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# Protective effects of anti-obesity and anti-diabetic activities of date pits powder on alloxan Induced diabetic rats

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***Abstract***
*The aim of the study was to evaluate the effects of date pits powder on body and fat weights, lipid profile, glucose, insulin, leptin hormones, liver enzymes, renal tissue antioxidant enzymes and histopathology of kidneys in obese diabetic rats. Forty five male Albino rats were randomized into 5 equal groups (n=9). Group A (negative control rats) was fed on basal diet, while the other 4 groups were fed on high-fat diet (HFD) for 4 weeks to induce acute obesity and hyperlipidemia. The obese rats were then rendered diabetic by intraperitoneal injection of alloxan (120 mg/kg/day) for 5 days. On becoming diabetic, group B was kept obese diabetic as positive control and while groups C, D and E were fed on basal diet containing 5%, 7.5% and 10% date pits powder respectively replaced equal amount of starch for 6 weeks. Blood samples were collected for biochemical analyses. Kidneys were dissected out for histopathology and renal homogenates were prepared to assay activities of tissue antioxidant enzymes. The results showed that the obese diabetic rats fed on 5, 7.5 and 10% date pits powder were significantly reduced in body, fat weights, serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total cholesterol, triglycerides and low density lipoprotein. It also decreased blood urea, creatinine, glucose and leptin hormone. On the other hand the obese diabetic rats fed on 5, 7.5 and 10% date pits powder were significantly increased in insulin levels, activities of superoxide dismutase, glutathione peroxidase and catalase antioxidant enzymes in renal tissues and alleviated kidney histopathological lesions induced by diabetes. The results denote that date pits extracts possess anti-obesity, antidiabetic effects, and consequences in obese diabetic rats.*

***Ker words: date pits powder, anti-diabetic, anti-obesity, lipid profile, glucose, insulin, leptin hormones, liver enzymes, renal tissue antioxidant.***

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## I. Introduction

Obesity is the most common health problem to become an epidemic on a global scale, especially in the developed countries of the world including Europe, the United States of America (USA) and Japan, which represents an increase in the risk of disease and death. Obesity is defined according to the World Health Organization (WHO) as an increase in fat accumulation that affects human health. Obesity has also been defined as an increase in adipose tissue mass (Sahib *et al.,* 2012). Moreover, obesity is associated with many diseases such as type 2 diabetes, atherosclerosis, cardiovascular disease, hypertension, osteoporosis and some types of cancer (Yun, 2010).

Diabetes is the most common endocrine disease and heterogeneous metabolic disorder. It affects 5% of the world's population. It is characterized by a lack of secretion and / or action of insulin, insulin resistance, and abnormal metabolism of glucose, fats and protein. Globally, diabetes causes a high death rate and is the second most common cause of death after cancer. It is known to cause a variety of complications such as kidney failure, blindness, amputations, neurological complications, and vascular complications of coronary artery disease, cerebral vascular disease and / or premature death (Middha *et al.,* 2014 and Shaikh and Shrivastava, 2014).

Date seeds contain many active compounds in the form of antioxidants, such as phenolic compounds, which may reduce free-radical levels by virtue of their anti-inflammatory and immune stimulant activities (Yasin *et al.,* 2015 and Zhang *et al.,* 2013). The phenolic content of date seeds includes protocatechuic acid, p-hydroxybenzoic, gallic acid, vanillic acid, caffeine acid, p-coumaric acid, m-coumaric, and o-coumaric (Takaeidi *et al.,* 2014). The content of phenolic acid as antioxidant reduces free radicals induced by both cancer and anti-cancer treatment. In addition, date seeds contain quercetin, which can increase the synthesis of T and B lymphocytes (Puri *et al.,* 2000 and Habib *et al.,* 2014). The date pits contains 3.1–7.1% moisture, 2.3–6.4% protein, 5.0–13.2 fat, 0.9–1.8% ash and 22.5–80.2% dietary fiber. Also, date pits contain high levels of phenolic compounds (3102– 4430 mg gallic acid equivalents/ 100 g), antioxidants (580–929 lm trolox equivalents/g) and dietary fiber (78–80 g/100 g) (Platat *et al.,* 2014). The good nutritional value of date pits is based on their

dietary fiber content, which makes them suitable for the preparation of fiber-based foods and dietary supplements. Since a large quantity of date pits are being produced as a waste material and the date pits contain a significant amount of bioactive phenolic compounds and dietary fiber. (Al- Farsi *et al.,* 2007). Date pits as a source of dietary fiber. Finely milled date seed fiber had a total dietary fiber content of 71% while the coarsely milled fraction contained 80% total dietary fiber. (Larrauri *et al.,* 1995). The aim of the study was to evaluate the anti-obesity and anti-diabetic activities of date pits powder on alloxan Induced diabetic rats.

## II. Materials and Methods

**Materials**

Dates pits were obtained from Al Alwani Memoni Dates Factory located in Al Khumra Industrial City, Jeddah, Kingdom, Saudi Arabia.

The date pits were washed with water to remove date flesh and dried at 50 ◦C under low pressure for 24 hours. The dried date pits were ground using a hammer mill. Then again ground into fine powder using a commercial home milling machine to produce fine date pits powder. A final 0.21 mm sieve was used to obtain the date pits powder. The final drying step was repeated for 2 hours to remove moisture from the powder. Then it was vacuum packed and kept frozen until use.

**Preparation of basal diet:**

The dietary supply of protein, fat, carbohydrates, vitamins and minerals was prepared recommended by (Reeves *et al.,* 1993). Basal diet consisted of 20 % protein, 10 % sucrose, 4.7 % fat, 2% choline chloride, 1% vitamin mixture, 3.5 % salt mixture and 5% fibers (cellulose). The remainder was corn starch up to 100 %.

**High-fat diet formula**

The high-fat diet was a hyper-caloric diet prepared by mixing its ingredients in a fixed proportion. The feed was prepared, dried, powdered and given every day in the morning to the animals, with water *ad libitum*. The diet was given and weight gain was observed in the rats on third day, confirming the development of obesity in the mice. The diet contained casein 20 g; DL-Methionine 0.3 g; Corn starch, 15 g; Sucrose, 10.5 g; Cellulose powder, 5 g; Mineral mixture, 3.5 g; Vitamin mixture, 1 g; Choline Bitartrate, 0.2 g; Corn oil, 9.9 g; Lard oil 17.6 g. This diet gave a total energy content of 17.03 kJ g-1.8 thus HFD, compared to the normal diet, was hyper-caloric and it contained less carbohydrates but more fat with a net energy difference of 4.37 kJ g-1. To avoid auto oxidation of the fat components, the food was stored at -24 ° C.

Forty-five Albino males rats (Westar strain) weighing approximately 175-185 g body weight and 8-10 weeks old were used in this study. Rats were obtained from King Fahd Center for Medical Research, King Abdulaziz University, Jeddah, Saudi Arabia. All animal experiments were performed under protocols approved by the Institutional Animal House of King Abdulaziz University, Jeddah, Saudi Arabia.

Rats were housed in standard laboratory conditions at (25 ± 3 ° C), relative humidity (50-55%) and a 12-hour light / dark cycle (five mice / cage) two weeks prior to the start of the experiment. Cages, bedding, and glass water bottles (equipped with stainless steel tubes) were replaced twice a week. The stainless steel feed containers are changed once a week. All animals are fed standard nutritionally balanced diet, drinking water and libitum.

Induction of obesity and diabetes:

Obesity was induced by feeding rats on high-fat diet (HFD) for 4 weeks which provided 45 % calories from lard. This obesity model in rats is very similar to the reality of obesity in humans according to (Bhatt *et al.,* 2006). The obese rats were rendered diabetic by intraperitoneally injection of alloxan in a dose of 120 mg/kg/day for 5 days according to (Ashok *et al.,* 2007). Then, fasting blood glucose levels were estimated, and rats with blood glucose level higher than 180 mg/dl were only used in the study.

Experience design

Forty five Albino male rats (Westar strain) rats were randomized into 5 groups, of 9 rats each. Group A was fed on basal diet (negative control), while the other 4 groups were fed on HFD for 4 weeks to induce obesity. Thereafter, obese rats were rendered diabetic by intraperitoneally injection of alloxan (120 mg/kg/day) for 5 days. After induction of diabetes, group B was kept obese diabetic and continued as positive control, while groups C, D and E were fed on basal diet containing 5%, 7.5% and 10% date pits powder respectively replaced equal amount of starch for 6 weeks.

At the end of experiment, the rats were weighed and body fats were carefully removed and weighed. The adiposity index was calculated by dividing the total weight of mesenteric, visceral, epididymis and retroperitoneal adipose tissues by the body weight and multiplied by 100 i.e. adiposity index = fat weight/body weight x100 according to (Pichon *et al.,* 2006). Rats were anesthetized by prolonged exposure to ether and

blood samples were withdrawn for separating the serum which was kept frozen until biochemical analyses. Kidneys were dissected out, divided into two portions; one portion was used for preparing renal homogenates to assay the activity of tissue antioxidant enzymes, the other portion of kidneys was preserved in 10 % formalin solution till processed for histopathological examination

Moisture, protein, fat, ash content Total dietary fiber and the insoluble in date pits powder were determined according the method described by using (AOAC, 2007).

The total phenolic content in date pits powder was determined following the Folin-Ciocalteu method described by (Singleton *et al.*, 1998).

Total flavonoids content in date pits powder were determined according to the method described by (Singleton, 1998 and Yi *et al.*, 2008) using colorimetric method.

Serum aspartate aminotransferase and alanine aminotransferase were estimated according the method described by (Bergmeyer *et al.*, 1978).

Alkaline phosphatase was determined according to (Roy, 1970).

Total cholesterol and High density lipoprotein cholesterol were determined according to the method described by (Richmond, 1973).

Triglycerides and Low density lipoprotein cholesterol and Very low density lipoprotein cholesterol were estimated and calculated according to the method described by (Friedewald *et al.*, 1972).

Formula:

1-LDL = TC – (HDL + TG\5).

2-VLDL = TC-(LDL+ HDL).

Blood urea nitrogen was measured according to the method described by (Patton and Crouch, 1977), uric acid and creatinine were measured according to the method described by (Fossati *et al.*, 1980) and (Husdan and Rapoport, 1968) respectively. Blood glucose was determined according to (Siest *et al.*, 1981), using glucose enzymatic kit**.**

Insulin was estimated according to the method described by (Yallow and Bauman, 1983), using specific antibody radioimmunoassay (RIA) kit

Leptin hormone was determined according to (Xiong *et al.*, 2005*)* using enzyme-linked immunosorbent assay (ELISA)

Renal antioxidant enzymes:

One gram of renal tissue was washed with ice-cooled 0.9% sodium chloride solution and homogenized in 100 ml of ice cooled 1.5% solution of potassium chloride and 50 mMol of potassium phosphate buffer solution (pH 7.4) to yield 10% homogenate (N/V). Renal homogenates were centrifuged at 8000 rpm for 10 minutes at 4°C and the supernatants were used to assay the activity of antioxidant enzymes catalase (CAT) were determined according to the method described by (Sinha, 1972), glutathione peroxidase (GPx) were determined according to the method described by (Paglia and Valentaine, 1979) and superoxide dismutase (SOD) were determined according to the method described by (Spitz and Oberley, 1989).

**Statistical Analysis**

Statistical analysis of the data was carried out by ANOVA using SAS statistical software (SAS, 1998). The significant differences among means were assessed by Duncan's multiple range tests (Duncan, 1955).

## III. Results and Discussion

The chemical constituents of date pits powder are shown in Table (1). Moisture content, fat, protein, ash and Total dietary fiber of date pits powder were 5.66, 8.74, 4.29, 1.44 and 79.14% respectively. These results are confirmed by (Amany *et al*. 2012) stated that the date seed was composed of 3.10-7.10% moisture, 2.30-6.40% protein, 5-13.20% fat, 0.9-1.80% ash and 22.50-80.20% dietary fiber. Date seeds are a very good source of dietary fiber, which was reported as 77.8–80.2 g/100 g fresh weight (Al-Farsi *et al*., 2007). On the other hand, total phenolic content and Flavonoids in date pits powder were 35.83 mg gallic acid equivalents/g date pits powder and 13.75 mg quercetin equivalents/g date pits powder respectively. These results are agreement with (Guizani *et al*., 2014) reported that Polyphenol contents in date seeds were in the range of 21-62 mg gallic acid equivalents/g date seed, Date seeds are an excellent source of phenolic compounds (3102-4430 mg gallic acid equivalents/100g fresh weight) (Al-Farsi *et al.*, 2007).

**Table 1. Chemical constituents of date pits powder**

| Components | Date pits powder |
|---|---|
| Moisture | 5.66 |
| Protein | 4.29 |
| Fat | 8.74 |
| Ash | 1.44 |
| Insoluble dietary fiber | 75.70 |

| | |
|---|---|
| Soluble dietary fiber | 3.44 |
| Total dietary fiber | 79.14 |
| Flavonoids (mg quercetin equivalents/g). | 13.75 |
| Total phenolic compounds (mg gallic acid equivalents/g). | 35.83 |

Effect of feeding of date pits powder on body weight, fat weight and adiposity index in obese diabetic rats are presented in Table (2). Results of present work indicate that, the obese diabetic rats positive control rats (Group B) were significantly ($p<0.05$) increased in body weight, fat weight and adiposity index by 23.22 %, 119.17 and 77.78 % respectively compared with negative control group (Group A) . Results also indicate that, the obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were significantly ($P<0.05$) decreased in body weight, fat weight and adiposity index compared with obese diabetic control rats (Group B) by 6.76, 12.16, 18.92 % for body weight, while the decrease values were 25.39, 35.63.46.33% for fat weight and 19.91, 26.62. 33.80% for adiposity index respectively. The feeding on date pits powder were regulation and decreasing in body weight. These results were confirmed with (Hursel and Westerterp-Plantenga, 2013),who found that Date seeds are rich in catechins, such as those found in green tea, which several studies have shown can affect body weight regulation by increasing energy expenditure.

**Table 2. Effect of feeding of date pits powder on body weight, fat weight and adiposity index in obese diabetic rats**

| Treatments | Body weight | fat weight | adiposity index |
|---|---|---|---|
| Group A (Negative control rats) | $240^{d}$ | $5.84^{e}$ | $2.43^{e}$ |
| Group B (Positive control rats) | $296^{a}$ | $12.80^{a}$ | $4.32^{a}$ |
| Group C | $276^{b}$ | $9.55^{b}$ | $3.46^{b}$ |
| Group D | $260^{c}$ | $8.24^{c}$ | $3.17^{c}$ |
| Group E | $240^{d}$ | $6.87^{d}$ | $2.86^{d}$ |

Values with different letters in the same column are significantly different at P<.0.05. Group C were fed on basal diet containing 5% date pits powder ,Group D were fed on basal diet containing 7.5% date pits powder ,Group E were fed on basal diet containing 10% date pits powder.

Effect of feeding of date pits powder on blood glucose, leptin and insulin hormone levels in obese diabetic rats are presented in table (3). Results of present work indicate that, the obesity diabetic control rats (Group B) were significantly ($p< 0.05$) increased in blood glucose, leptin hormone and significantly ($p< 0.05$) decreased in insulin hormone compared with the negative control rats (Group A) by 181.84, 138.10 and 75.24 % respectively. Results also indicate that, Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were significantly ($P<0.05$) increased in insulin hormone levels compared with the obesity diabetic control rats (Group B) by 136.36, 177.92 and 289.61 % respectively. on the other side, the Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were significantly ($P<0.05$) decreased in blood glucose and leptin hormone compared with obese diabetic control rats (Group B) by 34.56, 46.11 and 53.89% for blood glucose respectively, while the decrease values of leptin hormone were 28.93, 35.73 and 50.67% for ( Group C), ( Group D)and ( Group E) respectively. Findings of our study showed that date pits powder produced a marked decrease in blood glucose level in diabetic rats after 6 weeks of treatment. The antidiabetic effect may be due to release of insulin from existing pancreatic beta cells. Our findings agree with those reported by (El Fouhil *et al.*, 2013 and Manoharan *et al.*, 2007). Date seed extract can decrease inflammation in pancreatic beta cells, increase the production of insulin (El Fouhil *et al.*, 2013) and decrease the proliferation of pancreatic cancer cells, superoxide dependent iron release and DNA damage (Habib *et al.*, 2014).

**Table 3. Effect of feeding of date pits powder on blood glucose, leptin hormone and insulin hormone levels in obese diabetic rats**

| Treatments | Blood glucose (mg/dl) | Insulin (mg/dl) | Leptin (mg/dl) |
|---|---|---|---|
| Group A (Negative control rats) | $92.50^{e}$ | $3.11^{a}$ | $3.15^{d}$ |
| Group B (Positive control rats) | $260.70^{a}$ | $0.77^{d}$ | $7.50^{a}$ |
| Group C | $170.60^{b}$ | $1.82^{c}$ | $5.33^{b}$ |
| Group D | $140.50^{c}$ | $2.14^{b}$ | $4.82^{c}$ |
| Group E | $120.20^{d}$ | $3.00^{a}$ | $3.70^{d}$ |

Values with different letters in the same column are significantly different at P<.0.05. Group C were fed on basal diet containing 5% date pits powder ,Group D were fed on basal diet containing 7.5% date pits powder ,Group E were fed on basal diet containing 10% date pits powder.

Effect of feeding of date pits powder on total triglycerides and total cholesterol levels in obese diabetic rats are shown in Fig (1). Results of present work indicate that, obese diabetic rats (Group B) were increased in total triglycerides and total cholesterol by 98.22 % and 87.77 % respectively, compared with healthy control rats

(Group A). Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were decreased in triglycerides and total cholesterol compared with obese diabetic control rats (Group B) by 16.14, 32.63, 42.85 % for total triglycerides and 11.85, 29.47, 40.98% for total cholesterol respectively. (Salama *et al.,* 2019), found that, Rats fed on date pits powder showed significantly reduction in total cholesterol levels compared to the positive control group; this means that the lowering effect is due to the presence high content of polyphenols in date pits powder, which may help reduce total cholesterol levels in rats. (Ayatollahi *et al.,* 2019), found that, date seed reduced blood glucose levels and body weight of alloxan-induced diabetic rats when compared to control.

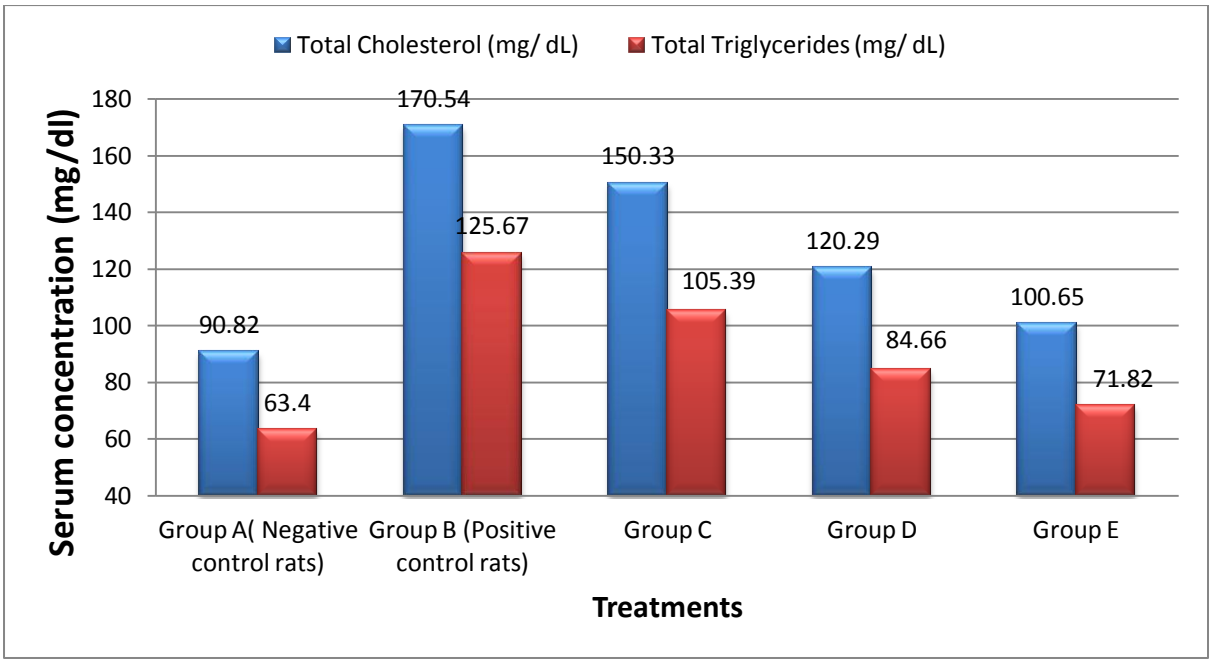


**Fig 1. Effect of feeding of date pits powder on total triglycerides and total cholesterol levels in obese diabetic rats**

Effect of feeding of date pits powder on high-density lipoprotein cholesterol HDLc, low- density lipoprotein cholesterol LDLc and very low density lipoprotein cholesterol VLDLc in obese diabetic rats are presented in Fig (2). Results of present work indicate that, the obesity diabetic control rats (Group B) were increased in low- density lipoprotein cholesterol LDLc , very low density lipoprotein cholesterol VLDLc and deceased in high-density lipoprotein cholesterol HDLc compared with the negative control rats (Group A) by 533.81 , 98.19 and 50.98 % respectively. Results also indicate that, Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were increased in high density lipoprotein cholesterol HDLc compared with the obesity diabetic control rats (Group B) by 36.97, 73.26 and 97.37 % respectively. on the other side, the Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were decreased in LDLc and VLDLc by 26.00, 54.41 and 75.97% for LDLc respectively, while the decrease values of VLDLc were 16.11, 32.59 and 42.86% for ( Group C), ( Group D)and ( Group E) respectively compared with obese diabetic control rats (Group B). Date pits contain several active compounds in the form of antioxidants, such as flavones. Polyphenols, polyunsaturated fatty acids, vitamin C, vitamin E, and fiber, which may reduce free radical levels thanks to their anti-inflammatory and immune stimulating activities. Antioxidants stop free radical oxidation and reduce oxidative low- density lipoprotein cholesterol. (Saryono *et al.*, 2017 and Salama *et al.*, 2019), founds that, Rats fed on date pits powder showed significantly reduction in LDL-C compared to the positive control group; this means that the lowering effect is due to the presence high content of polyphenols in date pits powder, which may help reduce LDL-C levels in rats. High fat diet supplementation resulted in dyslipidaemic changes, as illustrated by increasing triglycerides, very low density lipoprotein cholesterol, total cholesterol and low- density lipoprotein cholesterol, and a decrease in serum level of high-density lipoprotein cholesterol. (Park *et al.*, 2004 and Ayatollahi *et al.*, 2019), perceived that date seeds have the potential to reduce LDL and cholesterol levels in diabetic rats as compared to the control group. (Abiola *et al.*, 2018 and Khalil *et al.*, 2015), also detected decrease in the levels of total cholesterol, Triglycerides, and LDL with improved levels of HDL in diabetic treated rats.

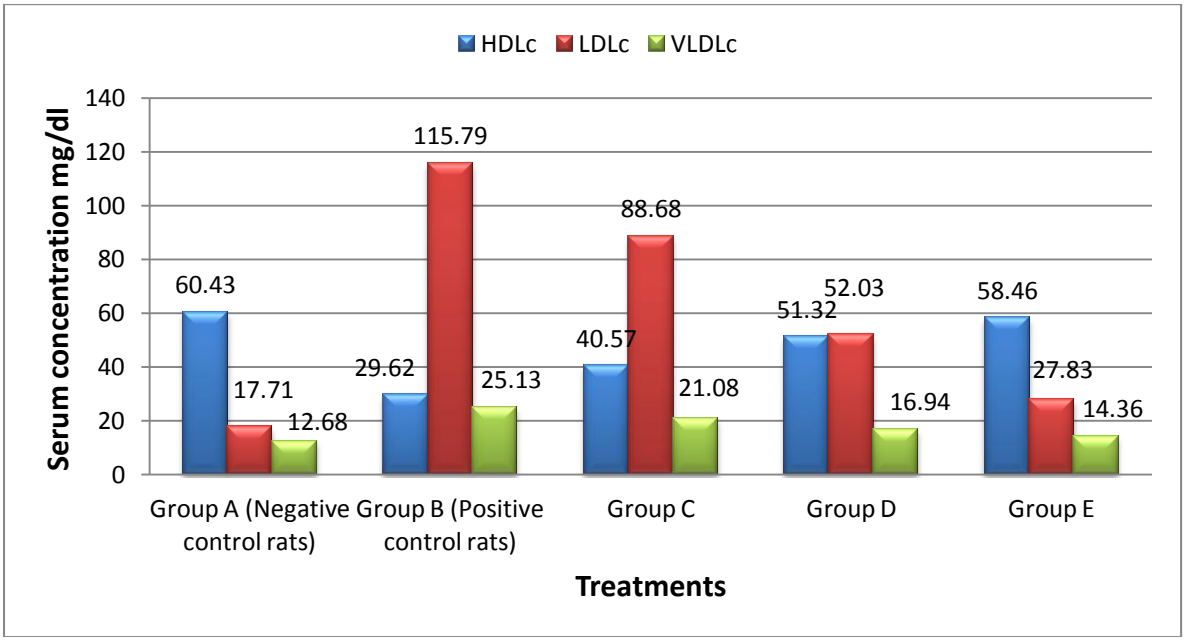


**Fig. 2. Effect of feeding of date pits powder on high-density lipoprotein cholesterol HDLc, low- density lipoprotein cholesterol LDLc and very low density lipoprotein cholesterol VLDLc in obese diabetic rats.**

Effect of feeding of date pits powder on serum Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) in obese diabetic rats are presented in Fig (3). Results of present work indicate that, the obese diabetic rats positive control rats (Group B) were increased in levels of alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) enzymes comparing with healthy control (Group A) by 120.96 % , 84.07 and 31.66 % respectively. these results are agreements with Harris 2005 who found that, The increased of serum biomarker liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) has been observed in diabetic rats compared with normal rats indicating impaired liver function that may be due to hepatic damage induced by hyperglycaemia. On the other side, Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were decreased in alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) compared with obese diabetic rats (Group B) by 22.26, 38.20 and 52.64 % for alanine aminotransferase (ALT),while the decrease values were 21.92, 34.54 and 44.12 % for Aspartate aminotransferase (AST) and 12.50, 19.86 and 34.28% for alkaline phosphatase (ALP) respectively. These results are confirmed with (Ayatollahi *et al.*, 2019 and Halaby *et al.*, 2014), found that, date seeds exhibited the potential to reduce serum levels of ALP in diabetic rats indicating date seeds can ameliorate kidney and liver functions in T2DM.

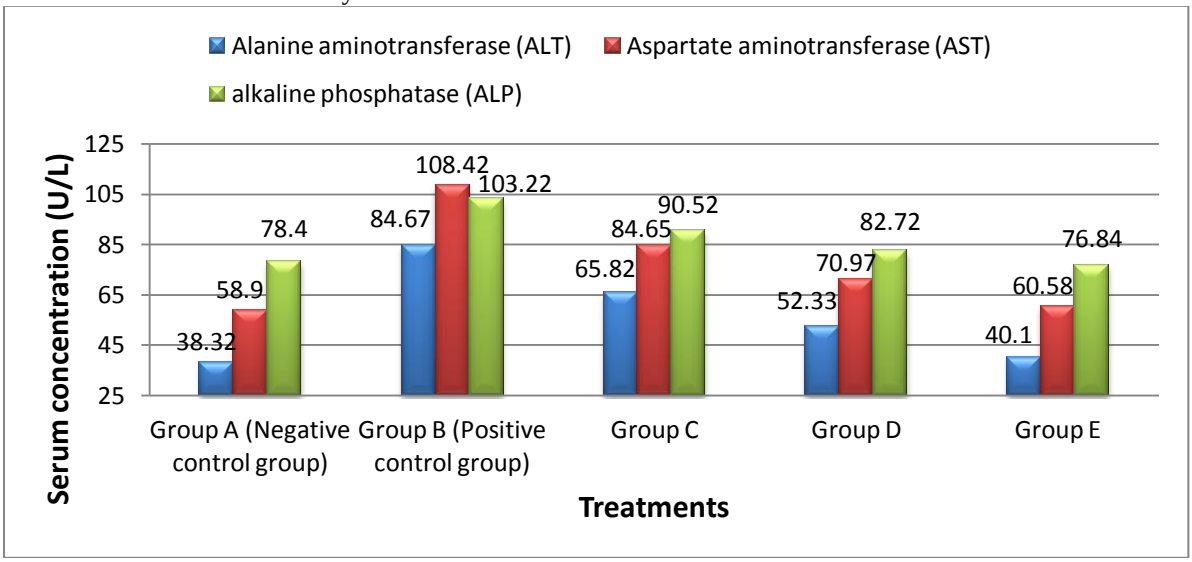


**Fig 3. Effect of feeding of date pits powder on serum Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) in obese diabetic rats.**

Effect of feeding of date pits powder on serum catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx) in obese diabetic rats are presented in Table (4). Results of present work indicate that, the in obese diabetic control rats (Group B) had a significantly ($p< 0.05$) decreased in catalase activity (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx) compared with the healthy control rats (Group A) by 94.64 , 67.07 and 65.7 % respectively. Results also indicate that, Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were significantly ($P<0.05$) increased in catalase activity (CAT), Superoxide dismutase (SOD), glutathione peroxidase (GPx) compared with the obesity diabetic control rats (Group B) by 18.85, 37.70 and 52.46 %for catalase activity, while the increased values of Superoxide dismutase and glutathione peroxidase were 28.16% , 44.10% , 62.38% and 104.76%. 175.19%, 300.00% respectively. These results are agreement with (Abdelaziz *et al.,* 2015), showed that treating diabetic rats with date seeds were improved levels of antioxidant enzymes including glutathione S-transferase, CAT and SOD compared with untreated rats.

**Table 4.Effect of feeding of date pits powder on serum catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx) in obese diabetic rats**

| Treatments | catalase (CAT) | superoxide dismutase (SOD) | glutathione peroxidase (GPx) |
|---|---|---|---|
| Group A (Negative control rats) | $0.194^{a}$ | $60.44^{a}$ | $0.95^{a}$ |
| Group B (Positive control rats) | $0.122^{e}$ | $35.62^{e}$ | $0.21^{e}$ |
| Group C | $0.145^{d}$ | $45.56^{d}$ | $0.43^{d}$ |
| Group D | $0.168^{c}$ | $51.33^{c}$ | $0.58^{c}$ |
| Group E | $0.186^{b}$ | $57.84^{b}$ | $0.84^{b}$ |

Values with different letters in the same column are significantly different at P<.0.05. Group C were fed on basal diet containing 5% date pits powder ,Group D were fed on basal diet containing 7.5% date pits powder ,Group E were fed on basal diet containing 10% date pits powder.

Effect of feeding of date pits powder on uric acid, creatinine and Blood urea nitrogen in obese diabetic rats are presented in Table (5). Results of present work indicate that, the obese diabetic rats positive control rats (Group B) were significantly ($p<0.05$) increased in levels of on uric acid , creatinine and Blood urea nitrogen comparing with healthy control (Group A) by 4.43 % , 201.61 and 76.37 % respectively. On the other side, Obese diabetic rats were fed on basal diet fortified with date pits powder at 5% (Group c), 7.5% (Group D) and 10% (Group E) were decreased in uric acid, creatinine and Blood urea nitrogen compared with obese diabetic rats (Group B) by 1.21, 2.42 and 3.64 % for uric acid, while the decrease values were 34.76, 50.27 and 60.43 % for creatinine and 16.33, 28.75 and 39.87% for Blood urea nitrogen respectively. These results are agreement with (Ayatollahi *et al.,* 2019 and Halaby *et al.,* 2014) found that, date seeds exhibited the potential to reduce serum levels of creatinine and urea in diabetic rats indicating date seeds can ameliorate kidney and liver functions in T2DM.

**Table 5. Effect of feeding of date pits powder on uric acid, creatinine and Blood urea nitrogen in obese diabetic rats**

| Treatments | uric acid (mg/dl) | creatinine (mg/dl) | Blood urea nitrogen (mg/dl) |
|---|---|---|---|
| Group A (Negative control rats) | $1.58^{c}$ | $0.62^{e}$ | $38.85^{e}$ |
| Group B (Positive control rats) | $1.65^{a}$ | $1.87^{a}$ | $68.52^{a}$ |
| Group C | $1.63^{ab}$ | $1.22^{b}$ | $57.33^{b}$ |
| Group D | $1.61^{b}$ | $0.93^{c}$ | $48.82^{c}$ |
| Group E | $1.59^{bc}$ | $0.74^{d}$ | $41.20^{d}$ |

Values with different letters in the same column are significantly different at P<.0.05. Group C were fed on basal diet containing 5% date pits powder ,Group D were fed on basal diet containing 7.5% date pits powder ,Group E were fed on basal diet containing 10% date pits powder

**Histopathological examination**:-

Histopathological examination of renal of normal control rats showed normal histological structure of renal parenchyma photo 1. renal of obese diabetic rats (positive control group) Group B revealed congestion of renal blood vessels, vacuolation of endothelial Lining glomerular tuft and vacuolation of epithelial lining renal tubules (photo 2). However the renal of rats from group C (obese diabetic rats were feed on 5 % date pits powder for 6 weeks revealed presence of focal regenerating renal tubules (photo 3). On the other hand, group D (obese diabetic rats were feed on 7.5 % date pits powder for 6 weeks) and group E (diabetic rats treated with 10% date pits powder for 6 weeks) revealed no histopathological changes (photo 4 and photo 5) respectively.

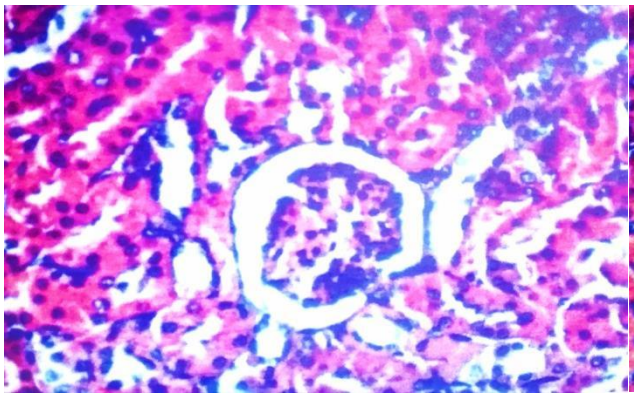

**Photo 1. Kidney of rats from group A (normal control group) showing the normal histological structure of renal parenchyma.**

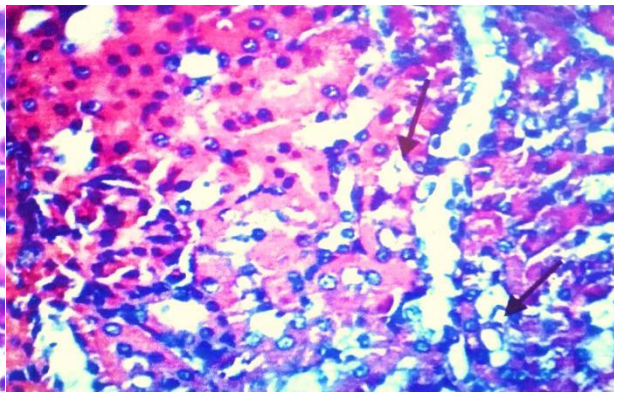

**Photo 2. Kidney of rats from group B (positive control group) showing the vacuolation of epithelial renal tubules.**

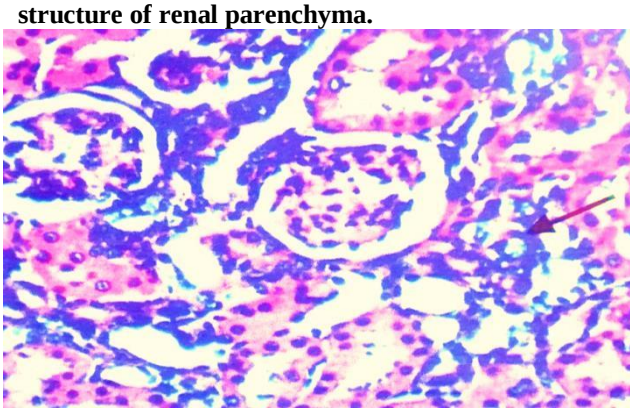

**Photo 3. Kidney of rats from group C showing focal regenerating renal tubules.**

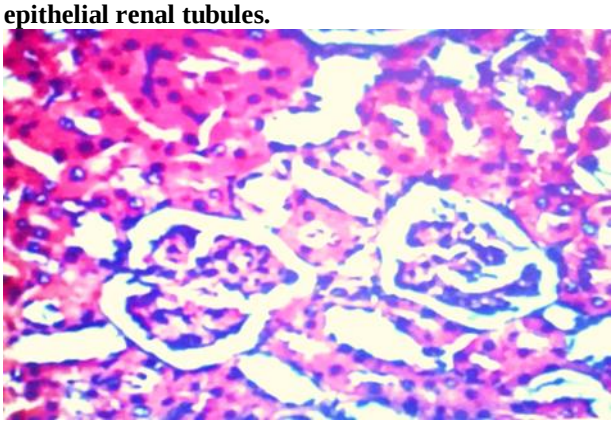

**Photo 4. Kidney of rats from group D showing no histopathological changes.**

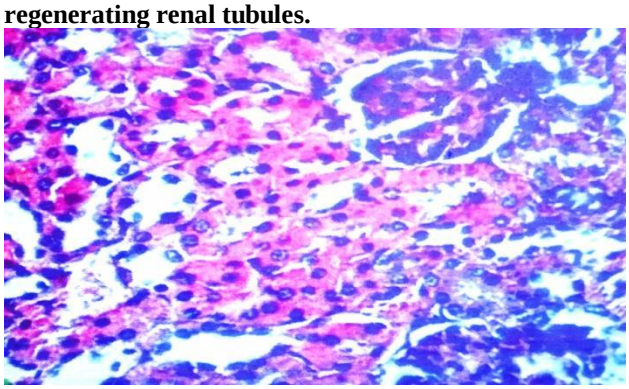

**Photo 5. Kidney of rats from group E showing no histopathological changes**

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