

Complex formation equilibria of Cu^{2+} and Zn^{2+} with Irbesartan and Losartan.

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Streszczenie

We conducted a thorough study of Cu^{2+} complex formation equilibria with Irbesartan and Losartan, the two primary drugs for the cure of cardiovascular diseases, with the aim of recognising if these drugs could exert a chelating action towards Cu^{2+} . We used different complementary techniques to gain a clear picture of the involved protonation and complexation equilibria. The low solubility in water of the ligands and of the formed metal complexes prevented the use of water as solvent, so we had to perform the measurements in mixed methanol-water solvents. Further, we studied the related equilibria with Zn^{2+} for evaluating a potential interference of this essential metal ion, largely present in biological fluids. Our study provided a strong evaluation of the formed complexes and of the relative stability constants. The binding of both metal ions takes place through the tetrazole moiety except for the Zn^{2+} -Irbesartan system. In this last case, NMR measurements gave evidence of a tautomeric equilibrium involving the imidazole ring and the aliphatic chain. The estimated complexation model, and the related stability constants, allowed a speciation study in human plasma, based on a number of simplifying assumptions, which remarked that both drugs, Losartan and Irbesartan, could exert a chelating action, scavenging non-negligible amounts of Cu^{2+} from the organism.

Słowa kluczowe

Diabetes, Sartans, Tautomers, spectroscopy, Metal coordination

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