QSAR analysis of tumor-specificity of newly synthesized 3-styrylchromone derivatives against human oral squamous cell carcinoma cell lines

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Introduction: Chromone ring constitutes basic skeleton of secondary metabolites in various plants. We have previously investigated 16 groups of chromone derivatives (239 compounds) for their tumor-specificity against human oral squamous cell carcinoma (OSCC) cell lines. Since 3-styrylchromone derivative showed prominent tumor-specificity, we performed here QSAR analysis with 14 newly synthesized 3-styrylchromones. ***Method:*** Tumor-specificity (TS) was calculated by dividing the mean 50% cytotoxic concentration (CC_{50}) for three human oral normal cells (gingival fibroblast, periodontal ligament fibroblast, pulp cell) (A) by that for four OSCC cells (Ca9-22, HSC-2, HSC-3, and HSC-4) (B) (T =A/B). PSE value that ☒☒reflects both tumor-specificity and cytotoxicity against cancer cells were calculated as follow: PSE= TS×100/B. Induction of apoptosis was evaluated by cell sorter. QSAR analysis was performed to determine the correlation between cytotoxicity and tumor-specificity of test compounds with 3,167 chemical descriptors, calculated from the most stabilized structure of 3-styrylchromone derivatives. ***Results and Discussion:*** Two compounds [**7, 14**] showed higher tumor-specificity (TS = 301, 182; PSE = 49842, 27898) than doxorubicin (TS = 55, PSE = 24954) and 5-FU (TS = 16; PSE = 26). When the 6 and 7th positions of chromone ring was H and OCH3 group, respectively, higher tumor-specificity was observed. Tumor-specificity was not increased, by introduction of OH, OCH3, Cl, or F into the 3, 4, 5 positions of the benzene ring. Treatment of HSC-2 cells with [**7,14**] induced the accumulation of HSC-2 cells in the subG1 and G2/M phases, suggesting the induction of apoptosis. The tumor-specificity of 3-styrylchromone derivatives were most correlated with descriptors for molecule shape and electronic charge. The present study suggests the applicability of 3-styrylchromone derivatives as seed compounds for exploring new anticancer drugs.