NITRIC OXIDE INVOLVEMENT IN MRP1 ACTIVITY IN L-1210 LYMPHOBLASTIC LEUKEMIA CELLS

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The multidrug resistance related protein (MRP1) is responsible for chemotherapy drug extrusion from the cells. This process normally depends on high GSH amounts. GSH is related to apoptosis induced by different agents such as nitric oxide (NO). In the present work, we studied the involvement of GSH in NO-induced cytotoxicity and its relationship with MRP1 activity and expression in L-1210 cell line. Murine L-1210 cells almost did not retain CFDA intracellularly and MRP inhibitor (probenecid) as well as BSO (an inhibitor of GSH synthesis) or SNAP increased CFDA accumulation in a concentration-dependent manner. In addition, co-incubation of SNAP (1 mM) with BSO (0,1 mM) highly increased CFDA accumulation exhibiting remarkable synergism. Moreover, the co-treatment with BSO and SNAP decreased MRP1 expression by approximately 15%. Our results suggest that NO and BSO decrease MRP1 activity directly through the reduction of MRP1 expression and also indirectly through the depletion of GSH.

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