New Analogues of AHMA as Potential Antitumor Agents: Synthesis and Biological activity

陳國棟

Chang JY;Lin CF;Pan WY;Bacherikov V;Chou CT;「CHC;HD;SYC;TJT;YWL;Chen KT;LTC;Su TL

Abstract

A series of new analogues of 3-(9-acridinylamino)-5-hydroxymethylaniline (AHMA, 1) and AHMA-ethylcarbamate (2) were synthesized by introducing an O-alkylcarboxylic acid esters to the CH(2)OH function, displacing the CH(2)OH function with a dimethylaminocarboxamido group or with a methyl function introduced at the meta-, para- or ortho-position to the NH(2) group to form 5-(9-acridinylamino)-m-toluidines (AMTs), 5-(9-acridinylamino)-p-toluidines (APTs) or 5-(9-acridinylamino)-o-toluidines (AOTs), respectively. The inhibitions of a variety of human tumor cell growth, interactions with DNA as well as inhibitory effect against topoisomerase II (Topo II) of these new agents were studied. Among AMT, APT and AOT derivatives with dimethylaminoethylcarboxamido and Me at C4 and C5 of acridine moiety (i.e., 21c, 23c and 26c) were more cytotoxic than AHMA (1) and AHMA-ethylcarbamate (2), depending upon the tumor cell line tested. Detailed structure-activity relationships of the new analogues were studied.