Investigation of Cobalt(III) Complexes for Hypoxia-Activated Drug Delivery

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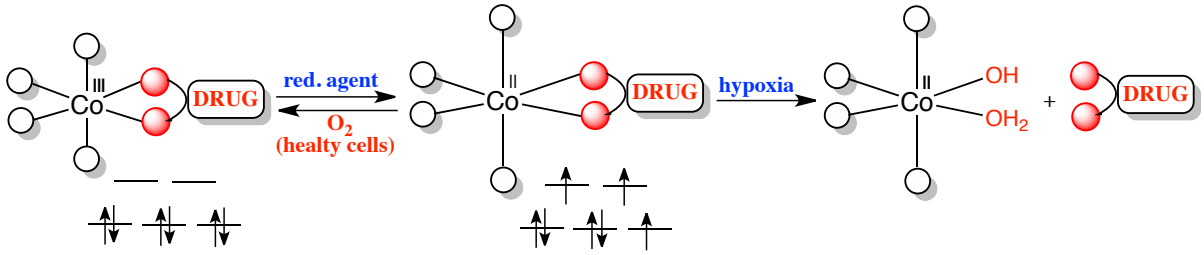
Investigation of cobalt(III) complexes as hypoxia-activated carriers for selective drug delivery to solid tumors may lead to more efficient treatments for cancer.[1] Hypoxia is a condition present in solid tumours, caused by inefficient vascularization that creates regions of low pO_2. The low levels of oxygen differentiate hypoxic cells from normoxic tissues. This differentiation holds the key for the development of more selective therapies.[1] Cobalt complexes, in general, have two accessible oxidation states: Co^{3+} that is chemically inert due to its low spin $3d^6$ configuration, and Co^{2+} that is labile (high spin $3d^7$). Thus, cobalt(III) complexes can work as carriers for selective delivery of anticancer agents to hypoxic regions of a tumor.[1] It has been demonstrated that coordination of anticancer agents to Co^{3+} can inhibit their cytotoxic properties. When reduced to Co^{2+} in a hypoxic environment, the active molecule is released and restored to its active form, killing the surrounding cells. If reduction takes place in oxygenated tissues, the complex is oxidized back to Co^{3+} by O_2 prior to dissociation, avoiding damage to normal cells.[1]



Our group has initiated an investigation of a series of cobalt(III) complexes with N_4-tetradentate ancillary ligands as carriers for hypoxia-activated drug deliver.[2] Catechol, 1,4-Naphthoquinone and 1,2,3-triazole derivatives were used as models of related anticancer agents in order to evaluate their coordination to Co^{3+} and the redox and reactivity properties of their complexes. All complexes were fully characterized by IR, UV-Visible and ^{1}H NMR spectroscopies, mass spectrometry, CHN elemental analysis and single crystal X-ray crystallography (for those obtained as single crystals). Cyclic voltammetry was used to evaluate the redox potential and reversibility of the pair Co^{3+}/Co^{2+}. To simulate reactivity under biological hypoxic and normoxic conditions, phosphate buffered solutions of the complexes were treated with ascorbic acid (a biologically relevant reducing agent) under different $[O_2]$.[2] A hypoxia-dependent dissociation of 1,4-naphthoquinone and 1,2,3-triazole derivatives from the cobalt(III) carriers was achieved.

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