

Methods for the accurate description of Platinum–DNA interaction

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Paul Ehrlich, who initiated an extensive search for the “Zauberkegel” a selective anti-infective drug in the beginning of the 20th century, introduced the age of inorganic chemotherapeutics.[1] Sixty years later Rosenberg discovered the biological activity of cis-diamminedichloridoplatin(II) and in 1969 reported its anti-tumor activity in mice.[2] Meanwhile Iridium, Rhodium, Ruthenium, Gold and other transition metal complexes have been screened for cytostatic and cytotoxic activity on cancer cells, some of them with very promising results.[3,4,5]

Cisplatin is still a widely used chemotherapeutic drug in case of cancer, but due to serious adverse effects the search for new platinum compounds with increased selectivity for cancer cells is continued.

Molecular modeling is a powerful tool to support and guide this research. As the accurate description of transition metal complexes puts high demands on the applied methods, we created a representative dataset of platinum complexes and performed a thorough benchmarking of available ab initio methods. For the future we are aiming on the detailed description of the interaction between Platinum complexes and biomolecules by QM/MM methods.

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