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Designed monofunctional platinums found to have significant antitumor activity

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Abstract

Although cisplatin is used in the clinic, its use has also been limited due to the presence of side effects and development of drug resistance. Currently much research efforts are being applied in designing new platinums that would interact with DNA differently than cisplatin. In this study, we designed four new platinum(II) complexes of the form $[PtL_3Cl]Cl$ coded as LH1, LH2, LH3 and LH4 where L= 3-hydroxy pyridine, imidazole, 8-hydroxy quinoline and benzimidazole respectively. Activity of the compounds against human ovarian cancer cell lines: A2780, $A2780^{cisR}$ and $A2780^{ZD0473R}$, cell uptake, levels of DNA□binding and nature of interaction with pBR322 plasmid DNA have been determined. In addition, combinations of LH1, LH2, LH3 and LH4 with cisplatin and selected phytochemicals were applied to the ovarian cancer cell lines as a function of concentration and sequence of administration. Although LH1 and LH2 are found to be much less active than cisplatin and result into lower intracellular platinum accumulation than cisplatin, LH3 and LH4 are significantly more active than cisplatin especially against the resistant cell lines. Combinations of LH1, LH2 and LH3 with cisplatin are found additive to synergistic against A2780, $A2780^{cisR}$ and $A2780^{ZD0473R}$ cell lines. When combined with phytochemicals genistein and curcumin, LH3 is found to produce sequenced dependent synergism with the bolus showing the greatest synergism. The results of the study can be seen to illustrate structure activity relationships and provides a rational basis for the design of novel platinum-based anticancer drug candidates.

Biography

Laila Arzuman is a PhD candidate at the age of 32 years from University of Sydney, Sydney Medical School under the supervision of Professor Fazlul Huq. Her research interest lies in designing new planaramineplatinum(II) compounds for antitumor activity. She received BSc (Honours) in Chemistry (2006) and MSc in Chemistry (2008) from Dhaka University Bangladesh.