



Title	INHIBITION OF THE REPAIR OF DNA DAMAGE BY THE HALOGENATED NUCLEIC ACID DERIVATIVE, 2-CHLORODEOXYADENOSINE, IN X-IRRADIATED CHINESE HAMSTER V79 CELLS
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INHIBITION OF THE REPAIR OF DNA DAMAGE BY THE HALOGENATED  
NUCLEIC ACID DERIVATIVE, 2-CHLORODEOXYADENOSINE, IN  
X-IRRADIATED CHINESE HAMSTER V79 CELLS

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2-Chlorodeoxyadenosine (2CldAdo) was found to have the ability to enhance the lethal effects of X-irradiation on Chinese hamster V79 cells. An examination of DNA damage using the filter-elution technique proved that 2CldAdo inhibited the repair of X-ray-induced DNA double-strand breaks but did not inhibit the repair of X-ray-induced DNA single-strand breaks. These results suggest that the inhibition of repair of DNA double-strand breaks by 2CldAdo was responsible for the enhancement of X-ray-induced cell killing. In order to elucidate the mechanisms by which 2CldAdo serves as a radiosensitizer, the effects of 2CldAdo on cellular metabolism were investigated. A method combining <sup>3</sup>H-labeled 2CldAdo and high performance liquid chromatography showed that 2CldAdo was phosphorylated to the triphosphate form by deoxycytidine kinase. The phosphorylation of 2CldAdo resulted in the reduction of the deoxyribonucleotide pool size and lowering of DNA synthesis.

Moreover, it was found that 2CldAdo suppressed the activity of cellular DNA synthesis, although it was incorporated into DNA. When the structural integrity of synthesized DNA was examined by the alkaline-filter elution method, a decrease in the molecular weight of DNA was observed, suggesting that the incorporation of 2CldAdo blocked the chain elongation of DNA synthesis or the ligation between the synthesized DNA fragments. However, the enhancement of the lethal effects of X-irradiation by 2CldAdo could not be explained by these findings because no effects of 2CldAdo were observed on the repair of single-strand breaks. The enhancement of X-ray-induced cell lethality by 2CldAdo must be explained by mechanisms other than the interference of DNA synthesis by 2CldAdo.