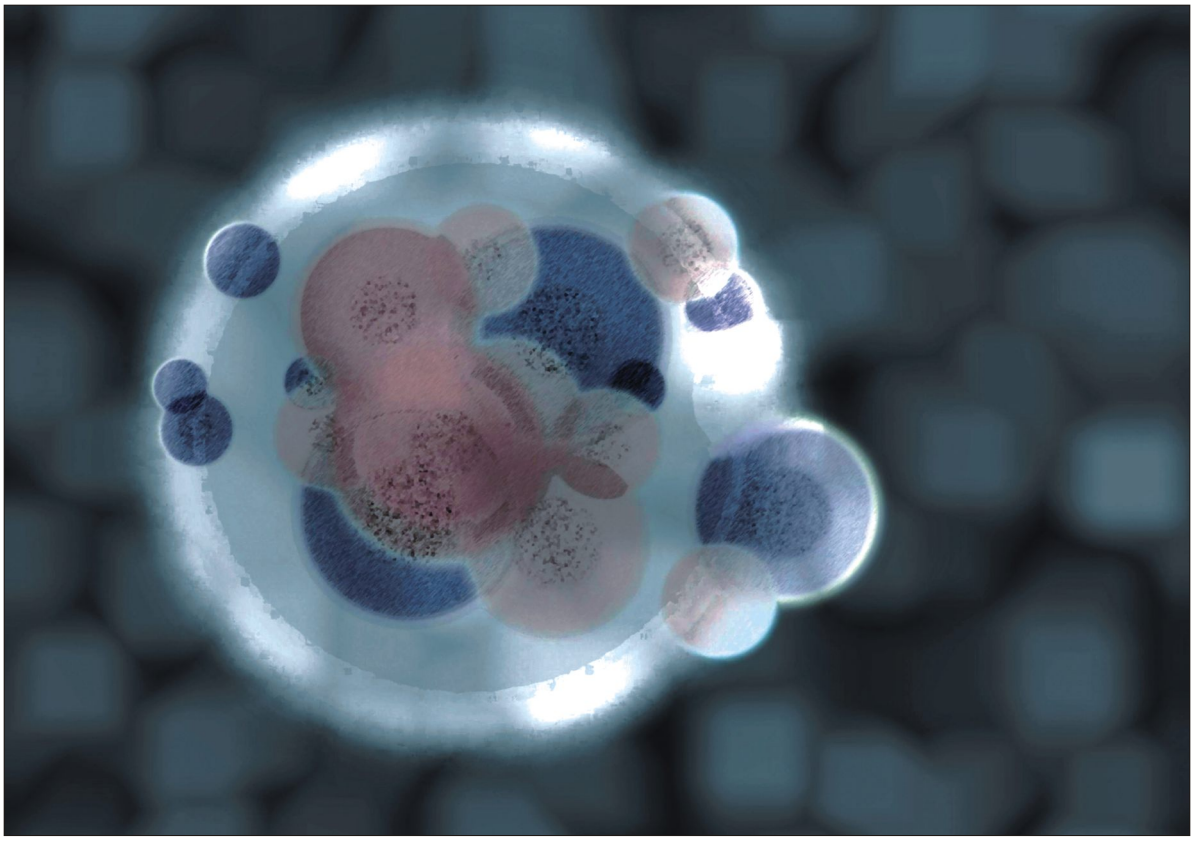

Journal of Biological Sciences

ISSN 1727-3048

science alert

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OPEN ACCESS Journal of Biological Sciences

ISSN 1727-3048
DOI: 10.3923/jbs.2018.364.372

Research Article
Therapeutic Effects of Parsley Extract in Streptozotocin-induced Gestational Diabetic Rats

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Abstract

Background and Objective: Gestational diabetes mellitus (GDM) seriously impairs the health of maternity and infant and it leads to pregnancy outcome. Antioxidants are matters that keep the cell injury caused by free radicals. Plants with antioxidant properties have been consumed for centuries as supportive therapy in the diabetes treatment. The present work was designed to assess effect of parsley extract on kidney of diabetic mellitus rats. **Materials and Methods:** Pregnant albino rats (n = 50) were divided after mating into five groups: First group (control group, C), second group (pregnant rats injected with intraperitoneal single dose of STZ (40 mg kg^{-1} b.wt.) in the 1st day of pregnancy (D1), third group: Pregnant rats were treated with parsley extract (1 m/150 g b.wt.) from the 1st to the 19th day of gestation post injection with STZ (40 mg kg^{-1} b.wt.) (D1+P), fourth group: Pregnant rats were injected with STZ (40 mg kg^{-1} b.wt.) on day 7 of gestation (D7), fifth group: Pregnant rats were treated with parsley extract (1 m/150 g b.wt.) from the 7th to the 19th day of gestation post injection with STZ (40 mg kg^{-1} b.wt.) (D7+P). The pregnant rats were dissected on the 19th day of gestation, any morphological or anatomical changes were photograph and blood sample were collected to estimate the hematological parameters. In addition, kidney samples of pregnant rats were taken for the histopathological study. **Results:** Diabetic rats showed some morphological and anatomical changes such as deep neck abscesses, cancer and bleeding in the lung. On the other hand, diabetic mothers, which were treated with parsley leaves extract showed normal morphological structure. According to the haematological and histopathological studies, the parsley leaf extract ameliorate the damage were occurred due to diabetes mellitus. **Conclusion:** Administration of the parsley extract has the ability to decrease the injury of hyperglycemia.

Key words: Diabetes mellitus, kidney, pregnant rats, hyperglycemia, parsley extract

Received: May 12, 2018 Accepted: August 02, 2018 Published: September 15, 2018

Citation: Mervat Ahmed Abd Rabou, 2018. Therapeutic effects of parsley extract in streptozotocin-induced gestational diabetic rats. J. Biol. Sci., 18: 364-372.

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Competing Interest: The author has declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Diabetes mellitus is one of the five leading causes of death over the world. It is a group of metabolic sicknesses result from a flaw in insulin secretion leading to disturbance of sugar, fat and protein metabolism[1]. Excessive amount of glucose circulates in the blood plasma include the stable consumption of inexpensive carbohydrate rich processed nutrients, binge eating, financial constraints to the filling of diabetes medication prescriptions[2].

The overall occurrence of diabetes mellitus was 12.5% and it was almost twice higher in the urban residents (16.3%) than in the rural population (8.6%), It prevalence was associated with sex, age, obesity hypertension and Russian ethnicity[3].

Gestational diabetes mellitus may lead to obesity and type 2 diabetes in young later in life[4].

Pancreatic islet β-cell destruction produced by streptozotocin (STZ) and it is widely used experimentally to produce diabetes mellitus[5].

Natural antioxidants are considered important nutrition constituents and it useful to human body. It plays an important role in overall health. They are natural compounds found in some foods that help neutralize free radicals in the bodies[6]. The natural antioxidants from plant materials exchange synthetic ones. Plants are being used to treat a number of health concerns and conditions. About 80% of people worldwide relying on them for some part of main healthcare[7]. Medical plant have beneficial effects on several animal models of lung irritation. It include coumarins, flavonoids, phenolics, iridoids, monoterpenes, diterpenes and triterpenoids[8].

Parsley is herbal plant used as food preservative[9]. It is used for different medicinal resolves in traditional and folklore medicine of different nations. Different pharmacological events have been attributed to this plant[10]. It is considered an antioxidant[11], calcium-channel-blocker in intestine and uterus force, anti-inflammatory proxy[12], purgative[13], cancer prevention[14], hypoglycemic assets[15], antiulcerogenic[16].

Type 2 diabetes lead to weakening in beta-cell function and chronic insulin conflict[17]. A decline in b-cell mass caused by disruption of b-cell duplication or increased rates of b-cell death and that reduce insulin secretion[18].

Various kidney bugs are common chronic circumstances due to kidney disease attributable to diabetes. Thus, people with diabetes may have chronic kidney disease in addition to diabetes. Chronic kidney disease is one of the most problems of diabetes and end-stage kidney disease occurred due to diabetes[19]. Approximately 5000 Australians obtain renal additional therapy because of diabetes[20].

Recent studies evidences suggest that haematological directories are altered in diabetes and numerous haematological changes disturbing the RBCs, WBCs and the clotting factors are shown to be directly related with diabetes mellitus[21].

Parsley can decreasing urinary calcium emission, increasing urinary pH, dieresis, declining urinary protein excretion because it act as antiurolithiatic drug[22]. It has a number of possible therapeutic attributes such as antimicrobial[23] and it can treat backache, blood pressure, eczema, knee, ache[24]. Parsley with geese resulted in significant advance in most of blood characters[25]. This study engrossed on the parsley which explored the antioxidant activity of parsley extract and its role in decreasing diabetes complications.

MATERIALS AND METHODS

Animals: This study was conducted on 50 female albino rats and 25 male, their weight 200-220 g. Animals fed on measured diet and some taters. All pregnant rats were stayed for 2 weeks in metallic cages under normal laboratory settings of light (12 h light and 12 h dark), at room temperature before the experiment was ongoing.

Pregnancy course: For induction of breeding, estrous cycle were determined by vaginal smears collection daily, then the estrous rats were captive with non-diabetic male in the ratio of 2:1. Mating established on the following morning by presence of vaginal plug or sperm in vaginal smear and that considered day zero of gestation[26].

The pregnant rats labeled and separated for complete the trial, after 1 weak of mating, nonpregnant rats were departed from the research[27].

Extraction of plant materials: The fresh parsley leave were ordered from market ,washed with tap water, cut into minor pieces and left to parched in the shadow at room fever. Dried leaves (100 g) were extracted by totaling 1000 mL of boiled distilled water for 30 min, then the extract was filtered and the filtrates were given to rats at dose 1 mL/150 g orally by digestive tube[9].

Induction of diabetes mellitus: Single intraperitoneal dose of freshly prepared STZ solution (40 mg kg^{-1} b.wt.) were injected

in rats on day one of gestation[26]. STZ dissolved in citrate buffer (0.1 mol L^{-1}, ph = 4.5)[28]. Blood glucose levels were checked after 24 h of STZ dose by using a glucometer (ACCUCHEK® Active Glucometer, Roche Diagnostics, Germany). If glucose levels more than 120 mg dL^{-1}, the rats were selected and used as gestational diabetes mellitus (GDM)[26].

Experimental design: Pregnant rats were divided into five groups after mating: Group C (control group), group D1 (pregnant rats treated with single interperitonal dose of STZ (40 mg kg^{-1} b.wt.) in the first day of pregnancy , group D1+P: pregnant rats treated with parsley extract (1m/150 g b.wt.) from first to 19 day of pregnancy one h post injection with single interperitonal dose of STZ (40 mg kg^{-1} b.wt.), group D7: Pregnant rats injected with interperitonal dose of STZ (40 mg kg^{-1} b.wt.) on day seven of pregnancy, group D7+P: Pregnant rats treated with parsley extract (1 m/150 g b.wt.) from seven to nineteen day of pregnancy one h post injection with single interperitonal dose of STZ (40 mg kg^{-1} b.wt.). The pregnant females were dissected on 19 day of pregnancy.

Morphological study: Any morphological changes were noted during experiment were photographed and any anatomical changes in the internal organs of mothers on day of slain were also photographed.

Heamatological studies: Blood was collected from the heart puncture of pregnant rats after deaden by plastic syringes in EDTA tube for determination of Hb, RBCs, HCT and WBCs in all preserved and control groups.

Histopathological studies: The samples of kidney of mothers fixed in 10% neutral buffer formol and Carnoy's fluid for the histopathological studies. The samples were washed and dehydrated in ascending grades of alcohol, then cleared in xylene and embedded in paraffin wax. Sections thickness were 5 mm and stained by haematoxylin and eosin allowing to the method of[29] to assess the kidney damage, collagen fibers were demonstrated by Mallory's trichrome stain[30].

Data statistics: Data were expressed as mean±SE. Contrasts between groups were analyzed by one-way analysis of variance (ANOVA). A P value of equal or less than 0.05 was considered statistically significant.

RESULTS

Morphological studies: Appearance of deep neck abscesses (Fig. 1a) and lung cancer (Fig. 1b) and bleeding (Fig. 1c) in the diabetic mothers received STZ on day 1 and on day 7 of gestation (groups D1 and D7) but normal morphological and anatomical structure were noted in groups D1+P and D7+P.

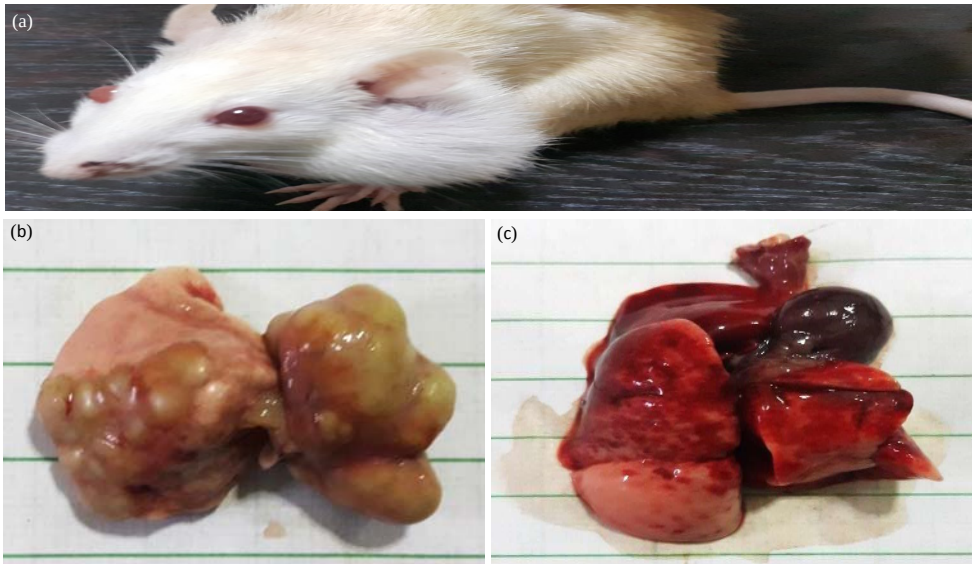

Fig. 1(a-c): Photographs showing some morphological and anatomical changes were appeared in diabetic groups (D1 and D7), (a) Deep neck abscesses, (b) Lung cancer and (c) Bleeding in lung

Table 1: Statistical analysis of the hematological parameters in different experimental groups

	Groups				
Parameters	C	D1	D1+p	D7	D7+P
RBCs (106 m^{-3})	6.49±0.24	4.83±0.45**	6.16±0.64	4.93±0.97**	6.40±0.53
Hb (g dL^{-1})	13.46±0.37	11.45±0.50**	12.72±0.81	11.30±0.52**	12.93±0.65
HCT (%)	41.34±1.14	34.20±1.49**	40.00±1.22	36.00±1.58**	39.60±1.51
WBCs (103 mm^{-3})	8.75±0.57	5.97±0.59**	7.66±1.10	6.20±0.66**	8.30±1.20

Each value represented the Mean±Standard deviation (SD). The values were considered significant at *$p \leq 0.05$ and highly significant at **$p \leq 0.01$ compared to the control group. C: Control, D1: Diabetic pregnant rats on day 1 of gestation, D1+P: Diabetic and parsley leave extract on day 1 of gestation, D7+: Diabetic pregnant rats on day 7 of gestation, D7+P: Diabetic and parsley leave extract on day 7 of gestation

Hematological studies: The diabetic groups D1 and D7 showed highly significant decrease in RBCs, respectively compared to the control group and in Hb, respectively compared to the control group and in HCT, respectively compared to the control group and in WBCs, respectively compared to the control group. But no significant change were recorded in groups D1+P and D7+P in RBCs, respectively and in Hb, respectively and in HCT, respectively and in WBCs, respectively as shown in Table 1.

Histopathological studies: Histological pattern of the maternal kidney cortex of the control group showed normal architecture of the glomeruli, Bowman's capsule and distal and proximal convoluted tubules (Fig. 2a) with thin scattered collagen fibres support the glomeruli, convoluted tubules and the capsule (Fig. 3a). Maternal kidney tissue of group D1 showed numerous hemorrhagic areas, lobulated and congested glomeruli (Fig. 2b), highly atrophied glomeruli, some of them are absent, Some nuclei of the convoluted tubules show pyknosis in D1+P group (Fig. 2d). Reduced collagen fibres was detected in the cortex with brightly red stained hemorrhagic areas and fibrotic convoluted tubules in maternal kidney cortex of group D1 and D1+P (Fig. 3b,d). Well-developed appearance of kidney tissue was demonstrated in maternal kidney tissue of group D1+P (Fig. 2c) but few hemorrhagic areas were still detected in group D7+P (Fig. 2e). Some what normal distribution of collagen fibres in the kidney cortex but brightly red stained blood cells were still detected in the small hemorrhagic areas in groups D1+P and D7+P (Fig. 3c,e).

DISCUSSION

The chronic hyperglycemia of diabetes mellitus lead to failure of numerous organs, especially eyes, kidneys, nerves, heart and blood pots[31]. Elevated blood glucose cause unfavourable changes in biochemical and haematological catalogues due to uncontrolled hyperglycemia and is a major cause development of problems due to diabetes[32]. Gestational elevated blood glucose is associated with increased injury (hypoglycemia, hypocalcemia, polycythemia, hyperbilirubinemia) and fetal death[33]. Gestational diabetes mellitus is a state of glucose bigotry and hyperglycemia with first beginning during pregnancy and is the most public complication of pregnancy, affecting up to 10% of expectant mothers[34].

Antioxidants can protect the cell damage caused by free radicals[31]. It can cooperate with stabilize and scavenge free radicals and stopping their noxious effects[35]. Medicinal plants are dreadful reserve for drug advance. It produces bioactive complexes via tissue culture equipment[36]. It have biological actions, low toxicity and economic possibility[37].

In the present study, there were no change in the morphological structure of pregnant rats in control and parsley groups but noticed appearance of deep neck abscesses and lung cancer and bleeding in the diabetic mothers treated by STZ on day 1 and on day 7 of gestation. Increased risk of lung tumor in diabetic patients was found in a large united kingdom[38].

Diabetes mellitus may be more susceptible to facial cellulitis and deep neck infections caused by odontogenic infections[39]. Diabetic cause higher DNA injury confirming the interaction between hyperglycemia-induced genotoxicity and teratogenesis[40]. Oxygen and nitrogen classes, the products of free radicals, which are needy on fatty acid oxidation, can tempt chromosome injury in STZ- induced diabetes mellitus[41]. STZ increase the diabetogenic effect of gestation which cause a lot of changes in the morphology of pregnant rats[42].

Parsley is one medicinal plant has beneficial properties for dealing of diabetes mellitus[43]. This may be due to its chemical building including ascorbic acid[44], flavonoid[11], these phytochemicals recover total antioxidant capacity, unhelpful oxygen free radicals and stops oxidative damage[45]. Current research evidences suggest that haematological changes are found in diabetes[31,45].

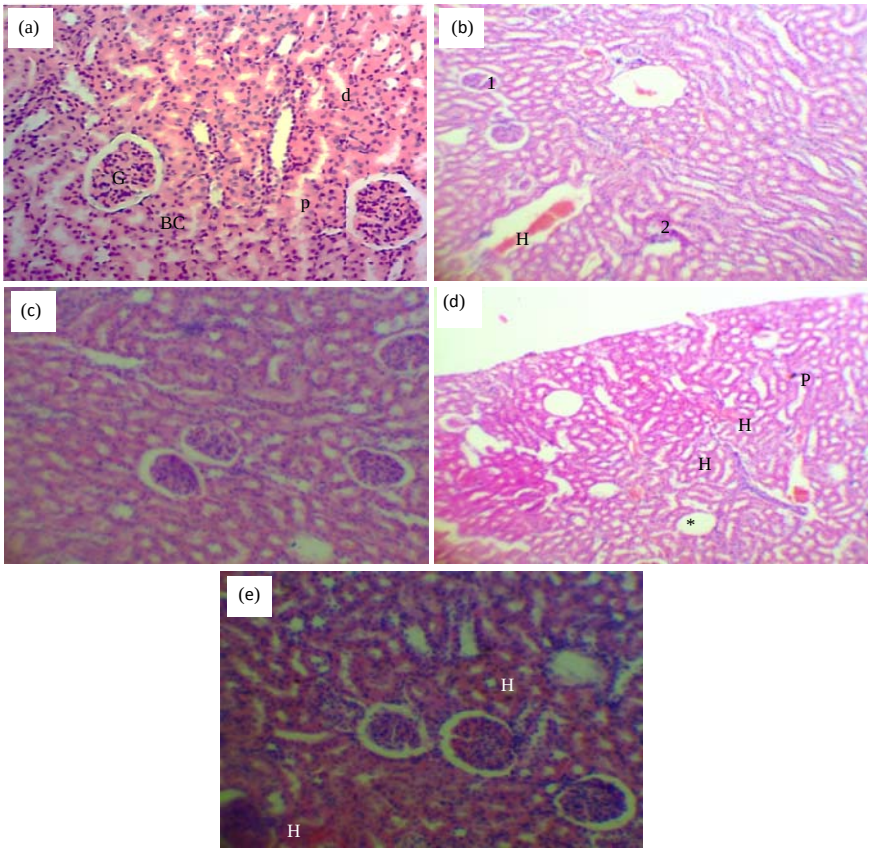

Fig. 2(a-e): Maternal kidney tissue of the control and different treated groups stained with hematoxylin and eosin, (a) Group C showing well developed architecture of the glomeruli (G), distal convoluted tubules, proximal convoluted tubules and BC-Bowman's capsule, (b) Group D1 showing numerous hemorrhagic areas (H), glomeruli were lobulated (1) congested (2), (c) Group D1+P showing well developed architecture of the kidney cortex, (d) Group D7 showing highly atrophied glomeruli, some of them were absent (*) in the kidney cortex with numerous hemorrhagic areas (H),Some nuclei of the convoluted tubules(CT) show pyknosis and (e) Group D7+P showing signs of improvement in the kidney cortex, but few hemorrhagic areas (H) were still detected

The present study showed that the mean RBC, HGB, WBC and HCT values of the parsley extract supplemented diabetic group are near control values compared to the unsupplemented diabetic group. Several haematological vagaries affecting the RBCs, WBCs and the coagulation factors are exposed to be directly connected with diabetes mellitus[31]. Supplementing the ration of parsley resulted in significant advance in most of blood traits involved in the present study[25]. This improvement in haematological traits as a result of the actions may be explained by the way that parsley is a decent source of iron, beta carotene and vitamin C, useful for improvement of general health status[46]. Flavonoids and quercetin which found in Petroselinum crispum contains often covers a major sections of the medicinal actions and have numerous caring effects[47]. It improves hyperglycemia- induced heart and aorta oxidative damage due to its antioxidant activity in the heart and aorta tissue[48].

Histological results of this study showed well developed architecture of kidney cortex of the control pregnant rats. The microscopic examination of kidney cortex of the diabetic rats showed severe changes. These changes include: Numerous hemorrhagic areas, lobulated and congested glomeruli, highly atrophied glomeruli, some of them are absent, some nuclei of the convoluted tubules show pyknosis. Highly decreased collagen fibres in the kidney cortex with bright red stained hemorrhagic areas and fibrotic CTs in the diabetic groups. These results agree with[49]. The kidney sections in diabetes mellitus showed damaged proximal convoluted tubules, glomeruli and interstitial inflammation[50]. Nephropathic

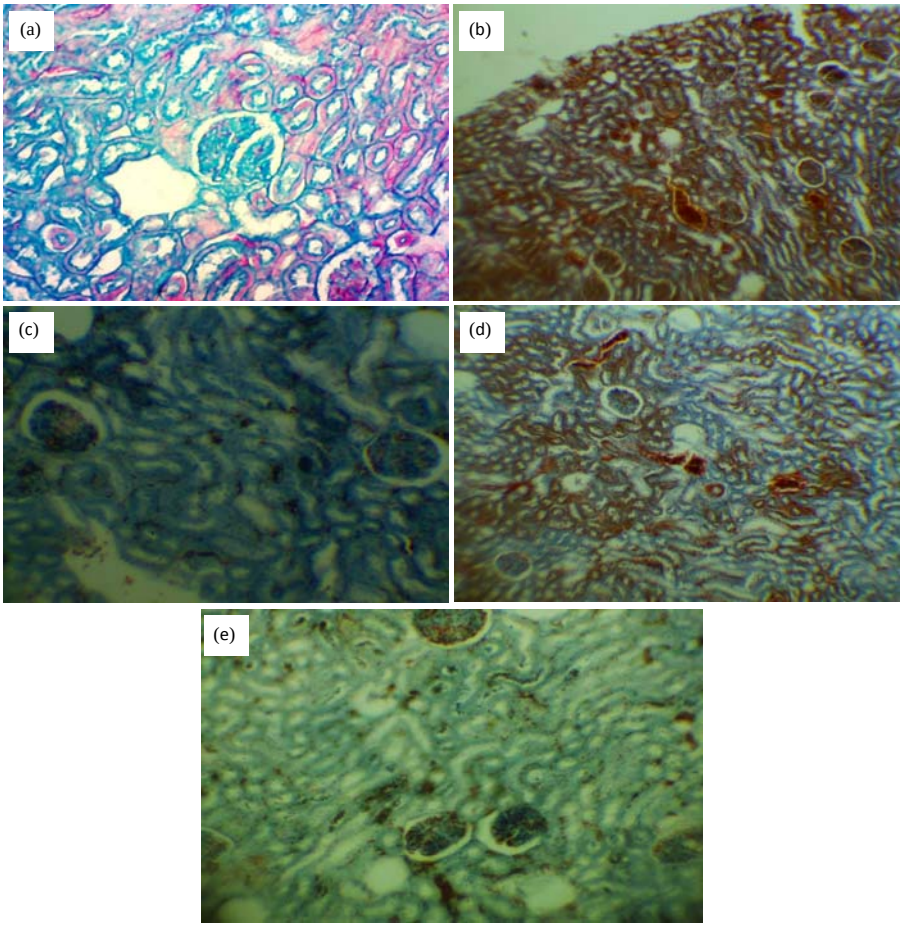

Fig. 3(a-e): Maternal kidney tissue of the control and different treated groups stained with mallory trichrome stain, (a) Group C showing thin scattered collagen fibres support the capsule, glomeruli and CTs, (b) Group D1 highly decreased collagen fibres in the kidney cortex with bright red stained hemorrhagic areas and fibrotic CTs, (c) Group D1 +P somewhat normal distribution of collagen fibres in the kidney cortex but brightly red stained blood cells are still detected in the small hemorrhagic areas, (d) Group D7 showing decreased collagen fibres in some CT of kidney cortex with brightly stained hemorrhagic areas and fibrotic CT and (e) Group D7+P showing nearly normal distribution of collagen fibres with brightly stained RBCs in the glomeruli and in between CTs

changes in the renal tissue of the diabetic rats and attributed the swelling of mitochondria and endoplasmic reticulum of convoluted tubules and the cell becomes water logged due to swelling of the some organelles[51]. Metabolic changes associated with diabetes lead to glomerulosclerosis, glomerular hypertrophy, tubulointerstitial inflammation and fibrosis[52]. Diabetic kidney disease seems to be one of the most frequent complications of diabetes mellitus. Based on increased free radical formation and/or diminished antioxidant defenses induce oxidative stress that is implicated in the pathogenesis of diabetic kidney disease. It induces oxidative stress as well as reactive oxygen species (ROS) formation that attributes to the activation of various downstream signaling cascade leading to structural the way to structural and functional changes in kidney[53].

In the present study diabetic rats treated with parsley leaf extract showed well developed kidney architecture with no inflammatory infiltration and normal distribution of collagen fibers was demonstrated in kidney cortex of group D1+P and D1+7. Parsley extract from the medical plants which have antiinflammatory role was noticed by several authors[37,54]. A biological mechanism that may explain these anti-inflammatory and anticancer belongings[54]. This mechanism involves the shutting down of an intercellular signaling system called cancer necrosis. Parsley reduced fatty degeneration, cytoplasmic vascularization and necrosis[9].

Flavonoids can scavenge free radicals and chelate metals for example, pro-anthocyanidin and luteolin to possess antioxidant actions which protect from diabetic kidney disease[55]. Parsley considered anti-hypertensive, antimicrobial, anti-diabetic, laxative in digestive tract, balance enzyme activities, increase glutathione in the kidney and clean kidney tissue after nephrotoxicity[56].

In this study kidney cortex of control group showed normal architecture of the glomeruli, capsule and CTs and thin scattered collagen fibres in the glomeruli, capsule and CTs. Normal kidney were observed by[57]. Some studies have shown that antioxidants are real and cheaper than conventional treatment in management of certain illnesses[58] Antioxidant possessions of parsley are likely to be responsible for its properties[11]. Parsley is used in clinical locations to treat diabetes complications and its side effects on kidney[16].

CONCLUSION

Diabetic mothers showed some morphological changes but diabetic rats which were administrated parsley extract showed somewhat normal morphological architecture. According to the hematological, histopathological clarifications of kidney, the parsley leaf extract succeeded to minimize the severe changes, which were observed in the diabetic rats. Finally parsley leaf extract has the facility to minimize the injury of hyperglycemia in pregnant rats.

SIGNIFICANT STATEMENT

The present study demonstrated that the parsley can succeed in the protection from destroy of gestational diabetic mellitus, decrease hyperglycemia in rats and minimize hazards of diabetes in the morphological, anatomical, hematological and histopathological studies in pregnant rats. This study will help the researcher to uncover the benefits of parsley and its effect during pregnancy.

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