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Lipoic acid ameliorates arsenic trioxide-induced cytotoxicity, HO-1 expression and oxidative stress in THP-1 cells

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Inorganic arsenic is a common environmental contaminant; chronic exposure to arsenic can alter the physiology of various key immune cells, particularly macrophages. The aim of this research is to elucidate the key parameters associated with arsenic-induced toxicity and investigate the potential and mechanism of α-lipoic acid (LA), a potent thioreducant, for reducing the toxicity in human promonocytic THP-1 cells. We found that a non-lethal concentration of arsenic trioxide (1 μM) significantly induced the expression of heme oxygenase-1 (HO-1), a response biomarker to arsenic, without stimulating measurable superoxide production. Co-treatment of cells with the HO-1 competitive inhibitor zinc protoporphyrin (Znpp) potentiated arsenic-induced cytotoxicity, indicating that HO-1 confers a cytoprotective effect against arsenic toxicity. In addition, low concentrations of arsenic trioxide (1 and 2.5 μM) markedly inhibited monocyte-to-macrophage differentiation and expression of macrophage markers. Treatment of cells with LA attenuated arsenic trioxide-induced cytotoxicity and HO-1 over-expression and restored the redox state. In addition, LA neutralized arsenic trioxide-inhibition of monocyte maturation into macrophages and reversed the expression and activity of scavenger receptors. In conclusion, the cytotoxicity of arsenic trioxide is associated with an imbalance of the cellular redox state, and LA can protect cells from arsenic-induced malfunctions either through its reducing activity, direct interacting with arsenic or stimulating other unidentified signaling pathways.