

SUPPLEMENTARY DATA

SUPPLEMENTARY TABLES

S1: Structures of yodium leaf active compounds and comparative drugs

No.	Compounds	Chemical structure	No.	Compounds	Chemical structure
1.	Ciprofloxacin Pubchem CID: 2764		8.	C7 (Pectolarigenin Pubchem CID: 5320438)	
2.	C1 (Multifidone Pubchem CID: 25181402)		9.	C8 (Jatrophone Pubchem CID: 5281373)	
3.	C2 (Multidione Pubchem CID: 101477139)		10.	C9 (Multifidanol Pubchem CID: 57390908)	
4.	C3 (Multifolone Pubchem CID: 102025875)		11.	C10 (Fraxidin Pubchem CID: 3083616)	
5.	C4 (Multifidol Glucoside Pubchem CID: 14412552)		12.	C11 (Jatrothrin Pubchem CID: )	
6.	C5 (Citlitrione Pubchem CID: 6449926)		13.	C12 (Jatropheneone Pubchem CID: 15923201)	
7.	C6 (cleomiscosin A Pubchem CID: 442510)		14.	C13 (Japodagrone Pubchem CID: 101437129)	

### S2: Parameters of Lipinski's rule of five

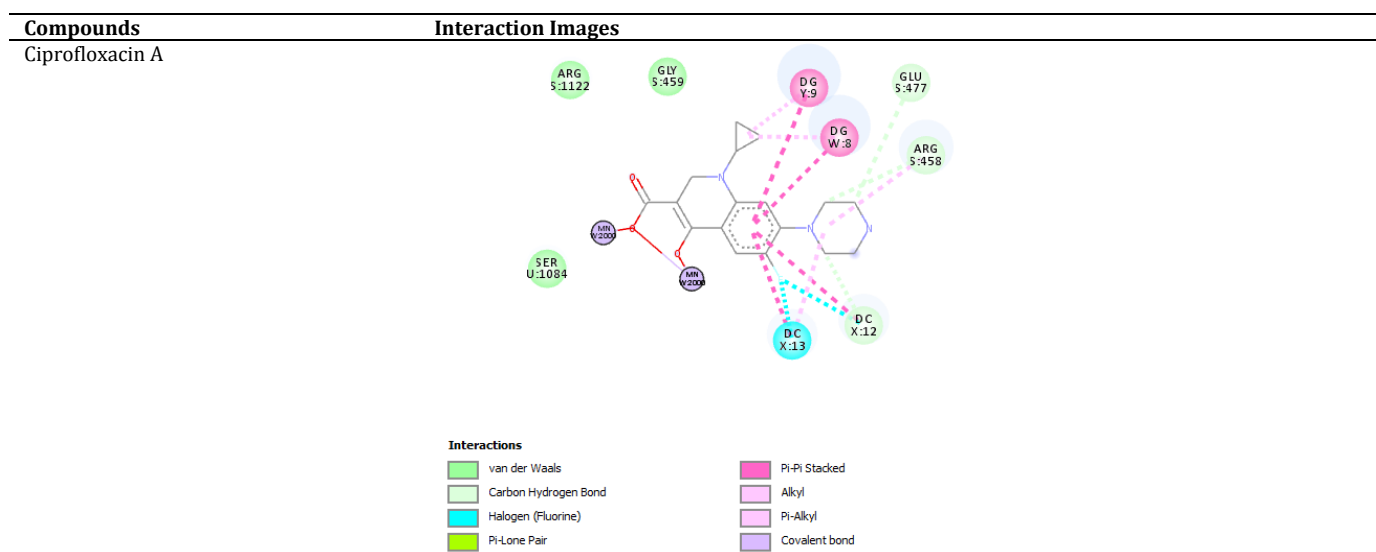
No	Compounds	Hydrogen donor	Hydrogen acceptor	Molecular weight	Log P	Eligible/Not eligible
1	Ciprofloxacin	2	6	331	1.368900	Eligible
2	C1 (Multifidone)	0	3	314	3.630799	Eligible
3	C2 (Multidione)	1	3	316	4.550920	Eligible
4	C3 (Multifolone)	2	3	318	3.406199	Eligible
5	C4 (Multifidol Glucoside)	6	9	372	-0.494700	Eligible
6	C5 (Citlaltirione)	0	4	330	2.889700	Eligible
7	C6 (cleomiscosin A)	2	8	386	2.29	Eligible
8	C7 (Pictolarigenin)	2	6	314	2.025	Eligible
9	C (Jatrophone)	0	3	312	4.02	Eligible
10	C9 (Multifidanol)	1	4	336	4.6	Eligible
11	C10 (Fraxidin)	1	5	222	1.167	Eligible
12	C11 (Jatrothrin)	5	6	312	-0.053	Eligible
13	C12 (Jatropheneone)	0	4	358	4.06	Eligible
14	C13 (Japodagrone)	1	4	332	3.135	Eligible

### S3: ADME prediction profile and toxicity

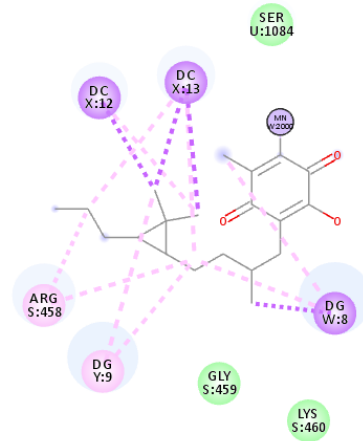
Compounds	Absorption		Distribution		Metabolism				Toxicity
	HIA (%)	Caco-2 (nm/sec)	BBB	PPB (%)	Cyp3A4 inhibition	Cyp2D6 inhibition	Cyp2C9 inhibition	Cyp2C19 inhibition	Ames test
Ciprofloxacin	96.27	21.28	0.01	31.05	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor	Mutagen
C1 (Multifidone)	98.00	41.96	0.85	100.00	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Mutagen
C2 (Multidione)	95.47	26.72	1.38	100.00	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Nonmutagen
C3 (Multifolone)	92.52	25.49	3.93	100.00	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Nonmutagen
C4 (Multifidol Glucoside)	23.63	2.51	0.04	59.30	Inhibitor	Non-Inhibitor	Inhibitor	Inhibitor	Mutagen
C5 (Citlaltirione)	98.13	23.9	1.47	81.79	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Mutagen
C6 (cleomiscosin A)	93.81	17.77	0.02	83.40	Non-Inhibitor	Non-Inhibitor	Inhibitor	Inhibitor	Mutagen
C7 (Pictolarigenin)	93.37	8.37	0.06	87.68	Inhibitor	Non-Inhibitor	Inhibitor	Inhibitor	Mutagen
C8 (Jatrophone)	97.78	50.36	0.84	98.63	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Mutagen
C9 (Multifidanol)	87.33	19.97	1.68	97.93	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Non-mutagen
C10 (Fraxidin)	93.30	0.29	0.73	57.04	Non-Inhibitor	Non-Inhibitor	Inhibitor	Inhibitor	Mutagen
C11 (Jatrothrin)	98.26	43.74	1.42	96.42	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Mutagen
C12 (Jatropheneone)	98.40	33.21	0.03	95.34	Inhibitor	Non-Inhibitor	Inhibitor	Inhibitor	Mutagen
C13 (Japodagrone)	95.98	14.95	0.84	96.03	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor	Non-mutagen

<sup>a</sup>Blood-brain barrier (BBB): high absorption ( $C_{br}/C_{bl} > 2.0$ ), middle absorption ( $C_{br}/C_{bl} = 2.0-0.1$ ), and low absorption ( $C_{br}/C_{bl} < 1.0$ ), <sup>b</sup>Protein-plasma binding (PPB): strongly bound ( $>90\%$ ), and weakly bound ( $<90\%$ ), <sup>c</sup> $P_{Caco-2}$  (nm/sec): low permeability ( $<4$ ), middle permeability (4-70), high permeability ( $>70$ ), <sup>d</sup>Human intestinal absorption (HIA), poorly absorbed (0-20%), moderately absorbed (20-70%), well absorbed (70-100%)

### S4: Interaction of amino acids with receptors at active site A



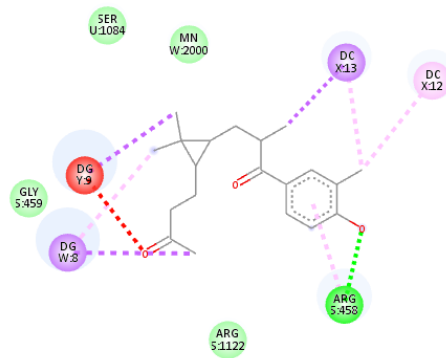
C1 (Multifidone)



Interactions

- van der Waals
- Pi-Sigma
- Pi-Alkyl
- Alkyl
- Covalent bond

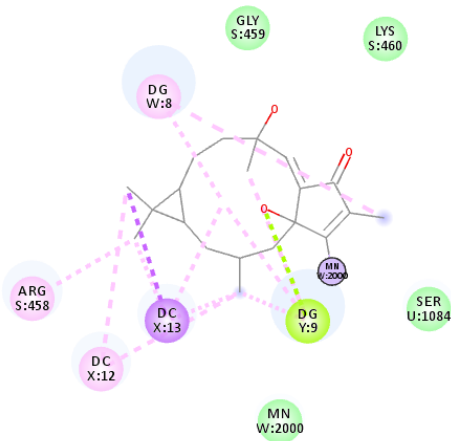
C2 (Multidione)



Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Unfavorable Acceptor-Acceptor
- Pi-Sigma
- Pi-Alkyl

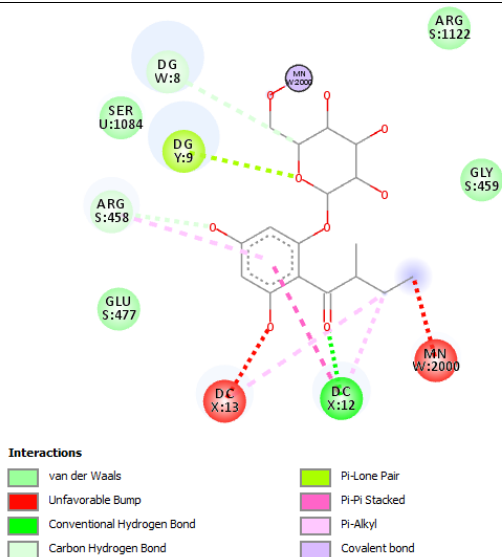
C3 (Multifolone)



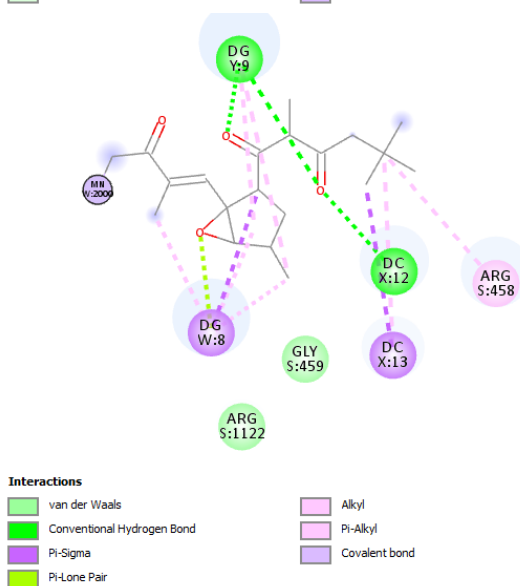
Interactions

- van der Waals
- Pi-Sigma
- Pi-Lone Pair
- Alkyl
- Pi-Alkyl
- Covalent bond

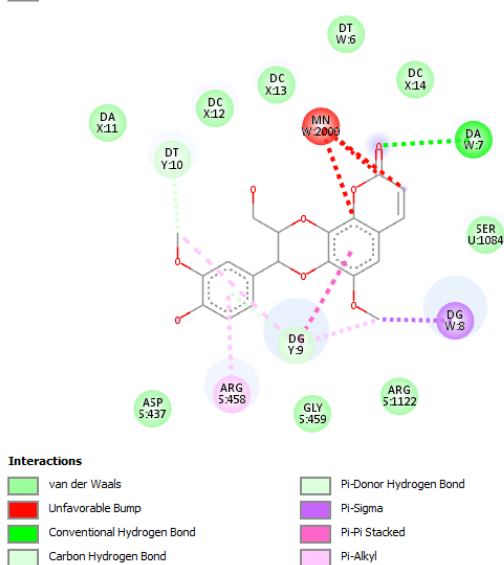
C4 (Multifidol Glucoside)



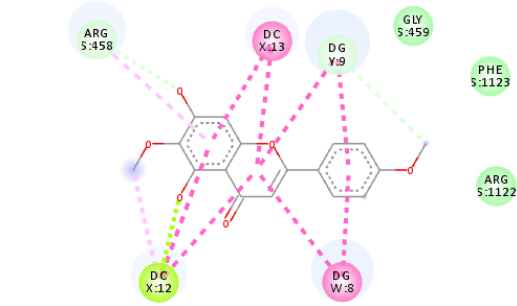
C5 (Citlitrione)



C6 (Cleomiscosin A)



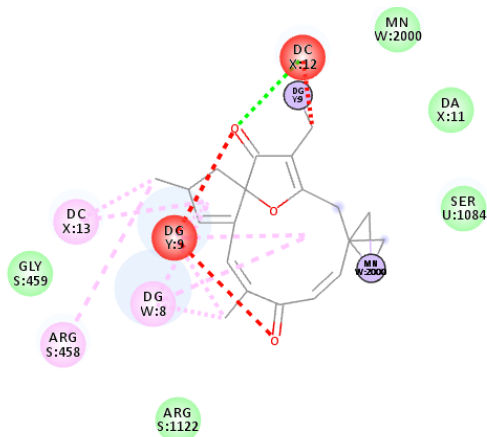
C7 (Pictolarigenin)



Interactions

- van der Waals
- Carbon Hydrogen Bond
- Pi-Lone Pair
- Pi-Pi Stacked
- Pi-Alkyl

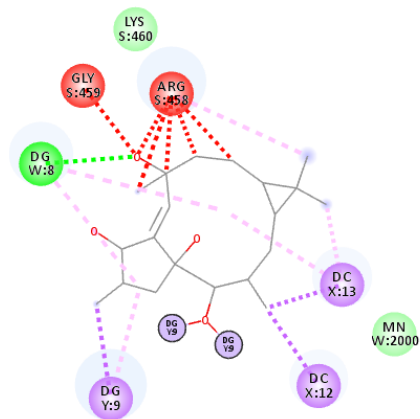
C8 (Jatrophone)



Interactions

- van der Waals
- Unfavorable Bump
- Conventional Hydrogen Bond
- Alkyl
- Pi-Alkyl
- Covalent bond

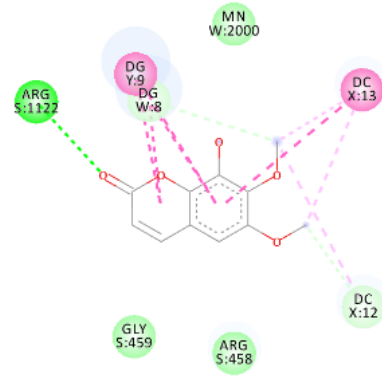
C9 (Multifidanol)



Interactions

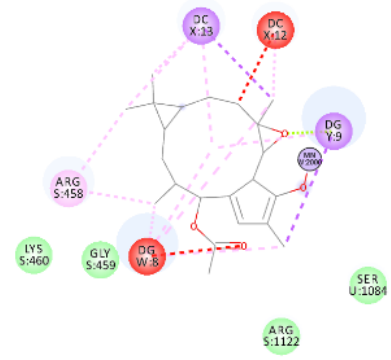
- van der Waals
- Unfavorable Bump
- Conventional Hydrogen Bond
- Pi-Sigma
- Alkyl
- Pi-Alkyl
- Covalent bond

C10 (Fraxidin)



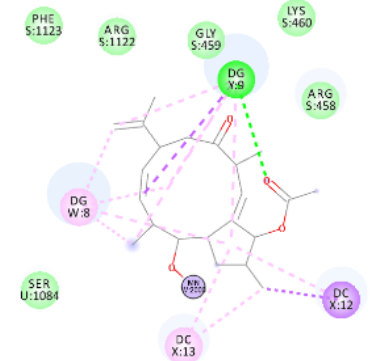
**Interactions**  
 von der Waals  
 Wasserstoffbrückenbindung  
 Kohlenstoff-Wasserstoff-Bindung  
 Pi-Pi Stacked  
 Pi-Pi  
 Pi-Kation

C11 (Jatrothrin)



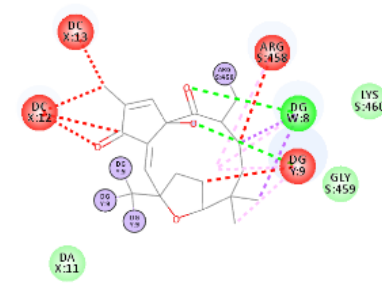
**Interactions**  
 von der Waals  
 Wasserstoffbrückenbindung  
 Pi-Pi  
 Pi-Kation  
 Pi-Pi  
 Pi-Kation  
 Wasserstoffbrückenbindung

C12 (Jatrophene)



**Interactions**  
 von der Waals  
 Wasserstoffbrückenbindung  
 Pi-Sigma  
 Pi-Pi  
 Pi-Kation  
 Wasserstoffbrückenbindung

C13 (Japodagrone)



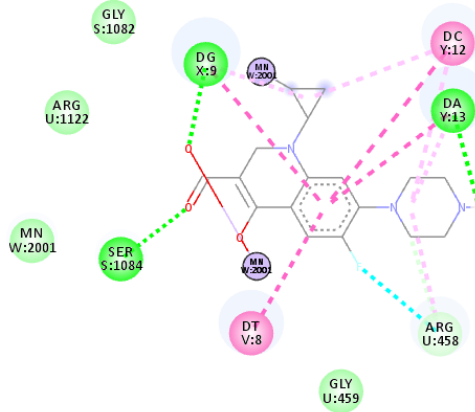
**Interactions**  
 von der Waals  
 Wasserstoffbrückenbindung  
 Kohlenstoff-Wasserstoff-Bindung  
 Pi-Sigma  
 Pi-Pi  
 Pi-Kation  
 Wasserstoffbrückenbindung

S5: Interaction of amino acids with receptors at active site B

Compounds

Interaction images

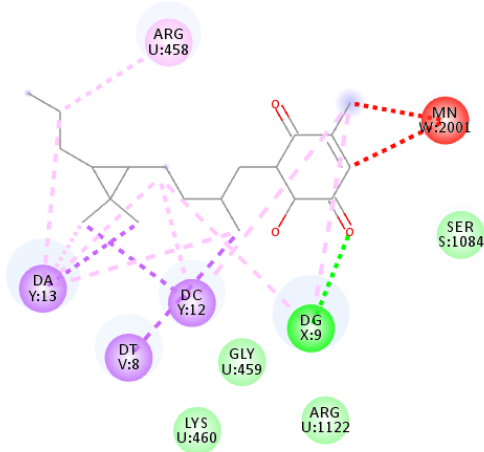
Ciprofloxacin B



Interactions

- |                            |               |
|----------------------------|---------------|
| van der Waals              | Pi-Pi Stacked |
| Conventional Hydrogen Bond | Alkyl         |
| Carbon Hydrogen Bond       | Pi-Alkyl      |
| Halogen (Fluorine)         | Covalent bond |

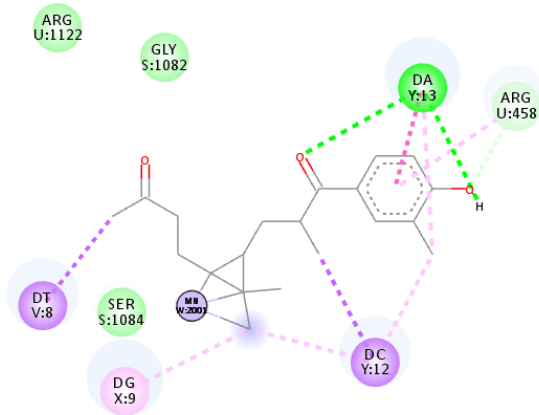
C1 (Multifidone)



Interactions

- |                            |          |
|----------------------------|----------|
| van der Waals              | Pi-Sigma |
| Unfavorable Bump           | Alkyl    |
| Conventional Hydrogen Bond | Pi-Alkyl |

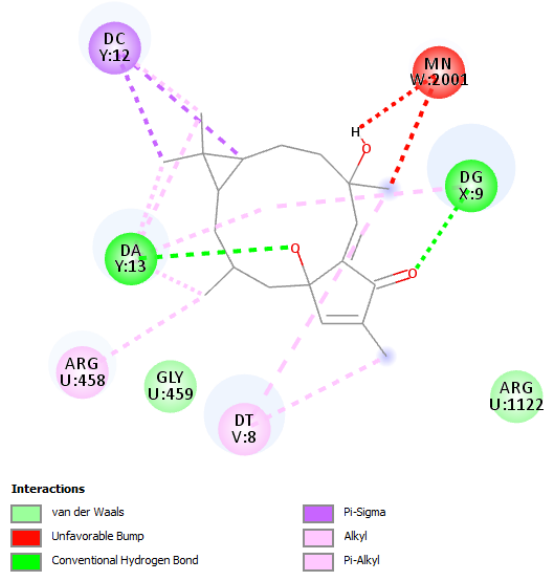
C2 (Multidione)



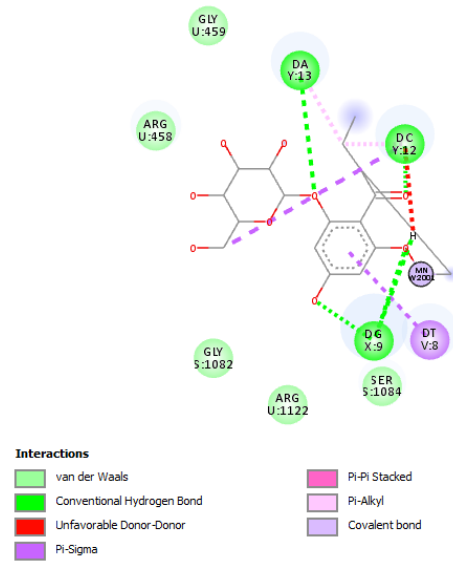
Interactions

- |                            |               |
|----------------------------|---------------|
| van der Waals              | Pi-Pi Stacked |
| Conventional Hydrogen Bond | Pi-Alkyl      |
| Carbon Hydrogen Bond       | Covalent bond |
| Pi-Sigma                   |               |

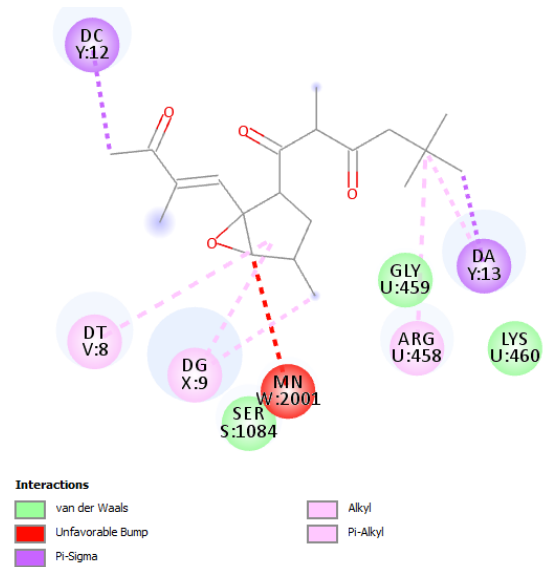
C3 (Multifolone)



C4 (Multifidol Glucoside)

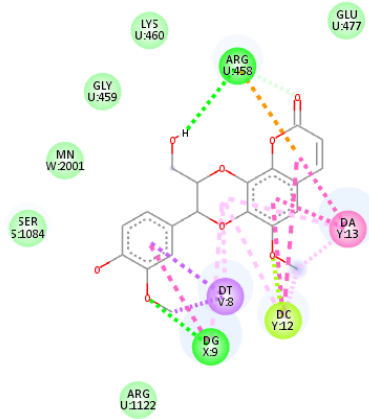


C5 (Citlitrione)





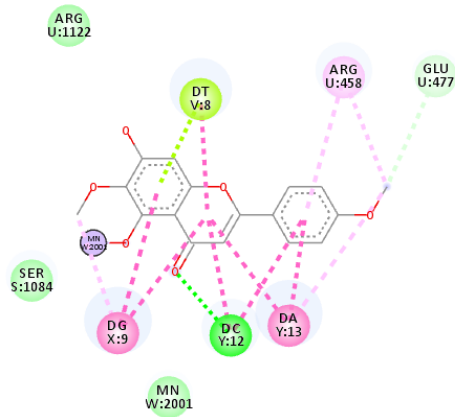
C6 (cleomiscosin A)



Interactions

- |                            |               |
|----------------------------|---------------|
| van der Waals              | Pi-Sigma      |
| Conventional Hydrogen Bond | Pi-Lone Pair  |
| Carbon Hydrogen Bond       | Pi-Pi Stacked |
| Pi-Cation                  | Pi-Alkyl      |

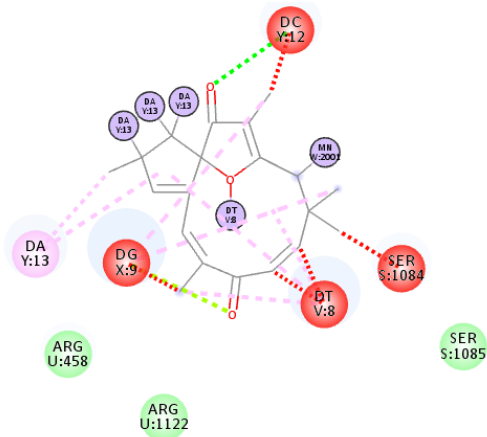
C7 (Pictolarigenin)



Interactions

- |                            |               |
|----------------------------|---------------|
| van der Waals              | Pi-Pi Stacked |
| Conventional Hydrogen Bond | Alkyl         |
| Carbon Hydrogen Bond       | Pi-Alkyl      |
| Pi-Lone Pair               | Covalent bond |

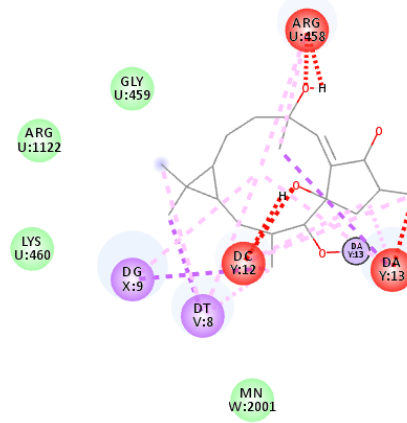
C8 (Jatrophone)



Interactions

- |                            |               |
|----------------------------|---------------|
| van der Waals              | Pi-Lone Pair  |
| Unfavorable Bump           | Pi-Alkyl      |
| Conventional Hydrogen Bond | Covalent bond |

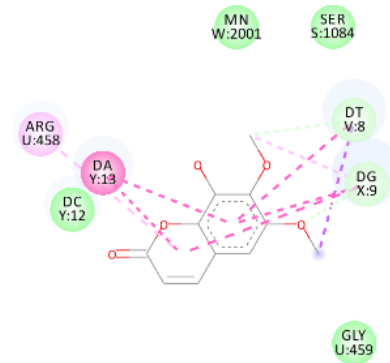
C9 (Multifidanol)



Interactions

- van der Waals
- Unfavorable Bump
- Unfavorable Donor-Donor
- Pi-Sigma
- Alkyl
- Pi-Alkyl
- Covalent bond

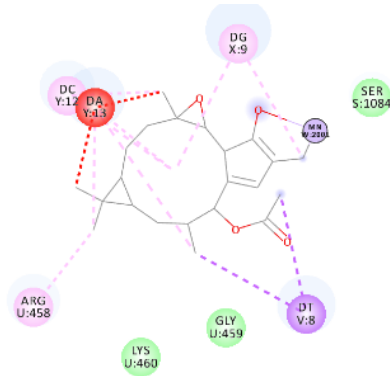
C10 (Fraxidin)



Interactions

- van der Waals
- Carbon-Hydrogen Bond
- Pi-Sigma
- Pi-Pi Stacked
- Pi-Alkyl

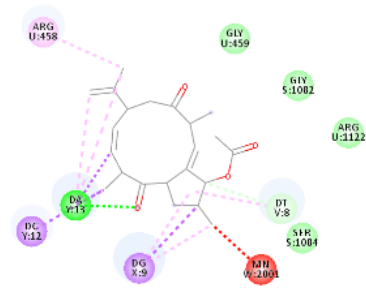
C11 (Jatrothin)



Interactions

- van der Waals
- Unfavorable Bump
- Pi-Sigma
- Alkyl
- Pi-Alkyl
- Covalent bond

C12 (Jatrophenone)

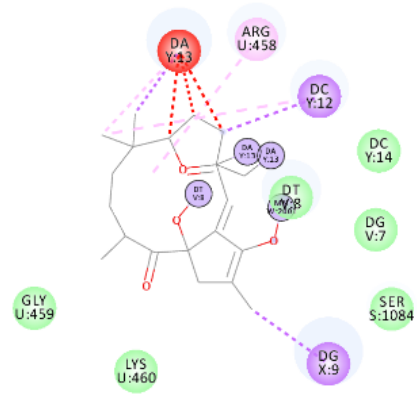


Interactions

- Van der Waals
- Intermolecular Pump
- Conventional Hydrogen Bond
- Carbon-Hydrogen Bond

π-Sigma  
Allyl  
π-Allyl

C13 (Japodagrone)



Interactions

- Van der Waals
- Intermolecular Pump
- π-Sigma

Allyl  
π-Allyl  
Conjugated bond