

Analysis of Cisplatin Adducts to Oligonucleotides of Enzymatically digested DNA using HPLC-ESI-Iontrap-MS

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Cisplatin is one of the leading metal based drugs which is widely used in treatment of cancer, especially effective against genitourinary tumors (1).

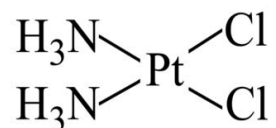


Fig. (1) Structure of Cisplatin

By aquation of the Cisplatin inside the cell, the two chloroligands, as shown in Fig. (1), are replaced by the nucleophilic N7 positions of the purine bases of the DNA to afford primarily 1,2- or 1,3-intrastrand and a lower number of interstrand cross-links (2).

In our study, calf thymus DNA was incubated with Cisplatin for about 72 hrs resulting in the formation of various platinated-oligonucleotides adducts, which were then digested by a combination of benzonase, unspecific nuclease, alkaline phosphatase, to remove the terminal phosphate group, for 24 hrs and nuclease S1, the endonuclease specific for single stranded polynucleotides, for only a short time, 30 min at 37°C

Separation and structure identification of platinated trinucleosides diphosphates either intrastrand or interstrand cross linked adducts was carried out using micro HPLC/ ESI-MS. In addition to the trimers, platinated tetranucleosides tri- and diphosphates adducts were also separated chromatographically and their structures were characterised as doubly charged.

Structure elucidation for each adduct was performed through the interpretation of the fragmentation data obtained from MS-MS and MSⁿ experiments.

References:

- (1) C.X. Zhang, S.J. Lippard, *Curr. Opin. Chem. Biol.*, 7 (2003) 481-489.
- (2) D. Wang, S.J. Lippard, *Nat. Rev. Drug Discov.*, 4 (2005) 307-320.

