DNA DAMAGE AND APOPTOSIS INDUCTION IN L1210
CELLS BY CIS-DIAMMINEDICHLOROPLATINUM(II)
AND ITS NEW AMINOFLAVONE ANALOGUE

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In this work we compared biological properties of cis-
diamminedichloroplatinum (cis-DDP) and its new analogue cis-[Pt(AF)₂Cl₂]
(AF stands for 3-aminoflavone) containing two aminoflavone ligands, as non
leaving ligands, instead of ammine groups. Both compounds were tested for
their antiproliferative activity against cultured L1210 cells, and their DNA in-
terstrand crosslinking activity in cells, and in a cell-free system. Cis-DDP was
found to be more cytotoxic drug than its new analogue. In terms of IC₅₀ (the
drug concentration effective in inhibiting 50% of the cell growth after 72 hours
exposure of L1210 cells to the drug) cis-DDP was about 4 times more active.
Both complexes reacted with purified calf thymus DNA in a cell-free system
producing of DNA interstrand crosslinks. Kinetics of crosslinks formation was
very similar for both compounds but maximal level of crosslinks was higher for
cis-DDP (crosslinked DNA fractions were 0.59 and 0.40 for cis-DDP and cis-
[Pt(AF)₂Cl₂], respectively. In cells, however, as assayed by DNA alkaline elu-
tion, crosslinks formation was very similar for both compounds.
At higher concentrations of drugs strong degradation of DNA was observed in
L1210 cells treated with cis-[Pt(AF)₂Cl₂] but not in the cells incubated with cis-
DDP. This DNA degradation seems to reflect very efficient apoptosis induction
by cis-[Pt(AF)₂Cl₂] as electrophoretic patterns of DNA from cells incubated
with this drug showed a ladder typical for apoptotic cells. An additional confir-
mation of this result was obtained by microscopic analysis of cells stained by
standard Giemsa procedure while in cells treated with cis-[Pt(AF)₂Cl₂] a signifi-
cant increase of the number of fragmented nuclei was found.