



EGCG Inhibits Angiotensin II Induced Activations of Extracellular Signal-regulated Kinases 1 and 2 (ERK1/2) and Akt/PKB Associated with ROS in the High Glucose Conditions

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Renal disease in diabetic patients is costly in terms of morbidity, mortality and expenditure. Therefore, prevention and treatment of diabetic nephropathy has become a prominent goal in the treatment of patients with diabetes mellitus. Renin-angiotensin II - aldosterone system plays a crucial role in the process of diabetic nephropathy. ACE inhibitors or ARBs, they are particularly beneficial in diabetic nephropathy. Recently, the pathogenesis of diabetic nephropathy associated with ROS system and MAPK activation is well-known. Although the underlying mechanisms remain incompletely understood, epigallocatechin-3-gallate (EGCG) has antioxidant effect. So, We designed this study to explore the effects of EGCG on angiotensin II induced activation of MAPK and Akt/PKB activity of rat podocyte under high glucose condition.

To investigate a generation of ROS in podocytes, various concentrations of glucose were treated. Intracellular ROS production was measured using 2',7'-dichlorofluorescein (DCFH) which is oxidized to the fluorescent product 2',7'-dichlorofluorescein (DCF) by ROS. Glucose-treated cells increase ROS production dose dependently. The highest generation of ROS showed at 30 mM glucose. EGCG treatment decreases ROS production dose dependently. and EGCG treatment suppress angiotensin II induced activation of MAPK activity in high glucose condition. EGCG-mediated suppression was also observed for Akt/PKB activity. Our results suggest that EGCG suppress angiotensin II induced activation of MAPK and Akt/PKB activity in high glucose condition. whole-cell membrane potentials were recorded at room temperature by using standard patch-clamp techniques. In a current clamp mode, resting membrane potential of the podocyte was -53 ± 7.02 mV under control conditions. 100 nM angiotensin II depolarized the cell (n=10) to -38.5 ± 6.83 mV from the control level.

These results provided a novel insight into the mechanisms by which EGCG inhibits podocyte injury associated with diabetic nephropathy. The inhibitory effect of the natural antioxidant, its long history of beverage consumption without adverse health effects and higher potent antioxidant capability make it a good candidate for therapeutic treatment and prevention of diabetic nephropathy.