XXX Symposium on Bioinformatics and Computer-Aided Drug Discovery

MOLECULAR DOCKING OF SECONDARY METABOLITE COMPOUNDS OF KAWISTA (LIMONIA ACIDISSIMA L.) AS HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 (HER-2) INHIBITORS

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INTRODUCTION

Data from the Global Cancer Observatory (GLOBOCAN) in 2018 shows that breast cancer is the second largest case in the world and the most cases in Indonesia, which is 58,256 cases or 16.7% of the total cancer cases (Ferlay et al., 2018).

20% of breast cancer patients are affected by HER2, which is abundant in the plasma membrane of SKBR3 cells (Fehling-Kaschek et al., 2019).

Kawista fruit (Limonia acidissima L.) is able to inhibit the proliferation of breast cancer derived from SKBR3 and MDA-MB345 (Pradhan, Tripathy and Patanaik, 2012).

Testing with in silico methods to predict the activity of secondary metabolite compounds of L. acidissima against HER2 receptors found in breast cancer

METHODS

Kawista (Limonia acidissima L.)

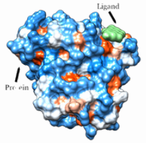
to determine the bioavailability, affinity and interaction of secondary metabolite compounds of L. acidissima fruit against HER2 receptor in silico

Dr. Duke's Phytochemical and Ethnobotanical databases

to search for secondary metabolites of plants

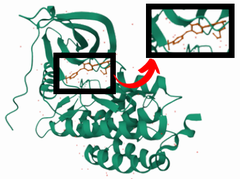
Knapsack Family

to search for secondary metabolites of plants



Molecular Docking

to see the prediction of affinity and interaction secondary metabolite compounds of L. acidissima against HER-2 target receptor



HER2

3PP0
target protein in the form of HER2 receptor obtained from the Protein Data Bank (PDB) webserver. 3PP0 is an x-ray protein found in the Protein Data Bank (PDB)

Secondary Metabolite

Ligands in the form of secondary metabolite compounds of L. acidissima plants obtained from the PubChem webserver. then obtained 31 secondary metabolite compounds tested using the SwissADME webserver

Secondary Metabolite

Compound Name

7-Methylporiol-Beta-D-Xylopyranosyl-D-Glucopyranoside
Ascorbic-Acid
Aurapten
Bergapten
Eo
Estragole
Isopimpinellin
Marmesin
Orientin
Pectin
Psoralen
Riboflavin
Stigmasterol
Ursolic-acid
Vitexin
Nb-Acetyl-Nb-methyltryptamine
Limodissimin A
Integriquinolone
Dihydroxyacidissiminol
Dihydrosuberenol
Acidissiminol epoxide
Acidissiminol
Acidissiminin epoxide
Acidissiminin
Acidissimin
9'',10''-didehydrodihydroxyacidissiminin
9'',10''-Didehydroacidissiminin epoxide
10,20-Dihydroxyeicosanoic acid
1-(1H-Indol-3-yl)-3-methyl-2,3-butanediol

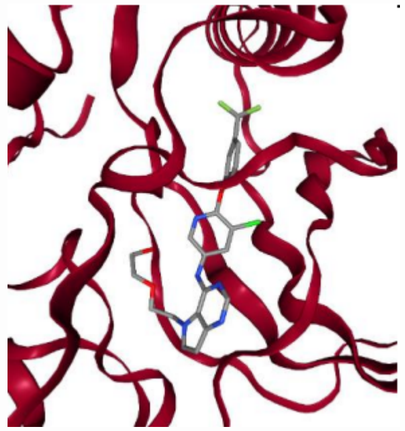
No.	Kode Senyawa	Jumlah Cluster	Jumlah Pose dalam Cluster Terbesar	Binding Energy (Kkal/Mol)	pKi (Prediksi Konstanta Inhibisi)
1	P1	21	25	-9.84	60.87 nM
2	P2	14	27	-3.38	3.34mm
3	P3	19	35	-6.22	27.36 uM
4	mol2	12	31	-4.55	461.86µm
5	mol3	11	61	-9.34	143.57nm
6	mol4	5	61	-6.1	33.61 µm
7	mol5	3	78	-8.34	769.04nm
8	mol6	4	50	-5.24	144.77 µm
9	mol7	4	48	-6.2	28.31 µm
10	mol8	2	99	-7.52	3.08 µm
11	mol11	4	67	-6.6	14.63 µm
12	mol16	9	63	-7.23	5 µm
13	mol17	5	52	-10.16	35.69nm
14	mol18	9	38	-5.64	73.66 µm
15	mol19	26	28	-10.08	40.97nm
16	mol20	7	22	-7.56	2.89 µm
17	mol21	23	23	-10.12	38.47nm
18	mol22	17	25	-10.42	23.07nm
19	mol25	2	50	-5.12	178.03 µm
20	mol28	28	17	-6.26	25.84 µm
21	mol29	15	26	-6.99	7.52 µm
22	mol30	5	86	-7.92	1.58 µm
23	mol31	3	87	-7.85	1.77 µm

ANALYSIS RESULT

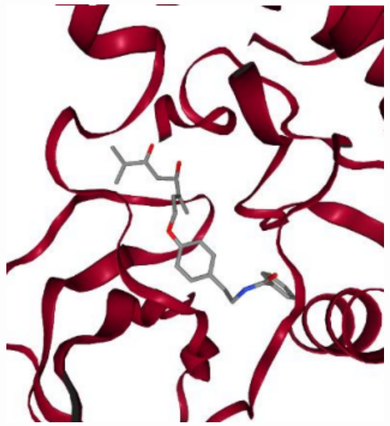
Compound Name	Binding Energy (Kkal/Mol)	Inhibition Constant (Ki)
Acidissiminol	-10.42	23.07nM
Limodissimin A	-10.16	35.69nM
Acidissiminol epoxide	-10.12	38.47nM
Dihydroxyacidissiminol	-10.08	40.97nM
SYR127063	-9.84	60.87nM

Compounds with the Same Binding Energy and Predicted Inhibition Constants or Less than Positive Control

DOCKING RESULT



a



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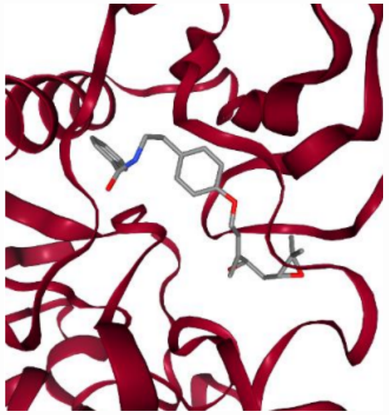

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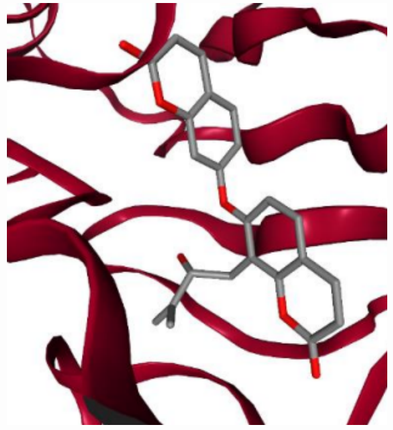

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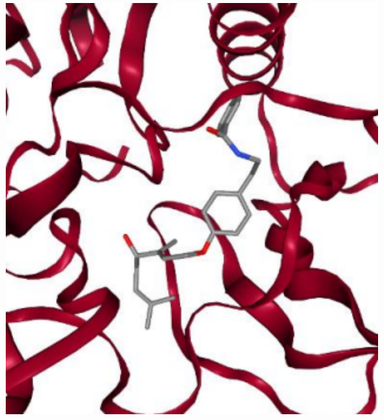
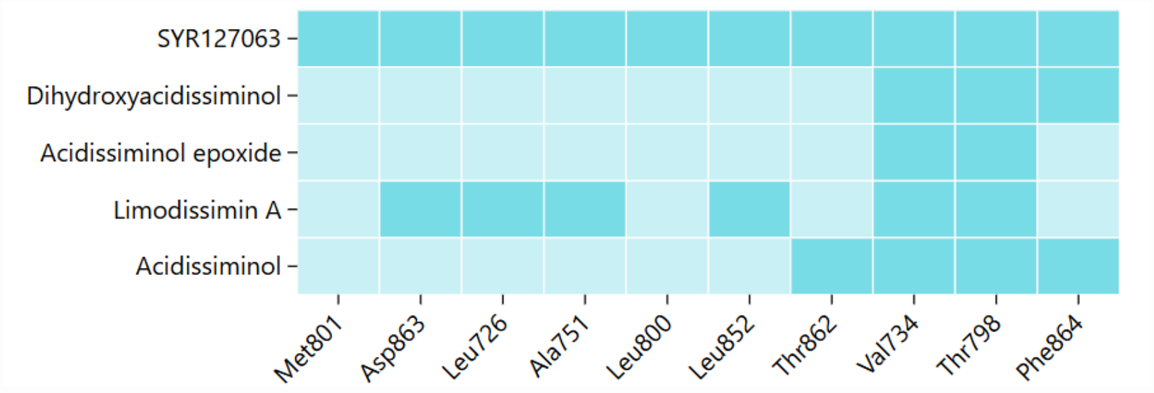


e

Visualization of docking results of positive control and secondary metabolite compounds of L. acidissima plant against HER2 receptor (3PP0) :
(a) SYR127063,
(b) Dihydroxyacidissiminol,
(c) Acidissiminol epoxide,
(d) Limodissimin A,
(e) Acidissiminol



CONCLUSION

01 Based on the research results obtained, of the 31 secondary metabolite compounds of Limonia acidissima plants, 20 compounds are predicted to have a good bioavailability profile.

02 There are 4 compounds, namely limodissimin A, dihydroxyacidissiminol, acidissiminol and acidissiminol epoxide which are predicted to have potential affinity as HER-2 positive breast anticancer.

03 There are 8 compounds namely aurapten, bergapten, isopimpinellin, marmesin, limodissimin A, intergriquinolone, acidissimin and 10,20-dihydroxyeicosanoic acid which are predicted to have the same interaction with SYR127063 as HER-2 positive breast anticancer.

THANK YOU FOR YOUR ATTENTION