Prevention of AQ-induced toxicity in vitro with SKF-525A and MP-induced toxicity in vitro and in vivo with ABT suggests that P450-catalysed activation is involved in the toxicity of both compounds. GSH depletion was seen to precede MP-induced toxicity in vitro, and would therefore suggest that GSH depletion may be involved in the mechanism of cytotoxicity and is not only a consequence of cell damage.

241. DELTAMETHRIN-INDUCED REACTIVE OXYGEN SPECIES IN PC12 CELLS AND RATS: ROLE OF N-ACETYL-L-CYSTEINE

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The mechanisms leading to deltamethrin (DM) neurotoxicity are not yet fully understood. Reactive oxygen species (ROS) overproduction is a common mechanism involved in chemical toxicity. The aim of this study was to investigate whether in vitro or in vivo exposure to DM produced reactive oxygen species (ROS). ROS production in rat pheochromocytoma (PC12) cells were measured by a molecular probe, 2′, 7′-dichlorofluorescein diacetate (DCFH-DA), and ROS production in hippocampus of Sprague–Dawley rats was measured by electron spin resonance (ESR). The results showed that DM induced a concentration and time-dependent increase in ROS production and lipid peroxidation in cultured PC12 cells and increase in ROS production in hippocampus of Sprague-Dawley rats. Furthermore, the antioxidant N-acetyl-L-cysteine (NAC) protected cells from ROS production stimulation induced by DM. In conclusion, our in vitro or in vivo study demonstrates that oxidative stress, evidenced by enhanced ROS production, is a mechanism involved in DM neurotoxicity. Moreover, NAC is effective in preventing DM-induced oxidative stress.

242. EFFECT OF CARBAMAZEPINE ON THE EXPRESSION OF THE HSP-70 GENES IN B CELLS FROM HYPERSENSITIVE PATIENTS

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The mechanisms of hypersensitivity to carbamazepine (CBZ), the most commonly used antiepileptic, are not fully understood. However, an immune aetiology has been implicated. Polymorphisms in the heat shock protein (HSP70) gene cluster, located in the class III region of the major histocompatibility complex (MHC), have been recently associated with CBZ hypersensitivity. The aim of our study is to investigate the effect of CBZ on expression of the HSP70 genes (HSPA1A, HSPA1B, HSPA1L) in B cells from CBZ hypersensitive patients. Epstein-Barr virus-transformed B-lymphoblastoid cell lines (B-LCL) were generated from CBZ hypersensitive patients (n = 4). Cells were treated with CBZ and samples analysed at different time points. Heat shock experiments (420°C for 2 hours) were performed as a positive control. Quantification of gene expression was performed using real-time RT-PCR normalised to the endogenous control (HPRT). All three genes (HSPA1A, HSPA1B, HSPA1L) showed an increase in mRNA levels following heat shock, with HSPA1B mRNA levels being the highest. CBZ, however, induced the expression of HSPA1L, but not of the other two genes. Our data show that only HSPA1L was induced following treatment with CBZ. Heat shock, however,

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ABSTRACTS

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