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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 IC_{50} 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 (IC_{50}: 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.