البحث رقم (٩)

Effect of adjusting Omega6:Omega3 ratio through flaxseed and flaxseed oil on blood and histological parameters in diabetic rats

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Abstract

Background: Diabetes is one of the major health concerns . Omega 3 and Omega 6 balanced ratio is important to maintain good health . Omega 3 and Omega 6 correct imbalances in modern diet that lead to health problems . The higher the ratio of Omega 6| Omega 3 the higher the health rate from many diseases. The optimum ratio must be less than 4: 1 that was related to less mortality(70% less). Flaxseed is noted one of the richest non animal source of Omega 3 fatty acids .

Objective: This study aimed to: Investigate the effect of adjusting dietary

Omega 6 : Omega 3 (2.17: 1) fatty acids ratio in diabetic rats on blood glucose, lipids and histopathological parameters with focus on pancreas and kidney .

This ratio is occurred in the experiment diets by adding either flaxseed or flaxseed oil .

Design: 27 diabetic rats were divided into 3 groups (9 rats each), first group was diabetic positive control, the second was flaxseed and the third was flaxseed oil . Nine normal rats were fed basal diet and served as negative control group. Blood samples were collected weekly for glucose monitoring while blood lipids were measured each two weeks. All animals were sacrificed after 6 weeks, organs were weighed and specimens from the kidney and pancreas were taken.

Results: Results showed that treatment with balance ratio of Omega 6 : Omega 3 by flaxseed and flaxseed oil brought sugar level back to near normal level as negative control and had also an effective role in controlling , the increase in total cholesterol in diabetic rats compared with (PC) group . It also has great histopathological effect through stopping and limiting damage in langerhans islet moreover can restore pancreas cells as mitosis division was shown in histopathology . Marked regression was also found in kidney cells of both treated group.

Conclusions:A ratio of (2.17: 1) Omega 6 : Omega 3 by flaxseed and flaxseed oil improve blood sugar in diabetic rats and restore pancreas cells. The study recommended that the addition of seeds and flaxseed oil to adjust ratio of omega-6: omega-3 (2.17: 1) in diet of diabetic patients, to improving the health status

Introduction

Diabetes mellitus became one of the greatest health concerns worldwide(Stolar , et al,2008;Kruger,et al,2012).

Both healthy nutrition and physical activity when included to daily program can decrease the prevalence of type 2 diabetic (T2D) by 60% (Tuomilehto et al .2001;Knowler et al ,2002) . A new area of promising research in therapeutic approaches against obesity and related metabolic diseases including insulin resistance , dyslipidemia , nonalcoholic fatty liver disease (NAFLD) and hypertension is the use of anti-inflammatory nutrients provided through diet.(Browning and Horton 2004 , Staels 2006 ,Weiss et al , 2004 , Lazic et al , 2014)

Omega 3 and Omega 6 fatty acids are polyunsaturated fats essential for human health because they cannot been made in the body. For this reason , people must obtain Omega 3 fatty acids from food sources either animal sources as fishor plant sources like nuts and flaxseed , while Omega-6 fatty acids is obtained from foods such as meat, poultry, and eggs as well as nuts and plant-based oils such as canola and sunflower oils.

By finding a balance between Omega-3 and Omega-6 fatty acids in the diet, both substances can work together to promote health.(Simopoulos,2006).

The average western style diet is highly enriched in polyunsaturated Omega-6 fatty acids and relatively deficient in Omega -3 fatty acids reaching the estimated dietary w6 \ w3 ratio of (10-20 :1) , (Simopoulos,2008).Omega6 and Omega 3 fatty acids are functionally distinct and their metabolites often have the opposing physiologic functions. While diets rich in W6 are generally proinflammatory and promote insulin resistance , the converse is true for W3 enriched diets , the converse is true for Omega 3 fatty acids – enriched diets. (Shmitz and Ecker 2008).

Omega-3 and Omega-6 fatty acids correct imbalances in modern diets that lead to health problems. Eating foods rich in Omega-3 and Omega-6 fatty acids can help lower the risk of chronic diseases such as heart disease, stroke, cancer , asthma, arthritis, as well as lower LDL or “bad” cholesterol. . (Simopoulos,2006).

Increasing Omega-6/Omega-3 fatty acids ratio is associated with increasing the ratio of cardiovascular disease. (Simopoulos and Cleland,2003).

It was shown that Omega 6 /Omega 3 equal to 4/1 was associated with a 70% decrease in total mortality.A ratio of 2.5/1 reduced rectal cell proliferation in patients with colorectal cancer. The lower Omega-6/Omega-3 ratio in women with breast cancer was associated with decreased risk. A ratio of 2-3/1 suppressed inflammation in patients with rheumatoid arthritis, and a ratio of 5/1 had a beneficial effect on patients with asthma, whereas a ratio of 10/1 had adverse consequence (Simopoulos ,2006).

Flaxseed is alternative to plant source of Omega3 fatty acid.It is one of the richest plant source of Omega 3 fatty acid α linolenic(ALA ,C 18:3n-3).(Soltan 2012).

Flaxseed have many nutritional values beside its rich content of Omega 3 ,it also contain fibers, lignans ,protein and antioxidants(Ivanova et al,2011);which have potential effect in decreasing prevalence of many diseases such as cardiovascular diseases , atherosclerosis , cancer , diabetes, arthritis, osteoporosis , autoimmune and neurological disorders . (Goyal et al , 2014)

Flaxseed is considered from the richest plant sources of the Omega 3 fatty acid i.e. αlinolenic acid (ALA)(Tonon et al .2011) and lignans,phytoestrogens, (Singh et al.2011)

The percent of αlinoleic acid in flaxseed oil is 39.00 -60.42% that make an excellent Omega6:Omega 3 fatty acid ratio of 0.3:1.(Pellizon , et al .2007).

High antioxidant content in flaxseed oil like tocopherols and beta-carotene can not prevent its oil from auto oxidation (Holstun and Zetocha1994).

AimsIn this study we aimed to: Investigate the effect of adjusting dietary omega 6 : omega 3 (2.17: 1) fatty acids ratio by using flaxseed or flaxseed oil on blood glucose and lipids in diabetic rats as well as study the effect of adjusting such ratio on histopthological parameters with focus on pancreas and kidney inflammation.

Careful consideration on the design of the diets, so that the ratio of omega 6: omega 3 is balanced in the experiment diets, balanced are occurred by adding either flaxseed or flaxseed oil.

Martials and Methods

Experimental design and diet planning:

A total number of 40 adults Albino male normal rats, weighing 150-180 g, obtained from Agriculture research institute.

Table (1): composition of positive control (PC) , negative control (NC), flaxseed(FS) and flaxseed oil (FSO) diets (g /100g):

Ingredient	PC&NC	FS	FSO
Skim milk	36.4	32.99	36.40
Fiber	1	1	1
Starch	47.60	47.70	47.60
Salt mixture	4	4	4
Vitamin mixture	1	1	1
Corn oil	10	7.60	7.64
flaxseed	-	5.71	-
flaxseed oil	-		2.36

All experiments were carried in the Agriculture research institute.

Composition of experimental diets are shown in table (1).
Diets in all experiment groups contain 12% protein, 4%salt mixture, 1% vitamin mixture and 10%fat.

In all diet, skim milk was served as the main source of protein. Both salt and vitamin mixtures were prepared according to A.O.A.C(2000).
Diets were designed with careful consideration so that Omega6:Omega3 ratio was balanced in both experimental diets to a ratio of 2.17:1 by adding 5.71 g/100g flaxseed side to 7.6 g corn oil in flaxseed group and 2.36 g/100g flaxseed oil side to 7.64 g corn oil in flaxseed oil group .While in both groups feeding basal diet (NC,PC) corn oil served as the only source of fat (10g) so that Omega6:Omega 3 ratio was (69.10:1).

Animal studies

Rats were fed on basal diet for two weeks as an adaption period. Rats were housed under controlled light (12: 12 light dar),temperature were maintained at 25 °C and humidity at 60%respectively with unlimited access to food and water . Rats weight were monitored.All efforts were made to minimize pain and distress during animal husbandry and experiments assessments .Protocol is approved by the institutional Animal Care and Use Committee. Cairo University.(CU-IACUC) approved number(CU II F 32 17).

Induction of diabetes:

The method of Battu et al 2011 , and Sangeetha et al 2011) were used to induce diabetic in rats . two grams of crystalline powdered alloxan monohydrate was dissolved in 50 ml of normal saline to yield a concentration of 40 mg \ ml . 150 mg \ kg body weight of alloxan per rat was administered intraperitoneally after overnight fast. After (72 hr) of injection fasting blood glucose level was measured .An activation dose was also given . The animals showing blood glucose level more than 200 mg \ dl) were considered diabetic (Suma, et al . 2011)

Diabetic rats were (27 rats) divided into 3 groups (9 rats each group),the first group was diabetic positive control (PC),the second group was flaxseed group (FS) and the third one was flaxseed oil group (FSO). Nine normal rats were fed basal diet and served as negative control group(NC) .Blood samples were collected weekly for glucose monitoring while blood lipids were measured each two weeks.

At the end of the experiment rats were sacrificed in a matched way so that the average length of the feeding period was the same in each group.

Biochemical assay:

Blood samples were obtained at intervals as mentioned before. Before blood sampling, rats were fasted for 16 hours. All blood samples were collected by capillary tube from vein pleascus in the eye and centrifuged at 3000 r.p.m. to obtain serum that was stored at -20oC until assayed for the determination of blood glucose, triglyceride , total cholesterol and high density lipoprotein (HDL).

Blood serum sample were analyzed using an enzymically spectrophotometric method as described by Rifai and King (1986).
The absorbance of sample and the standard were measured at 500 nm against the blank using standard solution.

Histopathological techniques

All animals were sacrificed after 6 weeks;organs were weighed and specimens from the kidney and pancreas were taken.

Haematoxylin and eosin stain

The specimens were fixed in 10% formalin, then processed to obtain paraffin blocks. Sections of 4 micron thickness were obtained and stained with haematoxylin and eosin stain (H+F) according to the methods described by Durary and Walington (1980). Sections were examined by light microscopy. The histopathological results of the different groups were tabulated and photographed.

Statistical analysis:
Results were statistically analyzed by the L.S.D.(least significant differences) according to Snedecor and Cochran (1980).

Results:
Table (2) showed blood glucose levels for negative control (NC), positive control (diabetic) group (PC) and both treated groups that had balance ratio of Omega 6 : Omega 3 (2.17:1) with either flaxseed (FS) or flaxseed oil (FSO).From table (2) it could be noticed that there was no significant differences among blood glucose level before induction between the four groups . While after alloxan induction results showed a significant difference between (NC) and each of (PC) and treated groups (FS , FSO) while no significant difference was showed between (PC) , (FS) and (FSO) groups. A gradually decrease occurred in blood glucose level from weak1 for (FS) and (FSO) groups such decrease was 22.46 % and 16.51 % after 3 weeks respectively, while after 6 weeks (the end of the experiment) a marked decrease was shown in glucose level for FS and FSO groups till reached 67.8 % for flaxseed and 68.5% for flaxseed oil groups. On the other hand positive control group (PC) showed a marked increase in blood glucose level after one week, then, glucose level fluctuated till reached 390mg/dl after 6 weeks (6.8%higher than zero time after induction).The great influence of FS and FSO on serum glucose levels of diabetic rats could be seen after 6 weeks as no significant difference was shown between glucose level after 6 weeks between (NC) and each of (FS) and (FSO) groups , while highly significant difference was showed between such groups and (PC) group

Table 2: The effect of feeding of FS and FSO on serum glucose of diabetic rats (mg/dl).

time / Treatment	Gluc. Bef.	Gluc. Aft.	week1	week2	week3	week4	week5	week6
NC	90.7a ± 2.75	92.6d ± 5.4	94.8d ± 5.4	95.2e ± 7.9	101.8d ± 5.9	98.6d ± 1.1	103.2e ± 3.4	103.0e ± 2.6
PC	90.0a ± 7.0	365.0a ± 2.6	455.6a ± 23.8	430.2a ± 35.8	418.8a ± 38.2	407.6a ± 36.9	393.2a ± 34.1	390.0a ±2.6
FS	88.4a ± 7.5	369.6a ± 48.3	351.8b ±45.6	343.6b ±43.8	286.6bc ± 23.6	178.2c ± 5.7	129.0c ± 2.6	119.0c ±2,6
FSO	84.2ab ± 3.3	348.8ab ± 11.1	333.4b ±14.6	310.6bc ±9.3	291.2b ± 9.8	180.4c ± 7.8	119.0d ± 1.6	110.0d ±2.6
Mean	88.31a ± 5.2	229.1c ±12.4	308.9bc ±19.7	294.9cd ±22,4	274.6c ±17.8	216.2b ± 14.7	186.1b ±9,7	180.5b ±2.5

NC=negative control PC=positive controlFS=flaxseed group FSO=flaxseed oil group
Mean values in each column having different superscript (a, b, c & d) are significantly different at $P < 0.05$

It is worthy to mention that the treatment with a balance ratio (2.17:1) of Omega 6: 3 by flaxseed and flaxseed oil brought sugar level back to near normal level as negative control (119± 2.6, 110±2.6 and 103±2.6) in respective order.

In this respect, Adlercreutz,(2007) declared that Dietary fibers lignans and alpha 3 fatty acids, in flaxseed have a role in decreasing diabetes complications.It was found that flaxseed lignin secoisolariciresinoldiglucoside (SDG), causeinhabitation in the expression of the phosphoenolpyruvatecarboxykinase gene, into the enzyme that cause glucose synthesis in the liver (Prasad 2002).

Mani et al (2011) mentioned that we can decrease fasting blood glucose by 19.7% in type 2 diabetics by daily intake of 10 g of flaxseed powder for 1 month. Omega 3 was reported to have a great effect on insulin sensitivity and glucose metabolism (Flachs and Rossmeisl, 2014). Many authors have noticed that the benefit of 6%linolenic acid

(LA) in the high fat (HF) diet in the protectionfrom the development of insulin resistance (IR) it also controlled the increase of adipose tissue (Lombardo and Chicco 2016). Studies on dietary obese mice fed corn- oil based HF diet indicate that replacement of 5 to 44% of dietary lipids by Omega -3 in the form of either triacylglycerols (TAG) or phospholipids can protect against the development of dyslipidemia impaired glucose homeostasis and IR (insulin resistance). (Rossmeisl et al, 2012, Janovska et al, 2013). In contrast to that, it was found that neither flaxseed intake Dodin et al, (2008) nor flaxseed oil (Barre et al,2008) caused decrease in fasting blood glucose or insulin levels.

Although some studies noted an effect of each of dietary fiber, lignin and Omega 3 on lowering blood glucose level in diabetic, our results ensure that proper ratio of Omega 6: Omega 3 had the greatest effect on controlling blood glucose level in diabetics rats.

Table (3) showed Total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL) in negative control (NC) , positive control (PC) and both treated groups that had balanced ratio of Omega 6 : Omega 3 (2.17:1) by flaxseed (FS) and flaxseed oil (FSO) . From these results , it could be noticed that after diabetic induction by aloxan, positive control group (PC) and both treatment groups, showed significant higher increase in TC compared with negative control group as there was a significant different between such groups and (NC) . While TC in negative control (NC) group showed insignificant difference between zero time and after 2,4 and 6 weeks . It is important to mention that TC values in positive control group (PC) showed statistically gradually increase after 2,4 and 6 weeks such increase reached 46.6 % at 6 weeks compared with TC after induction .It could be noticed from table(3)that no significant differences was noticed between TC content in FS and FSO at zero,2,4 weeks ,while there was significant difference between FS and FSO after 6 weeks.FS had a significant cholesterol lowering action in the serum of diabetic rats.

In this respect, previous study demonstrated that Omega 3 fatty acids correct imbalances in modern diets that lead to health problems .Eating food rich in Omega 3 fatty acids can help lower the risk of chronic diseases such as heart disease ,stroke and cancer as well as lowering LDL. Alpha linolenic acid (ALA) studies showed that a diet high in ALA helps reduce heart disease and stroke by reducing cholesterol and TG levels ,enhancing the elasticity of blood vessels and preventing the build-up of harmful fat deposits in the arteries.
(Lazic, et al,2014).
It is worthy to mention that balance level of Omega6 and Omega 3 by addition of flaxseed and flaxseed oil had an effective role in controlling the increase in total cholesterol compared with (PC) group that had higher Omega 6 and low quantity of Omega 3.
From results in table (3) it could be noticed that there was no significant difference between TG in negative control (NC) at zero time and after 2 , 4 and 6 weeks. On the other hand a significant increase in TG in positive control (PC) occurred after induction and at weeks 2, 4 and 6 .Regarding (FS) and (FSO)groups results showed a gradually decrease in TG level from week two , moreover such decrease reached 19.2and 10.99% after 6 weeks when compared with TG in zero time after induction. It is important to mention that (FS) group showed a significant higher decrease in TG than (FSO) group.

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Table 3: Total cholesterol(T.C) , triglyceride(T.G) and high density lipoprotein (HDL) for 6w in negative control(NC) , positive control(PC), Flaxseed(FS) and Flaxseed oil(FSO) groups

Treatment	Time	NC	PC	FS	FSO	interaction
T.C	Zero	79.2 f ±3.5	93.4 e ± 2.4	94.8 de ±3	95.4 de ±2.4	3.57
	2 wk	79.6 f ±2.3	107 c ± 1.6	96.6 de ±2.3	96.8 de ±1.9	
	4wk	79.2 f ± 2.8	135 b ±3.8	96.2 de ±2.4	98 d ±1.6	
	6wk	82.2 f ± 2.9	175 a ±4.2	94.4 e ±2.1	97 d ±1.8	
T.G	Zero	63.4 j ±1.8	117.4 e ±7.2	91.6 efg ±2.1	94.6 e ±3.6	5.76
	2 wk	64.6 j ±2.1	125.4c ±5.9	88.2 fgh ±5	92.8 ef ±3.1	
	4wk	63.8 j ±2.3	135.8 b ±9.1	82.6 h ±4.7	87.0 gh ±1.9	
	6wk	66.4 j ±1.8	144 a ±10.5	74 i ±2.9	84.2 h ±2.8	
HDL	Zero	35.6 ghi ±2.1	36.8 fgh ±1.9	36.6 fga ±2.1	37 fgh ±1.6	3.38
	2 wk	40.8 de ±10.3	35.4 ghi ±1.1	39.2 ef ±0.8	41.2 de ±1.3	
	4wk	38.2 efg ±1.3	34 hi ±1	43 cd ±1.4	45.4 bc ±1.1	
	6wk	39.8 def ±1.3	33 i ±0.7	49 a ±1	47.4 ab ±1.1	

Mean values in each column having different superscript (a, b, c & d) are significantly different at $P < 0.05$

Flach and Rossmeisl (2014) reported the effects of long – chain polyunsaturated fatty acids Omega 3 on insulin sensitivity and glucose homesthomeostasis which are improved by Omega 3 in many animal moderns of metabolic syndrome .They also mentioned that results of a majority of clinical trials performed in T2D patient found that Omega-3 has none or marginal effect on metabolic control, while effectively reduce hypertriglyceridemia in these patients.

With regard to HDL after 6 weeks, results showed that treated diabetic rats with flaxseed (FS) and flaxseed oil (FSO) had significant higher level of HDL compared with (NC) and (PC) groups. These values were 49± 1 and 47.4 ± 1.1 mg /dl for flaxseed (FS) and flaxseed oil (FSO) compared with 39.8 ± 1.3 and 33 ± 0.7 for (NC) and (PC) respectively. It is worthy to mention that the greatest effect was shown for flaxseed group (FS) it could be concluded that diabetic rats treated with a proper ratio of Omega 6 :Omega 3 by flaxseed and flaxseed oil led to a marked decrease in TC and TG compared with PC. On the other hand diabetic rats treated with flaxseed and flaxseed oil led to marked increase in HDL with respect to PC diabetic rates and also NC groups.

The initial and final body weights of the experimental rats are illustrated in table (4). Data showed that initial body weights for all the groups at zero time ranged from 157.6 ± 17.2 to 183.4 ± 25.9 without significant differences among all groups. Regarding the final body weight it ranged between 188.2 ± 24.4 in PC group to 234 ± 33.1 in (NC) group. It is important to mention that weight gain showed the lowest value in (PC) group (11.9 ± 2.4) and the highest value was for NC group(29.7 ± 9.3) while weight gain in both treated group fluctuated between (24.4 ± 2.3 in FSO and 19.9 ± 2 in FS groups).

Table 4: Initial , final weight and weight gain in basal diet control , diabetic control flaxseed and flaxseed oil groups

Treatment	Initial weight	Final weight	Weight gain
NC	183.4a ±25.9	234 a ±33.1	29.7 a ±9.3
PC	168,8a ±20	188.2b ±24.4	11.9c ±2.4
FS	157.6 a ±17.2	189.2 b ±22.7	19.9b ±2.0
FSO	172.2 a ±26.6	214.4 ab ±35.3	24.4ab ±2.3
LSD	NS	34.11	6.79

Mean values in each column having different superscript (a, b, c & d) are significantly different at $P < 0.05$

Data in table (5) showed the effect of different experimental diets on weight and relative weight of pancreas, kidney heart, liver and spleen. From results in this table, it could be noticed that mean weight of pancreas, kidney, liver and spleen didn't differ significantly between groups, while relative weight of all organs was statically higher in (PC) group than other groups.

Table 5 : Organs weight and relative weight in basal diet control, diabetic control, flaxseed and flaxseed oil groups

	Pancreas		Kidney		heart		Liver		spleen	
Treatment	Weight	relative	weight	relative	weight	relative	weight	relative	weight	relative
NC	0.3 ±0.04 A	0.1 B	1.3 ±0.12 A	0.55 D	0.7 ±0.05 A	0.28 B	6.7 ±1.04 A	2.9 C	0.8 ±0.09 A	0.32 C
PC	0.3 ±0.04 A	0.14 A	1.5 ±0.21 A	0.77 A	0.6 ±0.07 AB	0.33 A	6.9 ±1.02 A	3.6 A	0.8 ±0.13 A	0.42 A
FS	0.2 ±0.05 A	0.09 B	1.4 ±0.27 A	0.67 C	0.6 ±0.1 BC	0.26 B	6.5 ±0.86 A	3.1 BC	0.8 ±0.13 A	0.38 B
FSO	0.2 ±0.04 A	0.12 B	1.4 ±0.23 A	0.72 B	0.5 ±0.06 C	0.26 B	6.3 ±0.93 A	3.3 B	0.7 ±0.1 A	0.35 BC
Interaction LSD	NS	0.02	NS	0.04	0.09	0.03	NS	0.31	NS	0.04

Mean values in each column having different superscript (a, b, c & d) are significantly different at $P < 0.05$

It is important to mention that no significant difference was found in relative heart and pancreas weight between (NC) group and both treated groups.

Relative weight of liver showed no significant difference between (NC) and (FS) group , with concern to relative weight of kidney and spleen, a significant difference was found between (NC) and (FS) groups. While an increase of relative weight was found in (FSO) group in relative

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weight of these organs compared with (NC) group but these values were statistically lower than (PC).
It could be noticed from the same table that a significant difference was showed between groups in relative kidney. A significant difference was showed between PC and each of NC, (FS) and FSO concerning liver and spleen relative weight . Moreover insignificant difference was showed between (FSO) and NC group in spleen relative weight. Moreover relative liver weight in Flaxseed group showed no significant different compared with (NC) group.

Results on histopathological parameters are shown in figure (1) and (2).
Figure 1 represent histopathological parameters of Pancreas. From this figure it could be revealed that negative control rats (NC) showed normal islets of langerhans embedded in the exocrine portion (fig. 1a). Meanwhile pancreas of alloxan treated group (PC) revealed deleterious histopathological alterations varying from cytoplasmic vacuolation and necrosis of β cells (fig. 1b) to severe atrophy of langerhans islet and massive loss of β cells (fig. 1c). In addition ,to vacuolation of exocrine pancreatic acinar cells (fig. 1d). The blood vessels revealed hyalinization of arteriolar wall associated with cystic dilatation of pancreatic duct (fig. 1e). Pancreatitis with congestion of blood vessels and per vascular as well as interacinar mononuclear cell infiltration (fig. 1f) was also demonstrated. In other study a morphological change in pancreatic tissue of rats after the administration of alloxan characterized most pronounced degenerative change in the central regions of the islets of langerhans. The number and size of islets umen-sheny shape them wrong. The number of B-cells in the islets of sharply reduced, in most of them marked vacuolization of the cytoplasm, reducing the size of the nuclei, Chromatin condensation, in some cells kariopik-noz. Presence of a lymphocytic infiltrate along the periphery of the islets, interlobular connective tissue edema, congestion of the capillaries, Vascular stasis traced. (Gati, 2016) (FSO) group revealed

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less damaged langerhans islet with mild cytoplasmic vacuolation (fig. 1g). Marked restoration of langerhans islet with presence of mitotic figure (fig. 1h) was characteristically demonstrated in (FSO) group. In this respect it was found that increased dietary intake of fish oil (rich in omega 3)restored the activity of insulin receptor tyrosine kinase towards control value (Flckova et al, 1994) . Riccillo et al (2011) reported that type 2- diabetics induce markrdly abnormal change in rat islets of pancreas

Soltan 2012 studied the effect of varieties sources of Omega 3 fatty acids on diabetics rats and noted that Omega 3 supplies to had a protective effect on pancreatic B –cell which may due to the decrease of oxidation stress.

Results on histopathological parameters of kidney are presented in figure (2). From figure (2) it could be noticed that kidneys of negative control (NC) rats showed normal renal parenchyma with normal glomeruli and renal tubules (fig. 2a). Whereas those of alloxan treated group (PC) revealed severe histopathological alterations in renal glomeruli, tubules and interstitial tissue. Glomerular lesions was characterized by glomerular hypertrophy associated with congestion and thickening of glomerular basement membrane (fig. 2b) and mesangial expansion with intraluminal aggregation of protein cast in the surrounding renal tubules (fig. 2c) . Extensive vacuolar degeneration of renal tubular epithelium associated with mononuclear cell infiltration (fig. 2d) was frequently demonstrated. Blood vessels revealed medial and adventitial degeneration with mild perivascular edema and hemorrhage (fig. 2e) Group (FSO) revealed marked regression of the histopathological lesions compared to alloxan treated one and the lesions were confined to glomerular congestion and presence of few protein cast in some renal tubular lumina (fig. 2f). Group(FS) revealed glomerular congestion and the renal tubules appeared normal except for some renal tubules showed cytoplasmic vacuolation (fig. 2g).

This finding is in agreement with Lazic et al , (2014) who noted that diets enriched with Omega 3 have been shown to improve renal function in type 2 diabetics.

From both histopathological steam and blood analysis it could be deduced that balanced ratio of Omega 6 : Omega 3 have a great effect on the treatment of diabetic and the control of both blood glucose and blood lipids in rats treated with alloxan through stopping and limiting damage in langerhans islet and restoration of pancreas cells which was noted through mitosis division as shown in histopathology . Marked regression was also found in kidney cells in both(FS) and (FSO) groups with renal tubules that appeared nearly normal as negative control group (NC) compared with (PC) group that showed severe histopathological alterations in renal glomeruli ,tubules and interstitial tissue in kidney . In this respect , Simopoulos, (2006), mentioned that lower ratio of ω-6/ω-3 fatty acids is desirable as it is likely to reduce the risk of many of the chronic diseases of high prevalence in western societies, as well as in the developing countries. When comparing the above effect with great deterioration in blood and histopathological parameters seen in severe atrophy, necrosis and massive loss of β langerhans cells in pancreas and also severe histopathological alteration in renal glomeruli, tubules and interstitial tissue in kidney in positive control group. It is recommended to adjust Omega 6 :Omega 3 in diets for people with diabetics mellitus to stop, control and treat deterioration caused by diabetics in organs specially pancreas thus controlling sugar and lipid levels in blood thus, maintaining normal blood parameters and normal life for diabetic patients.

Conclusion

It can be concluded that the consumption of

1) Omega 3 is very important for the prevention management of coronary disease , hypertension , diabetes and other inflammatory and autoimmune condition.
2) As results of revolution at the last decade Omega 6 consumption increase through the high intake of some plant oil rich in Omega 6 and poor in Omega 3 (saturated oils- corn oil). On the other hand consumption of Omega 3 decrease as consequence of less consumed fish, flaxseed and other sources Of Omega 3 that lead to imbalance ratio of Omega 6: Omega 3 (20 , 30 :1) rather than (1:1) as was in the past , which caused an increase and prevalence of many diseases .

Our study insure that balanced can easily and cheaply be achieved through flaxseed and flaxseed oil and that balanced ratio had a great effect not only in adjusting blood glucose level in diabetic but also helps repairing renovating B cells in pancreas showed in mitotic division (Candela et al , 2011)

The study recommended the addition of seeds and flaxseed oil to adjust ratio of omega-6: omega-3 (2.17: 1) in diet of diabetic patients, to improve their health status .

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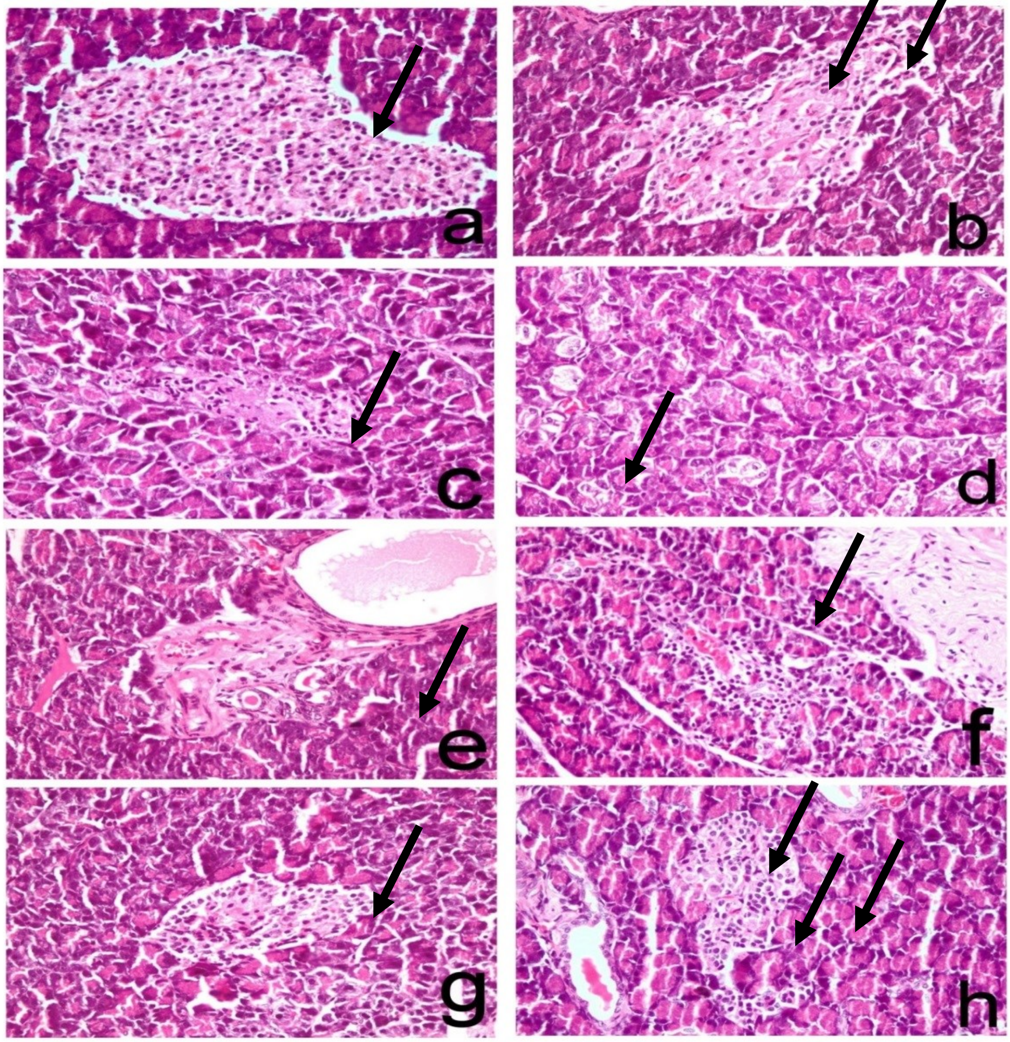
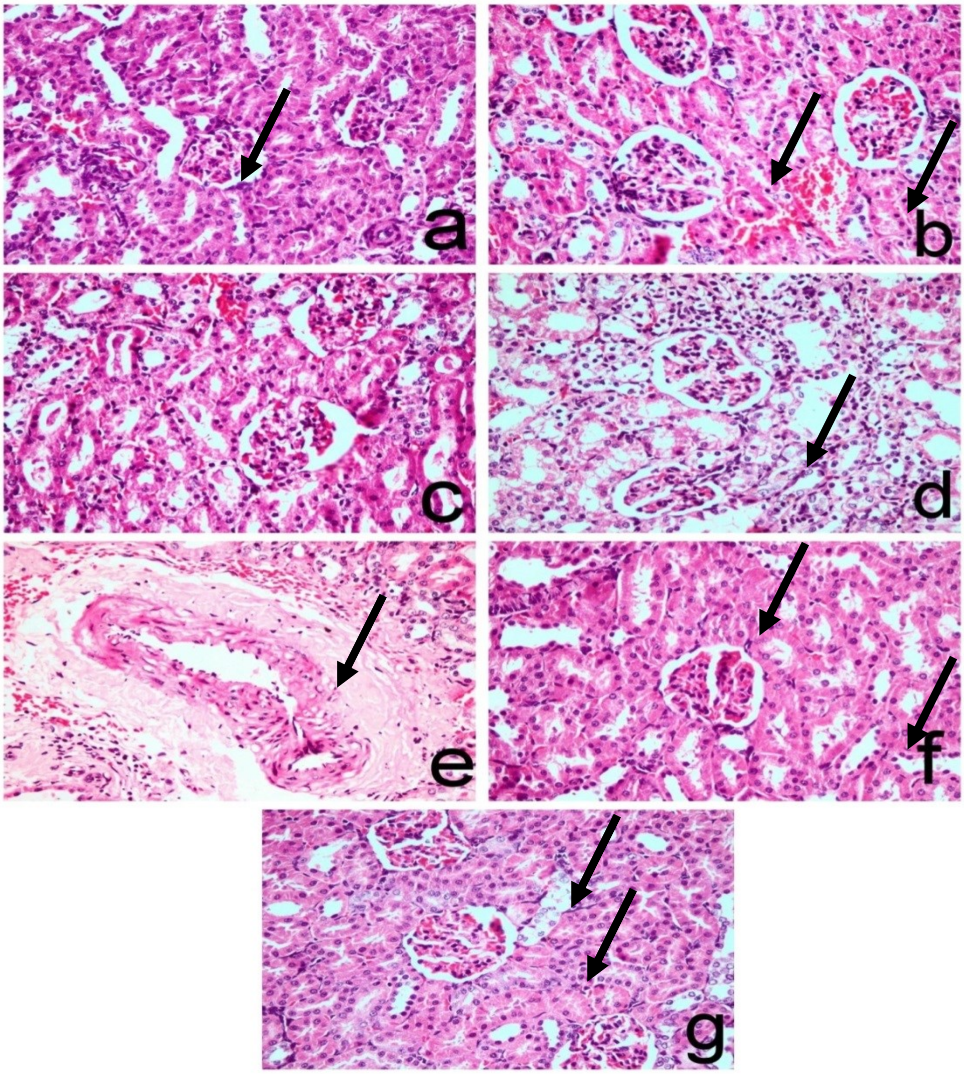
(Fig. 1):Pancreas of negative and positive control and bothtreated groups.



(Fig. 2) :Kidney of negative and positive control and both treatedgroups.



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الملخص

تأثير تعديل نسبة أوميجا ٦ الي اوميجا ٣ باستخدام زيت و بذور الكتان على الدم والهستوباثولوجي للفئران المصابة بداء السكري.

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يعد مرض السكر احد أهم المخاوف الصحية المسببة للعديد من المشاكل الصحية .و قد وجد إن التوازن بين أوميجا ٦ وأوميجا ٣ هام للحفاظ على صحة جيدة و الأنظمة الغذائية الحديثة غير السليمه تؤدي لاختلال النسبة بينهما مما يتسبب في انتشار العديد من المشاكل الصحية حيث انه كلما ارتفعت نسبة اوميجا ٦ عن اوميجا ٣ كلما زاد معدل الاصابه بالعديد من الأمراض.

و قد وجد أن نسبه اوميجا ٦: اوميجا ٣ المثلى يجب ان تكون أقل من ٤: ١ حيث ارتبطت هذه النسبة في كثير من الدراسات بمعدل وفيات أقل (٧٠٪).

و تعد بذور الكتان واحدة من أغنى المصادر غير الحيوانية للحمض الدهني اوميجا ٣.

ويهدف البحث إلى دراسة تأثير ضبط نسبه اوميجا ٦: اوميجا ٣ (٢.١٧: ١) في فئران التجارب المصابة بمرض السكر على جلوكوز الدم والدهون والحالة الهستوباثولوجية للبنكرياس والكلى.تم ضبط هذه النسبة في وجبات التجربة عن طريق إضافة زيت او بذور الكتان حيث اجريت التجربه علي ٣٦ فأر: تسعة فئران سليمة تم تغذيتها علي العليقه الاساسيه كمجموعة ضابطة سلبية بينما ٢٧ فأرا تم إصابتهم مرض السكر و تم تقسيمهم عشوائيا إلى ٣ مجموعات (٩ فأر كل منهم) : اول مجموعه منهم الضابطة الإيجابية لمرض السكر ، اما ألمجموعه الثانية و الثالثة فقد تم ضبط نسبه اوميجا ٦: اوميجا ٣ عن طريق

أضافه بذور او زيت الكتان علي التوالي. وتم جمع عينات من الدم أسبوعيا لمتابعه الجلوكوز بينما قياس دهون الدم كل أسبوعين.

أنهيت التجربه بذبح الفئران بعد ٦ أسابيع ثم وزنت الأعضاء و أخذت عينات من الكلى والبنكرياس للتشريح ..

أظهرت النتائج أن المعاملة بنسب متوازنة من اوميجا ٦: اوميجا ٣ بواسطة بذور الكتان وزيت بذرة الكتان قد عادت بمستوى السكر إلى مستوى قريب من المجموعه الضابطه السلبية وكان لها دور فعال في السيطرة على زيادة الكوليسترول الكلي في الفئران المصابة بمرض السكر مقارنة بالمجموعة الضابطه الموجبه. كما أن له تأثيرا هستوباثولوجي كبير من خلال التوقف والحد من الأضرار في جزر لانجرهانز علاوة على ذلك تم إعادة بناء البنكرياس حيث اوضح الفحص التشريحي حدوث انقسام ميتوزي في خلاياها. كما لوحظ ايضا تحسن ملحوظ في خلايا الكلى في كل المجموعات المعالجة..

الخلاصه: ضبط نسبة اوميجا ٦: اوميجا ٣ (٢.١٧: ١)بواسطة بذور الكتان وزيت بذور الكتان يحسن نسبة السكر في الدم لدى مرضى السكري ويعيد بناء خلايا البنكرياس

وتوصي الدراسة بضرورة إضافة بذور وزيت الكتان لضبط نسبة اوميجا ٦: اوميجا ٣ (٢.١٧: ١) في وجبات مرضي السكر لما لها من تأثيرات في تحسين الحالة الصحية