

Isatin-Hydrazones with Multiple Receptor Tyrosine Kinases (RTKs) Inhibitory Activity and In-Silico Binding Mechanism

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Supplementary Materials

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Table S1. Enzyme assays for compounds **1** and **2**.

Compounds	Conc. (μ M)	Log Conc	% Inhibition*		
			EGFR ^a	VEGFR-2 ^b	FLT-3 ^c
1	10	4	88.32868	84.37254	74.25952
	1	3	69.07922	53.50145	38.96826
	0.1	2	44.60802	32.28704	19.49138
	0.01	1	5.631365	4.897566	4.386743
	0	0	0	0	0
2	10	4	85.82672	86.81035	83.51873
	1	3	64.37524	70.38339	51.80122
	0.1	2	36.87912	38.94649	30.51339
	0.01	1	5.67763	11.52302	11.68087
	0	0	0	0	0
Control Drugs	10	4	93.94549	91.37509	91.30169
	1	3	83.30032	74.77711	63.95949
	0.1	2	60.25763	54.45391	34.19259
	0.01	1	28.48952	26.19801	18.64113
	0	0	0	0	0

^aErlotinib, ^bSorafenib and ^cSunitinib were used as control for protein kinase enzymes EGFR, VEGFR-2 and FLT-3 inhibitory test, respectively. * Here, average experimental data (from triplicate values) is given, and the calculated IC₅₀ values from the average (triplicated values) values are provided in the table 1.

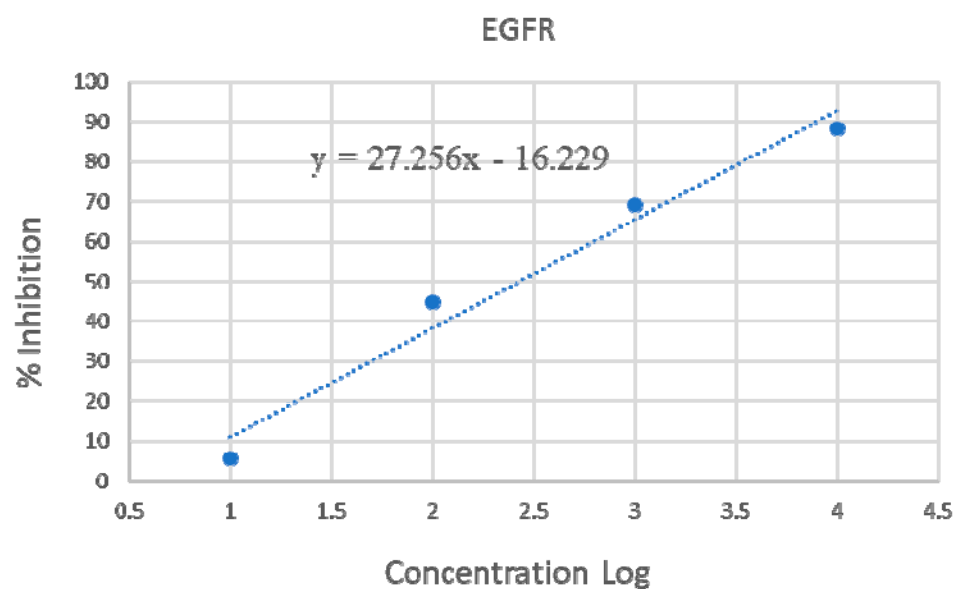


Figure S1. Calculation of the IC₅₀ Values of Protein Kinase Enzyme EGFR for compound 1.

$$\begin{aligned}
 y &= 27.256 \cdot x - 16.229 \\
 50 &= 27.256 \cdot x - 16.229 \\
 50 + 16.229 &= 27.256 \cdot x \\
 66.229 &= 27.256 \cdot x \\
 x &= 66.229 / 27.256 \\
 x &= 2.4299 \\
 \text{So, IC}_{50} &= 2.4299 \text{ (conc. log)} = 0.269 \mu\text{M}
 \end{aligned}$$

Experimental data for compounds 1 and 2

Synthesis of 3-((2,6-dichlorobenzylidene)hydrazono)indolin-2-one (1) [5].

Orange powder (98%). Mp. = 286–287 °C. IR (KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3165 (N-H), 2812 (C-H), 1730 (C=O), 1618 (C=N). ^1H NMR (DMSO- d_6 , 600 MHz) (ppm), δ 6.89 (t, 1H, ArH), 6.97 (t, 1H, ArH), 7.39–7.55 (m, 2H, ArH), 7.65 (t, 2H, ArH), 7.83 (t, 1H, ArH), 8.71 (s, 1H), 10.91 (s, 1H, -NH). ^{13}C NMR (DMSO- d_6 , 150 MHz) (ppm), δ 164.67, 155.50, 150.49, 145.80, 134.76, 134.72, 133.03, 129.98, 128.85, 122.77, 116.48 and 111.46. ESI mass m/z = 318 $[\text{M}(^{35}\text{Cl}) + \text{H}]^+$, 320 $[\text{M}(^{37}\text{Cl}) + \text{H}]^+$; 340 $[\text{M}(^{35}\text{Cl}) + \text{Na}]^+$, 342 $[\text{M}(^{37}\text{Cl}) + \text{Na}]^+$.

Synthesis of 3-((2-chloro-6-fluorobenzylidene)hydrazono)indolin-2-one (2) [5].

Reddish brown (75%). Mp. = 277–278 °C. IR (KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3165 (N-H), 2852 (C-H), 1732 (C=O), 1620 (C=N). ^1H NMR (DMSO- d_6 , 600 MHz) (ppm), δ 6.89 (t, 1H, ArH), 6.99 (t, 1H, ArH), 7.39–7.45 (m, 2H, ArH), 7.52 (t, 1H, ArH), 7.62 (t, 1H, ArH), 7.94 (t, 1H, ArH), 8.73 (s, 1H), 10.90 (s, 1H, -NH). ^{13}C NMR (DMSO- d_6 , 150 MHz) (ppm), δ 164.80, 162.18, 160.46, 154.25, 150.99, 145.77, 135.57, 134.74, 134.35, 134.29, 128.86, 127.07, 122.78, 119.84, 119.76, 116.67, 116.58, 116.44 and 111.43. ESI mass m/z = 302 $[\text{M}(^{35}\text{Cl}) + \text{H}]^+$, 304 $[\text{M}(^{37}\text{Cl}) + \text{H}]^+$; 324 $[\text{M}(^{35}\text{Cl}) + \text{H}]^+$, 326 $[\text{M}(^{37}\text{Cl}) + \text{H}]^+$.