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Genotoxicity study of a new tetraalkylammonium derivative of 6-methyluracil (agent No. 547)

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Abstract

Agent No. 547 (1,3-bis[x-(diethyl-ortho-nitrobenzylammonio)-pentyl]-6-methyluracil dibromide), a newly synthesized inhibitor of mammalian-specific acetyltcholinesterase (EC 3.1.1.7) was investigated for genotoxicity using the DNA-repair test, Ames test and in vivo micronucleus test with mouse peripheral blood erythrocytes. Agent No. 547 did not cause significant changes in growth of repair-deficient Escherichia coli tester strains. The compound was non-mutagenic in Salmonella typhimurium strains TA98 and TA100 with and without rat microsomal activation mixture. However, we observed a marked increase in number of His+ revertants for both tester strains in preincubation assays. The results obtained in the micronucleus test indicate that agent No. 547 possesses significant clastogenic activity. At the high dose tested (0.5 mg/kg), the compound induced a seven-fold increase in the number of micronuclei over the spontaneous background 48 h after treatment. The results suggest that further work should be promoted to identify the metabolic pathways involved in genotoxicity of agent No. 547 in mammalian cells and to evaluate the real risk of its exposure.

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Keywords

1,3-Bis[ω-(diethyl-ortho-nitrobenzylammonio)-pentyl]-6-methyluracil dibromide, Acetyltcholinesterase inhibitor, Genotoxicity