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Structure-cytotoxic activity relationships of simple hydroxylated coumarins.

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Several hydroxylated and/or methoxylated coumarin derivatives were tested for their relative cytotoxicity on four human tumor cell lines (oral squamous cell carcinoma HSC-2, HSC-3, melanoma A-375 and promyelocytic HL-60) and three normal human cells (gingival fibroblast HGF, periodontal ligament fibroblast HPLF and pulp cell HPC). Tumor cell-specific cytotoxicity was detected in all 6,7-dihydroxy-substituted coumarins only. The observations indicate that the tumor-specific cytotoxicity of the naturally occurring coumarin esculetin can be further enhanced by proper substitutions at 3- and/or 4-position(s) of the molecule. Agarose gel electrophoresis revealed that esculetin and its derivatives with tumor-specific cytotoxicity induce internucleosomal DNA fragmentation in HL-60 cells.