

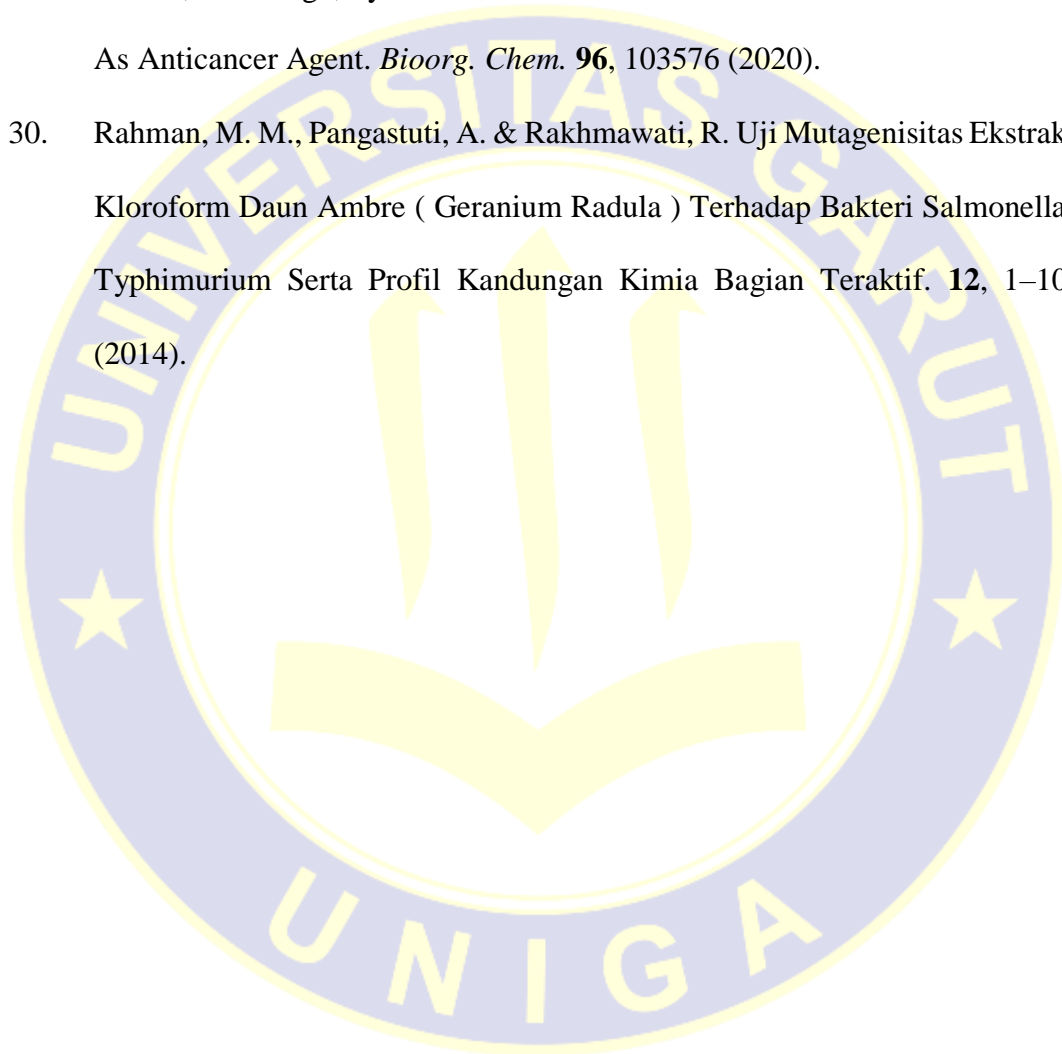
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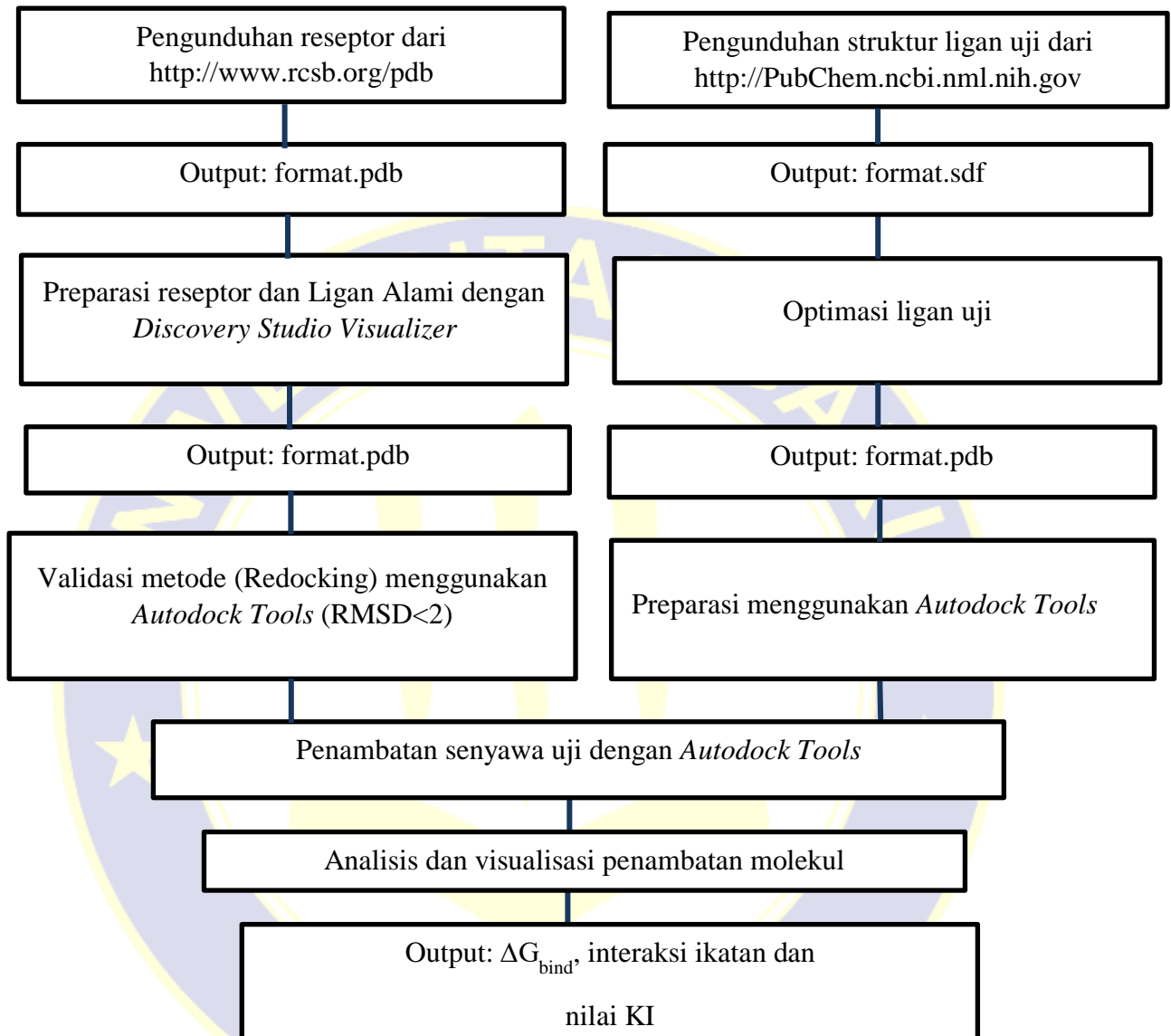
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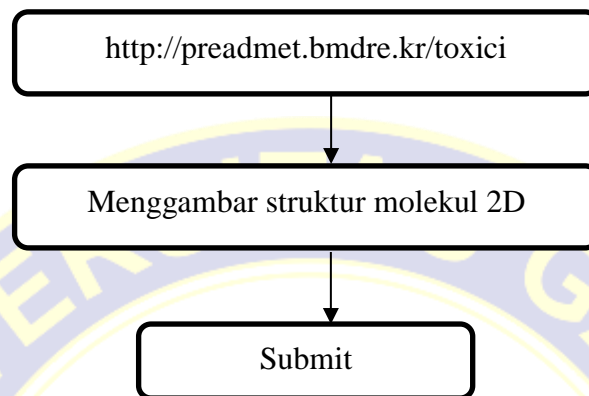
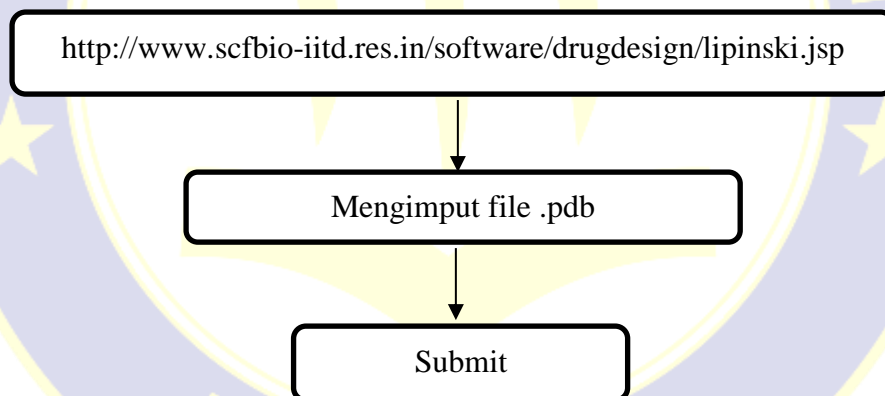


LAMPIRAN 1

ALUR PENELITIAN



Gambar III.1 Alur penelitian

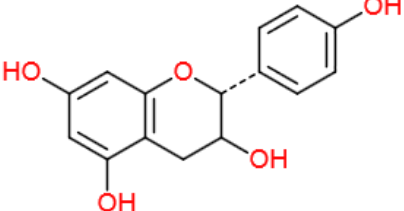
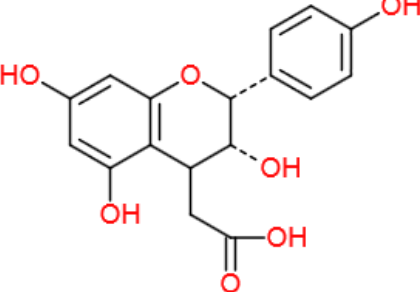
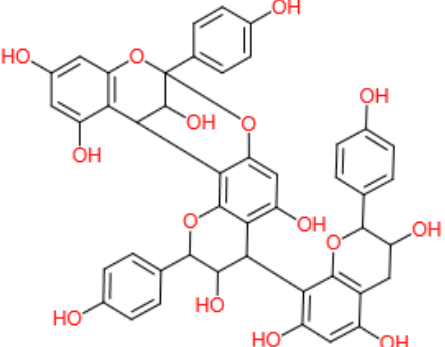
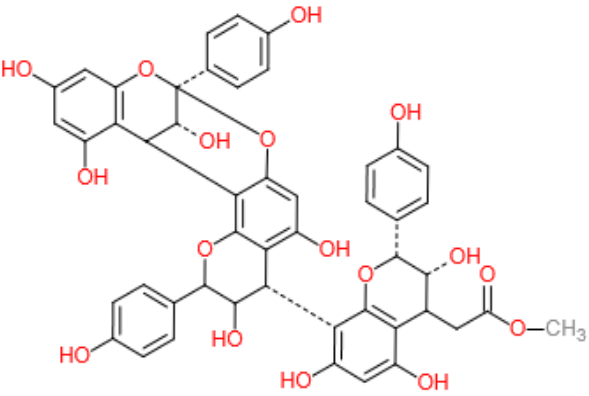
LAMPIRAN 1**(LANJUTAN)****Gambar III.2** Analisis preADME dan toksisitas**Gambar III.3** Analisis *lipinski's rule of five*

LAMPIRAN 2
AKAR PAKIS TANGKUR

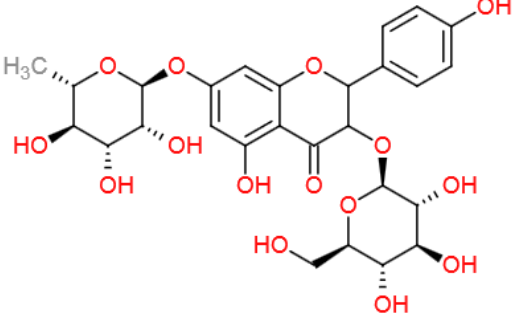
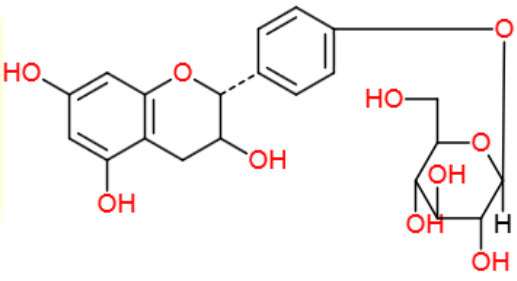
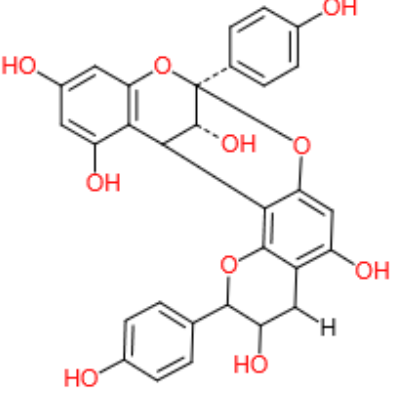


Gambar IV.1 Tanaman akar pakis tangkur

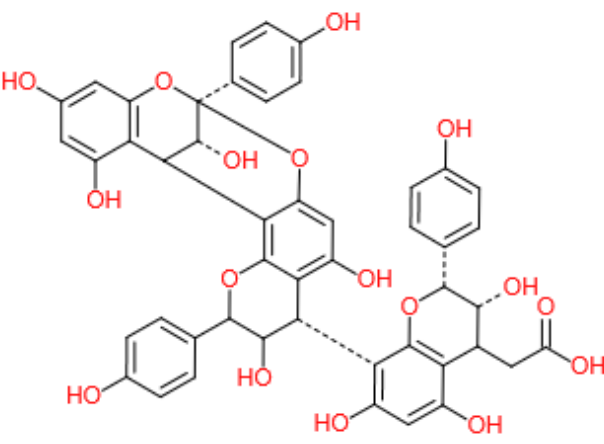
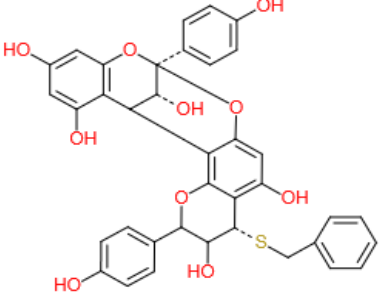
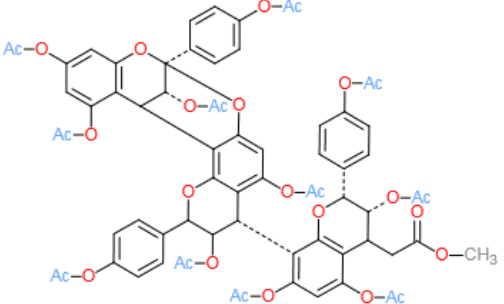
LAMPIRAN 3
SENYAWA AKAR PAKIS TANGKUR

No.	Nama Senyawa	Struktur
Gambar IV.2	(+) -afzelechin	
Gambar IV.3	3'-deoxydryopterin acid	
Gambar IV.4	Selligueain A	
Gambar IV.5	Selligueain B	

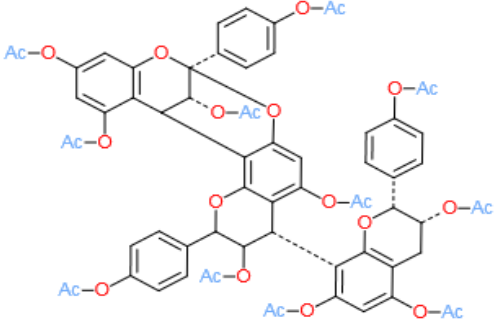
LAMPIRAN 3
(LANJUTAN)

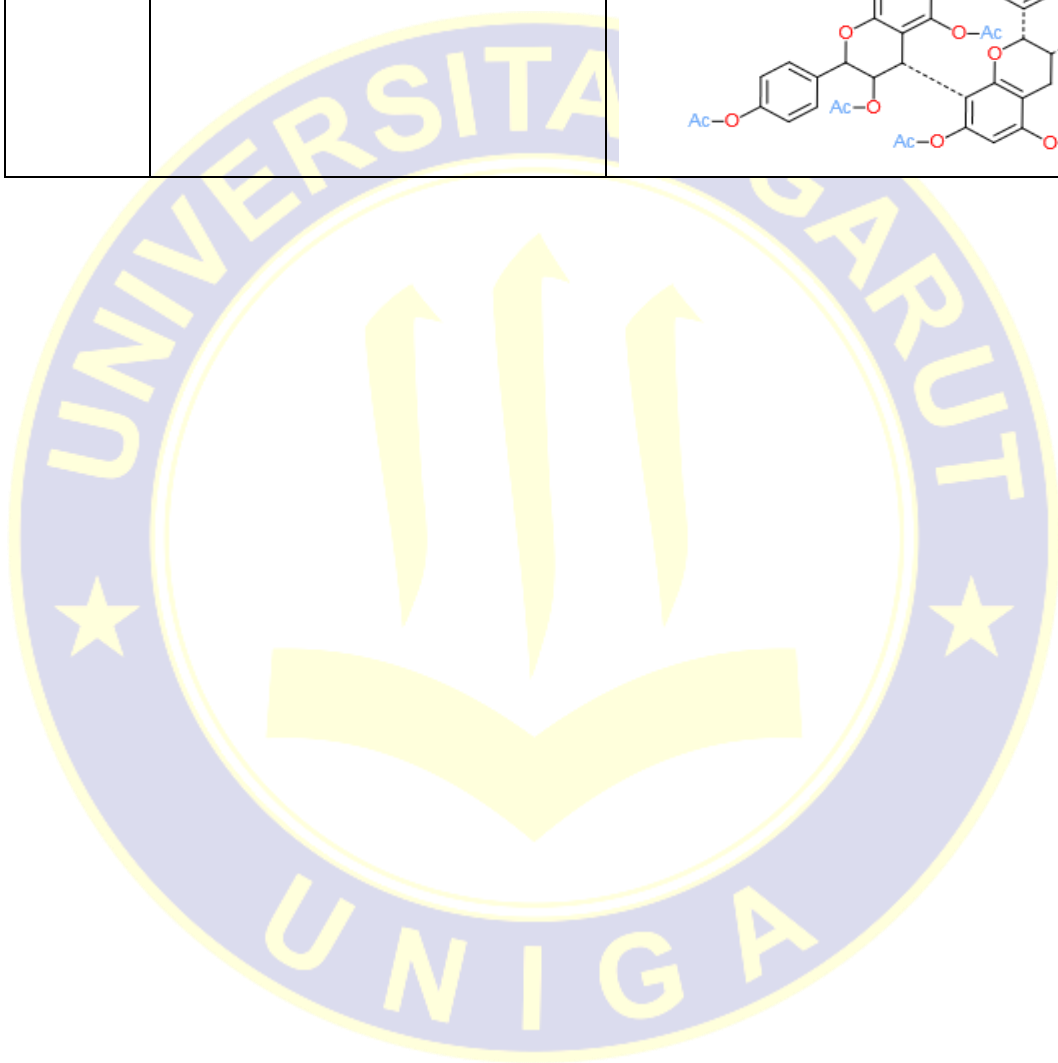
Gambar IV.6	Kaempferol-3-O- β -D-glukopyranoside-7-O- α -L-rhamnopyranoside	
Gambar	(+)-afzelechin-O- β -4'D-glukopyranoside	
Gambar IV.8	Geranin A	

**LAMPIRAN 3
(LANJUTAN)**

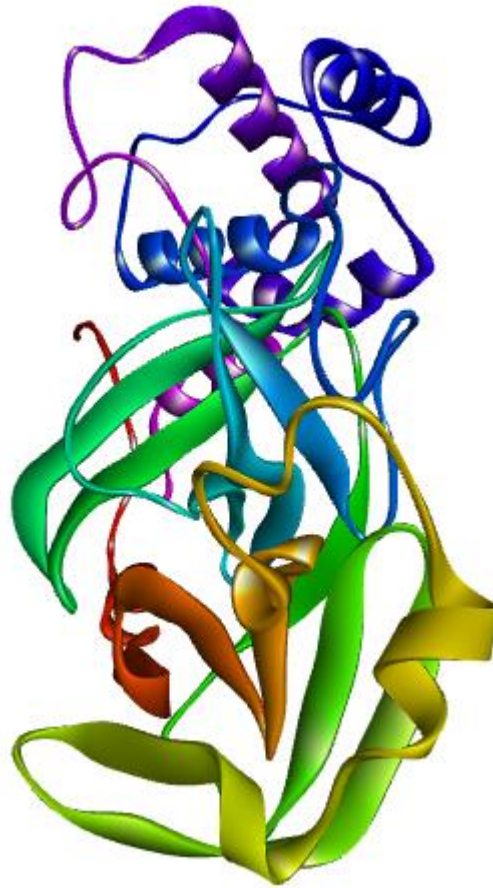
<p>Gambar IV.9</p>	<p>2-((2R,3R)-3,5,7-trihydroxy-2-(4-hydroxyphenyl)-8-((6R,10R,15R)-1,3,9,11,15-pentahydroxy-6,12-bis(4-hydroxyphenyl)-11,12,13,14-tetrahydro-10H-6,14-methanobenzo[d]naphtho[1,2-g][1,3]dioxocin-10-yl) chroman-4-yl)acetic acid</p>	
<p>Gambar IV.10</p>	<p>(4S,8S,15R)-4-(benzylthio)-2,8-bis(4-hydroxyphenyl)-3,4-dihydro-2H,14H-8,14-methanobenzo[7,8][1,3]dioxocin o[4,5-H]chromene-3,5,11,13,15-pentaol</p>	
<p>Gambar IV.11</p>	<p>Undecaacetate of epiafzelechin-(4β→8,2β→O→7)-epiafzelechin-(4β→8)-3'deoxydryopterac methyl ester</p>	

**LAMPIRAN 3
(LANJUTAN)**

Gambar IV.12	Undeacetylepiafzelechin- (4 β →8,2 β →O→7)- epiafzelechin-(4 β →8)-afzelechin	
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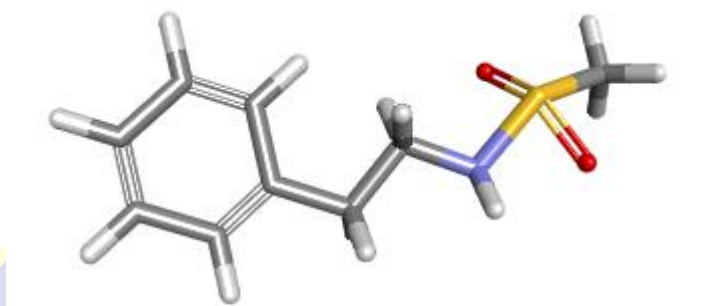


LAMPIRAN 4
STRUKTUR 3D RESEPTOR

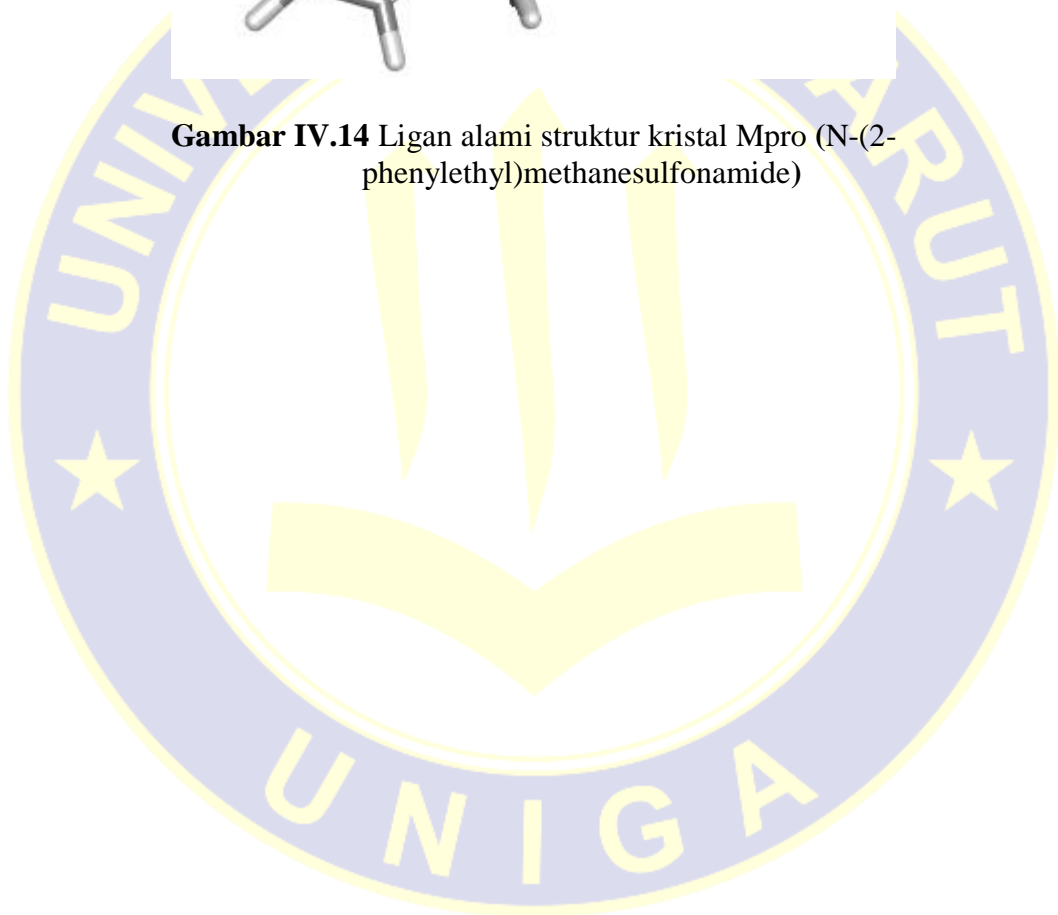


Gambar IV.13 Struktur kristal Mpro dengan PDB ID 5R7Y

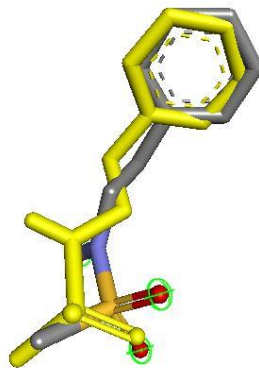
LAMPIRAN 5
STRUKTUR 2D LIGAN ALAMI



Gambar IV.14 Ligan alami struktur kristal Mpro (N-(2-phenylethyl)methanesulfonamide)



LAMPIRAN 6
VALIDASI METODE

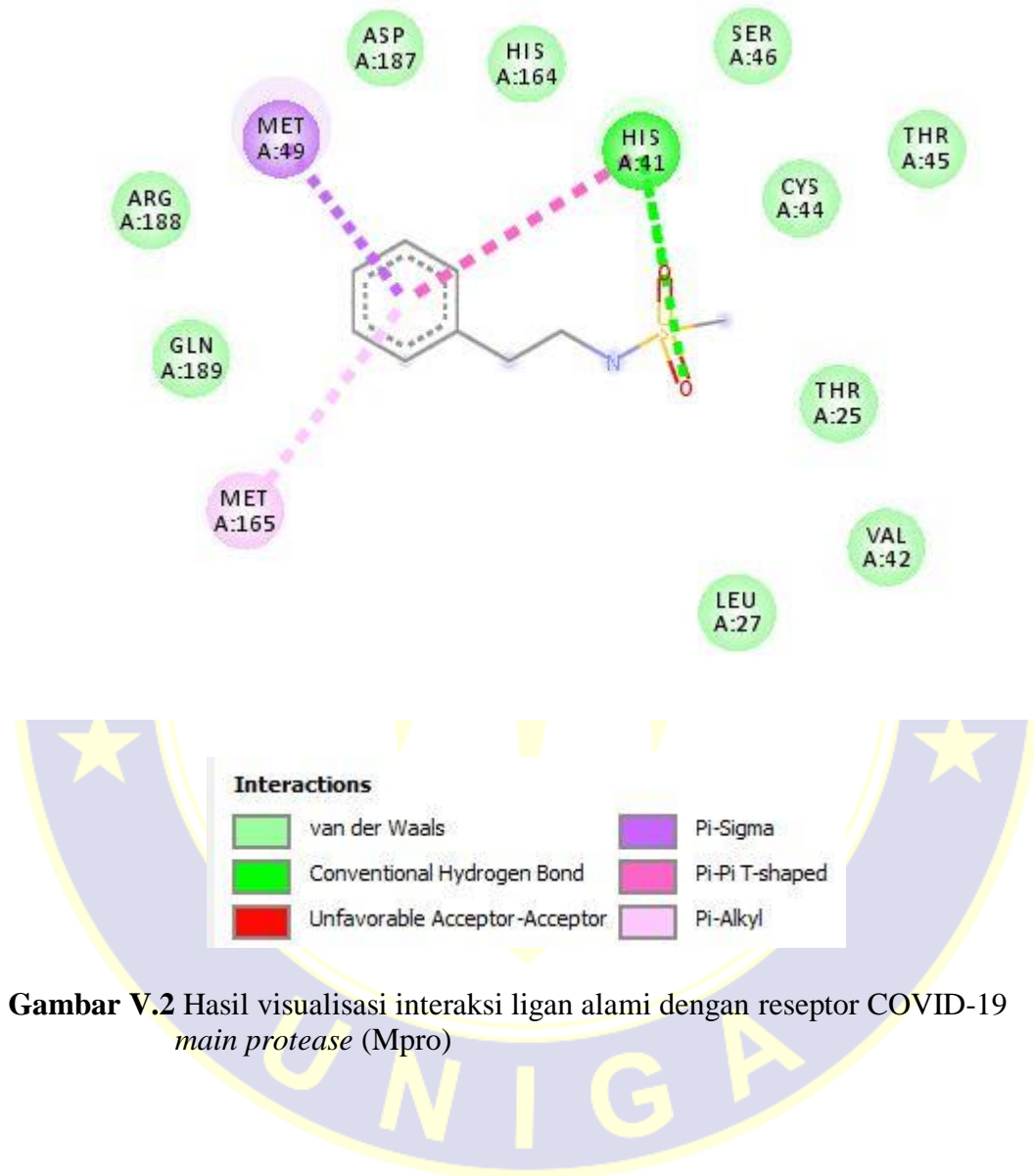


Gambar V.1 Hasil visualisasi tumpang tindih ligan alami dari reseptor COVID-19 *main protease* (Mpro) dari hasil kristalografi sinar-X (berwarna abu) dengan ligan hasil redocking (kuning).

Tabel V.1
Grid Box, RMSD, Nilai Energi Ikatan Ligan Alami

Kode Reseptor	Grid Box	RMSD (Å)	Nilai Energi Ikatan Ligan Alami
5R7Y	X: 10.301 Y: -2.386 Z: 24.735	1.604	-4.77

LAMPIRAN 6 (LANJUTAN)



Gambar V.2 Hasil visualisasi interaksi ligan alami dengan reseptor COVID-19 main protease (Mpro)

LAMPIRAN 7

HASIL PENAMBATAN MOLEKUL

Tabel V.2

Nilai Ikatan Energi dari Ligan Alami dan Senyawa Uji Pada Reseptor COVID-19
main protease (Mpro)

No	Senyawa/Ligan	Energi Ikatan (ΔG) kcal/mol	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI (uM)
Ligan alami					
1.	N-(2-phenylethyl)methanesul fonamide	-4.77	1	HIS A:41	316.40
Ligan uji					
1.	(+)-afzelechin	-5.10		HIS A:41 HIS A:164 GLU A:166	182.79
2.	Geranin A	+3.86e+005	2	GLN A:189 ARG A:188	-
3.	(+)-afzelechin-O- β -4'D-glukopyranoside	+5.37	2	GLU A:166 CYS A:145	-
4.	3'-deoxydryopteris acid	-3.23	3	CYS A:145 GLU A: 166 SER A: 46	4300.000
5.	Kaempferol-3-O- β -D-glucopyranoside-7-O- α -L-rhamnopyranoside	+1.39e+005	-	-	-

**LAMPIRAN 7
(LANJUTAN)**

**Tabel V.2
Lanjutan**

No	Senyawa/Ligan	Energi Ikatan (ΔG) kcal/mol	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI (uM)
6.	(4S,8S,15R)-4-(benzylthio)-2,8-bis(4-hydroxyphenyl)-3,4-dihydro-2H,14H-8,14methanobenzo[7,8][1,3]dioxocino[4,5-h]chromene-3,5,11,13,15-pentaol	+3.81e+005	3	CYS A:145 GLN A: 192 THR A: 24	-
7.	Selligueain A	+6.54e+005	2	ASN A: 142 GLN A:189	-
8.	Selligueain B	+7.39e+005	2	CYS A: 22 THR A: 45	-
9.	Undeca acetate of epiafzelechin-(4 β →8, 2 β →O→7)-epiafzelechin-(4 β →8)-3'-deoxydryopteris acid methyl ester	+1.57e+006	-	CYS A: 22 CYS A:145	-
10.	Undeca acetate of epiafzelechin-(4 β →8, 2 β →O→7)-epiafzelechin-(4 β →8)-3'-deoxydryopteris acid methyl ester	+1.57e+006	-	CYS A: 22 CYS A:145	-

**LAMPIRAN 7
(LANJUTAN)**

**Tabel V.2
Lanjutan**

No	Senyawa/Ligan	Energi Ikatan (ΔG) kcal/mol	Jumlah Ikatan Hidrogen	Residu Asam Amino	KI (uM)
11.	2-((2R,3R)-3,5,7-trihydroxy-2-(4-hydroxyphenyl)-8-((6R,10R,15R)-1,3,9,11,15-pentahydroxy-6,12-bis(4-hydroxyphenyl)-11,12,13,14-tetrahydro-10H-6,14-methanobenzo[d]naphtho[1,2-g][1,3]dioxocin-10-yl)chroman-4-yl)acetic acid.(7-9)	+7.33e+005	3	CYS A: 22 CYS A:145 THR A:45	-

LAMPIRAN 8

PREDIKSI DRUG LIKENESS BERDASARKAN ATURAN *LIPINSKI'S**RULE OF FIVE*

Tabel V.3

Sifat Fisiko Kimia Senyawa yang Terkandung Didalam Akar Pakis Tangkur
Berdasarkan Aturan *Lipinski's Rule of Five*

Senyawa Uji	Donor Ikatan Hidrogen	Akseptor Ikatan Hidrogen	Bobot Molekul (Dalton)	LogP	Memenuhi Syarat/Tidak
(+)-Afzelechin	4	5	274	1,84	Memenuhi
Geranin A	7	10	544	3,38	Tidak memenuhi
3'-deoxydryopteris acid	5	7	332	1,86	Memenuhi
Kaempferol-3-O- β -D-glucopyranoside-7-O- α -L-rhamnopyranoside	9	14	592	-1,48	Tidak memenuhi
(4S,8S,15R)-4-(benzylthio)-2,8-bis(4-hydroxyphenyl)-3,4-dihydro-2H,14H-8,14-methanobenzo[7,8][1,3]dioxocino[4,5-h]chromene-3,5,11,13,15-pentaol	7	10	652	5,67	Tidak memenuhi
2-((2R,3R)-3,5,7-trihydroxy-2-(4-hydroxyphenyl)-8-((6R,10R,15R)-1,3,9,11,15-pentahydroxy-6,12-bis(4-hydroxyphenyl)-11,12,13,14-tetrahydro-10H-6,14-methanobenzo[d]naphtho[1,2-g][1,3]dioxocin-10-yl)chroman-4-yl)acetic acid.(7-9)	12	16	872	5,35	Tidak memenuhi

**LAMPIRAN 8
(LANJUTAN)**

**Tabel V.3
Lanjutan**

Senyawa Uji	Donor Ikatan Hidrogen	Akseptor Ikatan Hidrogen	Bobot Molekul (Dalton)	LogP	Memenuhi Syarat/Tidak
Selligueain A	11	15	816	3,98	Tidak memenuhi
Selligueain B	11	16	886	5,44	Tidak memenuhi
(+)-afzelechin-O- β -4'D-glukopyranoside	7	10	436	-0,69	Tidak memenuhi
Undeca acetate of epiafzelechin-(4 β →8, 2 β →O→7)-epiafzelechin-(4 β →8)-3'-deoxydryopteris acid methyl ester	0	27	1348	8,91	Tidak memenuhi
Undecaacetyl epiafzelechin -(4 β -8,2 β -0-7)-epiafzelechin-(4 β -8)-afzelechin	0	25	1276	8,80	Tidak memenuhi

Keterangan: Berat Molekul tidak lebih dari 500 Dalton

Donor ikatan hidrogen tidak lebih dari 5

Akseptor ikatan hidrogen tidak lebih dari 10

Log P tidak lebih dari 5

LAMPIRAN 9

HASIL PENGUJIAN PreADME

Tabel V.4
Uji PreADME (Absorpsi dan Distribusi)

No	Senyawa/Ligan	Absorpsi		Distribusi
		Caco-2 cell (nm sec-1)	HIA (%)	Protein Plasma Binding (%)
1	(+)-Afzelechin	1,29	80,41	100,0
2	Geranin A	11,80	73,11	100,0
3	3'-deoxydryopteris acid	13,87	69,23	87,44
4	(+)-afzelechin-O-β-4'D-glukopyranoside	2,40	31,42	65,20
5	Kaempferol-3-O-β-D-glucopyranoside-7-O-α-L-rhamnopyranoside	6,99	5,43	40,36
6	(4S,8S,15R)-4-(benzylthio)-2,8-bis(4-hydroxyphenyl)-3,4-dihydro-2H,14H-8,14-methanobenzo[7,8][1,3]dioxocino[4,5-h]chromene-3,5,11,13,15-pentaol	17,64	86,09	100,0
7	Selligeanin B	16,81	48,56	100,0
8	2-((2R,3R)-3,5,7-trihydroxy-2-(4-hydroxyphenyl)-8-((6R,10R,15R)-1,3,9,11,15-pentahydroxy-6,12-bis(4-hydroxyphenyl)-11,12,13,14-tetrahydro-10H-6,14-methanobenzo[d]naphtho[1,2-g][1,3]dioxocin-10-yl)chroman-4-yl)acetic acid.(7-9)	16,73	38,26	100,0
9	Selligeanin A	15,40	54,23	100,0
10	Undeca acetate of epiafzelechin-(4β→8, 2β→O→7)-epiafzelechin-(4β→8)-3'-deoxydryopteris acid methyl ester	21,00	98,13	100,0

**LAMPIRAN 9
(LANJUTAN)**

**Tabel V.4
Lanjutan**

No	Senyawa/Ligan	Absorpsi		Distribusi
		Caco-2 cell (nm sec-1)	HIA (%)	Protein Plasma Binding (%)
11	Undecaacetyl epiafzelechin -(4 β -8,2 β -0-7)-epiafzelechin-(4 β -8)-afzelechin	21,02	98,04	100,0

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 10

UJI TOKSISITAS

Tabel V.5
Uji Toksisitas

No	Senyawa/Ligan	Ames Test	Karsinogenik
		Mutagen / Non-Mutagen	(-) / (+)
1	(+)-Afzelechin	Mutagen	(-)
2	Geranin A	Non-Mutagen	(-)
3	3'-deoxydryopteris acid	Mutagen	(-)
4	(+)-afzelechin-O-β-4'D-glukopyranoside	Mutagen	(-)
5	Kaempferol-3-O-β-D-glucopyranoside-7-O-α-L-rhamnopyranoside	Non-Mutagen	(-)
6	(4S,8S,15R)-4-(benzylthio)-2,8-bis(4-hydroxyphenyl)-3,4-dihydro-2H,14H-8,14-methanobenzo[7,8][1,3]dioxocino[4,5-h]chromene-3,5,11,13,15-pentaol	Non-Mutagen	(-)
7	Selliguaein B	Non-Mutagen	(-)
8	2-((2R,3R)-3,5,7-trihydroxy-2-(4-hydroxyphenyl)-8-((6R,10R,15R)-1,3,9,11,15-pentahydroxy-6,12-bis(4-hydroxyphenyl)-11,12,13,14-tetrahydro-10H-6,14-methanobenzo[d]naphtho[1,2-g][1,3]dioxocin-10-yl)chroman-4-yl)acetic acid.(7-9)	Non-Mutagen	(-)
9	Selliguaein A	Non-Mutagen	(-)
10	Undeca acetate of epiafzelechin-(4β→8, 2β→O→7)-epiafzelechin-(4β→8)-3'-deoxydryopteris acid methyl ester	Mutagen	(+)

LAMPIRAN 10
(LANJUTAN)

Tabel V.5
Lanjutan

No	Senyawa/Ligan	Ames Test	Karsinogenik
		Mutagen / Non- Mutagen	(-) / (+)
11	Undecaacetyl epiafzelechin -(4 β -8,2 β -0-7)-epiafzelechin-(4 β -8)-afzelechin	Mutagen	(+)

