VOL. 3, NO. 12, December 2013 ISSN 2225-7217
ARPN Journal of Science and Technology

http://www.ejournalofscience.org

In Silico Screening of Chemical Compounds from Roselle (Hibiscus Sabdariffa) as Angiotensin-I Converting Enzyme Inhibitor Used PyRx Program

[1] Dewi Yuliana, [2] Fachrul Islami Bahtiar ,[3] Ahmad Najib
[1] Department of Pharmacology, Faculty of Pharmacy, Universitas Muslim Indonesia
[2,3] Department of Natural Product Chemistry, Faculty of Pharmacy, Universitas Muslim Indonesia

[1] yuliaeman@gmail.com, [3] ahmad.najib@ymail.com

ABSTRACT

The research was conducted by in silico screening of Angiotensin-I Converting Enzyme (ACE) inhibitors from Roselle (Hibiscus sabdariffa) chemical compounds. The objective research was to determine the active compounds Roselle (Hibiscus sabdariffa) as a potential inhibitor of Angiotensin-I Converting Enzyme (ACE) by using in silico screening method.The research was conducted using chemical compounds Roselle (Hibiscus sabdariffa) downloaded via Take Out "Jamu" Knapsack and models of Angiotensin-I Converting Enzyme downloaded via Protein Data Bank (PDB) with code 1O86, then performed docking process using the PyRx program, and then evaluated of the free energy (ΔG) as docking process results. Result show that 3 of the Roselle (Hibiscus sabdariffa) chemical compounds have the lowest free energy value and potential as inhibitors of Angiotensin-I Converting Enzyme better than Lisinopril. Those are Hibiscetin, Hibiscetin 3-glucoside, and delphinidin 3-sambubioside with free energy (ΔG) are respectively -8.1 kcal / mol, -9.1 kcal / mol and -9.4 kcal / mol.

Keywords: *In Silico, Hibiscus sabdariffa, Angiotensin-I Converting Enzyme, Docking, PyRx*

1. INTRODUCTION

Chemical compound is a process which requires funds about 800 million U.S. dollars, according to records submitted by Dimasi et al. certainly a huge cost, much higher than the economic capability of developing countries, such as Indonesia. Strategy approach, directed efforts and economic support is needed to enable Indonesia to contribute in the discovery of drugs [3].

Recently An interesting offered is the utilization of computers as a tool in drug discovery. Increasing capabilities of computer is an opportunity to develop simulations and calculations in drug design. Computers offer the in silico methods as complementary in vitro and in vivo methods that are commonly used in the drug discovery process. Terminology in silico, is analogous to the in vitro and in vivo, refers to the utilization of computers for the study of drug discovery [3].

Screening of pharmacological activity on the active ingredients of medicinal plants is an expensive process and required a long time with laboratory experiments. Currently the drug design process through a revolution with the knowledge of bioinformatics, virtual screening, de novo design, etc have done. Using computer as media is -called in silico methods, in order to help identify drug targets through bioinformatics equipment. In silico methods can also be used to analyze the structure of macromolecular targets that might binding to the active site and binding to the target molecule, etc [3].

Previous photochemical studies on Hibiscus sabdariffa have reported the presence of phenolics, organic acids, sterols, terpenoids, polysaccharides and some minerals. The phenolic content in the plant consists mainly of anthocyanins like delphinidin- 3-O-glucoside, delphinidin-3-O-sambubioside, and cyanidin-3-Osambubioside [1].

Hibiscus sabdariffaextracts have demonstrated to have a broad range of therapeutic effects such as antioxidant, and antihypertensive [1,7,5]

A Different method have been shown that Hibiscus sabdariffa extracts can reduce blood pressure in humans, and has been Another possible mechanism may be inhibition of angiotensin I converting enzyme (ACE). The latter action has been demonstrated in vitro with a hydro ethanol crude extract of Hibiscus sabdariffa calyces demonstrated that HSE has a vasodilator effect in the isolated aortic rings of hypertensive rats. Recently, a clinical trial on 193 patients with hypertension stages I and II was carried out by our research group [2].

From the active aqueous extract of Hibiscus sabdariffa, an anthocyanin-rich fraction (HSFM) was obtained; this fraction inhibited the ACE activity in a dose-dependent manner with IC50 = 91.2_g//mL. RP-HPLC purification of this fraction afforded two pure anthocyanins which were characterized as delphinidin-3-O-sambubioside and cyanidin-3-O-sambubioside. The structures of these compounds were determined on the basis of the spectral data (1H NMR and 13C NMR) identical with those previously described, and which were obtained at the same conditions [4].

There are various reports that demonstrated that flavonoids inhibit the ACE [6].

2. RESEARCH METHOD

Model of the enzyme Angiotensin-I Converting Enzyme was obtained through the protein data bank with the code **1O86** in the download RSCB (PDB) website. Models of chemical compounds contained in Roselle (Hibiscus sabdariffa) obtained through the site Take out "jamu" Knapsack4 and made in the formula structures of 2D and 3D using the program ACD / ChemSketch. Then docking used Pyrx program and then visualized.

3. RESULT AND DISCUSSION

The docking result as shown on table 1 below

Table 1: Docking result between ligand with the receptor Angiotensin-I Converting Enzyme

No	Ligan / chemical compound	Gibbs Free Energy (ΔH)
1.	Hibiscetin	-8,1
2.	Hibiscetin 3-glucoside	-9,1
3.	Delphinidin 3-sambubioside	-9,4
4.	Lisinopril	-7,9

The objective of the research was to determine the active compounds from plants Roselle (Hibiscus sabdariffa) other than lisinopril as potential inhibitors of angiotensin-I converting enzyme. by in silico with PyRX software program.

This study used chemical compounds from plants Roselle (Hibiscus sabdariffa) due to the chemical compounds in plants has been reported that have anti hypertensive activity which is delphinidin-3-O sambubioside Those chemical compounds obtained by downloading the model chemical compounds from the site Take Out "Herbal" knapsack that MDL mol format files [V2000] (* mol) [2].

For the 3D structure of angiotensin-I converting enzyme can be downloaded from the website Protein Data Bank (PDB) with the code 1O86. Angiotensin-I converting enzyme is an enzyme that forms a complex with Zn 2 and Cl as an essential component of the binding site catalysis Angiotensin-I converting enzyme.

PyRX is a program used to docking between chemical compounds as ligands and proteins as receptors. In this docking process, 3 chemical compounds from Roselle plant (Hibiscus sabdariffa) and reference compounds, namely 1 didocking lisinopril binding site on the enzyme that is Zn701

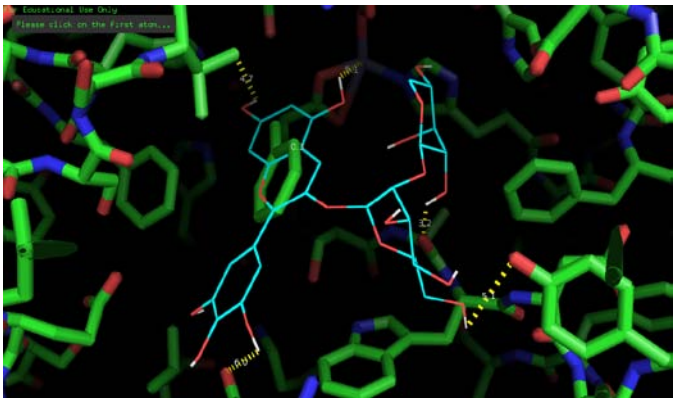

Fig 1: Delphinidin 3-sambubioside on the binding pocket

From the research we can find three chemical compounds that have synergistic activity with lisinopril (-7.9 kcal / mol) Hibiscetin , (ΔG) -8.1 kcal / mol, Hibiscetin 3-glucoside with a free energy change (ΔG) -9.1 kcal / mol, and delphinidin 3-sambubioside with the free energy (ΔG) -9.4 kcal / mol (Fig.1). ΔG Indicated the stability of the interaction (bonding) Angiotensin receptor with ligands Angiotensin converting enzyme in the binding site. AG showed the lowest energy conformation of bond is the most stable and optimum for drug design because have the highest affinity

4. CONCLUSION

Docking results showed activity of chemical compounds delphinidin-3-O-sambubioside have AG -9.4 kcal / mol. showed the lowest energy conformation of bond is the most stable and optimum for drug design because have the highest affinity

REFERENCES

[1] Ali, B.H., Wabel, N.A., Blunden, G., 2005. Pharmacological and toxicological aspects of Hibiscus sabdariffa L. Phytotheraphy Research 19, 369–375.

[2] Ajay, M., et al., 2007. Mechanism of the antihypertensive effect of Hibiscus sabdariffa L. calyces. Journal of Ethnopharmacology 109, 388–393.

[3] Dimasi, J.A., et al., 2003. The price of innovation: new estimates of drug development costs. J. Health. Econ., 22, 151-185.

[4] Du, Q., Jerz, G., Winterhalter, P., 2004. Isolation of two anthocyanin sambubiosides from bilberry (Vaccinium myrtillus) by high-speed counter-current chromatography. Journal of Chromatography A 1045, 59–63.

[5] Herrera, Arellano, A., et al., 2007. Clinical effects produced by a standarized herbal medicinal product of Hibiscus sabdariffa on patients with hypertension. A randomized, double-blind,

lisinopril-controlled clinical trial. Planta Medica 73, 6–12.

[6] Loizzo, M.R., et al., 2007. Inhibition of angiotensin converting enzyme (ACE) by flavonoids isolated from Ailanthus excelsa (Roxb) (Simaroubaceae). Phytotherapy Research 21, 32–36.

[7] Ramakrishna, B.V., et al., 2008. Antioxidant activities of roselle (Hibiscus sabdariffa) calyces and fruit extracts. Journal of Food Science and Technology 45, 223–227.

AUTHOR PROFILES

Dewi Yuliana, Receive the degree on Pharmaceutical Science 2005 and Magister of Pharmaceutical Science 2011, currently she is the researcher and lecturer at faculty of pharmacy, Universitas Muslim Indonesia-Indonesia

Fachrul Islami Bahtiar, Fresh graduate from under graduate program of Pharmaceutical Science. Receive the degree 2013 from faculty of pharmacy Universitas Muslim Indonesia-Indonesia.

Ahmad Najib, Senior lecturer at Faculty of pharmacy. Receive degree on Pharmaceutical Science 2001 and Magister of Pharmaceutical Science 2010. Currently he is the head of Natural Product Chemistry Laboratory.