In Vitro Investigations of Novel Imidazole-Coordinated Cisplatin Analogues Exhibiting High Cytostatic Activity and Minimized Nephrotoxicity

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Since the successful introduction of the antineoplastic drug cisplatin in cancer chemotherapy the occurrence of severe side effects such as peripheral neurotoxicity and cumulative nephrotoxicity as well as the development of resistances have strongly limited its clinical application. The synthesis of analogous compounds has long been dominated by strictly defined structure-activity relationships (SAR), which often led to complexes exhibiting the same disadvantages as the parent drug.

In order to overcome the two major drawbacks of cytostatic cisplatin analogues we focus on the synthesis of novel Pt(II) and Pd(II) complexes with tertiary amine ligands deviating from the classical SAR.[1,2] Novel imidazole-coordinated Pt(II) complexes were synthesized to specifically circumvent nephrotoxic side effects. Structural investigations were carried out by X-ray single crystal analysis on the homologous Pd(II) complexes. The biological characterization of the corresponding Pt(II) complexes included the standardized MTT Assay, monitoring of the impact on renal epithelial cells and measurement of caspase-3 activity.[3]

The presented compounds show promising biological properties in combining significant cytostatic activity with very low intrinsic kidney toxicity.

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[2] M. J. Rauterkus, S. Fakih, C. Mock, I. Puscasu, B. Krebs, *Inorg. Chim. Acta* **2003**, *350*, 355.
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