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ARSENIC TOXICITY IN HUMAN KERATINOCYTES.

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Arsenic, a human carcinogen and drinking water contaminant, is encountered in the environment in the trivalent(AsIII) and pentavalent(AsV) oxidation states. AsV, the most prevalent form, usually appears much less toxic with its potency being enhanced by reduction to AsIII. To understand the importance of reduction in elucidating arsenic mechanisms we evaluated the responsiveness of human keratinocyte cultures to different oxidation states using Northern and quantitative PCR analysis of heme oxygenase-1 induction. We found AsV to be as efficacious as AsIII; however a longer time was required for AsV to reach maximal effect. These observations were correlated with ICP-MS measurements of cellular uptake and conversion rates. In parallel experiments, we found pentavalent antimony (SbV) to have limited biological activity, uptake, and conversion compared to the trivalent form (SbIII). These findings emphasize the importance of intracellular reduction of metalloids for biological activity.