Study of Human Immunodeficiency Virus Type-1 Reverse Transcriptase (HIV-1 RT) Inhibitors by using Drug Design Alignment Patrons

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Abstract
Now a days, drug design and conformational studies are rapidly expanding fields to achieve bioactive drugs against different clinical disorders. In this work, three-dimensional quantitative structure activity relationship (3D-QSAR) was perform on 1-[(2-hydroxyethoxy) methyl]-6-(phenylthio) thymine analogues by using comparative molecular field analysis (CoMFA), comparative molecular similarity Indices analysis (CoMSIA) on three different alignments. The model inhibitors derived from CoMFA and CoMSIA analysis were found in significant range of cross-validated correlation coefficients (q^2) as well as conventional correlation coefficient (r^2) and would be consider potent as anti-AIDS compounds that can block reverse transcription process by obstructing the movement of HIV-1 reverse transcriptase's domains under predictive drug design guidelines.

Key Words
Drug design, Conformational analysis, Acquired immunodeficiency syndrome (AIDS), HIV-1 reverse transcriptase (HIV-1 RT), Three-dimensional quantitative structure activity relationship (3D-QSAR), comparative molecular field analysis (CoMFA), comparative molecular similarity Indices analysis (CoMSIA) and hydrogen bond donor.

1 INTRODUCTION
Acquired immunodeficiency syndrome or acquired immune deficiency syndrome (AIDS) is a retroviral and sexually transmitted disease caused by human immunodeficiency virus (HIV) [14, 18, 19, 29]. It is a severe cluster of multiple opportunistic infections (OIs) catch by opportunistic organisms that cause death of CD4 cells (cluster of differentiation-4), macrophages as well as neuronal cells toward complete distraction of immune system and development of AIDS [44, 54, 55, 59, 60]. HIV encodes reverse transcriptase enzyme to transcribe single stranded RNA into double stranded DNA, then reverse transcribe RNA into complementary DNA that further integrated into host chromosomal DNA and replicate along it. Without this enzyme, the HIV can not able to replicate and infect host [3, 12, 16, 19, 25, 29, 31, 55]. After passing approximately 30 years still there is no treatment for HIV positive patients except fewer antiretroviral therapies which based on anti-HIV-1 RT drugs or inhibitors [34]. These anti-HIV-1 RT candidates can disable HIV-1 reverse transcriptase [40, 43, 48, 56] and terminate DNA synthesis by obstructing domains moment or

incorporating with viral DNA. For instance, one hundred twenty analogues of 1-[(2-hydroxyethoxy) methyl]-6-(phenylthio) thymine were selected from literatures [26, 49] for three-dimensional quantitative structure activity relationship (3D-QSAR) by using comparative molecular field analysis (CoMFA), comparative molecular similarity indices analysis (CoMSIA) and partial least squares (PLS) on three different manual alignment patrons. The main object of conducting this research is to design potent anti-AIDS candidates within low energy conformations that would block HIV's infectious activity by disabling HIV-1 retroviral reverse transcriptase functions.

The 3D-QSAR correlates the structure of medicinal substance with bioactivity that must be based on absorption, distribution, metabolism, and excretion, (ADME) [17, 20] properties, detect functional groups and best fit low energy potent candidates within low energy conformations [1, 2, 4, 5, 7, 8, 30, 36, 38]. It is based on reliable quality assuring methods CoMFA and CoMSIA. The CoMFA is use to find out bioactive co-generic compounds by over lapping them into three dimensional grid via placement of probes and calculating possible grid points in favorable or non-favorable regions of lowest energy conformations [8, 10, 21]. While CoMSIA compares molecular structures among group of structures with five different similarities such as steric, electrostatic, hydrophobic, hydrogen bond donor and hydrogen bond acceptor [21, 32, 33, 41, 46]. On the other hand, the partial least squares or projection to latent structures is use to account the possible variation in achieved drug models by extraction of latent factor through rotation estimation checks (cross validation or leave one out validation) [11, 13, 57, 58]. These checks are uses to estimate quality or accuracy or capacity of new compound and out the un-fitted one by using validation parameters [35, 47].

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2 RESULTS

2.1 COMFA STUDY

2.3 CROSS VALIDATION TEST

CoMFA cross-validated correlation coefficients (q^2) = 0.512.
Number of component (N) = 6.

Column filtering (CF) 2.0.

2.4 CoMFA CROSS-VALIDATION PROPERTIES

CoMFA-Norm of coefficient (Steric) = 4.132.
CoMFA-Norm of coefficient (Electrostatic) = 3.729.
CoMFA-Fractions (Steric) = 0.526.
CoMFA-Fractions (Electrostatic) = 0.474.

2.5 NO VALIDATION/CONVENTIONAL CORRELATION TEST

CoMFA conventional correlation coefficient (r^2) = 0.873.
Number of component (N) = 6.
Column filtering (CF) 2.0.
Standard error of estimation (SEE) = 0.580.
F-values (N1=6, N2=103), 117.879.
Prob. of r^2 (N1=6, N2=103) = 0.000.

2.6 CoMFA CROSS-VALIDATION PROPERTIES

CoMFA-Norm of coefficient (Steric) = 4.130.
CoMFA-Norm of coefficient (Electrostatic) = 3.733.
CoMFA-Fractions (Steric) = 0.525.
CoMFA-Fractions (Electrostatic) = 0.475.

2.7 COMSIA STUDY

2.8 CROSS VALIDATION TEST

CoMSIA cross-validated correlation coefficients (q^2) = 0.710.
Number of component (N) = 6.
Column filtering (CF) 2.0.

2.9 CoMSIA CROSS-VALIDATION PROPERTIES

Norm of coefficient (Steric) = 0.820.
Norm of coefficient (Electrostatic) = 0.852.
Norm of coefficient (Hydrophobic) = 1.586.
Norm of coefficient (Donor) = 1.107.
Norm of coefficient (Acceptor)= 1.121.
Fractions (Steric) = 0.149.
Fractions (Electrostatic) = 0.155.
Fractions (Hydrophobic) = 0.289.
Fractions (Donor) = 0.202.
Fractions (Acceptor) = 0.204.

2.10 NO VALIDATION/CONVENTIONAL CORRELATION TEST

CoMSIA conventional correlation coefficient (r^2) = 0.898.
Number of component (N) = 6.
Column filtering (CF) 2.0.
Standard error of estimations (SEE) = 0.517.
F-values (N1=6, N2=103) = 151.800.
Prob. of r^2 (N1=6, N2=103) = 0.000.

2.11 CoMSIA CONVENTIONAL PROPERTIES

Norm of coefficient (Steric) = 0.812.
Norm of coefficient (Electrostatic) = 0.864.
Norm of coefficient (Hydrophobic) = 1.568.
Norm of coefficient (Donor) = 1.092.
Norm of coefficient (Acceptor) = 1.105.
Fractions (Steric) = 0.149.
Fractions (Electrostatic) = 0.159.
Fractions (Hydrophobic) = 0.288.
Fractions (Donor) = 0.201.
Fractions (Acceptor) = 0.203.

3 TABLES

INHIBITORS	ACTUAL PIC_{50}	RMSD	CoMFA PREDICTED PIC_{50}	CoMFA RESIDUAL PIC_{50}	CoMSIA PREDICTED PIC_{50}	CoMSIA RESIDUAL PIC_{50}

TABLE-1: TRAINING SET OF HEPT COMPOUNDS FOR 3D-QSAR (COMFA AND COMSIA)

H1	4.15	0.362	4.803	-0.65	5.306	-1.15
H2	3.85	0.366	4.195	-0.34	4.271	-0.42
H3	4.72	0.386	4.987	-0.26	5.071	-0.35
H4	5.59	0.380	4.844	0.75	5.376	0.22
H5	5.57	0.384	4.800	0.75	5.458	0.12
H6	4.92	0.380	4.785	0.14	5.506	-0.58
H7	4.35	0.380	4.755	-0.40	5.182	-0.83
H8	5.48	0.380	4.766	0.72	5.061	0.42
H9	4.89	0.377	4.822	0.07	5.090	-0.20
H10	5.24	0.377	5.764	-0.52	5.413	-0.17
H11	5.00	0.374	5.761	-0.76	5.385	-0.38
H12	4.47	0.374	4.879	-0.40	4.419	0.06
H13	4.09	0.379	4.816	-0.72	4.779	-0.68
H14	4.66	0.376	5.083	-0.42	5.374	-0.71
H15	6.59	0.336	6.471	0.12	5.444	1.15
H16	5.89	0.379	6.076	-0.18	5.136	0.76
H17	6.66	0.380	6.867	-0.20	6.651	0.01
H18	5.10	0.365	5.138	-0.03	4.602	0.50
H19	5.14	0.002	4.792	0.35	5.216	-0.07
H20	5.00	0.374	4.026	0.98	4.826	0.18
H31	7.89	0.498	7.862	0.03	7.650	0.24
H32	8.57	0.513	8.248	0.33	7.589	0.99
H33	7.85	0.498	6.572	1.28	7.151	0.70
H34	3.66	0.531	5.666	-2.00	5.485	-1.82
H35	5.15	0.529	4.931	0.22	5.295	-0.14
H36	6.01	0.057	5.977	0.04	5.896	0.12
H37	5.44	0.566	4.779	0.67	5.254	0.19
H38	5.69	0.031	5.811	-0.12	5.083	0.61
H39	5.22	0.568	5.376	-0.15	5.789	-0.56
H40	4.37	0.013	4.781	-0.41	5.041	-0.41
H41	6.07	0.562	6.073	0.00	6.436	-0.36
H42	5.06	0.377	4.859	0.21	5.074	-0.01
H43	5.17	0.570	5.118	0.06	5.662	-0.49
H44	5.12	0.022	5.228	-0.10	5.062	0.06
H45	6.48	0.245	6.556	-0.07	6.080	0.40
H46	5.82	0.378	6.131	-0.31	5.590	0.23
H47	5.24	0.018	5.084	0.16	4.866	0.38
H48	5.96	0.008	5.083	0.88	5.515	0.45
H49	5.48	0.011	4.918	0.57	5.709	-0.22
H50	7.06	0.377	6.557	0.51	6.217	0.85
H51	7.72	0.558	6.745	0.98	6.748	0.98
H52	7.58	0.585	7.635	-0.05	7.738	-0.15
H53	8.24	0.556	7.844	0.40	7.660	0.58
H54	8.30	0.580	7.883	0.42	8.531	-0.23
H55	8.23	0.558	7.686	0.55	7.652	0.58

H56	8.55	0.317	8.906	-0.35	8.337	0.22
H57	8.09	0.586	8.073	0.02	8.496	-0.40
H58	8.14	0.536	7.844	0.30	8.726	-0.58
H59	7.99	0.514	7.591	0.40	7.635	0.36
H60	8.51	0.514	8.015	0.50	8.108	0.41
H61	7.89	0.531	7.965	-0.07	8.215	-0.32
H62	8.14	0.248	8.511	-0.37	8.297	-0.15
H63	5.68	0.666	5.768	-0.08	6.385	-0.70
H64	5.33	0.393	5.658	-0.35	5.446	-0.11
H65	5.66	0.638	4.902	0.76	5.383	0.28
H66	5.92	0.538	5.562	0.36	6.206	-0.28
H67	7.89	0.099	8.057	-0.16	8.196	-0.30
H68	6.66	0.710	6.298	0.39	6.955	-0.29
H69	5.79	0.076	6.276	-0.48	6.198	-0.40
H70	6.45	0.806	6.173	0.28	7.118	-0.66
H71	7.11	0.806	6.178	0.94	7.145	-0.03
H72	7.92	0.034	7.248	0.68	7.250	0.67
H73	7.04	0.047	7.031	0.01	7.068	-0.02
H74	8.13	0.103	8.038	0.10	7.489	0.65
H75	6.47	0.680	5.822	0.65	6.177	0.30
H76	5.40	0.575	5.474	-0.07	6.146	-0.74
H77	6.35	0.564	6.779	-0.42	6.370	-0.02
H78	7.02	0.033	6.910	0.11	6.565	0.46
H79	7.02	0.556	6.803	0.22	7.226	-0.2
H80	7.00	0.554	6.636	0.37	6.696	0.31
H81	4.46	0.571	4.418	0.05	4.514	-0.05
H82	3.89	0.165	4.204	-0.31	4.161	-0.27
H83	3.53	0.899	3.079	0.46	3.126	0.41
H84	3.60	0.015	4.195	-0.59	3.957	-0.35
H85	3.60	0.032	4.389	-0.78	4.218	-0.61
H86	3.72	0.568	4.202	-0.48	3.092	0.63
H87	3.60	0.529	3.073	0.53	3.324	0.23
H88	3.56	0.570	4.101	-0.54	3.686	-0.12
H89	3.60	0.569	4.111	-0.51	3.863	-0.26
H90	3.96	0.574	3.979	-0.05	3.724	0.24
H91	3.45	0.000	3.507	-0.90	3.211	0.24
H92	3.51	0.571	4.412	0.23	3.452	0.06
H93	5.18	0.480	4.959	-0.66	4.687	0.50
H94	4.74	0.568	5.404	-0.34	4.238	0.51
H95	4.68	0.559	5.027	0.12	5.133	-0.45
H96	4.74	0.567	4.625	-0.59	4.481	0.26
H97	5.47	0.051	6.067	-1.75	5.538	-0.06
H98	3.60	0.529	5.355	-0.79	3.761	-0.16
H99	4.92	0.684	5.713	-0.72	5.171	-0.25
H100	4.89	0.574	5.616	-0.75	5.194	-0.30

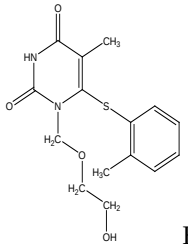
H101	4.72	0.566	5.475	0.42	4.771	-0.05
H102	4.00	0.573	3.586	0.50	4.187	-0.18
H103	4.52	0.570	4.029	0.61	4.395	0.13
H104	4.70	0.568	4.098	0.45	4.454	0.25
H105	4.70	0.613	4.256	0.01	4.267	0.44
H106	3.60	0.777	3.593	-0.36	2.742	0.86
H107	3.82	0.775	4.186	0.91	4.431	-0.61
H108	4.64	0.914	3.730	0.68	4.758	-0.11
H109	6.49	0.549	5.811	0.41	6.048	0.45
H110	6.68	0.552	6.275	-0.13	7.299	-0.61
H111	7.20	0.577	7.332	0.70	7.047	0.16
H112	7.38	0.858	6.687	1.29	6.959	0.43
H113	7.39	0.150	6.102	0.30	6.777	0.62
H114	7.89	0.549	7.593	0.06	7.840	0.05
H115	8.38	0.778	8.327	0.35	7.913	0.47
H116	8.57	0.544	8.220	-1.21	8.300	0.27
H117	6.60	0.598	7.814	-1.04	7.900	-1.30
H118	7.28	0.778	8.327	-0.46	7.913	-0.63
H119	8.80	0.782	9.263	-0.13	8.496	0.31
H120	9.22	0.782	9.351	-0.14	8.807	0.42

TABLE-2: TEST SET OF HEPT COMPOUNDS FOR 3D-QSAR (COMFA AND COMSIA)

4 FIGURES

Scheme: Two-dimensional structures of 1-[(2-hydroxyethoxy) methyl]-6-(phenylthio) thymine (HEPT)

INHIBITORS	ACTUAL PIC_{50}	RMSD	CoMFA PREDICTED PIC_{50}	CoMFA RESIDUAL PIC_{50}	CoMSIA PREDICTED PIC_{50}	CoMSIA RESIDUAL PIC_{50}
H21	5.60	0.023	6.372	-0.77	5.270	0.33
H22	6.96	0.051	7.305	-0.61	6.353	0.34
H23	5.00	0.584	8.034	-3.03	7.423	-3.72
H24	7.23	0.673	6.188	1.05	6.404	0.83
H25	8.11	0.092	6.447	1.67	7.165	0.95
H26	8.30	0.341	8.732	-0.43	7.800	0.50
H27	7.37	0.694	5.795	1.58	6.828	0.55
H28	6.92	0.498	6.117	0.81	6.094	0.83
H29	5.47	0.497	6.706	-1.23	6.549	-1.07
H30	7.20	0.524	7.082	0.12	6.791	0.41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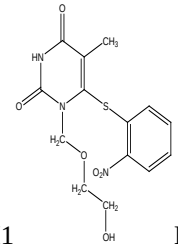
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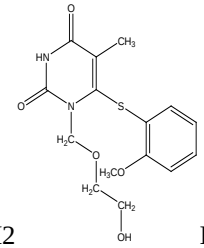
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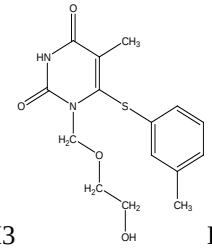
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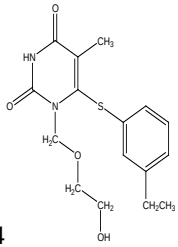
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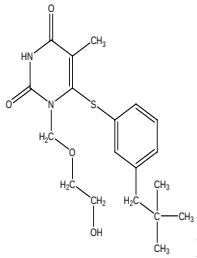
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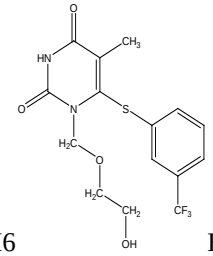
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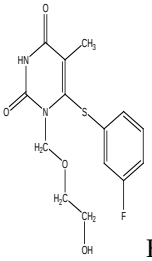
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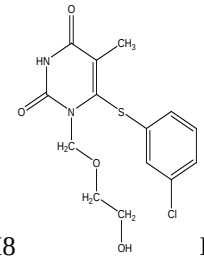
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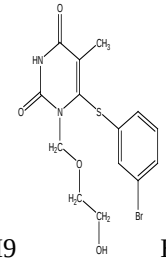
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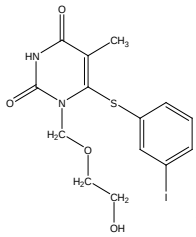
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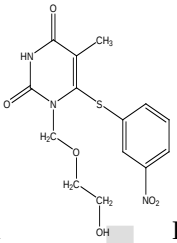
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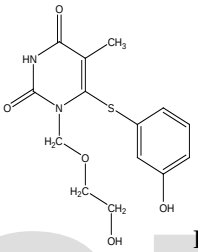
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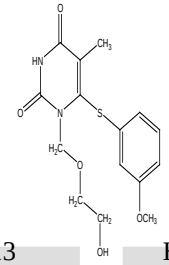
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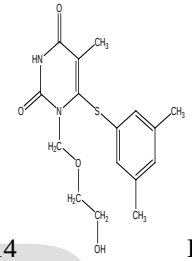
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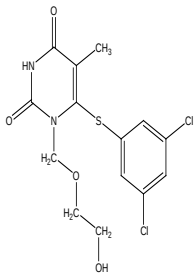
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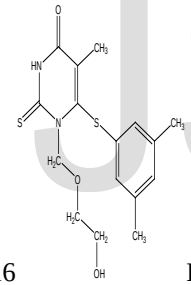
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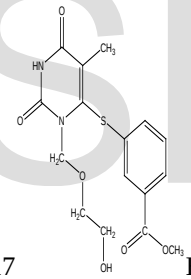
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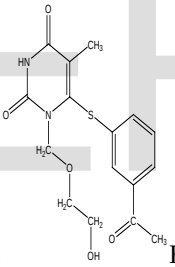
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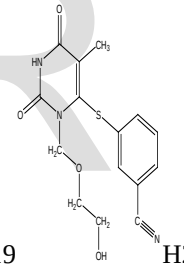
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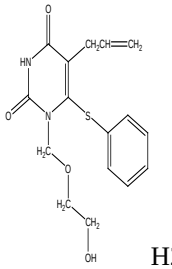
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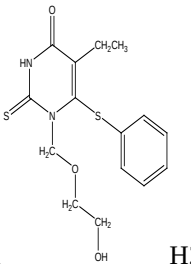
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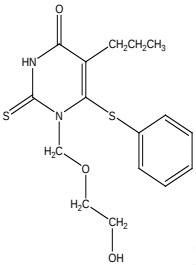
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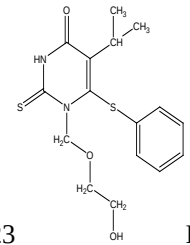
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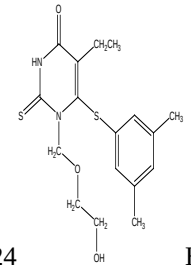
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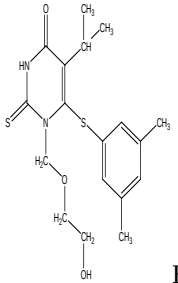
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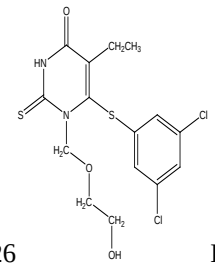
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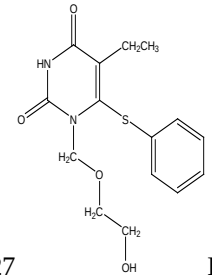
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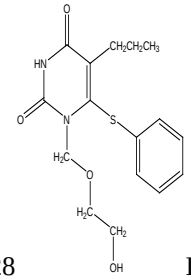
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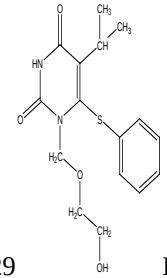
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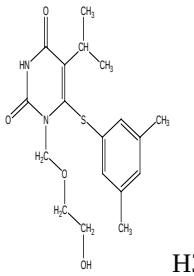
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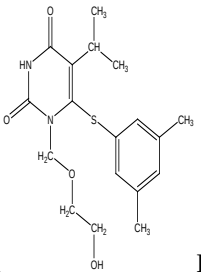
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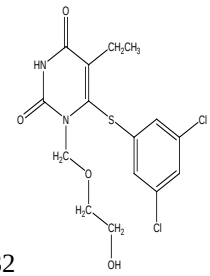
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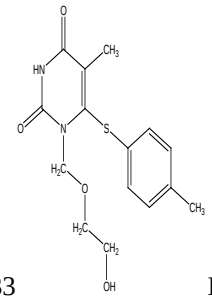
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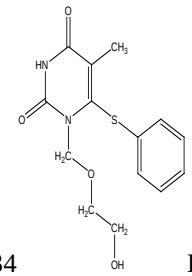
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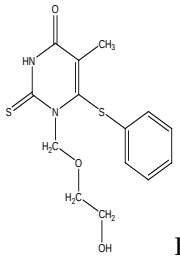
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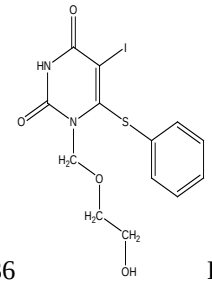
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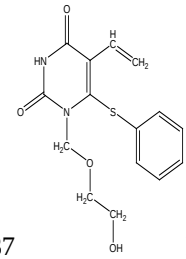
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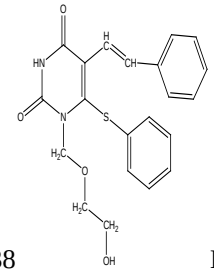
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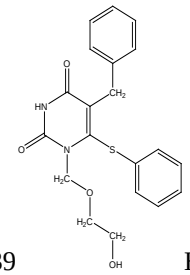
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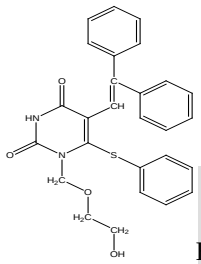
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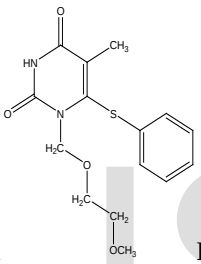
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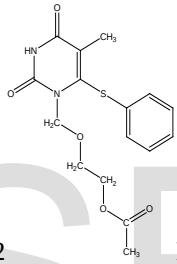
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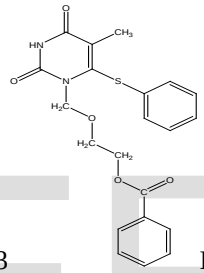
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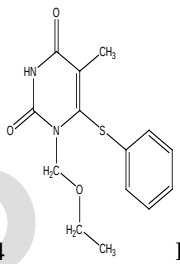
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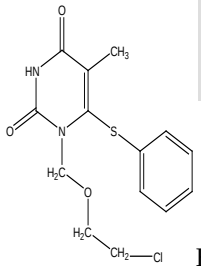
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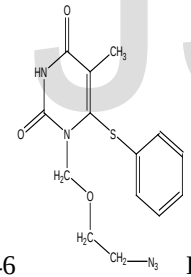
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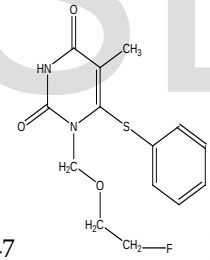
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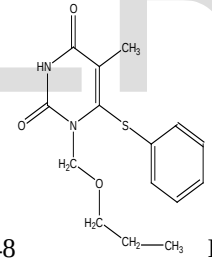
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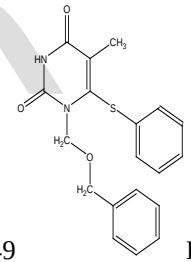
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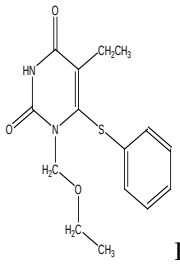
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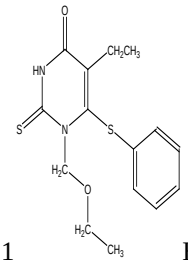
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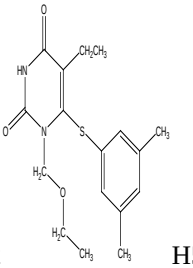
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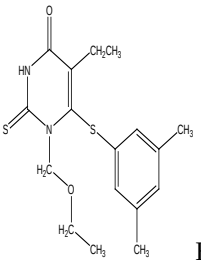
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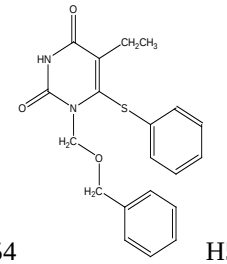
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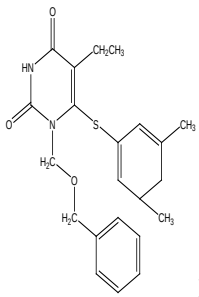
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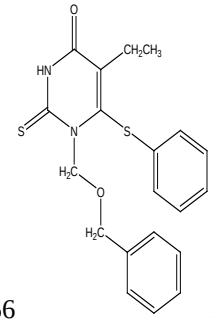
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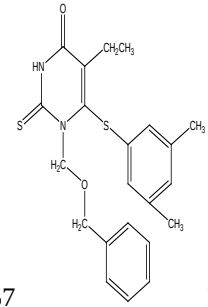
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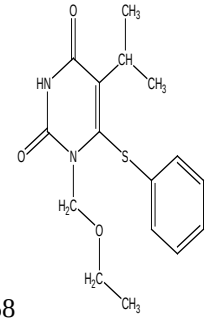
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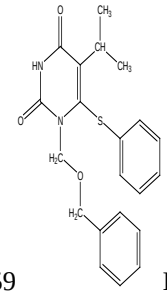
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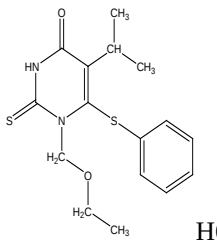
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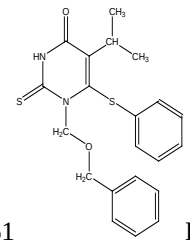
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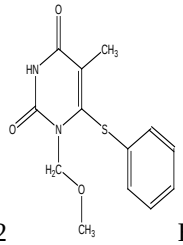
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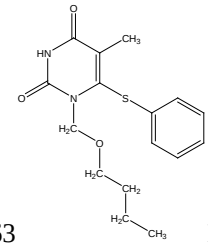
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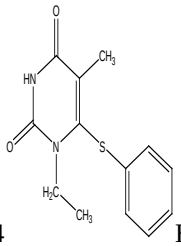
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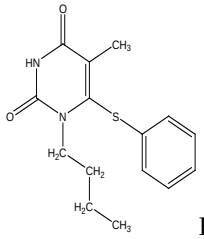
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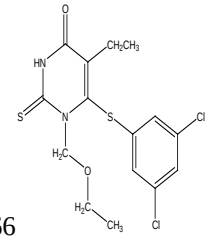
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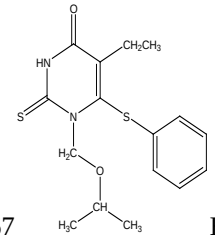
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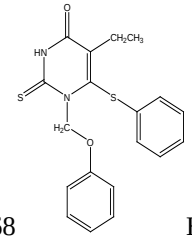
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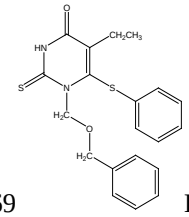
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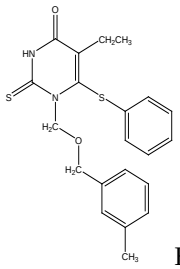
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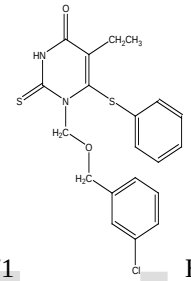
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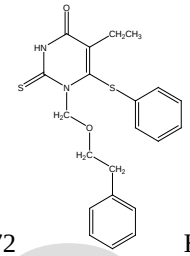
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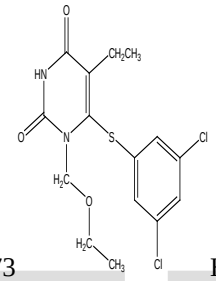
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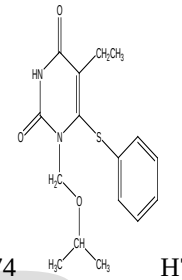
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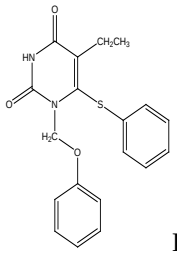
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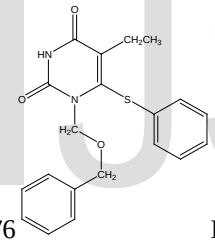
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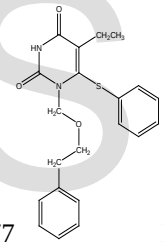
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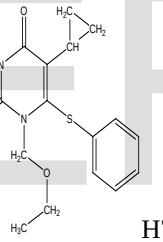
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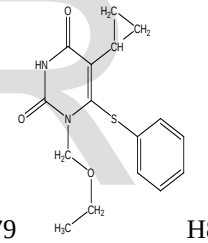
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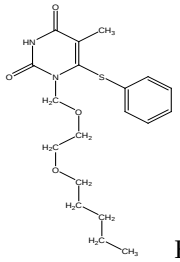
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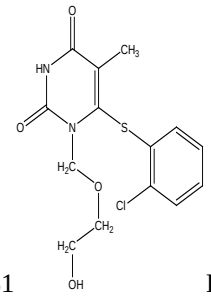
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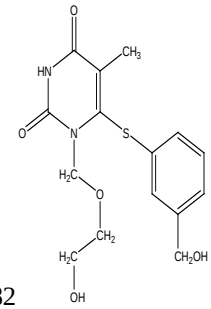
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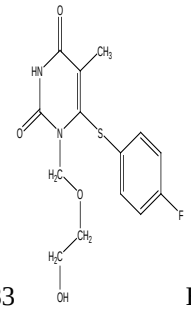
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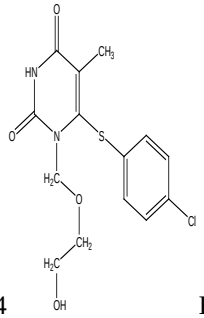
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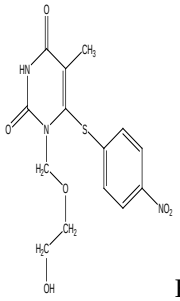
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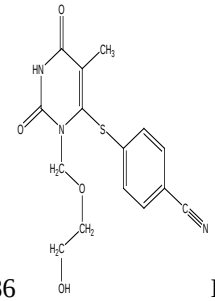
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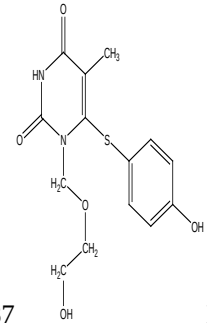
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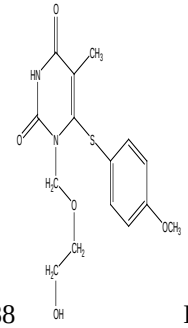
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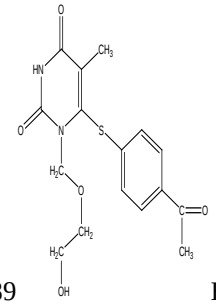
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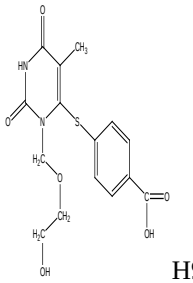
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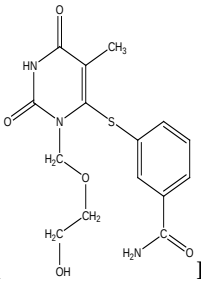
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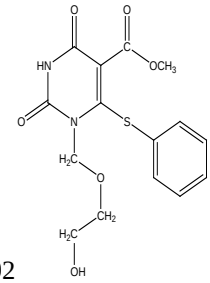
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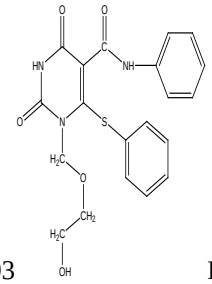
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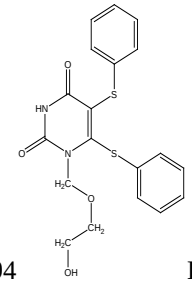
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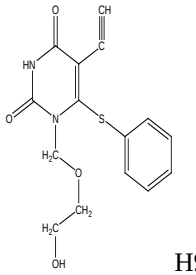
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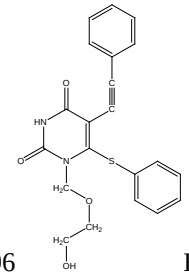
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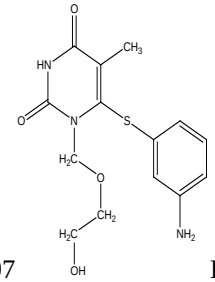
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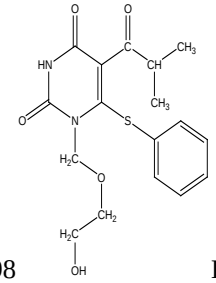
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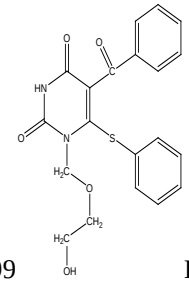
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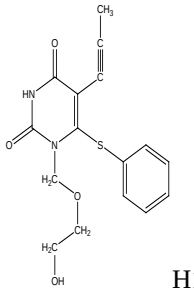
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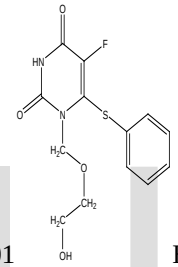
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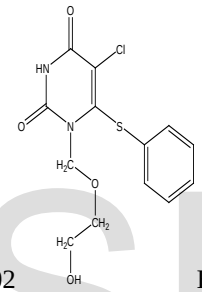
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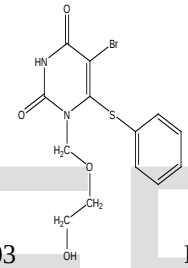
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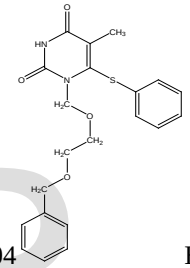
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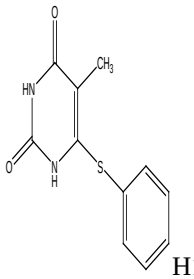
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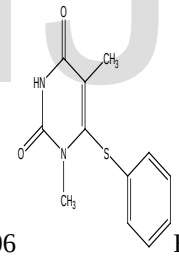
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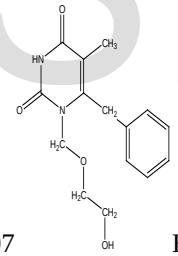
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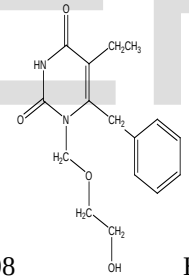
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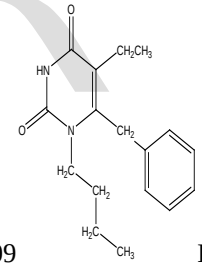
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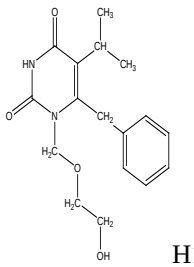
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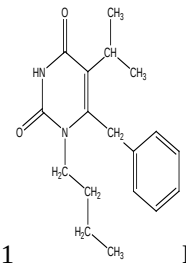
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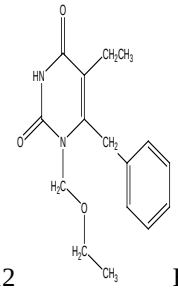
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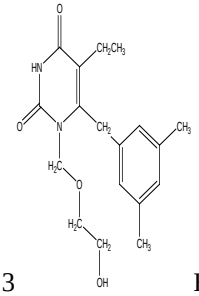
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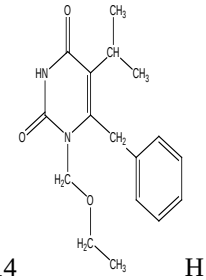
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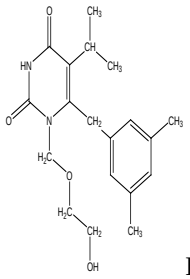
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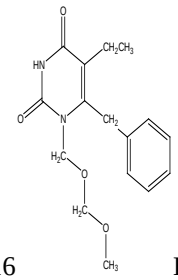
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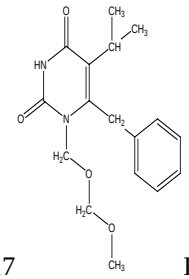
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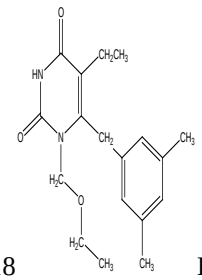
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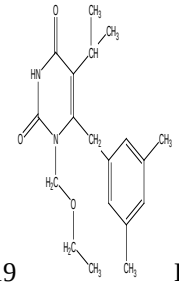
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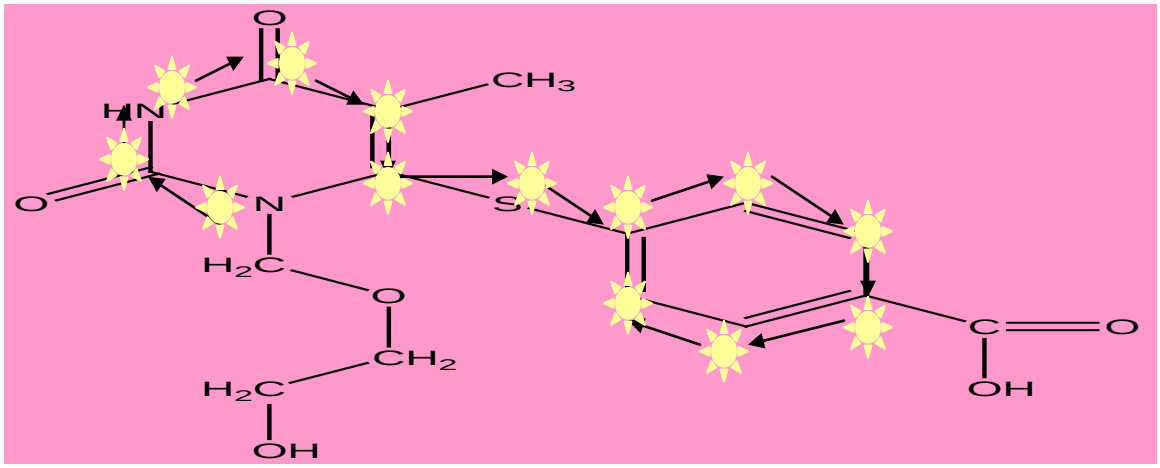

Fig-1: The sun sequence fit atoms alignment of bioactive template H-91 shows rough root mean square deviation (RMSD).

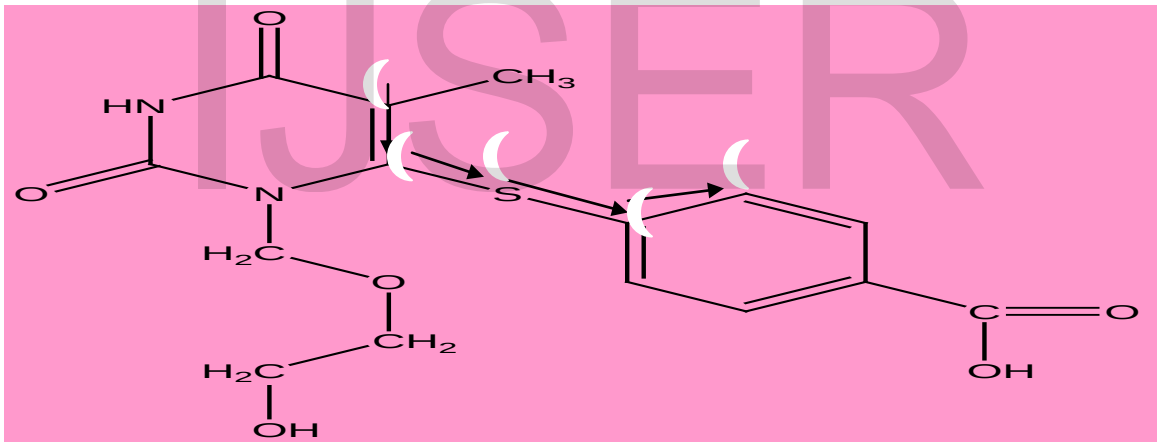

Fig-2: The moon sequence fit atoms alignment of bioactive template H-91 shows average root mean square deviation (RMSD) after removal of one compound as out layer.

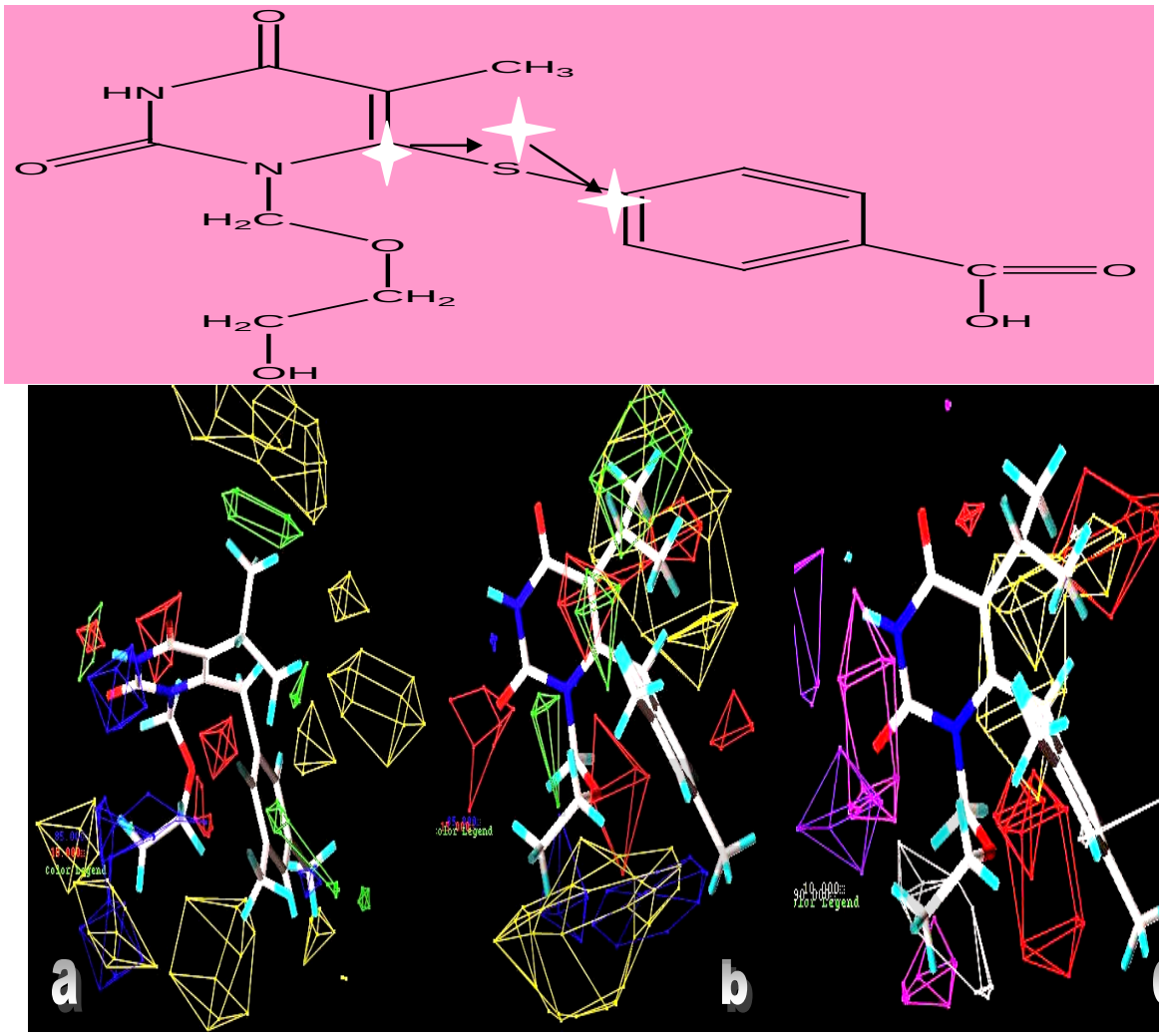

Fig-3: The star sequence fit atoms alignment of bioactive template H-91 shows excellent root mean square deviation (RMSD) after removal of two compounds as out layers.

Fig.4: 3Q-QSAR-CoMFA Steric-electrostatic (a), 3Q-QSAR-CoMSIA Steric-electrostatic (b) and hydrophobic, hydrogen bond donor plus acceptor (c) mapping of HEPT inhibitors.

5 DISCUSSION AND CONCLUSION

Drugs or inhibitors designed with conformational drug design methods were introduced after wide spread of clinical misuses of plant or animal derived products [17, 20, 30, 38, 42]. Therefore *in-silico* approaches are beneficial for calculating molecular properties, complementing three-dimensional structures of bio-molecules, to find out binding between target inhibitor and receptor protein, identifying receptor site and cost effective novel anti-AIDS candidates against HIV infection, [6, 9, 28, , 36, 37, 50, 52].

In this study, three-dimensional structures of 1-[(2-hydroxyethoxy) methyl]-6-(phenylthio) (thymine)] (HEPT) analogues were constructed by Gaussion-03 [15, 24, 27, 51] and Sybyl 6.9., [45, 53] (scheme). The experimental biological activities (EC50) of all

compounds were converted into log1/EC_{50} that used as dependent variable for training and test sets (table-1). After that, all analogues of HEPT were aligned on H-91 bioactive template (figure-1, 2 and 3) within receptor pocket by using field fit manual alignment through three patrons. The purpose of align inhibitors was to achieve difference in the sum of steric-electrostatic interaction energies across lattice between minimized inhibitors in term of root mean square deviation (RMSD) to find out bioactive minimum energy conformers in favorable region of inhibitors to produce pharmacological effects. H-25 and H-27 compounds were taken out from analysis to obtain potent drugs within significant range of cross-validated correlation coefficients (q^2), conventional correlation coefficient (r^2) and RMSD (figure-3 and table-1).

The 1-[(2-hydroxyethoxy) methyl]-6-(phenylthio) (thymine)] (H) inhibitors within low energy conformations derived from CoMFA cross validation gave q^2 (0.512/6) and no validation gave r^2 (0.873/6), SEE (0.580), F (117.879) were significant or satisfactory along steric and electrostatic properties. While inhibitors derived from of CoMSIA cross validation gave q^2 (0.710/6) and no validation gave r^2 (0.898/6), SEE (0.517), F (151.8) were found strongly potent within favorable steric, electronic, hydrophobic, hydrogen bond acceptor and hydrogen bond donor properties.

These results were further validated with experimental biological activities, predicted biological activities and field properties (steric, electrostatic, hydrophobic, hydrogen bond donor and hydrogen bond acceptor) by using regression contour maps. These maps are also use to mark favor or disfavor locations in inhibitors where chemical groups increases or decreases biological activities. With respect of CoMFA and CoMSIA steric-electrostatic contour; the hydrophobic groups (green) would enhance the biological activity of inhibitor to receptor as favor steric bulk. While electronegative groups (red) oxygen, florin or nitrogen enhanced bioactivity because of high electron density within disfavor region of receptor. On the other hand, electropositive groups (blue) were favored to biological activity. Instead of that the hydrophobic groups (yellow) marked less steric bulk is in favor of receptor with detrimental to the biological activity, (figure-4a and 4b). Further more, in CoMSIA, hydrophobic, hydrogen bond donor and hydrogen bond acceptor contours; hydrophilic groups (white), hydrophilic groups (yellow), hydrogen bond acceptor groups (magenta), hydrogen bond donor (purple) polyhedra) and hydrogen bond donor groups (cynes) would enhance, decreases, favored to receptor with increased biological activity biological activity of inhibitors, disfavored to receptor with enhanced biological activity, favored to receptor protein with enhanced biological activity (figure-4c). Here, oxygen atom or sp^2 or sp hybridized nitrogen atoms with lone pair can by hydrogen bond acceptor groups. While ooxygen or nitrogen atom bonded with hydrogen atom may involve as hydrogen bond donor.

The inhibitors derived from CoMFA and CoMSIA analyses are found in satisfactory range of q^2 values but CoMSIA's model compounds have favorable molecular properties (steric, electrostatic, hydrophobic, H-bond acceptor as well as H-bond donor) to the receptor. Finally, concluded that derived inhibitors of HIV-1 RT (HEPT) within low energy conformations from both analyses would be potent anti-AIDS candidates that can halt the DNA synthesis by obstructing the movement of HIV-1 reverse transcriptase's

domains, block reverse transcription (transcribes single stranded RNA into double stranded DNA and form double helix DNA when RNA has reverse transcribed into a single strand complementary DNA (cDNA) and stop HIV-1 to infect host cell.

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