, Faculty of Food, Nutrition & Home Sciences, University of Agriculture, Faisalabad, Pakistan

*Corresponding author: faiqa_javeed@yahoo.com

ABSTRACT

Diabetes mellitus is an important metabolic disorder and, owing to its significant health impacts, is a leading cause of death around the globe. According to WHO estimates, Pakistan is the 7th highest diabetes-affected population globally, where almost 7 million people are suffering from the disease. Flaxseed lignan and β-glucan have a constructive role in controlling diabetes. In connection to their enhanced insulin sensitivity, dietary supplementation of flaxseed fiber has shown potential results in postmenopausal diabetic women. Fed the subject population with lignan and β-glucan capsules and monitored hypoglycemic activity daily and weekly. Blood samples were taken to observe the blood glucose using flaxseed lignan and β-glucan in postmenopausal women. Fasting and random glucose levels of postmenopausal diabetic women in 4 weeks fed on flaxseed lignan and β-glucan ($P<0.01$). Liver and kidney functioning tests are found to be non-significant. This research indicates that flaxseed lignan and β-glucan reduce random and fasting blood glucose levels in postmenopausal patients.

***Keywords*:** Diabetes, Functional food, Flaxseed lignan, β-glucan

Article History (2020-1152) || Received: 21 Nov 2020 || Revised: 18 Dec 2020 || Accepted: 29 Dec 2020 || Published Online: 02 Feb 2021

1. INTRODUCTION

Diabetes mellitus is an endocrine disorder described by hyperglycemia and inadequate discharge of endogenous insulin. The beta islets cells of the pancreas produce insulin hormone (Pan et al. 2017; American Diabetes Association 2019). Hyperglycemia is notably a serious and alarming health concern of developed and underdeveloped world communities. Prevalence of diabetes mellitus has enormously increased in developing countries particularly in Pakistan during last few decades. In adequacy or lack of control over hyperglycemia in diabetic patients promote micro- and macro-vascular complication. Effective management of diabetes absolutely includes blood glucose monitoring, nutrition, exercise and medication (Piemonte 2011; De Boer et al. 2017).

According to the present data more than 7.5 million people in Pakistan are suffering from diabetes, whereas WHO has ranked Pakistan as 7th on the world diabetes prevalence chart. The International diabetes federation has alarmed that prevalence level of diabetes and its deleterious outcomes are expected to rise by 2030 if no effective and preventive strategies are undertaken (Bukhsh et al. 2019).

Functional foods have been suggested as more promising glycemia preventive strategies in diabetic patients (Passmore and Eastwood 1986; Ohr 2005; Oomah and Mazza 2000; Tharwat et al. 2017) and recommended to be included in dietary habits on regular basis. Flaxseed, belonging to Linaceae family is tiny, flat and elliptical shaped seed (Safdar et al. 2019) and has been highlighted as one of the best plant sources used as a functional food. The seed and its individual fractions bearing food properties are also recommended as nutraceutical owing to their protective and curative properties in glycemia, cardiovascular disorders, inflammation and oxidative changes (Mohamed et al. 2003; Akhtar et al. 2013).

It has been validated that flaxseed is a rich source of alpha linolenic acid; a good combination of omega 3 fatty acids and hydrolysable, phyto-estrogenic fibers i.e., lignan which make it attractive functional food for regulating blood sugar level (Rodriguez-Leyva et al. 2010; Bashir and Choi 2017). Lignans, a class of phytoestrogens, is present in flaxseed - a concentrated source of this hydrolysable fiber. Food based on plant sources particularly from flaxseed are thought to be rich source of dietary lignans (Cui et al. 2020). Secoisolariciresinol diglucoside are indicators of mammalian metabolites of lignan i.e., enterodiol and enterolactone. Production of mammalian isoflavoniods and lignans are gut microbiota mediated structurally altered products of lignans and isofalvones. It has been reported that this very active flaxseed fiber i.e., lignans may have a beneficial role in regulating blood sugar level (De Silva and Alcorn 2019). Flaxseed lignans due to their estrogenic, anti-estrogenic, antitumerogenic and antioxidant characteristics

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

may also support normal regulation of serum sugar levels. Therefore, it has been proposed that daily consumption of flaxseed can improve glucose status of postmenopausal women (Chen and Thompson 2003; Chen et al. 2004; Tan et al. 2004).

In postmenopausal women, production of estrogen by the body is suppressed that could complicate if not renewed from alternative resources (Gambacciani et al. 1997; Bhathena and Velasquez 2002; Louet et al. 2004; Rossi et al. 2004). Estrogen rich diets are thought to be sustainable source of estrogen in relieving postmenopausal complications (breast cancer, cardio vascular disorders, central nervous system damage, depression, anxiety) specifically in diabetic patients. It has also been confirmed that expanded usage of anti-diabetic drug therapy can adversely affect the body in the form of reduction in blood sugar levels, increase in body weight and initiation of lactic acidosis (Alkhalil et al. 2002; Rendell 2004; Scheen 2004).

Therefore, functional foods and nutraceutical supplements have the ability to combat systemic and chronic outcomes of long-term drug therapy of diabetes (Barnes et al. 2007). Owing to their investigated promising features in controlling diabetes, current study was aimed to exploit hypoglycemic effects of flaxseed lignan and β glucan in diabetic postmenopausal women. This was executed with objectives to assess the hypoglycemic effect of flaxseed lignan and β glucan in post-menopausal diabetic patients, to evaluate any possible side effects of lignan and β glucan supplementation on blood biochemistry of postmenopausal women and recommend effective dietary doses of flaxseed lignan and β glucan in controlling diabetes without posing any significant health hazard.

2. MATERIALS AND METHODS

The pure flaxseed lignan and β-glucan was provided by the Meat Technology Laboratory, National Institute of Food Science and Technology, University of Agriculture, Faisalabad (UAF). Ethical approval of the project was approval was taken from Institutional Biosafety/Bioethics Committee, UAF.

2.1. Treatment

Fifteen post-menopausal diabetic subjects were randomly divided into three groups. The control group was given capsule filled with base. A quantity of 0.1g/day of flaxseed lignan and 0.3g/day β glucan was provided to each patient in the form of capsules. The treatment was administered for the period of 30 days.

2.2. Sample Collection

Samples were collected from the postmenopausal women of age between 45-60 years from urban areas of Faisalabad. Zero sampling was done before start of research period. Blood Sampling for blood glucose and blood insulin was done on daily and weekly basis. A Blood sample was taken from each individual to be analyzed for different biochemical parameters such as liver tests.

Fifteen post-menopausal diabetic subjects were selected with their will. Each group was comprised of five subjects. The group 1 was control and fed on capsule filled with base. The group II was treated with flaxseed lignan and provided with daily dietary dose of 0.1g. The group III was β glucan treated group and was fed on daily dietary allowance of 0.3g β glucan for a period of one month. Blood samples were drawn from each individual to be analyzed for different biochemical parameters i.e., blood glucose, urea, creatinine on 7th, 14th, 21st and 28th days, respectively. The blood glucose of patients was checked daily during fasting and after two hours of flaxseed lignan and β-glucan intake.

2.3. Serum Biochemistry

The blood glucose concentration was calculated by GOD_PAP method as explained by Thomas and Labor (1992). The serum insulin concentration was determined by following the method of (Besch et al. 1987). The blood creatinine and urea were analyzed by the Jaffe method and GLDH method using the commercial kits (Jacobs et al. 1996; Thomas and Labor 1992), respectively.

The levels of Aspartate aminotransferase (AST) and Alanine amino transferase (ALT) were calculated by the dinitrophenylhydrazene (DNPH) method (Thomas and Labor 1992; Moss and Henderson 1999). The levels of Alkaline phosphatase (ALP) of the patients fed on lignan and β glucan was analyzed by alkaline phosphatase DGKC method (Thomas and Labor 1992; Moss and Henderson 1999).

The serum total proteins, albumins, Bilirubin and globulins was determined by using respective kits and methods. The blood total protein was analyzed by Biuret method as explained by Josephson and Gyllensward (1957). The albumin level was calculated by method described by Bradford (1976). The total blood bilirubin was analyzed by using the Jendrassik Grof method (Tietz 1999). The globulin was determined by method as described by (Bradford 1976).

2.4. Statistical Analysis

The data was statistically analyzed following the method described by (Steel et al. 1997).

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

3. RESULTS AND DISCUSSION

The current research was conducted with objective to assess the hypoglycemic effect of flaxseed lignan and β glucan in post-menopausal diabetic patients. The women were given flaxseed lignan and β glucan in capsulated form for a period one month. The blood glucose was checked daily and on weekly basis after the consumption of capsule. The blood of patients was tested on weekly basis for different biochemical analysis such as liver tests, blood proteins in order to assess the toxicity of flaxseed lignan and β glucan.

3.1. Glucose

Glucose is a major source of energy for most cells of the body. They are quickly turned into glucose in body. This raises blood glucose level. Hormones made in the body called insulin and glucagon help control blood glucose levels. A blood glucose test measures the amount of a sugar in a sample of blood. The result was found to be highly significant. Lemay et al. (2002) proved that flaxseed supplements helps to decrease blood glucose level in postmenopausal women. The research support facts that consuming 10g of β glucan helps to reduce peak glucose significantly and postponed the rate of glucose response. It was checked by blood samples for glucose (Kim et al. 2009). The current study confirmed that fed of flaxseed lignan helps to control blood glucose in postmenopausal diabetic patients.

***3.1.1. Fasting Blood Sugar*:** This is performed after a person has eaten nothing for eight hours is called fasting blood sugar test. It measures blood glucose level. In fasting condition sugar level of 100 to125mg/dl or above level is considered as diabetic (Walker and Colledge 2013). The fasting blood sugar for hypoglycemic effect of flaxseed lignan and β glucan in post-menopausal diabetic patients was highly significant.

It showed that flaxseed lignan and β glucan significantly reduce fasting blood sugar. These results are in accordance with (Bays et al. 2011) who reported that consumption of 6g/d β glucan for a time period of 12 weeks had significantly decreased fasting blood sugar as shown in (Fig 1; Table 1). In a study carried out on 90 patients with type 2 diabetes for a duration of 12 weeks. The study group was divided into three each containing 30 participants. The purpose of the study was to determine the effect of bakery product supplemented with flaxseed or flaxseed oil on patients having type 2 diabetes. The control group 1 was given regimen diet. Group 2 was provided with regimen diet same as group (1) along with a dose of flaxseed oil bakery regimen diet. For the group (3) was also given regimen diet the same as group (1) additional supplementation with flaxseed bakery product. The result showed significant changes in group 2 and 3 as compared to control. It showed that flaxseed is a remarkable alternative for treatment of diabetes (Tharwat et al. 2017).

Flaxseed lignan supplementation significantly reduced fasting plasma glucose concentration due to its anti-oxidant and anti-inflammatory activity (Rhee and Brunt 2011). Therefore, it can be concluded that functional foods such as flaxseed lignan and β glucan helps in controlling fasting blood sugar.

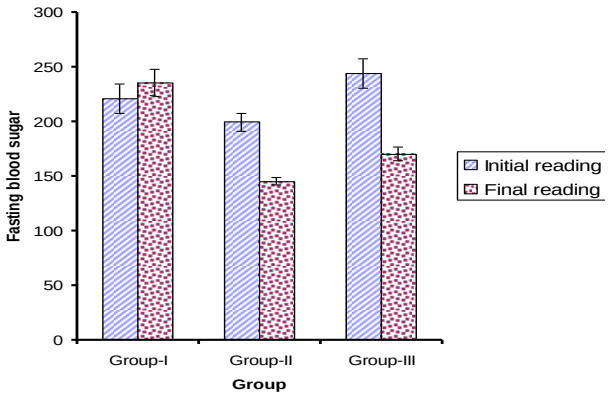

Fig 1: Fasting blood sugar (Mean+SE) of control (group I), hypoglycemic effect of flaxseed lignan (group II) and β glucan post-menopausal (group III) diabetic patients.

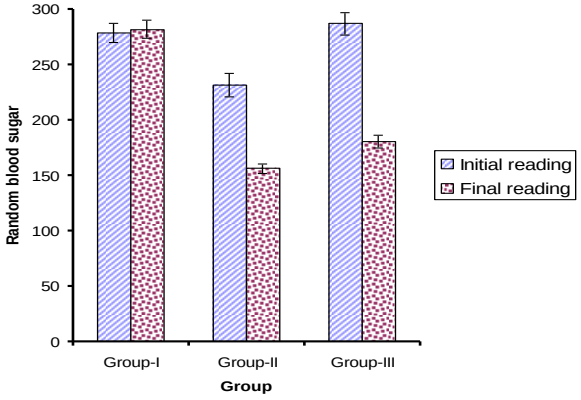

Fig 2: Random glucose level (Mean±SE) of control (group I) hypoglycemic effect of flaxseed lignan (group II) and β glucan post-menopausal (group III) diabetic patients.

3.1.2. Random Blood Sugar: In random glucose test patient's glucose is checked without regarding the time of meal. Normal glucose level is 85-100mg/dl (Walker and Colledge 2013). This level indicates the sugar management capabilities and hormonal balance. In diabetes, the random or fasting blood sugar level varies (Behall et al. 2006; Kim et al. 2009; Rhee and Brunt 2011). A diagnosis of diabetes is made if random blood sugar reading is 200mg/dl or higher as given in (Table 2; Fig. 2).

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

The hypoglycemic effect of flaxseed lignan and β glucan in post-menopausal diabetic patients' results showed that readings among groups was highly significant. Katare et al. (2012) confirmed that regular consumption of flaxseed lignan products help decrease random blood sugar in humans. In healthy females, fed of 25g flaxseed lignan lowered postprandial glucose upto 27%. The overall results show that consuming flaxseed lignan and β glucan for one month helps to control random blood sugar. Therefore, it can be concluded that flaxseed lignan and β glucan possess hypoglycemic effect on postmenopausal diabetic patients.

Table 1: Fasting blood sugar levels (mg/dl) in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Reading	Groups			Mean±SE
	I	II	III	
Initial	221.20+13.78a	199.60+8.30ab	243.80+13.50a	221.53+08.08A
Final	236.00+12.44a	145.60+3.53c	170.60+06.19bc	184.07+11.11B
Mean	228.60+9.09A	172.60+9.95B	207.20+14.07A	

Mean±SE sharing similar letters in a row or in a column are statistically non-significant (P>0.05). Small letters represent comparison among interaction mean±SE and capital letters are used for overall mean comparison.

Table 2: Random glucose levels (mg/dl) in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Reading	Group			Mean±SE
	I	II	III	
Initial	278.80±8.88a	231.60±10.65b	287.20±9.97a	265.87±08.40A
Final	282.20±8.21a	156.40±04.48c	181.00±5.60c	206.53±14.93B
Mean	280.50±5.73A	194.00±13.67C	234.10±18.50B	

Mean±SE sharing similar letters in a row or in a column are statistically non-significant (P>0.05). Small letters represent comparison among interaction mean±SE and capital letters are used for overall mean comparison.

3.2. Biochemical Parameters

***3.2.1. Insulin*:** Insulin is the main hormone secreted by pancreas regulating glucose uptake from blood into muscle and fat cells (Schinner et al. 2005; Lanner et al. 2008). In liver and muscles glucose is stored in the form of glycogen (Benedict et al. 2004). After 2 to 3 hours of meal, insulin is released from pancreas not continuously, but concentration changes with time. It alters the blood insulin concentration more than about 800pmol/l to less than 100pmol/l. It is supposed to escape down-regulation of insulin receptors in target cells and to help the liver to take out insulin from blood (Hellman et al. 2007; Pan et al. 2017). Determination of response to β glucan is suggested by studies showing that consumption of β glucan per day decreased serum insulin significantly in healthy postmenopausal women (Behall et al. 2006). The result was found to be non-significant between groups. It is obvious from data that Insulin for post-menopausal diabetic women consuming flaxseed lignan and β glucan varied non-significantly from 5.01 to 5.71 as shown in (Table 3).

The random variation in Insulin also indicate that flaxseed lignan and β glucan have non-detrimental effect on Insulin of diabetic patient means that change in Insulin content is not due to consumption of flaxseed lignan and β glucan. Therefore, it can be concluded that flaxseed lignan and β glucan have non-significant effect on insulin in postmenopausal diabetic patients.

Table 3: Blood insulin in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	4.20±0.071	5.38±0.442	5.44±0.347	5.01±0.232AB
2nd	4.20±0.063	5.50±0.412	4.90±0.624	4.87±0.272B
3rd	4.50±0.071	5.72±0.450	5.94±0.298	5.39±0.238AB
4th	4.34±0.068	6.38±0.248	6.40±0.341	5.71±0.290A
Mean	4.31±0.042B	5.75±0.202A	5.67±0.233A	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

***3.2.2. Creatinine*:** Creatinine (mg/dl) is a chemical waste product that's produced by muscle metabolism and to a smaller extent by eating meat. Creatinine helps evaluate kidney functions (Buysschaert et al. 2003). Walker and Colledge 2013) explained the normal range of blood creatinine for human and describe that blood creatinine varies from 0.8 to 1.1mg/dl. The result was found to be non-significant between groups. It is obvious from the data that creatinine of post-menopausal diabetic women is non-significantly flaxseed lignan and β glucan varying 0.77±0.049 to 0.71±0.043mg/dl (Table 4). Our value for creatinine fall in the normal range described by Buysschaert et al. (2003) and Walker and Colledge (2013). Our studies showed the total mean of blood creatinine to be non-significant.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

***3.2.3. Blood Urea*:** Urea, is an organic chemical compound, and is essentially the waste produced by the body after metabolizing protein. Physicians can use urea levels to detect diseases and disorders that affect the kidneys, such as acute kidney failure (Xie et al. 2018). The normal range of blood urea is 20-40 mg/dl (Walker and Colledge 2013). It is verified from results that flaxseed lignan and β glucan has non-significant effect on the blood urea in postmenopausal diabetic patients. It is obvious from data that blood urea for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 32.47 to 29.93mg/dl (Table 5).

However, the change in blood urea was non-significant indicating the safety of flaxseed lignan and β glucan. It shows that consumption of flaxseed lignan and β glucan for postmenopausal diabetic patients is helpful in curing diabetes without causing any complications and side effects. In our study, the urea level of subjects fed on flaxseed lignan and β glucan for one month are in the range described by Walker and Colledge (2013).

Table 4: Serum creatinine in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	0.74±0.040	0.86±0.112	0.70±0.089	0.77±0.049A
2nd	0.70±0.032	0.84±0.121	0.72±0.086	0.75±0.050A
3rd	0.64±0.051	0.80±0.095	0.70±0.063	0.71±0.042A
4th	0.64±0.040	0.82±0.107	0.68±0.049	0.71±0.043A
Mean	0.68±0.021B	0.83±0.050A	0.70±0.034AB	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

Table 5: Blood urea in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	31.20±1.71	34.20±1.16	32.00±1.22	32.47±0.82A
2nd	30.60±1.40	33.60±0.87	31.00±2.12	31.73±0.90A
3rd	30.60±2.14	33.40±1.08	30.80±2.03	31.60±1.03A
4th	28.40±2.16	32.20±2.85	29.20±2.52	29.93±1.42A
Mean	30.20±0.90B	33.35±0.79A	30.75±0.96B	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

3.2.4. Serum Total Protein: Total protein is a combination of albumin and globulin. Generally little more albumin is present than globulin and the ratio is more than 1. A ratio is less than or more than 1 indicates the problem in the body (Josephson and Gyllensward 1957; Bradford 1976). The normal level range of albumin/globulin ratio is 2.0 (Sinagra et al. 1997; Walker and Colledge, 2013). The result was found to be non-significant among groups. It is obvious from data that total protein for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 7.01 to 6.73 mg/100ml as given in (Table 6).

The random variation in total protein also indicates that consumption of flaxseed lignan and β glucan have non-detrimental effect on total protein of diabetic patient. According to our study the level of total protein falls in the range described by the Walker and Colledge (2013). So, flaxseed lignan and β does not have deleterious effects on total protein level of postmenopausal diabetic patients.

Table 6: Serum total protein in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	7.46±0.121	6.92±0.468	6.64±0.370	7.01±0.209A
2nd	7.44±0.068	6.84±0.524	6.46±0.387	6.91±0.229A
3rd	7.44±0.117	6.82±0.503	6.40±0.330	6.89±0.221A
4th	7.50±0.084	6.54±0.440	6.14±0.344	6.73±0.232A
Mean	7.46±0.046A	6.78±0.225B	6.41±0.170B	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

***3.2.4.1. Albumin*:** Albumin is made mainly in the liver using dietary protein. It helps to check how well the liver and kidneys are working (Mantovani et al. 2019). The Optimal Range is 4.5 to 4.8g/dl (Walker and Colledge, 2013).

The result was found to be non-significant between groups. It is obvious that albumin for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 4.42 to 4.15g/dl. In our present research, albumin levels of subjects after consuming flaxseed lignan and β glucan for duration of one month vary within the range described by Walker. This shows that flaxseed lignan and β glucan had non-significant effect on albumin level.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

***3.2.4.2. Globulin*:** Globulin is made up of different proteins and are important in antibodies formation. Some globulins are made by the liver, while others are made by the immune system (Mantovani et al. 2019). The optimum level of globulins in humans is described by (Walker and Colledge 2013) that is 2.3 to 3.0g/dl.

The results were found to be non-significant between groups. It is obvious from data that globulin for post-menopausal diabetic women consuming flaxseed lignan and β glucan varied non-significantly 3.27 to 3.11g/dl (Table 8). According to the range, described by Walker and Colledge (2013), globulin level that was checked after one week throughout the month is within the normal range. So, flaxseed lignan and β glucan has no significant effects on the globulin levels.

***3.2.5. Bilirubin*:** Bilirubin, an orange-yellow pigment, is a waste product of the normal breakdown of red blood cells. In most cases, the elevated bilirubin levels may indicate certain diseases such as an increased rate of destruction of red blood cells and might be associated with diabetes type 2 (Nano et al. 2016). The normal level of bilirubin in humans is 0.1 to 1.2mg/dl (Walker and Colledge, 2013). The result was found to be non-significant between groups. It is obvious from data that bilirubin for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 0.83 to 0.79mg/dl (Table 9).

However, the change in bilirubin was non-significant indicating the safety of flaxseed lignan and β glucan. The random variation in bilirubin also represent unaltered results. It does not shows deleterious effects on diabetic patients. It means that change in bilirubin content is not due to consumption of flaxseed lignan and β glucan. In our study, the levels of bilirubin of subjects, provided with flaxseed lignan and β glucan. Month, are falling within the normal range described by Walker and Colledge (2013).

Table 7: Serum albumin in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	4.66±0.098	4.56±0.236	4.04±0.150	4.42±0.117A
2nd	4.70±0.105	4.50±0.224	3.94±0.169	4.38±0.126A
3rd	4.68±0.111	4.38±0.218	3.82±0.136	4.29±0.129A
4th	4.76±0.093	4.04±0.236	3.64±0.129	4.15±0.152A
Mean	4.70±0.048A	4.37±0.115B	3.86±0.076C	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

Table 8: Serum globulin levels in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	3.40±0.045	3.18±0.058	3.22±0.058	3.27±0.039A
2nd	3.36±0.060	3.14±0.040	3.06±0.103	3.19±0.052AB
3rd	3.2±0.073	3.04±0.040	3.04±0.093	3.12±0.049AB
4th	3.34±0.10	2.96±0.068	3.02±0.092	3.11±0.065B
Mean	3.35±0.035A	3.08±0.031B	3.09±0.044B	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

Table 9: Serum bilirubin in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Week	Group			Mean±SE
	I	II	III	
1st	0.98±0.058	0.84±0.103	0.68±0.124	0.83±0.062A
2nd	1.00±0.071	0.78±0.066	0.66±0.133	0.81±0.063A
3rd	0.96±0.087	0.84±0.103	0.64±0.157	0.81±0.073A
4th	0.98±0.080	0.78±0.097	0.62±0.146	0.79±0.071A
Mean	0.98±0.034A	0.81±0.043AB	0.65±0.065B	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

3.3. Enzymes

3.*3.1. Alanine Aminotransferase*: An alanine aminotransferase (ALT) test measures the amount of this enzyme in the blood. ALT is found mainly in the liver. It is measured to check liver damage or diseases. The optimum level of ALT is (20-30U/L) (Walker and Colledge 2013). The regarding data of alanine aminotransferase for consuming flaxseed lignan and β glucan in post-menopausal diabetic patients was found to be non-significant between groups. It is obvious from data that alanine aminotransferase for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 27.60 to 24.13U/L (Table 10). However, the change in alanine aminotransferase was non-significant representing the safe use of flaxseed lignan. Data suggests that flaxseed enriched with lignan does not

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

altered ALT level of patients (Hemmings and Barker 2004). It does not cause any toxicity in patients. Our studies showed that the levels of ALT of our subjects, fed on flaxseed lignan and β glucan for duration of one month, are following the normal range described by Walker.

***3.3.2. Aspartate Aminotransferase*:** An aspartate aminotransferase test measures the amount of this enzyme in the blood. The normal range of AST is 20 to 30U/L (Walker and Colledge 2013). The result was found to be non-significant for post-menopausal diabetic patients between groups. Aspartate aminotransferase for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 24.27 to 22.07U/L as shown in (Table 11). According to the data, patients after consuming flaxseed lignan and β glucan there is not an increase in ALP proportions (Prasad 2004). In our study AST level of subjects fed on flaxseed lignan and β glucan for 1 month showed non-significant result. The values of subject are within the normal range as described by (Walker and Colledge 2013).

Table 10: Serum alanine aminotransferase levels in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Weeks	Group			Mean±SE
	I	II	III	
1st	28.60±0.51	26.80±0.92	27.40±1.08	27.60±0.51A
2nd	26.20±0.80	25.00±0.45	26.40±1.33	25.87±0.52AB
3rd	25.80±0.37	24.00±0.63	25.40±1.50	25.07±0.56B
4th	25.40±0.68	22.60±0.60	24.40±1.21	24.13±0.56B
Mean	26.50±0.40A	24.60±0.47B	25.90±0.64AB	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

Table 11: Serum aspartate aminotransferase in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Weeks	Group			Mean±SE
	I	II	III	
1st	25.80±2.08	23.80±2.78	23.20±3.97	24.27±1.65A
2nd	24.40±2.20	23.40±2.71	22.40±3.93	23.40±1.64A
3rd	24.80±2.29	22.60±2.93	22.20±3.48	23.20±1.60A
4th	22.80±1.88	21.80±2.67	21.60±3.36	22.07±1.45A
Mean	24.45±1.00A	22.90±1.29A	22.35±1.70A	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

***3.3.3. Alkaline Phosphatase*:** An alkaline phosphatase (ALP) test measures the amount of the enzyme ALP in the blood. A test for alkaline phosphatase (ALP) is done to check for liver disease or damage to the liver. The optimum level of alkaline phosphatase is (20 to 30U/L). The result was found to be non-significant between groups. It is obvious from data that alkaline aminotransferase for post-menopausal women consuming flaxseed lignan and β glucan varied non-significantly 121.20 to 118.87U/L (Table 12). According to the Prasad (2004) after use of flaxseed lignan and β glucan for 4 weeks. It does not have deleterious effects on the liver function. The level of ALP of our subjects fed on flaxseed lignan and β glucan for 1 month varied within the normal range described by Walker and Colledge (2013). These researches are in accordance with results of our study.

Table 12: Alkaline phosphatase concentration in post-menopausal diabetic patients treated with flaxseed lignan and β glucan

Weeks	Group			Mean±SE
	I	II	III	
1st	123.60±2.11	117.00±2.17	123.00±4.18	121.20±1.78A
2nd	122.60±2.25	116.80±2.08	122.20±4.04	120.53±1.72A
3rd	121.80±2.48	115.80±2.13	120.80±4.08	119.47±1.76A
4th	121.40±2.79	116.00±4.97	119.20±4.22	118.87±2.27A
Mean	122.35±1.13A	116.40±1.42B	121.30±1.93AB	

Mean±SE sharing similar letter in a row or in a column are statistically non-significant (P>0.05).

Conclusion: It was concluded that flaxseed Lignan and β glucan supplementation in capsule form significantly reduced the fasting and random glucose level of post-menopausal diabetic women. Flaxseed Lignan and β glucan supplementation also has a positive and significant effect on the initial blood glucose and final blood glucose reading of post-menopausal diabetic women. Flaxseed Lignan and β glucan has non-significant effect on insulin level, total protein, albumin and globulin levels bilirubin, urea, creatinine and liver function test of post-menopausal diabetic women was observed.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

Author's Contribution: MKS and NA conceptualized and supervised the study. FJ executed the study, collected data and drafted manuscript. MKS and NA finalized the manuscript. All authors approved the final version of the manuscript.

Acknowledgement: This project was financially supported by HEC titled "Tackling of metabolic syndrome by developing functional foods".

ORCID

Faiqa Javed https://orcid.org/0000-0001-6062-1165
Mian Kamran Sharif https://orcid.org/0000-0001-6244-1002

REFERENCES

Akhtar S, Ismail T and Riaz M, 2013. Flaxseed-A miraculous defense against some critical maladies. Pakistan Journal of Pharmaceutical Sciences 26: 199-208

Alkhalil C, Zavros G, Bailony F and Lowenthal DT, 2002. Clinical pharmacology physiology conference: metformin and lactic acidosis (LA). International Urology and Nephrology 34: 419-423.

American Diabetes Association, 2019. Obesity management for the treatment of type 2 diabetes: standards of medical care in diabetes-2019. Diabetes Care 42: S81–S89. https://doi.org/10.2337/dc19-S008

Barnes PM, Bloom B and Nahin RL, 2007. Complementary and alternative medicine use among adults and children; United States.

Bashir KM and Choi JS, 2017. Clinical and physiological perspectives of β-glucans: The past, present, and future. International Journal of Molecular Sciences18: 1906.

Bays H, Frestedt JL, Bell M, Williams C, Kolberg L, Schmelzer W and Anderson JW, 2011. Reduced viscosity Barley β-Glucan versus placebo: a randomized controlled trial of the effects on insulin sensitivity for individuals at risk for diabetes mellitus. Nutrition & Metabolism 8: 58. https://doi.org/10.1186/1743-7075-8-58

Behall KM, Scholfield JG, Hallfrisch JG and Liljeberg-Elmståhl HGM, 2006. Consumption of both resistant starch and β glucan improves postprandial plasma glucose and insulin in women. Diabetes Care 29: 976-981. https://doi.org/10.2337/dc05-2012

Benedict C, Hallschmid M, Hatke A, Schultes B, Fehm HL, Born J and Kern W, 2004. Intranasal insulin improves memory in humans. Psychoneuroendocrinology 29: 1326-1334. https://doi.org/10.1016/j.psyneuen.2004.04.003

Besch W, Woltanski KP, Keilacker H, Diaz-Alonso JM, Schulz B, Amendt P, Kohnert KD and Ziegler M, 1987. Measurement of Insulin in Human Sera Using a New RIA Kit. 1. Insulin determination in the absence of insulin antibodies—conventional assay and micro modification. Experimental and Clinical Endocrinology & Diabetes 90: 264-270. https://doi.org/10.1055/s-0029-1210700

Bhathena SJ and Velasquez MT, 2002. Beneficial role of dietary phytoestrogens in obesity and diabetes. The American Journal of Clinical Nutrition 76: 1191-1201.

Bradford MM, 1976. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Analytical Biochemistry 72: 248-254. https://doi.org/10.1016/0003-2697(76)90527-3

Bukhsh A, Khan TM, Nawaz MS, Ahmed HS, Chan KG, Goh BH, 2019. Association of diabetes knowledge with glycemic control and self-care practices among Pakistani people with type 2 diabetes mellitus. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 12: 1409-1417. https://doi.org/10.2147/DMSO.S209711

Buysschaert M, Joudi I, Wallemacq P and Hermans MP, 2003. Comparative performance of serum cystatin-c versus serum creatinine in diabetic subjects. Diabetes & Metabolism 29: 377-383. https://doi.org/10.1016/S1262-3636(07)70048-4

Chen J and Thompson LU, 2003. Lignans and tamoxifen alone or in combination, reduce human breast cancer cell adhesion, invasion and migration in vitro. Breast Cancer Research and Treatment 80: 163-170.

Chen J, Hui E, Ip T and Thompson LU, 2004. Dietary flaxseed enhances the inhibitory effect of tamoxifen on the growth of estrogen-dependent human breast cancer (mcf-7) in nude mice. Clinical Cancer Research 10: 7703-7711.

Cui Q, Du R, Liu M, Rong L, 2020. Lignans and their derivatives from plants as antivirals. Molecules 25: 183. https://doi.org/10.3390/molecules25010183

De Boer IH, Bangalore S, Benetos A, Davis AM, Michos ED, Muntner P, Rossing P, Zoungas S, Bakris G, 2017. Diabetes and hypertension: a position statement by the American Diabetes Association. Diabetes Care 40: 1273-1284. https://doi.org/10.2337/dci17-0026

De Silva SF, Alcorn J, 2019. Flaxseed lignans as important dietary polyphenols for cancer prevention and treatment: Chemistry, pharmacokinetics, and molecular targets. Pharmaceuticals 12: 68. https://doi.org/10.3390/ph12020068

Gambacciani M, Ciaponi M, Cappagli B, Piaggesi L, De Simone L, Orlandi R and Genazzani AR, 1997. Body weight, body fat distribution, and hormonal replacement therapy in early postmenopausal women. The Journal of Clinical Endocrinology & Metabolism 82: 414-417.

Hellman B, Gylfe E, Grapengiesser E, Dansk H and Salehi A, 2007. Insulin oscillations--clinically important rhythm. Antidiabetics should increase the pulsative component of the insulin release. Lakartidningen 104: 2236-2239.

Hemmings SJ and Barker L, 2004. The effects of dietary flaxseed on the Fischer 344 rat: I. Development, behaviour, toxicity and the activity of liver γ-glutamyltranspeptidase. Cell Biochemistry and Function 22: 113-121. https://doi.org/10.1002/cbf.1058

Jacobs DS, Kasten BL, Demott WR and Wolfson WL, 1996. Laboratory test handbook. Lexi-Comp Incorporated.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

Josephson B and A Gyllensward, 1957. The development of the protein fractions and of cholesterol concentration in the serum of normal infants and children. Scandinavian Journal of Clinical and Laboratory Investigation 9: 29-38. https://doi.org/10.3109/00365157090881l0

Katare C, Saxena S, Agrawal S, Prasad GB and Bisen PS, 2012. Flax seed: a potential medicinal food. Journal of Nutrition and Food Sciences 2: 120-127. https://doi.org/10.4172/2155-9600.100012

Kim H, Stote KS, Behall KM, Spears K, Vinyard B and Conway JM, 2009. Glucose and insulin responses to whole grain breakfasts varying in soluble fiber, β-glucan. European Journal of Nutrition 48:170-175.

Lanner JT, Bruton JD, Katz A and Westerblad H, 2008. Ca2+ and insulin-mediated glucose uptake. Current Opinion in Pharmacology 8: 339-345. https://doi.org/10.1016/j.coph.2008.01.006

Lemay A, Dodin S, Kadri N, Jacques H and Forest JC, 2002. Flaxseed dietary supplement versus hormone replacement therapy in hypercholesterolemic menopausal women. Obstetrics & Gynecology 100: 495-504. https://doi.org/10.1016/S0029-7844(02)02123-3

Louet JF, LeMay C and Mauvais-Jarvis F, 2004. Antidiabetic actions of estrogen: insight from human and genetic mouse models. Current Atherosclerosis Reports 6: 180-185.

Mantovani A, Sani E, Fassio A, Colecchia A, Viapiana O, Gatti D, Idolazzi L, Rossini M, Salvagno G, Lippi G, Zoppini G, Byrne CD, Bonora E and Targher G, 2019. Association between non-alcoholic fatty liver disease and bone turnover biomarkers in post-menopausal women with type 2 diabetes. Diabetes & Metabolism 45: 347-355. https://doi.org/10.1016/j.diabet.2018.10.001

Mohamed DA, Ismail AI and Ibrahim HE, 2003. Evaluation of the anti-inflammatory and biochemical effect of flaxseed oil in inflammed rats. In First International Congress of Pharmaceutical & Drug Industries Division, National Research Centre, Egypt. 24-26.

Moss DW and Henderson AR, 1999. Clinical enzymology. Titez Textbook of Clinical Chemistry. Edited by: Brutis CA, Ashwood ER.

Nano J, Muka T, Cepeda M, Voortman T, Dhana K, Brahimaj A, Dehghan A and Franco OH, 2016. Association of circulating total bilirubin with the metabolic syndrome and type 2 diabetes: A systematic review and meta-analysis of observational evidence. Diabetes & Metabolism 42: 389-397. https://doi.org/10.1016/j.diabet.2016.06.002

Ohr LM, 2005. Nutraceuticals & Functional Foods-Functional Fatty Acids. Food Technology-Chicago 59: 63-65.

Oomah BD and Mazza G, 2000. Functional foods. The Wiley Encyclopedia of Science and Technology 2: 1176-1182.

Pan CY, Sinnassamy P, Chung KD and Kim KW, 2007. Insulin glargine versus NPH insulin therapy in Asian type 2 diabetes patients. Diabetes Research and Clinical Practice 76: 111-118. https://doi.org/10.1016/j.diabres.2006.08.012

Passmore R and Eastwood MA, 1986. Davidson and Passmore human nutrition and dietetics: 8th Ed continued. Churchill Livingstone

Piemonte L, 2011. Diabetes Atlas released on World Diabetes Day. IDF Diabetes Atlas.

Prasad K, 2004. Saskatchewan University of Technologies Inc, assignee. Lignan complex derived from flaxseed as hypercholesterolemic and anti-atherosclerotic agent. United States patent US 6,673,773.

Rendell M, 2004. The role of sulphonylureas in the management of type 2 diabetes mellitus. Drugs 6: 1339-1358.

Rhee Y and Brunt A, 2011. Flaxseed supplementation improved insulin resistance in obese glucose intolerant people: a randomized crossover design. Nutrition Journal 10: 1-7. https://doi.org/10.1186/1475-2891-10-44

Rodriguez-Leyva D, Bassett CM, McCullough R and Pierce GN, 2010. The cardiovascular effects of flaxseed and its omega-3 fatty acid, alpha-linolenic acid. Canadian Journal of Cardiology 26: 489-496.

Rossi R, Origliani G and Modena MG, 2004. Transdermal 17-β-estradiol and risk of developing type 2 diabetes in a population of healthy, nonobese postmenopausal women. Diabetes Care 27: 645-649.

Safdar B, Pang Z, Liu X, Jatoi MA, Mehmood A, Rashid MT, Ali N, Naveed M, 2019. Flaxseed gum: Extraction, bioactive composition, structural characterization, and its potential antioxidant activity. Journal of Food Biochemistry 43: e13014. https://doi.org/10.1111/jfbc.13014

Scheen AJ, 2004. Combined thiazolidinedione-insulin therapy. Drug Safety 27: 841-856.

Schinner S, Scherbaum WA, Bornstein SR and Barthel A, 2005. Molecular mechanisms of insulin resistance. Diabetic Medicine 22: 674-682. https://doi.org/10.1111/j.1464-5491.2005.01566.x

Sinagra D, Scarpitta AM, Brigandì M and Binanti G, 1997. Alterazioni sieroproteiche nel diabete mellito [Serum protein changes in diabetes mellitus]. Minerva Medicine 88: 75-79. Italian.

Steel RG, 1997, Analysis of variance II: multiway classifications. Principles and procedures of statistics: A biometrical approach. McGraw Hill Book Co. Inc. New York, USA. 204-52.

Tan KP, Chen J, Ward WE and Thompson LU, 2004. Mammary gland morphogenesis is enhanced by exposure to flaxseed or its major lignan during suckling in rats. Experimental Biology and Medicine 229: 147-157. https://doi.org/10.1177/153537020422900203

Tharwat S, Shaheen D, El-Megeid A, Salam R, Rashed L, 2017. Effectiveness of adding flaxseed to type 2 diabetic patient's regimen. Endocrinology and Metabolic Syndrome 6: 267. https://doi.org/10.4172/2161-1017.1000267

Thomas L, Labor U, 1992. Enzymateischer kinetischer colorimetrischer test (GOD-PAP). Biocon Diagnostik Hecke 8: 169-174.

Tietz NW, 1999. Textbook of Clinical Chemistry, CA Burtis and ER Ashwood, Eds. W.B. Saunders, Philadelphia, United States.

Walker BR and Colledge NR, 2013. Davidson's principles and practice of medicine E-book. 22nd Ed., Ralston SH and Penman ID (eds). Elsevier Health Sciences. ISBN: 0702051039, 9780702051036

Xie Y, Bowe B, Li T, Xian H, Yan Y and Al-Aly Z, 2018. Higher blood urea nitrogen is associated with increased risk of incident diabetes mellitus. Kidney International 93: 741-752. https:/doi.org/10.1016/j.kint.2017.08.033