Insight into the inhibitory mechanism of Aryl Formyl Piperidine derivatives on Monoacylglycerol Lipase through Molecular Dynamics Simulations

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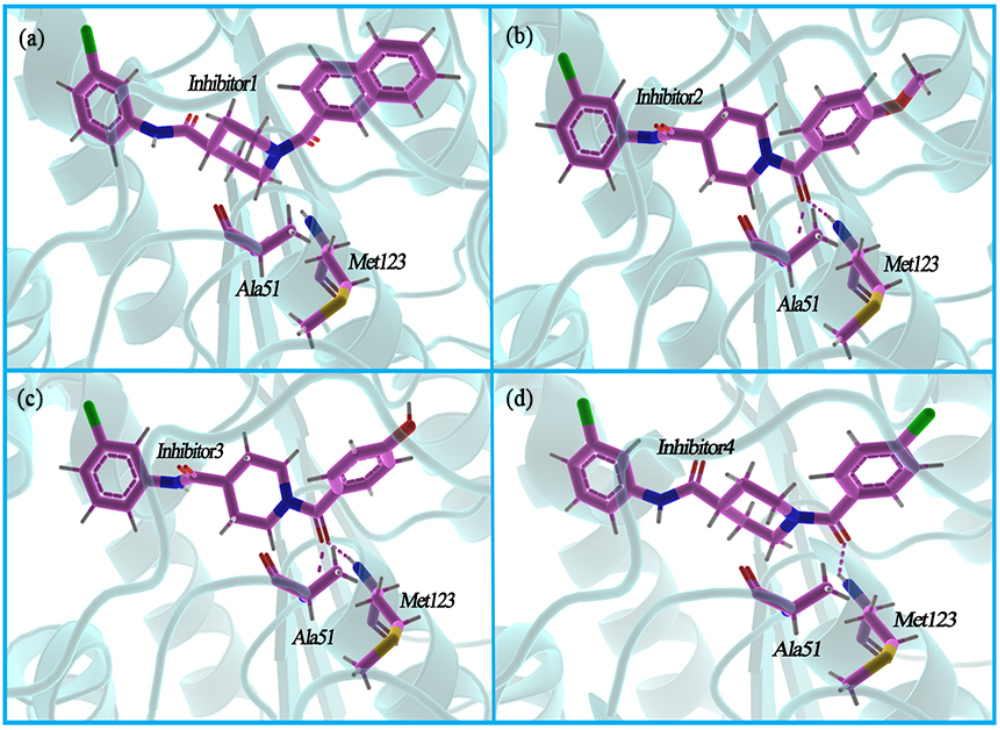

Figure S1. A diagram of the initial conformational patterns of the four complexes obtained by docking,(a)Complex 1, (b)Complex 2, (c)Complex 3, (d)Complex 4.

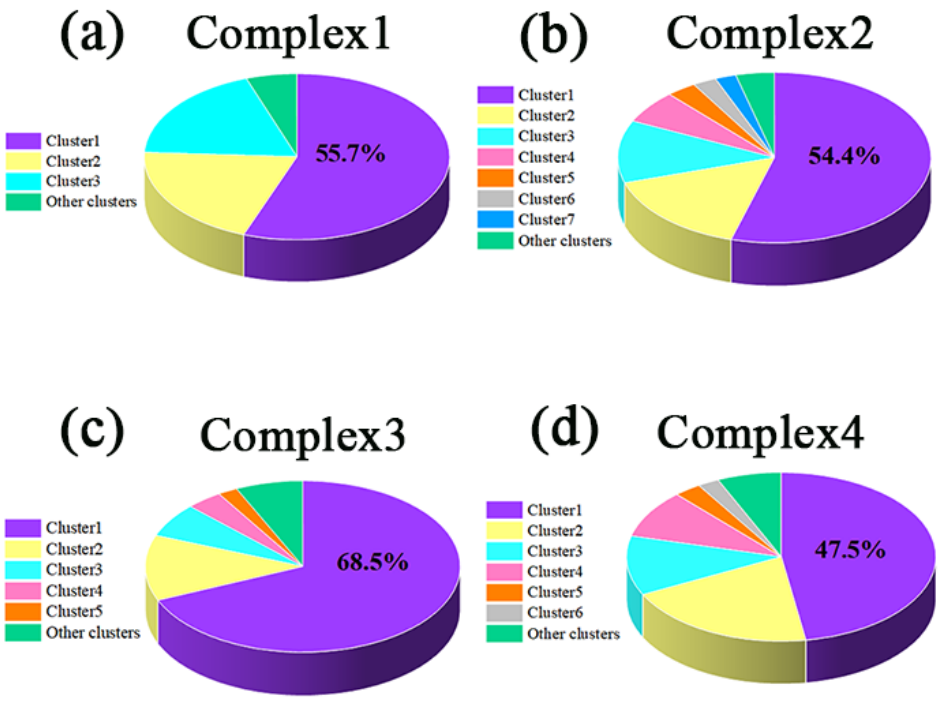

Figure S2. The results of the RMSD-based clustering of the four complexes are shown in the figure, with each complex obtaining its corresponding representative clusters and the "other clusters" being representative clusters that have less than 2% of the capacity.

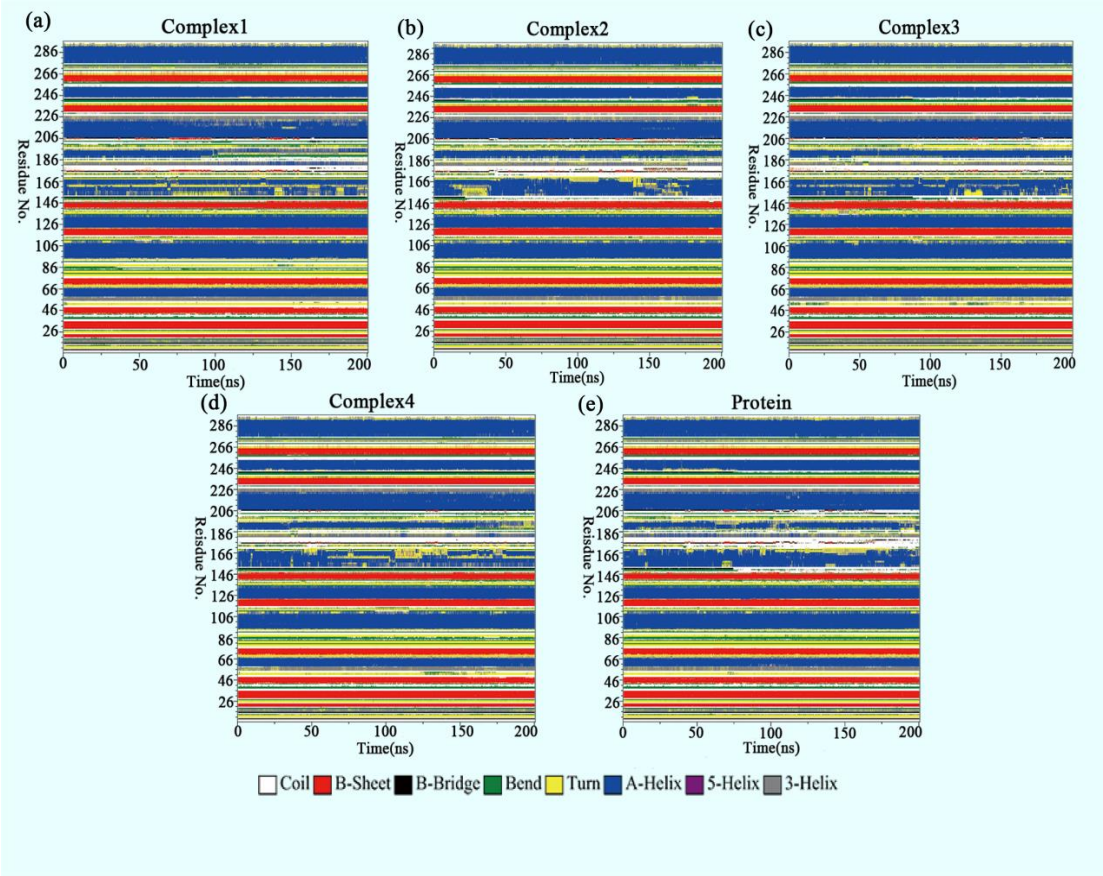

Figure S3. The plot of the whole secondary structure species of the four complexes and the protein with simulation time.

Table S1. The percentages of the first five eigenvectors of the four complexes.

Systems	PC1	PC2	PC3	PC4	PC5	Total
Complex1	25.2%	11.1%	7.0%	4.3%	10.3%	57.9%
Complex2	22.9%	12.8%	7.3%	4.1%	10.9%	58.0%
Complex3	16.8%	13.4%	7.4%	4.6%	12.6%	54.8%
Complex4	22.5%	13.3%	8.2%	5.2%	11.0%	60.2%

Table S2. The various decomposition energies of the important residues in the four complexes (kJ·mol^{-1}).

Residues	Complex1	Complex2	Complex3	Complex4
Gly50	**-4.5096[a]**	**-9.6398**	**-9.9206**	**-2.3282**
	3.9624[b]	**4.1893**	**4.6423**	**1.3702**
	-0.0540[c]	**-0.0389**	**-0.0563**	**-0.0095**
	-0.6027[d]	**-5.4894**	**-5.3370**	**-0.9684**
Ala51	**-14.2399**	**-16.0677**	**-16.6692**	**-5.8165**
	13.0334	**11.5887**	**11.8617**	**7.6964**
	-0.5967	**-0.5691**	**-0.7097**	**-0.3685**
	-1.8033	**-5.0454**	**-5.5175**	**1.5163**
Glu53	**-32.3265**	**-34.2925**	**-21.4421**	**4.0425**
	41.2708	**42.1167**	**35.9210**	**3.8122**
	-0.5069	**-0.4377**	**-0.3528**	**-0.0755**
	8.4268	**7.3743**	**14.1181**	**7.7922**
Ser122	**-18.9881**	**-11.1333**	**-11.9032**	**-3.8783**
	11.3517	**7.7205**	**7.0439**	**4.9793**
	-0.2698	**-0.4522**	**-0.4570**	**-0.1786**
	-7.9111	**-3.8577**	**-5.3147**	**0.9229**
Met123	**-12.1313**	**-12.1920**	**-14.5132**	**-2.5306**
	4.5824	**4.7105**	**4.9351**	**2.0820**
	-0.0435	**-0.1036**	**-0.1205**	**-0.0425**
	-7.5908	**-7.5904**	**-9.7019**	**-0.4924**
Ser155	**-4.7892**	**0.4058**	**-0.2051**	**-4.4302**
	6.7868	**-0.2715**	**0.4622**	**3.6556**
	-0.2302	**-0.0339**	**-0.0647**	**-0.1329**
	1.7672	**0.1004**	**0.1920**	**-0.9096**
Ile179	**-1.7921**	**-1.2348**	**-2.1505**	**-3.5604**
	0.3510	**0.0132**	**-0.1957**	**1.4116**
	-0.0209	**-0.2416**	**-0.5795**	**-0.3671**
	-1.4618	**-1.4659**	**-2.9276**	**-2.5138**
Ser181	**-1.0483**	**-2.9446**	**-6.8193**	**-4.2465**
	1.2266	**3.4855**	**3.8107**	**3.2641**
	-0.0692	**-0.1588**	**-0.1808**	**-0.1717**
	0.1074	**0.3838**	**-3.1917**	**-1.1514**
Leu184	**-6.6556**	**-4.9022**	**-6.3498**	**-2.7562**
	0.4401	**0.7352**	**0.8384**	**-0.2558**
	-0.3767	**-0.3838**	**-0.4904**	**-0.3527**
	-6.5920	**-4.5502**	**-6.0014**	**-3.3643**
Glu190	**-5.1072**	**-1.6855**	**0.6049**	**1.6572**
	4.6991	**3.1748**	**2.5685**	**1.1958**
	-0.1103	**-0.0657**	**-0.0988**	**-0.0642**

	-0.5189	1.4289	3.0747	2.7899
Val191	-2.5694	-2.0690	-2.0039	-1.9634
	0.9545	0.8746	0.6006	0.5774
	-0.0904	-0.0994	-0.1061	-0.1592
	-1.7028	-1.2950	-1.5110	-1.5430
Tyr194	-12.0189	-14.0364	-17.6955	-7.3541
	6.2679	8.2303	9.6291	4.9009
	-0.8757	-1.0501	-1.1365	-0.9373
	-6.6294	-6.8613	-9.2035	-3.3842
Asp197	-5.0952	-0.6685	1.2170	-0.6643
	3.2962	1.1557	0.4084	0.9553
	0.0002	0.0006	0.0000	-0.0008
	-1.7977	0.4862	1.6243	0.2916
Leu205	-1.3405	-3.7223	-1.8572	-4.4476
	-0.1636	-0.0461	-0.2341	0.3072
	-0.3953	-0.5987	-0.4126	-0.4852
	-1.9001	-4.3660	-2.5040	-4.6279
Leu213	-4.9730	-2.7714	-3.6157	-2.4997
	0.2927	0.1268	0.2246	0.2716
	-0.4793	-0.3252	-0.4528	-0.2283
	-5.1605	-2.9704	-3.8434	-2.4593
Asp239	6.1861	-0.0979	-4.4447	2.4919
	-5.8245	-2.3503	-2.5186	-3.0454
	0.0004	0.0004	0.0000	0.0001
	0.3575	-2.4502	-6.9640	-0.5526
Leu241	-11.1951	-8.5101	-5.2921	-7.0123
	4.4685	4.3976	1.0552	2.6352
	-0.8278	-1.1393	-0.8066	-0.6989
	-7.5579	-5.2549	-5.0399	-5.0822
His269	-25.4018	-3.1805	7.0066	-11.3696
	26.7227	14.4599	16.4347	14.0516
	-0.1303	-0.0409	-0.0975	-0.0323
	1.2032	11.2382	23.3346	2.6477
Val270	-5.5963	-6.0451	-4.7169	-4.5508
	0.3910	0.4089	0.1763	0.5846
	-0.5290	-0.6817	-0.7396	-0.4795
	-5.7358	-6.3203	-5.2817	-4.4466
Lys273	0.8941	-0.2677	-3.7450	-7.3273
	2.7429	1.1238	3.3418	5.5281
	-0.2031	-0.3149	-0.1260	-0.1850
	3.4319	0.5412	-0.5295	-1.9815

(a:ΔE_{MM} b:ΔG_{polar} c:$\Delta G_{nonpolar}$ d:$\Delta G_{binding}$)