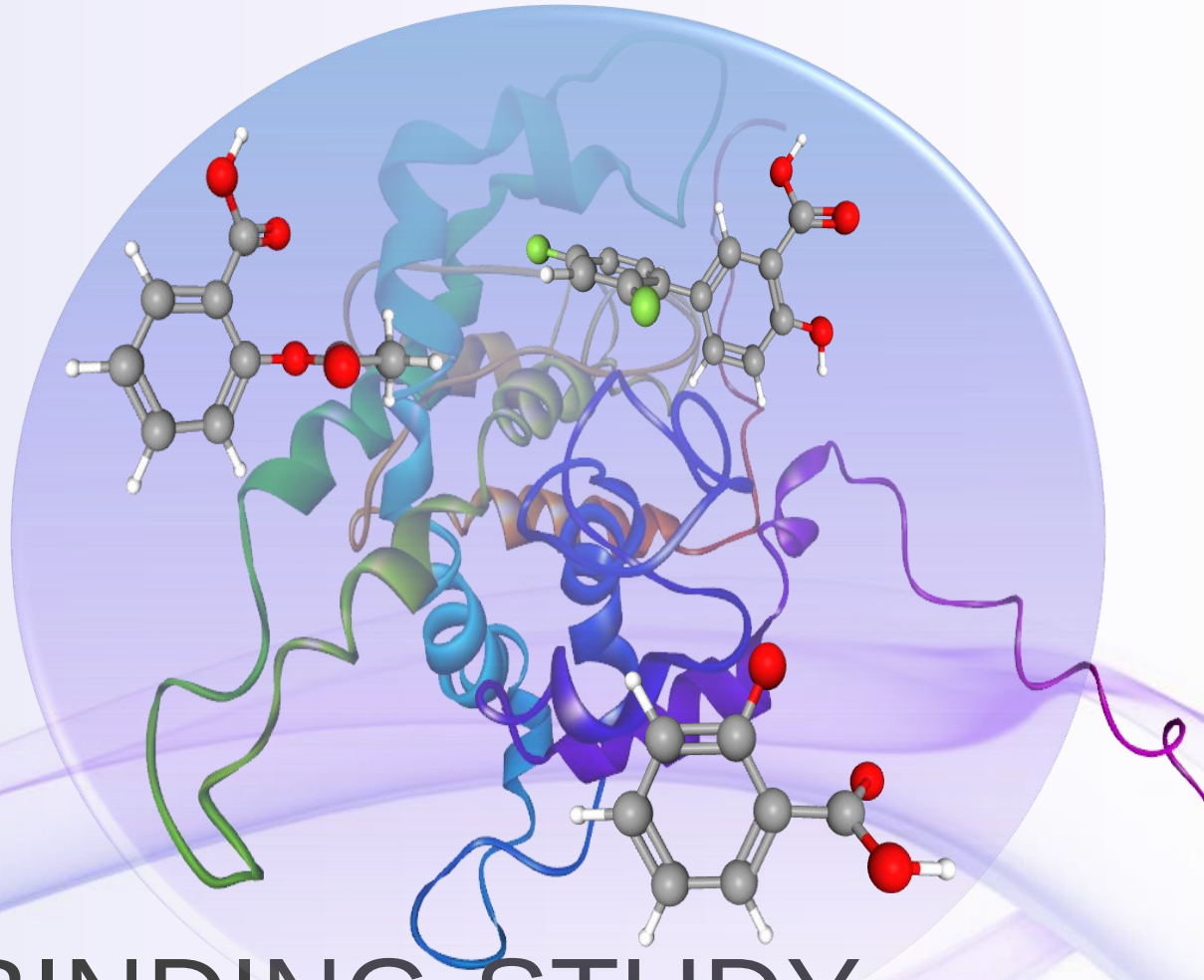
UBAYA
UNIVERSITAS SURABAYA



DRUG-PROTEIN BINDING STUDY

COMPUTATIONAL MODELLING APPROACH

A COLLABORATION STUDY BETWEEN

UNIVERSITY OF SURABAYA, INDONESIA AND DEFENSE UNIVERSITY, INDONESIA

Ratih

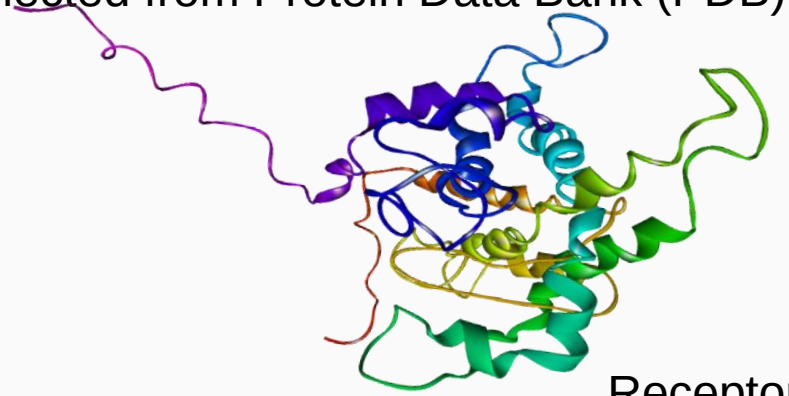
Department of Pharmaceutical Chemistry
Faculty of Pharmacy
University of Surabaya, Indonesia

Okta Nursanti

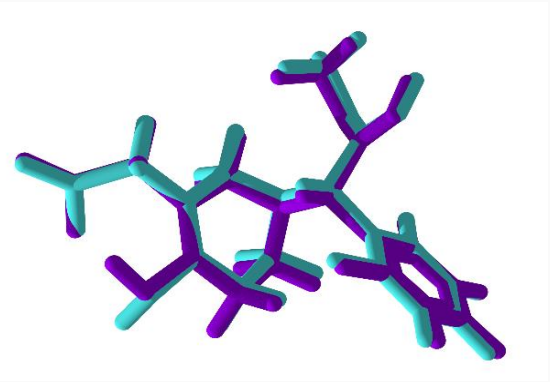
Medicinal Chemistry Laboratory
Faculty of Military Pharmacy Republic of Indonesia
Defense University, Indonesia

SCHEME OF REDOCKING SIMULATION

Selected from Protein Data Bank (PDB)

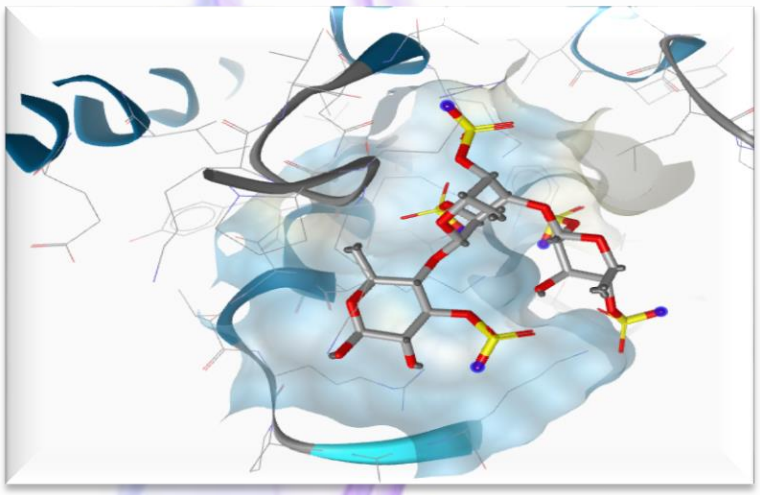


Receptor



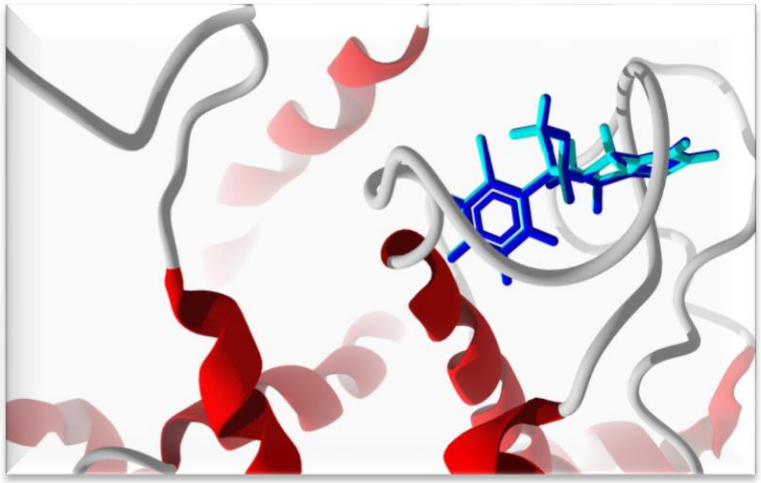
Ligand cocrystal

Redocking



Docking Pose

RMSD



SOFTWARE

Docking and protein preparation

MOE
Molecular
Operating
Environment

SMILES conversion to SYBYL.mol2

Open Babel

2D and 3D structures

WEB SERVER

RCSB PDB PROTEIN DATA BANK

3D protein
https://www.rcsb.org

D U D • E
A Database of Useful Decoys: Enhanced

Control negative preparation

DRUGBANK

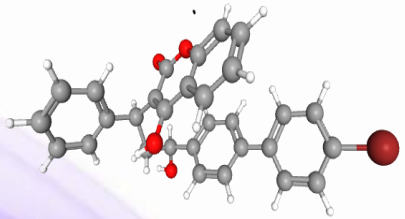
Information about the selected drugs
https://go.drugbank.com

PubChem

2D drug and ligand structures
https://pubchem.ncbi.nlm.nih.gov

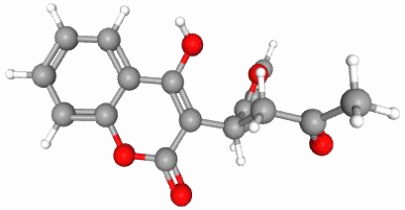
Training set

Bromadiolone



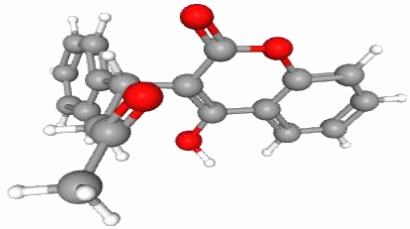
CID 9854012

Coumafuryl



CID 54689800

Warfarin



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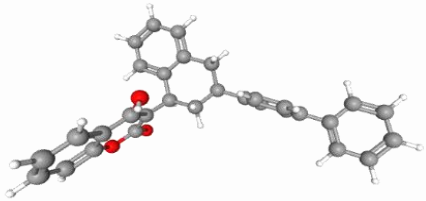
Difenacoum



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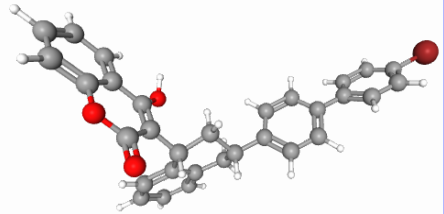
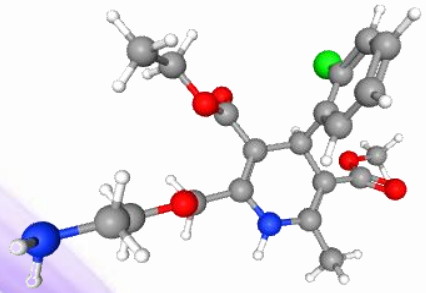
Brodifacoum



CID 54680676

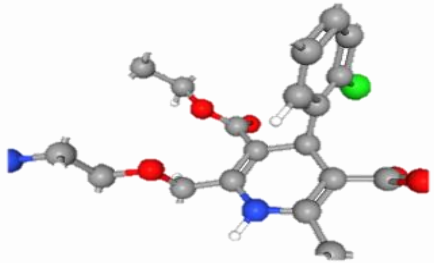
Tested Drugs

R-AMLODIPINE



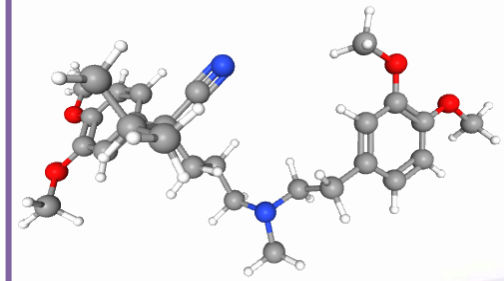
CID_9801597

S-AMLODIPINE



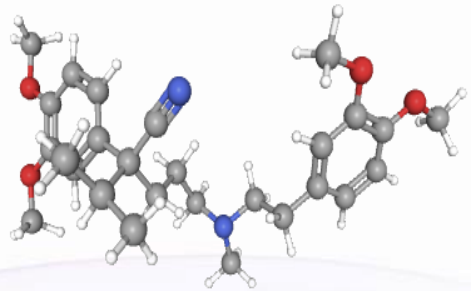
CID_9822750

R-VERAPAMIL



CID_65808

S-VERAPAMIL



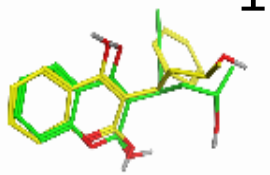
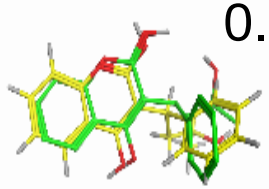
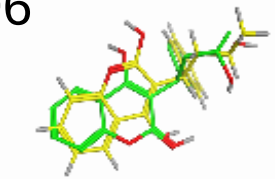
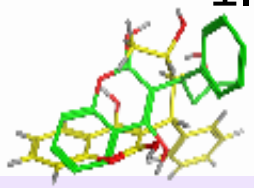
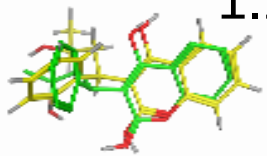
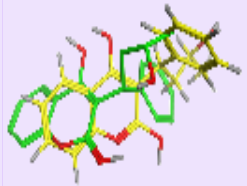
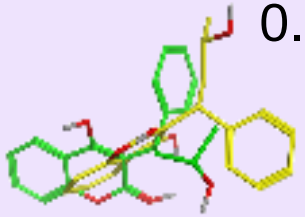
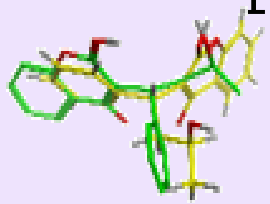
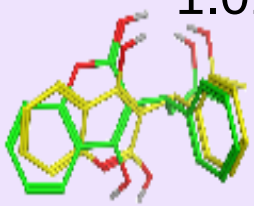
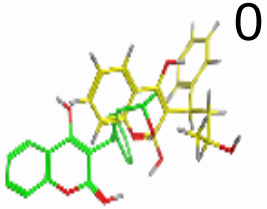
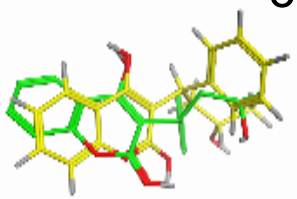
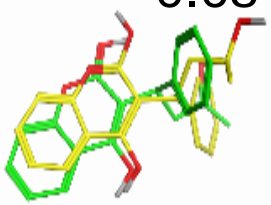
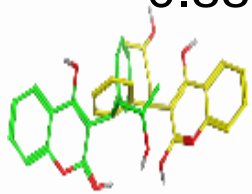
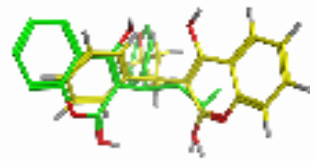
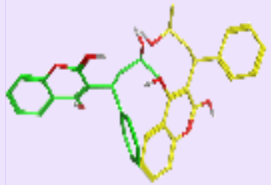
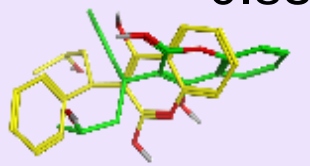
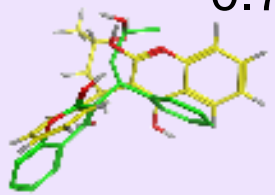
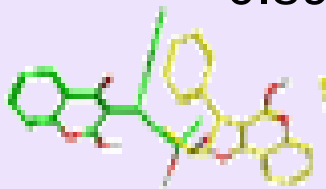
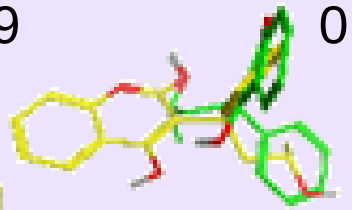
CID_92305

1H9Z PROTEIN

Scoring→ / Placement↓	Affinity dG	Alpha HB	ASE	GBVI/WSA dG	London dG
Alpha PMI	0.644245	0.655915	0.675115	0.738896	0.591763
AlphaTriangle	0.745413	0.745413	1.105186	1.205972	1.301725
Proxy Triangle	0.939548	1.187672	1.026441	1.164792	0.838274
Triangle Matcher	1.159916	0.968157	0.997675	1.011589	0.866555

Scoring Function Tambahan	Pose training/pose traning + decoy
Affinity dG	26/2435
ASE	28/2440
Alpha HB	28/2461
GBVI/WSA dG	28/2450
London dG	26/2451

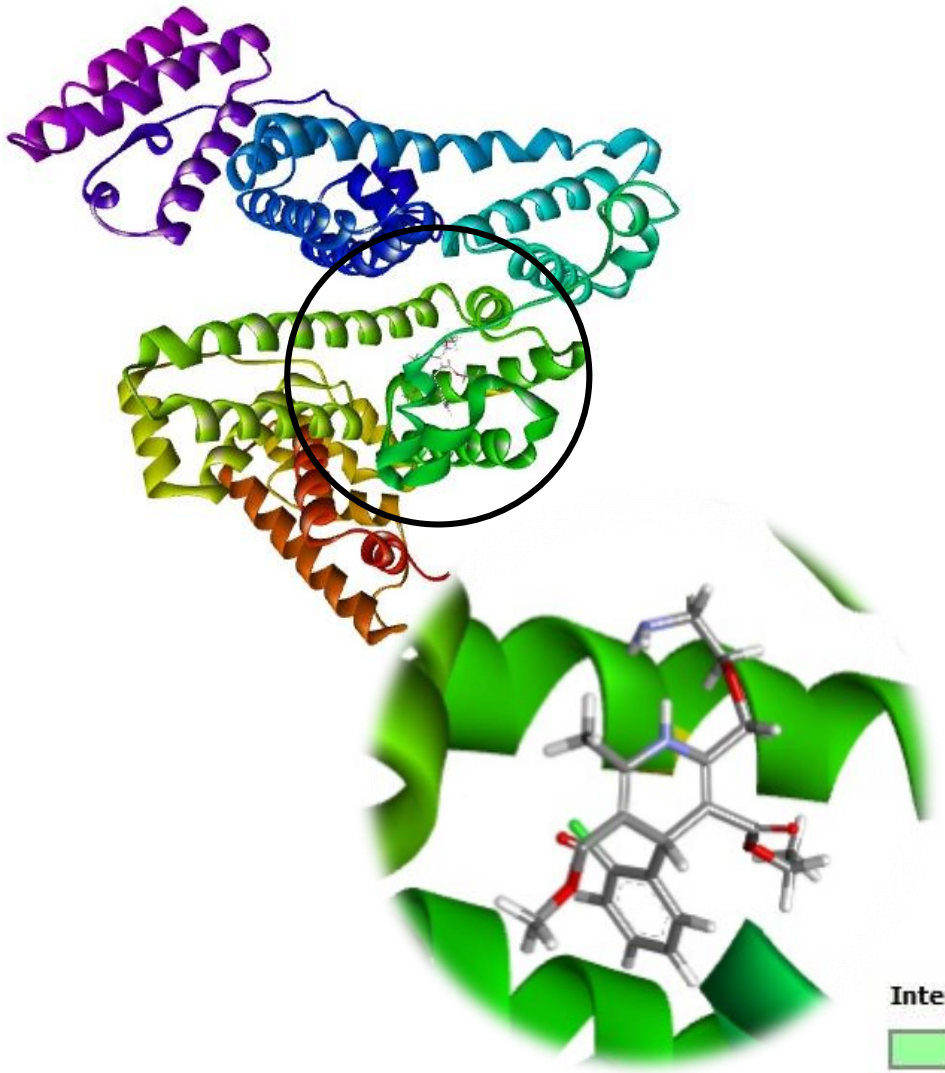
RESULTS

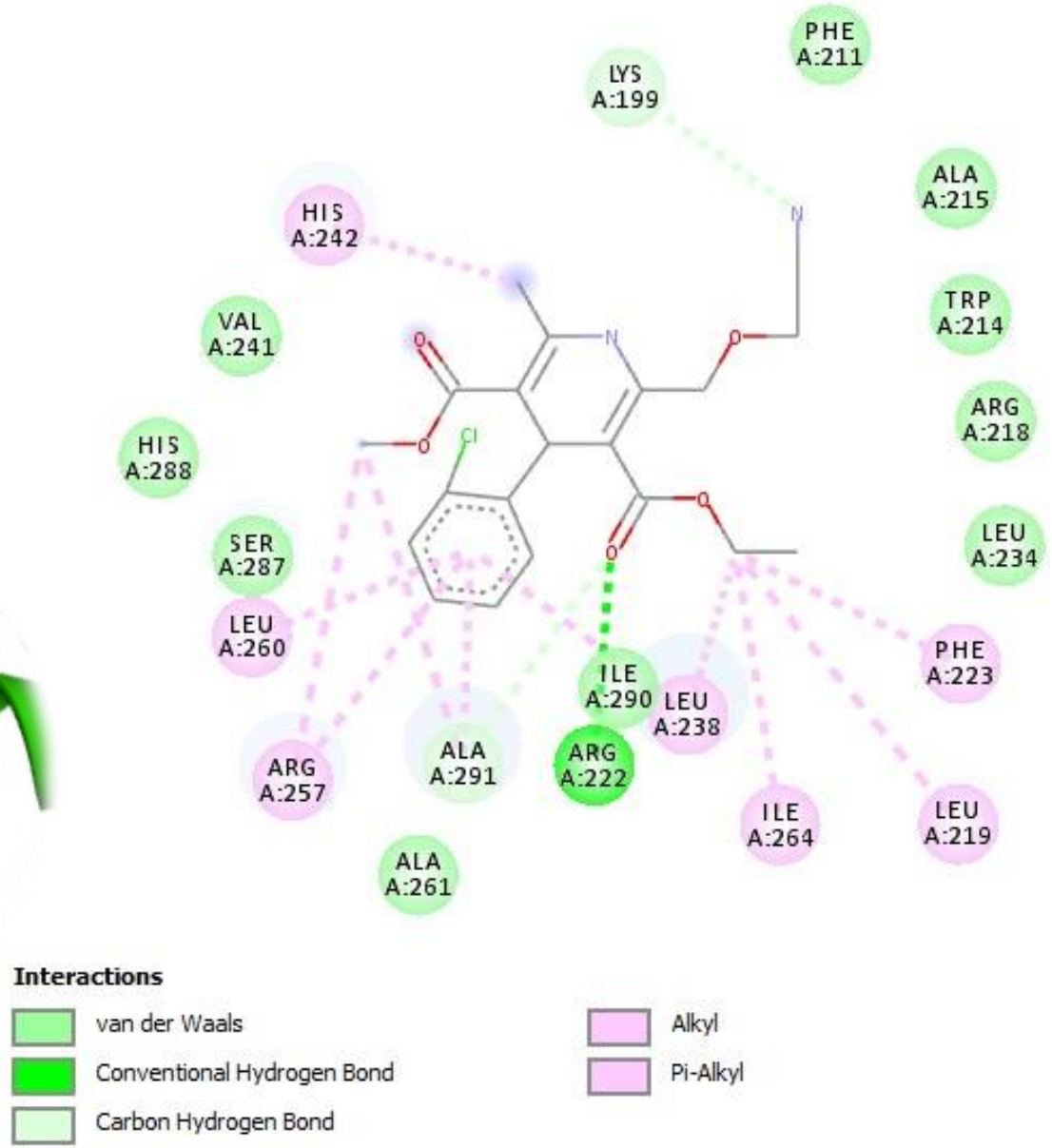
Scoring→ / Placement↓	Affinity dG	Alpha HB	ASE	GBVI/ WSA dG	London dG
Alpha PMI	1.11 	0.96 	1.76 	1.11 	1.11 
AlphaTriangle	1.04 	0.60 	1.09 	1.01 	0.85 
Proxy Triangle	0.89 	0.79 	0.68 	0.88 	0.74 
Triangle Matcher	0.87 	0.83 	0.73 	0.89 	0.86 

SUMMARY

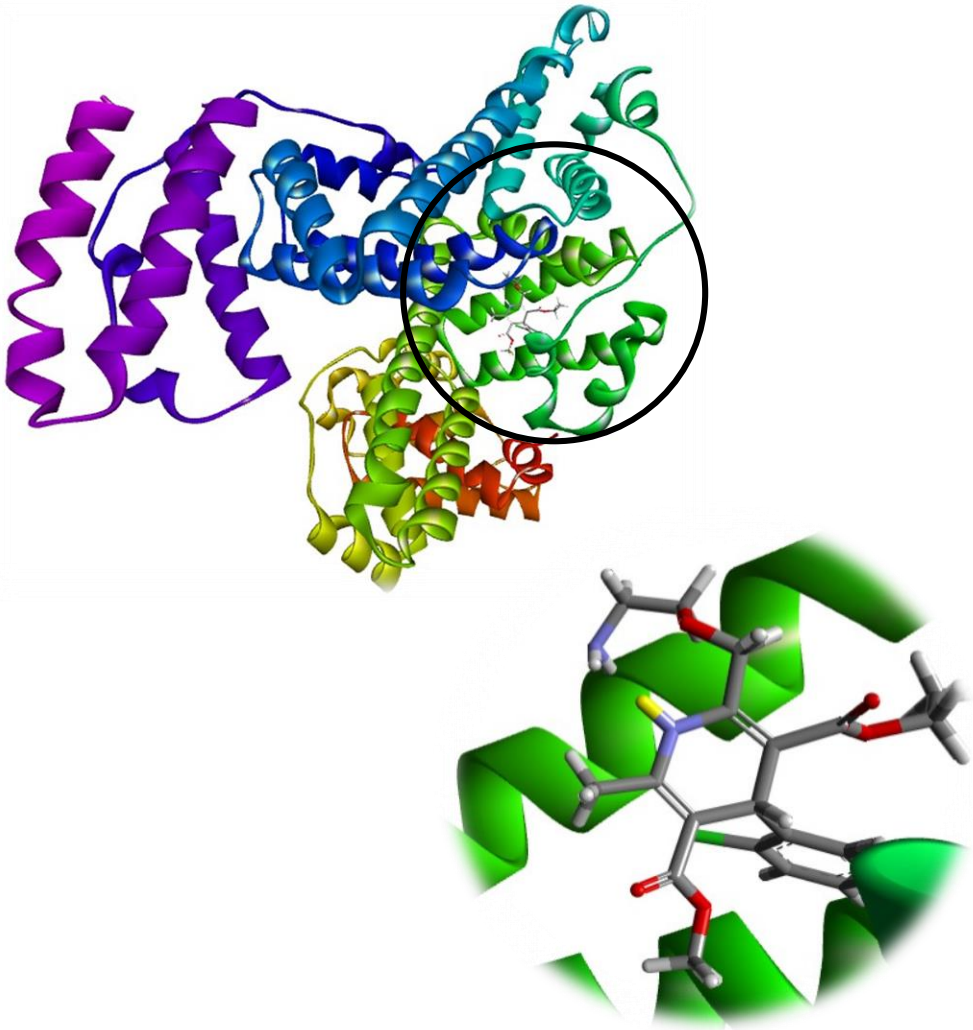
Additional scoring function	Drug molecule	Binding affinity
Affinity dG	Conformer3D_CID_65808_*R*-VER	-6.378026
	Conformer3D_CID_92305_*S*-VER	-6.971819
	Conformer3D_CID_9801597_*R*-AML	-5.783911
	Conformer3D_CID_9822750_*S*-AML	-5.783911
ASE	Conformer3D_CID_65808_*R*-VER	-33.720531
	Conformer3D_CID_92305_*S*-VER	-32.440483
	Conformer3D_CID_9801597_*R*-AML	-26.490945
	Conformer3D_CID_9822750_*S*-AML	-27.488300
Alpha HB	Conformer3D_CID_65808_*R*-VER	-151.42279
	Conformer3D_CID_92305_*S*-VER	-150.75346
	Conformer3D_CID_9801597_*R*-AML	-139.16114
	Conformer3D_CID_9822750_*S*-AML	-145.07617
GBVI/WSA dG	Conformer3D_CID_65808_*R*-VER	-9.856130
	Conformer3D_CID_92305_*S*-VER	-9.122101
	Conformer3D_CID_9801597_*R*-AML	-9.018595
	Conformer3D_CID_9822750_*S*-AML	-8.139161
London dG	Conformer3D_CID_65808_*R*-VER	-12.280153
	Conformer3D_CID_92305_*S*-VER	-11.002061
	Conformer3D_CID_9801597_*R*-AML	-11.790844
	Conformer3D_CID_9822750_*S*-AML	-10.848207

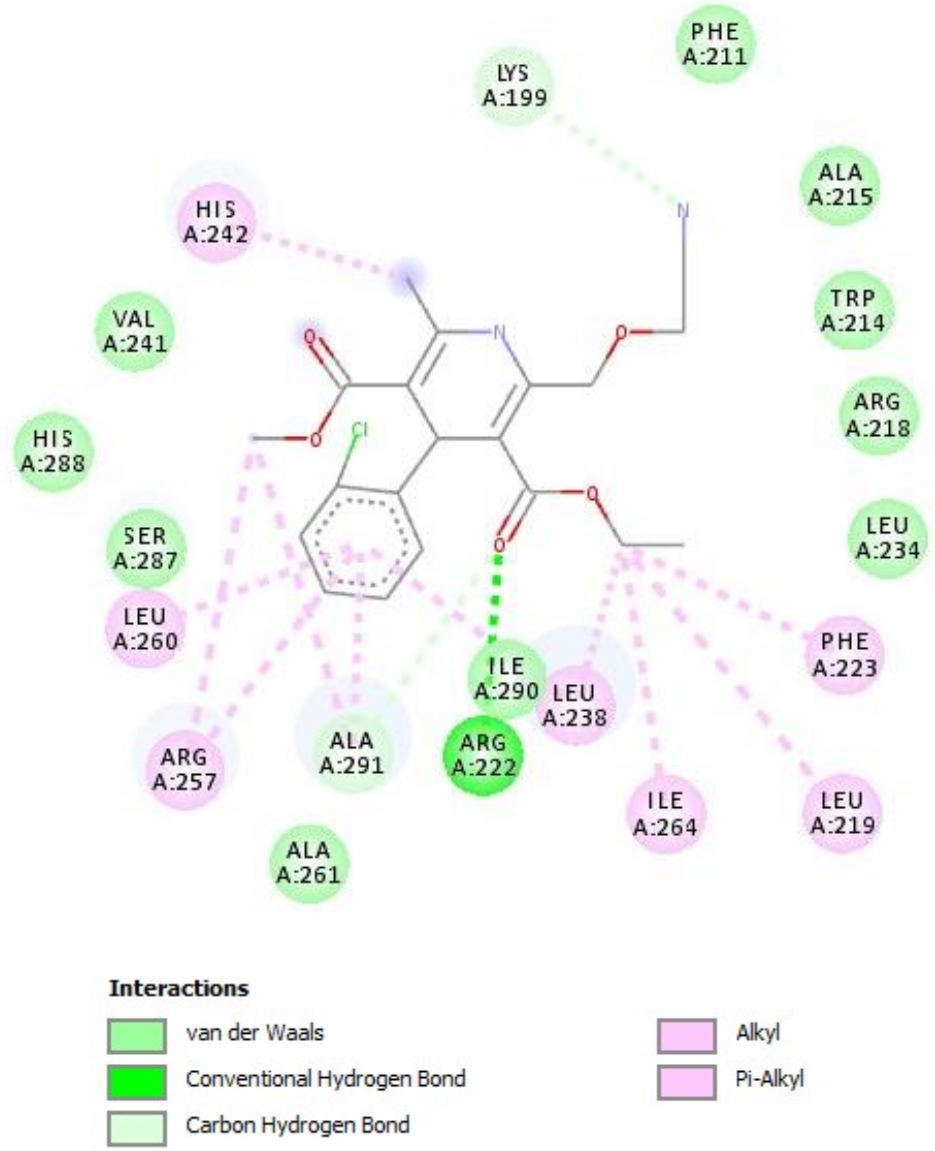
Conformer 3D_CID_9801597
***R*-Amlodipine**



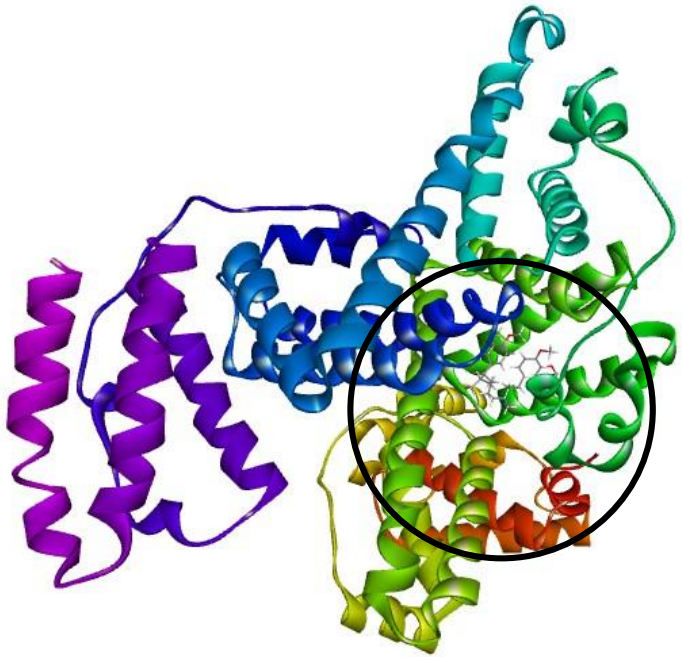


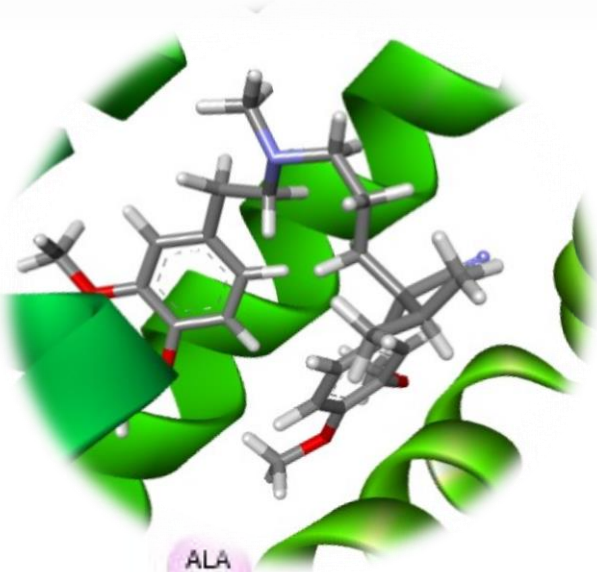
Conformer 3D_CID_9822750
S-Amlodipine

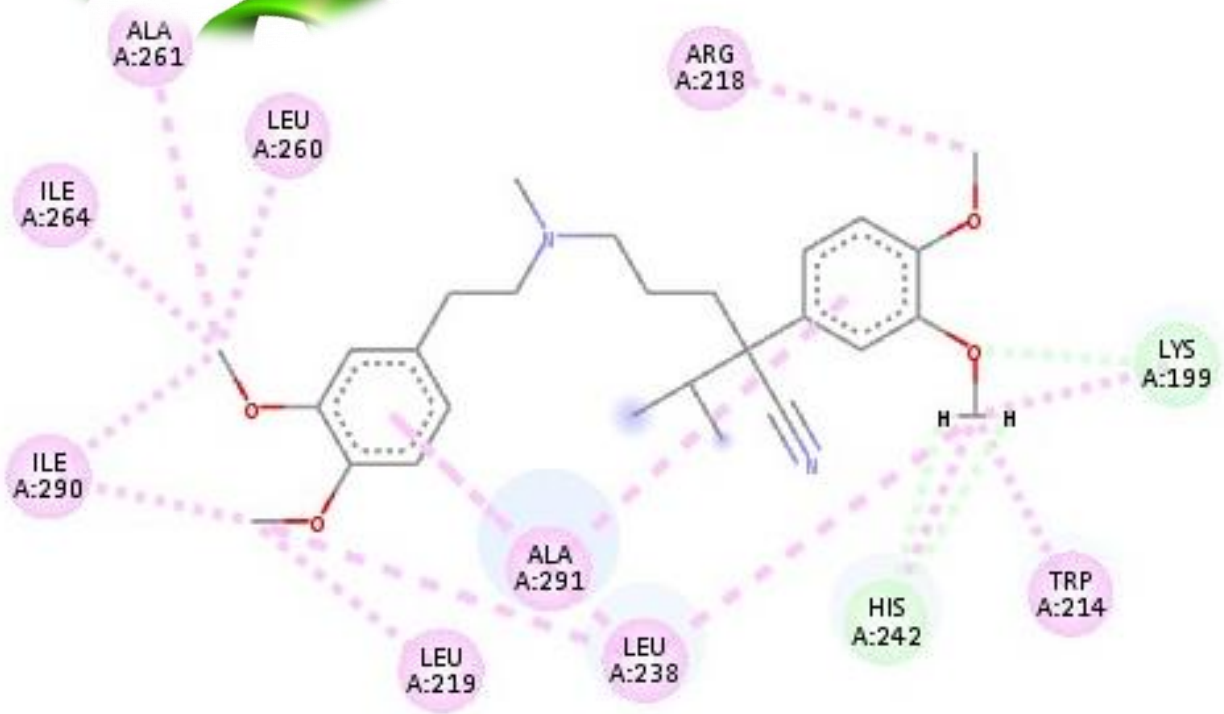




Conformer 3D_CID_65808
***R*-Verapamil**







Interactions

Carbon Hydrogen Bond

Alkyl

Pi-Alkyl

Conformer 3D_CID_92305
S-Verapamil