

Biological Chemistry of Platinum-Anthraquinone Complexes

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The successful role of the anthracyclins and platinum drugs in the treatment of cancer is well documented.^{1,2} In an attempt to eliminate the known side effects and increase the activity of these drugs, many have investigated the structure-activity relationships of platinum complexes, substituted anthraquinones and the effect of combining these two moieties.³

While the mechanism of the cytotoxicity of these types of complexes is multifaceted, they are generally known to bind tightly to DNA and in a sequence selective manner.

We have prepared a series of positively charged platinum-anthraquinone complexes, varying in the position of substitution to the anthraquinone and in the coordination of the platinum, and then examined their cytotoxicity.

For one of these complexes, we have investigated the binding affinity and any sequence selectivity for DNA, using UV-spectrophotometric titrations with salmon sperm DNA, as well as crystallography and 2D-NMR with the hexamers d(TGGCCA)₂ and d(CGTCCG)₂.

The intracellular targets of these complexes were further examined using cellular uptake studies and AAS.

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- (2) Crul, M.; van Waardenburg, R. C.; Beijnen, J. H.; Schellens, J. H. *Cancer Treat. Rev.* **2002**, *28*, 291-303.
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