Supplemnetary materials

Table S1. Results of functional assay towards 5-HT$_6$.

Agonist Mode*						Antagonist Mode**											
	E max (%)	SEM	EC50 M	pEC50	SEM pEC50		E max (%)	SEM	IC50 M	IC50 nM	pIC50	SEM	Kb M	Kb nM	pKb	SEM pKb	R2 Kb
Serotonin	100	0.5	2.76×10^{-9}	8.6	0	Serotonin	0.0	1.0	N.C	N.C	N.C	N.C	N.C	N.C	N.C	N.C	N.C
SB 258585	2	0.5	N.C.	N.C.	N.C.	SB 258585	100	0.7	6.01×10^{-9}	6.0	8.22	0,10	1.20×10^{-9}	1.2	8.92	0.10	0.945
Mianseri	2	0.5	N.C.	N.C.	N.C.	MI-AN-SER-IN	91	4.0	4.15×10^{-6}	4152.0	5.38	0,05	8.31×10^{-7}	830.5	6.08	0.05	0.988
1	4	0.5	N.C.	N.C.	N.C.	**1**	98	1.3	1.40×10^{-10}	1400.0	9.87	0.065	2.70×10^{-11}	0.027	10.57	0.0065	0.907
2	5	1.1	N.C.	N.C.	N.C.	**2**	96	3.1	6.33×10^{-8}	63.3	7.12	0,33	6.46×10^{-9}	6.5	8.19	0.33	0.903
3	9	3.3	N.C.	N.C.	N.C.	**3**	100	0.7	1.07×10^{-7}	106.6	6.97	0,20	2.13×10^{-8}	21.3	7.67	0.20	0.972

*Results were normalized as percentage of maximal agonist response (Serotonin 10^{-5} M) **Results were normalized as percentage of reference antagonist (SB258585 10$_{-5}$ M) Emax is the maximum possible effect.
N.C.—not calculable.

Table S2. Results of functional assay towards 5-HT$_{2A}$.

Agonist Mode*					Antagonist mode**										
	E_{max} (%)	SEM	EC$_{50}$ M	pEC$_{50}$		E_{max} (%)	SEM	IC$_{50}$ M	IC$_{50}$ nM	pIC$_{50}$	K$_b$ M	K$_b$ nM	pK$_b$	R^2
Serotonin	100	0.3	1.45 E-09	8.84	Serotonin	1	0.3	N.C.	N.C.	N.C.	N.C.	N.C.	N.C.	N.C.
SB 258585	N.T.													
Mianserin	1	0.3	N.C.	N.C.	Mianserin	1	0.3	1.01×10^{-9}	1.01	9.00	2.01×10^{-10}	0.20	9.70	0.928

1	58	9.7	4.49×10^{-8}	7.35	1	0	0	N.C.	N.C.	N.C.	N.C.	N.C.	N.C.	N.C.
2	21	0.6	5.84×10^{-7}	6.22	2	1	0.3	1.24×10^{-8}	12.36	7.90	2.47×10^{-9}	2.47	8.61	0.984
3	N.T.													

*Results were normalized as percentage of maximal agonist response (Serotonin 10^{-5} M) **Results were normalized as percentage of reference antagonist (SB258585 10^{-5} M) Emax is the maximum possible effect.

N.C.—not calculable N.T.—not tested.

Table S3. The metabolic pathways of compounds **2** and **3**.

Substrate	Molecular Mass (m/z)	Retention Time (min.)	Molecular Mass of the Metabolite (m/z)	Metabolic Pathway	Probable Structures of Metabolites*
2	397.31		413.07 (**M1**) 413.07 (**M2**) 383.03 (**M3**)	hydroxylation hydroxylation demethylation	Fig. S1B Fig. S1C Fig. S1D
3	328.42		279.22 (**M1**) 345.28 (**M2**)	decomposition and triple hydroxylation hydroxylation	Fig. S2B Fig. S2C

Table S4. The impact of compounds **1–3** on the MK-801-induced memory impairment in the NOR test.

Treatment	Dose (mg/kg)		Discrimination Index
Vehicle	0	+ 0	0.37 ± 0.03
MK-801 + Vehicle [17]	0.1+0		-0.07 ± 0.01; $p < 0.05$ vs veh
1 + MK-801 [17]	0.3	+ 0.1	0.29 ± 0.04; ns vs veh,; ns vs MK
	1+0.1		0.13 ± 0.08; ns vs veh; ns vs MK
	3+0.1		0.42 ± 0.18; ns vs veh; $p < 0.05$ vs MK $F_{(4,30)} = 3.9851$; $p < 0.01$
Vehicle + Vehicle	0	+ 0	0.21 ± 0.05
MK-801 + Vehicle	0.1+0		-0.05 ± 0.03; $p < 0.01$ vs veh
2 + MK-801	0.3	+ 0.1	0.26 ± 0.04; ns vs veh; $p < 0.01$ vs MK
	1+0.1		0.19 ± 0.04; ns vs veh; $p < 0.05$ vs MK
	3+0.1		0.30 ± 0.06; ns ve veh, $p < 0.001$ vs MK $F_{(4,27)} = 7.5715$; $p < 0.001$

Vehicle	0	+ 0	0.27 ± 0.04
MK-801 + vehicle	0.1+0		-0.11 ± 0.07; $p < 0.05$ vs veh
3 + MK-801	0.1	+ 0.1	0.26 ± 0.04; ns vs veh; $p < 0.01$ vs MK
	0.3	+ 0.1	0.30 ± 0.04; ns vs veh, $p < 0.001$ vs MK
	1+0.1		0.18 ± 0.15; ns vs veh, $p < 0.05$ vs MK
	3+0.1		0.31 ± 0.05, ns vs veh, $p < 0.001$ vs MK
			$F_{(5,47)} = 8.1658$; $p < 0.0001$

Compounds **1**, **2**, **3** were given *i.p.* 60 min while MK-801 was given *i.p.* 30 min before the T1 session. Values represent the mean ± SEM of the discrimination index during 3-min test session compared to the respective vehicle group (one-way ANOVA followed by Bonferroni's post-hoc test); NS—non-significant. N=6-7.

Table S5. Effect of compounds **1**, **2**, **3** on the immobility time in FST in rats.

| Treatment	Dose (mg/kg)	Immobility Time (s)
Vehicle	0	259.86 ± 5.4
1	1	241.80 ± 18.7
	3	175.29 ± 18.1; $p < 0.01$
	10	163.63 ± 11.2; $p < 0.001$
		$F_{(3,26)} = 10.615$; $p < 0.001$
Vehicle	0	227.71 ± 12.7
2	1	223.13 ± 11.4
	3	220.71 ± 4.7
	10	171.38 ± 12.80; $p < 0.01$
		$F_{(3,26)} = 5.8561$; $p < 0.01$
Vehicle	0	211.00 ± 9.3
3	1	177.50 ± 6.1
	3	159.13 ± 13.3; $p < 0.05$
	10	134.63 ± 16.7; $p < 0.001$
		$F_{(3,26)} = 6.8104$; $p < 0.01$

Decreased immobility time denotes antidepressant-like activity. Compounds **1**, **2**, **3** were given *i.p.* 60 min before the test. Values represent the mean ± SEM of immobility time during 5-min test session compared to the respective vehicle group (one-way ANOVA followed by Bonferroni's post-hoc test); *N*=6-8.

Table S6. Effects of compounds **1**, **2**, **3** in the EPM test in rats.

Treatment	Dose (mg/kg)	Open Arms				
		Time (s)	% of time	Entries	% of entries	Distance (cm)
Vehicle	0	31.39 ± 10.11	15.00 ± 4.29	9.14 ± 1.98	29.44 ± 4.82	456 ± 137
1	1	58.90 ± 14.20	25.76 ± 6.11	9.88 ± 1.99	32.59 ± 4.23	788 ± 175
	3	24.81 ± 5.24	10.27 ± 2.05	6.14 ± 0.77	29.49 ± 3.48	307 ± 78
	10	43.36 ± 9.08	18.34 ± 4.19	7.20 ± 1.66	42.23 ± 9.09	538 ± 104
		$F_{(3,23)} = 2.1368$;	$F_{(3,23)} = 2.3504$; NS	$F_{(3,23)} = 1.0379$; NS	$F_{(3,23)} = 1.2608$; NS	$F_{(3,23)} = 2.3440$; NS

NS

Vehicle	0	32.63 ± 9.50	12.67 ± 3.40	5.00 ± 1.20	24.90 ± 1.90	390 ± 116
	0.3	36.85 ± 8.90	14.85 ± 3.30	6.50 ± 1.60	23.97 ± 4.97	423 ± 87
	1	24.75 ± 3.19	10.10 ± 1.20	5.86 ± 0.90	26.53 ± 3.69	279 ± 45
2		72.23 ± 7.30; $p < 0.05$	30.00 ± 3.60; $p < 0.01$	13.00 ± 2.30; $p<0.05$	41.89 ± 3.37	914 ± 126; $p < 0.01$
	3	$F_{(3,23)} = 6.9314$; $p < 0.01$	$F_{(3,23)} = 7.7627$; $p < 0.001$	$F_{(3,23)} = 5.0274$; $p < 0.01$	$F_{(3,23)} = 3.9489$; NS	$F_{(3,23)} = 8.2188$; $p< 0.001$
Vehicle	0	32.63 ± 9.50	12.67 ± 3.50	5.00 ± 1.20	24.90 ± 1.90	390 ± 116
	0.3	24.27 ± 3.41	9.84 ± 1.50	5.28 ± 0.42	28.54 ± 6.70	340 ± 59
3	1	44.24 ± 9.71	18.30 ± 4.10	8.43 ± 1.36	33.64 ± 2.70	646 ± 145
		19.00 ± 5.50	7.03 ± 2.00	4.17 ± 1.10	24.39 ± 7.60	231 ± 87
	3	$F_{(3,22)} = 2.1964$; NS	$F_{(3,22)} = 2.6159$; NS	$F_{(3,22)} = 3.0956$; NS	$F_{(3,22)} = 0.6565$; NS	$F_{(3,22)} = 2.7192$; NS

Increased open-arm exploration denotes reduced anxiety. Compounds **1**, **2**, **3** were given *i.p.* 60 min before the test. Values represent the mean ± SEM of the time and percentage of time spent in open arms, entries and percentage of entries into the open arms during 5-min test session compared to the respective vehicle group (one-way ANOVA followed by Bonferroni's post-hoc test); NS—non-significant. N=6-7.
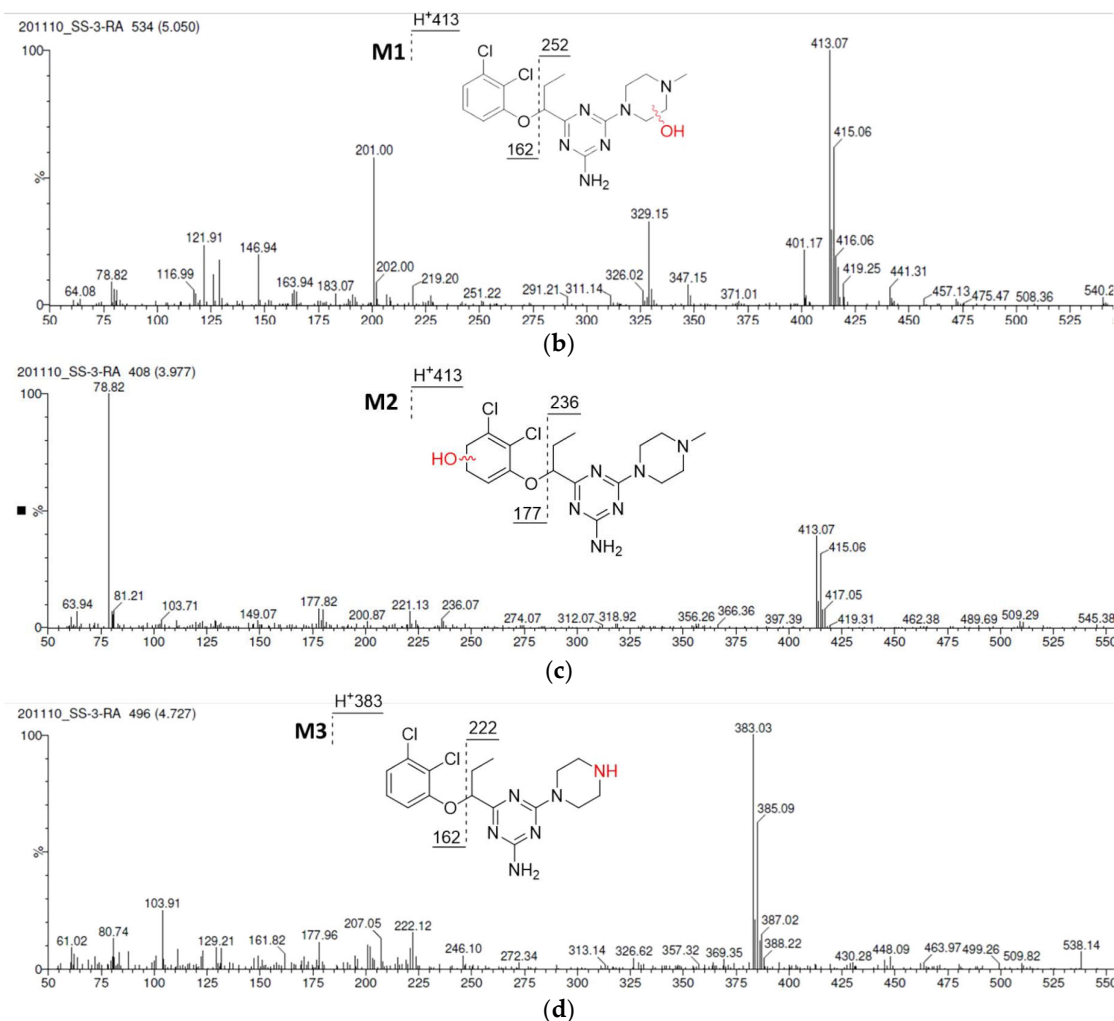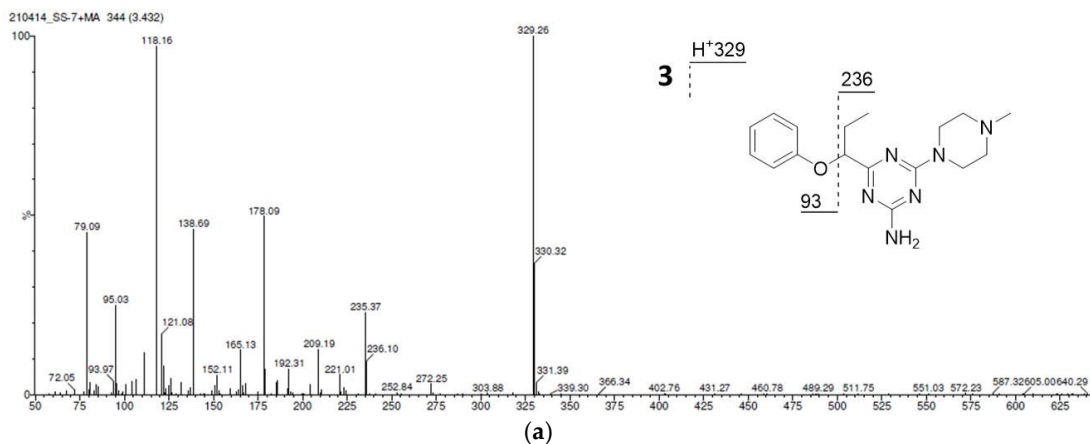

(**a**)
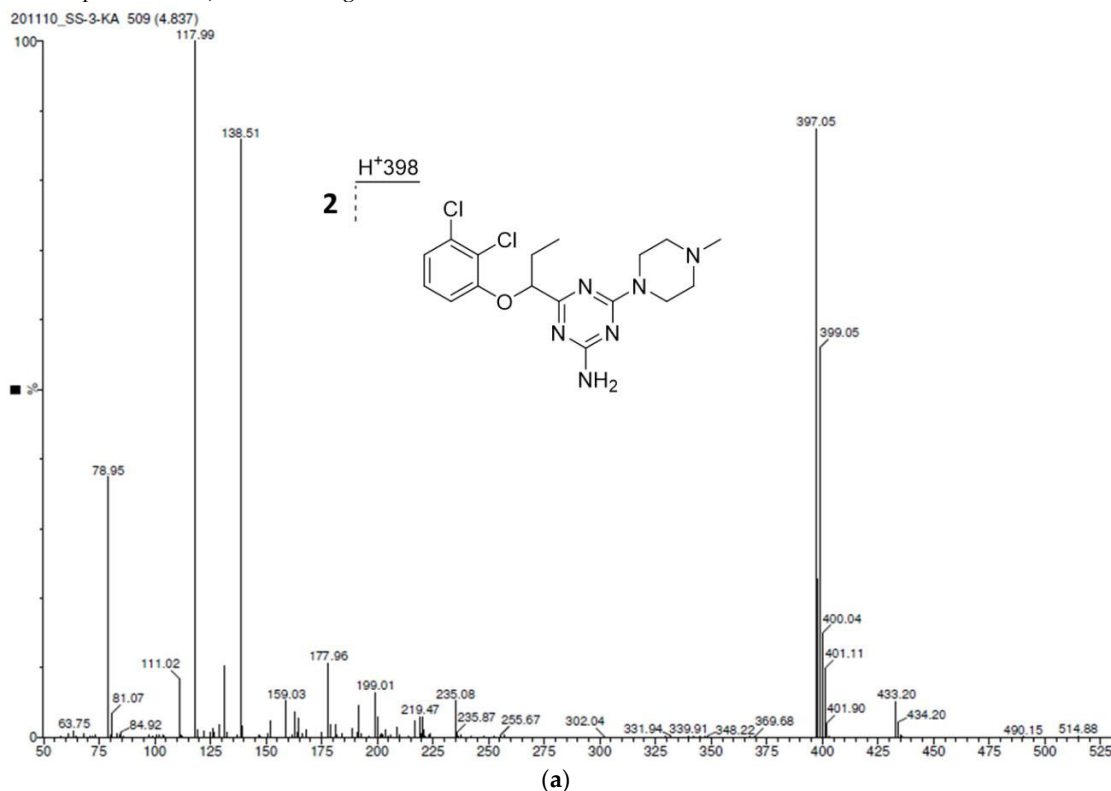
Figure S1. (**a**) MS spectra of compound **2**, control. (**b**) MS spectra and the most probable structure of compound's **2** metabolite M1 obtained after 120 min incubation with RLMs. (**c**) MS spectra and the most probable structure of compound's **2** metabolite M2 obtained after 120 min incubation with RLMs. (**d**) MS spectra and the most probable structure of compound's **2** metabolite M3 obtained after 120 min incubation with RLMs.
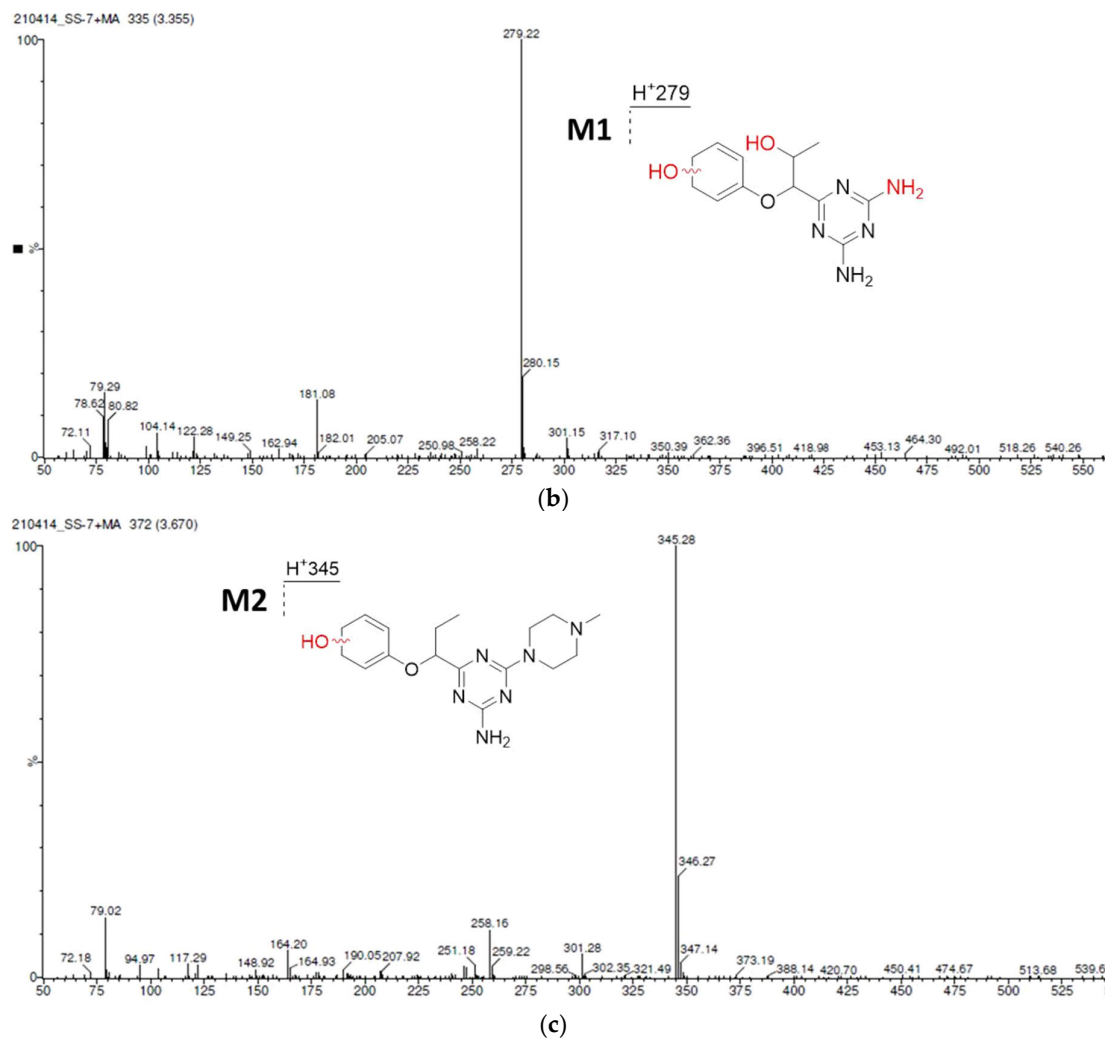
(b)

(c)

Figure S2. (**a**) MS spectra of compound **3**, control. (**b**) MS spectra and the most probable structure of compound's **3** metabolite M1 obtained after 120 min incubation with RLMs. (**c**) MS spectra and the most probable structure of compound's **9** metabolite M2 obtained after 120 min incubation with RLMs.