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Evaluation of effects of *Opuntia elatior* Mill. fruit juice and quercetin on biochemical parameters and histopathological changes in diabetic rats

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The present study was carried out to evaluate safety profile following administration of *Opuntia elatior* Mill. fruit juice (OEFJ) and quercetin for 28 days in diabetic rats. OEFJ (4 mL/kg p.o. for 28 days) and quercetin (50 mg/kg p.o. for 28 days) treatment shown restoring effect on haemoglobin, packed cell volume and total erythrocyte count in diabetic rats. Alterations in levels of alanine aminotransferase, creatinine, total bilirubin and lactate dehydrogenase observed in diabetic rats which were restored to normal level when diabetic rats were treated with OEFJ and quercetin alone and in combination. The mean values of total protein, albumin, globulin, total bilirubin, BUN and ALP were found unaltered in all groups. Damage induced by streptozotocin in pancreas, liver and kidney were lesser compared to diabetic control group when rats were treated with OEFJ and quercetin. However, no appreciable histopathological lesions have been observed in the spleen, heart, lung and intestine of rats in all treatment groups. In conclusion, *Opintia elatior* Mill. fruit juice have shown protective effect against alterations in biochemical parameters and pathological lesions of pancreas and liver in diabetic rats

Keywords: Histopathology, Diabetes mellitus, *Opuntia elatior,* Quercetin
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Diabetes mellitus is a complex heterogeneous metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both[1]. Various medicinal plants like *Trigonella foenum-graecum* L., *Glycyrrhiza glabra* L., *Carica papaya* L. have been evaluated to have antidiabetic or protective effects in diabetes[2-4]. *Opuntia elatior* Mill. is a folklore medicinal plant, and its ripen fruits are used by the local people of Gujarat for treatment of anemia and general debility. Fruit of *Opuntia elatior* Mill. is reported for its hematinic, analgesic and antiasthmatic activity[5]. Quercetin, is a plant compound (flavonoid) commonly found in many plants and fruits. Quercetin is used to treat conditions of heart and blood vessels including atherosclerosis, high cholesterol, heart disease and diabetes. It is an efficient antioxidant as evidenced by both *in vitro* and *in vivo* studies, and in parallel, it has also been shown to improve diabetes-related damages in animals[6]. Despite the use of *Opuntia elatior* Mill. fruit and quercetin as a herbal medicine and its efficacy in the treatment of various ailments, little is known about the possible effect, either of short term or long term usage on the haematological and biochemical parameters and histological architecture of the liver, heart, kidney and pancreatic tissues after streptozotocin induced damage. Therefore, the study was designed to evaluate the effects of *Opuntia elatior* Mill. fruit juice and quercetin treatment on biochemical parameters and histopathological changes in diabetic rats.

Materials and methods

Experimental animals

Forty two albino rats (6-8 weeks of age, Body weight ranging from 200 to 240 g) obtained from Zydus Research Centre, Cadila Healthcare Pvt. Ltd., Ahmedabad, Gujarat, India were used in the present study. All animals were maintained as per standard husbandry described in Committee for the Purpose of Control and Supervision of Experiments on Animal's standard guidelines. During entire study period, the animals were housed in the cool environment (23 to 26 °C) with relative humidity ranging from 40 to 55 %. Twelve hour dark and light cycle was

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maintained in animal room. Rat pelleted feed (VRK biological system, Vadodara, Gujarat, India) containing 18 % protein was provided *ad libitum* to animals throughout the study period, except overnight (16-20 h) fasting prior to termination stage. The experimental protocol No. JAU/JVC/IAEC/SA/02/2015 was approved by the Institutional Animal Ethics Committee (IAEC), College of Veterinary Science and Animal Husbandry, Junagadh Agricultural University, Junagadh, Gujarat, India.

Collection of plant materials and other drugs

Opuntia elatior Mill. plant is commonly grown in the region of Junagadh and fruits are used by local people for anaemic condition. The fruits of *Opuntia elatior* Mill. plant was obtained from local market and verified by Mr. Punit Bhatt, Pharmacognosist, Department of Veterinary Pharmacology and Toxicology, Veterinary College, Junagadh as well as confirmed by Dr Nitin B. Patel, Department of Genetics and Plant Breeding, College of Agriculture, Junagadh. Juice from fruits was made and used for the experiment. The specimen was submitted for preservation in the Herbarium, Department of Veterinary Pharmacology and Toxicology, College of Veterinary Science and A.H., Junagadh Agricultural University, Junagadh, Gujarat (Specimen No. JVC/VPT/SP/02/2015). Quercetin (QCT), streptozotocin (STZ) and glibenclamide (GLB) were purchased from the Sigma Aldrich.

Induction of diabetes

Streptozotocin (STZ) was dissolved in citrate buffer previously adjusted to *p*H 4.5 with 0.1 M citric acid with final concentration of 40 mg/mL. This solution was administered by single intraperitoneal injection to rats at a dose of 50 mg/kg body weight in all animals except animals of normal control and vehicle control groups. Diabetes was confirmed after 48 h by measuring level of glucose using biochemical kit (Biosystems S.A., Barcelona). Rats with blood glucose level above > 150 mg/dL were considered as diabetic.

Experimental design

Forty two albino rats were divided in seven groups (C1, C2, C3, C4, T1, T2 and T3). Animals of groups C3, C4, T1, T2 and T3 were injected with STZ to produce diabetes. Rats of group C1, C2, and C3 were kept as normal, vehicle and diabetic control, respectively. Rats of group C4 were administrated with glibenclamide solution (2 mg/mL) at dose rate of 5 mg/kg, p.o. for 28 days (control). Rats of group T1 and T2 were treated with freshly prepared OEFJ at dose rate of 4 mL/kg, p.o. (Volume not more than 1.5 mL) and quercetin (25 mg/mL solution) at dose rate of 50 mg/kg, p.o. respectively for 28 days. Rats of group T3 were administrated with OEFJ at dose rate of 4 mL/kg, p.o. along with quercetin at dose rate of 50 mg/kg, p.o. for 28 days. Volume of test compounds was varied based on body weight of animals.

Collection of samples

At the end of 28 days, blood samples were collected from retro-orbital plexus from all animals for haematological and biochemical analysis. Blood smears for determination of differential leukocyte count (DLC) were prepared from fresh blood at the time of blood collection. All rats were then humanely sacrificed using CO_2 and were subjected to gross pathological examination. The pancreas, liver, kidney, spleen, heart and lung were collected, cleaned and then weighed using analytical balance. For histopathological examinations, pancreas, liver, spleen, kidney, heart, lung, stomach, small and large intestine were collected in 10 % formalin.

Parameters studied

Hematological parameters

Hematological parameters like hemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leucocyte count, (TLC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH) were estimated using automated hematology analyzer. Differential leukocyte count was carried out after staining of blood smears using standard method.

Biochemical parameters

Biochemical parameters like blood glucose, aspartateaminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), blood urea nitrogen (BUN), creatinine, total protein (TP), albumin, and total bilirubin were estimated using standard kits on semi-automatic biochemistry analyzer.

Gross and histopathological lesions

Organ body weight ratio for major organs was calculated based on body weight of animals at the last

day of experiment and organ weight of organs recorded. For pathological evaluation, the formalin fixed tissues were subjected to paraffin wax embedding for tissue sectioning. Sections of each tissue collected were cut at 6-8 µ thickness with automatic section cutting machine semi-automated rotary microtome and were stained with haematoxyline and eosin (H & E) stain. The H & E stained slides were observed under microscope and histo-pathological lesions were recorded.

Statistical analysis

All the data obtained were presented as means ± standard error (SE). Data were analyzed statistically by one way ANOVA followed by Duncan's Multiple Range Tests to observe difference among the treatments.

Results and discussion

The mean values of hematological and biochemical parameters in animals of different groups after daily oral administration of OEFJ and quercetin for 28 days in diabetic rats are presented in (Tables 1&2), respectively. Effects of daily oral administration of OEFJ and quercetin for 28 days on histopathological findings pancreas and liver have been presented in (Figs 1-7). Clinical symptoms like dullness, sluggish movement, weight loss, polyuria, polydipsia, and polyphagia were observed in rats of diabetic control group. Reduction in body weight in diabetes might be due to breakdown of tissue proteins in diabetic rats[7].

Significant ($p < 0.05$) decrease in body weight of diabetic animals was observed after one week compared to other groups. The body weight of

Table 1 — Effect of daily oral administration of OEFJ (4 mL/kg/day) and quercetin (50 mg/kg/day) for 28 days on mean values of body weight and hematological parameters in diabetic rats.

Parameters	Treatment groups						
	C1	C2	C3	C4	T1	T2	T3
Body weight (g)	283.65 ± 9.42^{cd}	293.33 ± 8.95^{d}	212.03 ± 15.03^{a}	232.20 ± 26.69^{abc}	222.83 ± 25.05^{ab}	246.68 ± 16.90^{abcd}	275.77 ± 8.47^{bcd}
HB (g/dL)	14.53 ± 0.70^{ab}	15.05 ± 0.57^{abc}	13.90 ± 0.40^{a}	15.08 ± 0.97^{abc}	18.17 ± 0.42^{d}	16.75 ± 0.70^{cd}	15.97 ± 0.48^{bc}
PCV (%)	50.08 ± 2.32^{bc}	51.37 ± 3.20^{bc}	42.96 ± 2.09^{a}	45.83 ± 2.87^{ab}	53.13 ± 0.94^{c}	47.01 ± 1.10^{abc}	47.11 ± 1.25^{abc}
TEC (10^6/µL)	8.40 ± 0.87^{ab}	9.19 ± 1.19^{b}	7.45 ± 0.97^{a}	8.46 ± 1.34^{ab}	9.74 ± 0.33^{b}	8.51 ± 0.50^{ab}	8.58 ± 0.58^{ab}
WBC (10^3/cmm)	4.79 ± 0.75	4.20 ± 0.70	5.47 ± 0.38	5.56 ± 0.61	6.86 ± 0.29	6.45 ± 0.56	6.78 ± 0.36
MCV (fl)	57.83 ± 0.31	55.67 ± 0.92	57.75 ± 0.82	54.75 ± 0.79	54.53 ± 0.39	55.38 ± 0.47	54.95 ± 0.34
MCHC (%)	29.78 ± 0.43^{a}	29.67 ± 1.49^{a}	32.50 ± 0.77^{b}	33.07 ± 0.15^{b}	34.17 ± 0.28^{b}	34.53 ± 0.19^{b}	33.87 ± 0.20^{b}
MCH (pg)	17.28 ± 0.28^{a}	16.50 ± 0.73^{a}	18.76 ± 0.45^{c}	18.05 ± 0.26^{c}	18.63 ± 0.21^{c}	19.13 ± 0.18^{c}	18.62 ± 0.08^{c}
Lymphocyte (%)	76.33 ± 2.93	77.83 ± 3.33	75.50 ± 1.63	73.83 ± 1.25	71.67 ± 1.48	74.00 ± 0.82	75.17 ± 0.87
Neutrophils (%)	19.83 ± 1.54^{a}	19.67 ± 1.63^{a}	22.00 ± 1.24^{ab}	22.67 ± 1.50^{ab}	25.67 ± 1.12^{b}	23.33 ± 1.12^{ab}	21.83 ± 1.25^{ab}
Eosinophil (%)	0.33 ± 0.21	0.33 ± 0.21	0.17 ± 0.17	0.33 ± 0.21	0.17 ± 0.17	0.33 ± 0.21	0.17 ± 0.17
Monocytes (%)	3.50 ± 0.43	2.17 ± 0.31	2.33 ± 0.56	3.17 ± 0.60	2.50 ± 0.56	2.67 ± 0.61	2.83 ± 0.60

Note: Values (Mean ± SE) with different superscript in a row were significantly different ($p > 0.05$).

Table 2 — Effect of daily oral administration of OEFJ (4 mL/kg/day) and quercetin (50 mg/kg/day) for 28 days on mean values of biochemical parameters in diabetic rats.

Parameters	Treatment groups						
	C1	C2	C3	C4	T1	T2	T3
Blood glucose (mg/dL)	96.62 ± 5.18^{a}	91.95 ± 9.34^{a}	229.25 ± 54.58^{b}	147.58 ±31.81^{ab}	188.55 ±38.34^{ab}	180.70 ±38.09^{ab}	159.95±17.88^{ab}
AST (IU/L)	122.17 ± 7.34	127.83 ± 14.10	170.83 ± 15.15	138.50 ± 5.52	130. 67 ± 17.03	131.33 ± 5.19	128.00 ± 6..86
ALT (IU/L)	37.17 ± 1.70	39.83 ± 2.96	43.67 ± 2.60	37.67 ± 1.48	35.83 ± 2.14	35.00 ± 1.93	38.33 ± 1.89
ALP (IU/L)	126.83 ± 4.69	125.50 ± 5.03	124.33 ± 5.64	125.83 ± 5.41	126.17 ± 4.04	127.17 ± 3.64	126.17 ± 5.58
LDH (IU/L)	201.33 ± 4.09^{a}	202.83 ± 5.38^{a}	396.33±20.19^{b}	212.00 ± 13.88^{a}	222.83 ± 11.16^{a}	224.33 ±18.54^{a}	214.17 ±12.76^{a}
BUN (mg/dL)	12.58 ± 0.99	12.31 ± 0.62	15.49 ± 1.39	14.45 ± 1.05	15.73 ± 1.22	17.13 ± 1.88	17.58 ± 2.73
Creatinine (mg/dL)	0.36 ± 0.01	0.35 ± 0.01	0.39 ± 0.02	0.35 ± 0.02	0.34 ± 0.03	0.32± 0.01	0.38 ± 0.02
Total protein (g/dL)	5.48 ± 0.26	5.52 ± 0.31	5.38 ±0.13	5.28 ± 0.1	5.72 ± 0.27	5.75 ± 0.19	5.87 ± 0.16
Albumin (g/dL)	4.52 ± 0.24	4.61 ± 0.12	4.30 ± 0.09	4.44 ± 0.11	4.45 ± 0.19	4.36 ± 0.23	4.16 ± 0.23
Globulin (g/dL)	0.96 ± 0.22	0.74 ± 0.22	1.09 ± 0.08	0.84 ± 0.16	1.28 ± 0.36	1.39 ± 0.27	1.71 ± 0.29
Total Bilirubin (mg/dL)	0.18 ± 0.03	0.22 ± 0.05	0.27 ± 0.03	0.23 ± 0.03	0.21 ± 0.04	0.25 ± 0.04	0.22 ± 0.04

Note: Values (Mean ± SE) with different superscript in a row were significantly different ($p < 0.05$).

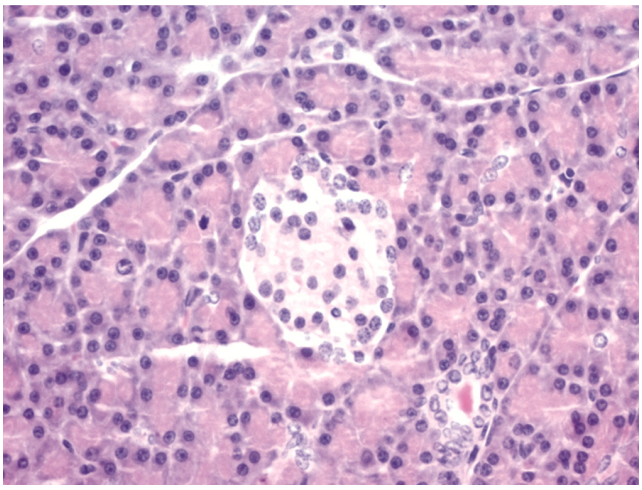

Fig. 1 — Microscopic view of pancreas showing small islets of Langerhans were with loss of its normal cell cord arrangement and vacuolar degeneration in many of serous acini and islet of Langerhans in group C3 (H & E stain X 480).

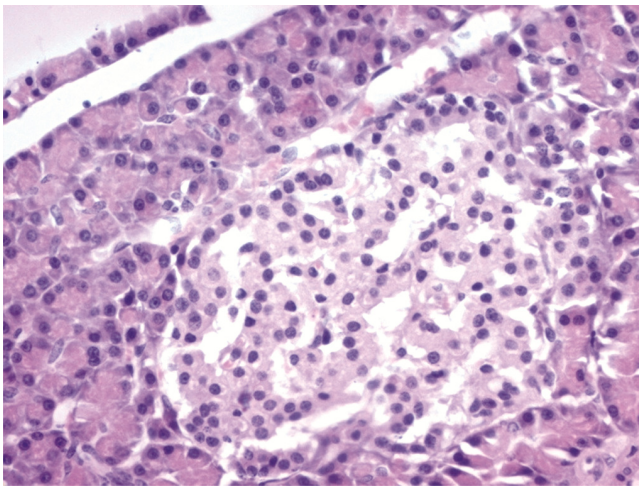

Fig. 2 — Microscopic view of pancreas showing an apparent increase in the size of an islet of Langerhans with loss of few cords of endocrine cells in group C4 (H & E stain X 480).

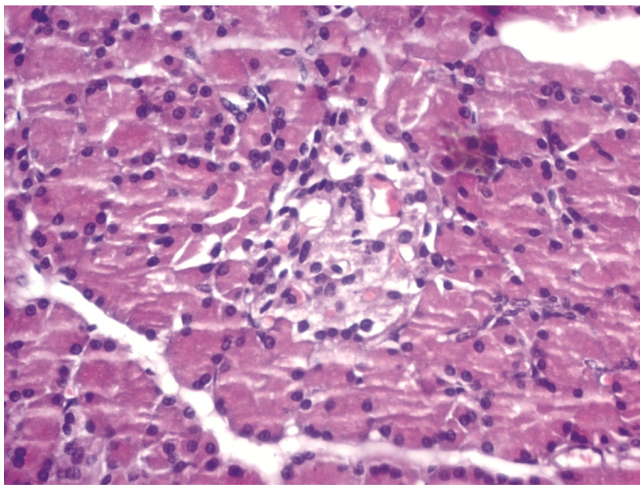

Fig. 3 — Microscopic view of pancreas showing distorted shrunken islets of Langerhans with less cellularity but larger in size in group T1 (H & E stain X 480).

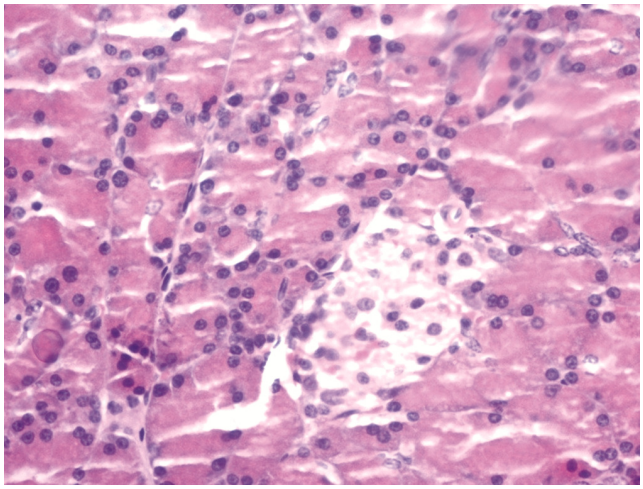

Fig. 4 — Microscopic view of pancreas showing shrunken distorted islet of Langerhans with marked loss of its cells in group T2 (H & E stain X 480).

diabetic rats treated with glibenclamide, OEFJ and quercetin were significantly ($p < 0.05$) restored near to normal level. Rats treated with OEFJ along with quercetin also shown significantly ($p < 0.05$) higher body weight. Similar findings of decreased body weight in streptozotocin-induced hyperglycemic rats were reported earlier[8,9]. OEFJ administration to diabetic rats improved the body weight which might be due to a better control of the hyperglycemic state in diabetic rats. Similar to *Opuntia elatior* Mill. in the present study, *Opuntia dillenii (*Ker-Gawl*)* Haw fruit juice also shown to improve body weight in streptozotocin induced diabetic rats[10]. Restoration of body weight in streptozotocin–induced diabetic mice by polysaccharides from *Opuntia dillenii (*Ker-Gawl*)* Haw was also reported[11]. The body weight restoration in diabetic rats treated with quercetin as well as OEFJ along with quercetin might be due to interactive effect of both treatments.

In the present experiment significant reduction in level of Hb, PCV and TEC have been observed in diabetic rats compared to rats in control groups. The findings are in agreement with earlier reports of increased level of glycated hemoglobin in diabetic rats with subsequent decrease in the levels of total hemoglobin[12]. The diabetic animal showed marked reduction in hematological parameters acquiescent with existing literature that anaemia is a common pathophysiology associated with diabetes mellitus[13].

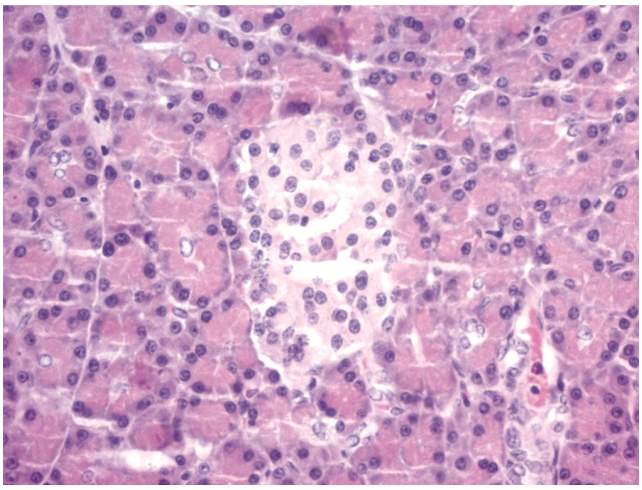

Fig. 5 — Microscopic view of pancreas showing an apparent increase in the size of an islet of Langerhans with few cords of normal endocrine cells in group T3 (H & E stain X 480).

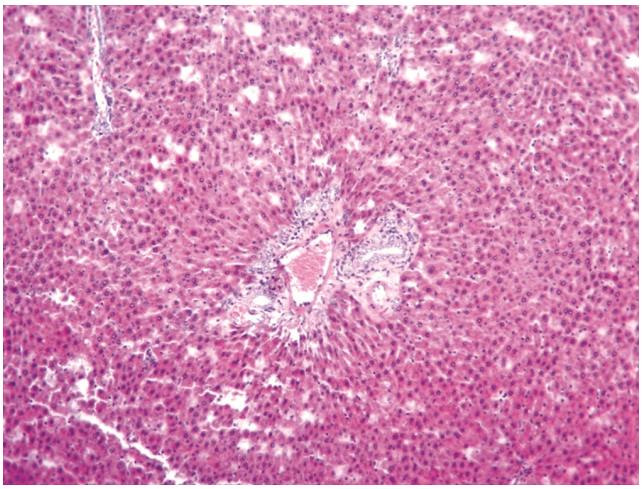

Fig. 6 — Microscopic view of liver showing varying degree of degenerative changes, vascular changes and infiltration of inflammatory cells with loss of normal architecture of parenchyma in group C3 (H & E stain X 480).

Similarly, Colak[14] also reported that diabetes mellitus causes the development of hypochromic anaemia due to a fall in the iron content of the body resulting from oxidative stress associated with the condition. The significant decrease in the level of packed cell volume (PCV) in diabetic control rats may be as a result of the cellular damage on the erythrocyte membrane as a result of oxidative stress by streptozotocin[15]. The altered haematological parameters due to STZ in the present study were restored to normal range after treatment with OEFJ and quercetin alone and in combination in diabetic rats. This finding is in agreement with reports from Chauhan *et al.*[16] that anemic rats recovered progressively from anemia

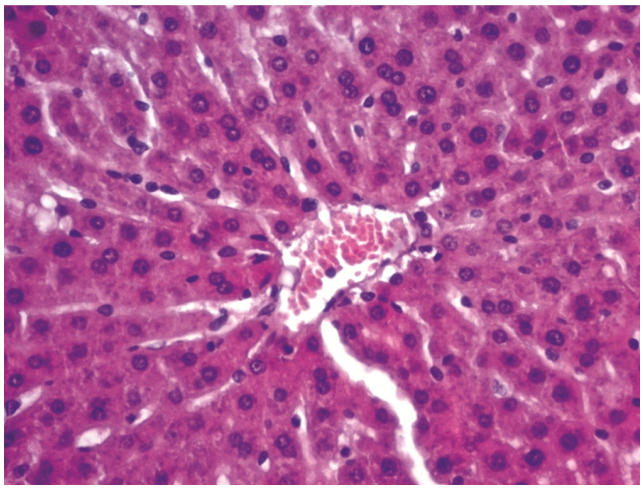

Fig.7 — Microscopic view of liver showing apparently normal architecture of hepatic lobes with slightly hydropic degeneration in group T3 (H & E stain X 480).

following administration of OEFJ. Similarly, Akacha *et al.*[17] also observed re-establishment of methotrexate altered hematological parameters by *Opuntia ficus-indica* (L.) Mill. in rats. In the present study OEFJ and quercetin alone and in combination significantly mitigate hematological turbulences in STZ induced diabetic rats. This protective effect of OEFJ might be due to presence of polyphenols, flavonoids, ascorbic acid, carotenoids and betalains compounds. Selvakumar *et al.*[18] reported that the values of Hb, PCV, RBC, WBC, neutorphils and platelet were significantly decreased in polychlorined biphenyls treated rats (anemic rats) which were restored to normal when quercetin (50 mg/kg) was administered along with polychlorined biphenyls.

In the present study, slight increase in the values of ALT and AST have been observed in diabetic control compared to normal rats, which might be due to increased cell membrane permeability or cell membrane damage of hepatocytes. However, these alterations were not significant. The level of ALP was not significantly altered in all groups of animals. The increased level of ALT and AST (43.67 ± 2.60 and 170.83 ± 15.15 IU/L) in the present study have been restored when diabetic rats treated with OEFJ (35.83 ± 2.14 and 130.67± 17.03 IU/L) and quercetin alone (35.00 ± 1.93 and 131.33± 5.19 IU/L) and in combination (38.33 ± 1.89 and 128.00± 6.86 IU/L). Increased levels of ALT and AST in diabetic rats indicated that diabetes may induce hepatic dysfunction. The increase in the activities of AST, ALT and ALP in serum may be mainly due to the leakage of these enzymes from the liver cytosol into

the blood stream. Abd El-Razek & Hassan[19] observed that treatment of alloxan-induced diabetic rats with cactus fruit juice at a single or repeated dose for 5 weeks caused reduction in the activity of ALT, AST and ALP enzymes in serum to their normal levels which might be due to revival of insulin secretion. Likewise, earlier studies revealed that when *Opuntia ficus-indica* (L.) Mill. juice administered with ethanol in rats, level of ALT was nearer to its normal range[20]. A possible explanation for the restoration of serum AST, ALT and ALP to their normal levels after the treatment may be due to revival of insulin secretion[21]. Selvakumar *et al.*[18] also observed retrieval effect of quercetin on liver enzymes such as AST, ALT, ALP and GGT, which were significantly increased by polychlorined biphenyls treatment in rats which supports the finding of reversal effect of quercetin on ALT, AST and ALP levels in the present study.

The mean value of total bilirubin in diabetic control group was non-significantly increased compared to other groups. Whereas, mean values of bilirubin in other treatment groups were not significantly differ from each other. In agreement to our finding, level of bilirubin was significantly increased in diabetic rats which was reversed to normal level when diabetic rats treated with *Opuntia ficus-indica* (L.) Mill. juice for eight weeks[22]. In favor of our findings, Chauhan *et al.*[16] also reported decrease in level of total bilirubin following administration of OEFJ at dose rate of 15 mL/kg in mercuric chloride induced high level of total bilirubin in rats.

The LDH level in rats of diabetic control group was significantly ($p < 0.05$) increased compared to other groups. Whereas, the mean value of LDH in rats of other treatment groups were non-significantly differ from each other. However, the enzyme released from other organs may contribute to the change in levels in enzyme. Our results indicating the fact that plasma LDH levels were significantly higher in diabetic rats than those in the control group support these possibilities. The levels of the enzyme in diabetic rats treated with OEFJ and quercetin were comparable to those of control rats.

The level of creatinine in diabetic control group was non-significantly increased compared to other groups. Whereas, level of creatinine in other treatment groups were not significantly differ from each other. The mean levels of creatinine in diabetic rats treated with glibenclamide, OEFJ and quercetin were reduced to almost normal level. The mean value of BUN was slightly higher in diabetic control as well as OEFJ and quercetin treated groups. An increase in creatinine and BUN levels in STZ-diabetic rats indicate diminished ability of the kidneys to filter these waste products from the blood and excrete them in the urine, is characteristic change in diabetes.

Detailed post-mortem examinations of all experimental animals of different groups were performed at the end of experiment. Upon gross examination of pancreas no appreciable lesions in all treatment groups have been observed. Macroscopic examination of pancreas in the experimental rats belonging to diabetic control revealed congestion and enlargement. Liver of the experimental diabetic rats treated with only OEFJ shown lesser enlargement and congestion which is considered as sign of effective treatment.Whereas, macroscopic view of kidneys shown mild to moderate enlargement and paleness in rats of diabetic control. Kidneys of diabetic rats treated with only OEFJ shown slight congestion and enlargement. Gross examination of spleen, heart, lung and intestine revealed no appreciable lesions in rats of all treatment groups.

Upon microscopic examination, no pathological changes were observed in pancreas of control (C1) and vehicle control (C2) groups. The histopathological changes of pancreas of rats of diabetic control group (C3) revealed varying degree of structural changes as well as degenerative changes. Small islets of Langerhans were with loss of its normal cell cord arrangement and vacuolar degeneration in many of serous acini and islet of Langerhans (Fig. 1). Pancreas from glibenclamide treated group (C4) showing an apparent increase in the size of an islet of Langerhans with loss of few cords of endocrine cells compare to control group (Fig. 2). While histopathological changes in pancreas of diabetic rats treated with OEFJ (T1) were distorted shrunken islets of Langerhans with less cellularity but larger in size compared to diabetic control group (Fig. 3). Microscopic view of pancreas of rats treated with quercetin (T2) shown shrunken distorted islet of Langerhans with marked loss of its cells compared to control group as well as OEFJ alone treated group (Fig. 4). In pancreas collected from rats treated with OEFJ along with quercetin (T3) shown an apparent increase in the size of an islet of Langerhans with few cords of normal endocrine cells (Fig. 5) compared to diabetic control group as well as other treatment groups (group T1 and T2). Abd El-Razek & Hassan[19] observed that

oral administration of cactus fruit juice, particularly, repeated dose (5 mL/four times daily/rat) to alloxan-induced diabetic rats improved the previous changes and brought back the normal architecture of the pancreatic tissue, as the islets of Langerhans increased in size and the serous acini appeared normal in size and shape and the connective tissue septae were close to normal. Diabetic rats fed with 2.5 % and 5 % prickly pear seedless pulp (*Opuntia dillenii (*Ker-Gawl*)* Haw improved the effect damage of streptozotocin or alloxan as the majority of the islets of Langerhans tended to be normal or with moderate expansion of pancreatic islets[10,23].

The effect of quercetin on histopathological findings in the present study was also supported by report from Vessal *et al.*[24], that quercetin brings about the regeneration of pancreatic islets and propably increases insulin release in STZ-induced diabetic rats. STZ administration has been reported to cause marked degeneration of β cells with inflammatory cells infiltration, which were reversed with treatment of quercetin (most of the pancreatic morphological changes, and interestingly some islets with pancreatic ducts)[25]. They proposed possible role of quercetin as protective effect against β cell damage by its anti-inflammatory, anti-apoptotic and antioxidant effects; and aids regeneration of β cells which might through stimulation of the ductal stem cells.

The histopathological changes in liver of rats of diabetic control group (C3) revealed varying degree of degenerative changes, vascular changes and infiltration of inflammatory cells with loss of normal architecture of parenchyma (Fig. 6). While histopathological changes in liver of rats treated with OEFJ along with quercetin (T3) rats shown apparently normal architecture of hepatic lobes with slightly hydropic degeneration compared to diabetic control group (Fig. 7). In accordance with our findings, Abd El-Razek & Hassan[19] observed marked structural alterations in the liver as a result of absence of insulin in alloxan-induced diabetic rats. The major alterations were severe dilatation of the portal vein with fibrosis, cellular infiltration and slight sinusoids dilatation. While treatment with fruit OEFJ shown improvement, since there was restoration of normal architecture of liver tissue with slight dilatation and congestion of the central and portal vein. Kobori *et al.*[26] reported that long term dietary intake of quercetin reduced body weight gain, as well as visceral and liver fat accumulation, and improved systemic parameters related to metabolic syndrome (hyperglycemia, hyperinsulinemia and dyslipidemia), probably by decreasing oxidative stress and increasing PPAR-α expression.

Upon microscopic examination of kidney, increased bowman's capsular space, vacuolar degeneration and coagulative necrosis of tubular epithelium were observed in rats of diabetic control group (C3), while kidneys of rats treated with OEFJ along with quercetin rats (T3) showed slight degenerated epithelium of glomeruli as well as tubules compared to diabetic control group. In agreement with our findings, Abd El-Razek & Hassan[19] observed various cellular injuries in alloxan-induced diabetic rats which could be due to oxidative stress induced by hyperglycemia. Increased glycation in diabetes leads to accumulation of glycated plasma proteins which involves in the pathogenesis of diseases.They observed blood sugar lowering and free radical scavenging effect of cactus fruit juice (5 mL/rat/four times daily for 5 weeks) in diabetic rats.

Conclusion

In conclusion, administration of *Opuntia elatior* Mill. fruit juice at 4 mL/kg and quercetin at 50 mg/kg alone and in combination orally for 28 days have preventive effects against alterations in biochemical parameters as well as pathological lesions in pancreas and liver of diabetic rats. However, detail study on isolation and evaluation of *in vivo* effect of phytochemicals from *Opuntia elatior* Mill. responsible for protective effect in diabetes is required.

Conflict of interest

The author (s) declares no conflict of interest.

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