

LAMPIRAN

Lampiran 1. File gridbox dalam format txt (grid.txt)

```
receptor = protein.pdbqt
```

```
ligand = ligand.pdbqt
```

```
center_x = -4.055
```

```
center_y = -12.232
```

```
center_z = -17.416
```

```
out = hasil.pdbqt
```

```
size_x = 10
```

```
size_y = 20
```

```
size_z = 16
```

Lampiran 2. File ion.mdp pada tahap netralisasi

```

; LINES STARTING WITH ';' ARE COMMENTS
title           = Minimization      ; Title of run

; Parameters describing what to do, when to stop and what to save
integrator = steep      ; Algorithm (steep = steepest descent minimization)
emtol      = 1000.0     ; Stop minimization when the maximum force < 10.0 kJ/mol
emstep     = 0.01      ; Energy step size
nsteps     = 50000      ; Maximum number of (minimization) steps to perform

; Parameters describing how to find the neighbors of each atom and how to calculate
the interactions
nstlist = 1             ; Frequency to update the neighbor list and long range forces
cutoff-scheme = Verlet
ns_type      = grid     ; Method to determine neighbor list (simple, grid)
rlist        = 1.0      ; Cut-off for making neighbor list (short range forces)
coulombtype  = cutoff   ; Treatment of long range electrostatic interactions
rcoulomb     = 1.0      ; long range electrostatic cut-off
rvdw         = 1.0      ; long range Van der Waals cut-off
pbc          = xyz      ; Periodic Boundary Conditions

```

Lampiran 3. File em.mdp pada tahap minimisasi energi

```

; LINES STARTING WITH ';' ARE COMMENTS
title           = Minimization      ; Title of run

; Parameters describing what to do, when to stop and what to save
integrator      = steep ; Algorithm (steep = steepest descent minimization)
emtol = 1000.0   ; Stop minimization when the maximum force < 10.0 kJ/mol
emstep         = 0.01   ; Energy step size
nsteps         = 50000  ; Maximum number of (minimization) steps to perform

; Parameters describing how to find the neighbors of each atom and how to calculate
the interactions
nstlist        = 1      ; Frequency to update the neighbor list and long range forces
cutoff-scheme  = Verlet
ns_type        = grid   ; Method to determine neighbor list (simple, grid)
rlist          = 1.2    ; Cut-off for making neighbor list (short range forces)
coulombtype    = PME    ; Treatment of long range electrostatic interactions
rcoulomb       = 1.2    ; long range electrostatic cut-off
vdwtype        = cutoff
vdw-modifier   = force-switch
rvdw-switch    = 1.0
rvdw           = 1.2    ; long range Van der Waals cut-off
pbc            = xyz    ; Periodic Boundary Conditions
DispCorr      = no

```

Lampiran 4. File NVT.mdp pada tahap ekuilibrasi 1

```

title           = Protein-ligand complex NVT equilibration
define          = -DPOSRES ; position restrain the protein and ligand
; Run parameters
integrator      = md       ; leap-frog integrator
nsteps         = 50000    ; 2 * 50000 = 100 ps
dt             = 0.002    ; 2 fs

; Output control
nstenergy      = 500     ; save energies every 1.0 ps
nstlog         = 500     ; update log file every 1.0 ps
nstxout-compressed = 500 ; save coordinates every 1.0 ps
; Bond parameters
continuation    = no     ; first dynamics run
constraint_algorithm = lincs ; holonomic constraints
constraints     = h-bonds ; bonds to H are constrained
lincs_iter     = 1      ; accuracy of LINCS
lincs_order    = 4      ; also related to accuracy
; Neighbor searching and vdW
cutoff-scheme  = Verlet
ns_type        = grid   ; search neighboring grid cells
nstlist        = 20     ; largely irrelevant with Verlet
rlist          = 1.2
vdwtype        = cutoff
vdw-modifier   = force-switch
rvdw-switch    = 1.0
rvdw           = 1.2    ; short-range van der Waals cutoff (in nm)
; Electrostatics
coulombtype    = PME     ; Particle Mesh Ewald for long-range electrostatics
rcoulomb       = 1.2     ; short-range electrostatic cutoff (in nm)
pme_order      = 4      ; cubic interpolation
fourierspacing = 0.16   ; grid spacing for FFT
; Temperature coupling
tcoupl         = V-rescale ; modified Berendsen thermostat
tc-grps        = Protein_UNK Water_and_ions ; two coupling groups - more accurate

```

(Lanjutan)

```
tau_t      = 0.1 0.1      ; time constant, in ps
ref_t      = 310.15 310.15 ; reference temperature, one for each group, in K
; Pressure coupling
pcoupl     = no      ; no pressure coupling in NVT
; Periodic boundary conditions
pbc       = xyz      ; 3-D PBC
; Dispersion correction is not used for proteins with the C36 additive FF
DispCorr   = no
; Velocity generation
gen_vel    = yes     ; assign velocities from Maxwell distribution
gen_temp   = 300     ; temperature for Maxwell distribution
gen_seed   = -1     ; generate a random seed
```

Lampiran 5. File NPT.mdp pada tahap ekuilibrasi 2

```

title          = Protein-ligand complex NPT equilibration
define         = -DPOSRES ; position restrain the protein and ligand
; Run parameters
integrator     = md      ; leap-frog integrator
nsteps        = 50000   ; 2 * 50000 = 100 ps
dt            = 0.002   ; 2 fs
; Output control
nstenergy     = 500     ; save energies every 1.0 ps
nstlog        = 500     ; update log file every 1.0 ps
nstxout-compressed = 500 ; save coordinates every 1.0 ps
; Bond parameters
continuation   = yes    ; continuing from NVT
constraint_algorithm = lincs ; holonomic constraints
constraints    = h-bonds ; bonds to H are constrained
lincs_iter     = 1      ; accuracy of LINCS
lincs_order    = 4      ; also related to accuracy
; Neighbor searching and vdW
cutoff-scheme  = Verlet
ns_type        = grid   ; search neighboring grid cells
nstlist        = 20     ; largely irrelevant with Verlet
rlist          = 1.2
vdwtype        = cutoff
vdw-modifier   = force-switch
rvdw-switch    = 1.0
rvdw           = 1.2   ; short-range van der Waals cutoff (in nm)
; Electrostatics
coulombtype    = PME    ; Particle Mesh Ewald for long-range electrostatics
rcoulomb       = 1.2
pme_order      = 4      ; cubic interpolation
fourierspacing = 0.16  ; grid spacing for FFT
; Temperature coupling
tcoupl         = V-rescale ; modified Berendsen thermostat
tc-grps       = Protein_UNK Water_and_ions ; two coupling groups - more accurate
tau_t         = 0.1 0.1 ; time constant, in ps
ref_t         = 310.15 310.15 ; reference temperature, one for each group, in K

```

(Lanjutan)

```
; Pressure coupling
pcoupl      = C-rescale      ; pressure coupling is on for NPT

pcoupltype  = isotropic      ; uniform scaling of box vectors
tau_p       = 2.0            ; time constant, in ps
ref_p       = 1.0            ; reference pressure, in bar
compressibility = 4.5e-5      ; isothermal compressibility of water,
bar^-1
refcoord_scaling = com
; Periodic boundary conditions
pbc         = xyz            ; 3-D PBC
; Dispersion correction is not used for proteins with the C36 additive FF
DispCorr    = no
; Velocity generation
gen_vel     = no            ; velocity generation off after NVT
```

Lampiran 6. File md.mdp pada tahap produksi

```

title          = Protein-ligand complex MD simulation
; Run parameters
integrator      = md          ; leap-frog integrator
nsteps         = 25000000    ; 2 * 25000000 = 50000 ps (50 ns)
dt             = 0.002      ; 2 fs
; Output control
nstenergy      = 5000       ; save energies every 10.0 ps
nstlog         = 5000       ; update log file every 10.0 ps
nstxout-compressed = 5000    ; save coordinates every 10.0 ps
; Bond parameters
continuation    = yes       ; continuing from NPT
constraint_algorithm = lincs ; holonomic constraints
constraints     = h-bonds   ; bonds to H are constrained
lincs_iter     = 1         ; accuracy of LINCS
lincs_order    = 4         ; also related to accuracy
; Neighbor searching and vdW
cutoff-scheme  = Verlet
ns_type        = grid      ; search neighboring grid cells
nstlist        = 20        ; largely irrelevant with Verlet
rlist          = 1.2
vdwtype        = cutoff
vdw-modifier   = force-switch
rvdw-switch    = 1.0
rvdw           = 1.2      ; short-range van der Waals cutoff (in nm)
; Electrostatics
coulombtype    = PME        ; Particle Mesh Ewald for long-range electrostatics
rcoulomb       = 1.2
pme_order      = 4         ; cubic interpolation
fourierspacing = 0.16     ; grid spacing for FFT
; Temperature coupling
tcoupl         = V-rescale   ; modified Berendsen thermostat
tc-grps        = Protein_UNK Water_and_ions ; two coupling groups - more accurate
tau_t          = 0.1 0.1    ; time constant, in ps
ref_t          = 310.15 310.15 ; reference temperature, one for each group, in K

; Pressure coupling
pcoupl         = Parrinello-Rahman ; pressure coupling is on for NPT

```


(Lanjutan)

```
pcoupltype      = isotropic      ; uniform scaling of box vectors
tau_p           = 2.0            ; time constant, in ps
ref_p           = 1.0            ; reference pressure, in bar
compressibility = 4.5e-5         ; isothermal compressibility of water,
bar^-1
; Periodic boundary conditions
pbc             = xyz           ; 3-D PBC
; Dispersion correction is not used for proteins with the C36 additive FF
DispCorr        = no
; Velocity generation
gen_vel         = no           ; continuing from NPT equilibration
```

Lampiran 7. File Masukan MMPBSA.in

Sample input file for PB calculation building the Amber topologies from structures. Please refer to the section "How gmx_MMPBSA works"

```
&general  
startframe=1,  
endframe=5001,  
temperature=310.15  
forcefields="oldff/leaprc.ff99SB,leaprc.gaff2"  
/  
&pb  
istrng=0.15, fillratio=4.0  
/
```

Lampiran 8. File Masukan MMGBSA.in

Sample input file for GB calculation

#This input file is meant to show only that gmx_MMPBSA works. Although, we tried to use the

input files as recommended in the

#Amber manual, some parameters have been changed to perform more expensive calculations

in a reasonable amount of time. Feel free to change the parameters

#according to what is better for your system.

&general

sys_name="Prot-Lig-ST",

startframe=1,

endframe=5001,

temperature=310.15

forcefields="oldff/leaprc.ff99SB,leaprc.gaff2"

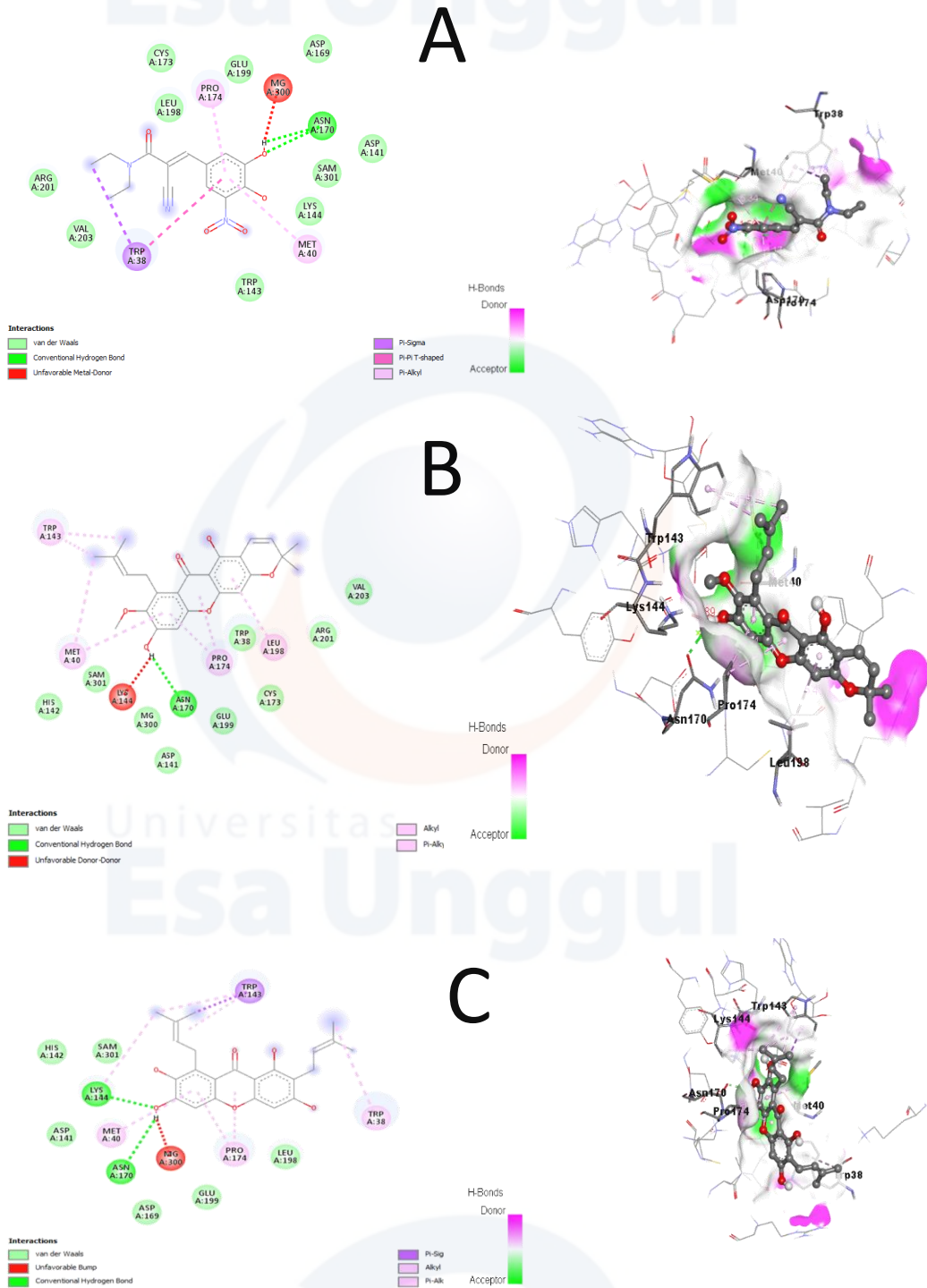
/

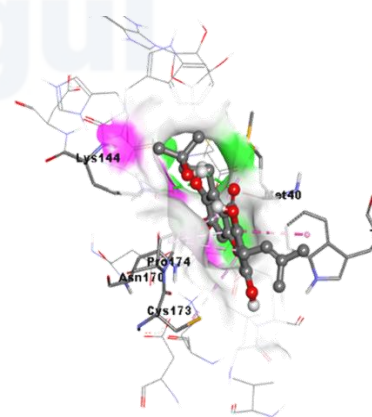
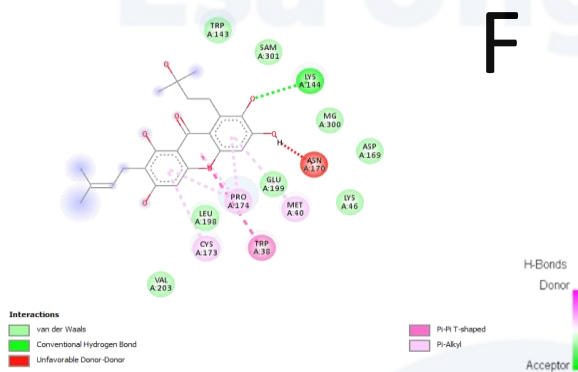
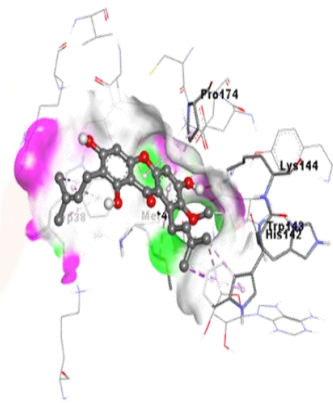
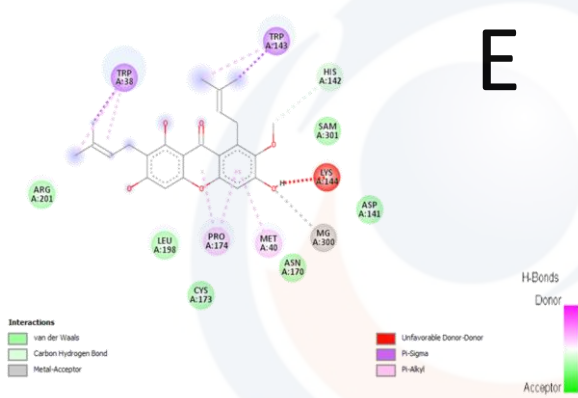
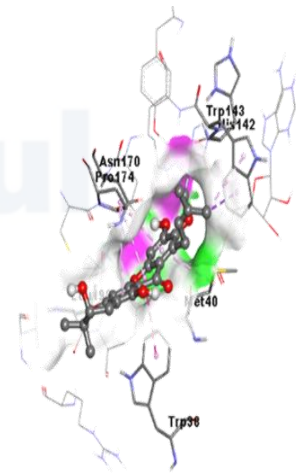
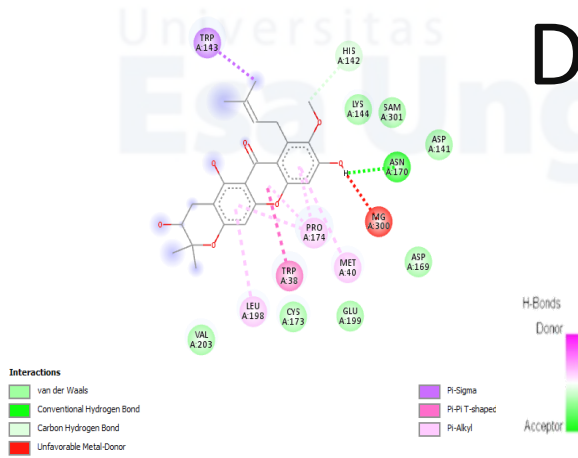
&gb

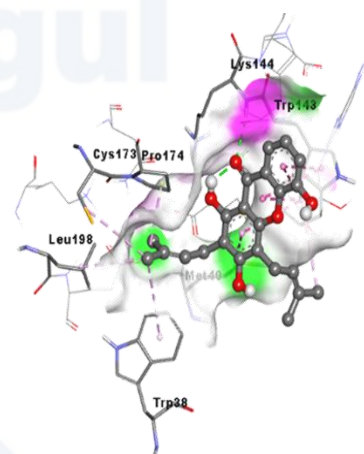
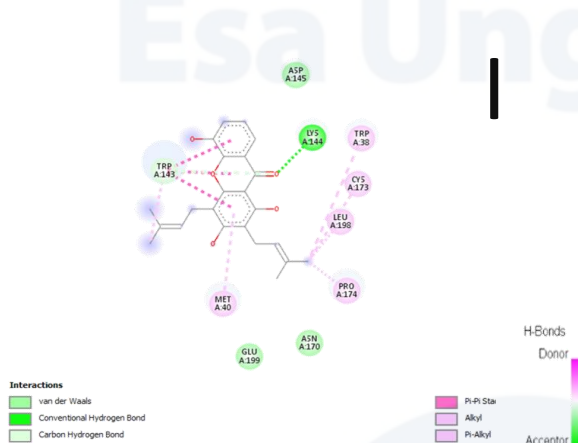
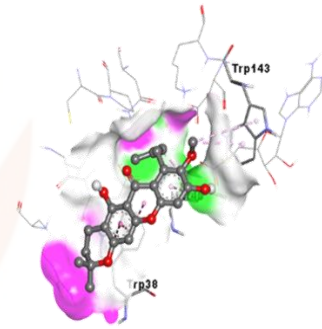
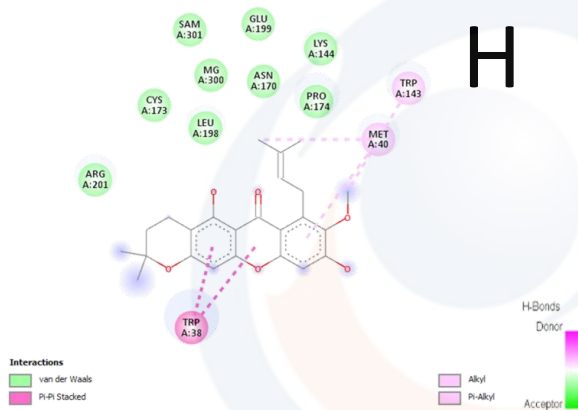
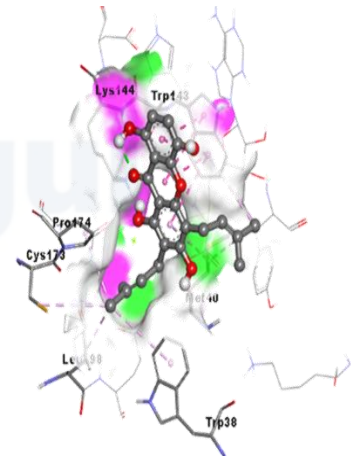
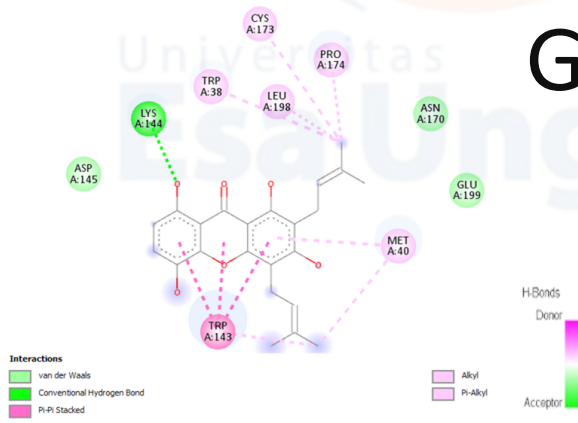
igb=5, saltcon=0.150,

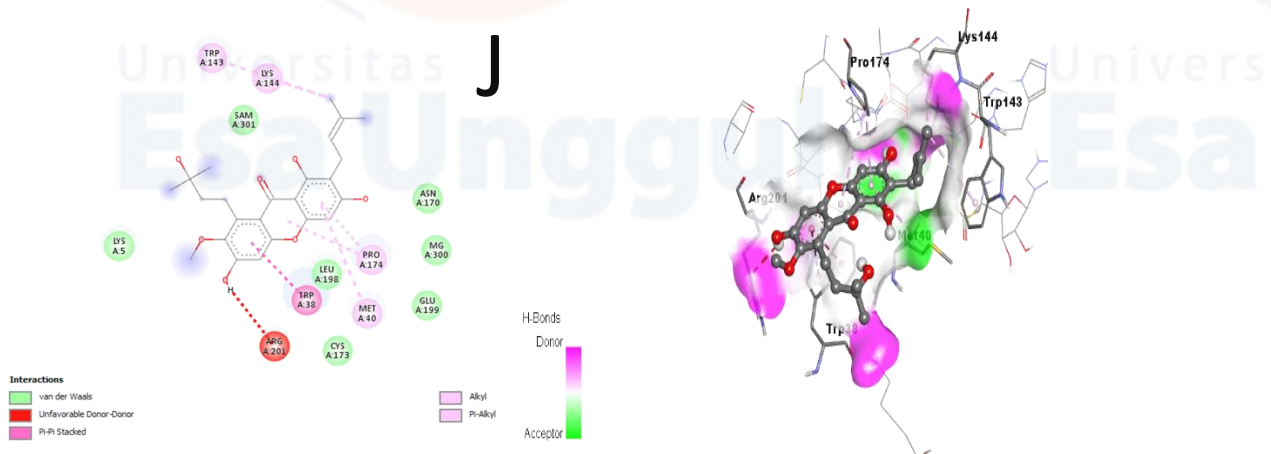
/

Lampiran 9. Hasil visualisasi 2D dan 3D interaksi antara ligan dengan protein reseptor COMT









(A) Entacapone, (B) Garciniafuran (C) γ -mangostin, (D) Mangostanol (E) α -mangostin, (F) Garcinone C, (G) Gartanin, (H) 3-Isomangostin, (I) 8-Deoxygartanin, (J) Garcinone D

Lampiran 10. File Notepad hasil penambatan molekuler (Energi afinitas)

```
Scoring function : vina
Rigid receptor: protein.pdbqt
Ligand: garciniafuran.pdbqt
Grid center: X -4.055 Y -12.232 Z -17.416
Grid size : X 10 Y 20 Z 16
Grid space : 0.375
Exhaustiveness: 8
CPU: 0
Verbosity: 1

Computing Vina grid ... done.
Performing docking (random seed: -379132837) ...
0% 10 20 30 40 50 60 70 80 90 100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
```

mode	affinity	dist from best mode	
	(kcal/mol)	rmsd l.b.	rmsd u.b.
1	-8.032	0	0
2	-7.449	2.387	8.076
3	-7.315	2.09	3.789
4	-7.274	2.872	8.161
5	-6.996	2.503	8.505
6	-6.416	1.996	7.912
7	-6.062	1.833	2.127
8	-5.337	3.374	8.409
9	-4.017	2.162	4.138

Garciniafuran

```
Scoring function : vina
Rigid receptor: protein.pdbqt
Ligand: Gammamangostin.pdbqt
Grid center: X -4.055 Y -12.232 Z -17.416
Grid size : X 10 Y 20 Z 16
Grid space : 0.375
Exhaustiveness: 8
CPU: 0
Verbosity: 1

Computing Vina grid ... done.
Performing docking (random seed: -1489154644) ...
0% 10 20 30 40 50 60 70 80 90 100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
```

mode	affinity	dist from best mode	
	(kcal/mol)	rmsd l.b.	rmsd u.b.
1	-7.057	0	0
2	-6.785	1.559	2.255
3	-6.246	2.469	8.565
4	-5.652	2.699	8.619
5	-5.596	1.459	7.647
6	-5.574	2.086	7.022
7	-5.462	2.431	8.167
8	-5.4	2.423	8.121
9	-5.238	2.628	4.386

γ-mangostin

```
Scoring function : vina
Rigid receptor: protein.pdbqt
Ligand: Mangostanol.pdbqt
Grid center: X -4.055 Y -12.232 Z -17.416
Grid size : X 10 Y 20 Z 16
Grid space : 0.375
Exhaustiveness: 8
CPU: 0
Verbosity: 1

Computing Vina grid ... done.
Performing docking (random seed: 533353877) ...
0% 10 20 30 40 50 60 70 80 90 100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
```

mode	affinity	dist from best mode	
	(kcal/mol)	rmsd l.b.	rmsd u.b.
1	-7.051	0	0
2	-6.58	3.227	8.079
3	-6.531	3.826	8.3
4	-6.494	2.201	8.379
5	-6.217	3.348	7.835
6	-4.628	2.478	8.2
7	-4.611	2.685	7.941
8	-4.386	1.821	2.223
9	-4.275	2.672	8.295

Mangostanol

```
Scoring function : vina
Rigid receptor: protein.pdbqt
Ligand: Entacapone.pdbqt
Grid center: X -4.055 Y -12.232 Z -17.416
Grid size : X 10 Y 20 Z 16
Grid space : 0.375
Exhaustiveness: 8
CPU: 0
Verbosity: 1

Computing Vina grid ... done.
Performing docking (random seed: -261749962) ...
0% 10 20 30 40 50 60 70 80 90 100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
```

mode	affinity	dist from best mode	
	(kcal/mol)	rmsd l.b.	rmsd u.b.
1	-6.915	0	0
2	-6.749	1.276	6.777
3	-6.359	3.5	5.928
4	-6.265	1.147	6.945
5	-6.232	3.667	6.113
6	-5.79	4.097	6.826
7	-5.534	4.718	7.383
8	-5.452	5.326	8.939
9	-5.351	3.181	4.563

Entacapone (Standard)

```
Scoring function : vina
Rigid receptor: protein.pdbqt
Ligand: Alphamangostin.pdbqt
Grid center: X -4.055 Y -12.232 Z -17.416
Grid size : X 10 Y 20 Z 16
Grid space : 0.375
Exhaustiveness: 8
CPU: 0
Verbosity: 1

Computing Vina grid ... done.
Performing docking (random seed: 1186651612) ...
0% 10 20 30 40 50 60 70 80 90 100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
```

mode	affinity	dist from best mode	
	(kcal/mol)	rmsd l.b.	rmsd u.b.
1	-6.729	0	0
2	-6.516	2.272	8.646
3	-6.486	1.604	2.149
4	-6.103	2.354	7.236
5	-5.999	2.261	8.085
6	-5.889	2.375	3.38
7	-5.851	1.449	2.27
8	-5.787	1.706	7.642
9	-1.246	2.707	8.072

α-mangostin

```
Scoring function : vina
Rigid receptor: protein.pdbqt
Ligand: GarcinoneC.pdbqt
Grid center: X -4.055 Y -12.232 Z -17.416
Grid size : X 10 Y 20 Z 16
Grid space : 0.375
Exhaustiveness: 8
CPU: 0
Verbosity: 1

Computing Vina grid ... done.
Performing docking (random seed: -361373806) ...
0% 10 20 30 40 50 60 70 80 90 100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
```

mode	affinity	dist from best mode	
	(kcal/mol)	rmsd l.b.	rmsd u.b.
1	-6.699	0	0
2	-5.743	4.504	5.885
3	-5.37	1.546	1.934
4	-5.115	3.413	4.596
5	-5.077	4.311	8.435
6	-5.018	5.527	6.448
7	-4.76	3.754	8.105
8	-4.674	4.468	8.449
9	-4.433	2.599	4.637

Garcinone C

(Lanjutan)

Scoring function : vina
 Rigid receptor: protein.pdbqt
 Ligand: Gartanin.pdbqt
 Grid center: X -4.055 Y -12.232 Z -17.416
 Grid size : X 10 Y 20 Z 16
 Grid space : 0.375
 Exhaustiveness: 8
 CPU: 0
 Verbosity: 1

Computing Vina grid ... done.
 Performing docking (random seed: -1008741948) ...
 0% 10 20 30 40 50 60 70 80 90 100%
-----	-----	-----	-----	-----	-----	-----	-----
-----	-----	-----	-----	-----	-----	-----	-----

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.671	0	0
2	-6.259	1.625	4.828
3	-6.18	5.403	9.306
4	-5.926	3.902	6.458
5	-5.738	4.969	8.892
6	-5.52	4.033	7.372
7	-5.402	4.46	8.085
8	-5.356	3.844	6.837
9	12.28	3.646	6.505

Gartanin

Scoring function : vina
 Rigid receptor: protein.pdbqt
 Ligand: 3_isomangostin.pdbqt
 Grid center: X -4.055 Y -12.232 Z -17.416
 Grid size : X 10 Y 20 Z 16
 Grid space : 0.375
 Exhaustiveness: 8
 CPU: 0
 Verbosity: 1

Computing Vina grid ... done.
 Performing docking (random seed: 2084557400) ...
 0% 10 20 30 40 50 60 70 80 90 100%
-----	-----	-----	-----	-----	-----	-----	-----
-----	-----	-----	-----	-----	-----	-----	-----

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.596	0	0
2	-6.523	2.585	8.385
3	-6.469	3.069	4.938
4	-5.864	2.348	7.654
5	-5.814	1.806	8.083
6	-5.265	2.528	8.088
7	-5.099	2.333	8.192
8	-4.596	2.993	3.949
9	-4.468	2.972	8.332

3-Isomangostin

Scoring function : vina
 Rigid receptor: protein.pdbqt
 Ligand: 8_deoxygartanin.pdbqt
 Grid center: X -4.055 Y -12.232 Z -17.416
 Grid size : X 10 Y 20 Z 16
 Grid space : 0.375
 Exhaustiveness: 8
 CPU: 0
 Verbosity: 1

Computing Vina grid ... done.
 Performing docking (random seed: 1445452280) ...
 0% 10 20 30 40 50 60 70 80 90 100%
-----	-----	-----	-----	-----	-----	-----	-----
-----	-----	-----	-----	-----	-----	-----	-----

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.53	0	0
2	-6.169	1.77	4.847
3	-6.15	5.279	9.211
4	-5.999	3.922	8.149
5	-5.579	3.591	8.294
6	-5.568	4.379	7.721
7	-5.513	4.863	10.01
8	-5.502	4.114	9.444
9	-5.477	3.773	5.86

8-Deoxygartanin

Scoring function : vina
 Rigid receptor: protein.pdbqt
 Ligand: GarcinoneD.pdbqt
 Grid center: X -4.055 Y -12.232 Z -17.416
 Grid size : X 10 Y 20 Z 16
 Grid space : 0.375
 Exhaustiveness: 8
 CPU: 0
 Verbosity: 1

Computing Vina grid ... done.
 Performing docking (random seed: 1098971865) ...
 0% 10 20 30 40 50 60 70 80 90 100%
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mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.185	0	0
2	-5.871	2.132	7.505
3	-5.397	2.636	7.226
4	-5.114	1.857	2.598
5	-5.097	1.82	7.772
6	-5.079	3.282	7.542
7	-4.765	2.272	4.568
8	-4.348	2.641	7.994
9	-4.096	2.219	4.717

Garcinone D