

DAFTAR PUSTAKA

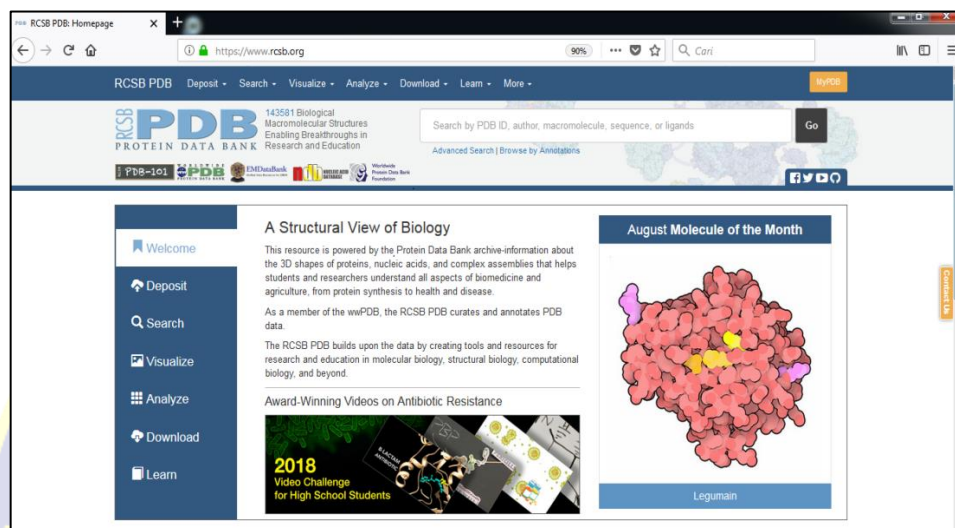
1. Kusteviani Fani. Jurnal Berkala Epidemiologi, Vol. 3, No. 1 Januari 2015; 45–56p.
2. KEMENKES RI. Riset Kesehatan Dasar. Jakarta: KEMENKES RI; 2013; 224-225p.
3. Virgianti, V.S. Aktivitas Antiobesitas Ekstrak Etanol Biji Dan Batang Tanaman Koro Benguk (*Mucuna pruriens* (L.) Pada Tikus Betina Galur Wistar. Tugas Akhir Sarjana Farmasi. Fakultas Matematika dan Ilmu Pengetahuan Alam. Garut : Universitas Garut; 2017.
4. Meilinah, dkk. Pengujian Aktivitas Inhibitor Lipase Ekstrak Etanol Dan Hasil Fraksionasi Dari Kedelai Detam 1 Dan Daun Jati Belanda. *Chimica et Natura Acta* Vo.2 No.1, April 2014:76-8p.
5. Achmad SA. Ilmu Kimia dan Kegunaan Tumbuh-tumbuhan Indonesia. Jilid II. Bandung: ITB; 2013.229p.
6. Yanuar A. Penambatan Molekular Praktek dan Aplikasi pada Virtual Screening. Jakarta: Fakultas Farmasi Universitas Indonesia; 2012. 8, 16-17,47p.
7. BPOM RI. Acuan Sediaan Herbal. Volume Ketiga. Edisi Pertama. Jakarta: BPOM RI; 2010. 47-48p.
8. Subardja Dedi. Obesitas Primer Pada Anak. Bandung: PT. Kiblat Buku utama; 2004. 17-23p.
9. Apriani Fitria. Studi Penambatan Molekul Senyawa-Senyawa Amidasi Etil Para Metokisinamat Pada Peroxisome Proliferator-Activated Receptor-Gamma (PPAR γ). Tugas Akhir Sarjana Farmasi, Jurusan Farmasi, Fakultas Kedokteran dan Ilmu Kesehatan, UIN Syarif Hidayatullah, Jakarta; 2015. 1, 2, 17-21p.
10. Tanto Chris, et al. Kapita Selekta Kedokteran. Jilid 1 Edisi IV. Jakarta: Media Aesculapius; 2014.126-127p.
11. Satyajit D. Sarker dan Lutfun Nahar. Kimia Untuk Mahasiswa Farmasi Bahan Kimia Organik Alam dan Umum. Yogyakarta: Pustaka Pelajar. 2009. 32-39p.

12. Sukandar Y.E, dkk. ISO Farmakoterapi 2. Jakarta: Ikatan Apoteker Indonesia; 2011. 110p.
13. Chirtopher A. Lipinski. Drug-like properties and the cause of poor solubility and poor permeability. J Pharmacol Toxicol Methods. 2001;44(1):44p.
14. Koolman J. Atlas Berwarna dan teks Biokimia. Jakarta: Hipokrates; 2000. 86-92p.

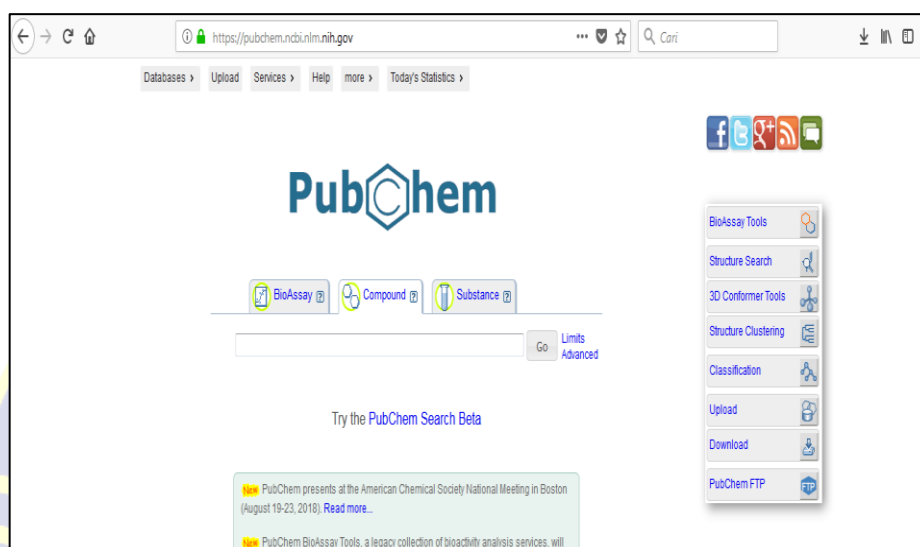


LAMPIRAN 2

PROTEIN DATA BANK

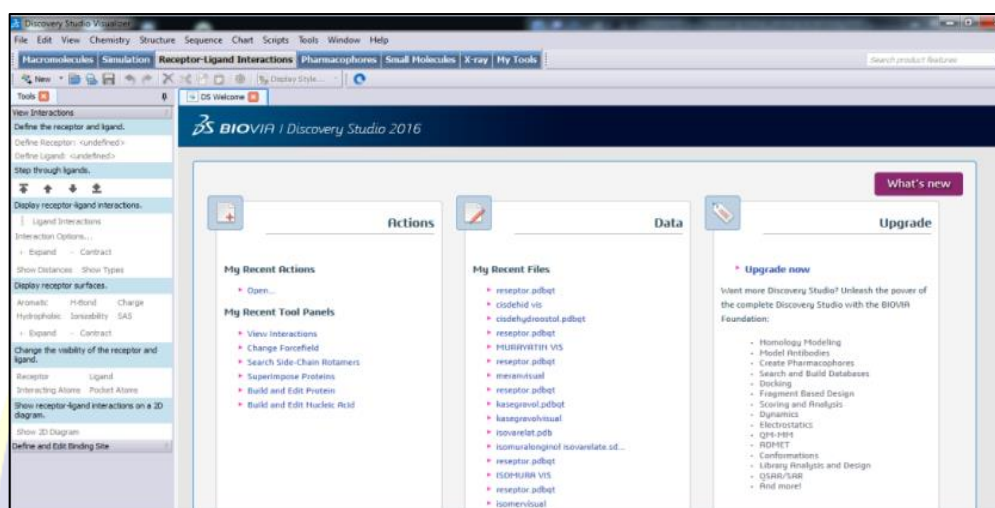


Gambar IV.2 Protein Data Bank

LAMPIRAN 3**PUBCHEM****Gambar IV.3 PubChem**

LAMPIRAN 4

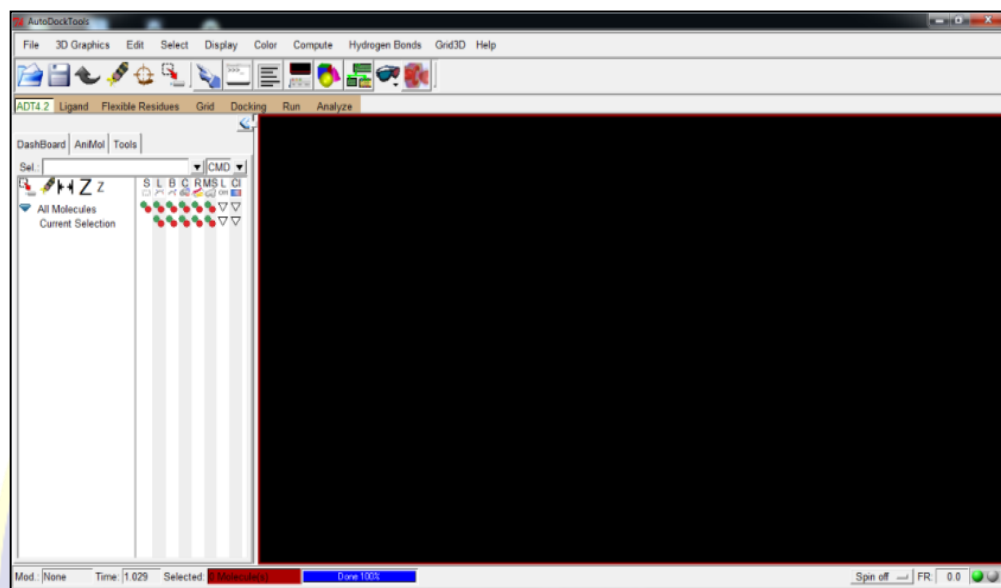
DISCOVERY STUDIO VISUALIZER



Gambar IV.4 Discovery Studio Visualizer

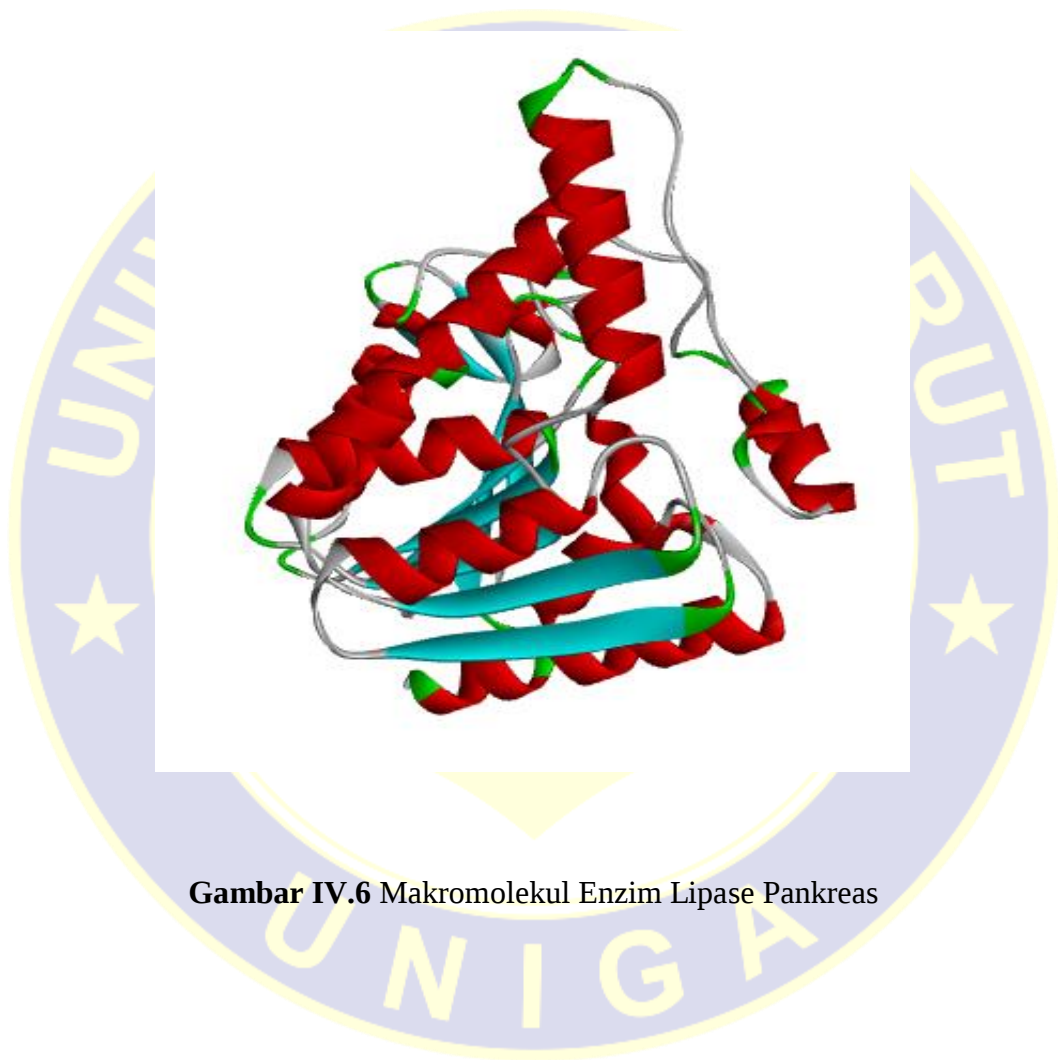
LAMPIRAN 5

AUTODOCK TOOLS

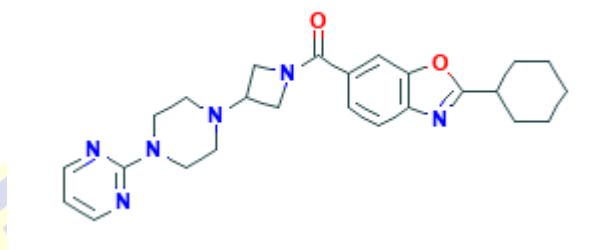


Gambar IV.5 AutoDock

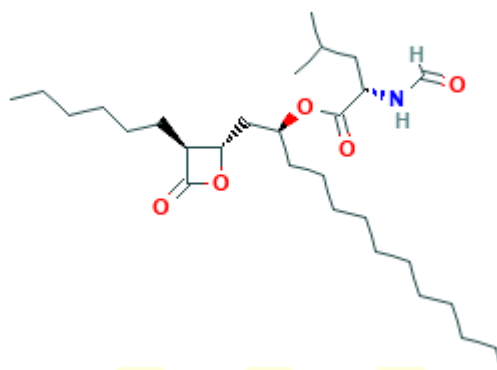
LAMPIRAN 6
MAKROMOLEKUL



Gambar IV.6 Makromolekul Enzim Lipase Pankreas

LAMPIRAN 7**LIGAN ALAMI****Gambar IV.7** Ligan alami dari 3PE6

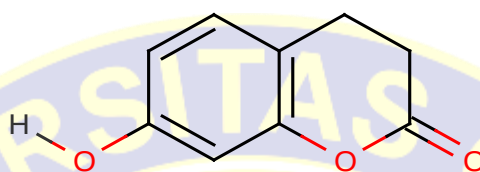
LAMPIRAN 8
SENYAWA PEMBANDING



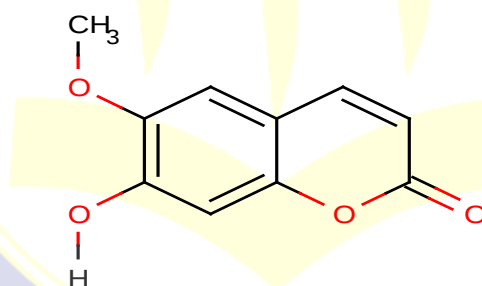
Gambar IV.8 Ligan pembanding (orlistat)

LAMPIRAN 9

SENYAWA DAUN KEMUNING

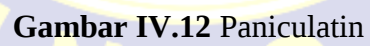
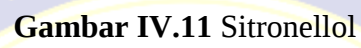


Gambar IV.9 Umbelliferon

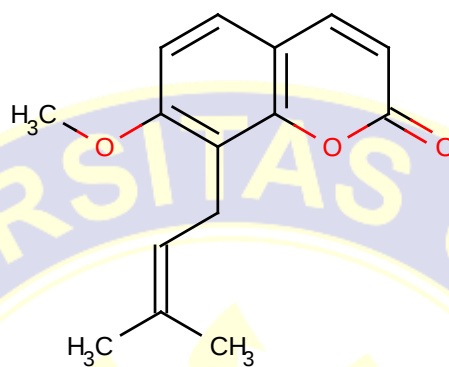


Gambar IV.10 Skopoletin

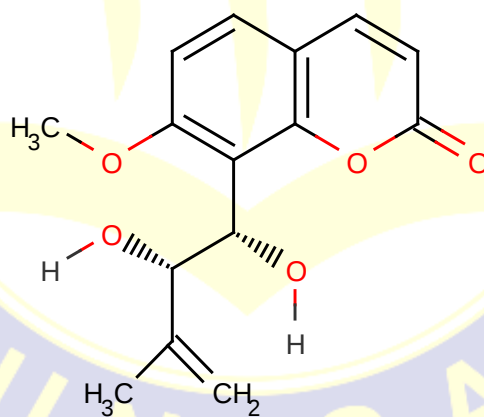
LAMPIRAN 9 (LANJUTAN)



**LAMPIRAN 9
(LANJUTAN)**

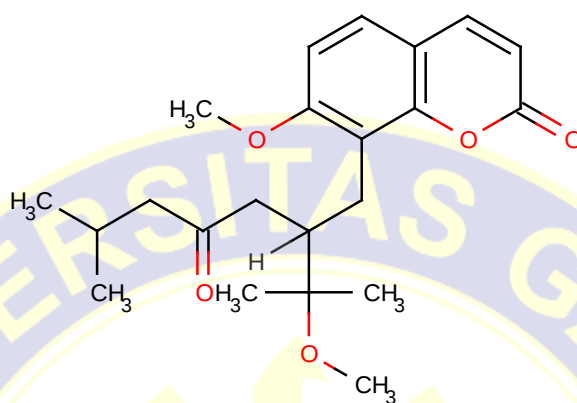


Gambar IV.13 Osthole

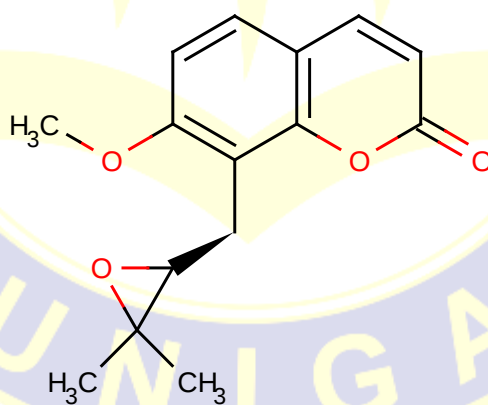


Gambar IV.14 Murpanikulol

**LAMPIRAN 9
(LANJUTAN)**

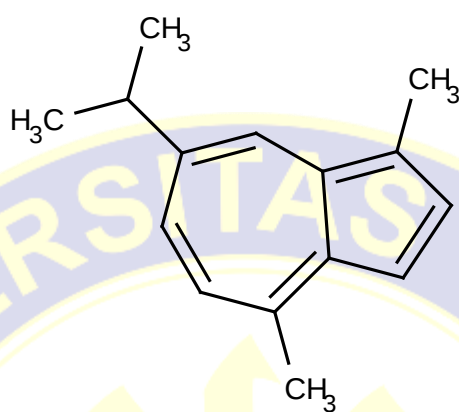


Gambar IV.15 Murrayatin

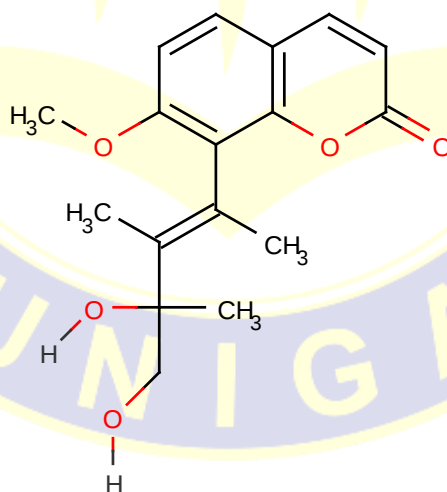


Gambar IV.16 Meranzin

**LAMPIRAN 9
(LANJUTAN)**

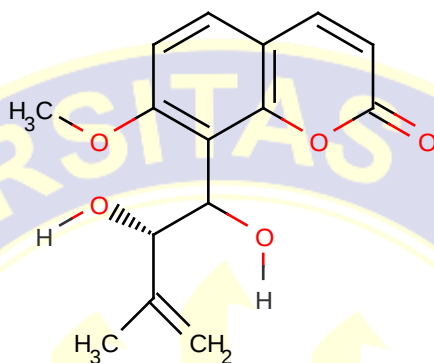


Gambar IV.17 S-guaiazulene

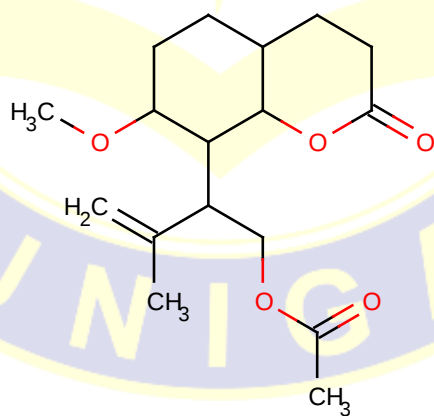


Gambar IV.18 Murpanidin

**LAMPIRAN 9
(LANJUTAN)**

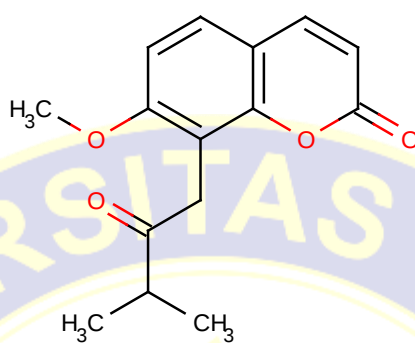


Gambar IV.19 Isomuralonginol asetat

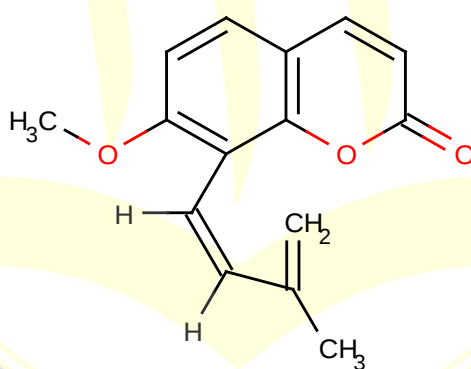


Gambar IV.20 Kasegravol

**LAMPIRAN 9
(LANJUTAN)**

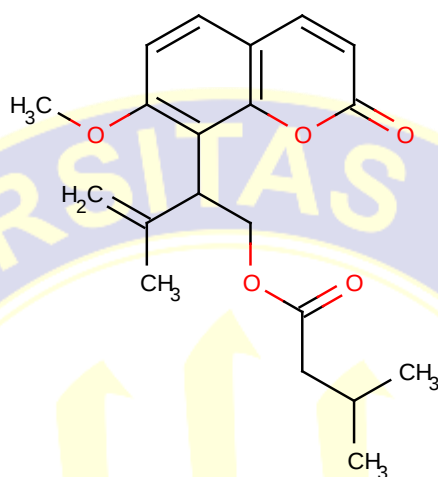


Gambar IV.21 Isomeranzin



Gambar IV.22 Cis-Dehydroosthol

**LAMPIRAN 9
(LANJUTAN)**



Gambar IV.23 Isomuralonginol isovalerat

LAMPIRAN 10

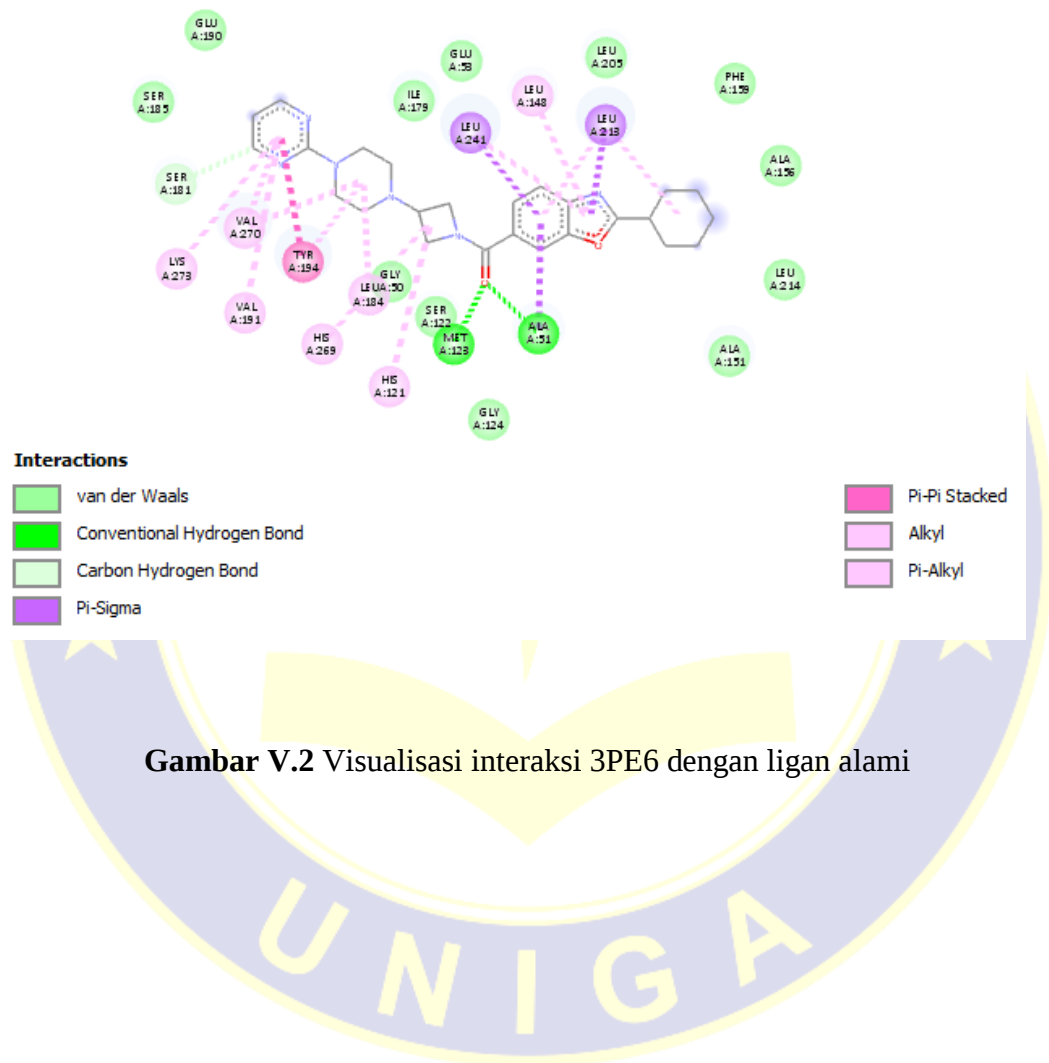
HASIL VALIDASI METODE

CLUSTERING HISTOGRAM						
Clus	Lowest	Run	Mean	Num	Histogram	
-ter	Binding		Binding	in		
Rank	Energy		Energy	Clus	5	10 15 20 25 30
35						
:					:	:
1	-12.89	8	-12.89	100		
#####						
#####						
Number of multi-member conformational clusters found = 1, out of 100 runs.						
RMSD TABLE						
Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Rep. Pattern
1	1	8	-12.89	0.00	0.38	RANKING
1	2	86	-12.89	0.02	0.37	RANKING
1	3	92	-12.89	0.31	0.51	RANKING
1	4	93	-12.89	0.30	0.50	RANKING
1	5	61	-12.89	0.02	0.37	RANKING

Gambar V.1 Hasil validasi metode re-docking 3PE6

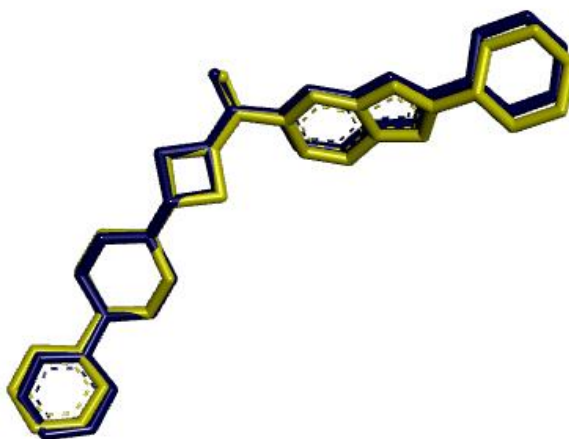
LAMPIRAN 11

INTERAKSI MAKROMOLEKUL



LAMPIRAN 12

HASIL *REDOCKING*



Gambar V.3 Hasil visualisasi tumpang tindih ligan alami dengan hasil kristalografi sinar-X (biru) dengan ligan hasil *redocking* kuning

LAMPIRAN 13

*ANALISIS LIPINSKI'S RULE OF FIVE***Tabel V.4**

Lipinski's Rule of Five Senyawa Daun Kemuning
(*Murraya paniculata*(L.)Jack)

No	Nama senyawa	BM (g/mol)	Log P	Donor ikatan H	Akseptor ikatan H	Molar refractivity
1	Ligan alami	466	3,31	0	8	125,34
2	Orlistat	495	6,88	1	6	140,91
3	Umbeliferon	162	1,32	1	3	42,77
4	Skopoletin	192	1,33	1	4	49,32
5	Meranzin	260	2,34	0	4	70,31
6	Isomerazin	260	2,39	0	4	21,21
7	Cis-dehidroostol	242	3,21	0	3	71,51
8	Murayatin	362	2,89	1	6	96,99
9	Kasegravol	267	1,38	2	5	74,40
10	Isomuranginol asetat	302	2,85	0	5	81,85
11	Murpanidin	276	1,59	2	5	73,44
12	Isomuranginol isovarelat	344	3,87	0	5	95,63
13	murpanikulol	358	3,40	0	6	95,77
14	Panikulatin	360	3,48	0	6	95,79
15	sitronellol	165	2,75	1	1	49,53
16	Osthole	244	3,13	0	3	70,79
17	S-guaiazulene	198	4,00	0	0	65,88

LAMPIRAN 14

HASIL PENAMBATAN MOLEKUL (MOLECULAR DOCKING)

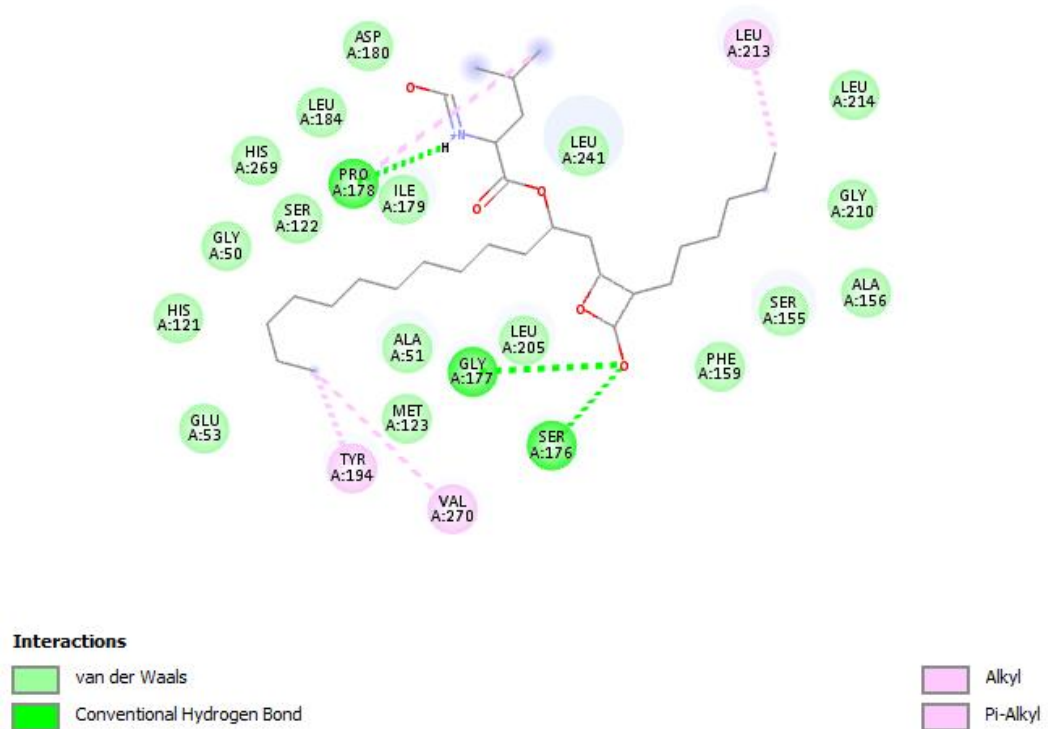
Tabel V.5

Hasil Penambatan Molekul senyawa Ligan Alami, Orlistat dan Senyawa daun kemuning

No	Nama Senyawa	Lowest Binding Energi	Nilai KI
1.	Ligan alami	-12,48	355,11
2.	ortlistat	-7,55	2.920
3	Umbeliferon	-5,90	47.040
4	Skopoletin	-6,06	66.240
5	Meranzin	-7,78	1.990
6	Isomeranzin	-7,90	1.610
7	Cis-Dehidroostol	-7.23	4.980
8	Murayatin	-8.48	604.43
9	Kasegravol	-7,59	2.710
10	Isomuranginol asetat	-7,45	3.480
11	Murpanidin	-6,65	13.430
12	Isomuranginol isovalerat	-8,44	647.36
13	Paniculatin	-7,71	2.230
14	Murpanikulol	-8,41	682.25
15	sitronellol	-5,29	131.750
16	s-guaiazulene	-7.13	5.980
17	Osthole	-7,16	5.600

LAMPIRAN 15

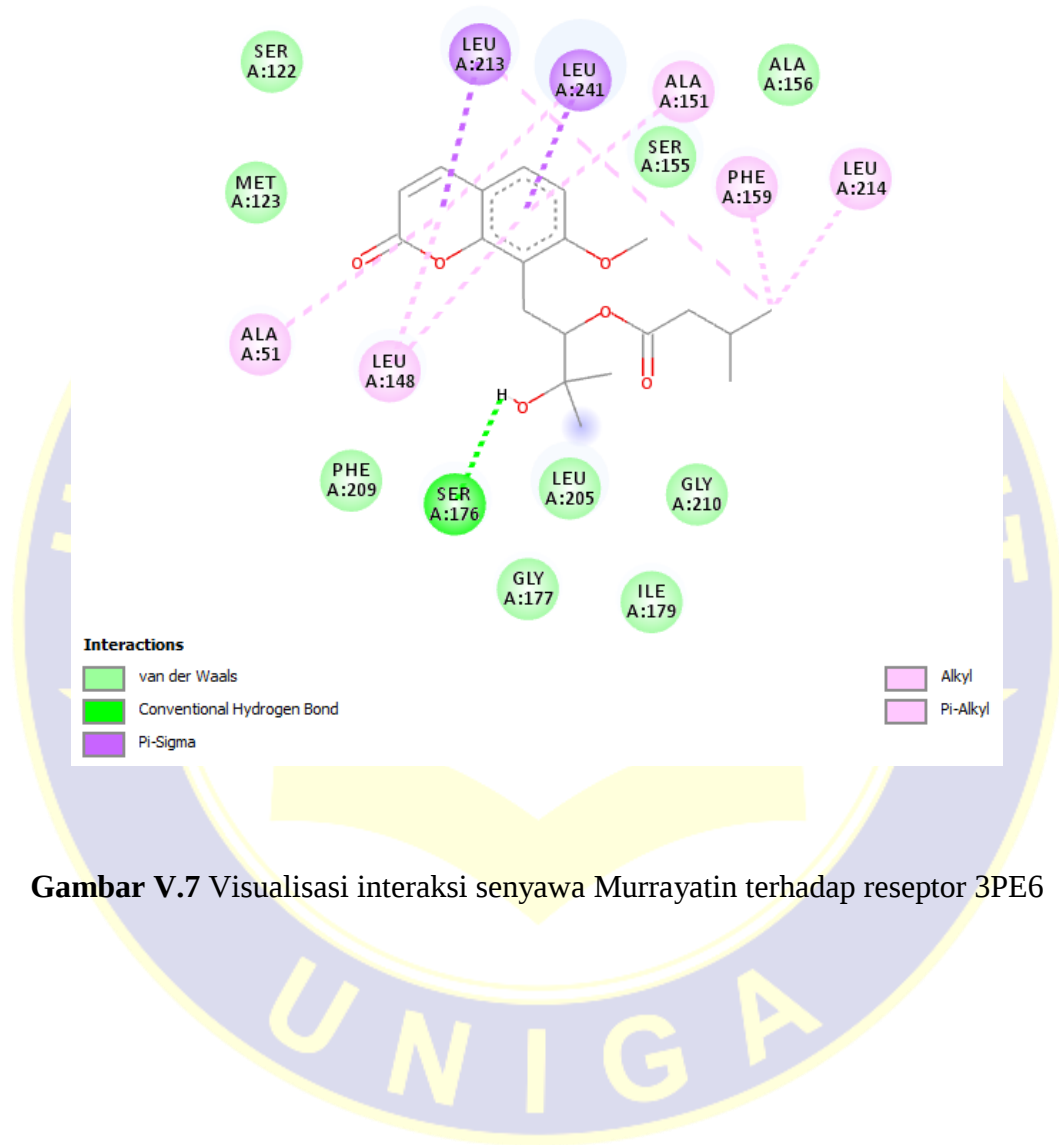
INTERAKSI SENYAWA ORLISTAT TERHADAP RESEPTOR 3PE6



Gambar V.6 Visualisasi interaksi Orlistat terhadap reseptor 3PE6

LAMPIRAN 16

INTERAKSI SENYAWA MURRAYATIN TERHADAP RESEPTOR 3PE6



Gambar V.7 Visualisasi interaksi senyawa Murrayatin terhadap reseptor 3PE6

LAMPIRAN 17

RESIDU ASAM AMINO

Tabel V.8
Hasil Analisis Residu Asam Amino

No	Senyawa Uji	Residu Asam Amino
1	Ligan alami	Ser181, Lys273, Val270, Val191, His269, Leu184, Leu148, Tyr194, Met123, Ala51, Leu213, Leu241.
2	Orlistat	Leu213, Tyr194, Val270, Gly177, Ser176, Pro178
3	Cis – dehydroosthol	Leu241, Met123, Ala51, Leu213, Ile179, His269, Tyr194, Val270, Leu184
4	Isomeranzin	Ile179, Leu241, Ala51, Met123, His269
5	Isomurralonginol acetat	Leu123, Leu205, Leu241, Cys242, Leu148, Ala51, Met123
6	kasegravol	Met123, Ala51, Tyr194, Leu213, Leu241, Ile179
7	Meranzine	Ser122, His269, Met123, Ala51, Ile179, His121, Val270, leu123
8	Murrayatin	Leu213, Leu241, Ala151, Phe159, Leu214, Ala51, Leu148, Ser176
9	Murpanidin	Met123, Ala213, Leu214, Ile179, His269, Tyr194, Val270, Leu184
10	Murpanikolol	Met123, Ala51, Ser122, Leu213, Leu148, Leu205, Leu214
11	Isomuralonginol isovalerat	Leu205, Leu241, Leu213, Cys242, Leu148, His269, His121, Val270, Met123, Ala51
12	osthole	His269, His121, Val270, Leu184, Leu213, Ile179, Leu241, Met123, Ala51
13	paniculatin	Ile179, Gly210, Leu205, Met123, Ala51
14	S-guaiazulene	Tyr194, Val270, Glu53, Ile179, His269, Arg57, Leu184, Lys27, Val191
15	sitronellol	Ala51, Ser122, Tyr194, Ile179, Val270, Leu241, His121
16	scopoletin	His269, Tyr194, Ile179, Met123, Ala51
17	Umbeliferon	His269, Ala51, Met123, Ile179, Val270, Glu53

LAMPIRAN 18
HASIL UJI PRE-ADME

Tabel V.9
Hasil uji Pre-Adme senyawa ligan alami, orlistat dan senyawa daun kemuning

NO	ligan	Caco-2 (nm.sec-1)	HIA (%)	Protein Plasma Binding
1	Ligan alami	55.74	98.28	86.67
2	Orlistat	43.80	96.55	89.38
3	Umbeliferon	19.51	94.17	42.39
4	Scopoletin	0.27	93.92	29.41
5	citronellol	4.95	100.00	100.00
6	s-guaiazulen	23.46	100.00	96.06
7	Paniculatin	33.35	98.77	90.44
8	Osthol	47.34	98.88	92.75
9	murpanikulol	31.69	98.64	90.23
10	Murpanidin	10.24	91.67	68.96
11	murayatin	30.84	96.55	89.38
12	meranzin	43.40	98.08	75.83
13	kasegravol	54.08	98.20	79.65
14	Isomuralonginol asetat	26.16	98.12	77.18
15	isomeranzin	23.29	97.99	85.68
16	Cis-dehydroosthol	47.32	98.79	88.79
17	Isomuralonginol isovalerat	40.17	98.52	90.46

Keterangan :

- 1 %HIA : 70-100% well absorbed, 20-70% moderately absorbed, 0-20% poorly absorbed.
- 2 *In Vitro* caco-2 cell permeability : > 70 higher permeability, 4-70 medium permeability, < 40 low permeability
- 3 % PPB : > 90% strongly bound, <90% weakly bound

LAMPIRAN 19

HASIL UJI TOKSISITAS

Tabel V.10

Hasil Prediksi Toksisitas Senyawa Ligan Alami, Orlistat dan Senyawa Daun Kemuning

No	Senyawa	Kroes TTC decision tree
1	Ligan alami	1
2	Orlistat	2
3	Cis – dehydroosthol	1
4	Isomeranzin	1
5	Isomurralonginol acetat	2
6	kasegravol	1
7	Meranzine	2
8	Murrayatin	1
9	Murpanidin	1
10	Murpanikolol	1
11	osthole	2
12	paniculatin	1
13	S-guaiazulene	1
14	Isomuralonginol isovalerat	2
15	sitronellol	1
16	Scopoletin	2
17	Umbeliferon	2

Kroes TTC decision tree:

- 1 = Substance Would not be expected to be a safety concern
- 2 = Negligible risk (low probably of a life-time cancer risk greater than in 10^{-6})
- 3 = Risk assesment requires compound-specific toxicity data