

Figure S1: The 2D-depiction generated from Ligand Scout 4.4.8 advance software, yellow color showing hydrophobic pocket. Hydrophobic type of interactions is mostly predominant in the 2D depiction model, indicated by black color. Red color showing the hydrogen bond acceptor features with several functional groups.

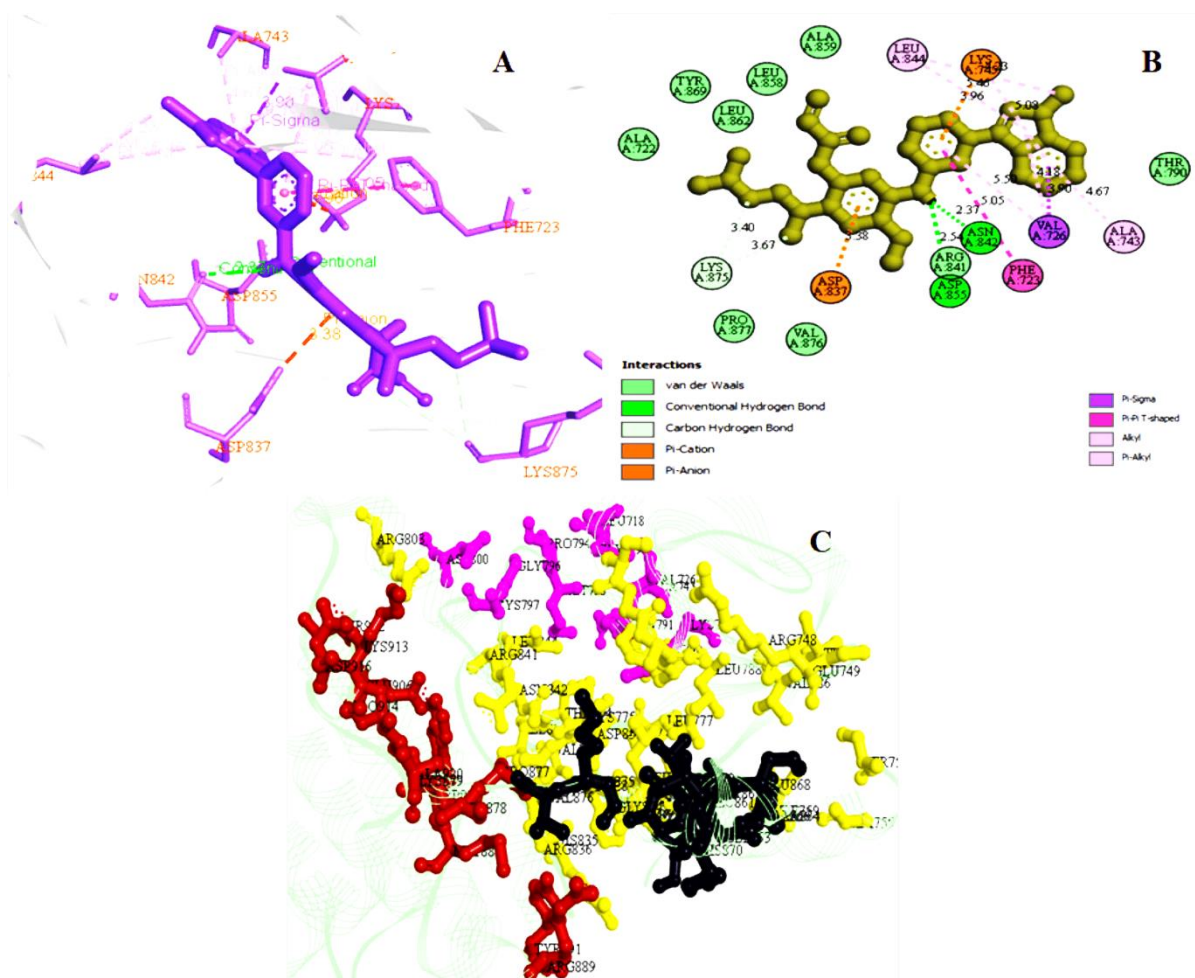


Figure S2: Describing protein ligand interaction generated from protein ligand interaction complex and the active site of the EGFR. (A) 3D Interaction of the protein ligand complex (B) Bond formation with attached ligand (C) the number of attached active site with 6JXT protein.

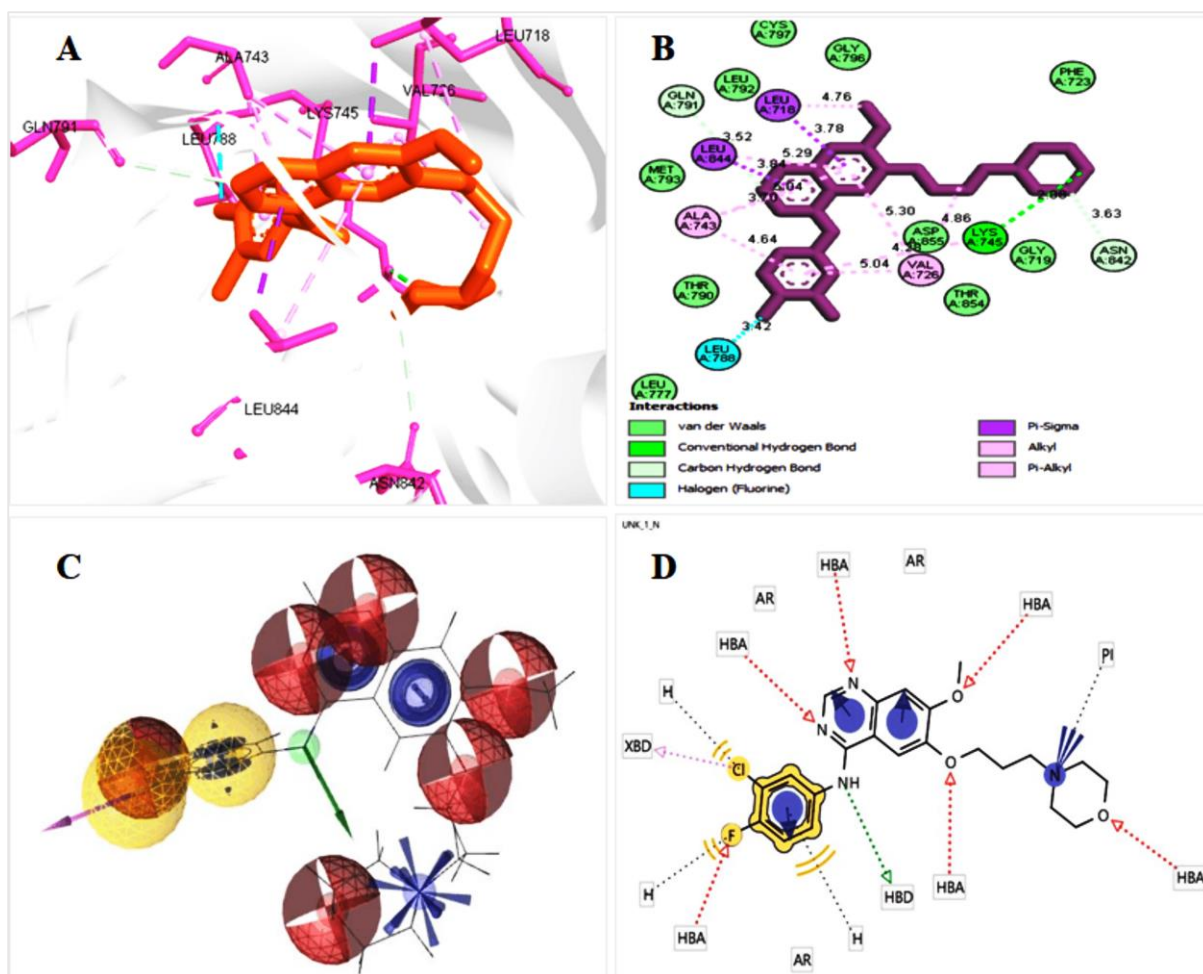


Figure S3: EGFR tyrosine kinase inhibitor (Gefitinib) with the 3D, 2D interaction, obtained pharmacophore features 3D and 2D. Gefitinib was docked with EGFR protein and generated all the features.

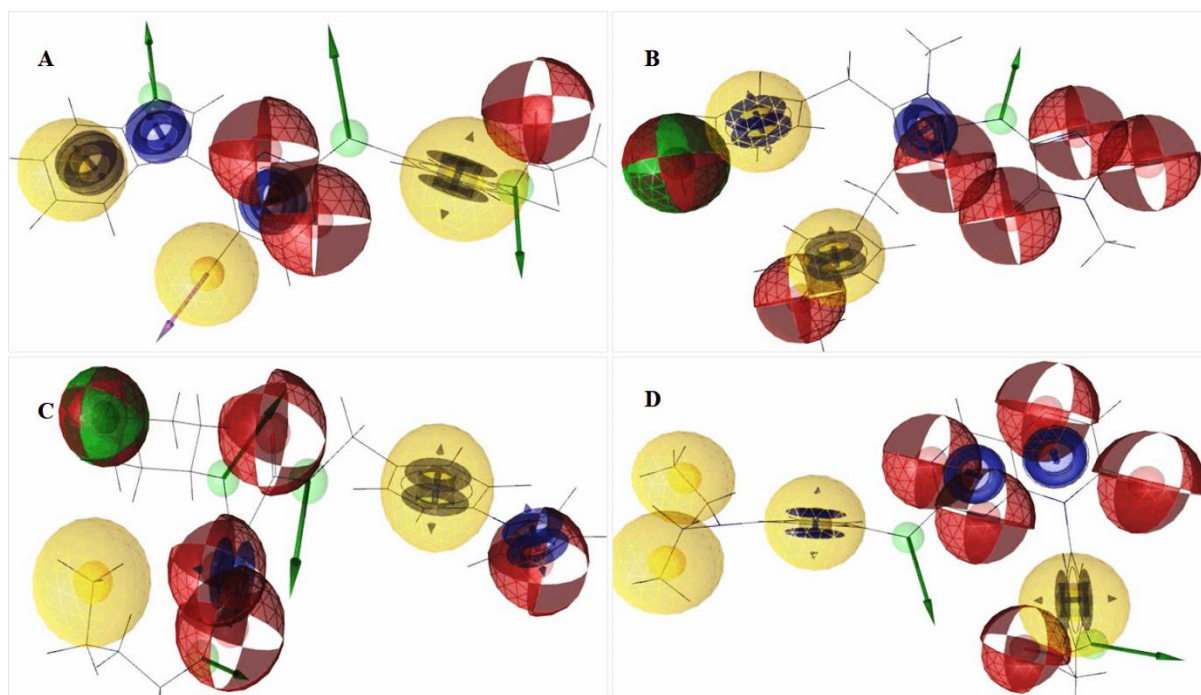


Figure S4: Several pharmacophore features of our selected compounds and ligand attach to EGFR protein. Selected protein attached to the ligand were indicated by pharmacophore features. Our natural compounds were showing more pharmacophore features and the binding capacity was higher with following the Lipinski rule of five (R05).

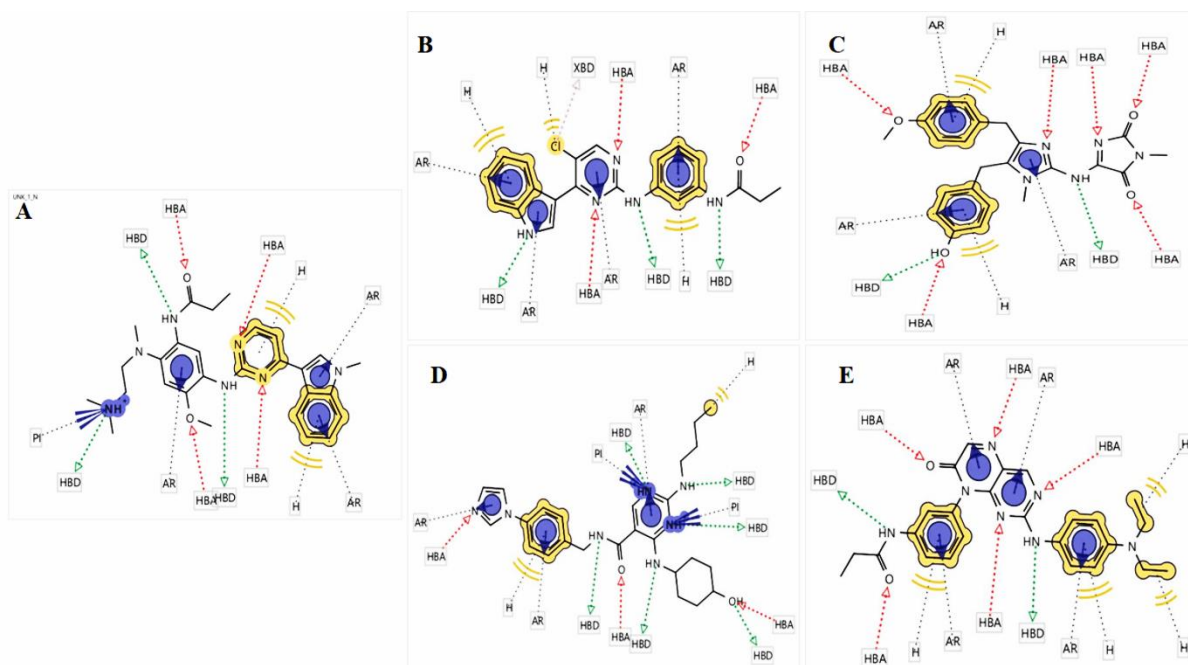


Figure S5: Analysis of 2d pharmacophore features of our selected antagonists and also control ligand. The result revealed that our compounds had more features than the current ligand attached to the selected protein and following the Lipinski rule of five.

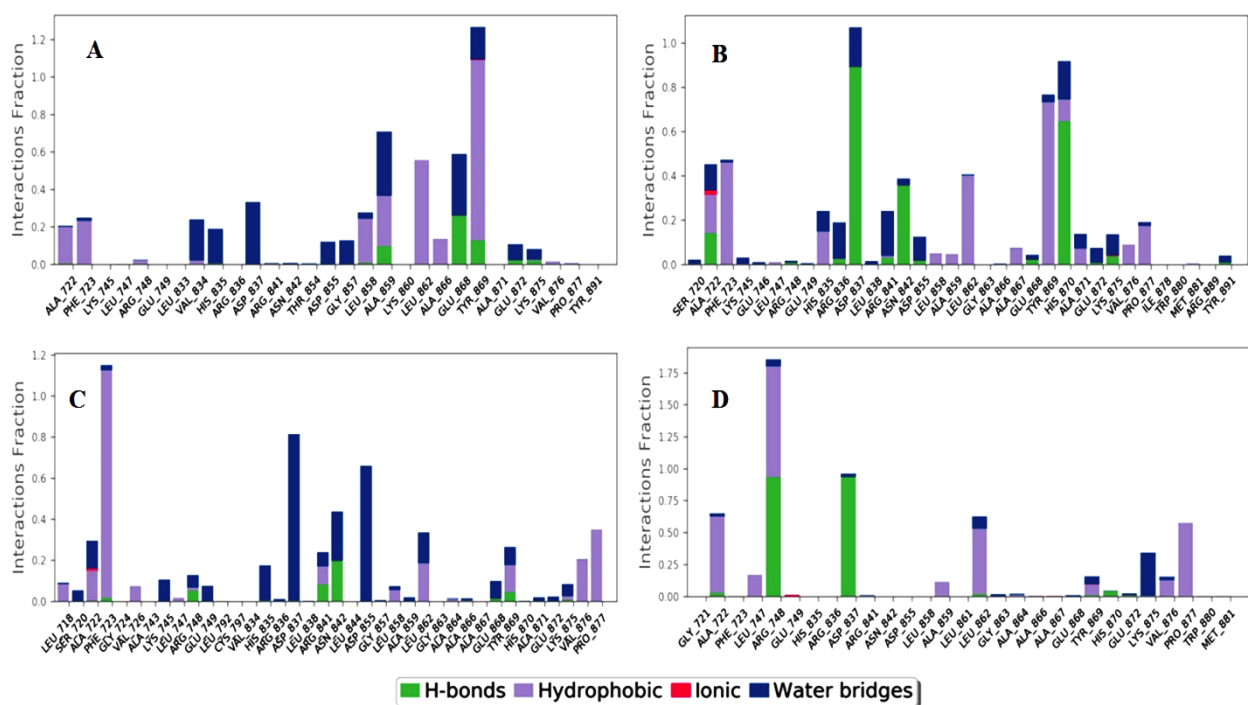


Figure S6: The column graph indicated the protein-ligand interaction during the molecular dynamic simulation at 100ns. The graph was showed the bond contact with several amino acids residue.

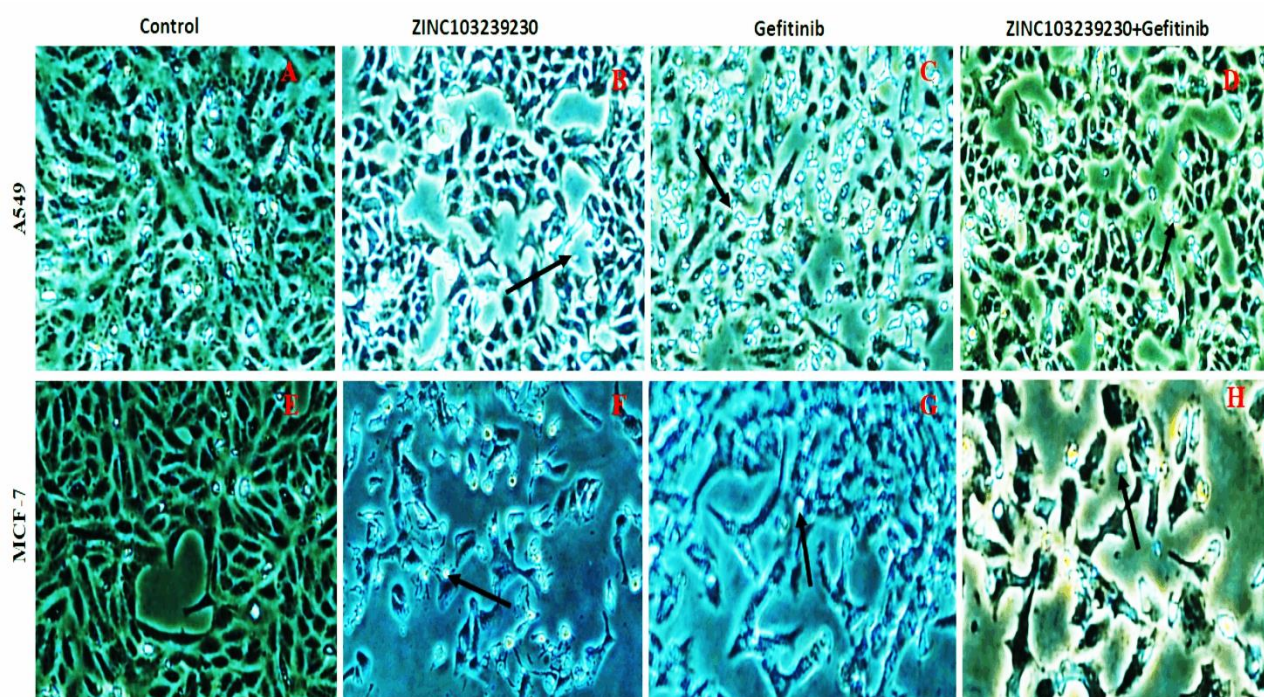


Figure S7: The cell death pattern through using different drugs with IC₅₀ concentration. (A) A549 cell without the treatment. (B, C, D) indicated the cell death by their structural changes (Elongation, cell shrinkage, cell membrane rupture). MCF-7 cell death indicated by F, G, H and E showed the MCF-7 cell line without treatment. Black arrows indicating the death cell. All photos were taken by phase contrast microscope (Scale bar 100µm)

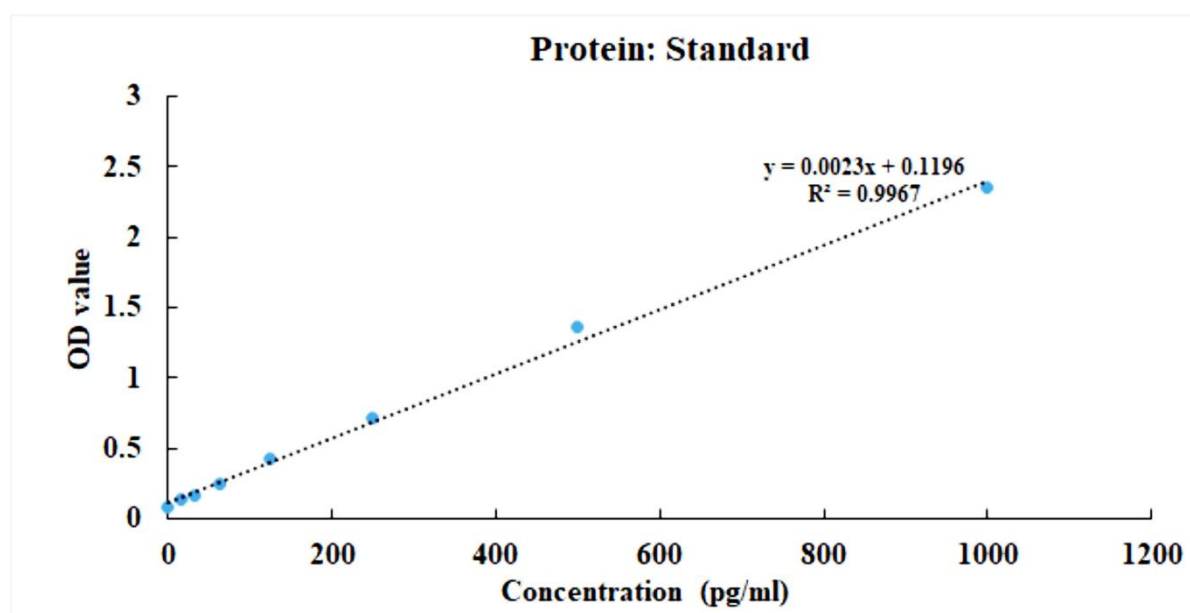


Figure S8: The standard curve preparation for the EGFR protein.

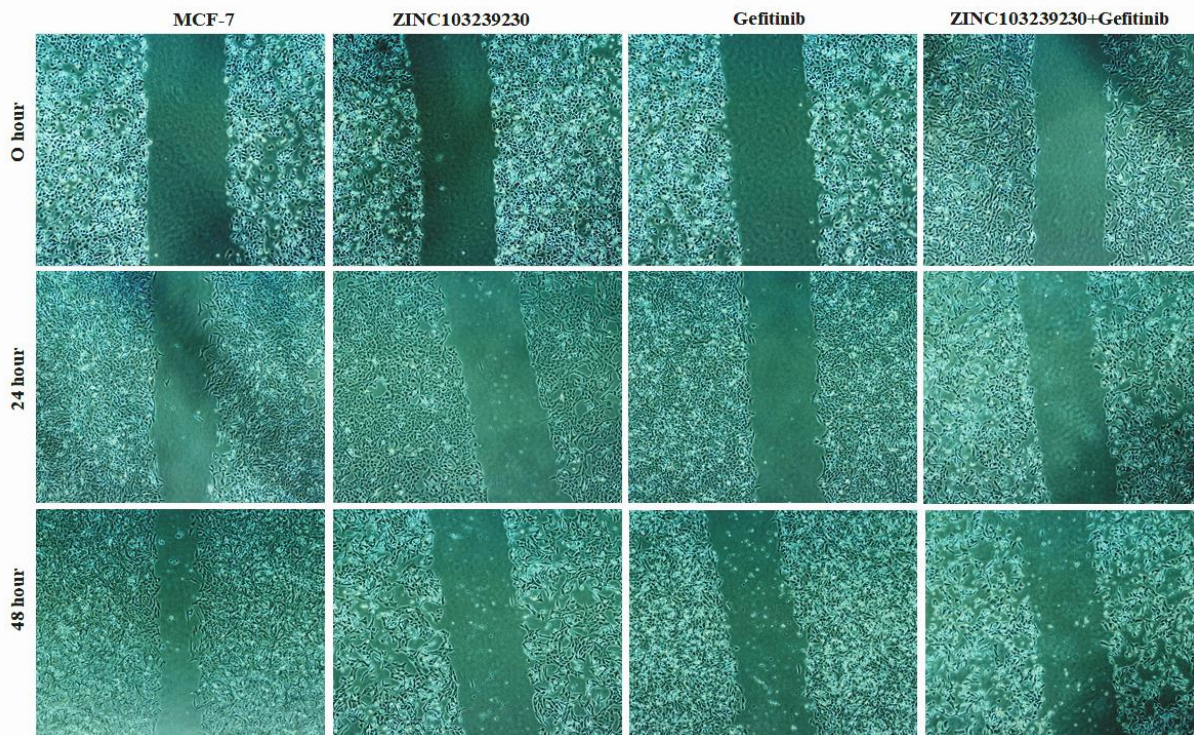
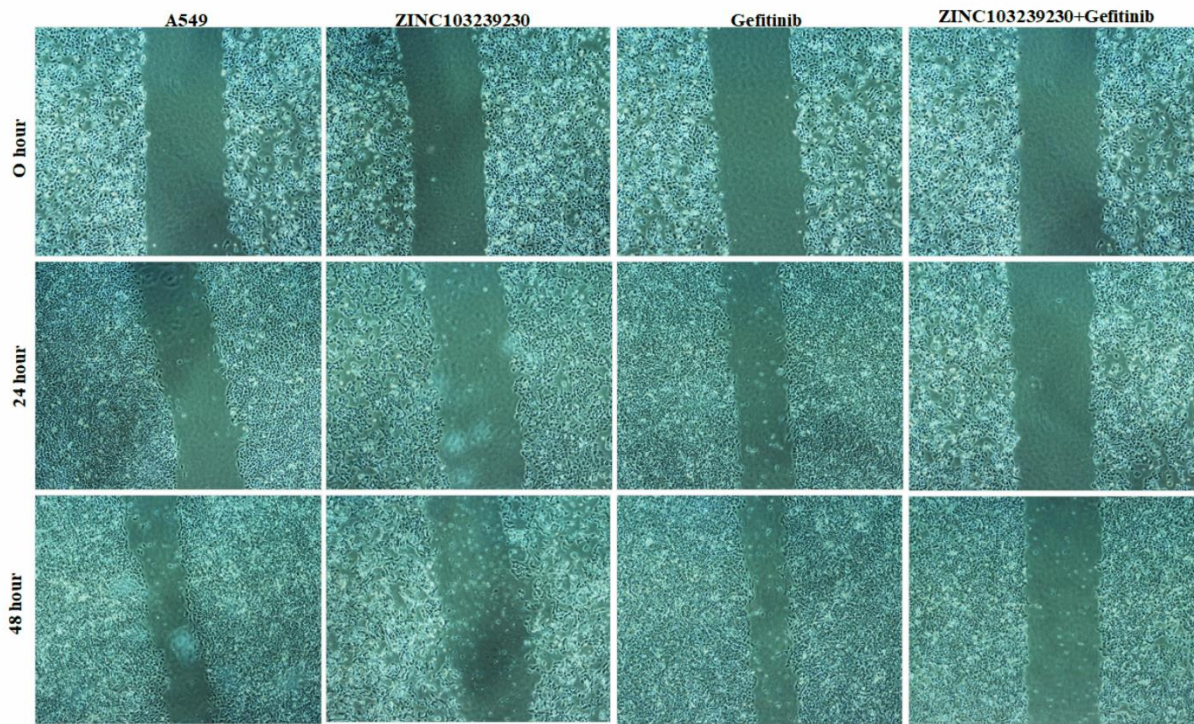
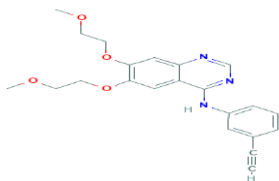
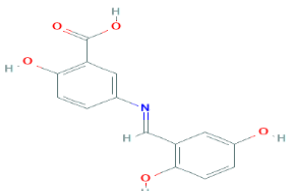


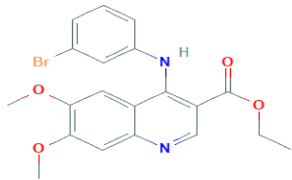
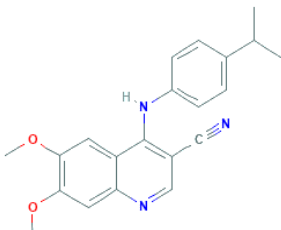
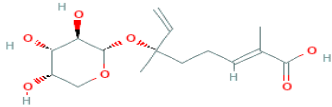
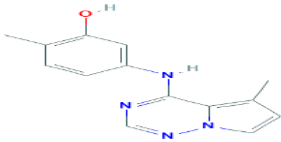
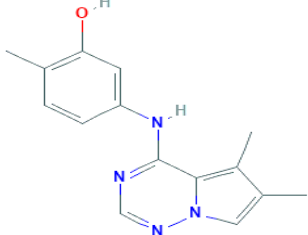
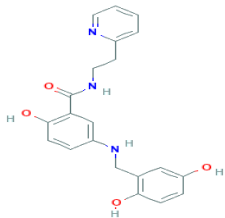
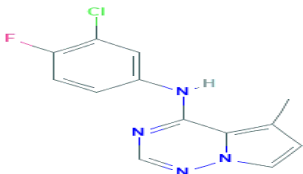
Figure S9: The migration of the cell with presence of antagonist and marketed drug gefitinib. A549 column were used as a control and was considered as untreated, at the same time MCF-7 column indicated control group without treatment.

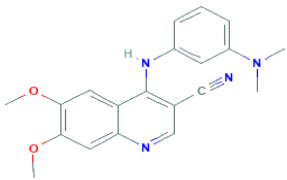
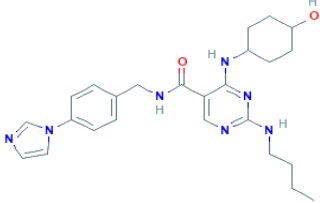
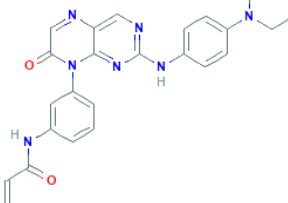
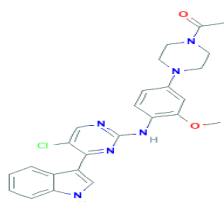
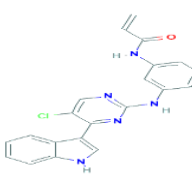
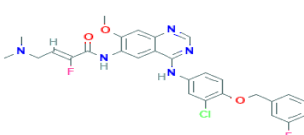
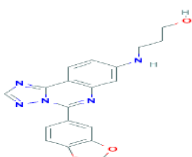
Table S1: The purchased of ZINC103239230 from the S Molecule. The gefitinib also purchased from the local pharmaceutical company of Bangladesh

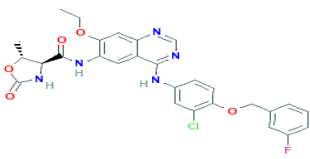
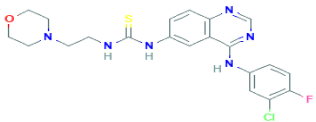
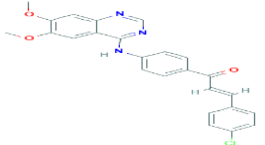
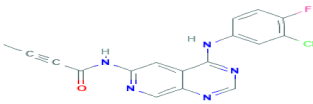
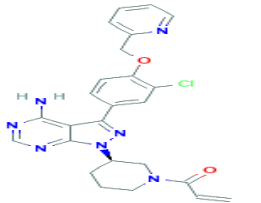
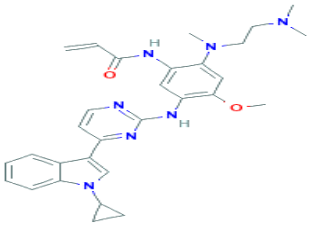
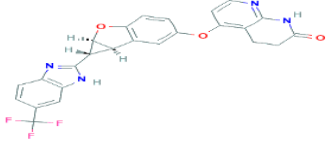
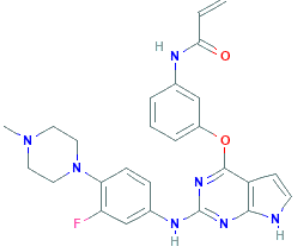
mcule.com Kft.		Quotation reference	Q-11505
Bartók Béla út 105-113.		Customer	Dain Md. Opu
H-1115, Budapest		Quotation date	July 21, 2021
Hungary		Valid until	August 20, 2021
Tax ID: HU23383540		Payment terms	30 days net or prepayment by credit card
		Estimated delivery time	14 working days after purchase order accepted
Email: order@mcule.com		Delivery format	Dry powder/film in supplier vial
Phone:		Shipping country	Saudi Arabia
+36-1-781-5983			
Quoted Mcule ID		Quoted product	
MCULE-3322057278		SMILES	
		CCCCNC1N=C(NC2CCC(O)CC2)C(C(NCC2C=CC(N3C=NC=C3)=CC=2)=O)=CN=1	
Item	Number of products	Amount / product (mg)	Average product price (USD)
Products	1	5	197.02
Shipping (from supplier to Mcule)			139.57
Shipping & handling			44.07
Total			380. 66
<i>New customers are eligible for 10% discount if indicated at the time of ordering (will be deduced from your first invoice).</i>			

Table S2: The number of selected known inhibitor with their IC₅₀ value, molecular formula and chemical structure

Number	PubChem ID	Molecular formula	Chemical Structure	IC ₅₀ (μ M)
1	176870	C ₂₂ H ₂₃ N ₃ O ₄		0.0001
2	375472	C ₁₄ H ₁₁ NO ₅		5

3	5328837	$C_{20}H_{19}BrN_2O_4$		6.94
4	5328863	$C_{21}H_{21}N_3O_2$		0.23
5	6438552	$C_{15}H_{24}O_7$		9.3
6	9859850	$C_{14}H_{14}N_4O$		0.34
7	10199254	$C_{15}H_{16}N_4O$		0.2
8	10499929	$C_{21}H_{21}N_3O_4$		0.015
9	11357877	$C_{13}H_{10}ClFN_4$		0.1

17	49860603	$C_{20}H_{21}ClN_4O_2$		0.85
18	71721525	$C_{25}H_{33}N_7O_2$		0.32
19	72202868	$C_{25}H_{25}N_7O_2$		0.00472
20	73294313	$C_{25}H_{25}ClN_6O_2$		0.77
21	73294314	$C_{21}H_{16}ClN_5O$		0.81
22	85471121	$C_{28}H_{26}ClF_2N_5O_3$		0.00156
23	118706214	$C_{19}H_{17}N_5O_3$		2.56

24	127050068	$C_{28}H_{25}ClFN_5O_5$		0.00257
25	127052091	$C_{21}H_{22}ClFN_6OS$		0.15
26	76900441	$C_{25}H_{20}ClN_3O_3$		0.027
27	11566580	$C_{17}H_{11}ClFN_5O$		0.0025
28	127264586	$C_{25}H_{24}ClN_7O_2$		0.0001
29	121280087	$C_{30}H_{35}N_7O_2$		0.53
30	89670174	$C_{25}H_{17}F_3N_4O_3$		0.029
31	72734520	$C_{26}H_{26}FN_7O_2$		0.18

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123631

 $\text{C}_{22}\text{H}_{24}\text{ClFN}_4\text{O}_3$

2.4

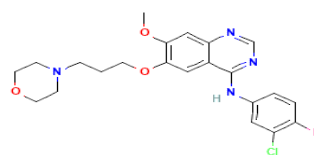


Table S3: Types of bond formed among the selected antagonist with their distance, category and the bond formation residue.

Zinc ID	Residue	Distance	Category	Type
ZINC96937394	MET793	2.6294	Hydrogen Bond	Conventional Hydrogen Bond
	ASP855	3.4444	Electrostatic	Pi-Anion
	LEU718	3.83771	Hydrophobic	Pi-Sigma
	THR790	3.68495	Hydrophobic	Pi-Sigma
	ALA743	5.13206	Hydrophobic	Pi-Alkyl
	LEU844	4.95436	Hydrophobic	Pi-Alkyl
	LYS745	4.81269	Hydrophobic	Pi-Alkyl
	LEU788	5.16262	Hydrophobic	Pi-Alkyl
	ALA743	4.70503	Hydrophobic	Pi-Alkyl
	LEU844	4.44865	Hydrophobic	Pi-Alkyl
	LEU718	5.18615	Hydrophobic	Pi-Alkyl
ZINC14611940	MET793	1.61032	Unfavorable	Unfavorable Donor-Donor
	LYS745	3.07377	Hydrogen Bond	Conventional Hydrogen Bond
	LYS745	2.80168	Hydrogen Bond	Conventional Hydrogen Bond
	THR790	2.29469	Hydrogen Bond	Conventional Hydrogen Bond
	LEU718	3.71047	Hydrogen Bond	Carbon Hydrogen Bond
	LEU788	3.47693	Hydrogen Bond	Carbon Hydrogen Bond
	ASP855	4.25467	Electrostatic	Pi-Anion
	LEU788	5.31726	Hydrophobic	Alkyl
	LYS745	3.86388	Hydrophobic	Alkyl
	LEU718	4.8807	Hydrophobic	Pi-Alkyl
	ALA743	5.01775	Hydrophobic	Pi-Alkyl
	LEU844	4.60319	Hydrophobic	Pi-Alkyl
	VAL726	4.51917	Hydrophobic	Pi-Alkyl
	ALA743	4.81401	Hydrophobic	Pi-Alkyl
	LYS745	5.44437	Hydrophobic	Pi-Alkyl
	MET793	1.06919	Unfavorable	Unfavorable Donor-Donor
	ARG841	2.34138	Hydrogen Bond	Conventional Hydrogen Bond
	MET793	2.21793	Hydrogen Bond	Conventional Hydrogen Bond
	GLN438	2.68776	Hydrogen Bond	Conventional Hydrogen Bond
ZINC103239230	THR503	2.77995	Hydrogen Bond	Conventional Hydrogen Bond
	ASP855	3.42001	Hydrogen Bond	Carbon Hydrogen Bond
	MET766	3.47288	Hydrogen Bond	Carbon Hydrogen Bond
	ASP855	3.72526	Electrostatic	Pi-Anion
	THR790	3.24363	Hydrophobic	Pi-Sigma
	LEU718	4.8546	Hydrophobic	Alkyl
	ALA743	4.67276	Hydrophobic	Alkyl
	LEU844	4.70735	Hydrophobic	Alkyl

ZINC96933670	VAL726	4.71853	Hydrophobic	Pi-Alkyl
	MET766	4.40067	Hydrophobic	Pi-Alkyl
	ARG841	2.82416	Hydrogen Bond	Conventional Hydrogen Bond
	TYR869	2.80397	Hydrogen Bond	Conventional Hydrogen Bond
	GLU868	3.5239	Hydrogen Bond	Carbon Hydrogen Bond
	ASP837	3.5371	Electrostatic	Pi-Anion
	PHE723	5.93153	Hydrophobic	Pi-Pi T-shaped
	ALA722	4.75293	Hydrophobic	Pi-Alkyl
	ALA722	4.24809	Hydrophobic	Pi-Alkyl
	ALA859	5.45543	Hydrophobic	Pi-Alkyl
