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Research Article

RENOPROTECTIVE EFFECT OF CHRYSIN (5,7 DIHYDROXY FLAVONE) IN STREPTOZOTOCIN INDUCED DIABETIC NEPHROPATHY IN RATS

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ABSTRACT

The present study was designed to investigate the effect of chrysin in experimentally induced diabetic nephropathy in rats. Wistar male albino rats were divided into four groups. Control rats (Group-I) received dimethyl sulfoxide, diabetic rats (Group- II) received STZ (50mg/kgbwt), (Group-III) rats received chrysin (20mg/kgbwt) and (Group-IV) rats received STZ (50mg/kgbwt and chrysin 20mg/kgbwt). Blood and urine samples were collected every four weeks to measure blood glucose, urea, serum creatinine, protein. Urine urea, creatinine, protein and glomerular filtration rate was determined. The levels of blood glucose, urea, serum creatinine total urinary protein, urine urea, creatinine were significantly ($p<0.001$) increased and Glomerular filtration rate was significantly ($p<0.001$) reduced in diabetic nephropathy rats. Coadministration of chrysin to STZ induced rats significantly ($p<0.001$) reduced the levels of blood glucose, urea, serum creatinine, urinary glucose, urea, creatinine, protein and elevated the level of Glomerular filtration rate. These results suggested that chrysin has renoprotective effect against STZ induced diabetic nephropathy in rats.

Keywords: Streptozotocin, Diabetic nephropathy, Hyperglycemia, Glomerular filtration rate, Chrysin.

INTRODUCTION

Diabetic Nephropathy is one of the most serious complications of diabetes and common cause of end- stage renal failure. At present 40% of the patients with type-11 diabetes suffer diabetic kidney diseases. The characteristic features of these diseases are persistent albuminuria, a decline in glomerular filtration rate and structural alterations such as thickened glomerular basement membrane and progressive accumulation of extra cellular matrix protein in the glomerular mesangium [1,2]

The involvement of various derangements associated with diabetes can be considered in the development of diabetic nephropathy. Among them hyperglycemia play an important role in renal injury. The magnitude of hyperglycemia correlates with the functional and structural changes of diabetic nephropathy. Clinically, strict glycemic control inhibits both the functional decline in GFR and the formation of characteristic structural lesions[3]. The restoration of glycemia reverses structural changes[4]. Exposure to high glucose causes an increase in matrix protein generation and cell cycle arrest by cultured cells[5,6], development of novel therapeutic agents inhibiting the afore mentioned factors is of particular interest as they represent potential treatments for the prevention of diabetic complications[7]. Several clinical trials and studies have shown that improved glycemic control is strongly associated with decreased development or regression of diabetic complications in both type1 and type11 diabetic mellitus and glomerulosclerosis with other clinical or pathologic evidence that sclerosis is attributable to diabetic nephropathy[8].

Flavonoids constitute the largest and most important group of polyphenolic compounds in plants. It is now widely accepted that dietary polyphenolics may play an important role in protecting the body against chronic diseases, such as cancer, cardiovascular diseases[9,10] and diabetes mellitus[11].

Chrysin (5, 7 dihydroxy flavone) is a polyphenolic compound derived from species like passiflora, pelargonium and pinaceae. It is naturally present in honey, plant extracts, propolis and pine wood[12]. Chrysin exhibits a strong complexing activity for clinical and therapeutic applications in various diseases. Like other flavonoids chrysin exhibits many beneficial effects and pharmacological activities such as an antiinflammatory[13], antioxidant[14], antihypertensive[15], antidiabetogenic[16] and anticancer[17]. Chrysin also has the potency for clinical and the therapeutic application against the physiological and biochemical effects of aging[18]. In vivo studies have indicated that chrysin offers protection against oxidative stress mediated ethanol-induced liver injury and also suggests the chemoprotective effects on breast and colon cancers[19,20]. Chrysin acts as a hepato-protective and antioxidant agent against D-galactosamine- induced hepatotoxicity[21]. The present study was undertaken to evaluate the renoprotective effect of chrysin in Streptozotocin induced diabetic nephropathy in rats.

MATERIALS AND METHODS

Animals

Healthy Wistar male albino rats, weighing 180-200g were obtained from Saveetha University, Chennai, India and maintained in a diurnal light and dark cycle of 12h each. Rats were fed with standard food pellets and given access to water ad libitum. Rats were left for one week for acclimatized before starting the study. The experimental designs were approved by the Institutional Ethical Committee of the Saveetha University, Chennai (009/2010/CPSEA).

Chemicals

Streptozotocin (STZ) and Chrysin were purchased from Sigma Chemicals Co (St. Louis, Mo, USA). All other chemicals used in this study were of analytical grade and obtained from SRL Chemicals, Mumbai, India.

Experimental induction of diabetic mellitus

Diabetes was induced by single injection of STZ at a dose of 50mg dissolved in 0.1M citrate buffer (PH 4.5)/kg body weight, intra peritonealy, after 16h fasting[22]. After injection the animals were free access to food and water. After 4h the animals were given with 10% glucose in their drinking water for the first 24h to counter any initial hypoglycemia. 72h after STZ injection diabetes was confirmed in rats by blood sugar level greater than 250mg/dl. Animals with blood glucose levels greater than 250mg/dl was considered for further study. Blood samples were collected every four weeks from orbital plexus by prickling a needle under ketamine anaesthesia. Blood glucose was determined by using o-toluidine reagent[23].

Experimental designs

Experimental animals were divided into four groups and each group consisting of six animals.

Group 1: Rats received Dimethy Sulphoxide (1% DMSO) as vehicle i .p for 20 weeks and referred as positive control rats

Group 11: Rats were administered i .p a single dose of STZ 50mg dissolved in 0.1M citrate buffer PH 4.5/kg body weight and served as a diabetic rats.

Group 111: Rats were treated with chrysin 20 mg dissolved in 1% DMSO/kg body weight i .p for 20 weeks to assess the toxicity if any induced by chrysin and rats were referred as drug control.

Group 1V: Rats were received STZ 50mg/kg body weight (as in Group 11) along with Chrysin 20mg/kg body weight (as in Group 111) and rats were referred as treated rats.

Sample collection

The change in body weight and level of glucose in all groups of rats were recorded at regular intervals throughout the study. During the experimental period the animals were placed in individual metabolic cages every 4 weeks and 24h urine samples were collected for the measurement of urea, creatinine, total protein and creatinine clearance. Rats had free access to water while in metabolic cages.

Biochemical Parameters

Nephropathy was evalvated by estimating blood urea and urinary protein. Further creatinine clearance was also determined as a measure of glomerular filtration rate (GFR)[24]. Creatinine clearance was assessed from the urinary and serum creatinine and expressed as ml/min/kg body weight. Blood and urinary urea was estimated by diacetyl monooxime method[25], serum and urinary creatinine were measured by alkaline picrate method[26]. Urinary protein was quantified by Lowry's method[27]. Glycosylated Hemoglobin was determined by the method of Nayak and Pattabiraman[28] and plasma insulin was estimated by ELISA kit (for rats) supplied by Lincoplex Ltd. (USA) method.

Statistical Analysis

The values are expressed as mean± SD for six animals in each group. Differences between groups were assessed by One-way analysis of variance (ANOVA) using SPSS software package for windows. Post hoc testing performed for inter-group comparisons using the least significance difference (LSD) test; Significance at p-value (<0.001, <0.01, <0.05) have been given respective symbols in the tables.

RESULT

Table 1 represents the changes in the body weight in control and experimental groups of rats. A gradual gain in body weight was observed in the control group of rats whereas there was a significant (p<0.001) decrease in STZ induced diabetic nephropathy rats when compared with control rats. Administration of chrysin alone in group III rats has significant (p<0.001) gain in body weight when compared with group II animals. Coadministration of chrysin with STZ induced rats led to significant gain in body weight in group 1V rats compared to group II rats. However significant difference was observed between group II and group IV animals.

Table 1: Effect of chrysin on the body weight of control and experimental groups of rats Body weight (g)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	205±3.74	211±2.44	219±3.28	228±5.09	235±7.74	245±4.47
II	205±3.52	196±2.09	192±1.67	a***	a***	a*** 172±4
				185±3.89	179±2.44	
III	207±3.74	214±3.80	221±3.74	ns	ns	ns
				c	c	c
				232±6.9	237±6.16	249±1.09
IV	202±1.78	207±1.09	213±2.09	b***	b***	b***
				220±1.78	232±5.65	241±1.09

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P values: ***<0.001, **<0.01, *<0.05, ns-non-significant.

Table 2 demonstrates that the level of blood glucose in control and experimental animals. Control rats did not have any significant variation in the blood glucose throughout the experiment. In STZ induced diabetic rats there was a significant (p<0.001) and sustained raise in blood glucose level when compared with control animals. There was no significant change in the level of blood glucose in chrysin alone treated animals, it was found to be similar to those of control group of rats. Coadministration of chrysin to STZ induced rats observed no significant change in blood glucose level when compared with STZ induced diabetic rats. This suggested that chrysin prevented the development of hyperglycemia and it has anti-diabetic property.

Table 2: Change in blood glucose levels in each experimental group of animals Blood Glucose (mg/dl)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	85±4.4	90±2.52	86±1.7	89±2.09	86.6±1.03	88±2.19
II	90±1.26	a***	a***	a***	a***	a***
		250±3.16	270±4.42	281.5±4.88	289±2.09	296±4.73
III	87±1.09	ns	ns	ns	ns	ns
		c	c	c	c	c
		93.5±0.54	89.66±1.36	88.66±2.06	90±1.78	85.5±3.01
IV	90±2.82	b***	b***	b***	b***	b***
		93±1.78	98±2.82	90.33±1.36	89.66±1.63	91.66±1.50

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P value: ***<0.001, **<0.01,*<0.05, ns-non-significant.

Table 3, 4 represents the level of blood urea and serum creatinine of control and experimental group of rats. The levels of blood urea and serum creatinine in control and group III animals were found to be near normal throughout the study. There was significant (p<0.001) increase in the levels of blood urea and serum creatinine in STZ induced diabetic rat from fourth week onwards when compared with control animals. The observed reduced level of blood urea and serum creatinine in group IV animals might be due to coadministration of chrysin, suppressed the elevation of urea and creatinine, suggested the renoprotective action of chrysin.

Table 3: Effect of chrysin on the level of blood urea of control and experimental group of rats Blood Urea (mg/dl)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	19±0.63	0.66±0.89	21±0.89	21.33±1.63	22.33±1.96	20±1.26
II	21±1.67	a***	a***	a***	a***	a***
		28.33±2.58	47.5±5.24	59.16±5.84	65.83±2.04	68±0.63
		ns	ns	ns	ns	Ns
III	20.66±1.21	c	c	c	c	c
		18.5±1.04	20.16±1.32	16.66±1.63	21.16±1.32	19±0.89
IV	20±1.41	b***	b***	b***	b***	b***
		22.66±1.21	24±1.26	19.16±0.98	22.5±1.57	23±2.09

Values are expressed as mean± SD of six animals from each group. Comparison between a -Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P values: ***<0.001, **<0.01, *<0.05, ns-non-significant.

Table 4: Effect of chrysin on the level of serum creatinine of control and experimental group of rats Serum creatinine (mg/dl)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	0.60±0.014	0.58±0.034	0.53±0.019	0.50±0.026	0.50±0.014	0.48±0.019
II	0.88±0.05	a***	a***	a***	a***	a***
		0.88±0.05	0.99±0.089	1.66±0.014	1.85±0.10	2.61±0.071
III	0.60±0.028	ns	ns	ns	ns	ns
		c	c	c	c	c
		0.58±0.030	0.57±0.033	0.55±0.034	0.50±0.026	0.46±0.041
IV	0.62±0.046	b***	b***	b***	b***	b***
		0.60±0.014	0.58±0.034	0.56±0.026	0.54±0.017	0.50±0.014

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P value: ***<0.001, **<0.01,*<0.05, ns-non-significant.

Table 5 indicates the level of serum protein in experimental animals. There was a significant (p<0.001) decrease in serum protein level in STZ induced diabetic animals from eighth week when compared to control group whereas the level of serum protein in group III and IV animals was similar to control animals. The observed level of serum protein in group IV animals might be due to chrysin coadministration.

Table 5: Effect of chrysin on the level of serum protein of control and experimental group of rats Serum Protein (mg/dl)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	7.75±0.27	7.95±0.33	7.97±0.35	8.10±0.22	8.15±0.30	8.23±0.22
II	7.62±0.41	a** 7.25±0.22	a***	a***	a***	a***
			6.87±0.39	6.41±0.25	5.87±0.26	4.91±.34
III	7.5±0.54	ns	ns	ns	ns	ns
		c	c	c	c	c
		7.76±0.57	7.90±0.54	8.125±0.51	8.20±0.51	8.36±0.48
IV	7.35±0.47	ns	b*	b***	b***	b***
		b	7.79±0.60	7.82±0.55	7.99±0.51	8.125±0.51
		7.61±0.57				

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P values: ***<0.001, **<0.01, *<0.05, ns-non-significant.

The levels of glycosylated hemoglobin and plasma insulin in experimental groups of rats represented in Table 6. A significant (p<0.001) increase in the level of glycosylated hemoglobin and significant (p<0.001) decrease in the level of plasma insulin were found in STZ induced diabetic rats from twelveth week when compared with control rats. The observed significant (p<0.001) decrease in the level of glycosylated hemoglobin and significant (p<0.001) increase in the level of insulin in group IV animals when compared with group II animals might be due to chrysin. The effect was more distinct in the group of rats treated with chrysin alone.

Table 6: Effect of chrysin on the levels of Glycosylated Hemoglobin and plasma Insulin of control and experimental group of rats

Parameters	Group I	Group II	Group III	Group IV
Glycosylated	7.16±0.06	a***	c***	b***
Hemoglobin		9.5±0.07	6.4±0.17	7.25±0.06
(%)				
Plasma Insulin	13.9±0.10	a***	ns	b***
(µu/ml)		6.5±0.17	c	12.75±0.27
			14.24±1.48	

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P values: ***<0.001, **<0.01, *<0.05, ns-non-significant.

The level of urinary glucose in experimental animals was indicated in Table 7. A significant (p<0.001) excretion of glucose in urine was found in STZ induced diabetic rats from fourth week onwards whereas there was no glucose in the urine of group I,III and IV animals.

Table 8, 9 represents the level of urinary urea and creatinine in experimental rats. There was a significant (p<0.001) increase in the level of urinary urea and significantly (p<0.001) reduced level of creatinine were found in group 11 animals from eighth week when compared with control animals. The level of urea and creatinine in urine of group III and IV animals were found to be as similar to control group of rats.

The levels of excretion of protein in urine of experimental animals were represented in Table 10. Excretion of protein in urine was not observed in any rat from group I, III and IV. However, there was a significant (p<0.001) and sustained increase in urinary protein after eight weeks in STZ induced diabetic rats.

Table 7: Effect of chrysin on the level of urinary glucose of control and experimental group of rats Urinary glucose (g/dl)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	Nil	Nil	Nil	Nil	Nil	Nil
II	Nil	a***	a***	a***	a***	a***
		0.5±0.06	1.0±0.14	1.45±0.13	2±0.14	2±0.2
III	Nil	Nil	Nil	Nil	Nil	Nil
IV	Nil	Nil	Nil	Nil	Nil	Nil

Values are expressed as mean± SD of six animals from each group. Comparison between a- Group I and Group II. P value: ***<0.001

Table 8: Effect of chrysin on the level of urinary urea of control and experimental group of rats Urinary Urea (mg/dl)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	37.8±0.44	38.5±0.44	38.1±0.56	38.5±0.58	37.6±0.40	38.25±0.82
II	36.5±0.42	ns	a***	a***	a***	a***
		a	56.5±0.57	68±0.44	74.5±0.10	96±0.89
		38.8±0.52				
III	36.5±1.04	ns	ns	ns	ns	ns
		c	c	c	c	c
		37.5±1.08	37.8±1.14	37.2±1	38.4±0.83	38.1±0.98
	37.4±0.74	ns				
IV		b	b***	b***	b***	b***
		37.7±0.81	39±0.83	39.6±0.83	39.2±0.56	38.5±0.74

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P values: ***<0.001, **<0.01, *<0.05, ns-non-significant.

Table 9: Effect of chysin on the level of urinary creatinine of control and experimental group of rats Urinary creatinine (mg/dl)

Groups	0 weeks	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	53.1±1.41	53.3±1.09	55.1±2	60.2±2.09	60±2.36	65.1±3.16
II	52.5±0.77	ns	a***	a***	a***	a***
		a	51.2±1.01	50.4±2.82	50.2±1.13	50±2.82
		52.2±1.2				
III	53.2±1.41	ns	ns	c*	c*	ns
		c	c	63.2±1.41	63±1.78	c
		53.4±2.09	56.1±1.41			65.1±2.82
IV	55±2.82					
		b*	b***	b***	b***	b***
		57.1±4	60±3.34	65.1±2.60	65.2±2.28	65±4.97

Values are expressed as mean± SD of six animals from each group. Comparison between a-Group I and Group II, b-Group II and Group IV, c-Group I and Group III

P values: ***<0.001, **<0.01, *<0.05, ns-non-significant.

Table 10: Effect of chrysin on the level of urinary protein of control and experimental group of rats Urinary Protein (g/L)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	Nil	Nil	Nil	Nil	Nil	Nil
			a***	a***	a***	a***
II	Nil	Nil	0.7±0.04	1.46±0.10	2±0.14	2.5±0.14
III	Nil	Nil	Nil	Nil	Nil	Nil
IV	Nil	Nil	Nil	Nil	Nil	Nil

Values are expressed as mean± SD of six animals from each group. Comparison between a- Group I and Group II, p value: ***<0.001

Table 11 indicates the level of creatinine clearance in experimental animals. Creatinine clearance was taken as a parameter to asses GFR. In the early weeks of diabetes there was a normal creatinine clearance and in the later weeks there was a gradual decline in GFR in group II animals. The GFR was found normal in early weeks in group III and IV animals and decreased rise in later weeks when compared to control animals and there was significant (p<0.001) rise GRF in later weeks when compared to group II animals.

Table 11: Effect of chrysin on the level of creatinine clearance of control and experimental groups of rats Creatinine Clearance (ml/min)

Groups	0 week	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks
I	1.19±0.017	1.20±0.019	1.31±0.018	1.46±0.01	1.41±0.01	1.53±0.017
II	1.21±.02	a**	a*** 1.12±0.025	a***	a***	a***
		1.26±0.037		0.68±0.032	0.63±0.02	0.46±0.038
III	1.18±0.026	ns				
		c	c***	c***	c***	c*
		1.18±0.03	1.23±0.014	1.37±0.02	1.50±0.014	1.57±0.04
IV	1.21±0.018	ns				
		b	b***	b***	b***	b***
		1.27±0.05	1.34±0.02	1.46±0.014	1.44±0.014	1.49±0.02

Values are expressed as mean± SD of six animals from each group. Comparison between a- Group I and Group II, b- Group II and Group IV, c- Group I and Group III.

P value: ***<0.001, **<0.01, *<0.05, ns- non-significant.

DISCUSSION

Diabetic nephropathy is a leading cause of end-stage renal failure, accounting for 35-40% of all new cases requiring dialysis therapy worldwide. Early diabetic nephropathy is characterized by hyper filtration, micro albuminuria, renal and glomerula hypertrophy, mesangial matrix accumulation and thickening of the glomerular basement membrane[29]. In the later stages, when diabetic nephropathy progresses, patients develop proteinuria and their glomerular filtrate rate decline, eventually leading to end- stage renal disease. Hyperglycemia, hyperlipidemia, hypertension and also proteinuria itself, contribute to progression of renal damage.

Results of the study confirm that STZ, commonly used diabetogenic agent in experimental animals[30], causes hyperglycemia, polyuria, macroproteinuria as well as decrease in GFR. Under such conditions hyperglycemia is due to the damage of the beta-cells.

Induction of diabetes with STZ is associated with the characteristic loss of body weight, which is due to increased muscle wasting[31] and due to catabolism of tissue proteins[32] leading to significant reduction in the body weight gain of diabetic nephropathy rats, which was observed in the present study. The reduction in the body weight of diabetic nephropathy rats might have occurred as a result of catabolism of structural proteins due to scarcity of carbohydrate as energy source[33]. Weight loss during diabetes is mainly related to urinary glucose excretion because cells are unable to utilize glucose. Another factor is the osmotic diuresis resulting in hyperosmotic dehydration[34]. A significant increase in the body weight was observed in STZ induced rats administered with chrysin which could be due to the protective effect of chrysin in controlling muscle wasting and protein turn over and may also due to the improvement in insulin secretion from the pancreatic beta cells and glycemic control The fundamental mechanism underlying hyperglycemia involves over production of glucose by excessive hepatic glycogenolysis and gluconeogenesis and decreased utilization by the tissues[35]. Persistent hyperglycemia, is a factor in the development and progression of the complications of diabetes mellitus[36]. Reports have shown that the level of the blood glucose was elevated in STZ induced diabetic rats. In the present study, we have also observed a marked elevation in blood glucose level of STZ induced rats and there was no rise in the level of blood sugar in chrysin coadministered STZ induced rats. This data suggested that coadministration of chrysin with STZ prevents the development of diabetic nephropathy by maintaining blood glucose level to normal suggesting insulin secretory effect and antihyperglycemic activity of chrysin.

Glycosylated hemoglobin remains the gold standard biochemical marker for the assessment of diabetes[37]. A high glucose present in the blood reacts with hemoglobin to form glycosylated hemoglobin[38]. This condition favours reduction in the level of total hemoglobin and elevation in glycosylated hemoglobin, which is directly proportional to blood glucose[39]. The observed high levels of glycated hemoglobin in STZ induced rats after twelve weeks reveals poor glycemic control. Coadministration of chrysin to STZ-induced rats reduced the formation of glycosylated hemoglobin by virtue of its normoglycemic activity. Since the glycosylation of protein is an oxidation reaction, flavonoids should be able to prevent this reaction as they are considered as effective antioxidants. Several researches have demonstrated that flavonoids attenuate hyperglycemia and there is reduced non-enzymatic glycation of proteins in animals[40].

In the present study, we have observed a significant decrease in the levels of insulin in STZ-induced diabetic rats. Insulin deficiency is manifested in a number of biochemical and physiological alterations. The simultaneous administration of chrysin and STZ prevented the deficiency of insulin and enhanced the insulin secretion which suggested the insulin secretory effect of chrysin.

Urine glucose estimation study revealed that animals administered with chrysin and STZ prevented the excretion of glucose in urine, whereas there was significant increase in the level of glucose in urine of STZ induced diabetic rats from the fourth week onwards. The observed normal level of blood glucose and total absence of urinary glucose in rats administered with chrysin alone suggested antidiabetic activity of chrysin.

The diabetic hyperglycemia induces the elevation of the blood urea and serum creatinine in diabetic rats, which are considered as significant makers of renal dysfunction[41]. Impaired balance of nitrogen coupled with lowered protein synthesis leads to increased concentration of urea in blood[42]. Increased plasma creatinine level and BUN are indication of the development of diabetic nephropathy in rats[43,44]. In the present investigation there was a significant elevation in the levels of blood urea and serum creatinine from the fourth week of the study in STZ induced diabetic rats. Our study revealed that coadministration of chrysin with STZ to rats prevented the development of diabetic nephropathy by lowering blood urea and serum creatinine. This could be explained that there was increased clearance of blood urea and creatinine by the kidney or that there where decreased protein degradation.

The observed increased excretion of urinary urea and decreased excretion of creatinine indicates the development of diabetic nephropathy in STZ induced rats. Whereas the rats coadministered with chrysin and STZ demonstrated reduced level of urinary urea and increased level of urinary creatinine. We also observed normal level of urea and creatinine in urine of rats administered with chrysin alone. This report suggested that chrysin prevented the progression of diabetic nephropathy and protected the kidney from further damage.

Serum creatinine concentration is widely interpreted as a measure of the GFR and is used as an index of renal function in clinical practice[45]. The end-stage of diabetic renal disease is usually characterized by changes in both proteinuria and subsequent decline in GFR. Development of lesions in the glomerular capillaries of the kidneys allows protein to escape because of changes in the basement membrane[46].

CONCLUSION

The results of the present study demonstrates that reduced level of protein in serum, GFR and development of proteinuria in STZ induced rats, clearly suggested that the development of diabetic

nephropathy and coadministration of chrysin attenuate the development of proteinuria and elevated the creatinine clearance level and there by maintains GFR to normal. This suggested that chrysin has antidiabetic and antidiabetic nephropathy effect. Further studies with the compound will help in designing pharmacological active compound that can be administered along with insulin in diabetic mellitus patients or administered in early diabetic nephropathy patients that will quench the secondary complications of diabetic mellitus.

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