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ALT-711이 고포도당에서 배양한 혈관간세포에 미치는 항산화효과

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Antioxidant Effect of ALT-711 in Mesangial Cells Cultured Under High Glucose

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Purpose : ALT-711 [(2-oxo-2-phenyl)ethyl-4,5-dimethylthiszolium chloride] was first introduced as an advanced glycation end-products (AGE) breaker but was shown to inhibit diabetic renal injury through inhibition of PKCα activation. Since cellular reactive oxygen species (ROS) amplify PKC signal during the development and progression of diabetic nephropathy, we examined if ALT-711 confer renoprotection in diabetes through its antioxidant effect.

Methods : Synchronized SV40-transformed mouse mesangial cells were stimulated with 30 mM D- glucose (high glucose) or 100 uM H_2O_2 for a given period. ALT-711 (10 ug/mL) was administered 1 hour before the addition of high glucose or H_2O_2. NADPH oxidase and PKC proteins in the membrane and cytosol were measured by Western blot analysis, dichlorofluorescein (DCF)-sensitive cellular ROS by FACS, and H_2O_2 by potassium iodide method.

Results : High D-glucose, but not L-glucose, significantly increased NADPH oxidase subunit p47 phox, p67 phox, and rac1 proteins in the membrane fraction without any effect on cytosol fraction in 30 minutes after high glucose. ALT-711 effectively prevented high glucose-induced membrane translocation of NADPH oxidase subunits and cellular ROS. H_2O_2 significantly increased translocation of rac1 as well as PKCα from the cytoplasm to the membrane, which was effectively inhibited by ALT-711. ALT-711 also reduced H_2O_2 in test tube in a dose-dependent manner.

Conclusion : The present study suggests that ALT-711 may attenuate renal injury in diabetes, in part, through inhibiting NADPH oxidase and scavenging H_2O_2.