Abstract:

The design and synthesis of novel azo-coumarin derivatives represent a promising area of research in medicinal chemistry due to their potential pharmacological activities. In this study, a series of novel azo-coumarin derivatives such as 6-[3-pyridyl]azocoumarin, 6-[Phenylazo]coumarin, 6-[2-Chlorophenylazo]coumarin, 6-[3-Chlorophenylazo]coumarin, and 6-[4-Chlorophenylazo]coumarin were synthesized using diazo-coupling reaction. The synthesized compounds were fully characterized using FT-IR, NMR, and mass spectrometry, and biological studies were carried out. The structures of the synthesized compounds were optimized using DFT calculation and the frontier molecular orbital calculations reveal that synthesized compounds were more biologically and chemically active than coumarin. The cytotoxicity of these derivatives was evaluated against human cancer cell lines LN-229 and the IC_{50} values were evaluated and it was found that 6-[4-Chlorophenylazo]coumarin was most effective. The interaction of these derivatives with CT-DNA was investigated using UV-visible and fluorescence spectroscopy. All the synthesized compounds bound at the minor groove of CT-DNA and the binding constant values showed the order of the binding affinities was 6-[4-Chlorophenylazo]coumarin > 6-[2-pyridyl]azocoumarin > 6-[3-Chlorophenylazo]coumarin > 6-[Phenylazo]coumarin > 6-[3-pyridyl]azocoumarin > coumarin and all the compounds bound with CT-DNA through minor groove. The BSA binding study of the synthesized compounds was also carried out using UV-visible and fluorescence spectroscopy which showed the same binding order of the compounds observed with the DNA binding study. *In silico* analysis supported all the experimental outcomes regarding CT-DNA and BSA binding.

Keywords: Azo-coumarins, DFT calculations, Cytotoxicity, BSA binding, DNA binding, Molecular docking.