9-Norbornyl-6-Chloropurine (NCP) induces Cell death through GSH Depletion-Associated ER stress and Mitochondrial Dysfunction

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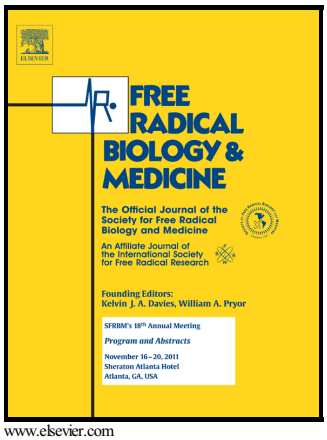

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Title

9-NORBORNYL-6-CHLOROPURINE (NCP) INDUCES CELL DEATH THROUGH GSH DEPLETION-ASSOCIATED ER STRESS AND MITOCHONDRIAL DYSFUNCTION

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Abbreviations: NCP, 9-norbornyl-6-chloropurine; GST, glutathione-*S*-transferase; GSH, L-glutathione reduced, MMP, mitochondrial membrane potential; GR, glutathione reductase; PI, propidium iodide; 4-PBA, sodium phenylbutyrate; QUER, quercetin; ALLO, allopurinol; ABT, 1-aminobenzotriazole; CCCP, carbonyl cyanide 3-chlorophenylhydrazone; CAPE, caffeic acid phenethyl ester; MDA, 1,1,3,3-tetraethoxypropane; DPI, diphenyleneiodonium chloride; TBA, 2-thiobarbituric acid; EDTA, ethylenediaminetetraacetic acid; TFA, trifluoroacetic acid; GSSG, L-glutathione oxidized; SA, sulfosalicylic acid; CDNB, 1-chloro, 2,4-dinitrobenzene; LO, lipoxygenase

Abstract

9-Norbornyl-6-chloropurine (NCP) is a representative of a series of antienteroviral bicycle derivatives with selective cytotoxicity towards leukemia cell lines. In this work we explored the mechanism of the antileukemic activity of NCP in T-cell lymphoblast cells (CCRF-CEM). Specifically, we searched for a potential link between its ability to induce cell death on the one hand and to modulate intracellular glutathione (GSH) that is necessary to its metabolic transformation via glutathione-*S*-transferase on the other hand. We have observed that GSH