

# Design, synthesis and biological evaluation of certain CDK2 inhibitors based on pyrazole and pyrazolo[1,5-a]pyrimidine scaffold with apoptotic activity

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## Abstract

Different series of novel pyrazole and pyrazolo[1,5-a] pyrimidine derivatives (2a-g), (3a-c), (7a-d) and (10a-e) were designed, synthesized and evaluated for their ability to inhibit CDK2/cyclin A2 enzyme in vitro. In addition, the cytotoxicity of the newly synthesized compounds was screened against four different human cancer cell lines. The CDK2/cyclin A2 enzyme inhibitory activity revealed that compounds (7d) and (10b) exhibited the highest activity among the newly synthesized derivatives against four tumor cell lines (HepG2, OEH/9, C76, and Eceq4) with IC<sub>50</sub> values of 0.49 M and 39034.32027.4;0;7 M, respectively. Flow cytometry cell cycle assay was carried for compounds (7d) and (10b) to investigate their apoptotic activity. The obtained results revealed that they induced cell-cycle arrest in the G<sub>0</sub>-G<sub>1</sub> phase and reinforced apoptotic DNA fragmentation. Molecular modeling studies have been carried out to gain further understanding the binding mode of the target compounds together with field alignment to define the similar field properties.

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