ABSTRACT

STUDY ON ANTITUMOR ACTIVIY OF SUBSTITUTED 4-ANILINO COUMARIN DERIVATIVES USING QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR)

By:

Daratu Eviana Kusuma Putri
16/403605/PPA/05122

Study on anti-hepatoma and anti-colon cancer activity of substituted 4-anilino coumarin derivatives using quantitative structure-activity relationship (QSAR) has been done. The structures and activities data were referred from Luo *et al*. experiment (Luo *et al.*, 2017). The molecular and electronic molecule properties were obtained from DFT/BPV86 6-31G basis set calculation method. The QSAR analysis were shown by Multiple Linear Regression method (MLR). The best models obtained for substituted 4-anilino coumarin derivatives were:

Anti-colon cancer activity:
$\text{Log } IC_{50} = 0.767 + (-1.768 \times qC15) + (2.182 \times qC17) + (0.208 \times \log P)$
$n = 23$; $r^2_{train} = 0.778$; $r^2_{test} = 0.8307$ $r^2_{overall} = 0.7559$; $F_{cal}/F_{tab} = 4.890$;
SEE = 0.193
Anti-hepatoma activity:
$\text{Log } IC_{50} = 0.34 + (0.717 \text{ x } qC2) + (1.012 \text{ x } qC17) + (4.961 \text{ x } qC18) + (0.385 \text{ x Log P})$
$n = 27$; $r^2_{train} = 0.747$; $r^2_{test} = 0.8223$ $r^2_{overall} = 0.6922$; $F_{cal}/F_{tab} = 4.249$;
SEE = 0.197

The models were used to calculate the inhibitory activities of anti-colon cancer and antihepatoma of 17 newly designed substituted 4-anilino coumarin derivatives. It resulted compounds 4-[(3-nitro-5- phosphanylphenyl) amino] -2-oxo-3-(3*H*-1,2,4-triazol-3-yl)-2*H*-chromene-6-carboxamide and 3-{[6-(formylamino) -2-oxo-3-(1*H*-tetrazol-5-yl) -2*H*-chromen-4-yl]amino} benzamide had the best predicted anti-colon cancer and anti-hepatoma activities, respectively.

Keywords: coumarin, anti-cancer, QSAR

INTISARI

STUDI AKTIVITAS ANTITUMOR DARI TURUNAN 4-ANILINO KUMARIN TERSUBSTITUSI MENGGUNAKAN QSAR (QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP)

Oleh:

Daratu Eviana Kusuma Putri
16/403605/PPA/05122

Studi tentang aktivitas antikanker kolon dan antihepatoma terhadap turunan 4-anilino kumarin tersubstitusi menggunakan QSAR telah diselesaikan. Struktur dan data aktivitas diambil dari penelitian yang dilakukan oleh Luo dkk.(Luo *et al.*, 2017). Sifat-sifat molekuler dan elektronik diperoleh dari perhitungan menggunakan metode DFT/BPV86 and 6-31G basis set setelah metode tersebut divalidasi. Analisis QSAR dilakukan dengan menggunakan metode Multiple Linier Regression (MLR). Model terbaik yang diperoleh untuk turunan 4-anilino kumarin tersubstitusi adalah:

Aktivitas antikanker kolon:
Log IC_{50} = 0.767 + (-1.768 × qC15) + (2.182 × qC17) + (0.208 × log P)
n = 23; r^2_{train} = 0.778; r^2_{test} = 0.8307 $r^2_{overall}$ = 0.7559; F_{cal}/F_{tab} = 4.890;
SEE = 0.193

Aktivitas antihepatoma:
Log IC_{50} = 0.34 + (0.717 x qC2) + (1.012 x qC17) + (4.961 x qC18)
+ (0.385 x Log P)
n = 27; r^2_{train} = 0.747; r^2_{test} = 0.8223 $r^2_{overall}$ = 0.6922 F_{cal}/F_{tab} = 4.249; SEE = 0.197

Kedua model digunakan untuk memprediksi nilai aktivitas penghambatan (IC_{50}) antikanker kolon dan antihepatoma dari 17 senyawa turunan 4-anilino kumarin tersubstitusi hasil. Dari hasil prediksi persamaan QSAR, senyawa 4-[(3-nitro-5-phosphanylphenyl)amino] -2-oxo-3-(3*H*-1,2,4-triazol-3-yl) -2*H*-chromene-6-carboxamide dan 3-{[6-(formylamino)-2-oxo-3-(1*H*-tetrazol-5-yl)-2*H*-chromen-4-yl]amino}benzamide memiliki prediksi aktivitas antikanker kolon dan anti hepatoma dengan nilai yang terbaik.

Kata Kunci: kumarin, anti-kanker, QSAR