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Recovery of 1-Chloro-2,4-dinitrobenzene Detoxification by N-acetyl- L-cysteine in Glutathione Predepleted Human Erythrocytes

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Abstract: Glutathione is an important thiol-containing compound involved in the detoxification process in erythrocytes. Its thiol group reacts with a variety of xenobiotics in a glutathione S-transferase catalyzed reaction to form conjugates that are effluxed from the erythrocytes by an ATP dependent transport mechanism. A well studied experimental system is the transport of the conjugate of glutathione and 1-chloro-2,4-dinitrobenzene. We investigated whether N-acetyl-L-cysteine protects the free-SH content and restores 1-chloro-2,4-dinitrobenzene detoxification in erythrocytes or replaces glutathione in detoxification process in glutathione predepleted erythrocytes. Our results indicate that N-acetyl-L-cysteine restores the intracellular free-SH content following depletion by 1-chloro-2,4-dinitrobenzene and N-ethylmaleimide. N-acetyl-L-cysteine (10 mM) increased the intraerythrocyte free-SH level to 14 ± 1 µmol/ml erythrocytes in 10 min in erythrocytes treated with N-ethylmaleimide. The control level was 5 ± 0.1 µmol/ml RBC. Results showed that N-acetyl-L-cysteine, in the presence and absence of L-buthioninesulfoximine, significantly recovered the 1-cloro-2,4-dinitrobenzene detoxification process in erythrocytes. The rate of conjugate transport in glutathione predepleted and N-acetyl-L-cysteine treated erythrocytes was 449 ± 38 nmol/ml erythrocytes. In the absence of N-acetyl-L-cysteine the rate of transport was 214 ± 21 nmol/ml erythrocytes which remained similar to the control. Our results suggest that N-acetyl-L-cysteine recovers the dinitrophenyl-glutathione transport and also replaces glutathione in the detoxification of 1-cloro-2,4-dinitrobenzene in glutathione predepleted erythrocytes.

Key Words: GSH, NAC, Erythrocytes, Xenobiotics, Detoxification, Free-SH

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