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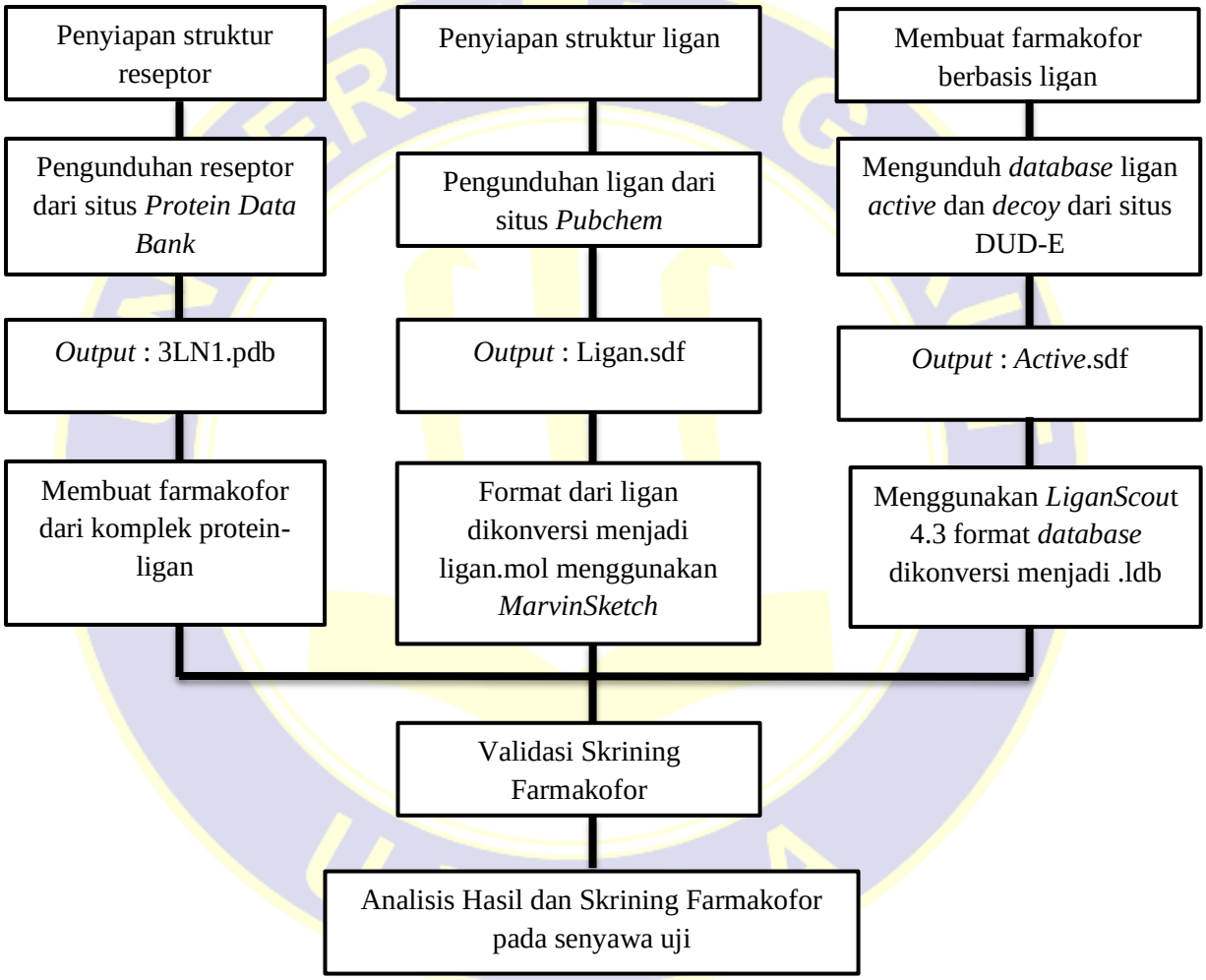
LAMPIRAN 1

ALUR PENELITIAN SKRINING FARMAKOFOR

Tabel IV.1

Alur Penelitian Skrining Farmakofor

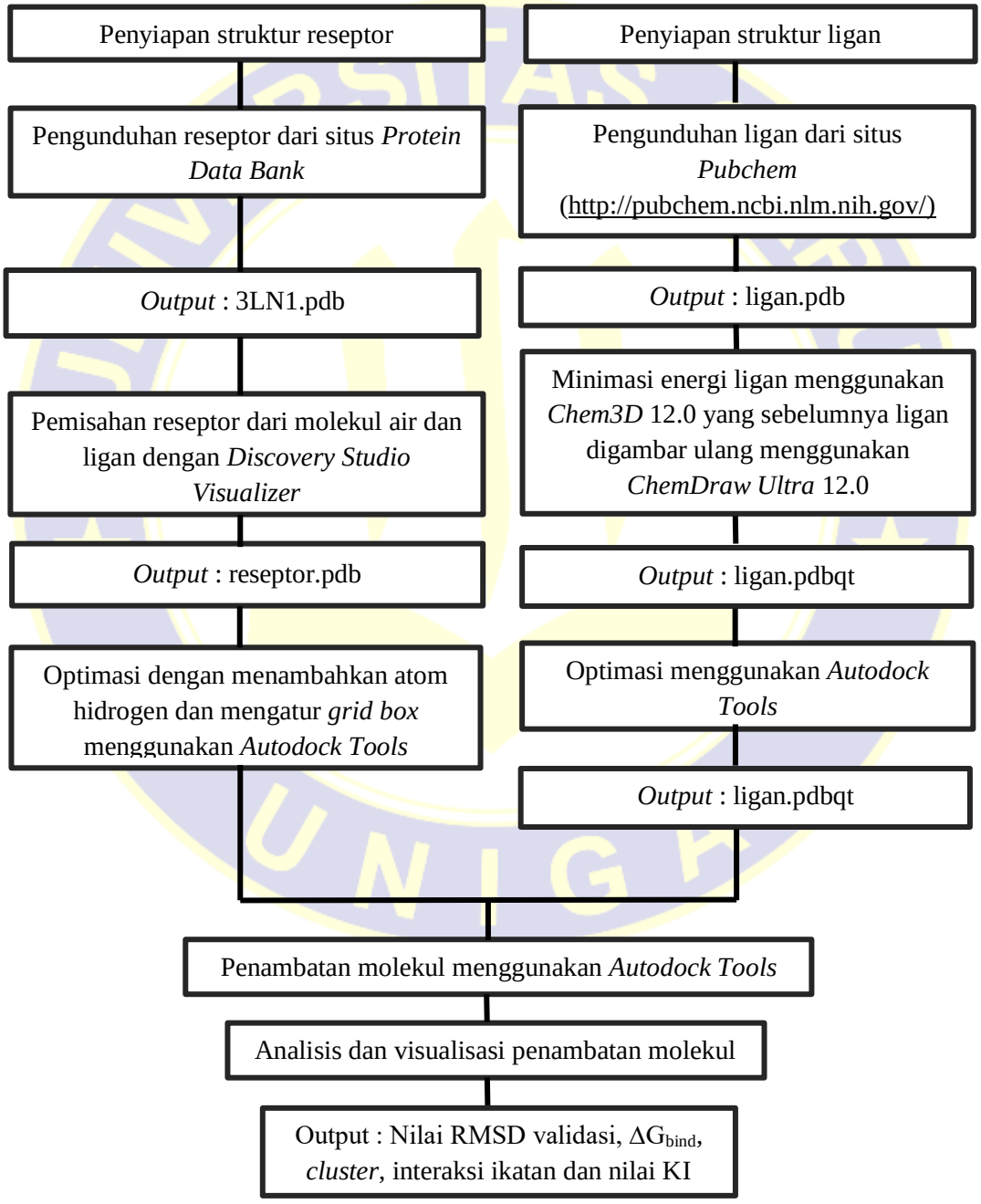


LAMPIRAN 2

ALUR PENELITIAN *MOLECULAR DOCKING*

Tabel IV.1

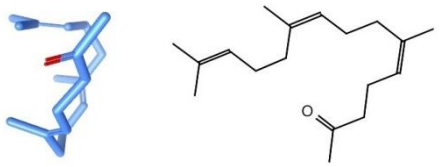
Alur Penelitian *Molecular Docking*



LAMPIRAN 3

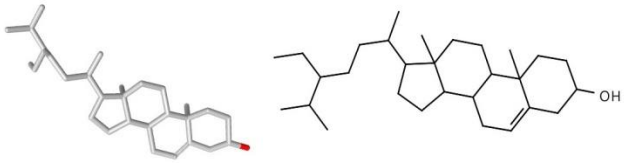
STRUKTUR 3D DAN 2D SENYAWA DAUN ASAM JAWA

1



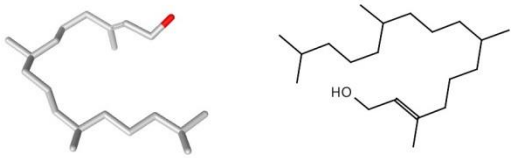
6,10,14-trimethylpentadeca-5,9,13-trien-2-one

2



β-Sitosterol

3



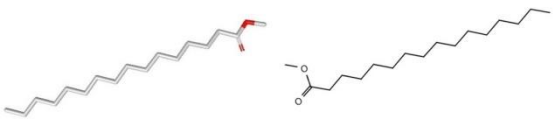
Phytol

4

Diphenyl-ether

5

6

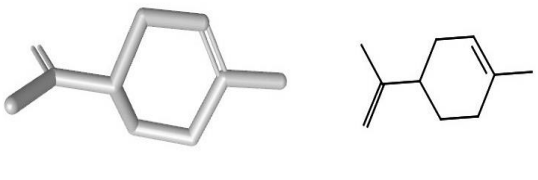


Methyl Hexadecanoate

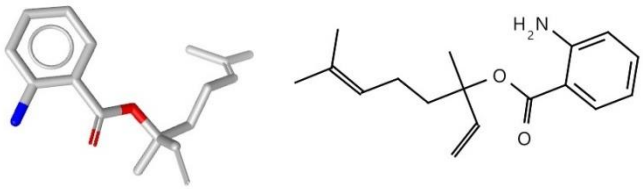
7

1-Methyl-4-propylbenzene (p-cymene)

8



Limonene

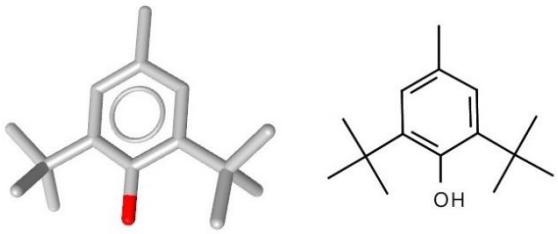


Linalool anthranilate

Gambar IV.1 Struktur kimia kandungan senyawa aktif dalam daun asam jawa (*Tamarindus indica* L.)

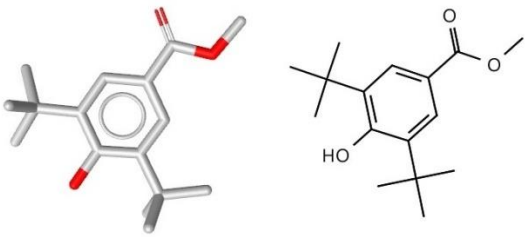
LAMPIRAN 3
(LANJUTAN)

9



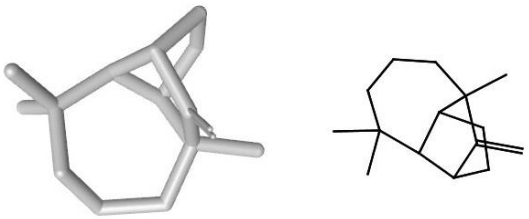
2,6-ditert-butyl-4-methylphenol

10



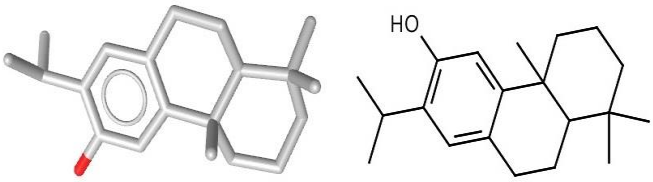
Methyl 3,5-ditert-butyl-4-hydroxybenzoate

11



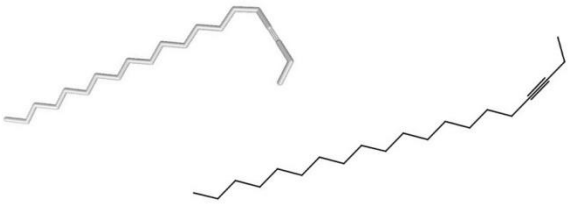
Longifolene

12



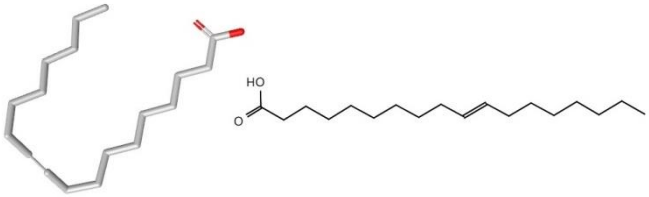
Cryptopinone

13



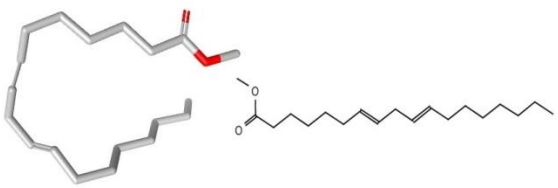
3-eicosyne

14



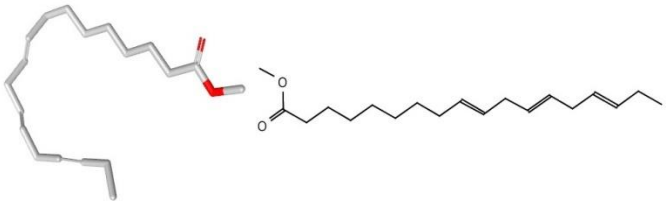
10-Octadecenoic acid

15



Methyl 7,10-Octadecadienoate

16

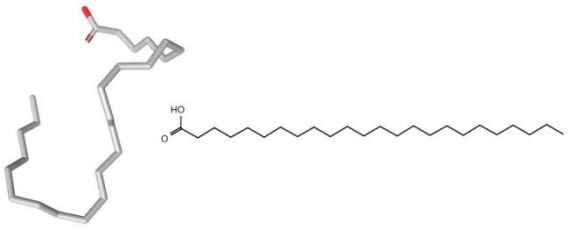


Ethyl 9,12,15-Octadecatrienoate

Gambar IV.1 Struktur kimia kandungan senyawa aktif dalam daun asam jawa (*Tamarindus indica* L.)

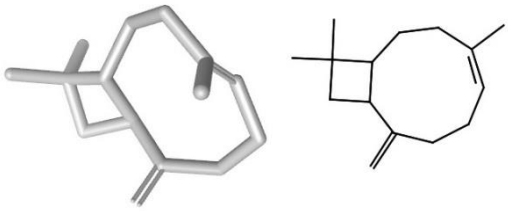
LAMPIRAN 3
(LANJUTAN)

17



Methyl 15-tricosenoate

18

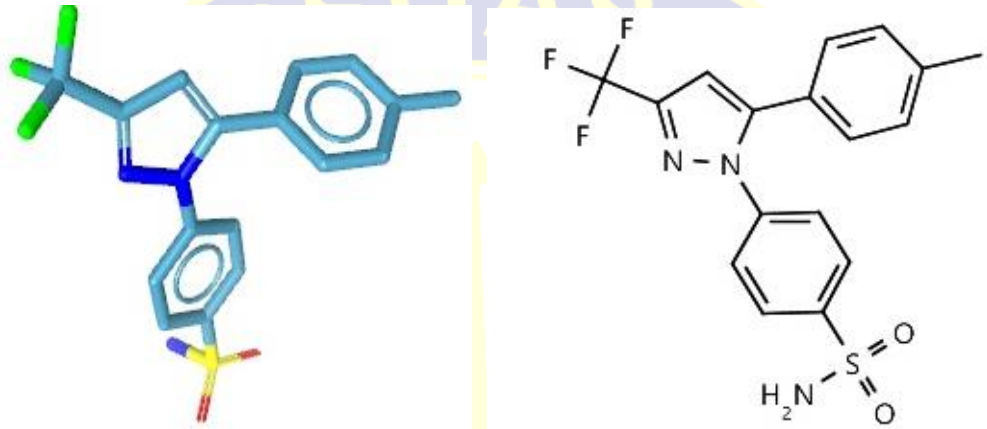


Caryophyllene

Gambar IV.1 Struktur kimia kandungan senyawa aktif dalam daun asam jawa (*Tamarindus indica* L.)

LAMPIRAN 4

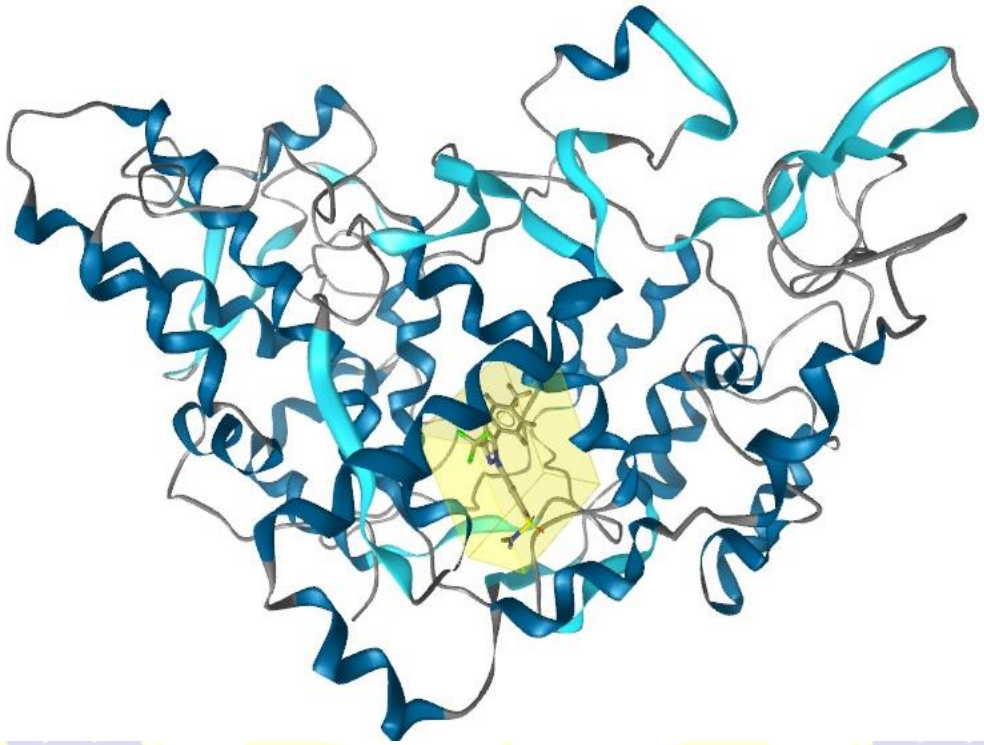
STRUKTUR 3D DAN 2D LIGAN ALAMI CELECOXIB



Gambar IV.2 Struktur kimia ligan alami Celecoxib

LAMPIRAN 5

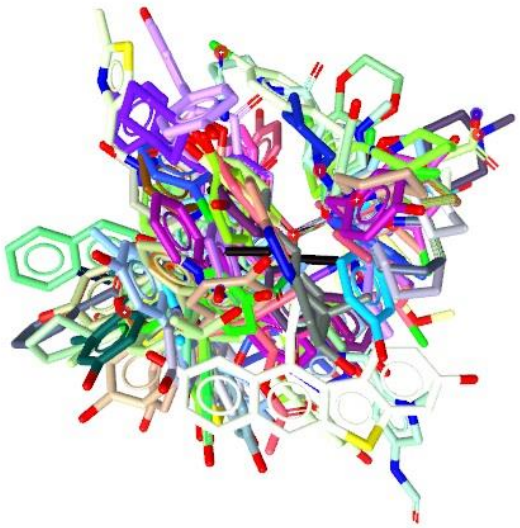
STRUKTUR 3D RESEPTOR SIKLOOKSIGENASE-2



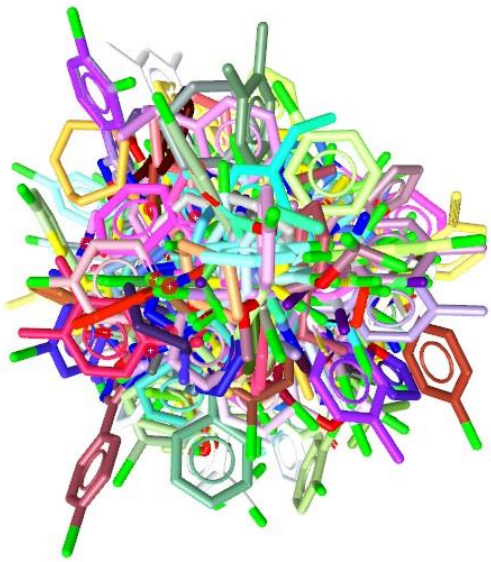
Gambar IV.3 Struktur tiga dimensi (3D) reseptor Siklooksigenase-2

LAMPIRAN 6

STRUKTUR 3D DATABASE *ACTIVE* DAN *DECOY*



Gambar IV.4 Kumpulan struktur tiga dimensi senyawa *active* yang didapatkan dari situs *DUD-E*



Gambar IV.5 Kumpulan struktur tiga dimensi senyawa *decoy* yang didapatkan dari situs *DUD-E*

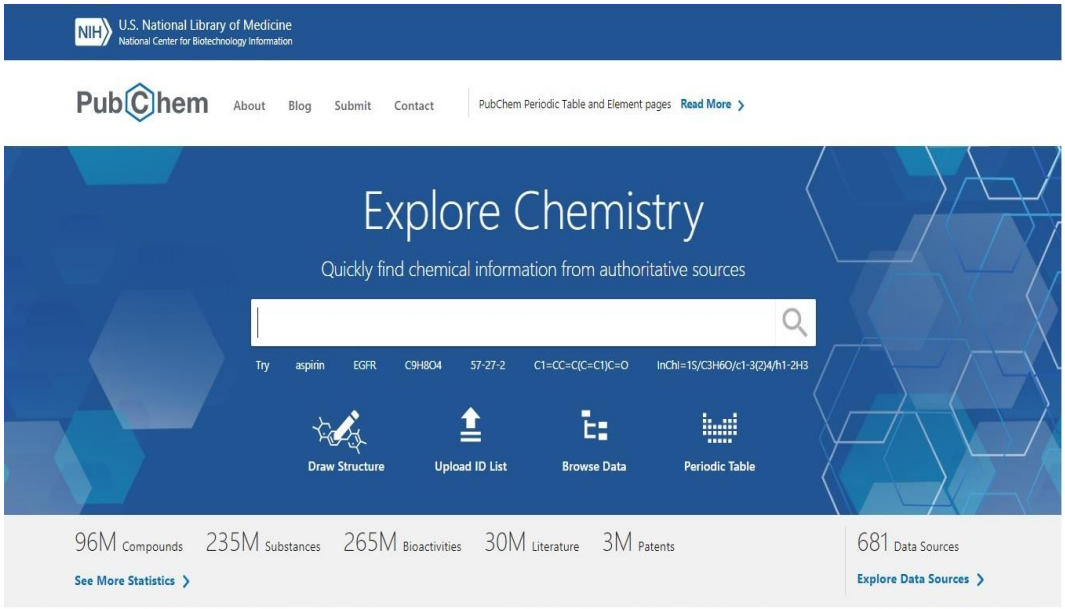
LAMPIRAN 7

SITUS *PROTEIN DATA BANK*

Gambar IV.6 Tampilan situs *Protein Data Bank* (PDB) sebagai tempat pengunduhan reseptor.

LAMPIRAN 8

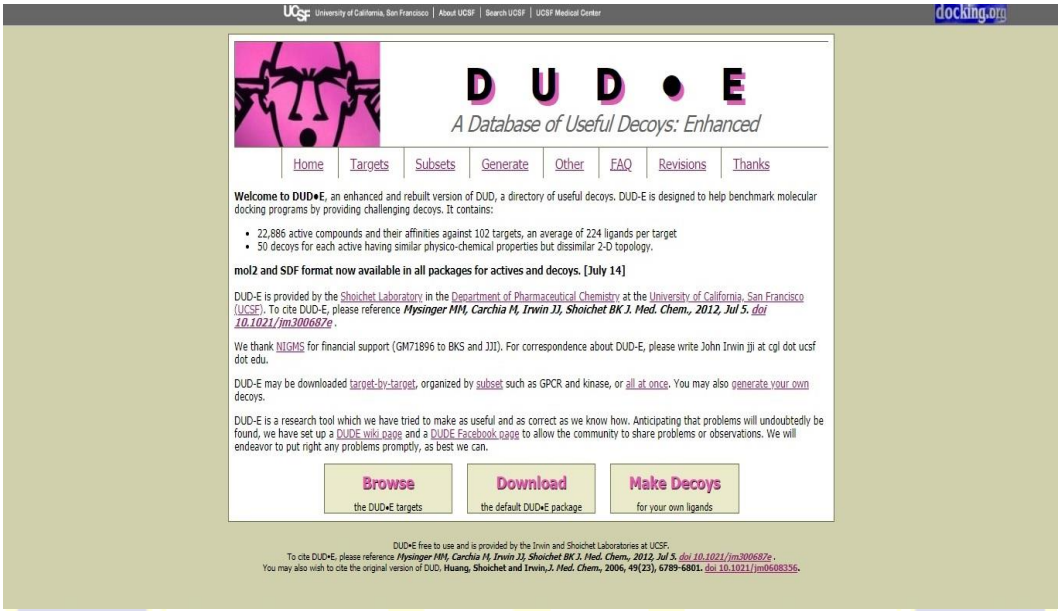
SITUS PUBCHEM



Gambar IV.7 Tampilan utama situs *PubChem* sebagai tempat pengunduhan beberapa senyawa dalam format .pdb

LAMPIRAN 9

SITUS DUD-E



Gambar IV.8 Tampilan utama situs *DUD-E* sebagai tempat pengunduhan senyawa *active* dan *decoy* dalam format .sdf

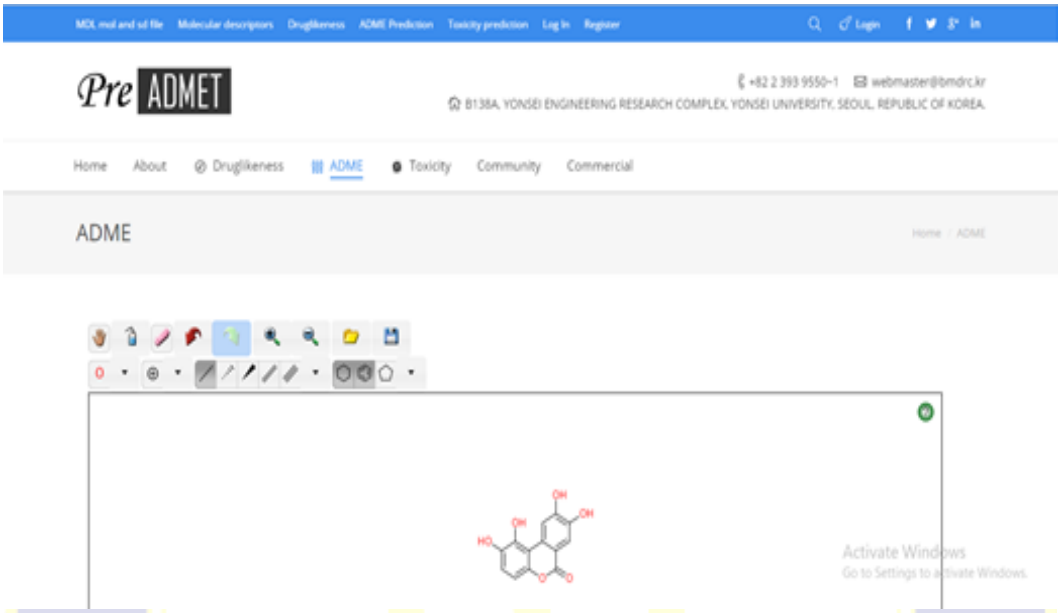
LAMPIRAN 10

SITUS LIPINSKI RULE OF FIVE

Gambar IV.9 Tampilan situs *Lipinski rule of five* untuk pengujian sifat fisikokimia

LAMPIRAN 11

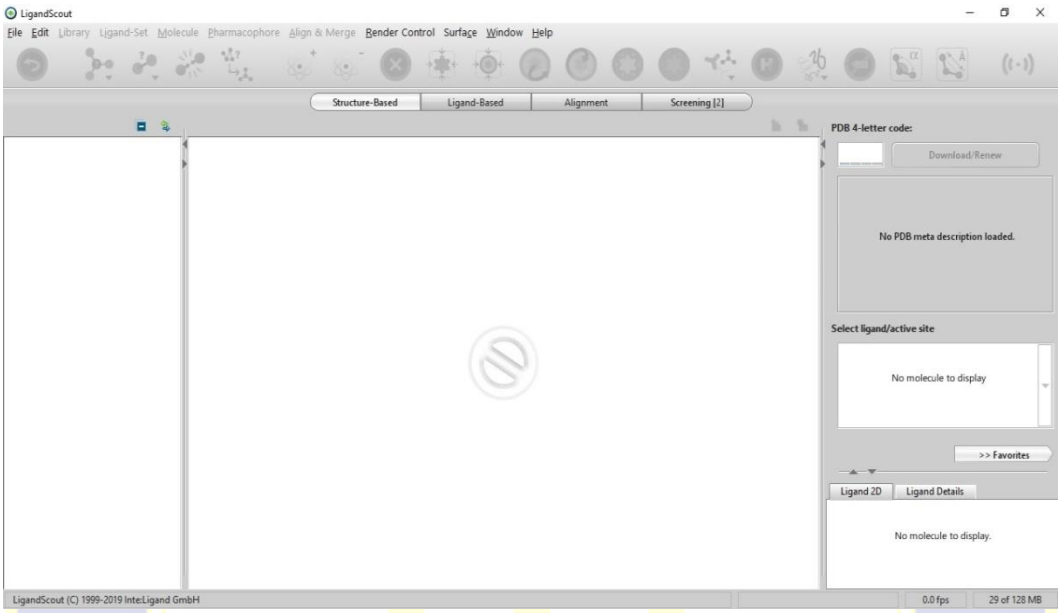
SITUS PREADMET



Gambar IV.10 Tampilan situs *PreADMET*

LAMPIRAN 12

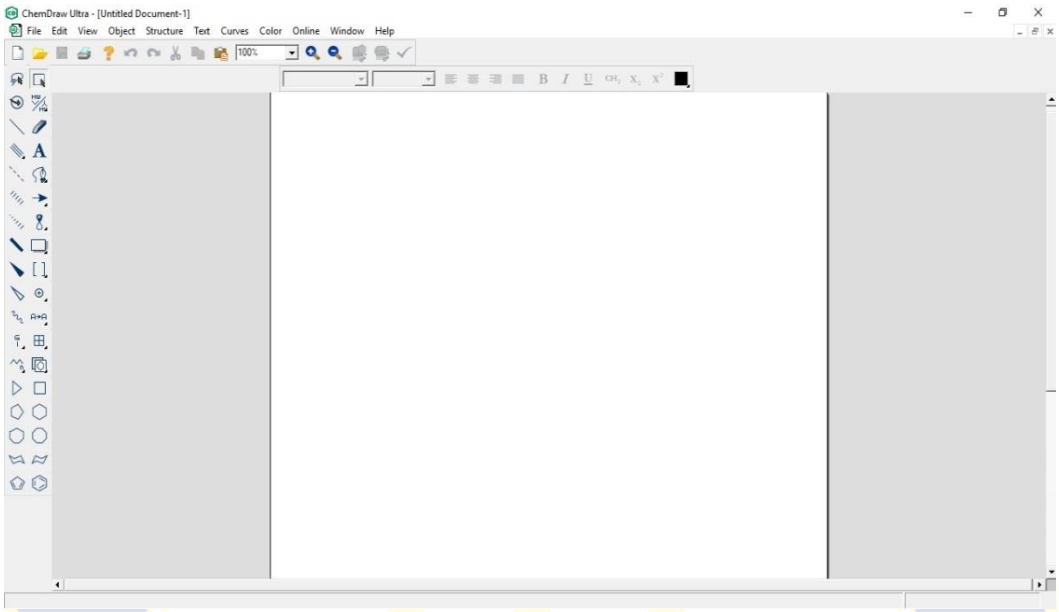
PERANGKAT LUNAK LIGANDSCOUT 4.3



Gambar IV.11 Tampilan utama perangkat lunak *LigandScout* 4.3

LAMPIRAN 13

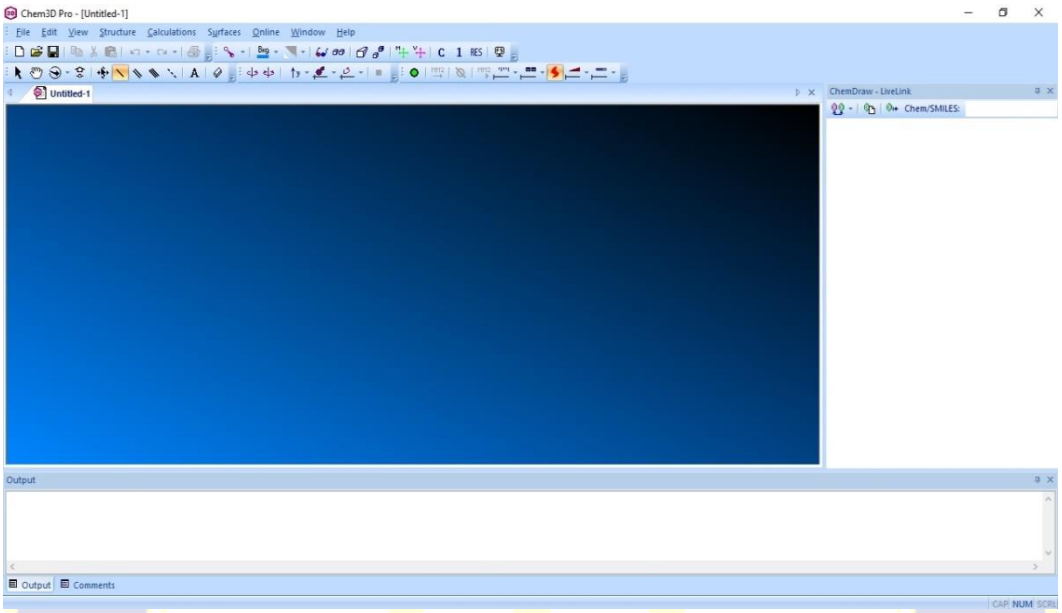
PERANGKAT LUNAK CHEMDRAW ULTRA 12.0



Gambar IV.12 Tampilan utama perangkat lunak *ChemDraw Ultra* 12.0

LAMPIRAN 14

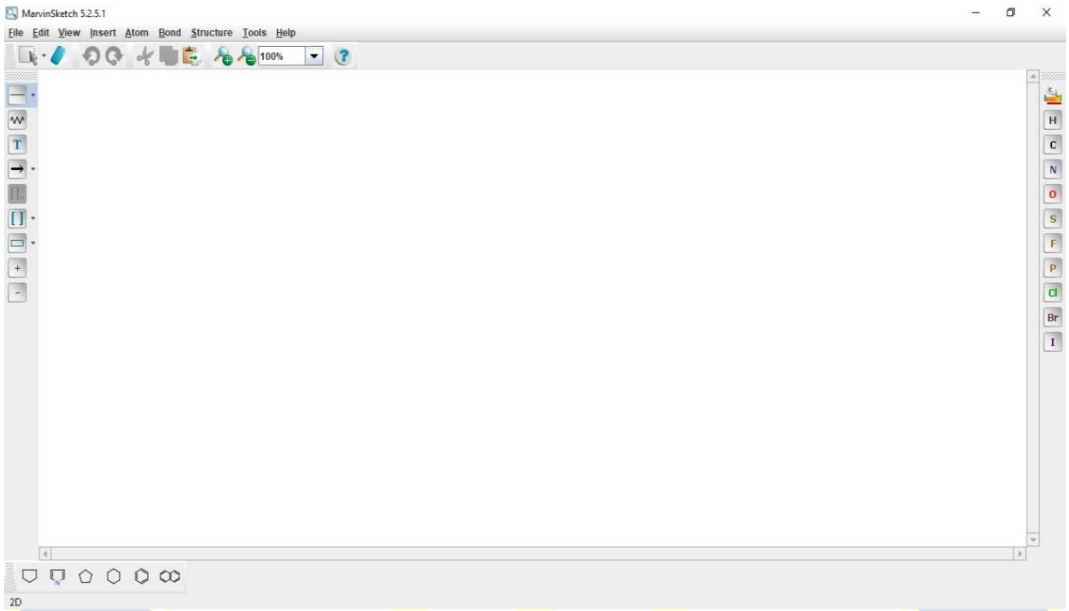
PERANGKAT LUNAK CHEM3D PRO 12.0



Gambar IV.13 Tampilan utama perangkat lunak *Chem3D Pro* 12.0

LAMPIRAN 15

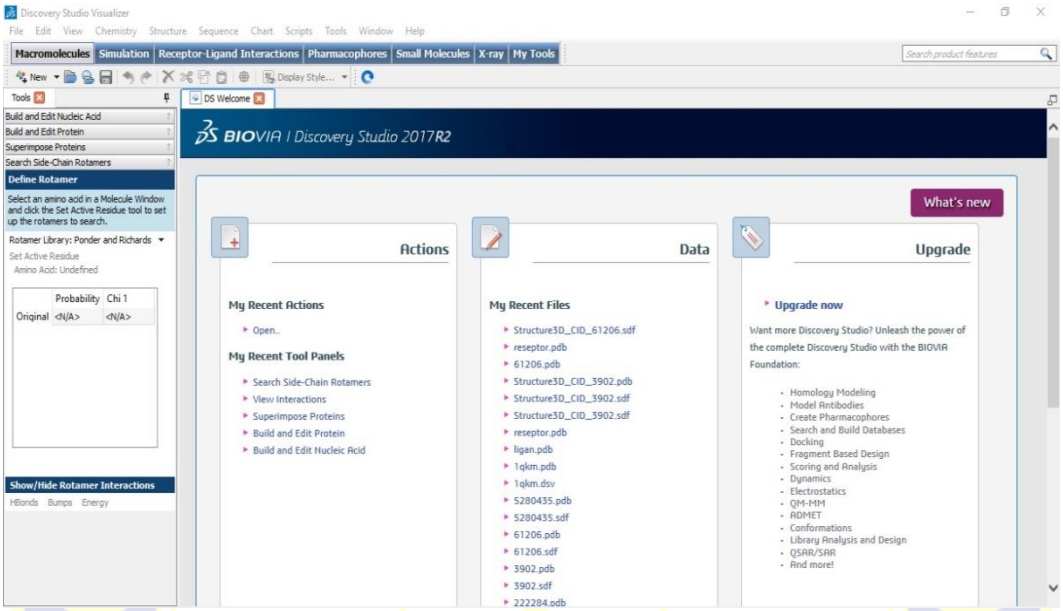
PERANGKAT LUNAK MARVINSKETCH



Gambar IV.14 Tampilan perangkat lunak *MarvinSketch*

LAMPIRAN 16

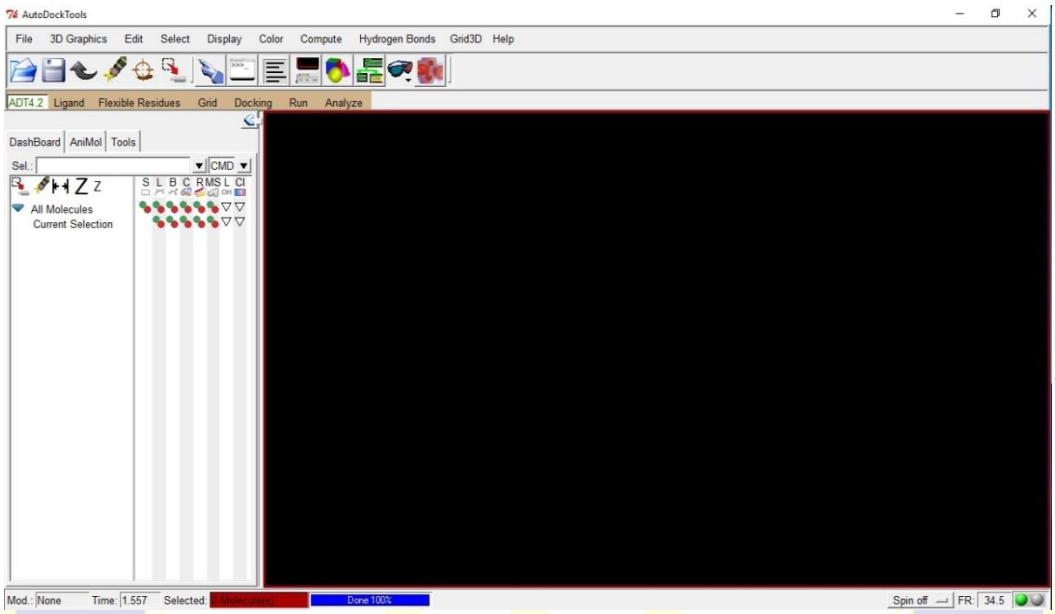
PERANGKAT LUNAK DISCOVERY STUDIO VISUALIZER 2017 CLIENT



Gambar IV.15 Tampilan utama perangkat lunak *Discovery Studio Visualizer*

LAMPIRAN 17

PERANGKAT LUNAK AUTODOCK TOOLS

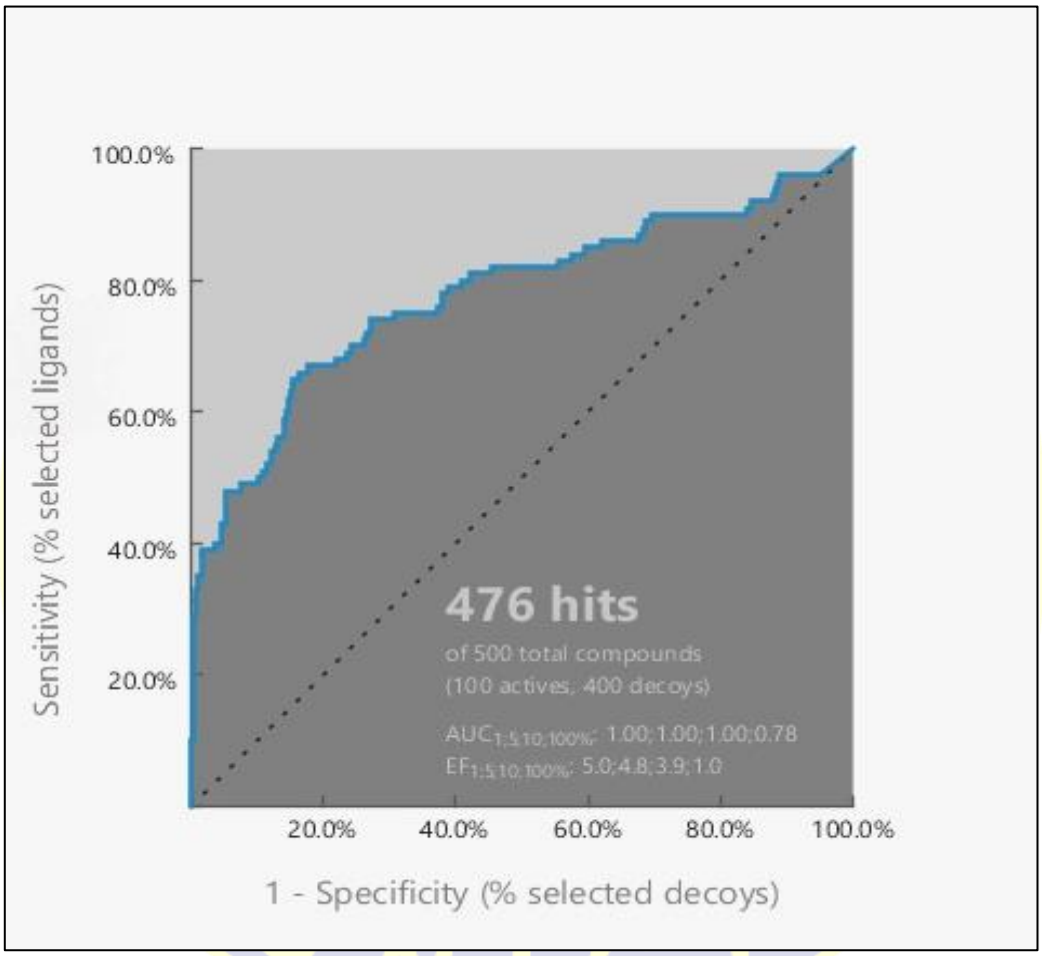


Gambar IV.16 Tampilan perangkat lunak *AutoDock Tools* sebagai tempat penambatan molekul antara ligan dengan reseptor

LAMPIRAN 18

KURVA VALIDASI SKRINING FARMAKOFOR

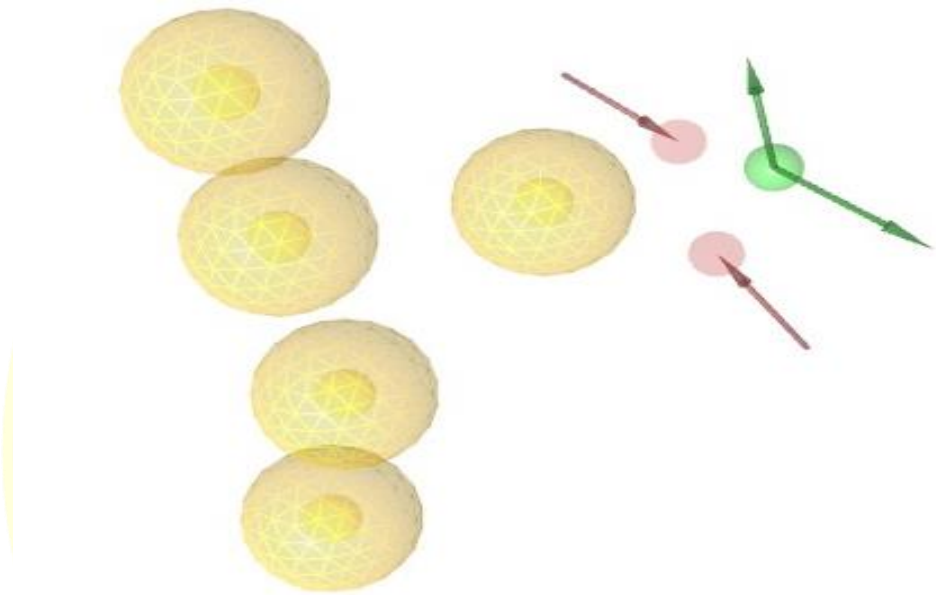
(KURVA *ROC*)



Gambar V.1 Kurva validasi (kurva *ROC*) model farmakofor

LAMPIRAN 19

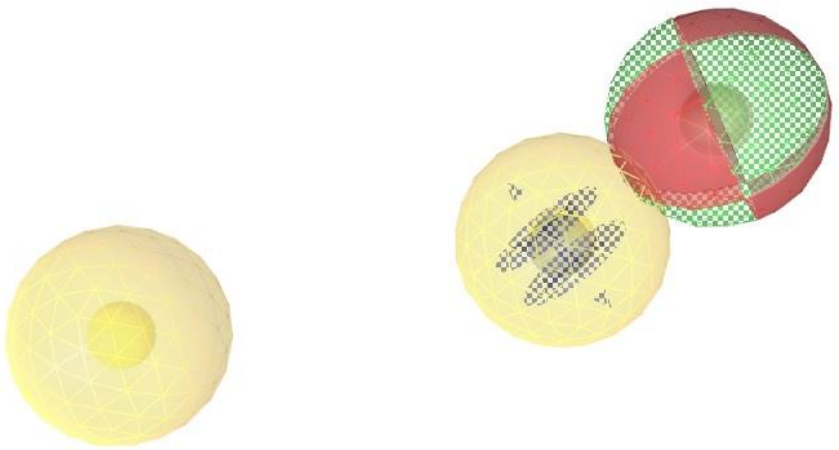
FARMAKOFOR RESEPTOR SIKLOOKSIGENASE-2



Gambar V.2 Farmakofor dari reseptor Siklooksigenase-2 yang terdiri dari donor ikatan hidrogen, akseptor ikatan hidrogen dan interaksi hidrofobik

LAMPIRAN 20

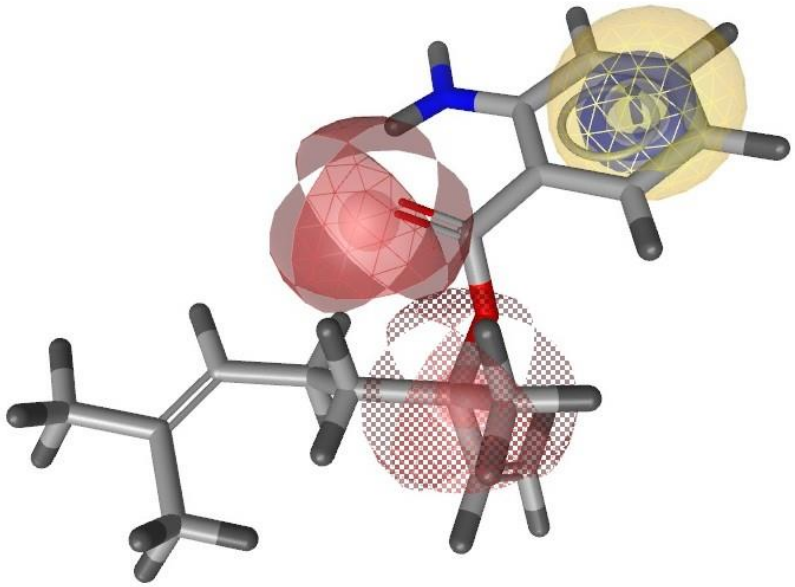
FARMAKOFOR MODEL 1 (MODEL TERBAIK)



Gambar V.3 Farmakofor dari model-1 yang terdiri dari donor ikatan hidrogen, akseptor ikatan hidrogen, interaksi hidrofobik dan cincin aromatik

LAMPIRAN 21

HASIL SKRINING FARMAKOFOR



Farmakofor model-1 hit dengan Linalool

Gambar V.4 Hasil Skrining Farmakofor Senyawa Daun Asam Jawa (*Tamarindus indica* L.)

LAMPIRAN 21
(LANJUTAN)

Tabel V.1

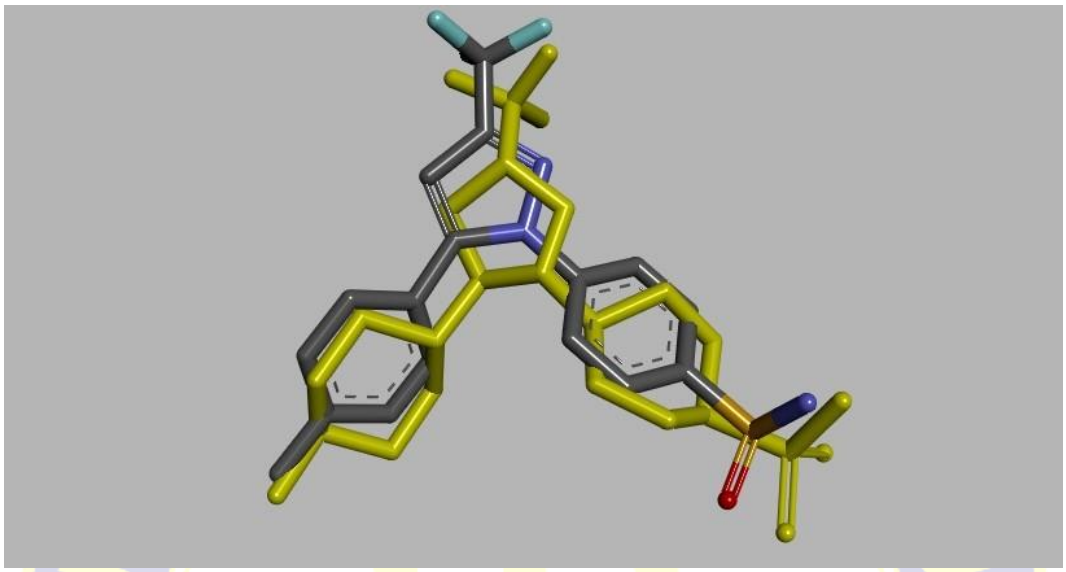
No	Nama Senyawa	Pharmacophore Depiction	Pharmacophore Fit Score
1	Linalool		52.11

Hasil Skrining Farmakofor Senyawa Daun Asam Jawa (*Tamarindus indica* L.)

Keterangan: warna kuning = interaksi hidrofobik
warna merah = akseptor ikatan hidrogen
warna hijau = donor ikatan hidrogen

LAMPIRAN 22

VALIDASI METODE RESEPTOR SIKLOOKSIGENASE-2



Gambar V.5 Visualisasi tumpang tindih ligan alami Celecoxib (warna abu gelap) dengan ligan hasil *redocking* (warna kuning)

Tabel V.2

Hasil validasi metode dengan *redocking* ligan alaminya didapatkan nilai RMSD < 2.4 Å yaitu 0.863 Å menunjukkan validitas metode dan reseptor yang sudah valid

Kode PDB	Grid Box	Tingkat Validasi	Validasi		Ikatan Energi (kkal/mol)
			RMSD Cluster (Å)	RMSD Reference (Å)	
3LN1	X: 77.870 Y: -15.391 Z: -7.855	2.500.000	0.00	0.863	-7.98

LAMPIRAN 23

HASIL PENAMBATAN MOLEKUL LIGAN ALAMI

DAN SENYAWA UJI

Tabel V.3

Hasil penambatan molekul berdasarkan nilai energi ikatan (ΔG) beserta nilai konstanta inhibisi (KI) dan residu asam aminonya

No	Senyawa/Ligan Uji	ΔG (kkal/mol)	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI
Ligan Alami					
Ligan Alami Celecoxib		-7.98	8	ILE503, GLN178, PHE504, HIS75, TYR371, SER339, ARG449.106	62.85 nM
Senyawa Aktif Asam Jawa (*Tamarindus indica* L.)					
1	6,10,14-trimethylpentadeca-5,9,13-trien-2-one	-.6.01	1	ARG346	55.48 nM
2	Phytol	-7.11	2	GLU305, ARG346	64.15. nM
3	β-Sitosterol	-6.92	1	GLU305	69.67 nM
4	Diphenyl-ether	-5.40	-	-	52.25 nM
5	Methyl Hexadecanoate	-6.26	1	ARG346	58.76 nM

LAMPIRAN 23
(LANJUTAN)

Tabel V.3
Hasil penambatan molekul berdasarkan nilai energi ikatan (ΔG) beserta nilai konstanta inhibisi (KI) dan residu asam aminonya

No	Senyawa/Ligan Uji	ΔG (kkal/mol)	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI
6	1-Methyl-4-propylbenzene (p-cymene)	-6.48	-	-	96.22 nM
7	Limonene	-5.91	-	-	96.3 nM
8	Linalool anthranilate	-9,21	1	TYR371	62.41 nM
9	2,6-ditert-butyl-4-methylphenol	-5.75	1	LEU298	52.07 nM
10	Methyl 3,5-ditert-butyl-4-hydroxybenzoate	-6.11	1	LEU298	11.14 nM
11	Longifolene	-6.99	-	-	21.4 nM
12	Cryptopinone	-8.21	1	SER339	89.13 nM
13	3-eicosyne	-6.78	-	-	51.99 nM
14	10-Octadecenoic acid	-6.12	2	GLU305, ARG346	63.09 nM

LAMPIRAN 23
(LANJUTAN)

Tabel V.3

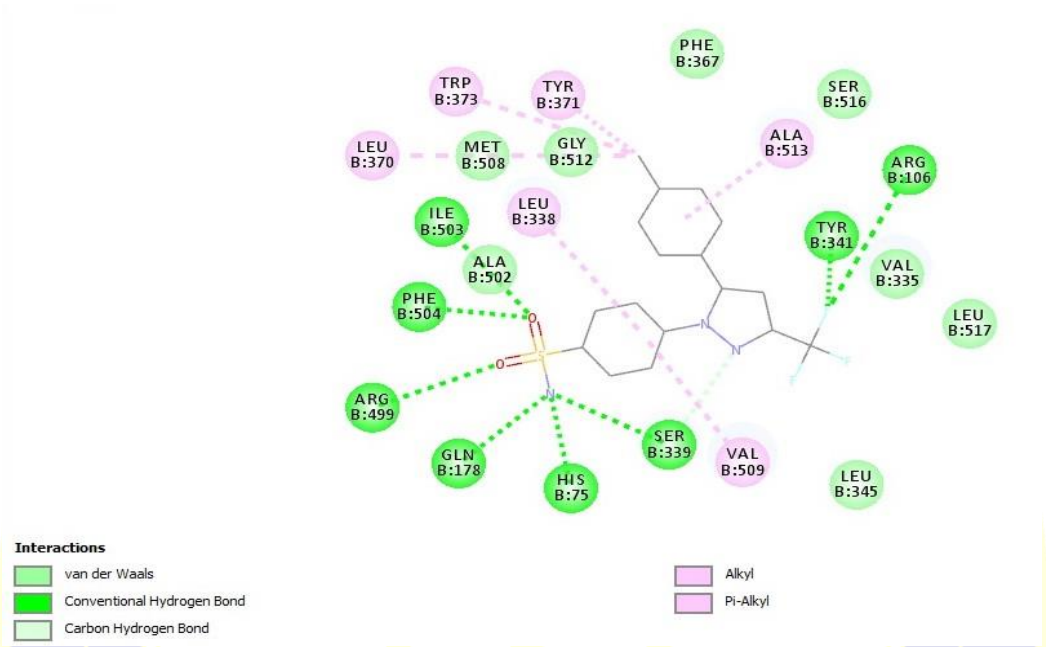
Hasil penambatan molekul berdasarkan nilai energi ikatan (ΔG) beserta nilai konstanta inhibisi (KI) dan residu asam aminonya

No	Senyawa/Ligan Uji	ΔG (kkal/mol)	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI
15	Methyl 7,10-Octadecadienoate	-6.96	1	HIS475	41.26 nM
16	Ethyl 9,12,15-Octadecatrienoate	-6.58	1	ARG346	72.28 nM
17	Methyl 15-tricosenoate	-5.44	-	-	63.55 nM
18	Caryophyllene	-6.15	-	-	41.07 nM

LAMPIRAN 24

VISUALISASI PENAMBATAN MOLEKUL CELECOXIB

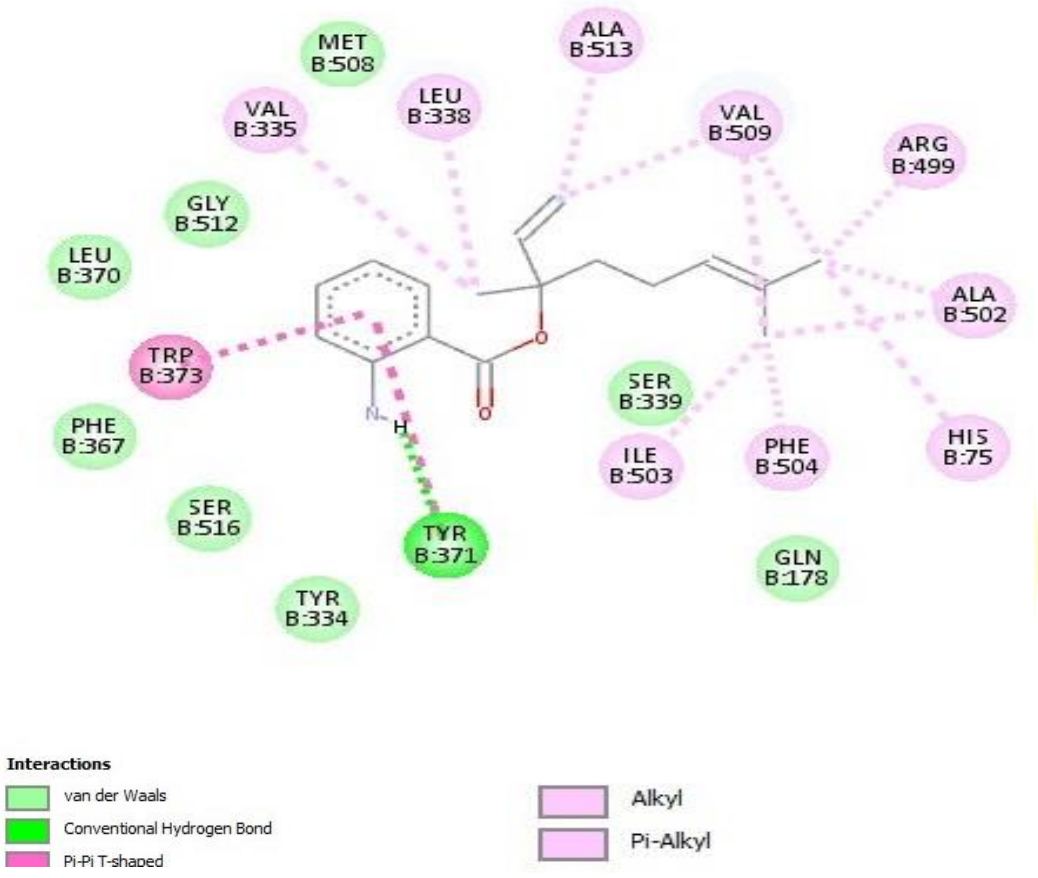
DENGAN RESEPTOR



Gambar V.6 Visualisasi residu asam amino dengan ikatan hidrogen pada ligan alami Celecoxib

LAMPIRAN 25

VISUALISASI HASIL PENAMBATAN LINALOOL DENGAN RESEPTOR SIKLOOKSIGENASE-2



Gambar V.7 Visualisasi residu asam amino dengan ikatan hidrogen pada Linalool

LAMPIRAN 26

SIFAT FISIKOKIMIA SENYAWA DAUN ASAM JAWA

BERDASARKAN *LIPINSKI'S RULE OF FIVE*

Tabel V.4

Data sifat fisikokimia senyawa uji berdasarkan *Lipinski's rule of five*

No	Senyawa/Ligan Uji	Donor Hidrogen	Akseptor Hidrogen	Bobot molekul	Log P	Memenuhi/Tidak Memenuhi Syarat
1	6,10,14-trimethylpentadeca-5,9,13-trien-2-one	0	1	262.437	5.775	Tidak memenuhi
2	β-Sitosterol	1	1	414.718	8.025	Tidak memenuhi
3	Phytol	1	1	296.539	6.364	Tidak memenuhi
4	Diphenyl-ether	0	0	170.211	3.479	Memenuhi
5	Methyl Hexadecanoate	0	1	270.457	5.641	Tidak memenuhi
6	1-Methyl-4-propylbenzene (p-cymene)	0	0	134.222	2.948	Memenuhi
7	Limonene	0	0	136.238	3.309	Memenuhi
8	Linalool anthranilate	1	1	273.376	3.885	Memenuhi
9	2,6-ditert-butyl-4-methylphenol	1	1	220.356	4.296	Memenuhi

LAMPIRAN 26
(LANJUTAN)

Tabel V.4

Data sifat fisikokimia senyawa uji berdasarkan *Lipinski's rule of five*

No	Senyawa/Ligan Uji	Donor Hidrogen	Akseptor Hidrogen	Bobot molekul	Log P	Memenuhi/Tidak Memenuhi Syarat
10	Methyl 3,5-ditert-butyl-4-hydroxybenzoate	1	2	264.365	3.542	Memenuhi
11	Longifolene	0	0	204.357	4.415	Memenuhi
12	Cryptopinone	1	1	286.459	5.546	Tidak memenuhi
13	3-eicosyne	0	0	278.524	7.351	Tidak memenuhi
14	10-Octadecenoic acid	0	2	282.468	6.109	Tidak memenuhi
15	Methyl 7,10-Octadecadienoate	0	1	294.479	5.973	Tidak memenuhi
16	Ethyl 9,12,15-Octadecatrienoate	0	1	292.463	5.749	Tidak memenuhi
17	Methyl 15-tricosenoate	0	2	368.646	8.673	Tidak memenuhi
18	Caryophyllene	0	0	204.357	4.725	Memenuhi

Syarat: 1. BM < 500 mg/mol
2. Log P < 5
3. Donor Hidrogen < 5
4. Akseptor Hidrogen < 10

LAMPIRAN 27

HASIL UJI PREADME (ABSORPSI DAN DISTRIBUSI)

Tabel V.5

Data hasil pengujian *PreADME* pada ke 18 senyawa aktif daun asam jawa (*Tamarindus indica* L.)

No	Nama Senyawa	Caco-2 cell (nm^{sec-1})	HIA (%)	Protein Plasma Binding
1	6,10,14-trimethylpentadeca-5,9,13-trien-2-one	56.6804[b]	100.00[a]	100.00[a]
2	β-Sitosterol	52.3734[b]	100.00[a]	100.00[a]
3	Phytol	38.7817[b]	100.00[a]	100.00[a]
4	Diphenyl-ether	22.5539[b]	100.00[a]	100.00[a]
5	Methyl Hexadecanoate	45.8362[b]	100.00[a]	100.0[a]
6	1-Methyl-4-propylbenzene (p-cymene)	23.4336[b]	100.00[a]	100.0[a]
7	Limonene	23.6317[b]	100.00[a]	100.00[a]
8	Linalool anthranilate	37.4763[b]	96.005494[a]	95.05476[a]
9	2,6-ditert-butyl-4-methylphenol	45.9116[b]	100.00[a]	100.00[a]
10	Methyl 3,5-ditert-butyl-4-hydroxybenzoate	22.8946[b]	95.001042[a]	100.00[a]
11	Longifolene	23.4939[b]	100.00[a]	92.352757[a]
12	Cryptopinone	44.363[b]	100.00[a]	100.00[a]
13	3-eicosyne	22.518[b]	100.00[a]	100.00[a]
14	10-Octadecenoic acid	28.1906[b]	98.436935[a]	100.00[a]
15	Methyl 7,10-Octadecadienoate	47.1151[b]	100.00[a]	100.00[a]

LAMPIRAN 27
(LANJUTAN)

Tabel V.5

Data hasil pengujian *PreADME* pada ke 18 senyawa aktif daun asam jawa (*Tamarindus indica* L.)

No	Nama Senyawa	Caco-2 cell (nm^{sec-1})	HIA (%)	Protein Plasma Binding
16	Ethyl 9,12,15-Octadecatrienoate	47.0406[b]	100.00[a]	100.00[a]
17	Methyl 15-tricosenoate	35.2315[b]	98.083030[a]	100.00[a]
18	Caryophyllene	23.6315[b]	100.00[a]	100.00[a]

Klasifikasi: *In Vitro Caco-2 cell permeability* (nm sec-1): >70 *higher permeability* (a), 4-70 *medium permeability* (b), <4 *low permeability* (c); *%human intestinal absorption* (%HIA): 70-100% *well absorbed* (a), 20-70% *moderately absorbed* (b), 0-20% *poorly absorbed* (c); *%plasma protein binding*: >90% *strongly bound* (a), <90% *weakly bound* (b).

LAMPIRAN 28

HASIL UJI TOKSISITAS

Tabel V.6

Data hasil pengujian toksisitas yang dilihat dari potensi mutagen dan karsinogen dari ke 18 senyawa uji

No	Nama Senyawa	Toksisitas	Karsinogenisitas
1	6,10,14-trimethylpentadeca-5,9,13-trien-2-one	Non-mutagen	Positif
2	β-Sitosterol	Non-mutagen	Negatif
3	Phytol	Non-mutagen	Negatif
4	Diphenyl-ether	Mutagen	Positif
5	Methyl Hexadecanoate	Non-mutagen	Positif
6	1-Methyl-4-propylbenzene (p-cymene)	Mutagen	Negatif
7	Limonene	Mutagen	Positif
8	Linalool anthranilate	Non-mutagen	Positif
9	2,6-ditert-butyl-4-methylphenol	Non-mutagen	Negatif
10	Methyl 3,5-ditert-butyl-4-hydroxybenzoate	Non-mutagen	Negatif
11	Longifolene	Mutagen	Positif
12	Cryptopinone	Non-mutagen	Positif
13	3-eicosyne	Non-mutagen	Positif
14	10-Octadecenoic acid	Mutagen	Positif
15	Methyl 7,10-Octadecadienoate	Non-mutagen	Positif
16	Ethyl 9,12,15-Octadecatrienoate	Non-mutagen	Positif
17	Methyl 15-tricosenoate	Non-mutagen	Positif
18	Caryophyllene	Mutagen	Positif