Electrospray ionisation mass spectrometry of higher order structures of DNA

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1. Background

- Binding of drugs to double-stranded (duplex) DNA hinders DNA replication.
- It is difficult to target DNA sequences without disrupting normal cell functions.
- Higher order structures of DNA are currently being investigated as potential targets for chemotherapy or pathogenic DNA.
- Quadruplex DNA is one such type of structure. There are many forms and it is thought to occur at the ends of telomeres.
- Drugs which bind to quadruplex DNA can do so with more specificity and hinder replication. This makes them potential anti-tumor and antimarial agents.
- These complexes can be studied using electrospray ionisation mass spectrometry (ESI-MS).

Aim: To test the drugs berberine and its derivatives o-SS14, m-SS14 and p-SS14 for their affinity towards a duplex DNA sequence (D2), and a quadruplex forming sequence (Q1).

2. DNA structures tested...

- Duplex (D2) and quadruplex (Q1) DNA were titrated with each drug. Appropriate volumes of stock solutions were prepared to give DNA/drug mixtures in the ratios 1:1, 1:6, and 1:9.

Methods

- ESI-MS was used to obtain negative ion ESI mass spectra of the drug/DNA complexes.
- Duplex (D2) and quadruplex (Q1) DNA were titrated with each drug. Appropriate volumes of stock solutions were prepared to give DNA/drug mixtures in the ratios 1:1, 1:6, and 1:9.

Results

- The graph shows a comparison of the relative amounts of complexed DNA as a percentage of all DNA (free + complexed) in reaction mixtures. Duplex DNA abundances are shown in green, quadruplex DNA in red.

Conclusions

- The compounds m-SS14 and p-SS14 were found to have significant specificity for quadruplex DNA.
- May lead to applications as quadruplex DNA specific anti-tumor and anti-pathogenic agents!

References: