

## **SINTESIS TURUNAN PIRAZOLINA DARI ASETOFENON DAN PREDIKSI AKTIVITAS SEBAGAI ANTI-COVID-19 MELALUI PENAMBATAN MOLEKUL**

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### **INTISARI**

Penelitian tentang Covid-19 menjadi perhatian dunia sejak pandemi Covid-19 dimulai, hal tersebut membuat para peneliti melakukan investigasi senyawa yang berpotensi sebagai obat Covid-19. Penelitian ini bertujuan melakukan sintesis dua turunan senyawa pirazolina dari kalkon dan hidrazin hidrat serta mengetahui aktivitas senyawa pirazolina yang diperoleh sebagai anti-Covid-19 melalui penambatan molekul.

Senyawa turunan kalkon diperoleh dari reaksi kondensasi Claisen-Schmidt senyawa asetofenon dengan benzaldehida dan 4-metoksibenzaldehida dengan penambahan katalis NaOH 30% melalui metode pengadukan yang menghasilkan produk kalkon A [3-(1,3-difenilprop-2-en-1-on)] dan kalkon A1 [3-(4-metoksifenil)-1-fenilprop-2-en-1-on]. Sintesis senyawa turunan pirazolina diperoleh dari reaksi sikloadisi kalkon A dan kalkon A1 dengan hidrazin hidrat dalam pelarut polar melalui metode refluks yang menghasilkan produk pirazolina A [3,5-difenil-4,5-dihidro-1H-pirazol] dan pirazolina A1 [5-(4-metoksifenil)-3-fenil-4,5-dihidro-1H-pirazol]. Karakterisasi produk dilakukan menggunakan GC-MS, FTIR, <sup>1</sup>H-NMR, dan <sup>13</sup>C-NMR. Uji aktivitas anti-Covid-19 dilakukan dengan metode penambatan molekul untuk mengkaji energi ikatan dan interaksi senyawa terhadap protein SARS-Cov-2 Mpro, ACE2, NSP16, dan PLpro menggunakan *software* Autodock4.

Senyawa kalkon A dan A1 memiliki karakteristik berupa padatan berwarna kuning dengan persentase hasil masing-masing 86,6% dan 70,5%. Senyawa pirazolina A dan A1 memiliki karakteristik berupa padatan berwarna putih dengan persentase hasil masing-masing 91% dan 95%. Hasil penambatan molekul menunjukkan bahwa senyawa pirazolina A kurang stabil dibandingkan ligan XX5, SNG, dan TTT karena memiliki energi ikatan lebih tinggi dari ligan-ligan tersebut. Sedangkan pirazolina A1 kurang stabil dibandingkan ligan X77, XX5, dan TTT. Senyawa pirazolina A memiliki energi ikatan lebih rendah daripada X77 (ligan utama SARS-CoV-2 Mpro) serta terjadi interaksi spesifik dengan Cys 145 dan His 41 yang merupakan residu asam amino utama SARS-CoV-2 Mpro, sedangkan pirazolina A1 memiliki energi ikatan lebih rendah daripada SNG (SARS-CoV-2 NSP16) dan terjadi interaksi spesifik dengan Tyr 6930 melalui ikatan hidrogen sehingga dimungkinkan pirazolina A dan A1 berpotensi digunakan sebagai anti-Covid-19.

Kata kunci: anti-Covid-19, kalkon, penambatan molekul, pirazolina

## ***SYNTHESIS OF PYRAZOLINE DERIVATIVES FROM ACETOPHENONE AND THEIR ANTI-COVID-19 ACTIVITIES PREDICTION WITH MOLECULAR DOCKING***

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### ***ABSTRACT***

*Research on Covid-19 has attention of world since Covid-19 pandemic began, this has made researcher investigate compounds that have potential as Covid-19 drugs. The research aimed to synthesize two of pyrazoline derivatives compounds from chalcone with hydrazine hydrate and to determine the anti-Covid-19 activity of the molecular docking.*

*The chalcone derivatives was obtained from the Claisen-Schmidt condensation of acetophenone compounds with benzaldehyde and 4-methoxybenzaldehyde the addition of 30% NaOH catalyst through stirring method, which resulted in the product chalcone A [3-(1,3-diphenylprop-2-en-1-one)] and chalcone A1 [3-(4-methoxyphenyl)-3-phenylprop-2-en-1-one]. The pyrazoline derivatives was obtained from the cycloaddition reaction of chalcone A and A1 with hydrazine hydrate in polar solvent in under reflux method, which resulted in the product pyrazoline A [3,5-diphenyl-4,5-dihydro-1H-pyrazole] and pyrazoline A1 [5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole]. Structure characterized of the product using GC-MS, FTIR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR. The anti-Covid-19 activity test was carried out using the molecular docking method to assess the binding energy and interaction of the compound to the SARS-CoV-2 Mpro, ACE2, NSP16, dan Plpro protein using Autodock4 software.*

*The result showed that chalcone A and A1 had the characteristics of yellow solid with the yield of 86.6% and 70.5%. Respectively pyrazoline A and A1 had the characteristics of white solid with the yield of 91% and 95%. Respectively molecular docking resulted in pyrazoline compound that were less stable than XX5, SNG, and TTT ligands because they had higher binding energy than these ligand. Pyrazoline A1 is less stable than X77, XX5, and TTT ligands. The pyrazoline compound has a lower binding energy than X77 (the mainligan from SARS-CoV-2 Mpro) and has specifically interacted with Cys 145 and His 41 which are the main amino acids residue of SARS-CoV-2 Mpro. The pyrazoline A1 compound has a lower binding energy than XX5 (the main ligan SARS-CoV-2 NSP16) and specifically interacts with amino acids Tyr 6930 through hydrogen bonds. This pyrazoline A and A1 were potential to be anti-Covid-19 agents.*

*Key word: anti-Covid-19, chalcone, molecular docking, pyrazoline*