Summary

Diabetes mellitus (DM) is a clinically and genetically heterogeneous group of metabolic disorders manifested by abnormally high levels of glucose in the blood. The hyperglycemia is the result of a deficiency of insulin secretion caused by pancreatic β-cell dysfunction (Type1) or of resistance to the action of insulin (Type 2) .

The prevalence and incidence of DM are increasing worldwide. Diabetes is associated with reduced life expectancy and increased morbidity and mortality.

Diabetic nephropathy is the leading cause of the end-stage renal disease. More than 30% of patients with diabetes mellitus develop clinically evident diabetic nephropathy 10–20 years from the onset of disease .

Diabetic nephropathy occurs as a consequence of the interaction between metabolic and hemodynamic factors. It is characterized as glomerulosclerosis and the major morphologic abnormality in Diabetic nephropathy is the thickening of the glomerular basement membrane (GBM) and the expansion of the mesangium . The natural history of type

1 and type 2 diabetic nephropathy is similar with regard to the progression from microalbuminuria to proteinuria .

The basis for the prevention of diabetic nephropathy is the treatment of its known risk factors: hypertension, hyperglycemia, smoking, and dyslipidemia .

The principal aim in the treatment of diabetic nephropathy is control of the glycaemia and aggressive antihypertensive therapy, decreasing the blood pressure below 130/85mmHg.

Many studies suggest promising steps in the development of therapeutic approaches to prevent or to decrease the rate of progression of diabetic nephropathy .

The measures described above might not be effective in some patients with diabetes, and novel therapeutic strategies are warranted. High doses of thiamine and its derivate benfotiamine have been shown to retard the development of microalbuminuria in experimental diabetic nephropathy, probably due to decreased activation of protein kinase C, decreased protein glycation, and oxidative stress. Treatment with ALT-711, a cross-link breaker of the advanced glycation end products, has been shown to result in a significant

reduction in urine albumin excretion, blood pressure, and renal lesions in experimental diabetes .

Treatment with a protein kinase C ß inhibitor (ruboxistaurin) normalized GFR, decreased albumin excretion rate, and ameliorated glomerular lesions in diabetic rodents .

In diabetes-induced glomerulosclerosis, administration of a modified heparin glycosaminoglycan prevented albuminuria, glomerular and tubular matrix accumulation and transforming growth factor ß1 mRNA overexpression. Very few studies have been conducted in humans. Sulodexide, a glycosaminoglycan, significantly reduced albuminuria in micro- or macroalbuminuric type 1 and type 2 diabetic patients. Pimagedine, a second-generation inhibitor of advanced glycation end products, reduced urinary protein excretion and the decline in GFR in proteinuric type 1 diabetic patients in a randomized, placebo-controlled study .