Pharm Anal Acta 2018, Volume 9
DOI: 10.4172/2153-2435-C3-040

Design and synthesis of formononetin-dithiocarbamate hybrids that inhibit growth and migration of PC-3 cells via MAPK/Wnt signaling pathways

Dong-Jun Fu[1,2]
[1]Zhengzhou University, Chine
[2]University of California, Irvine

Novel formononetin-dithiocarbamate derivatives were designed, synthesized and evaluated for antiproliferative activity against three selected cancer cell line (MGC-803, EC-109, PC-3). The first structure-activity relationship (SAR) for this formononetin-dithiocarbamate scaffold is explored with an evaluation of 14 variants of the structural class. Among these analogues, tert-butyl-4-(((3-((3-(4-methoxyphenyl)-4-oxo-4H-chromen-7-yl)oxy)propyl)thio)carbonothioyl)piperazine-1-carboxylate (8i) showed the best inhibitory activity against PC-3 cells (IC50=1.97μM). Cellular mechanism studies elucidated 8i arrests cell cycle at the G1 phase and regulate the expression of G1 checkpoint-related proteins in concentration-dependent manners. Furthermore, 8i could inhibit cell growth via the MAPK signaling pathway and inhibit migration via the Wnt pathway in PC-3 cells.

zzufdj@sina.com