

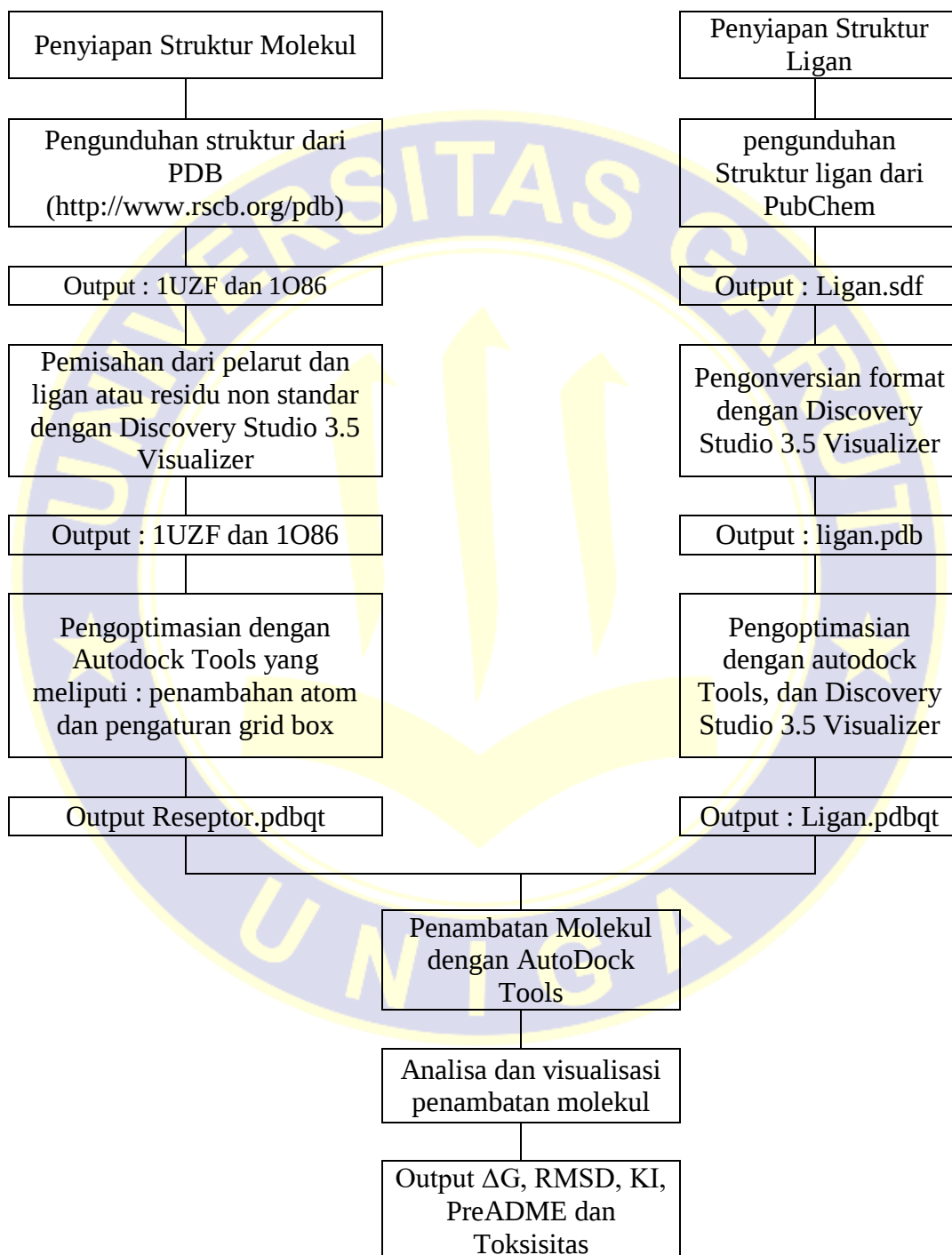
DAFTAR PUSTAKA

1. Persistence the, The IN, Of USE, As A, Predictor The, Rate I, et al. The Persistence In The USE of Anthypertension as the Predictor of. 2014;2014:200p.
2. Muhadi. JNC 8 : Evidence-based Guideline Penanganan Pasien Hipertensi Dewasa. Cermin Dunia Kedokt. 2016;43(1):54–59p.
3. Kusuma Mayasari S. Aktivitas Penghambatan Angiostensin-I Converting Enzyme oleh Fraksi Flavonoid Fenolik dari Infusa daun Singkong (*Manihot Utilissima pohl.*) Secara In Vitro. Yogyakarta; 2015.1-8p
4. Gunawan S dan N. Farmakologi dan Terapi. 5th ed. Gunawan S dan N, editor. Jakarta: FKUI; 2007. 341-360p.
5. Rohini K SP. Therapeutic Role of Coumarins and Coumarin-Related Compounds. J Biofertilizers Biopestic. 2014;05(01):1-3p.
6. Adelin T, Dwinna Aliza dan. Penambatan Molekuler Kurkumin Dan Analognya Pada Enzim Siklooksigenase-2 Molecular Docking of Curcumin and It's Analogue on Cyclooxigenase-2 Enzyme. J Med Vet. 2013;7(1)p.
7. Kemenkes.RI. Pusdatin Hipertensi. Infodatin. 2014;(Hipertensi):1–7p.
8. Satyajit D. Sarker dan Lutfun Nahar. Kimia Untuk Mahasiswa Farmasi Bahan Kimia Organik, Alam dan Umum. Inawati Wanandi S, editor. Yogyakarta: Pustaka Pelajar; 2009. 37-39, 247, 518-521p.

9. Koolman J. Atlas Berwarna dan teks Biokimia. Jakarta: Hipokrates; 2000. 86-92p.
10. Apriani F. Studi Penambatan Molekul Senyawa-Senyawa Amidasi etil Para Metoksisinamat Pada Peroxisome Poliferator-Activated Reseptor-Gamma (PPAR γ). Jakarta; 2015.12-13, 17-21p.
11. Yanuar A. Penambatan Molekul Praktek dan Aplikasi Pada Virtual Screening. Depok: Universitas Indonesia; 2012. 8, 16-17, 47p.
12. Nursamsiar, Tandi Toding, Alparida, Awaluddin A. Studi In Silico Senyawa Turunan Analog Kalkon dan Pirimidin Sebagai Antiinflamasi : Prediksi Absorpsi, Distribusi, dan Toksisitas. Pharmacy. 2016;13(1):92–100p.
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. Lestari T. Studi interaksi Senyawa Turunan 1,3-Dibenzoiltiourea sebagai Ribonukleotida Reduktase Inhibitor. J Farm Indones. 2015;7(3):163–169p.

LAMPIRAN 1

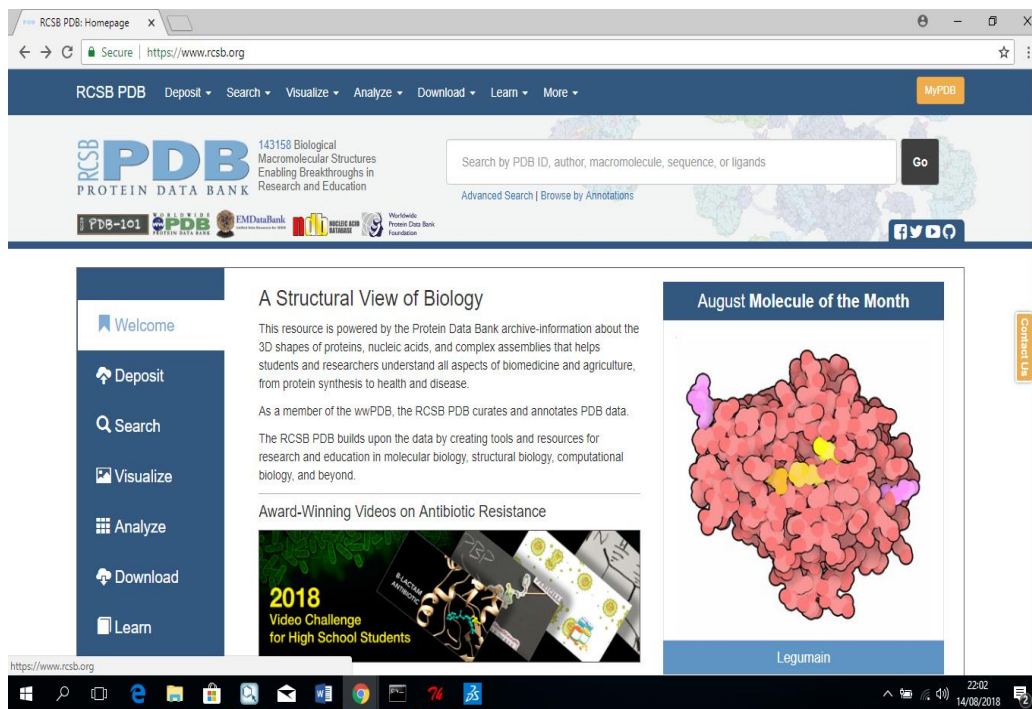
ALUR PENELITIAN



Gambar I.1 Alur penelitian secara umum

LAMPIRAN 2

PROTEIN DATA BANK



Gambar I.2 Protein Data Bank

LAMPIRAN 3

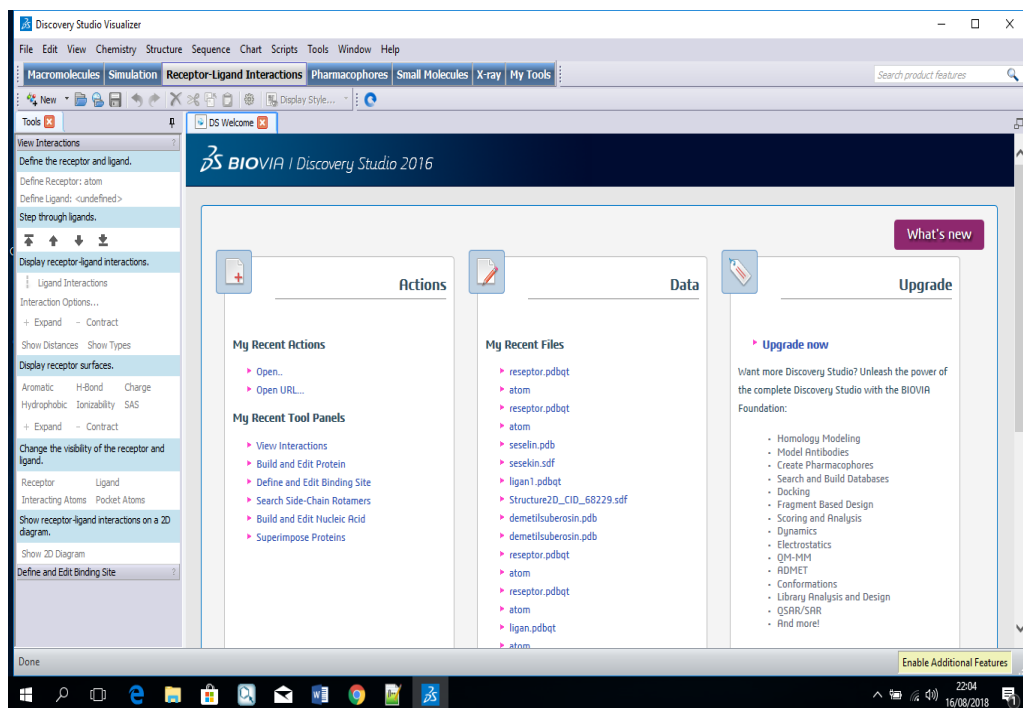
PUBCHEM



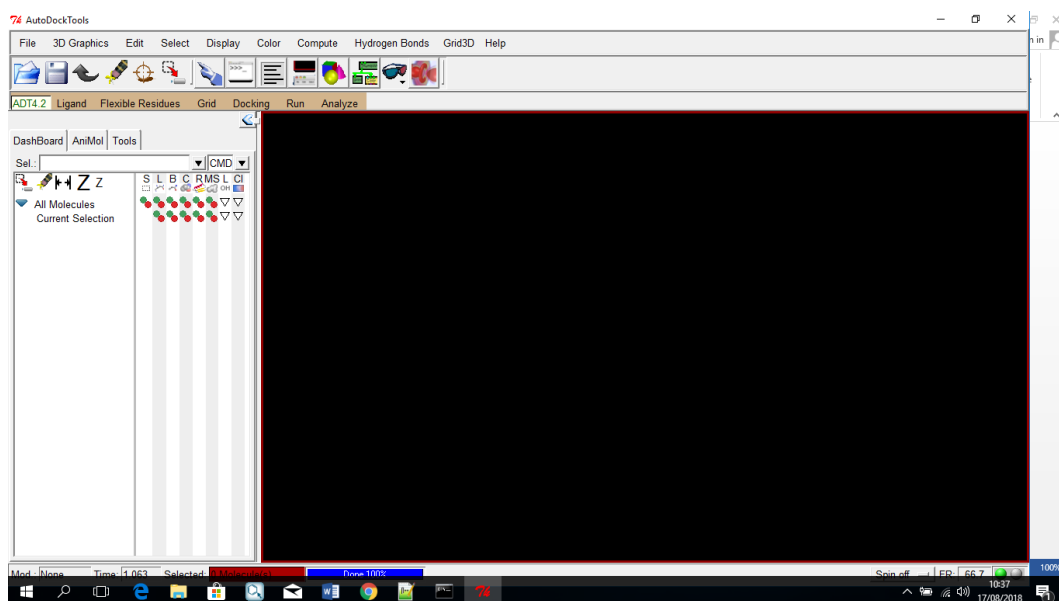
Gambar I.3 PubChem

LAMPIRAN 4

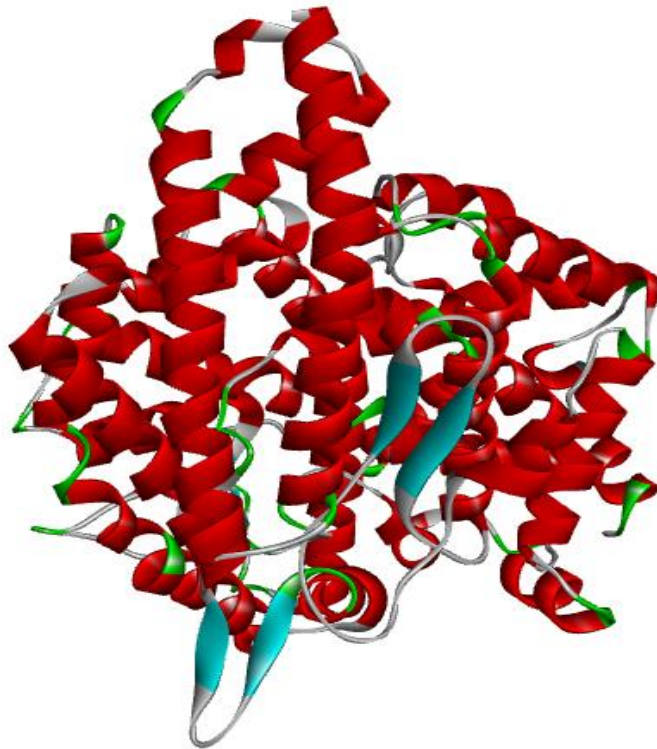
DISCOVERY STUDIO VISUALIZER



Gambar I.4 Discovery Studio Visualizer

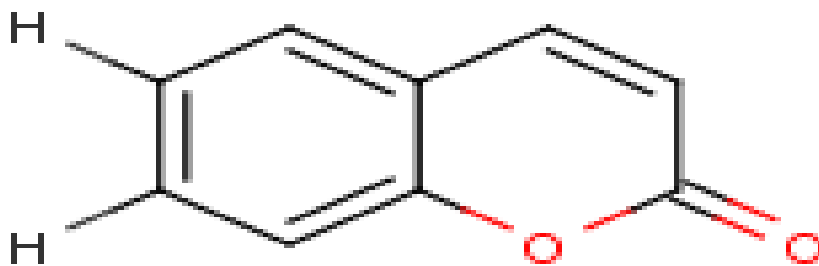
LAMPIRAN 5**AUTODOCK****Gambar I.5 AutoDock**

LAMPIRAN 6
MAKROMOLEKUL

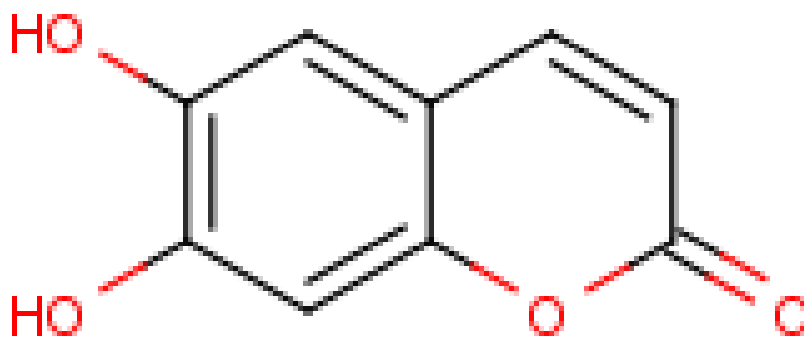


Gambar I.6 Makromolekul Angiotensin Converting Enzym

LAMPIRAN 7
STRUKTUR KUMARIN

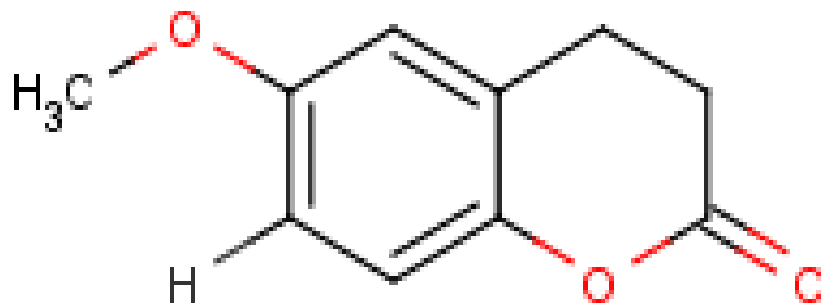


Gambar I.7 Umbelliferon

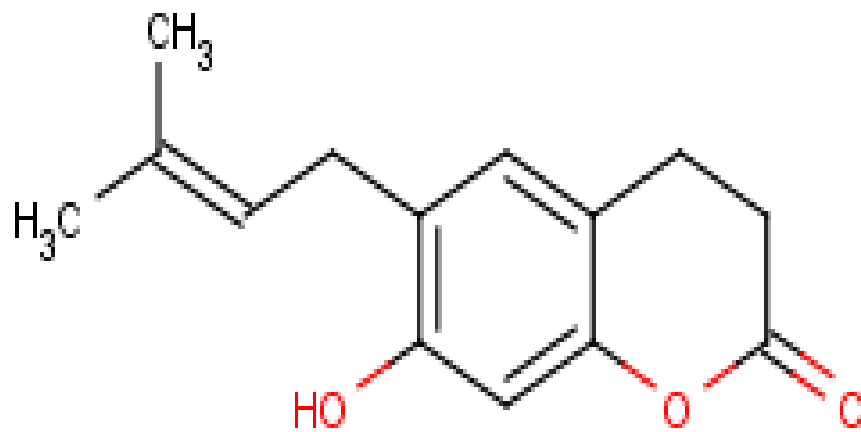


Gambar I.8 Esculetin

**LAMPIRAN 7
(LANJUTAN)**

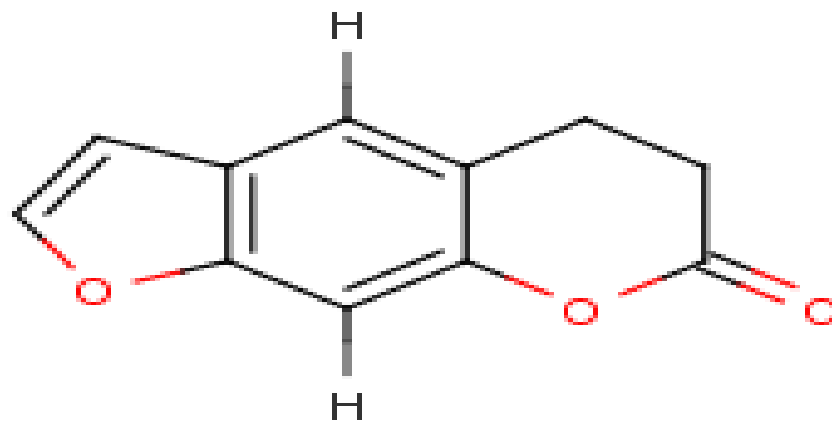


Gambar I.9 Scopoletin

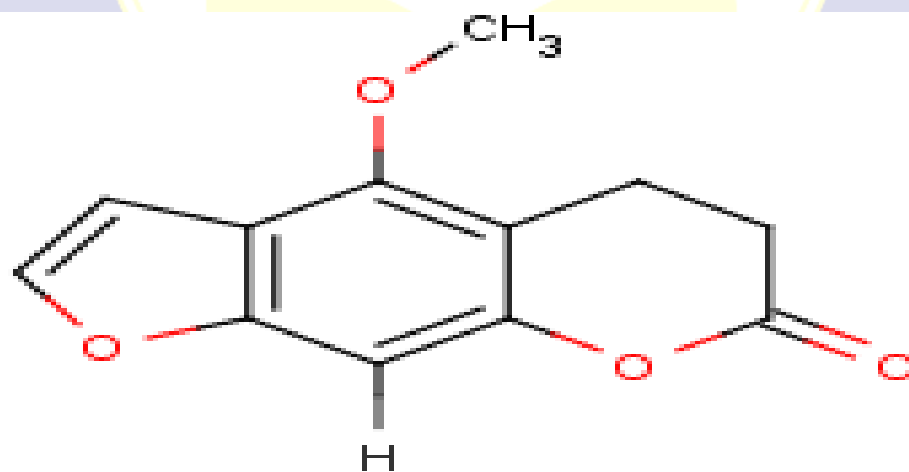


Gambar I.10 Demetilsuberosin

**LAMPIRAN 7
(LANJUTAN)**

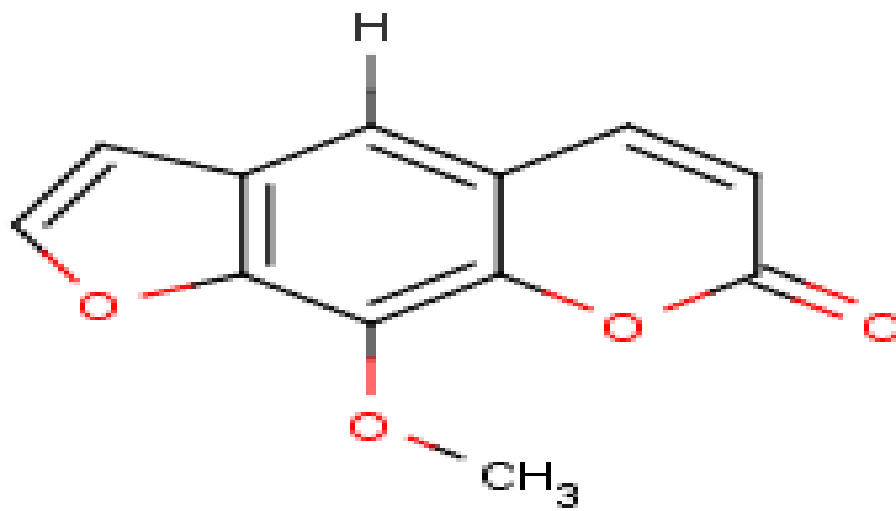


Gambar I.11 Psoralen

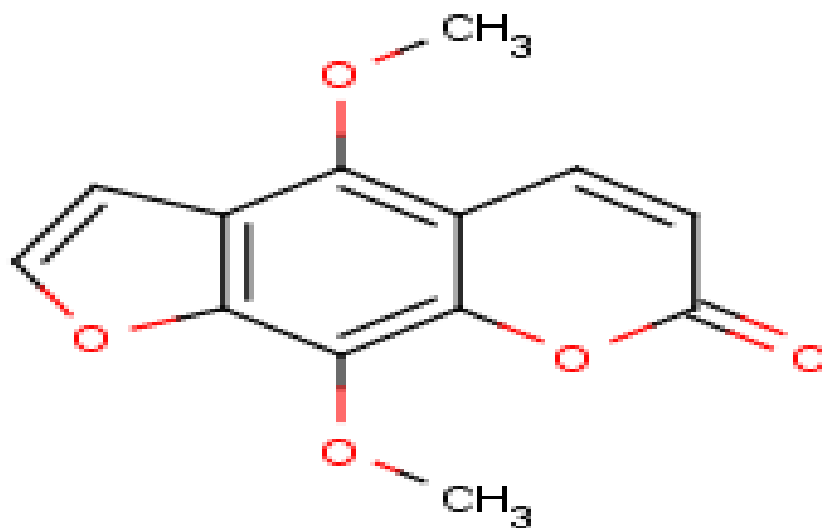


Gambar I.12 Bergapten

**LAMPIRAN 7
(LANJUTAN)**

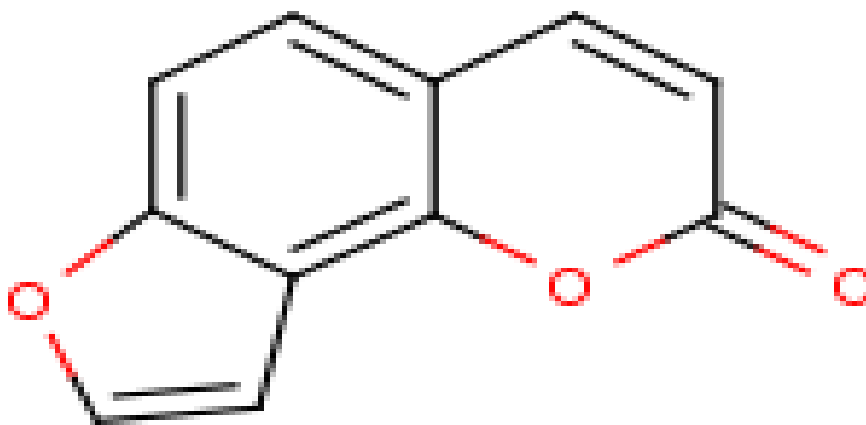


Gambar I.13 Xantotoksin

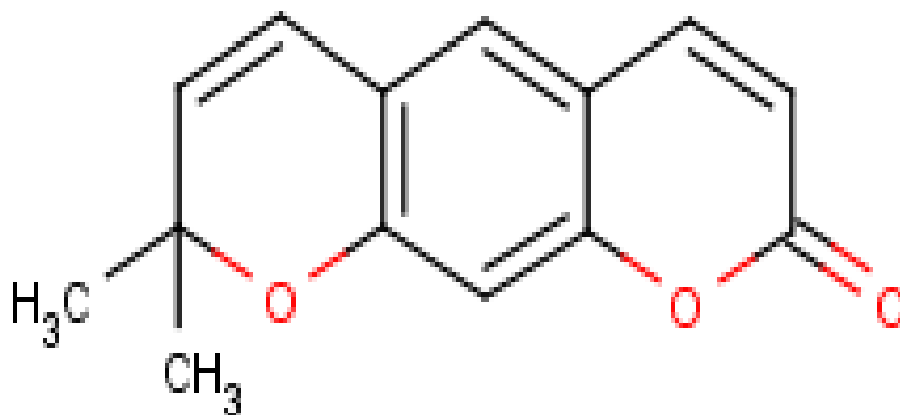


Gambar I.14 Isopimpinellin

**LAMPIRAN 7
(LANJUTAN)**

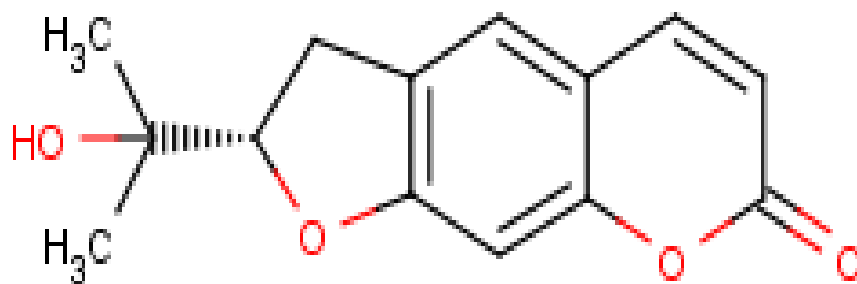


Gambar I.15 Angelisin

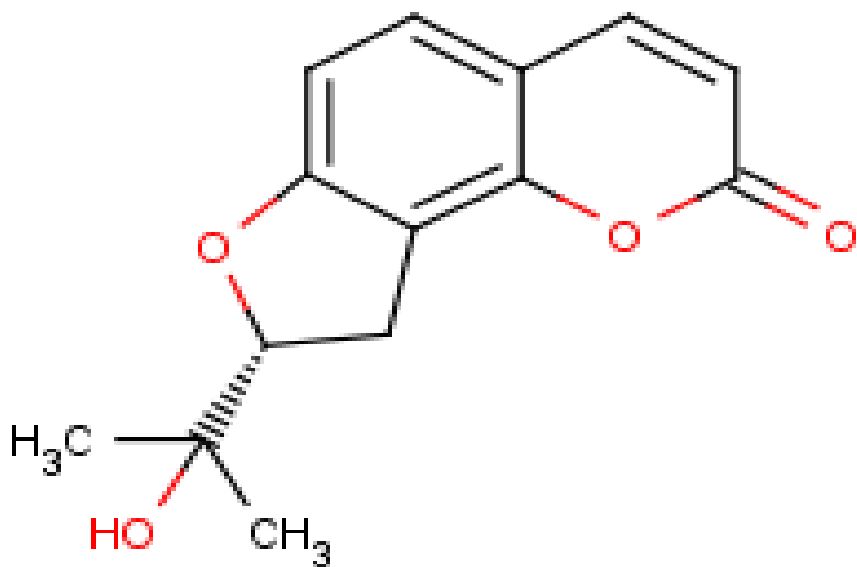


Gambar I.16 Xantiletin

**LAMPIRAN 7
(LANJUTAN)**

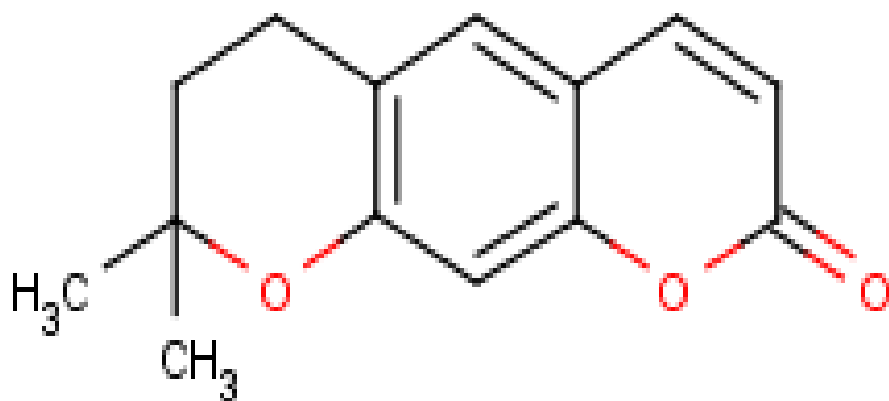


Gambar I.17 Marmesin

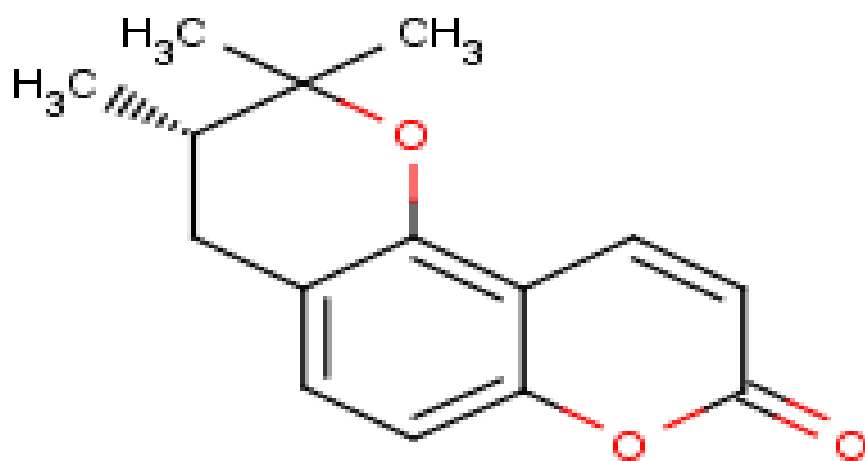


Gambar I.18 Dihydroorosenol

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(LANJUTAN)**

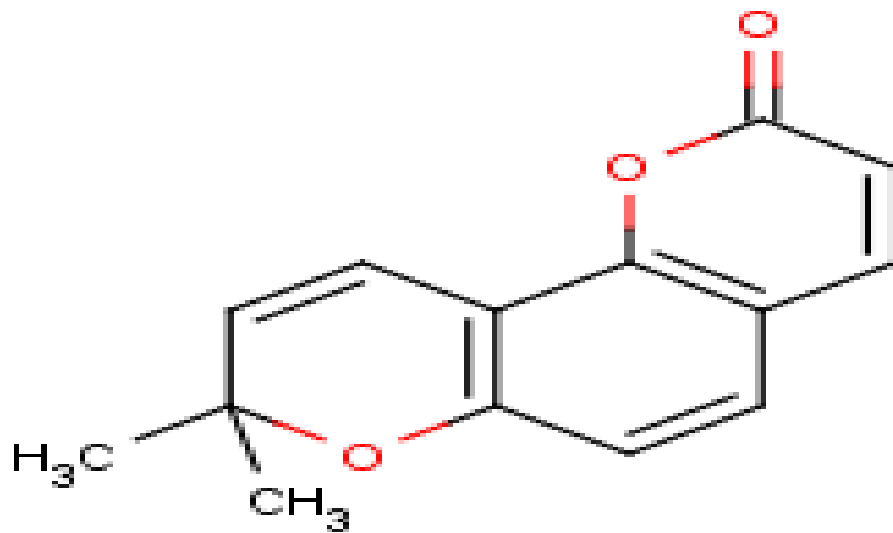


Gambar I.19 1'2'-dihydrosantiletin

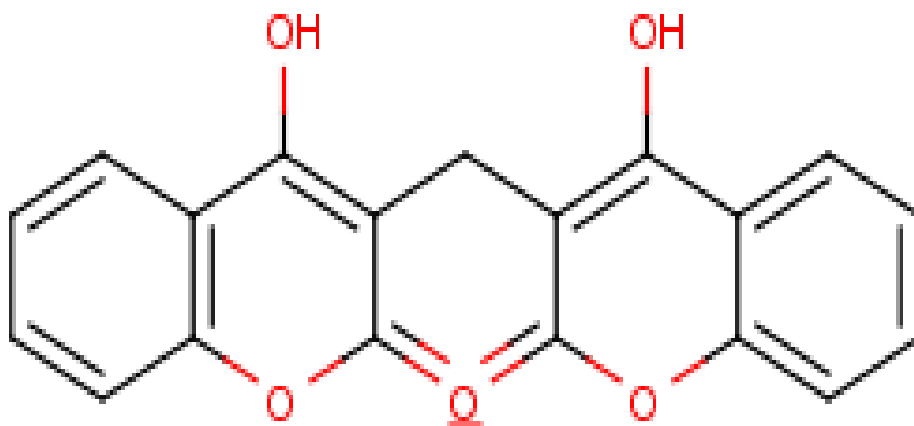


Gambar I.20 Libanotin

LAMPIRAN 7
(LANJUTAN)

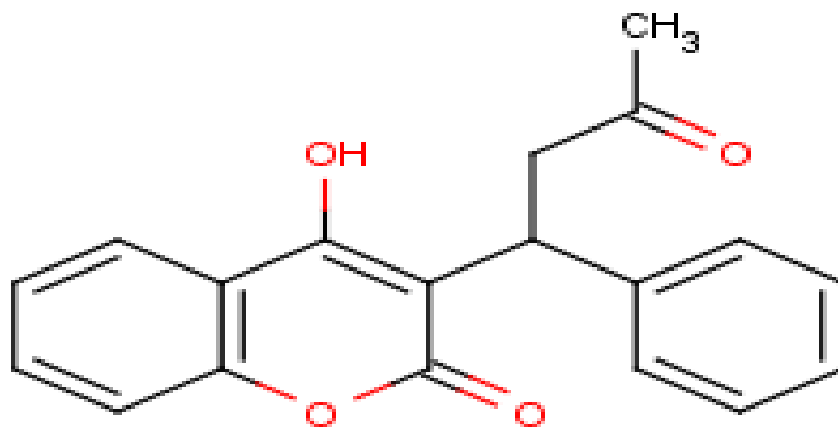


Gambar I.21 Seselin

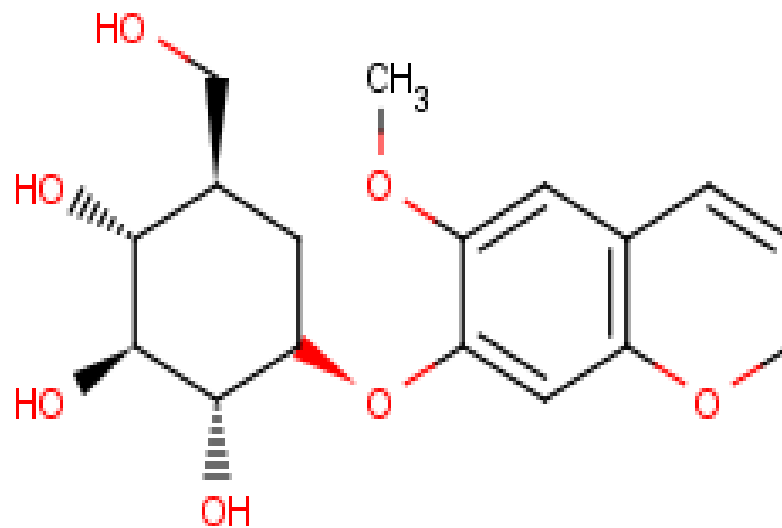


Gambar I.22 Dikumarol

**LAMPIRAN 7
(LANJUTAN)**

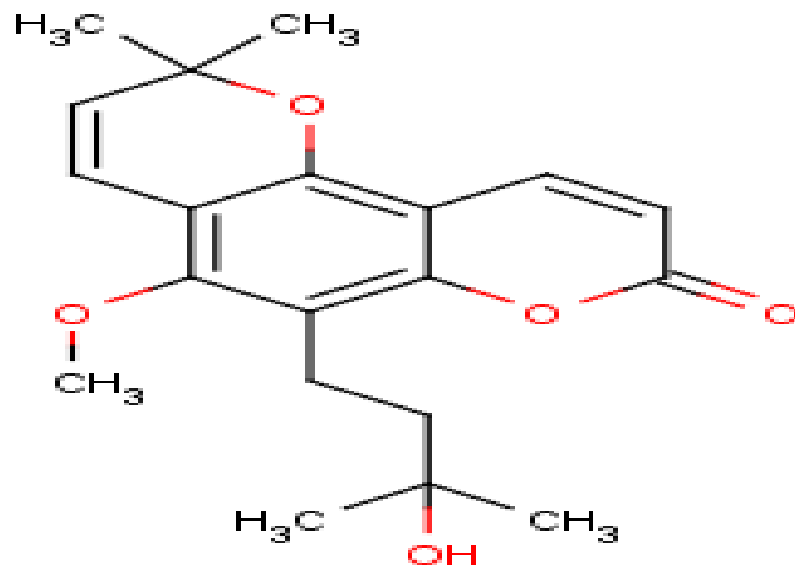


Gambar I.23 Warfarin



Gambar I.24 Skopolin

LAMPIRAN 7
(LANJUTAN)



Gambar I.25 Avisennol

LAMPIRAN 8

HASIL VALIDASI METODE

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13793
13794 Number of distinct conformational clusters found = 2, out of 100 runs,
13795 Using an rmsd-tolerance of 2.0 Å
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13798 CLUSTERING HISTOGRAM
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Clus	Lowest	Run	Mean	Num	Histogram
-ter	Binding		Binding	in	
Rank	Energy		Energy	Clus	
1	-6.84	79	-6.63	99	#####
2	-4.61	81	-4.61	1	#

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Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	79	-6.84	0.00	0.60	RANKING
1	2	43	-6.83	0.11	0.56	RANKING
1	3	25	-6.91	0.11	0.59	RANKING
1	4	42	-6.81	0.13	0.60	RANKING
1	5	83	-6.81	0.19	0.60	RANKING
1	6	39	-6.79	0.39	0.75	RANKING
1	7	89	-6.79	0.34	0.73	RANKING
1	8	22	-6.78	0.44	0.76	RANKING
1	9	31	-6.78	0.11	0.59	RANKING

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Gambar V.1 Hasil validasi 1UZf dengan Captopril

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Clus	Lowest	Run	Mean	Num	Histogram
-ter	Binding		Binding	in	
Rank	Energy		Energy	Clus	
1	-8.01	57	-8.00	100	#####

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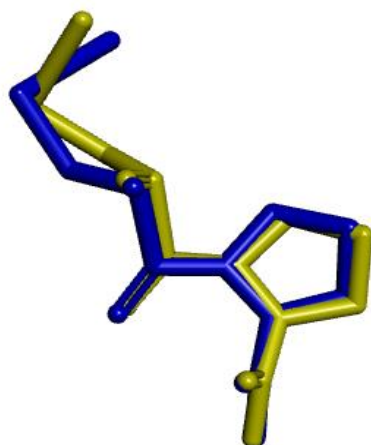
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Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	57	-8.01	0.00	0.72	RANKING
1	2	29	-8.01	0.01	0.72	RANKING
1	3	68	-8.01	0.01	0.72	RANKING
1	4	36	-8.01	0.02	0.72	RANKING
1	5	14	-8.01	0.00	0.72	RANKING
1	6	75	-8.01	0.02	0.72	RANKING
1	7	17	-8.01	0.01	0.72	RANKING

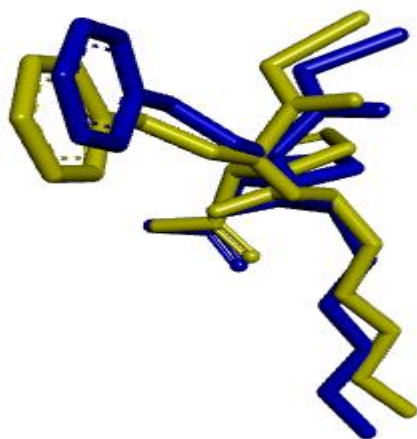
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Gambar V.2 Hasil validasi 1O86 dengan Lisinopril

LAMPIRAN 9

HASIL *RE-DOCKING* LIGAN ALAMI

Gambar V.3 Hasil visualisasi *re-docking* 1UZF (captopril) dengan ligan alami berwarna biru dan hasil kristalografi berwarna kuning



Gambar V.4 Hasil visualisasi *re-docking* 1O86 (lisinopril) dengan ligan alami berwarna biru dan hasil kristalografi berwarna kuning

LAMPIRAN 10

HASIL PENAMBATAN MOLEKUL SENYAWA UJI

Tabel V.1

Hasil Penambatan Molekul Berupa energi Bebas dan KI makromolekul 1UZF

no	Nama Senyawa	Lowest Binding Energi	Nilai KI (nM)
1.	Ligan Pembanding (Captopril)	-6,84	9.620
2.	Umbelliferon	-5,87	4.730
3.	Aesculetin	-5,14	9.130
4.	Skopoletin	-5,85	5.580
5.	Skopolin	-6,14	31.400
6.	Psoralen	-5,85	51.800
7.	Bergapten	-5,75	60.890
8.	Xantotoksin	-6,38	21.160
9.	Isopimpinellin	-6,39	20.790
10.	Angelisin	-5,80	45.490
11.	Marmesin	-6,67	12.800
12.	Dihidroorosenol	-6,78	10.670
13.	Xantiletin	-6,69	12.500
14.	Avisenol A	-6,00	40.290
15.	Dihidroksantiletin	-6,56	15.510
16.	Libanotin	-7,38	6.900
17.	Dikumarol	-6,94	8.210
18.	Warfarin	-8,07	1.710
19.	Demetilsuberosin	-6,50	25.190
20.	Seselin	-7,02	7.090

LAMPIRAN 10
(LANJUTAN)

Tabel V.2

Hasil Penambatan Molekul Berupa Energi Bebas dan KI makromolekul 1O86

No	Nama Senyawa	Lowest Binding Energi	Nilai KI (nM)
1.	Ligan Pembanding (Lisinopril)	-8,01	1.350
2.	Umbelliferon	-5,72	63.980
3.	Aesculetin	-5,54	86.980
4.	Skopoletin	-5,72	64.210
5.	Skopolin	-7,47	3.320
6.	Psoralen	-6,01	39.320
7.	Bergapten	-6,04	37.430
8.	Xantotoksin	-6,49	17.430
9.	Isopimpinellin	-6,65	13.340
10.	Angelicin	-6,21	27.860
11.	Marmesin	-6,90	8.760
12.	Dihidroorosenol	-7,25	4.870
13.	Xantiletin	-6,49	17.430
14.	Avisenol A	-6,58	15.100
15.	Dihidroksantiletin	-6,78	10.780
16.	Libanotin	-8,76	4.130
17.	Dikumarol	-6,95	8.000
18.	Warfarin	-8,37	728,22
19.	Demetilsuberosin	-6,60	14.520
20.	Seselin	-7,06	6.720

LAMPIRAN 11

PRE ADME

Tabel V.3
Hasil Pre-ADME

No	Ligan	Caco-2 (nm.sec-1)	HIA (%)	Protein Plasma Binding (%)
1.	Ligan Pembanding (Captopril)	21,03	79,47	60,47
2.	Ligan Pembanding (Lisinopril)	16,55	83,31	13,79
3.	Angelicin	37,74	98,42	82,52
4.	Avisenol	49,80	96,11	86,57
5.	Bergapten	43,47	98,16	91,65
6.	Dikumarol	-	-	-
7.	Dihidroorosenol	27,45	96,17	81,78
8.	Isopimpinellin	43,47	98,16	91,65
9.	Libanotin	43,49	98,98	89,07
10.	Marmesin	8,00	95,36	74,40
11.	Psoralen	37,74	98,42	91,06
12.	Aesculetin	18,57	88,19	11,46
13.	Scopoletin	0,27	93,92	29,41
14.	Umbelliferon	19,51	94,17	42,39
15.	Xantiletin	37,74	98,42	86,04
16.	1'2-Dihidroxantiletin	24,76	99,05	89,22
17.	Xantotoksin	43,47	98,16	93,04
18.	Demetilsuberosin	14,40	95,06	97,48
19.	Warfarin	22,15	96,05	88,42
20.	Seselin	32,26	98,96	85,70
21.	Skopolin	11,35	53,81	41,84

LAMPIRAN 12
HASIL TOKSISITAS

Tabel V.4
Hasil Toksisitas

No	Nama Senyawa	Mutagenik	Karsinogenik
1.	Captopril	Mutagenik	Negatif
2.	Lisinopril	Non-Mutagenik	Negatif
3.	Angiotensin	Mutagenik	Positif
4.	Amlodipine	Non-Mutagenik	Negatif
5.	Bergapten	Mutagenik	Negatif
6.	Dikumarol	-	-
7.	Dihidroorosenol	Non-Mutagenik	Positif
8.	Isopimpinellin	Mutagenik	Negatif
9.	Libanotin	Non-mutagenik	Negatif
10.	Marmesin	Mutagenik	Negatif
11.	Psoralen	Mutagenik	Negatif
12.	Scopolin	Non-mutagenik	Positif
13.	Scopoletin	Mutagenik	Negatif
14.	Umbelliferon	Mutagenik	Positif
15.	Xantiletin	Mutagenik	Negatif
16.	Dihidroxantiletin	Mutagenik	Negatif
17.	Xantotoksin	Mutagenik	Negatif
18.	Demetilsuberosin	Mutagenik	Negatif
19.	Aesculetin	Mutagenik	Negatif
20.	Seselin	Mutagenik	Negatif
21.	Warfarin	Mutagenik	Negatif

LAMPIRAN 13

SIFAT FISIKOKIMIA SENYAWA UJI

Tabel V.5

Sifat Fisikokimia Senyawa Uji

No	Nama senyawa	BM (g/mol)	Log P	Donor ikatan H	Akseptor ikatan H	Molar refractivity
1.	Aesculetin	178	1,03	2	4	44,44
2.	Angelisin	186	2,36	0	3	50,88
3.	Avisenol	304	2,42	2	5	82,72
4.	Bergapten	216	2,37	0	4	57,43
5.	Dicumarol	336	3,15	2	6	87,86
6.	dihidroorosenol	344	2,57	1	6	88,67
7.	isopimpinellin	246	2,38	0	5	63,98
8.	Libanotin	386	3,27	0	7	99,63
9.	Marmesin	246	1,69	1	4	65,52
10.	Psoralen	186	2,36	0	3	50,88
11.	Scopolin	354	-1,19	4	9	82,05
12.	Scopoletin	192	1,33	1	4	49,32
13.	Umbelliferon	162	1,32	1	3	42,77
14.	Xantiletin	228	2,80	0	3	64,85
15.	dihidroxantiletin	230	2,72	0	3	64,13
16.	xantotoksin	216	2,37	0	4	57,43
17.	demetilsuberosin	244	3,13	0	3	70,79
18.	Seselin	321	-0,05	5	6	77,14
19.	Warfarin	308	3,63	1	4	86,10

LAMPIRAN 14

HASIL RESIDU ASAM AMINO YANG TERBENTUK

Tabel V.6

Hasil Analisis Ikatan Hidrogen dan Asam Amino yang terikat

No	Senyawa uji	Jumlah Ikatan Hidrogen	Residu Asam Amino
1.	Kaptopril	5	His353, His513, Gln281, Tyr520, Lys511
2.	Esculetin	3	His353, Lys511, Tyr520
3.	Angelisin	2	His353, His513
4.	Avisennol	2	Gln281, Tyr520
5.	Bergapten	3	His353, His513, Gln281
6.	Dicumarol	2	His353, Lys511
7.	Dihidroorosenol	3	Glu376, Thr282, Gln281
8.	Dihidroxanthiletin	1	Lys511
9.	Isopimpinellin	3	His353, His513, Gln281
10.	Libanotin	4	Ala354, His353, Lys511, Gln281
11.	Marmesin	3	Gln281, His353, His513
12.	Psoralen	3	Gln281, His353, His513
13.	Scopoletin	4	His513, Lys511, Tyr520, Gln281
14.	Scopolin	4	His353, his513, Tyr520, Glu384
15.	Demetilsuberosin	1	His513
16.	Umbelliferon	5	Tyr520, Tyr523, His513, Gln281, Lys511
17.	Xantilethin	2	His353, His513
18.	Xanthotoxin	-	-
19.	Seselin	2	His353, His513
20.	Warfarin	2	Gln281, Lys511

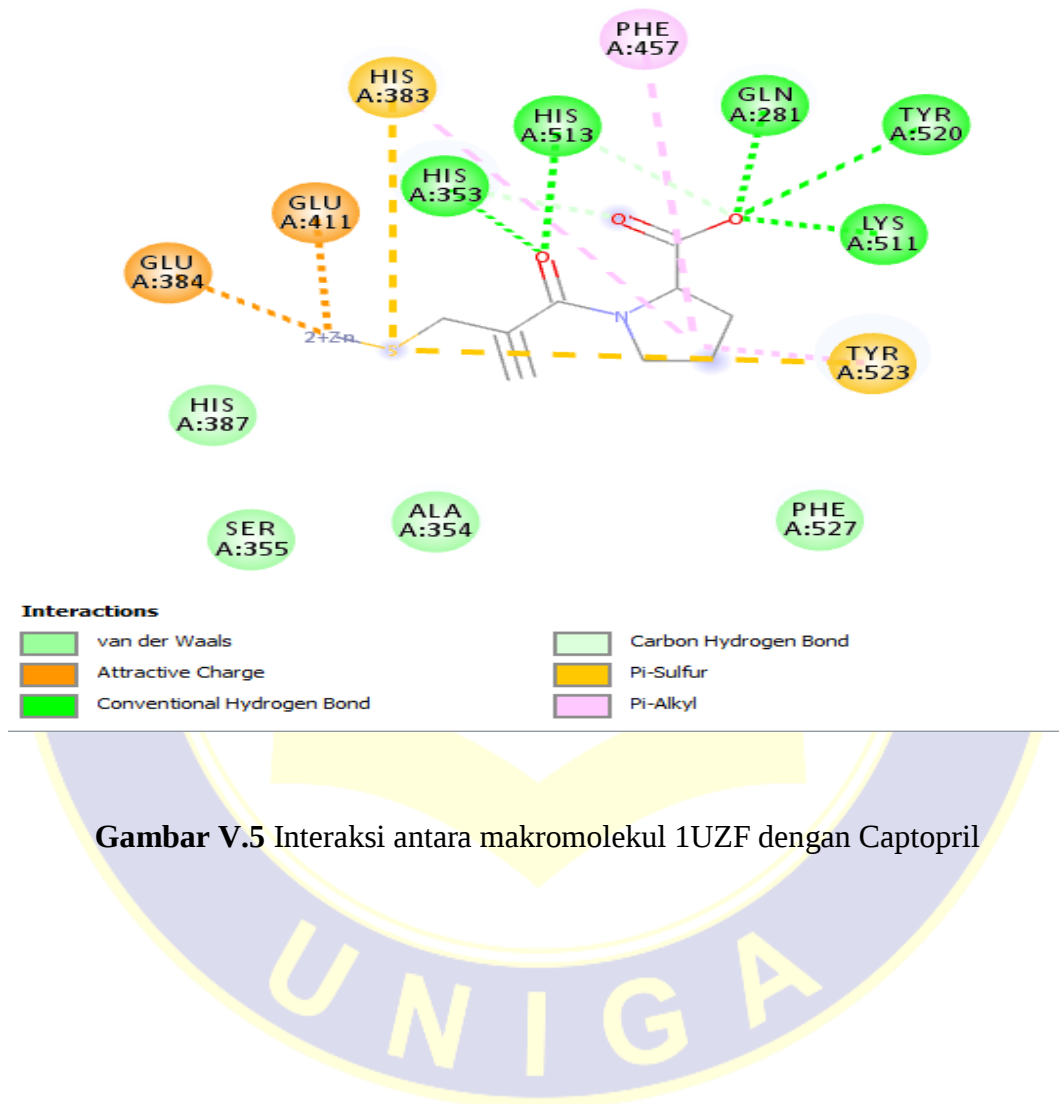
LAMPIRAN 14
(LANJUTAN)

Tabel V.7

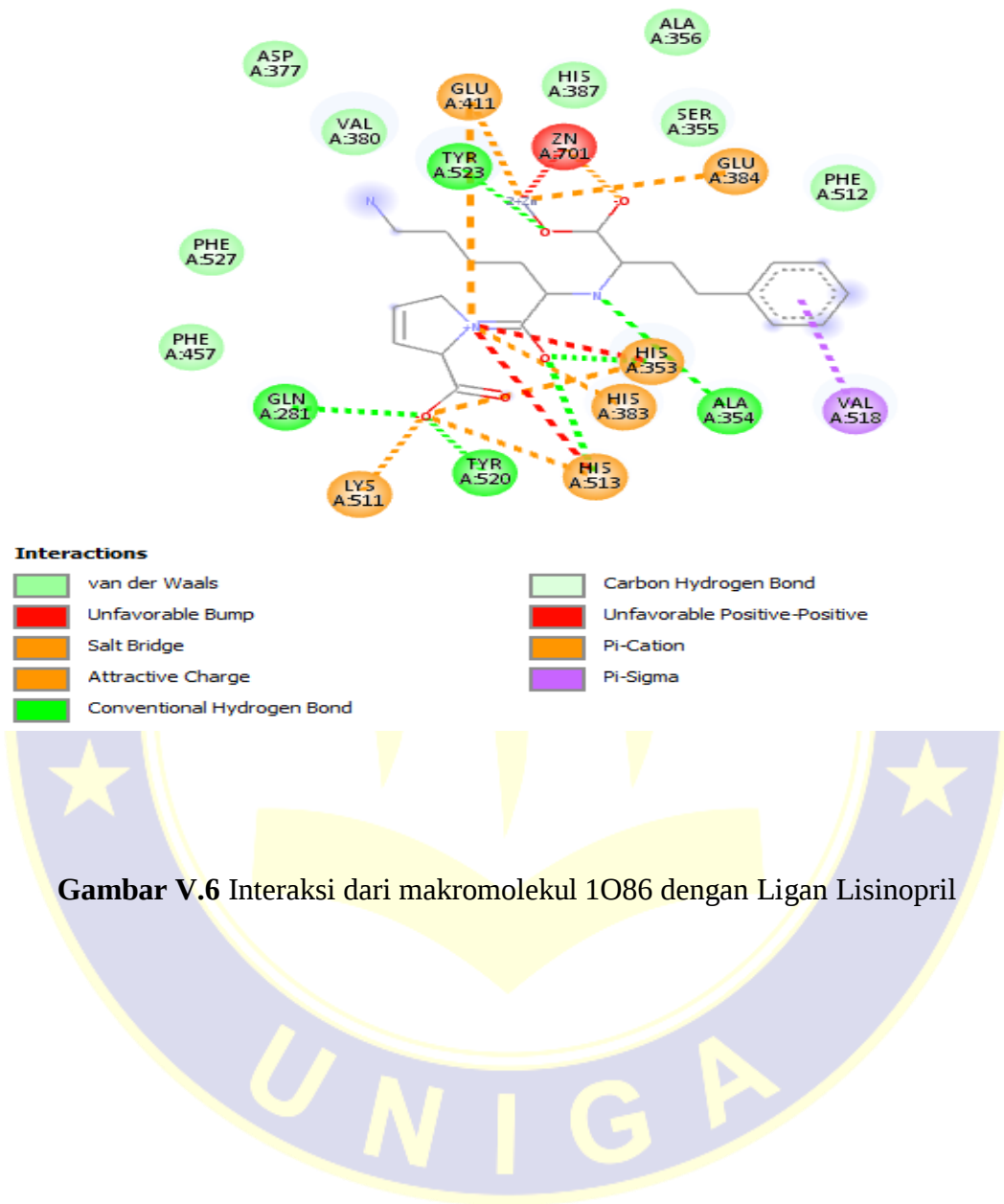
Hasil analisis Ikatan Hidrogen dan Asam Amino yang terikat

No.	Senyawa Uji	Jumlah Ikatan Hidrogen	Residu Asam Amino
1.	Lisinopril	6	Tyr520, Tyr523, His353, His513, Ala354, Gln281
2.	Esculetin	3	Lys511, Tyr520, asp415
3.	Angelisin	3	Tyr520, Gln281, Lys511
4.	Avisenol	3	Tyr523, Ala356, Glu411
5.	Bergapten	2	Tyr520, Lys511
6.	Dicumarol	5	His513, Tyr523, Glu384, Arg522, Ala356
7.	Dihidroorosenol	1	Ala356
8.	Dihidroxanthiletin	2	Lys511, Tyr520
9.	Isopimpinellin	3	Lys511, Tyr520, Gln281
10.	Libanotin	5	Lys511, Tyr520, Gln281, Thr282, Lys454
11.	Marmesin	3	Gln281, His353, His513
12.	Psoralen	3	Tyr520, Gln281, Lys511
13.	Scopoletin	1	Ala356
14.	Skopolin	5	Cys370, Ala354, Lys511, Gln281, Glu384
15.	Umbelliferon	4	Lys511, Tyr520, Gln281, Glu384
16.	Demetilsuberosin	1	His353
17.	Xanthiletin	2	Tyr520, Lys511
18.	Xanthotoxin	3	Lys511, Gln281, Tyr520
19.	Seselin	3	Tyr520, Gln281, Lys511
20.	Warfarin	4	Arg522, Glu384, His353, His513

LAMPIRAN 15
INTERAKSI MAKROMOLEKUL

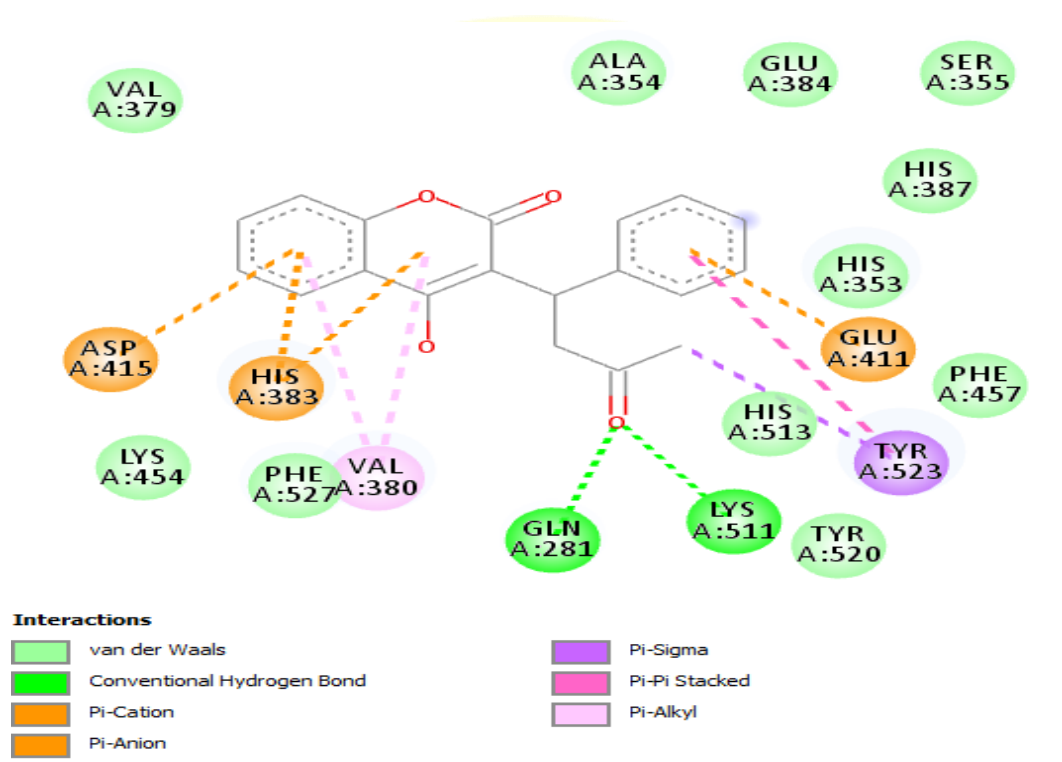


LAMPIRAN 15 (LANJUTAN)



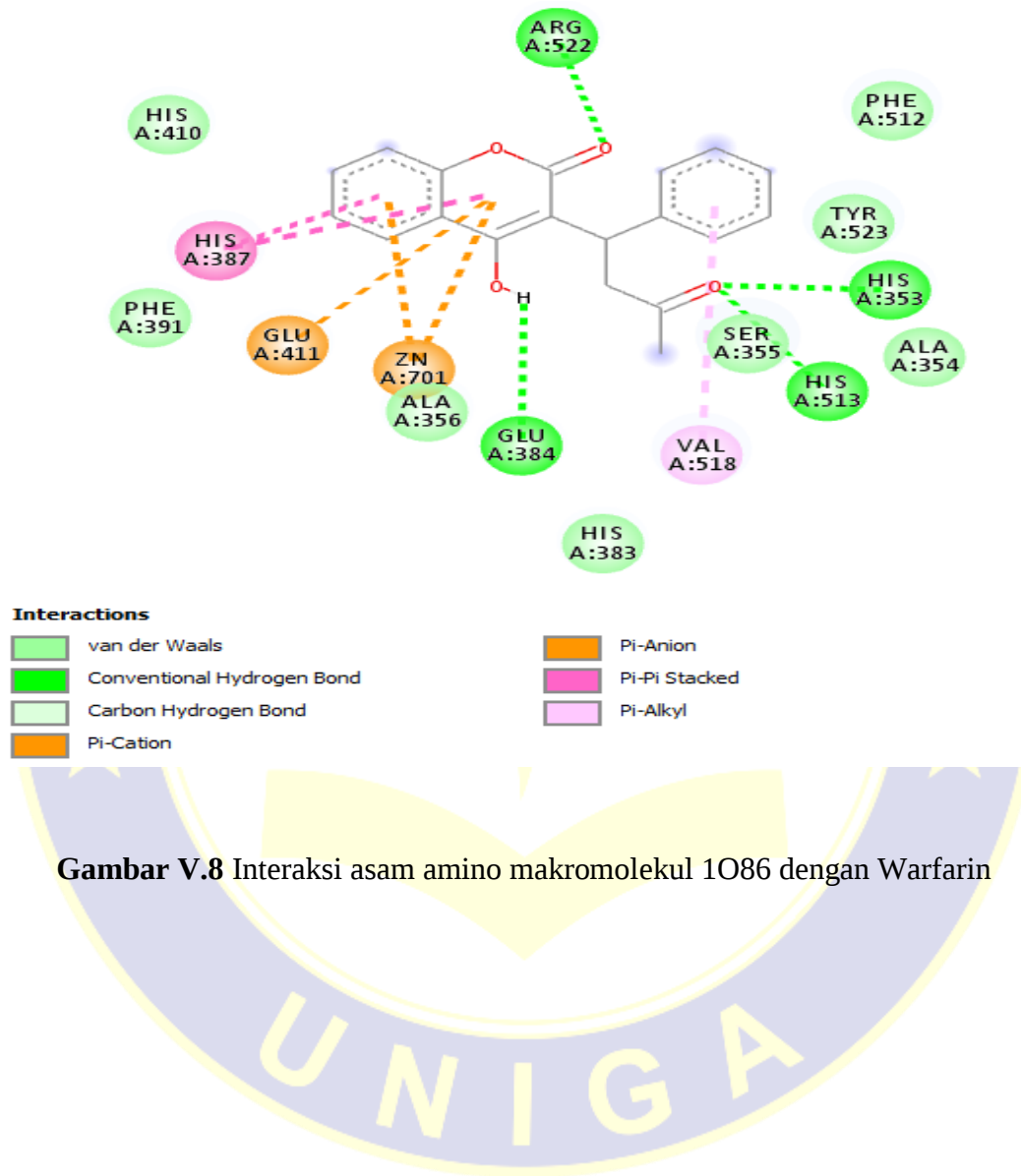
LAMPIRAN 16

INTERAKSI MAKROMOLEKUL SENYAWA UJI

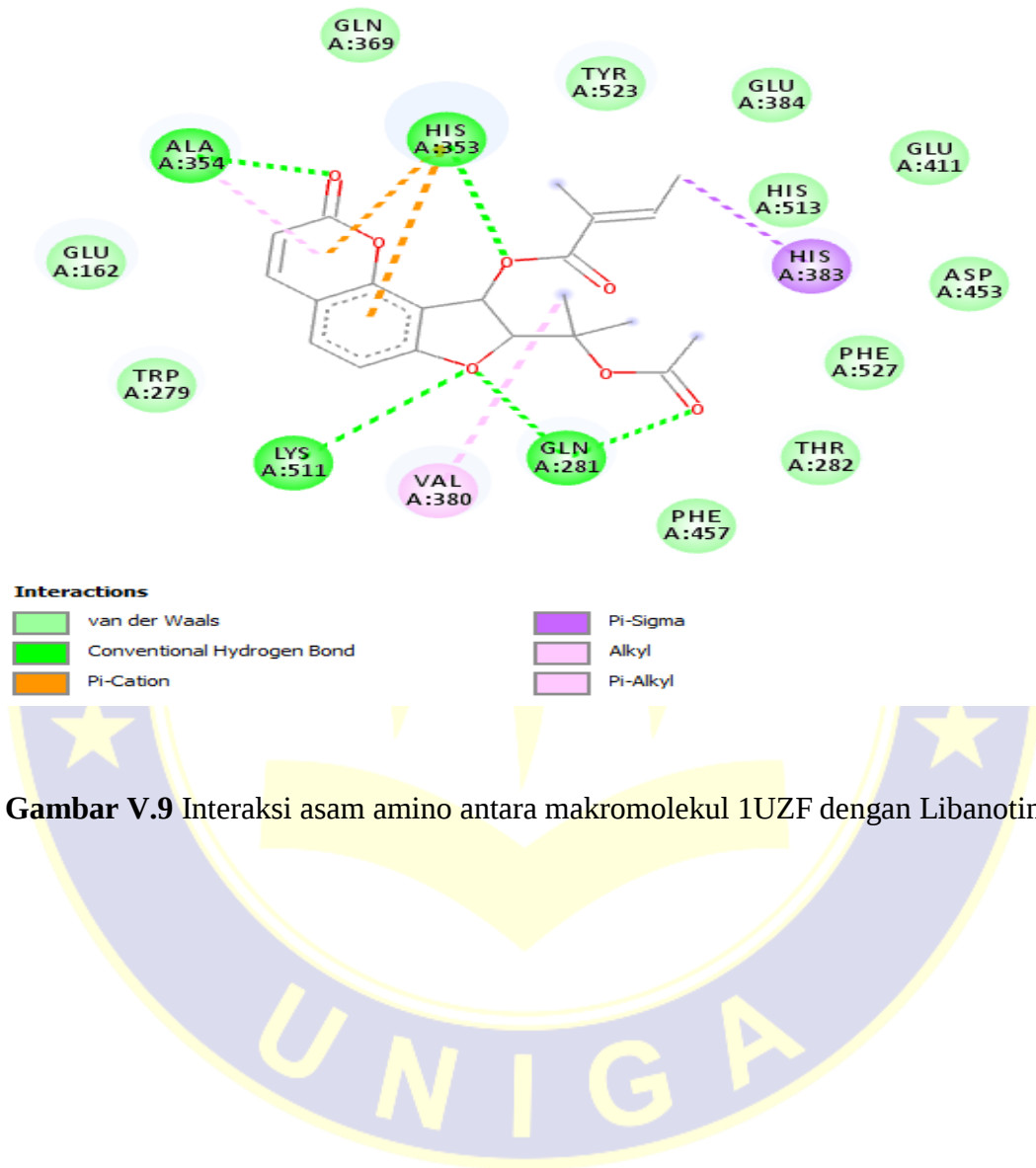


Gambar V.7 Interaksi asam amino antara makromolekul 1UZP dengan warfarin

LAMPIRAN 16 (LANJUTAN)



LAMPIRAN 16 (LANJUTAN)



Gambar V.9 Interaksi asam amino antara makromolekul 1UZF dengan Libanotin

LAMPIRAN 16 (LANJUTAN)

