

BAB V

PENUTUP

5.1 Kesimpulan

Berdasarkan hasil-hasil penelitian yang diperoleh serta pembahasannya maka dapat disimpulkan sebagai berikut:

1. Pada reseptor Mpro/3CLpro senyawa yang bersifat aktif dapat menghambat infeksi virus dan memiliki nilai *binding affinity* terkecil yaitu senyawa Amentoflavone dan Taiwanhomoflavone A dengan nilai sebesar -9,7 kkal/mol dan juga senyawa Catechin Gallate yang memiliki nilai *binding affinity* sebesar -9,1 kkal/mol. Pada reseptor *spike glikoprotein* senyawa yang memiliki nilai *binding affinity* terkecil yaitu senyawa Withaferin A dengan nilai sebesar -8,0 kkal/mol. Pada reseptor ACE2 senyawa yang dapat menghambat infeksi virus yaitu senyawa Amentoflavone, Catechin Gallate, Epicatechin gallate, Lactucopicrin 15-Oxalate, Rosmanol, Silibin, Withaferin A, dan Taiwanhomoflavone A dengan nilai *binding affinity* sebesar -8,0 hingga -8,9 kkal/mol. Senyawa 1,8-sineol memiliki nilai *binding affinity* sebanding yaitu -4,2 hingga -4,6 kkal/mol pada ketiga reseptor.
2. Dari hasil *molecular docking* yang dilakukan adanya ikatan antara senyawa ligan dan reseptor pada residu asam amino. Pada reseptor Mpro/3CLpro, residu asam amino Cys 145, Ser 144 dan Glu 166 merupakan residu yang paling sering berinteraksi dengan ligan. Pada reseptor *spike glikoprotein*, residu asam amino Val 367 merupakan residu yang paling sering berinteraksi

dengan ligan. Pada reseptor ACE2, residu asam amino Trp 349 dan Asp 350 merupakan residu yang paling sering berinteraksi dengan ligan.

5.2 Saran

Disarankan kepada pihak-pihak yang ingin melakukan penelitian serupa atau yang ingin melanjutkan penelitian ini agar dilakukan pengujian lebih lanjut untuk validasi menggunakan model *in vitro* dan *in vivo* agar diketahui apakah senyawa-senyawa tersebut dapat digunakan dalam studi untuk penemuan obat maupun vaksin COVID-19.

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LAMPIRAN-LAMPIRAN

Lampiran 1. Prosedur kerja *molecular docking* dengan *Autodock vina*

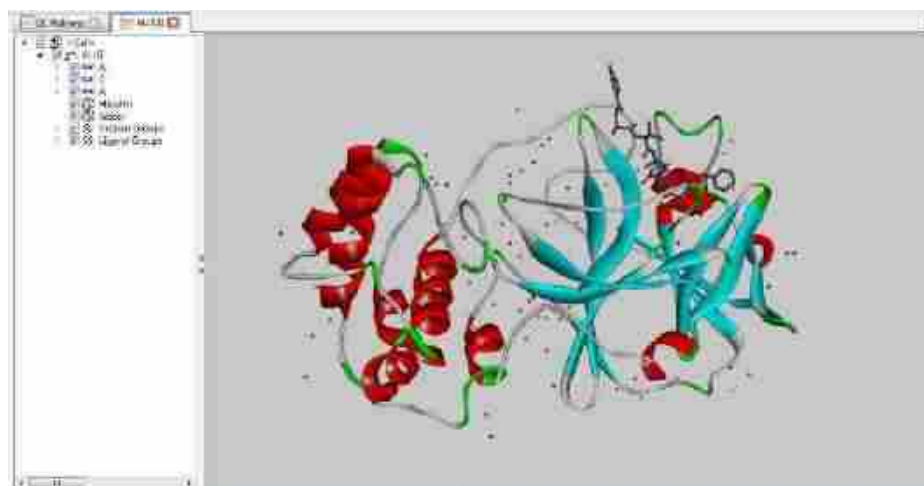
a. Penyiapan reseptor

1. Pengunduhan makromolekul dari Protein Data Bank dengan situs <https://www.rcsb.org/>. identitas molekul tersebut yaitu Mpro/3CLpro (6LU7), *Spike glikoprotein* (7BZ5), dan ACE2 (6M0J). makromolekul diunduh dalam format .pdb.



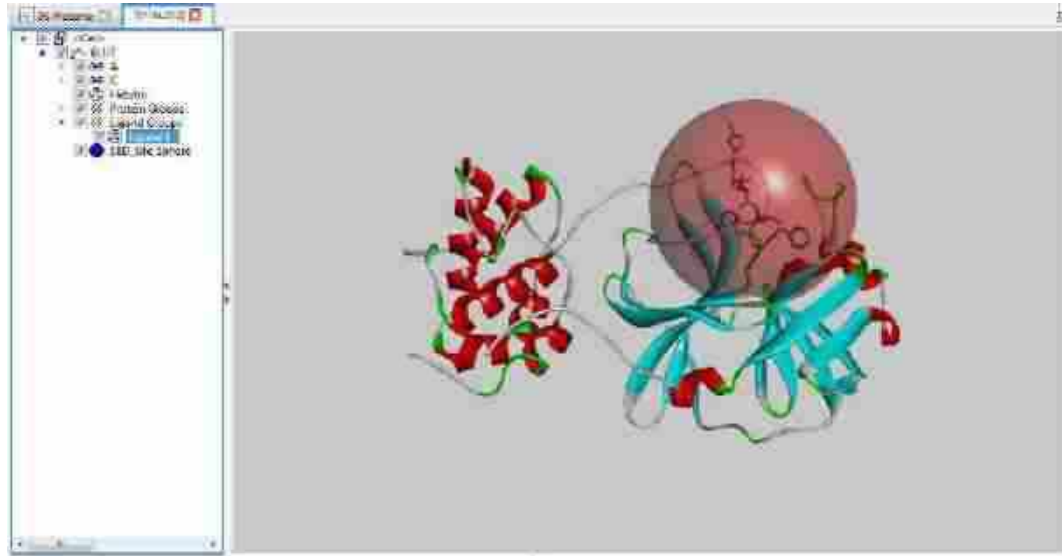
Pilih 'Download Files → PDB Format'

2. Pemisahan makromolekul dari molekul air dan ligan dengan *discovery studio*. Disimpan dalam format .pdb

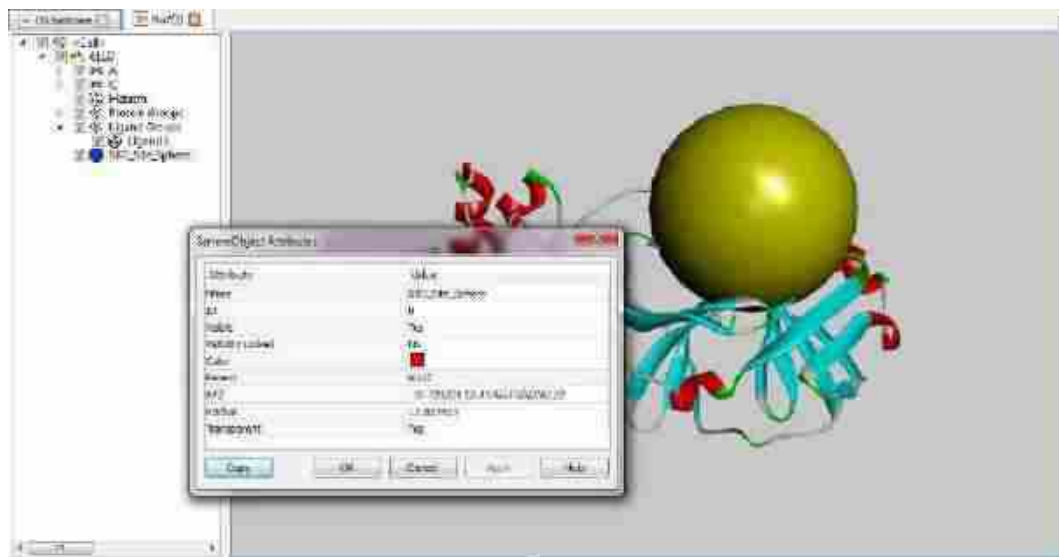


Pilih 'Water → Delete'

3. Pengaturan *grid box* yaitu nilai center X, Y, dan Z. disimpan dalam format .pdb



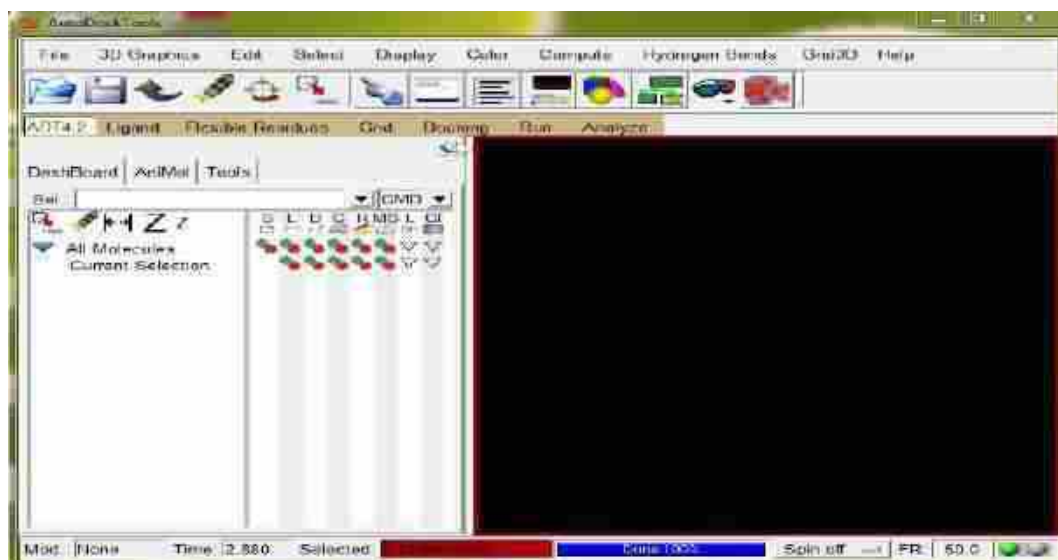
Pilih 'Ligan Groups → Define and Edit Binding Site → From Current Selection'



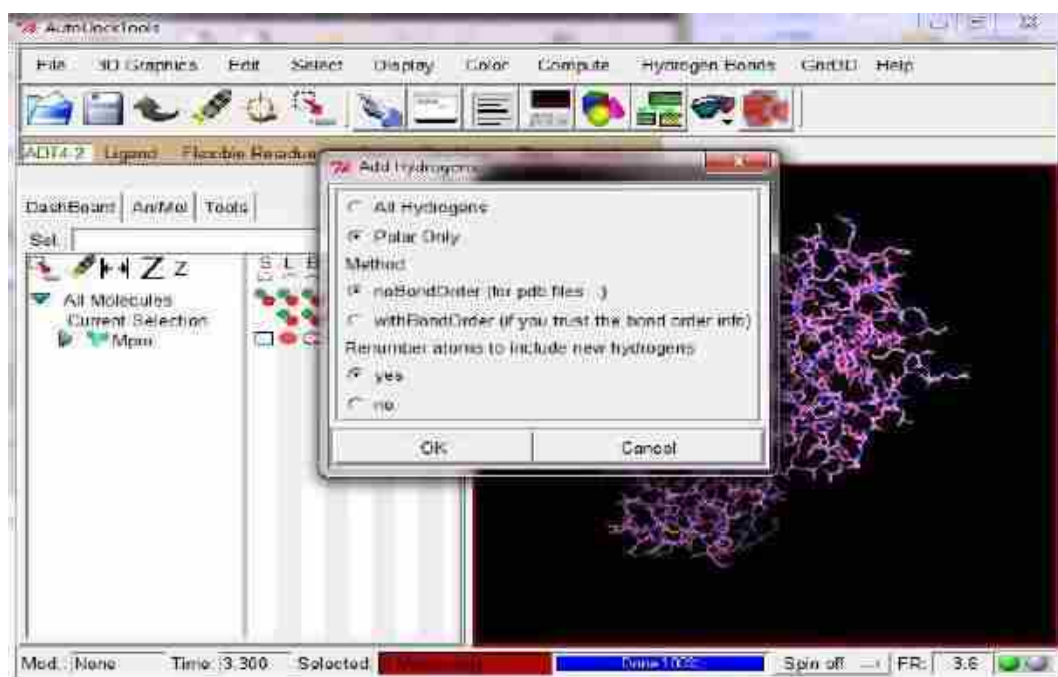
Klik Kanan pilih 'Artibuttes'

Save as 'Mpro.pdb'

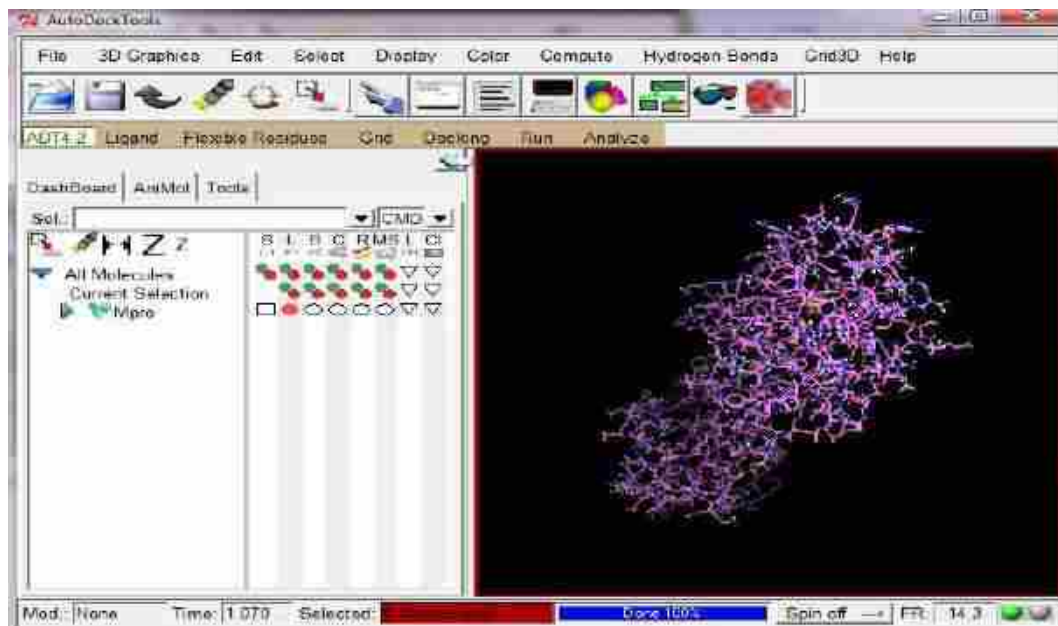
4. Optimasi Makromolekul dengan Autodock tools yaitu penambahan atom hidrogen. Disimpan dalam format .pdbqt



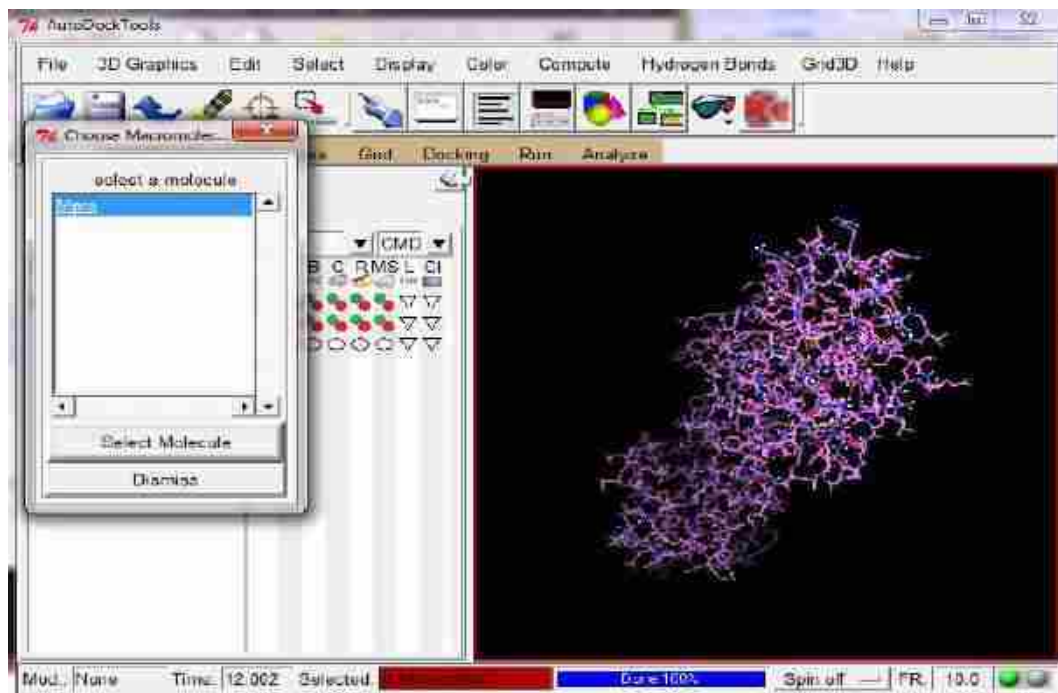
Pilih 'File → Read Molecule', pilih molekul yang akan digunakan.



Pilih 'Edit → Hydrogens → add → Polar Only → Ok'



Pilih 'Edit → Charges → Add Kollman charges'



Pilih 'Grid → macromolecule → Choose → Select Molecule → Ok'

Save as 'Mpro.pdbqt'

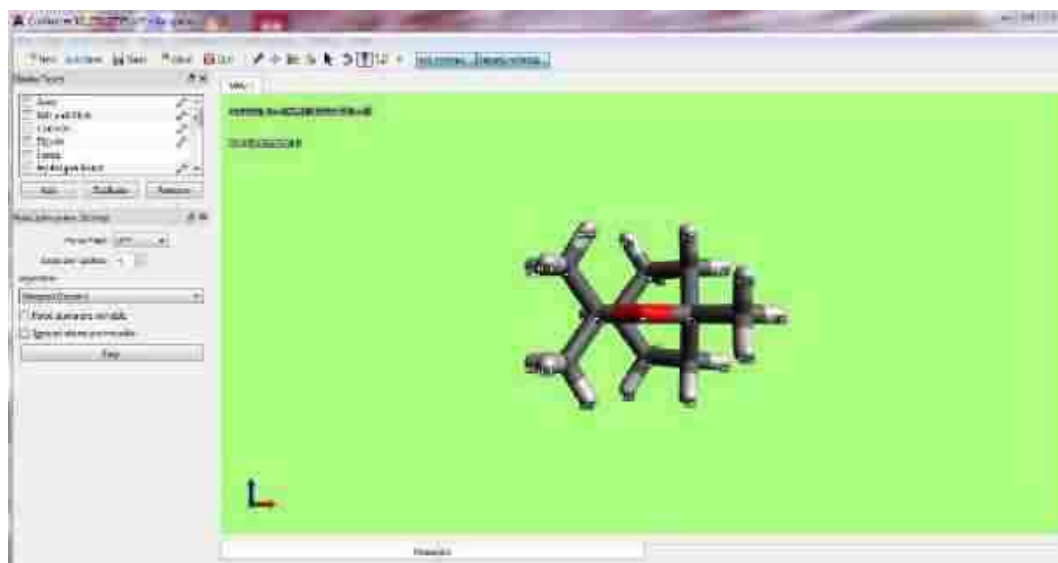
b. Penyiapan Ligan

1. Pengujian Hukum Lima Lipinski dengan SWISS ADME dengan situs <http://www.swissadme.ch/index.php>.



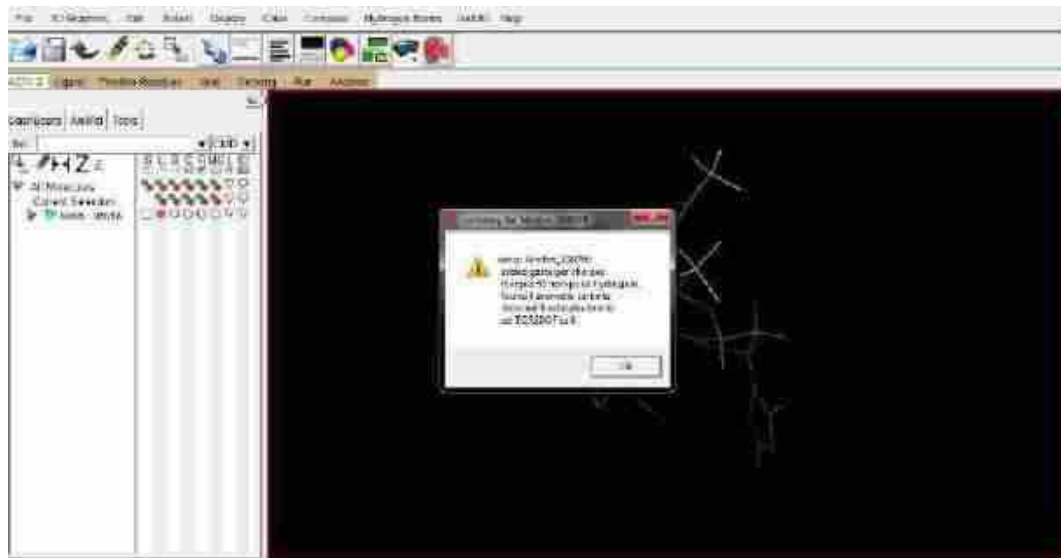
Pilih 'Download → 3D Conformer → SDF → Save'

3. Format ligan diubah menjadi .pdb dengan Advogardo

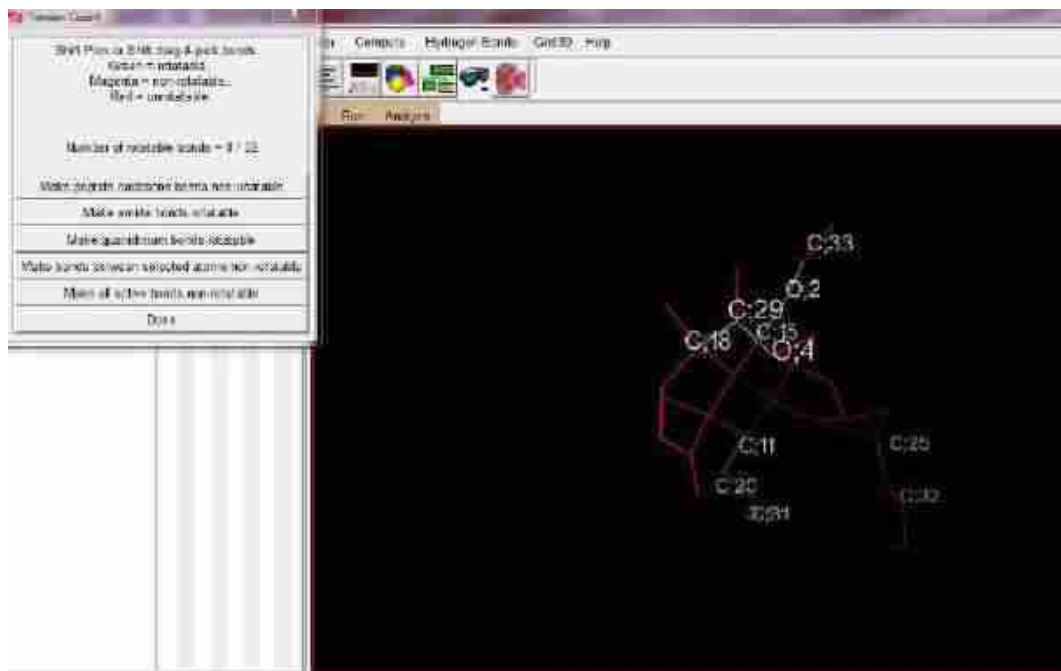


Pilih Save as 'Ligan.pdb'

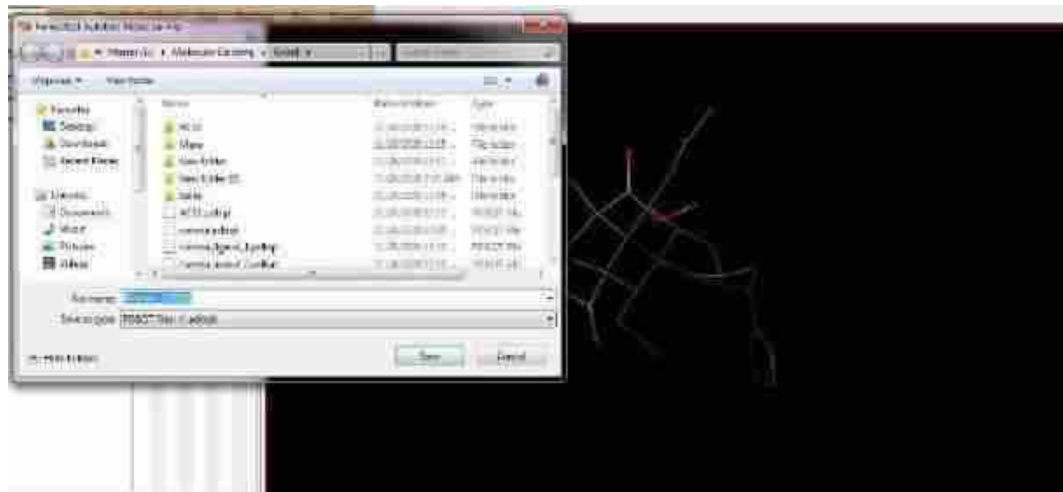
4. Optimasi struktur ligan dengan Autodock tools



Pilih 'Ligand → Input → Open → pilih ligan yang akan dipakai → Open → Ok'



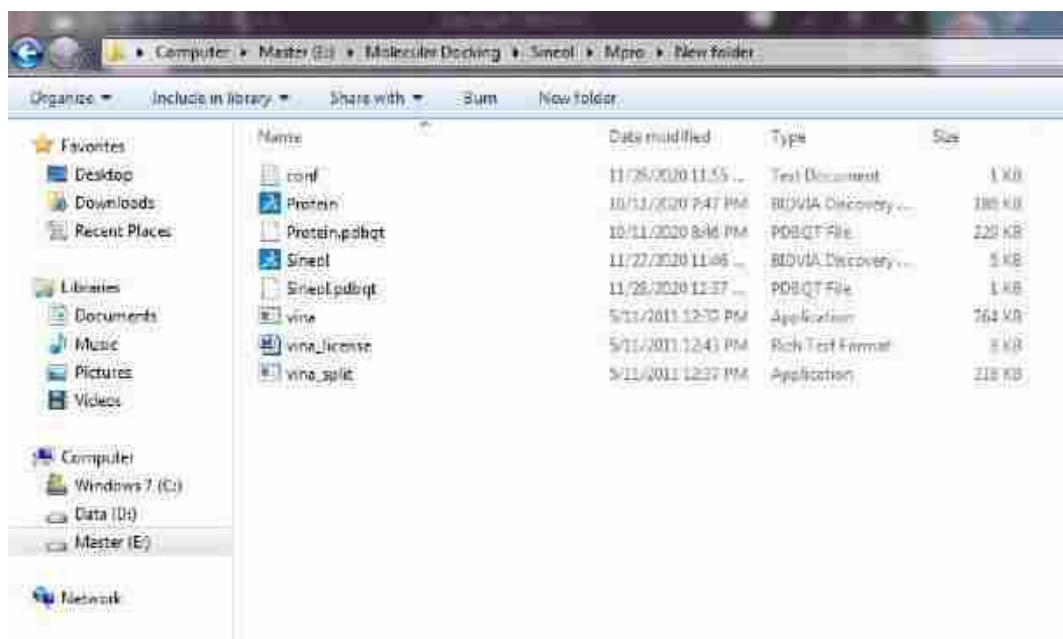
Pilih 'Torsion Tree → Choose Torsions → Done'



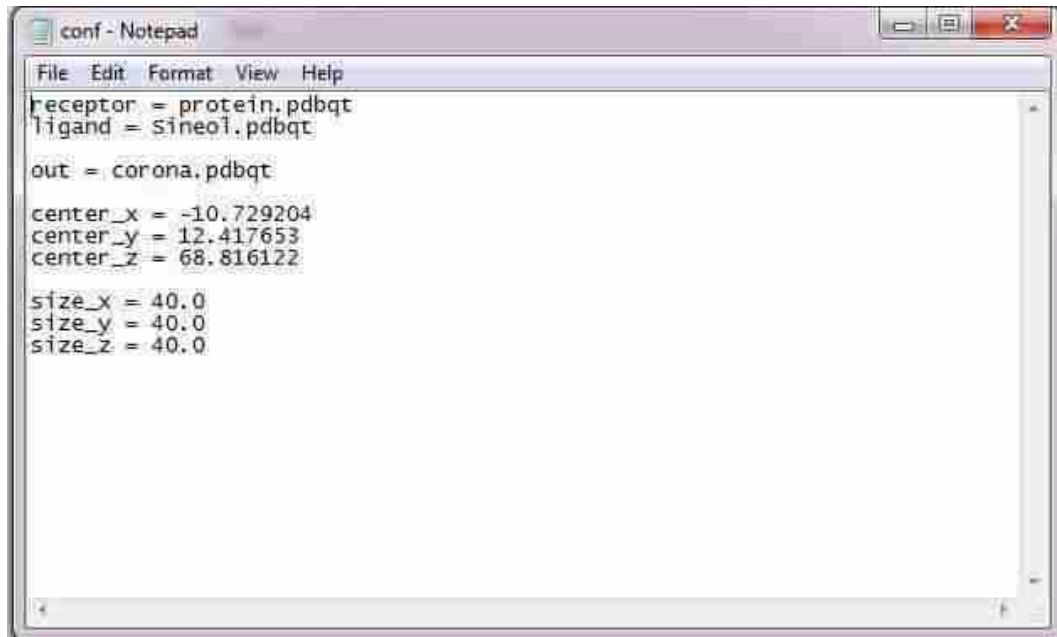
Pilih 'Ligan → Output → Save as PDBQT → save'

c. *Molecular docking* dengan *Autodock vina*

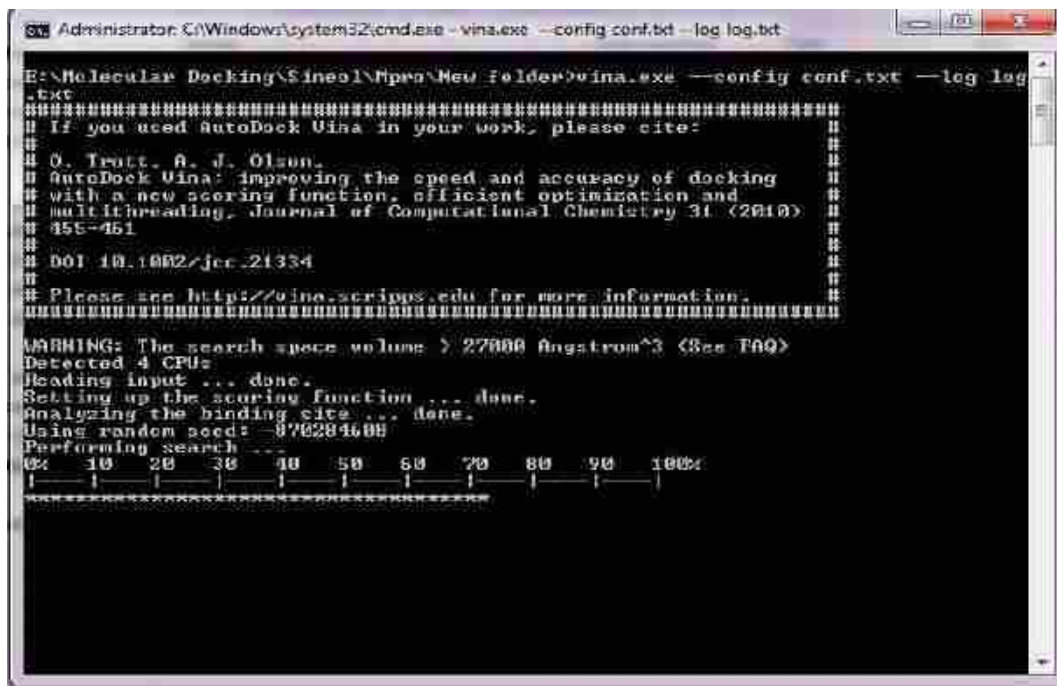
1. Menyimpan file ligan dan protein yang telah disiapkan dalam satu file kerja



2. Membuat file konfigurasi *vina* pada notepad, disimpan dengan nama conf.



3. *Autodock vina* dijalankan melalui perintah *command prompt*



Tekan 'Shift + Ctrl + Enter + Tombol kanan pada mouse / tombol kanan pada touchpad → Open command window here'

Ketik perintah '*vina.exe -config conf.txt -log log.txt* → Enter'

4. Hasil *Molecular docking*

```

Administrator: C:\Windows\system32\cmd.exe

E:\Molecular Docking\Bincal\Mpro\New folder>vina.exe --conf conf.txt --log log.txt
-----
If you used AutoDock Vina in your work, please cite:
-----
O. Trott, R. J. Olson,
AutoDock Vina: Improving the speed and accuracy of docking
with a new scoring function, efficient optimization and
multithreading, Journal of Computational Chemistry 31 (2010)
455-461
DOI: 10.1002/jcc.21334
Please see http://vina.scripps.edu for more information.
-----
WARNING: The search space volume is 270000 Angstrom^3 (See FAQ)
Detected 4 CPUs
Reading input ... done.
Sorting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -870384608
Performing search ...
|-----|
| 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% |
|-----|
done.
Refining results ... done.

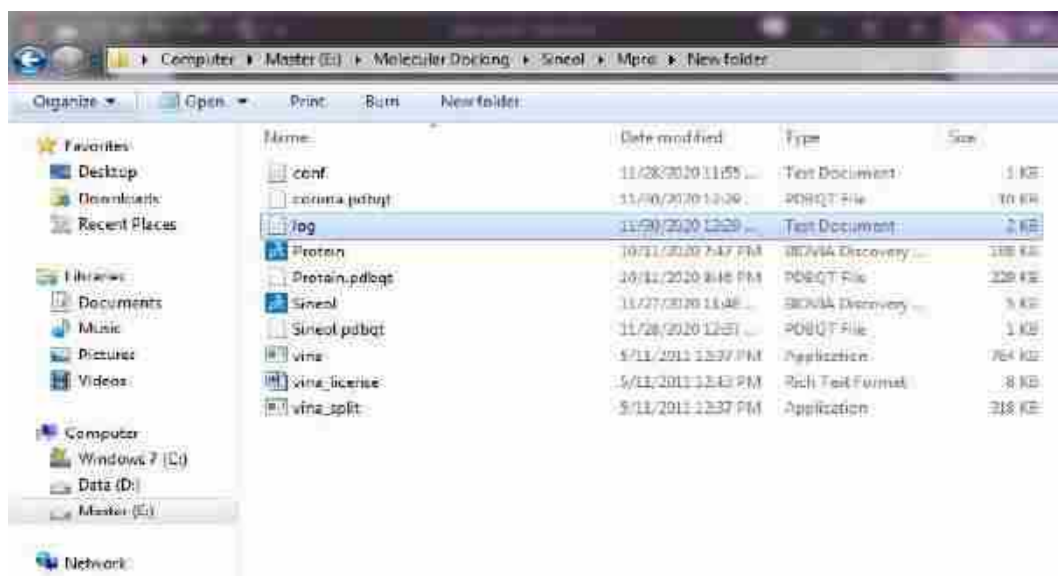
mode | affinity | dist from best mode
      | (local/global) | rmsd l.b. | rmsd h.b.
-----|-----|-----|-----|
1 | -4.2 | 0.000 | 0.000
2 | -4.2 | 1.520 | 2.033
3 | -4.1 | 0.200 | 5.257
4 | -4.1 | 3.629 | 4.420
5 | -4.1 | 1.755 | 3.451
6 | -4.0 | 15.231 | 17.544
7 | -4.0 | 3.961 | 6.380
8 | -3.9 | 0.960 | 3.360
9 | -3.9 | 16.203 | 19.519

Writing output ... done.

E:\Molecular Docking\Bincal\Mpro\New folder>

```

Dalam folder kerja akan muncul folder baru 'log.txt' setelah proses *docking* selesai



```

log - Notepad
File Edit Format View Help
#####
# If you used AutoDock Vina in your work, please cite:
#
# O. Trott, A. J. Olson,
# AutoDock Vina: improving the speed and accuracy of docking
# with a new scoring function, efficient optimization and
# multithreading, Journal of Computational Chemistry 31 (2010)
# 455-461
#
# DOI 10.1002/jcc.21334
#
# Please see http://vina.scripps.edu for more information.
#####
WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -870284608
Performing search ... done.
Refining results ... done.

mode | affinity | dist from best mode
      | (kcal/mol) | rmsd l.b. | rmsd u.b.
-----|-----|-----|-----
1 | -4.2 | 0.000 | 0.000
2 | -4.2 | 1.528 | 3.043
3 | -4.1 | 4.200 | 5.957
4 | -4.1 | 3.699 | 5.420
5 | -4.1 | 1.755 | 3.451
6 | -4.0 | 16.231 | 17.544
7 | -4.0 | 3.961 | 6.380
8 | -3.9 | 0.963 | 3.360
9 | -3.9 | 16.283 | 17.519

writing output ... done.

```

5. Visualisasi hasil moleculaf docking

```

Administrator: C:\Windows\system32\cmd.exe
E:\Molecular Docking\Singol\Huro>vina.exe --config conf.txt --log log.txt
#####
# If you used AutoDock Vina in your work, please cite:
#
# O. Trott, A. J. Olson,
# AutoDock Vina: improving the speed and accuracy of docking
# with a new scoring function, efficient optimization and
# multithreading, Journal of Computational Chemistry 31 (2010)
# 455-461
#
# DOI 10.1002/jcc.21334
#
# Please see http://vina.scripps.edu for more information.
#####
WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -422051100
Performing search ...
Progress: 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
#####
Refining results ... done.

mode | affinity | dist from best mode
      | (kcal/mol) | rmsd l.b. | rmsd u.b.
-----|-----|-----|-----
1 | -4.2 | 0.000 | 0.000
2 | -4.2 | 1.542 | 3.053
3 | -4.1 | 4.165 | 5.949
4 | -4.1 | 6.912 | 3.198
5 | -4.1 | 1.797 | 3.485
6 | -4.0 | 16.308 | 17.692
7 | -4.0 | 3.971 | 6.388
8 | -3.9 | 24.225 | 25.814
9 | -3.9 | 1.776 | 3.783

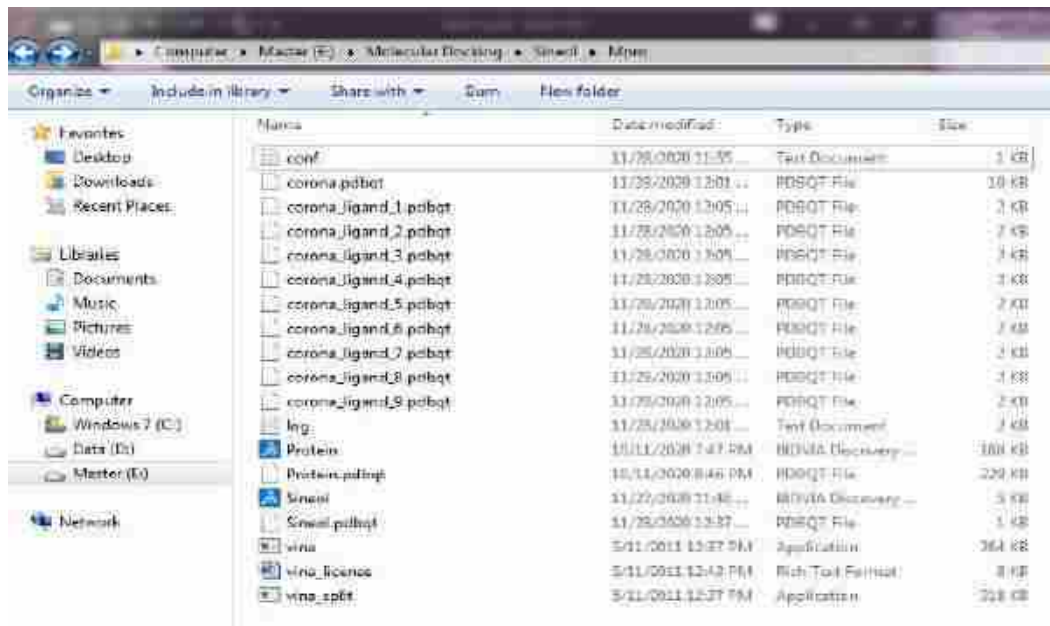
writing output ... done.

E:\Molecular Docking\Singol\Huro>vina_split --input corona.pdbqt
Prefix for ligands will be corona_ligand.
Prefix for flexible side chains will be corona_Flex_

E:\Molecular Docking\Singol\Huro>

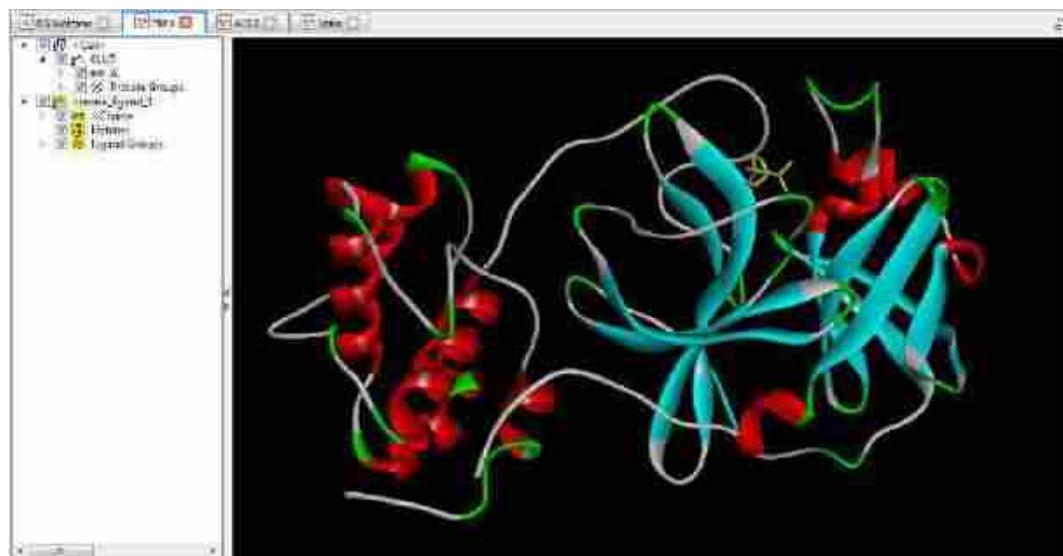
```

Ketik perintah 'vina_split --input corona.pdbqt (nama file output yang diinginkan)
→ enter'

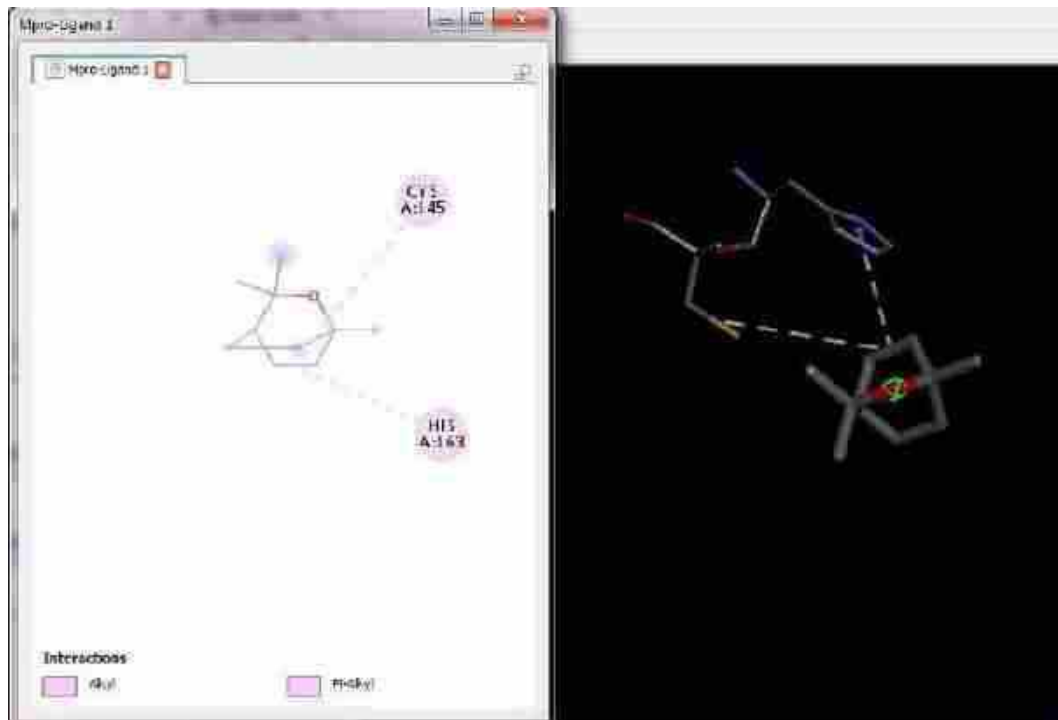


Akan muncul file output ligan dalam format .pdbqt dalam folder kerja.

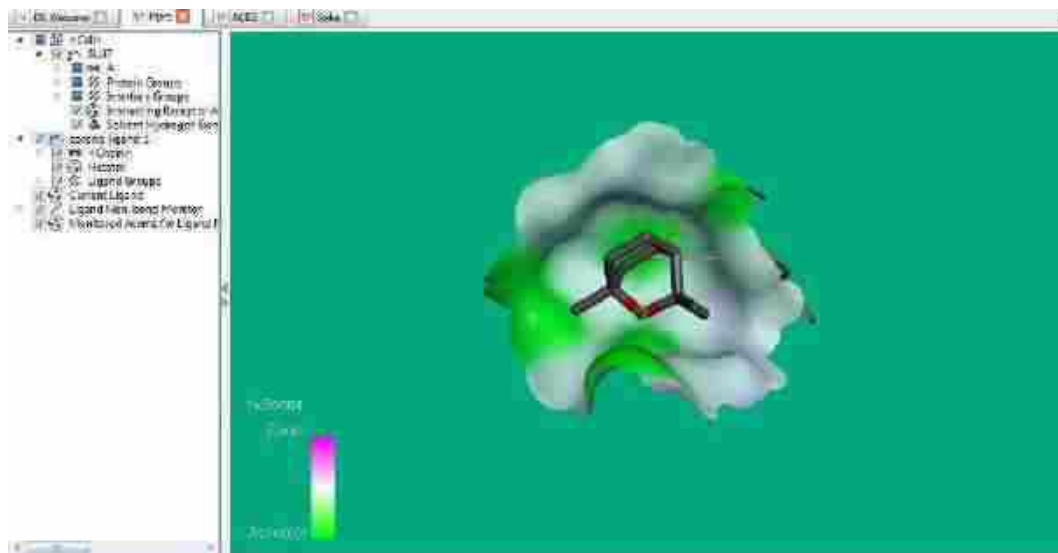
6. Melihat interaksi reseptor dan ligan dengan discovery studio



Pilih 'File → Open → pilih file reseptor yang telah dipreparasi → memasukan file output ligan'

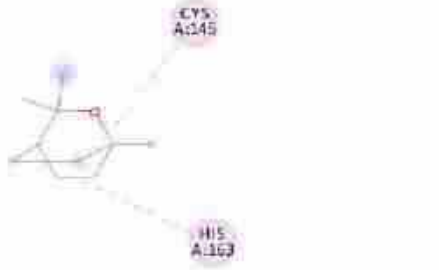
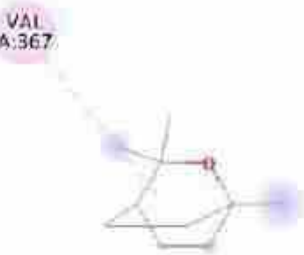
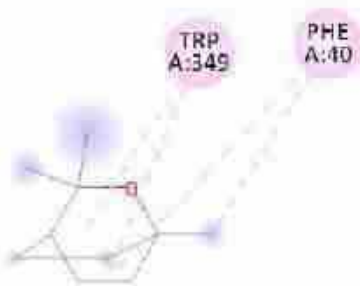

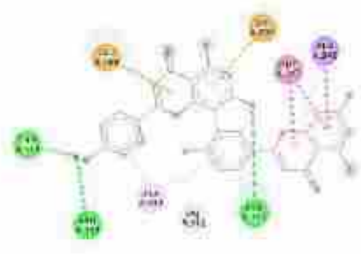
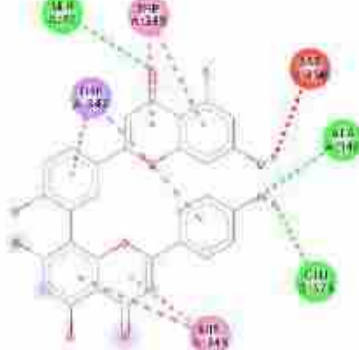


Untuk hasil 2D ‘Output Ligand → View Interactions → Ligand Interactions → Show 2D Diagram’

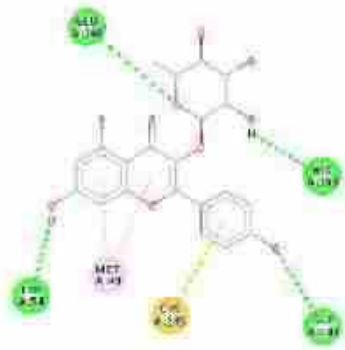


Untuk interaksi dengan ikatan hirogen ‘Display receptor surfaces → H-Bond’

Lampiran 2. Gambar 2D hasil *molecular docking* dengan *Autodock vina*

Ligan	Mpro	Spike	ACE2
1,8-Sineol	 <p>Interaksi: H-Bond</p>	 <p>Interaksi: H-Bond</p>	 <p>Interaksi: H-Bond</p>
Amentoflavone	 <p>Interaksi: H-Bond, Hydrophobic Contact, Pi-Stacking, Pi-Pi Stacking, Pi-Alkyl, Pi-Cation, Pi-Anion, Pi-Sulfur</p>	 <p>Interaksi: Hydrophobic Contact, Pi-Alkyl, Pi-Pi Stacking, Pi-Cation, Pi-Anion, Pi-Sulfur</p>	 <p>Interaksi: H-Bond, Hydrophobic Contact, Pi-Alkyl, Pi-Pi Stacking, Pi-Cation, Pi-Anion, Pi-Sulfur</p>

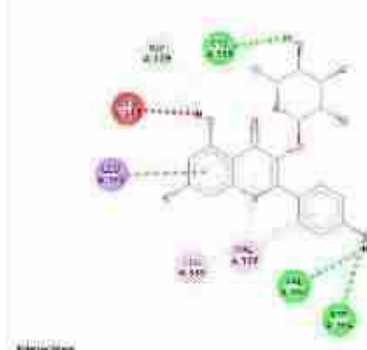
Afzelin



Interaktion

- Green circle: Conventional hydrogen bond
- Yellow circle: Hydrophobic

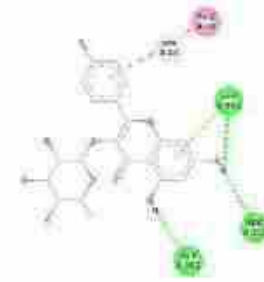
Phe A:40



Interaktion

- Green circle: Conventional hydrogen bond
- White circle: Other hydrogen bond
- Red circle: Unconventional hydrogen bond

Phe A:40

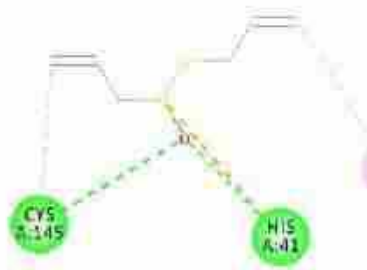


Interaktion

- Green circle: Conventional hydrogen bond
- Yellow circle: Hydrophobic

Phe A:40

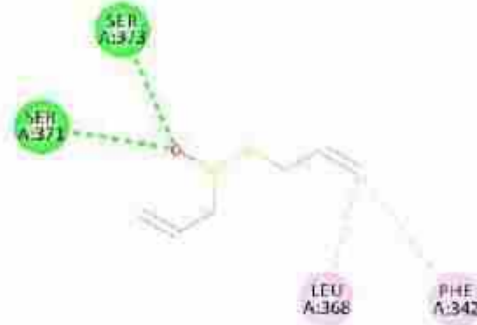
Alicin



Interaktion

- Green circle: Conventional hydrogen bond
- Yellow circle: Hydrophobic

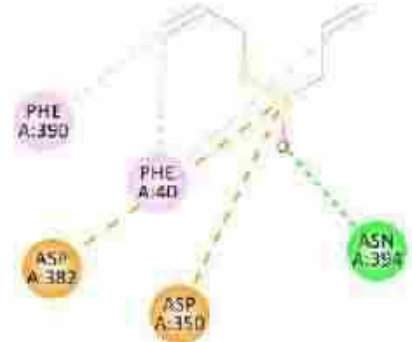
Phe A:40



Interaktion

- Green circle: Conventional hydrogen bond
- White circle: Other hydrogen bond

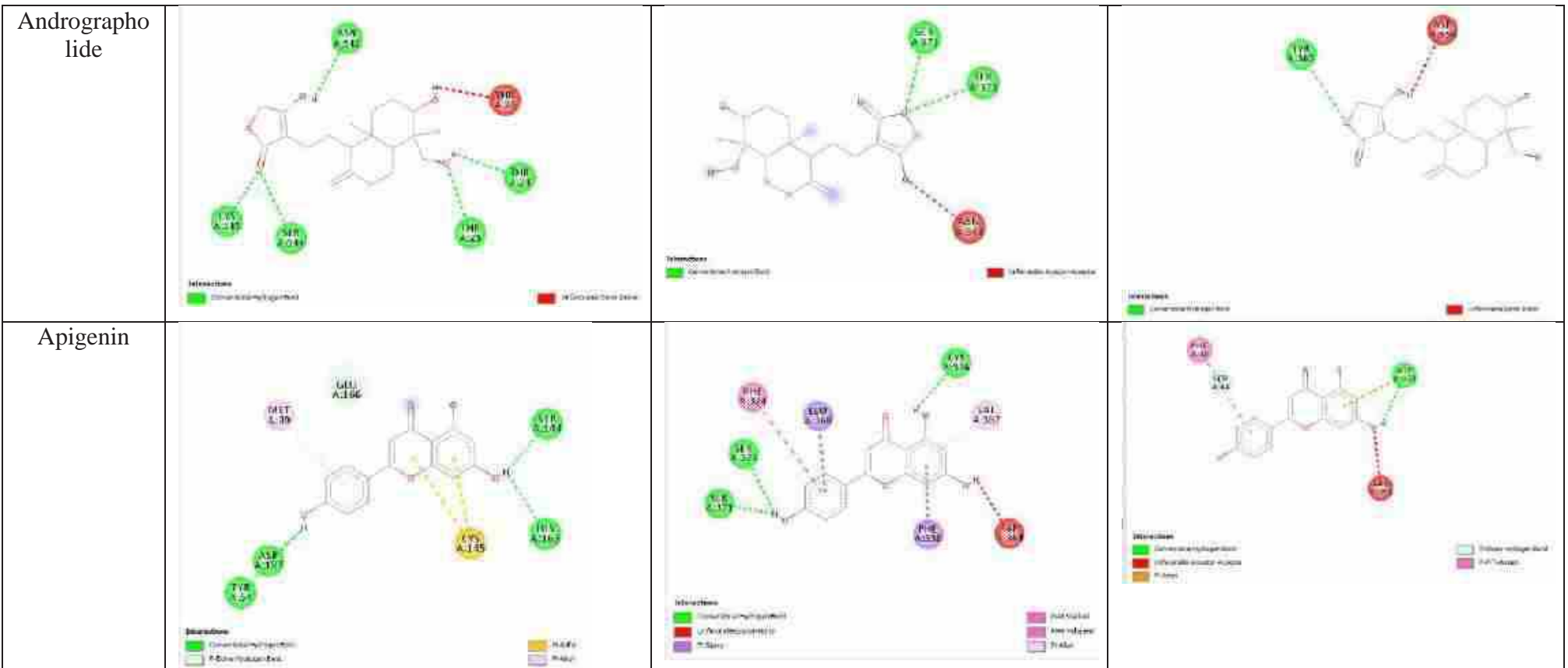
Phe A:40



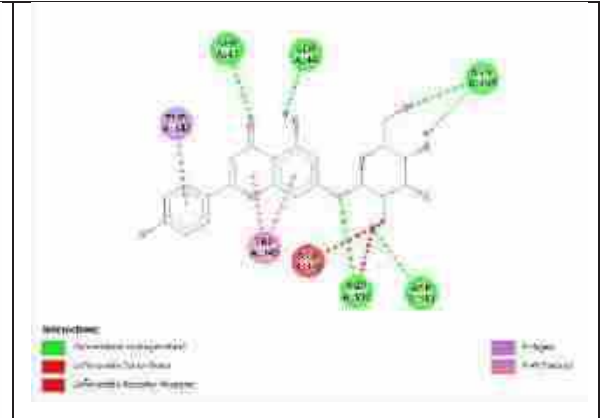
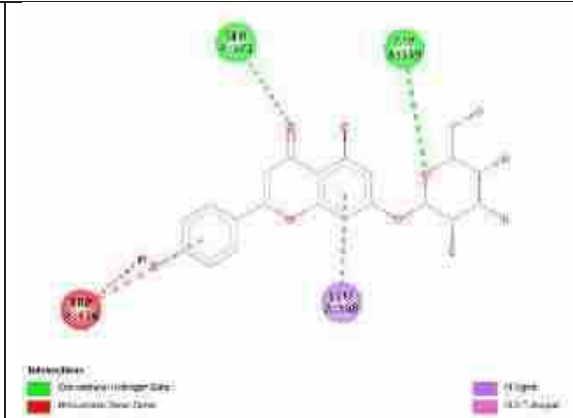
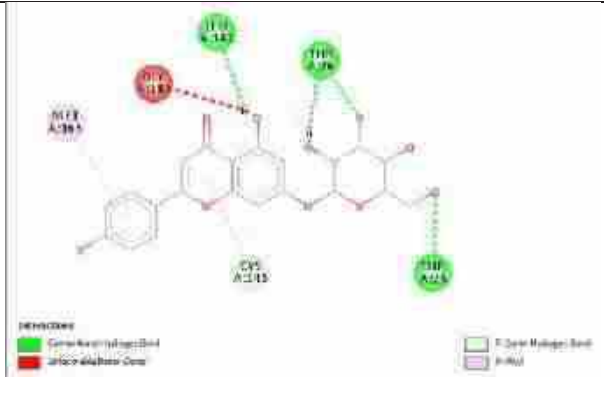
Interaktion

- Orange circle: Hydrophobic
- Green circle: Conventional hydrogen bond

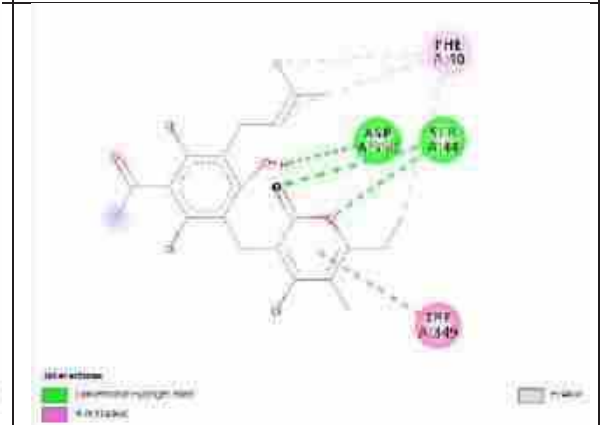
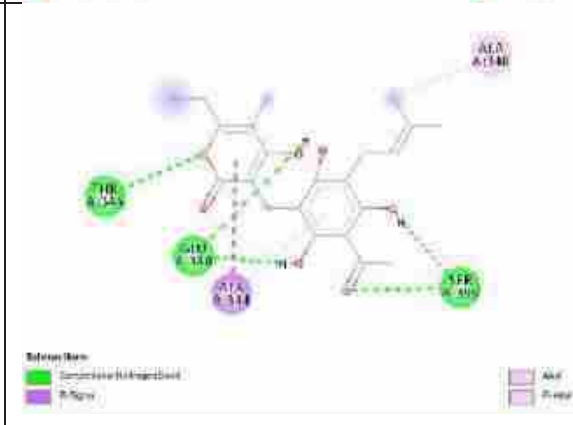
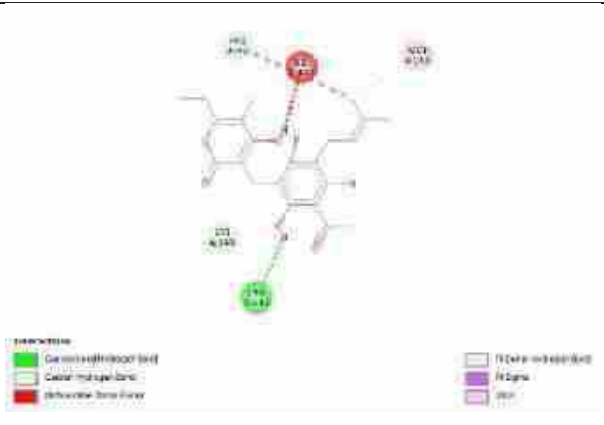
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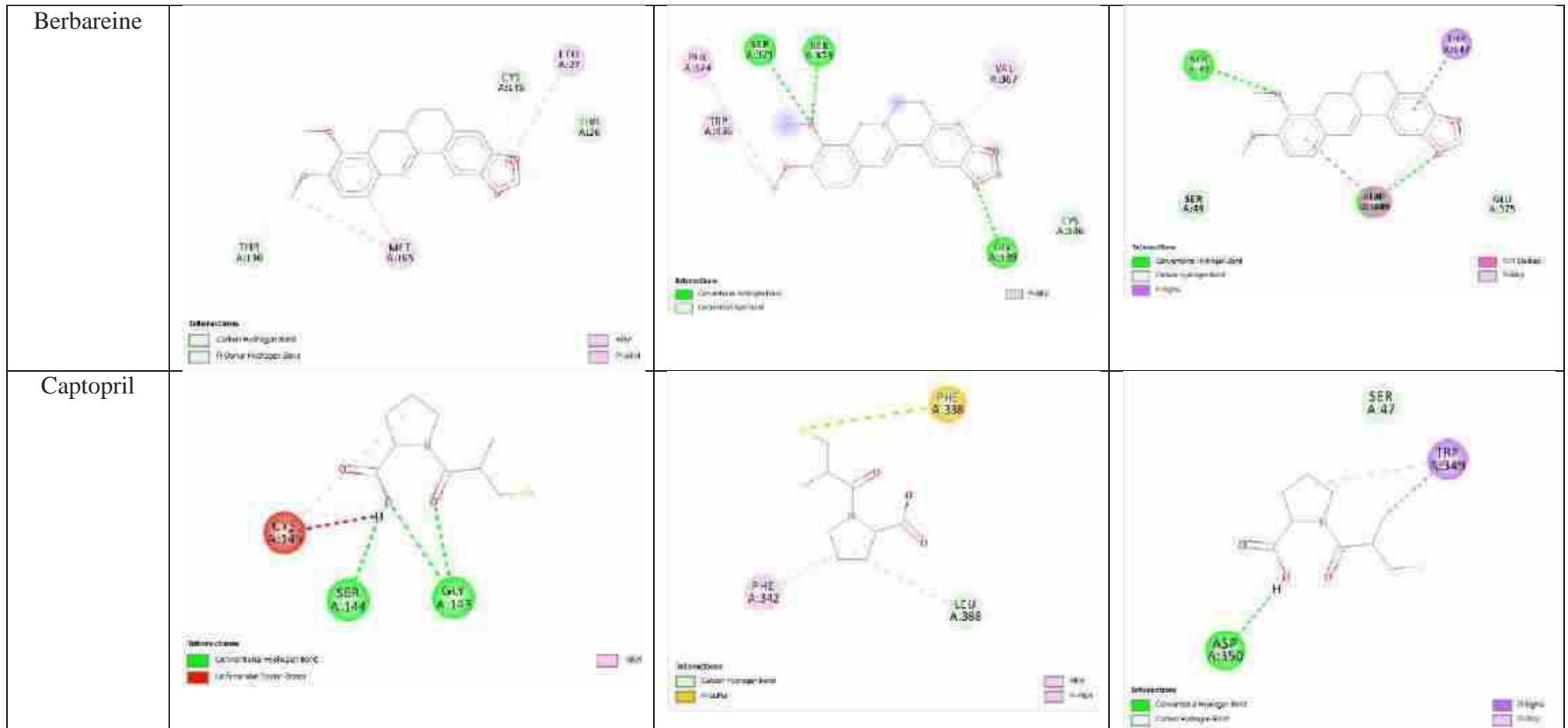


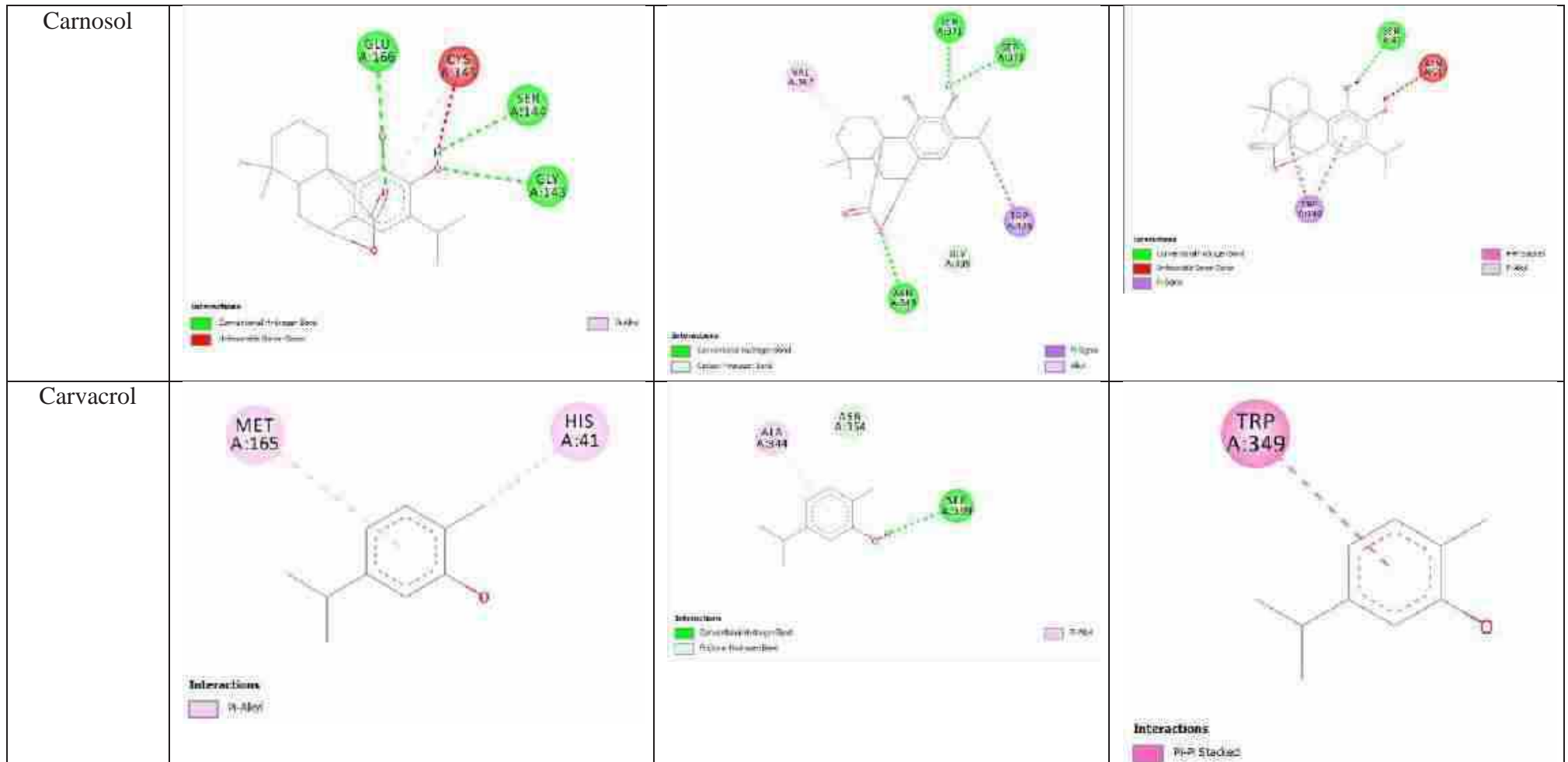
Apigetrin



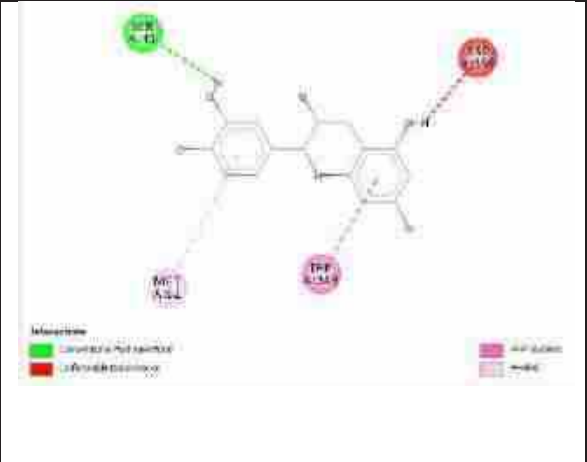
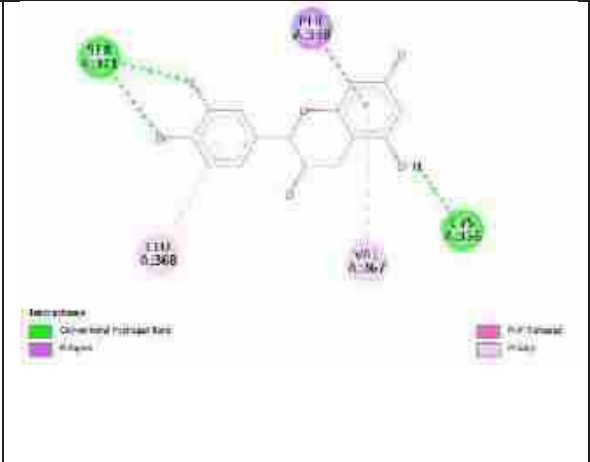
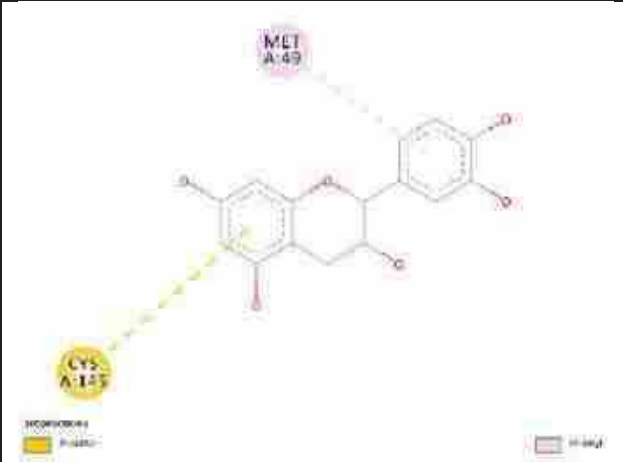
Arzanol



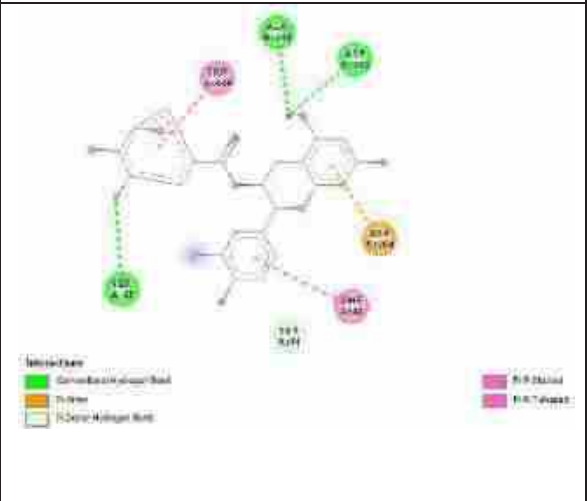
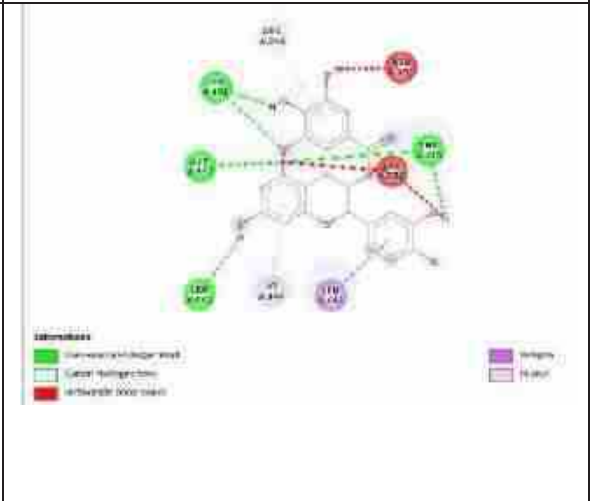
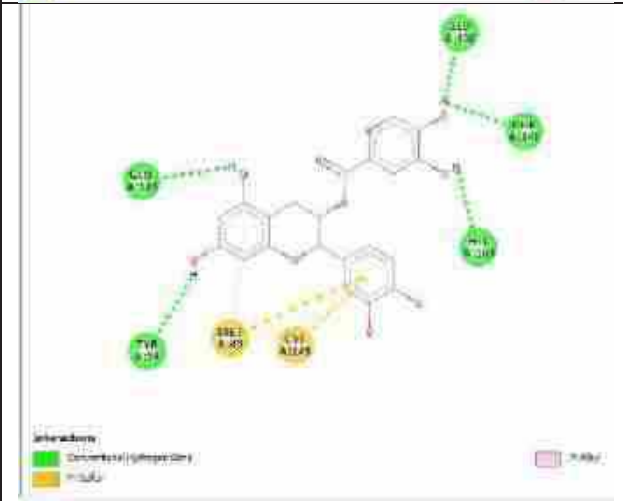


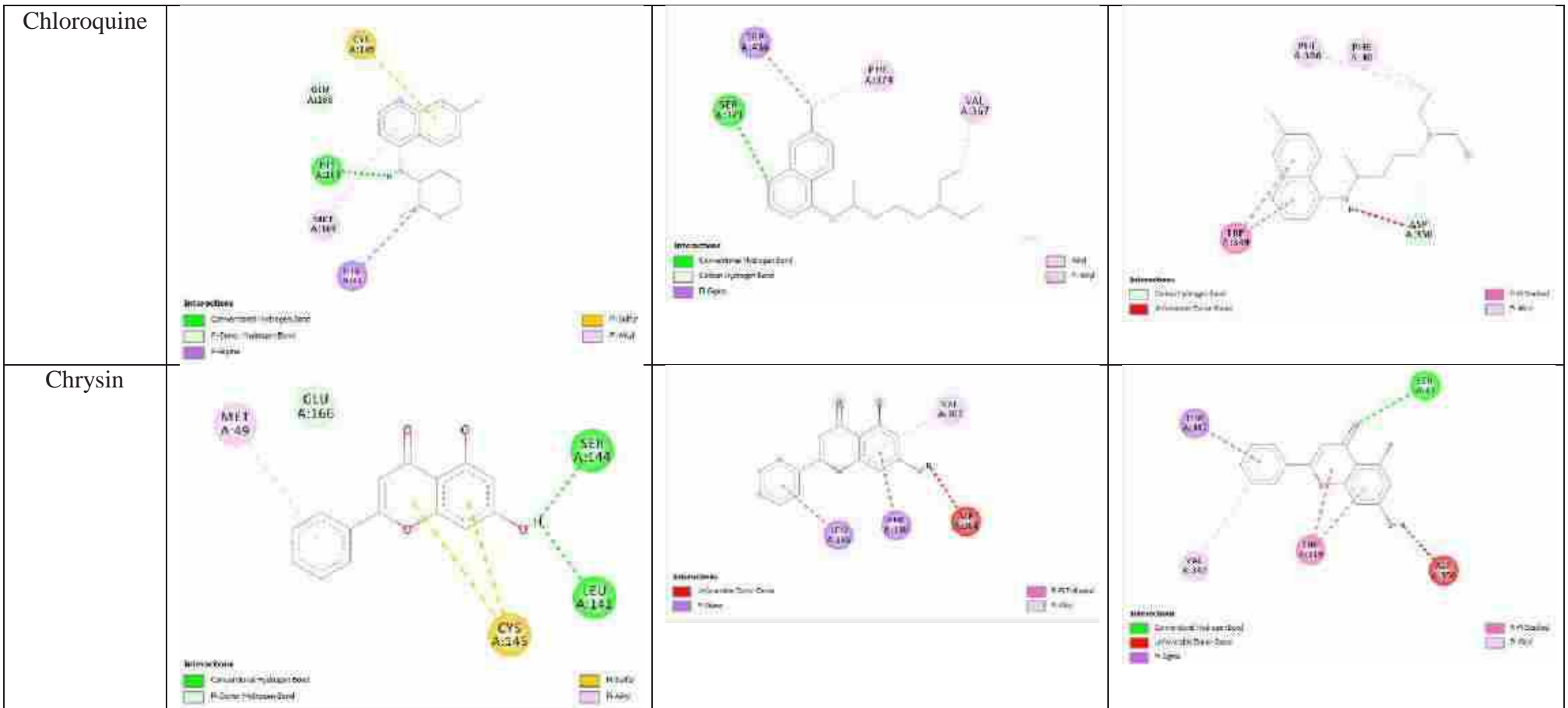


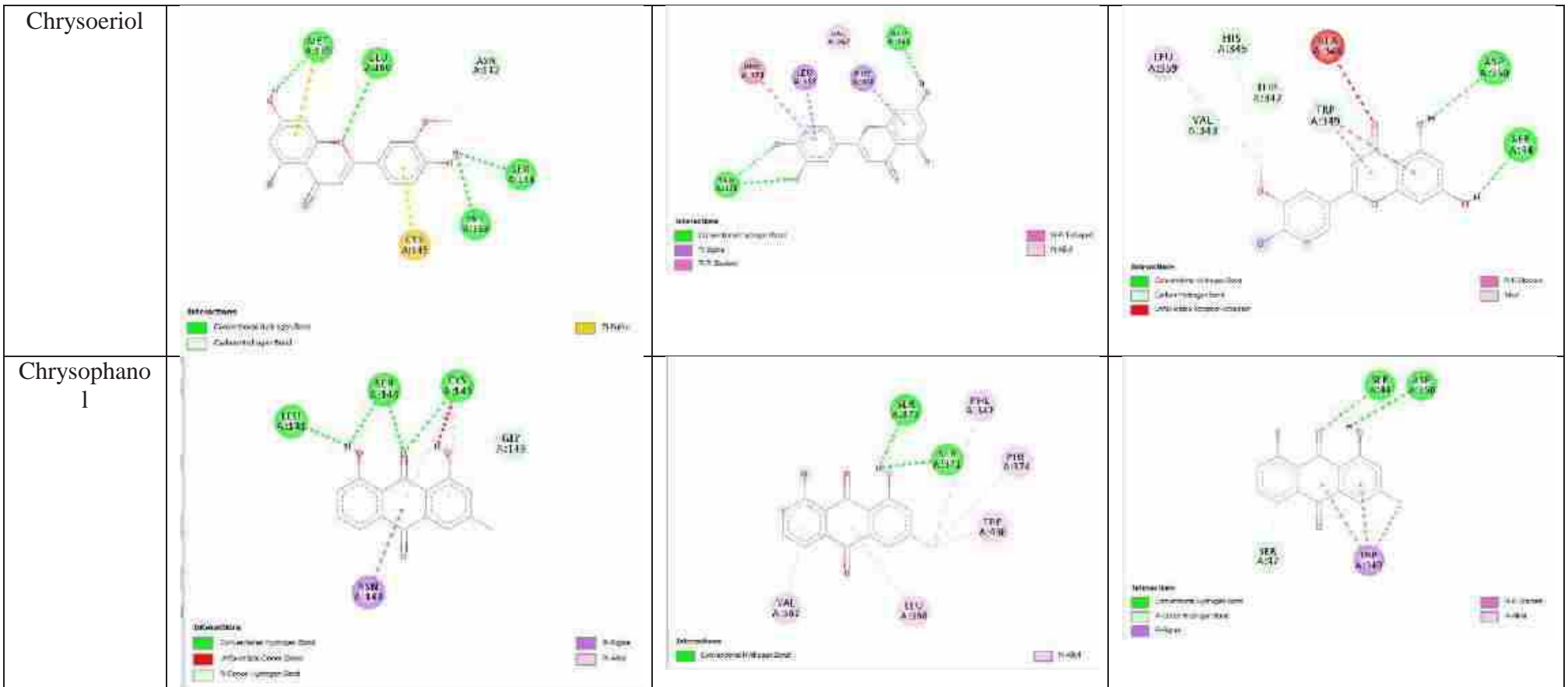
Catechin

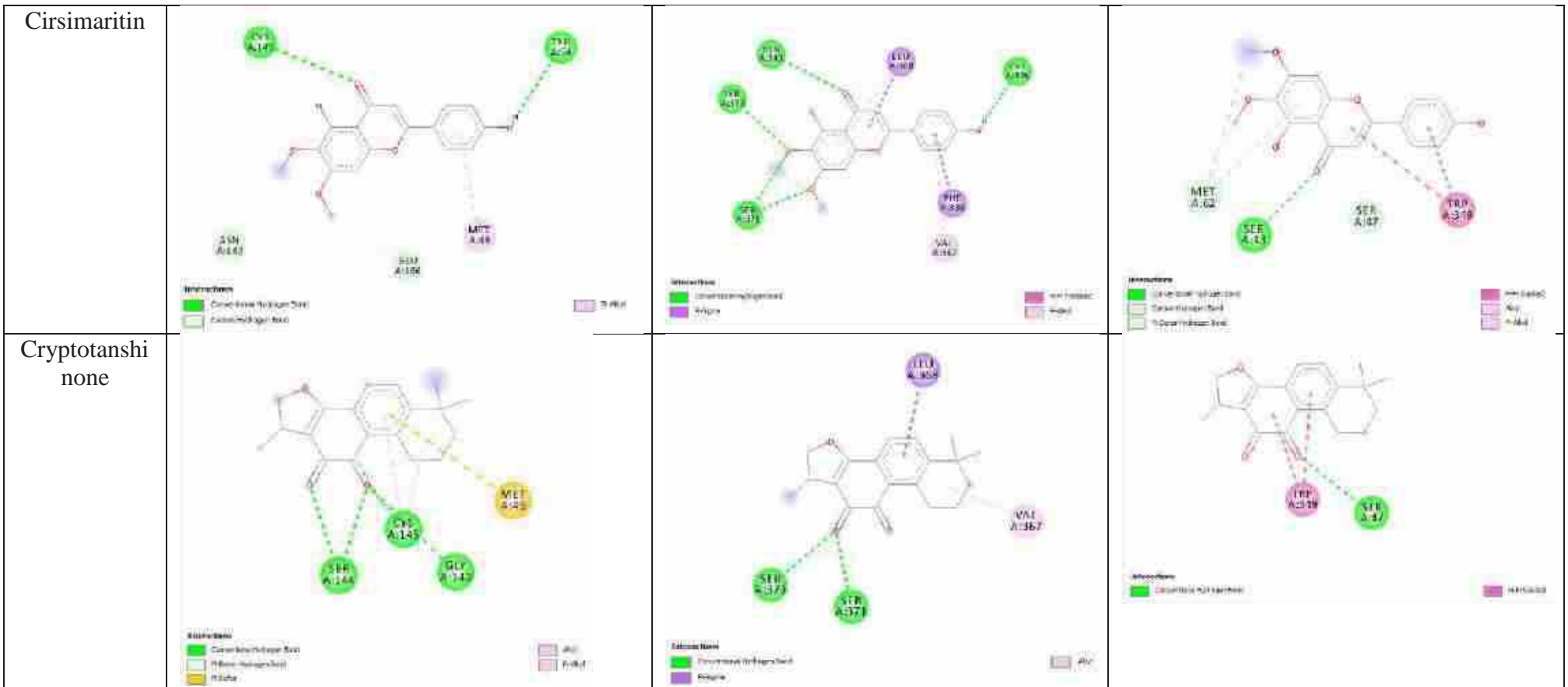


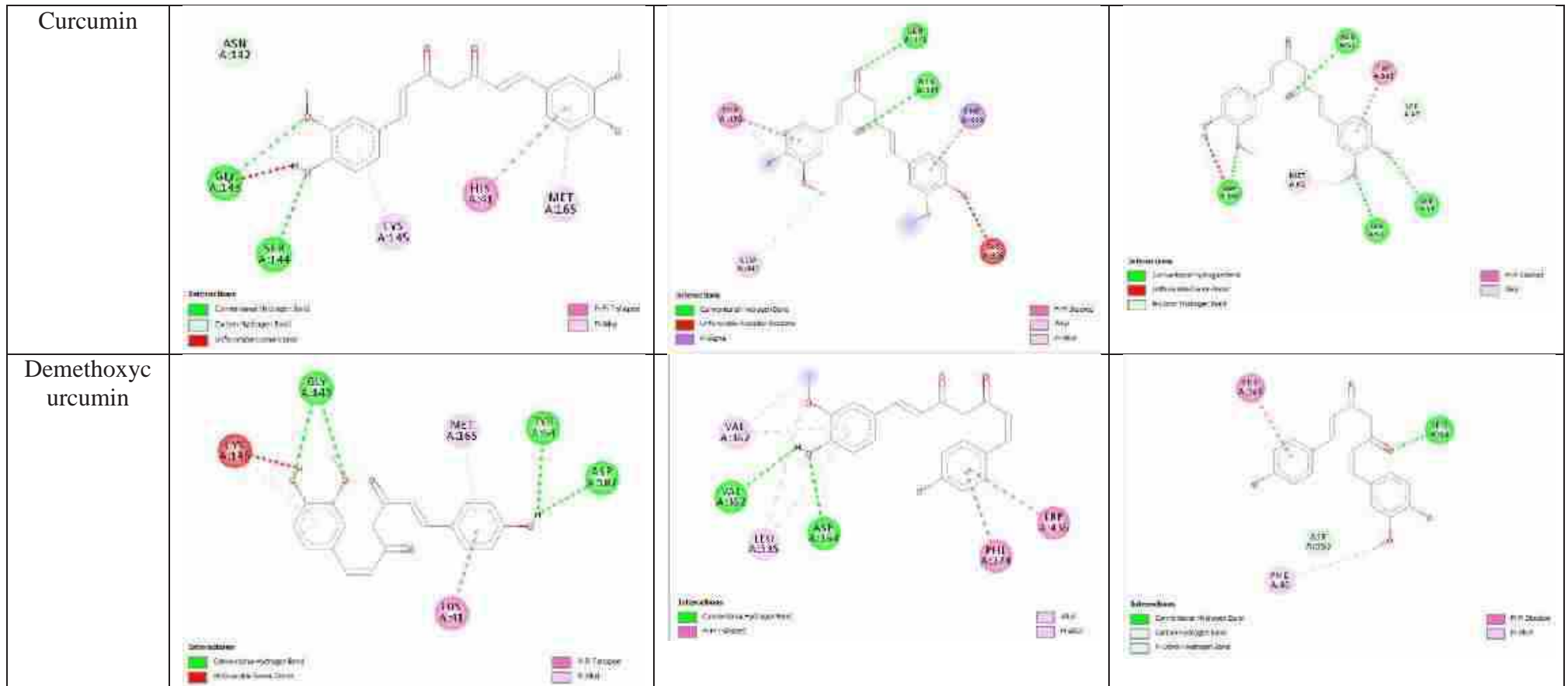
Catechin Gallate

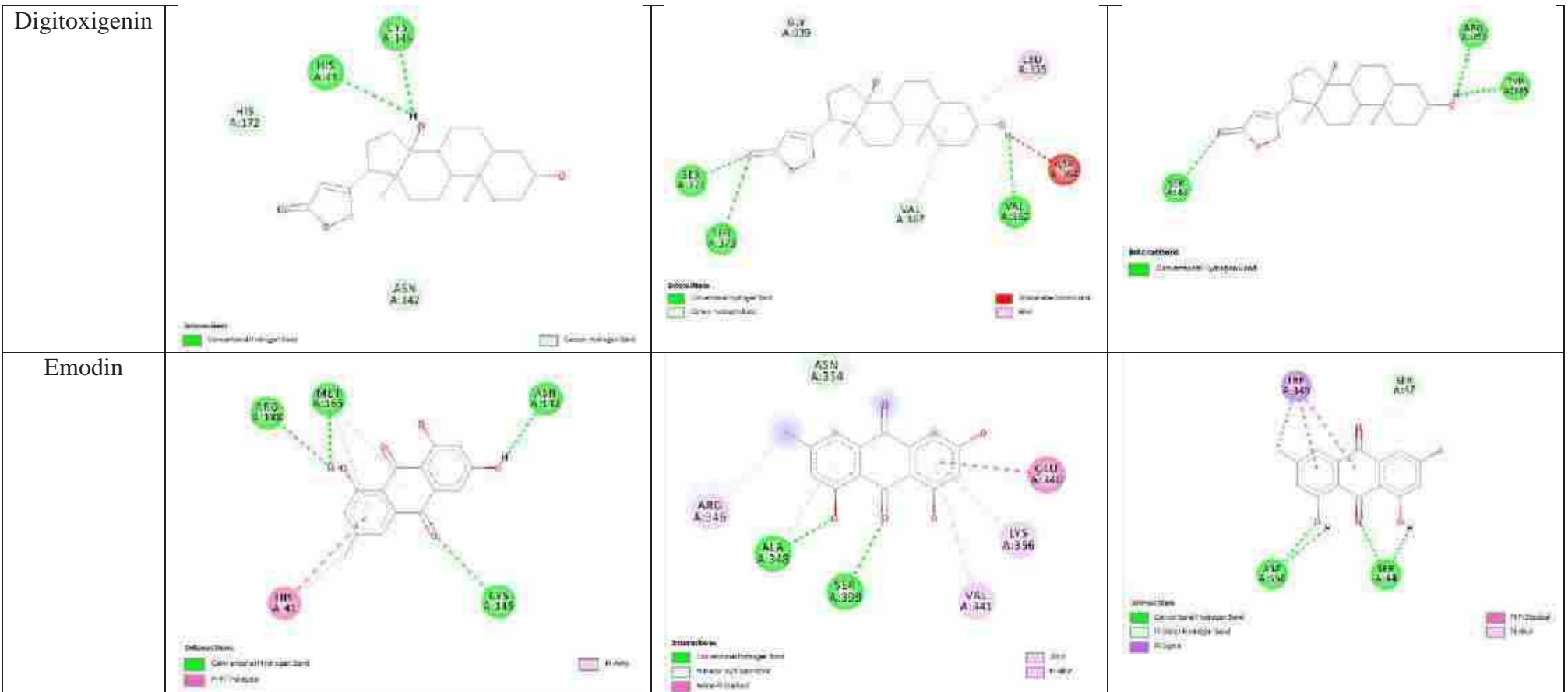




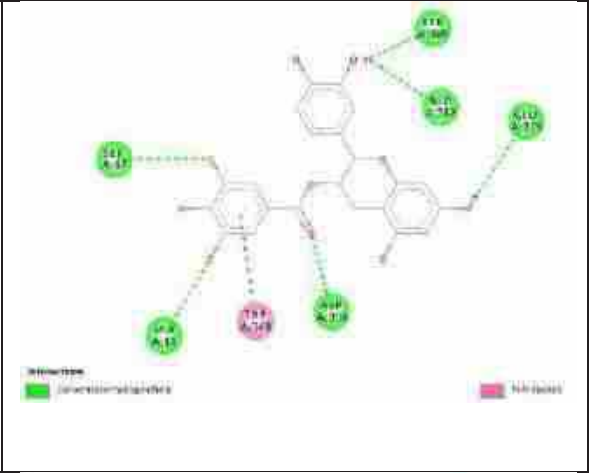
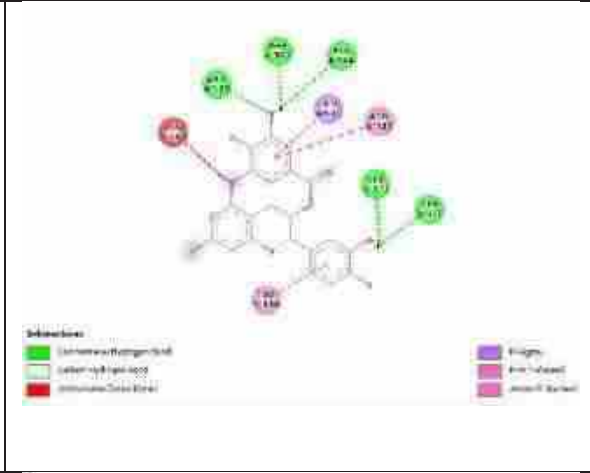
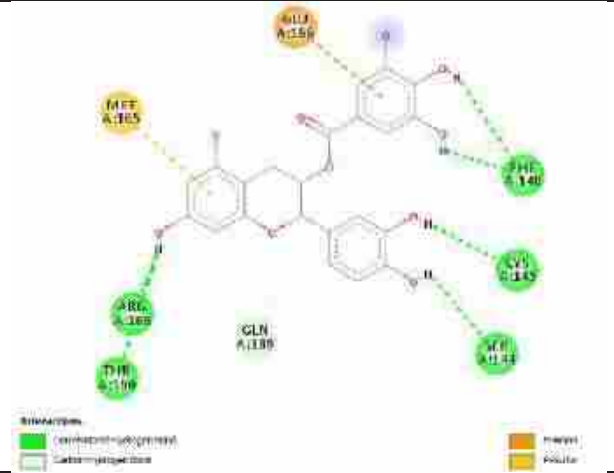




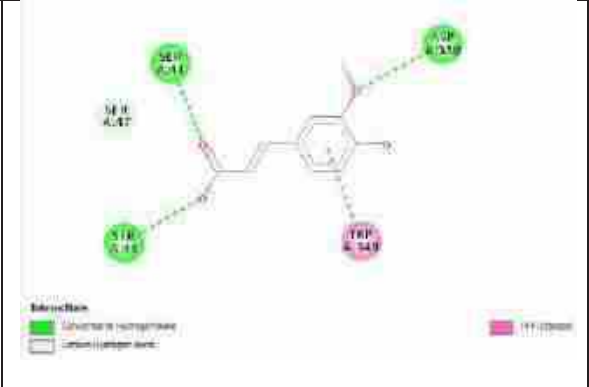
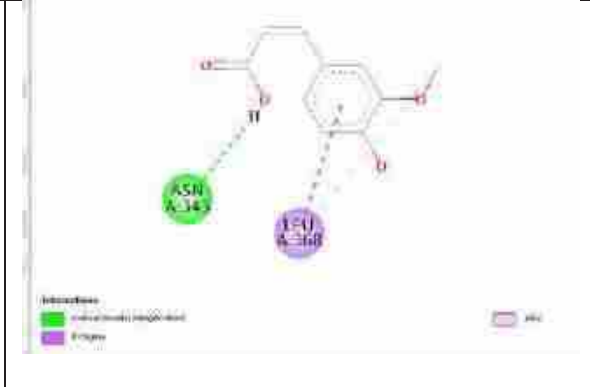
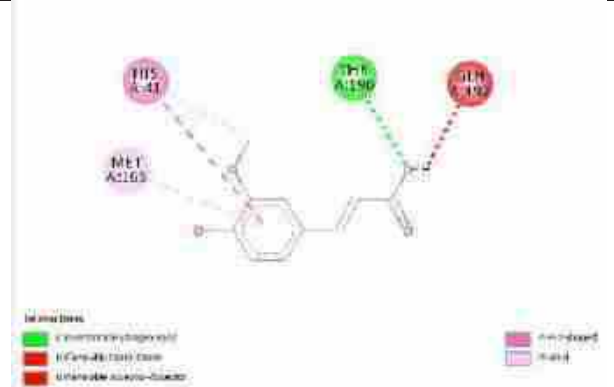


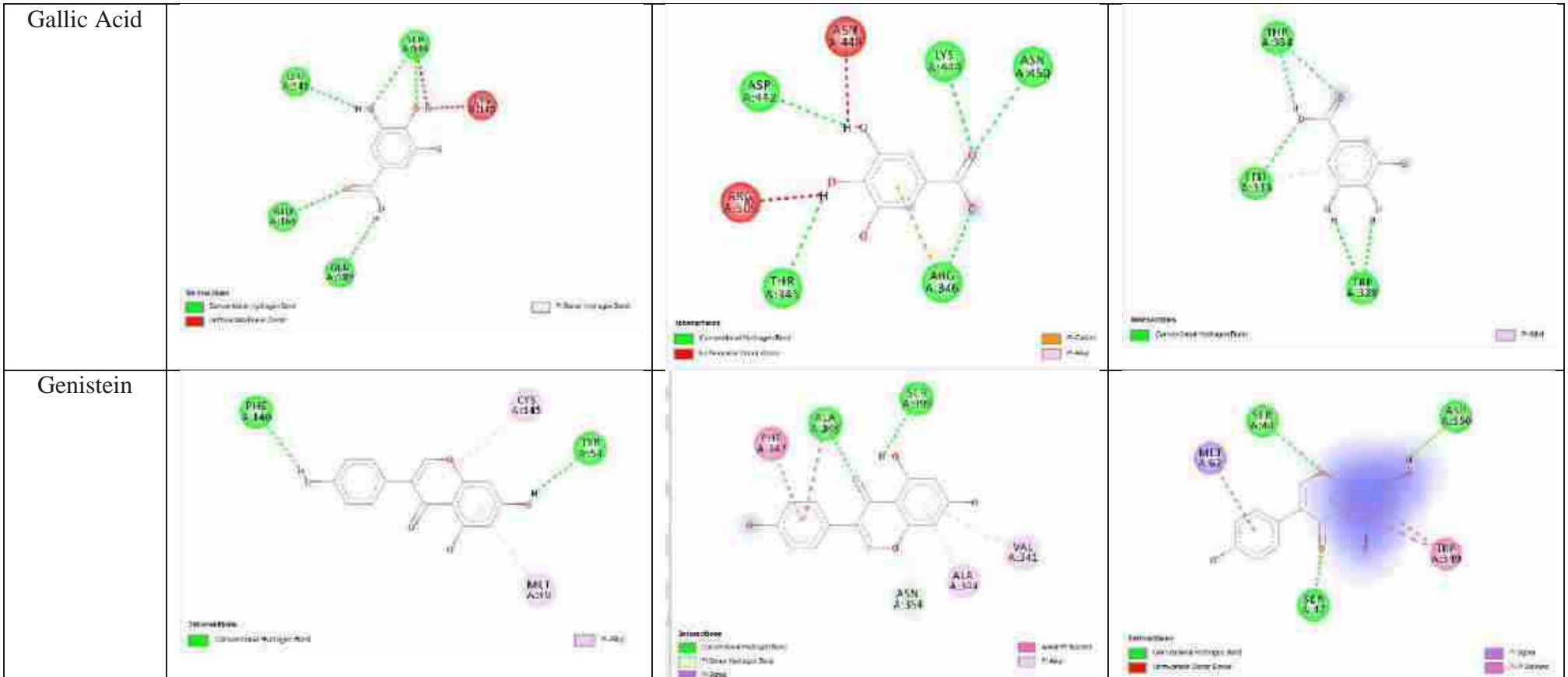


Epicateching allate

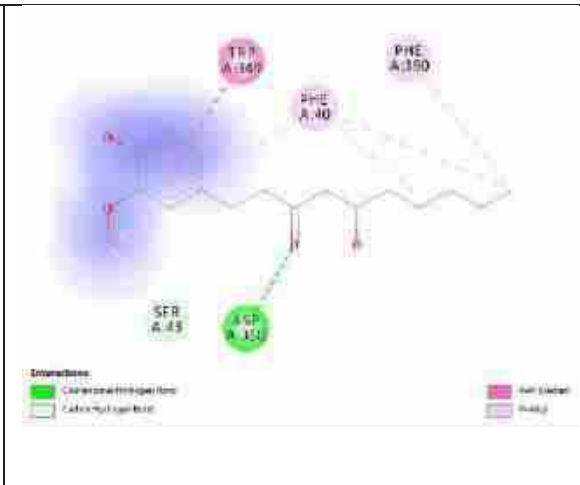
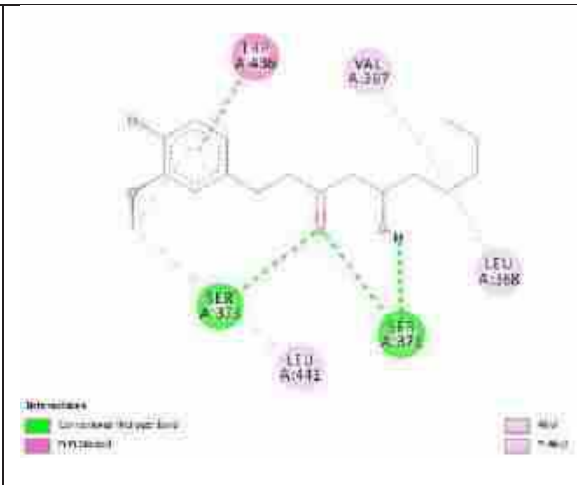
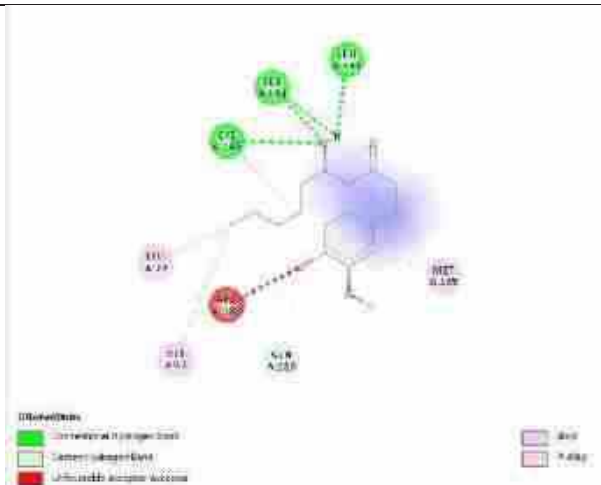


Ferulic Acid

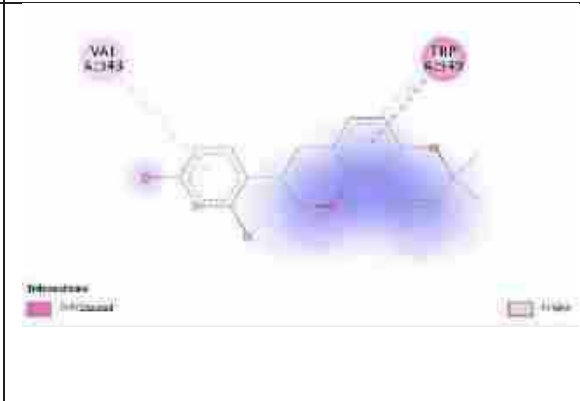
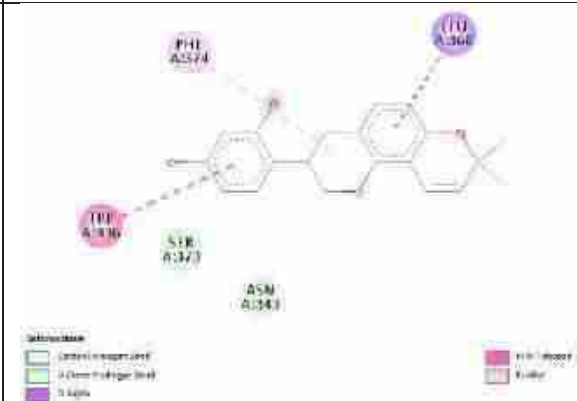
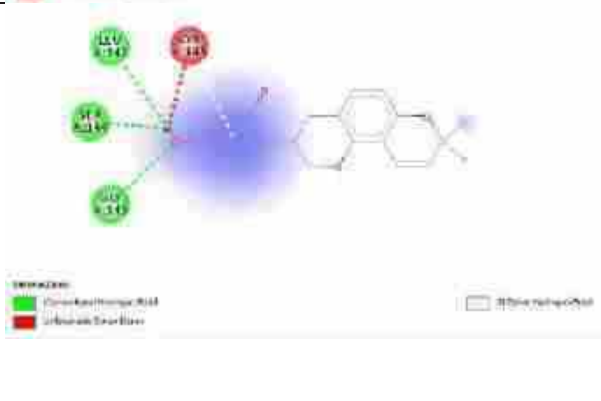




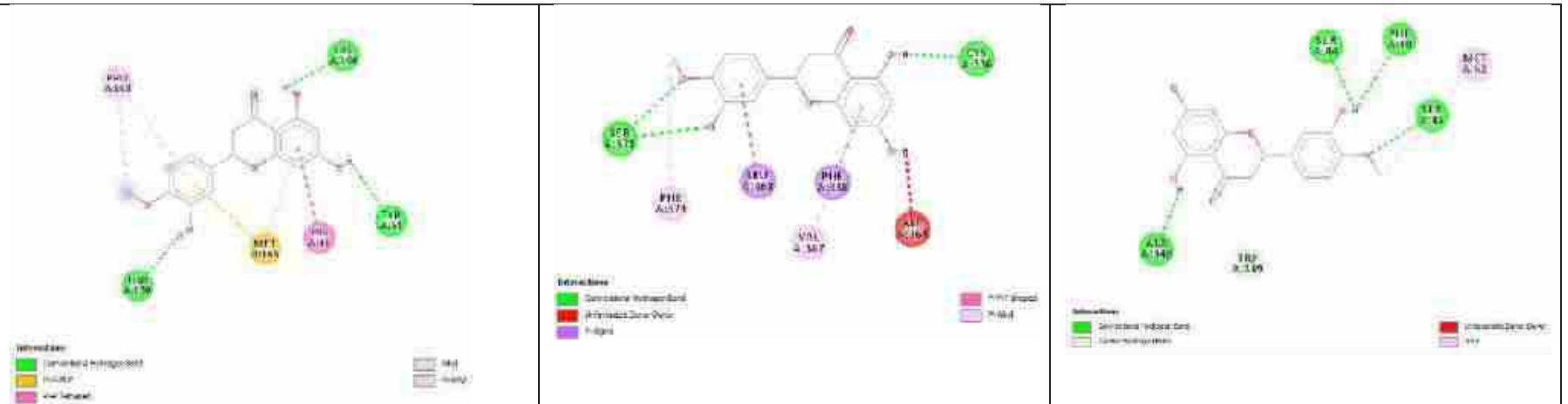
Gingerol



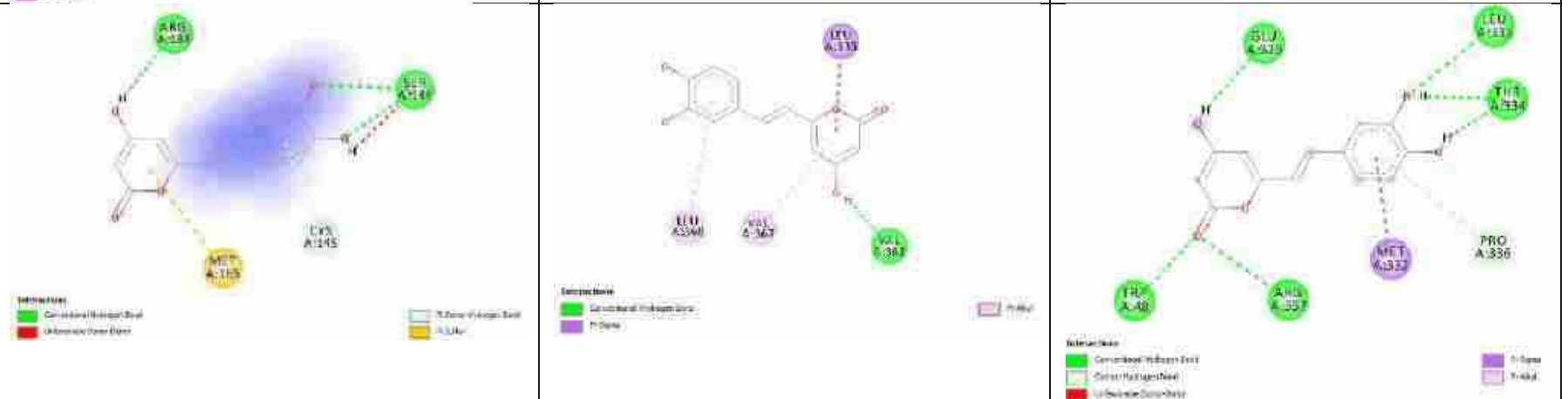
Glabridin

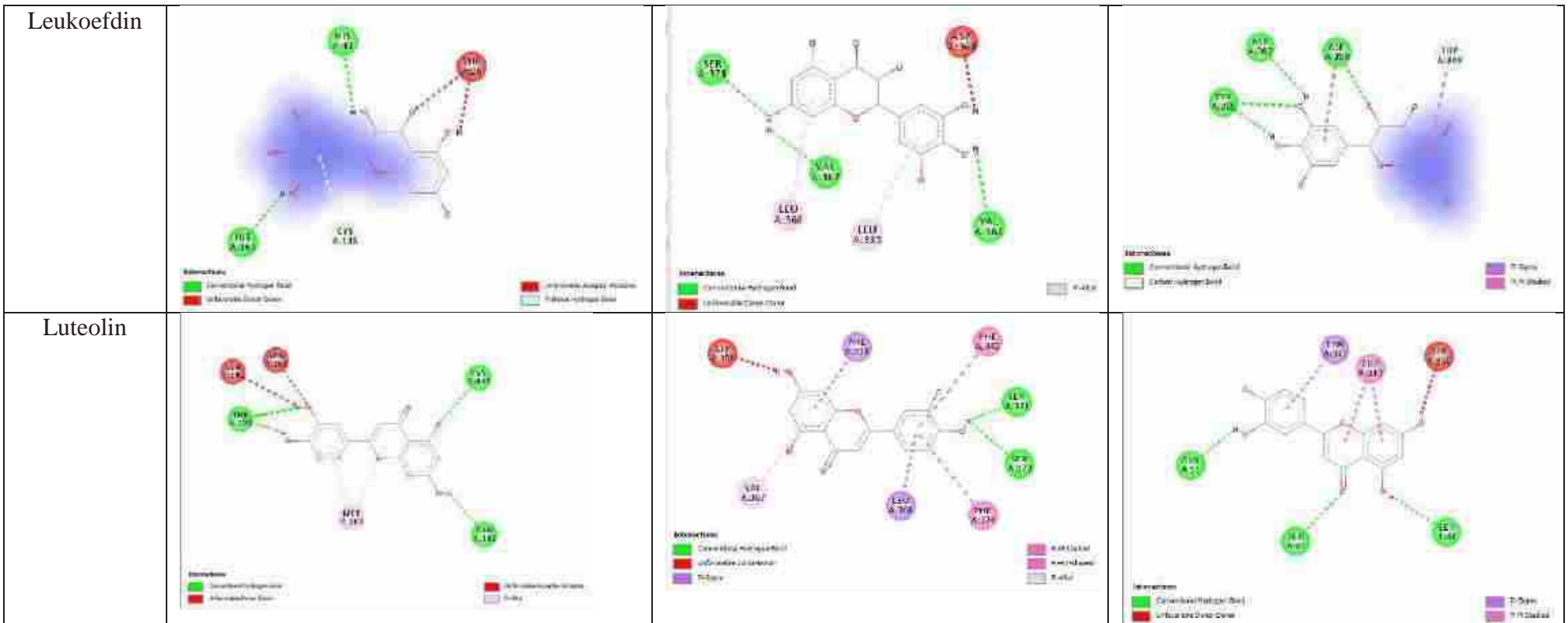


Hesperetin

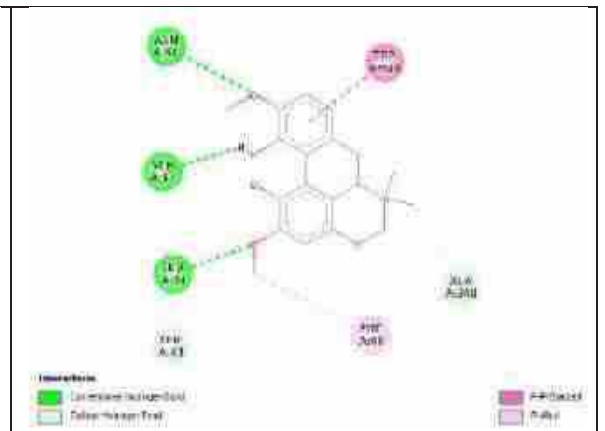
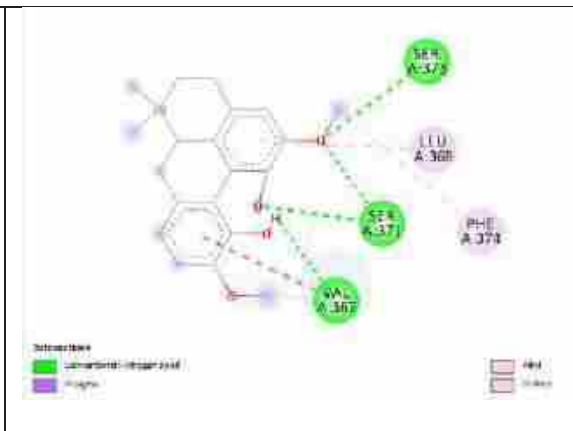
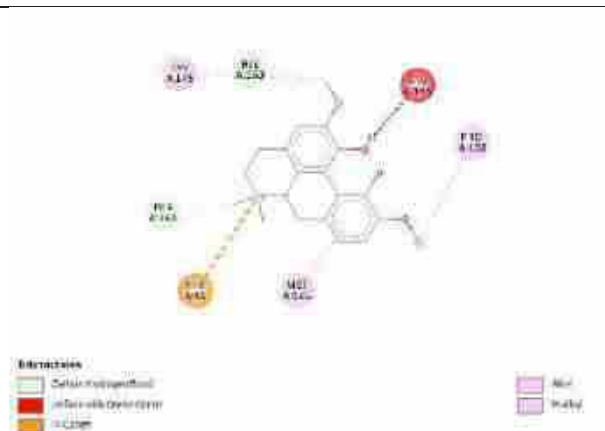


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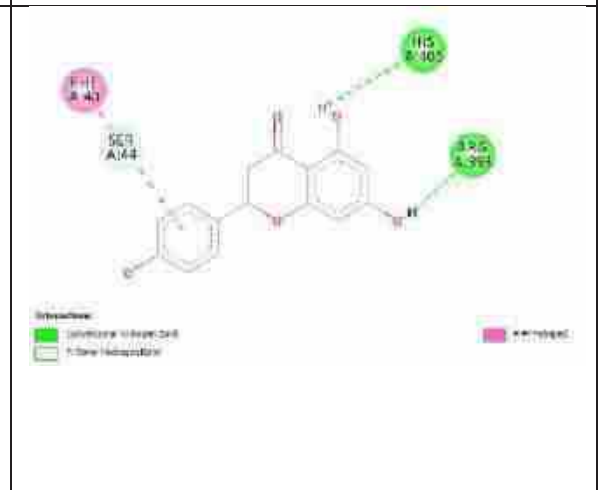
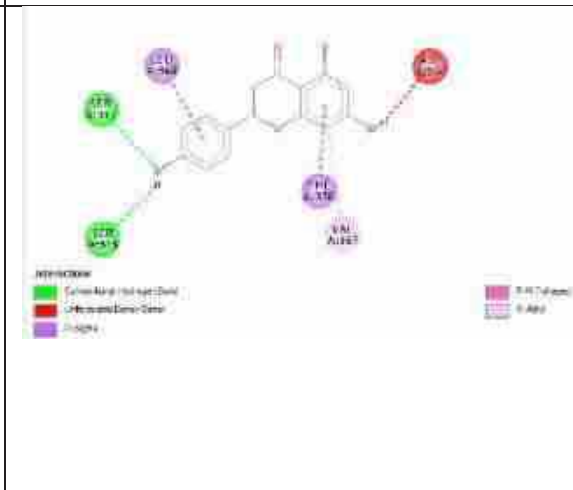
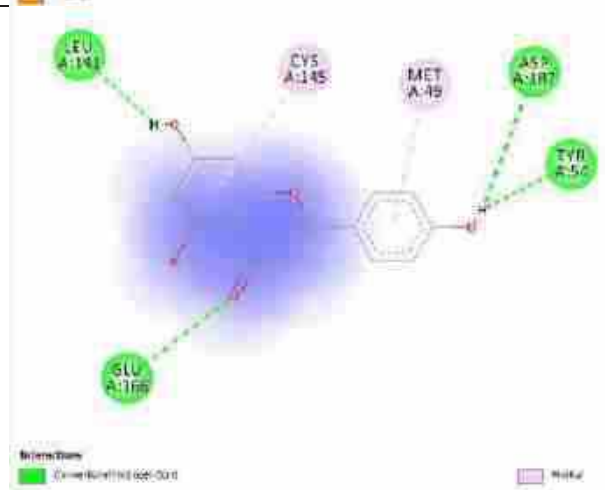


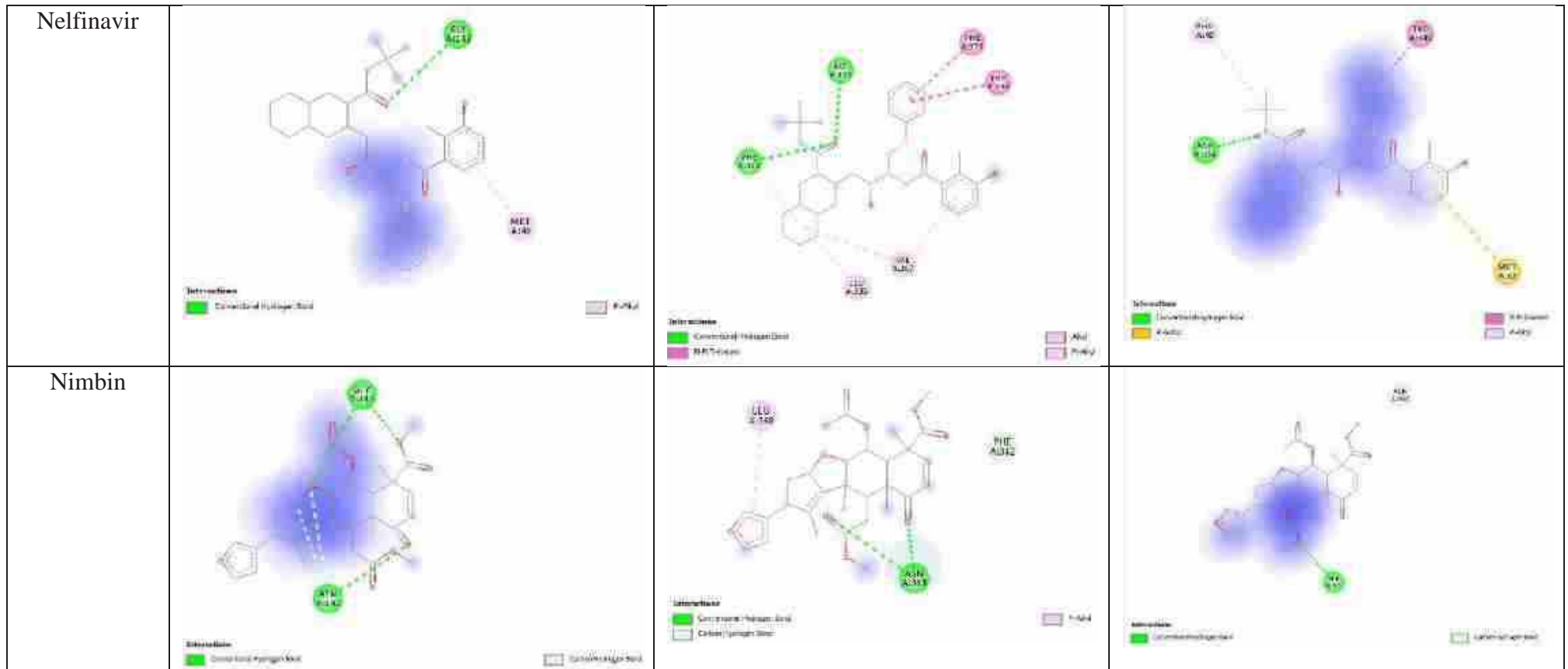


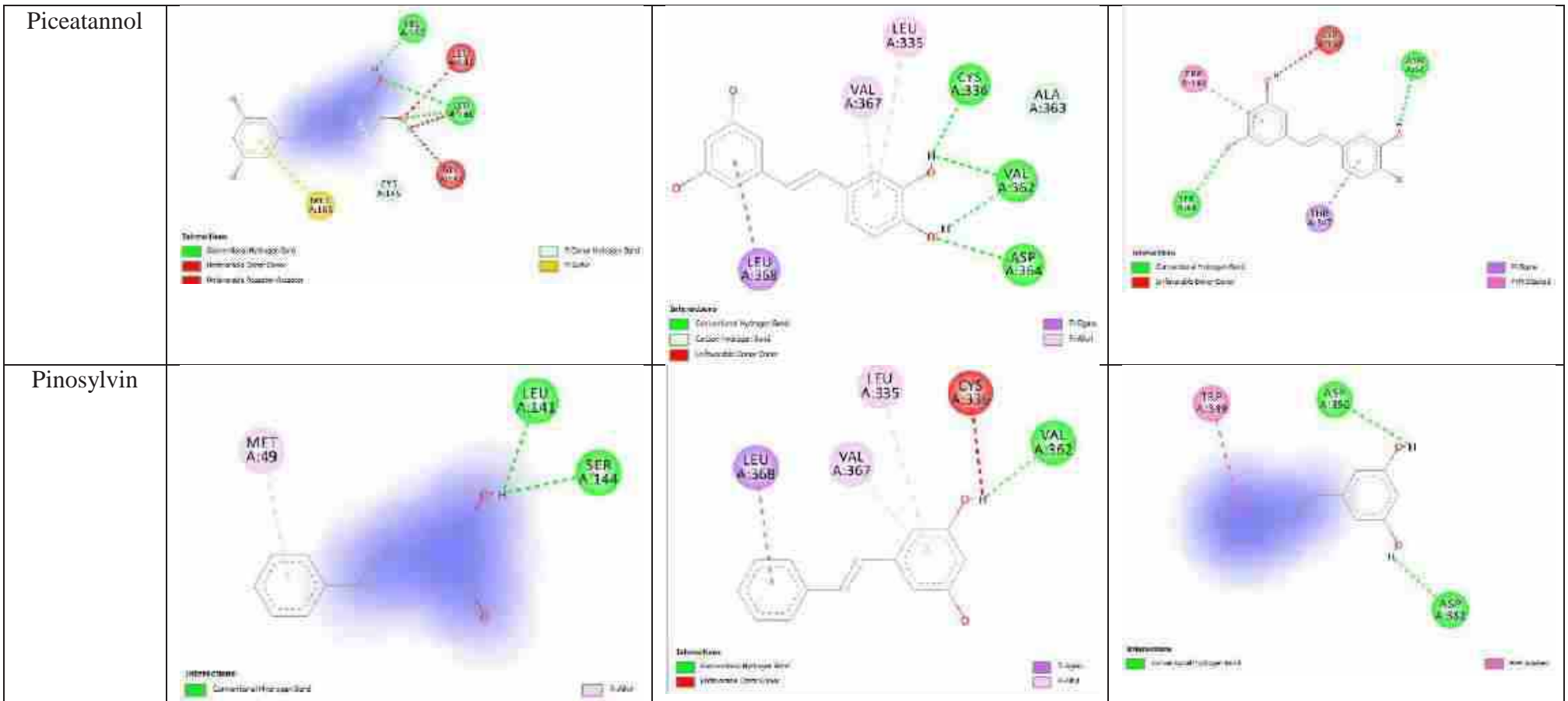
Magnoflorine

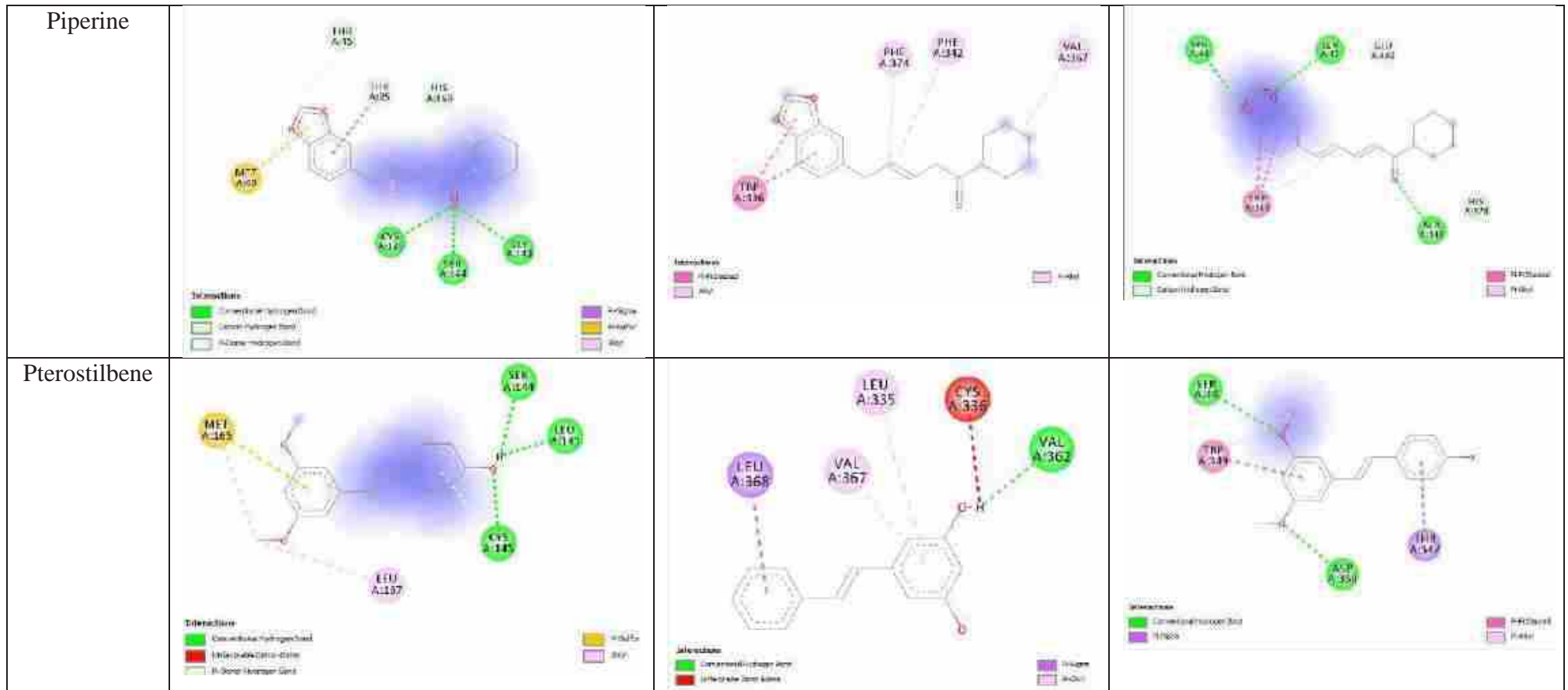


Narigenin

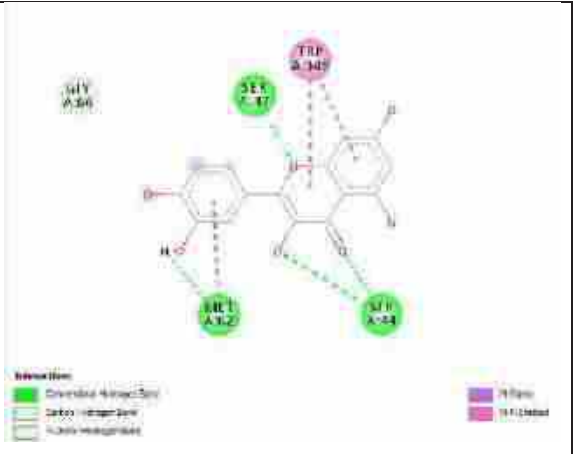
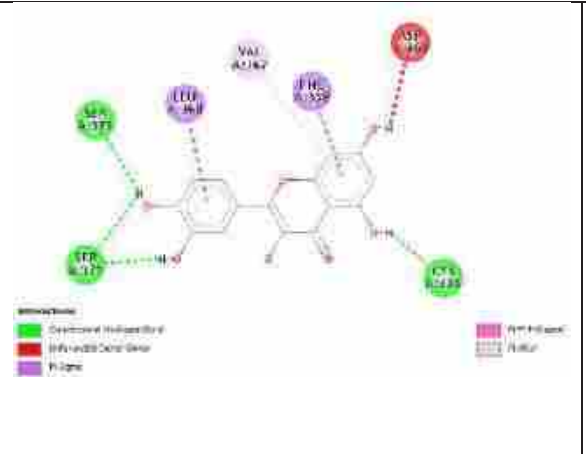
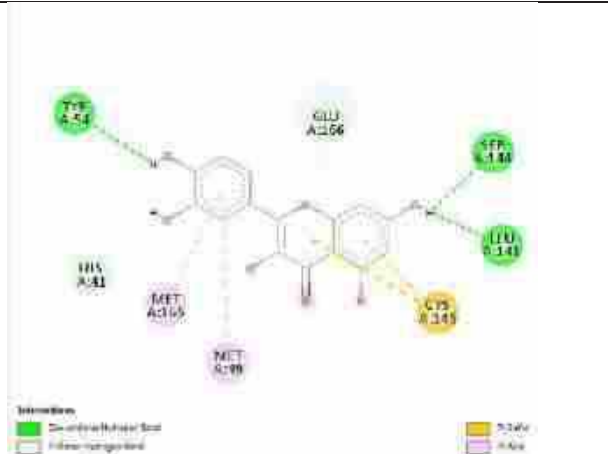




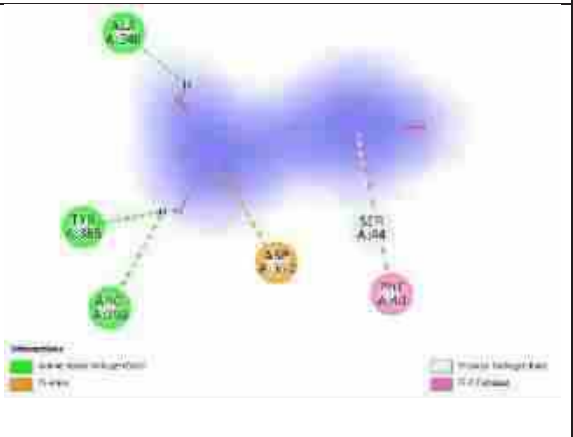
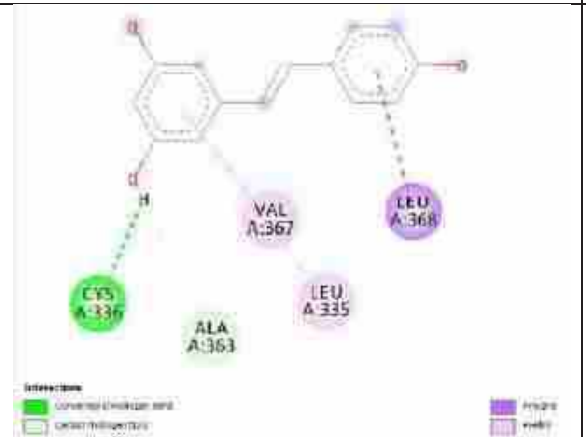
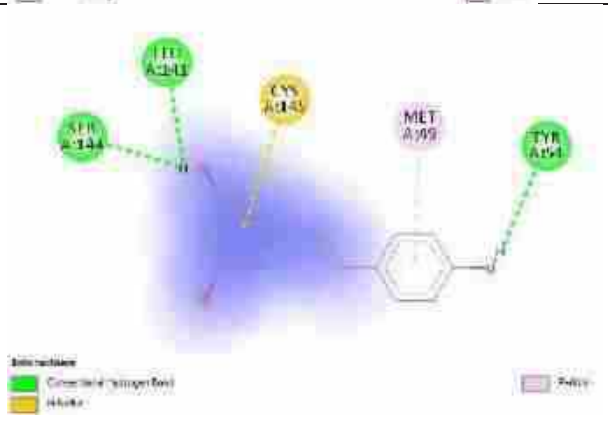


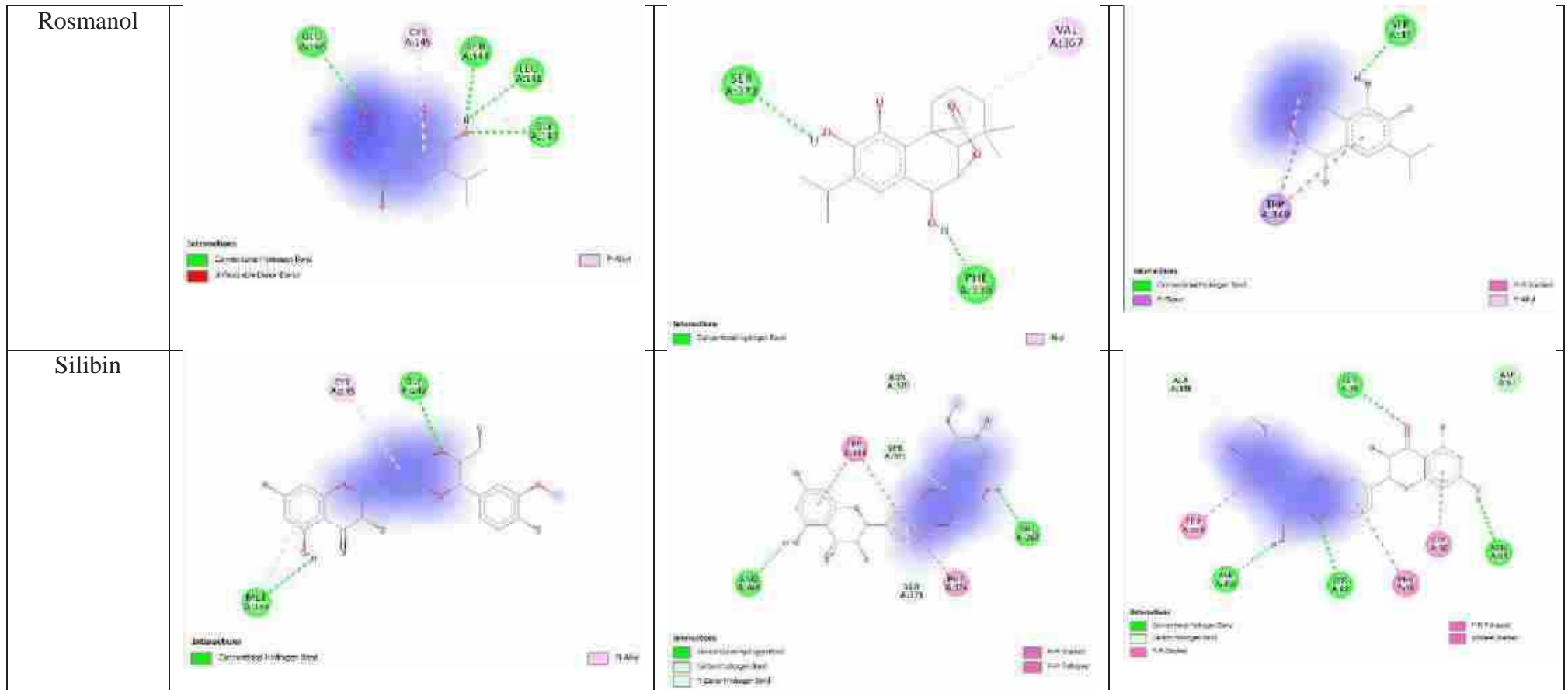


Quercetin

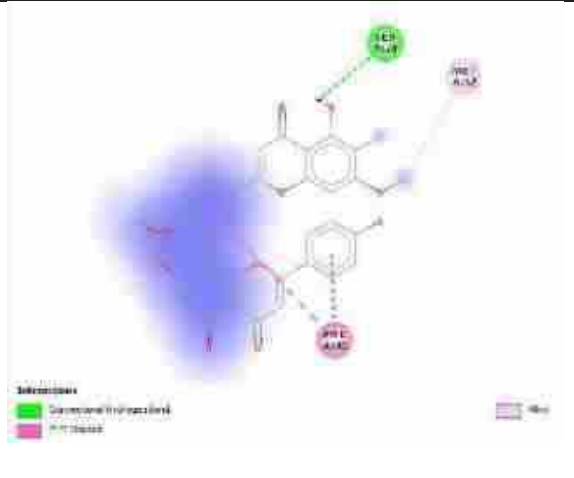
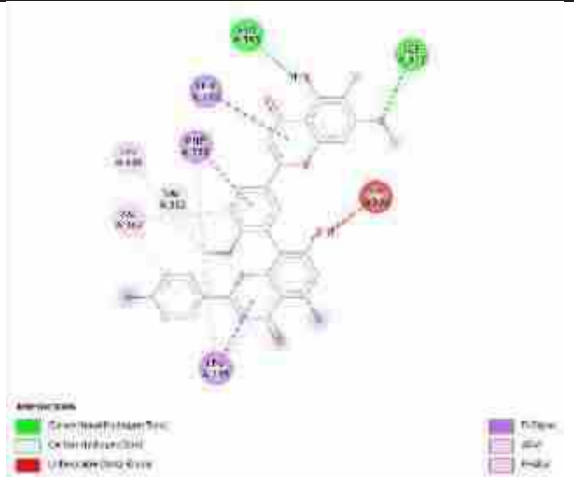
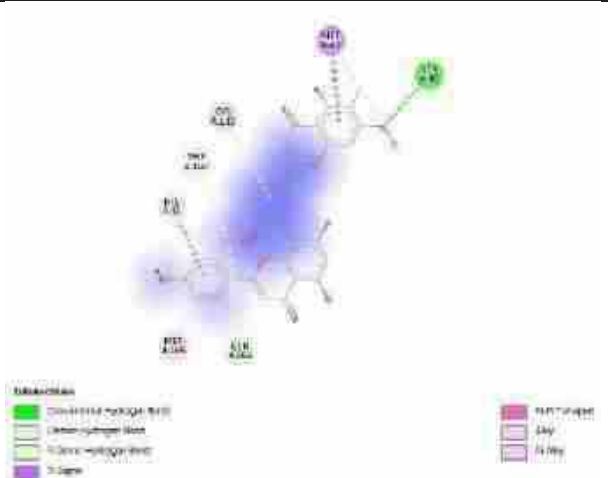


Resveratrol

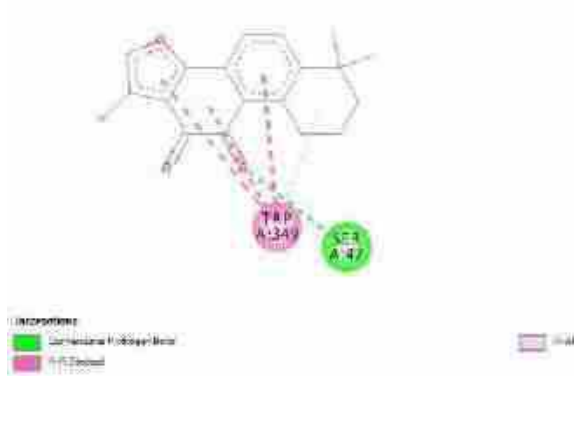
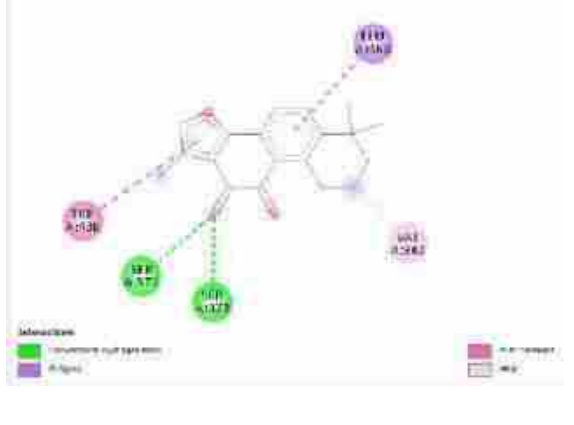
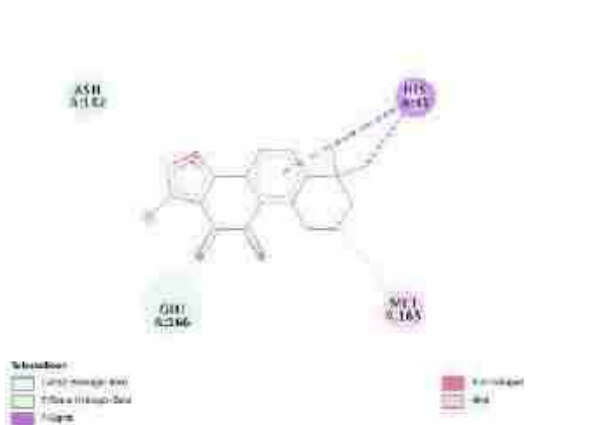




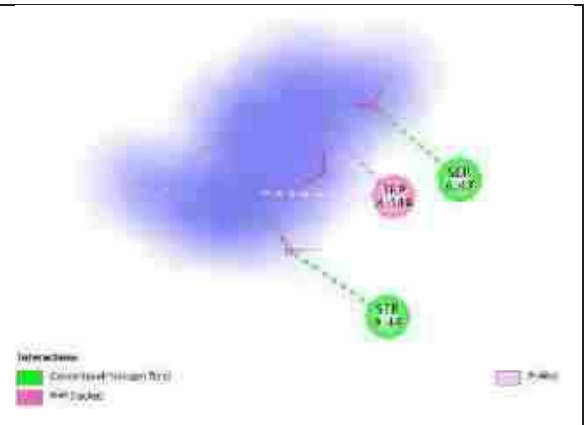
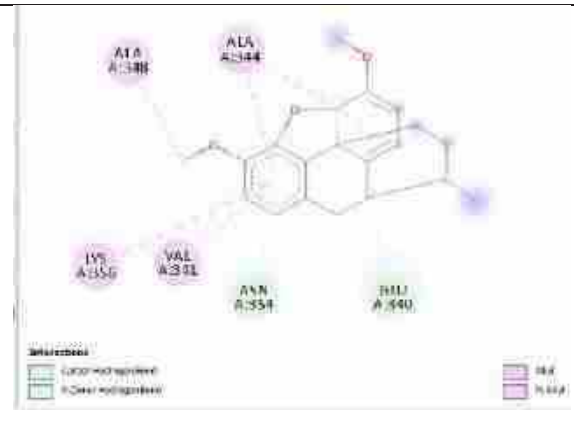
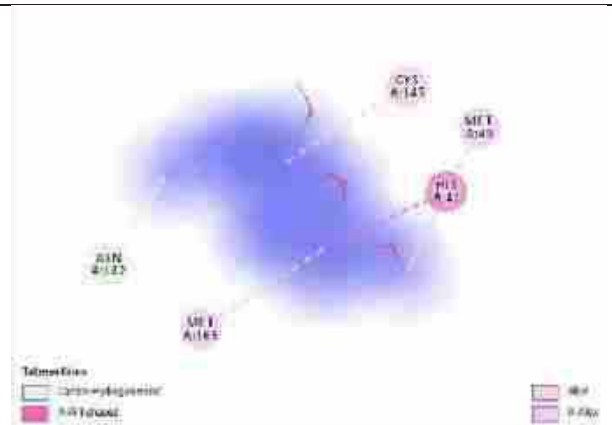
Taiwanhomo flavone A



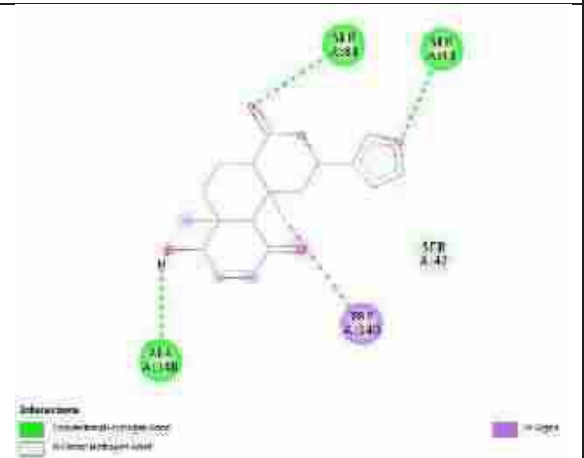
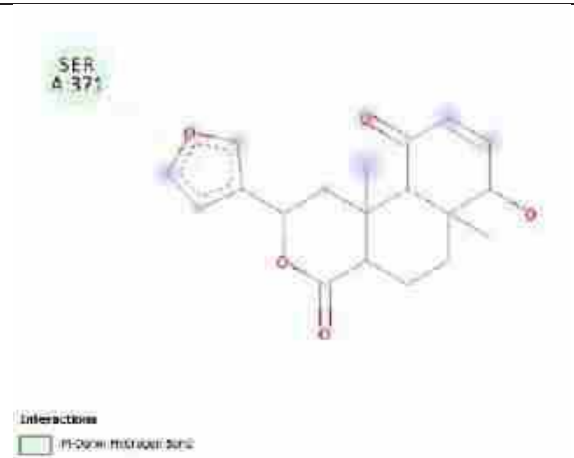
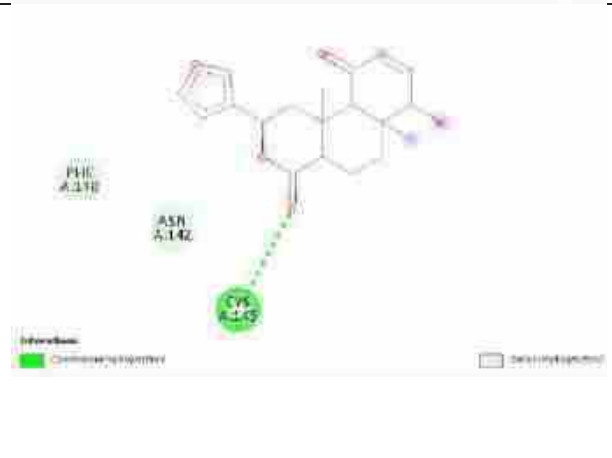
Tanshinone IIA



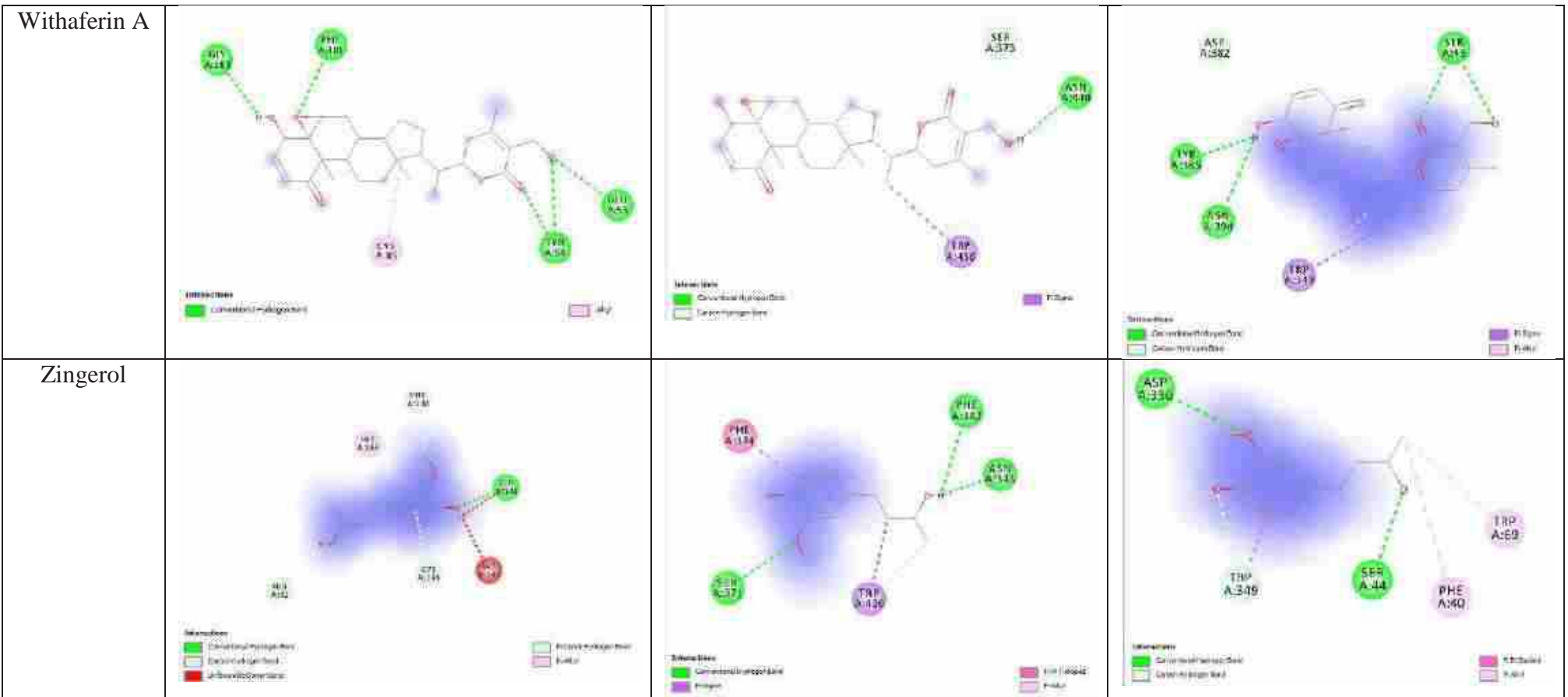
Thebaine



Tinosponone



<p>Ursolic Acid</p>	<p>Interactions: ■ Conventional hydrogen bond Cation-π interaction</p>	<p>Interactions: ■ π-π system</p>	
<p>Vasicinone</p>	<p>Interactions: ■ Conventional hydrogen bond ■ Unfavorable interaction ■ π-π system π-π system</p>	<p>Interactions: ■ Conventional hydrogen bond π-π hydrogen bond ■ π-π π-π</p>	<p>Interactions: ■ Conventional hydrogen bond ■ π-π</p>



Zingiberene

