Charge-State Dependence of Dissociation of Drug-DNA Complexes

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Overview

Objectives
- To correlate the CAD patterns of drug/duplex complexes with binding modes of drugs.
- To examine the charge-state dependence of dissociation of drug/duplex complexes.

Materials
- Formation of DNA duplexes in solution by annealing, then transferring to ion trap by ESI.
- CAD of drug/duplex complexes by collision-induced dissociation (CID).

Introduction

The dissociation pathways of DNA duplexes and drug/duplex complexes are sensitive to initial conditions greatly affect the competitive dissociation pathways. The identities of the drug and the DNA sequences are both found to affect the CAD patterns of drug/DNA complexes. General correlations have been drawn between the structural characteristics of the duplex and the CAD patterns of the drug/DNA complexes. The dissociation pathways of DNA duplexes and drug/duplex complexes are sensitive to initial conditions and are affected by the sequence of the drug and the DNA.

Results and Discussion

The dissociation pathways of DNA duplexes and drug/duplex complexes are sensitive to initial conditions greatly affect the competitive dissociation pathways. The identities of the drug and the DNA sequences are both found to affect the CAD patterns of drug/DNA complexes. General correlations have been drawn between the structural characteristics of the duplex and the CAD patterns of the drug/DNA complexes. The dissociation pathways of DNA duplexes and drug/duplex complexes are sensitive to initial conditions and are affected by the sequence of the drug and the DNA.

Conclusions

- Single-strand separation predominates at higher charge states and this stripping process is mediated through strand cleavage and strand displacement.
- For lower charge states, drug ejection predominates for intercalator/duplex complexes and the strand separation predominates for minor groove binder/duplex complexes.
- CAD analysis of the lower charge state complexes are more appropriate in evaluating gas-phase dissociation pathways.

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References