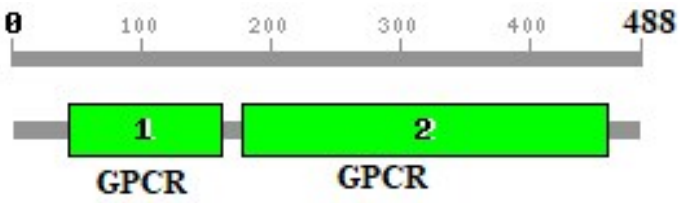


Figure 1: Histamine H1 receptor showed two similar domains of GPCR from 45-162 and 178-461 amino acids.

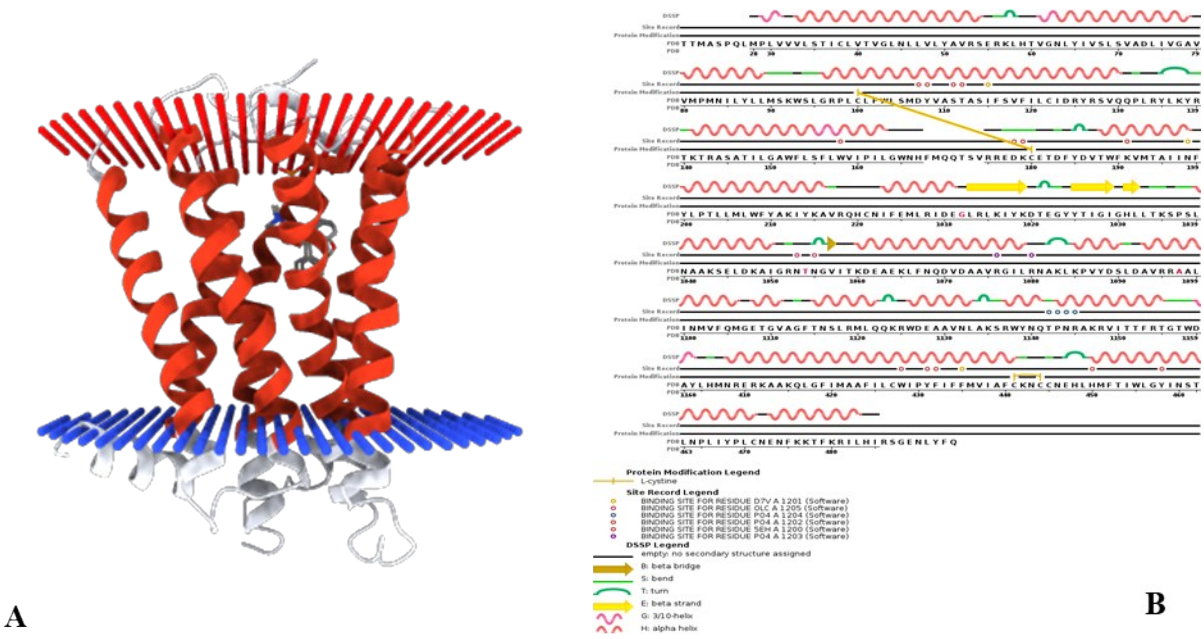
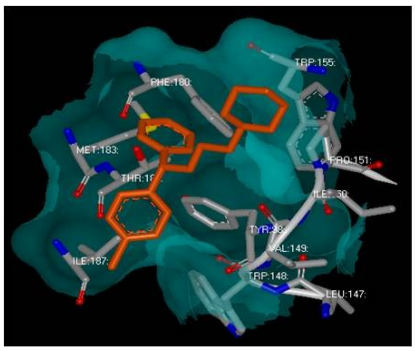
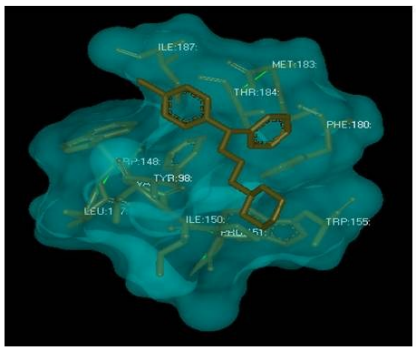


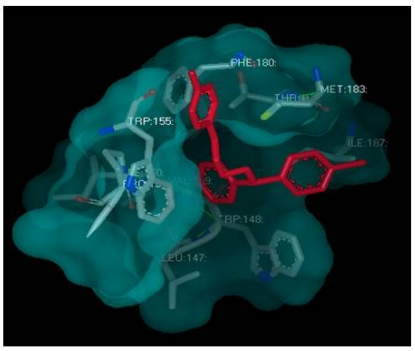
Figure 2:A) Structure of template 3RZE and B) Secondary structureprediction of 3RZE



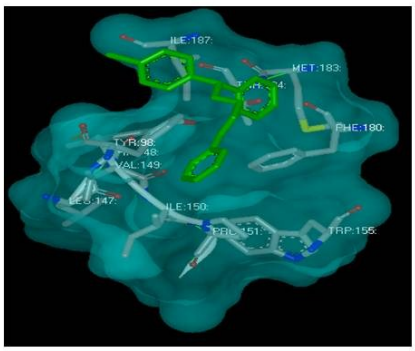
a) CLOPERASTINE



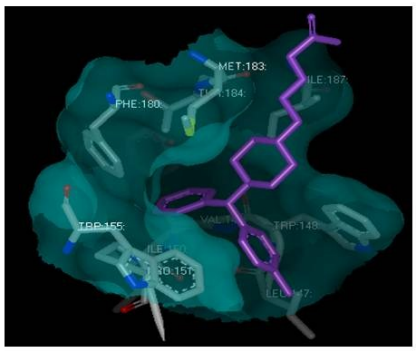
b) Derivative 1



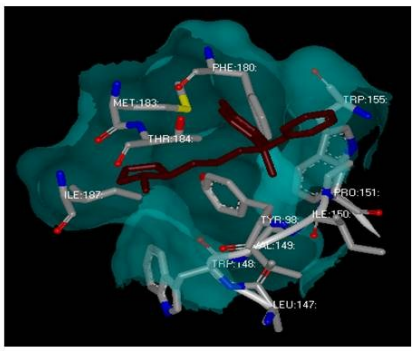
c) Derivative 4



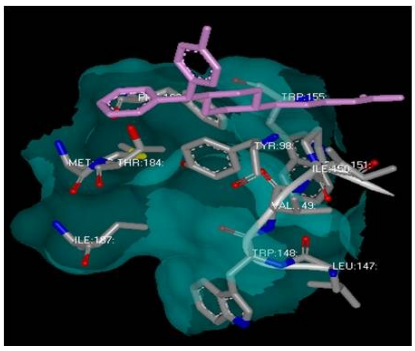
d) Derivative 5



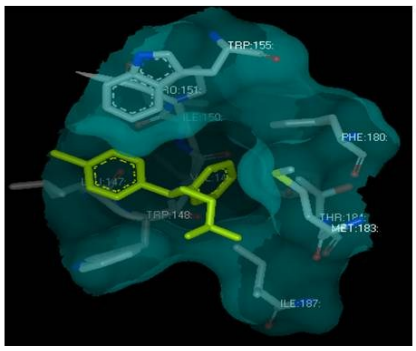
e) Derivative 6



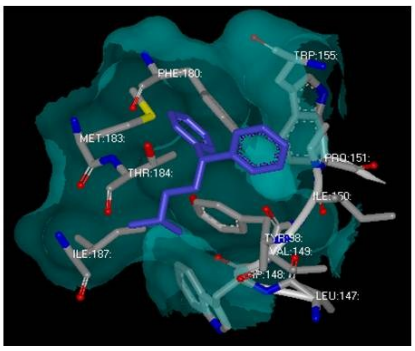
f) Derivative 7



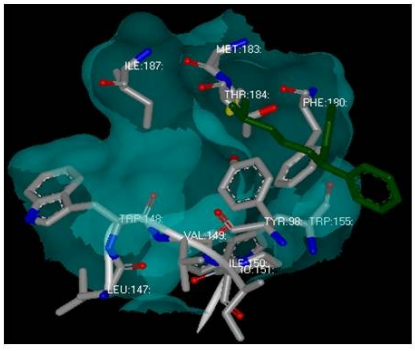
g) Derivative 8



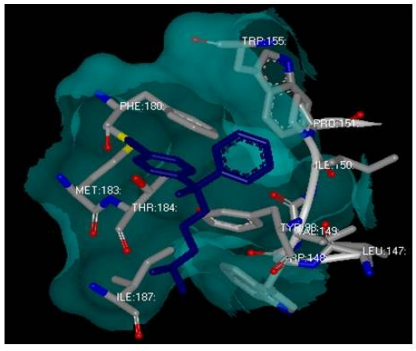
h) Derivative 9



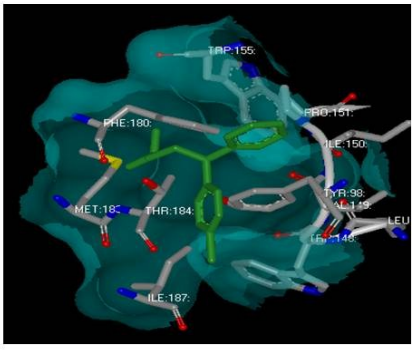
i) Derivative 10



j) Derivative 11



k) Derivative 13



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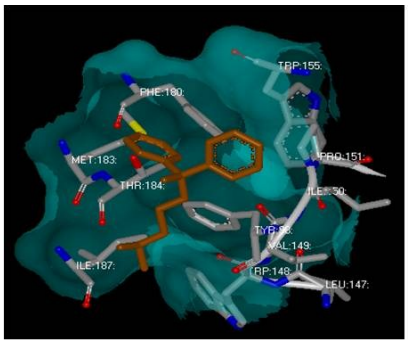
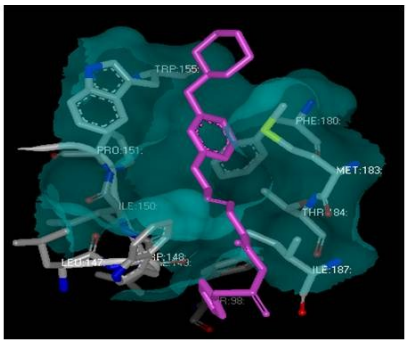
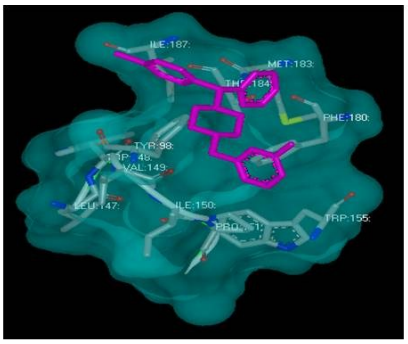


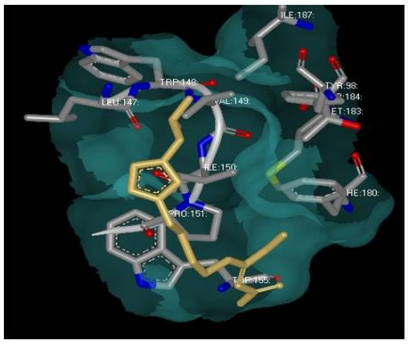
m) Derivative 16



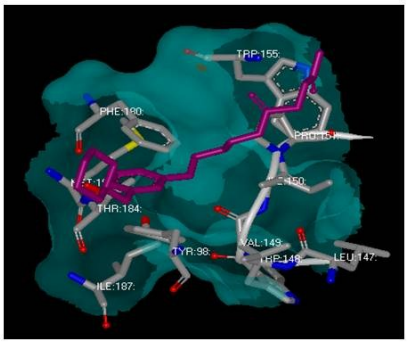
n) Derivative 17



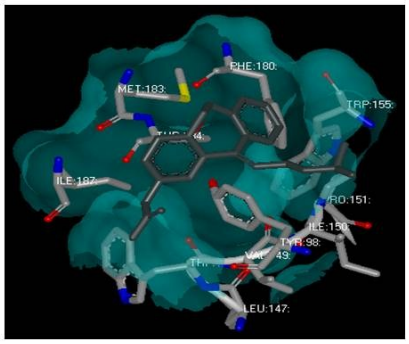
o) Derivative 18



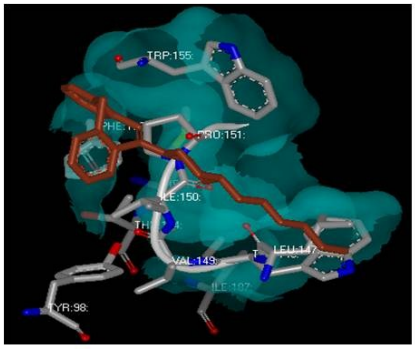
p) Derivative 19



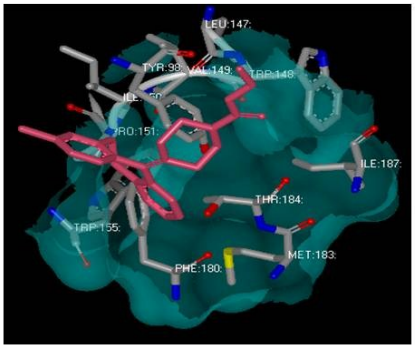
q) Derivative 20



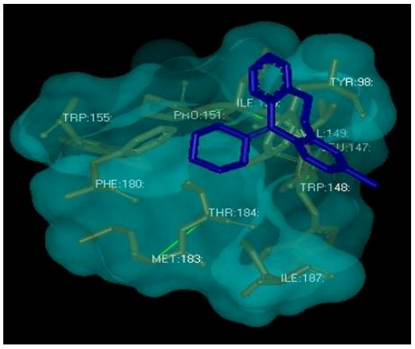
r) Derivative 23



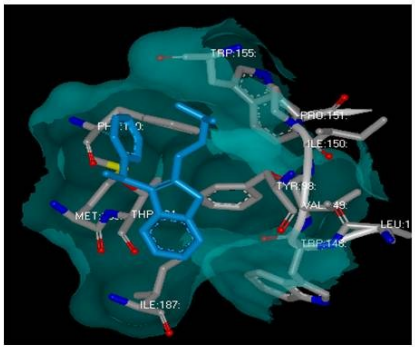
s) Derivative 24



t) Derivative 25



u) Derivative 26



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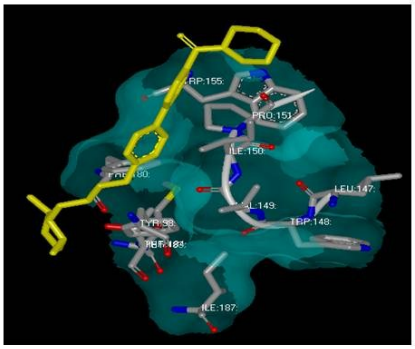
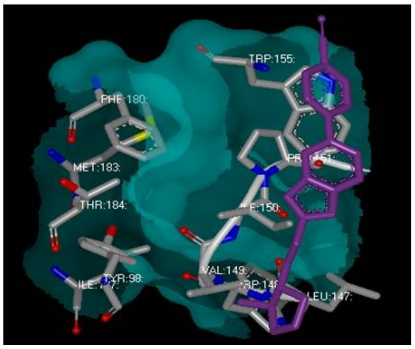
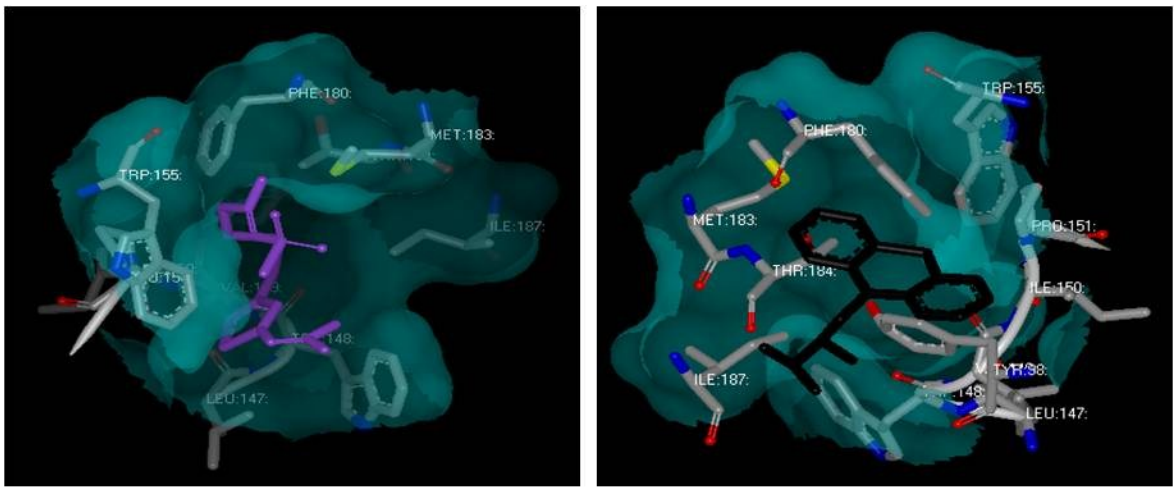


w) Derivative 28



x) Derivative 29



y) Derivative 33 z) Derivative 35

Figure 3 Docking studies of Histamine H1 receptor with Cloperastine derivatives (3a-3z)

Table 1 Molecular properties of Cloperastine derivatives

Compounds	**miLog P**	**TPSA**	**natoms**	**MW**	**nO N**	**nOH NH**	**nvio lati ons**	**nr otb**	**VOLUM E**
Cloperastine($C_{20}H_{24}ClNO$)	1.187	66.761	12.0	168.148	4	2	0	2	144.608
Derivative 1 ($C_{19}H_{22}ClNO_2$)	0.841	49.69	12.0	168.192	3	2	0	2	159.014
Derivative 2 ($C_{37}H_{35}Cl_2NO_2$)	-0.043	69.918	12.0	170.164	4	3	0	2	150.47
Derivative 3 ($C_{40}H_{41}Cl_2NO_4$)	0.614	49.69	11.0	154.165	3	2	0	2	142.42
Derivative 4 ($C_{21}H_{20}ClNO$)	0.254	41.533	11.0	135.149	2	1	0	3	145.591
Derivative 5 ($C_{22}H_{22}ClNO$)	1.204	75.995	14.0	198.174	5	2	0	3	170.154
Derivative 6 ($C_{23}H_{30}N_2O_2$)	0.027	79.152	14.0	200.19	5	3	0	3	176.016
Derivative 7 ($C_{21}H_{26}ClNO$)	0.631	58.924	13.0	184.191	4	2	0	3	167.972
Derivative 8 ($C_{21}H_{25}ClN_2O_3$)	-1.524	55.767	14.0	198.218	4	1	0	3	184.936
Derivative 9 ($C_{21}H_{28}ClNO$)	1.76	45.767	13.0	182.175	4	1	0	3	142.136
Derivative 10 ($C_{16}H_{20}N_2$)	0.641	39.69	10.0	143.192	4	2	0	1	144.014
Derivative 11 ($C_{17}H_{21}NO$)	-0.033	72.918	11.0	150.164	4	2	0	1	140.47
Derivative 12 ($C_{32}H_{39}NO_2$)	0.046	31.533	13.0	167.149	2	1	0	1	146.591
Derivative 13 ($C_{18}H_{22}BrNO$)	1.204	75.995	14.0	198.174	5	2	0	3	170.154
Derivative 14 ($C_{32}H_{39}NO_4$)	0.548	86.152	13.0	270.19	4	3	0	2	185.016
Derivative 15 ($C_{16}H_{19}ClN_2$)	0.512	53.69	13.0	148.165	2	2	0	2	152.42
Derivative 16 ($C_{17}H_{22}N_2O$)	1.322	32.21	13.0	145.149	2	1	0	1	125.23
Derivative 17 ($C_{22}H_{29}N_3O_4S$)	1.254	67.995	13.0	188.174	4	2	0	2	148.154
Derivative 18 ($C_{25}H_{27}ClN_2$)	0.127	48.152	13.0	210.19	4	2	0	2	155.016
Derivative 19 ($C_{13}H_{22}N_4O_3S$)	0.545	45.924	12.0	176.191	3	2	0	2	175.972
Derivative 20 ($C_{19}H_{28}N_2O_4$)	1.235	47.767	14.0	185.218	4	1	0	3	177.936

Derivative 21 ($C_{15}H_{24}N_4S$)	0.89	44.767	11.0	182.175	4	1	0	3	157.136
Derivative 22 ($C_{13}H_{15}ClN_4O$)	0.841	41.69	14.0	184.192	4	1	0	3	158.014
Derivative 23 ($C_{21}H_{23}NO_3$)	-0.53	42.918	11.0	154.164	3	2	0	1	148.47
Derivative 24 $C_{21}H_{25}N_3O_2S$	0.452	35.533	13.0	141.149	5	1	0	3	142.591
Derivative 25 ($C_{22}H_{23}ClN_2O_2$)	0.732	53.69	13.0	144.165	3	1	0	1	132.42
Derivative 26 ($C_{19}H_{19}ClN_2$)	0.527	33.542	12.0	146.149	4	1	0	1	145.591
Derivative 27 ($C_{20}H_{24}N_2$)	1.342	54.995	13.0	176.174	4	2	0	3	136.154
Derivative 28 ($C_{26}H_{34}N_2O_3$)	1.027	87.152	13.0	185.19	4	1	0	2	144.016
Derivative 29 ($C_{22}H_{22}N_2O$)	0.487	67.924	13.0	176.191	4	2	0	3	155.972
Derivative 30 ($C_9H_{16}N_6S$)	1.325	46.767	13.0	176.218	3	1	0	2	176.936
Derivative 31 ($C_{16}H_{18}N_2O_2$)	1.65	45.767	13.0	162.175	4	1	0	3	152.136
Derivative 32 ($C_{14}H_{17}ClN_4S$)	1.853	45.275	14.0	187.174	4	2	0	2	158.154
Derivative 33 ($C_8H_{15}N_7O_2S_3$)	0.477	32.152	12.0	416.19	4	3	0	2	155.016
Derivative 34 ($C_{14}H_{16}ClN_3O$)	1.456	76.924	13.0	175.191	4	2	0	2	174.972
Derivative 35 ($C_{17}H_{20}N_2S$)	1.624	65.767	12.0	163.218	4	1	0	3	146.936

Table 2 Bioactivity studies of Cloperastine derivatives

Compounds (Molecular Formula)	**GPCR ligand**	**Ion channel modulator**	**Kinase inhibitor**	**Nuclear receptor ligand**	**Protease inhibitor**	**Enzyme inhibitor**
Cloperastine($C_{20}H_{24}ClNO$)	-0.75	-0.46	-0.95	-0.63	-1.2	-0.34
Derivative 1 ($C_{19}H_{22}ClNO_2$)	-0.68	-0.35	-0.84	-0.55	-0.12	-0.33
Derivative 2 ($C_{37}H_{35}Cl_2NO_2$)	-0.76	-0.27	-0.93	-0.63	-0.09	-0.21
Derivative 3 ($C_{40}H_{41}Cl_2NO_4$)	-0.88	-0.24	-0.86	-0.78	-1.01	-0.39
Derivative 4 ($C_{21}H_{20}ClNO$)	-1.50	-0.56	-1.14	-0.92	-0.65	-0.65
Derivative 5 ($C_{22}H_{22}ClNO$)	-0.68	-0.24	-0.68	-0.45	-1.82	-0.12
Derivative 6 ($C_{23}H_{30}N_2O_2$)	-0.67	-0.07	-0.63	-0.43	-1.79	-0.08
Derivative 7 ($C_{21}H_{26}ClNO$)	-0.52	-0.14	-0.63	-0.56	-1.72	-0.07
Derivative 8 ($C_{21}H_{25}ClN_2O_3$)	-0.88	-0.26	-1.14	-0.67	-1.51	0.05
Derivative 9 ($C_{21}H_{28}ClNO$)	-0.56	-0.48	-0.93	-0.55	-0.41	-0.23
Derivative 10 ($C_{16}H_{20}N_2$)	-0.88	-0.22	-0.92	-0.64	-1.29	-0.12
Derivative 11 ($C_{17}H_{21}NO$)	-0.83	-0.25	-0.86	-0.73	-1.51	-0.19
Derivative 12 ($C_{32}H_{39}NO_2$)	-1.30	-0.56	-1.17	-0.98	-1.25	-0.63
Derivative 13 ($C_{18}H_{22}BrNO$)	-0.62	-0.24	-0.68	-0.45	-0.42	-0.14
Derivative 14 ($C_{32}H_{39}NO_4$)	-0.68	-0.03	-0.64	-0.44	-0.39	-0.08
Derivative 15 ($C_{16}H_{19}ClN_2$)	-0.75	-0.48	-0.93	-0.65	-1.02	-0.31
Derivative 16 ($C_{17}H_{22}N_2O$)	-0.66	-0.33	-0.82	-0.58	-1.32	-0.36
Derivative 17 ($C_{22}H_{29}N_3O_4S$)	-0.89	-0.23	-0.98	-0.64	-1.19	-0.28
Derivative 18 ($C_{25}H_{27}ClN_2$)	-0.82	-0.26	-0.82	-0.73	-0.11	-0.19
Derivative 19	-1.40	-0.51	-1.14	-0.98	-0.65	-0.65

($C_{13}H_{22}N_4O_3S$)						
Derivative 20 ($C_{19}H_{28}N_2O_4$)	-0.63	-0.07	-0.69	-0.43	-0.59	-0.08
Derivative 21 ($C_{15}H_{24}N_4S$)	-0.61	-0.13	-0.62	-0.54	-0.42	-0.07
Derivative 22 ($C_{13}H_{15}ClN_4O$)	-0.57	-0.22	-1.16	-0.66	-0.31	0.05
Derivative 23 ($C_{21}H_{23}NO_3$)	-0.45	-0.26	-0.84	-0.73	-1.31	-0.19
Derivative 24 $C_{21}H_{25}N_3O_2S$	-1.60	-0.55	-1.12	-0.98	-1.25	-0.65
Derivative 25 ($C_{22}H_{23}ClN_2O_2$)	-0.35	-0.26	-0.68	-0.43	-0.12	-0.18
Derivative 26 ($C_{19}H_{19}ClN_2$)	-0.74	-0.08	-0.64	-0.46	-0.59	-0.08
Derivative 27 ($C_{20}H_{24}N_2$)	-1.85	-0.45	-0.94	-0.65	-1.22	-0.38
Derivative 28 ($C_{26}H_{34}N_2O_3$)	-1.64	-0.34	-0.83	-0.55	-1.32	-0.39
Derivative 29 ($C_{22}H_{22}N_2O$)	-1.84	-0.25	-0.97	-0.64	-1.29	-0.26
Derivative 30 ($C_9H_{16}N_6S$)	-0.41	-0.28	-0.82	-0.73	-1.41	-0.19
Derivative 31 ($C_{16}H_{18}N_2O_2$)	-0.20	-0.55	-1.12	-0.98	-1.35	-0.65
Derivative 32 ($C_{14}H_{17}ClN_4S$)	-0.34	-0.23	-0.94	-0.65	-1.19	-0.24
Derivative 33 ($C_8H_{15}N_7O_2S_3$)	-0.71	-0.27	-0.85	-0.76	-1.21	-0.79
Derivative 34 ($C_{14}H_{16}ClN_3O$)	-1.40	-0.55	-1.17	-0.93	-1.25	-0.67
Derivative 35 ($C_{17}H_{20}N_2S$)	-0.88	-0.25	-0.88	-0.72	-1.11	-0.89