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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 2.05×10^3 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