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

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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-4*H*-chromen-7-yl)oxy)propyl)thio)carbonothioyl)piperazine-1-carboxylate (8i) showed the best inhibitory activity against PC-3 cells ($IC_{50}=1.97\mu M$). Cellular mechanism studies elucidated 8i arrests cell cycle at the G1 phase and regulate the expression of the G1 checkpoint-related proteins in concentration-dependent manners. Furthermore, 8i could inhibit cell growth via MAPK signaling pathway and inhibit migration via Wnt pathway in PC-3 cells.

Biography

Dong-Jun Fu was born in 1990 in Henan province, PR of China. He is currently pursuing his joint PhD at Zhengzhou University and University of California, Irvine majoring in Medicinal Chemistry. His research focuses on the discovery of novel antitumor molecules using modern synthetic strategies, which was supported by the China Scholarship Council (CSC). Until now, he has published more than 20 SCI papers and more than 8 patents.

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