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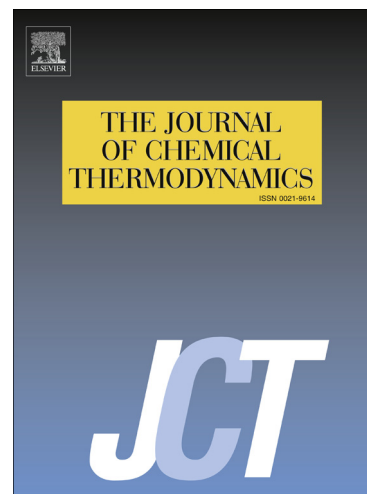
Direct DNA interaction and genotoxic impact of three metals: cadmium, nickel and aluminum

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Direct DNA interaction and genotoxic impact of three metals: cadmium, nickel and aluminum

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Abstract

This study simultaneously investigates direct DNA interaction and genotoxic impact of three typical metals: aluminum, cadmium and nickel, which the high concentration in soils and which the industries use, result in a daily significant exposure to humans. The three of them are suspected to be involved in carcinogenesis which implies genomic lesions. We propose to first study their genotoxic impact in vivo on primary normal human dermal fibroblast (NHDF) cells with comet assay at pH 7 to measure DNA breaks occurrence. Then, to characterize the metal/DNA interaction by isothermal titration calorimetry (ITC).

Comet assay shows that Cd and Ni are genotoxic, they are responsible for DNA breaks starting from 1.10^{-4} mol.L⁻¹ and 5.10^{-2} mol.L⁻¹, respectively whereas Al has no effect (on DNA at pH7) as studied by ITC at pH 7. Cd and Ni present an electrostatic interaction with DNA phosphate groups. At high Cd concentration, a DNA condensation is observed by contrast. Al has no interaction with DNA phosphate groups, but at pH 4 the electrostatic interaction is strong and the same DNA condensation phenomenon is observed. Metal genotoxic effect seems linked to the electrostatic interaction on DNA phosphate groups. Genotoxic power evolves in parallel to DNA phosphate interaction strength as Cd > Ni > Al. If this study shows that metals ions do not directly break DNA, this binding could be a preferential site for damage due to reactive oxygen species.

Key words: aluminum; cadmium; nickel; isothermal titration calorimetry; genotoxicity; DNA binding

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