UJI ANALISIS MLR-PCA PADA DESAIN TURUNAN PIRAZOL KARBOKSAMIDA SEBAGAI INHIBITOR SUKSINAT DEHIDROGENASE (SDH) DENGAN 2D-QSAR DAN *MOLECULAR DOCKING*

SKRIPSI

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

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ABSTRAK

Penyakit hawar pelepah pada umumnya disebabkan oleh jamur *R. solani*. Kemunculan jamur tersebut menyebabkan kerugian bagi para petani karena dapat menurunkan hasil produksi tanaman biji-bijian (serelia) seperti salah satunya padi. Oleh karena itu, penggunaan senyawa antijamur yang mengandung inhibitor suksinat dehidrogenase merupakan salah satu upaya untuk mengendalikan penyakit hawar pelepah dari jamur *R. solani*. Pada penelitian ini mengkaji turunan pirazol karboksamida baru yang didesain sebagai inhibitor suksinat dehidrogenase. Prediksi nilai aktivitas antijamur ditentukan menggunakan persamaan *Quantitative Structure-Activity Relationship* (QSAR) dan visualisasi interaksi senyawa turunan pirazol karboksamida dengan inhibitor suksinat dehidrogenase ditentukan menggunakan *molecular docking*. Sebanyak 29 senyawa turunan pirazol karboksamida dan aktivitas (EC_{50}) digunakan dalam penelitian ini untuk pemodelan QSAR dan *molecular docking*. Struktur dioptimasi menggunakan metode DFT/B3LYP/LanL2DZ sebagai perhitungan deskriptor elektronik (2D) dan pemodelan QSAR menggunakan metode *Multiple Linear Regression* (MLR) dan *Principal Component Analysis* (PCA). Uji MLR menunjukkan model persamaan QSAR yang valid dengan akurasi pemodelan yang baik dan menghasilkan persamaan:

$$\log EC_{50} = 2{,}3936\ (\pm 0{,}9447)\ [C13] + 9{,}1367\ (\pm 3{,}0682)\ [C10] + 2{,}2473\ (\pm 0{,}6055)\ [HOMO] - 48{,}1289\ (\pm 14{,}1289)\ [C4] + 1{,}3937\ (\pm 0{,}9465)\ [C14] + 28{,}3750\ (\pm 6{,}6731)$$

$$R^2_{tr} = 0{,}8911;\ Q^2 = 0{,}793; F = 28{,}079;\ R^2_{val} = 0{,}9908;\ RMSE = 0{,}3450$$

Pada uji PCA menunjukkan model persamaan QSAR yang valid menggunakan 14 deskriptor komponen utama dan menunjukkan akurasi pemodelan yang baik yaitu $R^2 = 0{,}82187$. Senyawa turunan pirazol karboksamida baru yang berpotensi sebagai inhibitor suksinat dehidrogenase ditentukan berdasarkan interaksi hasil docking yaitu senyawa A1 dengan *docking score* -4,9 kkal/mol, senyawa A5 dengan *docking score* -5,1 kkal/mol, dan senyawa A7 dengan *docking score* -5,3 kkal/mol.

Kata Kunci: MLR, *molecular docking*, PCA, QSAR

ABSTRACT

Sheath blight is generally caused by the fungus *R. solani*. The emergence of this fungus causes losses for farmers because it can reduce the production of grain crops (cerelia), for example rice. Thus, the use of antifungal compounds containing succinate dehydrogenase inhibitors is one of the efforts to control sheath blight of the fungus *R. solani*. This research examines a new pyrazole carboxamide derivative designed as a succinate dehydrogenase inhibitor. Antifungal activity value prediction was determined using Quantitative Structure-Activity Relationship (QSAR) equation and visualization of the interaction of pyrazole carboxamide derivatives with succinate dehydrogenase inhibitors was determined using molecular docking. As many as 29 pyrazole carboxamide derivatives and activities (EC_{50}) were used in this study for QSAR modeling and molecular docking. The structure was optimized using the DFT/B3LYP/LanL2DZ method for calculating electronic descriptors (2D) and QSAR modeling using the Multiple Linear Regression (MLR) and Principal Component Analysis (PCA) methods. The MLR test showed a valid QSAR equation model with good modeling accuracy and produces an equation

$$\begin{aligned}\log EC_{50} = {} & 2{,}3936\ (\pm 0{,}9447)\ [C13] + 9{,}1367\ (\pm 3{,}0682)\ [C10] \\ & + 2{,}2473\ (\pm 0{,}6055)\ [HOMO] - 48{,}1289\ (\pm 14{,}1289)\ [C4] \\ & + 1{,}3937\ (\pm 0{,}9465)\ [C14] + 28{,}3750\ (\pm 6{,}6731)\end{aligned}$$

$$R_{tr}^2 = 0{,}8911;\ Q^2 = 0{,}793; F = 28{,}079;\ R_{val}^2 = 0{,}9908;\ RMSE = 0{,}3450$$

The PCA test indicated that the QSAR equation model was valid using 14 principal component descriptors and showed good modeling accuracy, namely R^2 = 0.82187. The new pyrazole carboxamide derivative compounds that have the potential as succinate dehydrogenase inhibitors were determined based on the interaction of the docking results, namely compound A1 with a docking score of -4.9 kcal/mol, compound A5 with a docking score of -5.1 kcal/mol, and compound A7 with a docking score of - 5.3 kcal/mol.

Keyword: **MLR, *molecular docking*, PCA, QSAR**

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DAFTAR TABEL

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