DESAIN TURUNAN FENOKSIPIRIDIN SEBAGAI INHIBITOR PROTOPORFIRINOGEN OKSIDASE DENGAN QSAR DAN *MOLECULAR DOCKING*

SKRIPSI

diajukan untuk memenuhi sebagian dari syarat untuk memperoleh gelar Sarjana Sains Program Studi Kimia

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ABSTRAK

Herbisida sangat penting digunakan dalam produksi tanaman untuk melindungi mereka dari persaingan dengan gulma untuk meningkatkan hasil panen dan kualitas tanaman. Herbisida inhibitor protoporfirinogen oksidase (PPO, EC 1.3.3.4) bekerja pada enzim protoporfirinogen oksidase, yang mengkatalisis oksidasi protoporfirinogen IX menjadi protoporfirin IX. Penelitian ini mengkaji serangkaian turunan fenoksipiridin baru yang didesain sebagai inhibitor protoporfirinogen oksidase. *Quantitative Structure-Activity Relationship* (QSAR) digunakan untuk menentukan mode pengikatan dan stabilitas strukturalnya sebagai struktur inhibitor protoporfirinogen oksidase untuk membuat inhibitor protoporfirinogen oksidase berdasarkan senyawa yang disintesis. Sebanyak 21 senyawa turunan fenoksipiridin yang mengandung kumarin dan aktivitas (IC_{50}) yang diperoleh dari penelitian sebelumnya digunakan dalam penelitian ini. Struktur dioptimasi menggunakan metode semiempirik Austin Model 1 (AM1) dan pemodelan QSAR menggunakan metode *Multiple Linear Regression* (MLR). Diperoleh dua model persamaan QSAR dengan akurasi pemodelan yang baik (R^2_{tr} elektronik = 0,8208; R^2_{tr} 3D = 0,8892) dan memiliki kemampuan untuk memprediksi aktivitas biologis berupa log IC_{50} prediksi (R^2_{val} elektronik = 0,9575; R^2_{val} 3D = 0,9795). Senyawa turunan fenoksipiridin baru yang paling berpotensi sebagai inhibitor protoporfirinogen oksidase berdasarkan interaksi hasil *docking* yaitu senyawa A7 dengan *docking score* -6,83 kkal/mol, senyawa A8 sebesar -6,88 kkal/mol, dan B7 sebesar -6,71 kkal/mol.

Kata kunci: QSAR, *docking*, fenoksipiridin, inhibitor PPO

ABSTRACT

Herbicides are very important used in crop production to protect them from competition with weeds to increase crop yields and quality of crop. The herbicide protoporphyrinogen oxidase (PPO, EC 1.3.3.4) acts on the enzyme protoporphyrinogen oxidase, which catalyzes the oxidation of protoporphyrinogen IX to protoporphyrin IX. In this study, a series of new phenoxypyridine derivatives were developed as protoporphyrinogen oxidase inhibitors. In this case, Quantitative Structure-Activity Relationship (QSAR) was used to determine the binding mode and its structural stability as a structure of a protoporphyrinogen oxidase inhibitor, to make protoporphyrinogen oxidase inhibitors based on the synthesized compounds. A total of 21 phenoxypyridine derivatives compounds containing coumarin and activity (IC_{50}) obtained from previous studies were used in this study. The structure was optimized using the Austin Model 1 (AM1) semi-empirical method and QSAR modeling using the Multiple Linear Regression (MLR) method. Two models of QSAR equations were obtained with good accuracy (R^2_{tr} electronic = 0.8208, R^2_{tr} 3D = 0.8892) and have the ability to predict biological activity in the form of predictive log IC_{50} (R^2_{val} electronic = 0.9575, R^2_{val} 3D = 0.9795). The new phenoxypyridine derivatives that have the most potential as protoporphyrinogen oxidase inhibitors based on the interaction of the docking results are compound A7 with a docking score of -6.83 kcal/mole, compound A8 of -6.88 kcal/mole, and B7 of -6.71 kcal/mole.

Keywords: QSAR, docking, phenoxypyridine, PPO inhibitor

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AM1	: Austin Model 1
BCF	: Bioconcentration Bactors
F	: Variance Ratio
GB	: Giga Byte
GHz	: Giga Hertz
IC_{50}	: Median Inhibitory Concentration
Max	: Maksimum
Mean	: Rata-rata
Min	: Minimum
MLR	: Multiple Linear Regression
L	: Leverage
PPO	: Protoporfirinogen Oksiade
Q^2	: Cross validation coefficient
QSAR	: Quantitative Structure-Activity Relationship
R	: Koefisien korelasi
R^2	: Koefisien determinasi
R^2_{tr}	: Koefisien determinasi set pelatihan (training set)
R^2_{val}	: Koefisien determinasi set validasi (validation set)
RAM	: Random Access Memory
RMSE	: Root Mean Squared Error
SAR	: Structure Activity Relationship
SR	: Standardized Residual

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