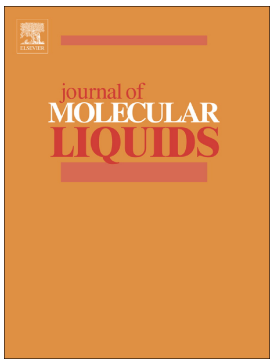

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DNA/protein interactions, cell cycle arrest and apoptosis study of potent cytotoxic Pt(II) complexes with reduced side-effects

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Abstract

A series of platinum(II) complexes (**C1**-**C6**), incorporating an intercalating substituted benzimidazole (2-aminomethylbenzimidazole) and varied leaving groups such as chloride, chelating carboxylates, and thiols, was synthesized to achieve more potent and specific metallodrugs. Spectroscopic titrations, viscosity and electrophoresis measurements revealed that the complexes bound to DNA via an intercalative mode. The complexes were also found to have high affinity towards serum albumin, BSA. Cell viability experiments against three human cancer cell lines (A549, MCF-7, MDA-MB-231) in vitro indicated that the antitumor activities were comparable with cisplatin and its successors, with the greatest efficiency towards A549. Interestingly, complexes **C1**-**C4** were 1.3-1.6 times more potent than cisplatin towards MDA-MB-231 cells. The complexes generate lower degrees of oxidative stress and are almost non-toxic to normal L6 myotubes, indicative of selective toxicity for tumor cells over normal cells. Further studies with A549 cell line revealed that the inhibition of cancer cell proliferation by the complexes is brought about by a combination of cell cycle arrest at the G2/M phase and induction of a caspase-mediated apoptosis.

Keywords: Pt(II) complexes ; DNA/BSA binding ; In vitro cytotoxicity ; Cell cycle arrest ; Apoptosis.