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Anti-Apoptotic Effect of Pueraria tuberosa in Rats with Streptozotocin Induced Diabetic Nephropathy

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Abstract : Diabetic nephropathy (DN) is characterized as diabetic kidney disease which involves many pathways e.g. hyperactivated protein kinase c (PKC), polyol pathway, excess production of advanced glycation end product (AGEs) & free radical accumulation etc. All of them results to hypoxia followed by apoptosis of podocytes, glomerulosclerosis, extracellular matrix (ECM) accumulation and fibrosis resulting to irreversible changes in kidney. This is continuously rising worldwide and there are not enough specific drugs, to retard its progress. Due to increasing side effects of allopathic drugs, interest in herbal remedies is growing. Earlier, we have reported that PTY-2 (a phytomedicine, derived from Pueraria tuberosa Linn.) inhibits the accumulation of extracellular matrix (ECM) through activation of MMP-9. Present study exhibited the therapeutic potential of Pueraria tuberosa in the prevention of podocytes apoptosis and modulation of nephrin expression in streptozotocin (STZ) induced DN rats. DN rats were produced by maintaining persistent hyperglycemia for 8 weeks by intra-peritoneal injection of 55 mg/kg streptozotocin (STZ). These rats were randomly divided in 2 groups, i.e. DN control, and DN+ water extract of Pueraria tuberosa (PTW). One group of age-matched normal rats served as non-diabetic control (group-1), The STZ induced DN rats (group-2) and DN+PTW treated rats (group-3). The PTW was orally administered (0.3g/kg) daily to group-2 rats and drug vector (1 ml of 10% tween 20) in control rats. The treatments were continued for 20 days and blood and urine samples were collected. Rats were then sacrificed to investigate the expression Bcl2, Bax and nephroprotective protein i.e. nephrin in kidney glomerulus. The effect of PTW was evaluated, we have found that the PTW significantly($p < .001$) reversed the raised serum urea, serum creatinine, urine protein and improved the creatinine clearance in STZ induce diabetic nephropathy in rats and also significantly($p < .001$) prevented the rise in urine albumin excretion. The Western blot analysis of kidney tissue homogenate showed increased expression of Bcl2 in PTW treated rats. The RT-PCR showed the increased expression and accumulation of nephrin mRNA. The confocal photomicrographs also supported the reduction of Bax and a simultaneous increase in Bcl2 and nephrin in glomerular podocytes. Hence, our finding suggests that the nephroprotective role of PTW is mediated via restoration of nephrin thus prevents the podocytes apoptosis and ameliorates diabetic nephropathy. The clinical trial of PTW would prove to be a potential food supplement/ drug of alternative medicine for patients with diabetic nephropathy in early stage.

Keywords : Pueraria tuberosa, diabetic nephropathy, anti-apoptosis, nephrin
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