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Induction of Heme Oxygenase-1 by 15-Deoxy-Δ12,14 Prostaglandin J2 in Pc12 Cells : Implications for Protection Against Oxidative cell Death

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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-Deoxy-⊿12,14 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.

H2O2 treatment caused oxidative PC12 cell death 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-XL ratio and decreased mitochondrial membrane potential, all of which were inhibited or restored by relatively low concentration of 15d-PGJ2 pretreatment. In another experiment, PC12 cells treated with 15d-PGJ2 exhibited transient activation of Akt/protein kinase B as well as extracellular signal-regulated kinase 1/2 and induction of heme oxygenase-1 (HO-1) expression and nuclear translocation of Nrf-2 as an adaptive response to oxidative insult.

In conclusion, H2O2 caused apoptosis in PC12 cells by inducing oxidative stress, which was effectively protected by 15d-PGJ2 through augmentation of the cellular antioxidant defence involving HO-1 and Nrf-2.

Keyword : ROIs, PGJ2, Akt, ERK1/2, HO-1, nrf-2