Photoactivated Platinum(IV) Anticancer Complexes

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Cisplatin is a highly effective anti-cancer drug which is used to treat a variety of different cancers. However, its use can also result in some serious side-effects. We are designing non-toxic, inert photoactive Pt(IV) cisplatin analogues, which after administration might remain inactive until selectively irradiated at the target site. Examples include the photoactive diazido complexes *cis, trans, cis*-$[Pt(N_3)_2(OH)_2(NH_3)_2]$ and *cis, trans*-$[Pt(en)(N_3)_2(OH)_2]$, which can be activated by UV or visible light to Pt(II) species with the loss of the two azide ligands, and have been shown to bind to guanine [1] and DNA [2] on photoactivation. The azide ligands are released as N_2 and therefore the complex may effectively be a prodrug for aqua cisplatin-type species.

1D [^{1}H] and 2D [^{1}H,^{15}N] HSQC NMR spectroscopy have been used to follow the courses of the reactions between ^{15}N-labelled Pt(IV) azide compounds and nucleotides. Reduction and binding to 5′-GMP has been observed after only 1 minute of irradiation for some compounds.

In vitro phototoxicity experiments carried out on several cell lines, including the bladder cancer cell line 5637 and ovarian cancer cell line A2780, have shown the compounds to be toxic upon irradiation but inactive in the dark.

These inert photoactivatable Pt(IV) compounds have the potential to act as anticancer agents, which could be selectively activated and thus reduce the side-effects of platinum therapy.

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