Mechanisms underlying the inhibition of the cytochrome P450 system by copper ions

Letelier, M. E.

Faúndez, M.

Jara-Sandoval, J.

Molina-Berríos, A.

Cortés-Troncoso, J.

Aracena-Parks, P.

Marín-Catalán, R.

Copper toxicity has been associated to the capacity of free copper ions to catalyze the production of superoxide anion and hydroxyl radical, reactive species that modify the structure and/or function of biomolecules. In addition, nonspecifi c Cu2+-binding to thiol enzymes, which modifi es their catalytic activities, has been reported. Cytochrome P450 (CYP450) monooxygenase is a thiol protein that binds substrates in the fi rst and limiting step of CYP450 system catalytic cycle, necessary for the metabolism of lipophilic xenobiotics. Therefore, copper ions have the potential to oxidize and bind to cysteinyl residues of this monooxygenase, altering the CYP450 system activity. To test this postulate, we studied the eff ect of Cu2+ alone and Cu2+/ascorbate in rat liver microsomes, to independently evaluate its nonspecifi c binding and its pro-oxidant eff ects, respectively. We assessed these eff ects on the absorbance spectrum of the monooxygenase, as a measure of structural damage, and p-