

STUDI HUBUNGAN KUANTITATIF STRUKTUR-AKTIVITAS
SENYAWA ANTIMALARIA TURUNAN 1,10-FENANTROLIN
MENGGUNAKAN METODE MLR, PCR DAN ANN

Dennis Ismudewa
11/316916/PA/14035

INTISARI

Analisis menggunakan metode *multilinear regression* (MLR), *principal component regression* (PCR) dan *artificial neural network* (ANN) untuk studi hubungan kuantitatif struktur-aktivitas (HKSA) telah dilakukan pada senyawa antimalaria turunan 1,10-fenantrolin. Tujuan penelitian ini adalah mengkaji hubungan aktivitas antimalaria dan deskriptor teoritik turunan senyawa 1,10-fenantrolin menggunakan metode linier, yaitu MLR dan PCR serta metode non linier, yaitu ANN untuk usulan desain senyawa antimalaria. Deskriptor teoritik yang digunakan berupa parameter elektronik, parameter sterik, dan parameter lipofilitas yang dianalisis pada struktur hasil optimasi menggunakan metode semiempirik PM3. Analisis statistik dilakukan dengan menggunakan metode MLR, PCR, dan ANN.

Hasil analisis QSAR dari metode statistik sebagai berikut:

MLR:

$$\log 1/IC_{50} = -24,242 - 13,441 \cdot qC_2 - 18,215 \cdot qC_5 + 8,552 \cdot qC_7 + 13,084 \cdot qC_8 - 7,910 \cdot qC_9 - 18,564 \cdot qN_{10} + 20,421 \cdot qC_{12} - 153,821 \cdot qC_{13} + 0,229 \cdot \mu - 1,879 \cdot E_{HOMO} + 0,534 \cdot \log P - 0,004 \cdot V$$

$n = 16$; $r = 0,9979$; $r^2 = 0,9958$; $SD = 0,4224$; $F_{hit}/F_{tab} = 41,4178$; $PRESS = 0,1895$

PCR:

$$\log 1/IC_{50} = 6,068 + 0,377 \cdot VL_1 + 0,017 \cdot VL_2$$

$n = 16$; $r = 0,636$; $r^2 = 0,405$; $SD = 1,726$; $F_{hit}/F_{tab} = 1,200$; $PRESS = 3,1461$

HKSA menggunakan metode ANN menunjukkan hasil yang relatif lebih baik, ditunjukkan dengan nilai koefisien korelasi sebesar 0,976 dan nilai PRESS, yaitu 0,260. Berdasarkan model senyawa yang diperoleh, telah dilakukan desain antimalaria baru yang mempunyai aktivitas prediksi lebih tinggi dari senyawa hasil sintesis sebelumnya, yaitu 1-butyl-7-hidroksi-8-(1-kloroetil)-9-metil-1,10-fenantrolin dengan nilai $\log 1/IC_{50}$ sebesar 7,07.

Kata kunci: HKSA, 1,10-fenantrolin, regresi multilinier, regresi komponen utama, jaringan syaraf tiruan

***QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP STUDY OF
ANTIMALARIAL 1,10-PHENANTHROLINE DERIVATIVE COMPOUNDS
USING MLR, PCR AND ANN METHODS***

Dennis Ismudewa
11/316916/PA/14035

ABSTRACT

The analysis of quantitative structure-activity relationship (QSAR) of 1,10-phenanthroline derivative compound using multilinear regression (MLR), principal component regression (PCR), and artificial neural network (ANN) methods as antimalarial has been performed. The aim of this research is to investigate the relationship between antimalarial activity and theoretical descriptor 1,10-phenanthroline derivative compounds using MLR and PCR linear methods and ANN as non-linear method which proposed a new design of antimalarial. The theoretical descriptors were used i.e. electronic parameter, steric parameter and lipophilicity parameter were calculated from the optimized geometry using semiempirical method, PM3. QSAR analysis was carried out using three methods i.e. MLR method, PCR and ANN.

The result of QSAR analysis from the statistical method was :

MLR:

$$\log 1/IC_{50} = -24.242 - 13.441 \cdot qC_2 - 18.215 \cdot qC_5 + 8.552 \cdot qC_7 + 13.084 \cdot qC_8 - 7.910 \cdot qC_9 - 18.564 \cdot qN_{10} + 20.421 \cdot qC_{12} - 153.821 \cdot qC_{13} + 0.229 \cdot \mu - 1.879 \cdot E_{HOMO} + 0.534 \cdot \log P - 0.004 \cdot V$$

$$n = 16; r = 0.9979; r^2 = 0.9958; SD = 0.4224; F_{cal}/F_{tab} = 41.4178; PRESS = 0.1895$$

PCR:

$$\log 1/IC_{50} = 6.068 + 0.377 \cdot VL_1 + 0.017 \cdot VL_2$$

$$n = 16; r = 0.636; r^2 = 0.405; SD = 1.726; F_{cal}/F_{tab} = 1.200; PRESS = 3.146$$

ANN results showed better result that was a coefficient constant of 0.976 and PRESS score of 0.260. Based on the obtained compound model, a new design of antimalarial has been proposed. Which have higher predicted activity than those of previously synthesized compound, i.e. 1-butyl-7-hydroxyl-8-(1-chloroethyl)-9-methyl-1,10-phenanthroline with predicted $\log 1/IC_{50}$ is 7.07.

Keywords: QSAR, 1,10-phenanthroline, multilinear regression, principal component regression, artificial neural network