

[P-40]**15-DEOXY- $\Delta^{12,14}$ PROSTAGLANDIN J₂ RESCUES PC12 CELLS FROM HYDROGEN PEROXIDE-INDUCED APOPTOSIS THROUGH POTENTIATION OF CELLULAR ANTIOXIDATIVE DEFENSE CAPACITY***Ji-Woo Kim, Jung-Hee Jang and Young-Joon Surh**Laboratory of Biochemistry and Molecular Toxicology, College of Pharmacy,
Seoul National University, Seoul 151-742, Korea*

Purpose of Study: Oxidative stress induced by reactive oxygen intermediates (ROIs) has been implicated in a variety of human diseases including cancer, diabetes, rheumatoid arthritis and neurodegenerative disorders. Hydrogen peroxide (H₂O₂), a representative ROI which is produced during the cellular redox process, can cause cell death via apoptosis and/or necrosis depending on its concentrations. 15-D prostaglandin J₂ (15d-PGJ₂), a dehydration product of prostaglandin D₂, has been reported to possess a number of biological activities such as anti-inflammatory, anticarcinogenic, and antioxidative properties. In this study, we have investigated the protective effect of 15d-PGJ₂ on H₂O₂-induced oxidative stress in rat pheochromocytoma (PC12) cells.

Methods: H₂O₂-induced oxidative cell damage was initially assessed by measuring cytotoxicity. The induction of programmed cell death was determined by characteristic morphological features, internucleosomal DNA fragmentation, disruption of mitochondrial membrane potential, in situ terminal end-labeling and the expression of apoptosis-related marker proteins. To examine the levels of anti-apoptotic and/or antioxidative proteins, Western blot analysis was conducted using specific antibodies.

Results: H₂O₂ treatment caused intracellular accumulation of ROIs and cytotoxicity in a concentration dependent manner. PC12 cells treated with H₂O₂

exhibited apoptotic cell death as determined by morphological features, internucleosomal DNA fragmentation, cleavage of poly (ADP-ribose)polymerase, an increased Bax/Bcl-X_L ratio and decreased mitochondrial membrane potential, which was protected by relatively low concentrations of 15d-PGJ₂ (< 3μM) pretreatment. In another experiment, H₂O₂ treatment led to transient activation of protein kinase B (Akt), extracellular signal-regulated kinase 1/2 and heme oxygenase-1 as an adaptive response of cells to oxidative insult, which was augmented by 15-dPGJ₂ pretreatment.

Conclusions: H₂O₂ caused apoptosis in PC12 cells by inducing oxidative stress, which was effectively protected by 15-dPGJ₂ through augmentation of the cellular antioxidant defence.