Supplementary Information

A Mid-Infrared Spectrophotometric Method for Simultaneous Quantification of Naltrexone and Bupropion with Multivariate Calibration

Andrea Cristina Novack,[a] Alexandre F. Cobre,[a] Camila Regina S. Madeira,[a] Thais M. Guimarães,[a] Mariana M. Fachi,[a] Mário Sérgio Piantavini[a] and Roberto Pontarolo *,[a]

[a]*Programa de Pós-Graduação em Ciências Farmacêuticas, Universidade Federal do Paraná, 80210-170 Curitiba-PR, Brazil*

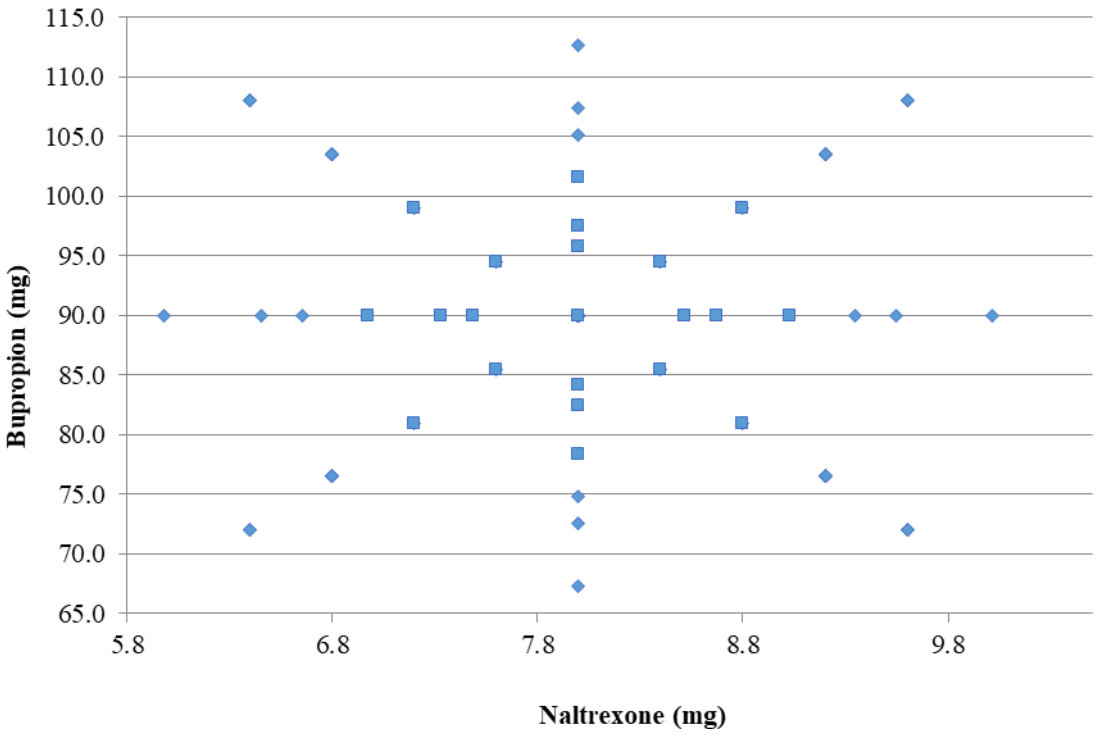

Figure S1. Graphic representation of central composite design of naltrexone and bupropion samples.

*e-mail: pontarolo@ufpr.br

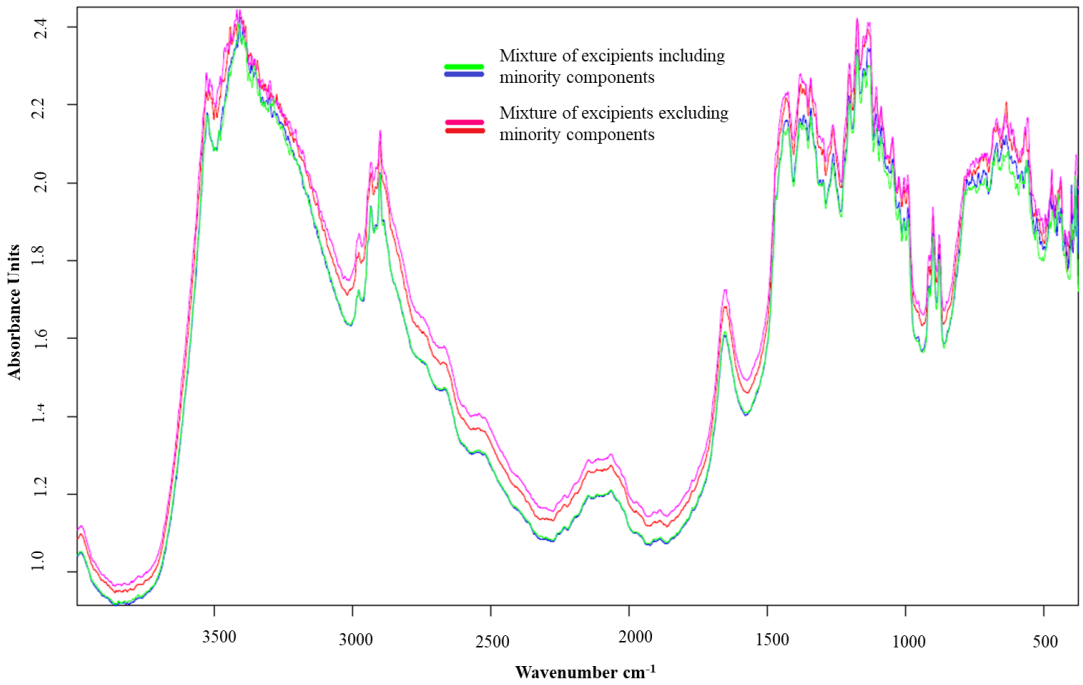

Figure S2. IR (obtained by the DRIFT technique) spectrum of mixing excipients with and without minority components.

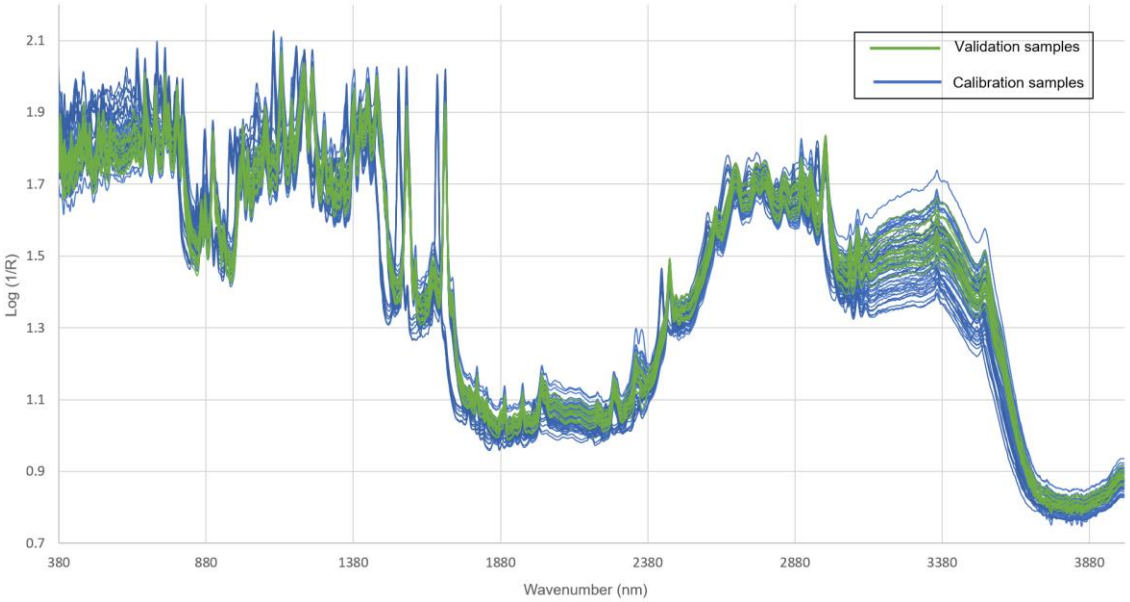

Figure S3. Mid-infrared spectra of naltrexone and bupropion samples used for calibration (represented by blue color) and validation (represented by green color) of the PLS model.

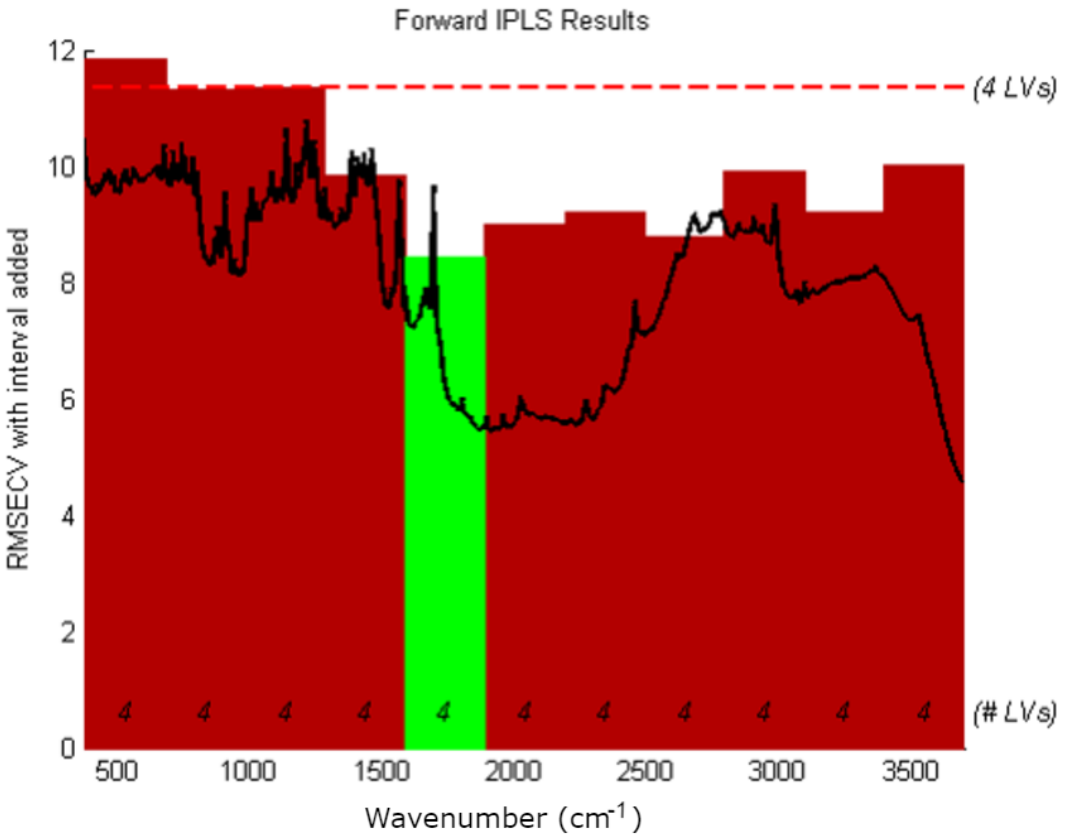

Figure S4. Mid-infrared spectrum region selected by PLS2-iPLS 213 cm^{-1}.

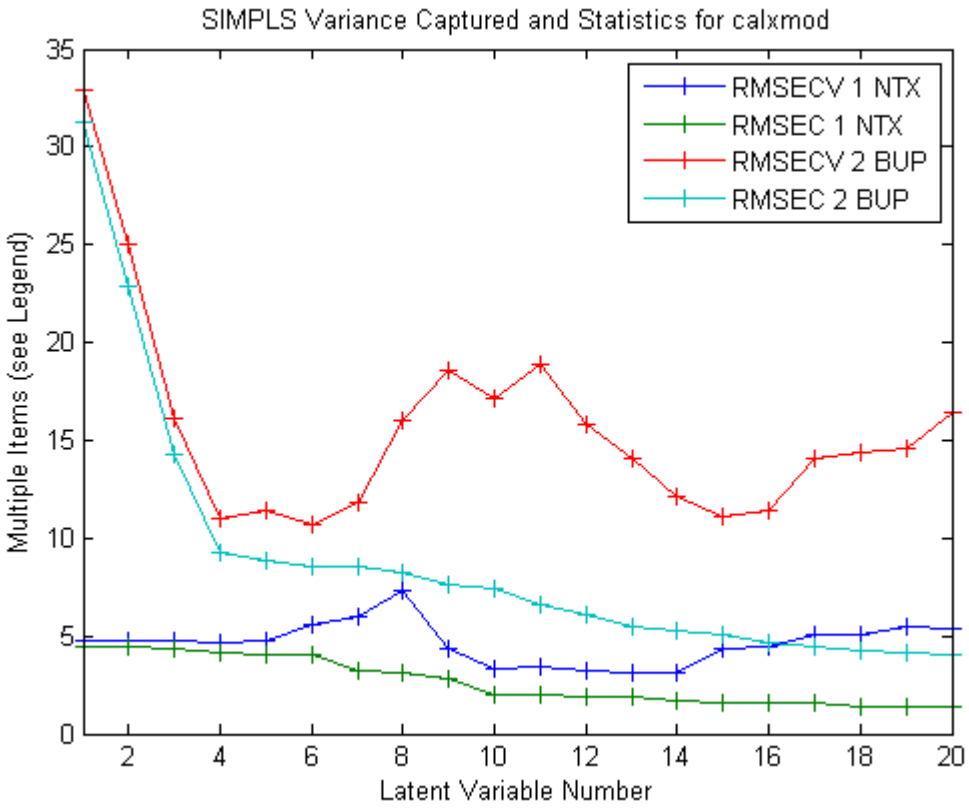

Figure S6. Latent variable chosen for MIR-PLS2.

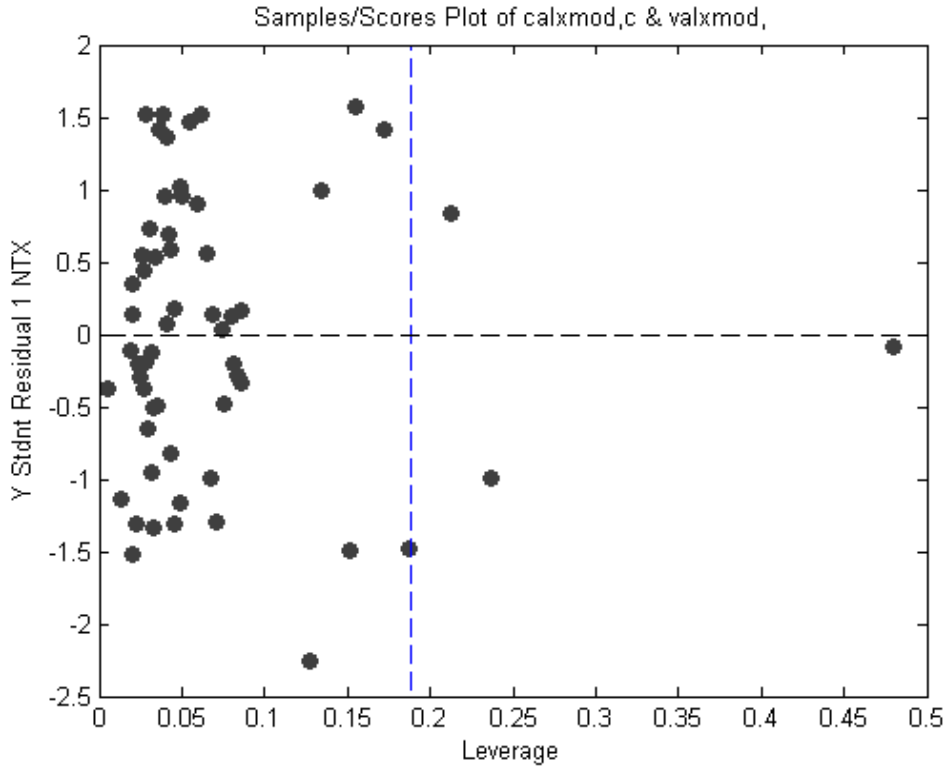

Figure S7. Outliers in naltrexone quantification, model MIR-PLS2.

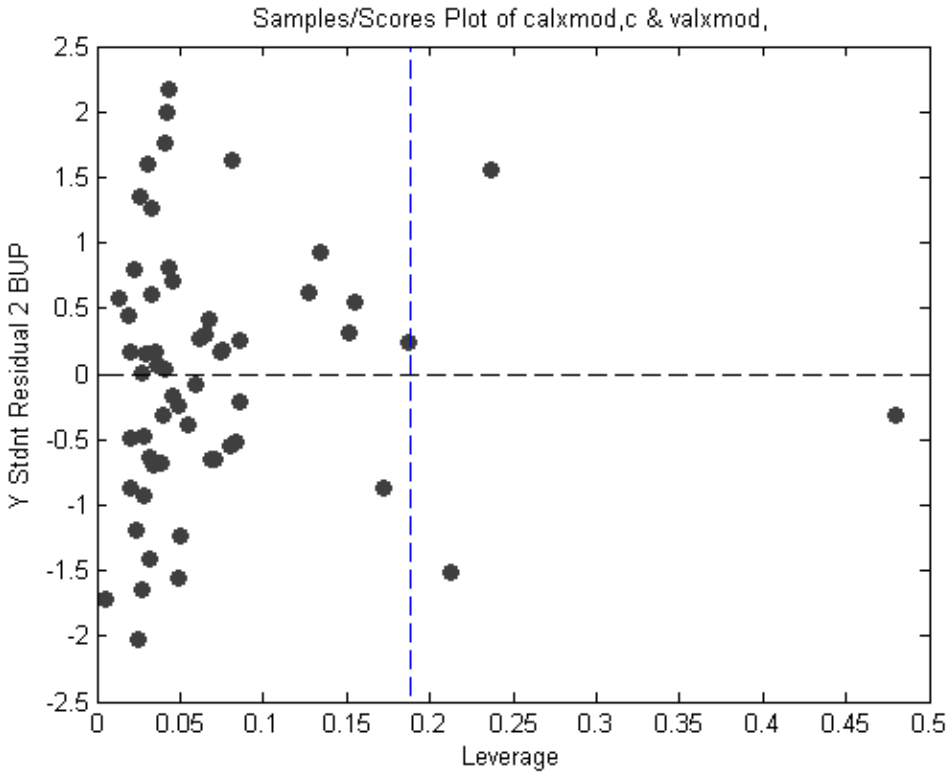

Figure S8. Outliers in bupropion quantification, model MIR-PLS2.

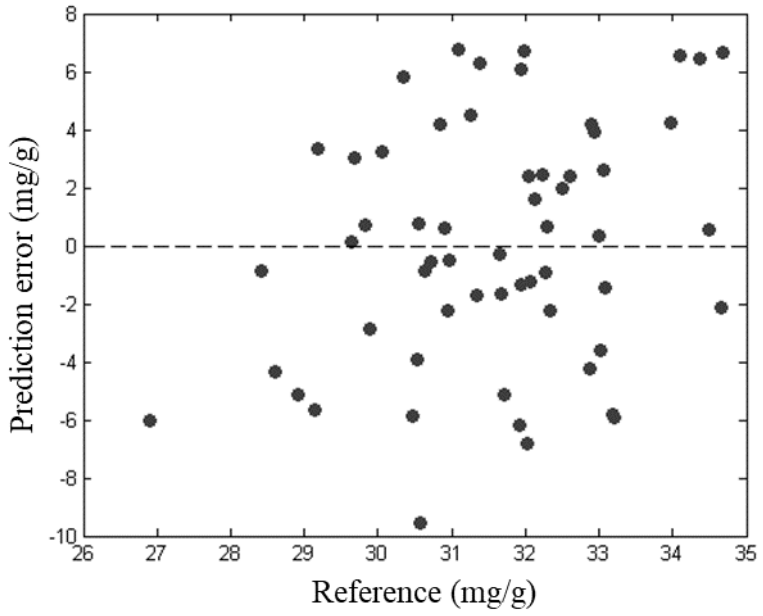

Figure S9. Linearity by error distribution on the i-PLS2-MID model for NTX.

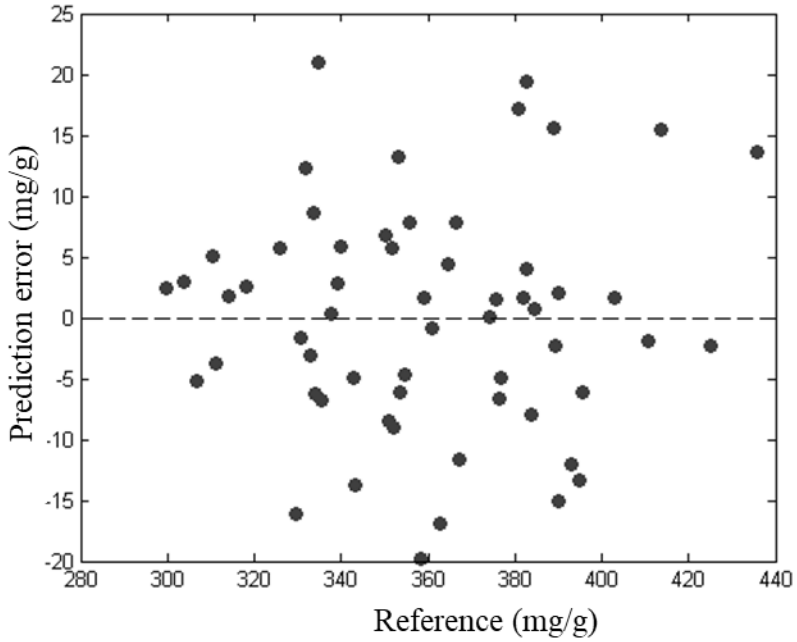

Figure S10. Linearity by error distribution on the i-PLS2-MID model for BUP.

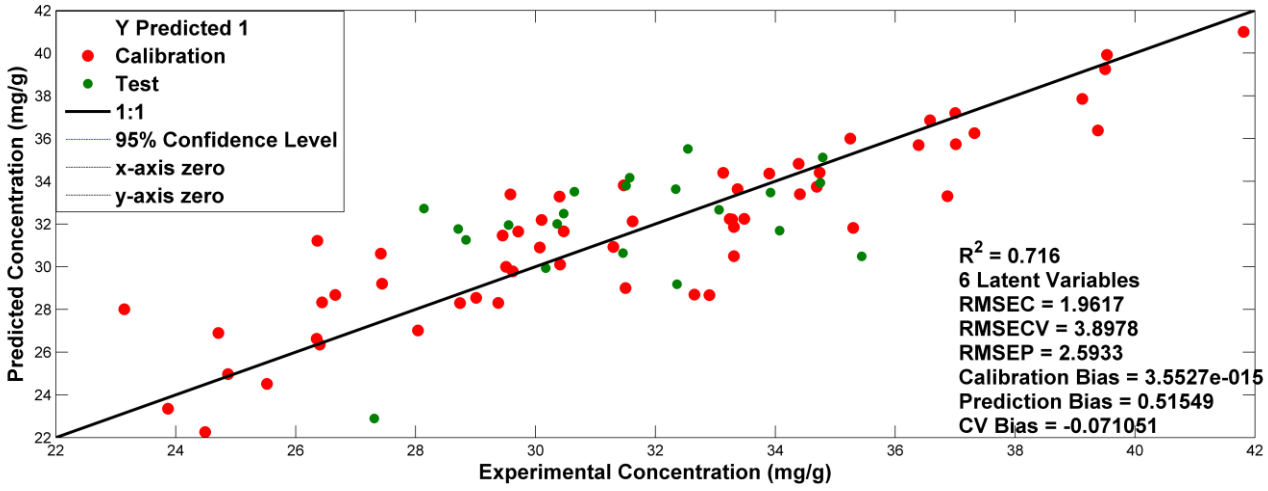

Figure S11. Linear analysis between experimental and predicted concentration of the PLS1 model for quantification of naltrexone. No samples were removed as an outlier.

Table S1. Matrix of the design central composite design. Samples with 5, 10, 15 and 20% variations provided by Statistica software[1]

Type	Sample	NTX	BUP	Excipients[a]	Type	Sample	NTX	BUP	Excipients[a]
V	1	8.00	90.00	152.00	C	40	8.00	90.00	161.78
V	2	8.00	82.43	152.00	V	41	8.00	101.58	152.00
V	3	7.60	94.50	144.40	V	42	9.03	90.00	152.00
V	4	8.40	85.50	144.40	C	43	8.00	90.00	164.78
V	5	7.33	90.00	152.00	C	44	6.80	76.50	159.60
V	6	7.60	85.50	144.40	C	45	5.98	90.00	152.00
V	7	8.40	94.50	159.60	C	46	8.00	90.00	152.00
C	8	7.60	85.50	159.60	C	47	8.00	67.30	152.00
C	9	8.40	94.50	144.40	C	48	9.20	103.50	159.60
C	10	7.60	94.50	159.60	C	49	8.00	90.00	139.22
V	11	8.00	97.57	152.00	C	50	9.20	76.50	144.40
C	12	8.00	90.00	164.78	C	51	6.80	103.50	159.60
C	13	8.40	85.50	159.60	C	52	10.02	90.00	152.00
C	14	8.00	90.00	139.22	C	53	6.80	103.50	144.40
V	15	8.67	90.00	152.00	C	54	9.20	76.50	159.60
V	16	8.00	84.21	152.00	C	55	6.80	76.50	144.40
V	17	7.49	90.00	152.00	C	56	8.00	112.70	152.00
V	18	8.00	95.79	152.00	C	57	9.20	103.50	144.40
C	19	8.00	90.00	161.78	C	58	6.80	76.50	159.60
C	20	8.00	90.00	142.22	C	59	6.46	90.00	152.00
V	21	8.51	90.00	152.00	C	60	8.00	72.62	152.00
C	22	8.00	90.00	152.00	C	61	9.20	103.50	159.60
C	23	6.65	90.00	152.00	C	62	9.20	76.50	144.40
C	24	8.00	90.00	139.22	C	63	6.80	103.50	159.60
V	25	8.80	81.00	159.60	C	64	9.54	90.00	152.00
V	26	7.20	81.00	159.60	C	65	6.80	103.50	144.40
C	27	8.00	74.86	152.00	C	66	9.20	76.50	159.60
V	28	7.20	99.00	144.40	C	67	6.80	76.50	144.40
C	29	8.00	90.00	164.78	C	68	8.00	107.38	152.00
V	30	8.80	99.00	159.60	C	69	9.20	103.50	144.40
C	31	7.20	99.00	159.60	C	70	6.40	72.00	144.40
C	32	8.00	105.14	152.00	C	71	6.40	108.00	144.40
C	33	7.20	81.00	144.40	C	72	6.40	108.00	159.60
C	34	9.35	90.00	152.00	C	73	6.40	72.00	159.60
C	35	8.80	81.00	144.40	C	74	9.60	108.00	159.60
C	36	8.80	99.00	144.40	C	75	9.60	72.00	159.60
V	37	6.97	90.00	152.00	C	76	9.60	72.00	144.40
C	38	8.00	90.00	142.22	C	77	9.60	108.00	144.40
V	39	8.00	78.42	152.00	C	78	8.00	90.00	152.00
						79	8.00	90.00	152.00

[a]Excipient 65% lactose, 20% cellulose, 15% hydroxypropylmethyl cellulose (HPMC). C: calibration; V: validation; NTX: naltrexone; BUP: bupropion.

Table S2. Weight quantity of drugs, excipients and calculation of theoretical concentration of NTX and BUP drugs in the mixture

Sample	Measured weight / mg				Theoretical concentration / (mg g^{-1})[a]	
	NTX	BUP	EXC	Total mass	NTX	BUP
1	16.03	180.14	304.03	500.20	31.51	361.11
2	16.05	164.78	304.02	484.85	32.54	340.78
3	15.29	189.29	288.78	493.36	30.47	384.71
4	16.87	171.06	288.81	476.74	34.79	359.78
5	14.63	180.04	304.04	498.71	28.84	361.99
6	15.20	170.98	288.78	474.96	31.46	360.96
7	16.86	189.01	319.19	525.06	31.57	360.95
8	15.23	171.07	319.22	505.52	29.62	339.32
9	16.87	189.69	288.83	495.39	33.48	383.94
10	15.32	189.48	319.23	524.03	28.74	362.56
11	15.93	195.85	304.08	515.86	30.36	380.68
12	16.10	180.08	329.60	525.78	30.10	343.43
13	16.84	171.00	319.21	507.05	32.65	338.16
14	16.08	180.06	278.37	474.51	33.31	380.49
15	17.38	180.00	304.09	501.47	34.07	359.91
16	16.07	168.45	303.99	488.51	32.34	345.76
17	15.00	179.94	304.02	498.96	29.55	361.60
18	15.96	192.13	303.78	511.87	30.65	376.36
19	16.07	179.98	323.65	519.70	30.40	347.25
20	16.20	180.03	284.54	480.77	33.13	375.47
21	17.30	180.36	303.80	501.46	33.92	360.64
22	16.01	180.08	304.01	500.10	31.47	361.06
23	13.38	180.05	304.08	497.51	26.44	362.88
24	16.08	180.04	278.40	474.52	33.31	380.44
25	17.65	162.38	319.25	499.28	34.75	326.11
26	14.51	162.66	319.73	496.90	28.71	328.23
27	16.62	149.67	303.97	470.26	34.74	319.13
28	14.34	197.82	288.74	500.90	28.14	396.00
29	15.89	180.25	329.60	525.74	29.71	343.78
30	17.61	198.06	319.33	535.00	32.36	371.21
31	14.42	198.05	319.19	531.66	26.66	373.52
32	15.85	210.36	304.08	530.29	29.38	397.76
33	14.43	161.96	289.16	465.55	30.47	348.83
34	18.71	180.09	303.98	502.78	36.58	359.16
35	17.63	161.86	288.78	468.27	37.01	346.59
36	17.64	197.75	288.85	504.24	34.39	393.23
37	13.85	180.12	304.67	498.64	27.31	362.20
38	16.09	180.18	284.49	480.76	32.90	375.79
39	16.03	156.68	303.96	476.67	33.06	329.58
40	16.08	180.15	323.58	519.81	30.41	347.50
41	16.06	203.05	304.17	523.28	30.17	389.08
42	18.12	180.30	304.20	502.62	35.44	359.69

Table S2. Weight quantity of drugs, excipients and calculation of theoretical concentration of NTX and BUP drugs in the mixture (cont.)

Sample	Measured weight / mg				Theoretical concentration / (mg g^{-1})[a]	
	NTX	BUP	EXC	Total mass	NTX	BUP
43	16.08	180.06	329.52	525.66	30.07	343.47
44	13.55	153.08	319.20	485.83	27.42	315.94
45	12.05	180.13	304.11	496.29	23.87	363.93
46	16.03	180.09	304.12	500.24	31.50	360.98
47	16.04	134.58	303.95	454.57	34.69	296.86
48	18.49	207.03	319.26	544.78	33.37	385.35
49	16.04	180.00	278.36	474.4	33.24	384.74
50	18.51	153.02	288.76	460.29	39.53	337.10
51	13.57	207.11	319.15	539.83	24.71	389.03
52	20.06	180.08	304.02	504.16	39.12	362.19
53	13.66	207.05	288.80	509.51	26.36	412.06
54	18.47	153.07	319.26	490.8	37.00	316.24
55	13.68	153.14	288.88	455.7	29.51	340.76
56	16.10	225.42	304.08	545.6	29.01	418.94
57	18.47	206.98	288.88	514.33	35.30	408.06
58	13.56	153.07	319.23	485.86	27.44	319.46
59	12.90	180.04	304.00	496.94	25.52	367.37
60	16.05	145.31	304.10	465.46	33.90	316.56
61	18.44	207.00	319.23	544.67	33.28	385.37
62	18.44	153.07	288.87	460.38	39.38	337.14
63	13.66	207.05	319.20	539.91	24.87	388.86
64	19.10	180.02	304.08	503.2	37.32	362.76
65	13.69	207.15	288.87	509.71	26.40	412.10
66	18.40	153.05	319.19	490.64	36.87	316.31
67	13.71	153.05	288.88	455.64	29.58	340.60
68	16.02	214.78	304.00	534.8	29.45	407.23
69	18.44	207.11	288.80	514.35	35.25	408.30
70	12.70	143.80	288.80	445.3	28.04	323.80
71	12.90	216.12	288.83	517.85	24.49	418.47
72	12.91	216.40	319.16	548.47	23.14	395.62
73	12.77	144.26	319.40	476.43	26.35	303.61
74	19.42	215.55	319.84	554.81	34.41	389.56
75	19.38	143.72	319.30	482.4	39.50	298.73
76	19.22	143.88	288.88	451.98	41.81	319.19
77	19.42	216.30	288.88	524.6	36.39	413.43
78	15.92	180.11	304.08	500.11	31.30	361.11
79	16.10	180.10	304.31	500.51	31.62	360.80

[a](drug mass (in mg) × drug content × 1000)/total mass (in mg); drug content = NTX content = 0.9831 and BUP content = 1.0027.

Table S3. Result of the chromatographic method validation

Figures of merit	Value	NTX	BUP
Precision / %	RSD repeatability	0.07	0.39
	RSD intermediate	0.12	0.40
Recovery / %	Recovery ± RSD	low: 95.08 ± 4.20 medium: 97.22 ± 3.69 high: 99.86±3.57	low: 98.40 ± 4.08 medium: 99.52 ± 1.48 high: 95.44 ± 2.04
Range / (μg mL^{-1})		4.80-12.20	54.00-126.00
Linearity	RSD of each level	r > 0.99	r > 0.99
	correlation coefficient	RSD < 2.3	RSD < 0.27
Robustness / %	RSD pH	1.14	3.22
	RSD temperature	1.75	0.43
	RSD volume injection	1.14	1.77
	RSD mobile phase	0.51	0.20
	RSD column batch	1.21	0.76

RSD: residual standard deviation; NTX: naltrexone; BUP: bupropion.

Reference

1. *Statistica*, version 10; StatSoft software, Tulsa, OK, USA, 2013.