Abstract

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Keratinocytes are part of the epidermis and represent the majority of cells in the upper layer of human skin. When these cells are damaged by mutagenic substances, changes in the composition of the genetic material may occur, and even cell death may occur. Such substances that induce changes in DNA and have mutagenic potential include the chemical warfare agent sulfur mustard.

The purpose of this study was to compare the HaCaT keratinocyte cell line with the experimentally derived 3HSM4 cell line in response to hydrogen peroxide-induced oxidative stress. The 3HSM4 cells were prepared by selecting resistant clones of HaCaT cells that were repeatedly exposed to the cytotoxic effects of sulfur mustard.

The results of the comparison show that 3HSM4 cells proved to be more resistant to hydrogen peroxide. When glutathione (GSH) synthesis was blocked in both cell types, the cytotoxic effect of hydrogen peroxide was the same. Although 3HSM4 cells were shown to be more resistant in terms of cytotoxicity, they were found to have much higher levels of free radicals than HaCaT cells. However, when intracellular GSH stores were analyzed, no significant differences were found between the two cell types. Hydrogen peroxide also induced cell death equally in the apoptotic death mode. Changes in mitochondrial membrane potential, changes in caspase 3/7 levels, and DNA damage were not significant because these changes were no longer detected after 24 hours.

These results suggest that sulfur mustard could induce permanent changes in the cellular response to oxidative stress in 3HSM4 cells. These changes then appear to be limited to the initial response of antioxidant protective mechanisms. However, it is conceivable that there are other unknown factors that may make the cell more resistant to hydrogen peroxide than the original HaCaT cells and that were not apparent in our analyses.