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Book Review

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Metal ions in biological systems, Vol. 42,
Metal complexes in tumor diagnosis and as anticancer agents

Marcel Dekker, 2004
£106 pp; price 0-8247-5498-8 (hardcover)

This is one of two recent volumes in a most successful series published since 1973 and which enjoys world renown and respect as both reference and as training material; the current volume is no exception.

Nowadays, magnetic resonance contrast agents for medical and molecular imaging allow tumours as small as 1 mm diameter to be detected and characterized without recourse to damaging ionizing radiation. Developments using pH switches (between pH 7 and 5) to increase the relaxivity and resolution use polymer-based sensitivity agents, and paramagnetic cations, predominantly gadolinium(III), Mn(II) and Fe(III).

Luminescent lanthanide probes as diagnostic and therapeutic tools use selection rules that dictate the transitions to be weak and not markedly affected by the surroundings, thus giving easily recognized lines. More than 60 years ago this led to phosphors being discovered and has now opened up the field of medical imaging. Lanthanide(III) ions, having high co-ordination number, can toxically challenge Ca and Zn *in vivo*. Synthetic strategies to shadow the steadily decreasing coordination number as atomic mass increases across the series and matching cation cavity fitting offer a wide range of options. These principles are clearly illustrated using coloured diagrams. Photodynamic therapies, photoangioplasty and macular degeneration repairs are emerging from such lutetium compounds.

Radiolanthanides used in therapy employ low tissue-range β particles and LET emission for radiosynovectomy and bone metastases treatment, the main challenge being portability of accelerator to form the doses and related dosimetry. Radiometal-labelled proteins using Mo, Tc, Re, W and others are widely used in research and development work *in vitro*.

Several chapters on *cis*platin and other platinum agents underline the remarkable achievements of this serendipitous discovery–US$1 billon per year sales, use for half of all patients undergoing chemotherapy, and up to 90% cure rates following three decades of improvements and serious side-effect reductions. This agent apparently enters cells by both active transport and passive diffusion and functions predominantly through intrastrand links, the DNA cross-linking inhibiting DNA replication, which triggers programmed cell death.

Statistically, about 10 000 compounds have to be synthesized and screened to lead to one clinically valuable compound; high-throughput synthetic methodology is still churning through such derivatives of Pt and of other metals.

Currently, one can select the (undesired!) side-effects which differ between *cis*platin, carboplatin and oxaliplatin. Acquisition of more mechanistic details of side-effect *modus operandi* could well lead to further reductions. A chapter discusses the effects of cytoprotective agents in Pt therapy to overcome the severe dose limitations and to fine-tune therapeutic regimens.

*trans*Platin compounds also show some antitumour activity (the *trans*Pt equivalent dates back to 1844, when it was prepared as 'Reiset's second chloride'). We are left with the molecular pharmacology challenge of why *trans*platin is less toxic to some cells or, perhaps more pertinently, why some cells are so extremely sensitive to the *cis* isomer?

Polynuclear Pt drugs, from trinuclear upwards, are reported to have expanded the range of tumours that are treatable and laid a foundation for Pt(IV) anticancer agents which use di- and tri-functional DNA binding; once again it appears that the spectrum of tumours responding and the choice of side effects is dependent upon metal speciation.

Ruthenium, gallium and gold antitumour agents have a range of interesting, and different from Pt, activities but the only tissue-natural metal discussed is titanium which, interestingly, was the first non-Pt metal researched through to clinical trials after *cis*platin was discovered. In such octahedral Ti complexes, *cis* ethoxy replaces the *cis* chloro of *cis*platin. Over and above any anticancer activity (mainly osteosarcomas), inorganic gallium nitrate has undergone trials for treating hypercalcaemia associated with chemotherapy.

Finally, the volume closes with a description of metal-dependent antibiotics, Fe(III), Cu(II) and Zn(II), already becoming established as essential requirements for antibiotic efficacy.

The book has 29 authors for 14 chapters and contains 1589 literature references. The standard of production is reasonably high but there are some frustrating glitches.

In the tradition of the previous 40+ volumes in the Sigel *cum* Sigel series, this is a gem of a book for both newcomers and established researchers in the field; long may they continue!

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