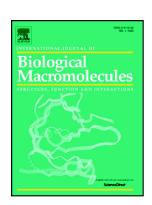
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DNA Binding, artificial nuclease activity and cytotoxic studies of newly synthesized steroidal pyrimidines

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ABSTRACT. The new steroidal pyrimidine derivatives (4-6) were synthesized by the reaction of steroidal thiosemicarbazones with (2-methyl) diethyl malonate in absolute ethanol. After characterization by spectral and analytical data, the DNA interaction studies of compounds (4-6) were carried out by UV-vis, fluorescence spectroscopy, hydrodynamic measurements, molecular docking and gel electrophoresis. The compounds bind to DNA preferentially through electrostatic and hydrophobic interactions with K_b ; 2.31×10^3 M⁻¹, 1.93×10^3 M⁻¹ and 2.05 $\times 10^3$ M⁻¹, respectively indicating the higher binding affinity of compound 4 towards DNA. Gel electrophoresis demonstrated that compound 4 showed a strong interaction during the concentration dependent cleavage activity with pBR322 DNA. The molecular docking study suggested the intercalation of steroidal pyrimidine moiety in the minor groove of DNA. During in vitro cytotoxicity, compounds (4-6) revealed potential toxicity against the different human cancer cells (MTT assay). During DAPI staining, the nuclear fragmentations on cells occurred after treatment with compounds 4 and 5. Western blotting analysis clearly indicates that compound 4 causes apoptosis in MCF-7 cancer cells. The results revealed that compound 4 has better prospectus to act as a cancer chemotherapeutic candidate, which warrants further in vivo anticancer investigations.

Key words: Pyrimidine; UV-vis; Fluorescence; Western blotting; MTT assay

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