

ASSESSMENT OF THE NEPHROPROTECTIVE EFFICACY OF RICINUS COMMUNIS L. (CASTOR) SEED ETHANOLIC EXTRACT ON RENAL DYSFUNCTION IN A DEXAMETHASONE AND HIGH-FAT DIET-INDUCED DIABETIC NEPHROPATHY RAT MODEL

Shivani Chauhan*, Rabia Choudhary¹, Surjeet Singh², Ram Dayal³

*Student Scholar, Sunder Deep Pharmacy College Dasna Ghaziabad

¹ Associate Professor, Sunder Deep Pharmacy College

² Assistant Professor, Sunder Deep Pharmacy College

³ Director, Sunder Deep Pharmacy College Dasna Ghaziabad

Received: July 15, 2025

Accepted: Aug 13, 2025

Published: Aug 14, 2025

ABSTRACT

Background: Characterized by advancing renal impairment, diabetic nephropathy (DN) is a critical Minute vascular complication of diabetes mellitus and the leading global contributor to concluding phase renal disease. Despite conventional therapeutic approaches, there is a critical need for novel nephroprotective agents with minimal adverse effects. Plant-based therapeutics offer promising alternatives; however, many species with potential nephroprotective properties remain scientifically unvalidated.

Objective: This study investigated the nephroprotective effects of castor seed ethanolic extract in experimentally induced diabetic nephropathy, evaluating its dose-dependent therapeutic potential against diabetes-associated renal complications.

Methods: Laboratory albino rats (Wistar strain) (150-200 g) were randomly allocated into six groups (n=6 each): control, diabetic control, three test groups receiving castor seed ethanolic extract (200, 300, and 400 mg/kg/day orally), and standard treatment (metformin 600 µg/kg/day). Diabetes was induced using a high-fat diet and dexamethasone (250 µg/kg subcutaneously) until blood glucose exceeded 250 mg/dL. Following diabetes confirmation, the treatments were administered for 28 days. Comprehensive assessments included glycemic parameters (blood glucose and HbA1c), lipid profile, renal function markers (serum creatinine, urea, uric acid, and BUN), urinary parameters (albumin, creatinine, protein excretion), histopathological examination, and antioxidant status (SOD and TBARS).

Results: Phytochemical analysis revealed the presence of flavonoids, glycosides, steroids, and cardenolides in the extract. Diabetic rats exhibited severe hyperglycemia (294.1 ± 5.56 mg/dL), dyslipidemia, elevated renal dysfunction markers, proteinuria, and oxidative stress. The castor seed extract demonstrated significant dose-dependent improvements across all parameters. The high-dose group (400 mg/kg) achieved near-normoglycemic levels (98.13 ± 2.99 mg/dL), comparable to metformin (92.15 ± 4.11 mg/dL). Treatment significantly reduced serum creatinine, urea, and BUN levels ($p < 0.001$) and decreased urinary albumin excretion and proteinuria. Histopathological examination revealed preserved glomerular and tubular architecture in the treated groups, with minimal structural damage compared to the severe nephropathic changes in untreated diabetic rats. Antioxidant parameters showed restored SOD activity and reduced TBARS levels, indicating the amelioration of oxidative stress.

Conclusions: Castor seed ethanolic extract exhibits potent dose-dependent nephroprotective effects in experimentally induced diabetic nephropathy through multiple mechanisms, including glycemic control, lipid profile normalization, preservation of renal function, and antioxidant activity. These findings suggest that castor seed extract is a promising therapeutic candidate for diabetic nephropathy management, warranting further clinical investigation to establish its therapeutic efficacy and safety profile in human subjects.

KEYWORDS: Diabetic nephropathy, castor seed, *Ricinus communis*, nephroprotection, oxidative stress, herbal medicine.

INTRODUCTION

Diabetic Kidney Disease (DKD) is a major complication of diabetes, marked by a gradual decline in kidney function. This condition is commonly characterized by a reduced glomerular filtration rate (GFR) and the presence of albumin in the urine, known as albuminuria (1) (2) (3). About 20-50% of individuals with diabetes have DN, and as the incidence of diabetes rises globally, so does its prevalence. DKD is the primary cause of ESRD and chronic kidney disease (CKD) worldwide. It is a serious microvascular consequence linked to diabetes (4) (5) (6).

The pathogenesis of DN involves multiple interconnected mechanisms such as metabolic changes due to hyperglycemia, Hemodynamic changes, activation of RAAS and transforming growth factor β (1) (7) (8). Lifestyle, clinical, and genetic factors all influence the development and progression of DN. The main causes of risk include hyperglycemia, high blood pressure, genetic disposition, obesity, and dyslipidemia (7) (9). Abnormal lipid levels, particularly disruptions in cholesterol metabolism, are believed to significantly contribute to both the onset and progression of DN. Cholesterol accumulates in renal cells due to abnormalities in cholesterol metabolism in DN. This deposit is cytotoxic and contributes to impaired renal function (10).

Both conventional and herbal medicines have nephroprotective effects. Some conventional medications used to treat Diabetic Nephropathy includes Angiotensin-converting enzyme inhibitors (enalapril, ramipril, captopril, lisinopril) (11), Angiotensin II receptor antagonists (telmisartan, losartan, irbesartan, candesartan) (12), Calcium channel blockers (Diltiazem, verapamil, amlodipine, nifedipine) (13), Diuretics (spironolactone, hydrochlorothiazide, chlorthalidone) (14), Beta-blockers (metoprolol, carvedilol, atenolol) (15). According to currently available research, approximately 400 plant species have been shown to possess antidiabetic properties. Many plant species, especially those with nephroprotective properties, have not yet been scientifically proven in traditional Indian medical systems (16). We selected castor seeds from several plant species for this study.

The plant yields three seeds in a brittle capsule, with kernels that are usually white and seed colors ranging from whitish to black. These seeds, measuring 5-16 mm wide, produce oil known for its cathartic, laxative, and anti-rheumatic effects (17). The seeds contain endosperm (65-75%) and coating (25-35%), with moisture (5.5%), carbohydrates (13%), fiber (12.5%), protein (17.9%), and ash (2.5%). Their oil has a high density, stable viscosity across temperatures, and a freezing point near -10 °C (18).

MATERIAL & METHOD

Reagents: Dexamethasone and metformin were purchased. A high-fat diet was prepared accordingly (19). Blood Glucose and SOD (super-oxide dismutase) commercial kits were used.

Extraction of castor seed ethanolic extract: Uncoated seeds was performed by keeping them in a hot air oven for two hours at 45–50 °C. Once cooled, the seeds were crushed using a mortar, creating a thick paste that resembled a pestle. The product was macerated with 95% ethanol for five days. For the filtration of the extract, a filter paper (Whatman No. 1) was used. A rotary evaporator was used to concentrate the filtrate at a temperature between 40 and 60 °C.

Castor seed extract also contains the toxic substance ricin, which is harmful to living organisms. To get rid of it, we use detoxification methods. In this method, the castor seed extract was autoclaved at 15 psi for 60 min (20).

Animals: Wistar Albino rats (150-200 gm) were used in the current experimental study. The rats were procured from Biotenic Pharma Private Limited, Greater Noida, (Uttar Pradesh, India) and kept under the space had 12-hour light-dark cycle, a controlled 22-25°C temperature, and relative humidity of 60-70%.

The animals had free access to food and water ad libitum. The Institutional Animal Ethics Committee examined all experimental approaches and techniques utilized in the study, and the laboratory animal care was conducted in accordance with the guidelines provided by the CCSEA, the Ministry of Government of India, and the Ministry of Environmental Affairs.

Induction of Diabetes- All rats were fasted overnight before starting the experiment. On day 0, a one-touch glucose meter was used to measure blood glucose levels, and weight was recorded. Dexamethasone was then administered subcutaneously at a dose of 250 µg/kg daily. To help the rats adjust to the high-fat diet, oral feeding of a high-fat diet was introduced gradually over the first five days, increasing from 1 ml to 5 ml, and then fixed at 5 ml on the fifth day. The HFD and dexamethasone doses were administered daily to induce diabetes.

Experimental Group- Animals with blood glucose concentrations greater than 250 mg/dL were included in the study. To mark the beginning of DN, measurements were made of serum creatinine, urea, uric acid, BUN, and albumin levels in urine were measured. After confirming elevated blood glucose levels, HFD and dexamethasone were discontinued.

Group I- Normal saline given orally considered as Control Group)

Group II- Normal saline given orally named as Diabetic Group

Group III- Low dose of Castor Seed Extract, 200 mg/kg/day orally

Group IV- Medium dose of Castor Seed Extract, 300 mg/kg/day orally

Group V- High dose of Castor Seed Extract, 400 mg/kg/day orally

Group VI- Standard group, metformin at the dose of 600 µg/kg/day

Blood and Urine parameters: On day 14 of treatment, blood samples were collected and centrifuged at $10 \times g$ rpm for 15 min to extract the serum. Serum samples were stored at -80°C in order to prepare them to estimate glycosylated hemoglobin (HbA1c), serum lipid profile and serum creatinine. Urine samples were collected for albumin, creatinine, protein excretion, and blood urea nitrogen (BUN) estimation.

Kidney Histopathological Examination- Chloroform scarring was applied to all group rats on the 14th day of the treatment investigation. The renal tissue was immediately removed and preserved in 10% formalin. For microscopic examination, a 5µm thick section was prepared using a rotating microtome and stained with hematoxylin and eosin (H&E) dye.

Kidney Homogenization Preparation- Both kidneys were dissected, washed with isotonic saline, and weighed immediately after sacrifice. The tissue was placed in a glass tube of 12 × 75 cm, and phosphate buffer was added at a ratio of 1:3. A motor-driven Teflon pestle homogenizer was used to homogenize the tissue on ice three times for 30 s. A 1.5 mL Eppendorf tube was filled with the sample and sonicated for 1 minute in 30-second bursts at 40% power for 1 min (with cooling on ice) using a Vibra Cell cup horn sonicator. All procedures were performed at 4 °C.

Antioxidant Parameters - Antioxidant parameters in diabetic nephropathy display a characteristic pattern: increased markers of oxidative damage and decreased antioxidant defenses (SOD). These changes underline the role of oxidative stress in DN pathogenesis and underscore the potential of antioxidant-based therapeutic strategies (21) (22).

Molecular Studies: Thiobarbituric acid reactive substances (TBARS) are widely used molecular biomarkers of lipid peroxidation and oxidative stress. Molecular studies examining TBARS provide insights into the role of oxidative damage in the development and progression of diabetic nephropathy (DN) (23).

RESULT & DISCUSSION

Phytochemical Screening

Preliminary qualitative phytochemical analysis indicated that the extract contains various amounts of alkaloids, glycosides, saponins, steroids, phenols, and cardenolides.

Table -Phytochemical screening of castor seed extract

S. No.	Phytochemicals	Result
1.	Flavonoids	Moderately present
2.	Glycoside	Moderately present
3.	Hydrogen Cyanide	Slightly present
4.	Resin	Absent
5.	Saponin	Slightly present
6.	Steroids	Moderately present
7.	Soluble Carbohydrate	Moderately present
8.	Tannin	Slightly present
9.	Reducing sugar	Highly present
10.	Terpenoids	Absent
11.	Phenols	Slightly present
12.	Cardinoloides	Highly present

Effect on Body Weight- Diabetic rats (Group II) showed significant weight loss, a typical symptom of uncontrolled diabetes. Treatment with the test drug, especially at higher doses (Group V), led to progressive weight gain similar to that in the standard drug group (Group VI), suggesting a dose-dependent antidiabetic and metabolic-restorative effect of the test drug.

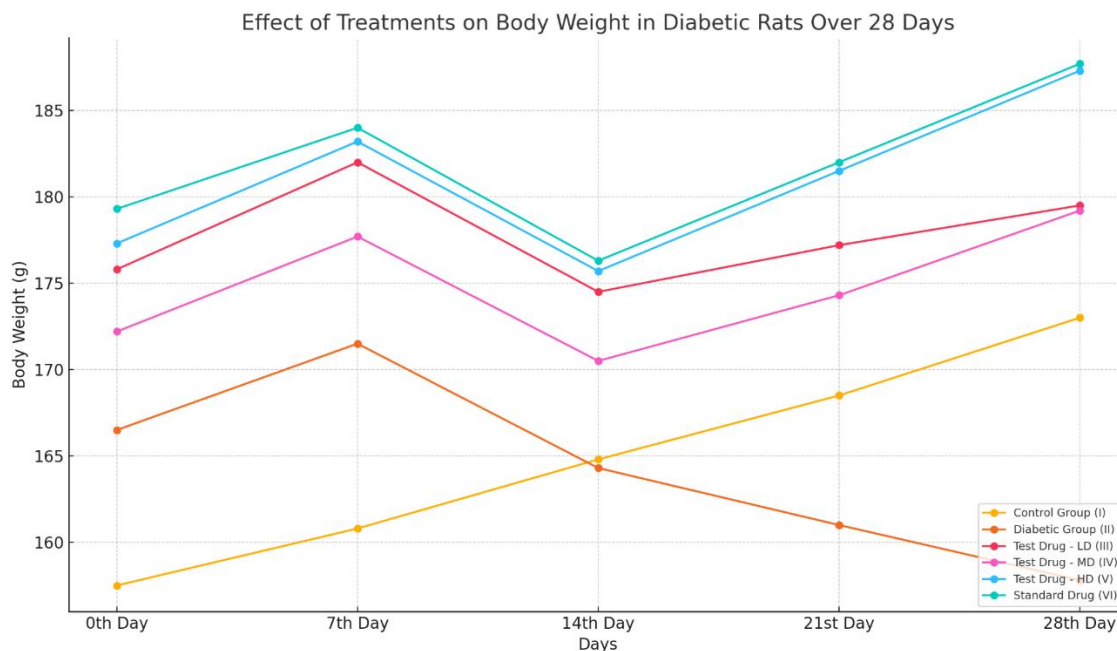


Fig- Changes in body weight (mean $\pm$ SEM) over a 28-day period

Effect on Blood Glucose Level- The untreated diabetic group exhibited a consistent and severe increase in the parameter (likely blood glucose), indicative of uncontrolled diabetes progression. All test drug groups initially mirrored the diabetic pattern, peaking on day 14. However, Groups IV (MD) and V (HD) showed significant reductions from Day 14 onwards. Group III (Low Dose) showed limited but noticeable improvement, suggesting that it may not be optimal for achieving full therapeutic efficacy. Groups V (High Dose) and VI (Standard Drug) achieved near-normal levels by day 28, suggesting that the test drug was dose-dependently effective in reversing or managing diabetes-induced abnormalities.

Groups	Day 0	Day 7	Day 14	Day 21	Day 28
I (Control Group)	87.33 $\pm$ 0.65	87.30 $\pm$ 0.69	87.28 $\pm$ 0.66	87.40 $\pm$ 0.61	87.45 $\pm$ 0.70
II (Diabetic Group)	87.37 $\pm$ 0.87	180.9 $\pm$ 3.46	284.3 $\pm$ 4.56	289.6 $\pm$ 4.65	294.1 $\pm$ 5.56
III (Test Drug-LD)	88.13 $\pm$ 0.93	188.3 $\pm$ 0.97	286.4 $\pm$ 4.70	237.2 $\pm$ 3.69	187.6 $\pm$ 8.89
IV (Test Drug-MD)	88.05 $\pm$ 1.01	188.2 $\pm$ 4.75	287.6 $\pm$ 2.32	204.0 $\pm$ 3.83	128.8 $\pm$ 4.69
V (Test Drug-HD)	89.55 $\pm$ 0.66	189.6 $\pm$ 1.49	292.2 $\pm$ 1.18	200.7 $\pm$ 7.00	98.13 $\pm$ 2.99
VI (Standard Drug)	87.17 $\pm$ 0.83	187.8 $\pm$ 3.39	290.7 $\pm$ 3.30	194.9 $\pm$ 3.74	92.15 $\pm$ 4.11

Food and water Intake- Compared to the control group, people with chronic diabetes consume more food and water. Metformin and castor seed extract enhanced the activity of these enzymes at different dosages.

Effect of HFD and Dexamethasone on Urea and Uric Acid- The levels increased levels of urea and uric acid indicate the presence of nephropathy. The urea and uric acid levels were significantly increased.

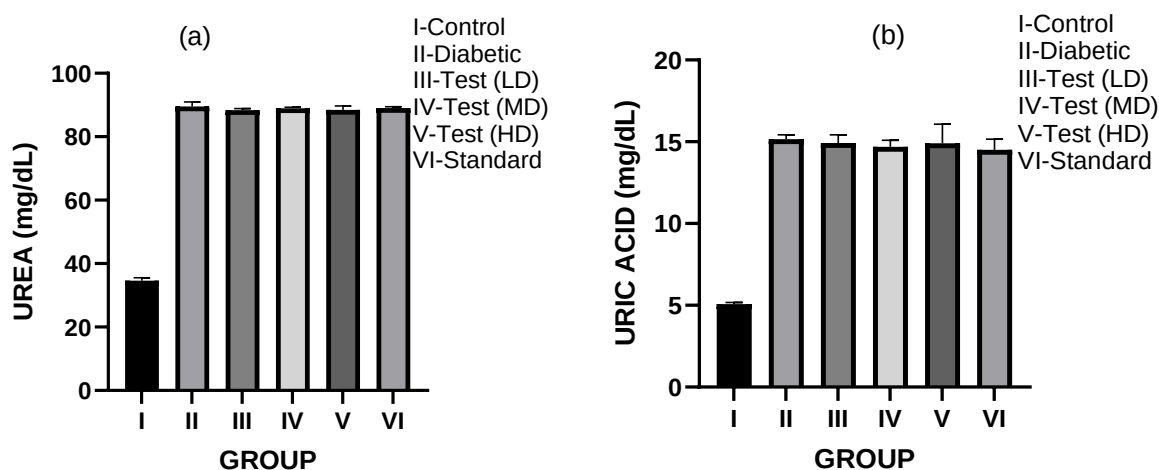


Fig- Effect on Urea and uric acid (a) A significant increase in urea levels ($p < 0.0001$) was observed in diabetic-induced groups (II–VI) relative to the normal group (I) **(b)** Uric acid levels were also

significantly elevated (, $p < 0.0001$) in the diabetic-induced groups (II–VI) compared to the normal group, based on one-way ANOVA with Tukey’s post hoc analysis

Blood test

- Effect on Glycosylated hemoglobin-** After diabetes induction, all groups except the control (I) showed a significant increase in HbA1c, with the diabetic (II), test (III, IV, V), and standard (VI) groups all at similarly high levels. This indicates the successful induction of hyperglycemia in all non-control groups due to HFD and dexamethasone. The level of HbA1C was considerably elevated (<0.001). Its level was considerably ($p<0.001$) decreased by metformin and castor seed extract.

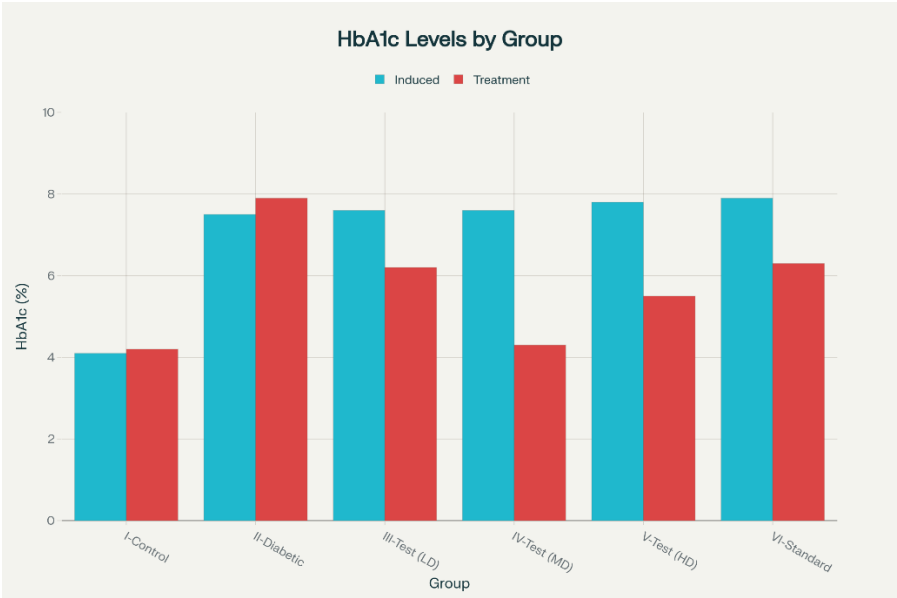


Fig- Comparison of HbA1c levels between Induced and Treatment groups

Effect on Serum Lipid Profile: The lipid changes observed in the diabetic group, including increased LDL, VLDL, and triglyceride levels and reduced HDL levels, mirror the typical patterns seen in human type 2 diabetes, driven by insulin deficiency/resistance affecting lipid metabolism. Treatments have improved glycemic control, often parallel to improvements in lipid profiles, as shown here, and contribute to reduced cardiovascular risk.

Table - Serum Lipid Profile

GROUPS	Total Cholesterol (mg/dL)		HDL- Cholesterol (mg/dL)		VLDL (mg/dL)		LDL (mg/dL)		Triglyceride (mg/dL)	
	DAY 14	DAY 28	DAY 14	DAY 28	DAY 14	DAY 28	DAY 14	DAY 28	DAY 14	DAY 28
I (Control Group)	102±10	105±5	55±8	60±4	17.2±5	18±6	29±12	23±2	87±8	91±5
II (Diabetic Group)	206±4	210±3	45±4	42±9	30±4	28±6	131±3	140±4	143±3	149±9

III (Test Drug- LD)	208±6	165±7	49±7	55±5	28±8	25±5	131±2	103±8	140±4	105±5
IV (Test Drug-MD)	210±8	153±10	48±11	52±3	31±12	29±9	145±8	99±6	138±6	96±7
V (Test Drug-HD)	209±2	122±4	42±8	50±7	33±7	28±11	140±6	86±5	143±3	91±2
VI (Standard Drug)	206±6	182±8	46±9	67±5	36±10	21±14	132±8	89±6	134±8	90±4

Effect on Serum Creatinine- The induction of diabetes with HFD and dexamethasone elevated the serum creatinine level. Compared to the diabetic and metformin groups, castor seed extract considerably ($p < 0.001$) lowered the serum creatinine level.

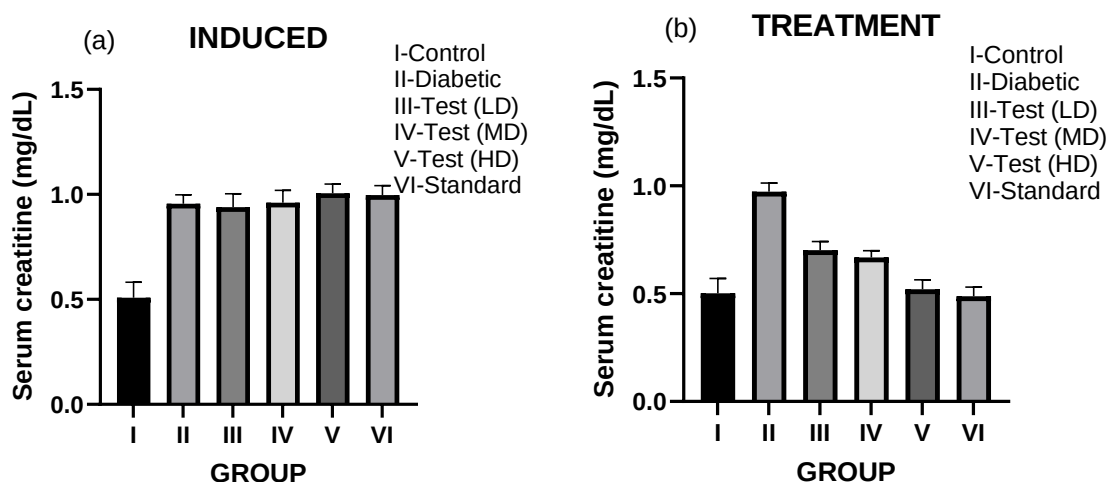


Fig- Effect on Serum creatinine- Statistical analysis using one-way ANOVA with Tukey's test revealed: (a) a significant difference between the induced and control groups ($p < 0.001$), and (b) significant differences between both test and standard groups compared to the diabetic group ($p < 0.001$)

Urine test

Effect on Urine Volume- The rapid and sustained rise in urine output following diabetes induction in all non-control groups (Group-II-VI) validates the effective modeling of diabetic nephropathy, with loss of normal renal regulation and onset of polyuria. The castor seed extract, especially at medium and high doses, significantly reduced urine output, indicating the restoration of renal concentrating ability, suppression of polyuria, and overall reno-protective action. These improvements are comparable to those of standard (metformin) antidiabetic therapy.

Effect on Albumin- Diabetic rats, regardless of later treatment allocation, rapidly developed albuminuria after induction, reflecting early stage diabetic nephropathy. Test drugs, especially at moderate and high doses, and standard treatment significantly reduced albumin excretion, reflecting the mitigation or reversal of diabetic nephropathy. Lower albuminuria indicates the preservation or restoration of glomerular function.

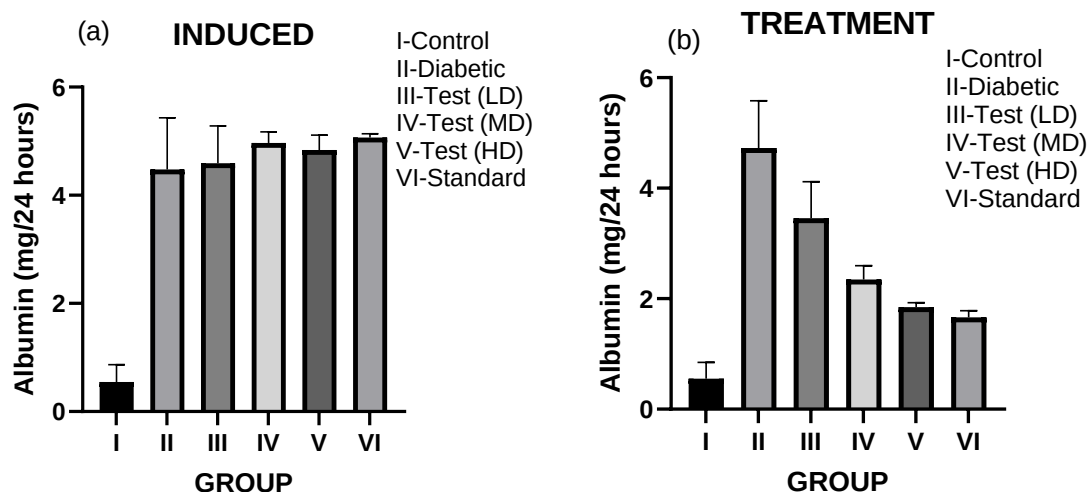


Fig- Effect on Albumin level (a) A significant difference was found between the induced and control groups ($p < 0.001$) **(b)** Significant differences were also observed in the test and standard groups compared to the diabetic group ($p < 0.001$), based on one-way ANOVA with Tukey's test

Effect on Creatinine- The reduction in urinary creatinine excretion in the diabetic and test groups reflects the onset of renal dysfunction, a hallmark of diabetic nephropathy, indicating compromised glomerular filtration. The test groups (especially at medium and high doses) and the standard treatment group exhibited increased urinary creatinine excretion post-treatment.

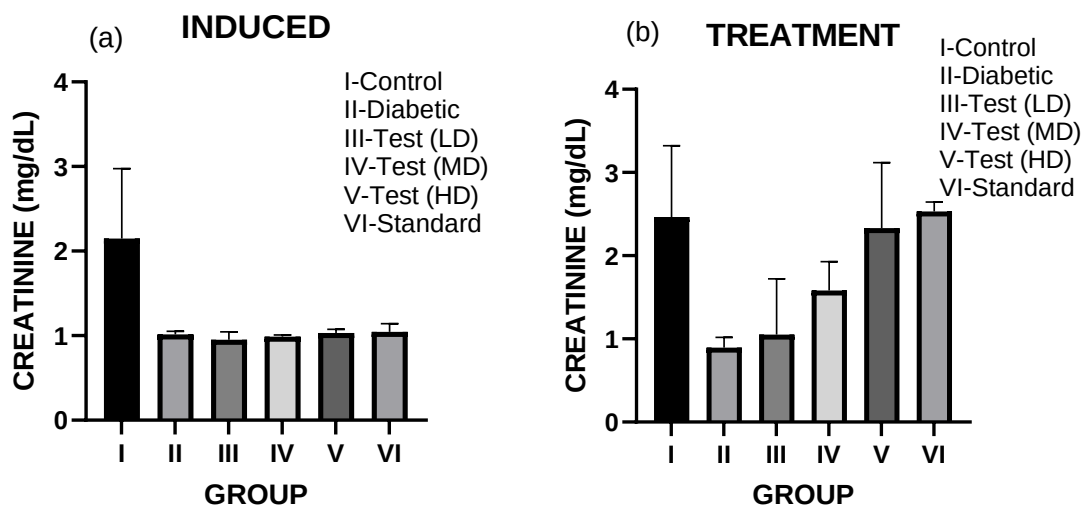


Fig -Effect on creatinine (a) The induced group showed a significant difference compared to the control group ($p < 0.001$) **(b)** Both the test and standard groups exhibited significant differences compared to the diabetic group ($p < 0.001$), as determined by one-way ANOVA with Tukey's post hoc test

Effect on Protein Excretion- All groups, except the control, exhibited a pronounced increase in protein excretion (proteinuria), as evidenced by significantly elevated values compared to the control group. This marked increase in urinary protein signals the successful induction of diabetic nephropathy. Untreated diabetic animals remain at risk for worsening kidney damage due to persistent proteinuria. Test drugs and

standard treatments provide renoprotective effects, and significant decreases in proteinuria suggest improved glomerular barrier function and reduced progression of diabetic nephropathy.

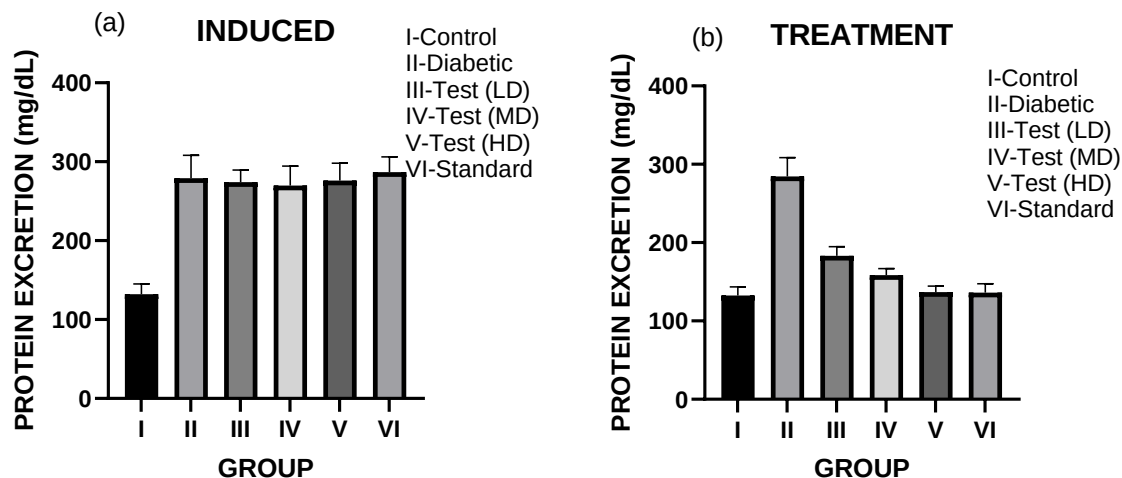


Fig-Effect on Protein Excretion (a) Induced group was compared with control group, *** ($p < 0.001$) (b) Test and standard group was compared with diabetic group, *** ($p < 0.001$), using one-way ANOVA (Tukey Test)

Effect on Blood Urea Nitrogen (BUN) level: A persistent and marked increase in BUN indicates the onset of renal dysfunction. At higher test drug doses and with standard therapy, BUN was restored toward normal, reflecting improved renal excretory function and attenuation of diabetic nephropathy.

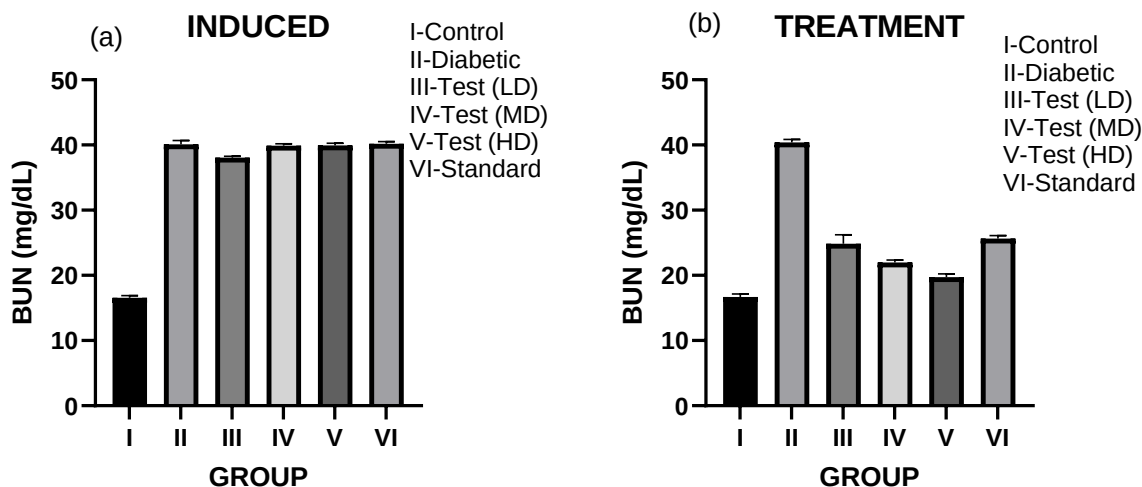


Fig-Effect on Blood Urea Nitrogen (a) The induced group showed a significant difference compared to the control group ($p < 0.001$) (b) Both the test and standard groups exhibited significant differences compared to the diabetic group ($p < 0.001$), as analyzed by one-way ANOVA with Tukey's test

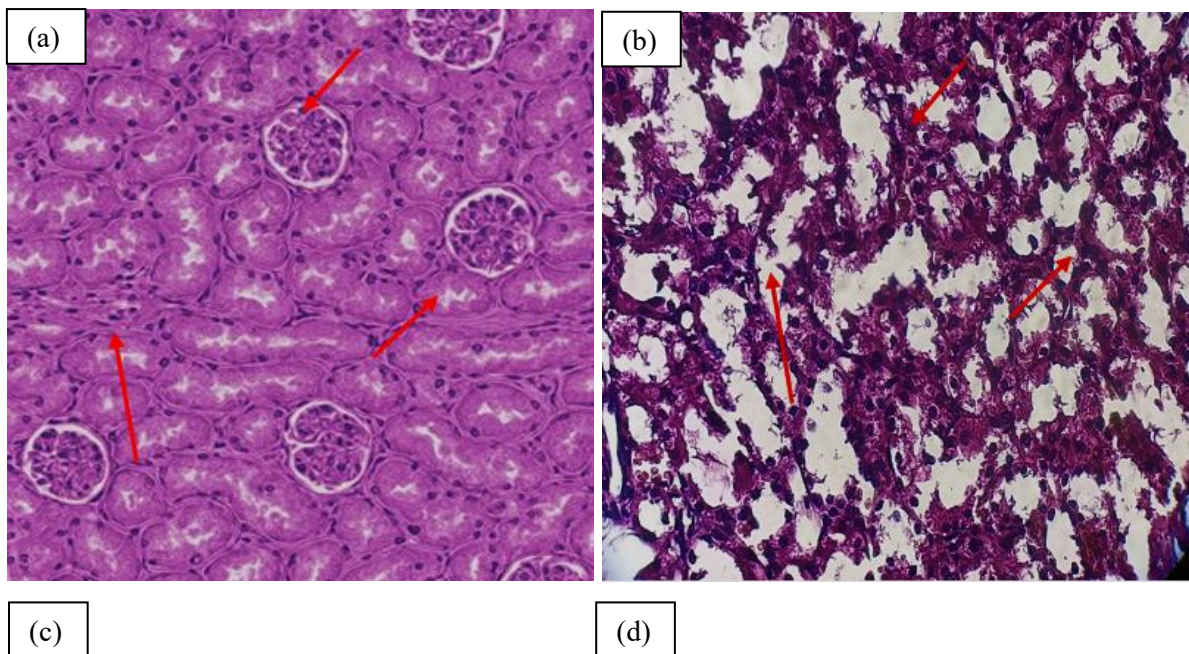
Histopathological Analysis

Kidney Weight- The weight of the kidneys of rats in the diabetic group was higher than that of the control group. The increase in kidney weight was due to diabetic nephropathy. The test (III-V) and standard (VI) groups had lower weights than the diabetic group.

Table - Weight of kidney

Group	Kidney weight (gm)
I (Control)	1.2± 0.07
II (Diabetic)	1.5±0.09
III (Test Drug-LD)	1.3 ±0.04
IV (Test Drug- MD)	1.4±0.06
V (Test Drug- HD)	1.27±0.05
VI (Standard)	1.26±0.06

Microscopic evaluation of histopathology: The kidney histology of diabetic Wistar rats demonstrated hallmark features of diabetic nephropathy, such as glomerular, tubular, and interstitial injury, edema and fibrosis, and loss of normal renal parenchymal organization. These changes confirm the presence and progression of diabetic nephropathy in animal models and serve as robust morphological evidence for studies assessing renoprotective interventions. Untreated diabetes leads to severe structural damage, whereas treatment with the test (400 mg/kg) and standard therapies results in marked structural preservation, supporting their efficacy in reducing or reversing diabetic kidney damage. There is a small preservation at low and medium doses of the test drug compared to the higher dose.



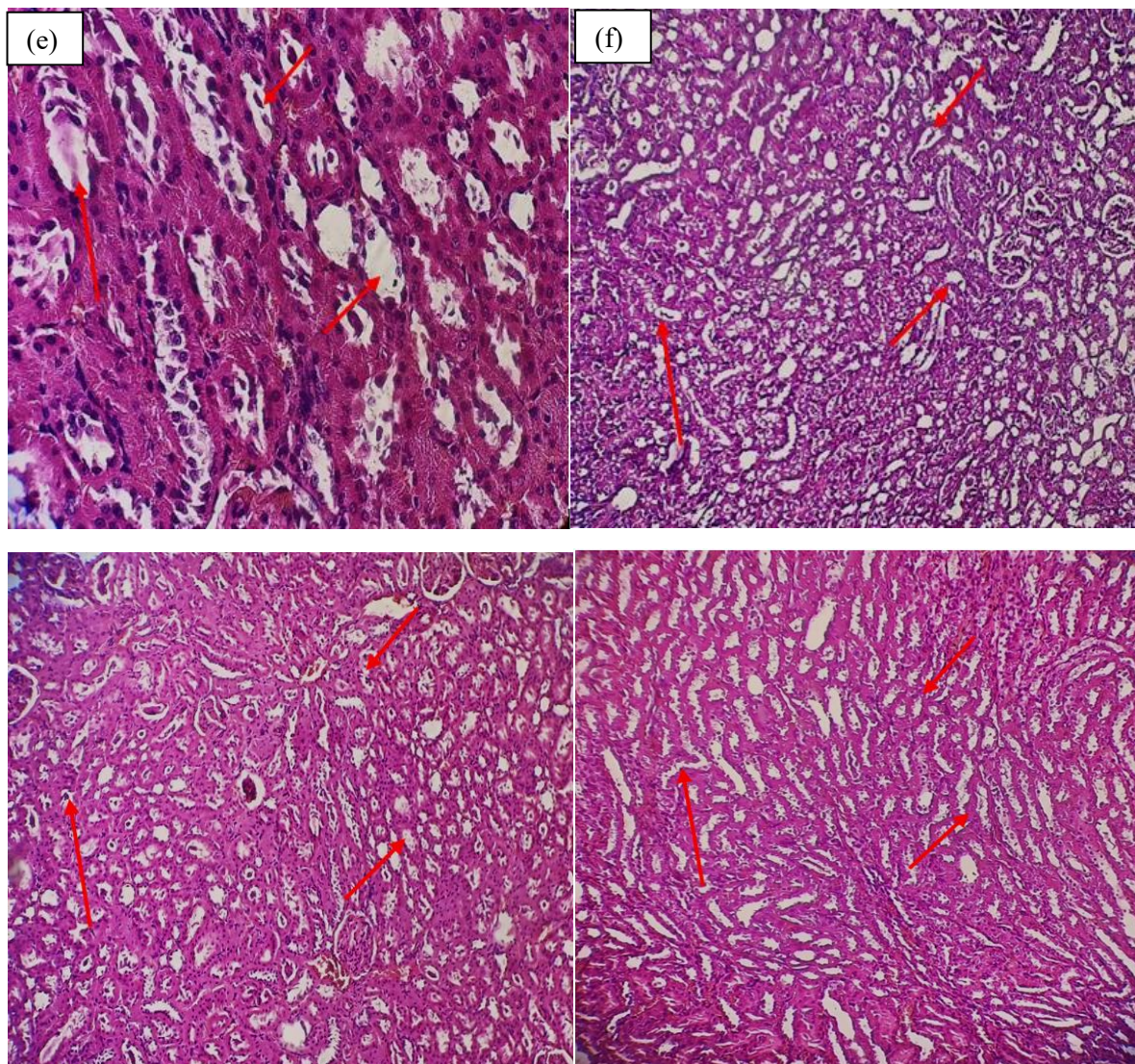


Fig- Histopathological examination of kidneys of rats (a) Control Group (b) Diabetic Group (c) Test Group I- Low Dose (d) Test Group II-Medium Dose (e) Test Group III- High Dose (f) Standard Group

Antioxidants Parameters

The SOD control group showed the highest SOD activity, representing a normal antioxidant status. The diabetic group exhibited a dramatic decline in SOD activity, indicating a significant reduction in antioxidant defense due to the induction of diabetic nephropathy. The test drug (LD) showed a slight increase in SOD compared to the diabetic group, but it was still much lower than that of the control group. The test drug (MD) showed a noticeable improvement in SOD near the mid-range. The test drug (HD) showed further increase in SOD activity, approaching the levels observed with the standard drug.

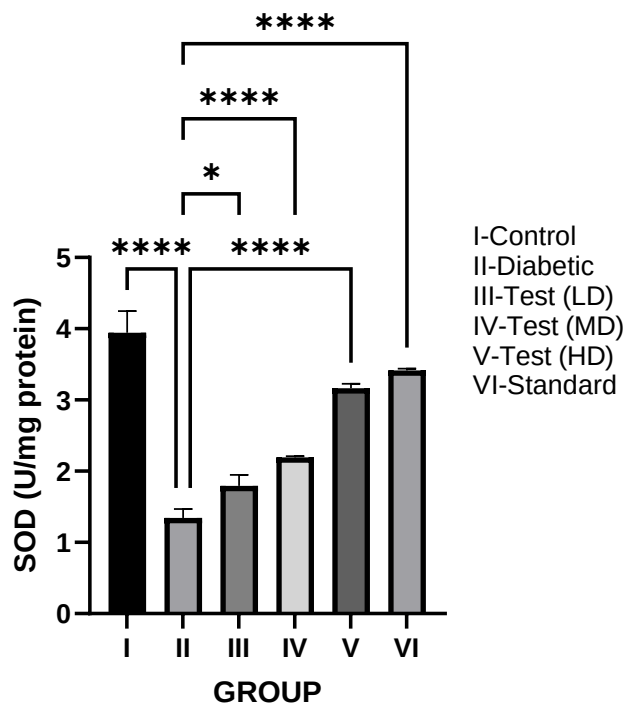


Fig- Effect on SOD- SOD levels were significantly decreased (****, $p < 0.0001$) in the diabetic group compared to the normal group, and significantly increased (**, $p < 0.0001$) in the treated groups (IV–VI) compared to the diabetic group, as assessed by one-way ANOVA with Tukey's test.

Molecular studies

TBARS- Control group reflects minimal oxidative damage, consistent with healthy renal tissue. High TBARS levels in the diabetic group reflect uncontrolled oxidative stress, contributing to kidney injury. The test compound and standard drug reduced TBARS, indicating the restoration of antioxidant capacity and protection against oxidative stress.

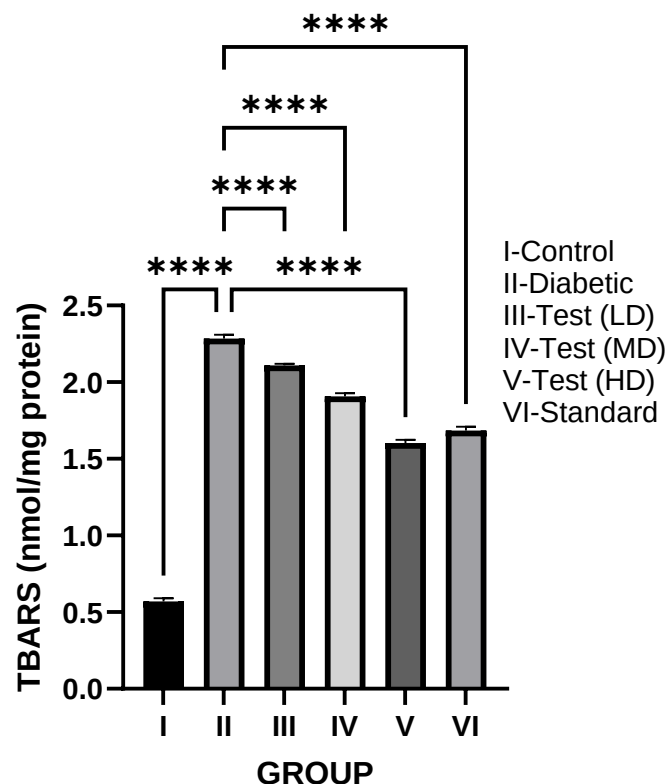


Fig- Effect on TBARS- Using one-way ANOVA with Tukey's test, TBARS was found to be significantly higher (****, $p < 0.0001$) in the diabetic group than in the normal group, and significantly lower (**, $p < 0.0001$) in the treatment groups (IV–VI) than in the diabetic group.

CONCLUSION

Castor seed phytoextract demonstrated significant antidiabetic effects in Wistar albino rats with diabetes induced by HFD and Dexamethasone. Diverse doses of the ethanolic extract produced diverse effects, but the high dose improved lipid profiles and lowered blood glucose levels, indicating that it might have inherent antidiabetic properties. The test drug (especially at medium and high doses) and standard treatment significantly reversed diabetic dyslipidemia, normalizing lipid parameters and suggesting potential cardiovascular benefits. Untreated diabetic animals maintained high serum creatinine levels, reflecting persistent kidney dysfunction. Castor seed extract treatments, particularly at moderate and high doses, and the standard drug effectively lowered serum creatinine levels, indicating potential reno-protective benefits. The data suggest that castor seed extract has the potential to attenuate or reverse the functional signs of diabetic nephropathy, specifically polyuria, which is a primary early symptom. Dose-dependent effects further support their utility in managing diabetic renal complications. The subsequent treatment especially with moderate/high doses of the test agent or standard therapy led to a pronounced decrease in urinary albumin excretion. These findings indicate that the Castor Seed extract provide significant protection against diabetes-induced kidney damage, supporting their potential for the management and prevention of diabetic nephropathy. They prevent or reverse key features of diabetic nephropathy, as shown by the normalization of urinary creatinine levels. Reductions in BUN achieved by test and standard therapies suggest these interventions help preserve renal function and may delay the onset or severity of diabetic nephropathy.

References

1. Habli, M.M., 2024. Comprehensive insights into diabetic nephropathy: pathophysiology, clinical features, and emerging treatments. *Journal of The Egyptian Society of Nephrology and Transplantation*, 24(4), pp.163-168.
2. Nadendla, R.R., K, K., Aziz, N., Pyne, C., Panigrahy, U.P., Wal, P., Kulkarni, M.H. and Rasheed, A., 2025. An updated review on diabetic nephropathy: potential mechanisms, biomarkers, therapeutic targets and interventional therapies. *Current Diabetes Reviews*, 21(9), p.e240624231266.
3. Joumaa, J.P., Raffoul, A., Sarkis, C., Chatrieh, E., Zaidan, S., Attieh, P., Harb, F., Azar, S. and Ghadieh, H.E., 2025. Mechanisms, Biomarkers, and Treatment Approaches for Diabetic Kidney Disease: Current Insights and Future Perspectives. *Journal of Clinical Medicine*, 14(3), p.727.
4. Hauwanga, W.N., Abdalhamed, T.Y., Ezike, L.A., Chukwulebe, I.S., Oo, A.K., Wilfred, A., Khan, A.R.A.K.A., Chukwuwike, J., Florial, E., Lawan, H. and Felix, A., 2024. The Pathophysiology and Vascular Complications of Diabetes in Chronic Kidney Disease: A Comprehensive Review. *Cureus*, 16(12).
5. Jha, R., Lopez-Trevino, S., Kankanamalage, H.R. and Jha, J.C., 2024. Diabetes and renal complications: an overview on pathophysiology, biomarkers and therapeutic interventions. *Biomedicines*, 12(5), p.1098.
6. Sinha, S.K. and Nicholas, S.B., 2023. Pathomechanisms of diabetic kidney disease. *Journal of Clinical Medicine*, 12(23), p.7349.
7. Kushwaha, K., Kabra, U., Dubey, R. and Gupta, J., 2022. Diabetic nephropathy: pathogenesis to cure. *Current Drug Targets*, 23(15), pp.1418-1429.
8. Bansal, D., & Dhiman, A. (2022). A Rationalized Overview of Diabetic Nephropathy. *EAS Journal of Medicine and Surgery*, 4(1), 15–18. <https://doi.org/10.36349/easjms.2022.v04i01.003>
9. Natesan, V. and Kim, S.J., 2021. Diabetic nephropathy—a review of risk factors, progression, mechanism, and dietary management. *Biomolecules & therapeutics*, 29(4), p.365.
10. Chen, X., Yin, Q., Ma, L. and Fu, P., 2021. The role of cholesterol homeostasis in diabetic kidney disease. *Current Medicinal Chemistry*, 28(36), pp.7413-7426.
11. Reboldi, G., Gentile, G., Angeli, F. and Verdecchia, P., 2009. Choice of ACE inhibitor combinations in hypertensive patients with type 2 diabetes: update after recent clinical trials. *Vascular Health and Risk Management*, pp.411-427.
12. Ej, L., 2001. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med*, 345, pp.851-860.
13. Tikkanen, I. and Johnston, C.I., 1997. Comparison of renin-angiotensin to calcium channel blockade in renal disease. *Kidney International Supplement*, (63).
14. Pahor, M., Psaty, B.M., Alderman, M.H., Applegate, W.B., Williamson, J.D. and Furberg, C.D., 2000. Therapeutic benefits of ACE inhibitors and other antihypertensive drugs in patients with type 2 diabetes. *Diabetes care*, 23(7), pp.888-892.
15. Strippoli, G.F., Craig, M.C., Schena, F.P. and Craig, J.C., 2006. Role of blood pressure targets and specific antihypertensive agents used to prevent diabetic nephropathy and delay its progression. *Journal of the American Society of Nephrology*, 17(4_suppl_2), pp.S153-S155.
16. Shafi, S., Tabassum, N. and Ahmad, F., 2012. Diabetic nephropathy and herbal medicines. *International Journal of Phytopharmacology*, 3(1), pp.10-7.
17. Abomughaid, M.M., Teibo, J.O., Akinfe, O.A., Adewolu, A.M., Teibo, T.K.A., Afifi, M., Al-Farga, A.M.H., Al-kuraishy, H.M., Al-Gareeb, A.I., Alexiou, A. and Papadakis, M., 2024. A phytochemical and pharmacological review of *Ricinus communis* L. *Discover Applied Sciences*, 6(6), p.315.

18. Yeboah, A., Ying, S., Lu, J., Xie, Y., Amoanimaa-Dede, H., Boateng, K.G.A., Chen, M. and Yin, X., 2020. Castor oil (*Ricinus communis*): a review on the chemical composition and physicochemical properties. *Food Science and Technology*, 41, pp.399-413.
19. Sivabalan, S., Renuka, S. and Menon, V.P., 2008. Fat feeding potentiates the diabetogenic effect of dexamethasone in Wistar rats. *International Archives of Medicine*, 1, pp.1-12.
20. Herrera, M.D., Jiménez-Ocampo, R., Rosales-Serna, R., Rodríguez-González, J.A., Santos-De la Cruz, J.L., Cruz-Bravo, R.K., Alvarado-Aguilar, P., Gamboa-Gómez, C.I. and Guerrero-Romero, F., 2021. A simple thermal-detoxified method for castor bean (*Ricinus communis* L.) cake, and its potential nutraceutical properties. *Industrial Crops and Products*, 174, p.114151.
21. Singla, H., Goyal, G., Garg, C. and Bhalla, K., 2019. Total antioxidant status in type 2 diabetes mellitus with diabetic nephropathy. *Int J Adv Med*, 6(3), p.673.
22. Vodošek Hojs, N., Bevc, S., Ekart, R. and Hojs, R., 2020. Oxidative stress markers in chronic kidney disease with emphasis on diabetic nephropathy. *Antioxidants*, 9(10), p.925.
23. Turk, H.M., Sevinc, A., Camci, C., Cigli, A., Buyukberber, S., Savli, H. and Bayraktar, N., 2002. Plasma lipid peroxidation products and antioxidant enzyme activities in patients with type 2 diabetes mellitus. *Acta diabetologica*, 39(3), pp.117-122.