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Cytotoxic Activity of Benzothiepins against Human Oral Tumor Cell Lines

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A total of 11 newly synthesized benzothiepins and structurally-related compounds were investigated for cytotoxic activity against both normal and tumor cells. All these compounds showed higher cytotoxic activity against three human oral tumor cell lines (HSC-2, HSC-3, HSG) than against normal human gingival fibroblast (HGF), suggesting tumor-specific cytotoxic action. In general, 3,4-dihydro-1-benzothiepin-5(2*H*)-ones [1-6] showed higher cytotoxic activity than 2,3-dihydro-1-benzothiepins [7-11]. Compounds 4 (4-bromo-3, 4-dihydro-2-(2-oxo-2-phenylethyl)-1-benzothiepin-5(2H)-one), 54-bromo-3,4-dihydro-2-(2-oxopropyl)-1-benzothiepin-5(2*H*)-one) and 6(4-bromo-3,4-dihydro-2-[1-(methoxycarbonyl)-1-methylethyl]-1-benzothiepin-5(2*H*)-one), showed higher cytotoxic activity than compounds 1, 2 and 3, respectively, which had Cl instead of Br at C-4 position. Agarose gel electrophoresis demonstrated that these compounds induced large DNA fragments in oral tumor cells, whereas they produced smear pattern of smaller DNA fragments in human promyelocytic leukemia cells HL-60. These data suggest the medicinal efficacy of benzothiepins.