Antiproliferative and proapoptotic activities of aza-annulated naphthoquinone analogs

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 1,4-Naphthoquinone derivatives have been widely documented with regard to their biological properties, and particularly their anticancer activities. In the 9,10-anthraquinone family, aza-annulation involving one of the carbonyl oxygen atoms has afforded more potent, possibly less toxic analogues. We recently carried out different modifications on the naphthoquinone skeleton to generate 3-chloro-2-amino- and 3-chloro-2-(N-acetamido)-1,4-naphthoquinone and 3,4-dihydrobenzo[f]quinoxalin-6(2H)-one derivatives. These three series of compounds were now tested against normal human fibroblasts and six human cancer cell lines. Some of the dihydrobenzoquinoxalinone derivatives were not only more potent than their 1,4-naphthoquinone counterparts, but also exhibited 10- to 14-fold selectivity between bladder carcinoma and normal cells and were equipotent with the non-selective reference drug used (etoposide). The fusion of an additional azaheterocycle to the 1,4-naphthoquinone nucleus modul