

Cytotoxic and genotoxic effects of β -(triphenylphosphonio)ethyl carboxylate and of N,N'-bis(dihexylphosphino)lmethyl)-1,4- diaminocyclohexane

Ilinskaya O., Zelenikhin P., Kolpakov A., Karamova N., Margulis A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

Background: Several organophosphorous compounds (OPs) are now being tested therapeutically. Cholinesterase inhibition, which in large doses makes these agents effective pesticides, may also be useful in other doses for treating dementia. Metrifonate, for example, has been used to treat schistosomiasis and is undergoing trials for the treatment of primary degenerative dementia. Material/Methods: Here we report the characterization of newly synthesized OPs from the group of phosphobetaines [β -(triphenylphosphonio)ethyl carboxylate, PB] and of alpha-aminophosphoryl compounds [N,N'- bis(dihexylphosphino)lmethyl)-1,-diaminocyclohexane, AP] according to their toxic and genotoxic properties determined in prokaryotic and eukaryotic test systems. Results: The absence of toxicity towards Gram-negative bacteria and of genotoxicity in Ames mutagenicity assay and in SOS-chromotest did not exclude the cytotoxic effect of PB towards NIH3T3 mouse fibroblasts, which supports the notion of an extremely diverse interspecies response to OPs. In contrast, AP demonstrated toxic properties detected by antibacterial effect as well as by the inhibition of the proliferation and respiration of fibroblasts. The enzymatic transformation of the compound is necessary to reveal the genotoxic properties of AP. The role of mammalian microsomal enzymes and of bacterial C-P lyase in the formation of AP genotoxic metabolites is under discussion. Conclusions: Neither toxicity nor genotoxicity of PB was found in bacterial tests. Cytotoxic and mutagenic effects of AP were detected. The data contribute to the investigation of the biological activity of novel organophosphates which could be useful for the future development of OP-based therapeutics.

Keywords

β -(triphenylphosphonio)ethyl carboxylate, Cytotoxicity, Metabolic activation, Mutagenicity, N,N'-bis(dihexylphosphino)lmethyl)-1,4-diaminocyclohexane, Organophosphorous compounds, SOS-response