

Structural speciation in binary-ternary metal ion-aromatic chelator systems mirrors tissue-specific in vitro cytotoxic selectivity.

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Metallotoxins (not endogenous) are encountered in the environment and emerge through physical and anthropogenic activities. Their entry in various organisms leads through water and the food chain to humans, thereby inducing a plethora of pathophysiologicals. Delineation of their interactive role with physiological and physiologically relevant substrates requires well-defined forms arising from such interactions along with the ensuing (bio)chemical reactivity accounting for toxic manifestations and health aberrations.

To pursue biological role delineation efforts, low molecular mass metabolic energy metal ion physiological binder α -hydroxycarboxylic acids (e.g. citric, mandelic, malic, HIBAH₂) were used in pH-specific syntheses involving toxic metal ions (thallium and cadmium) and bulky aromatic chelators 2,2'-bipyridine (2,2'-bipy) and 1,10'-phenanthroline (phen). The isolated crystalline materials were physicochemically characterized (elemental analysis, FT-IR, NMR, ESI-MS, and X-ray crystallography) in the solid state and solution. Their physicochemical characteristics subsequently led to tissue-specific biological toxicity studies in several cell lines representing well-defined tissue organs. Their emerging toxicity profile (cell viability, morphology, chemotacticity) was correlated via genetic biomarkers to apoptotic-necrotic processes, thereby shedding light on cellular toxicity mechanisms.

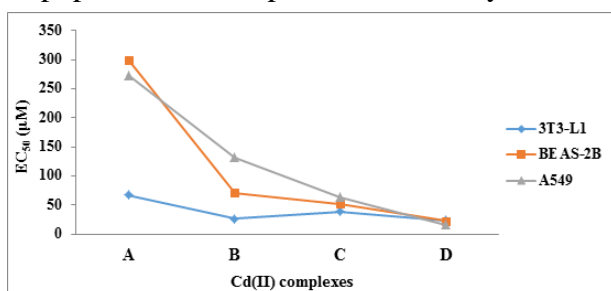


Figure 1: Representative plot of EC₅₀ change of Cd(II) compounds in 3T3-L1, BEAS-2B, and A549 cell lines.

Collectively, synthetic bioinorganic approaches woven into cellular molecular biology reveal metal ion structure- and tissue-specific

toxicity, a) portraying the contributions of thermodynamics to the formulation of bioactivity, and b) warranting further probing into the development of efficient chelators in metal-detoxification.

References:

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