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S-015 - SYNTHESIS, CHARACTERIZATION AND DNA INTERACTION OF NOVEL PLATINUM(II) COMPLEXES CONTAINING SUBSTITUTED BENZIMIDAZOLE LIGANDS

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Objectives: The fortuitous discovery of cisplatin in 1965, and by the 1978, it had been approved by FDA for treatment of the different types of cancer such as testicular, ovarian, head and neck, colon, bladder, gastric, and lung cancer. However, there are two considerable problems associated with clinical cisplatin usage: intrinsic or acquired resistance and side effects including nephrotoxicity, ototoxicity, nausea and emetogenicity. These have led to the development of cisplatin analogs that would be clinically effective without and/or less toxicity. From this context, we report on the synthesis and spectral characterization of eight new platinum(II) complexes of the type [Pt(L1-L4)2Cl2] C1-C4 and [Pt(L1-L4)2I2] C5-C8 (L1=5(6)-chlorobenzimidazole, L2=5(6)-methylbenzimidazole, L3=5(6)-chloro-2-methylbenzimidazole, L4=5(6)-methyl-2-methylbenzimidazole). The interactions with pBR322 plasmid DNA and inhibition of the BamHI and HindIII restriction enzyme activity through the synthesized complexes were also studied.

Methods: C1-C4 or C5-C8 were prepared by the reaction of the corresponding ligand and K2PtCl4 or K2PtI4 in ethanol/water solution. The plasmid DNA interactions and restriction enzyme activities of them were also investigated using Agarose Gel Electrophoresis method.

Results: An attempts of synthesizing new potent anticancer drugs were done by combining Pt(II) chlorido and iodo compounds with benzimidazole derivatives ligands L1-L4. The description of compounds after the synthesis was assumed by using spectroscopic characterization, pBr322 plasmid DNA interaction and then BamHI and HindIII restriction enzymes. Therefore, looking after plasmid DNA interacting outcomes, synthesized complexes modified the tertiary structure of pBR322 plasmid DNA, and the results showed that the complex C2 was highly active compound regarding to all synthesized complexes.

Conclusion: It was profound that the labile ligands containing chlorido (C1-C4) are more active than those containing iodo (C5-C8). Promising biological activity from synthesized complexes provides useful information for further cytotoxic evaluation including cisplatin resistant cell lines and future platinum-drug design strategies.

Keywords: benzimidazole, platinum complexes, synthesis, gel electrophoresis, cisplatin

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