

# Induction of DNA-Protein Cross-Links by Platinum Compounds

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The differences between *cis*- and *trans*-diamminedichloroplatinum II (DDP) in forming DNA-protein cross-links in isolated human lymphocytes were investigated. Both *cis*- and *trans*-DDP can induce DNA-protein cross-links. We show that *cis*-DDP forms complexes between DNA and proteins faster than *trans*-DDP. This results from an increase in the quantity of DNA and platinum together with an increase in drug concentration. Under the same conditions *trans*-DDP causes a decrease in DNA-forming complexes with proteins. After a 12 h incubation of lymphocytes we observe a similar level of DNA in DNA-protein cross-links induced by DDP isomers, but more platinum appears in complexes induced by *trans*-DDP. The results obtained demonstrate that the antitumor drug – *cis*-DDP and the clinically ineffective *trans*-DDP induce links between DNA and proteins in a different manner. We suggest that the therapeutic activity of *cis*-DDP can in part arise from rapidly forming DNA-protein complexes which can destroy the most important cellular processes, such as replication and transcription.