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Lampiran 1. Tabel nilai afinitas pengikatan (ΔG Binding) replikasi daun cocor bebek

Senyawa	ΔG Binding (kkal/mol) \pm SD									
	1YWN					6GL8				
	Rep 1	Rep 2	Rep 3	Rata-Rata	\pm SD	Rep1	Rep2	Rep 3	Rata-Rata	\pm SD
<i>Native Ligand</i>	-10,37	-10,37	-10,35	-10,36	0,04	-12,65	-12,66	-12,68	-12,66	0,02
Kalanchoside A	-7,48	-7,4	-7,43	-7,44	0,04	4022,18	4051,59	4066,37	4046,71	22,50
Kalanchoside B	-7,47	-7,44	-7,41	-7,44	0,03	-4,64	-4,66	-4,64	-4,65	0,01
Kalanchoside C	-6,58	-6,53	-6,45	-6,52	0,07	-5,71	-5,68	-5,03	-5,47	0,38
Thesiuside	-6,33	-7,33	-7,42	-7,03	0,61	-4,86	-4,61	-4,7	-4,72	0,13
Hellebrigenin	-7,32	-7,33	-7,34	-7,33	0,01	-6,32	-6,32	-6,32	-6,32	0,00
Hellebrigenin-3-acetate	-7,33	-7,25	-7,3	-7,29	0,04	-6,98	-6,95	-6,94	-6,96	0,02
Bryophyllin B	-6,48	-6,46	-6,94	-6,63	0,28	-7,42	-7,48	-7,43	-7,44	0,03
Myricitrin	-7,22	-7,21	-7,27	-7,23	0,03	-4,38	-4,71	-4,56	-4,55	0,17
Bersaldegenin-1,3,5- orthoacetate	-6,26	-6,26	-6,25	-6,26	0,01	-6,09	-6,09	-6,09	-6,09	0,00
Quercetin 3-O-alpha-L-rhamnopyranoside	-7,78	-7,77	-7,78	-7,78	0,01	-8,17	-8,17	-8,17	-5,99	0,04
Bufalin	-7,65	-7,9	-7,65	-7,73	0,14	-8,17	-8,17	-8,17	-8,17	0,00
1 β -hydroxylbufalin	-6,79	-6,72	-6,72	-6,74	0,040	-6,44	-6,44	-6,46	-6,45	0,01
12β-hydroxylbufalin	-7,55	-7,56	-7,55	-7,55	0,02	-7,7	-7,63	-7,63	-7,65	0,04
Dihydroquercetin	-7,54	-7,53	-7,55	-7,54	0,01	-5,05	-5,05	-5,05	-5,05	0,00
Kontrol Negatif	-4,69	-4,69	-4,69	-4,690	0,000	-3,91	-3,93	-3,91	-3,917	0,012

<i>ΔG Binding (kkal/mol)±SD</i>										
Senyawa	3POZ					4L6S				
	Rep 1	Rep 2	Rep 3	Rata-Rata	±SD	Rep1	Rep2	Rep 3	Rata-Rata	±SD
<i>Native Ligand</i>	-10,02	-9,93	-9,96	-9,970	0,046	-10,47	-10,47	-10,46	-10,467	0,006
Kalanchoside A	-3,83	-5,13	-4,35	-4,437	0,654	-3,3	-3,33	-3,31	-3,313	0,015
Kalanchoside B	-6,58	-6,57	-5,57	-6,240	0,580	-3,15	-3,17	-3,15	-3,157	0,012
Kalanchoside C	-7,76	-7,76	-7,77	-7,763	0,006	-9,27	-9,27	-9,27	-9,270	0,000
Thesiuside	-7,16	-6,94	-7,09	-7,063	0,112	-7,51	-7,52	-7,52	-7,517	0,006
Hellebrigenin	-8,64	-8,63	-8,64	-8,637	0,006	-9,85	-9,88	-9,87	-9,867	0,015
Hellebrigenin-3-acetate	-7,95	-7,95	-7,95	-7,950	0,000	-9,91	-9,93	-9,93	-9,923	0,012
Bryophyllin B	-7,71	-7,73	-7,72	-7,720	0,010	-10,22	-10,23	-10,26	-10,237	0,021
Myricitrin	-7,99	-7,97	-7,98	-7,980	0,010	-9,04	-9,04	-9,05	-9,043	0,006
Bersaldegenin-1,3,5- orthoacetate	-8,07	-8,07	-8,08	-8,073	0,006	-5,09	-5,09	-5,07	-5,083	0,012
Quercetin 3-O-alpha-L-rhamnopyranoside	-7,84	-7,86	-7,88	-7,860	0,020	-10,17	-10,05	-10,27	-10,163	0,110
Bufalin	-9,09	-9,09	-9,08	-9,087	0,006	-11,59	-11,59	-11,59	-11,590	0,000
1β-hydroxybufalin	-10,46	-10,45	-10,45	-10,453	0,006	-9,65	-9,67	-9,67	-9,663	0,012
12β-hydroxybufalin	-8,8	-8,83	-8,81	-8,813	0,015	-9,53	-9,55	-9,53	-9,537	0,012
Dihydroquercetin	-7,32	-7,3	-7,32	-7,313	0,012	-7,94	-7,94	-7,96	-7,947	0,012
Kontrol Negatif	-5,51	-5,5	-5,51	-5,507	0,006	-5,56	-5,57	-5,56	-5,563	0,006

<i>ΔG Binding (kkal/mol)±SD</i>										
Senyawa	4L23					4HVB				
	Rep 1	Rep 2	Rep 3	Rata-Rata	±SD	Rep1	Rep2	Rep 3	Rata-Rata	±SD
<i>Native Ligand</i>	-8,83	-8,84	-8,83	-8,833	0,006	-10,56	-10,56	-10,55	-10,557	0,006
Kalanchoside A	-4,7	-4,88	-4,8	-4,793	0,090	-6,37	-6,39	-6,37	-6,377	0,012
Kalanchoside B	-4,7	-4,68	-4,65	-4,677	0,025	-6,37	-6,37	-6,37	-6,370	0,000
Kalanchoside C	-5,23	-5,28	-5,24	-5,250	0,026	-6,65	-6,69	-6,66	-6,667	0,021
Thesiuside	-6,39	-6,41	-6,39	-6,397	0,012	-7,55	-7,57	-7,55	-7,557	0,012
Hellebrigenin	-6,89	-6,9	-6,88	-6,890	0,010	-7,64	-7,68	-7,66	-7,660	0,020
Hellebrigenin-3-acetate	-7,11	-7,13	-7,13	-7,123	0,012	-8,18	-8,17	-8,17	-8,173	0,006
Bryophyllin B	-6,47	-6,49	-6,46	-6,473	0,015	-8,95	-8,98	-8,95	-8,960	0,017
Myricitrin	-8,89	-8,54	-9,01	-8,813	0,244	-7,32	-7,35	-7,33	-7,333	0,015
Bersaldegennin-1,3,5-orthoacetate	-8,77	-8,77	-8,77	-8,770	0,000	-8,78	-8,78	-8,78	-8,780	0,000
Quercetin 3-O-alpha-L-rhamnopyranoside	-8,96	-8,82	-8,93	-8,903	0,074	-7,89	-7,9	-7,9	-7,897	0,006
Bufalin	-10,59	-10,59	-10,59	-10,590	0,000	-10,64	-10,65	-10,65	-10,647	0,006
1β-hydroxybufalin	-8,21	-8,23	-8,24	-8,227	0,015	-7,78	-7,75	-7,77	-7,767	0,015
12β-hydroxybufalin	-9,75	-9,77	-9,80	-9,773	0,025	-10,16	-10,18	-10,18	-10,173	0,012
Dihydroquercetin	-8,34	-8,36	-8,36	-8,353	0,012	-7,51	-7,54	-7,52	-7,523	0,015
Kontrol Negatif	-4,83	-4,83	-4,83	-4,830	0,000	-5,33	-5,33	-5,34	-5,333	0,006

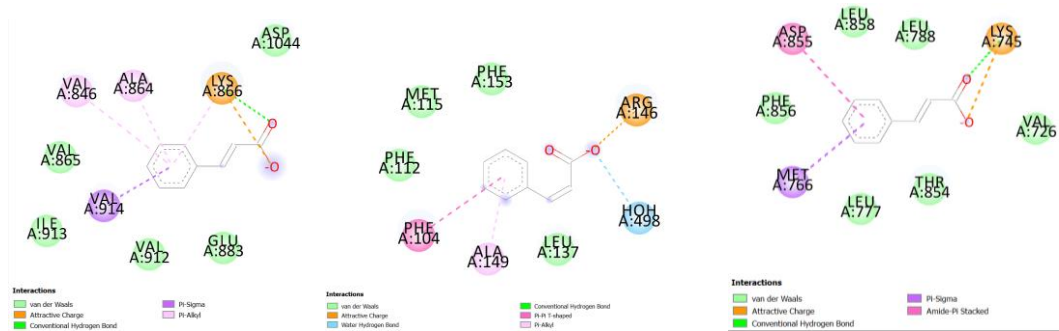
<i>ΔG Binding (kkal/mol)±SD</i>										
Senyawa	4W4Y					3L8X				
	Rep 1	Rep 2	Rep 3	Rata-Rata	±SD	Rep1	Rep2	Rep 3	Rata-Rata	±SD
<i>Native Ligand</i>	-10,84	-10,84	-10,83	-10,837	0,006	-9,99	-9,99	-9,99	-9,990	0,000
Kalanchoside A	-2,14	-2,14	-2,16	-2,147	0,012	1,11	1,15	1,13	1,130	0,020
Kalanchoside B	-1,87	-1,88	-1,86	-1,870	0,010	1,61	1,61	1,61	1,610	0,000
Kalanchoside C	-1,89	-1,89	-1,88	-1,887	0,006	-7,32	-7,32	-7,35	-7,330	0,017
Thesiuside	2,06	2,08	2,06	2,067	0,012	-6,8	-6,83	-6,82	-6,817	0,015
Hellebrigenin	-6,06	-6,08	-6,05	-6,063	0,015	-9,86	-9,86	-9,99	-9,903	0,075
Hellebrigenin-3-acetate	-3,76	-3,78	-3,78	-3,773	0,012	-8,75	-8,74	-8,75	-8,747	0,006
Bryophyllin B	-4,8	-4,83	-4,83	-4,820	0,017	-7,23	-7,25	-7,28	-7,253	0,025
Myricitrin	-6,56	-6,57	-6,55	-6,560	0,010	-7,89	-7,88	-7,88	-7,883	0,006
Bersaldegenin-1,3,5-orthoacetate	-6,32	-6,32	-6,33	-6,323	0,006	-6,11	-6,13	-6,13	-6,123	0,012
Quercetin 3-O-alpha-L-rhamnopyranoside	-6,55	-6,57	-6,57	-6,563	0,012	-6,99	-6,99	-6,96	-6,980	0,017
Bufalin	-6,33	-6,33	-6,33	-6,330	0,000	-8,53	-8,51	-8,54	-8,527	0,015
1β-hydroxylbufalin	-8,11	-8,13	-8,13	-8,123	0,012	-7,92	-7,93	-7,95	-7,933	0,015
12β-hydroxylbufalin	-5,67	-5,69	-5,69	-5,683	0,012	-7,71	-7,74	-7,72	-7,723	0,015
Dihydroquercetin	-7,19	-7,22	-7,2	-7,203	0,015	-7,87	-7,85	-7,88	-7,867	0,015
Kontrol Negatif	-5,46	-5,46	-5,47	-5,463	0,006	-5,18	-5,18	-5,18	-5,180	0,000

Lampiran 2. Tabel Hasil Validasi Metode Penambatan.

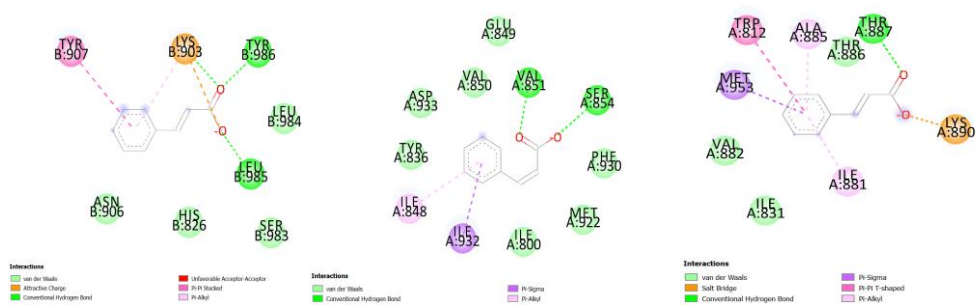
Makromolekul	RMSD (Å)				$\Delta G_{binding}$ (kkal/mol)			
	Rep 1	Rep 2	Rep 3	Rata-rata	Rep 1	Rep 2	Rep 3	Rata-rata \pm SD
1YWN	0,344	0,337	0,358	0,346	-10,37	-10,37	-10,35	-10,363 \pm 0,012
6GL8	0,140	0,102	0,103	0,115	-12,65	-12,66	-12,68	-12,663 \pm 0,015
3POZ	0,527	0,728	0,575	0,610	-10,02	-9,93	-9,96	-9,970 \pm 0,046
4L6S	0,342	0,350	0,342	0,342	-10,47	-10,47	-10,46	-10,467 \pm 0,006
4L23	0,000	0,001	0,000	0,000	-8,83	-8,84	-8,83	-8,833 \pm 0,006
4HVB	0,062	0,044	0,069	0,058	-10,56	-10,56	-10,55	-10,557 \pm 0,006
4W4Y	0,369	0,276	0,272	0,369	-10,84	-10,84	-10,83	-10,837 \pm 0,006
3L8X	0,552	0,550	0,548	0,550	-9,99	-9,99	-9,99	-9,990 \pm 0,000

Lampiran 3. Binding Site Kontrol negatif

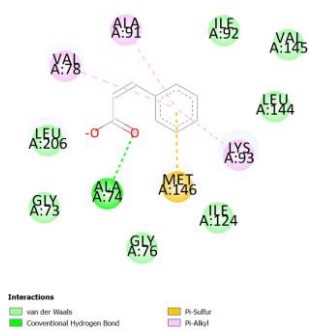
Cinnamic acid - (1YWN) *Cinnamic acid* - (6GL8) *Cinnamic acid* - (3POZ)



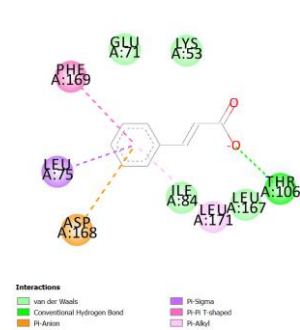
Cinnamic acid - (4L6S) *Cinnamic acid* - (4L23) *Cinnamic acid* - (4HVB)



Cinnamic acid - (4W4Y)



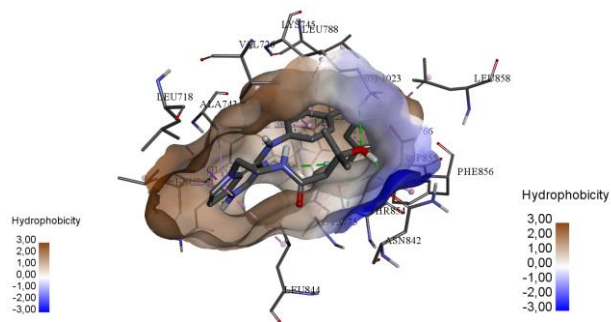
Cinnamic acid - (3L8X)



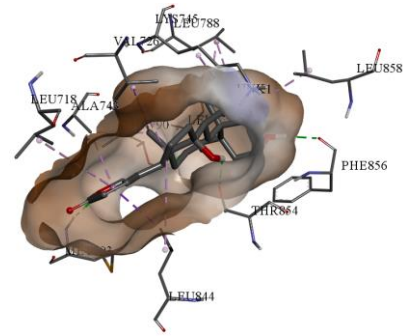
Lampiran 5. Interaksi ligan dan protein terpilih dalam ruang 3 dimensi

Epidermal growth factor receptor erbB1 (3POZ)

Native Ligand

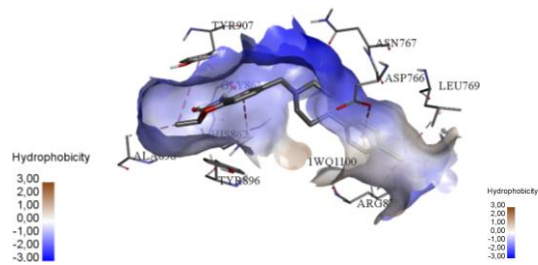


1 β -hydroxybufalin

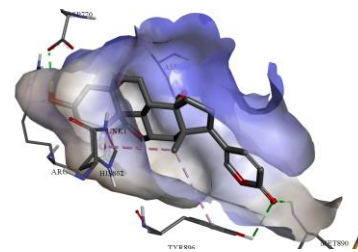


Poly(ADP-ribose) polymerase-1 (4L6S)

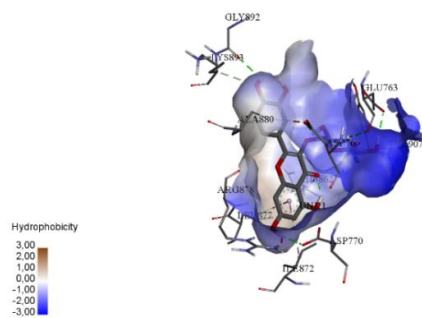
Native Ligand



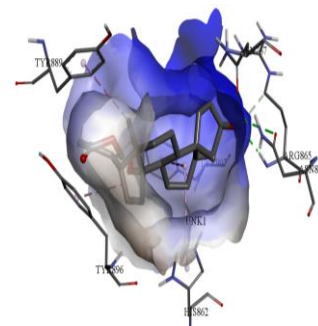
Bryophyllin B



Quercetin 3-O-alpha-L-rhamnopyranoside

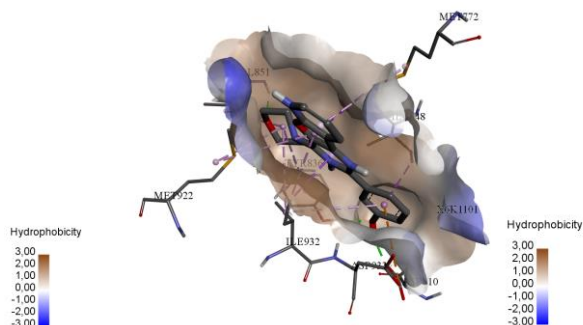


Bufalin

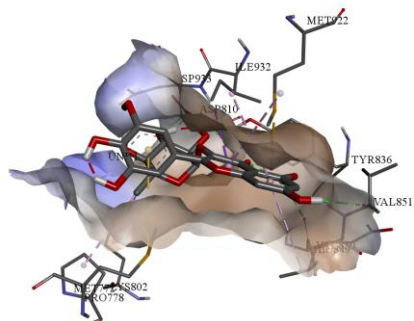


PI3K p110-alpha (4L23)

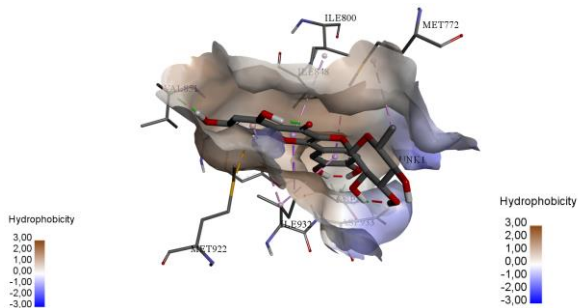
Native Ligan



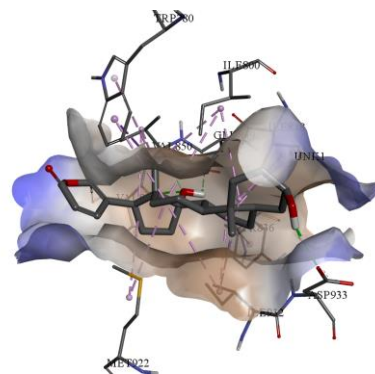
Myricitrin



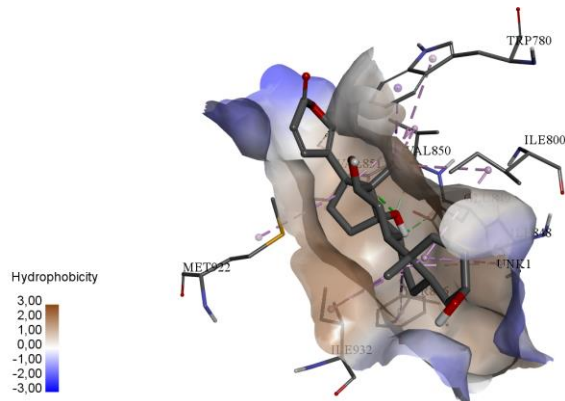
Quercetin 3-O-alpha-L-rhamnopyranoside

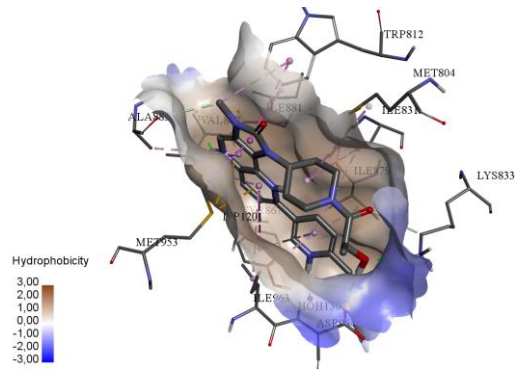
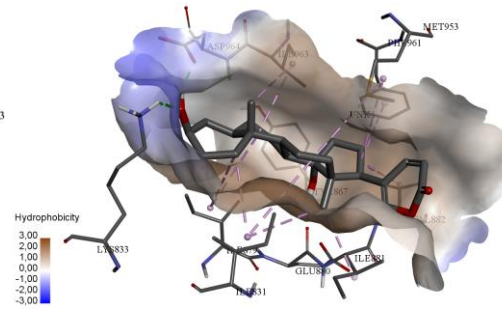
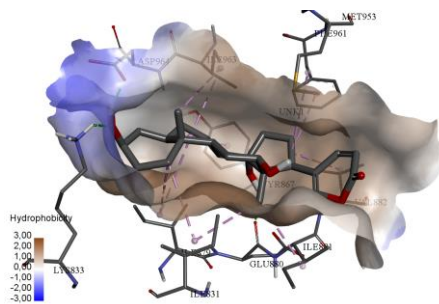
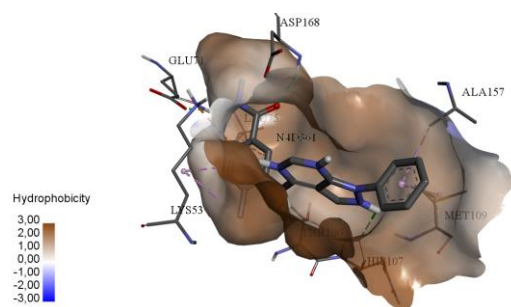
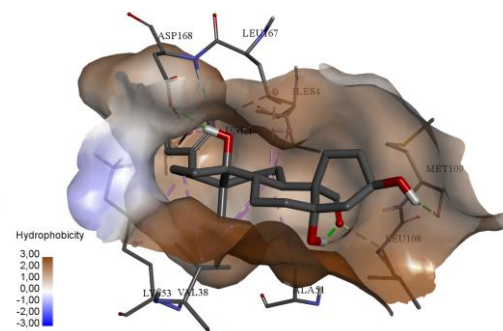


Bufalin

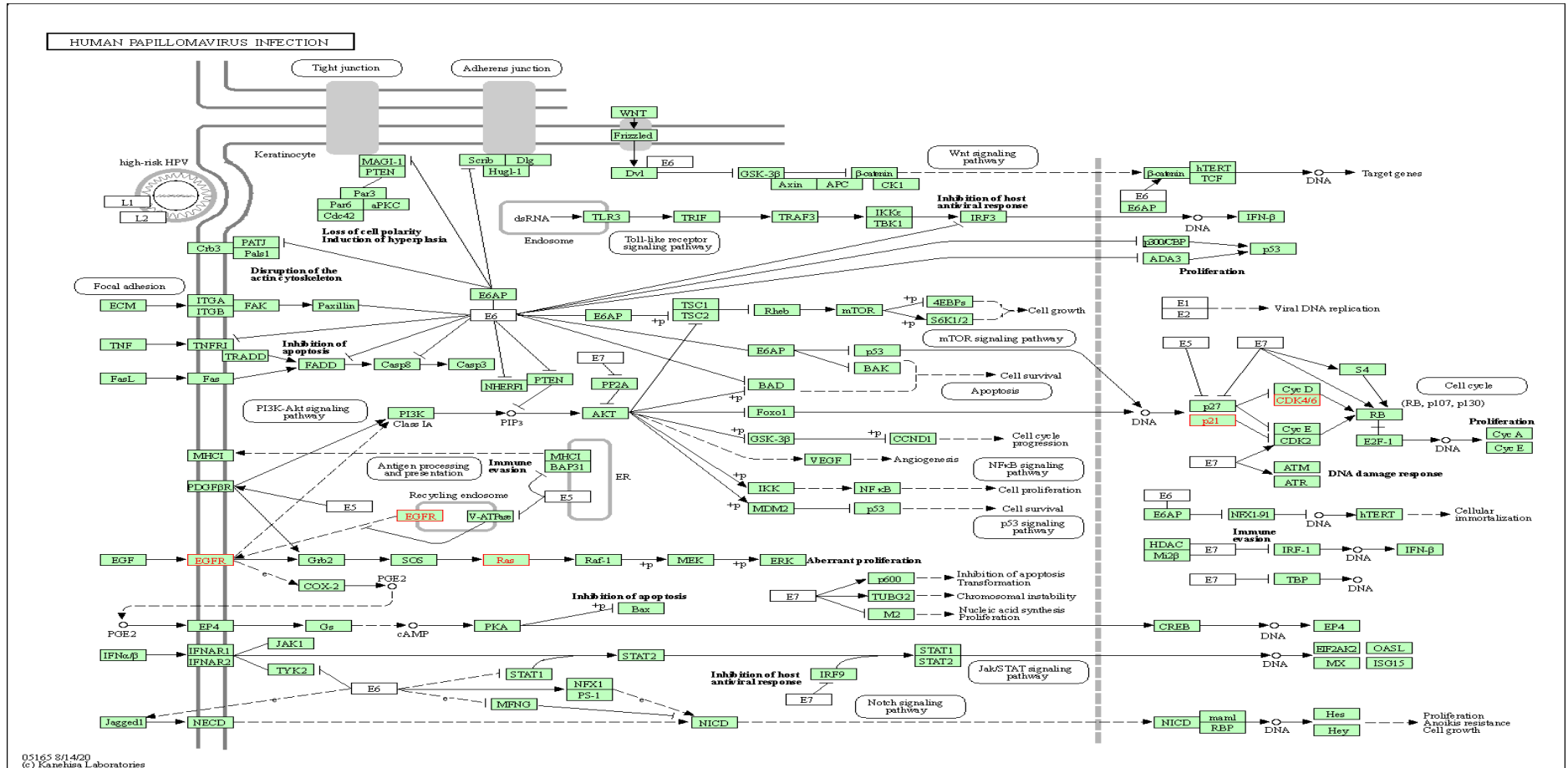


12β-hydroxybufalin



Serine/threonine-protein kinase mTOR (4HVB)*Native Ligand**Bufalin**12 β -hydroxybufalin****TNF-Alpha (3L8X)****Native Ligand**Hellebrigenin*

Lampiran 6. Pathway Kanker Serviks



Lampiran 7. Prosedur Penambatan Molekuler

1. Pencarian target makromolekul

Pencarian target molekuler dilakukan dengan screening awal terhadap struktur 3D tiap ligan uji menggunakan *SWISSPred* dan *SEA server* selanjutnya disesuaikan yang terdapat di KEGG pathway kanker serviks.



Webserver : Swiss Target Prediction

Query	Target Key	Target Name	Description	P-Value	MaxTC
compound_1	AT1A1_HUMAN	ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	1.259e-161	0.82
	AT1A1_MOUSE	ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	5.753e-84	0.82
	NOTCH1_MOUSE	Notch1	Neuronic locus notch homolog protein 1	1.648e-70	0.41
	AT1A1_HUMAN	ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	7.572e-61	0.82
	SDAC1_HUMAN	SLOCAC1	Solute carrier organic anion transporter family member 4C1	2.03e-54	0.47
	G6PD_HUMAN	G6PD	Glucose-6-phosphate 1-dehydrogenase	2.534e-53	0.43
	EPHA2_MOUSE	EphA2	Ephrin type-A receptor 2	2.259e-45	0.30
	SMT1_MOUSE	SMT1	Cycloartenol-C-24 methyltransferase	2.969e-41	0.35
	AT1A3_RAT	Alp1A3	Sodium/potassium-transporting ATPase subunit alpha-3	9.226e-36	0.82
	G6PDG1_RTRIP	g6pd	Glucose-6-phosphate 1-dehydrogenase	2.716e-34	0.43
	AT1A2_RAT	Alp1A2	Sodium/potassium-transporting ATPase subunit alpha-2	2.106e-32	0.82
	GERAA_RAT	CalcA4	Gamma-aminobutyric acid receptor subunit alpha-4	4.834e-32	0.49
	CBQ_HUMAN	SEPPIN6B	Corticosteroid-binding globulin	2.833e-30	0.43
	SH4B_RAT	SH4B2	OMP-N-acetylneuraminic-beta-galactosaminide-alpha-2,3-sialyltransferase 2	8.427e-30	0.29
	GPR94_HUMAN	GPR94	G-protein coupled bile acid receptor 1	3.156e-27	0.43
	SHBG_RAT	Shbg	Sex hormone-binding globulin	1.248e-24	0.30
	AT1A4_RAT	Alp1A4	Sodium/potassium-transporting ATPase subunit alpha-4	1.007e-23	0.40
	AT1B1_RAT	Alp1B1	Sodium/potassium-transporting ATPase subunit beta-1	1.007e-23	0.40
	AT1A1_PIG	ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	1.313e-23	0.29
	SHBG_HUMAN	SHBG	Sex hormone-binding globulin	1.262e-22	0.43
IF4A1_MOUSE	EIf4a1	Eukaryotic initiation factor 4A1	1.521e-22	0.32	
NRX3_MOUSE	Nrx3	Nuclear receptor subfamily 1 group 1 member 3	1.903e-22	0.30	
CAHL_BOVIN	CA4	Carbonic anhydrase 4	7.227e-19	0.33	
NTCP2_HUMAN	SLC19A2	Real sodium/bile acid cotransporter	7.772e-16	0.33	

Webserver : Sea Search Server

Prediksi target molekuler terpilih

1. *VEGFR-2*
2. *Bcl-2*
3. *erbB1*
4. *PARP-1*
5. *PI3K-Alpha*
6. *mTOR*
7. *ERK-1*
8. *TNF- α*

2. Pengunduhan makromolekul target

Pengunduhan makromolekul melalui (<http://www.rcsb.org/pdb/>). Identitas molekul tersebut yaitu *VEGFR-2* dengan kode PDB 1YWN, *Bcl-2* dengan kode 6GL8, *erbB1* dengan kode 3POZ, *PARP-1* dengan kode 4L6S, *PI3K-Alpha* dengan kode 4L23, *mTOR* dengan kode 4HVB, *ERK-1* dengan kode 4W4Y, *TNF- α* dengan kode 3L8X. Data makromolekul diunduh dalam format .pdb dan disimpan dalam folder untuk masing-masing protein.

RCSB PDB Deposit - Search - Visualize - Analyze - Download - Learn - More - Documentation - MyPDB -

Structure Summary 3D View Annotations Experiment Sequence Genome Versions

Biological Assembly 1

1YWN
Vegfr2 in complex with a novel 4-amino-furo[2,3-d]pyrimidine
DOI: 10.2210/pdb1YWN/pdb
Classification: TRANSFERASE
Organism(s): Homo sapiens
Expression System: Spodoptera frugiperda
Mutation(s): Yes

Deposited: 2005-02-18 Released: 2005-08-23
Deposition Author(s): Miyazaki, Y., Matsunaga, S., Tang, J., Maeda, Y., Nakano, M., Philippe, R.J., Shibahara, M., Liu, W., Sato, H., Wang, L., Nolte, R.T.

Experimental Data Snapshot
Method: X-RAY DIFFRACTION
Resolution: 1.71 Å
R-Value Free: 0.239
R-Value Work: 0.205
R-Value Observed: 0.206

wwPDB Validation

Metric	Percentile Ranks	Value
Rfree		0.239
Clashscore		4
Ramachandran outliers		0.4%
Sidechain outliers		0.4%
RSRZ outliers		27.2%

This is version 1.3 of the entry. See complete history.

Literature

Novel 4-amino-furo[2,3-d]pyrimidines as Tie-2 and VEGFR2 dual inhibitors
Miyazaki, Y., Matsunaga, S., Tang, J., Maeda, Y., Nakano, M., Philippe, R.J., Shibahara, M., Liu, W., Sato, H., Wang, L., Nolte, R.T., (2005) *Bioorg Med Chem Lett* 16: 2203-2207
PubMed: 16837284
DOI: 10.1016/j.bmcl.2005.03.034
Primary Citation of Related Structures: 1YWN

PubMed Abstract:
[Novel Furo\[2,3-d\]pyrimidines, New potent and potent dual inhibitors of PDS and VEGFR2 receptor tyrosine kinases \(TK\) and a diarylurea moiety at 5-position shows remarkably enhanced activity against both enzymes. One of the most active compounds, 4-amino-3-\(4-\(2-fluoro-5-\(trifluoromethyl\)phenyl\)amino-carbonyl\(aminophenyl\)-2-\(4-methoxyphenyl\)furo\[2,3-d\]pyrimidine \(7k\) is ~3 nM on both TK receptors and the activity is rationalized based on the X-ray crystal structure ...](#)

RCSB PDB Deposit - Search - Visualize - Analyze - Download - Learn - More - Documentation - MyPDB -

Structure Summary 3D View Annotations Experiment Sequence Genome Versions

Biological Assembly 1

3POZ
EGFR Kinase domain complexed with tak-285
DOI: 10.2210/pdb3POZ/pdb
Classification: TRANSFERASE/TRANSFERASE INHIBITOR
Organism(s): Homo sapiens
Expression System: Antheraea
Mutation(s): No

Deposited: 2010-11-23 Released: 2011-03-30
Deposition Author(s): Aertgeerts, K., Skene, R., Sogabe, S.

Experimental Data Snapshot
Method: X-RAY DIFFRACTION
Resolution: 1.50 Å
R-Value Free: 0.243
R-Value Work: 0.219
R-Value Observed: 0.220

wwPDB Validation

Metric	Percentile Ranks	Value
Rfree		0.247
Clashscore		3
Ramachandran outliers		0.4%
Sidechain outliers		1.3%
RSRZ outliers		14.7%

This is version 1.1 of the entry. See complete history.

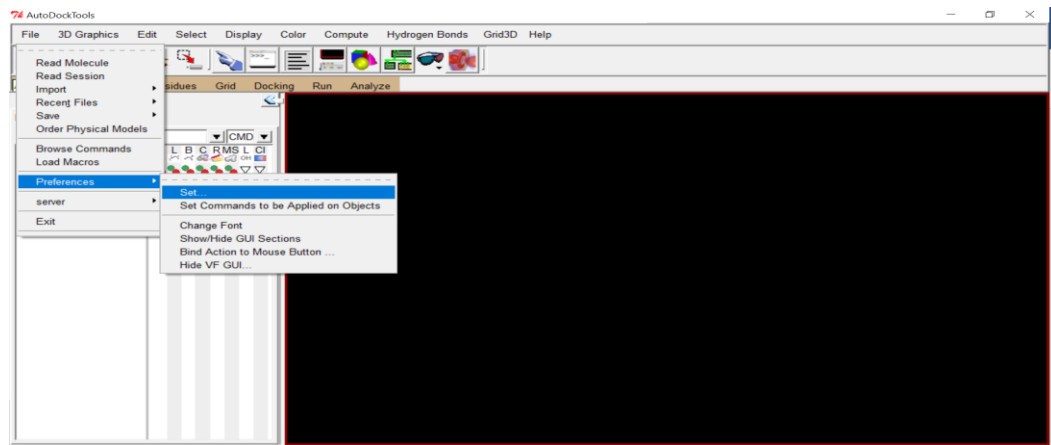
Literature

Structural Analysis of the Mechanism of Inhibition and Allosteric Activation of the Kinase Domain of HER2 Protein.
Aertgeerts, K., Skene, R., Yano, J., Sang, B.C., Zou, H., Snell, G., Jennings, A., Iwamoto, K., Habuka, N., Hirokawa, A., Ishikawa, T., Tanaka, T., Miki, H., Ohta, Y., Sogabe, S., (2011) *J Biol Chem* 286: 18756-18765
PubMed: 21454582
DOI: 10.1074/jbc.M110.206193
Primary Citation of Related Structures: 3PP0, 3POZ

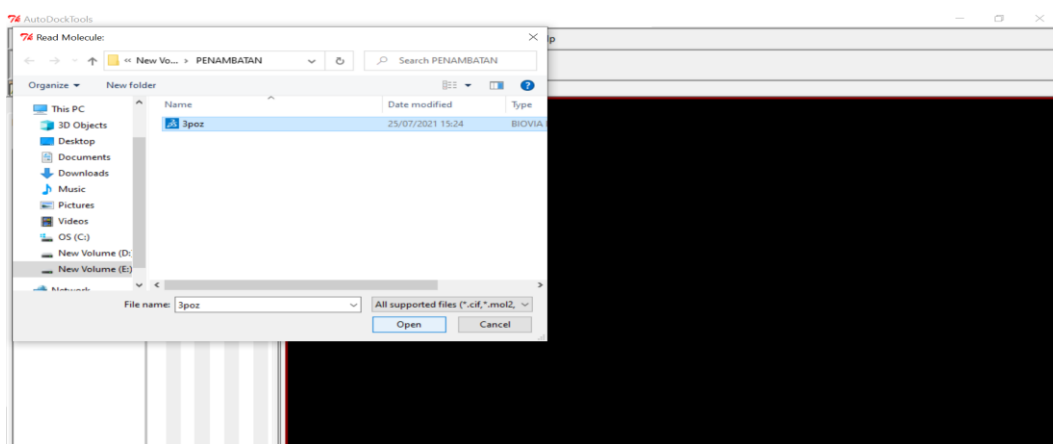
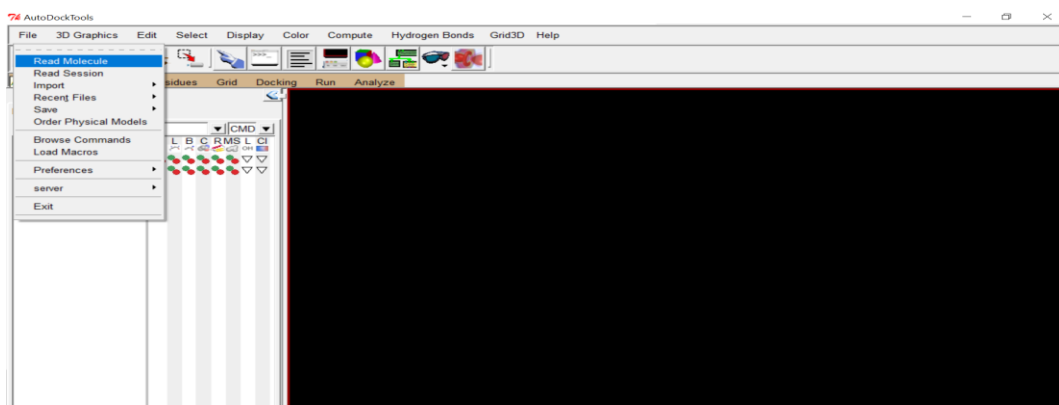
PubMed Abstract:
Aberrant signaling of ErbB family members human epidermal growth factor 2 (HER2) and epidermal growth factor receptor (EGFR) is implicated in many human cancers, and HER2 expression is predictive of human disease recurrence and prognosis. Small molecule kinase inhibitors of EGFR and of both HER2 and EGFR have received approval for the treatment of cancer ...

3. Pemisahan dan preparasi makromolekul dengan *native ligand*.

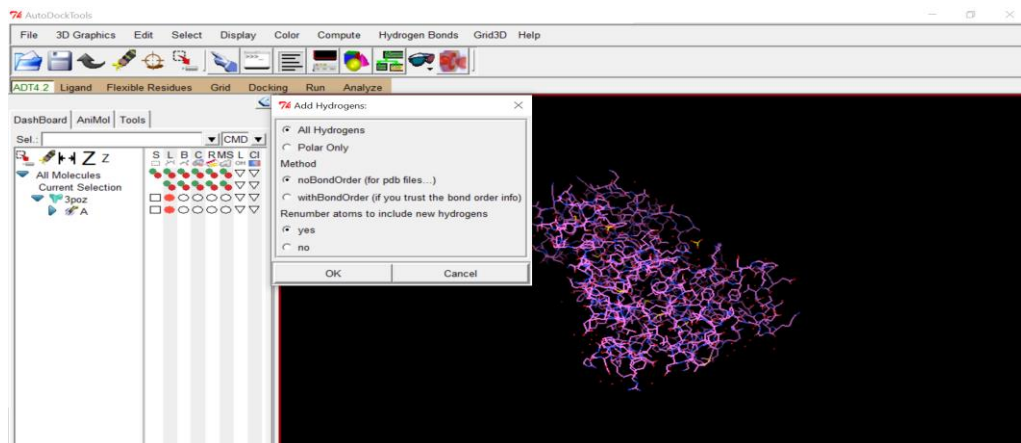
Pemisahan makromolekul protein dari pelarut dan ligan atau residu non standar dengan autodock tools. Disimpan dalam format .pdb.



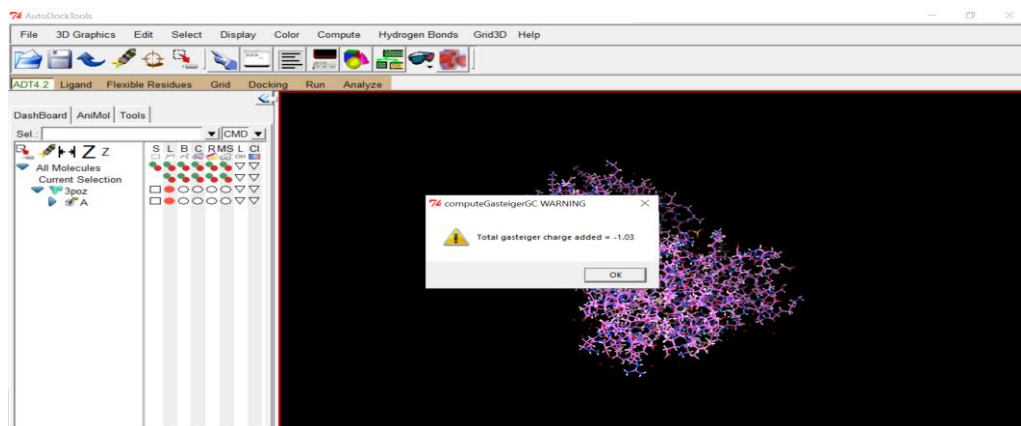
Set alamat folder makromolekul-File-Preference-Set



Klik *File-Open Molecule*-Dipilih makromolekul 3POZ

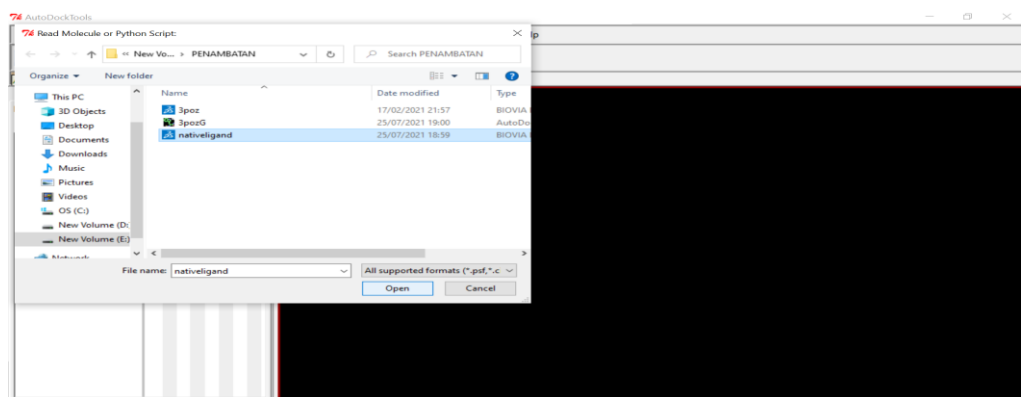


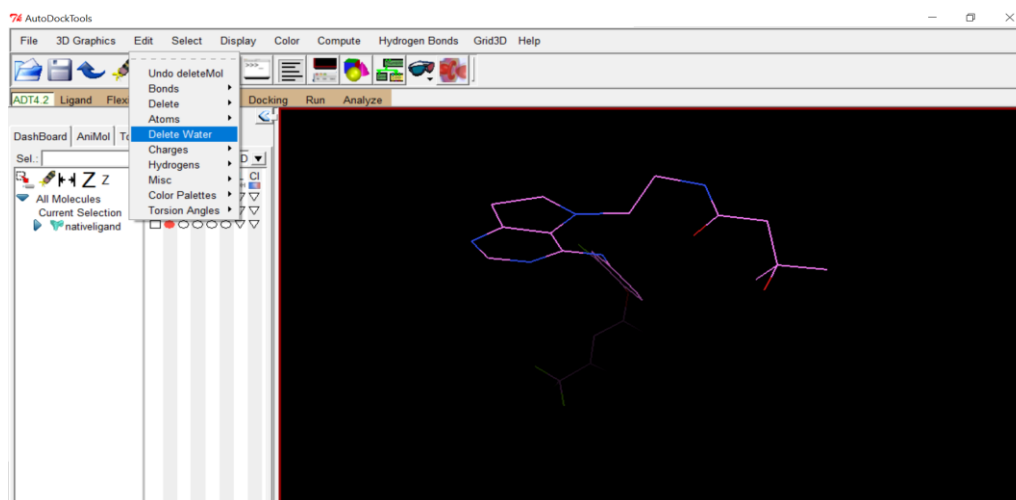
Edit-Add hydrogen-Add-Ok



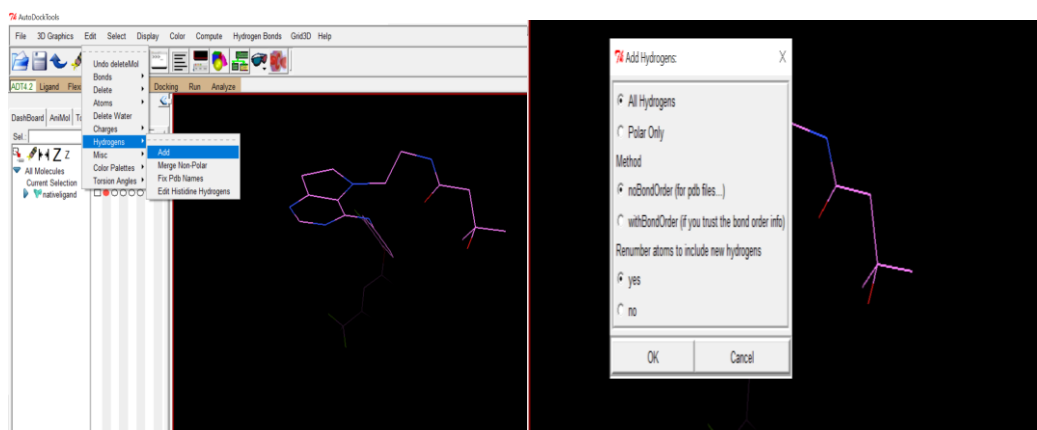
Edit-Charges-Compute gasteiger-Ok

➤ Preparasi *native ligand*

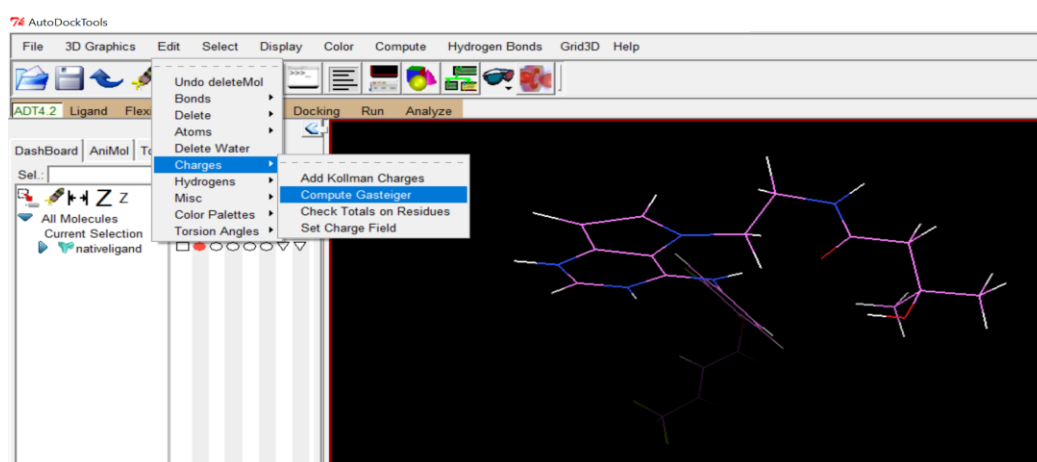
Membuka file *native ligand*-Read molecul-dipilih *native ligand*



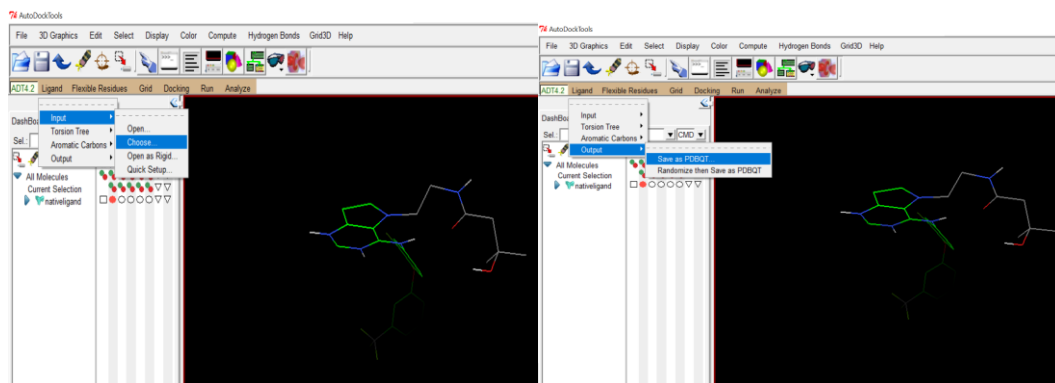
Edit-Delete water



Edit-Hydrogens-Add-Ok



Edit-Charges-Compute Gasteiger



Ligand-Output-Save as PDBQT

4. Penyiapan Struktur 3 dimensi Ligan Uji

Struktur ligan uji disiapkan dengan SMILES dari pubchem.

PubChem Bufalin (Compound)

2.1.4 Canonical SMILES ?

C2CCC(CC1CCC3C2CCC4(C3(CCC4C5=COC(=O)C=C5)O)C)O

Computed by OEChem 2.1.5 (PubChem release 2019.06.18)

2.1.5 Isomeric SMILES ?

C[C@]12CC[C@@H](C[C@H]1CC[C@@H]3[C@@H]2CC[C@]4([C@@]3(CC[C@@H]4C5=COC(=O)C=C5)O)C)O

Computed by OEChem 2.1.5 (PubChem release 2019.06.18)

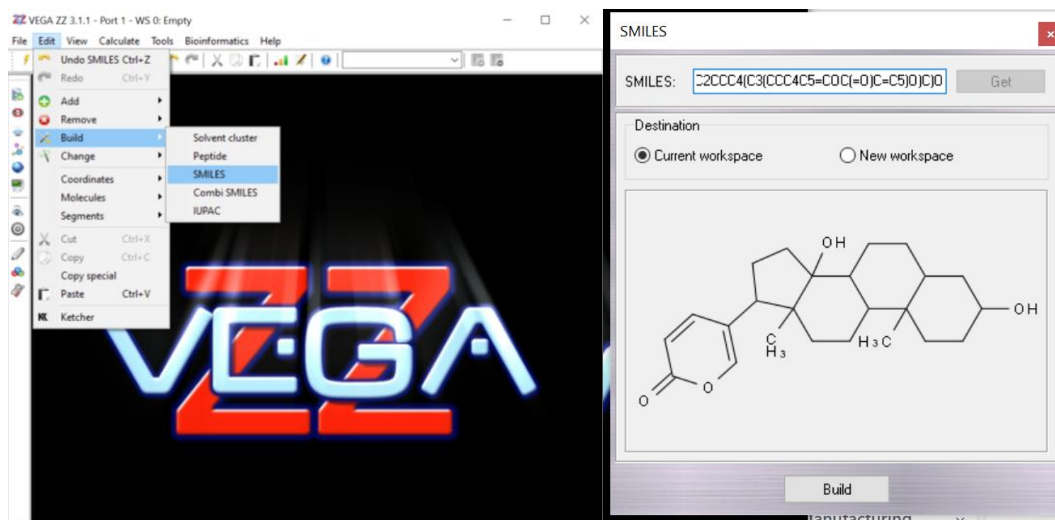
2.2 Molecular Formula ?

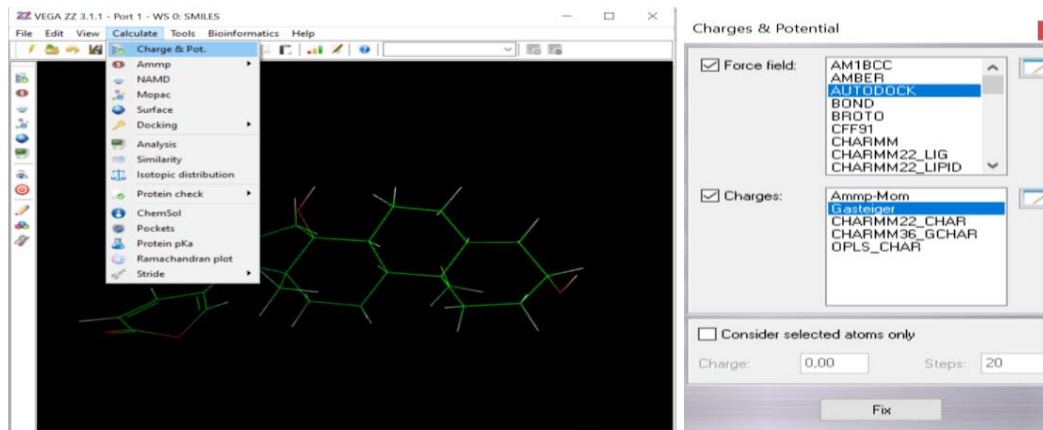
C₂₄H₃₄O₄

CONTENTS

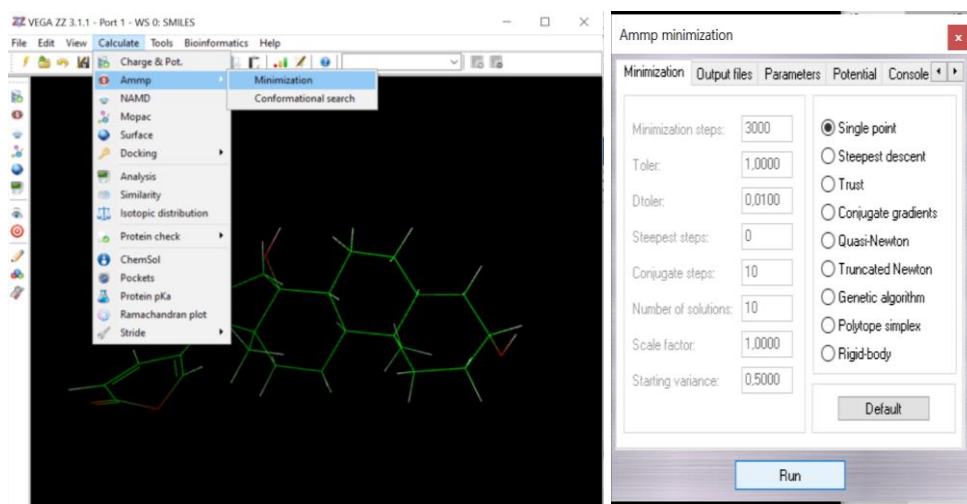
- Title and Summary
- 1 Structures
- 2 Names and Identifiers
- 3 Chemical and Physical Properties
- 4 Spectral Information
- 5 Related Records
- 6 Chemical Vendors
- 7 Pharmacology and Biochemistry
- 8 Use and Manufacturing
- 9 Safety and Hazards

Struktur ligan yang telah dibuat dioptimasi dengan VegaZZ





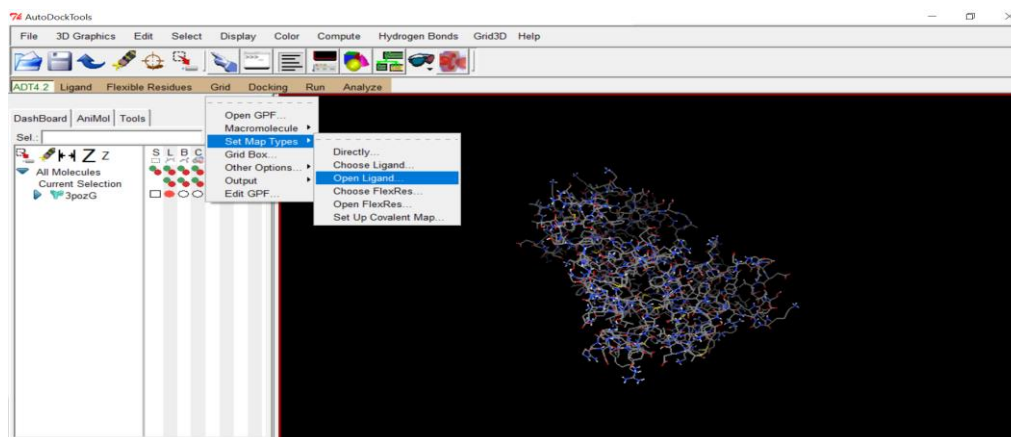
Pilih-*Calculate-Charge&Pot.-Pilih forcefield AUTODOCK-Charge Geisteger-Fix*



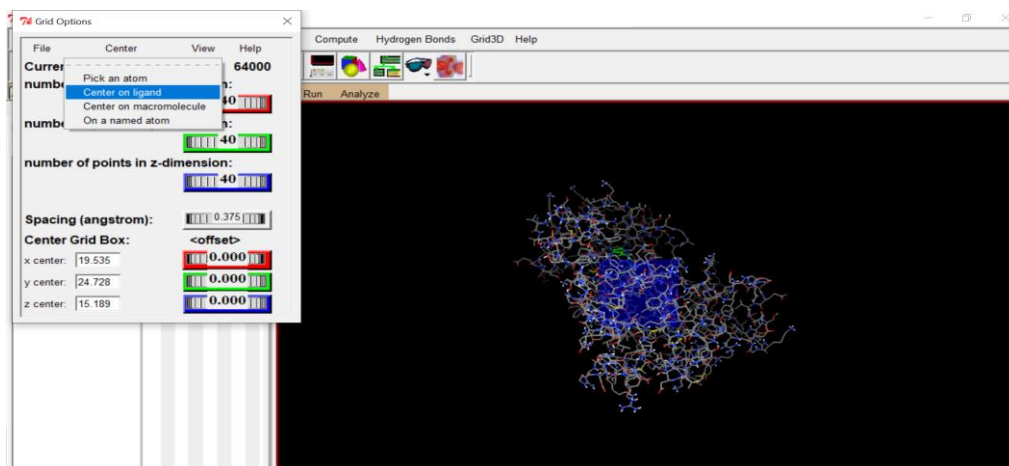
Pilih - *Calculate-Ammp-Minimization*

5. Penentuan *grid box* dari makromolekul.

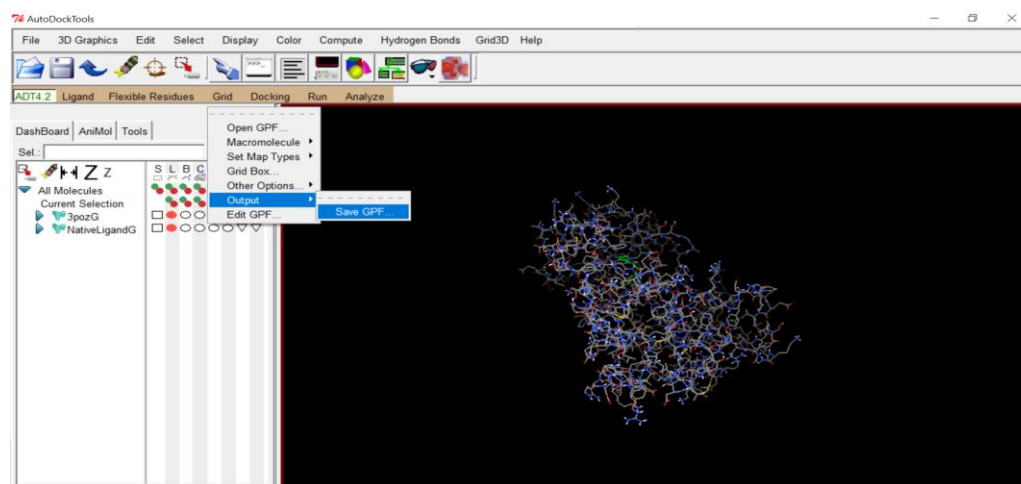
Grid box mengatur ruang bergerak ligan pada target



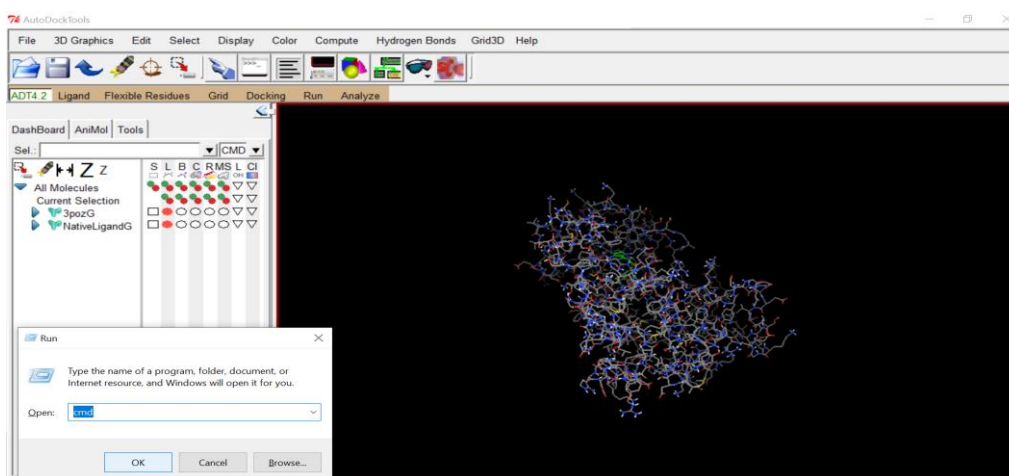
Grid- Macromolecul-Open-Set Map Types-Open Ligand



Dipilih grid-Gridbox-Center on Ligand-Close saving current-gpf.



Diklik Grid-Output-Save gpf.



Diklik windows+R- kemudian diketik cmd-Ok

```

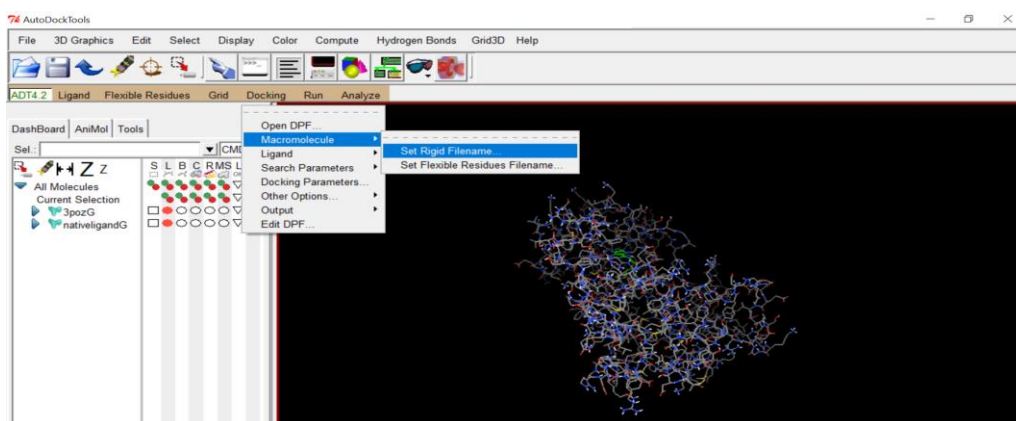
C:\WINDOWS\system32\cmd.exe - autogrid4.exe -p grid.gpf -l hasilgrid.glg
Microsoft Windows [Version 10.0.19042.1118]
(c) Microsoft Corporation. All rights reserved.
C:\Users\ASUS>E:
E:\>cd E:\PENAMBATAN
E:\PENAMBATAN>autogrid4.exe -p grid.gpf -l hasilgrid.glg

C:\WINDOWS\system32\cmd.exe
Microsoft Windows [Version 10.0.19042.1118]
(c) Microsoft Corporation. All rights reserved.
C:\Users\ASUS>E:
E:\>cd E:\PENAMBATAN
E:\PENAMBATAN>autogrid4.exe -p grid.gpf -l hasilgrid.glg
E:\PENAMBATAN>

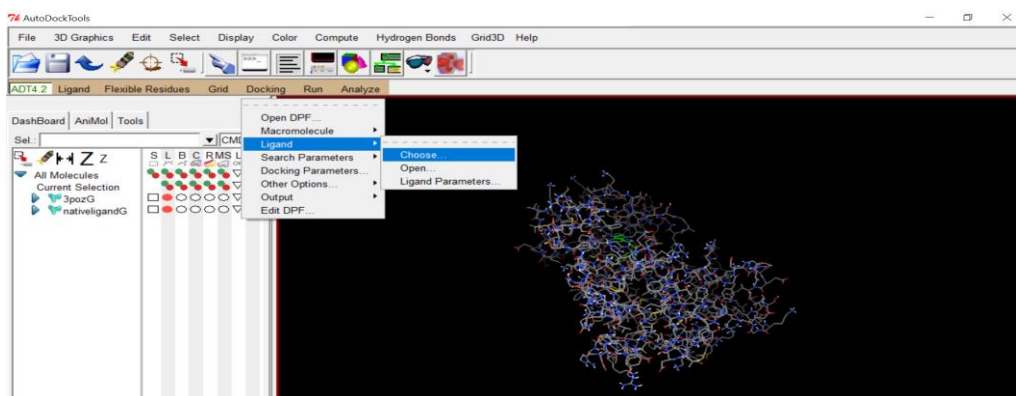
```

Proses grid selesai ditandai dengan kembali pada folder awal dan cmd.exe

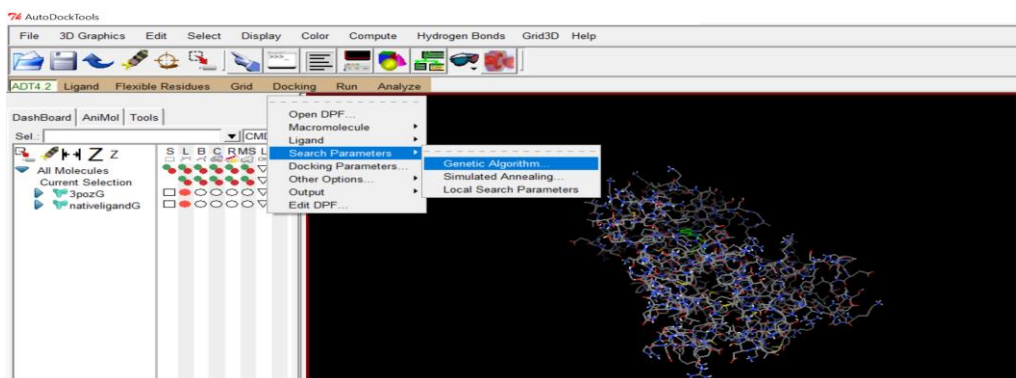
6. Validasi metode penambatan molekuler.



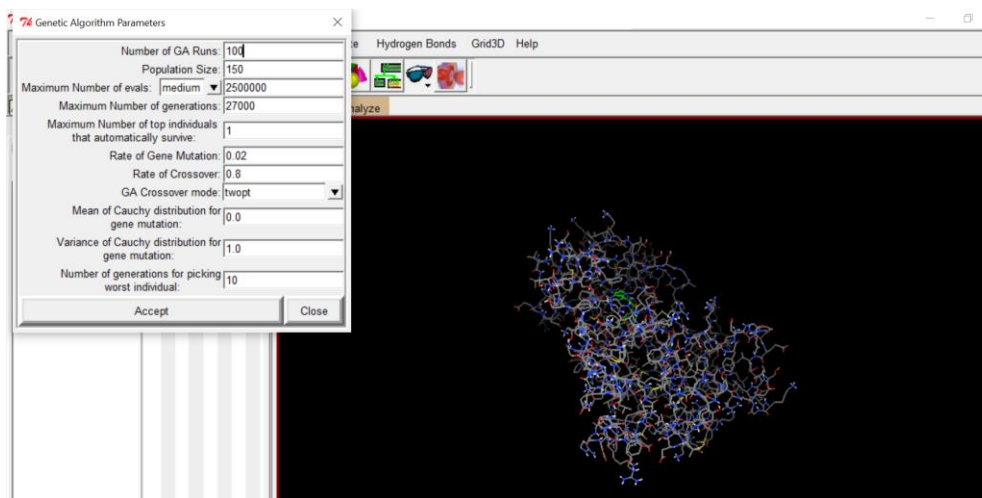
Docking- macromolecule- Set Rigit Filename



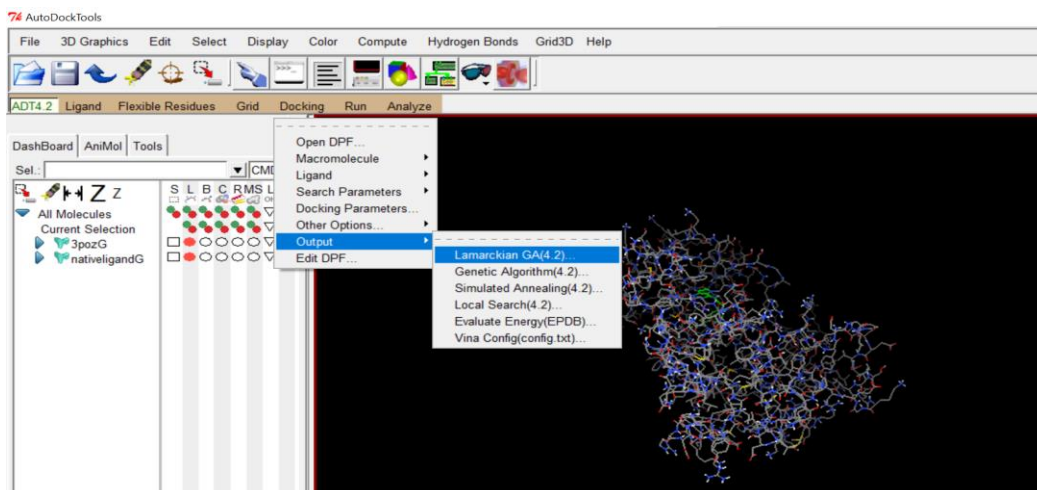
Docking-Ligand-Choose



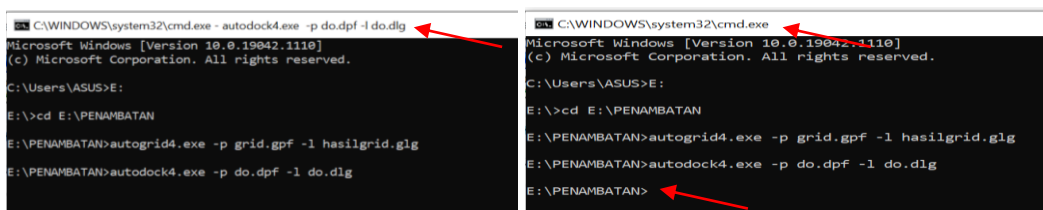
Docking-Search Parameters-Genetic Algorithm



Running di setting pada 100x dan population size 150.



Docking-Output-Lamarckian GA- dan file disimpan dengan format dpf.



Proses penambatan selesai ditandai dengan kembali pada folder awal dan cmd.exe

7. Analisis hasil penambatan molekuler

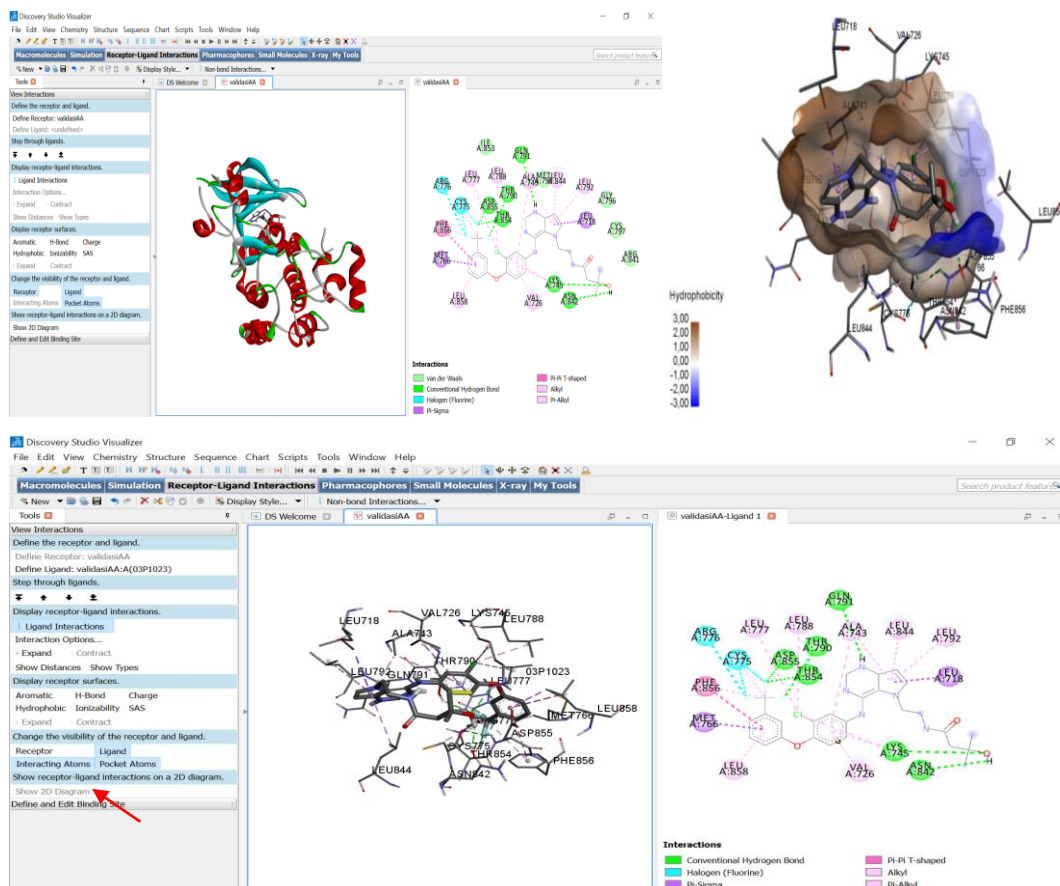
*do - Notepad
File Edit Format View Help
CLUSTERING HISTOGRAM

Clus-ter Rank	Lowest Binding Energy	Run	Mean Binding Energy	Num in Clus	Histogram							
					5	10	15	20	25	30	35	
1	-10.02	49	-8.94	37	#####	#####	#####	#####	#####	#####	#####	#####
2	-9.39	23	-8.29	18	#####	#####	#####	#####	#####	#####	#####	#####
3	-9.06	76	-9.06	1	##							
4	-8.82	64	-8.82	1	##							
5	-8.88	37	-8.01	4	####							
6	-8.48	46	-7.61	5	#####							
7	-8.48	45	-7.49	2	##							
8	-8.46	30	-8.46	1	##							
9	-8.02	13	-7.75	3	###							
10	-7.92	61	-7.58	8	#####							
11	-7.36	54	-7.36	1	##							
12	-7.21	56	-7.21	1	##							
13	-7.09	18	-6.90	7	#####							
14	-6.94	58	-6.39	2	##							
15	-6.88	9	-6.88	1	##							
16	-6.54	44	-6.54	1	##							
17	-6.45	63	-6.45	1	##							
18	-6.44	36	-6.44	1	##							
19	-6.11	83	-6.11	1	##							
20	-6.09	27	-6.09	1	##							
21	-5.78	1	-5.64	2	###							
22	-5.38	94	-5.38	1	##							

Number of multi-member conformational clusters found = 10, out of 100 runs.

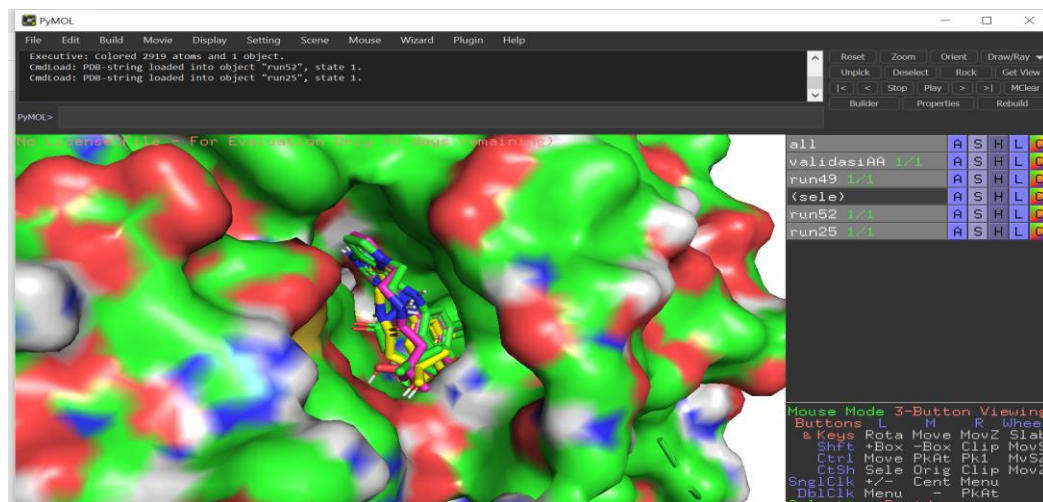
Energi binding terbaik dipilih pada *Num in Clus* terbanyak dan pada hasil *run*.

8. Visualisasi dengan PyMOL dan Discovery Studio Visualizer



Visualisasi dapat dilakukan secara 2D untuk mengetahui ikatan yang terjadi:

Klik show 2D Diagram-muncul 2D interaksi dan jenis ikatan yang terjadi



Pada PyMOL-dipilih-Surface