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Novel Carbazole Sulfonamide Derivatives of Antitumor Agent: Synthesis,

Antiproliferative Activity and Aqueous Solubility

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Abstract:

The current optimization of IG-105 (3) on the carbazole–ring provided a series of new carbazole sulfonamides derivatives 13a-13m. All of the compounds have been evaluated against HepG2 cells (hepatoma cancer) for antiproliferative activity. Compounds that showed activity better or comparable to that of 3 versus HepG2 were evaluated against MCF-7 (breast cancer), MIA PaCa-2 (pancreatic cancer), and Bel-7402 (hepatoma/liver cancer) for antiproliferative activity. Of the seven compounds selected for further study five (13b, 13g, 13j, 13k and 13l) were found to give IC₅₀ values against the four cell lines comparable to those for 3. Two compounds (13f and 13i) were more active than 3 and their activity against HepG2 and MCF-7 (IC₅₀: 0.01-0.07 μM) approached that of the positive controls podophyllotoxin (podo) and CA-4. Most of compounds showed aqueous solubility (0.11-19.60 μg/mL at pH 7.4 and 2.0) better than 3. These promising results warrant further development of new compounds 13f and 13i as potential potent antitumor drug candidates.

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