

Potential of Cellular Antioxidant Defenses by Koean Red Ginseng Extract: Implications for Protection Against PCB126-induced Apoptosis

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Polychlorinated biphenyls (PCBs) are ubiquitous environmental contaminants that display a complex spectrum of biological and toxicological properties including cognitive and motor dysfunctions. There has been compelling evidence supporting that PCB-induced cytotoxicity is mediated through generation of reactive oxygen (ROS). Considerable attention has recently been focused on identifying naturally occurring phytochemicals that are able to scavenge excess ROS, thereby protecting against oxidative cell death. Red ginseng, which has a variety of biological and pharmacological activities including antioxidant, anti-inflammatory, antimutagenic and anticarcinogenic properties, has been widely used in traditional herbal medicine for the treatment of various diseases. In this study, we have investigated the effect of red ginseng extract on PCB126-induced oxidative cell death. Rat pheochromocytoma (PC12) cells treated with PCB126 exhibited increased accumulation of intracellular ROS and underwent apoptotic death as determined by characteristic morphological alterations, positive *in situ* terminal end-labeling (TUNEL staining), and the perturbation of mitochondrial membrane potential. Red ginseng extract attenuated PCB126-induced cytotoxicity, apoptotic features, and intracellular ROS accumulation. To further explore the possible molecular mechanisms underlying the antioxidant effects of red ginseng extract, we focused on activation of NF-E2-related factor 2 (Nrf2) as a potential molecular target. Nrf2 is a transcription factor involved in the cellular protection against oxidative stress through antioxidant response element (ARE)-directed induction of several phase 2 detoxifying and antioxidant enzymes, such as heme oxygenase-1 (HO-1) and γ -glutamylcysteine ligase (GCL). Treatment of PC12 cells with antiapoptotic concentration of red ginseng extract increased nuclear translocation, DNA-binding and transcriptional activity of Nrf2, leading to up-regulation of HO-1 expression and cellular glutathione synthesis. Moreover, PC12 cells treated with red ginseng extract exhibited transient activation of Akt/ protein kinase B and extracellular signal-regulated kinase 1/2, which are upstream of Nrf2 activation. These results suggest that red ginseng extract could potentiate cellular antioxidant defenses through induction of HO-1 and GCL via Nrf2-ARE signaling,

thereby protecting PC12 cells from PCB126-induced oxidative cell death, which may provide a preventive or therapeutic potential in the management of neurotoxic damage caused by environmental contaminants.

Key words : apoptosis, GCL, glutathione, HO-1, Nrf2, PCB126, PC12 cells, ROS, red ginseng extract

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