BAB V
KESIMPULAN DAN SARAN

A. Kesimpulan

Berdasarkan penelitian yang telah dilakukan dapat diperoleh kesimpulan bahwa :

Pertama, prediksi profil farmakikinetika kulit jeruk manis dan bakung putih dapat di absorpsi dengan baik melalui oral, blood brain barier yang baik serta dapat di metabolisme pada CYP450.

Kedua, senyawa kimia 5-hydronoracronycine, citracridone III, limocitrine, hesperetin, hippacine, hippadine, dan lycorine memiliki affinitas tertinggi terhadap reseptor androgen dan CYP17A1 sebagai antikanker prostat.

Ketiga, Limocitrine dan Hippadine diprediksi memiliki interaksi yang baik terhadap target molekuler reseptor androgen serta Citracridone III terhadap target CYP17A1.

B. Saran

Pertama**,** hasil ini merupakan prediksi aktivitas biologis karena didapat dari simulasi pemodelan *software*. Sehingga perlu dilakukan uji *in vitro* dan *in vivo* untuk mengetahui aktivitas senyawa–senyawa tersebut.

Kedua, penelitian perbandingan dapat dilakukan dengan menggunakan kode PDB makromolekul yang berbeda serta *sofware docking* yang berbeda seperti GOLD, Glide, dan DOCK6.

Ketiga, Perlu dilakukan prediksi ADME menggunakan menggunakan sofware lain, karena pada sofware SwissADME ini hanya dapat menganalisis metabolisme pada sitokrom CYP450.

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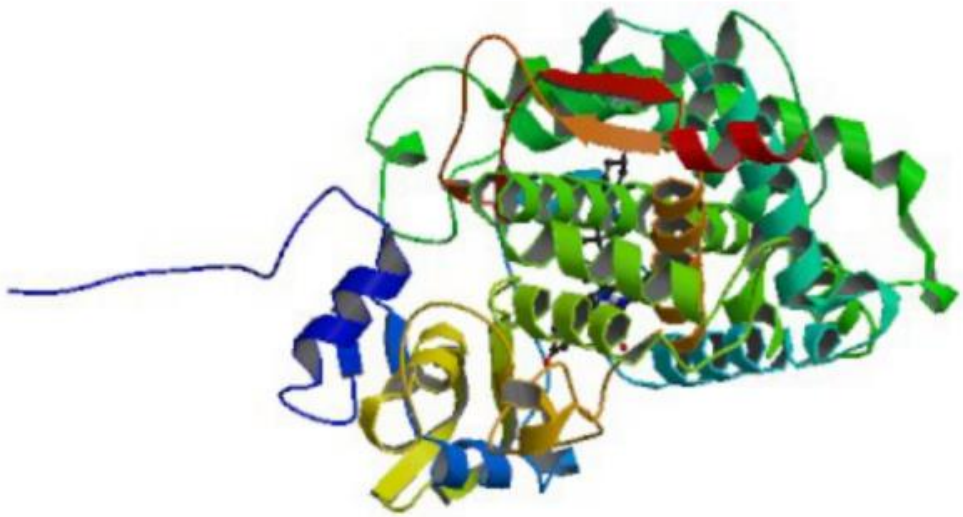
LAMPIRAN

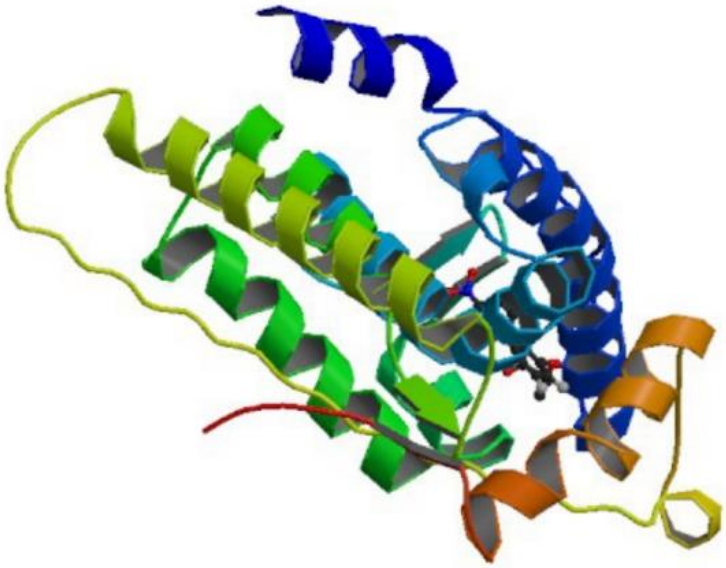
Lampiran 1. Struktur 3D makromolekul.

Struktur 3D Makromolekul AR dengan Kode PDB 3RUK



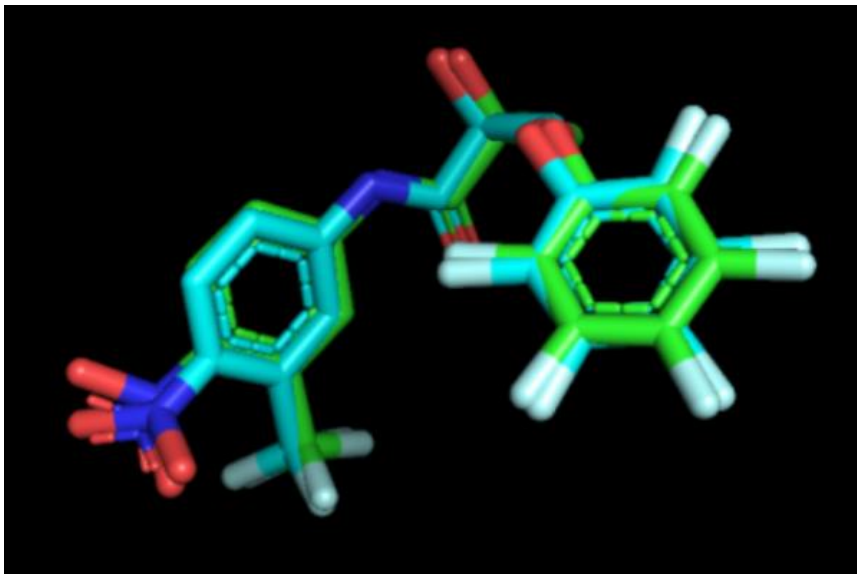
(Sumber : www.rscb.org)

Struktur 3D Makromolekul CYP17A1 dengan Kode PDB 3B67



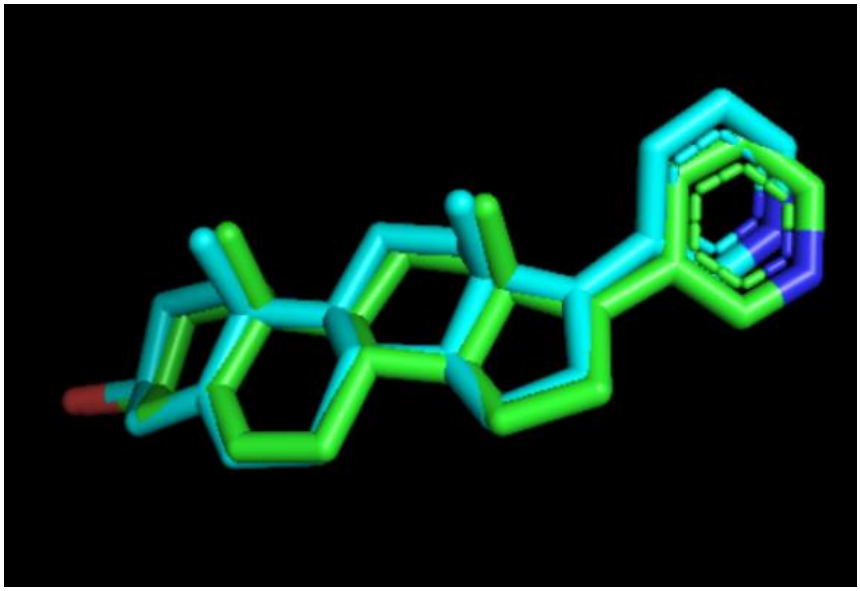
(Sumber : www.rscb.org)

Lampiran 2. *Overlay* hasil validasi motode *docking* dengan PyMol.



Warna hijau (hasil kristalografi) dan warna biru (hasil re-*docking*).

Ligan Asli Makromolekul Reseptor Androgen



Warna hijau (hasil kristalografi) dan warna biru (hasil re-*docking*).

Ligan Asli Makromolekul CYP17A1

Lampiran 3. Hasil *docking* nilai energi ikatan pada target AR.

NO	LIGAN	REPLIKASI					RATA-RATA	SD
		1	2	3	4	5		
1	3b67_11-Hydroxynoracronycine	-9.50	-9.50	-9.50	-9.50	-9.50	-9.50	0.00
2	3b67_11-O-Methylcrinamine	-6.00	-6.00	-6.00	-6.00	-6.00	-6.00	0.00
3	3b67_3-O-Acetylhamayne	-8.80	-8.80	-8.80	-8.80	-8.80	-8.80	0.00
4	3b67_4'-5-7-8-Tetramethoxyflavone	-6.60	-6.60	-6.60	-6.60	-6.60	-6.60	0.00
5	3b67_5-Hydroxy-3'-4-6-7-tetramethoxyflavone	-5.50	-5.50	-5.50	-5.60	-5.60	-5.54	0.05
6	3b67_6-Hydroxycrinamine	-8.30	-8.30	-8.30	-8.30	-8.30	-8.30	0.00
7	3b67_Bicalutamide	-10.00	-10.00	-10.00	-10.00	-10.00	-10.00	0.00
8	3b67_CRIWELLINE	-9.00	-9.00	-9.00	-9.00	-9.00	-9.00	0.00
9	3b67_CitracridoneIII	-9.70	-9.70	-9.70	-9.70	-9.70	-9.70	0.00
10	3b67_CitrusininеI	-8.60	-8.70	-8.70	-8.70	-8.70	-8.68	0.04
11	3b67_CitrusininеII	-8.50	-8.50	-8.50	-8.50	-8.50	-8.50	0.00
12	3b67_Curcumene	-7.30	-7.30	-7.30	-7.60	-7.60	-7.42	0.16
13	3b67_Hesperetin	-8.10	-8.10	-8.10	-8.10	-8.10	-8.10	0.00
14	3b67_Hesperidin	-2.30	-2.30	-2.40	-2.30	-2.30	-2.32	0.04
15	3b67_Limocitrin	-8.70	-8.70	-8.70	-8.70	-8.70	-8.70	0.00
16	3b67_Naringin	-1.80	-1.80	-1.80	-1.80	-1.80	-1.80	0.00
17	3b67_Nobiletin	-4.00	-4.00	-4.00	-4.00	-4.00	-4.00	0.00
18	3b67_Pentamethylquercetin	-7.20	-7.30	-7.20	-7.30	-7.30	-7.26	0.05
19	3b67_Retusin	-8.50	-8.50	-8.50	-8.50	-8.50	-8.50	0.00
20	3b67_Sinensetin	-3.40	-3.30	-3.30	-3.30	-3.30	-3.32	0.04
21	3b67_Tangeretin	-5.70	-5.60	-5.60	-5.70	-5.70	-5.66	0.05
22	3b67_allopurinol	-5.40	-5.40	-5.40	-5.40	-5.40	-5.40	0.00
23	3b67_crinamine	-8.10	-8.10	-8.10	-8.10	-8.10	-8.10	0.00
24	3b67_hippacine	-9.30	-9.40	-9.30	-9.30	-9.30	-9.32	0.04
25	3b67_hippadine	-9.80	-9.80	-9.80	-9.80	-9.80	-9.80	0.00
26	3b67_lycorine	-9.30	-9.30	-9.30	-9.30	-9.30	-9.30	0.00
27	3b67_natsucitrineII	-7.30	-7.20	-7.30	-7.20	-7.20	-7.24	0.05
28	3b67_ungeremine	-8.70	-8.70	-8.70	-8.70	-8.70	-8.70	0.00
29	3b67_3b67ligand	-11.20	-11.20	-11.20	-11.20	-11.20	-11.20	0.00

Lampiran 4. Hasil *docking* nilai energi ikatan pada target CYP17A1.

NO	LIGAN	REPLIKASI					RATA-RATA	SD
		1	2	3	4	5		
1	3ruk_11-Hydroxynoracronycine	-10.00	-10.20	-10.20	-10.20	-10.20	-10.16	0.09
2	3ruk_11-O-Methylcrinamine	-7.00	-7.40	-7.40	-7.40	-7.40	-7.32	0.18
3	3ruk_3-O-Acetylhamayne	-9.00	-9.00	-9.00	-9.00	-9.00	-9.00	0.00
4	3ruk_4'-5-7-8-Tetramethoxyflavone	-8.20	-8.10	-8.00	-8.20	-8.20	-8.14	0.09
5	3ruk_5-Hydroxy-3'-4-6-7-tetramethoxyflavone	-8.10	-8.00	-8.00	-8.00	-8.00	-8.02	0.04
6	3ruk_6-Hydroxycrinamine	-9.30	-9.30	-9.30	-9.30	-9.30	-9.30	0.00
7	3ruk_CRIWELLINE	-8.90	-9.20	-9.20	-9.20	-9.20	-9.14	0.13
8	3ruk_CitracridoneIII	-9.70	-9.70	-9.70	-9.70	-9.70	-9.70	0.00
9	3ruk_CitrusinineI	-8.90	-9.00	-8.90	-8.90	-8.90	-8.92	0.04
10	3ruk_CitrusinineII	-8.60	-8.90	-8.90	-8.90	-8.90	-8.84	0.13
11	3ruk_Curcumene	-7.40	-7.10	-7.10	-7.10	-7.10	-7.16	0.13
12	3ruk_Hesperetin	-9.30	-9.60	-9.60	-9.60	-9.60	-9.54	0.13
13	3ruk_Hesperidin	5.40	5.90	5.60	4.40	4.40	5.14	0.70
14	3ruk_Limocitrin	-8.70	-8.60	-8.60	-8.60	-8.60	-8.62	0.04
15	3ruk_Naringin	-3.30	-1.90	-5.60	-5.50	-5.50	-4.36	1.68
16	3ruk_Nobiletin	-7.20	-6.70	-7.10	-7.30	-7.30	-7.12	0.25
17	3ruk_Pentamethylquercetin	-6.60	-6.80	-6.90	-6.80	-6.80	-6.78	0.11
18	3ruk_Retusin	-7.40	-7.80	-7.80	-7.80	-7.80	-7.72	0.18
19	3ruk_Sinensetin	-7.30	-7.20	-6.80	-7.30	-7.30	-7.18	0.22
20	3ruk_Tangeretin	-8.20	-8.20	-8.10	-8.20	-8.20	-8.18	0.04
21	3ruk_allopurinol	-5.20	-5.20	-5.20	-5.20	-5.20	-5.20	0.00
22	3ruk_crinamine	-8.30	-8.70	-8.70	-8.70	-8.70	-8.62	0.18
23	3ruk_hippacine	-9.00	-9.40	-9.40	-9.40	-9.40	-9.32	0.18
24	3ruk_hippadine	-9.90	-9.90	-10.00	-10.00	-10.00	-9.96	0.05
25	3ruk_lycorine	-9.50	-9.50	-9.50	-9.50	-9.50	-9.50	0.00
26	3ruk_natsucitrineII	-8.50	-8.50	-8.50	-8.50	-8.50	-8.50	0.00
27	3ruk_ungeremine	-8.80	-8.90	-9.20	-9.30	-9.30	-9.10	0.23
28	3ruk_3rukligand	-11.10	-11.10	-11.10	-11.10	-11.10	-11.10	0.00

Lampiran 5. Aturan *Lipinski* ligan uji.

Ligan	Bobot Molekul	*H-Bond acceptors*	*H-Bond donors*	Log P	*Druglikeness*
***Citrus sinensis* L**					
5-Hydroxynoracronycine	323.34	4	2	2.84	Diterima
Tetra-O-methylscutellarein	342.34	6	0	3	Diterima
5-Desmethylsinensetin	358.34	7	1	2.89	Diterima
Citracridone-III	339.34	5	3	2.51	Diterima
Citrusinine-I	301.29	5	2	2.04	Diterima
Citrusinine-II	287.27	5	3	1.68	Diterima
Curcumene	202.34	0	0	4.86	Diterima
Hesperetin	302.28	6	3	1.91	Diterima
Hesperidin	610.56	15	8	-0.72	Ditolak
Limocitrine	346.29	8	4	1.76	Diterima
Naringin	580.53	14	8	-0.79	Ditolak
Nobiletin	402.39	8	0	3.02	Diterima
Retusin	358.34	7	1	2.86	Diterima
Sinensetin	372.37	7	0	3.1	Diterima
Tangeretin	372.37	7	0	3.02	Diterima
Pentamethylquercetin	372.37	7	0	3.04	Diterima
Natsucitrine-II	301.29	5	2	2.08	Diterima
***Crinum asiaticum* L**					
11-O-Methylcrinamine	315.36	5	0	1.98	Diterima
3-O-Acetylhamayne	329.35	6	1	1.45	Diterima
6-Hydroxycrinamine	317.34	6	2	0.99	Diterima
Criwelline	331.36	6	1	1.46	Diterima
Crinamine	301.34	5	1	1.48	Diterima
Hippacine	251.24	3	2	2.21	Diterima

Hippadine	263.25	3	0	2.85	Diterima
Lycorine	287.31	5	2	0.84	Diterima
Ungeremine	266.27	3	1	1.8	Diterima

Lampiran 6. Profil farmakokinetik *SWISSAdme* Ligan uji

Ligan Uji	GI Absorpsion	BBB Permeant	Pgp Substrate	Inhibitor					Bioavailability Score
				CYP3A4	CYPA12	CYP2C19	CYP2C9	CYPD6	
Citrus sinensis L									
5-Hydroxynoracronycine	Tinggi	Ya	Tidak	Ya	Tidak	Ya	Ya	Tidak	0.55
Tetra-O-methylscutellarein	Tinggi	Ya	Tidak	Ya	Ya	Ya	Ya	Ya	0.55
5-Desmethylsinensetin	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Ya	0.55
Citracridone-III	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Tidak	0.55
Citrusinine-I	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Ya	0.55
Citrusinine-II	Tinggi	Tidak	Tidak	Ya	Tidak	Tidak	Ya	Ya	0.55
Curcumene	Rendah	Tidak	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	0.55
Hesperetin	Tinggi	Tidak	Ya	Ya	Tidak	Tidak	Tidak	Ya	0.55
Hesperidin	Rendah	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	0.17
Limocitrine	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Ya	0.55
Naringin	Rendah	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	0.17
Nobiletin	Tinggi	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	Ya	0.55
Retusin	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Ya	0.55
Sinensetin	Tinggi	Ya	Tidak	Tidak	Ya	Ya	Tidak	Ya	0.55
Tangeretin	Tinggi	Ya	Tidak	Tidak	Tidak	Ya	Tidak	Ya	0.55
Pentamethylquercetin	Tinggi	Ya	Tidak	Tidak	Ya	Ya	Tidak	Ya	0.55
Natsucitrine-II	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Ya	0.55
Crinum asiaticum L									
11-O-Methylcrinamine	Tinggi	Ya	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	0.55
3-O-Acetylhamayne	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	0.55
6-Hydroxycrinamine	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Ya	Tidak	0.55
Criwelline	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	0.55
Crinamine	Tinggi	Ya	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	0.55
Hippacine	Tinggi	Ya	Tidak	Ya	Tidak	Tidak	Ya	Tidak	0.55
Hippadine	Tinggi	Ya	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	0.55
Lycorine	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Ya	Tidak	0.55
Ungeremine	Tinggi	Ya	Ya	Ya	Tidak	Tidak	Tidak	Tidak	0.55