Chapter 7

SUMMARY

&

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Medicinal plants are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds. The plant contains a large number of constituents such as flavonoids, alkaloids, steroids, triterpenoids, lipids, lignins, carbohydrates, proteins, and glycoprotein which are responsible for their activity. The World Health Organization (WHO) estimates that herbal medicines provide primary healthcare for approximately 3.5 to 4 billion people worldwide, and about 85% of traditional medicine involves the use of plant extracts, which may be called “modern herbal medicine.” and these medicine are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Diabetic nephropathy is microvascular complication affecting 25–40% of people of type 1 or type 2 diabetes and it increases by 6% per year characterized by thickening of basement membranes and mesangial expansion with progression into glomerulosclerosis, tubular necrosis and interstitial fibrosis, which ultimately result in renal failure. Albino Wistar rats of either sex were employed in present study because of their small size, low cost and easy availability, Moreover, other species like Sprague–Dawley rats resistant to renal lipid accumulation in high-fat diet model. Administration of STZ at a dose of 40 mg/kg, 50 mg/kg, 55 mg/kg, 60 mg/kg and 65 mg/kg i.p. induces hyperglycemia in rats. STZ-induced hyperglycemia activates PKC, aldose-reductase, NADPH oxidase, formation of AGEs and increases Angiotensin-II levels and leads to development of diabetic nephropathy in 4-8 weeks, assessed in terms of serum creatinine, BUN, proteinuria, creatinine clearance, extracellular matrix deposition, dyslipidemia and consequent development of glomerulosclerosis and
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tubulointerstitial fibrosis. The STZ (55 mg/kg i.p., once) was employed in the present study to induce experimental diabetes in overnight fasted rats. STZ develops hyperglycemia within 72 hours (serum glucose >180 mg/dl) and after 7 days of STZ administration, rats showed the blood glucose level >240 mg/dl are named as diabetic rats. In the present study, diabetic rat has been noted to increase the tissue TBARS and decrease reduced form of glutathione (GSH) suggesting development of diabetes-induced oxidative stress. The oxidative stress has been documented to play a major role in the progression of nephropathy. The increases in serum creatinine, blood urea, proteinuria, creatinine clearance, urinary output and pathological changes in glomeruli have been documented to be index of nephropathy which was noted to be increased in diabetic rats as compared with normal rats. The diabetes-induced alteration in lipid profile such as hypertriglyceridaemia and hypercholesterolemia affect the function of glomeruli and produces glomerulosclerosis, which also results in diabetic nephropathy. Further, diabetes induced hypertrophic and fibrotic changes in renal cortex were assessed by measuring kidney weight/body weight (%) and renal collagen contents, respectively. Furthermore, serum lipids and tissue lipids were measured. However, pharmacological treatment with Saraca asoca, Jasminum grandiflorum or Lisinopril or fenofibrate prevent diabetes-induced nephropathy by increasing the reduced form of glutathione (GSH) and decreasing tissue TBARS, serum creatinine, blood urea nitrogen and proteinuria and reducing pathological changes in glomeruli. Fenofibrate has been well reported to reduced triglyceride and cholesterol through activation of PPAR-α. Treatment with Saraca asoca and Jasminum grandiflorum extracts in diabetic rats markedly attenuated the development of diabetic nephropathy when compared to treatment with lisinopril or fenofibrate. Saraca asoca is documented to reduce the expression of TNF-α and act as anti-inflammatory and also
reported to reduce oxidative stress by scavenging the free radical generations. Moreover, it has been reported to have antidiabetic property which is consonant with result observed in present study. Further, Jasminum grandiflorum also have the ACE inhibitor effects. Thus, the observed beneficial effect of Saraca asoca and Jasminum grandiflorum extracts in preventing diabetes-induced nephropathy due to anti-inflammatory, antioxidant, antidiabetic and hypotensive effects. However, Saraca asoca treatment partially modulate lipid profile in diabetic Further, the renoprotective effect of lisinopril has been well reported in basic and clinical studies that’s why lisinopril has been employed as a standard drug. The beneficial effect of alcholic and aqueous extracts either Saraca asoca or Jasminum grandiflorum in preventing diabetic nephropathy has been observed to be almost similar to the effect produced by lisinopril. The various extracts of Saraca asoca or Jasminum grandiflorum has been observed to contains Alkaloids, Carbohydrates, Phytosterols, Phenols, Tannin, Flavonoids which has been reported to improves lipid profile, antioxidant, diabetic and nephropathy parameter and supporting the observed results.

On the basis of results obtained in the present study, the following salient findings may be summarized:

- The present study has been designed to investigate the phytochemical and pharmacological evaluation of Saraca asoca and Jasminum grandiflorum. The literature survey revealed that Saraca asoca and Jasminum grandiflorum have exhibited variety of biological effects like anti-oxidant, anti-microbial, and anti-inflammatory and also have beneficial effect in metabolic disorders. However, the antidiabetic potential and renoprotective of Saraca asoca and Jasminum grandiflorum has not been explored.
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- Rats were administered streptozotocin (55 mg/kg, i.p. once) to produce diabetes.
- *Saraca asoca* extracts, *Jasminum grandiflorum* extracts, and fenofibrate (30 mg/kg p.o., 7 weeks), glibenclamide (10 mg/kg p.o., 7 weeks) or Lisinopril (1 mg/kg p.o., 7 weeks) has been administered to diabetic rats to evaluate the various parameters of diabetic nephropathy used in the present study.
- Estimation of blood glucose, Insulin and HbA1c has been used as marker of hyperglycemia.
- STZ-induced diabetes is often associated with dyslipidemia. Therefore, estimation of total cholesterol, triglycerides and HDL has been used as a marker of dyslipidemia. Moreover, lipids get deposited in the kidney of diabetic patients in presence of fibrotic tissue leading to glomerulosclerosis, tubulointerstitial fibrosis, and increased collagen expression subsequently leading to proteinuria.
- STZ-induced diabetes has produced nephropathy which can be assessed as elevated level of proteinurea, serum creatinine and BUN.
- The administration of fenofibrate has produced ameliorative effect on STZ-induced nephropathy through activation of PPAR-α and consequent inhibition of accumulation of renal lipids.
- The extracts of *Saraca asoca* or *Jasminum grandiflorum* has also prevented STZ-induced nephropathy more markedly as compared to Lisinopril and fenofibrate perhaps due to decrease in oxidative stress, improve lipid profile and consequently prevents the morphological changes in diabetic glomeruli.