Design, synthesis and anticancer evaluation of novel spirobenzo[h] chromene and spirochromane derivatives with dual EGFR and B-RAF inhibitory activities

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A novel series of spirobenzo[h]chromene and spirochromane derivatives was designed, synthesized and evaluated as potential anticancer agents against MCF-7 (human breast carcinoma), HT-29 (human colorectal adenocarcinoma) and A549 (human lung carcinoma) cell lines using MTT assay. Eight compounds 7, 8e, 13a-e and 16 showed a better anticancer activity than that of sorafenib, the multi-kinase inhibitor with IC50 values between 1.78 and 5.47 mM or erlotinib with IC50 values over 20 mM. Representative compounds 8e, 13c and 16 were selected for further mechanistic investigation via EGFR, B-RAF and tubulin polymerization assays. Compound 16 was the most potent EGFR inhibitor (IC50 ¼1.2 mM), yet compounds 8e, 13c and 16 displayed moderate tubulin polymerization inhibition effects. Molecular docking studies of those compounds revealed their possible binding modes into the active sites of both EGFR and B-RAF kinases. The newly developed compounds represent a therapeutically promising approach for the treatment of different types of cancer.