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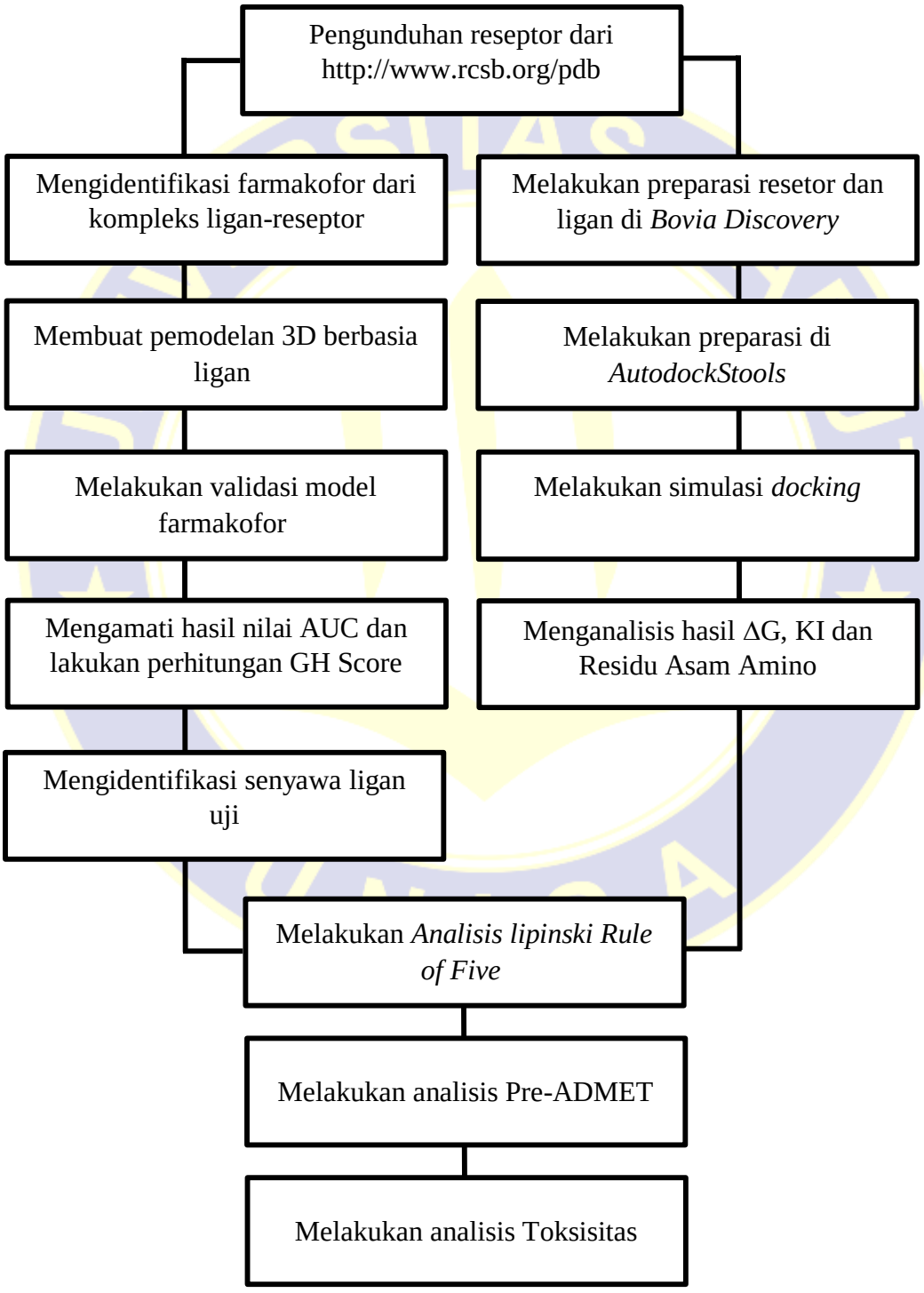
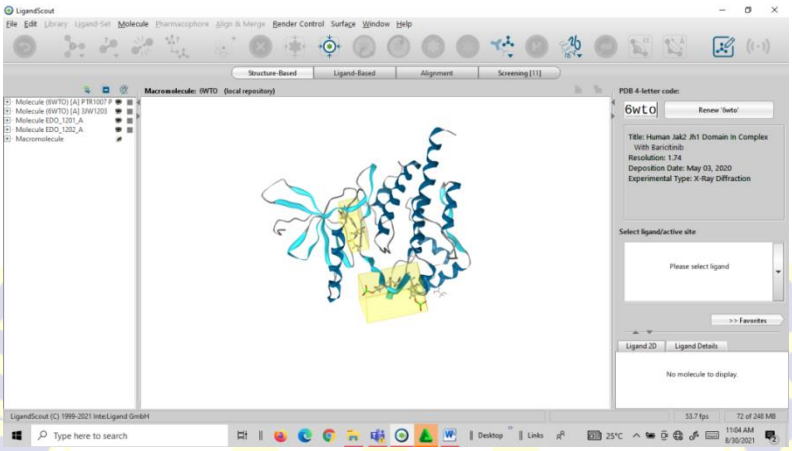
LAMPIRAN 1

ALUR PENELITIAN SKRINING FARMAKOFOR DAN PENAMBATAN

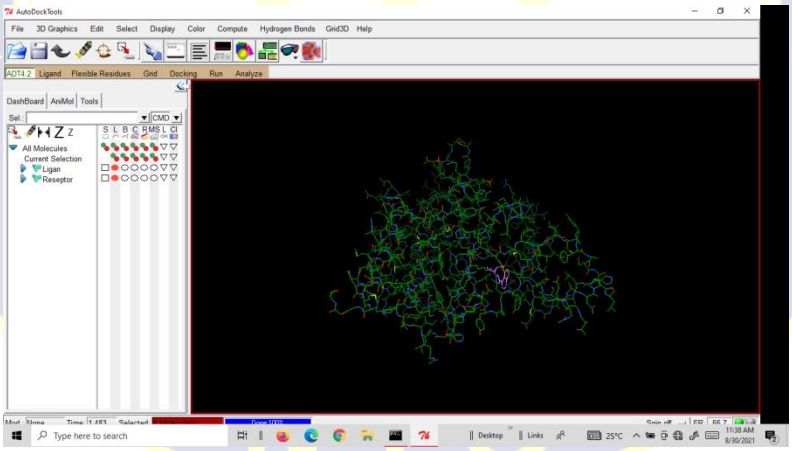


LAMPIRAN 2

APLIKASI DAN SITUS

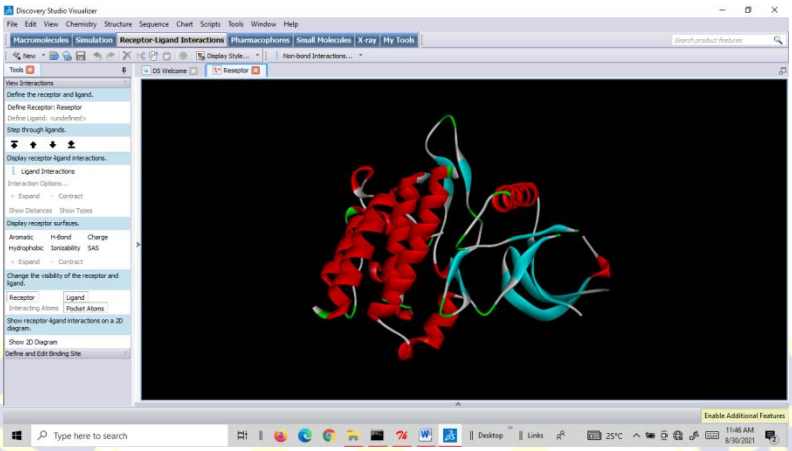


Gambar II.1 Tampilan *LigandScout*®

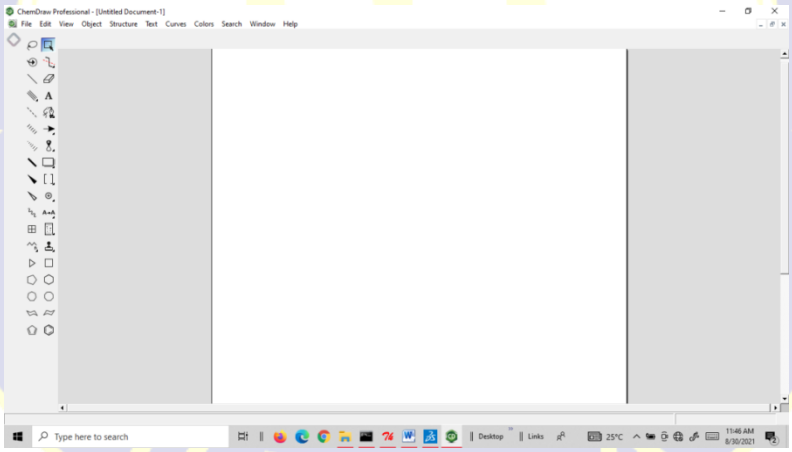


Gambar II.2 Tampilan *Autodock Tools*

LAMPIRAN 2
(LANJUTAN)

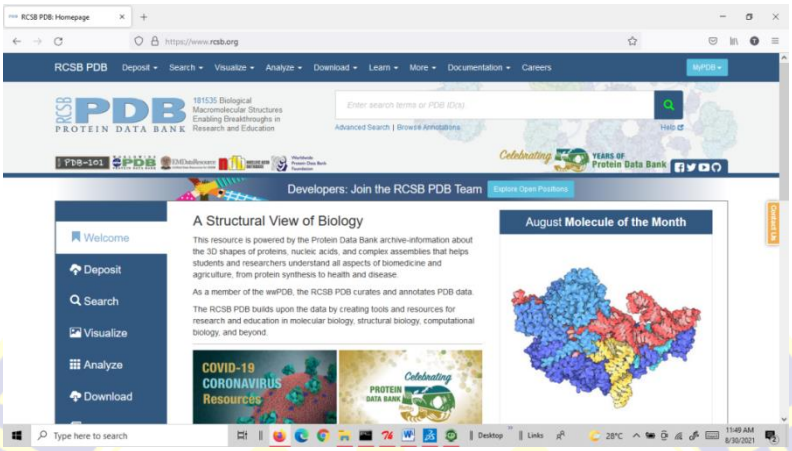


Gambar II.3 Tampilan *Discovery Studio*

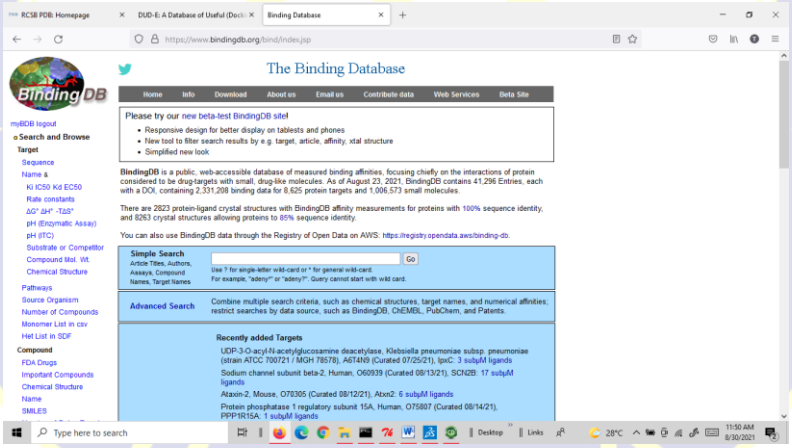


Gambar II.4 Tampilan *ChemDraw*

LAMPIRAN 2
(LANJUTAN)

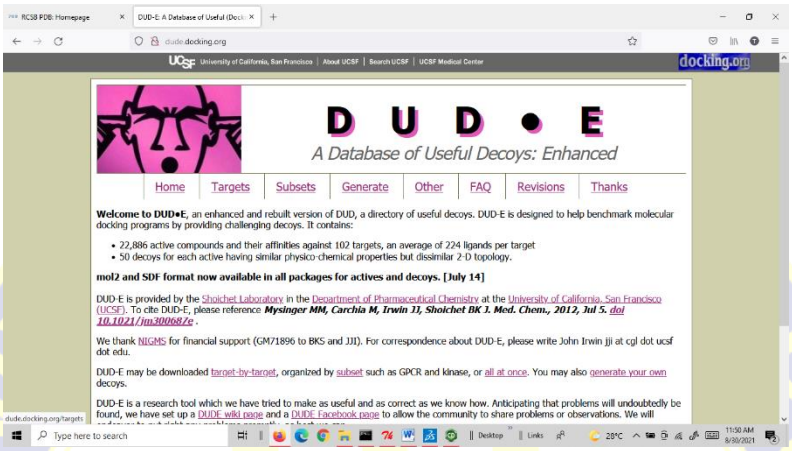


Gambar II.5 Tampilan situs *Protein Data Bank* (PDB)

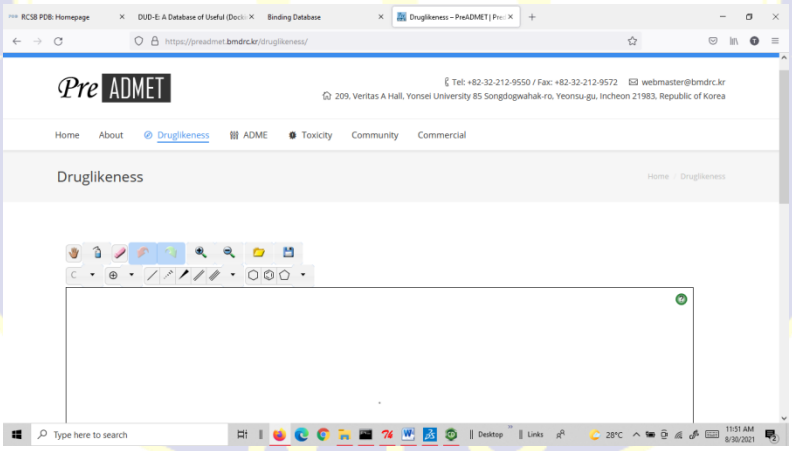


Gambar II.6 Tampilan situs *Binding Database*

LAMPIRAN 2
(LANJUTAN)

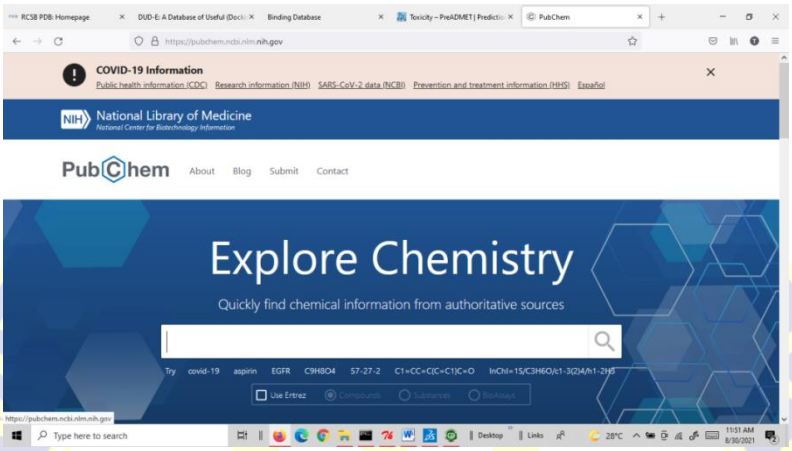


Gambar II.7 Tampilan situs DUD-E

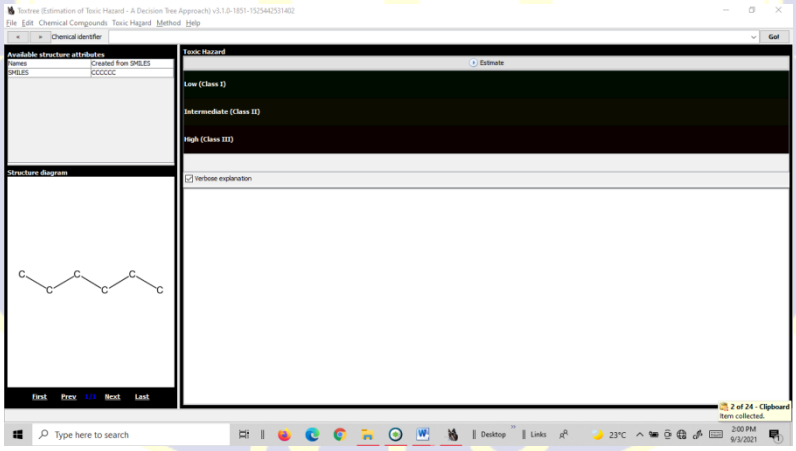


Gambar II.8 Tampilan situs *Pre-ADMET*

LAMPIRAN 2
(LANJUTAN)



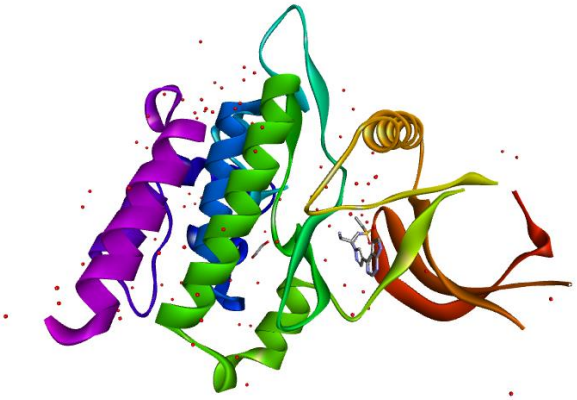
Gambar II.9 Tampilan situs *PubChem*



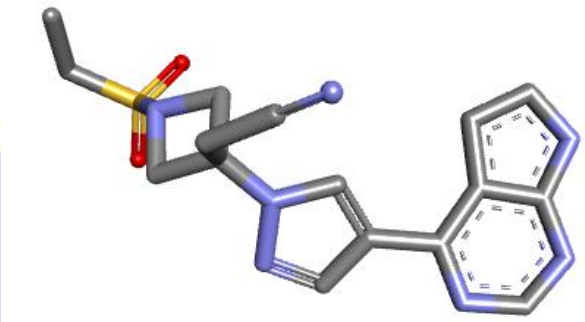
Gambar II.10 Tampilan *Toxtree*

LAMPIRAN 3

STRUKTUR 3D MAKROMOLEKUL PROTEIN DAN LIGAN ALAMI



Gambar III.1 *Tyrosine-protein kinase JAK2*



Gambar III.2 Ligan alami

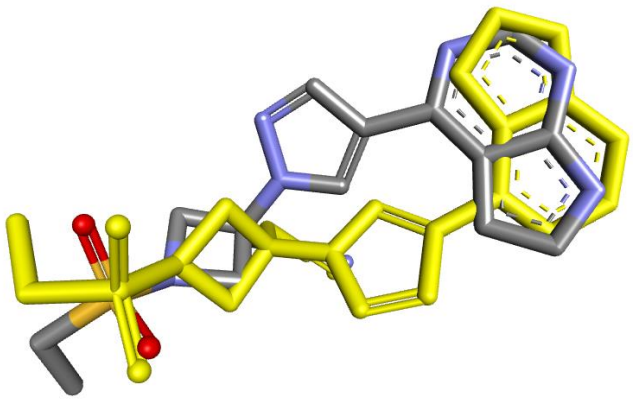
LAMPIRAN 4

VALIDASI METODE

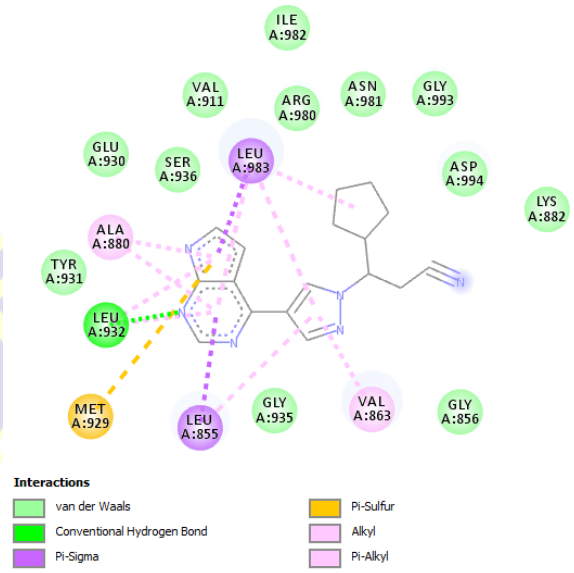
Tabel IV.1

Hasil Validasi Metode Penambatan Molekul

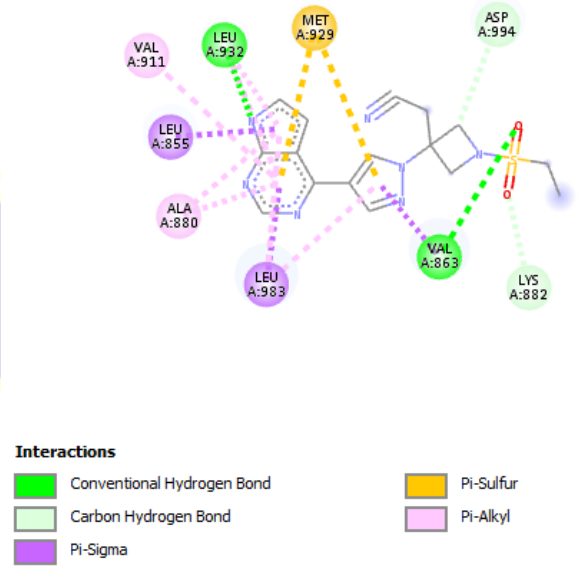
No	Kode PDB	Nilai RMSD	Grid Box
1.	6WTO	1.72Å	X = -21.227 Y = -13.767 Z = 7.785



Gambar IV.1 Visualisasi tumpang tindih ligan alami JAK2 (6WTO) dengan ligan hasil *redocking*

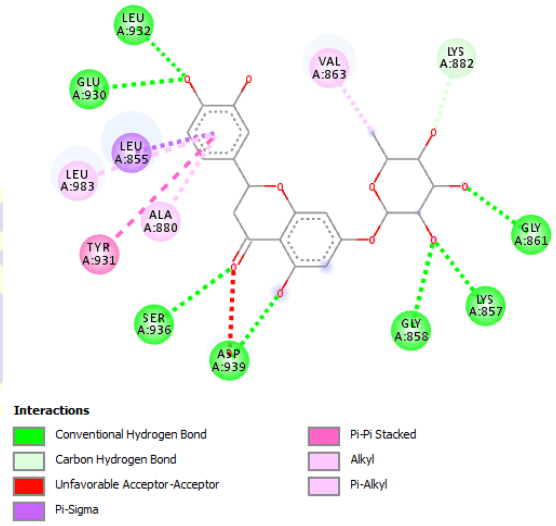


Gambar IV.2 Visualisasi ligan pembanding ruxolitinib

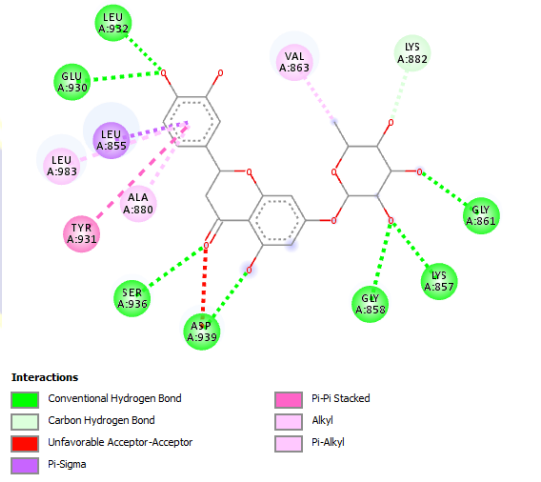


Gambar IV.3 Visualisasi *Native Ligand* terhadap JAK2

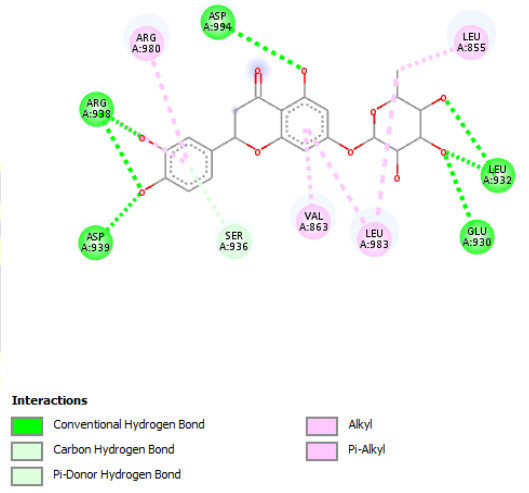
VALIDASI METODE
(LANJUTAN)



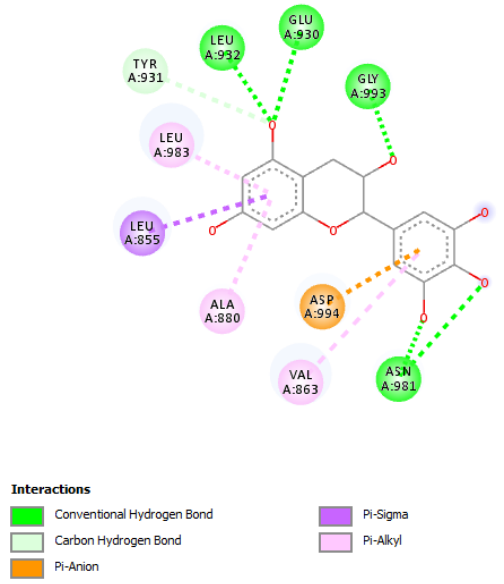
Gambar IV.4 Visualisasi struktur 2D residu asam amino penambatan senyawa *Astragalin* terhadap reseptor JAK2



Gambar IV.5 Visualisasi struktur 2D residu asam amino penambatan senyawa *Eriodictyol* terhadap reseptor JAK2

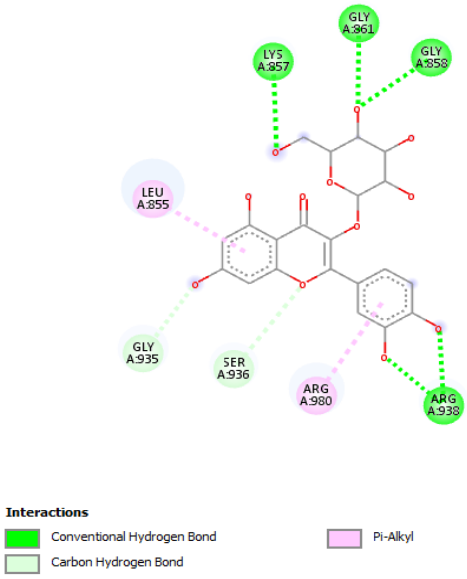


Gambar IV.6 Visualisasi struktur 2D residu asam amino penambatan senyawa *Fisetin* terhadap reseptor JAK2

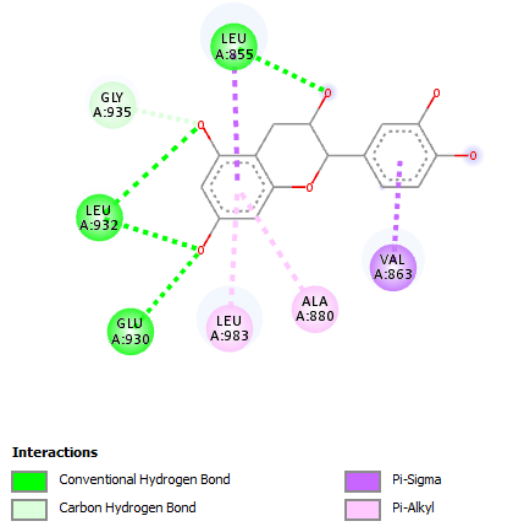


Gambar IV.7 Visualisasi struktur 2D residu asam amino penambatan senyawa *Gallocatechin* terhadap reseptor JAK2

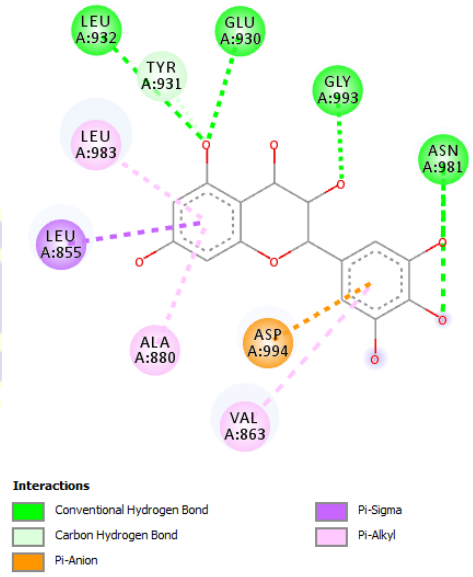
VALIDASI METODE
(LANJUTAN)



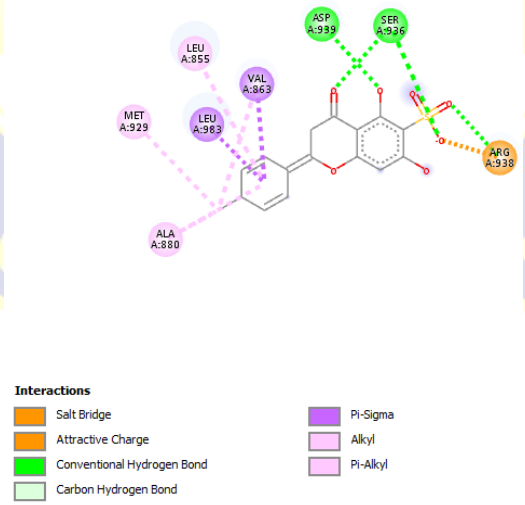
Gambar IV.8 Visualisasi struktur 2D residu asam amino penambatan senyawa *Isoquercitrin* terhadap reseptor JAK2



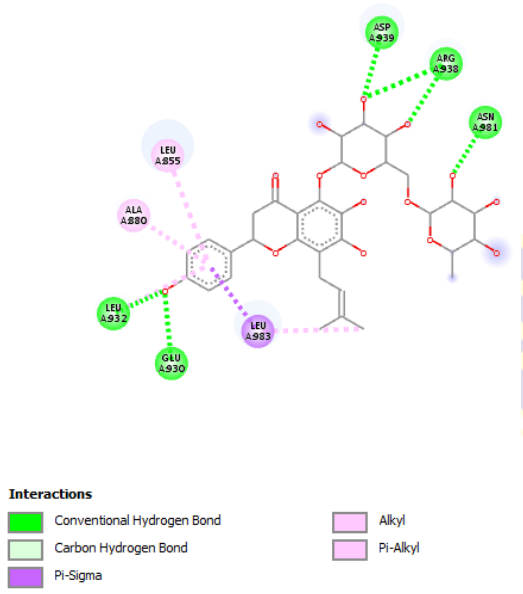
Gambar IV.9 Visualisasi struktur 2D residu asam amino penambatan senyawa *Katekin* terhadap reseptor JAK2



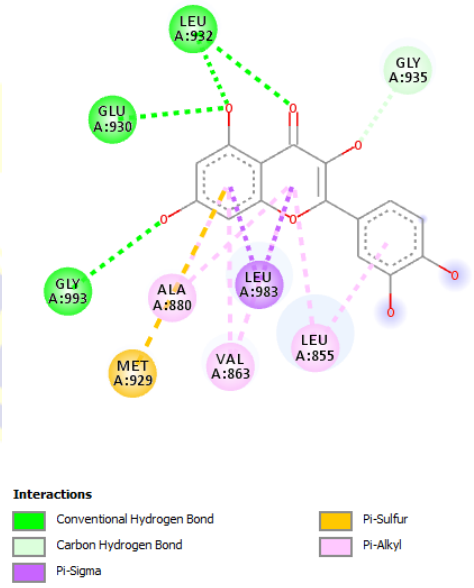
Gambar IV.10 Visualisasi struktur 2D residu asam amino penambatan senyawa *Leukodelfinidin* terhadap reseptor JAK2



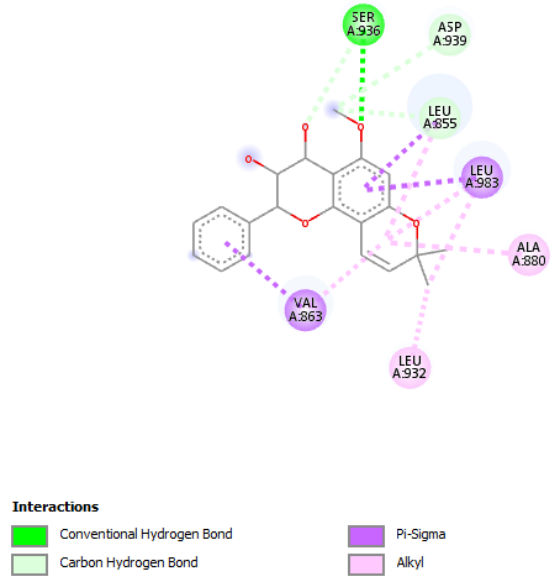
Gambar IV.11 Visualisasi struktur 2D residu asam amino penambatan senyawa *Niruriflavone* terhadap reseptor JAK2



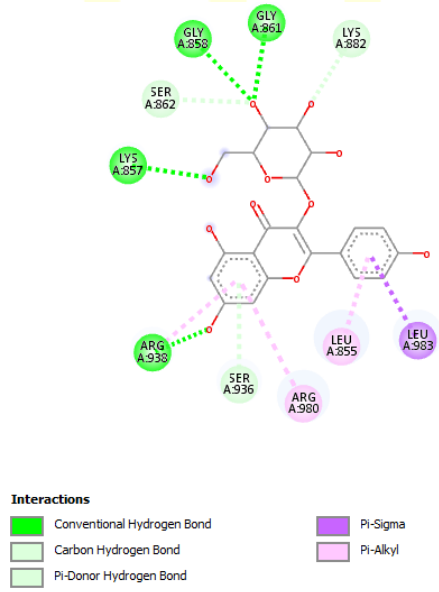
Gambar IV.12 Visualisasi struktur 2D residu asam amino penambatan senyawa *Nirurin* terhadap reseptor JAK2



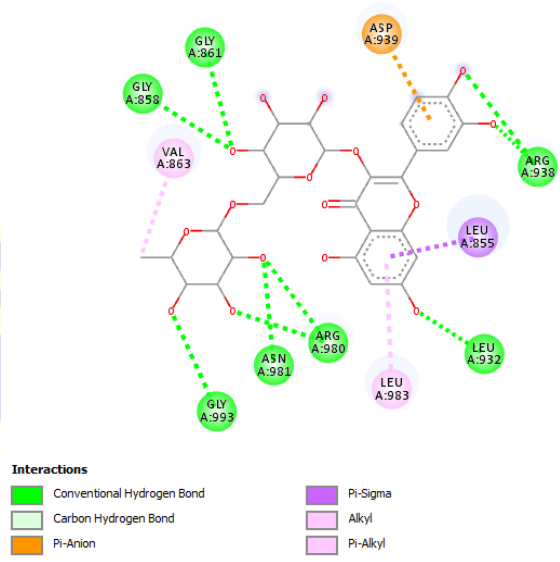
Gambar IV.13 Visualisasi struktur 2D residu asam amino penambatan senyawa *Quercetin* terhadap reseptor JAK2



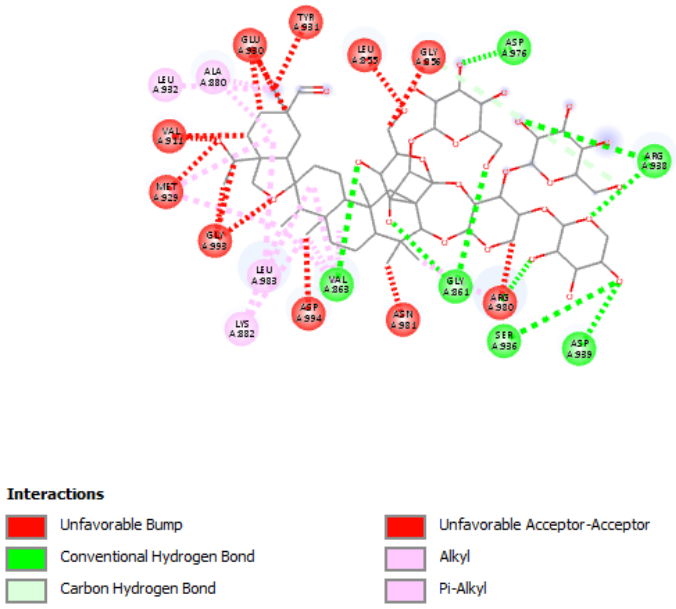
Gambar IV.15 Visualisasi struktur 2D residu asam amino penambatan senyawa *Quercetol* terhadap reseptor JAK2



Gambar IV.16 Visualisasi struktur 2D residu asam amino penambatan senyawa *Quercitrin* terhadap reseptor JAK2



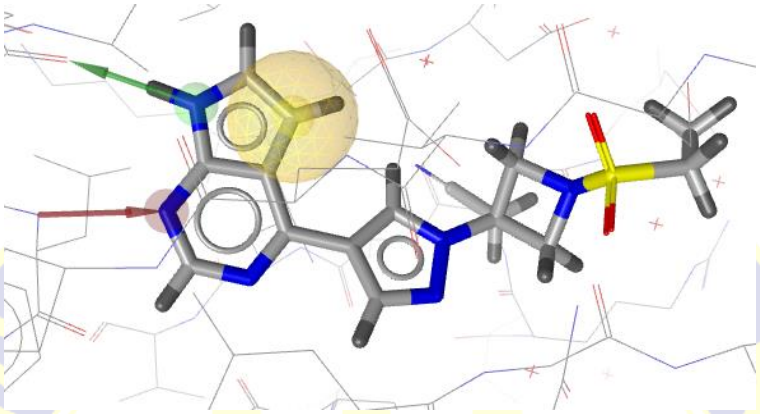
Gambar IV.17 Visualisasi struktur 2D residu asam amino penambatan senyawa *Rutin* terhadap reseptor JAK2



Gambar IV.18 Visualisasi struktur 2D residu asam amino penambatan senyawa *Saponin* terhadap reseptor JAK2

LAMPIRAN 5

SCREENING FARMAKOFOR



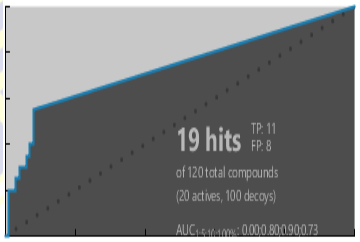
Gambar V.1 Visualisasi ligan alami

Gambar V.2 Model 1 farmakofor ligan *Tyrosine-kinase JAK2*

LAMPIRAN
(LANJUTAN)

Tabel IV.2

Hasil Validasi Farmakofor

Reseptor	**ROC *Curve***	**AUC**	**GH *Score***
JAK2		0,73	0,50

Tabel IV.3

Hasil *Screening* Farmakofor

No.	**Nama Senyawa**	***Matching Features***	***Fit Score***
1.	*Baricitinib* (Ligan pembanding 1)		-
2.	*Ruxolitinib* (Ligan pembanding 2)		-
2.	*Quercetol*		56.32

Keterangan :

Warna biru = cincin aromatik

Warna kuning = ikatan hidrofobik

Warna merah = akseptor ikatan hidrogen

Warna hijau = donor ikatan hidrogen

LAMPIRAN 6

PREDIKSI DRUG LIKENESS BERDASARKAN ATURAN LIPINSKI'S RULE OF FIVE

Tabel IV.4

Hasil Prediksi *Drug Likeness*

Senyawa	Berat Molekul (gr/mol)	Ikatan Hidrogen		Log p	Keterangan
		Donor	Akseptor		
Quercetin	302.23	5	7	1.5	Memenuhi Syarat
Rutin	610.5	10	16	-1.3	Tidak Memenuhi Syarat
Astragalin	448.4	7	11	0.7	Tidak Memenuhi Syarat
Quercitrin	448.4	7	11	0.9	Tidak Memenuhi Syarat
Isoquercitrin	464.4	8	12	0.4	Tidak Memenuhi Syarat
Gallocatechin	306.27	6	7	0	Tidak Memenuhi Syarat
Niruriflavone	348.3	3	7	1.8	Memenuhi Syarat
Quercetol	354.4	2	5	2.6	Memenuhi Syarat
Fisetin	448.4	7	11	0.2	Tidak Memenuhi Syarat
Nirurin	664.6	9	15	0	Tidak Memenuhi Syarat
Saponin	1223.3	15	27	-2.7	Tidak Memenuhi Syarat
Leukoldelfinidin	322.27	7	8	0	Tidak Memenuhi Syarat
Katekin	290.27	5	6	0.4	Memenuhi Syarat
Eriodictyol	434.4	6	10	0.7	Memnuhi Syarat

LAMPIRAN 7

Prediksi ADME Senyawa Aktif Tanaman Meniran *(Phyllanthus niruri L.)*

Tabel IV.5

Hasil prediksi Pre-ADME

No	Nama Senyawa	Absorbsi		Distribusi
		CaCo2 (nm. Sec-1)	HIA (%)	PPB (%)
1.	Baricitinib (ligan pembanding)	3.08	93.54	78.87
2.	Astragalin	11.14	25.18	57.58
3.	Eriodictol	5.62	41.97	77.86
4.	Fisetin	9.77	25.17	58.11
5.	Gallocatechin	0.38	45.95	100
6.	Isoquercitrin	9.43	11.77	59.15
7.	Katekin	0.65	66.70	100
8.	Leukodelfinidin	1	25.23	97.88
9.	Niruriflavone	0.42	89.62	100
10.	Nirurin	9.77	11.14	73.91
11.	Quercetin	3.41	63.48	92.23
12.	Quercetol	28.56	94.02	85.83
13.	Quercitrin	7.37	24.94	64.95
14.	Rutin	7.91	2.86	43.89
15.	Saponin	19.72	0	15.89

Keterangan :

% Human Intestinal Absorpsi (%HIA) = (a) 70-100% *well absorbed*
(b) 20-70% *moderately absorbed*
(c) 0-20% *poorly absorbed*

In Vitro CaCo-2 cell permeability (nm-sec 1) = (a) >70 *higher permeability*
(b) 4-70 *medium permeability*
(c) < 4 *low permeability*

Plasma Protein Binding = (a) > 90 *strongly bound*
(b) < 90 *weakly bound*

LAMPIRAN 8

HASIL ANALISIS TOKSISITAS

Tabel IV.6

Analisis Toksisitas Native Ligan

No	Nama Senyawa	Kroes TCC	Karsinogenik		Mutagen (Amest Test)
			Genotoksik	Non Genotoksik	
1	Baricitinib(Ligan Pembanding)	Tidak Beresiko	-	-	-
2	Astragalin	Tidak Beresiko	-	-	-
3	Eriodictyol	Tidak Beresiko	-	-	-
4	Fisetin	Tidak Beresiko	-	-	-
5	Gallocatechin	Tidak Beresiko	-	-	-
6	Isoquercitrin	Tidak Beresiko	-	-	+
7	Cathecin	Tidak Beresiko	-	-	-
8	Leucodelphinidin	Tidak Beresiko	-	-	-
9	Niruriflavone	Tidak Beresiko	-	-	-
10	Nirurin	Beresiko Rendah	+	-	+
11	Quercetin	Tidak Beresiko	-	-	+
12	Quercetol	Tidak Beresiko	-	-	-
13	Quercitrin	Tidak Beresiko	-	-	+
14	Saponin	Beresiko Rendah	+	-	+
15	Katekin	Beresiko Rendah	-	-	+

LAMPIRAN 9

PENAMBATAN MOLEKUL LIGAN UJI

Tabel IV.7

Hasil Penambatan Ligan Uji terhadap JAK2

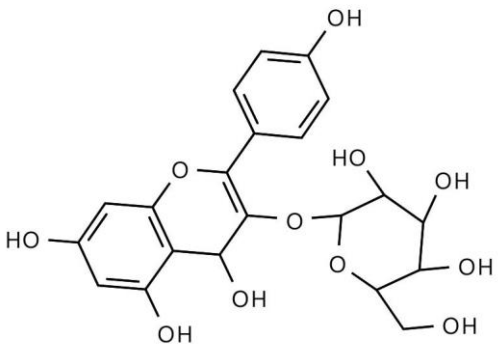
No	Senyawa	ΔG (kkal/mol)	KI (nM)	Residu Asam Amino
1	Baricitinib (Ligan Pembanding 1)	-8,40	691,02	LEU932A, VAL863A, ASP994A, LYS882A, VAL911A, LEU855A, ALA880A, LEU983A, MET929,
2.	Ruxolitinib (Ligan Pembanding 2)	-7,65	$246x10^{1}$	LEU932A, LEU983A, LEU 855A, MET929A, VAL863A, SER936A.
2	Astragalin	-7,83	1810	LEU932A,GLU930A, SER936A, ASP939A, GLY858A, LYS857A, GLY861A, LYS882A, LEU983A, LEU855A, TYR931A, ALA880A, VAL863A.
3	Eriodictyol	-8,32	801,20	LEU932A,GLU930A, SER936A, ASP939A, GLY858A, LYS857A, GLY861A, LYS882A, LEU983A, LEU855A, TYR931A, ALA880A, VAL863A.
4	Fisetin	-8,85	324,12	ARG938A, SER936A, ASP994A, ASP939A, LEU932A, GLU930A,

				ARG980A, VAL863A, LEU983A, LEU855A
5	Gallocatechin	-6,84	9640	LEU932A, GLU930A, GLY993A, TYR931A, ASN981A, LEU983A, LEU855A, ALA880A, VAL863A, ASP994A.
6	Isoquercirtin	-8,19	994,18	LYS857A, GLY861A, GLY858A, ARG938A, SER936A, GLY935A, LEU855A, ARG980A.
7	Katekin	-6,97	771	LEU855A, GLY935A, LEU932A, GLU930A, LEU983A, ALA880A, VAL863A.
8	Leukodelfinidin	-6,88	908	LEU932A, TYR931A, GLU930A, GLY993A, ASN981A, LEU983A, LEU855A, ALA880A, ASP994A, VAL863A.
9	Niruriflavone	-8,07	1220	ASP939A, SER936A, MET929A, LEU855A, LEU983A,VAL863A, ALA880A, ARG938A.
10	Nirurin	-8,49	594,38	ASP939A, ARG938A, ASN981A, LEU932A, GLU930A, LEU855A, ALA880A, LEU938A.
11	Quercetin	-7,24	4930	LEU932A, GLU930A, GLY935A, GLY993A, MET929A, ALA880A, VAL863A, LEU983A, LEU855A.

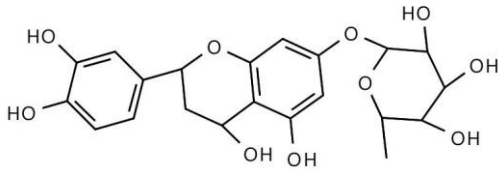
12	Quercetol	-8,53	561,93	SER936A, ASP939A, LEU855A, LEU983A, ALA880A, LEU932A, VAL863A.
13	Quercitrin	-7,56	2860	LYS882A, GLY861A, GLY858A, SER862A, LYS857A, ARG938A, SER936A, ARG980A, LEU855A, LEU983A.
14	Rutin	-9,02	244,42	GLY858A, GLY861A, ARG938A, LEU932A, ARG980A, ASN981A, GLY993A, ASP939A, VAL863A, LEU855A, LEU983A.
15	Saponin	+212,54	-	GLU930A, TYR931A, VAL911A, MET929A, GLY993A, ASP994A, LEU855A, GLY856A, LEU932A, ALA880A, LEU983A, LYS882A, VAL863A, ASP976A, GLY861A, SER936A, ASP939A, ARG938A, ASN981A, ARG980A.

LAMPIRAN 10

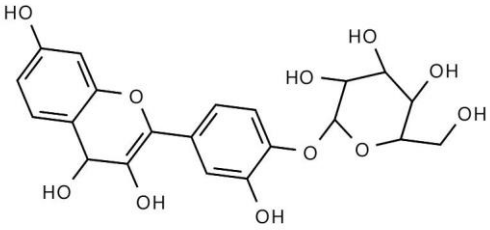
GAMBAR STRUKTUR LIGAN UJI



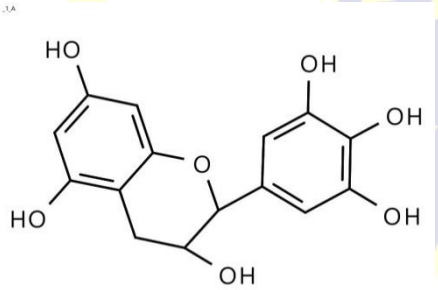
Astragalin



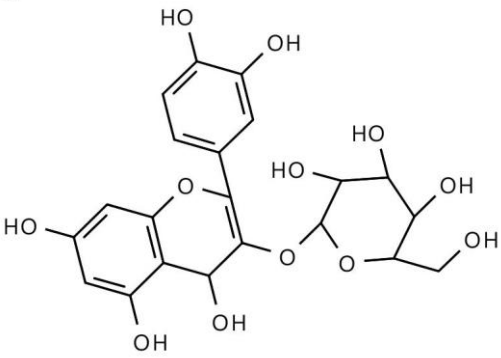
Eriodictyol



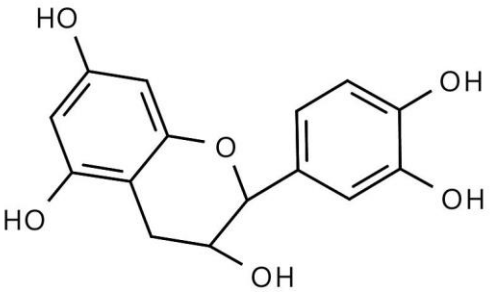
Fisetin



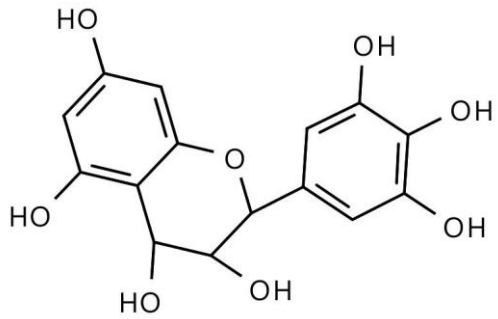
Gallocacethin



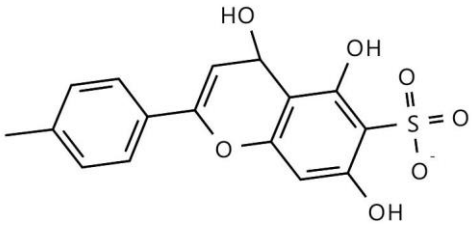
Isoquercitrin



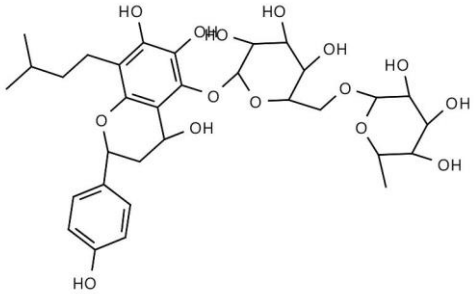
Katekin



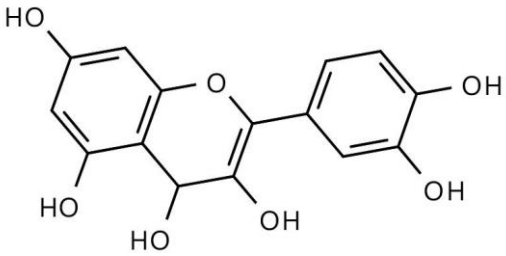
Leukodelfinidin



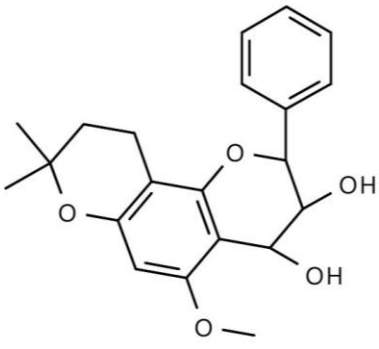
Niruriflavone



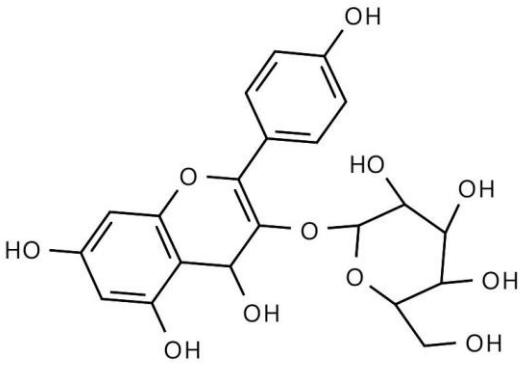
Nirurin



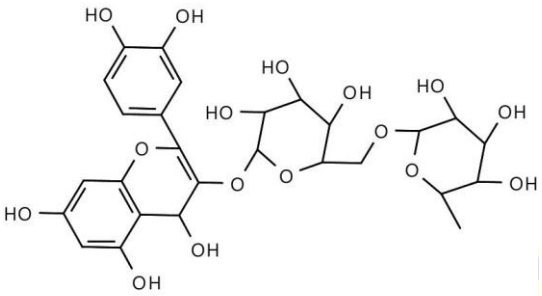
Quercetin



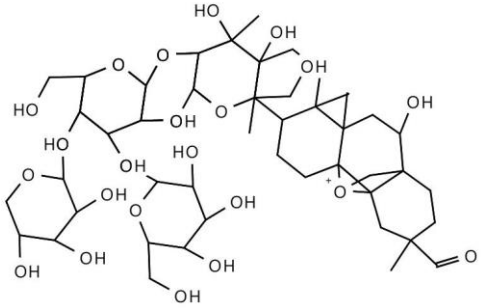
Quercetol



Quercitrin



Rutin



Saponin