Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

N-(7-chloroquinolinyl-4-aminoalkyl)arylsulfonamides as antimalarial agents: Rationale for the Activity with reference to Inhibition of Hemozoin Formation

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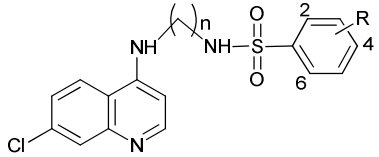
Table S1. β-hematin formation inhibition activity of N-(7-chloroquinolinyl-4-aminoalkyl) arylsulfonamides at different concentration.

Comd.	β-Hematin inhibitory activity			
	0.5 µg	1 µg	2 µg	2.5 µg
4	21	34	48	63
5	26	42	51	66
6	23	39	51	63
7	24	41	52	64
8	14	21	32	43
9	20	36	47	66
10	12	19	28	42
11	17	24	36	49
12	19	33	48	59
13	14	21	27	36
14	19	33	45	57
15	22	42	56	68
16	23	44	56	67
17	33	53	64	78
18	16	29	42	51
19	15	27	42	53
CQ	8	19	29	34

Table S2. Physicochemical characteristics of R group of N-(7-chloroquinolinyl-4-aminoalkyl) arylsulfonamides.



Comd.	Substitution		MR	MR	MR	π	π	π	σp	σp	σp	*R*	*R*	*R*	*F*	*F*	*F*	H-Accept
	R	**n**	**2**	**4**	**6**	**2**	**4**	**6**	**2**	**4**	**6**	**2**	**4**	**6**	**2**	**4**	**6**	**4**
4	H	3	1.03	1.03	1.03	0	0	0	0	0	0	0	0	0	0	0	0	0
5	H	2	1.03	1.03	1.03	0	0	0	0	0	0	0	0	0	0	0	0	0
6	*p*-F	3	1.03	0.92	1.03	0	0.14	0	0	0.06	0	0	-0.34	0	0	0.43	0	0
7	*p*-F	2	1.03	0.92	1.03	0	0.14	0	0	0.06	0	0	-0.34	0	0	0.43	0	0
8	*p*-Br	3	1.03	8.88	1.03	0	0.86	0	0	0.23	0	0	-0.17	0	0	0.44	0	0
9	*p*-Br	2	1.03	8.88	1.03	0	0.86	0	0	0.23	0	0	-0.17	0	0	0.44	0	0
10	*p*-NO_2	3	1.03	7.36	1.03	0	-0.28	0	0	0.78	0	0	0.16	0	0	0.67	0	1
11	*p*-NO_2	2	1.03	7.36	1.03	0	-0.28	0	0	0.78	0	0	0.16	0	0	0.67	0	1
12	*p*-CH_3	3	1.03	5.65	1.03	0	0.56	0	0	-0.17	0	0	-0.13	0	0	-0.04	0	0
13	*p*-CH_3	2	1.03	5.65	1.03	0	0.56	0	0	-0.17	0	0	-0.13	0	0	-0.04	0	0
14	*p*-*t*-butyl	3	1.03	19.62	1.03	0	1.98	0	0	-0.2	0	0	-0.13	0	0	-0.07	0	0
15	*p*-*t*-butyl	2	1.03	19.62	1.03	0	1.98	0	0	-0.2	0	0	-0.13	0	0	-0.07	0	0
16	2,4,6-tri-iPr	3	14.96	14.96	14.96	1.53	1.53	1.53	-0.15	-0.15	-0.15	-0.1	-0.1	-0.1	0.05	0.05	0.05	0
17	2,4,6-tri-iPr	2	14.96	14.96	14.96	1.53	1.53	1.53	-0.15	-0.15	-0.15	-0.1	-0.1	-0.1	0.05	0.05	0.05	0
18	*p*-C_6H_5	3	1.03	25.36	1.03	0	1.96	0	0	0.01	0	0	-0.08	0	0	0.08	0	0
19	*p*-C_6H_5	2	1.03	25.36	1.03	0	1.96	0	0	0.01	0	0	-0.08	0	0	0.08	0	0

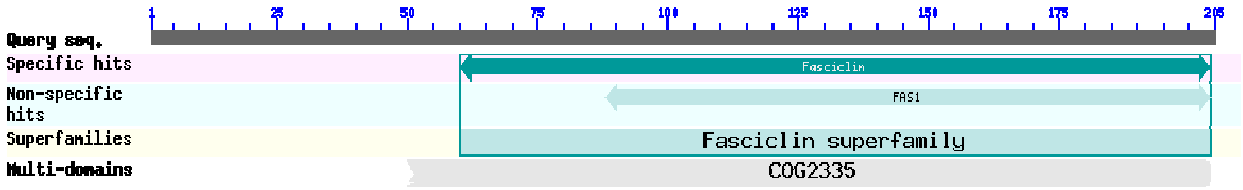


Figure S1. Conserved fasciclin domains of the *P.f* HDP in protein sequence.

GenTHREADER Scores (alignments displayed against the first of the input sequences)

Conf.	Net Score	p-value	PairE	SolvE	Aln Score	Aln Len	Str Len	Seq Len	View Alignment	SCOP Codes	CATH Codes	Structure	CATH Entry
HIGH	51.549	3e-04	-159.1	-13.0	199.0	140	146	205	Display 1x3bA0 Alignment	Search SCOP for 1x3bA	Search CATH for 1x3b		CATH Summary
MEDIUM	41.813	0.003	-129.9	-4.9	155.0	137	297	205	Display 1o70A0 Alignment	Search SCOP for 1o70A	Search CATH for 1o70		CATH Summary
MEDIUM	39.735	0.005	-41.4	-1.8	167.0	133	137	205	Display 1w7dA0 Alignment	Search SCOP for 1w7dA	Search CATH for 1w7d		CATH Summary
LOW	35.903	0.012	-129.2	-7.4	110.0	131	131	205	Display 2vxpA0 Alignment	Search SCOP for 2vxpA	Search CATH for 2vxp		CATH Summary
LOW	31.382	0.034	-139.9	-9.4	64.0	179	373	205	Display 2fgtA0 Alignment	Search SCOP for 2fgtA	Search CATH for 2fgt		CATH Summary

Figure S2. Gen THREADER Scores for the selection of templates for HDP modeling.

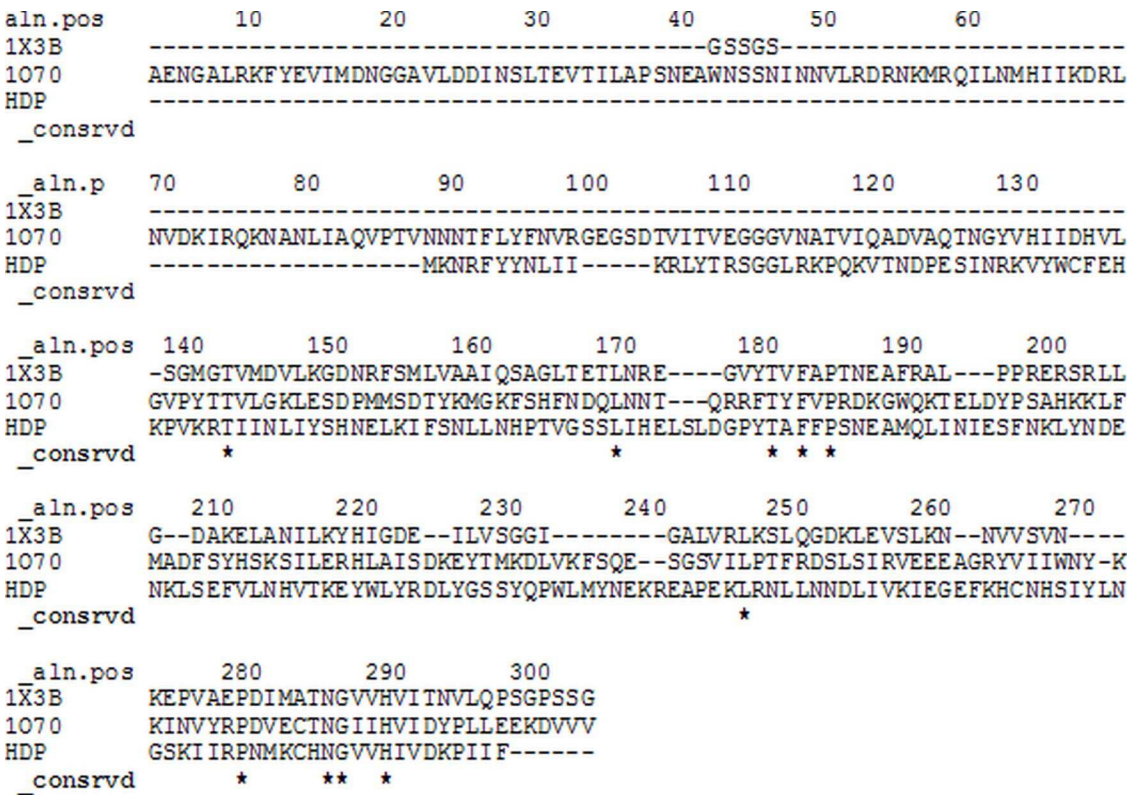


Figure S3. Multiple sequence alignment of *P.f*-HDP with FAS1 domain of human (PDB; 1X3B) and FAS1 domain of drosophila melanogaster (PDB; 1O70).

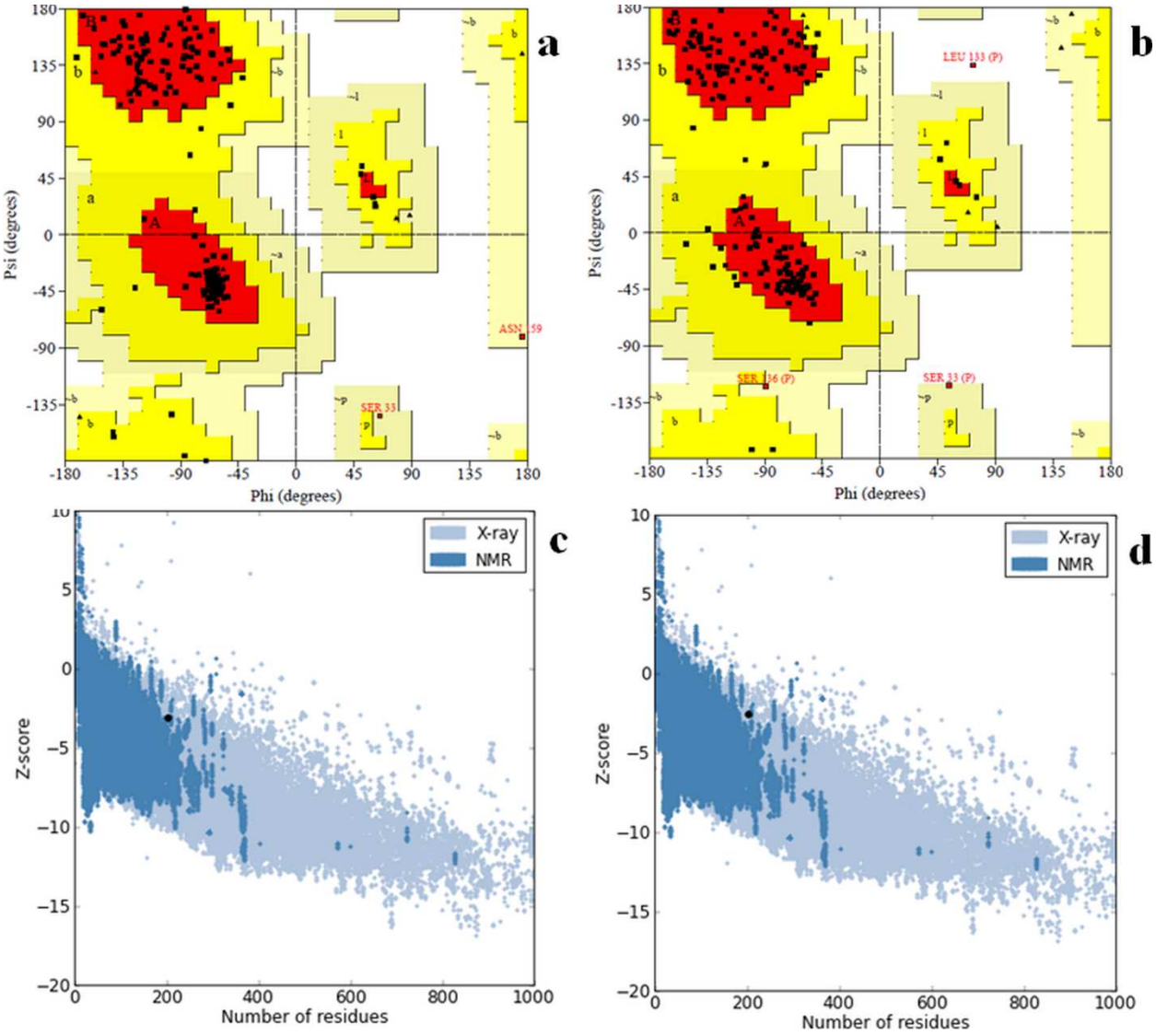


Figure S4. (a, b) Ramchandran (φ, ψ angle) plots and (c, d) PROSA plots of *Pf*-HDP homology model and model after MD simulations (10ns). In Ramchandran plots red, dark yellow, light yellow and white regions represent the favored, allowed, “generously allowed" and disallowed regions as defined by ProCheck. In ProSA plot, the z-score indicates overall model quality. Its value is displayed in a plot that contains the z-scores of all experimentally determined protein chains in current PDB. Black dot indicate the comparable quality of homology structure of *Pf*-HDP to experimentally developed structures.

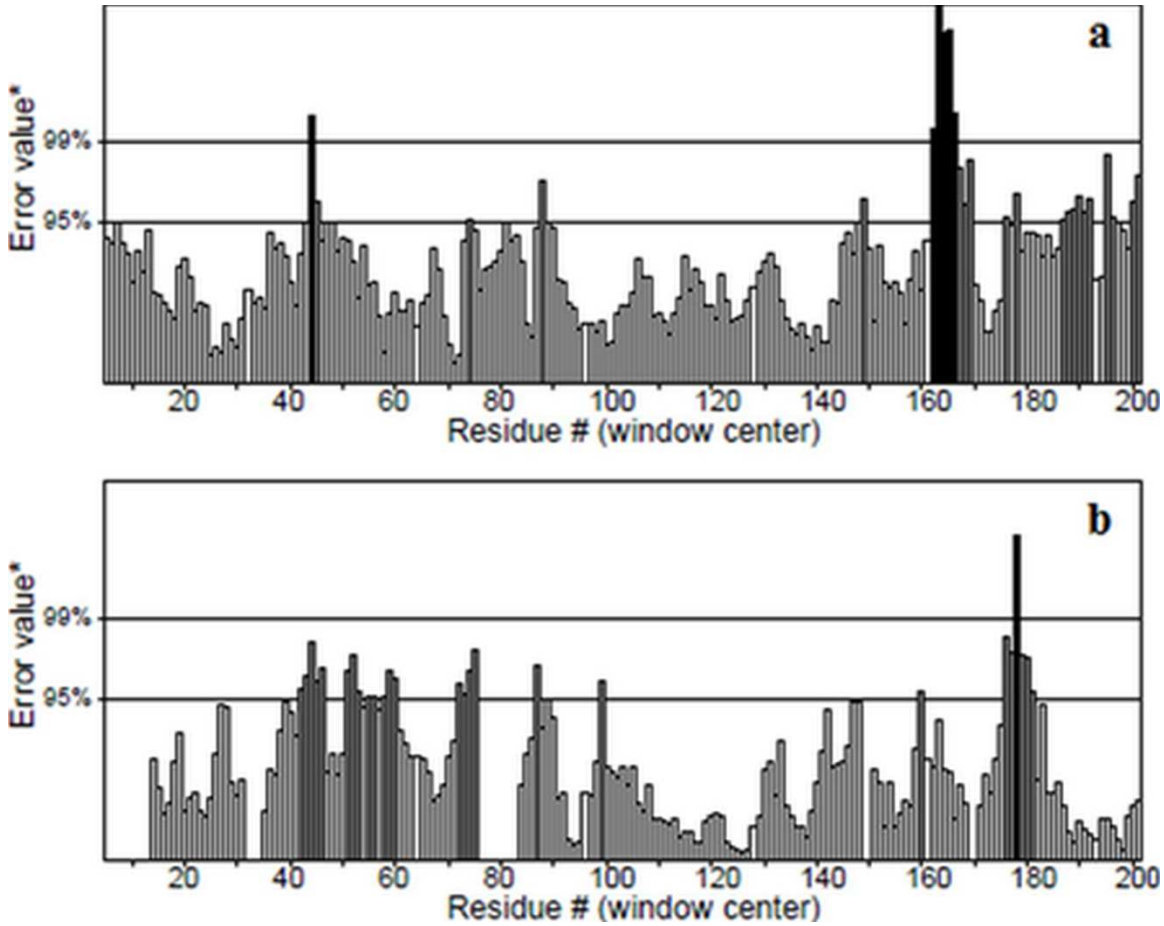


Figure S5. *Pf*-HDP ERRAT plot after (a) homology modeling and (b) molecular dynamic simulation of 10 ns.

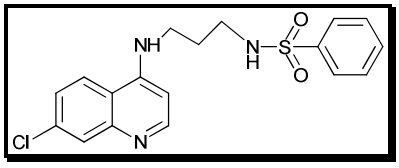
Table S3. *Pf* -HDP 3-D structural variation data during molecular dynamic simulation (3-10 ns). The bold text residues maintained their structural characteristics during MD simulation.

Equilibration time	**Ramachandran plot:**				**Errat plot**	**Free energy of folding (VADAR)**	**Variation in 3-D structure**	
ns	Core	Allow	Gener	Disall	Overall quality factor	K cal/mol	Alpha	Beta
3	84.30%	13.50%	2.20%	0.00%	84.70	-166.64	**I51INLI**YS, **S65NLL**N, S75SLI, N94E**AMQ**LIN, **F105NKLY**NDE, **K114LSEFVLNHVTK**, **Q139PWL**	**Y7NLI, L14YTR**, **Y87TAFF**P, **K153LR, D161LI**, I166EG, K171HC, **G194VVHI**V
4	91.90%	7.60%	0.50%	0.00%	90.36	-167.65	P46VK, **I51INLI**, N59ELKIF**SNLL**N, S75SL, E95**AMQ**LINI, **F105NKLY**, **K114LS**, **V119LNHVTK**EY, **Q139PWL**MYNE	**Y7NLI, L14YTR**, D30PE, N35RK, **Y87TAFF**P, **K153LR**, **D161LI**, M189KC, **G194VVHI**V
5	89.20%	10.30%	0.50%	0.00%	81.10	-174.61	P46VK, **I51INLI**YS, N59EL, I63F**SNLL**N, N94E**AMQ**LINIE, **F105NKLY**, **K114LSEFVLNHVTK**EY, Y138**QPWL**MYNE	**Y7NLI**, **L14YTR**, Q25KVT, V38YW, **Y87TAFF**P, **K153LR**, **D161LI**, I166EG, K171HC, **G194VVHI**V
6	89.70%	8.60%	1.60%	0.00%	86.56	-172.7	**I51INLI**YS, K62IF**SNLL**N, S75SLI, N94E**AMQ**LINIE, **F105NKLY**, **K114LSEFVLNHVTK**EY, **Q139PWL**MYNE	**Y7NLI, L14YTR**, D30PE, N35RK, **Y87TAFF**P, **K153LR**, **D161LI**, **G194VVHI**V
7	91.90%	7.00%	1.10%	0.00%	86.40	-172.35	**I51INLI**YS, N59ELKIF**SNLL**N, S75SLI, N94E**AMQ**L, **F105NKLY**ND, **K114LSEFVLNHVTK**EY, **Q139PWL**MYNE,	**Y7NLI**, **L14YTR**, D30PE, N35RK, **Y87TAF**F, **K153LR**, **D161LI**, I166EG, K171HC, M189KC, **G194VVHI**
8	90.80%	7.60%	1.10%	0.50%	88.83	-177.08	**I51INLI**YS, N59ELKIF**SNLL**N, S75SLI, **A96MQ**L, **F105NKLY**, **K114LSEFVLNHVTK**EY, Y138**QPWL**MYNE,	**Y7NLI**, **L14YTR**, D30PE, N35RK, Y**87TAF**F, **K153LR**, **D161LI** , M189KC, **G194VVHI**
9	88.60%	10.30%	0.00%	1.10%	83.53	-175.13	**I51INLI**YS, N59ELKIF**SNLL**N, N94E**AMQ**L, **F105NKLY**ND, **K114LSEFVLNHVTK**EY, Q139PWLMYN	**Y7NLI**, **L14YTR**, D30PE, N35RK, **Y87TAFF**P, **K153LR**, **D161LI**, M189KC, **G194VVHI**V
10	89.2%	9.2%	1.1%	0.5%	84.97	-173.23	**I51INLI**YS, K62IF**SNLL**N, S75SL, N94E**AMQ**, **F105NKLY**, **K114LSEFVLNHVTK**EY, Y138**QPWL**MYNE	**Y7NLI, L14YTR**, D30PE, N35RK, **Y87TAFF**P, **K153LR**, **D161LI**, M189KC, **G194VVHI**V

6. Synthesis

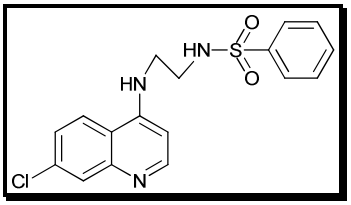
Experimental: Synthesis: The ^{1}H NMR (300, 400 MHz) and ^{13}C NMR (100MHz) spectra were recorded in $CDCl_3$ and DMSO-d_6, used as solvents on DPX-400 Bruker FT-NMR spectrometer. Chemical shifts are reported in parts per million d (ppm) with the residual protons of the solvent as reference. The splitting pattern abbreviations are as follows: s (singlet), d (doublet), dd(double doublet) and m (multiplet). Coupling constants are given in hertz. Mass Spectra (ESI-MS), high resolution mass spectra HRMS (ESI-HRMS) were recorded on Jeol (Japan)/SX-102, Agilent 6520 Q-Tof (ESI HRMS) spectrometers correspondingly. Analytical thin-layer chromatography (TLC) was carried out on Merck's precoated silica-gel plates 60 F254 and spots were visualized by irradiation with UV light (254 nm). Iodine was used as developing agent. Column chromatographic purification was performed over silica gel (230–400 mesh) using a gradient solvent system (hexene/ethylacetate) as the eluent unless otherwise specified. All chemicals and reagents were obtained from Aldrich (USA), Lancaster (UK) or Spectrochem Pvt. Ltd (India) and were used without further purification.

N-(3-(7-chloroquinolin-4-ylamino)propyl)benzenesulfonamide (4).



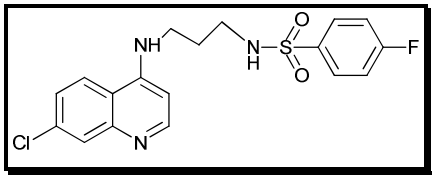
White solid; Yield 70%; Mp: 192-194°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ= 8.38 (d, 1H, *J* = 5.2 Hz), 8.22 (d, 1H, *J* = 9.0 Hz), 7.79-7.77 (m, 3H), 7.71-7.61 (m, 1H), 7.61-7.53 (m, 2H), 7.46 (dd, 1H, *J* = 2.0 Hz, *J* = 8.9 Hz), 7.23 (brs, 1H), 6.41 (d, 1H, *J* =5.4 Hz), 3.25-3.23 (m, 2H), 2.90-2.86 (m, 2H), 1.78-1.74 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.9, 150.2, 148.9, 140.4, 133.6, 132.5, 129.3, 127.3, 126.5, 124.2, 124.1, 117.5, 98.8, 40.6. 40.1. 27.9; ESI-MS: m/z 376 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{18}H_{18}ClN_3O_2S + H^+]$ 376.0881 found 376.0884.

N-(2-(7-chloroquinolin-4-ylamino)ethyl)benzenesulfonamide (5).



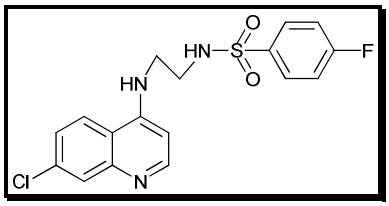
White solid; Yield 73%; Mp: 162-165°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=8.40 (d, 1H, *J* = 5.3 Hz), 7.92-7.88 (m, 3H), 7.74 (d, 1H, *J* = 8.9 Hz), 7.61.7,50(m, 3H), 7.34 (dd, 1H, *J* = 1.8 Hz, *J* = 8.8 Hz), 6.21 (d, 1H, *J* = 5.3 Hz), 3.20-3.19 (m, 2H), 1.3-1.27 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.6, 150.1, 148.6, 140.3, 133.8, 132.5, 129.3, 127.2, 126.5, 124.4, 124.0, 117.4, 98.6, 42.2, 40.8; ESI-MS: m/z 362 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for [$C_{17}H_{16}ClN_3O_2S$ + H^+] 362.0752 found 362.0754.

N-(3-(7-chloroquinolin-4-ylamino)propyl)-4-fluorobenzenesulfonamide (6).



White solid; Yield 73%; Mp: 197-199°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ= 8.39(d, 1H, *J* = 5.4 Hz), 8.21 (d, 1H, *J* = 9.0 Hz), 7.85-7.72 (m, 4H), 7.46-7.35 (m, 3H), 6.41 (d, 1H, *J* = 5.3 Hz), 3.25-3.23 (m, 2H), 2.90-2.88 (m, 2H), 1.78-1.74 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ =163.2, 152.3, 150.3, 149.5, 137.2 133.8, 129.9, 129.8, 127.9, 124.4, 117.9, 116.8, 116.6, 99.1, 40.9, 40.6, 28.2; ESI-MS: m/z 394 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for [$C_{18}H_{17}ClFN_3O_2S$ + H^+] 394.0787found 394.0756.

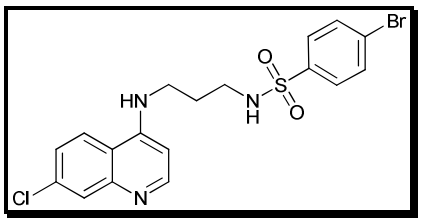
N-(2-(7-chloroquinolin-4-ylamino)ethyl)-4-fluorobenzenesulfonamide (7).



Pale yellow; Yield 75%; Mp: 179-182°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ= 8.38 (d, 1H, *J* = 5.0 Hz), 8.14 (d, 1H, *J* = 9.0 Hz), 7.89-7.88 (m, 4H), 7.36-7.26 (m, 3H), 6.42 (d, 1H *J* = 5.3 Hz), 3.38-3.18 (m, 2H), 3.05-3.02 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 162.9, 151.8, 150.0,

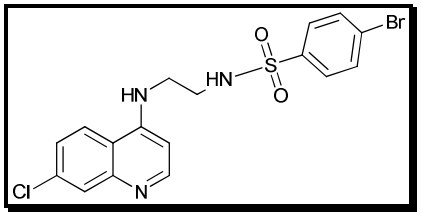
148.8, 136.7, 133.7, 129.6, 129.5, 127.3, 124.4, 124.0, 117.4, 116.5, 116.3, 98.7, 42.1, 40.8; ESI-MS: m/z 380 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{17}H_{15}ClFN_3O_2S + H^+]$ 380.0630 found 380.0636.

4-bromo-N-(3-(7-chloroquinolin-4-ylamino)propyl)benzenesulfonamide (8).



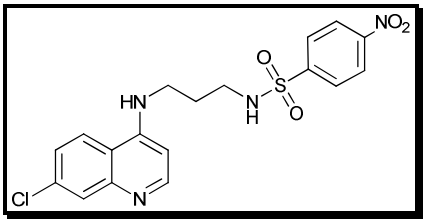
White solid; Yield 68%; Mp: 168-170 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ= 8.39 (d, 1H, *J* = 5.4 Hz), 8.21(d, 1H, *J* = 9.0 Hz), 7.80-7.77(m, 4H), 7.70 (d, 2H, *J* = 8.6 Hz), 7.45 (dd, 1H, *J* = 2.1 Hz, *J* = 8.9 Hz), 7.25-7.22 (m, 1H), 6.40 (d, 1H, *J* = 5.5 Hz), 3.26-3.20 (m, 2H), 2.92-2.87 (m, 2H), 1.79-1.74 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.9, 150.6, 149.1, 140.1, 134.0, 132.7, 128.9, 127.6, 124.6, 124.5, 117.8, 99.1, 40.9, 40.2 28.2; ESI-MS: m/z 454 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{18}H_{17}BrClN_3O_2S + H^+]$ 453.9886 found 453.9979.

4-bromo-N-(2-(7-chloroquinolin-4-ylamino)ethyl)benzenesulfonamide (9).



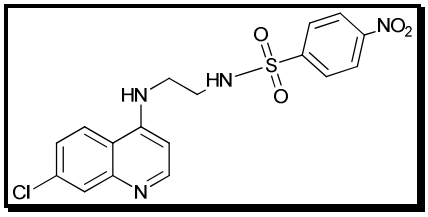
Pale yellow; Yield 71%; Mp: 155-153°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.39 (d, 1H, *J* = 5.2 Hz), 8.13 (d, 1H, *J* = 9.0 Hz), 7.98-7.95 (m, 1H), 7.79 (d, 1H, *J* =2.9 Hz), 7.73-7.68 (m, 4H), 7.47 (dd, 1H, *J* = 2.1 Hz, *J* =9.0 Hz), 7.28-7.25 (m, 1H), 6.41 (d, 1H, J= 5.4 Hz), 3.38-3.35 (m, 2H), 3.07-3.02 (m, 2H),; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.4, 150.2, 148.5, 139.7, 133.9, 132.3, 128.5, 127.1, 126.3, 124.5, 124.0, 117.4, 98.7, 42.1, 40.8; ESI-MS: m/z 440 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{17}H_{15}BrClN_3O_2S + H^+]$ 439.9830 found 439.9822.

N-(3-(7-chloroquinolin-4-ylamino)propyl)-4-nitrobenzenesulfonamide (10).



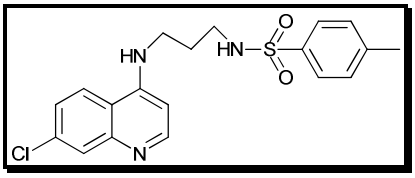
Pale yellow; Yield 64%; Mp: 149-150°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.35-8.33 (m, 3H), 8.21-8.18 (m, 2H), 8.15-8.12 (m, 1H), 8.03-8.00 (m ,2H), 7.84-7.83 (m, 1H), 7.62 (dd, 1H, *J* = 2.1 Hz, *J* =9.0 Hz), 6.60 (d, 1H, *J* = 6.3 Hz), 3.39-3.34 (m, 2H), 3.00-2.97 (m, 2H), 1.83-1.76(m, 2H), ^{13}C NMR (100 MHz, DMSO-d_6) δ =152.8, 149.5, 147.4, 146.0, 143.6, 136.0, 129.6, 128.2, 127.0, 125.7, 124.8, 123.5, 116.4, 98.7, 40.4, 40.2, 27.6; ESI-MS: m/z 421 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{18}H_{17}ClN_4O_4S + H^+]$ 421.0732 found 421.0726.

N-(2-(7-chloroquinolin-4-ylamino)ethyl)-4-nitrobenzenesulfonamide (11).



Pale yellow; Yield 60%; Mp: 151-152°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ == 8.36-8.34 (m, 3H), 8.26-8.21 (m, 3H), 8.05-8.01 (m, 1H), 7.75(s, 1H), 7.45 (d, 1H, *J* =8.9 Hz), 6.54 (d, 1H, *J* =5.3 Hz), 4.16-4.12 (m, 2H); 3.70-3.65 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ =152.3, 151.0, 150.0, 149.3, 143.8, 134.1, 129.9, 127.9, 126.2, 125.2, 124.8, 124.2, 123.1, 117.7, 99.0, 48.2, 42.7; ESI-MS: m/z 407 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{17}H_{15}BrClN_4O_4S + H^+]$ 407.0575 found 407.0564.

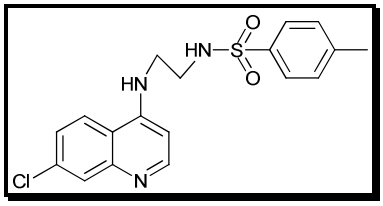
N-(3-(7-chloroquinolin-4-ylamino)propyl)-4-methylbenzenesulfonamide (12).



White solid; Yield 69%; Mp: 160-162°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ= 8.44 (d, 1H, *J* = 5.3 Hz), 8.13 (d, 1H, *J* = 8.9 Hz), 7.86 (s, 1H), 7.74 (d, 2H, *J* = 7.8 Hz) , 7.40-7.32 (m, 3H), 6.49

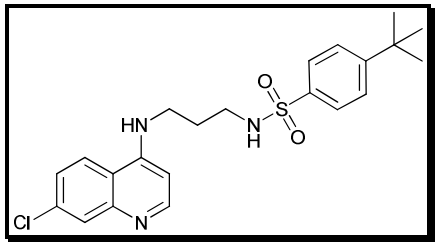
(d, 1H, *J* = 5.2 Hz), 3.48-3.42 (m, 2H), 3.12-3.06 (m, 2H), 2.37 (s, 3H), 1.99-1.90 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.8, 150.2, 148.9, 142.7, 137.5, 133.6, 129.7, 127.3, 126.6, 124.2, 124.1, 117.5, 98.8, 40.6, 40.1, 27.8, 21.0; ESI-MS: m/z 390 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{19}H_{20}ClN_3O_2S + H^+]$ 390.1038 found 390.1075.

N-(2-(7-chloroquinolin-4-ylamino)ethyl)-4-methylbenzenesulfonamide (13).



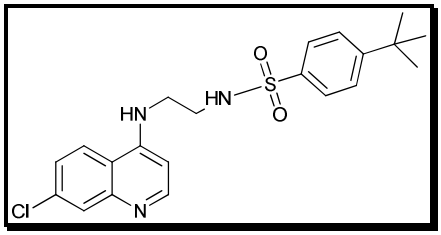
Pale yellow; Yield 63%; Mp: 156-158°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ= 8.38 (d, 1H, *J* = 5.4 Hz), 8.16 (d, 1H, *J* = 9.0 Hz), 7.79(s, 1H), 7.75 (d, 1H, *J* = 5.6 Hz), 7.67(d, 2H, *J* = 8.2 Hz), 7.49 (dd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz), 7.35-7.24 (m, 2H), 6.42 (d, 1H, *J* = 5.5 Hz), 3.34-3.31 (m, 2H), 3.01-2.99 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.5, 150.3, 150.3, 148.2, 142.8, 139.3, 137.4, 133.9, 129.7, 128.2, 126.9, 126.5, 125.0, 124.5, 124.1, 117.3, 98.6, 42.1, 40.8, 34.4, 30.5, 21.1; ESI-MS: m/z 376 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{18}H_{18}ClN_3O_2S + H^+]$ 376.0881 found 376.0890.

4-tert-butyl-N-(3-(7-chloroquinolin-4-ylamino)propyl)benzenesulfonamide (14).



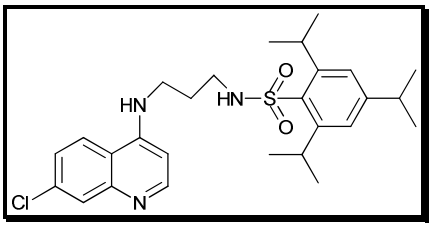
White solid; Yield 72%; Mp: 163-165°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46 (d, 1H, *J* = 5.3 Hz), 7.90 (d, 1H, *J* = 2.0 Hz), 7.78-7.74 (m, 3H), 7.51-7.49 (m, 2H), 7.36 (dd, 1H, *J* = 2.1 Hz, *J* = 8.9 Hz), 6.32 (d, 1H, *J* = 5.3 Hz), 5.74-5.72 (m, 1H), 3.56-3.52 (m, 2H), 3.13 (t, 2H, *J* = 6.0 Hz), 1.93-1.87 (m, 2H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ =155.5, 151.8, 149.9, 149.0, 137.4, 133.3, 127.4, 126.3, 125.9, 124.0, 117.4, 98.6, 40.5, 34.7, 30.7, 27.8; ESI-MS: m/z 432 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{22}H_{26}ClN_3O_2S + H^+]$ 432.1507 found 432.1502.

4-tert-butyl-N-(2-(7-chloroquinolin-4-ylamino)ethyl)benzenesulfonamide (15).



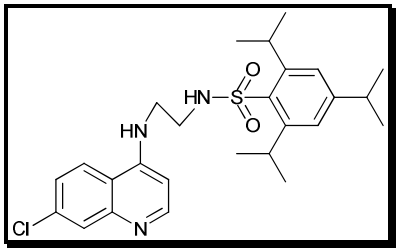
White solid; Yield 68%; Mp: 161-162°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.37 (d, 1H, *J* = 6.4 Hz), 8.18 (d, 1H, *J* = 9.7 Hz), 7.82 (t, 1H, *J* = 5.9 Hz), 7.78 (d, 1H, *J* =2.2 Hz), 7.72-7.69 (m, 2H), 7.52-7.50 (m, 2H), 7.47 (dd, 1H, *J* = 2.2 Hz, *J* =9.0 Hz), 7.33-7.30 (m, 1H), 6.39(d, 1H, *J* =5.5 Hz), 3.38-3.33 (m, 2H), 3.04-2.99 (m, 2H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 155.9, 152.3, 150.3, 149.5, 138.0, 134.0, 128.0, 126.9, 126.5, 124.7, 117.9, 99.1, 42.6, 41.3, 35.3, 31.3; ; ESI-MS: m/z 418 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{21}H_{24}ClN_3O_2S + H^+]$ 418.1351 found 418.1342.

N-(3-(7-chloroquinolin-4-ylamino)propyl)-2,4,6-triisopropylbenzenesulfonamide (16).



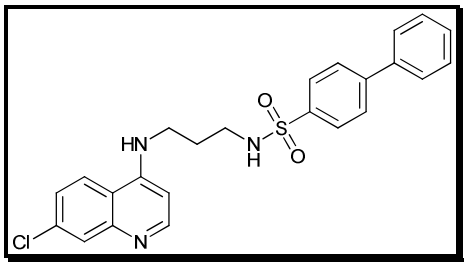
White solid; Yield 68%; Mp: 179-181°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ =8.47 (d, 1H, *J* = 7.5 Hz), 7.93-7.92 (m, 1H), 7.81-7.78 (d, 1H, *J* = 8.9 Hz), 7.37 (dd, 1H, *J* = 1.9 Hz, *J* = 8.8 Hz), 7.18(s, 2H), 6.35 (d, 1H, *J* = 5.3 Hz), 5.88 (s, 1H), 4.18-4.09 (m, 2H), 3.58-3.56 (m, 2H), 3.14 (s, 2H), 2.95-2.86 (m,1H),1.96-1.93 (m, 2H), 1.27-1.25 (m,18H);^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.0, 151.5, 150.3, 149.7, 148.6, 133.7, 133.3, 127.1, 124.2, 124.1, 123.6, 117.4, 98.7, 40.1, 40.0, 33.3, 28.8, 28.1, 24.8, 23.5; ESI-MS: m/z 502 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{27}H_{36}ClN_3O_2S + H^+]$ 502.2290 found 502.2311.

N-(2-(7-chloroquinolin-4-ylamino)ethyl)-2,4,6-triisopropylbenzenesulfonamide (17).



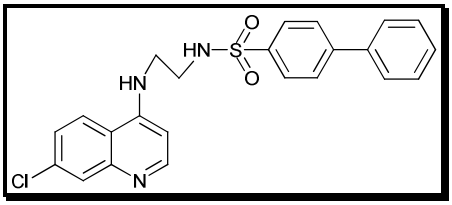
White solid; Yield 75%; Mp: 198-200°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 8.39 (s, 1H), 7.95 (d, 1H, *J* = 8.6 Hz), 7.86 (s, 1H), 7.40 (d, 1H, *J* = 8.6 Hz), 7.20 (s,3H) 6.80 (brs, 1H), 6.31 (d, 1H, *J* = 4.7 Hz), 4.18-4.14 (m, 2H), 3.48 (s, 2H), 3.43(3H, d, *J* = 5.3 Hz), 1.30-1.27 (m, 18H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 152.6, 151.1, 151.0, 150.1, 148.0, 134.6, 133.4, 126.7, 125.0, 124.5, 124.0, 117.6, 98.8, 42.8, 40.2, 33.7, 29.3, 25.1, 23.8; ESI-MS: m/z 488 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{26}H_{34}ClN_3O_2S + H^+]$ 488.2133 found 488.2122.

N-(3-(7-chloroquinolin-4-ylamino)propyl)biphenyl-4-sulfonamide (18).



White solid; Yield 67%; Mp: 150-152°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.39 (d, 1H, *J* = 5.2 Hz), 8.29 (d, 1H, *J* = 9.0 Hz), 7.86-7.81 (m, 4H), 7.80-7.79 (m, 1H), 7.77-7.74 (m, 1H), 7.69-7.67 (m, 2H), 7.53-7.50 (m, 2H), 7.49-7.48 (m, 1H), 7.46-7.41 (m, 1H), 6.52 (d, 1H, *J* = 5.8 Hz), 3.26-3.33 (m, 2H), 2.96-2.91(m, 2H), 1.82-1.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.6, 149.3, 146.1, 143.3, 138.6, 137.9, 133.8, 128.5, 127.9, 126.8, 126.6, 126.4, 125.0, 124.1, 123.9, 116.4, 98.1, 39.9, 39.8, 27.2; ESI-MS: m/z 452 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{24}H_{22}ClN_3O_2S + H^+]$ 452.1194 found 452.1217.

N-(2-(7-chloroquinolin-4-ylamino)ethyl)biphenyl-4-sulfonamide (19).



White solid; Yield 70%; Mp: 151-153°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ= 8.36 (d, 1H, *J* = 5.1 Hz), 8.16 (d, 1H, *J* = 9.0 Hz), 7.88 (d, 2H, *J* = 8.25 Hz), 7.78 (s, 1H), 7.75 (d, 1H, *J* = 5.9 Hz) , 7.66 (d, 1H, *J* =7.1 Hz), 7.51-7.41 (m, 6H), 6.42 (d, 1H, *J* = 5.3 Hz), 3.41-3.32 (m, 2H), 3.11-3.09 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 152.0, 150.4, 149.0, 140.7, 134.1, 132.9, 129.6, 127.5, 126.8, 124.7,124.3,117.7, 99.0, 42.5, 42.1 ESI-MS: m/z 438 $[M+H]^+$. HRMS (ESI TOF (+)) calcd for $[C_{23}H_{20}ClN_3O_2S + H^+]$ 438.1038 found 438.1027.