

SUPPLEMENTARY MATERIAL

Insights into Flibanserin Stress Degradation Pathway: *In silico* – *In vitro* Toxicity Assessment of Its Degradates

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Figure S1- UV Spectrum of Flibanserin

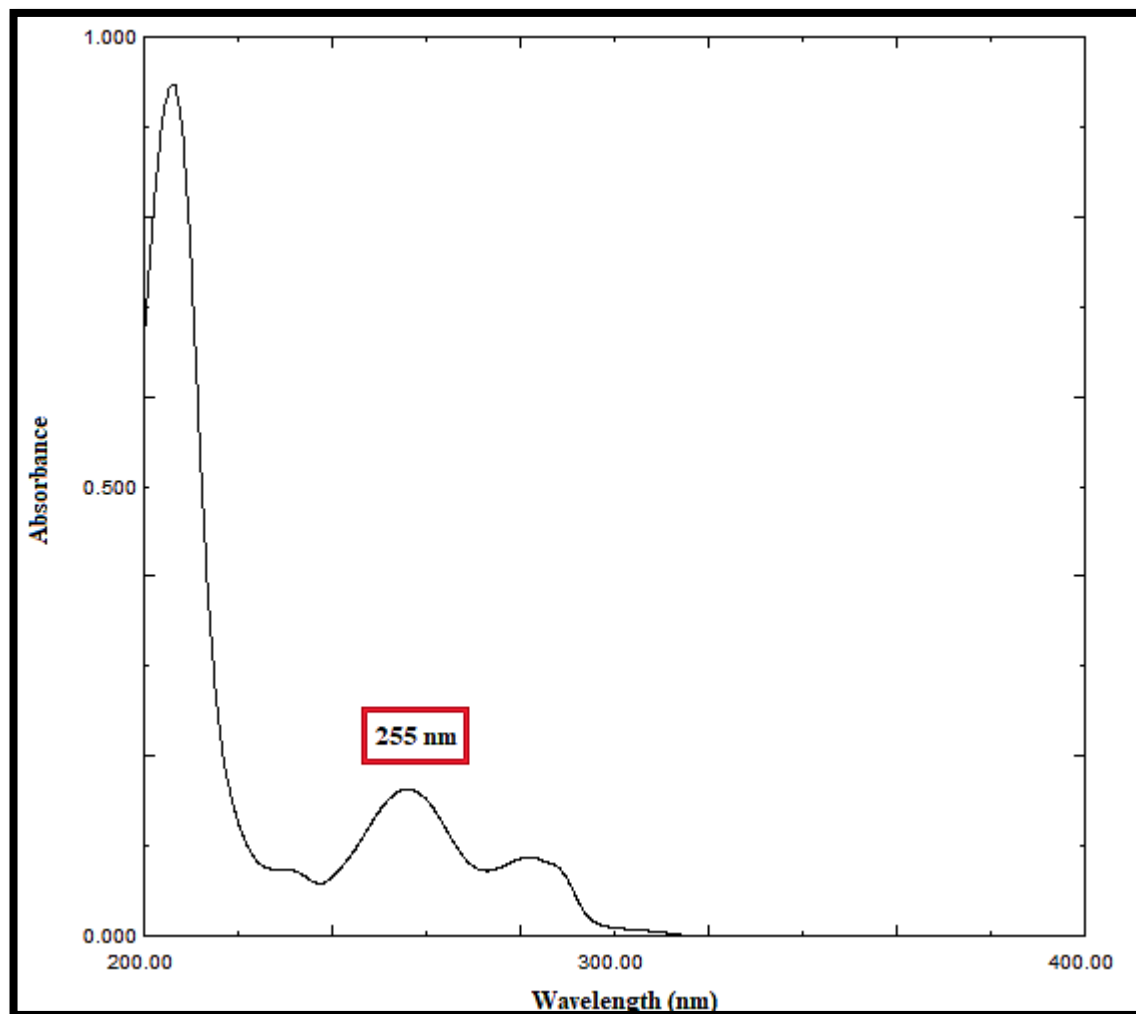
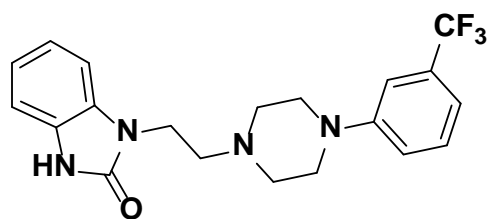


Figure S2-¹H NMR Spectrum of Flibanserin



Flibanserin

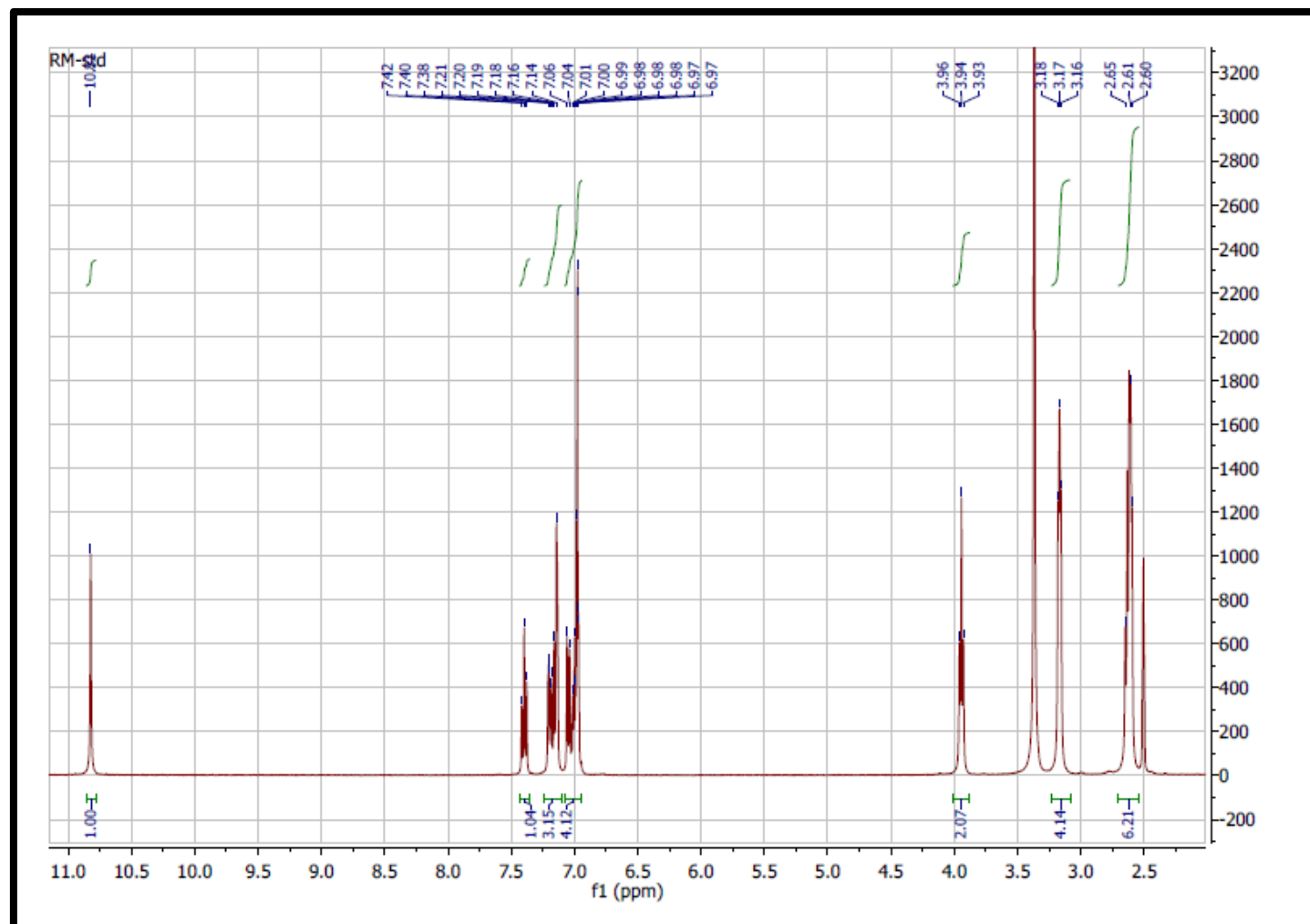
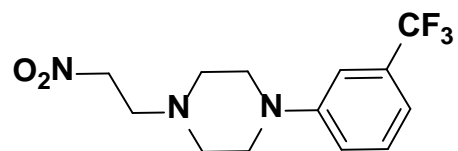


Figure S4-¹H NMR Spectrum of DP 2



DP 2

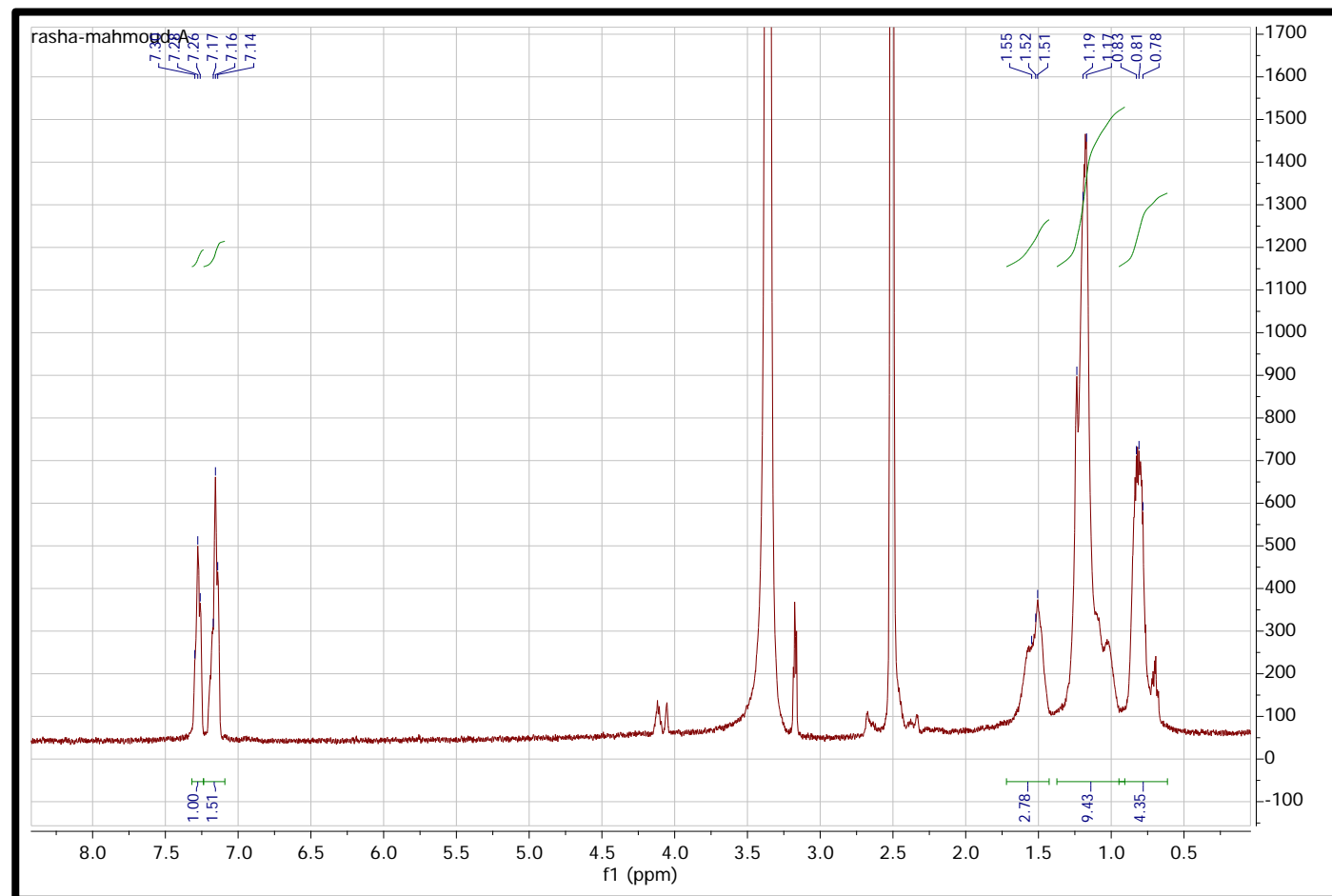


Figure S5- Postulated Mechanism of formation of DP 1&2

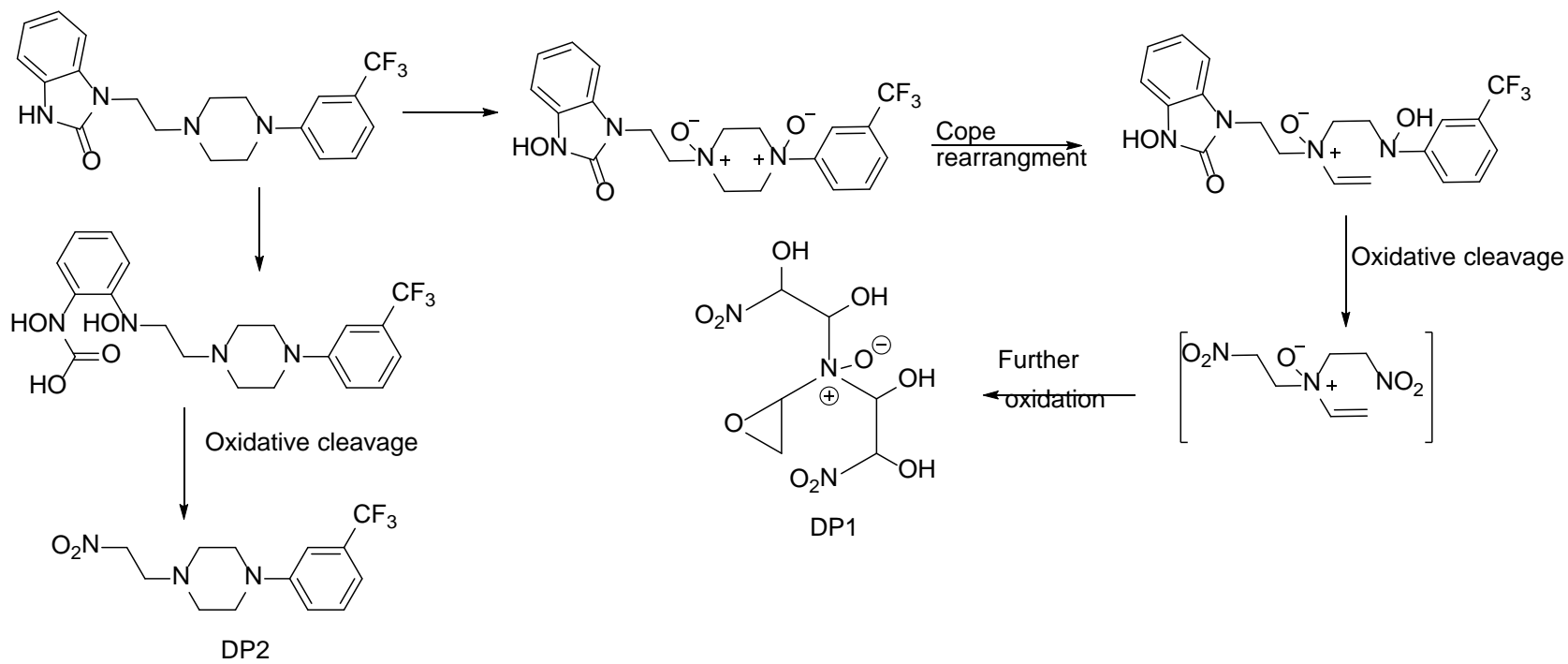


Figure S6- Coefficient plots for method robustness

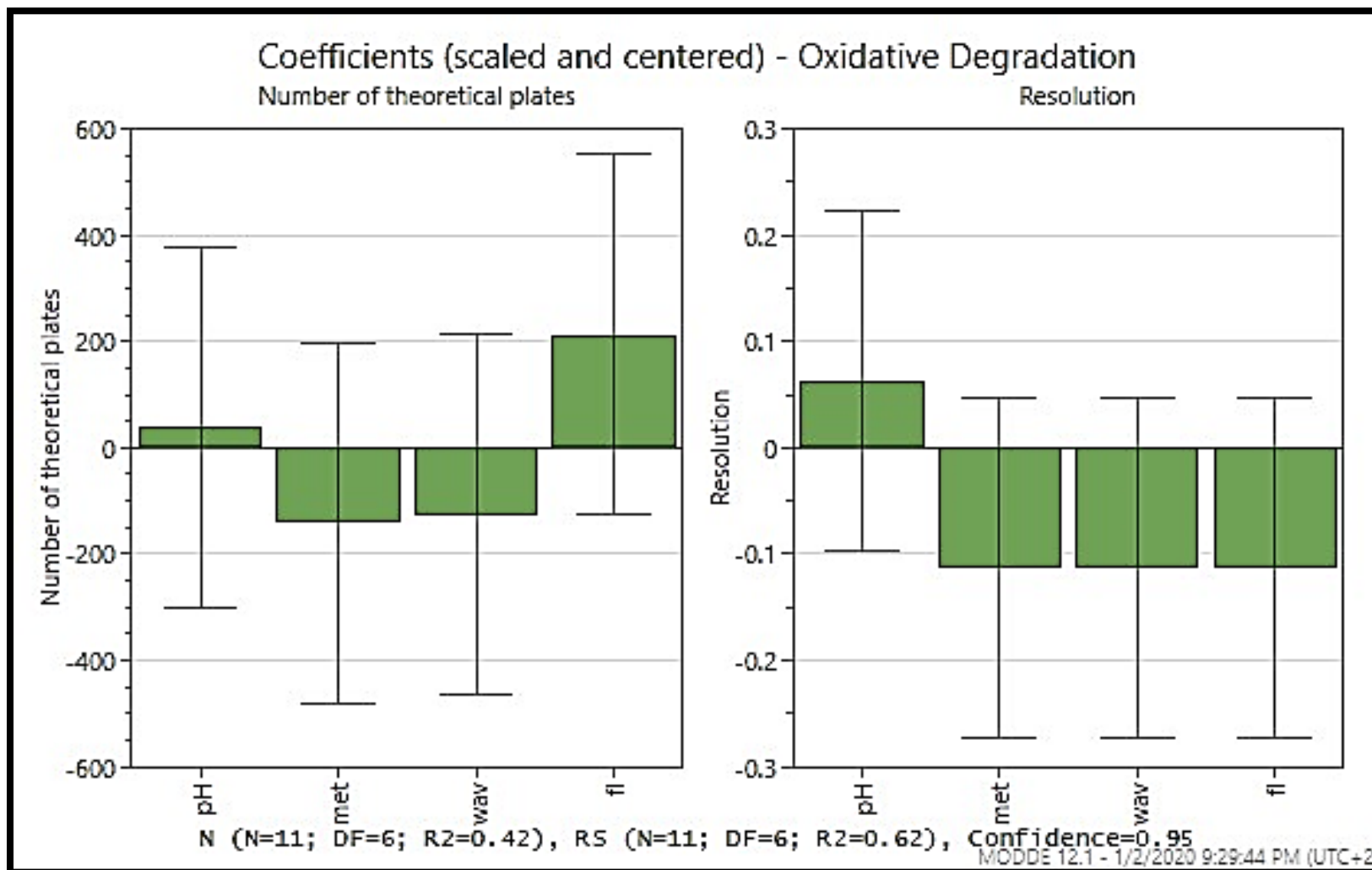


Figure S7- The expected ADMET study

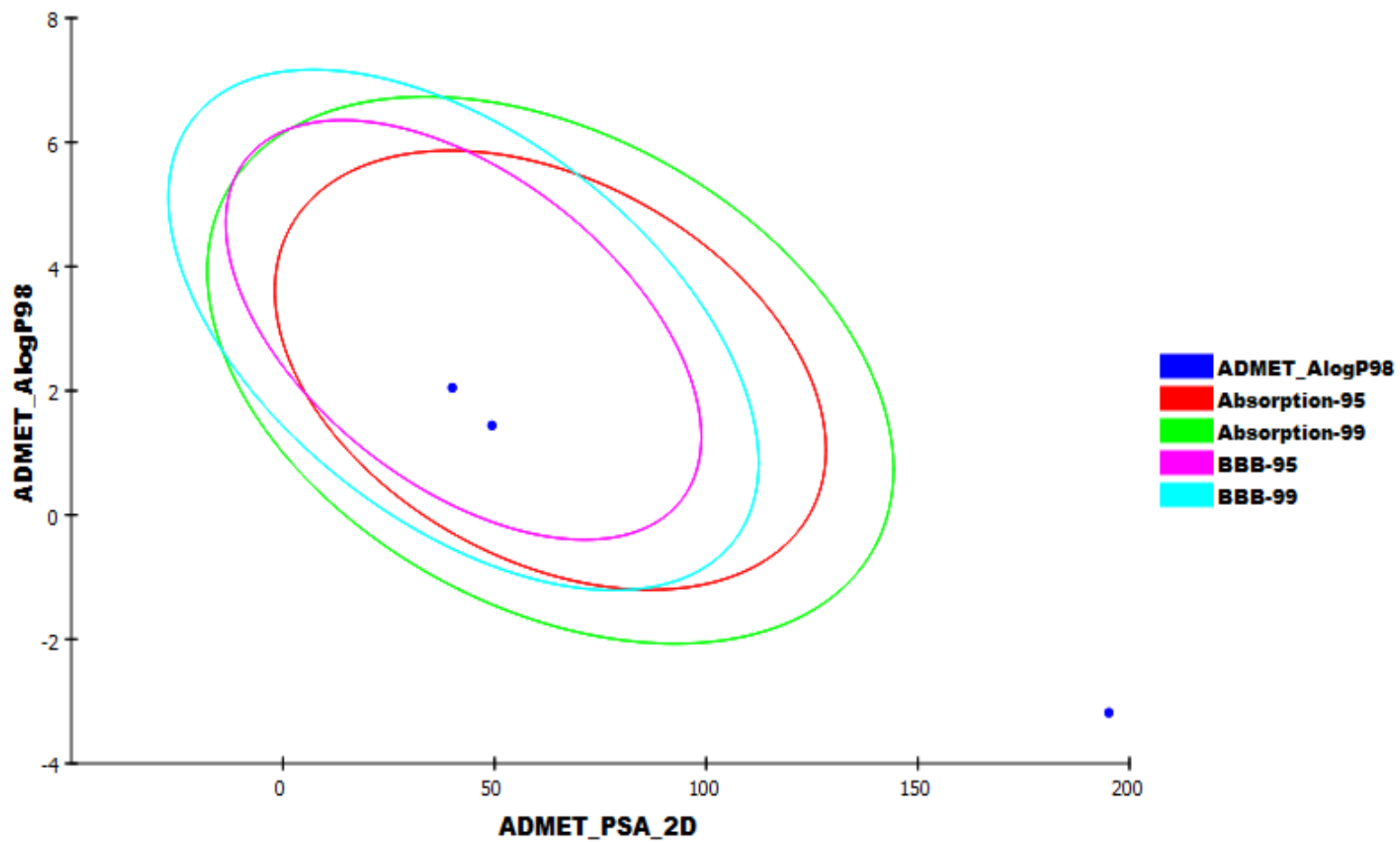


Table S1- System suitability parameters for Flibanserin in the presence of its oxidative DPs

Parameter	Flibanserin
Resolution	4.7
No. of theoretical plates	4339
Capacity factor	2.2
Symmetry	0.83

Table S2- Design of experiment (DOE) for Flibanserin robustness testing

Exp. No	pH	methanol	Wavelength	Flow rate
1	4.2	88	253	1.2
2	4.2	92	253	0.8
3	4.2	92	257	0.8
4	3.8	92	257	1.2
5	4.2	88	257	1.2
6	3.8	92	253	1.2
7	3.8	88	257	0.8
8	3.8	88	253	0.8
9	4	90	255	1
10	4	90	255	1
11	4	90	255	1

Table S3- *In vitro* cytotoxicity of Fibanserin and its degradation products on HSF cell line

Fibanserin	Raw data			Blank Corrected Data			Viability %			Mean	STD
	1	2	3	1	2	3	1	2	3		
Conc.											
c	2.285	2.257	2.271	2.254	2.226	2.24	100	100	100	100	0
0.01	2.284	2.281	2.287	2.253	2.25	2.256	100.58	100.45	100.71	100.58	0.1093522
0.1	2.2675	2.262	2.273	2.2365	2.231	2.242	99.844	99.598	100.09	99.844	0.2004791
1	2.201	2.196	2.207	2.17	2.165	2.176	96.875	96.652	97.143	96.89	0.200755
10	2.188	2.177	2.166	2.157	2.146	2.135	96.295	95.804	95.313	95.804	0.4009581
100	2.151	2.13	2.1405	2.12	2.099	2.1095	94.643	93.705	94.174	94.174	0.3827328
Blank	0.031	0.031	0.031	Blank Average		0.031	Control average		2.24		

DP 1	Raw data			Blank Corrected Data			Viability %			Mean	STD
	1	2	3	1	2	3	1	2	3		
Conc.											
c	2.249	2.275	2.301	2.218	2.244	2.27	100	100	100	100	0
0.01	2.209	2.2315	2.244	2.178	2.2005	2.213	97.059	98.061	98.619	97.913	0.645356
0.1	2.151	2.155	2.147	2.12	2.124	2.116	94.474	94.652	94.296	94.474	0.1455431
1	2.11	2.157	2.204	2.079	2.126	2.173	92.647	94.742	96.836	94.742	1.710131
10	2.079	2.071	2.061	2.048	2.04	2.03	91.266	90.909	90.463	90.879	0.328145
100	2.008	2.047	2.091	1.977	2.016	2.06	88.102	89.84	91.8	89.914	1.5109223
Blank	0.031	0.031	0.031	Blank Average		0.031	Control average		2.244		

DP 2	Raw data			Blank Corrected Data			Viability %			Mean	STD
	1	2	3	1	2	3	1	2	3		
Conc.											
c	2.362	2.363	2.362	2.331	2.332	2.331	100	100	100	100	0
0.01	2.286	2.274	2.298	2.255	2.243	2.267	96.726	96.211	97.24	96.726	0.4202728
0.1	2.195	2.244	2.147	2.164	2.213	2.116	92.822	94.924	90.764	92.837	1.6986325
1	2.1665	2.171	2.162	2.1355	2.14	2.131	91.6	91.793	91.407	91.6	0.1576023
10	2.136	2.164	2.109	2.105	2.133	2.078	90.292	91.493	89.134	90.306	0.9631781
100	2.083	2.082	2.085	2.052	2.051	2.054	88.018	87.975	88.104	88.033	0.0534981
Blank	0.031	0.031	0.031	Blank Average		0.031	Control average		2.3313		

Dox	Raw data			Blank Corrected Data			Viability %				
Conc.	1	2	3	1	2	3	1	2	3	Mean	STD
c	2.146	2.133	2.159	2.115	2.102	2.128	100	100	100	100	0
0.01	1.845	1.848	1.842	1.814	1.817	1.811	85.768	85.91	85.626	85.768	0.1158151
0.1	1.476	1.432	1.454	1.445	1.401	1.423	68.322	66.241	67.281	67.281	0.8493109
1	0.707	0.723	0.691	0.676	0.692	0.66	31.962	32.719	31.206	31.962	0.6176806
10	0.072	0.073	0.072	0.041	0.042	0.041	1.9385	1.9858	1.9385	1.9543	0.0222886
100	0.0545	0.055	0.054	0.0235	0.024	0.023	1.1111	1.1348	1.0875	1.1111	0.0193025
Blank	0.031	0.031	0.031	Blank Average		0.031	Control average		2.115		