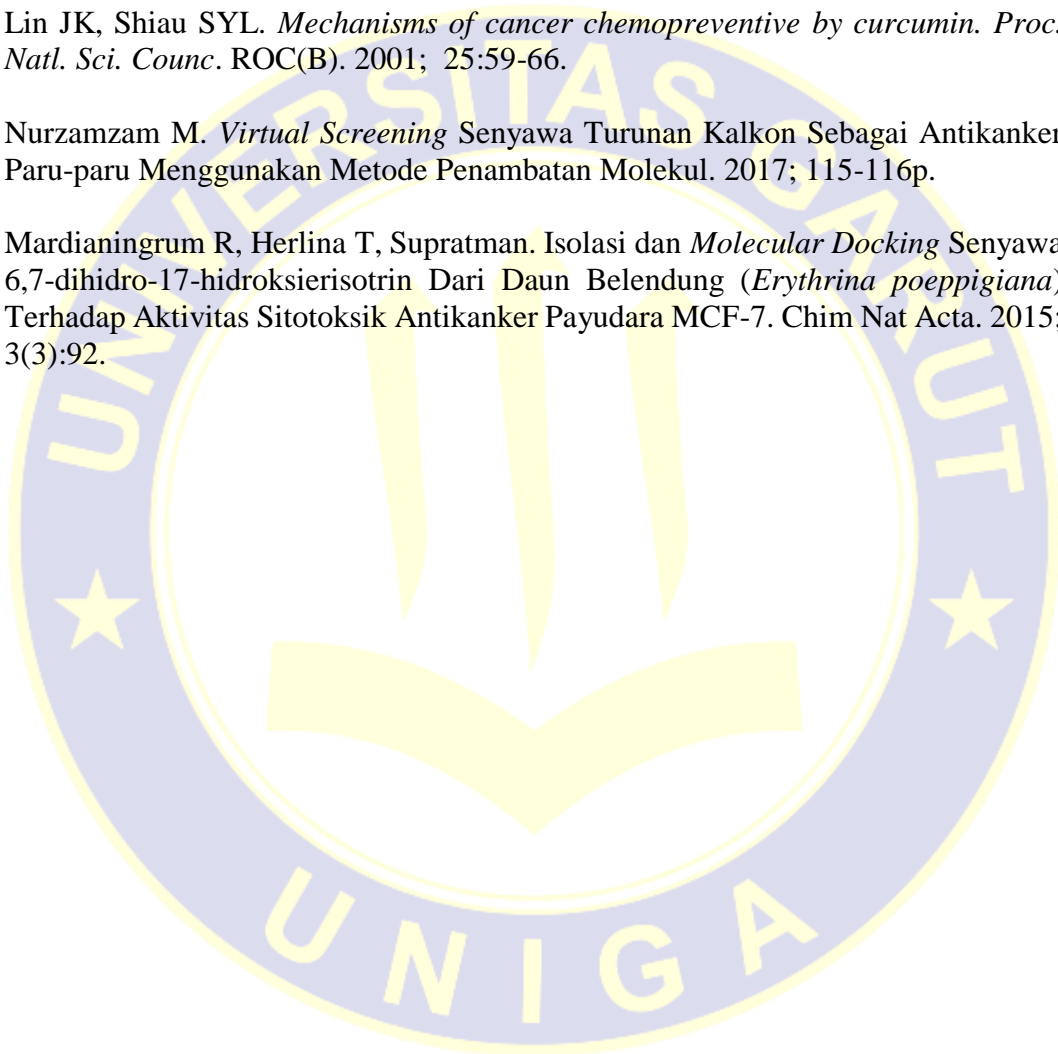


## DAFTAR PUSTAKA

1. Zebua Y. Fajar, Mulyani Hasta Sri, dan H. Endah Marselina. 2012. "Pemodelan Deteksi Penyakit Sirosis Hati dengan Menggunakan Jaringan Syaraf Tiruan". Vol. 2 nomor 2. Universitas Respati Yogyakarta.
2. Yunarto Nanang. Prospek Tanaman Obat sebagai Antihepatitis. Pusat Biomedis dan Teknologi Dasar Kesehatan. Kemenkes RI; 2013; 3(2): 60-69.
3. World Health Organization. Global Hepatitis Report 2017. *Department of Communicable diseases Surveillance and Response*; 2017.
4. Firdayani, Kususmaningrum Susi, dan Miranti Ria Yosephine. Potensi Senyawa Bioaktif Tanaman Genus *Phyllanthus* Sebagai Inhibitor Replikasi Virus Hepatitis B. Tangerang Selatan: Pusat Teknologi Farmasi dan Medika; 2017; 4(2).
5. World Health Organization. Hepatitis B. *Department of Communicable diseases Surveillance and Response*; 2002.
6. Gani A. Rino. Pengobatan Terkini Hepatitis Kronik B dan C". Tangerang: RSUPN Cipto Mangunkusumo; 2005.
7. Thedja, M. D., Ie, S. I., Narita, V., Nurainy, N., & Muljono, D. H. Karakteristik *Reverse Transcriptase Gen Polymerase* Virus Hepatitis B Pada Penderita Hepatitis B Kronis Asimtomatik Pra-Pengobatan. Universitas Al-Azhar Indonesia: Lembaga Biologi molekuler Eijkman; 2017; 5(3): 183-190. <https://doi.org/10.23886/ejki.5.8046>.
8. Aswani Tuti, Manalu Wasmen, dkk. Potensi Ekstrak Pegagan (*Centella asiatica*) dan Kunyit (*Curcuma longa*) Untuk Meningkatkan Aktivitas Enzim Glutation Peroksidase (GSH-Px) pada Jaringan Hati Tikus. Kementerian Kesehatan Republik Indonesia; 2015.
9. Candra Agung Adi. Aktivitas Hepaprotektor temulawak pada Ayam yang Diinduksi Pemberian Parasetamol. Bandar Lampung: Jurusan Peternakan Politeknik Negeri Lampung; 2013; 13(2):137-143.
10. Marinda Dwi Ferinna. 2014. *Hepatoprotective Effect of Curcumin in Chronic Hepatitis*". Lampung University: Faculty of Medicine; 2014; 3(7).
11. Badan Pengawas Obat dan Makanan. Gerakan nasional minum temulawak. Info POM. 2005; 6(6): 1-12.

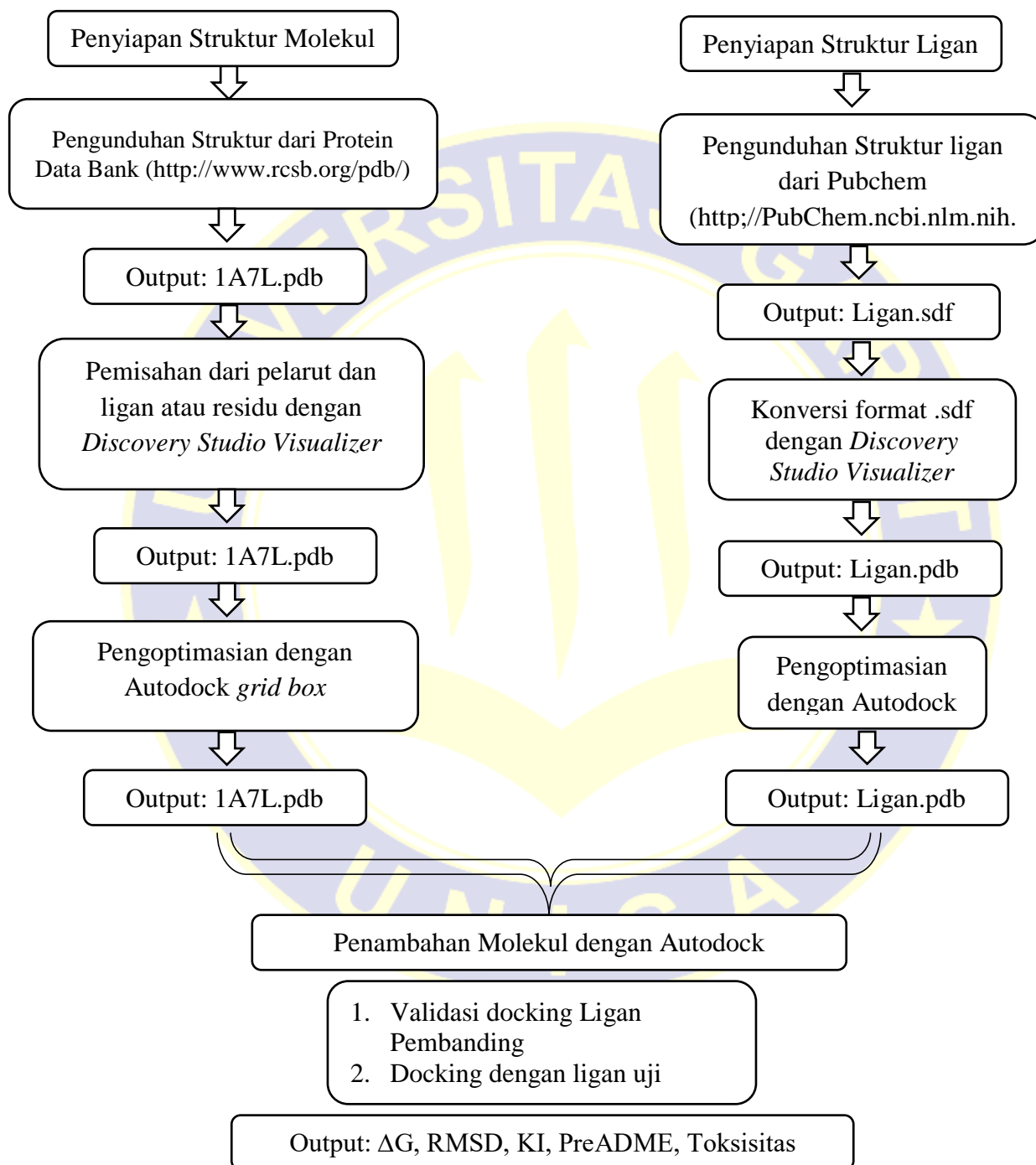
12. Rohaimi, Mohd bin Ab Halim. *Validation of GC-MC Method for Standardization of Curcuma xanthorrhiza Extracts Using Biochemical Markers, Ar-Curcumene and Xanthorrhizol*. Universiti Sains Malaysia; 2014.
13. Suhud Farida. Uji Aktivitas *In silico* Senyawa Baru 1-Benzil-3-benzoilurea Induk dan Tersubstitusi sebagai Agen Antiproliferatif. Universitas Surabaya: Departemen Kimia Farmasi; 2015; 7(4).
14. Achmad Sjamsul Arifin, Hakim Euis Holisotan, Makmur Lukman, Syah Yana Maolana, Juliawaty Lia Dewi, Mujahidin Dindin. Ilmu Kimia dan Kegunaan Tumbuh-tumbuhan Obat Indonesia. Jilid 1. Bandung: Penerbit ITB; 2009.
15. Dermawaty Dessy Eva. *Potential Extract Curcuma (Curcuma xanthorrhizal, Roxb) as Antibacterials. Faculty of Medicine*. University of Lampung: Faculty of Medicine; 2015; 4(1).
16. Pracoyo Endah Noer dan Wibowo. Faktor-faktor yang Berhubungan dengan Tingkat Kekebalan Hepatitis B (anti-HBs) pada Anak Umur 1-14 tahun dari Data Hasil Riskesdas 2007. Pusat Biomedis dan Teknologi Dasar Kesehatan; 2016.
17. Siregar Agustina Fazidah. Hepatitis B Ditinjau dari Kesehatan Masyarakat dan Upaya Pencegahan”. Universitas Sumatra Utara: Fakultas Kesehatan Masyarakat; *Library USU*; 2007; 1–8.
18. Gani A. Rino. Pengobatan Terkini Hepatitis Kronik B dan C”. Tangerang: RSUPN Cipto Mangunkusumo; 2005.
19. Prianto Bayu. *Pemodelan Kimia Komputasi. Penelitian Bidang Material Dirgantara*. LAPAN.
20. Muchtaridi. Teori dan praktek penambatan molekul (*molecular docking*). Bandung: Unpad Press; Cetakan 1. 2018; hal 142; xii.
21. Agustina Widiastuti, Susanti Elfi, Yunita Nurma, dan Yamtinah Sri. Modul Chem Office: Chem draw & Chem 3D. Program studi Pendidikan kimia. Surakarta: Universitas Sebelas Maret; 2018.
22. Yanuar Arry. Penambatan Molekul: Praktek dan Aplikasi pada Virtual Screening. Laboratorium Komputasi Biomedik dan Rancangan Obat. Jakarta: Fakultas Farmasi Universitas Indonesia; 2012; 1-3p.
23. Kartasasmit, Rahmana Emran, Anugrah Rina, dan Tjahjono Daryono Hadi. *Kajian Docking dan Prediksi Beberapa Aspek Farmakokinetika Desain Molekul Turunan Kuinin Sebagai Upaya Menemukan Kandidat Senyawa Antimalaria yang Baru*. Cimahi: Institut Teknologi Bandung; 2015.

24. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings. *Adv Drug Deliv Rev.* 1997; 23:3– 25.
25. Yustika FP, Riza H, Fajriaty I. Studi *Molecular Docking* Hasil Modifikasi Struktur Senyawa Atorvastatin Untuk Meningkatkan Efek Antihiperlipidemia.
26. Lin JK, Shiau SYL. *Mechanisms of cancer chemopreventive by curcumin.* *Proc. Natl. Sci. Counc. ROC(B).* 2001; 25:59-66.
27. Nurzamzam M. *Virtual Screening* Senyawa Turunan Kalkon Sebagai Antikanker Paru-paru Menggunakan Metode Penambatan Molekul. 2017; 115-116p.
28. Mardianingrum R, Herlina T, Supratman. Isolasi dan *Molecular Docking* Senyawa 6,7-dihidro-17-hidroksierisotrin Dari Daun Belendung (*Erythrina poeppigiana*) Terhadap Aktivitas Sitotoksik Antikanker Payudara MCF-7. *Chim Nat Acta.* 2015; 3(3):92.

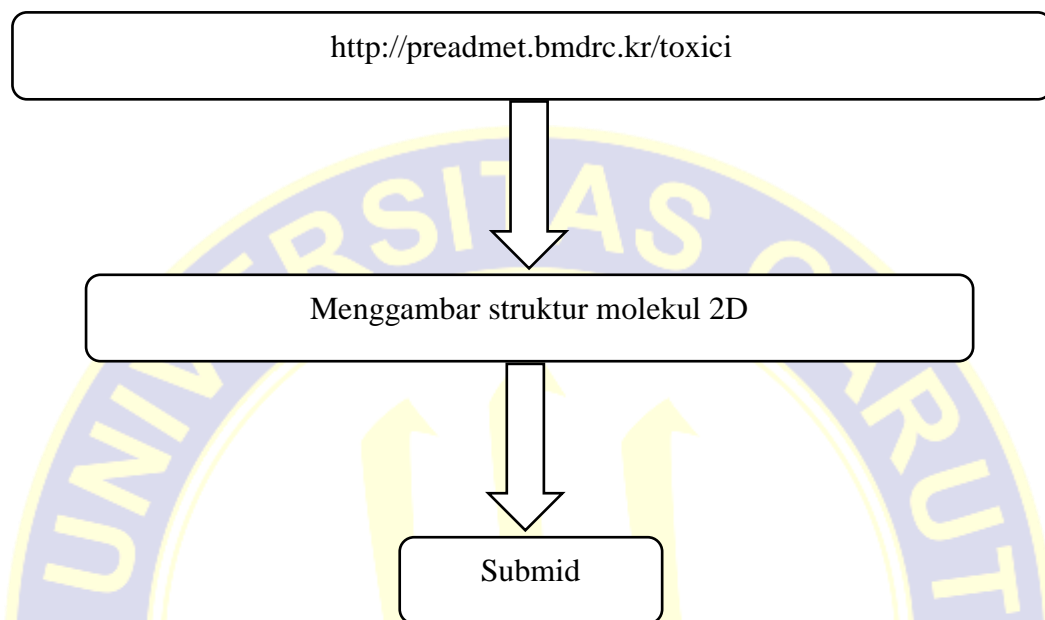
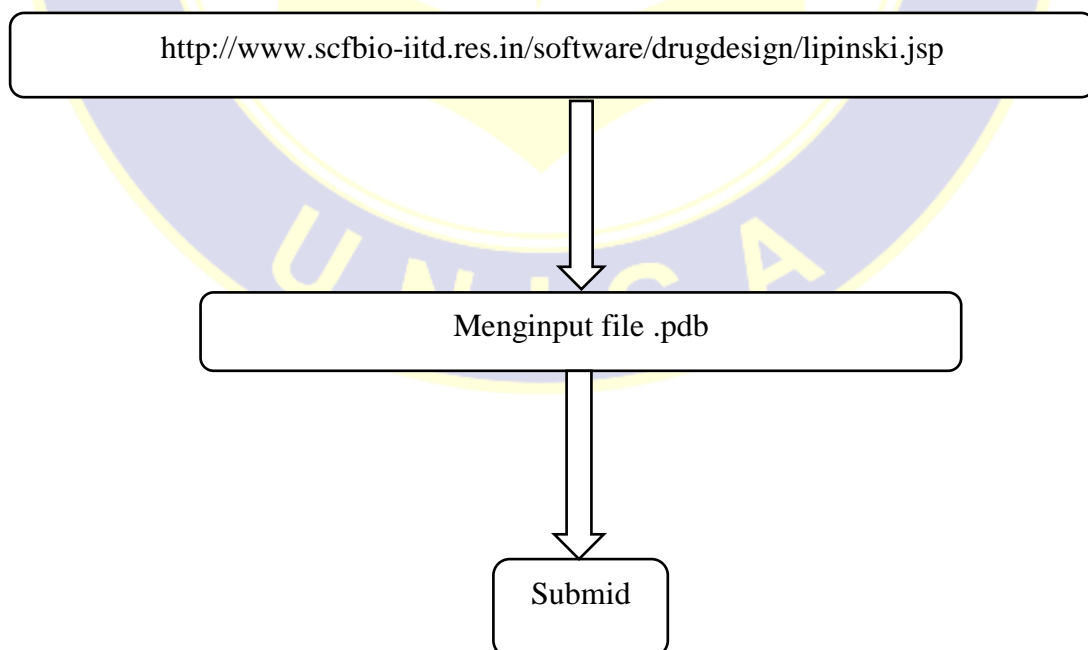


## LAMPIRAN 1

### ALUR PENELITIAN

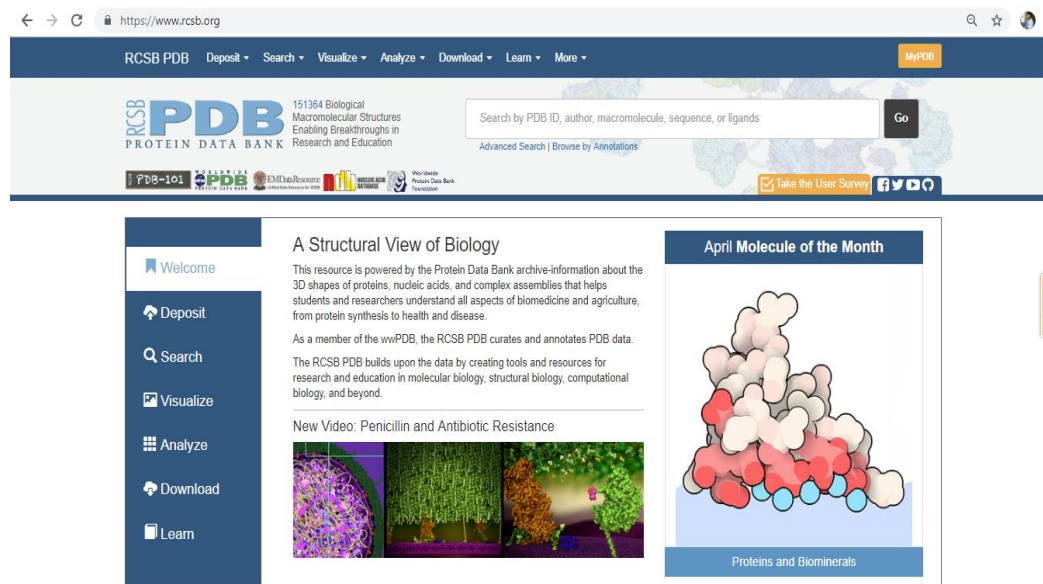


**Gambar V.3** Alur penelitian

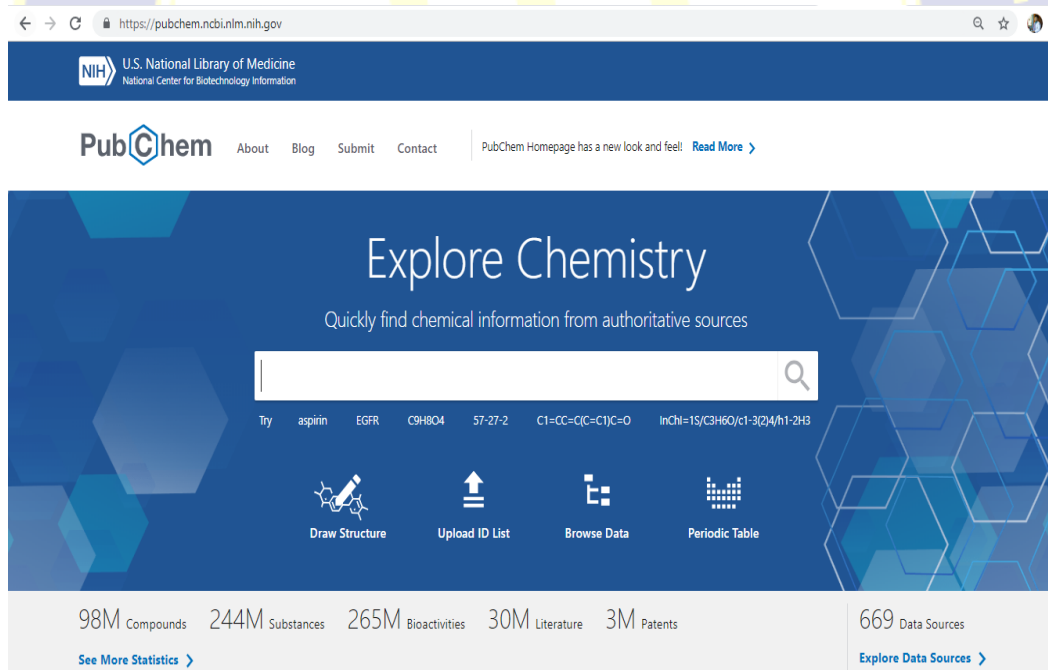
**LAMPIRAN 1****(LANJUTAN)****Gambar V.4** Analisis preADME dan Toksisitas**Gambar V.5** Analisis Lipinski's rule of five

## LAMPIRAN 2

### SITUS DAN APLIKASI

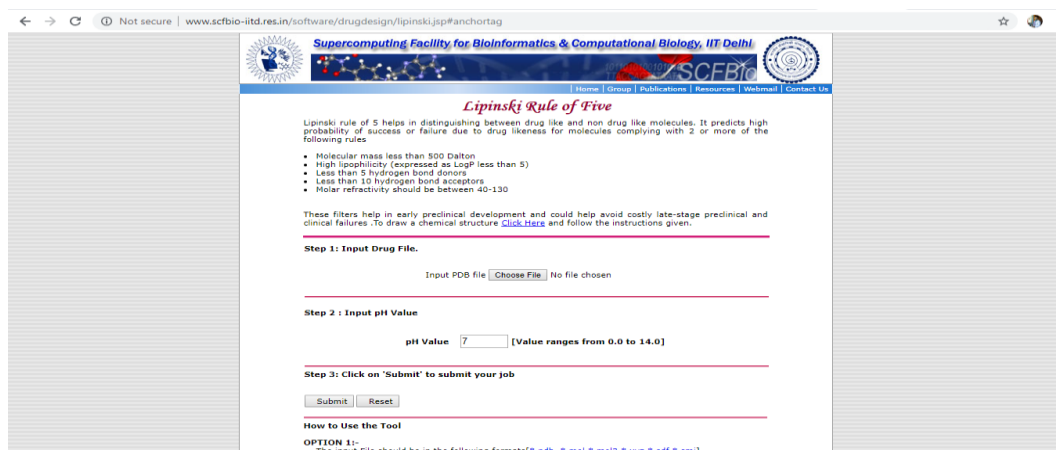


**Gambar V.6** Tampilan situs *Protein Data Bank*

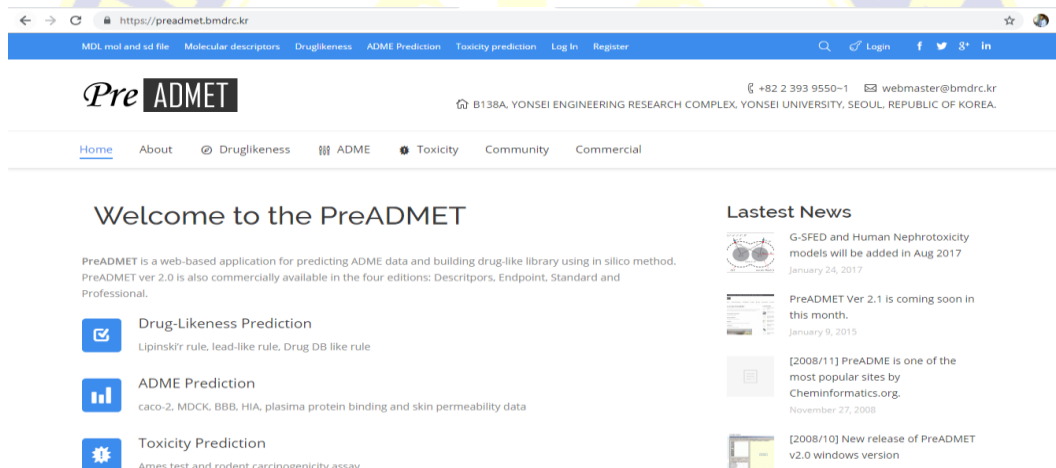


**Gambar V.7** Tampilan situs *Pubchem*

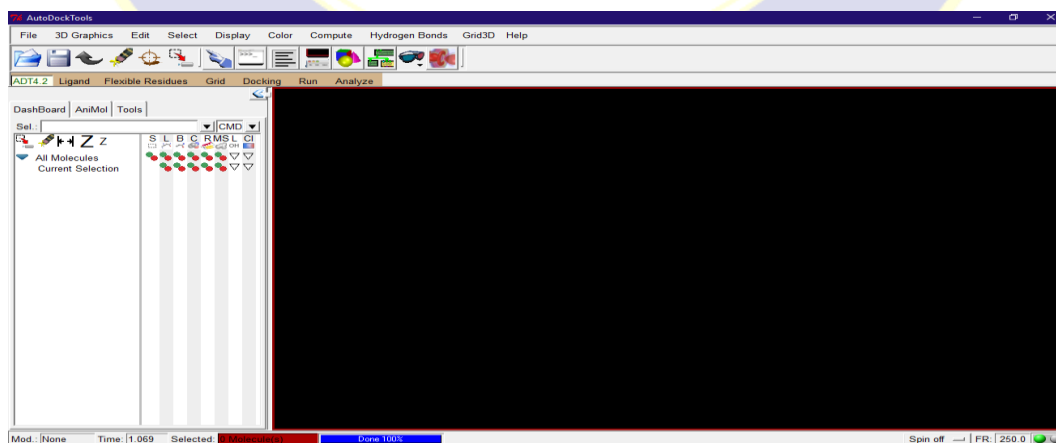
## LAMPIRAN 2 (LANJUTAN)



Gambar V.8 Tampilan situs *Lipinski Rule of Five*

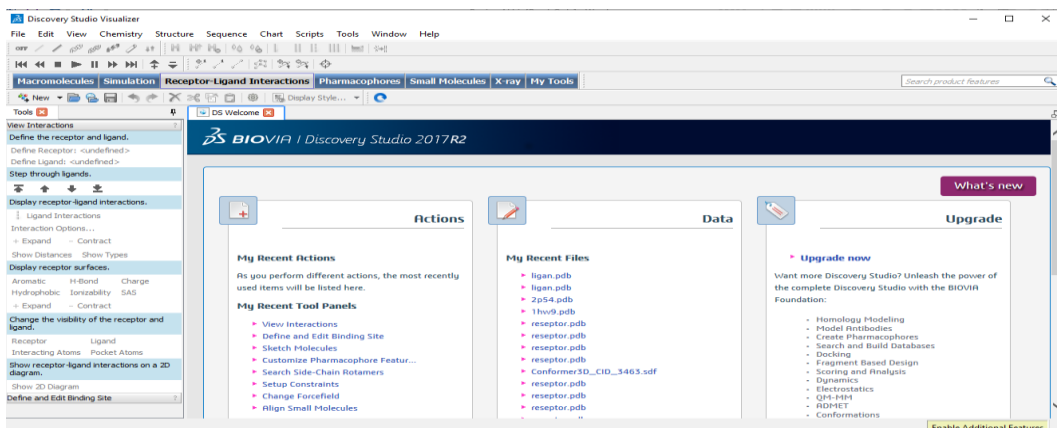


Gambar V.9 Tampilan situs Pre-ADME dan Toksisitas

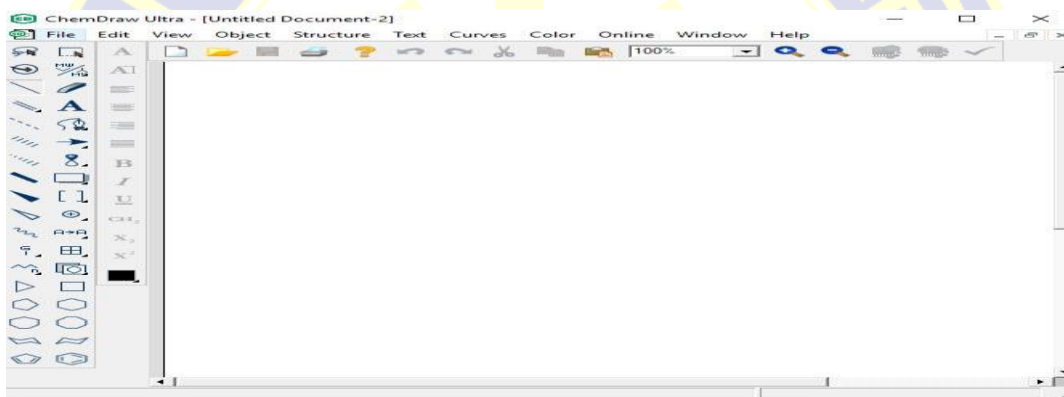


Gambar V.10 Tampilan aplikasi *AutoDock Tools*<sup>®</sup>

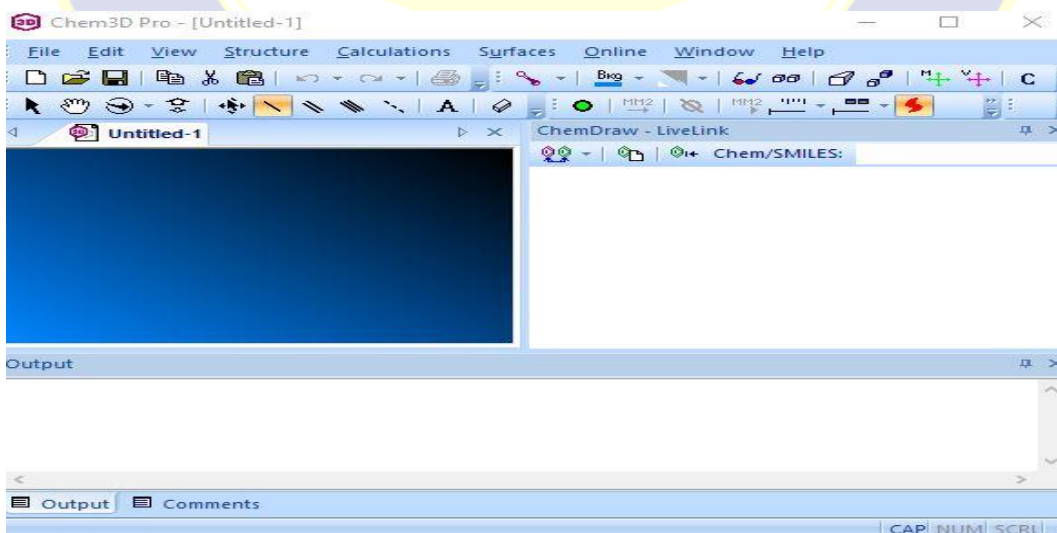
## LAMPIRAN 2 (LANJUTAN)



Gambar V.11 Tampilan aplikasi *Discovery Studio Visualizer*<sup>®</sup>



Gambar V.12 Tampilan aplikasi *ChemDraw ultra*<sup>®</sup>



Gambar V.13 Tampilan aplikasi *ChemDraw 3D*<sup>®</sup>

## LAMPIRAN 3

### RESEPTOR VIRUS HEPATITIS B (HBV)

The image shows two screenshots of the RCSB PDB website for entry 1A7L. The top screenshot displays the 'Biological Assembly 1' view of the protein structure, which is a ribbon model colored by domain. The right side of the page provides detailed information about the entry, including its title, DOI, classification, organism, and experimental data. A 'wwPDB Validation' section shows a bar chart comparing metrics like Clashscore, Ramachandran outliers, and Sidechain outliers against percentile ranks. The bottom screenshot shows the '3D View' of the structure, which is a ribbon model colored by domain, with a control panel on the right for adjusting the view (e.g., Assembly, Model, Symmetry, Style, Color, Ligand, Quality, Water, Hydrogens, Clashes).

**1A7L**  
 DOMINANT B-CELL EPITOPE FROM THE PRES2 REGION OF HEPATITIS B VIRUS IN THE FORM OF AN INSERTED PEPTIDE SEGMENT IN MALTODEXTRIN-BINDING PROTEIN

DOI: 10.2210/pdb1A7L/pdb

Classification: [TRANSPORT](#)

Organism(s): [Escherichia coli \(strain K12\)](#)

Expression System: [Escherichia coli](#)

Deposited: 1998-03-16 Released: 1998-06-17

Deposition Author(s): [Saul, F.A.](#), [Vulliez-Lenormand, B.](#), [Lema, F.](#), [Bentley, G.A.](#)

**Experimental Data Snapshot**

Method: X-RAY DIFFRACTION

Resolution: 2.9 Å

R-Value Free: 0.286

R-Value Work: 0.192

**wwPDB Validation**

Metric	Percentile Ranks	Value
Clashscore	9	9
Ramachandran outliers	0.1%	0.1%
Sidechain outliers	3.9%	3.9%

This is version 1.2 of the entry. See complete history.

**1A7L**  
 DOMINANT B-CELL EPITOPE FROM THE PRES2 REGION OF HEPATITIS B VIRUS IN THE FORM OF AN INSERTED PEPTIDE SEGMENT IN MALTODEXTRIN-BINDING PROTEIN

Note: Use your mouse to drag, rotate, and zoom in and out of the structure. Mouse-over to identify atoms and bonds. [Mouse controls documentation.](#)

Structure View | Electron Density Maps | Ligand View

Structure View Documentation

Assembly: Bioassembly 1

Model: Model 1

Symmetry: None

Style: Cartoon

Color: Rainbow

Ligand: Ball & Stick

Quality: Automatic

Water:

Hydrogens:

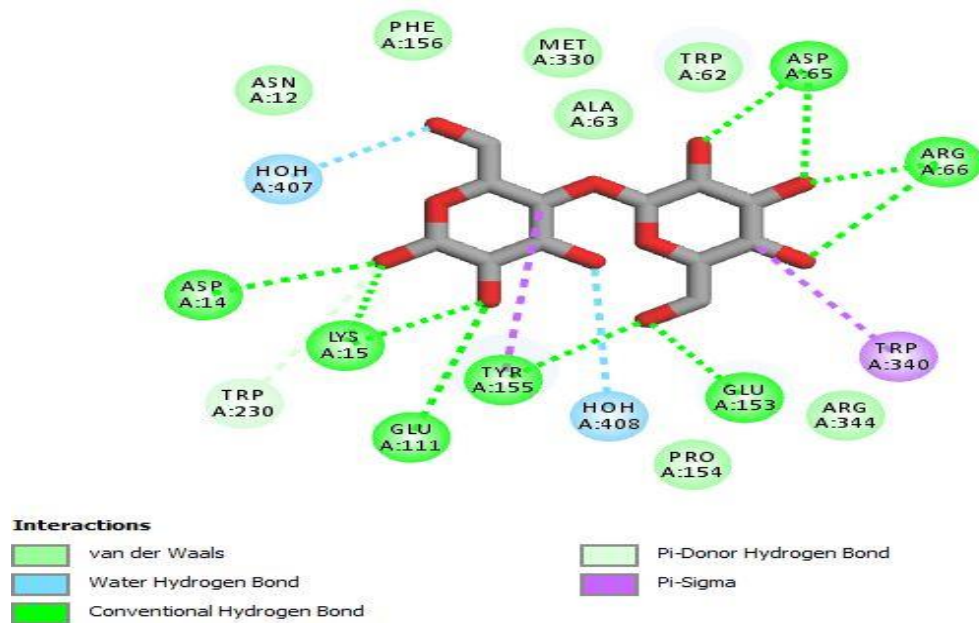
Ions:

Clashes:

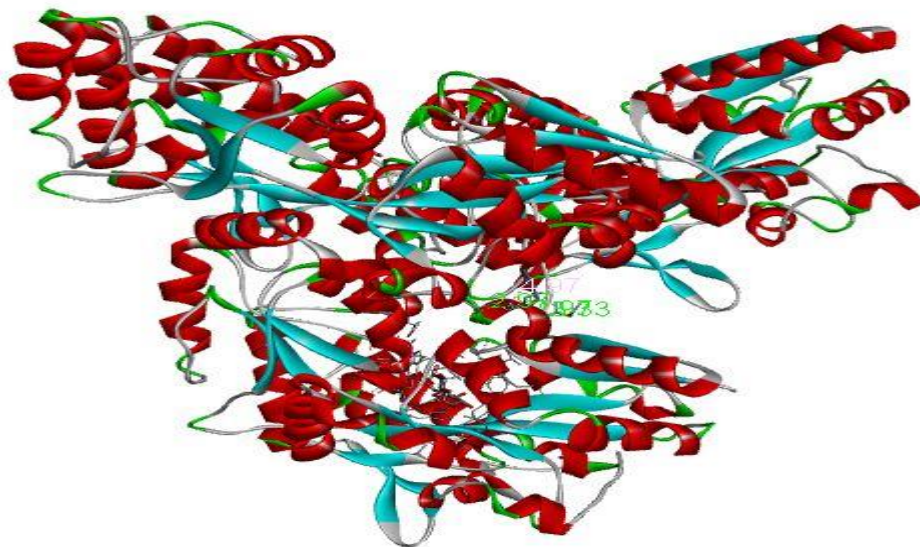
**Gambar V.14** Reseptor Virus Hepatitis B (*Wildtype*)

## LAMPIRAN 4

### STRUKTUR 2D DAN 3D LIGAN ALAMI

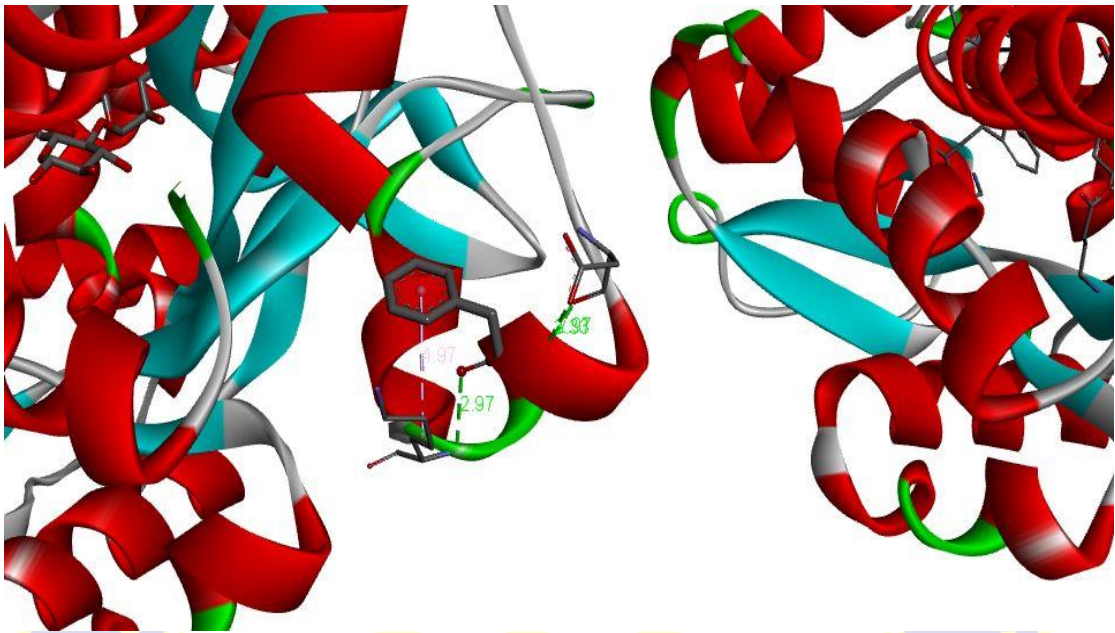


Gambar V.15 Struktur 2D Ligan Alami dengan HBV

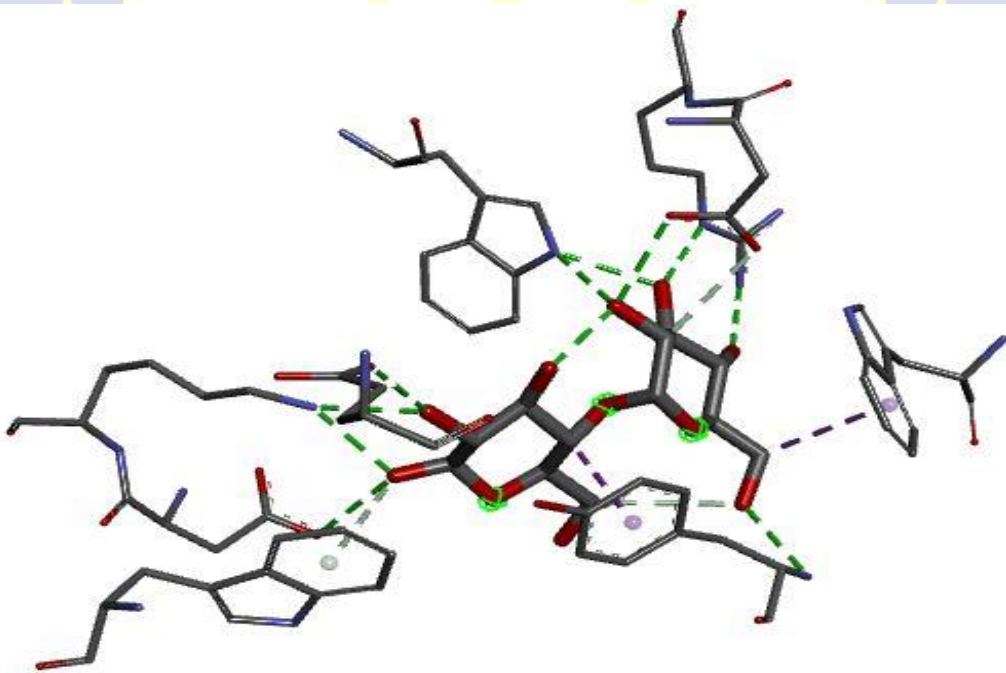


Gambar V.16 Struktur 3D Ligan Alami dengan HBV

#### LAMPIRAN 4 (LANJUTAN)



Gambar V.17 Pembesaran Struktur 3D Ligan Alami dengan reseptor HBV



Gambar V.18 Interaksi HBV dengan Ligan Alami

## LAMPIRAN 5

### RESEPTOR VIRUS HEPATITIS B (HBV *mutant*)

RCSB PDB - 1IUD: MALTODEXTRIN

https://www.rcsb.org/structure/1iud

RCSB PDB Deposit Search Visualize Analyze Download Learn More MyPDB

Structure Summary 3D View Annotations Sequence Sequence Similarity Structure Similarity Experiment

Biological Assembly 1

1IUD

MALTODEXTRIN-BINDING PROTEIN INSERTION/DELETION MUTANT WITH AN INSERTED B-CELL EPITOPE FROM THE PRES2 REGION OF HEPATITIS B VIRUS

DOI: 10.2210/pdb1IUD/pdb

Classification: [HYBRID PROTEIN](#)

Organism(s): [Escherichia coli \(strain K12\)](#)

Expression System: [Escherichia coli](#)

Deposited: 1996-05-29 Released: 1997-06-05

Deposition Author(s): [Saul, F.A.](#), [Vulliez-Le Normand, B.](#), [Lema, F.](#), [Bentley, G.A.](#)

Experimental Data Snapshot

Method: X-RAY DIFFRACTION

Resolution: 2.7 Å

R-Value Free: 0.281

R-Value Work: 0.178

wwPDB Validation

Metric	Percentile Ranks	Value
Clashscore		19
Ramachandran outliers		1.9%
Sidechain outliers		9.4%

3D View: Structure | Ligand Interaction

Standalone Viewers

RCSB PDB - 1IUD: MALTODEXTRIN

https://www.rcsb.org/3d-view/1IUD

RCSB PDB Deposit Search Visualize Analyze Download Learn More MyPDB

1IUD

MALTODEXTRIN-BINDING PROTEIN INSERTION/DELETION MUTANT WITH AN INSERTED B-CELL EPITOPE FROM THE PRES2 REGION OF HEPATITIS B VIRUS

Note: Use your mouse to drag, rotate, and zoom in and out of the structure. Mouse-over to identify atoms and bonds. Mouse controls documentation.

Structure View Electron Density Maps Ligand View

Structure View Documentation

Assembly Bioassembly 1

Model Model 1

Symmetry None

Style Cartoon

Color Rainbow

Ligand Ball & Stick

Quality Automatic

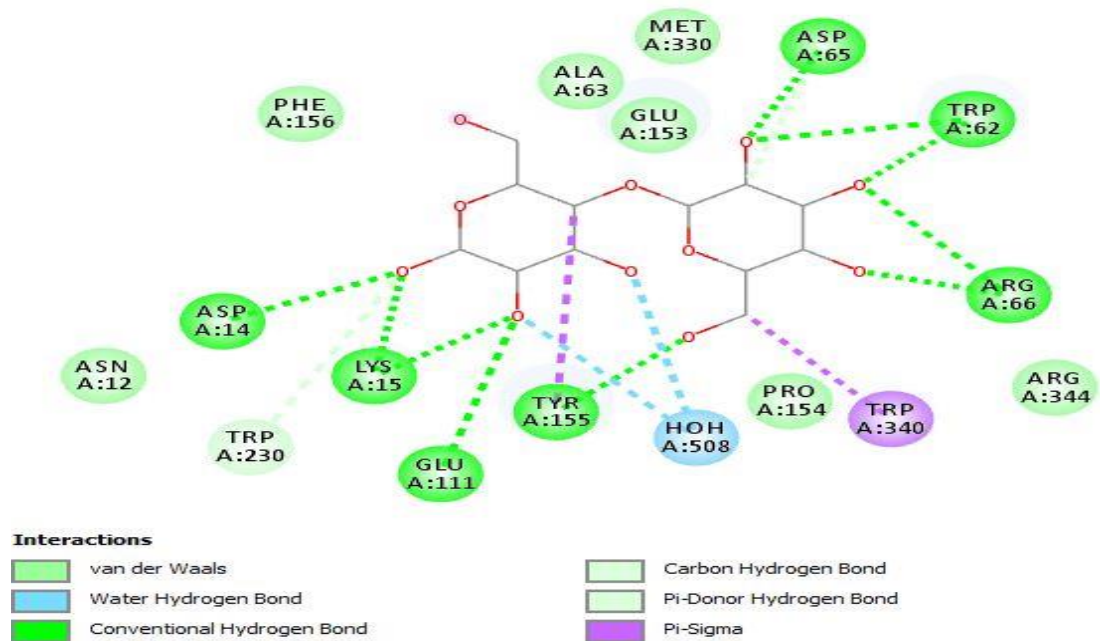
Water  Ions

Hydrogens  Clashes

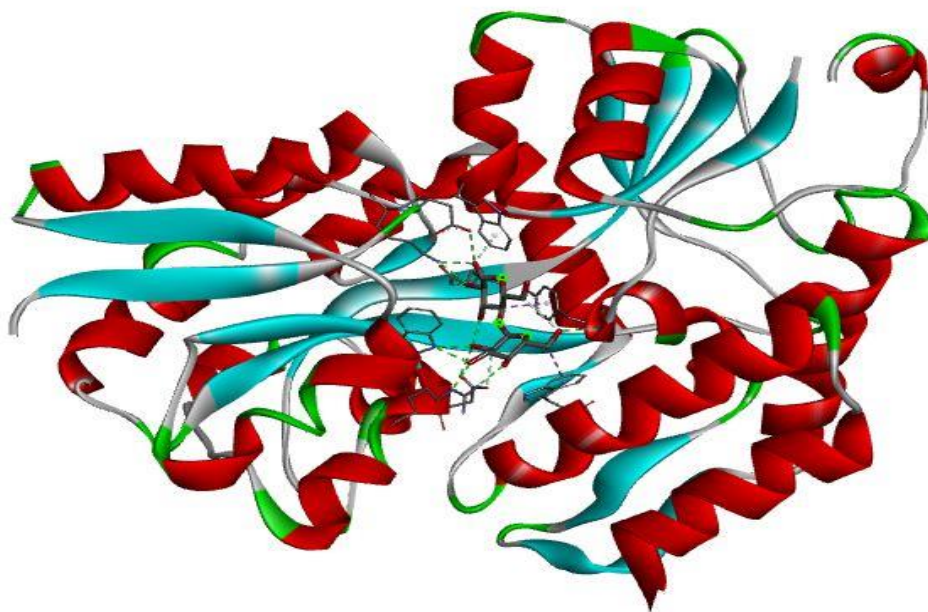
Gambar V.19 Reseptor Virus Hepatitis B (*Mutant*)

## LAMPIRAN 6

### STRUKTUR 2D DAN 3D LIGAN ALAMI

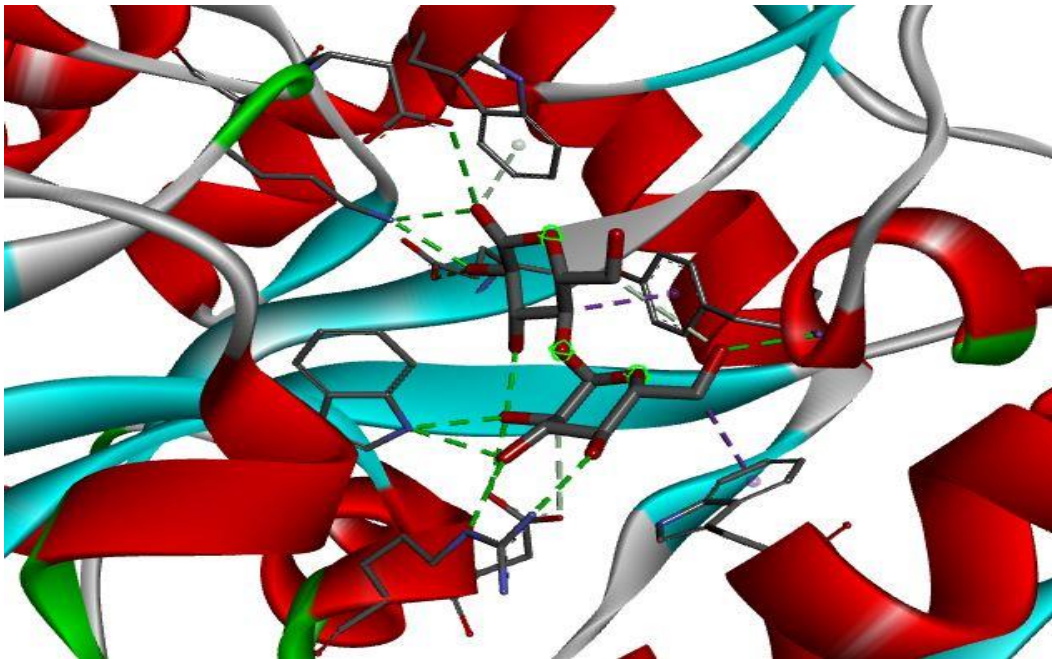


Gambar V.20 Struktur 2D Ligan Alami dengan HBV

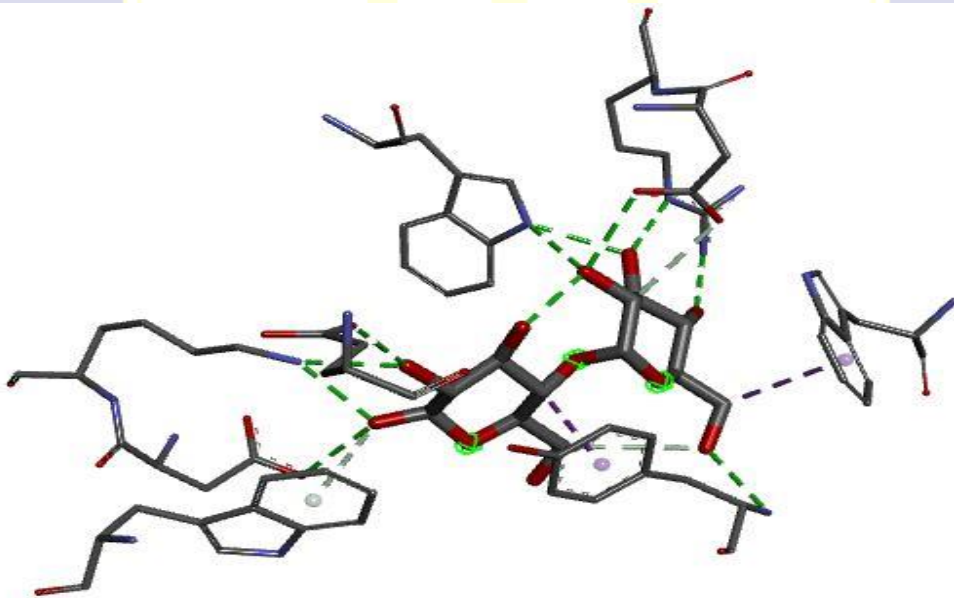


Gambar V.21 Struktur 3D Ligan Alami dengan HBV (*Mutant*)

**LAMPIRAN 6  
(LANJUTAN)**



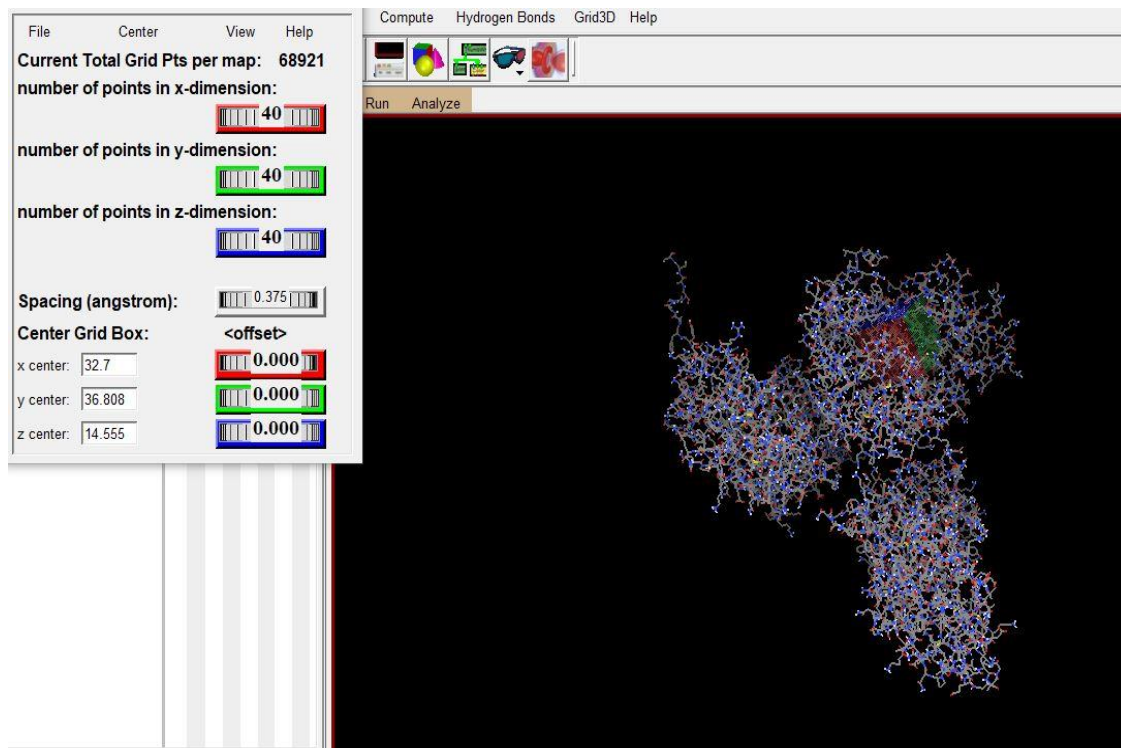
**Gambar V.22** Pembesaran Struktur 3D Ligan Alami dengan reseptor HBV



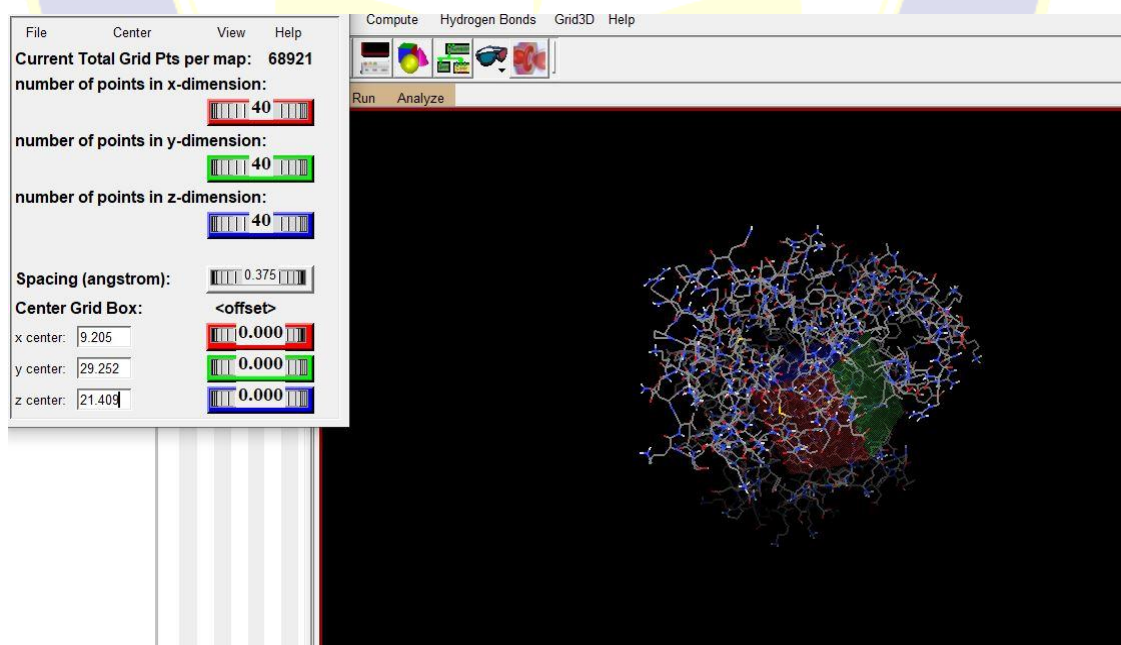
**Gambar V.23** Pembesaran Struktur 3D Ligan Alami dengan reseptor HBV

## LAMPIRAN 7

### PARAMETER *GRIDBOX*



**Gambar V.24** Tampilan parameter *gridbox* HBV *wildtype*

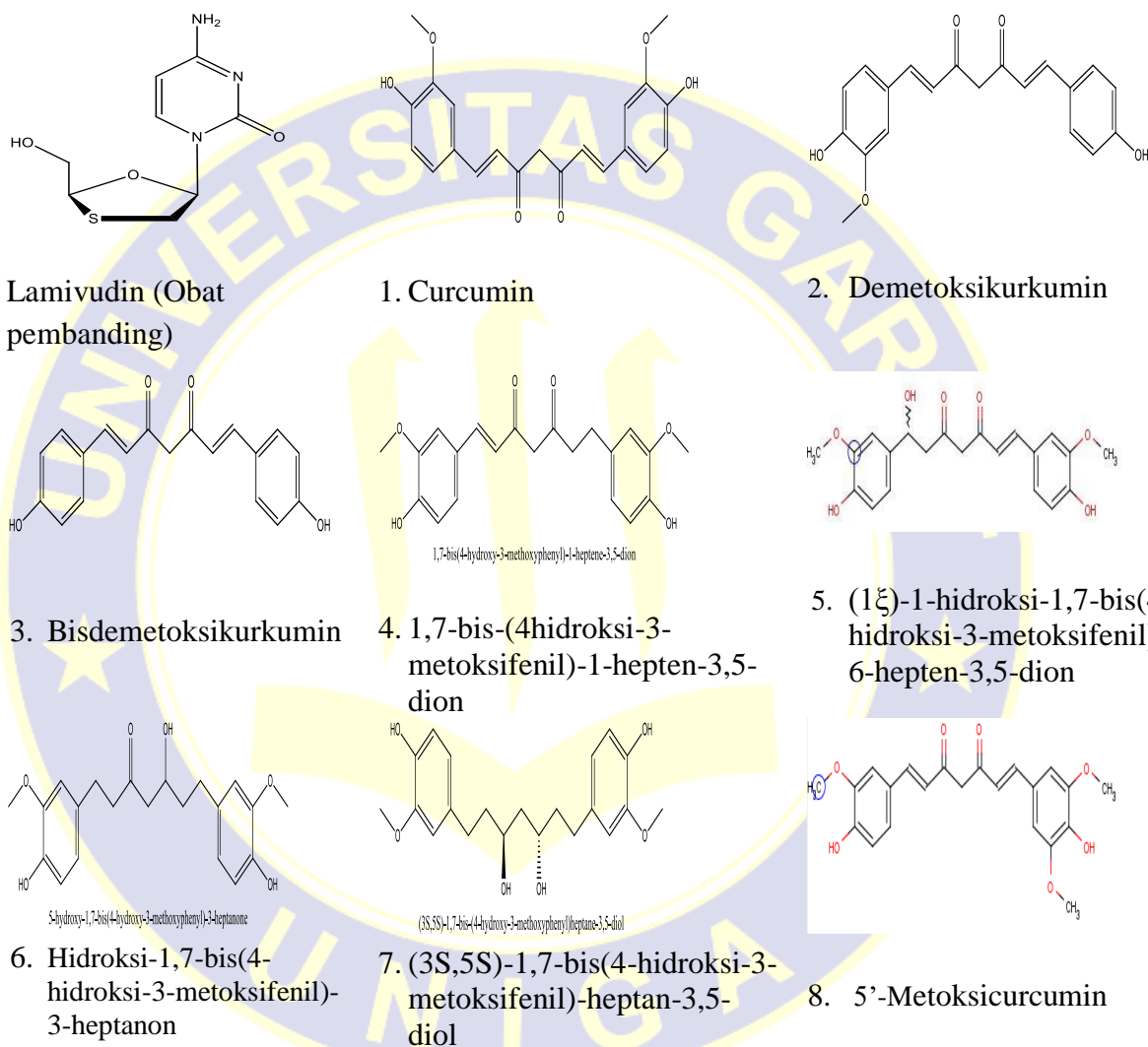


**Gambar V.25** Tampilan parameter *gridbox* reseptor HBV *mutant*

## LAMPIRAN 8

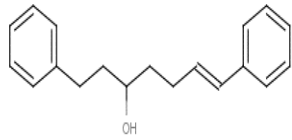
## STRUKTUR 2D SENYAWA UJI

## A. Struktur Senyawa yang Dilakukan Penambatan Molekul

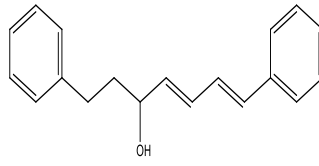


Gambar V.26 Senyawa Uji 2D

## LAMPIRAN 8 (LANJUTAN)

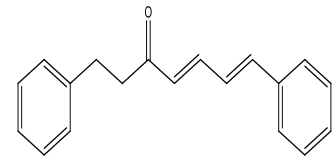


9. *Trans*-1,7-difenil-1-hepten-5-ol

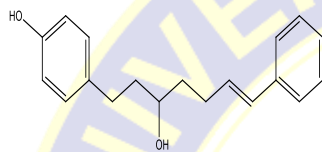


*trans,trans*-1,7-difenil-1,3-heptadien-5-ol

10. *Trans, trans*-1,7-difenil-1,3-heptadien-5-ol

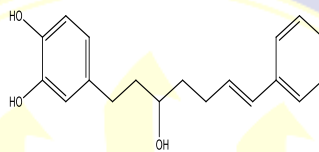


11. Alnuston



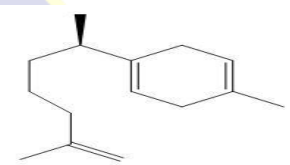
1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol

12. 1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol

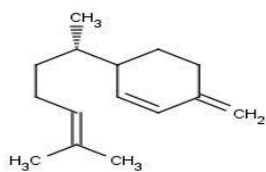


1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol

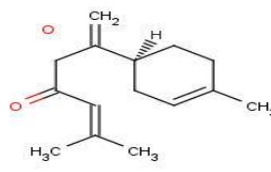
13. 1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol



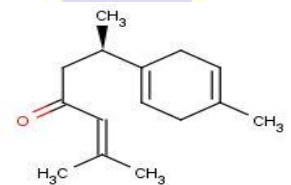
14.  $\beta$ -Kurkumen



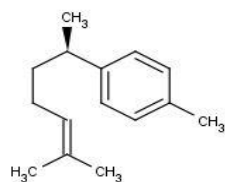
15.  $\beta$ -seskuifelandren



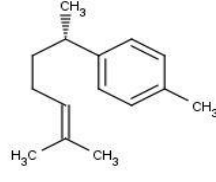
16.  $\beta$ -Atlanton



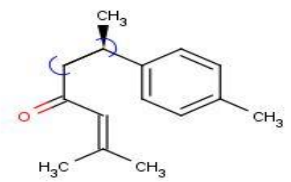
17. Turmeron



18. Ar-Kurkumen



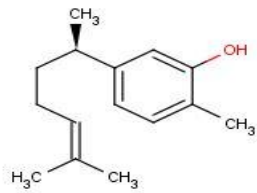
19.  $\alpha$ -Kurkumen



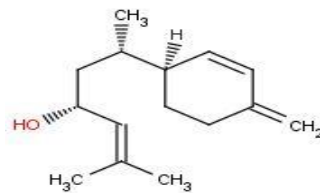
20. ar-Turmeron

Gambar V.27 Lanjutan

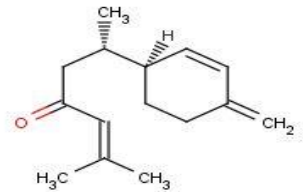
## LAMPIRAN 8 (LANJUTAN)



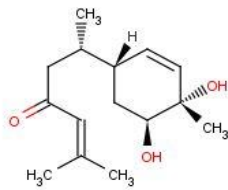
21. Santorizol



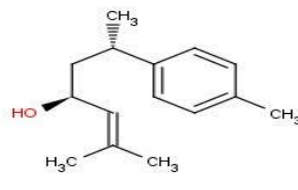
22. Bisakurul



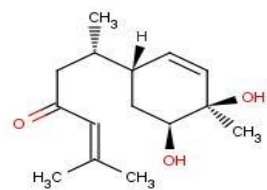
23. Kurlon



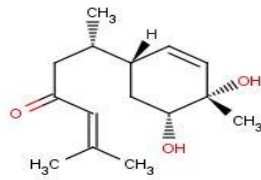
24. Bisakuron



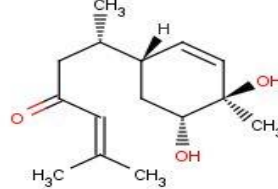
25. Bisakumul



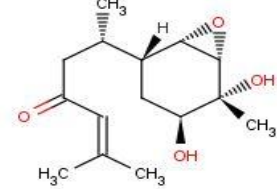
26. Bisakuron A



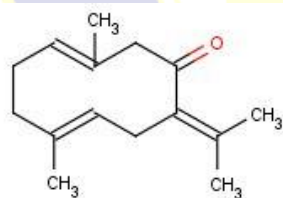
27. Bisakuron B



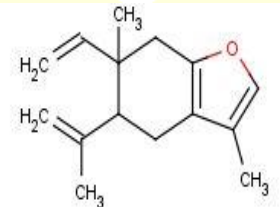
28. Bisakuron C



29. Bisakuron epoksida



30. Germakron

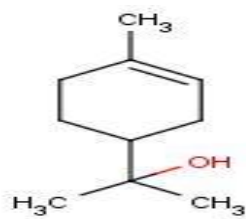
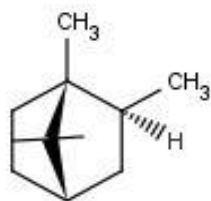


31. Kurzeren

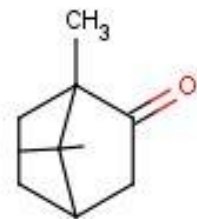


32. Kurzerenon

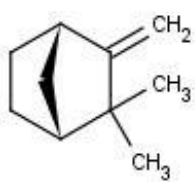
Gambar V.28 Lanjutan

**LAMPIRAN 8  
(LANJUTAN)**33.  $\alpha$ -Terpineol

34. Isoborneol



35. Kamfor

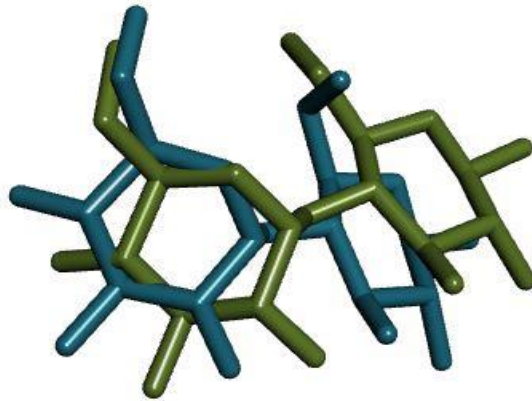


36. Kamfen

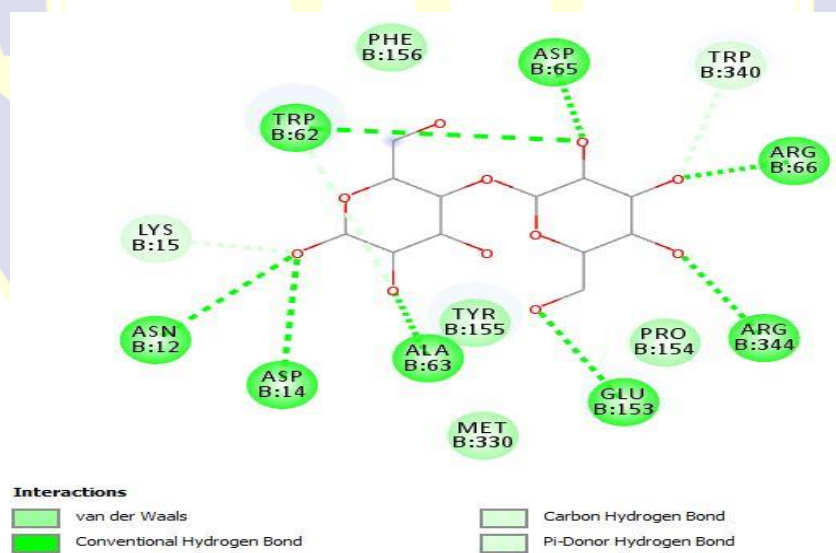
**Gambar V.29 Senyawa Uji 2D**

## LAMPIRAN 9

### VALIDASI METODE (*REDOCKING*)

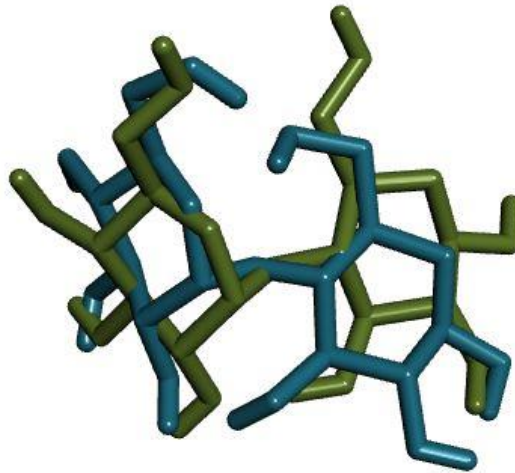


**Gambar V.30** Hasil visualisasi tumpang tindih ligan alami dari HBV (1A7L) dari hasil kristalografi sinar-X (hijau) dengan ligan hasil *redocking* (biru)

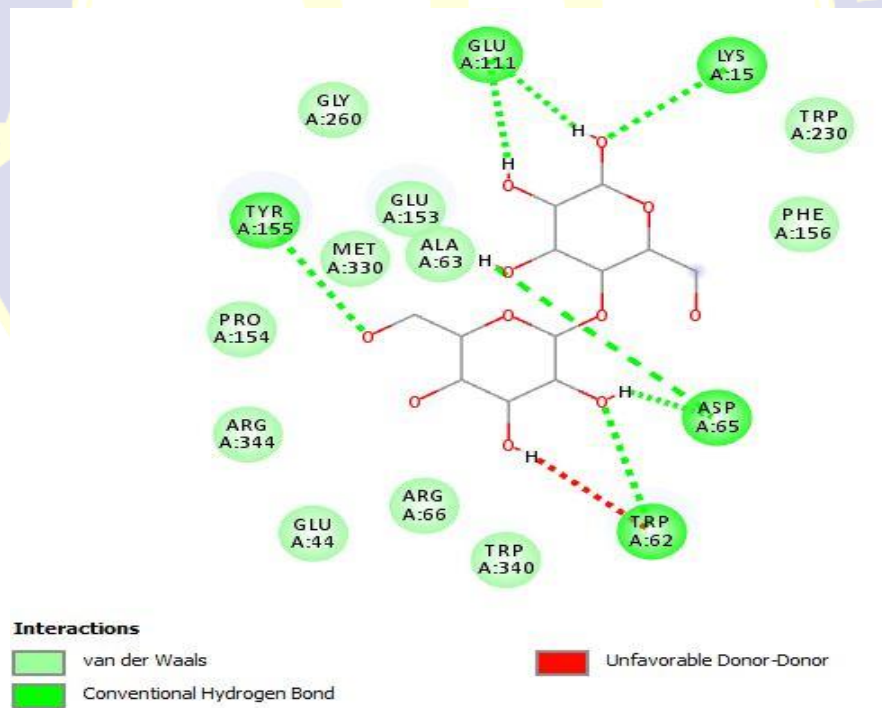


**Gambar V.31** Hasil visualisasi interaksi ligan alami dengan HBV (1A7L)

## LAMPIRAN 9 (LANJUTAN)



**Gambar V.32** Hasil visualisasi tumpang tindih ligan alami dari reseptor HBV dari hasil kristalografi sinar-X (hijau) dengan ligan hasil *redocking* (biru)



**Gambar V.33** Hasil visualisasi interaksi ligan alami dengan reseptor HBV (1IUD)

## LAMPIRAN 10

## HASIL PENAMBATAN MOLEKUL

Tabel V.2

Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada HBV (1A7L)

Senyawa/Ligan	Ikatan Energi ( $\Delta G$ ) kcal/mol	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI (nM)
Ligan Alami	-8,17	9	TRP62, ASP65, ARG66, ARG344, GLU153, TYR155, ALA63, ASP14, ASN12	1,03 $\mu\text{M}$
Curcumin	-8,05	4	GLU111, ALA63, ASP65, ASP14	1,26 $\mu\text{M}$
5'-Metoksicurcumin	-8,00	3	ASP14, ASP65, TRP62	1,38 $\mu\text{M}$
<i>Trans, trans</i> -1,7-difenil-1,3-heptadien-5-ol	-7,98	2	ASP65, TRP,62	1,62 $\mu\text{M}$
Bisakuron B	-7,73	3	TYR155, GLU153, ARG344	2,16 $\mu\text{M}$
Demetoksicurcumin	-7,61	6	LYS42, ARG344, ARG66, GLU111, ASN12, ASP14	2,65 $\mu\text{M}$
1,7-bis-(4hidroksi-3-metoksifenil)-1-hepten-3,5-dion	-7,59	3	ASP14, GLU111, ARG66	2,75 $\mu\text{M}$
Bisakuron A	-7,58	3	TYR155, GLU153, ARG344	2,77 $\mu\text{M}$
1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol	-7,57	6	LYS42, ARG344, ARG66, GLU111, ASN12, ASP14	2,82 $\mu\text{M}$
<i>Trans</i> -1,7-difenil-1-hepten-5-ol	-7,57	3	ASP14, ASP65, TRP62	2,82 $\mu\text{M}$
Bisdemetoksikurkumin	-7,56	3	GLU111, ARG66, ASP14	2,86 $\mu\text{M}$

## LAMPIRAN 10 (LANJUTAN)

**Tabel V.2**  
Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada HBV (1A7L)  
(Lanjutan)

Senyawa/Ligan	Ikatan Energi ( $\Delta G$ ) kcal/mol	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI (nM)
(3S,5S)-1,7-bis(4-hidroksi-3-metoksifenil)-heptan-3,5-diol	-7,55	5	TRP62, LYS15, ASP14, ARG66	18,70 $\mu\text{M}$
Alnuston	-7,51	1	ALA63	2,63 $\mu\text{M}$
Bisakuron epoksida	-7,44	2	GLU153, ARG66	4,09 $\mu\text{M}$
1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol	-7,38	4	ASP14, ASP65	5,27 $\mu\text{M}$
Bisakurool	-7,31	2	ARG66, ASP65	7,06 $\mu\text{M}$
5-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-3-heptanon	-7,24	6	TRP62, ASP65, ARG344, ARG66, ASP14, ASN12	4,91 $\mu\text{M}$
(1 $\xi$ )-1-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-6-hepten-3,5-dion	-7,14	4	GLU111, ALA63, ASP65, ASP14	3,73 $\mu\text{M}$
$\beta$ -Atlanton	-7,09	1	ALA63	6,33 $\mu\text{M}$
Kurlon	-7,04	1	ALA63	6,97 $\mu\text{M}$
Ligan pembanding	-7,02	1	TYR155	7,13 $\mu\text{M}$
Bisakuron	-7,01	2	ARG66, ASP65	7,29 $\mu\text{M}$
Bisakumol	-6,78	2	ASP65, ARG66	17,65 $\mu\text{M}$
Santorizol	-6,77	2	ASP65, TRP62	10,89 $\mu\text{M}$
$\beta$ -seskuifelandren	-6,75	0	-	10,75 $\mu\text{M}$
Germakron	-6,61	1	LYS15	14,27 $\mu\text{M}$
ar-Turmeron	-6,52	1	ARG66	15,30 $\mu\text{M}$
Kurzerenon	-6,47	0	-	18,20 $\mu\text{M}$
Kurzeren	-6,42	0	-	19,72 $\mu\text{M}$
$\alpha$ -Kurkumen	-6,34	0	-	22,59 $\mu\text{M}$
Ar-Kurkumen	-6,31	0	-	9,39 $\mu\text{M}$
Turmeron	-6,27	1	ARG66	22,42 $\mu\text{M}$
$\beta$ -Kurkumen	-6,14	0	-	31,70 $\mu\text{M}$

## LAMPIRAN 10 (LANJUTAN)

**Tabel V.2**

Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada Reseptor HBV (1A7L)  
(Lanjutan)

Senyawa/Ligan	Ikatan energi ( $\Delta G$ ) kcal/mol	Jumlah ikatan hidrogen	Residu asam amino	KI (nM)
$\alpha$ -Terpineol	-6,04	2	ASP65, TRP62	37,54 $\mu$ M
Isoborneol	-5,84	2	ASP65, TRP62	52,48 $\mu$ M
Kamfor	-5,75	1	ARG66	60,84 $\mu$ M
Kamfen	-5,18	0	-	158,61

**Tabel V.3**

Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada Reseptor HBV (1IUD)

Senyawa/Ligan	Ikatan energi ( $\Delta G$ ) kcal/mol	Jumlah ikatan hidrogen	Residu asam amino	KI (nM)
Bisdemetoksikurkumin	-8,76	4	ARG66, ASP14, TYR155, GLU111	381,08
Curcumin	-8,44	4	ARG66, TYR155, ASP14, GLU111	647,75
Bisakuron A	-8,21	3	ASP65, TRP62, LYS15	5,28 $\mu$ M
<i>Trans</i> -1,7-difenil-1-hepten-5-ol	-8,19	2	LYS15, GLU111	997
1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol	-8,17	4	ASP65, TRP62, LYS15, ASP14	1,03 $\mu$ M
Demetoksicurcumin	-8,11	4	GLU111, TYR155, ARG66, ASP14	1,13 $\mu$ M
1,7-bis-(4hidroksi-3-metoksifenil)-1-hepten-3,5-dion	-8,03	4	GLU111, LYS15, TYR155, ASP14	1,29 $\mu$ M

## LAMPIRAN 10 (LANJUTAN)

**Tabel V.3**

Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada Reseptor HBV (1IUD)  
(Lanjutan)

Senyawa/Ligan	Ikatan energi ( $\Delta G$ ) kcal/mol	Jumlah ikatan hidrogen	Residu asam amino	KI (nM)
5'-Metoksicurcumin	-8	6	ARG344, ARG66, TRP62, LYS15, GLU111, ASN12	1,38 $\mu\text{M}$
1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol	-7,99	3	ASP14, LYS15, ASP65	1,40 $\mu\text{M}$
Bisakuron C	-7,96	4	ASP65, TRP62, LYS15, ASP14	1,46 $\mu\text{M}$
<i>Trans, trans</i> -1,7-difenil-1,3-heptadien-5-ol	-7,9	2	TRP62, ASP65	1,62 $\mu\text{M}$
Bisakuron B	-7,85	3	LYS15, ASP14, TRP62	2,99 $\mu\text{M}$
Alnuston	-7,62	1	TRP62	2,61 $\mu\text{M}$
5-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-3-heptanon	-7,5	5	TYR155, ASN15, ASP14, GLU111, GLU153	3,17 $\mu\text{M}$
Bisakuron epoksida	-7,44	2	GLU153, ARG66	4,09 $\mu\text{M}$
(1 $\xi$ )-1-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-6-hepten-3,5-dion	-7,36	3	LYS15, ASP14, TRP62	3,73 $\mu\text{M}$
Bisakurool	-7,13	3	ARG66, TRP62, ASP65	5,96 $\mu\text{M}$
$\beta$ -Atlanton	-7,13	2	ALS15, GLU111	5,98 $\mu\text{M}$
Bisakuron	-7,11	3	ARG66, TRP62, ASP65	6,15 $\mu\text{M}$
ar-Turmeron	-7,07	1	TRP62	6,53 $\mu\text{M}$
$\beta$ -seskuifelandren	-7,01	0	-	7,28 $\mu\text{M}$
$\alpha$ -Kurkumen	-6,96	0	-	7,96 $\mu\text{M}$
(3S,5S)-1,7-bis(4-hidroksi-3-metoksifenil)-heptan-3,5-diol	-6,94	6	TRP62, ASP65, ASP14, ARG66, GLU111, LYS15	8,25 $\mu\text{M}$

## LAMPIRAN 10 (LANJUTAN)

**Tabel V.3**

Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada Reseptor HBV (1IUD)  
(Lanjutan)

Senyawa/Ligan	Ikatan energi ( $\Delta G$ ) kcal/mol	Jumlah ikatan hidrogen	Residu asam amino	KI (nM)
Kurlon	-6,9	2	TRP62	8,80 $\mu$ M
Ligan Alami	-6,9	5	GLU111, LYS15, ASP65, TRP62, TYR155	8,78 $\mu$ M
Ar-Kurkumen	-6,86	0	-	9,39 $\mu$ M
Kurzerenon	-6,75	2	TYR155	7,48 $\mu$ M
Santorizol	-6,68	2	ASP14, LYS15	12,69 $\mu$ M
Turmeron	-6,6	2	TRP62, ARG66	27,03 $\mu$ M
Bisakumol	-6,59	2	ASP665, ARG6	14,71 $\mu$ M
Kurzeren	-6,54	0	-	11,92 $\mu$ M
Germakron	-6,23	2	TRP62, ARG66	27,03 $\mu$ M
Isoborneol	-6,19	1	ASP65	32,82 $\mu$ M
$\beta$ -Kurkumen	-6,14	0	-	31,70 $\mu$ M
Kamfor	-6,04	1	TYR155	37,10 $\mu$ M
$\alpha$ -Terpineol	-6,04	2	ASP65, TRP62	37,54 $\mu$ M
Kamfen	-5,18	0	-	158,61 nM
Ligan pembanding	-5,01	4	ASP14, ASN12, LYS15, GLU111	211,47 nM

## LAMPIRAN 11

SIFAT FISIKOKIMIA BERDASARKAN ATURAN *LIPINSKI'S**RULE OF FIVE*

Tabel V.4

Sifat Fisikokimia Senyawa yang Terkandung di dalam Rimpang Temulawak Berdasarkan Aturan 5 Lipinski

No	Ligan	Berat Molekul	Log P	H-Donor	H-Akseptor	Memenuhi Syarat/Tidak
1.	Curcumin	368	3,37	2	6	Memenuhi
2.	Demetoksicurcumin	338	3,36	2	4	Memenuhi
3.	Bisdemetoksikurkumin	308	3,35	2	3	Memenuhi
4.	1,7-bis-(4hidroksi-3-metoksifenil)-1-hepten-3,5-dion	370	3,29	2	6	Memenuhi
5.	(1ξ)-1-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-6-hepten-3,5-dion	386	2,78	3	7	Memenuhi
6.	5-hidroksi-1,7-bis(4-hidroksi-3-heptanon	374	3,00	3	6	Memenuhi
7.	(3S,5S)-1,7-bis(4-hidroksi-3-metoksifenil)-heptan-3,5-diol	376	2,79	4	6	Memenuhi
8.	5'-Metoksicurcumin	398	3,38	2	7	Memenuhi
9.	<i>Trans</i> -1,7-difenil-1-hepten-5-ol	266	4,47	1	1	Memenuhi
10.	<i>Trans, trans</i> -1,7-difenil-1,3-heptadien-5-ol	264	4,25	1	1	Memenuhi
11.	Alnuston	262	4,46	0	1	Memenuhi
12.	1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol	282	4,18	2	2	Memenuhi

## LAMPIRAN 11 (LANJUTAN)

**Tabel V.4**  
Sifat Fisikokimia Senyawa yang Terkandung di dalam Rimpang Temulawak Berdasarkan Aturan 5 Lipinski (Lanjutan)

No	Ligan	Berat Molekul	Log P	H-Donor	H-Akseptor	Memenuhi Syarat/Tidak
13.	1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol	266	4,47	1	1	Memenuhi
14.	$\beta$ -Kurkumen	204		0	0	Memenuhi
15.	$\beta$ -seskuifelandren	204	5,04	0	0	Memenuhi
16.	$\beta$ -Atlanton	218	4,89	0	1	Memenuhi
17.	Turmeron	218	4,21	0	1	Memenuhi
18.	Ar-Kurkumen	202	4,21	0	0	Memenuhi
19.	$\alpha$ -Kurkumen	202	4,84	0	0	Memenuhi
20.	ar-Turmeron	216	4,84	0	1	Memenuhi
21.	Santorizol	218	4,02	1	1	Memenuhi
22.	Bisakurol	220	4,55	1	1	Memenuhi
23.	Kurlon	218	3,86	0	1	Memenuhi
24.	Bisakuron	252	4,07	2	3	Memenuhi
25.	Bisakumol	218	2,24	1	1	Memenuhi
26.	Bisakuron A	218	3,82	2	3	Memenuhi
27.	Bisakuron B	252	2,24	2	3	Memenuhi
28.	Bisakuron C	252	2,24	2	3	Memenuhi
29.	Bisakuron epoksida	252	2,24	2	4	Memenuhi
30.	Germakron	268	1,45	0	1	Memenuhi
31.	Kurzeren	218	4,36	0	1	Memenuhi
32.	Kurzerenon	230	3,84	0	2	Memenuhi
33.	$\alpha$ -Terpineol	154	3,48	1	1	Memenuhi
34.	Isoborneol	154	2,50	1	1	Memenuhi
35.	Kamfor	152	2,19	0	1	Memenuhi
36.	Kamfen	136	2,40	0	0	Memenuhi

## LAMPIRAN 12

## UJI PreADME

**Tabel V.5**  
Uji PreADME (Absorpsi dan Distribusi)

No	Senyawa/Ligan	Absorpsi		Distribusi
		Caco-2 cell (nm sec-1)	HIA (%)	Protein Plasma Binding (%)
1	Curcumin	20.07	94	88
2	Demetoksicurcumin	21.01	94	89
3	Bisdemetoksikurkumin	21.40	93	94
4	1,7-bis-(4hidroksi-3-metoksifenil)-1-hepten-3,5-dion	20.16	94	88
5	(1 $\xi$ )-1-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-6-hepten-3,5-dion	15.93	90	83
6	5-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-3-heptanon	19.26	90	91
7	(3S,5S)-1,7-bis(4-hidroksi-3-metoksifenil)-heptan-3,5-diol	18.65	85	91
8	5'-Metoksicurcumin	18.77	95	87
9	<i>Trans</i> -1,7-difenil-1-hepten-5-ol	55.25	100	98
10	<i>Trans, trans</i> -1,7-difenil-1,3-heptadien-5-ol	55.22	100	95
11	Alnuston	56.50	100	96
12	1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol	38.72	94	92
13	1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol	23.09	91	98
14	$\beta$ -Kurkumen	23.41	100	100
15	$\beta$ -seskuifelandren	23.40	100	100
16	$\beta$ -Atlanton	55.68	100	100
17	Turmeron	55.69	100	100
18	Ar-Kurkumen	23.40	100	100
19	$\alpha$ -Kurkumen	23.40	100	100

**LAMPIRAN 12**  
**(Lanjutan)**

**Tabel V.5**  
Uji PreADME (Absorpsi dan Distribusi)  
(Lanjutan)

No	Senyawa/Ligan	Absorpsi		Distribusi
		CaCo-2 cell (nm sec-1)	HIA (%)	Protein Plasma Binding (%)
20	ar-Turmeron	55.50	100	100
21	Santorizol	53.28	100	100
22	Bisakurol	53.27	100	100
23	Kurlon	55.57	100	100
24	Bisakuron	24.61	91	88
25	Bisakumol	53.11	100	100
26	Bisakuron A	24.61	91	88
27	Bisakuron B	24.61	91	88
28	Bisakuron C	24.61	91	88
29	Bisakuron epoksida	19.02	89	61
30	Germakron	55.88	100	100
31	Kurzeren	57.02	100	100
32	Kurzerenon	55.48	100	100
33	$\alpha$ -Terpineol	50.81	100	23
34	Isoborneol	51.71	100	100
35	Kamfor	50.45	100	100
36	Kamfen	23.49	100	100

*Keterangan: HIA (Human Intestinal Absorpsi) = 70-100% well absorbed*

*20-70 moderately absorbed*

*0-20% poorly absorbed*

*In Vitro CaCo-2 cell permeability = > 70 higher permeability*

*4-70 medium permeability*

*< 4 low permeability*

*Plasma Protein Binding = > 90% strongly bound*

*< 90% weakly bound*

## LAMPIRAN 13

## UJI TOKSISITAS

**Tabel V.6**  
Uji Toksisitas

No	Senyawa/Ligan	Ames Test	Karsinogenik
		Mutagen / Non Mutagen	(-) / (+)
/	Ligan pembanding (Lamivudin)	Mutagen	Positif
2	Curcumin	Non-Mutagen	Negatif
3	Demetoksicurcumin	Non-Mutagen	Negatif
4	Bisdemetoksikurkumin	Non-Mutagen	Negatif
5	1,7-bis-(4hidroksi-3-metoksifenil)-1-hepten-3,5-dion	Non-Mutagen	Negatif
6	(1ξ)-1-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-6-hepten-3,5-dion	Non-Mutagen	Negatif
7	5-hidroksi-1,7-bis(4-hidroksi-3-metoksifenil)-3-heptanon	Non-Mutagen	Negatif
8	(3S,5S)-1,7-bis(4-hidroksi-3-metoksifenil)-heptan-3,5-diol	Mutagen	Negatif
9	5'-Metoksicurcumin	Non-Mutagen	Positif
10	<i>Trans</i> -1,7-difenil-1-hepten-5-ol	Mutagen	Positif
11	<i>Trans, trans</i> -1,7-difenil-1,3-heptadien-5-ol	Mutagen	Positif
12	Alnuston	Mutagen	Positif
13	1-fenil-7-(4-hidroksifenil)-1-hepten-5-ol	Non-Mutagen	Negatif
14	1-fenil-7-(3,4-dihidroksifenil)-1-hepten-5-ol	Mutagen	Positif
15	β-Kurkumen	Mutagen	Positif
16	β-seskuifelandren	Mutagen	Positif
17	β-Atlanton	Non-Mutagen	Positif
18	Turmeron	Mutagen	Positif
19	Ar-Kurkumen	Mutagen	Positif
20	α-Kurkumen	Mutagen	Positif
21	ar-Turmeron	Mutagen	Negatif

**LAMPIRAN 13**  
**(Lanjutan)**

**Tabel V.6**  
Uji Toksisitas  
(Lanjutan)

No	Senyawa/Ligan	Ames Test	Karsinogenik
		Mutagen / Non Mutagen	(-) / (+)
22	Santorizol	Mutagen	Positif
23	Bisakurol	Mutagen	Positif
24	Kurlon	Non-Mutagen	Positif
25	Bisakuron	Non- Mutagen	Negatif
26	Bisakumulol	Mutagen	Positif
27	Bisakuron A	Non-Mutagen	Negatif
28	Bisakuron B	Non-Mutagen	Negatif
29	Bisakuron C	Non-Mutagen	Negatif
30	Bisakuron epoksida	Non-Mutagen	Negatif
31	Germakron	Mutagen	Positif
32	Kurzeren	Mutagen	Positif
33	Kurzerenon	Mutagen	Positif
34	$\alpha$ -Terpineol	Mutagen	Negatif
35	Isoborneol	Mutagen	Negatif
36	Kamfor	Mutagen	Negatif
37	Kamfen	Mutagen	Negatif