Introduction

Diabetic nephropathy *(DN)* is the most common cause of end-stage renal disease in the world, and accounts for a significant increase in morbidity and mortality in patients with diabetes. According to the World Health Organization *(WHO)*, it is expected that the number of patients with diabetes will rise to 370 million by 2030 in the world ***(Wild et al. ,2004).***

It has also been reported that about 25-40% of type 1 or type 2 diabetic patients develop diabetic nephropathy within 20-25 year of the onset of diabetes ***(Remuzzi et al. ,2002)***, therefore, development of novel therapeutic strategies for diabetic nephropathy is urgently needed.

From large clinical trials such as United Kingdom Prospective Diabetes Study ***(UKPDS ,1998)*** and Diabetes Control and Complication Trial ***(DCCT ,1993)***, intensive control of blood pressure or glucose reduced the development and progression of diabetic nephropathy, however, number of diabetic patients with end-stage renal failure is still increasing despite of strict blood pressure and/or glycemic control.

Recently, advanced glycation end products *(AGEs)* have been focused as a new therapeutic target for the treatment of diabetic nephropathy because there are accumulating evidence that AGEs play a central role in the pathogenesis of diabetic nephropathy. AGEs accumulate in the glomeruli and tubulointerstitium as a result of hyperglycemia, aging, and/or uremia in patients with diabetes. In addition, it is suggested that AGEs elicit reactive oxygen species *(ROS)* generation through the interaction with the receptor for AGEs *(RAGE)*, thereby being involved in the progression of diabetic nephropathy ***(Yamagishi et al. ,2007).***

Further, numerous data have demonstrated the active participation of ROS and AGEs in diabetic nephropathy, which could be an initial trigger for the morphological changes characteristic in diabetic nephropathy. ROS generation itself has also been known to stimulate the formation of AGEs such as pentosidine and *N*-carboxymethyllysine *(CML)* in diabetic kidney, Therefore, it is assumed that AGEs could alter the structure and function of kidney, thus leading to the development of glomerular hyperfiltration, basement membrane thickening, glomerulosclerosis and/or tubulointerstitial fibrosis in diabetes ***(Yamagishi et al. ,2002).***

Renin-angiotensin system *(RAS)* is also activated under diabetic conditions and thought to play an important role in the pathogenesis of diabetic nephropathy ***(Cooper ,2001).***

Recent data have shown that AGEs could modulate the RAS pathway and stimulate production of various growth factors and cytokines in diabetic nephrropathy through the interaction with AGE receptors *(RAGE)* including , AGE-receptor 1 *(AGE-R1)*, AGE-receptor 2 *(AGE-R2)*, AGE-receptor 3 *(AGE-R3)*, and macrophage scavenger receptor *(MSR)* ; In particular, the interaction between the metabolic pathways and the hemodynamic ones such as the cross-talk between the AGE-receptor system and the RAS, is proposed to play a critical role in diabetic nephropathy ***(Yamagishi et al. ,2002).***

Moreover, several *in vivo*- and *in vitro*-studies have also suggested that transforming growth factor-β *(TGF-β)*, a profibrogenic factor, vascular endothelial growth factor *(VEGF)*, known as a vascular permeability factor, connective tissue growth factor *(CTGF)*, platelet-derived growth factor *(PDGF)*, and pigment epithelium-derived growth factor *(PEDF)* are implicated in the AGEs-induced renal damage in diabetes ***(Cooper ,2001).***

Inhibitors of AGEs formation and/or AGEs cross-link breaker may ameliorate renal injury in patients with diabetic nephropathy, renoprotective properties of the inhibitors of the RAS could be ascribed partly to its inhibitory effects on AGEs formations and/or its downstream pathways, blockade of the cross-talk between the metabolic pathway and the hemodynamic one will be a promising therapeutic strategy for the treatment of diabetic patients with nephropathy ***(Fukami et al. ,2008).***

Aim of The Essay

This essay aims at clarifing the role of advanced glycation end products *(AGEs)* in the pathogenesis of diabetic nephropathy and the role AGE inhibitors in the better management of diabetic nephropathy.