The administration of *Fumaria parviflora* extract to regulate glucose and insulin level, alongside iron accumulation and renal histopathological alterations in male rats induced by diabetes.

Alaa Ali Mahmoud Atiyah[1] , Assistant Professor Dr. Qays Assi Ahmed[2]
[1.2] Department of Biology, College of Education for Pure Sciences, University of Kirkuk, Kirkuk, Iraq

*Corresponding author's email: : fualaa775@gmail.com[1]
Email addresses of coauthors: fualaa775@gmail.com[1] qaysassi77@uokirkuk.edu.iq[2]

Abstract

Background and Objective: Diabetes is a major cause of kidney disorders and iron metabolism disturbances, leading to tissue damage due to oxidative stress. Therefore, this study aimed to evaluate the therapeutic efficacy of the plant extract *Fumaria parviflora* alone or combined with vitamin E, and compare it with insulin, in normalizing glucose and insulin levels, and reducing iron deposition and tissue damage in the kidneys of diabetic rats. **Experimental design**: 35 male rats (Sprague Dawley) were randomly divided into 7 equal groups (5 rats per group) as follows: 1) the healthy control. 2) The diabetic control (induced by alloxan 135 mg/kg). And the diabetic treatment groups treated with: 3) insulin (6 international units). 4) Vitamin E (150 mg/kg). 5) Royal jello extract (250 mg/kg). 6) Insulin + Vitamin E. 7) Royal jello extract + Vitamin E. The experiment lasted for 4 weeks before blood sampling and kidney excision for biochemical and histological examination. **Results**: The diabetic group showed a significant increase in glucose, a sharp decrease in insulin, with dense iron deposition, and severe histological changes including tubular necrosis, glomerular congestion, and interstitial hemorrhage. In contrast, the therapeutic treatments led to a reduction in glucose levels and an improvement in insulin, with a clear distinction for the plant extract. Histologically, the combination of Royal jello extract + Vitamin E extract and Vitamin E (group 7), as well as insulin with Vitamin E (group 6), showed a remarkable superiority in restoring the natural structure of renal corpuscles and tubules, and reducing iron deposition to rare levels. **Conclusion**: The study concludes that the extract of the plant *Fumaria parviflora* has a high therapeutic and preventive capacity against diabetic nephropathy, and this physiological and histological efficiency is doubled when the extract is combined with vitamin E, due to their synergistic antioxidant role and regulation of iron and insulin pathways.

Keywords: Diabetes, *Fumaria parviflora*, Insulin hormone, Iron deposition, Kidneys.

Introduction

Diabetes is primarily characterized by hyperglycemia, polyuria, and increased appetite [1]. It can be classified into Type 1 Diabetes Mellitus (T1DM) or insulin-dependent diabetes, which is the less common type, characterized by the autoimmune destruction of pancreatic beta cells [2]. Type 2 Diabetes Mellitus (T2DM), or non-insulin-dependent diabetes, is a common chronic disease resulting from the interaction between genetic and environmental factors, accounting for about 90–95% of diabetes cases [3]. And gestational diabetes mellitus, which affects more than 10% of pregnancies [4].

The therapeutic approaches for diabetes are diverse, including dietary regulation, pharmaceutical drug treatments, and the use of medicinal plants

ISSN 2072-3857

within therapeutic dietary systems that reduce carbohydrates and replace them with healthy and balanced nutrition patterns [5]. Recent studies indicate that effective plant compounds, including flavonoids, polyphenols, and alkaloids, possess a significant ability to lower blood glucose levels and improve insulin sensitivity and function by regulating cellular signaling pathways associated with glucose absorption and reducing oxidative stress. This makes them candidates for development into future clinical treatments that reduce reliance on traditional chemical medications [6] . The plant *Fumaria parviflora* is an annual herbaceous medicinal plant with branched stems, known for its recent efficacy as an antimicrobial and antiviral agent, liver protector, and anti-diabetic and anti-inflammatory. These activities are primarily attributed to alkaloids and secondary compounds. Studies have demonstrated its impact on proteins associated with various diseases [7]. Therefore, this study aimed to extract the effective dose of *Fumaria parviflora* extract and evaluate the therapeutic effect of insulin hormone and vitamin E, as well as the *Fumaria parviflora* extract alone or in combination with vitamin E, to normalize glucose and insulin hormone levels along with iron deposition and histopathological changes in the kidneys induced by diabetes in male rats

Material and Methods

1.2: Insulin, Vitamin E, and the plant *Fumaria parviflora*

Insulin was purchased from local pharmacies in the form of pens for subcutaneous injection with a concentration of 100 units/ml from the commercial product Lantus SoloStar, manufactured by Sanofi [8]. Vitamin E, specifically DL-α-Tocopherol, was also purchased from the Chinese company Macklin with a purity of 96%, a chemical formula of C29H50O2, and a molecular weight of 430.71 [9].

The plant *Fumaria parviflora* was collected in April 2025 from the city of (Taq Taq/Erbil Governorate). The plant parts were thoroughly washed to remove dirt and impurities, then left to dry in the shade for seven days at room temperature, with proper ventilation and continuous stirring from time to time to speed up the drying process and prevent fungal growth. After that, the dried sample was ground using an electric blender to obtain a fine powder. which was later stored in airtight containers until used in the extraction process, and was extracted in 1000 ml of an alcoholic solvent prepared with a dilution ratio of 70% ethanol and 30% distilled water [10].

2.2: Preparation of Experimental Animals

This study was conducted from mid-October 2025 to mid-November 2025, using 35 male white rats aged 8-9 weeks and weighing 180-230 grams. They were obtained from the animal house of the College of Veterinary Medicine at Tikrit University and were monitored for two weeks before the experiment to ensure their health status, adaptation to new conditions, and absence of diseases before being used in the experiment. The groups of animals were placed in cages measuring 60×30×25 cm, with the cage floors covered with sawdust. The cages were equipped with specially designed metal covers for these cages and experiments. The appropriate environmental conditions for the experimental animals were prepared before the study began, as they were placed in a special laboratory animal room with a light cycle of 12 hours of light and 12 hours of darkness daily. The animals were also kept at a moderate

temperature of (25 ± 2) °C with good ventilation. The cleanliness of the cages and the surrounding environment of the animals was maintained, as the cages were regularly disinfected using appropriate disinfectants such as a 90% Dettol solution and 70% ethyl alcohol. The bedding inside the cages was also changed regularly every 3 days to maintain a healthy environment for the animals [11].

3.2: Induction of Diabetes

Five rats were isolated for the control group (non-diabetic), and the animals were injected once, intraperitoneally, with Chinese-origin alloxan to induce diabetes. The alloxan was prepared at the time of injection with a concentration of 135 mg/kg body weight, by dissolving 1 g of alloxan in 10 ml of normal saline. After withholding food from the animals for 12 hours, they were immediately provided with food post-injection, and their drinking water was replaced with a 5% glucose solution for 24 hours to mitigate the shock from the alloxan treatment. After an hour and a half, blood sugar was tested using a German-made glucose meter to confirm their induced diabetes.

4.2: Division of Experimental Animals

After the completion of the acclimatization period for the Sprague Dawley rats, which lasted two weeks to adapt to the conditions, their weight was measured before the start of the experiment and divided into similar weights for each group. The rats underwent a two-week acclimatization period to adapt to the new environment and ensure their health. During this period, the weights of the rats were measured and divided to be similar among the groups. The study included 35 male rats aged 8–9 weeks and weighing between 180–230 grams, which were randomly divided into 7 equal groups, with five rats in each group. During the experimental period, all rats, whether healthy or diabetic, were fed a standard diet consisting of (200g soy, 250g yellow corn, 200g flour, 20g premix, 200g barley, 100g bran, and limestone, in addition to antifungal substances at a ratio of 25g to ensure their basic nutritional needs were met). After confirming diabetes in the tested groups, the animals were distributed as follows:

1. The first group (the control group): This group was treated with a standard diet and distilled water throughout the 4-week experimental period. The first group (the healthy control): This group was treated with a standard diet and distilled water throughout the 4-week experimental period.

2. The second group (diabetic): This group was treated with a standard diet, and diabetes was experimentally induced by injecting the rats with alloxan at a concentration of 135 mg/kg body weight, along with providing them with distilled water throughout the experiment. The second group (diabetic): This group was treated with a standard diet, and diabetes was experimentally induced by injecting the rats with alloxan at a concentration of 135 mg/kg body weight, while providing them with distilled water throughout the experiment.

3. The third group (diabetic with insulin): This group was treated with a standard diet, and diabetes was induced experimentally by injecting the rats with alloxan at a concentration of 135 mg/kg body weight, while they were given distilled water throughout the experiment. The third group (diabetic with insulin): This group was treated by giving it a standard diet, and diabetes was experimentally induced by injecting the rats with alloxan. Subsequently, they were injected with insulin hormone at a concentration of 6 international units, while continuing to provide them with a

standard diet throughout the experimental period.

4. The fourth group (diabetic with vitamin E) was treated by giving it a standard diet, and diabetes was induced experimentally by injecting the rats with alloxan. Then, they were administered vitamin E at a concentration of 150 mg/kg while continuing to provide them with a standard diet throughout the experimental The fourth group (diabetic with vitamin E) was treated by giving it a standard diet. Diabetes was experimentally induced by injecting the rats with alloxan, followed by administering vitamin E at a concentration of 150 mg/kg while continuing to provide them with a standard diet throughout the experimental period.

5. The fifth group (diabetic with *Fumaria parviflora* extract): This group was treated with a standard diet, and diabetes was induced experimentally by injecting the rats with alloxan. They were then administered *Fumaria parviflora* extract at a concentration of 250 mg/kg, Group five (diabetic with *Fumaria parviflora* extract): This group was treated with a standard diet, and diabetes was experimentally induced by injecting the rats with alloxan. Subsequently, they were administered an extract of the plant *Fumaria parviflora* at a concentration of 250 mg/kg, while continuing to provide them with a standard diet throughout the experiment.

6. The sixth group (diabetic with insulin + vitamin E): This group was treated with a standard diet, and diabetes was induced experimentally by injecting the rats with alloxan. Subsequently, they were injected with insulin and given vitamin E, while continuing to provide them with a standard diet throughout the experimental period Group six (diabetic with insulin + vitamin E): This group was treated with a standard diet, and diabetes was experimentally induced by injecting the rats with alloxan. They were then injected with insulin and given vitamin E, while continuing to receive a standard diet throughout the experiment.

7. The seventh group (diabetic with *Fumaria parviflora* extract + Vitamin E): This group was treated with a standard diet, and diabetes was experimentally induced by injecting the rats with alloxan. They were then administered *Fumaria parviflora* extract along with Vitamin E, while Group Seven (Diabetic with *Fumaria parviflora* Extract + Vitamin E): This group was treated with a standard diet, and diabetes was experimentally induced by injecting rats with alloxan. Subsequently, they were administered *Fumaria parviflora* extract with Vitamin E while continuing to receive a standard diet throughout the experimental period.

5.2: Blood Sample Collection

After four weeks from the start of the experiment, blood samples were collected from the experimental animals. Before the blood collection process, the rats were fasted for 12 hours, allowing them only water, to reduce variability in measuring biochemical indicators. After that, the animals were anesthetized using general anesthesia thru intraperitoneal injection with a mixture of ketamine and xylazine at doses appropriate for the animal's weight, to ensure sufficient anesthesia allowing for blood withdrawal without causing pain to the animal. After ensuring complete anesthesia, the animal was secured on the dissection platform, and a surgical incision was made in the thoracic region using scissors and surgical forceps to access the thoracic cavity. After that, blood samples were drawn directly from the heart using a sterile syringe with a long needle thru the cardiac puncture technique. Blood samples were collected in gel tubes and left at room temperature for 15 minutes to allow clotting to occur. Then, the serum was separated using a centrifuge at a speed of 3000 RPM for 15 minutes. Then, the

ISSN 2072-3857

serum was transferred to clean test tubes and stored at a temperature of (-20°C) until it was used for various tests. After completing the blood collection, the kidneys were excised for histological study.

The kidneys were immediately washed with Normal Saline to remove blood residues, then cut into small pieces and placed in closed containers submerged in a previously prepared 10% neutral formalin solution for the purpose of fixing the organs, remaining for 24 hours. After the fixation period, the samples were thoroughly washed of formalin, then stored in 70% ethyl alcohol until used in preparing tissue sections using Prussian Blue Iron stain to measure iron deposition, and hematoxylin and eosin stain to study histological changes.

6.2: Biochemical Analyzes

The blood glucose test was conducted according to the method described by the manufacturer Rossmax and using the cobas device. Insulin in the blood was determined by enzyme immunoassay for quantitative estimation in the laboratory in serum using a kit manufactured by SUNLONG, China, used for the quantitative measurement of insulin hormone in rats.

7.2: Statistical analysis

The statistical analysis of the results was conducted using a One-Way ANOVA test, and the significant tests were determined according to Duncan's Multiple Range Test at a significance level of ($P \leq 0.05$) using SPSS version 25.

Results and Discussion

1.3: Determination of active dose

Table (1) shows that the dose of 250 mg/kg body weight of the alcoholic extract of the plant *Fumaria parviflora* is the most effective in reducing glucose (97.00± 5.15 ^{c}) in the serum of the treated rats compared to the groups treated only with glucose and those treated with concentrations of (100, 150, 200, and 250) mg of the alcoholic extract of the plant *Fumaria parviflora*, where the glucose concentrations were (113.40 ± 5.08 ^{b}), (111.60 ± 8.20^{b}), (109.00 ± 3.54^{b}), (97.00±5.15^{c}). This dose was adopted to evaluate the effect of the plant *Fumaria parviflora* under study in male rats

2.3: Glucose Concentration in Blood Serum

The results of the current study, as shown in Figure (1) and Table (2), indicated a significant increase ($p \leq 0.005$) in glucose levels in the diabetes group (192.00± 9.67 ^{a}) compared to the control group (91.20± 5.07 ^{e}). In contrast, there was a significant decrease in glucose levels in the insulin and vitamin E treatment groups, the *Fumaria parviflora* plant extract group, the insulin and vitamin E group, and the *Fumaria parviflora* plant extract with vitamin E group, respectively (141.00 ± 22.12^{b}),(131.80±10.26^{bc}),(114.60±12.60^{cd}), (131.40 ±28.99^{bc}), (104.20 ± 4.09^{de}), compared to the diabetes group (192.00± 9.67 ^{a}). This indicates a clear improvement in glucose homeostasis with single and dual treatments, with a relative preference for combined treatments in restoring glucose levels closer to the control group.

3.3: Insulin Concentration in Serum

The current results, as shown in Figure (1) and Table (2), indicated significant differences at a significance level of ($p \leq 0.005$) in insulin levels among the experimental groups. The diabetic group recorded a notable decrease in insulin levels (456.00±117.12^{d}) compared to the control group (1626.40 ±98.36 ^{a}), reflecting the clear impact of diabetes induction on insulin regulation. The results showed a significant increase in the groups treated with *Fumaria parviflora* extract,

the insulin with vitamin E group, and the *Fumaria parviflora* extract with vitamin E group (782.80 ±78.80[c]), (957.60 ±118.35[b]), (950.00 ±46.54 [b]) respectively, indicating a clear functional improvement in insulin regulation with both single and dual treatments. However, the groups that were administered insulin and vitamin only did not show a significant decrease compared to the diabetic group.

4.3: Iron Deposition in the Kidneys

The results of the current study for the kidneys of the healthy control group showed rare iron deposition (Iron Deposition, ID) as in (Figure 2a), while in the diabetic group, significant iron deposition was observed as in (Figures 2b, c). In the diabetic group injected with insulin, moderate iron deposition was observed as in (Figure 2d). In the diabetic group administered Vitamin E, moderate iron deposition was observed as in (Figure 2e). In the diabetic group administered *Fumaria parviflora* extract, rare iron deposition was observed as in (Figure 2f). In the diabetic group injected with insulin and administered Vitamin E, moderate iron deposition was observed as in (Figure 2g). In the diabetic group administered *Fumaria parviflora* extract and Vitamin E, rare iron deposition was observed as in (Figure 2h).

5.3: Histological study of the kidneys

The kidneys in the healthy control group showed the renal corpuscle containing the glomerulus (G), Bowman's space (BS), proximal convoluted tubules (PCT), and distal convoluted tubules (DCT) normally as in (Figure 3a). In the diabetic group, hemorrhage (He) was observed within the urinary tubules and interstitial tissue, with severe congestion (Co) in the capillaries surrounding the urinary tubules, along with hemolysis (H) and partial Bowman's space obstruction (Bso), which is noted in various inflammatory conditions. The renal tubules show signs of degeneration (D), with some swollen tubular epithelial cells (S), acute renal tubular injury or necrosis (N), and small, dense clusters of inflammatory cells (Ic) scattered in the interstitial tissue as seen in (Figure 3b). Blood cell overcrowding (Bco) and blood accumulation (Ba) outside the blood vessels between the renal tubules, necrosis (N), and protein leakage (Pl) from damaged glomeruli or remnants of dead renal tubular cells appeared as shown in (Figure 3c).

In the group with diabetes and injected with insulin, there is still moderate hemorrhage (He) and hemolysis (H), and Bowman's space narrows (Bsn) slightly. However, the glomeruli (G), proximal convoluted tubules (Pct), and distal convoluted tubules (Dct) appeared normal as shown in (Figure 3d). The group with diabetes and administered vitamin E shows cloudy swelling (CS) of the epithelial cells lining the renal tubules and glomerular congestion (GC), which may indicate an inflammatory response. Interstitial Edema (IE) is also observed between the tubules, while the glomeruli (G), Bowman's space (Bs), proximal convoluted tubules (Pct), and distal convoluted tubules (Dct) appear normal in some areas as shown in (Figure 3e). In the diabetic group treated with *Fumaria parviflora* extract, Bowman's Space Narrows (BSN) appears somewhat narrowed, which may indicate Cloudy Swelling (CS), a type of hydropic degeneration of the epithelial cells lining the tubules. Meanwhile, the glomeruli (G), proximal convoluted tubules (Pct), and distal convoluted tubules (Dct) were observed to be normal in some areas, as shown in (Figure 3f). In the group with diabetes, injected with insulin and administered vitamin E, the renal corpuscle appears containing the glomerulus (G) and Bowman's space (BS). The proximal convoluted tubules (PCT) and distal convoluted tubules (DCT) were also

observed to be normal as shown in (Figure 3g). In the group with diabetes treated with *Fumaria parviflora* extract and vitamin E, the renal corpuscle appears containing the glomerulus (G) and Bowman's space (BS). The proximal convoluted tubules (PCT) and distal convoluted tubules (DCT) were also observed to be normal as shown in (Figure 3h).

The results of our study showed an increase in glucose levels and a decrease in insulin levels in the diabetic group, which is consistent with what [12]. indicated, where it was shown that the induction of diabetes with alloxan leads to hyperglycemia with a clear deterioration in beta cell function and an increased need for external insulin. As for the increased iron deposition in the renal tissues of diabetic cases compared to the healthy control group, our results are consistent with the study by [13] , which indicated that excessive iron accumulation plays a pivotal role in the development of diabetic nephropathy, as it contributes to enhancing the pathological mechanisms associated with renal tissue damage. The process of measuring iron deposition in the kidneys of diabetic patients is of great importance due to its role in improving therapeutic intervention strategies and monitoring disease progression. Hyperglycemia leads to the disruption of iron transport protein regulation within renal cells, which enhances iron absorption while inhibiting its release, resulting in its accumulation in renal tissue. This explains the marked increase in its levels in diabetic kidneys. This accumulation is associated with increased oxidative stress and mitochondrial dysfunction, directly contributing to the accelerated progression of diabetic nephropathy [14]. Our results are consistent with the study by [15], which showed that alloxan-induced diabetes leads to damage to the renal tubules and stimulates a clear inflammatory response in the interstitial tissue, characterized by the infiltration of inflammatory cells. This corresponds to the accumulation of inflammatory cells, degeneration of epithelial cells, and loss of the normal organization of renal tissue. Additionally, the study by [16] demonstrated that oxidative stress and inflammation play a major role in the development of diabetic nephropathy, as they lead to podocyte injury, extracellular matrix accumulation, and glomerulosclerosis. They also contribute to epithelial-mesenchymal transition and renal tubular atrophy, increasing protein loss in the urine.

As for the role of insulin, the study's results align with what [17] demonstrated, as they found that administering exogenous insulin in diabetic animal models leads to the regulation of glucose levels within normal limits, as well as improved glycemic stability. This reflects the fundamental role of insulin in reducing blood glucose concentration and compensating for its secretion deficiency, thereby improving the overall metabolic state. As for the role of insulin in alleviating tissue imbalances, our results are consistent with the study by [18] , which induced diabetes in rats. The study showed that insulin-treated rats maintained the structure of the glomeruli and mesangial cells similarly to the control group, with only minor changes in the renal tubules. In contrast, the untreated group exhibited expansion of mesangial cells, atrophy of the renal tubules, and irregular cellular changes. The partial improvement in the histological structure of the glomeruli and tubules indicates that insulin provides protective benefits to the kidneys in diabetes, although some moderate histological changes such as hemorrhage, hemolysis, and narrowing of Bowman's space persist. This confirms that insulin treatment improves renal structure but does not fully restore it to normal within a short period of treatment. Our

ISSN 2072-3857

results are also consistent with the study by [19], which showed that insulin therapy protects the kidneys in diabetic rats by reducing the leakage of NEP and KIM-1 fragments in the urine. Insulin also contributed to alleviating hyperglycemia, reducing urinary albumin, and limiting glomerulosclerosis, demonstrating its protective role in maintaining renal function and the tissue balance of the kidney. As for the role of vitamin E, the results of the current study align with what was shown by [20], where studies found that elevated levels of vitamin E are associated with reduced insulin resistance in diabetic patients, which in turn reflects on improved blood glucose regulation. The results indicate that vitamin E deficiency may be an independent factor that enhances insulin resistance and elevated glucose levels, highlighting the potential role of vitamin E in improving diabetic metabolism and reducing insulin resistance. In the group with diabetes treated with vitamin E, a significant reduction in iron deposition within the renal tissue was recorded. In this context, antioxidants play a pivotal role in mitigating these effects, as vitamin E, being one of the most important fat-soluble antioxidants, inhibits lipid peroxidation and reduces the formation of free radicals resulting from iron reactions. It also contributes to reducing the inflammatory response associated with hyperglycemia, which is one of the factors that stimulate increased hepcidin expression. Therefore, the protective effect of vitamin E may not be limited to reducing oxidative stress alone, but also extends to improving iron metabolism balance, reducing its deposition within the kidney, and decreasing the structural changes and functional impairments associated with the development of diabetic nephropathy [21]. As for the histopathological lesions, our results are consistent with the study by [22], which was conducted on male rats treated with vitamin E at a dose of 100 mg/kg for 56 days. This study revealed significant degenerative changes in the renal tubular epithelial cells in the treated groups, indicating that vitamin E contributed to alleviating the severity of these changes compared to the untreated diabetic group, although it could not completely eliminate them due to the continued high blood glucose levels. The granular appearance of the cytoplasm reflects the accumulation of degraded proteins and dysfunctional organelles, which is a characteristic feature of cellular stress conditions below the lethal threshold in chronic hyperglycemia.

As for the role of the alcoholic extract of the plant *Fumaria parviflora*, it indicates that this effect is related to the pathological condition of diabetes and confirms the plant's effectiveness as a potential supplement for treating hyperglycemia in animal models [23]. Some recent studies also support the potential role of *Fumaria parviflora* in improving diabetes-related indicators in humans. A randomized clinical trial showed that the alcoholic extract of the plant improved levels of inflammatory markers and oxidative stress in patients with type 2 diabetes, which are factors associated with improved insulin sensitivity and glucose regulation [24]. Therefore, the observed improvement in the treated group can be explained by the role of vitamin E as an antioxidant that inhibits lipid peroxidation and protects cell membranes, in addition to the role of *Fumaria parviflora* in enhancing antioxidant defenses and reducing oxidative stress, which is reflected in the reduction of renal changes and the improvement of tissue structure. As for the role of *Fumaria parviflora* extract, it reflects a state of partial protection against oxidative stress, which is consistent with the study by [25]on the alloxan-induced diabetic rat model, where plant extracts rich in antioxidant compounds showed the ability to alleviate glomerular changes

ISSN 2072-3857

caused by elevated glucose levels, with some minor changes remaining. Meanwhile, the cloudy swelling of the epithelial cells lining the tubules appeared swollen with granular cytoplasm, partially obscuring the tubular lumens. This is an early reversible change resulting from sodium-potassium pump disturbance and ionic imbalance. This aligns with what [26] indicated, as the review showed that flavonoids exert a protective effect in diabetic nephropathy by regulating oxidative stress and inflammation pathways [27]. They reduce the production of reactive oxygen species (ROS) and activate antioxidant systems such as Nrf2/HO-1, as well as inhibit inflammatory cytokines like TNF-α, IL-1β, and IL-6 by regulating NF-κB and TGF-β pathways, ultimately leading to reduced renal cell damage and improved structural function of glomeruli and tubular cells. These compounds possess antioxidant and anti-inflammatory activities by inhibiting inflammatory cytokines such as TNF-α, IL-6, and IL-1, and activating antioxidant enzymes such as CAT and GPx. These results align with the heterogeneous nature of diabetic nephropathy, where the severity of renal lesions varies according to the degree of oxidative stress exposure and the efficiency of antioxidant protection in different regions of the kidney [28]

Table (1) Determination of the effective dose of *Fumaria parviflora* plant extract on glucose concentration.

Parameters Groups	**Test Glucose M±SD**
Control	5.1±135.60[a]
100 Mg/Kg	±113.405.08[b]
150 Mg/Kg	8.20±111.60[b]
200 Mg/Kg	±109.003.54[b]
250 Mg/Kg	±97.005.15[c]
F	30.85
P-Value	p <.0001***

- The values expressed as mean ± standard error
- The number of rats (5) in each group
- The numbers followed by different letters vertically indicate a significant difference at a probability level of ($p \leq 0.005$).

.

Table (2): The effect of *Fumaria parviflora* extract, vitamin E, and insulin on glucose and insulin concentration.

Parameters / Groups	Glucose(mg\dl) M±SD	Insulin(ng\ml) M±SD
Control	91.20±5.07[e]	1626.40±98.36[a]
Diabetes	192.00±9.67[a]	456.00±117.12[d]
Diabetes + Insulin	141.00±22.12b	486.40±62.44[d]
Diabetes + Vitamin E	131.80±10.26[bc]	509.20±121.96[d]
Diabetes + *Fumaria parviflora*	114.60±12.60[cd]	782.80±78.80[c]
Diabetes + (Insulin+ Vitamin E)	131.40±28.99[bc]	957.60±118.35[b]
Diabetes + (*Fumaria parviflora* + Vitamin E)	104.20±4.09[de]	950.00±46.54[b]

- The values are expressed as the mean ± standard deviation.
- The number of rats (5) in each group.
- Vertical letters indicate significant differences at a probability level of ($P \leq 0.05$).

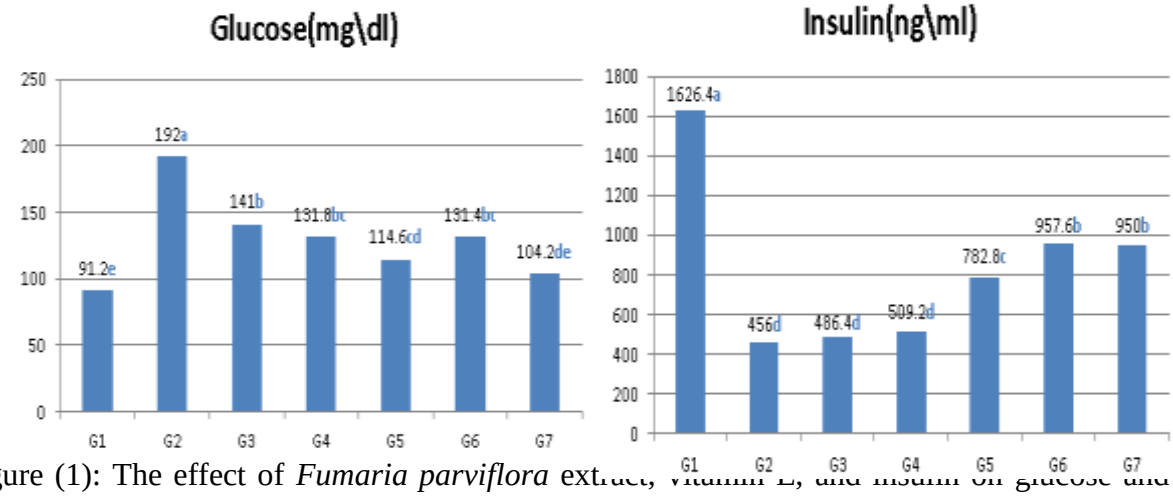
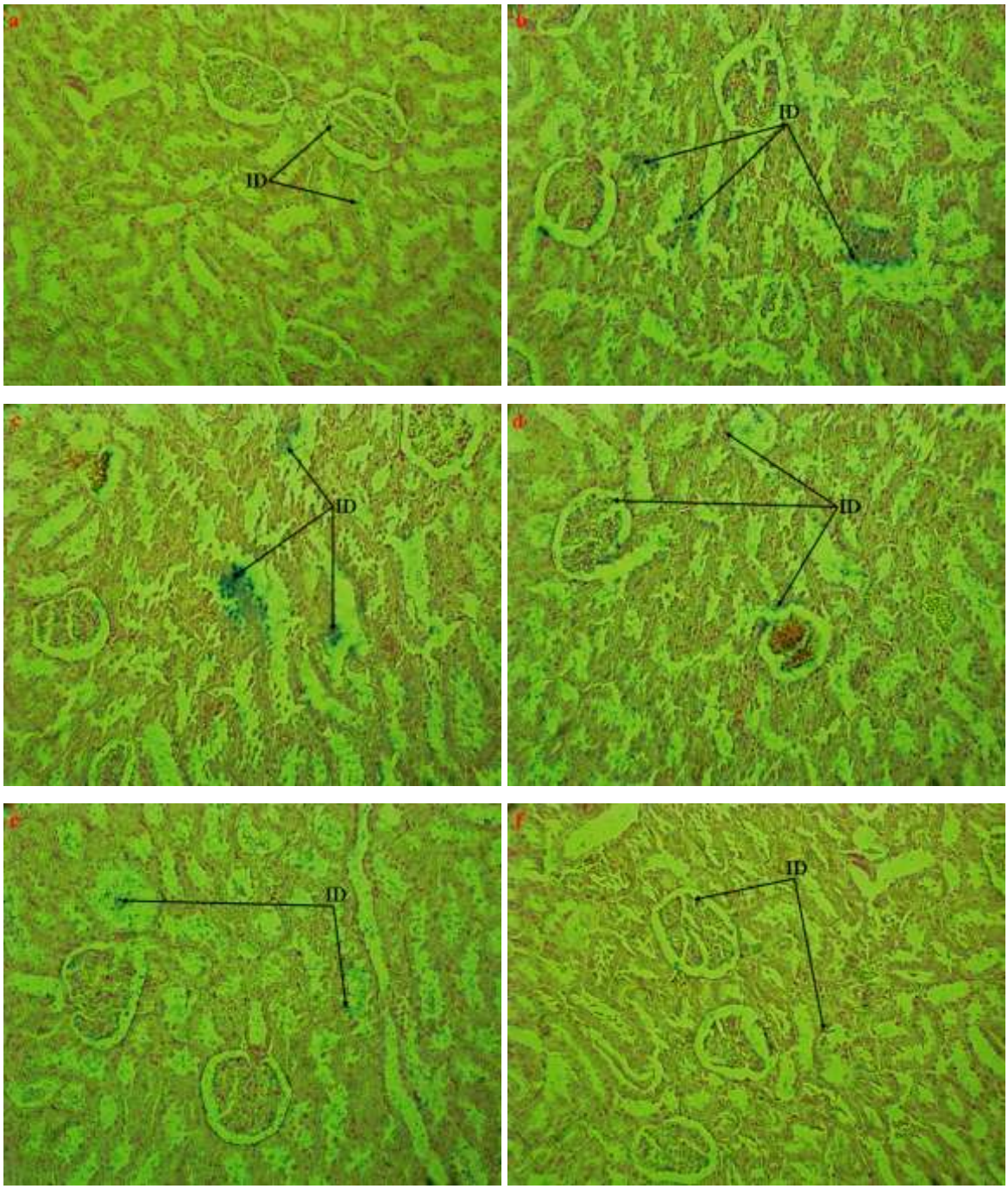
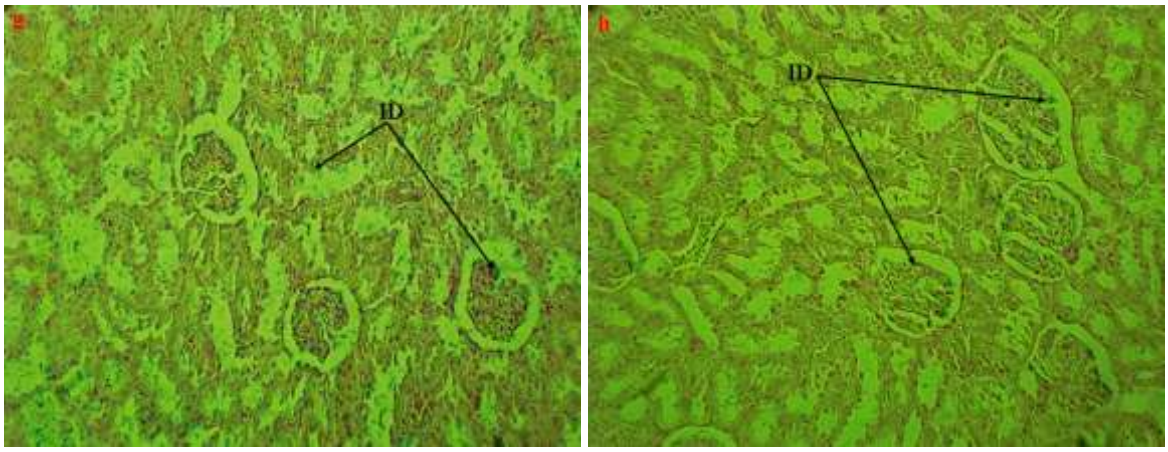


Figure (1): The effect of *Fumaria parviflora* extract, vitamin E, and insulin on glucose and insulin concentration.

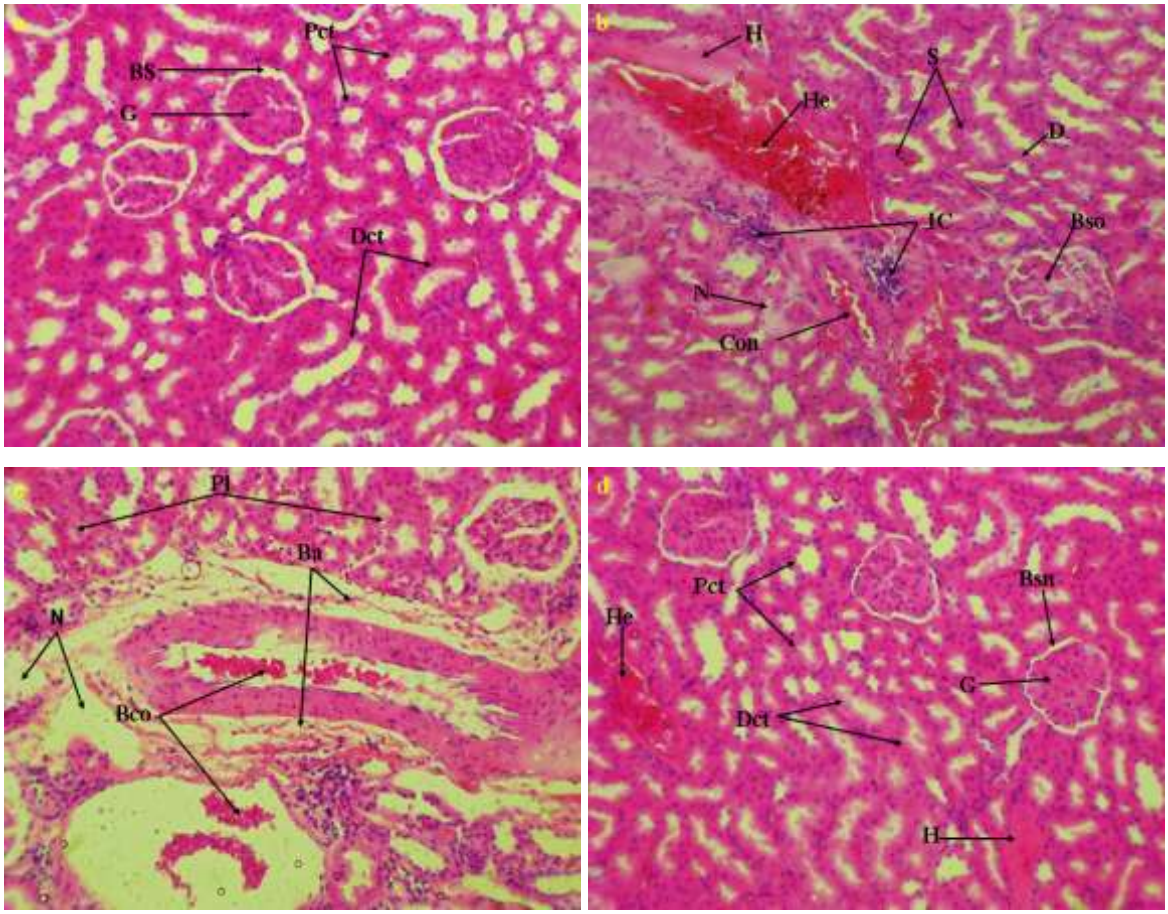
ISSN 2072-3857

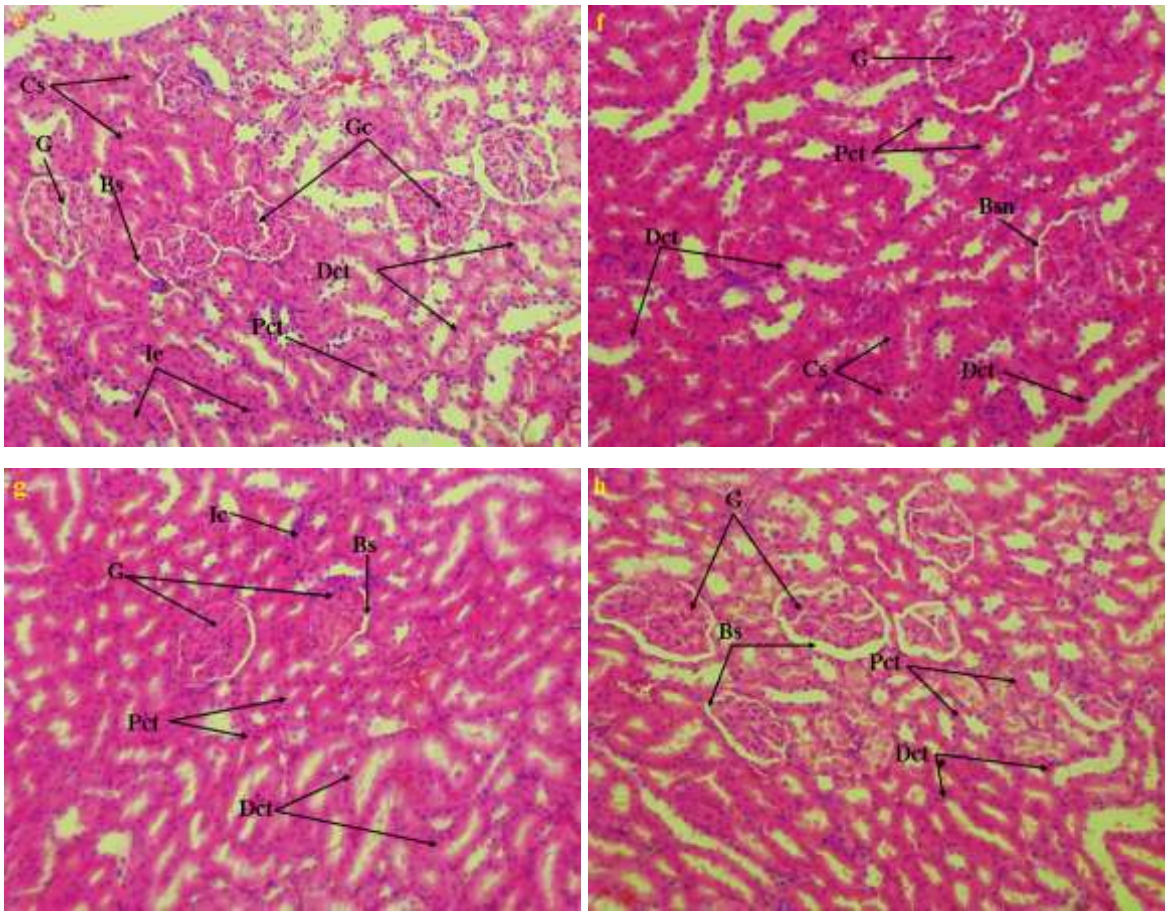


ISSN 2072-3857



(Figure 2) a. Kidney section of the healthy control group. b,c. Kidney sections of the diabetic group. d. Kidney section of the diabetic group treated with insulin hormone only. e. Kidney section of the diabetic group treated with vitamin E only. f. Kidney section of the diabetic group treated with *Fumaria parviflora* extract only. g. Kidney section of the diabetic group treated with (insulin hormone + vitamin E). h Kidney section of the diabetic group treated with (*Fumaria parviflora* extract + vitamin E) (blue Iron stain 20X).





(Figure 3) a. Kidney section of the healthy control group. b,c. Kidney sections of the diabetic group. d. Kidney section of the diabetic group treated with insulin hormone only. e. Kidney section of the diabetic group treated with vitamin E only. f. Kidney section of the diabetic group treated with *Fumaria parviflora* extract only. g. Kidney section of the diabetic group treated with (insulin hormone + vitamin E). h. Kidney section of the diabetic group treated with (*Fumaria parviflora* extract + Vitamin E) (H&E, 20X) .

Conclusion

The induction of diabetes (type 1) leads to significant functional and pathological disturbances; ranging from hormonal metabolic disorders (hyperglycemia and decreased insulin secretion) to the development of acute kidney injury characterized by tissue deposition of toxic iron, and the stimulation of destructive histological changes in the glomeruli and renal tubules due to oxidative stress. In contrast, the treatments used have shown remarkable efficacy in reducing these disorders; insulin contributed to regulating the physiological balance of sugar, while vitamin E distinguished itself with a protective antioxidant role that reduced the deposition of granular iron. The extract of the plant *Fumaria parviflora* has also proven to be highly effective in protecting the kidneys and inhibiting cellular damage. This protection reaches its peak in terms of tissue and functional aspects when combining *Fumaria parviflora* extract or insulin with vitamin E, reflecting an excellent synergistic effect that almost completely restores the physiological and tissue structural levels of the kidneys to their natural balance.

ISSN 2072-3857

Acknowledgment: We extend our sincere gratitude to University of Kirkuk and the Department of Biology for their support and cooperation. This research did not receive any specific grant or financial support from funding agencies in the public, commercial, or non-profit sectors

References

[1] Alam, S., M. K. Hasan, S. Neaz, N. Hussain, M. F. Hossain and T. Rahman. 2021. Diabetes Mellitus: Insights from Epidemiology, Biochemistry, Risk Factors, Diagnosis, Complications and Comprehensive Management. Diabetology. 2(2): 36–50.
[2] Grattoni, A., G. Korbutt, A. A. Tomei, A. J. García, A. R. Pepper, C. Stabler, et al. 2025. Harnessing Cellular Therapeutics for Type 1 Diabetes Mellitus: Progress, Challenges, and the Road Ahead. Nature Reviews Endocrinology. 21(1): 14–30.
[3] Młynarska, E., W. Czarnik, N. Dzieża, W. Jędraszak, G. Majchrowicz, et al. 2025. Type 2 Diabetes Mellitus: New Pathogenetic Mechanisms, Treatment and the Most Important Complications. International Journal of Molecular Sciences. 26(3): 1094.
[4] Lee, J., N. K. Lee and J. H. Moon. 2025. Gestational Diabetes Mellitus: Mechanisms Underlying Maternal and Fetal Complications. Endocrinology and Metabolism. 40(1): 10–25.
[5] Mitaki, N. B., I. V. Fasogbon, O. V. Ojiakor, W. Makena, E. O. Ikuomola, et al. 2025. A Systematic Review of Plant-Based Therapy for the Management of Diabetes Mellitus in the East Africa Community. Phytomedicine Plus. 5(1): 100717.
[6] Mammen, M. V., A. Suman, A. Kumar, D. P. Singh, A. Anand and S. Parveen. 2025. Recent Advances in Antidiabetic Phytochemicals: Bridging Traditional Remedies and Next-Generation Therapeutics. The Review of Diabetic Studies. pp. 197–218.
[7] Sharma, A., P. Yadav, R. Jangra, S. Singh, V. Kumar, et al. 2025. From Roots to Remedies: Exploration of Medicinal Potential of *Fumaria parviflora* Lam. in Drug Discovery. Pharmacological Research–Natural Products. 100319.
[8] Lucier, J., P. M. Mathias and C. Doerr. 2024. Type 1 Diabetes (Nursing). In: StatPearls [Internet]. StatPearls Publishing.
[9] Ichsan, A. M., A. Bukhari, S. Lallo, U. A. Miskad, A. A. Dzuhry, et al. 2022. Effect of Retinol and α-Tocopherol Supplementation on Photoreceptor and Retinal Ganglion Cell Apoptosis in Diabetic Rats Model. International Journal of Retina and Vitreous. 8(1): 40.
[10] Domínguez Oliva, A., I. Hernández Avalos, A. Bueno Nava, C. Chávez, A. Verduzco Mendoza, et al. 2025. Environmental Enrichment for Laboratory Rats and Mice: Endocrine, Physiological, and Behavioral Benefits of Meeting Rodents' Biological Needs. Frontiers in Veterinary Science. 12: 1622417.
[11] Rizvi, W., M. Fayazuddin, O. Singh, S. N. Syed, S. Moin, et al. 2017. Anti-Inflammatory Effect of *Fumaria parviflora* Leaves Based on TNF-α, IL-1, IL-6 and Antioxidant Potential. Avicenna Journal of Phytomedicine. 7(1): 37–45.
[12] Kim, Y. K., K. C. Won and L. Sussel. 2024. Glucose Metabolism Partially Regulates β-Cell Function Through Epigenomic Changes. Journal of Diabetes Investigation. 15(6): 649–655.
[13] Geng, W., L. Pan, L. Shen, Y. Sha, J. Sun, et al. 2022. Evaluating Renal Iron Overload in Diabetes Mellitus by Blood Oxygen Level-Dependent Magnetic Resonance Imaging: A Longitudinal Experimental Study. BMC Medical Imaging. 22(1): 200.
[14] Kumar, R., D. Kulshreshtha, A. Aggarwal, S. Asthana, A. Dinda and C. K. Mukhopadhyay. 2024. Glucose Induced Regulation of Iron Transporters Implicates Kidney Iron Accumulation. Biochimica et Biophysica Acta–General Subjects. 1868(11): 130713.
[15] Almuttairi, R. S. 2023. The Effects of

Metformin Treatment on Diabetic Albino Rats' Pancreas, Liver, and Kidney Histology. Archives of Razi Institute. 78(1): 459–463.
[16] Jin, Q., T. Liu, Y. Qiao, D. Liu, L. Yang, et al. 2023. Oxidative Stress and Inflammation in Diabetic Nephropathy: Role of Polyphenols. Frontiers in Immunology. 14: 1185317.
[17] Goez-Mora, J. E., N. Arbelaez-Córdoba, N. Balcazar-Morales and P. S. Rivadeneira. 2025. Study of Insulin Infusion in Diabetic Rats with an Ultra-Low-Cost Insulin Pump for Managing Blood Glucose Levels. Journal of Diabetes Investigation. 16(10): 1782–1793.
[18] Akbas, F. 2018. Protective Effect of Insulin Treatment on Early Renal Changes in Streptozotocin-Induced Diabetic Rats. Acta Endocrinologica. 14(2): 169–174.
[19] Gill, R. K., E. S. Salem, N. Grobe and K. M. Elased. 2025. Insulin Restores Renal Neprilysin and Attenuates the Shedding of Urinary NEP and KIM-1 in Diabetic Akita Mice. Frontiers in Pharmacology. 16: 1679651.
[20] Zhang, X., J. Lu, Y. Wu, B. Huang, K. Chen and J. Li. 2024. Anti-Inflammatory Properties of Biflavonoids Derived from Selaginella moellendorfii: Targeting NLRP3 Inflammasome-Dependent Pyroptosis. SSRN Electronic Journal.
[21] Chu, J., K. Wang, L. Lu, H. Zhao, J. Hu, et al. 2024. Advances of Iron and Ferroptosis in Diabetic Kidney Disease. Kidney International Reports. 9(7): 1972–1985.
[22] Ayaz, H., S. Kaya, U. Seker and Y. Nergiz. 2023. Comparison of the Anti-Diabetic and Nephroprotective Activities of Vitamin E, Metformin, and Nigella sativa Oil on Kidney in Experimental Diabetic Rats. Iranian Journal of Basic Medical Sciences. 26(4): 395–399.
[23] Fathiazad, F., S. Hamedeyazdan, M. K. Khosropanah and A. Khaki. 2013. Hypoglycemic Activity of *Fumaria parviflora* in Streptozotocin-Induced Diabetic Rats. Advanced Pharmaceutical Bulletin. 3(1): 207–210.
[24] Karimi, A., E. Dalir Abdollahinia, S. Ostadrahimi, M. Vajdi, M. Mobasseri, et al. 2024. Effects of Hydroalcoholic Extract of *Fumaria parviflora* Lam on Gene Expression and Serum Levels of Inflammatory and Oxidative Stress Parameters in Patients with Type 2 Diabetes: A Randomized Controlled Clinical Trial. Journal of Functional Foods. 122: 106528.
[25] Arabnozari, H., F. Shaki, A. Saberi Najjar, M. Hosseini, M. Shokrzadeh and E. Habibi. 2024. The Effect of Polygonum hyrcanicum Hydroalcoholic Extract on Oxidative Stress and Nephropathy in Alloxan-Induced Diabetic Mice. Scientific Reports. 14: 18117.
[26] Hu, Q., C. Qu, X. Xiao, W. Zhang, Y. Jiang, et al. 2021. Flavonoids on Diabetic Nephropathy: Advances and Therapeutic Opportunities. Chinese Medicine. 16(1): 74.
[27] Bhargava, A., P. Shrivastava and A. Tilwari. 2021. HPTLC Analysis of *Fumaria parviflora* (Lam.) Methanolic Extract of Whole Plant. Future Journal of Pharmaceutical Sciences. 7(1): 1.
[28] Sharma, A., R. Singh, R. Gill and S. S. Gill. 2025. From Roots to Remedies: Exploration of Medicinal Potential of *Fumaria parviflora* Lam. in Drug Discovery. Industrial Crops and Products (In press).

.

ISSN 2072-3857