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P210. DNA BINDING AND ANTICANCER ACTIVITY OF NOVEL SPIRO-CYCLOTRIPHOSPHAZENES

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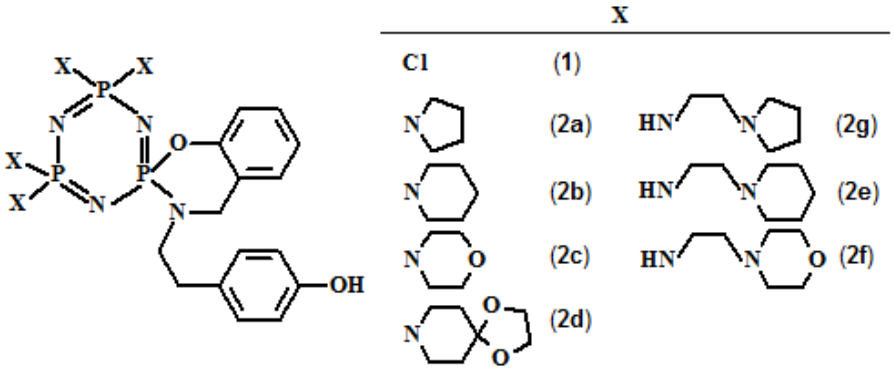
This study describes anticancer activity and DNA binding properties of partly (1) and fully (2a–g) substituted spiro-cyclotriphosphazenes with a nitrogen-attached 4-hydroxyphenylethyl pendant arm. The reaction of hexachlorocyclotriphosphazene, N3P3Cl6, with tyramine podand afforded phosphazene (1). Heterocyclic amine substituted derivatives (2a–g) were prepared by the replacement reactions of the Cl–atoms in 1 with pyrrolidine, piperidine, morpholine, 1,4-dioxa-8-azaspiro[4,5]decane, 1-(2-aminoethyl)pyrrolidine, 1-(2-aminoethyl) piperidine, and 4-(2-aminoethyl)morpholine in dry THF, respectively. The DNA cleavage activity of the compounds was studied on pBR322 DNA using gel electrophoresis experiments. It was found that 2e and 2f had caused the highest level of damage to DNA. The interactions of 1 and 2e with calf thymus DNA were also investigated using absorption spectrometry. Computational studies were carried out using DFT/B3LYP/6-31G method to know energies and the orientation of HOMO and LUMO frontier orbitals of 1 and 2b. The obtained results revealed that cyclotriphosphazene (1) interacted with DNA, further, this was also confirmed by molecular docking evaluations. Molecular docking of 1 with the DNA gyrase protein (PDB ID: 3U2D) exhibited the binding affinity with energy of −8.4 having an interaction with amino acids GLU-50 and ASN54. Cell death was measured by using propidium iodide and Annexin V method on flow cytometry. Most of cyclotriphosphazenes showed moderate cytotoxicity, while 2e and 2g had a weak cytotoxicity on MDA-MB 231 human mammary cancer cell line.



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