Supplementary Data

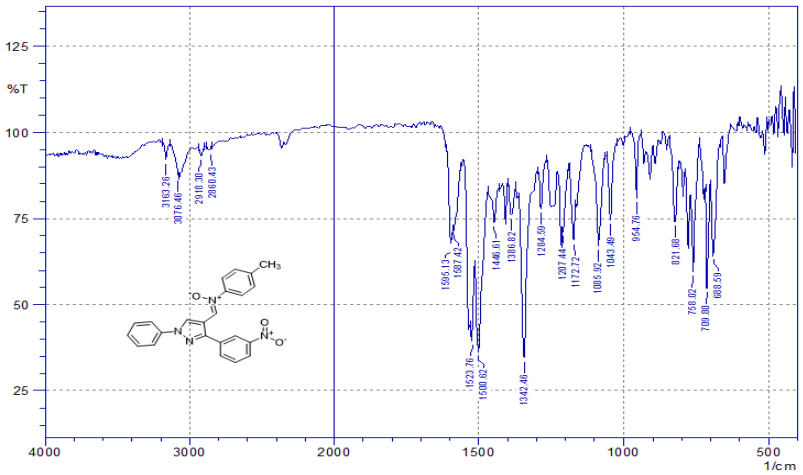

Figure 1: FT-IR spectra of compound (7a)

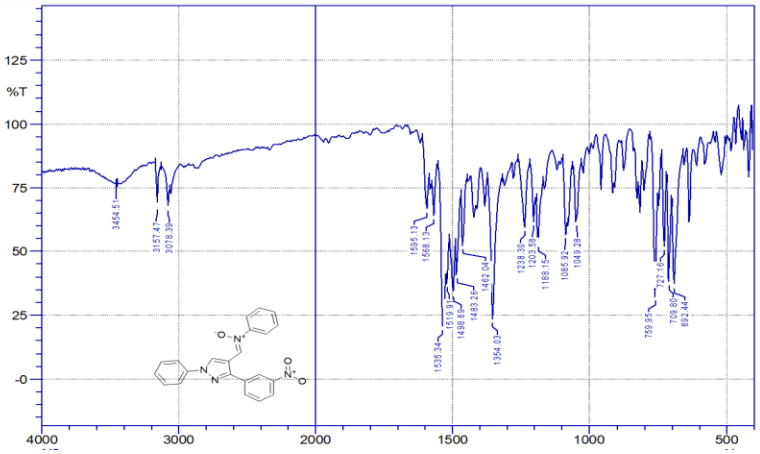

Figure 2: FT-IR spectra of compound (7b)

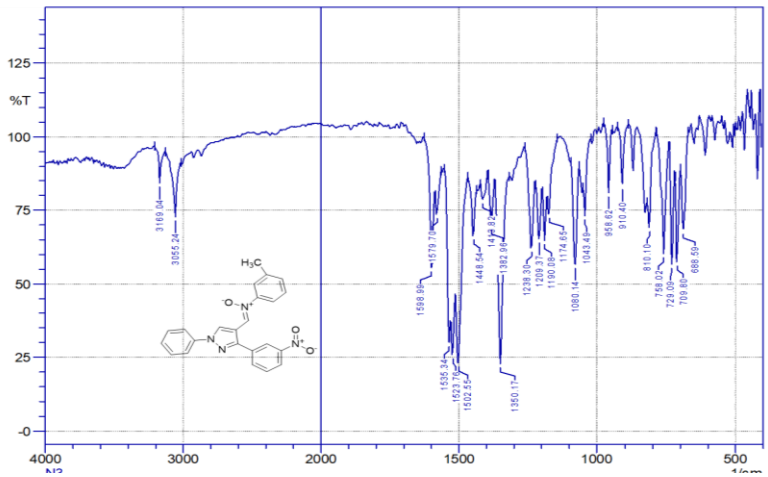

Figure 3: FT-IR spectra of compound (7c)

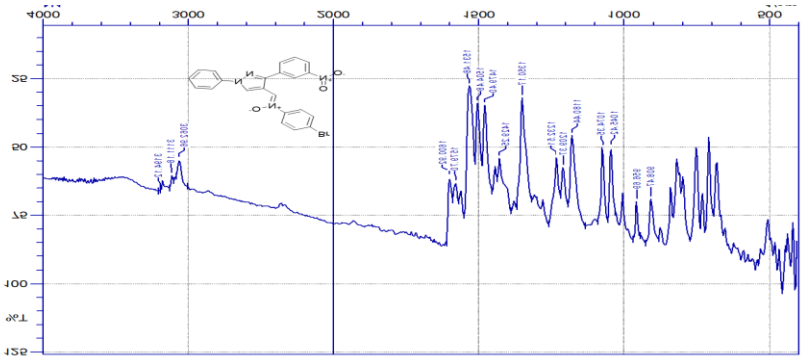

Figure 4: FT-IR spectra of compound (7d)

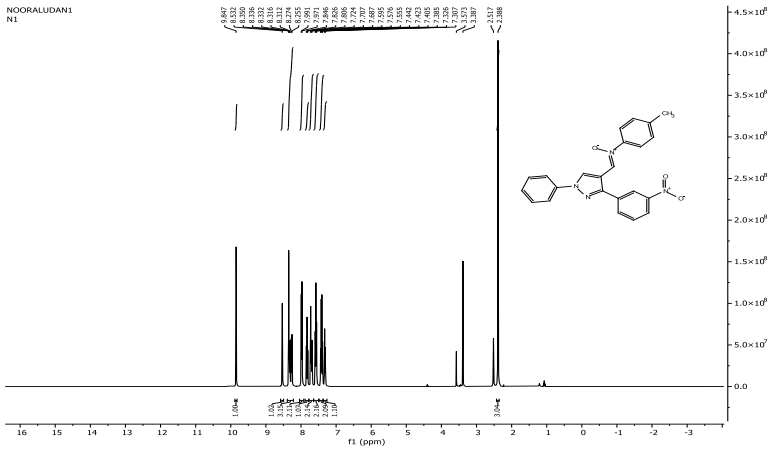

Figure 5: ^{1}H-NMR spectrum of compound 7a

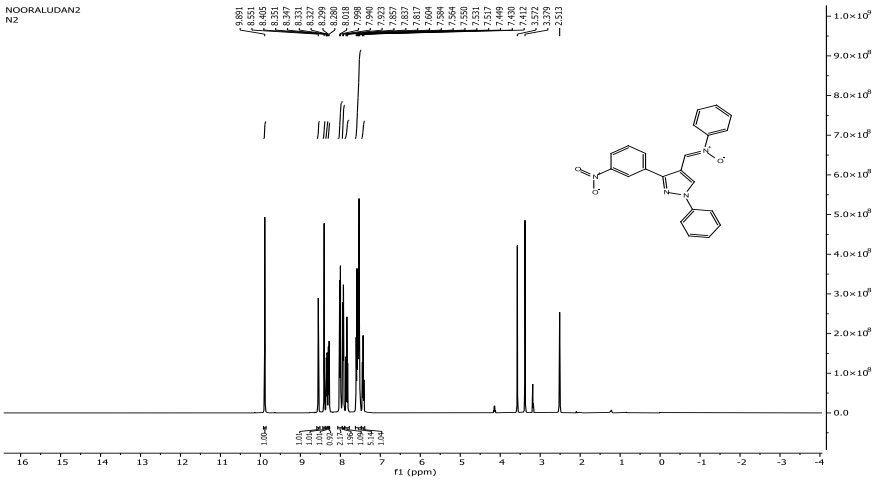

Figure 6: ^{1}H-NMR spectrum of compound 7b

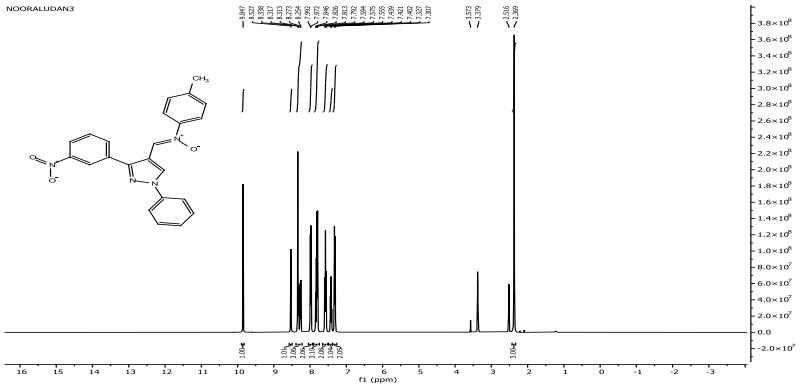

Figure 7: ^{1}H-NMR spectrum of compound 7c

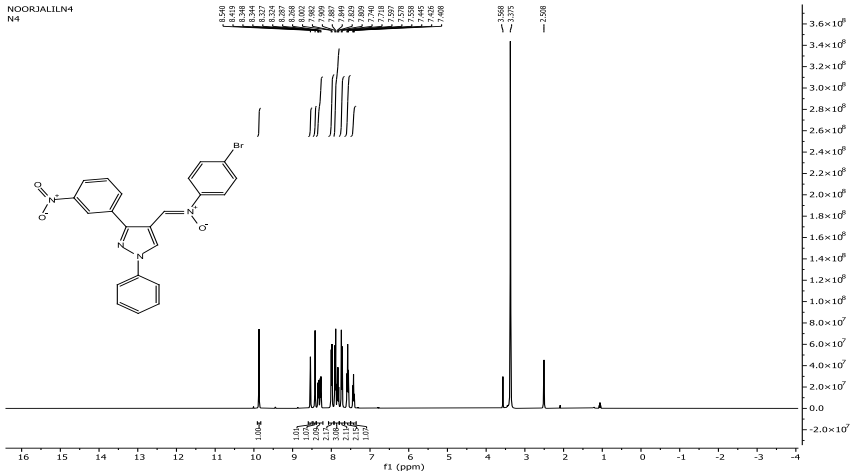

Figure 8: ^{1}H-NMR spectrum of compound 7d

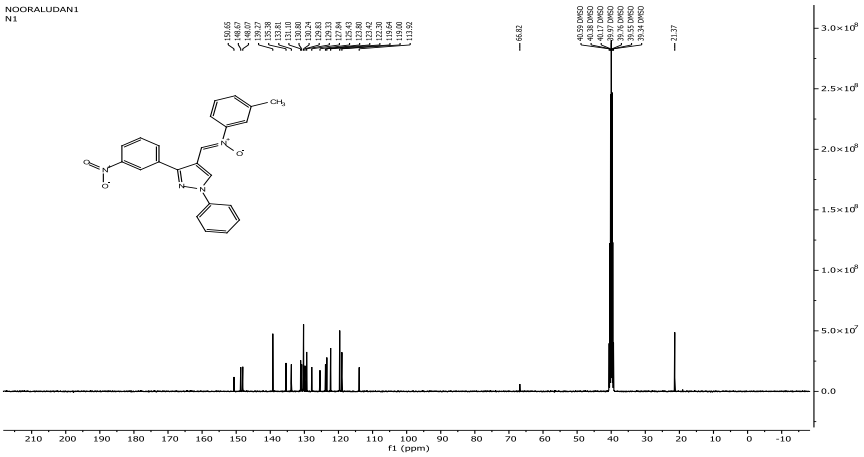

Figure 9: ^{13}C-NMR spectrum of compound 7a

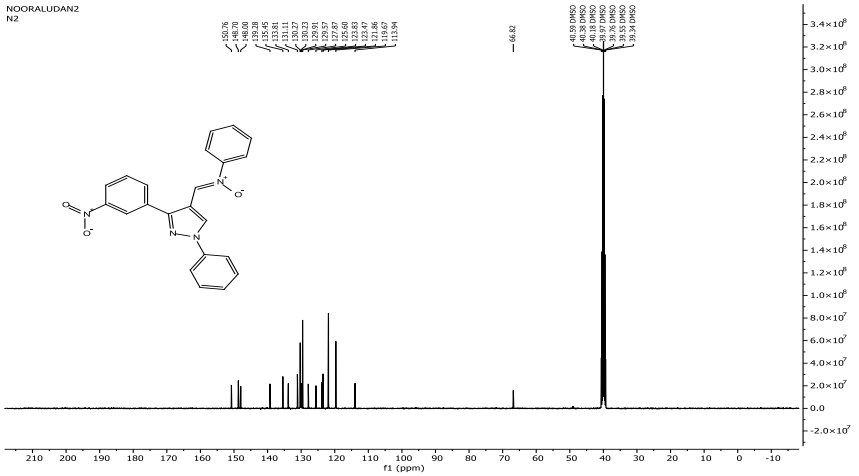

Figure 10: ^{13}C-NMR spectrum of compound 7b

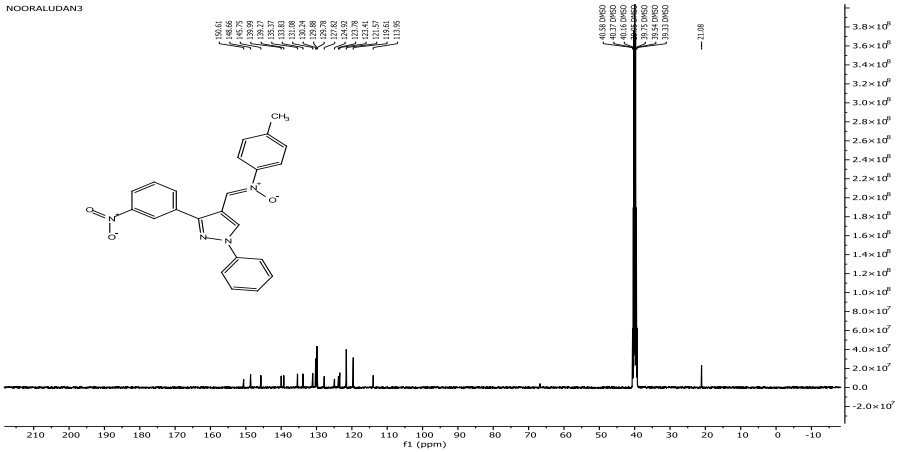

Figure 11: ^{13}C-NMR spectrum of compound 7c

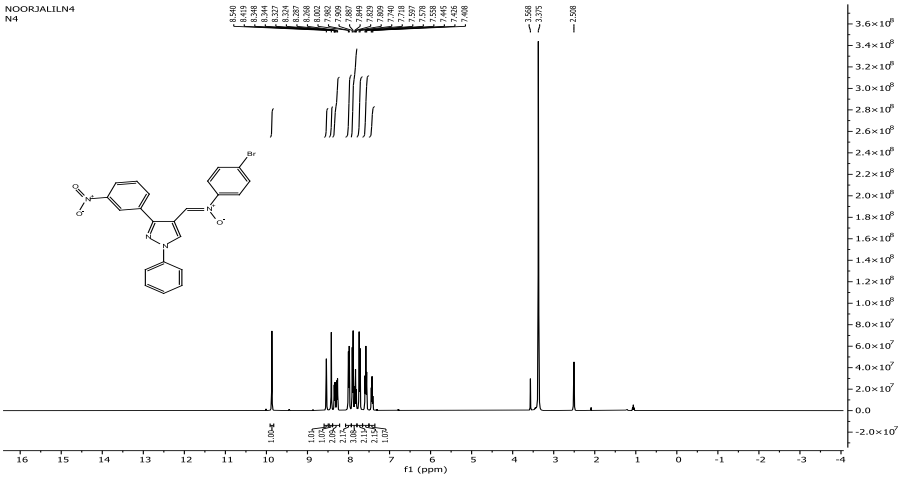

Figure 12: ^{13}C-NMR spectrum of compound 7d

Biological activity data

Erlotinib	HdFn		A549	
Conc.	mean	SD	mean	SD
400	70.332	1.136225	29.128	2.224263
200	77.469	2.744673	39.54433	2.384233
100	86.26567	1.390614	50.03867	1.856837
50	93.59567	0.570728	62.77033	1.400022
25	94.98467	0.176647	74.18967	2.208107

7a	HdFn		A549	
Conc.	mean	SD	mean	SD
400	70.756	1.971927	41.20367	1.97465
200	81.983	1.011401	47.994	1.371279
100	88.85033	1.830761	64.699	2.736053
50	93.171	0.703874	74.537	4.356447
25	94.329	0.80194	87.46133	1.923728

7b	HdFn		A549	
Conc.	mean	SD	mean	SD
400	61.304	2.215092	38.85067	1.165191
200	73.843	2.780171	51.312	1.351383
100	87.23	1.182011	65.625	2.438719
50	93.05567	0.2315	77.315	2.162482
25	94.329	0.463	85.60967	1.794162

7c	HdFn		A549	
Conc.	mean	SD	mean	SD
400	67.78567	0.547066	60.764	1.389
200	73.997	1.456125	67.901	1.571414
100	83.75767	5.290427	77.43067	2.323653
50	93.673	0.876269	88.31033	2.374614
25	94.869	0.876269	94.17433	0.884001

N4	HdFn		A549	
Conc.	mean	SD	mean	SD
400	70.409	0.637395	37.96267	0.30634
200	77.54633	1.408324	50.116	2.69683
100	85.76367	0.601599	62.46133	2.256966
50	93.32567	0.570491	76.42767	2.208861
25	94.75333	0.868646	87.307	2.17226

Molecular docking data

The binding mode of the crystal ligand Erlotinib exhibited an energy binding of -8.303 kcal/ mol against EGFR tyrosine kinase. Erlotinib formed two hydrophobic interactions between aromatic rings and Lys 721 and Val 702. Additionally, it formed two hydrogen bonds between the O-atom and NH with Met769 and Asp 831, respectively, as shown in Figure 17.

The binding mode of compound **7a** exhibited an energy binding of -7.014 kcal/ mol against EGFR tyrosine kinase. The aromatic ring forms one hydrophobic interaction bond with Leu 694, as shown in Fig. 13.

Whereas Compound **7b** shows binding energy -7.516 kcal/ mol. It forms one hydrophobic binding interaction between the pyrazole ring and Val 702. In addition to two hydrogen bonds, one formed between the N-atom of pyrazole and Lys 721, and the other one formed between the O- of the nitro group and Asp 831, as shown in Figure 14.

Compound **7c** shows binding energy -7.522 kcal/ mol. The O- of nitro generate one hydrogen bond with Lys 721 as shown in Fig. 15.

The binding energy of Compound **7d** was -6.481 kcal/ mol. The binding mode shows two hydrophobic interactions between aromatic rings and Asp 831, as shown in Figure. 16.

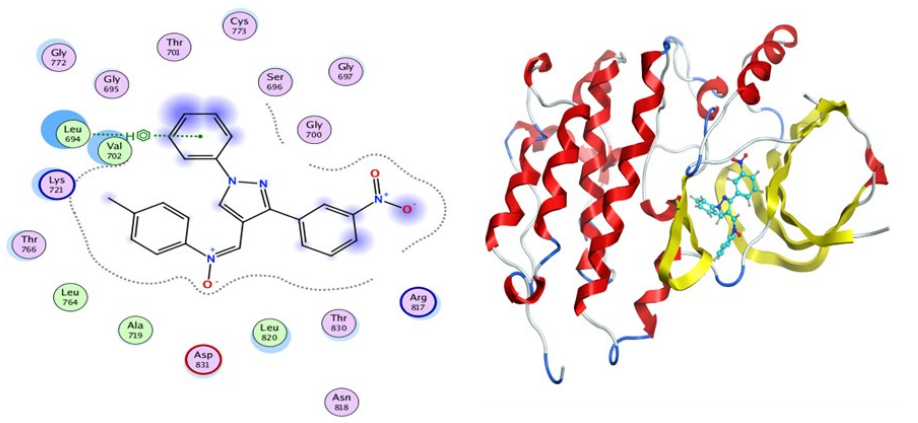

Fig 13: 2D and 3D orientation of compound 7a docked in EGFR tyrosine kinase

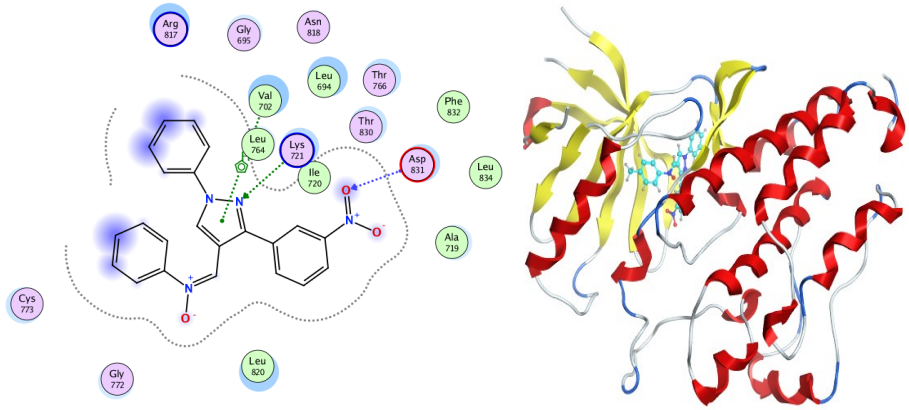

Fig 14: 2D and 3D orientation of compound 7b docked in EGFR tyrosine kinase

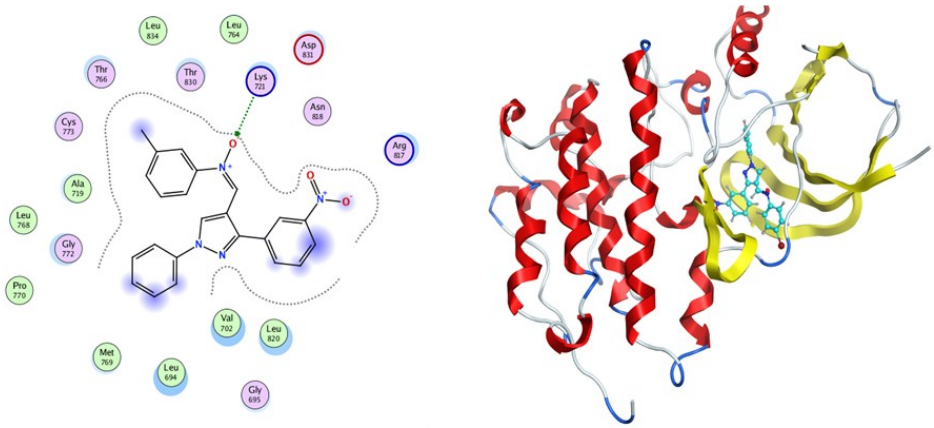

Fig 15: 2D and 3D orientation of compound 7c docked in EGFR tyrosine kinase

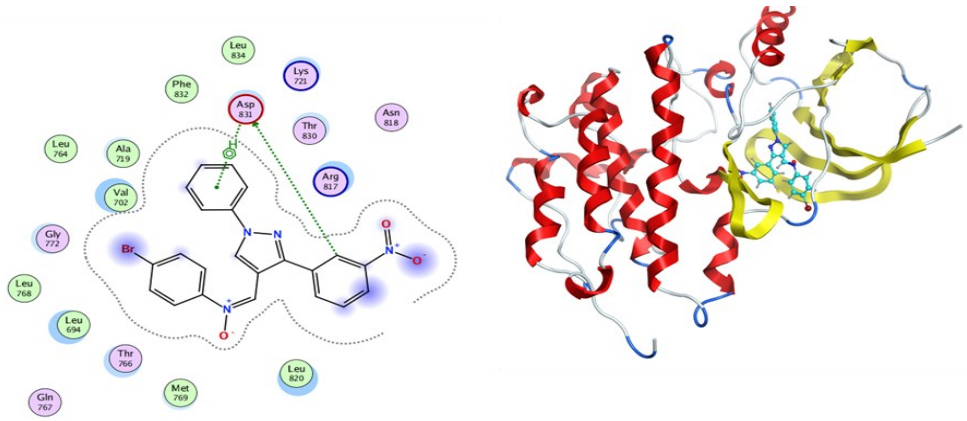

Fig 16: 2D and 3D orientation of compound 7d docked in EGFR tyrosine kinase

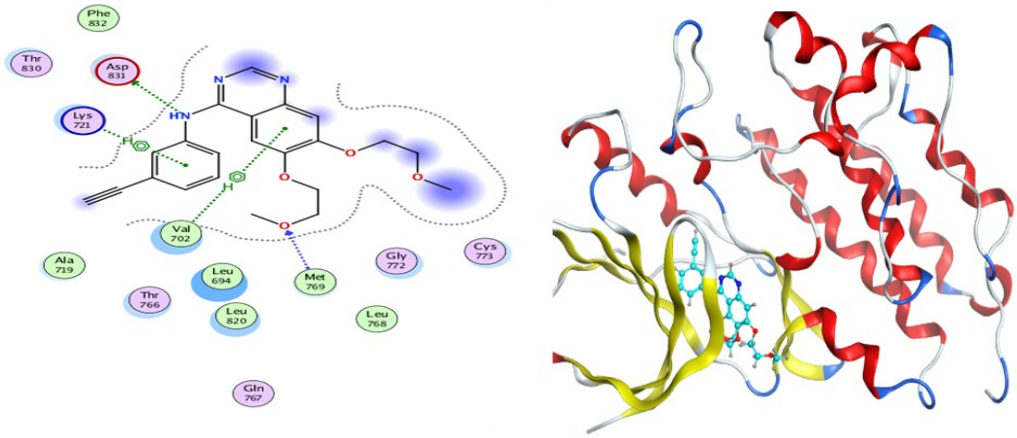

Fig 17: 2D and 3D orientation of Erlotinib docked in EGFR tyrosine kinase