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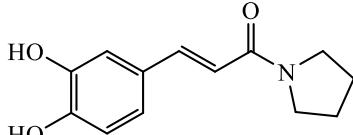
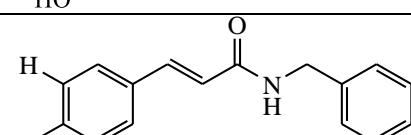
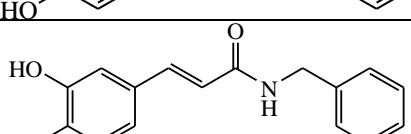
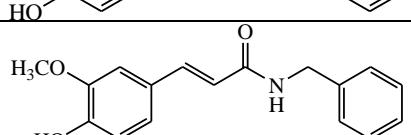
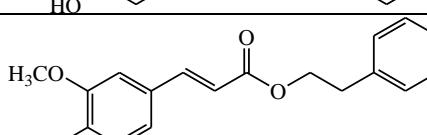
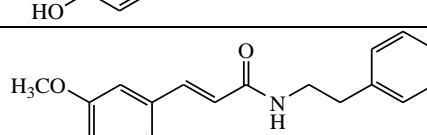
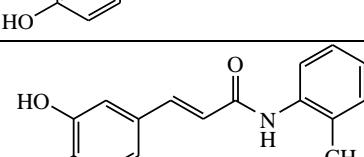
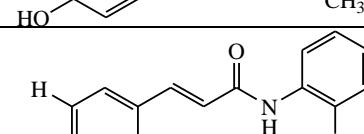
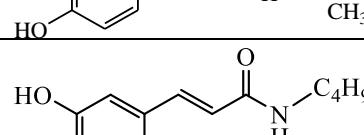
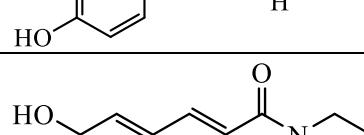
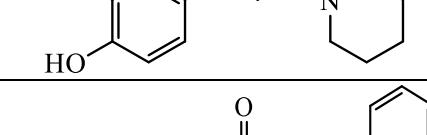
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Lampiran 1. Daftar Senyawa Turunan Asam Sinamat dan Aktivitasnya

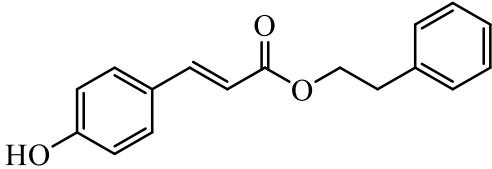
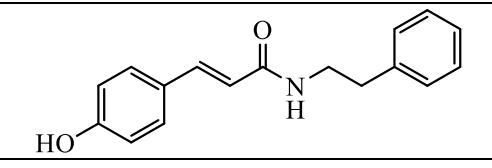
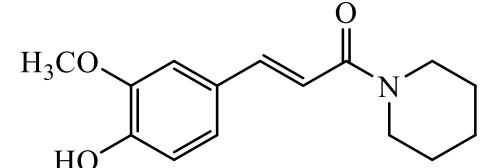
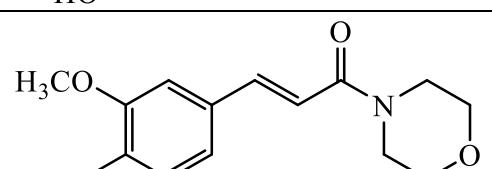
Tabel 11. Struktur senyawa hasil modifikasi beserta nilai aktivitasnya

No	Struktur Senyawa	Nama Senyawa	IC ₅₀ (µg/mL)
1		<i>p</i> -kumaramida (Firdaus dkk., 2009)	44,0
2		N-propil- <i>p</i> -kumaramida (Firdaus dkk., 2012)	53,56
3		N,N-dietil- <i>p</i> -kumaramida (Firdaus dkk., 2012)	23,50
4		N-Piperidinil- <i>p</i> -kumaramida (Firdaus dkk., 2012)	5,34
5		Metil <i>p</i> -kumarat (Rasyid dkk., 2014)	16,15
6		Metil <i>p</i> -metoksisinamat (Rasyid dkk., 2014)	21,18
7		N-morfolinil- <i>p</i> -kumaramida (Firdaus dkk., 2021)	19,35
8		N-morfolinil kafeamida (Firdaus dkk., 2021)	1,48
9		N-pirolidinil- <i>p</i> -kumaramida (Firdaus dkk., 2021)	53,46

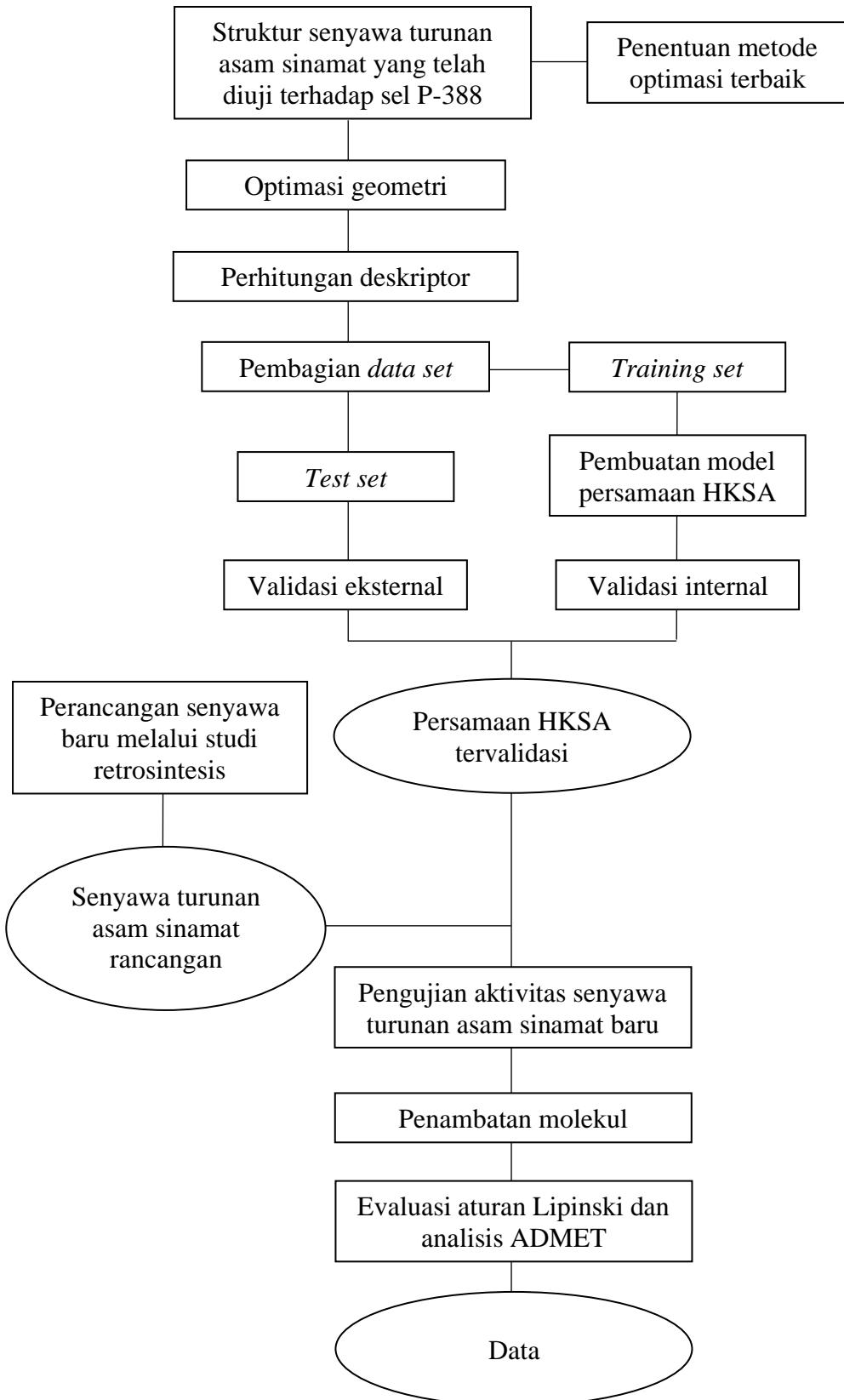
Lanjutan Tabel 11.

No	Struktur Senyawa	Nama Senyawa	IC₅₀ ($\mu\text{g/mL}$)
10		N-pirolidinil kafeamida (Firdaus dkk., 2021)	11,35
11		N-benzil kumaramida (Firdaus dkk., 2022)	16,15
12		N-benzil kafeamida (Firdaus dkk., 2022)	674,38
13		N-benzil ferulamida (Firdaus dkk., 2022)	179,56
14		fenetil <i>trans</i> -3-(4-hidroksi-3-metoksifenil) akrilat (Firdaus dkk., 2018)	10,79
15		<i>trans</i> -3-(4-hidroksi-3-metoksifenil)-N-fenetil akrilamida (Firdaus dkk., 2018)	29,14
16		<i>trans</i> -N-(<i>o</i> -tolil) kafeamida (Firdaus dkk., 2019)	0,91
17		<i>trans</i> -N-(<i>o</i> -tolil)- <i>p</i> -kumaramida (Firdaus dkk., 2019)	16,97
18		N-butil kafeamida (Tahir, 2020)	0,609
19		N-piperidinil kafeamida (Firdaus dkk., 2020)	0,861
20		N-fenetil-2-(3,4-diasetoksifenil) akrilamida (Fattah dkk., 2020)	0,5

Lanjutan Tabel 11.

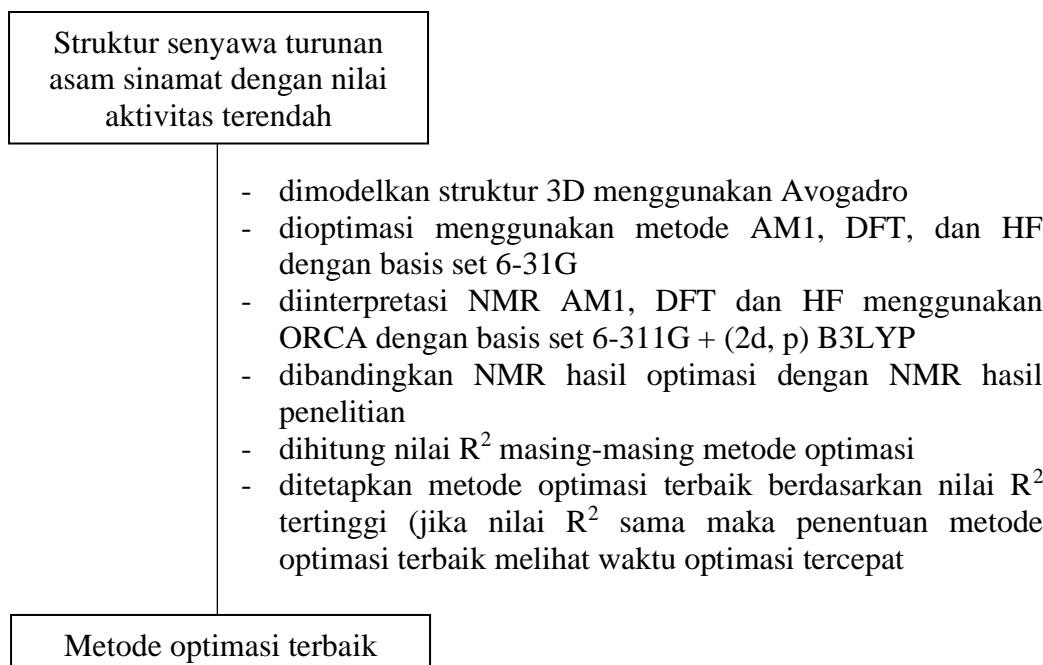
No	Struktur Senyawa	Nama Senyawa	IC₅₀ ($\mu\text{g/mL}$)
21		Fenetyl kumarat (Firdaus dkk., 2022)	1,0
22		N-fenetyl kumaramida (Firdaus dkk., 2022)	5,89
23		N-piperidinil ferulamida (Firdaus dkk., 2017)	46,67
24		N-morfolinil ferulamida (Firdaus dkk., 2017)	57,10

Lampiran 2. Diagram Alir

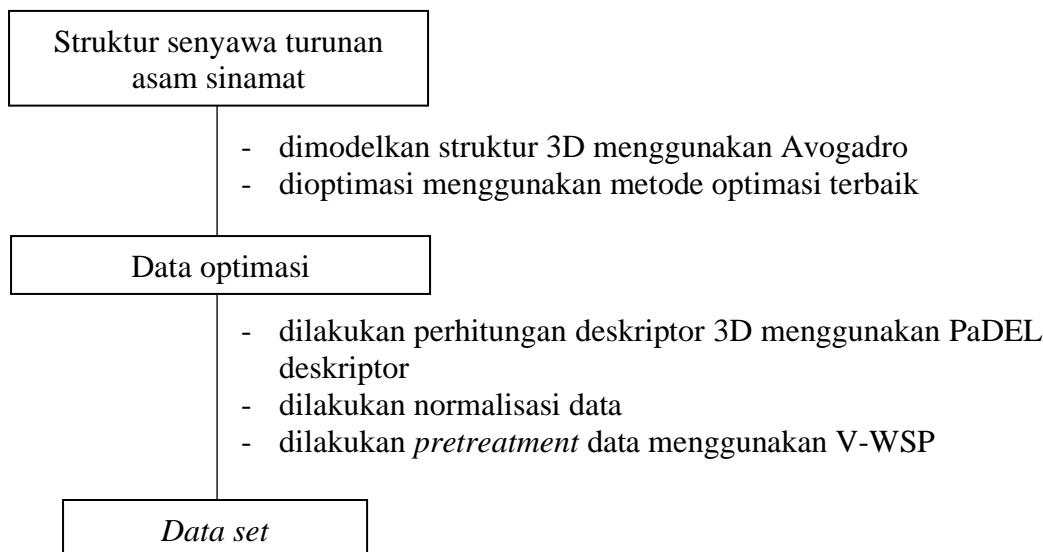


Lampiran 3. Bagan Kerja

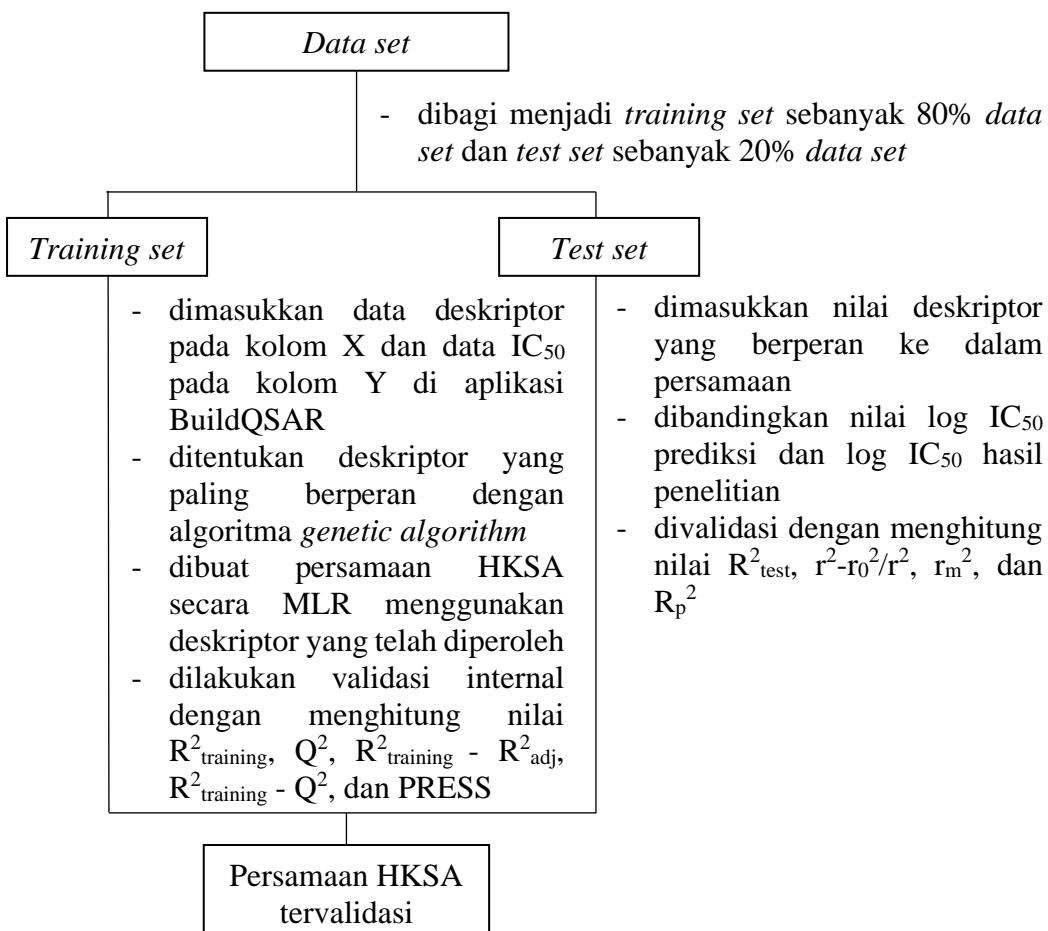
1. Pemilihan Metode Perhitungan Komputasi



2. Optimasi Geometri dan Perhitungan Deskriptor

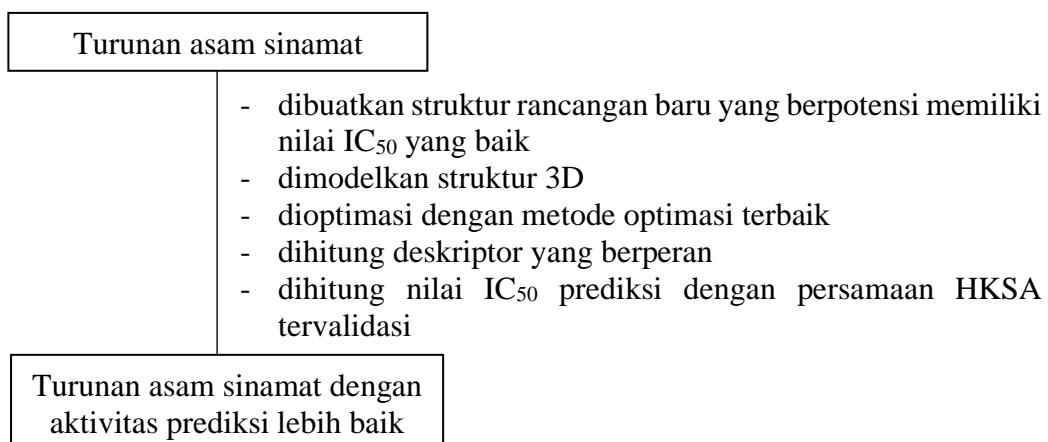


3. Menentukan Persamaan HKSA



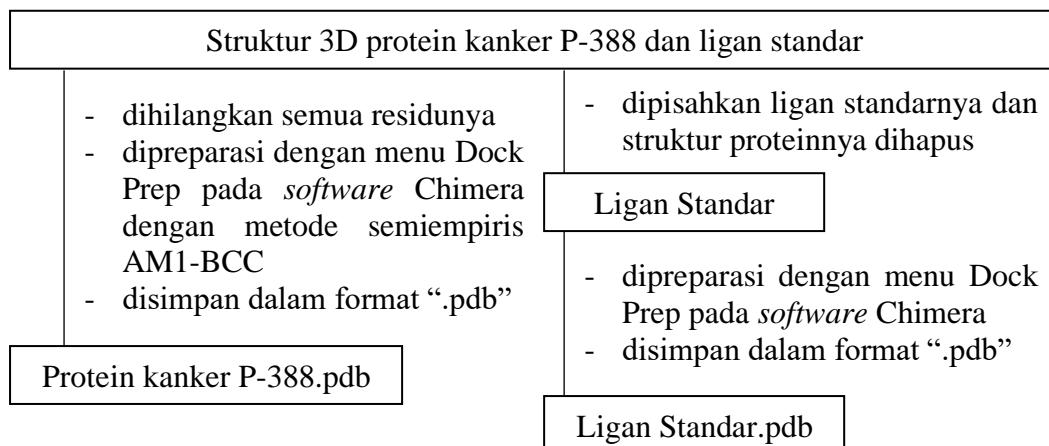
Catatan: Jika persamaan HKSA yang diperoleh memenuhi standar tervalidasi maka dilanjutkan ke tahap perancangan senyawa, jika tidak maka proses diulangi dari pembagian *data set*

4. Merancang Senyawa Turunan Asam Sinamat Baru

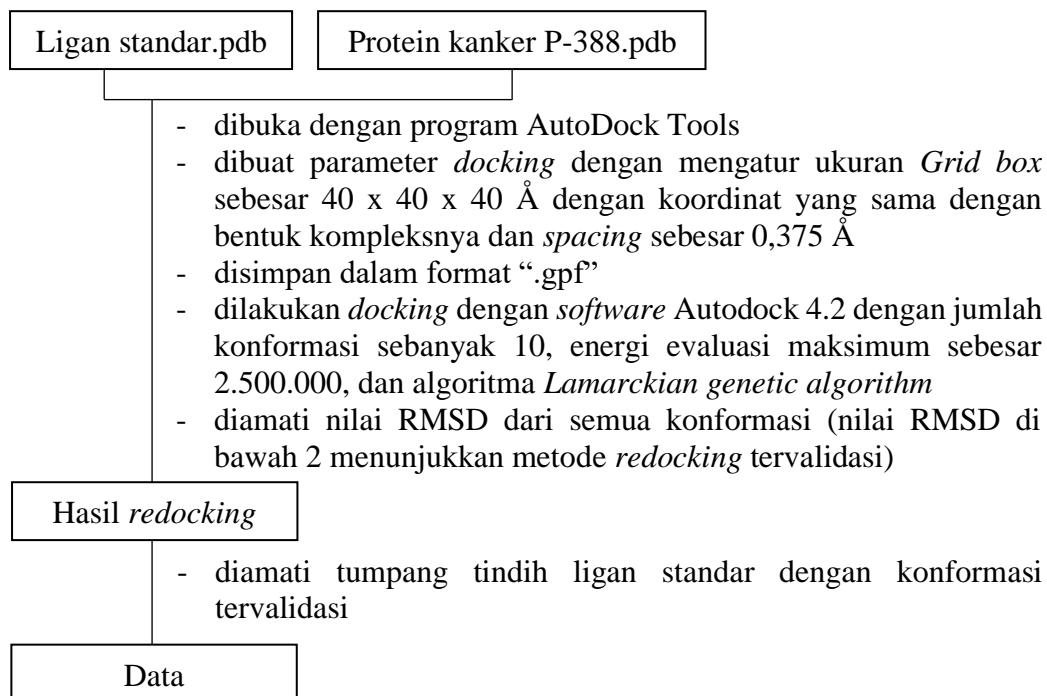


5. Molecular Docking Senyawa Rancangan

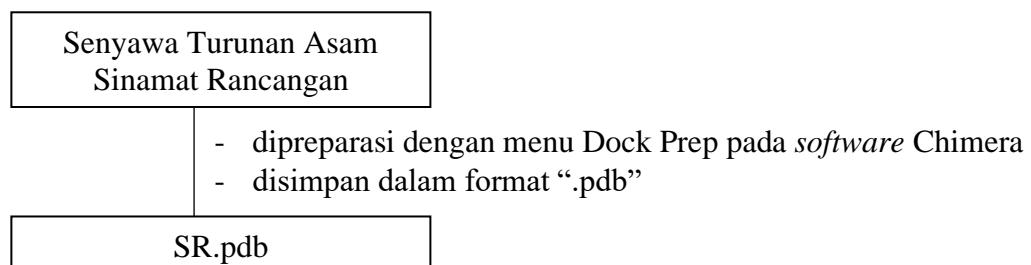
a. Preparasi Protein dan Ligan Standar



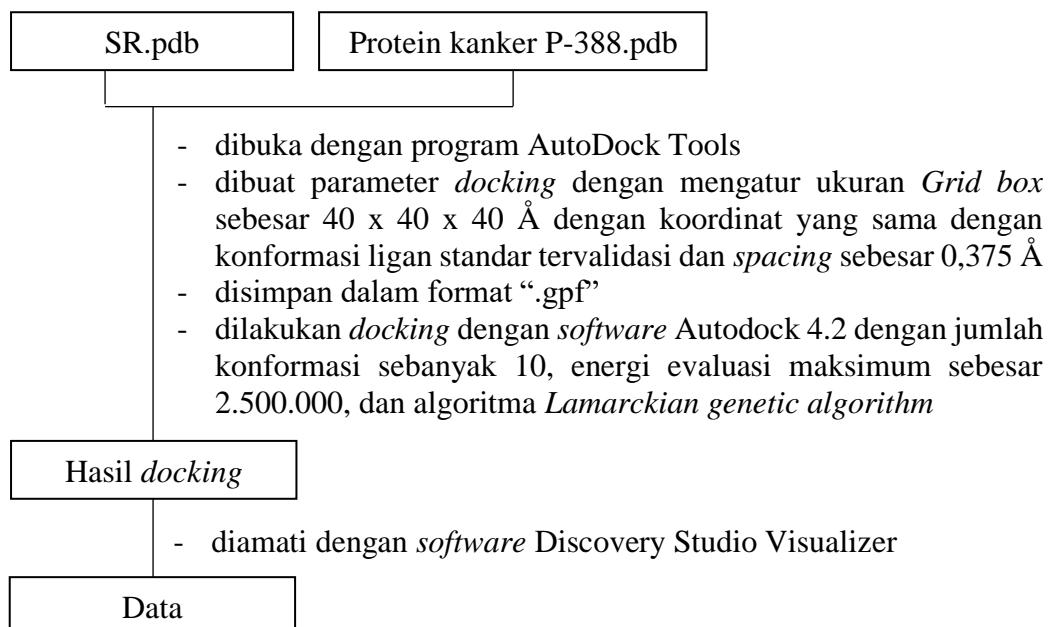
b. Proses Redocking Ligan Standar



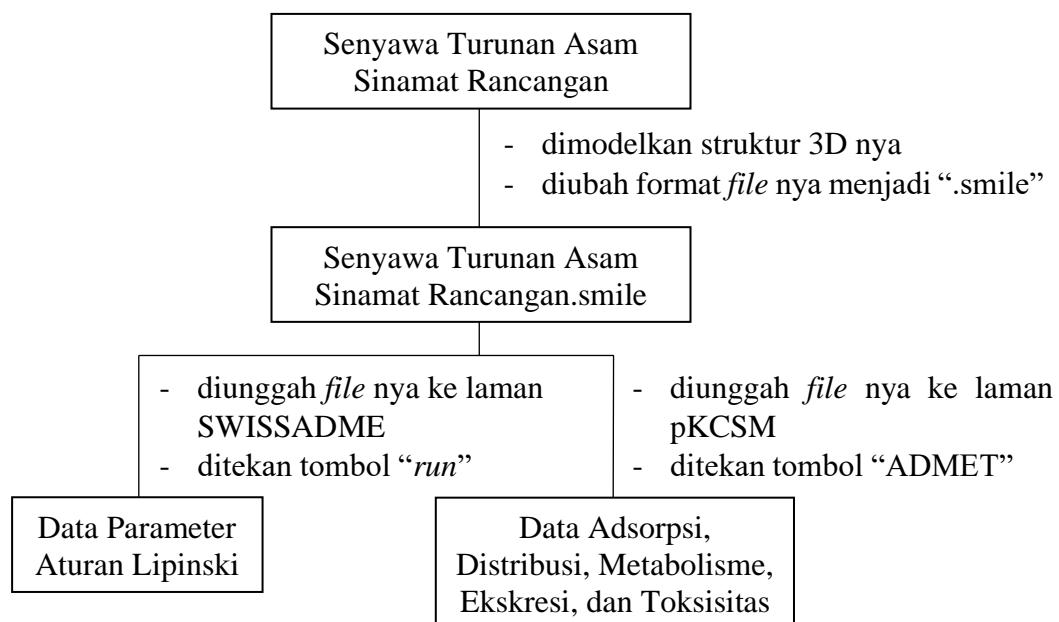
c. Preparasi Senyawa Turunan Asam Sinamat Rancangan



d. Proses *Molecular docking*



6. Evaluasi Aturan Lipinski dan Analisis ADMET



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	KV	KW	KX	KY	KZ	LA	LB	LC	LD	LE	LF	LG	LH	U	U	LK	LL	LM
1	Dv	E1e	E2e	E3e	L2p	E1p	E2p	E3p	Dp	E11	E21	Di	E1s	Ds				
2	0.872	0.394	0.544	1	0.28	0	0.4		1	0.871	0.215	0.787	1	0.404	1			
3	0.551	0.678	0.521	0.299	0.153	0.686	0.379	0.2	0.578	0.632	0.534	0.417	0.757	0.446				
4	0.835	0.301	0.749	0.46	0.69	0.532	0.866	0.438	0.869	0.051	0.766	0.524	0.36	0.586				
5	0.917	0.637	0.92	0.378	0.576	0.752	0.853	0.341	0.911	0.447	0.941	0.561	0.718	0.638				
6	0.056	0.232	0.121	0.057	0.09	0.101	0.112	0.042	0.001	0.173	0.208	0	0.243	0				
7	0	0	0	0.195	0	0.037	0	0.132	0	0	0	0	0.063	0	0.041			
8	0.758	0.609	0.778	0.336	0.621	0.625	0.825	0.219	0.721	0.404	0.818	0.488	0.639	0.542				
9	0.829	0.956	0.921	0.313	0.717	0.656	0.862	0.214	0.749	0.716	1	0.574	0.975	0.638				
10	0.697	0.62	0.79	0.229	0.457	0.644	0.724	0.167	0.65	0.517	0.749	0.381	0.687	0.46				
11	0.753	0.942	0.889	0.212	0.554	0.671	0.736	0.164	0.668	0.808	0.871	0.451	1	0.54				
12	0.7	0.566	0.749	0.006	0.654	0.87	0.611	0.001	0.599	0.377	0.785	0.135	0.66	0.233				
13	0.743	0.775	0.851	0	0.717	0.871	0.655	0	0.615	0.539	0.931	0.198	0.856	0.301				
14	0.628	0.602	0.693	0.1	0.696	0.812	0.512	0.061	0.581	0.542	0.717	0.247	0.677	0.306				
15	0.676	0.65	0.603	0.19	0.467	0.915	0.512	0.119	0.69	0.669	0.666	0.357	0.764	0.381				
16	0.696	0.626	0.638	0.186	0.464	0.893	0.527	0.115	0.68	0.51	0.669	0.321	0.709	0.371				
17	0.594	0.806	0.661	0.001	1	0.764	0.538	0.001	0.51	0.639	0.789	0.176	0.876	0.245				
18	0.539	0.627	0.546	0.008	0.97	0.805	0.446	0.002	0.502	0.47	0.699	0.128	0.71	0.18				
19	0.711	0.712	0.627	0.366	0.176	0.658	0.523	0.257	0.663	0.603	0.482	0.474	0.787	0.546				
20	0.829	0.68	1	0.258	0.633	0.586	0.97	0.205	0.739	0.478	0.946	0.463	0.745	0.564				
21	1	0.696	0.458	0.429	0.91	1	0.568	0.311	0.926	0.684	0.593	0.431	0.831	0.564				
22	0.686	0.584	0.625	0.113	0.368	0.985	0.456	0.065	0.665	0.464	0.773	0.267	0.722	0.309				
23	0.688	0.525	0.649	0.11	0.323	0.945	0.441	0.063	0.634	0.247	0.767	0.22	0.627	0.287				
24	0.959	0.855	0.879	0.489	0.664	0.706	0.944	0.438	1	0.899	0.791	0.701	0.896	0.767				
25	0.971	1	0.88	0.462	0.701	0.69	1	0.416	0.992	1	0.883	0.713	0.986	0.77				

Lampiran 7. Data Hasil *Docking* Senyawa Rancangan dan Senyawa 20

Tabel 12. Hasil *docking* senyawa SR1

Konformasi	Konstanta Inhibisi (mM)	Energi Ikat (kkal/mol)	Residu interaksi ikatan H
1	0,52854	-4,47	Arg831, Gln881 dan Ser992
2	0,94197	-4,13	Arg831, Gln881 dan Ser992
3	0,40439	-4,63	Arg831 dan Ala994
4	0,3669	-4,69	Arg831 dan Gln881
5	1,43	-3,88	Arg831, Val990, Ser991, dan Ala994
6	0,40158	-4,63	Arg831, Asn838, Val990, dan Pro995
7	0,3532	-4,71	Arg831, Val990 dan Pro995
8	0,38187	-4,66	Arg831 dan Ser992
9	0,23775	-4,94	Arg831, Ser992 dan Asp 996
10	0,72541	-4,28	Arg831, Gln881 dan Ala994

Tabel 13. Hasil *docking* senyawa SR2

Konformasi	Konstanta Inhibisi (mM)	Energi Ikat (kkal/mol)	Residu interaksi ikatan H
1	2,94	-3,45	Ser991
2	3,23	-3,40	Asn838 dan Ala868
3	3,36	-3,37	Ala868 dan Ser991
4	2,03	-3,67	Ser991
5	3,52	-3,35	Ala868
6	2,65	-3,51	Ala868
7	2,54	-3,54	Ala868
8	2,61	-3,53	Ala868
9	3,00	-3,44	Ala868 dan Ser991
10	3,48	-3,35	Ala868

Tabel 14. Hasil docking senyawa SR7

Konformasi	Konstanta Inhibisi (mM)	Energi Ikat (kkal/mol)	Residu interaksi ikatan H
1	1,26	-3,96	Asn838 dan Ala868
2	1,35	-3,92	Asn838 dan Ala868
3	0,75056	-4,26	Ala868
4	1,22	-3,97	Ala868
5	1,18	-3,99	Asn838 dan Ala868
6	0,44056	-4,58	Arg831, Asn838 dan Val990
7	0,67913	-4,32	Ala868
8	1,07	-4,05	Asn838 dan Ala868
9	0,87121	-4,17	Asn838 dan Ala868
10	0,56056	-4,44	Val990 dan Ala994

Tabel 15. Hasil docking senyawa SR8

Konformasi	Konstanta Inhibisi (mM)	Energi Ikat (kkal/mol)	Residu interaksi ikatan H
1	0,35907	-4,7	Arg831, Gln881 dan Ser992
2	1,35	-3,92	Ser991
3	0,76427	-4,25	Arg831, Gln881 dan Ser992
4	1,2	-3,99	Ser991
5	0,37185	-4,68	Arg831, Gln881 dan Ser992
6	1,05	-4,07	Ala868
7	0,35866	-4,7	Arg831, Gln881 dan Ser992
8	1,02	-4,08	Asn838 dan Val990
9	0,97281	-4,11	Arg831 dan Pro995
10	0,45631	-4,56	Arg831 dan Ser992

Tabel 16. Hasil *docking* senyawa 20

Konformasi	Konstanta Inhibisi (mM)	Energi Ikat (kkal/mol)	Residu interaksi ikatan H
1	0,95725	-4,12	Ala868 dan Ser991
2	0,56281	-4,43	-
3	2,00	-3,68	-
4	0,87066	-4,17	Ala868 dan Ser991
5	0,49642	-4,51	Asn838
6	0,85508	-4,19	Ala868 dan Ser991
7	0,94277	-4,13	Ser991
8	1,10	-4,04	Ser991
9	0,41457	-4,61	Ser991
10	0,95218	-4,12	-

Lampiran 8. Dokumentasi Penelitian

Three Notepad windows showing NMR spectra data:

```
20-1H-NMR-AM1.txt - Notepad
# Summary of NMR spectra ( SCF GIAO Magnetic shielding)
# Values for element H only
# Reference: TNS B3LYP/6-311+G(2d,p) GIAO
# Reference shielding: 31.8821 ppm
# Degenerate peaks are condensed together (Degeneracy Tolerance 0.05)
#
# Shift (ppm) Degeneracy Atoms
8.6555000000 1.0000 9
8.5592000000 1.0000 11
8.0924000000 1.0000 28
7.9990000000 1.0000 7
7.7980000000 1.0000 32
7.6938000000 1.0000 34
7.6137000000 2.0000 33,38
7.5456000000 1.0000 8
6.5856000000 1.0000 13
6.5452000000 1.0000 17
4.3984000000 1.0000 15
3.6891000000 1.0000 28
3.4461000000 1.0000 18
3.3146000000 1.0000 45
3.1639000000 1.0000 40
3.0684000000 1.0000 41
2.9524000000 2.0000 42,21
2.8847000000 1.0000 46
2.8033000000 1.0000 44
Ln 7, Col 16 100% Windows (CRLF) UTF-8
```

```
20-1H-NMR-HF.txt - Notepad
# Summary of NMR spectra ( SCF GIAO Magnetic shielding)
# Values for element H only
# Reference: TNS B3LYP/6-311+G(2d,p) GIAO
# Reference shielding: 31.8821 ppm
# Degenerate peaks are condensed together (Degeneracy Tolerance 0.05)
#
# Shift (ppm) Degeneracy Atoms
8.6555000000 1.0000 9
8.5592000000 1.0000 11
8.0924000000 1.0000 28
7.9990000000 1.0000 7
7.7980000000 1.0000 32
7.6938000000 1.0000 34
7.6137000000 2.0000 33,38
7.5456000000 1.0000 8
6.5856000000 1.0000 13
6.5452000000 1.0000 17
4.3984000000 1.0000 15
3.6891000000 1.0000 28
3.4461000000 1.0000 18
3.3146000000 1.0000 45
3.1639000000 1.0000 40
3.0684000000 1.0000 41
2.9524000000 2.0000 42,21
2.8847000000 1.0000 46
2.8033000000 1.0000 44
Ln 12, Col 40 100% Windows (CRLF) UTF-8
```

```
20-1H-NMR-DFT.txt - Notepad
# Summary of NMR spectra ( SCF GIAO Magnetic shielding)
# Values for element H only
# Reference: TNS B3LYP/6-311+G(2d,p) GIAO
# Reference shielding: 31.8821 ppm
# Degenerate peaks are condensed together (Degeneracy Tolerance 0.05)
#
# Shift (ppm) Degeneracy Atoms
8.2653000000 1.0000 11
7.8951500000 2.0000 7,28
7.6598000000 2.0000 33,32
7.5246000000 2.0000 34,9
7.4404000000 1.0000 30
7.2874000000 1.0000 8
6.5458000000 1.0000 13
5.4135000000 1.0000 15
4.2491000000 1.0000 17
3.5976000000 1.0000 20
2.8358000000 1.0000 42
2.7549000000 1.0000 18
2.6219000000 1.0000 45
2.4862000000 1.0000 46
2.3778500000 2.0000 21,40
2.0539000000 1.0000 44
1.9815000000 1.0000 41
Ln 5, Col 16 100% Windows (CRLF) UTF-8
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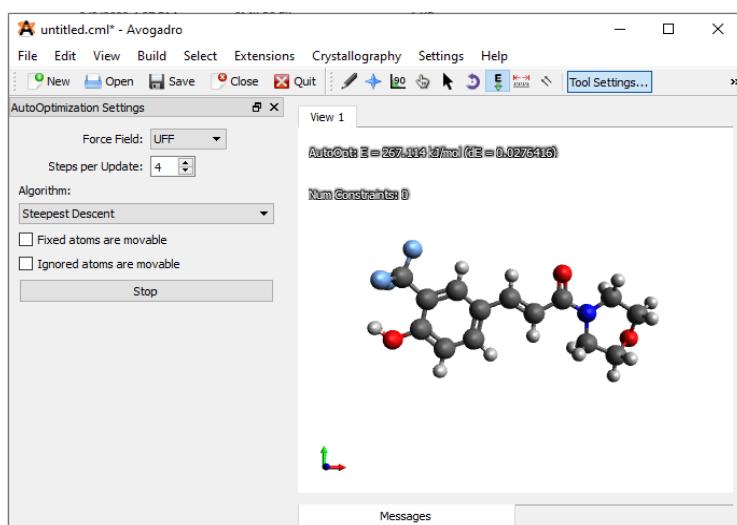
Pemilihan optimasi terbaik

Two Notepad windows showing input (.inp) and output (.out) files for ORCA DFT calculation:

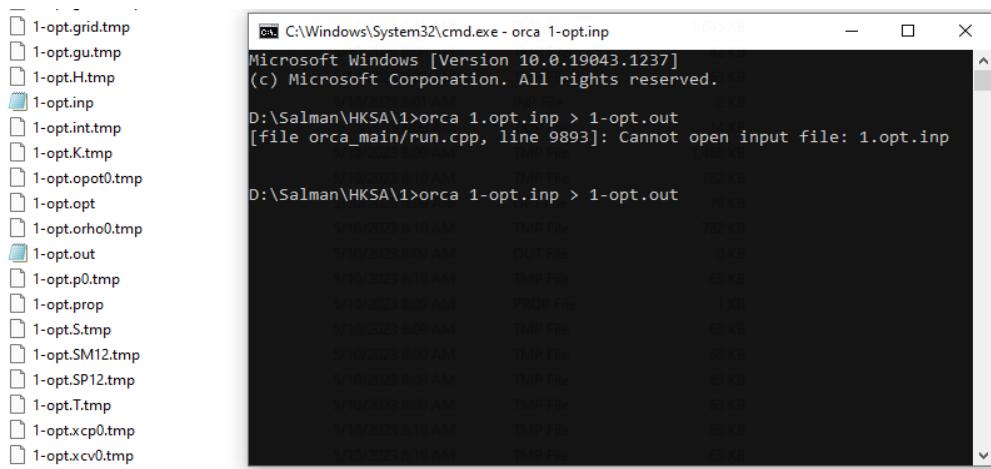
```
1-opt.inp - Notepad
File Edit Format View Help
# avogadro generated ORCA input file
# Basic Mode
#
! B3LYP OPT 6-31G NormalPrint NormalSCF
%
%scf
MaxIter 125
end
%
%output
end
*
* xyz 0 1
C -5.21865 1.80028 -0.08067
C -5.38811 0.41388 -0.06796
C -3.93534 2.35350 -0.05439
C -2.79636 1.52909 -0.01486
C -2.97724 0.12918 -0.00229
C -4.26325 -0.42004 -0.02869
C -1.45682 2.18312 0.01163
C -0.27957 1.52856 0.05010
O -6.63264 -0.10429 -0.09367
Ln 38, Col 1 100% Windows (CRLF) UTF-8
```

```
1-opt.out - Notepad
File Edit Format View Help
*****
* O R C A *
*****
--- An Ab Initio, DFT and Semiempirical electronic structure package ---
#####
# _***-
# Department of theory and spectroscopy #
# Directorship: Frank Neese #
# Max Planck Institute fuer Kohlenforschung #
# Kaiser Wilhelm Platz 1 #
# D-45470 Muelheim/Ruhr #
# Germany #
# All rights reserved #
# _***-
#####
Program Version 4.2.1 - RELEASE -
With contributions from (in alphabetic order):
Ln 42, Col 43 100% Windows (CRLF) UTF-8
```

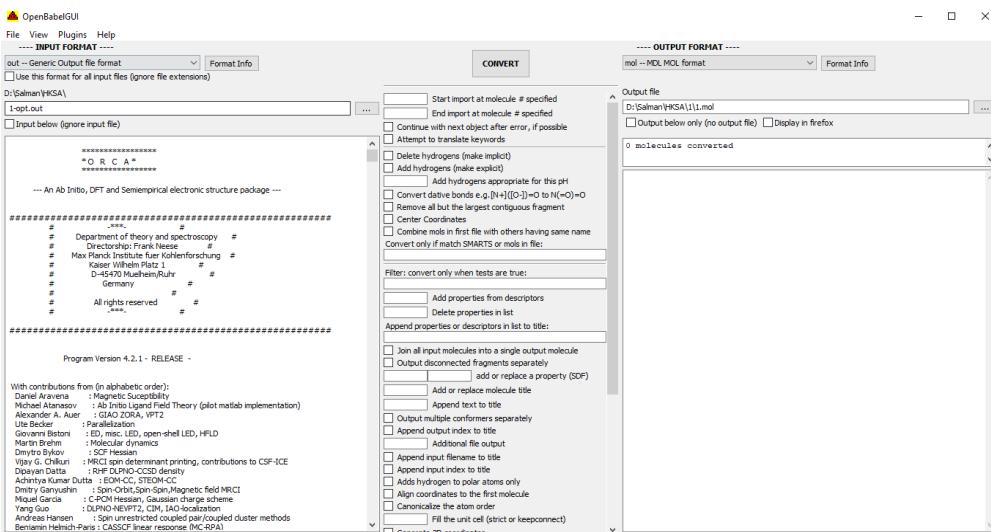
Tampilan file .inp dan .out



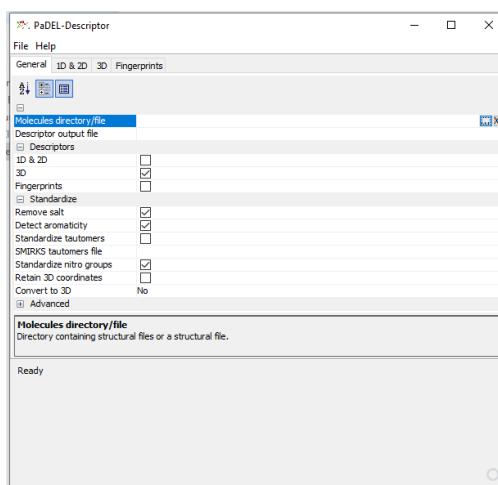
Tampilan aplikasi Avogadro



Proses optimasi dengan ORCA



Konversi format file menggunakan Open Babel



Tampilan aplikasi PaDEL-Descriptor

DTC lab
Drug Theoretical and Cheminformatics Laboratory

DR. KUNAL ROY SEARCH ALL TOOLS JOURNAL MORE

Cheminformatics Tools

A QSAR Tools

Important Note: The same software tools are now also available from the official Website of Jadavpur University (Kolkata, INDIA). Although you can freely access the software tools from any one of the sites, you are advised to cite the link http://teqip.jdu.ac.in/QSAR_Tools/

```

graph TD
    1[1. Select dataset  
Literature survey  
Database] --> 2[2. Calculate descriptors  
Elemental Descriptors - (Metal, Nonmetal, Semimetal)  
(Other freely available software like PdID, CTK Descriptor calculator, etc)]
    2 --> 3[3. Normalize the data  
(optional step)  
Normalize Data * Standardize*]
    3 --> 4[4. To Evaluate Dataset  
A. Dataset Modifiability  
MDModifiability Index (MDI)*  
B. Dataset diversity  
Diversity Validator*  
Mahalanobis-Distance*]
    4 --> 5[5. Data Pre-Treatment  
Data Pre-Treatment GUI  
(VWSP)*]
    5 --> 6[6. Dataset Division  
Dataset Dividers GUI*  
Euclidean Based Kennard-Stone*  
Mahalanobis Distance Based Kennard-Stone*  
Clustering Methods:  
k-Means GUI (free)*  
Modified k-Means GUI (paid version)]
    6 --> 7[7. QSAR Model Development  
Stepwise MLR*  
Genetic Algorithm*  
MLR-BestSubsetSelection*]
    7 --> 8[8. Model Validation/Evaluation  
MLR/Logistic Regression GUI*  
Kruskal Wallenks Marke-Cake*  
MLR-Versus-Decision Tree*  
MLE-Lowes Many-Out*  
CrossValidation Validation*]
    8 --> 9[9. To Define Applicability Domain (AD)  
AD-Using Standardization Approach*  
Evaluating AD*  
AD-MDI*]
  
```

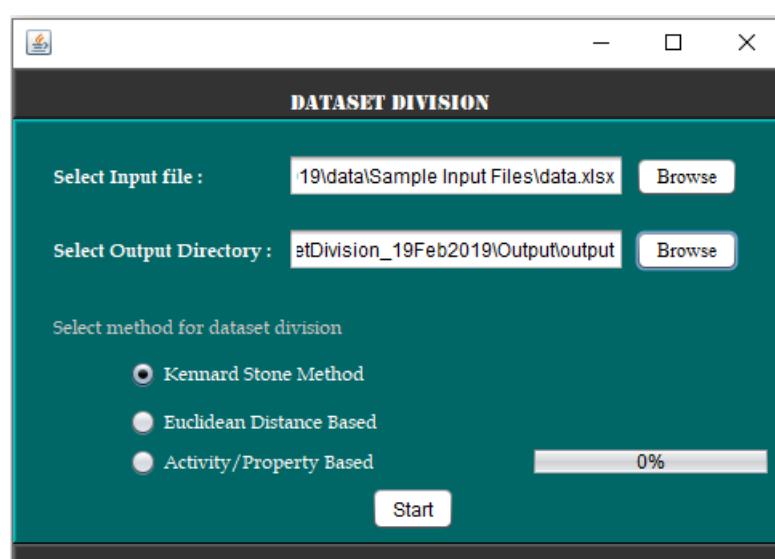
*Software Tools (Java Programming Language) available at DTC lab website
†Software Tools (C++ Programming Language) available at DTC lab website

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 • Department of Physics, SCSVMV University, Tamil Nadu, INDIA.
 • Institute of Pharmaceutical Sciences, Guru Chaudhary Vishwavidyalaya, Bihar, INDIA.

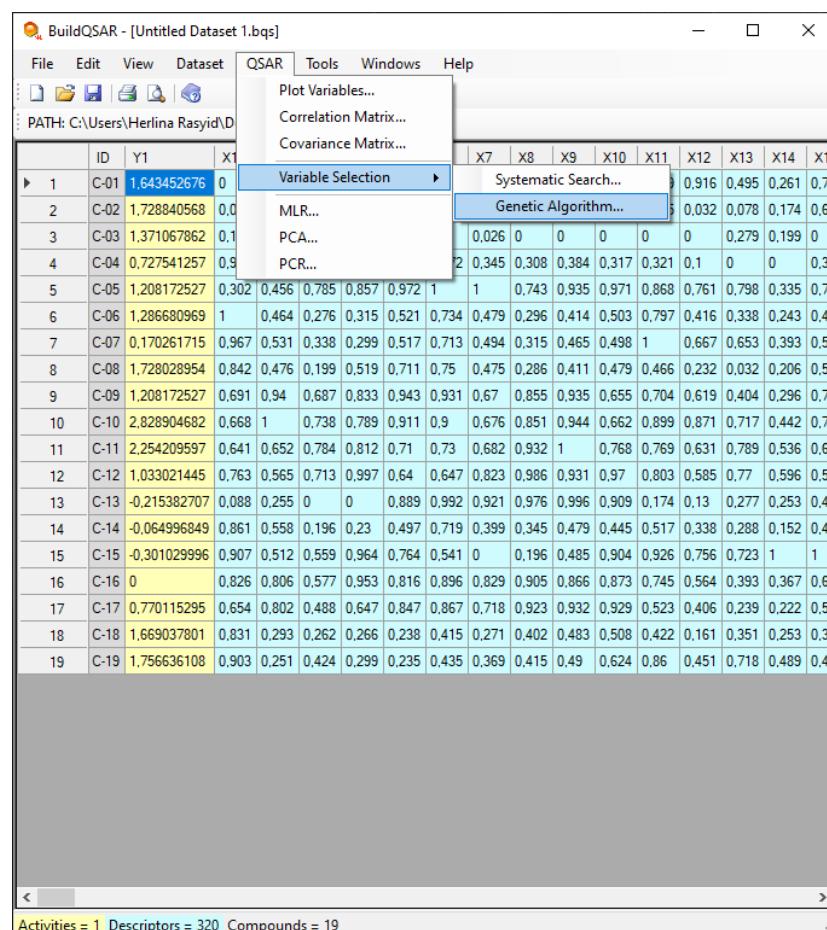
Tampilan laman situs DTC LAB



Tampilan aplikasi pembagi *data set*

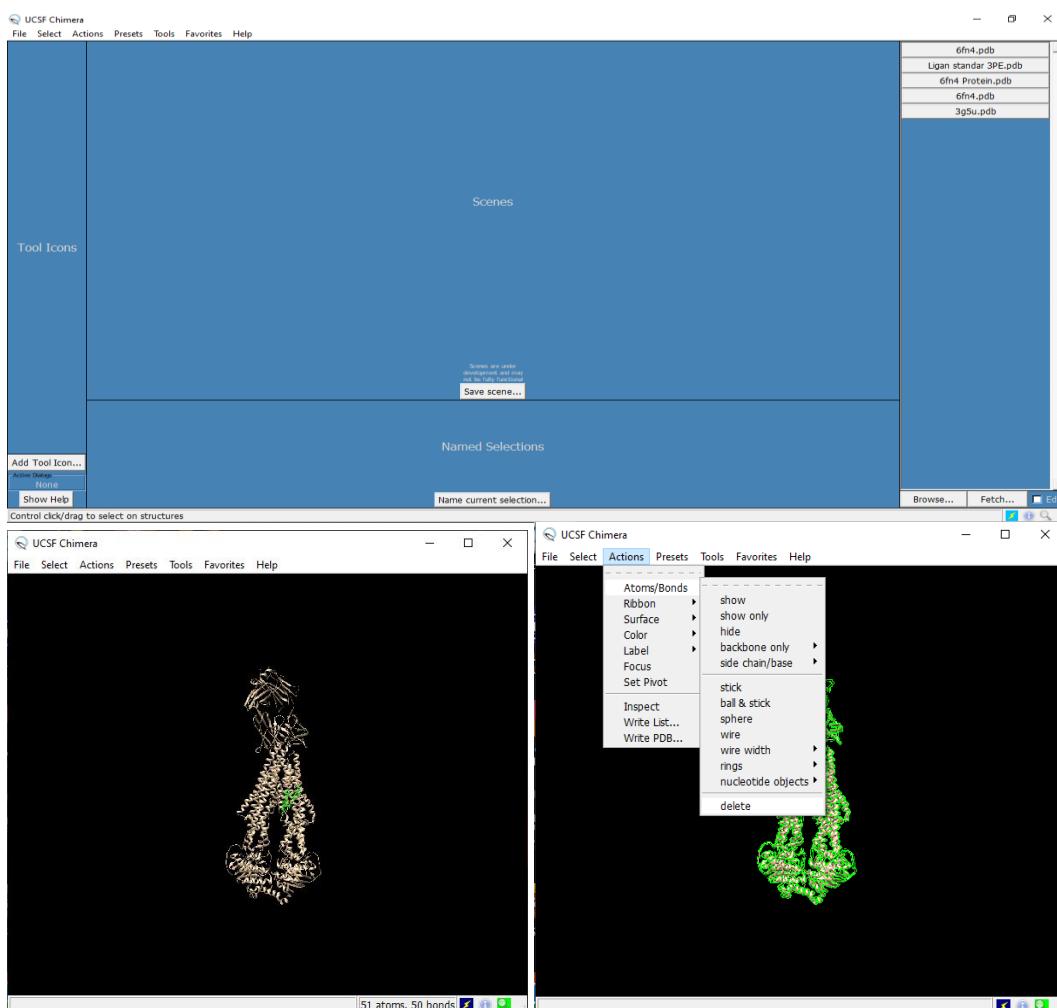


Tampilan aplikasi *pretreatment* V-WSP

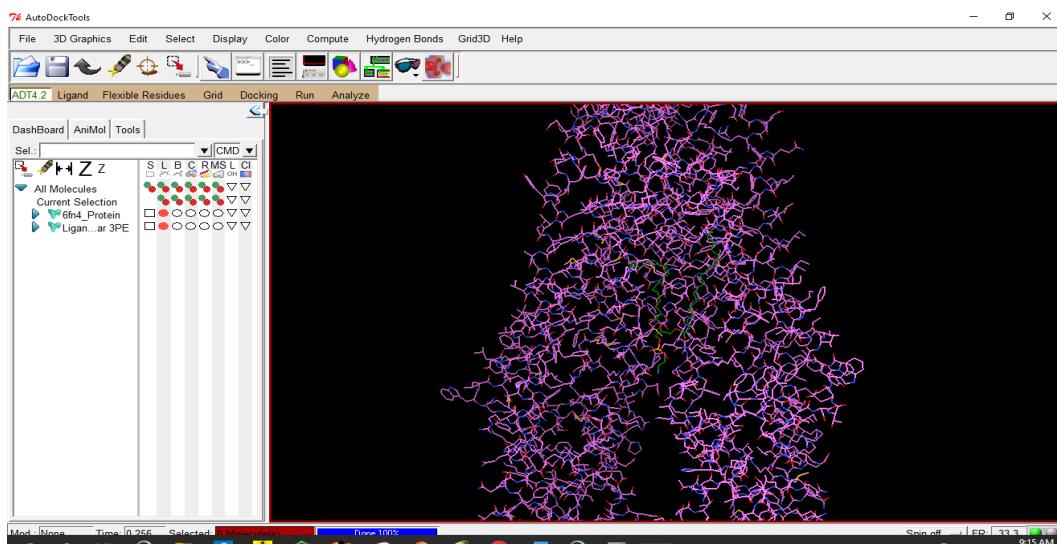


Tampilan BuildQSAR

Tampilan laman situs protein data bank (PDB)

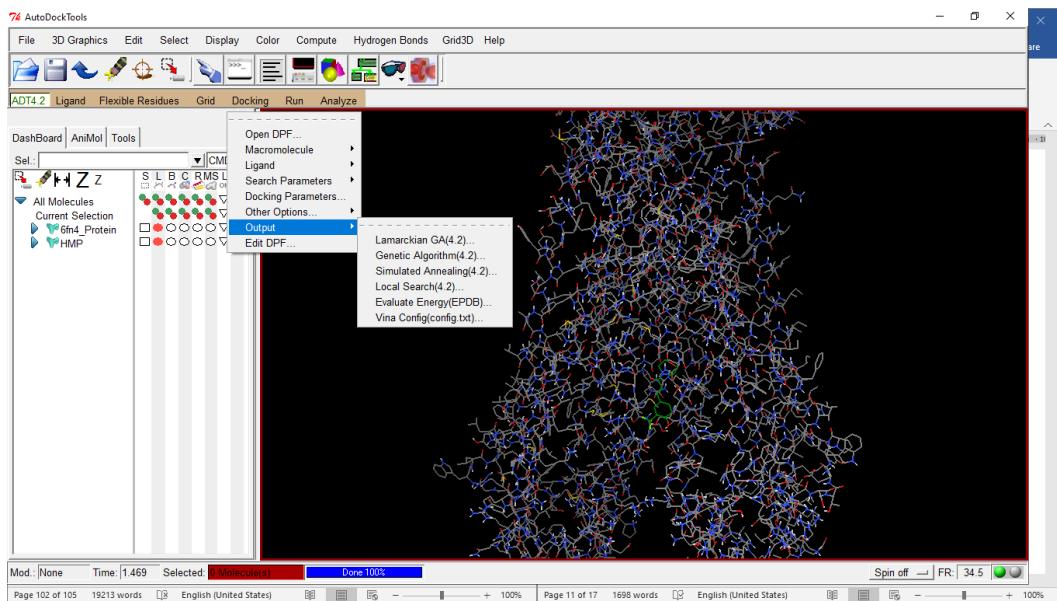


Proses preparasi protein dan ligan di chimera



Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	3	+3.11	0.00	1.16	RANKING
1	2	47	+3.17	0.25	1.10	RANKING
1	3	41	+3.17	0.25	1.09	RANKING
1	4	19	+3.18	0.24	1.14	RANKING
1	5	7	+3.18	0.25	1.10	RANKING
1	6	37	+3.18	0.25	1.09	RANKING
1	7	32	+3.18	0.28	1.08	RANKING
1	8	50	+3.19	0.26	1.09	RANKING
1	9	20	+3.19	0.25	1.11	RANKING
1	10	49	+3.22	0.36	1.10	RANKING

Proses redocking ligan standar dan perhitungan nilai RMSD



Proses docking senyawa dengan autodock tools

```

C:\Windows\System32\cmd.exe
Microsoft Windows [Version 10.0.19043.1237]
(c) Microsoft Corporation. All rights reserved.

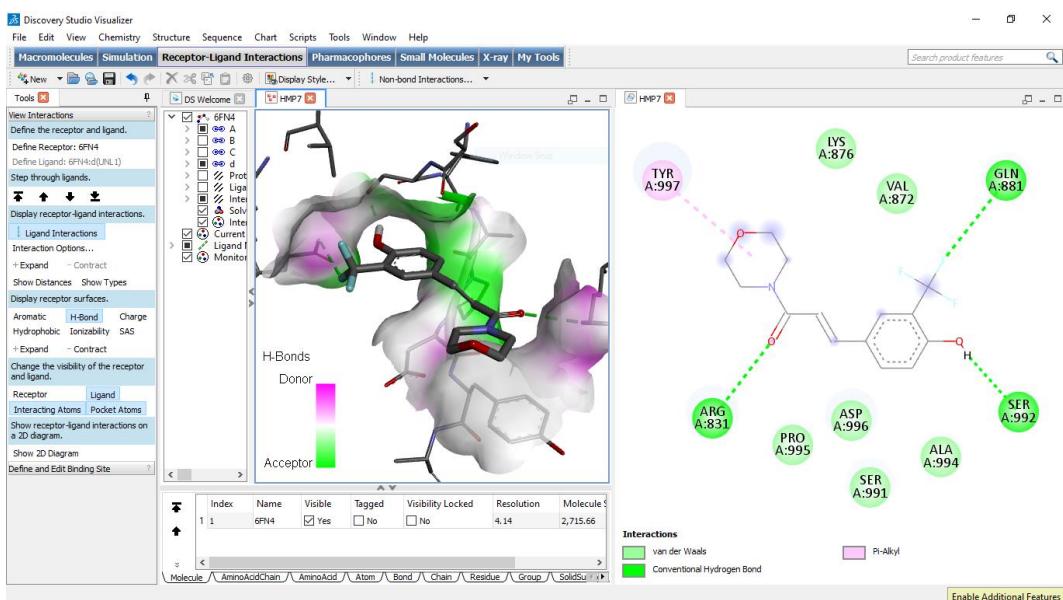
D:\Salman\Penelitian\Kelengkapan Hasil\3D model new comp\Docking HMP\proses running>autogrid4 -p HMP.gpf -l HMP.glg

D:\Salman\Penelitian\Kelengkapan Hasil\3D model new comp\Docking HMP\proses running>autodock4 -p HMP.dpf -l HMP.dlg

D:\Salman\Penelitian\Kelengkapan Hasil\3D model new comp\Docking HMP\proses running>

```

Proses *running docking* senyawa rancangan dengan autodock4



Visualisasi interaksi 2D dan 3D menggunakan Discovery Studio Visualizer

SwissDrugDesign | SwissDock SwissParam SwissSidechain SwissBiocentre SwissTargetPrediction SwissADME SwissSimilarity | About us

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This website allows you to compute physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties, druglike nature and medicinal chemistry friendliness of one or multiple small molecules to support drug discovery.

The main article describing the web service and its underlying methodologies is **SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules**. *Sci. Rep.* (2017) 7:42717.

For details about development and validation of iLOGP, please refer to this article: **iLOGP: a simple, robust, and efficient description of *n*-octanol/water partition coefficient for drug design using the GB/SA approach**. *J. Chem. Inf. Model.* (2014) 54(12):3284-3301.

For details about development and validation of the BOILED-Egg, please refer to this article: **A BOILED-Egg to predict gastrointestinal absorption and brain penetration of small molecules**. *ChemMedChem* (2016) 11(11):1117-1121.

Developed and maintained by the **Molecular Modeling Group** of the SIB | Swiss Institute of Bioinformatics.

Enter a list of SMILES here:
`c1(cc(c1)/C=C/C(=O)N1CCOCC1)O)C(F)(F)F`

Fill with an example Clear Run!

Tampilan laman situs SwissADME

Pharmacokinetic properties

Step 1: Please provide a set of molecules (SMILES format)

Description
Upload your SMILES file: Choose File No file chosen
Files are expected to have headers Identifying the columns File limits

OR

Description
Provide a SMILES string:
`c1(cc(c1)/C=C/C(=O)N1CCOCC1)O)C(F)(F)F`
Example:
`CC(=O)OC1=CC=CC=C1C(=O)O`

Step 2: Please choose the prediction mode

Description
Prediction of pharmacokinetic properties
Absorption Distribution Metabolism Excretion Toxicity ADMET

Disclaimer
No molecule information will be retained on the system after being uploaded by the user.

Tampilan laman situs pkCSM

Lampiran 9. Perhitungan

1. Pembuatan dan validasi persamaan HKSA algoritma Kennard stone method

Persamaan HKSA:

$$pIC_{50\ pred} = -0,0003 \times WNSA-1 + 49117,718$$

Data *test set* algoritma Kennard stone method

Senyawa	WNSA-1	pIC ₅₀ obs
1	0,044	1,6435
4	0,121	0,7275
16	0,660	-0,0409
18	0,405	-0,2154
22	0,457	0,7701

$$pIC_{50\ pred}\ (1) = -0,0003 \times 0,044 + 49117,718 = 49117,71799$$

$$pIC_{50\ pred}\ (4) = -0,0003 \times 0,121 + 49117,718 = 49117,71796$$

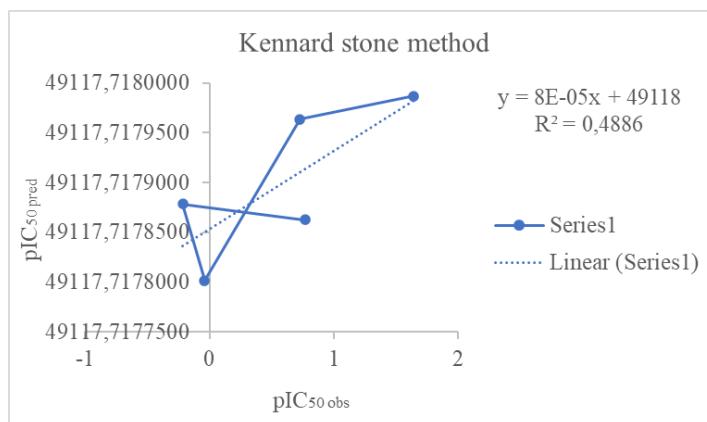
$$pIC_{50\ pred}\ (16) = -0,0003 \times 0,66 + 49117,718 = 49117,71780$$

$$pIC_{50\ pred}\ (18) = -0,0003 \times 0,405 + 49117,718 = 49117,71788$$

$$pIC_{50\ pred}\ (22) = -0,0003 \times 0,457 + 49117,718 = 49117,71786$$

Data dan grafik regresi algoritma Kennard stone method

Senyawa	pIC ₅₀ obs	pIC ₅₀ pred
1	1,6435	49117,71799
4	0,7275	49117,71796
16	-0,0409	49117,71780
18	-0,2154	49117,71788
22	0,7701	49117,71786



2. Pembuatan dan validasi persamaan HKSA algoritma Euclidean *distance based*

Persamaan HKSA:

$$pIC_{50\ pred} = -0,0003 \times WNSA-1 + 44856,4021$$

Data *test set* algoritma Euclidean *distance based*

Senyawa	WNSA-1	pIC ₅₀ obs
2	0,310	1,7288
5	0,003	1,2082
10	0,246	1,0549
20	1,000	-0,3010
21	0,454	0

$$pIC_{50\ pred}(2) = -0,0003 \times 0,31 + 44856,4021 = 44856,4020$$

$$pIC_{50\ pred}(5) = -0,0003 \times 0,003 + 44856,4021 = 44856,4021$$

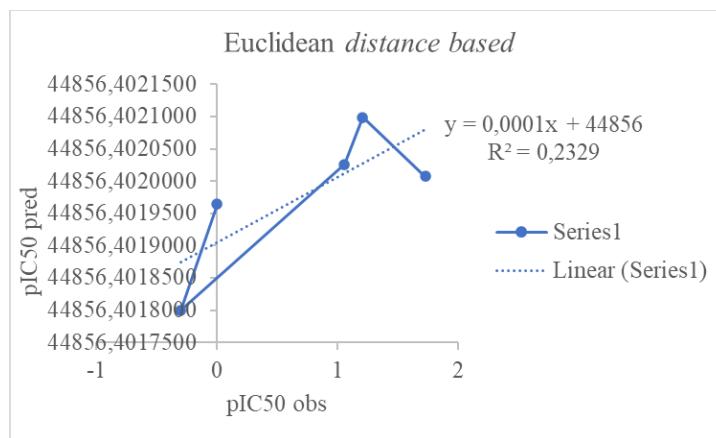
$$pIC_{50\ pred}(10) = -0,0003 \times 0,246 + 44856,4021 = 44856,4020$$

$$pIC_{50\ pred}(20) = -0,0003 \times 1 + 44856,4021 = 44856,4018$$

$$pIC_{50\ pred}(21) = -0,0003 \times 0,454 + 44856,4021 = 44856,4019$$

Data dan grafik regresi algoritma Euclidean *distance based*

Senyawa	pIC ₅₀ obs	pIC ₅₀ pred
2	1,7288	44856,4020
5	1,2082	44856,4021
10	1,0549	44856,4020
20	-0,3010	44856,4018
21	0	44856,4019



3. Pembuatan dan validasi persamaan HKSA algoritma *activity/property based*

Persamaan HKSA:

$$pIC_{50\ pred} = -0,0002 \times WNSA-1 + 59598,155$$

Data *test set* algoritma *activity/property based*

Senyawa	WNSA-1	pIC ₅₀ obs
1	0,044	1,6435
2	0,310	1,7288
8	0,268	0,1703
13	0,530	2,2542
18	0,405	-0,2154

$$pIC_{50\ pred}\ (1) = -0,0002 \times 0,044 + 59598,155 = 59598,15499$$

$$pIC_{50\ pred}\ (2) = -0,0002 \times 0,31 + 59598,155 = 59598,15494$$

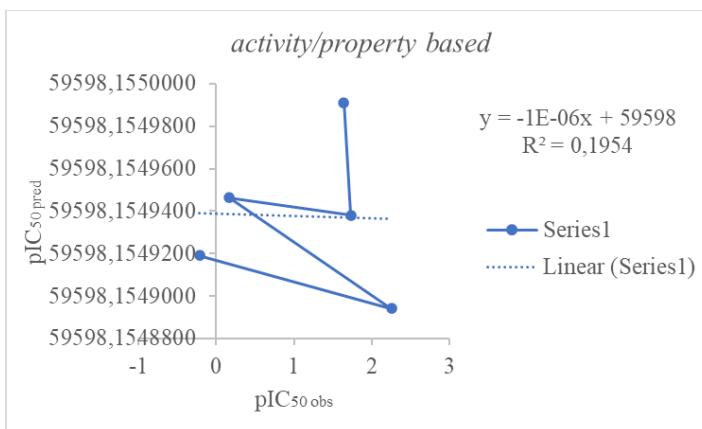
$$pIC_{50\ pred}\ (8) = -0,0002 \times 0,268 + 59598,155 = 59598,15495$$

$$pIC_{50\ pred}\ (13) = -0,0002 \times 0,53 + 59598,155 = 59598,15489$$

$$pIC_{50\ pred}\ (18) = -0,0002 \times 0,405 + 59598,155 = 59598,15492$$

Data dan grafik regresi algoritma *activity/property based*

Senyawa	pIC ₅₀ obs	pIC ₅₀ pred
1	1,6435	59598,15499
2	1,7288	59598,15494
8	0,1703	59598,15495
13	2,2542	59598,15489
18	-0,2154	59598,15492



4. Pembuatan dan validasi persamaan HKSA manual (1)

Persamaan HKSA:

$$pIC_{50\ pred} = 1.2380 \times TDB1r + 2.8572 \times RDF130s - 3.8733 \times E1v + 2.7195 \times E2v + 1.0071$$

Data *test set* manual (1)

Senyawa	TDB1r	RDF130s	E1v	E2v	pIC₅₀ obs
16	1	0,435	0,832	0,421	-0,0409
18	0,070	0,775	0,673	0,664	-0,2154
19	0,508	0,008	0,670	1	-0,0650
20	0,790	1	0,932	0,400	-0,3010
21	0,877	0,419	0,981	0,366	0

$$\begin{aligned} pIC_{50\ pred}(16) &= 1.2380 \times 1 + 2.8572 \times 0,435 - 3.8733 \times 0,832 + 2.7195 \times 0,421 \\ &\quad + 1.0071 \\ &= 1,4103 \end{aligned}$$

$$\begin{aligned} pIC_{50\ pred}(18) &= 1.2380 \times 0,070 + 2.8572 \times 0,775 - 3.8733 \times 0,673 + 2.7195 \times 0,664 + 1.0071 \\ &= 2,5071 \end{aligned}$$

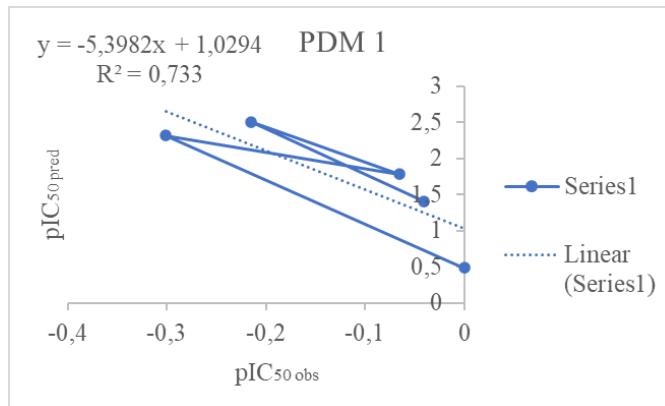
$$\begin{aligned} pIC_{50\ pred}(19) &= 1.2380 \times 0,508 + 2.8572 \times 0,008 - 3.8733 \times 0,670 + 2.7195 \times 1 \\ &\quad + 1.0071 \\ &= 1,7833 \end{aligned}$$

$$\begin{aligned} pIC_{50\ pred}(20) &= 1.2380 \times 0,790 + 2.8572 \times 1 - 3.8733 \times 0,932 + 2.7195 \times 0,4 + 1.0071 \\ &= 2,3202 \end{aligned}$$

$$\begin{aligned} pIC_{50\ pred}(21) &= 1.2380 \times 0,877 + 2.8572 \times 0,419 - 3.8733 \times 0,981 + 2.7195 \times 0,366 + 1.0071 \\ &= 0,4856 \end{aligned}$$

Data dan grafik regresi manual (1)

Senyawa	pIC₅₀ obs	pIC₅₀ pred
16	-0,0409	1,4103
18	-0,2154	2,5071
19	-0,0650	1,7833
20	-0,3010	2,3202
21	0	0,4856



5. Pembuatan dan validasi persamaan HKSA manual (2)

Persamaan HKSA:

$$\begin{aligned} \text{pIC}_{50\text{ pred}} &= 3.3951 \times \text{RDF115u} + 1.6324 \times \text{RDF35m} - 2.8094 \times \text{RDF25s} - 4.3888 \\ &\quad \times \text{RDF120s} + 1.8731 \end{aligned}$$

Data *test set* manual (2)

Senyawa	RDF115u	RDF35m	RDF25s	RDF120s	pIC _{50 obs}
5	0,018	0,007	0	0	1,2082
6	0,204	0	0,013	0,077	1,3259
7	0,178	0,222	0,471	0,096	1,2867
11	0,540	0,075	0,372	0,177	1,2082
17	0,359	0,090	0,439	0,235	1,2297

$$\begin{aligned} \text{pIC}_{50\text{ pred}} (5) &= 3.3951 \times 0,018 + 1.6324 \times 0,007 - 2.8094 \times 0 - 4.3888 \times 0 + \\ &\quad 1.8731 \\ &= 1,9456 \end{aligned}$$

$$\begin{aligned} \text{pIC}_{50\text{ pred}} (6) &= 3.3951 \times 0,204 + 1.6324 \times 0 - 2.8094 \times 0,013 - 4.3888 \times 0,077 \\ &\quad + 1.8731 \\ &= 2,1912 \end{aligned}$$

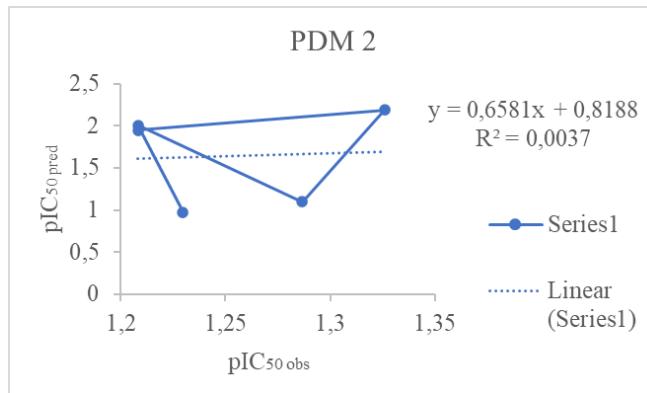
$$\begin{aligned} \text{pIC}_{50\text{ pred}} (7) &= 3.3951 \times 0,178 + 1.6324 \times 0,222 - 2.8094 \times 0,471 - 4.3888 \times \\ &\quad 0,096 + 1.8731 \\ &= 1,0953 \end{aligned}$$

$$\begin{aligned} \text{pIC}_{50\text{ pred}} (11) &= 3.3951 \times 0,540 + 1.6324 \times 0,075 - 2.8094 \times 0,372 - 4.3888 \times \\ &\quad 0,177 + 1.8731 \\ &= 2,0070 \end{aligned}$$

$$\begin{aligned} \text{pIC}_{50\text{ pred}} (17) &= 3.3951 \times 0,359 + 1.6324 \times 0,090 - 2.8094 \times 0,439 - 4.3888 \times \\ &\quad 0,235 + 1.8731 \\ &= 0,9742 \end{aligned}$$

Data dan grafik regresi manual (2)

Senyawa	pIC ₅₀ obs	pIC ₅₀ pred
5	1,2082	1,9456
6	1,3259	2,1912
7	1,2867	1,0953
11	1,2082	2,0070
17	1,2297	0,9742



6. Pembuatan dan validasi persamaan HKSA manual (3)

Persamaan HKSA:

$$\text{pIC}_{50} \text{ pred} = -1.5503 \times \text{TDB7s} - 2.8093 \times \text{RDF95u} - 0.9302 \times \text{RDF135m} + 1.4041 \times \text{RDF45p} + 2.8199$$

Data *test set* manual (3)

Senyawa	TDB7s	RDF95u	RDF135m	RDF45p	pIC ₅₀ obs
2	0,130	0,272	0,026	0,040	1,7288
9	0,097	0,549	0	0,289	1,7280
12	1	0,489	0,404	0,312	2,8289
13	0,488	0,407	0,543	0,407	2,2542
24	0,227	0,662	0,001	0,500	1,7566

$$\begin{aligned} \text{pIC}_{50} \text{ pred (2)} &= -1.5503 \times 0,130 - 2.8093 \times 0,272 - 0.9302 \times 0,026 + 1.4041 \times 0,040 + 2.8199 \\ &= 1,8862 \end{aligned}$$

$$\begin{aligned} \text{pIC}_{50} \text{ pred (9)} &= -1.5503 \times 0,097 - 2.8093 \times 0,549 - 0.9302 \times 0 + 1.4041 \times 0,289 \\ &\quad + 2.8199 \\ &= 1,5330 \end{aligned}$$

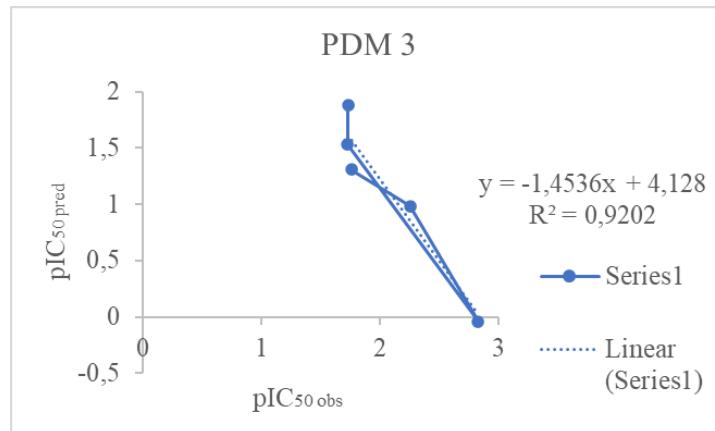
$$\begin{aligned} \text{pIC}_{50} \text{ pred (12)} &= -1.5503 \times 1 - 2.8093 \times 0,489 - 0.9302 \times 0,404 + 1.4041 \times 0,312 \\ &\quad + 2.8199 \\ &= -0,0419 \end{aligned}$$

$$\begin{aligned}
 pIC_{50\text{ pred}}(13) &= -1.5503 \times 0,488 - 2.8093 \times 0,407 - 0.9302 \times 0,543 + 1.4041 \times \\
 &\quad 0,407 + 2.8199 \\
 &= 0,9863
 \end{aligned}$$

$$\begin{aligned}
 pIC_{50\text{ pred}}(24) &= -1.5503 \times 0,227 - 2.8093 \times 0,662 - 0.9302 \times 0,001 + 1.4041 \times \\
 &\quad 0,500 + 2.8199 \\
 &= 1,3093
 \end{aligned}$$

Data dan grafik regresi manual (3)

Senyawa	$pIC_{50\text{ obs}}$	$pIC_{50\text{ pred}}$
2	1,7288	1,8862
9	1,7280	1,5330
12	2,8289	-0,0419
13	2,2542	0,9863
24	1,7566	1,3093



7. Pembuatan dan validasi persamaan HKSA manual (4)

Persamaan HKSA:

$$\begin{aligned}
 pIC_{50\text{ pred}} = & 2,689 * \text{RDF155u} + 1,8678 * \text{RDF45m} - 1,8747 * \text{RDF25s} - \\
 & 4,5706 * \text{RDF120s} + 1,4509
 \end{aligned}$$

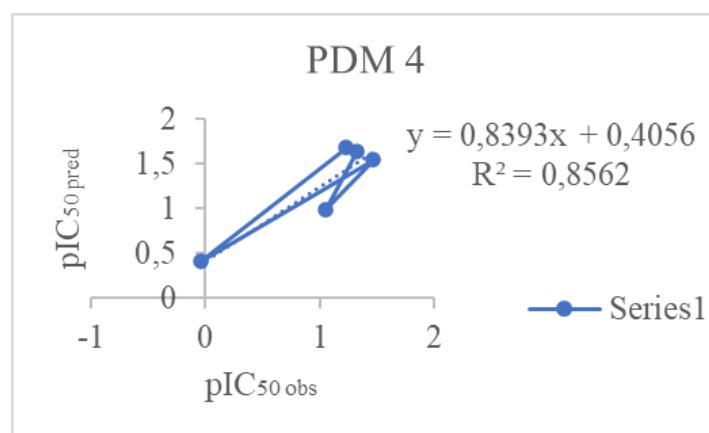
Data *test set* manual (4)

Senyawa	RDF155u	RDF45m	RDF25s	RDF120s	$pIC_{50\text{ obs}}$
6	0,204	0,01	0,013	0,077	1,3259
10	0,219	0,508	0,489	0,237	1,0550
15	0,975	0,48	0,804	0,42	1,4645
16	0,412	0,643	0,646	0,469	-0,0410
17	0,359	0,619	0,439	0,235	1,2297

$$\begin{aligned}
pIC_{50\text{ pred}}(6) &= 2,689*0,204 + 1,8678*0,01 - 1,8747*0,013 - 4,5706*0,077 + \\
&\quad 1,4509 \\
&= 1,641827 \\
pIC_{50\text{ pred}}(10) &= 2,689*0,219 + 1,8678*0,508 - 1,8747*0,489 - 4,5706*0,237 + \\
&\quad 1,4509 \\
&= 0,988673 \\
pIC_{50\text{ pred}}(15) &= 2,689*0,975 + 1,8678*0,48 - 1,8747*0,804 - 4,5706*0,42 + \\
&\quad 1,4509 \\
&= 1,542308 \\
pIC_{50\text{ pred}}(16) &= 2,689*0,412 + 1,8678*0,643 - 1,8747*0,646 - 4,5706*0,469 + \\
&\quad 1,4509 \\
&= 0,405096 \\
pIC_{50\text{ pred}}(17) &= 2,689*0,359 + 1,8678*0,619 - 1,8747*0,439 - 4,5706*0,235 + \\
&\quad 1,4509 \\
&= 1,675335
\end{aligned}$$

Data dan grafik regresi manual (4)

Senyawa	pIC ₅₀ obs	pIC ₅₀ pred
6	1,3259	1,6418
10	1,0550	0,9887
15	1,4645	1,5423
16	-0,0410	0,4051
17	1,2297	1,6753



8. Validasi eksternal persamaan model 1

$$r_m^2 = r^2 \times (1 - \sqrt{r^2 - r_0^2}) \quad r_0^2 = 1 - \frac{\sum(y_{\text{obs}} - k \times y_{\text{pred}})^2}{\sum(y_{\text{obs}} - \bar{y}_{\text{obs}})^2} \quad k = \frac{\sum(y_{\text{obs}} \times y_{\text{pred}})}{\sum(y_{\text{pred}})^2}$$

Data persamaan model 1

No	y _{obs}	y _{pred}	(y _{obs} x y _{pred})	(y _{pred}) ²
16	-0,0409	1,4103	-0,0578	1,9890
18	-0,2154	2,5071	-0,5399	6,2856
19	-0,0650	1,7833	-0,1159	3,1799
20	-0,3010	2,3202	-0,6985	5,3833
21	0	0,4856	0	0,2358
Σ			-1,4121	17,0737

$$k = \frac{-1,4121}{17,0737} = -0,08271$$

No	(k x y _{pred})	(y _{obs} - k x y _{pred})	(y _{obs} - k x y _{pred}) ²
1	-0,1166	0,0757	$0,5728 \times 10^{-2}$
6	-0,2074	-0,0080	$0,0064 \times 10^{-2}$
8	-0,1475	0,0825	$0,6805 \times 10^{-2}$
20	-0,1919	-0,1091	$1,1910 \times 10^{-2}$
21	-0,0402	0,0402	$0,1613 \times 10^{-2}$
Σ			0,0261

No	y _{obs}	\bar{y}_{obs}	y _{obs} - \bar{y}_{obs}	(y _{obs} - \bar{y}_{obs}) ²
1	-0,0409	-0,1245	0,0835	$0,6975 \times 10^{-2}$
6	-0,2154	-0,1245	-0,0909	$0,8264 \times 10^{-2}$
8	-0,0650	-0,1245	0,0595	$0,3537 \times 10^{-2}$
20	-0,3010	-0,1245	-0,1766	$3,1172 \times 10^{-2}$
21	0	-0,1245	0,1245	$1,5494 \times 10^{-2}$
Σ			0,0654	

$$r_0^2 = 1 - \frac{0,0261}{0,0654}$$

$$= 1 - 0,3991$$

$$= 0,6009$$

$$r^2 - r_0^2/r^2 = \frac{0,733 - 0,6009}{0,733}$$

$$= \frac{0,1321}{0,733}$$

$$= 0,1802$$

$$\begin{aligned}
r_m^2 &= 0,733 \times (1 - \sqrt{0,733 - 0,6009}) \\
&= 0,733 \times (1 - \sqrt{0,1321}) \\
&= 0,733 \times (1 - 0,3635) \\
&= 0,733 \times 0,6365 \\
&= 0,4666
\end{aligned}$$

9. Validasi eksternal persamaan model 3

$$r_m^2 = r^2 \times (1 - \sqrt{r^2 - r_0^2}) \quad r_0^2 = 1 - \frac{\sum(y_{\text{obs}} - k \times y_{\text{pred}})^2}{\sum(y_{\text{obs}} - \bar{y}_{\text{obs}})^2} \quad k = \frac{\sum(y_{\text{obs}} \times y_{\text{pred}})}{\sum(y_{\text{pred}})^2}$$

Data persamaan model 3

No	y _{obs}	y _{pred}	(y _{obs} × y _{pred})	(y _{pred}) ²
9	1,7288	1,8862	3,2609	3,5578
10	1,7280	1,5330	2,6490	2,3501
11	2,8289	-0,0419	-0,1185	0,0018
19	2,2542	0,9863	2,2233	0,9728
20	1,7566	1,3093	2,2999	1,7143
Σ			10,3146	8,5966

$$k = \frac{10,3146}{8,5966} = 1,1998$$

No	(k × y _{pred})	(y _{obs} - k × y _{pred})	(y _{obs} - k × y _{pred}) ²
9	2,2631	-0,5343	0,2855
10	1,8394	-0,1114	0,0124
11	-0,0503	2,8792	8,2896
19	1,1834	1,0708	1,1466
20	1,5709	0,1856	0,0345
Σ			9,7686

No	y _{obs}	\bar{y}_{obs}	y _{obs} - \bar{y}_{obs}	(y _{obs} - \bar{y}_{obs}) ²
9	1,7288	2,0593	-0,3305	0,1092
10	1,7280	2,0593	-0,3313	0,1098
11	2,8289	2,0593	0,7696	0,5923
19	2,2542	2,0593	0,1949	0,0380
20	1,7566	2,0593	-0,3027	0,0916
Σ				0,9409

$$\begin{aligned}
r_0^2 &= 1 - \frac{9,7686}{0,9409} \\
&= 1 - 10,3822 \\
&= -9,3822 \\
r^2 - r_0^2/r^2 &= \frac{0,9202 - (-9,3822)}{0,9202} \\
&= \frac{10,3024}{0,9202} \\
&= 11,1958 \\
r_m^2 &= 0,9202 \times (1 - \sqrt{0,9202 - (-9,3822)}) \\
&= 0,9202 \times (1 - \sqrt{10,3024}) \\
&= 0,9202 \times (1 - 3,2097) \\
&= 0,9202 \times (-2,2097) \\
&= -2,0334
\end{aligned}$$

10. Validasi eksternal persamaan 4

$$r_m^2 = r^2 \times (1 - \sqrt{r^2 - r_0^2}) \quad r_0^2 = 1 - \frac{\sum(y_{obs} - k \times y_{pred})^2}{\sum(y_{obs} - \bar{y}_{obs})^2} \quad k = \frac{\sum(y_{obs} \times y_{pred})}{\sum(y_{pred})^2}$$

Data persamaan 4

No	y _{obs}	y _{pred}	(y _{obs} × y _{pred})	(y _{pred}) ²
6	1,3259	1,6418	2,1769	2,6956
10	1,0550	0,9887	1,0430	0,9775
15	1,4645	1,5423	2,2587	2,3787
16	-0,0410	0,4051	-0,0166	0,1641
17	1,2297	1,6753	2,0601	2,8067
Σ			7,5222	9,0226

$$k = \frac{7,5222}{9,0226} = 0,8337$$

No	(k x ypred)	(yobs - k x ypred)	(yobs - k x ypred) ²
6	1,3688	-0,0429	0,0018
10	0,8243	0,2307	0,0532
15	1,2858	0,1787	0,0319
16	0,3377	-0,3787	0,1434
17	1,3967	-0,1671	0,0279
Σ			0,2583

No	yobs	\bar{y}_{obs}	$y_{obs} - \bar{y}_{obs}$	$(y_{obs} - \bar{y}_{obs})^2$
6	1,3259	1,0068	0,3191	0,1018
10	1,0550	1,0068	0,0482	0,0023
15	1,4645	1,0068	0,4577	0,2095
16	-0,0410	1,0068	-1,0478	1,0979
17	1,2297	1,0068	0,2229	0,0497
Σ				1,4611

$$r_0^2 = 1 - \frac{0,2583}{1,4611}$$

$$= 1 - 0,1768$$

$$= 0,8232$$

$$r^2 - r_0^2/r^2 = \frac{0,8562 - 0,8232}{0,8562}$$

$$= \frac{0,0330}{0,8562}$$

$$= 0,0385$$

$$r_m^2 = 0,8562 \times (1 - \sqrt{0,8562 - 0,8232})$$

$$= 0,8562 \times (1 - \sqrt{0,0330})$$

$$= 0,8562 \times (1 - 0,1816)$$

$$= 0,8562 \times 0,8184$$

$$= 0,7007$$

11. Perhitungan nilai pIC₅₀ dan IC₅₀ prediksi senyawa rancangan

$$pIC_{50\text{ pred}} = 2,689 * RDF155u + 1,8678 * RDF45m - 1,8747 * RDF25s - 4,5706 * RDF120s + 1,4509$$

Data deskriptor senyawa rancangan

Senyawa	RDF155u	RDF45m	RDF25s	RDF120s
SR1	0	0,163	0,223	0,445
SR2	0	0	0,325	0,485
SR3	1	1	0,616	0,634
SR4	0,661	0,836	0	0,613
SR5	0	0,842	1	0,063
SR6	0	0,682	0,275	0
SR7	0	0,851	0,757	1
SR8	0	0,689	0,037	0,902

$$\text{pIC}_{50 \text{ pred}} \text{ SR1} = 2,689*0 + 1,8678*0,163 - 1,8747*0,223 - 4,5706*0,445 + 1,4509 \\ = -0,69662$$

$$\text{IC}_{50 \text{ pred}} \text{ SR1} = 10^{-0,69662} \\ = 0,2011$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR2} = 2,689*0 + 1,8678*0 - 1,8747*0,325 - 4,5706*0,485 + 1,4509 \\ = -1,37512$$

$$\text{IC}_{50 \text{ pred}} \text{ SR2} = 10^{-1,37512} \\ = 0,0422$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR3} = 2,689*1 + 1,8678*1 - 1,8747*0,616 - 4,5706*0,634 + 1,4509 \\ = 1,955124$$

$$\text{IC}_{50 \text{ pred}} \text{ SR3} = 10^{1,955124} \\ = 90,1829$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR4} = 2,689*0,661 + 1,8678*0,836 - 1,8747*0 - 4,5706*0,613 + 1,4509 \\ = 1,988032$$

$$\text{IC}_{50 \text{ pred}} \text{ SR4} = 10^{1,988032} \\ = 97,2819$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR5} = 2,689*0 + 1,8678*0,842 - 1,8747*1 - 4,5706*0,063 + 1,4509 \\ = 0,86094$$

$$\text{IC}_{50 \text{ pred}} \text{ SR5} = 10^{0,86094} \\ = 7,2601$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR6} = 2,689*0 + 1,8678*0,682 - 1,8747*0,275 - 4,5706*0 + 1,4509 \\ = 2,209197$$

$$\text{IC}_{50 \text{ pred}} \text{ SR6} = 10^{2,209197} \\ = 161,8815$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR7} = 2,689*0 + 1,8678*0,851 - 1,8747*0,757 - 4,5706*1 + 1,4509 \\ = -2,94935$$

$$\text{IC}_{50 \text{ pred}} \text{ SR7} = 10^{-2,94935} \\ = 0,0011$$

$$\text{pIC}_{50 \text{ pred}} \text{ SR8} = 2,689*0 + 1,8678*0,689 - 1,8747*0,037 - 4,5706*0,902 + 1,4509 \\ = -1,45423$$

$$\text{IC}_{50 \text{ pred}} \text{ SR8} = 10^{-1,45423} \\ = 0,0351$$

Data nilai pIC_{50} dan IC_{50} prediksi senyawa rancangan

Senyawa	pIC₅₀	IC₅₀ prediksi
SR1	-0,6966	0,2011
SR2	-1,3751	0,0422
SR3	1,9551	90,1829
SR4	1,9880	97,2819
SR5	0,8609	7,2601
SR6	2,2092	161,8815
SR7	-2,9494	0,0011
SR8	-1,4542	0,0351