# A Role of Reactive Oxygen Species in Organophosphate Induced Neuronal Cell Cytotoxicity

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Organophosphate (OP) pesticides are used in agriculture, veterinary and public settings worldwide to control pests. Oxidative stress induced by pesticide in neuronal cells is one of the underpin mechanism that induced neurotoxicity. Therefore, role of reactive oxygen species induced by oxon metabolites of commonly used organophosphate pesticides in human neuronal progenitor cortical neuronal cells (hNPCs) has been examined. Undifferentiated and differentiated human progenitor cortical neuronal cells were exposed to oxon metabolites of chlorpyrifos and azamethiphos for 24 hours over a concentration range of 0.3-200 μM and cell viability measured using Thiazolyl Blue Tetrazolium Bromide (MTT) and lactate dehydrogenase (LDH) assays. Low and high inhibition concentrations of each pesticide interpolated from viability curves were further assessed by ATP assay to evaluate the impact of pesticides upon cellular bioenergetics. Cellular reactive oxygen species (ROS) generation was assessed using 2',7'-dichlorofluorescin diacetate (DCFDA) assays while cellular oxidative stress markers such as protein carbonylation, glutathione, and lipid peroxidation levels were also quantified. Specific targets of cytosolic oxidative damage were characterized by gel electrophoresis and oxyblots. Both cell phenotypes experienced pesticide-induced cell viability loss, ATP depletion and ROS generation that was pesticide concentration dependent. There was a concentration-dependent increase of protein carbonylation levels, and lipid peroxidation associated with the oxidative stress and GSH depletion. A protein of 50 kDa was a major target for oxidative stress damage after exposure to either pesticide and in both undifferentiated and differentiated hNPCs. This study concluded that cytotoxic responses are associated with ROS generation with concomitant increased of lipid peroxidation, antioxidant depletion and protein carbonylation.

***Keywords:*** *hNPC, Organophosphates, Reactive Oxygen Species*