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The Role of Chitosan and Wheat Germ as Antidiabetic Substances in Diabetic Rats

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ABSTRACT

Diabetes mellitus (DM) is a complex and multivarious group of disorders that disturbs the metabolism of carbohydrate, fat and protein. Anti-diabetic effect of chitosan and wheat germ in alloxan diabetic rats was studied. Five groups of rats (Sprague-Dawley) were used; group 1 was normal (negative control) fed on a standard diet whereas groups (2, 3, 4 and 5) were diabetic and fed on a standard diet. Group 2 was considered as positive control. Chitosan (CH) (5%) was added to diet 3, wheat germ (WG) (10%) to diet 4 and a mixture of chitosan and wheat germ (7.5%) was added to diet 5. Feeding period continued for 6 weeks. At the end of the experiment fasting blood samples were obtained from animals in all groups and analyzed for several biochemical parameters. The results showed that rats in groups 3, 4 and 5 attained more body weight than group2. Serum glucose, malondialdhyde, total lipids, total cholesterol, LDL cholesterol and triglycerides were all increased in diabetic positive control group. The total antioxidant capacity and HDL cholesterol were decreased. Also Liver and kidney functions were elevated. Addition of either chitosan or wheat germ to the diet caused a marked improvement of all these parameters and returned back to near normal values. Histopathological examination showed that positive control rats have hypertrophy, hyperplasia, congestion and vacuolations of islets of Langerhans compared with negative control and treated groups. The conclusion is chitosan and the mixture of chitosan and wheat germ supplementation can protect against health hazards exerted due to diabetes mellitus.
Keywords: Diabetes mellitus, chitosan, wheat germ, lipid profile, liver function, malondialdhyde.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic disease with complex underlying etiologies. It is a group of metabolic disorder characterized by elevated blood glucose level resulting from the defects in insulin secretion, insulin action or both [1]. The incidence of diabetes mellitus is on the rise world wise. Based on the World health organization (WHO) report, the number of diabetic patients is expected to increase from 171 million in year 2000 to 366 million or more by the year 2030 [2]. Diabetes is affecting approximately 3% of the population worldwide [3]. Increasing evidences from both experimental and clinical studies suggest that oxidative stress plays a major role in the pathogenesis of DM. Abnormally high level of free radicals and the simultaneous decline in antioxidant defense mechanisms may lead to the damage of cellular organelles and enzymes, increased lipid peroxidation and development of insulin resistance [4].

Current drugs used for the treatment of diabetes are associated with several side effects and hence there is need for effective, safe and better oral hypoglycemic agents [5]. Chitosan is a natural nontoxic biopolymer produced by the deacetylation of chitin, a major component of the shells of crustaceans such as crab, shrimp and crawfish. Currently, chitosan has received considerable attention for its commercial applications in the biomedical, food and chemical industries [6,7]. It is a hydrophilic, biocompatible and biodegradable polymer with low toxicity [8]. Because of its bioadhesive properties, chitosan has also received substantial attention in novel bioadhesive drug delivery systems with aim to improve the bioavailability of drugs by prolonging the residence time at the site of absorption [9].

Wheat germ is a by-product of the flour milling industry and is the most potential and excellent sources of vitamins, minerals, fiber and proteins at a relative low cost [10]. It contains 3 times as much protein of high biological value, 7 times as much fat, 50 times as much sugar and 6 times as much mineral as compared to flour content from the endosperm [11]. In addition to wheat germ is the richest known natural source of tocopherols and also abundant in B-group vitamins [12]. Wheat germ protein has been classed with effectively better animal proteins and is rich in seventeen amino acids, especially the essential amino acids lysine, methionine and threonine, in which many cereals are deficient [13]. Wheat germ is the most important nutritious part of wheat grain separated by ultra-modern milling technology which keeps free radical in check which in turn helps to prevent heart diseases, cancers and diabetes. It is also very important for vitality and healthy heart, further lowering the risk of coronary heart diseases and helps to reduce obesity and delays ageing process. The presence of sugar in germ makes it acceptable and tasty. Over 80 percent of fat present in wheat germ is made up of polyunsaturated fatty acids (PUFAs). Wheat germ is a good source of phytosterol and one such as phytosterol is beta sistosterol which is a plant sterol found in almost all plants. According to Cara et al. [14], beta sistosterol regulates of insulin in the presence of non-stimulatory glucose concentrations and inhibiting glucose -6-phosphatase. Hence, the objective of the current study was to evaluate the effects of chitosan and wheat germ against hazards of diabetes mellitus in experimental rats.

MATERIALS AND METHODS

MATERIALS

Chitosan preparation: Isolation of chitin and preparation of chitosan were prepared according to the method described by [15].

Wheat germ: was obtained from South Cairo and Giza flour Mills &Bakeries Company.

Reagents: All kits were purchased from Bio-diagnostic Company, Egypt.

Experimental animals:

Forty Sprague-Dawley male albino rats weighing 130±10g were obtained from the laboratory animal house, National Research Centre, Egypt. The animals were housed individually in stainless steel cages in a controlled environment (25±2 °C, 50-60% relative humidity and 12-hour light-dark cycle). The animals were fed ad libitum with a basal diet and water for two weeks, and were then randomly assigned to 5 groups (8 rats each). Animal experiments were conducted according to the guidelines of Animal Care and Ethics Committee of the National Research Centre, Egypt.

Induction of hyperglycemia in rats:

Hyperglycemia was induced in the rats by intra-peritoneal injection of 5% solution of alloxan in saline (125mg/kg body weight) [16]. Before induction of hyperglycemic fasting blood samples were taken from rats for estimation the level of blood glucose.

After one week of the induction blood sample was taken for analysis of fasting blood glucose which fallow up for 3 weeks to insure the induction of hyperglycemia. For recorded the initial reading blood samples were taken for estimation of serum total lipid, triglycerides, total cholesterol, HDL- cholesterol, LDL- cholesterol, ALT, AST, ALP activity, creatinine and urea.

Experimental design: Thirty two of diabetic rats were divided into 4 groups each contain 8 rats. In addition 8 normal rats were fed basal diet without any treatment (negative control). All the rats were kept individually in stainless steel cages. The diets and water were given for 6 weeks. The body weight and food consumption during the experimental period were followed weekly.

Group 1: (negative control): normal rats received basal diet consisting of corn starch 65%, casein 15%, corn oil 10%, salt mixture 4%, vitamins mixture 1% and cellulose 5% [17].
Group 2: (positive control): diabetic rats received basal diet.
Groups 3, 4 and 5 are diabetic rats fed on basal diet and receiving 5% chitosan, 10 % wheat germ and 7.5 % mixture of them respectively.

Blood sampling: After 6 weeks (period of treatment), the rats were fasted overnight. All the animals were scarified by cervical decapitation. Blood samples were collected from each rat from the retro-orbital vein and were received into clean dry centrifuge tubes. Serum was separated by centrifugation at 3000 rpm for 15 minutes and kept in deep-freezer at -20 °C until used for estimation of glucose level, total lipid, triglycerides, total cholesterol, HDL-cholesterol, LDL-cholestreol, serum ALT, AST, ALP activity, creatinine, urea, malondialdhyde and total antioxidant capacity.

METHODS

Calculation of body weight gain (BWG) and feed efficiency ratio (FER)

Body weight and food consumption were measured according to Hsu et al. [18]. Using following equation:

$$BWG = Final\ body\ weight - initial\ body\ weight$$

$$Feed\ efficiency\ ratio\ (FER) = \frac{Weight\ gain\ (g)}{Food\ intake\ (g)}$$

Determination of Serum glucose

Serum glucose was determined according to Trinder [19].

Lipid profile

Serum total lipids (TL), triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were determined according to [20-24] respectively.

Determination of Liver function biomarkers

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were measured calorimetrically in serum according to the method described by [25]. Alkaline phosphatase (ALP) activity in serum was determined according to Rec [26].

Determination of Kidney function biomarkers

Determination of urea

Urea content was determined according to the method described by [27].

Determination of creatinine

Creatinine level content determined according to the method described by [28].

Determination of Total antioxidant capacity

Total antioxidant was determined according to the method described by [29].

Determination of lipid peroxide (Malondialdehyde)

Lipid peroxide was determined according to the method described by [30].

Histopathological examination

Pancreas of the sacrificed rats was taken and immersed in 10 % formalin solution. The specimens were then trimmed, washed and dehydrated in ascending grades of alcohol. Dehydrated specimens were cleared in xylol, embedded in paraffin, sectioned at 4-6 microns thickness and stained with heamtoxylin and eosin for histopathological examination according to the method described by [31].

Statistical analysis

Statistical analysis (standard deviation ''SD'' and standard error ''SE'') was carried out according to [32]. LSD (Least significant difference) test was used to compare the significant differences between means of treatment [33]. The statistical package for social science SPSS [34] program version was used for all analysis.

RESULTS AND DISCUSSION

Body weight gain, food intake and feed efficiency ratio:

Mean values of body weight gain, food intake and feed efficiency ratio of the different experimental groups are shown in table (1).

Table 1: Body weight gain, food intake and feed efficiency ratio of the different experimental groups.

Parameters / Treatments	Body weight gain (BWG)(g)	Food intake(FI)(g)	FER
G-1 Negative control	74.25±4.52a	563.12±6.85b	0.13±0.007a
G-2 Positive control	61.50±2.06b	595.37±18.10a	0.10±0.005b
G-3 Chitosan	78.25±1.84a	582.87±7.04ab	0.13±0.003a
G-4 Wheat germ	77.37±2.27a	585.25±4.75ab	0.13±0.003a
G-5 CH+WG	77.62±2.54a	592.75±9.52ab	0.13±0.003a

All values are represented as mean ±S.E. Means with different letters are significantly different (p<0.05).

Tabulated data show that diabetic rats (positive control) had significant decrease in body weight BW (61.50±2.06g) as compared to normal negative control (74.25±4.52g). Addition of chitosan (5%), wheat germ (10%) and the mixture of them (7.5%) to the diets of diabetic groups (3,4 and 5) significantly increased body weight gain as compared to positive control group (78.25±1.84, 77.37±2.27, 77.62±2.54 and 61.50±2.06 g respectively). However there were no significant differences between the three supplemented groups. Concerning food intake (FI) results revealed that positive control group showed significant increase (595.37±18.10g) as compared to negative control group (563.12±6.85g). Groups (3,4,5) recorded non-significant changes in FI as compared to positive control group. The present results showed that addition of chitosan, wheat germ and the mixture of them significantly increased feed efficiency ratio (FER) as compared to positive control group. Our finding demonstrated that our supplements (chitosan, wheat germ and the mixture of them) significantly improved BWG, FI and FER of the diabetic groups (3,4 and5) as compared to positive control group. Diabetes is characterized by sever weight loss was observed in the present study and this result was in agreement with Al-Shamaony et al. and Katiyar et al. [35, 36]. The decrease in body weight gain in diabetic rats might be the result of protein wasting due to unavailability of carbohydrate as an energy source [37]. Chitosan and wheat germ administration controlled the body weight loss in diabetic animals, though there were no significant differences between them and their mixture. These results coincided with Hsien et al. [38]. Hsien et al. [38] also reported that there was no significant change in food consumption among the dietary groups in both non-diabetic and diabetic rats.

Table 2: Serum glucose (mg/dl), total antioxidant capacity (mM/L) and malondialdehyde (nmol/ml) of the different experimental groups.

Parameters / Treatments	Glucose(mg/dl)	Total antioxidant capacity (mM/L)	Malondialdehyde (nmol/ml)
G-1Negative control	69.46±4.95c	1.57±0.013a	3.41±0.04b
G-2Positive control	116.56±4.78a	1.52±0.013b	4.50±0.37a
G-3Chitosan	70.80±3.47c	1.54±0.020ab	1.86±0.10d
G-4 Wheat germ	83.82±1.85b	1.55±0.016ab	2.53±0.23c
G-5CH+WG	73.22±4.51bc	1.56±0.008ab	2.56±0.15c

All values are represented as mean ±S.E. Means with different letters are significantly different (p<0.05).

Data in table (2) showed mean values of serum glucose, total antioxidant capacity and malondialdehyde of diabetic rats fed on different levels of chitosan, wheat germ and their mixture. Tabulated data illustrated that serum glucose level of group 1 (negative normal control) was significantly lower (p<0.05) when compared with diabetic positive control group 2 (69.46±4.95 and 116.46±4.78 mg/dl respectively). On the other hand diabetic groups 3, 4 and 5 which fed on diets containing chitosan, wheat germ and the mixture of them showed significant decrease (p<0.05) in serum glucose level as compared to the positive control group (70.80±3.47, 83.82±1.85, 73.22±4.51 and 116.56±4.78 mg/dl respectively). The best response for serum glucose was obtained in groups 3 (that fed on chitosan) followed by group 5 and group 4 respectively. With regard to the effect of feeding chitosan, wheat germ and their

mixture on serum level of total antioxidant capacity (TAC) in diabetic rats, the present data demonstrated that positive control group had significant decrease in total antioxidant capacity (1.52±0.013 mM/L) as compared to the negative control (1.57±0.013 mM/L). Diabetic groups (3,4,5) fed on basal diet with different levels of chitosan, wheat germ and their mixture showed no significant differences in total antioxidant capacity level as compared to the positive control (1.54±0.020, 1.55±0.016, 1.56±0.008 and 1.52±0.013 mM/L respectively). Concerning malondialdehyde level (MDA), data revealed that positive control group showed significant increase in MDA level as compared to the negative control (4.5±0.37 and 3.41 ±0.04 nmol/ml respectively). Adding chitosan, wheat germ and their mixture to the diets of diabetic groups 3, 4 and 5 significantly decreased the level of MDA as compared to the positive control (1.86±0.10, 2.53±0.23, 2.56±0.15 and 3.41±0.44 nmol/ml respectively). The previous results showed that addition of chitosan, wheat germ and the mixture of them to the diets of rats significantly improved serum glucose level of the diabetic rats. These results are in agreement with Cara et al.[15] who reported that wheat germ is a good source of pyhtosterol and one such phytosterol in beta sistosterol regulates blood sugar and insulin levels in type 2 diabetic by stimulating the release of insulin concentrations and inhibiting glucose -6-phosphatase. Also several studies conducted on animals and patients [39, 40] with diabetes have shown that the intestinal disaccharidase activities are greater than non-diabetic animals or subjects. Many viscous soluble dietary fibers (e.g. chitosan) are capable of reducing the activity of intestinal disaccharidase and delaying the gastric emptying. This will then slow down the absorption of glucose and increase the insulin sensitivity of the peripheral tissue and hence reduce the plasma glucose [41]. Moreover chitosan oligosaccharides can be used as an antidiabetic agent because it increases glucose tolerance and insulin secretion [42]. In addition, Kondo et al. [43] reported that long term (22-week) administration of low molecular weight chitosan prevents the progressive of diabetes mellitus in mice. They suggested that the putative mechanism of the antidiabetic action of chitosan was the prevention of the decrease in B cells in pancreatic islets. Also it has been reported that chitosan may possess a potential for alleviating type 1 diabetic hyperglycemia through the decrease in liver gluconeogenesis and increase in skeletal muscle glucose uptake and use [44]. Moreover chitosan administration to diabetic rats significantly decreased the level of blood glucose and glycosylated hemoglobin (HbA1c) and reduced the activities of gluconeogenic enzymes such as glucose -6-phospahtase and fructose-1,6.bisphospahtase [45].

Malondialdehyde is a good indicator of lipid peroxidation and reflects the degree of oxidation in the body [46]. In the current study remarkable increase in MDA level was observed in the diabetic positive control group as compared to normal negative control group. Also, data showed a significant decrease in total antioxidant capacity level in the positive control as compared to negative control. Addition of chitosan and wheat germ to diets of diabetic rats groups (3, 4 and 5) caused a marked reduction in MDA concentration and an improvement in total antioxidant capacity. These results coincided with Boros et al. and Juskiewicz et al. [47,48]. Juskiewicz et al. [48] demonstrated that wheat germ contains compounds such as benzoquinones and other plant flavonoids which increase the antioxidant potential of serum and control oxidative stress and cell damage. Moreover chitosan and its oligosaccharides

showed antioxidant effects and regulate the antioxidant enzyme activities and reduce lipid peroxidation [49, 50, 36].

Lipid profile

The values of serum total lipid, total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides of the different experimental groups are shown in table (3).

Table 3: Mean values of lipid Parameters of different experimental groups.

Parameters Treatments	Total lipid (mg/dl)	Total cholesterol (mg/dl)	Triglycerides (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)
G-1 Negative control	204.22±20.52c	94.06±10.36b	67.47±6.17b	39.67±1.86b	49.77±2.53b
G-2 Positive control	311.75±11.45 a	123.42±11.19a	83.30±5.15a	53.13±6.18a	39.48±1.26c
G-3 Chitosan	243.18±10.61bc	95.40±12.92ab	48.23±2.88c	36.55±3.43b	55.75±1.92a
G-4 Wheat germ	245.66±7.14b	89.61±2.38b	56.36±3.68bc	37.63±3.50b	50.01±1.78ab
G-5 CH+WG	216.26±15.64bc	91.65±8.88b	45.81±2.35c	33.52±2.80b	54.88±1.02ab

All values are represented as mean ±S.E. Means with different letters are significantly different (p<0.05).

The values reported for serum total lipid were 204.22±20.52 mg/dl for negative control group, 311.75 ±11.45 mg/dl for positive control group, 243.18±10.61 mg/dl for diabetic rats fed on chitosan diet (G3), 245.66±7.14 mg/dl for diabetic rats fed on wheat germ (G4) and 216.26±15.64 mg/dl for rats fed on the mixture of chitosan and wheat germ (G5). Serum total cholesterol was 94.06±10.36 mg/dl in negative control increased to 123.42±11.19 mg/dl for diabetic rats (positive control), 95.40±12.92, 89.61±2.38 and 91.65±8.88 mg/dl for groups (3,4 and 5) respectively. The values reported for serum triglycerides were 67.47± 6.17, 83.30± 5.15, 48.23± 2.88, 56.36±3.68 and 45.81± 2.35 mg /dl for the negative control and groups 2, 3, 4 and 5 respectively. It can be noticed that all lipid parameters except HDL-cholesterol significantly elevated in diabetic control group (positive control) as compared to normal control group (negative control). After addition of chitosan, wheat germ and the mixture of them, the alternation in lipid metabolism was partially modulated as evidenced by decrease levels of serum total lipid, total cholesterol, triglycerides, LDL-cholesterol level and at the same time increased level of HDL-cholesterol in diabetic groups. Although there were no significant differences in the results of lipid parameters between groups 3, 4 and 5, the best values for lipid parameters were obtained by feeding a mixture of wheat germ and chitosan to diabetic rats (group 5).

Diabetes mellitus is usually associated with hyperlipidemia [51]. The current results are supported by Xia et al. [50] who reported that chitosan significantly lowered serum total triglycerides (TG), total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) concentrations and elevated the high density lipoprotein cholesterol (HDL-C) level. This result suggested that chitosan could effectively prevent hypercholesterolemia. Moreover chitosan has been shown to possess the hypolipidemic and hypoglycemic (major in type 2 diabetic model)

effects in vitro and in vivo [52,43]. Also our data coincided with those of Katiyar et al. [36] who demonstrated that serum lipids showed significant decrease in diabetic rat treated with chitooligosaccharides. Also, chitosan reduced the concentration of plasma cholesterol in animals [53] and in type 2 diabetic patients in combination with hypercholesterolemia [54]. With regard to the effect of wheat germ, the present results agreed with previous study established that addition of 7% wheat germ to a high fat and high cholesterol diet improved lipoprotein in rats [55]. In rats the absorption of triacylglycerol and cholesterol was delayed and reduced by wheat germ and other wheat fraction in part as a result of the inhibition of pancreatic lipase and the reduction in triacylglycerol lipolysis [56]. In addition to, Louts et al. [57] showed that wheat germ plays a beneficial role in the dietary management of hyperlipidemia. Moreover, Cara et al. [58] reported that inclusion of wheat germ in a meal reduced plasma chylomicron cholesterol concentration by 27%. Wheat germ contains fibers, it has been thought that some effect on cholesterol metabolism might be mediated by dietary fiber. In addition, wheat germ has a high content of phytosterol relative to total fat. Phytosterols intrinsic to wheat germ are biologically active and have a prominent role in reducing cholesterol absorption, consequently reducing cholesterol absorption would be lower serum cholesterol level and LDL-cholesterol [59,60].

Liver and kidney functions:

Results of liver and kidney functions of the different experimental groups are shown in table (4).

Table4: Liver and Kidney functions of the different experimental groups.

Parameters \ Treatments	AST (IU/L)	ALT (IU/L)	ALP(IU/L)	Urea (mg/dl)	Creatinine (mg/dl)
G-1 Negative control	37.83±4.53c	35.87±4.04b	83.37±5.85b	26.15±3.045b	0.95±0.06b
G-2 Positive control	50.41±3.01a	55.12±3.11a	135.32±3.74a	50.30±4.14a	1.67±0.11a
G-3 Chitosan	41.40±2.86b	21.50±2.63c	73.26±4.69b	24.98±1.75b	0.96±0.096b
G-4 Wheat germ	37.06±4.72c	39.75±4.14b	79.81±5.73b	28.77±3.19b	1.05±0.15b
G-5 CH+WG	39.50±2.95bc	31.62±3.69bc	77.46±3.84b	26.11±1.84b	0.90±0.071b

All values are represented as mean ±S.E. Means with different letters are significantly different (p<0.05).

Data in this table showed a significant increase of aspartate amino transferase (AST) in the diabetic positive control (50.41± 3.01 IU/L) as compared to the negative control group (37.83±4.53IU/L). Addition of chitosan, wheat germ and their mixture lead to alternation of AST value in these groups. AST levels significantly decreased in all groups compared to positive control. The most decrease was obtained in group 4 (37.06±4.72 IU/L), followed by group 5 (39.50±2.95IU/L) and group 3 (41.40±2.86IU/L) respectively. With regard to alanine amino transeferase level (ALT) data showed significant increase in positive control group (55.12±3.11 IU/L) as compared to negative control (35.87±4.04 IU/L). Our experimental groups (3, 4 and 5) exhibited significant decreases in ALT level as compared to positive control group. (21.50±2.63, 39.75±4.14, 31.62±3.69 and 55.12±3.11 IU/L respectively).

Alkaline phosphatase (ALP) level showed a significant increase in positive control group (135.32±3.74 IU/L) as compared to negative control group (83.37±5.85 IU/L). Addition of chitosan, wheat germ and their mixture significantly decreased ALP level (73.26±4.69, 79.81± 5.73 and 77.46 ±3.84 IU/L respectively) as compared to positive control. In diabetic animals the changes in the levels of AST, ALT, ALP are directly related to changes in metabolism in which the enzymes are involved. The increased activities of transaminases, which are active in the absence of insulin due to the availability of amino acids in the blood of diabetes mellitus and also responsible for the increased gluconeogenesis and ketogensis. Diabetes caused lipid peroxidation that mediated tissues damage in pancreas, liver, kidney and heart. The increase in the level of these enzymes in diabetes may be as a result of the leaking out from the tissue and then migrating into the blood stream [61]. The restoration of AST, ALT and ALP to their respective normal levels was observed in our experimental groups. Our results were compatible with Barakat et al. [62], who revealed that induction of liver injury with chloropyrifos (CPF) intake is reflected by significant increase in all hepatic serum enzyme activites than control and treated groups. There is a noticeable improvement in all studied enzyme activites by fermented wheat germ treatment. Katiyar et al.[36] demonstrated that serum glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT) activity were increased significantly in alloxan induced diabetic mice in respect to control group. These two parameters in serum were come towards control level after treatment with chitooligosaccharides (COS). Data concerning kidney function are shown also in the same table (4). Serum urea and creatinine levels in diabetic rats (positive control) were very high when compared with normal rats and diabetic rats supplemented with chitosan, wheat germ and the mixture of them. Addition of chitosan, wheat germ and the mixture of them to the diets of diabetic groups (3, 4 and 5) decreased significantly the level of serum urea and creatinine as compared to the positive control, and this decrease reach to the normal range. The diabetic hyperglycemia induced by alloxan produces elevation of serum levels of urea and creatinine which are considered as significant markers of renal dysfunction [63,36]. Barakat et al. [62] reported that supplementation of wheat germ to the diet of nephrotoxic rats caused significant improvement in kidney function.
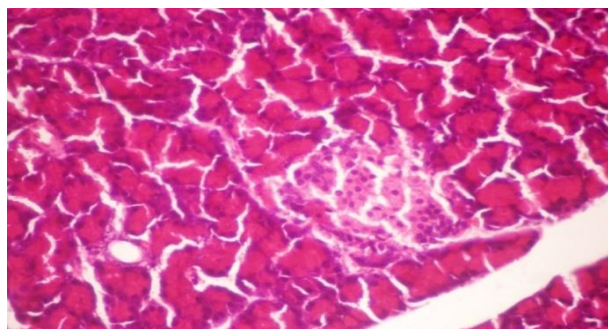
Histopathological examination

Fig.1: pancreas of rat from group 1 showing the normal histological structure of pancreas (H and E x 400).
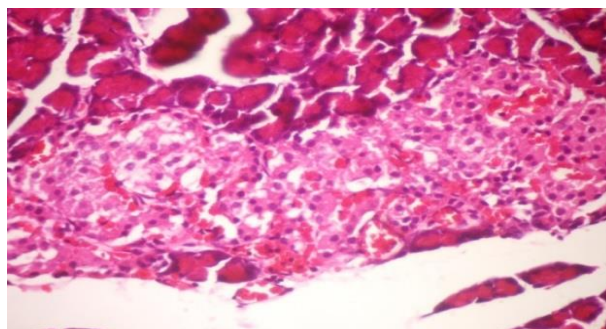

Fig.2: pancreas of rat from group 2 showing hypertrophy,hyperplasia,congestion and vacuolations of islets of langerhan's(H and E x 400).
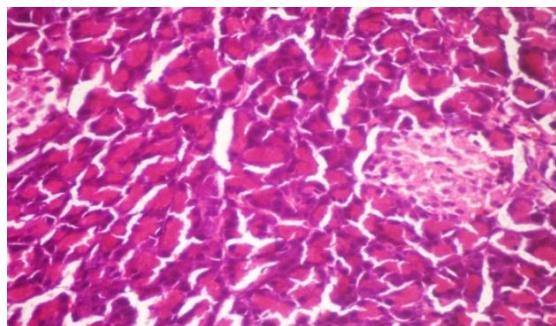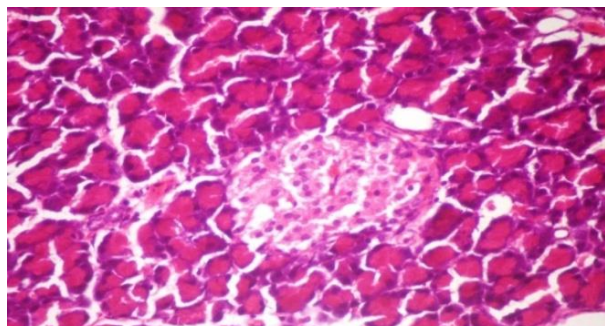
Fig.3: pancreas of rat from group 3 showing vacuolations of some B cells of islets of lanerghan's (H and E x400).

Fig.4: pancreas of rat from group 4 showing no histopathological changes(H and E x400).
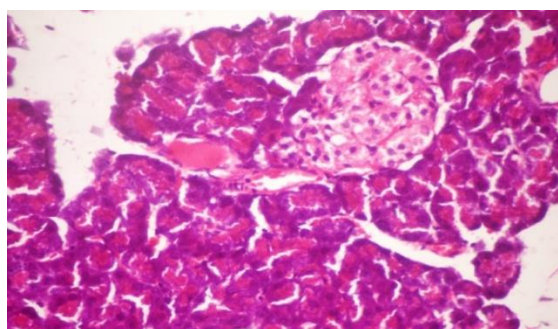

Fig.5: pancreas of rat from group 5 showing no histopathological changes (H and E x400).

CONCLUSION

Our data have shown that chitosan, wheat germ and the mixture of them can improve blood glucose level, lipid profile, liver and kidney functions, decreasing oxidative stress and ameliorate histological alteration.

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