

TITLE: Polyamine-Anthracene Conjugates: the Correlation between Interaction with DNA, PAT Activity, and Cytotoxicity.

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Introduction: A series of cytotoxic polyamine-anthracene conjugates (Ants) was evaluated based on the ability to bind to calf thymus (CT) DNA. Polyamine transporter(s) (PATs) are also able to interact with Ants, enabling them to penetrate the phospholipid bilayer of cells. While they constitute a potential category of new drugs, the basis for the cytotoxicity of the Ants is still a mystery.

Method: Using UV-visible spectroscopy, each Ant was compared based on the range of absorbance values it produced at increasing amounts of DNA until each reached the saturation point. The DNA binding data were then compared to the cytotoxicity level (IC_{50}) of each Ant in two cell lines, CHO (Chinese hamster ovary) and CHO-MG (mutated cell line, no PAT). This enabled us to compare the cytotoxicity level of each Ant to DNA binding and PAT activity.

Results: The number of positively charged amino groups, the number of carbons between each amino group, the type of intercalation, and methylation of the terminal amino group all affected the affinity of Ants for DNA. Compounds with threading intercalation capacity were found to have high affinity compared to mono intercalation. In the case of certain Ants, trends were found regarding the Ants' affinity for DNA, PAT activity, and cytotoxicity. For example, Ant34 was highly toxic to both cell lines (CHO-MG and CHO) and had high affinity for DNA. Alternatively, Ant44 showed high toxicity in the CHO line and high affinity for DNA, but showed low toxicity in CHO-MG cells, which have no PAT activity.

Discussion: PATs may be a potential drug delivery system with the ability to transport polyamine Ants across the phospholipid bilayer of cells. However, not all Ants are delivered into the cell by PATs. The ability of certain Ants to bind to DNA may be related to cytotoxicity. By studying and understanding the effect of Ants, we may gain a better understanding of how PAT systems may work.