ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: www.pharmascope.org/ijrps

# Insilico screening chemical compounds $\alpha$-glucosidase inhibitor from Cordia myxa L.

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*Article History:*

Received on: 14.03.2019
Revised on: 20.06.2019
Accepted on: 25.06.2019

*Keywords:*

Cordia myxa L,
Diabetes Mellitus,
Docking,
Insilico,
Pyrex Program

ABSTRACT

One mechanism to maintain blood glucose level for diabetes mellitus is the inhibitor of the $\alpha$-glucosidase enzyme to reduce the increased level. The research aimed to determine the chemical compound of *Cordia myxa* L. that can inhibit an $\alpha$-glucosidase by insilico screening using the computer simulation with some docking program. The 3 D enzyme target receptor downloaded from Protein Bank Data (PDB) with 1LWJ code, and the macromolecules of a chemical compound from the sample were resulted from GC-MS analysis and optimizing the 3D conformation by. Screening of chemical compound by Autodock Vina on Pyrex Program. The results showed that 19's chemical compounds of (*Cordia myxa* L.) having the value of free bonding energy ($\Delta$G) in the range of -5.3 kcal/mol to -9.3 kcal/mol, two compound with the higher $\Delta$G value than the others are Bis (2-ethylhexyl) phthalate ($\Delta$G -7.8 kcal/mol) and 2,2,4-Trimethyl-3-(3,8,2,16-tetramethylheptadeca, 3,7,11,15, tetraenyl-cyclohexanol) ($\Delta$G -9.3 kcal/mol).

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ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v10i3.1421

Production and Hosted by

Pharmascope.org


## INTRODUCTION

Diabetes mellitus is a disease of malfunction body process, usually due to a combination of hereditary a d environmental causes, resulting in hyperglycemia due to defects in either insulin ecretion or in ulin action in the ody (Elavarasi *et al.*, 2013). *Cordia myxa* L. has been reported to have potential activity as an anti-diabetic. This mechanism is based on the inhibition of the alpha-glucosidase enzyme (Najib *et al.*, 2019a). Some compounds involved in this plant activity. The previous research showed that 19 compounds can determine as enzyme inhibitor (Najib *et al.*, 2019b) . Insilico is the method to Investigate the interaction of the compound with the enzyme by a computer program. Insilico screening can be made as the preliminary process to determine the drugs candidates (Yuliana *et al.*, 2013).

## MATERIALS AND METHODS

### Insilico Screening

Model of the 3D macromolecule (alpha-glucosidase enzyme) was downloaded from the protein data bank (code 1LWJ) on the NCBI website.

### Compounds Preparation

Compounds are results from GC-MS determination of n-hexane fraction of *Cordia myxa* L (Yuliana *et al.*, 2013). All 2D chemical structure are drawn by

chemskecth then convert to 3D with minimizing energy conformation.

**Docking Process**

Docking on the compounds to enzyme target by Autodock Vina embedded on PyRx program (Yuliana *et al.*, 2013). Docking results on each compounds are recorded the free bonding energy (ΔG). Results of docking visualized by PyMol (Yuliana *et al.*, 2013).

**Data Analysis**

Data analysis from ranked the from free bonding energy (ΔG). The lowest energy showed a stable compound, and the highest energy showed unstable compounds.

**RESULTS AND DISCUSSION**

Docking results showed in Table 1.

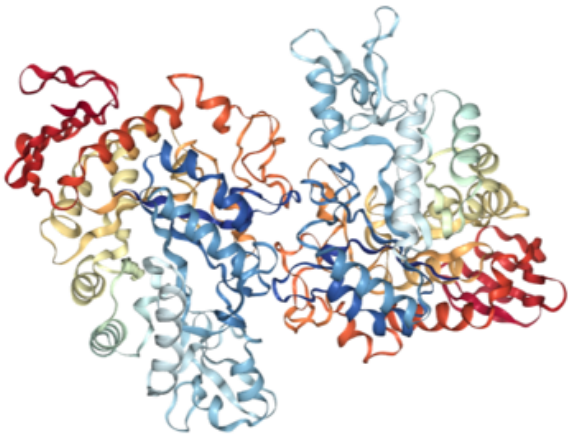

**Figure 1: 2,2,4-Trimethyl-3-(3,8,2,16-tetramethyl heptadeca, 3,7,11,15, tetraenyl-cyclohexanol) (ΔG -9.3 kcal/mol).**

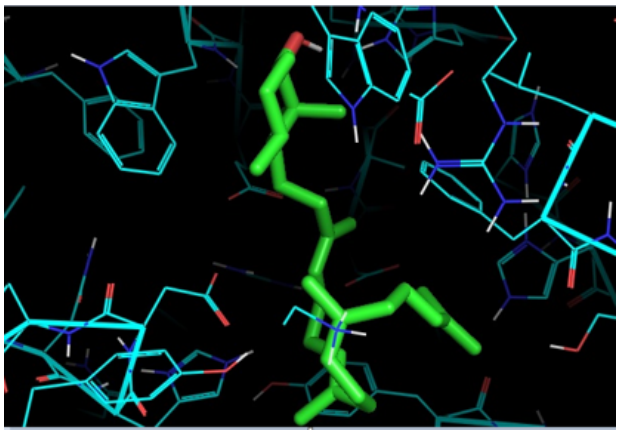

**Figure 2: Bis (2-ethylhexyl) phthalate (ΔG -7.8 kcal/mol)**

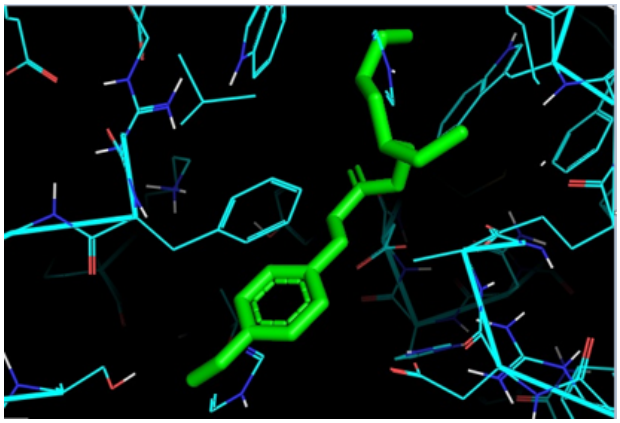

**Figure 3: Target Enzyme 1 LWJ**

Sample for docking target on the compounds as enzyme alpha-glucosidase (1 LWJ) on protein data bank web sites showed in Figure 3 .

Diabetes mellitus (DM) is a hyperglycemia illness which is indicated by inadequate of insulin or a decrease in insulin insensitivity (Corwin and Corwin, 2008). DM causes by the abnormal condition, whereas the body mechanism cannot control the blood glucose level on normal condition. Diabetics correlated with the malfunction on the insulin production. As a consequence, the blood glucose level steady in the up normal condition (Feng *et al.*, 2011).

Alpha-glucosidase inhibitors are one of the antidiabetic compounds on the plants that can inhibit the enzyme target. There is several research to conduct for seeking the new compounds that has the ability as a potential agent for crude drugs for curing DM (Najib *et al.*, 2011).

Our research before finding that the purpose of the chemical compound in the n-hexane fraction of *Cordia myxa* L. on leaves indicated that alpha-glucosidase enzyme could have inhibited by those compounds (Najib *et al.*, 2019a). GC-MS profiling for determining the compounds on this fraction was conduct and find some chemical substances (Najib *et al.*, 2019b).

To determine if potential substance as an enzyme inhibitor for further research, we use the insilico method. This method will describe to find it more about drugs candidate by the computer program (Yuliana *et al.*, 2013). On the compounds docking with a target enzyme as the natural substance on the body system. Docking results indicated that one compound with the lowest free bonding energy approximately the free bonding energy of acarbose. This result from the sample still above the acarbose free bonding energy. It is contrary with the in-vitro results showed that n-hexane fraction on the sample has the higher potency than acarbose (Na-

**Table 1: Docking Results from Compounds with 1LWJ as Target Enzyme**

| Ligand | Binding Energy |
|---|---|
| 1,3-Benzenedicarboxylic_acid,_bis(2-ethylhexyl)_ester_uff_E= 155.60 | -7.2 |
| 1-Docosene_uff_E= -10.54 | -5.6 |
| 1-Hexadecanol,_2-methyl_uff_E= 195.12 | -5.3 |
| 1lwj_uff_E= 1895.67 | -10.2 |
| 1-Nonadecene_uff_E= -7.50 | -5.9 |
| 2,2,4-Trimethyl-3-cyclohexanol_uff_E= 119.98 | -9.3 |
| 2-Propenoic_acid,_3-(4-methoxyphenyl)-,_2-ethylhexyl_ester_uff_E= 137.93 | -7.8 |
| 3,7,11,15 -tetramethyl-2-hexadecen-1_uff_E= 51.16 | -6.7 |
| 7-Tetradecyne_uff_E= 26.81 | -5.6 |
| 9,12,15-Octadecatrienoic_acid,_methyl_ester_uff_E= 7.32 | -6.3 |
| benzene,_1,2,3-trimethyl_uff_E= 59.36 | -6.0 |
| benzene,_1-ethyl-3-methyl_uff_E= 57.91 | -6.1 |
| Bis(2-ethylhexyl)_phthalate_uff_E= 226.94 | -7.8 |
| Cetene_uff_E= -6.41 | -5.6 |
| Decane,_5,6-bis_uff_E= 111.47 | -7.1 |
| Hexadecanoic_acid,_methyl_ester_uff_E= 32.65 | -5.9 |
| Isophytol_uff_E= 55.46 | -6.8 |
| Isopropyl_myristate_uff_E= 22.70 | -6.2 |
| Isopropyl_palmitate_uff_E= 32.96 | -6.2 |
| Octadecanoic_acid,_ethyl_ester_uff_E= 18.48 | -6.0 |
| phenol,_2,4-bis_uff_E= 1618.15 | -7.7 |

Note: 1lwj_uff_E (Acarbose as a comparator)
Binding Energyon Kcal/mol
Docking visualization on the 2 compounds with lower biding energy showed in Figure 1 andFigure 2.

jib *et al.*, 2011). This condition can occurs because of the interaction two or more compound on the fraction can increase the potency on sample (Li and Lou, 2018) It is different from the docking process because the compounds docked with target protein one by one (Munhoz and Frode, 2017).

## CONCLUSIONS

Nineteen's chemical compounds of (*Cordia myxa* L.) having the value of free bonding energy ($\Delta$G) in the range of -5.3 kcal/mol to -9.3 kcal/mol, two compounds with the higher $\Delta$G value than the others are Bis (2-ethylhexyl) phthalate ($\Delta$G -7.8_kcal/mol)_and_2,2,4-Trimethyl-3- (3,8,2,16-tetramethylheptadeca, 3,7,11,15, tetraenyl-cyclohexanol) ($\Delta$G -9.3 kcal/mol). *Cordia myxa* L. as a plant for the potential for DM drugs, need more advance research to proofing the effectiveness and efficacy to the patient.

## ACKNOWLEDGEMENT

Thank you to Directorate Research, Technology and High Education, Ministry of Research, Technology and the High Education Republic Indonesia for funding this research for grant Basic Research for University Institution (PDUPT-RISTEK DIKTI) 2019.

## REFERENCES

Corwin, E. J., Corwin 2008. *Handbook of pathophysiology*. Wolters Kluwer Health/Lippincott Williams & Wilkins.

Elavarasi, S., Saravanan, K., Renuka, C. 2013. A SYSTEMATIC REVIEW ON MEDICINAL PLANTS USED TO TREAT DIABETES. MELLITUS. International Journal of Pharmaceutical, Chemical & Biological Sciences, 3(3).

Feng, J., Yang, X. W., Wang, R. F. 2011. Bioassay guided isolation and identification of $\alpha$-glucosidase inhibitors from the leaves of Aquilaria Sinensis. Phytochemistry, 72(2–3):242–247.

Li, G., Lou, H. X. 2018. Strategies to diversify natural products for drug discovery. Medicinal Research Reviews, 38(4):1255–1294.

Munhoz, A. C. M., Frode, T. S. 2017. Isolated Compounds from Natural Products with Potential An-

tidiabetic Activity -. A Systematic Review. Current Diabetes Reviews, 14(1).

Najib, A., Ahmad, A. R., Handayani, V. 2019a. ELISA Test on Cordia myxa L. Leaf Extracts for alpha-Glucosidase Inhibitor. Pharmacognosy Journal, 11(2):358–361.

Najib, A., Handayani, V., Ahmad, A. R., Hamidu, L., Anisa, R. 2019b. Chemoprofiling of active n-hexane fraction as alpha-glucosidase inhibitors from kanunang (Cordia myxa L.) leaves from enrekang south Sulawesi. Journal of Global Pharma Technology.

Najib, A., Hartati, S., Elya, B. 2011. In vitro bioassay of an n-buthanol isolate of Acorus calamus L. on inhibitory of activity a-glucosidase. International Journal of PharmTech Research.

Yuliana, D., Bahtiar, F. I., Najib, A. 2013. In silico screening of chemical compounds from roselle (Hibiscus Sabdariffa) as angiotensin-I converting enzyme inhibitor used PyRx program. ARPN J. Sci. Technol, 3:1158–1160.