Introduction and Aim of work:

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 deficiency of insulin secretion caused by pancreatic β-cell dysfunction (Type1) or of resistance to the action of insulin (Type 2) **(Mealey & Ocampo, 2007)**.

The prevalence and incidence of DM are increasing worldwide. Diabetes is associated with reduced life expectancy and increased morbidity and mortality **(Cohen & Shaw, 2007)**.

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 **(Zhang et al., 2005).**

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 (**Zhang et al., 2005**). The natural history of type 1 and type 2 diabetic nephropathy is similar with regard to the progression from microalbuminuria to proteinuria **(Sonkodi & Mogyorósi, 2003)**.

Important secondary mediators for the development of renal damage are transforming gross factor β (TGFβ) , locally generated angiotensin II , endothelin and several other cytokines Recent insights into podocye function and identification of proteins of the slit membrane have led to the concept that the podocyte is aprime player in the genesis of protienuria **(Gross et al, 2003)**.

The basis for the prevention of diabetic nephropathy is the treatment of its known risk factors: hypertension, hyperglycemia, smoking, and dyslipidemia **(Gross et al., 2005)**.

The principal aim in the treatment of diabetic nephropathy is to control the blood glucose level 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 **(Sonkodi & Mogyorósi, 2003).**

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

(Vicki et al., 2004)

Treatment with protein kinase C β inhibitor (**ruboxistaurin**) normalized GFR, decreased albumin excretion rate and ameliorated glomerular lesions in diabetic rodents (**Katherine et al., 2005**)

In diabetes induced glomerulosclerosis , administration of moadified heoarin glycosaminoglycan (**Sulodexide**) prevented albuminuria, glomerular and tubular matrix accumulation and transforming growth factor β1 mRNA overexpression. Very few studies have been conducted in humans. **(Joost et al., 2005)**