Synthesis and in vitro antiproliferative activity of novel pyrazolo[3,4-d]pyrimidine derivatives,

Nasser Saad ,Nermin S. Abdou, Rabah A. T. Serya, Ahmed Esmat, Mai F. Tolba, Nasser S. M. Ismail and Khaled A. M. Abouzid

Associate Professor of Pharmaceutical Chemistry

Abstract

A novel series of pyrazoloij3,4-d]pyrimidine derivatives were designed, synthesized and evaluated for their
antiproliferative activity. Among the five compounds selected by NCI, compound 11a showed a distinctive
pattern of selectivity on cell line panels and was further screened for a 5-log dose range, where it showed
potent antiproliferative activity with median growth inhibition (GI50) equal to 1.71 μM against the CNS cancer
SNB-75 cell line. The tested derivative showed remarkably the highest cell growth inhibition against
non-small cell lung cancer HOP-62, CNS cancer SNB-75, breast cancer HS578T, and melanoma MALME-
3M cell lines. Flow cytometric analysis revealed that compound 11a could significantly induce apoptosis in
A549 cells in vitro at low micromolar concentrations. Further investigation showed that compound 11a
induced significant cell cycle arrest at G0/G1 phase partly due to its ability to downregulate cyclin D1 and
upregulate p27kip1 levels

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