

**Table S1.** Genebank accession numbers, name, function and detailed primer information for the studied target and reference genes.

Gene	Accession number	Function	Primers Sequence (5'→3')	Final Concentration (nM)	Amplicon Length (bp)	Efficiency (%)
<i>5-ht1aa</i>	NM_001123321.1	Serotonin receptor	F: ATGAGGATGAGCGGGATGTAG R: CAATCAGCCAGGACCACG	300	80	125
<i>5-ht2c</i>	NM_001129893.1	Serotonin receptor	F: GCGCTCTCTGCTCTATTTGG R: GTAGCGGTCGAGAGAAATGG	1000	89	126.4
<i>abcb4</i>	JQ014001	ABC transporter	F: TACTGATGATGCTTGGCTTAATC R: TCTCTGGAAGGTGAAGTTAGG	300	159	110.6
<i>abcc1</i>	XM_002661199	ABC transporter	F: GCTCGAGCTCTCCTCAGAAA R: TCGGATGGTGGACTGTATCA	300	99	125.1
<i>abcc2</i>	NM_200589	ABC transporter	F: GCACAGCATCAAGGGAAACA R: CCTCATCCACTGAAGAACCGA	300	87	116.5
<i>abcg2a</i>	NM_001042775.1	ABC transporter	F: AAGGGTATCGAGGACCGTCT R: AATCCTGACCCTGAACGATG	300	97	113.1
<i>adra2a</i>	NM_207637.2	Norepinephrine receptor	F: AGCGTTTTGTGACTGCTGTG R: TAATGGGATTGAGGGAGCTG	300	86	114
<i>adra2b</i>	NM_207638.1	Norepinephrine receptor	F: GTCTGCCTGGCCACACTAAT R: GTACGGGGCGAGTTTATCA	1000	80	119.7
<i>adra2c</i>	NM_207639.1	Norepinephrine receptor	F: CTATTCTCCGCCACCATT R: CCAGCACATCCCCACTATT	1000	80	133.8
<i>ahr2</i>	NM_001007789.2	Aryl hydrocarbon nuclear receptor	F: TTCTGTTGCCGATTGAGATG R: CTTGTTTTGCCCATGGAGAT	300	96	113.8
<i>cat</i>	NM_130912.1	Antioxidant enzyme	F: CAGGAGCGTTTGGCTACTTC R: ATCGGTGTCGTCTTCCAAC	300	91	113
<i>Cu/Zn sod</i>	Y12236	Antioxidant enzyme	F: GTCGTCTGGCTGTGAGAGTG R: TGTCAGCGGGCTAGTGCTT	300	113	110
<i>cyp1a1</i>	NM_131879.1	Phase I biotransformation enzyme	F: AACTCTTCGCAGGTGCTCAT R: ACAAATGCCATTGGAGACC	300	97	102
<i>cyp3a65</i>	NM_001037438.1	Phase I biotransformation enzyme	F: TGACCTGCTGAACCTCTCT R: AAGGGCGAAAATCCATCTCT	300	82	91
<i>dat</i>	NM_131755.1	Dopamine transporter	F: ACGTCAATTCTCTTTGGAGT R: TCCTCGATATCATCACTGAA	150	86	97
<i>drd1b</i>	NM_001135976.2	Dopamine receptor	F: CTGCGACTCCAGCCTTAATC R: AGATGCGGGTGTAAGTGACC	600	98	117.2
<i>drd2b</i>	NM_197936.1	Dopamine receptor	F: ACGCCGAATATCAGTCCAAC R: GCAGTGCCTGAGTTTCAACA	300	96	110.7
<i>gstπ</i>	NM_131734	Phase II biotransformation enzyme	F: TCTGGACTCTTTCCCGTCTCTCAA R: ATTCACTGTTGCCGTTGCCGT	300	105	119
<i>mao</i>	NM_212827.2	Monoamine oxidase	F: ACCAACTCAAAACCGCATTC R: GTAGGCAAAAAGGTTCCACA	300	151	105
<i>net</i>	XM_689046.5	Norepinephrine transporter	F: AGTCCAGCGTTCTTGCTGTT R: TCTGCCAGTATGGGAAAAC	300	92	117
<i>ppara</i>	NM_001161333.1	Peroxisome proliferator activated nuclear receptor	F: CATCTTGCCTTGACAGACATT R: CACGCTCACTTTTCATTTCAC	600	81	88.3
<i>pparβ</i>	AF342937.1	Peroxisome proliferator activated nuclear receptor	F: GCGTAAGCTAGTCGCAGGTC R: TGCACCAGAGAGTCCATGTC	600	204	81.6
<i>ppary</i>	DQ839547.1	Peroxisome proliferator activated nuclear receptor	F: GGTTCATTACGCGTTCAC R: TGGTTCACGTCACTGGAGAA	600	250	87
<i>pxr</i>	DQ069792.1	Pregnane X nuclear receptor	F: CTTTTTCAGACGTGCGATGA R: TTGGCACTGTCTTCTGTTGC	300	94	112.7
<i>raraa</i>	NM_131406.2	Retinoic acid nuclear receptor	F: GTAGTGGAGTGTGGATGTGAA R: GTGCTGATGTCTGATGGATGA	300	118	108.7
<i>rarab</i>	NM_131399.1	Retinoic acid nuclear receptor	F: ATGGATTACTACCACCAGAAC R: TCTCCACAGAGTGATTCCGAGC	300	115	109.4
<i>rarga</i>	NM_131339.1	Retinoic acid nuclear receptor	F: CCCGCCAACTGTACGATGTCA R: GGGTCCAGTCCAGCATAGAAA	300	79	117.6
<i>rxraa</i>	NM_001161551.1	Retinoid X receptor	F: ATTCAATGGCATCTCCTG R: GCGGCTTAATATCCTCTG	600	99	101.8

<i>rxrab</i>	NM_131153.1	Retinoid X receptor	F: CGCCGCATCAAATCACATAAAC R: TGAATGGGTTGGACAGTATTAGC	300	87	109.4
<i>rxrbb</i>	NM_131238.1	Retinoid X receptor	F: TCACAACTTGGGCGTGGAGGC R: CGCATCTTGACAGACCAGCTCAG	300	105	100.7
<i>rxrga</i>	NM_131217.2	Retinoid X receptor	F: ATCTCAGTTCTTCGTTGCAGGTAG R: CGTTGATGATGGATGGGTGATGG	300	105	99.6
<i>rxrgb</i>	NM_001002345.1	Retinoid X receptor	F: CGCGGAATGGATACTCACG R: GCTGATGACGGACGGATGAC	300	114	97.7
<i>serta</i> / <i>slc6a4a</i>	NM_001039972.1	Serotonin transporter	F: CATCTATGCTGAGGCTATTG R: AAGAATATGATGGCGAAGA	300	73	100
<i>vmat2</i>	NM_001256225.2	Vesicular monoamine transporter	F: CTA AAAAGCTCCGCATCCAG R: TGTCCAAGAGCAAAGCAATG	150	231	133
<i>actb1</i>	NM_131031.1	Reference gene	F: TCCCAAAGCCAACAGAGAGAAG R: GTCACACCATCACCAGAGTCC	10	147	100.5
<i>efl</i>	NM_131263.1	Reference gene	F: GGACACAGAGACTTCATCAAGAAC R: ACCAACACCAGCAGCAACGT	300	84	116.8
<i>rpl8</i>	NM_200713.1	Reference gene	F: CAATGACGACCCGACCG R: CGCCAGCAACTCAGTCACT	10	136	96

Gene	F(4,15)	p
<b>Cluster e</b>		
<i>cyp3a65</i>	5.309	0.007
<i>drd2b</i>	6.791	0.003
<i>dat</i>	23.323	<0.000001
<i>mao</i>	9.44	0.001
<i>5-HT1a</i>	2.74	0.068
<b>Cluster g</b>		
<i>net</i>	0.792	0.548
<i>serta</i>	5.115	0.008
<i>ppar<math>\beta</math></i>	8.198	0.001
<i>ahr2</i>	6.305	0.003
<b>Cluster h</b>		
<i>abcc2</i>	6.512	0.003
<i>gst</i>	3.654	0.029
<i>rarab</i>	19.45	<0.000001
<i>raraa</i>	2.182	0.121
<i>rarga</i>	24.729	<0.000001
<i>rxrga</i>	11.348	<0.000001
<i>rxraa</i>	7.282	0.002
<i>5-HT2c</i>	7.547	0.002
<i>drd1b</i>	2.568	0.081

Nominal concentration (ng/L)	Real concentration (ng/L)	Recovery (%)	Sampling time	Media replacement	Quantification method	Reference
racemic-fluoxetine						

100	94.6 (46.4+48.2)	>80%	Every renewal	Daily	UPLC-ESI- MS/MS	[29]
<b>fluoxetine</b>						
100	104					
1000	1000					
10000	9830	Not reported	24 hours	Daily	LC-MS/MS	[44]
100000	94300					
1000000	971000					
500	440					
10000	8720	>87%	Daily	Daily	UPLC-MS/MS	[45]
<b>(s)-fluoxetine</b>						
100	105.4	>80%	Every renewal	Daily	UPLC-ESI- MS/MS	[29]
<b>(r)-fluoxetine</b>						
100	89.4	>80%	Every renewal	Daily	UPLC-ESI- MS/MS	[29]
<b>(s)-norfluoxetine</b>						
3500		62.5				
15000	Not reported	84.1	day 1, 2 and 3	Not reported	SPE-HPLC-FD	[46]
28000		91.1				
<b>(r)-norfluoxetine</b>						
3500		99.1				
15000	Not reported	102	day 1, 2 and 3	Not reported	SPE-HPLC-FD	[46]
28000		103				
<b>racemic- norfluoxetine</b>						
100	102 (46.4+48.2)	>80%	Every renewal	Daily	UPLC-ESI- MS/MS	[29]

The above mentioned studies were conducted under controlled laboratorial conditions. UPLC-ESI-MS/MS, ultra-performance liquid chromatography-electrospray tandem mass spectrometry; LC-MS/MS, liquid chromatography tandem mass spectrometry; UPLC-MS/MS,

ultra-performance liquid chromatography tandem mass spectrometry; SPE-HPLC-FD, Solid-phase extraction with high-performance liquid chromatography coupled with Chirobiotic V and fluorescence detection