LOW-LEVEL LEAD, CADMIUM AND VANADIUM: "IN VITRO" EVALUATION OF THEIR GENOTOXIC POTENTIAL AS INFLUENCED BY COPPER, ZINC OR SELENIUM

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Inorganic lead (Pb), cadmium (Cd) and vanadium (V, mostly as vanadyl) are considered to be potential (Pb) or sure (Cd, V) mutagenic and/or carcinogenic agents in exposed humans, also by actions involving copper (Cu), zinc (Zn) and/or selenium (Se). Clinical and epidemiological studies, however, did not establish clear relationships among times/levels of exposure to Pb, Cd and V, plasma and/or tissue concentrations of Cu, Zn and Se and appearance of tumors. On the other hand, too high concentrations or doses of Pb, Cd and V were often employed in experimental "in vitro" and "in vivo" researches; the obtained results on genotoxic potential of such elements, therefore, do not seem extrapolable to human people occupationally or environmentally exposed to Pb, Cd or V compounds. In the present study, cultured human normal dermal Hs 27 fibroblasts and B-mel melanoblasts were used. Cell proliferation was preliminarly assessed in the presence, until 120 hours, of Pb acetate (30-300 μM), Cd acetate (0.50-15 μM) and V (as sodium metavanadate, 1-10 μM). Such experiments allowed to select a dose for each of the three elements (100 μM Pb, 3 μM Cd and 2 μM V) for evaluating effects on cell viability (Trypan blue dye exclusion assay), apoptosis (Acridine orange/ethidium bromide assay; DNA fragmentation assessment) and chromosome and DNA damage (Cytokinesis-block micronucleus assay/CBMN and Single cell gel electrophoresis/Comet test, respectively). In this regard, Cd and V, but not Pb, were shown to reduce cell viability; Pb increased formation of micronuclei in Hs 27 annd B-mel cells without changing the percentage of cells with damaged DNA (comets), thus altering chromosome segregation and inducing aneuploidy; Cd and V increased formation of both micronuclei and comets in Hs 27 and B-mel cells, respectively, thus showing a remarkable selective genotoxic action; Pb, Cd and V did not evidence effects on apoptosis. Pre-exposure for 10 days of Hs 27 fibroblasts and B-mel melanoblasts to a selected concentration (1 μM) of Cu acetate or Zn acetate or sodium selenite or –selenate unaffected the increased micronuclei formation that was induced when giving 100 μM Pb for 2 days at the end of the same pre-exposure; in such experimental conditions, only Zn was able to prevent the 3 μM Cd-induced genotoxic effects (increased frequency of micronuclei and comets) in the Hs 27 cells, in which sodium selenate opposed the Cd effects only as well as the increased frequency of comets was concerned.
This study shows that low-level Pb causes aneuploidy effects in the absence of direct genotoxicity, whereas low-level Cd and V are provided with different genotoxic potential depending on cell type (normal or tumoral) and, only for Cd, on (reduced) levels of Zn and Se, but not of Cu.