

Special Issue on Transition Metal Complexes as Chemotherapeutic Anticancer Agents

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Interest in metal-based anticancer drugs skyrocketed following the serendipitous discovery of cisplatin (*cis*-diamminedichloroplatinum(II)). Today, cisplatin and its analogues are among the most frequently prescribed chemotherapeutic anticancer drugs. Unfortunately, the road to perfection is always a long journey, which is also true for metal-based drugs. Commercially available drugs are associated with severe dose limiting side effects such as nephrotoxicity, cardiotoxicity, inherited or acquired resistance, and poor activity against certain types of cancer. These drawbacks have motivated medicinal chemists and pharmacologists to search for substitutes. Transition metal complexes with rationally designed ligands have emerged as potential anticancer agents because of their tunable coordination geometry and versatile redox properties. In a metal-based drug, the ligands play important roles in modulating the membrane permeability and tuning the redox properties of the system, which can be used for directional delivery of the complex to specific subcellular organelles. Under certain instances, the metal ion may stabilize the drug ligand and act as a carrier until it reaches the target site. Therefore, the overall effect of metal ion and ligand in a complex may result in enhanced selectivity and efficacy of the complex while initiating new mechanism of drug action. Metal complexes of bioessential metal ions such as vanadium, iron, cobalt, copper, and zinc have attracted a great deal of attention as potential anticancer agents in recent years due to their low intrinsic toxicity.

Photocytotoxic metal complexes have attracted considerable attention for their potential use in the photodynamic therapy (PDT) of cancer. In PDT, a photoactivable drug is administered to a cancer patient and the target tissue is irradiated with light in the presence of molecular oxygen, thereby resulting in the generation of cytotoxic molecular species. Photofrin® is currently the FDA approved and clinically frequently prescribed organic PDT drug. Unfortunately, the limitations such as skin sensitivity and hepatotoxicity of Photofrin have provided motivation to search for its alternatives. Consequently, the photoactive metal complexes with nonporphyrinic ligands have emerged as potential candidates in the PDT of cancer. Metal complexes can cause cell death via photo-redox and/or type-I pathways besides generating cytotoxic singlet oxygen species in a type-II process. Thus, “metal-based phototoxic agents” is another growing area of research.

Potential topics include but are not limited to the following:

- ▶ Designing of novel transition metal complexes with enhanced selectivity and efficacy
- ▶ Metal complexes that can overcome cisplatin resistance and target specific cellular organelles
- ▶ Studies on the mechanism of action of such complexes
- ▶ Photocytotoxic transition metal complexes as potential PDT agents
- ▶ DNA photo-cleaving metal complexes and their mechanism of action
- ▶ Dual function metal complexes for cellular imaging and anticancer activity
- ▶ Pharmacological aspects of metal complexes

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