INTISARI

Analisis Hubungan Kuantitatif Struktur Aktivitas (HKSA) modulator reseptor asetilkolin nikotinik $\alpha 4\beta 2$ berdasarkan parameter teoritis hasil perhitungan semiempiris AM1 telah dilakukan. Penelitian ini didasari oleh peralihan fokus pengembangan obat dari reseptor asetilkolin muskarinik ke reseptor asetilkolin nikotinik yang diduga mempunyai fungsi relatif sama dan peranannya dalam timbulnya beberapa penyakit syaraf. Tujuan penelitian ini adalah untuk mengetahui hubungan kuantitatif antara struktur dan afinitas senyawa-senyawa modulator reseptor asetilkolin nikotinik berdasarkan konsentrasi yang dapat menghambat ikatan antara [^{3}H]*cytisine* dengan reseptor sebanyak 50% (IC_{50}).

Penelitian ini menggunakan rancangan eksperimental kuasi. Data parameter teoritis diperoleh dari hasil perhitungan semiempiris AM1 menggunakan program komputer *HyperChem 6.0*. Sembilan belas deskriptor digunakan dalam penelitian ini. Data tersebut diolah secara statistik menggunakan analisis regresi multivariat metode *backward* dengan program *SPSS 12.0 for Windows*. Tujuh belas model persamaan diperoleh dan dianalisis berdasarkan kriteria statistik untuk memperoleh model persamaan terbaik.

Hasil penelitian menunjukkan bahwa model persamaan 9 memenuhi kriteria statistik dan merupakan model persamaan terbaik, dengan persamaan :

$$\log(1/IC_{50}) = 3{,}853 + 15{,}121(\mathbf{qC_2}) + 38{,}399(\mathbf{qN}) + 9{,}730(\mathbf{qC_4}) + 1{,}299(\mathbf{qC_5}) + 0{,}305(\boldsymbol{\mu}) - 0{,}06228(\mathbf{SA}) + 0{,}03484(\mathbf{V}) - 0{,}721(\mathbf{logP}) + 0{,}02912(\mathbf{M}) - 0{,}005354(\mathbf{E_b}) + 0{,}00004223(\mathbf{E_e})$$

(n = 29; m = 11; R = 0,799; R^2 = 0,638; SE = 0,693; F_{hitung}/F_{tabel} = 1,131; $PRESS$ = 8,246)

Model persamaan terbaik tersebut dapat digunakan untuk memprediksikan nilai afinitas senyawa-senyawa baru modulator reseptor asetilkolin nikotinik yang merupakan analog nikotin.

Kata kunci : **HKSA, analog nikotin, AM1, regresi linier multivariat**

ABSTRACT

A Quantitative Structure Activity Relationship (QSAR) analysis of the $\alpha 4\beta 2$ nicotinic acetylcholine receptors modulators has already been done based on the theoretical parameters from AM1 semiempirical method. This research based on the focus of drugs development that changed from muscarinic acetylcholine receptors to the nicotinic acetylcholine receptors which has similar function and having role related to several neuronal diseases. The aim of the research is to find out the quantitative relationship between structure and affinity of nicotinic acetylcholine receptors modulator compounds based on concentration which could inhibited the 50% affinity of [^{3}H]*cytisine* with the receptor.

This research used quasi experimental design. The theoretical parameters data were taken from AM1 semiempirical method using *HyperChem 6.0*. Nineteen descriptors have been used in this research. The data were statistically calculated using *backward* method of the multivariate linear regression with *SPSS 12.0 for Windows*. Seventeen equation models have been obtained and analyzed based on statistical criteria to find the best equation model.

The results showed that the 9th equation model was the best model because fulfill the statistical analysis criteria and represented with equation below :

$$\begin{aligned}\log(1/IC_{50}) = {} & 3.853 + 15.121(\mathbf{qC_2}) + 38.399(\mathbf{qN}) + 9.730(\mathbf{qC_4}) + 1.299(\mathbf{qC_5}) \\ & + 0.305(\boldsymbol{\mu}) - 0.06228(\mathbf{SA}) + 0.03484(\mathbf{V}) - 0.721(\mathbf{logP}) \\ & + 0.02912(\mathbf{M}) - 0.005354(\mathbf{E_b}) + 0.00004223(\mathbf{E_e})\end{aligned}$$

(n = 29; m = 11; R = 0.799; R^2 = 0.638; SE = 0.693; F_{hitung}/F_{tabel} = 1.131; $PRESS$ = 8.246)

The best equation model may be applied to predict the affinity of new nicotinic acetylcholine receptors modulator compounds which are nicotine analogue.

Keywords : **QSAR, nicotine analogue, AM1, multivariate linear regression.**