Supplementary Materials: *In Silico* ADME Profiling of Salubrinal and its Analogues
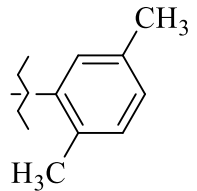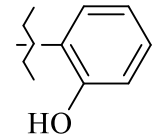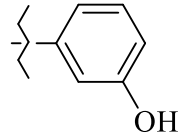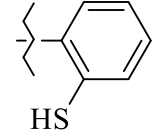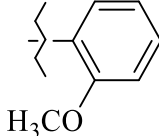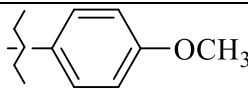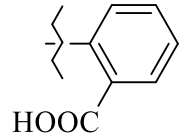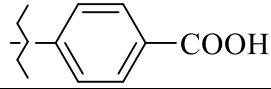
Pavlo V. Zadorozhnii, Vadym V. Kiselev and Aleksandr V. Kharchenko

Table S1. Structures of Salubrinal analogues containing a cinnamic acid residue.
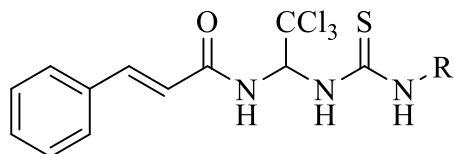
Comp.	R	CAS No	SMILES
S1		405060–59–9	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)\C=C\C1=CC=CC=C1
S2		863036–22–0	ClC(Cl)(Cl)C(NC(=S)NC1=CC=C2C=CC=NC2=C1)NC(=O)\C=C\C1=CC=CC=C1
S3		294654–78–7	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1C=CC=C2)NC(=O)\C=C\C1=CC=CC=C1
S4		324769–18–8	ClC(Cl)(Cl)C(NC(=S)NC1=CC=C2C=CC=CC2=C1)NC(=O)\C=C\C1=CC=CC=C1
S5		405060–99–3	NC(=O)CNC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl

Comp.	R	CAS No	SMILES
S6		405060–96–0	COC(=O)CNC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S7		863036–35–5	CC(C)(C)OC(=O)NCCCCNC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S8		301359–85–3	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC=C1)NC(=O)\C=C\C1=CC=CC=C1
S9		301359–95–5	CC1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S10		301359–86–4	CC1=CC(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=CC=C1
S11		301359–87–5	CC1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C=C1
S12		1429483–71–5	CC1=C(C)C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=CC=C1
S13		301359–93–3	CC1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C(C)=C1

Comp.	R	CAS No	SMILES
S14		301359–94–4	CC1=CC=C(C)C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=C1
S15		294657–79–7	OC1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S16		3037775–31–7	OC1=CC(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=CC=C1
S17		405060–94–8	SC1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S18		301359–88–6	COC1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S19		1346508–38–0	COC1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C=C1
S20		303775–35–5	OC(=O)C1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S21		294655–14–4	OC(=O)C1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C=C1

Comp.	R	CAS No	SMILES
S22		294655–12–2	COC(=O)C1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S23		294654–81–2	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC(=C1)N(=O)=O)NC(=O)\C=C\C1=CC=CC=C1
S24		294654–82–3	ClC(Cl)(Cl)C(NC(=S)NC1=CC=C(C=C1)N(=O)=O)NC(=O)\C=C\C1=CC=CC=C1
S25		301359–89–7	ClC1=CC=CC=C1NC(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl
S26		301359–90–0	ClC1=CC(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=CC=C1
S27		301359–91–1	ClC1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C=C1
S28		301359–92–2	ClC(Cl)(Cl)C(NC(=O)\C=C\C1=CC=CC=C1)NC(=S)NC1=CC=C(Br)C=C1
S29		301359–97–7	ClC1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C(Cl)=C1

Comp.	R	CAS No	SMILES
S30		301359–98–8	ClC1=CC=C(Cl)C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=C1
S31		301359–96–6	FC(F)(F)C1=CC=C(Cl)C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)=C1
S32		301815–13–4	CC(=O)NC1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C=C1
S33		294653–17–1	ClC(Cl)(Cl)C(NC(=S)NC1=CC=C(C=C1)\N=N\C1=CC=CC=C1)NC(=O)\C=C\C1=CC=CC=C1
S34		294654–77–6	NS(=O)(=O)C1=CC=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)C=C1
S35		863036–23–1	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC=N1)NC(=O)\C=C\C1=CC=CC=C1
S36		1349267–41–9	CC1=CC(Br)=C(NC(=S)NC(NC(=O)\C=C\C2=CC=CC=C2)C(Cl)(Cl)Cl)N=C1
S37		1349267–41–9	ClC(Cl)(Cl)C(NC(=O)\C=C\C1=CC=CC=C1)NC(=S)NC1CCS(=O)(=O)C1
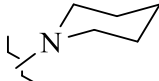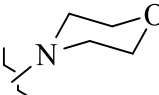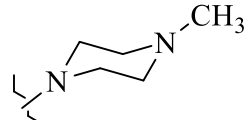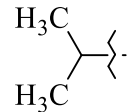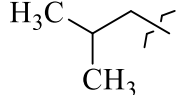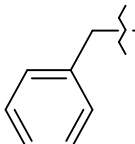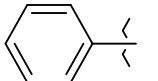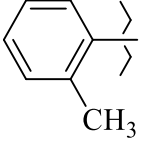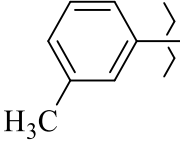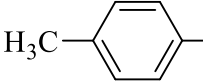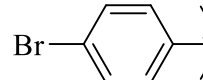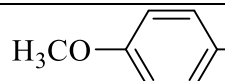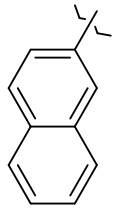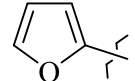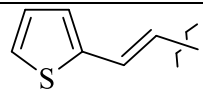
Comp.	R	CAS No	SMILES
S38		1346508–37–9	ClC(Cl)(Cl)C(NC(=O)\C=C\C1=CC=CC=C1)NC(=S)N1CCCCC1
S39		1346508–36–8	ClC(Cl)(Cl)C(NC(=O)\C=C\C1=CC=CC=C1)NC(=S)N1CCOCC1
S40		1429483–72–6	CN1CCN(CC1)C(=S)NC(NC(=O)\C=C\C1=CC=CC=C1)C(Cl)(Cl)Cl

Table S2. Structures of Salubrinal analogues containing quinoline ring.
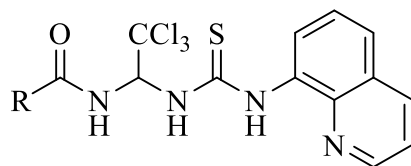
Comp.	R	CAS No	SMILES
S41	CH₃–	294658–37–0	CC(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S42		324769–75–5	CC(C)C(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S43		294658–28–9	CC(C)CC(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S44	(CH₃)₃C–	412962–51–7	CC(C)(C)C(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S45		305856–11–5	ClC(Cl)(Cl)C(NC(=O)CC1=CC=CC=C1)NC(=S)NC1=CC=CC2=C1N=CC=C2

Comp.	R	CAS No	SMILES
S46		294646–80–3	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)C1=CC=CC=C1
S47		324017–95–0	CC1=C(C=CC=C1)C(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S48		330684–99–6	CC1=CC=CC(=C1)C(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S49		294658–30–3	CC1=CC=C(C=C1)C(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S50		330567–60–7	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)C1=CC=C(Br)C=C1
S51		294658–45–0	COC1=CC=C(C=C1)C(=O)NC(NC(=S)NC1=CC=CC2=C1N=CC=C2)C(Cl)(Cl)Cl
S52		405060–98–2	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)C1=CC2=C(C=CC=C2)C=C1
S53		324017–57–4	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)C1=CC=CO1
S54		1346508–21–1	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)\C=C\C1=CC=CS1
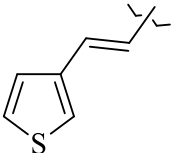
Comp.	R	CAS No	SMILES
S55		1346508−22−2	ClC(Cl)(Cl)C(NC(=S)NC1=CC=CC2=C1N=CC=C2)NC(=O)\C=C\C1=CSC=C1

Table S3. List of online servers used in the work.

No	Online resource	E−link
1	ADMETlab	http://admet.scbdd.com/
2	admetSAR	http://lmmd.ecust.edu.cn/admetsar2/
3	ALOGPS 2.1	http://www.vcclab.org/lab/alogps/start.html
4	Molinspiration	https://www.molinspiration.com/
5	pkCSM	http://biosig.unimelb.edu.au/pkcsm/
6	SuperCYPsPred	http://insilico−cyp.charite.de/SuperCYPsPred/
7	SciFinder	https://scifinder.cas.org
8	SwissADME	http://www.swissadme.ch/
9	Vienna LiverTox	https://livertox.univie.ac.at/

Table S4. Prediction results of the absorption of Salubrinal and its analogues in the human intestine.

Comp.	ADMETLab		admetSAR 2.0 *		SwissADME	Lipinski rules				Veber rules	
	result	prob.	result	prob.		M_w **	$N_{H bond donors}$**	$N_{H bond acceptors}$**	LogP ***	$N_{rot. bonds}$ **	PSA ****, Å²
S1	++	0.735	+	0.916	High	479.82	3	5	2.71	8	69.78
S2	++	0.727	+	0.920	High	479.82	3	5	2.71	8	72.02
S3	+	0.693	+	0.944	High	478.83	3	4	3.87	8	60.17
S4	+	0.693	+	0.944	High	478.83	3	4	3.87	8	60.74
S5	+	0.598	+	0.922	High	409.73	5	6	1.33	9	84.08
S6	+	0.520	+	0.930	High	424.74	3	6	1.98	10	85.72
S7	−	0.497	+	0.948	High	523.91	4	7	2.91	14	89.34
S8	+	0.675	+	0.931	High	428.77	3	4	3.20	8	56.65
S9	+	0.679	+	0.955	High	442.80	3	4	3.82	8	57.56
S10	+	0.689	+	0.955	High	442.80	3	4	3.82	8	57.58

Comp.	ADMETLab		admetSAR 2.0 *		SwissADME	Lipinski rules				Veber rules	
	result	prob.	result	prob.		M_w **	$N_{H\ bond\ donors}$ **	$N_{H\ bond\ acceptors}$ **	LogP ***	$N_{rot.\ bonds}$ **	PSA ****, $Å^2$
S11	+	0.689	+	0.955	High	442.80	3	4	3.82	8	57.27
S12	+	0.673	+	0.955	High	456.83	3	4	4.04	8	56.96
S13	+	0.673	+	0.955	High	456.83	3	4	4.04	8	56.60
S14	+	0.673	+	0.955	High	456.83	3	4	4.04	8	58.61
S15	+	0.570	+	0.929	High	444.77	4	5	3.04	8	70.63
S16	+	0.554	+	0.929	High	444.77	4	5	3.04	8	71.70
S17	+	0.650	+	0.913	Low	460.84	3	4	3.87	8	83.09
S18	+	0.552	+	0.946	High	458.80	3	5	3.26	9	68.41
S19	+	0.541	+	0.946	High	458.80	3	5	3.26	9	68.78
S20	−	0.467	+	0.831	High	472.78	4	6	2.08	9	85.86
S21	−	0.483	+	0.835	High	472.78	4	6	2.08	9	88.08
S22	+	0.516	+	0.918	High	486.81	3	6	3.40	10	80.13
S23	+	0.616	+	0.863	Low	473.77	3	7	2.16	9	101.18
S24	+	0.616	+	0.863	Low	473.77	3	7	2.16	9	100.34
S25	+	0.649	+	0.937	High	463.22	3	4	4.09	8	57.58
S26	+	0.658	+	0.937	High	463.22	3	4	4.09	8	57.51
S27	+	0.658	+	0.937	High	463.22	3	4	4.09	8	57.34
S28	+	0.628	+	0.915	High	507.67	3	4	3.79	8	57.61
S29	+	0.649	+	0.937	High	497.66	3	4	4.57	8	57.17
S30	+	0.649	+	0.937	High	497.66	3	4	4.57	8	57.40
S31	+	0.66	+	0.930	Low	531.21	3	4	4.89	9	56.87
S32	+	0.642	+	0.955	High	485.82	4	6	3.00	9	80.83
S33	+	0.678	+	0.931	Low	532.88	3	6	3.87	10	79.21
S34	+	0.666	+	0.869	Low	507.85	5	7	2.10	9	110.44
S35	++	0.709	+	0.900	High	429.76	3	5	2.16	8	69.08
S36	+	0.650	+	0.914	High	522.68	3	5	2.98	8	68.30
S37	+	0.585	+	0.903	High	470.83	3	6	1.33	8	102.54
S38	++	0.728	+	0.936	High	420.79	2	4	2.55	7	58.87
S39	+	0.690	+	0.928	High	422.77	2	5	1.49	7	68.78
S40	++	0.739	+	0.949	High	435.81	2	5	2.12	7	62.40
S41	++	0.737	+	0.950	High	391.71	3	5	1.84	6	69.92

Comp.	ADMETLab		admetSAR 2.0 *		SwissADME	Lipinski rules				Veber rules	
	result	prob.	result	prob.		M_w **	$N_{H\ bond\ donors}$**	$N_{H\ bond\ acceptors}$**	LogP ***	$N_{rot.\ bonds}$ **	PSA ****, $\mathring{A}^2$
S42	++	0.726	+	0.961	High	419.76	3	5	2.31	7	69.36
S43	++	0.704	+	0.955	High	433.79	3	5	2.54	8	69.65
S44	++	0.723	+	0.949	High	433.79	3	5	2.54	7	68.58
S45	++	0.702	+	0.901	High	467.81	3	5	2.57	8	70.02
S46	++	0.732	+	0.946	High	453.78	3	5	2.62	7	72.74
S47	++	0.730	+	0.970	High	467.81	3	5	3.24	7	71.77
S48	++	0.737	+	0.964	High	467.81	3	5	3.24	7	72.69
S49	++	0.737	+	0.964	High	467.81	3	5	3.24	7	71.57
S50	+	0.683	+	0.932	High	532.68	3	5	5.39	7	73.17
S51	+	0.572	+	0.962	High	483.81	3	6	2.70	8	83.18
S52	++	0.732	+	0.946	High	503.84	3	5	3.28	7	72.41
S53	+	0.675	+	0.936	High	443.74	3	6	1.40	7	81.98
S54	++	0.734	+	0.843	Low	485.85	3	5	2.32	8	91.55
S55	++	0.734	+	0.843	Low	485.85	3	5	2.32	8	93.48

* The obtained values of the probability for the unification of the results were rounded to thousandths; ** The parameter was calculated using Molinspiration; *** The LogP value obtained by the Moriguchi method (MLogP) (see Table S5 below); **** The polar surface area was calculated using the 3D PSA method in the PyMOL 0.99rc6 program (see Table S6 below).

Table S5. Lipophilicity (LogP$_{o/w}$) prediction results for Salubrinal and its analogues using various online servers.

Comp.	admetSAR 2.0 (ALOGP)	ADMETLab * (ALOGP)	SwissADME					Molinspiration (miLOGP)	ALOGPS 2.1 (ALOGPs)	Consensus LogP **
			iLOGP	XLOGP3	WLOGP	MLOGP	SILICOS–IT			
S1	5.05	5.05	3.18	5.21	4.75	2.71	5.32	4.59	4.94	4.47
S2	5.05	5.05	3.61	5.21	4.75	2.71	5.32	4.61	4.95	4.53
S3	5.65	5.65	3.40	6.19	5.35	3.87	5.88	5.79	5.63	5.22
S4	5.65	5.65	3.25	6.19	5.35	3.87	5.88	5.81	5.63	5.20
S5	1.46	1.46	2.04	2.33	1.35	1.33	2.81	2.30	2.76	2.05
S6	2.15	2.15	3.11	3.30	2.04	1.98	3.60	3.43	3.22	2.85
S7	4.28	4.28	3.81	4.80	4.17	2.91	5.00	4.93	4.50	4.30
S8	4.50	4.50	3.25	4.94	4.20	3.20	4.80	4.63	4.65	4.27
S9	4.81	4.81	3.56	5.30	4.51	3.82	5.34	5.03	4.85	4.65

Comp.	admetSAR 2.0 (ALOGP)	ADMETLab * (ALOGP)	SwissADME					Molinspiration (miLOGP)	ALOGPS 2.1 (ALOGPs)	Consensus LogP **
			iLOGP	XLOGP3	WLOGP	MLOGP	SILICOS–IT			
S10	4.81	4.81	3.40	5.30	4.51	3.82	5.34	5.05	4.87	4.64
S11	4.81	4.81	3.66	5.30	4.51	3.82	5.34	5.08	4.88	4.68
S12	5.12	5.12	3.70	5.67	4.82	4.04	5.87	5.43	5.10	4.97
S13	5.12	5.12	3.63	5.67	4.82	4.04	5.87	5.46	5.11	4.97
S14	5.12	5.12	3.44	5.67	4.82	4.04	5.87	5.46	5.10	4.94
S15	4.20	4.20	2.69	4.58	3.90	3.04	4.34	4.36	4.62	3.97
S16	4.20	4.20	3.24	4.58	3.90	3.04	4.34	4.13	4.62	4.01
S17	4.79	4.79	3.02	5.09	4.49	3.87	5.11	4.81	5.53	4.59
S18	4.51	4.51	3.48	4.91	4.21	3.26	4.89	4.64	4.69	4.32
S19	4.51	4.51	3.17	4.91	4.21	3.26	4.89	4.69	4.73	4.30
S20	4.20	4.20	2.56	5.02	3.90	2.08	4.31	4.67	4.55	3.91
S21	4.20	4.20	2.80	4.47	3.90	2.08	4.31	4.54	4.46	3.85
S22	4.29	4.29	3.23	5.34	3.99	3.40	4.86	4.93	4.57	4.33
S23	4.41	4.41	3.43	4.77	4.63	2.16	3.10	4.57	4.85	3.99
S24	4.41	4.41	2.68	4.77	4.63	2.16	3.10	4.59	4.87	3.90
S25	5.15	5.15	3.10	5.57	4.85	4.09	5.46	5.26	5.21	4.84
S26	5.15	5.15	3.55	5.57	4.85	4.09	5.46	5.28	5.19	4.89
S27	5.15	5.15	3.19	5.57	4.85	4.09	5.46	5.31	5.18	4.85
S28	5.26	5.26	3.15	5.63	4.96	3.79	5.50	5.44	5.25	4.87
S29	5.81	5.81	3.34	6.20	5.51	4.57	6.13	5.91	5.80	5.41
S30	5.81	5.81	3.52	6.20	5.51	4.57	6.13	5.91	5.80	5.43
S31	6.17	6.17	3.72	6.45	7.02	4.89	6.61	6.13	5.93	5.87
S32	4.46	4.46	3.15	4.12	3.97	3.00	4.54	3.85	4.48	3.95
S33	6.91	6.91	4.08	6.72	6.61	3.87	6.66	6.82	6.01	5.96
S34	3.15	3.15	2.10	3.50	3.93	2.10	3.01	3.32	3.91	3.13
S35	3.89	3.89	2.81	4.20	3.59	2.16	4.25	4.37	4.20	3.68
S36	4.96	4.96	3.73	5.26	4.67	2.98	5.48	5.56	5.09	4.72
S37	2.16	2.16	2.40	2.96	3.14	1.33	3.38	3.09	2.84	2.66
S38	3.87	3.87	3.10	4.41	3.38	2.55	4.56	4.72	4.33	3.87
S39	2.72	2.72	2.87	3.19	2.23	1.49	3.94	3.66	3.24	2.92
S40	2.63	2.63	3.12	3.38	1.76	2.12	3.57	3.71	3.27	2.95

Comp.	admetSAR 2.0 (ALOGP)	ADMETLab * (ALOGP)	SwissADME					Molinspiration (miLOGP)	ALOGPS 2.1 (ALOGPs)	Consensus LogP **
			iLOGP	XLOGP3	WLOGP	MLOGP	SILICOS–IT			
S41	3.35	3.35	2.42	3.67	3.16	1.84	3.60	2.28	3.37	2.96
S42	3.99	3.99	2.84	4.71	3.80	2.31	4.22	3.36	4.08	3.66
S43	4.38	4.38	2.94	4.93	4.19	2.54	4.62	3.89	4.26	3.97
S44	4.38	4.38	3.41	5.07	4.19	2.54	4.46	4.27	4.46	4.10
S45	4.58	4.58	2.76	4.72	4.39	2.57	5.09	4.04	4.60	4.09
S46	4.65	4.65	3.18	4.78	4.46	2.62	4.70	3.95	4.61	4.12
S47	4.96	4.96	3.15	5.15	4.77	3.24	5.23	4.35	4.78	4.45
S48	4.96	4.96	3.69	5.15	4.77	3.24	5.23	4.37	4.77	4.52
S49	4.96	4.96	3.30	5.15	4.77	3.24	5.23	4.40	4.78	4.48
S50	5.41	5.41	3.16	5.22	3.21	5.39	4.49	4.76	5.16	4.60
S51	4.66	4.66	3.39	4.75	4.47	2.70	4.78	4.00	4.56	4.16
S52	5.80	5.80	3.46	6.03	5.61	3.28	5.74	5.13	5.58	5.08
S53	4.24	4.24	2.63	4.18	4.05	1.40	4.09	3.21	4.01	3.48
S54	5.11	5.11	3.38	4.92	4.81	2.32	5.94	4.31	4.85	4.46
S55	5.11	5.11	3.38	4.89	4.81	2.32	5.94	4.00	4.84	4.41

* admetSAR 2.0 and ADMETLab gave the identical ALOGP values. When calculating the LogP$_{Consensus}$, the resulting ALOGP value was used only once; ** LogP-$_{Consensus}$ was calculated as the arithmetic mean of the LogP values obtained by different methods.
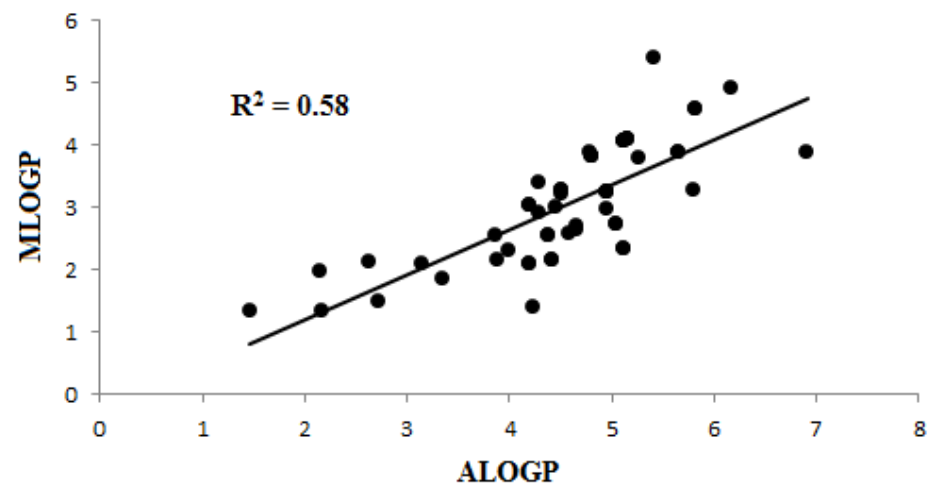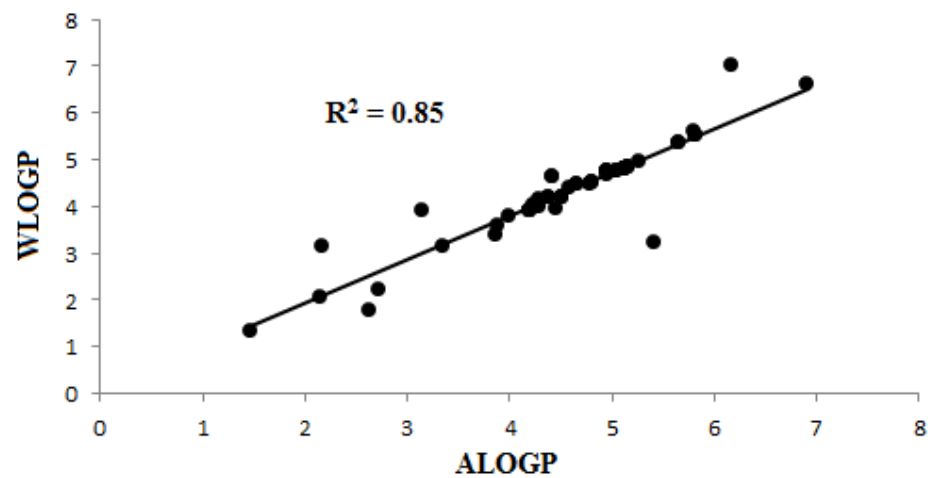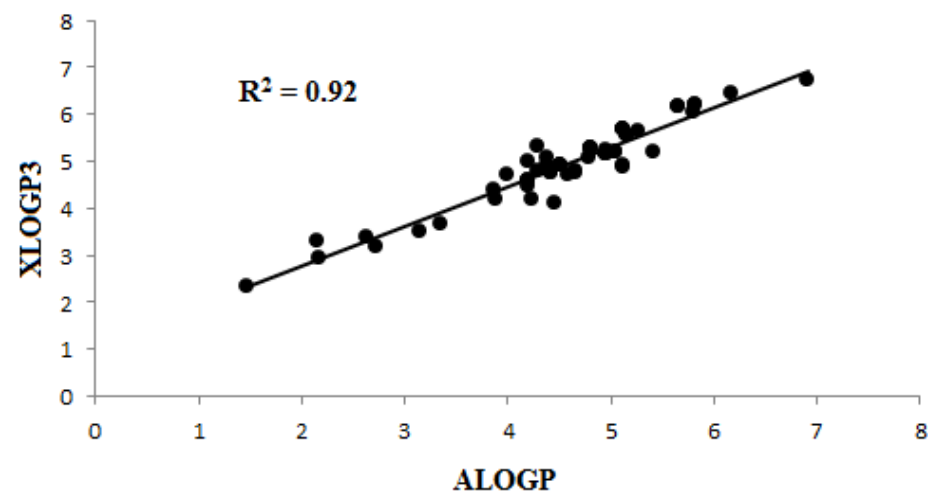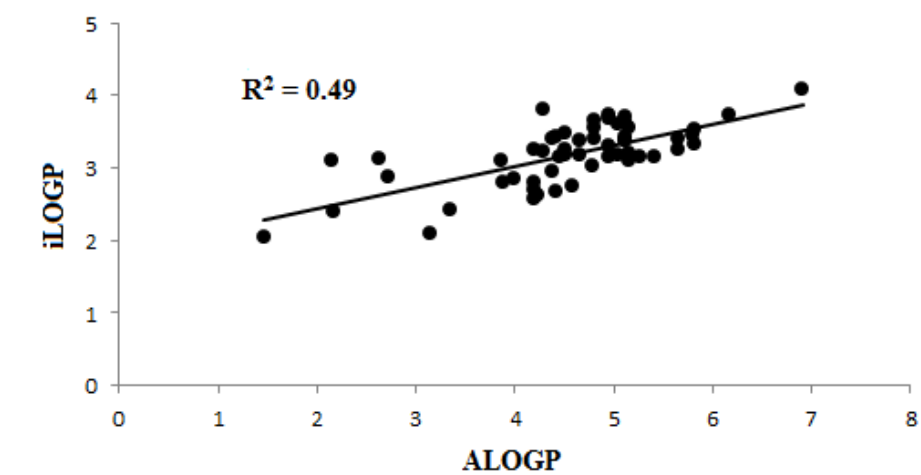
Figure S1. Correlation of the LogP values for Salubrinal and its analogues calculated by different methods (continued follows below).
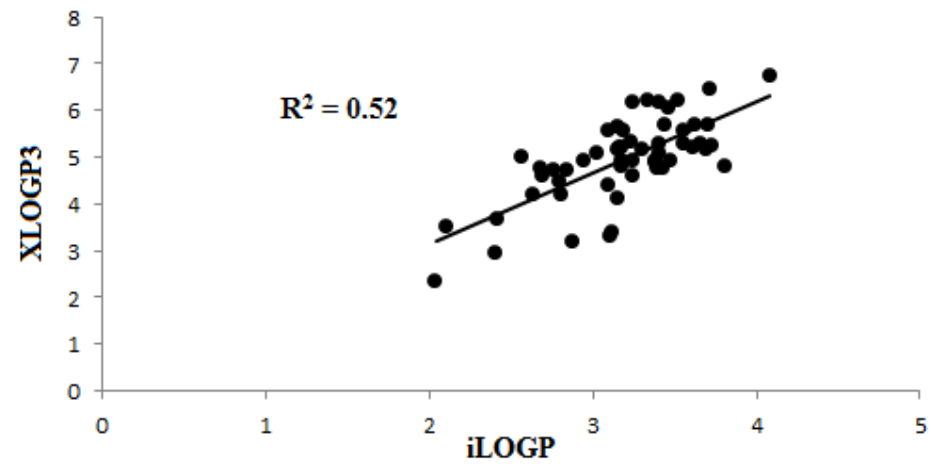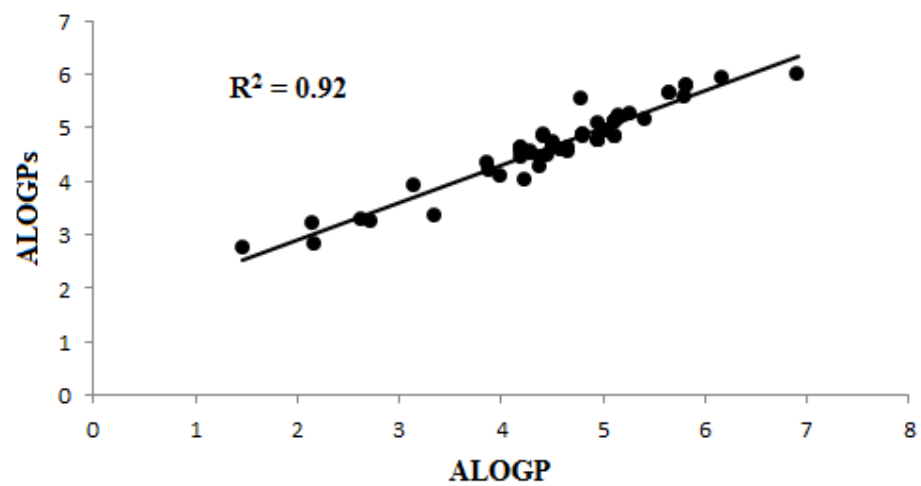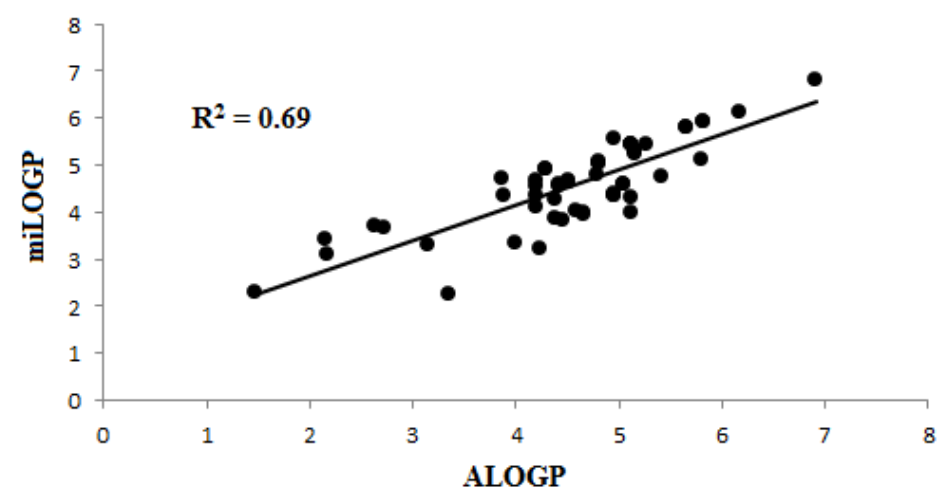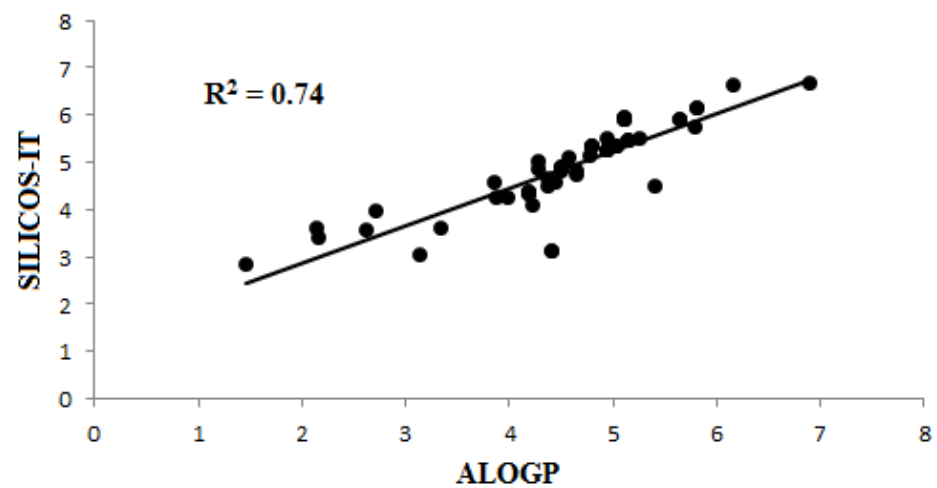
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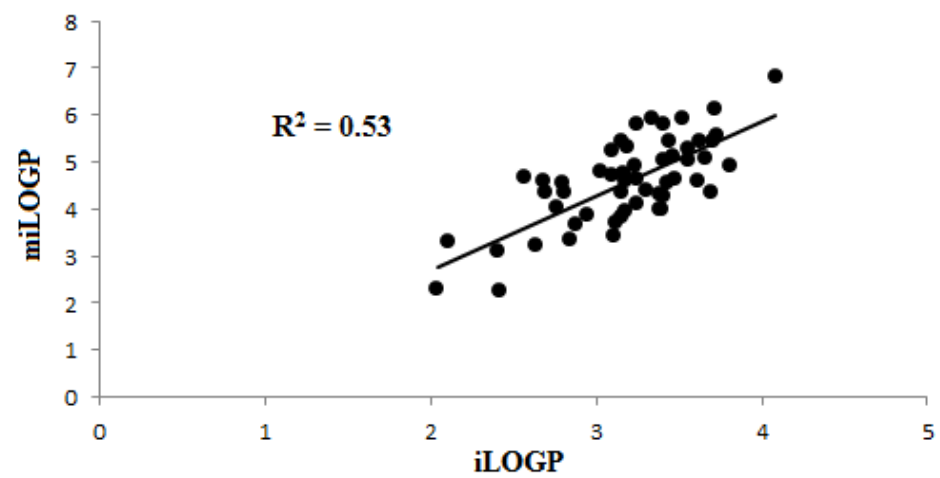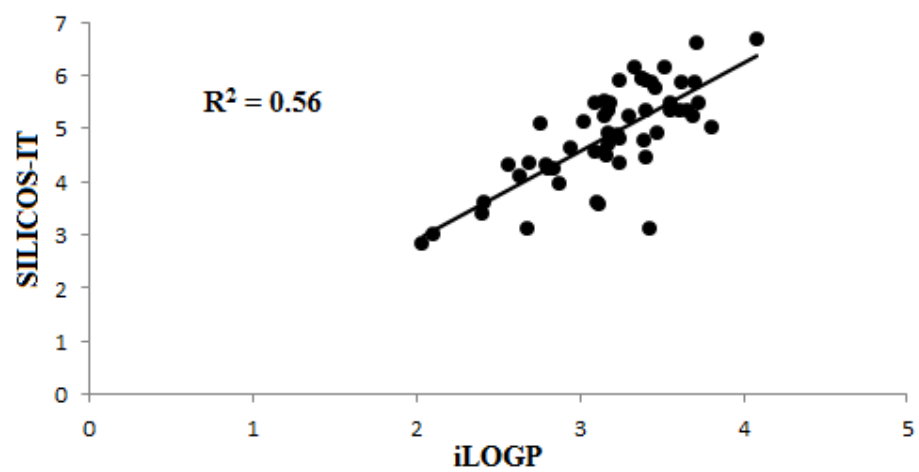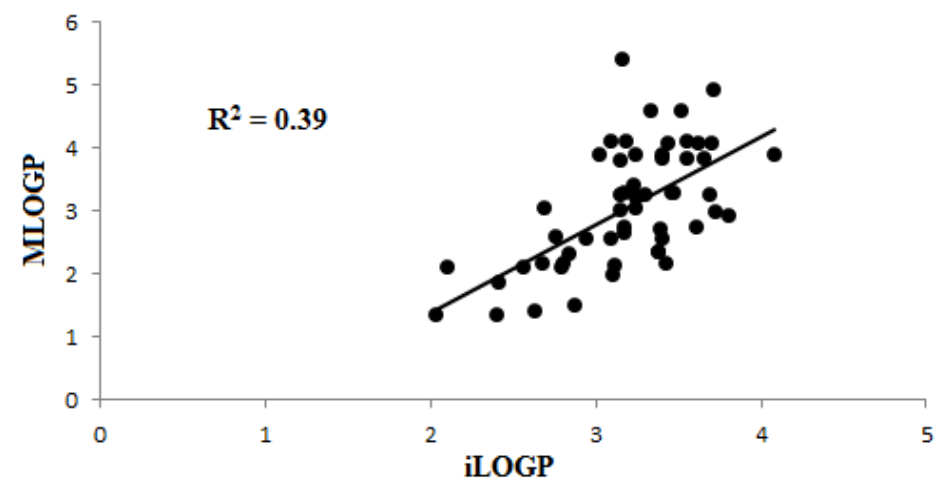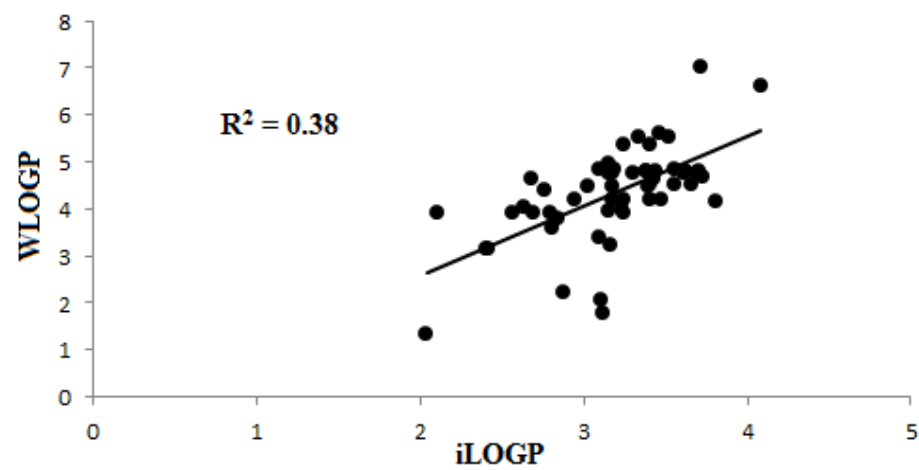
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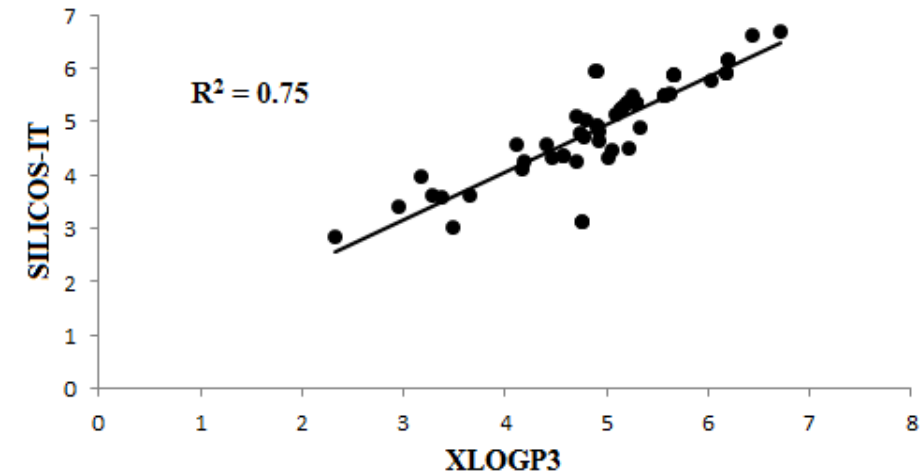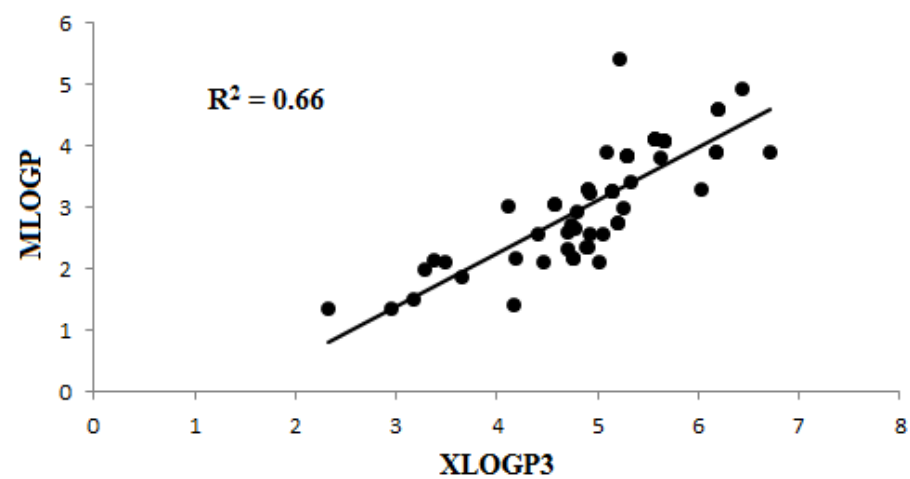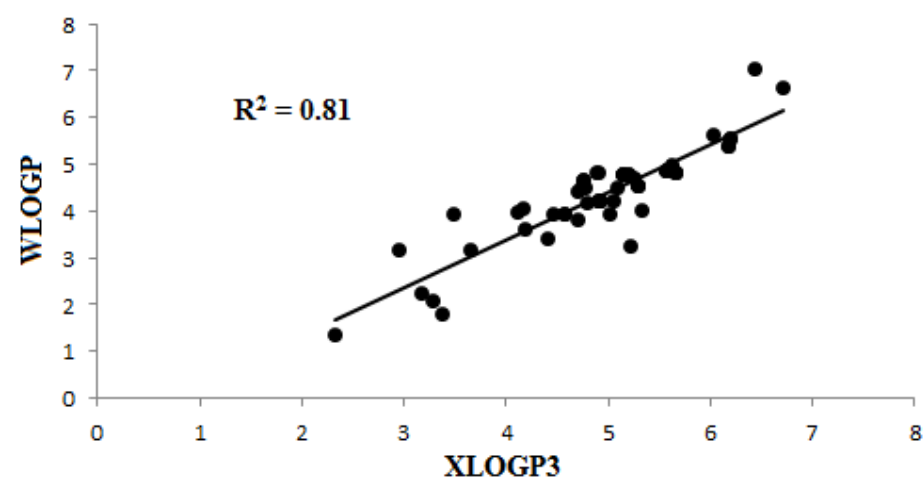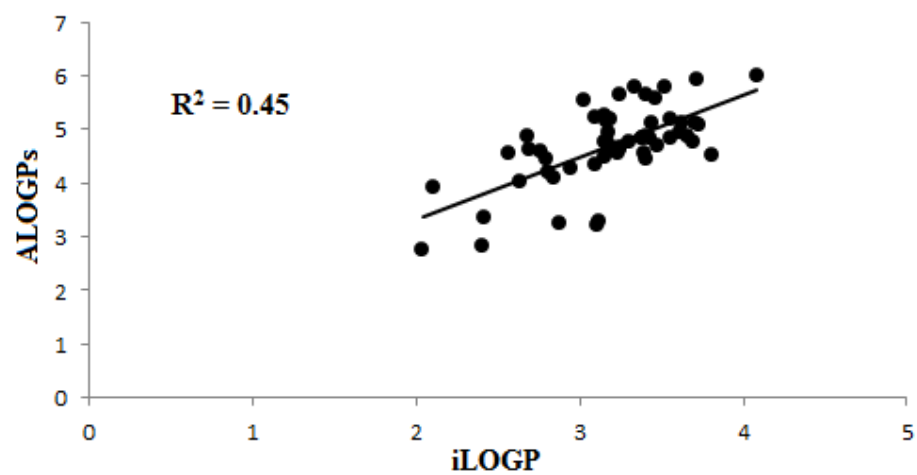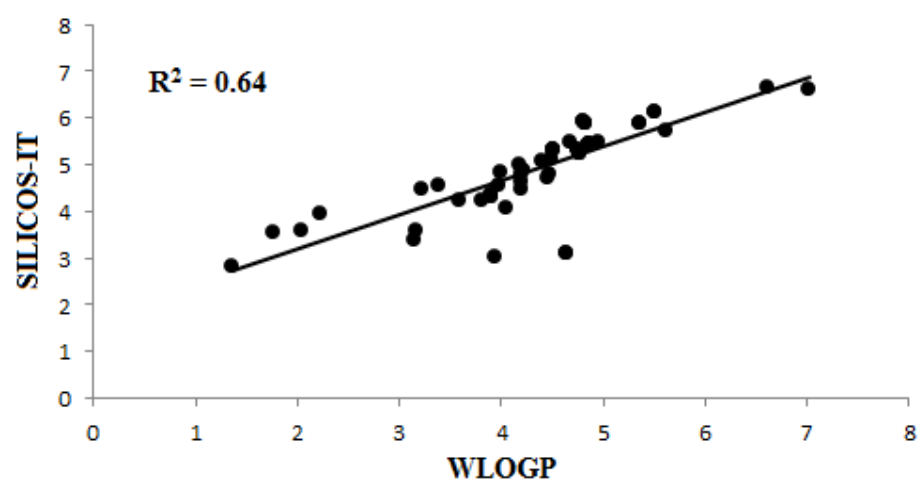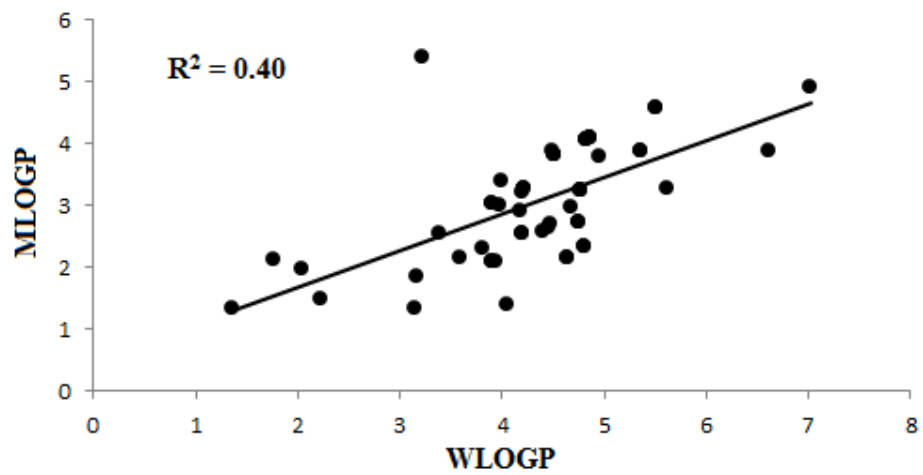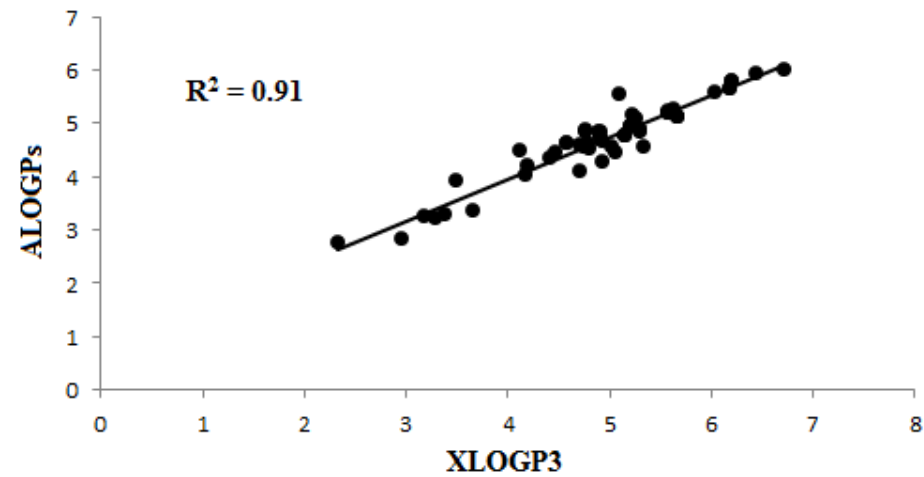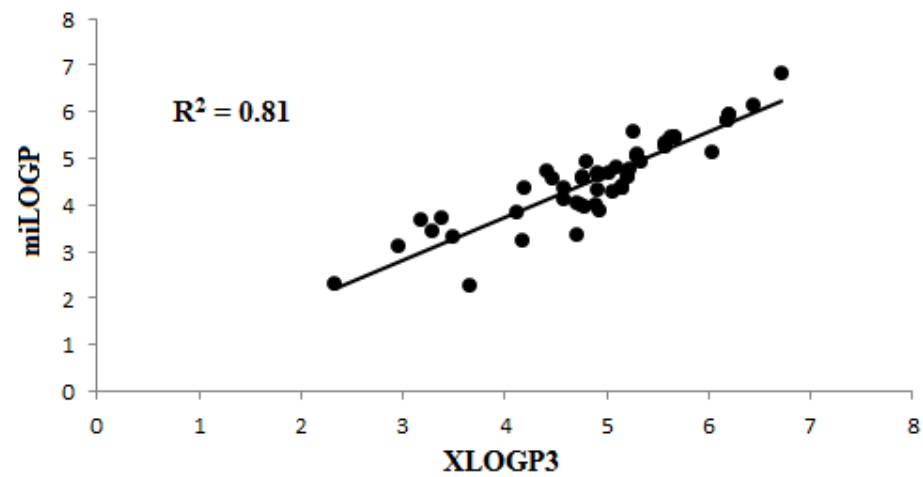
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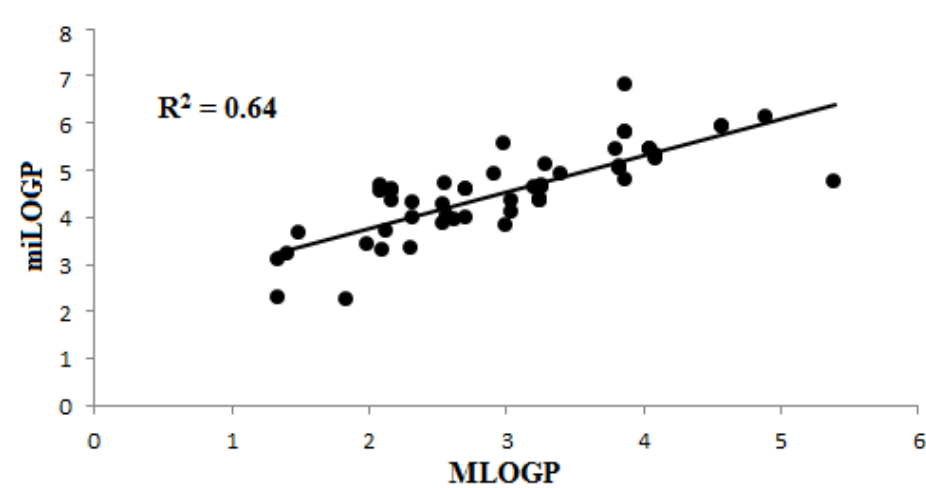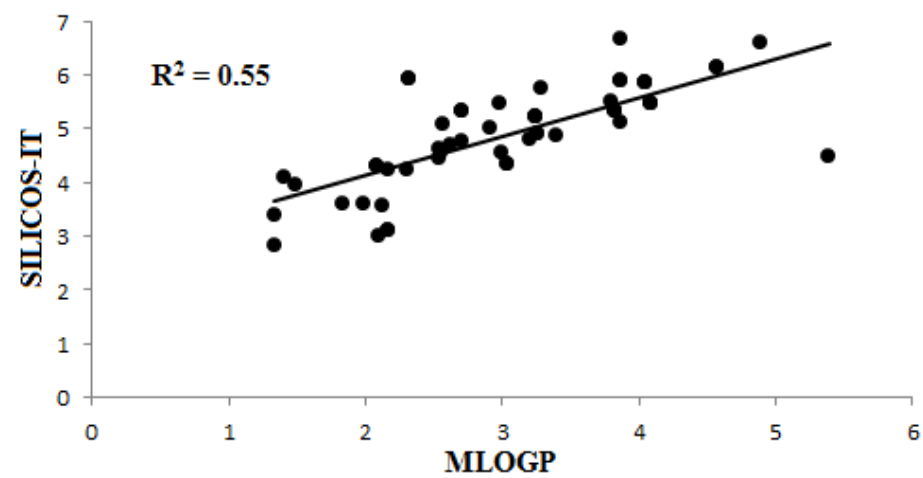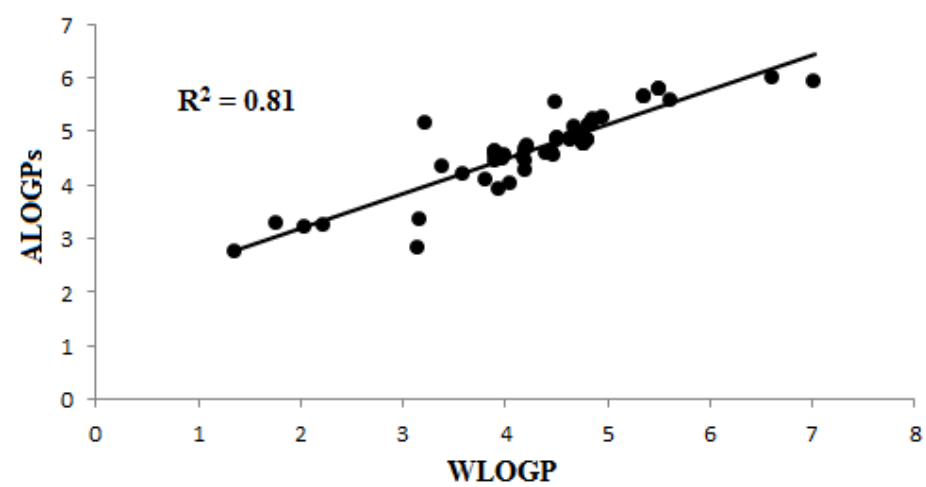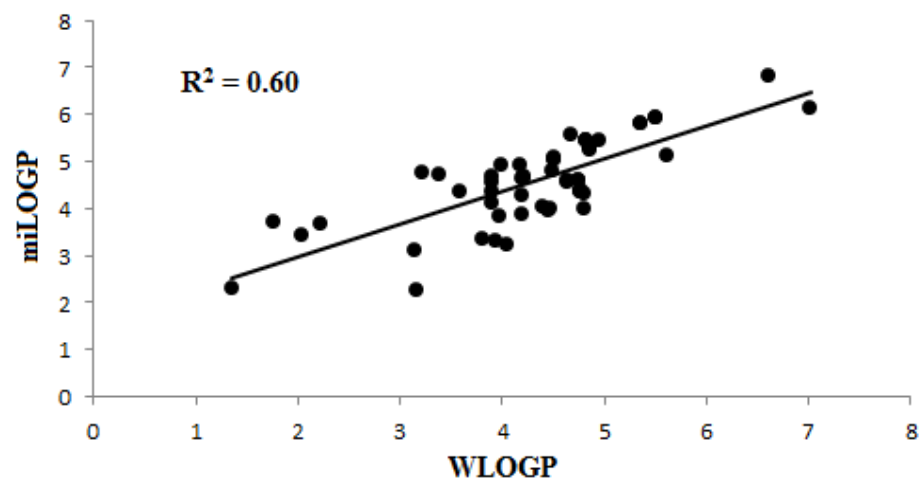
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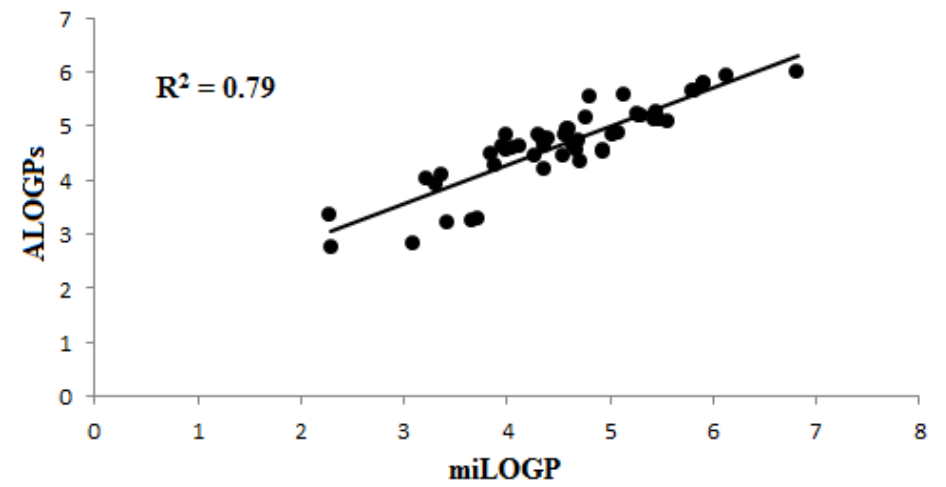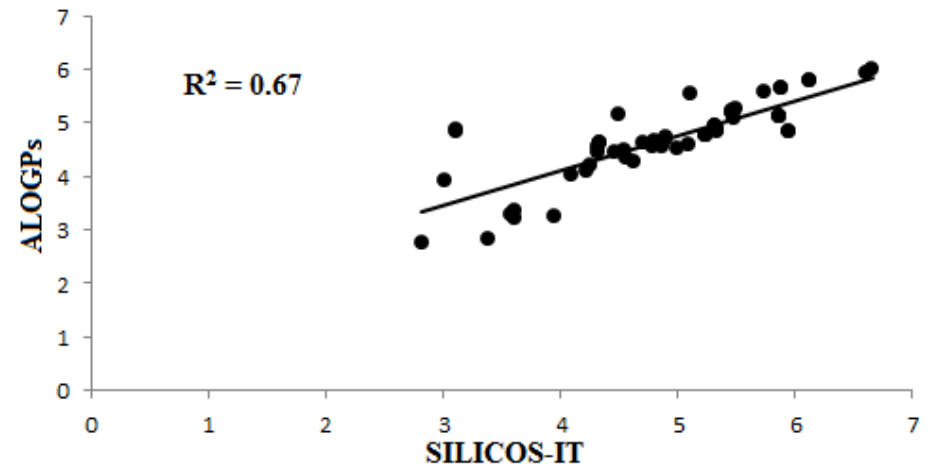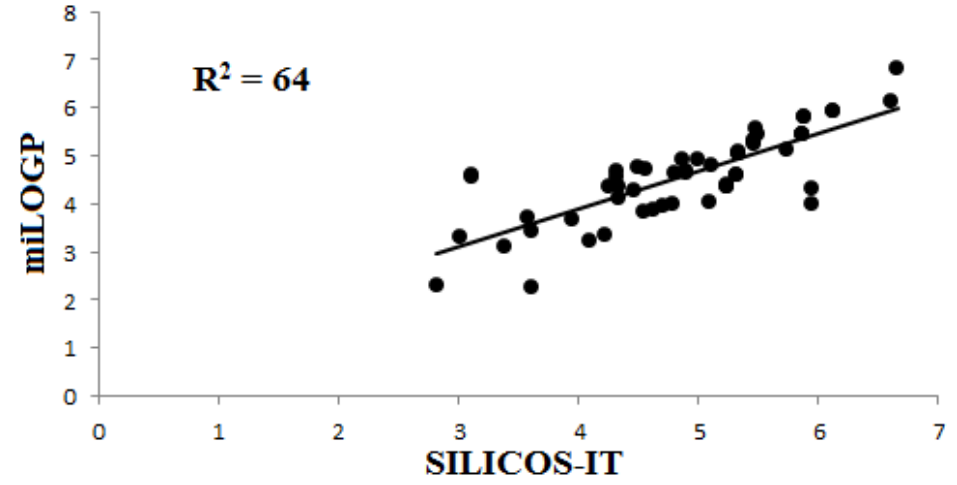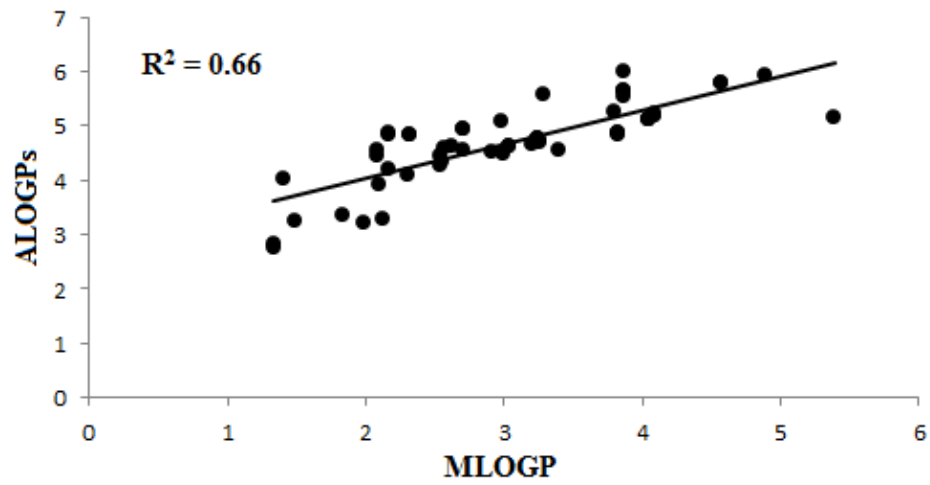
Figure S1. Cont.

Figure S1. Cont.
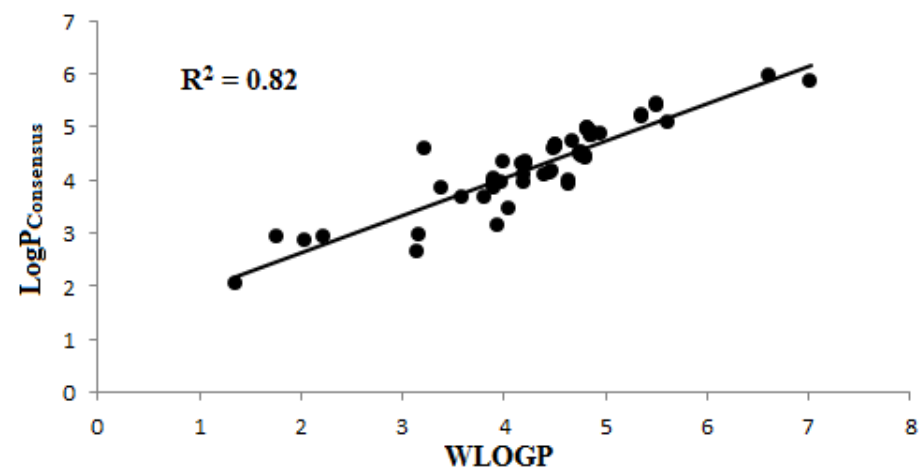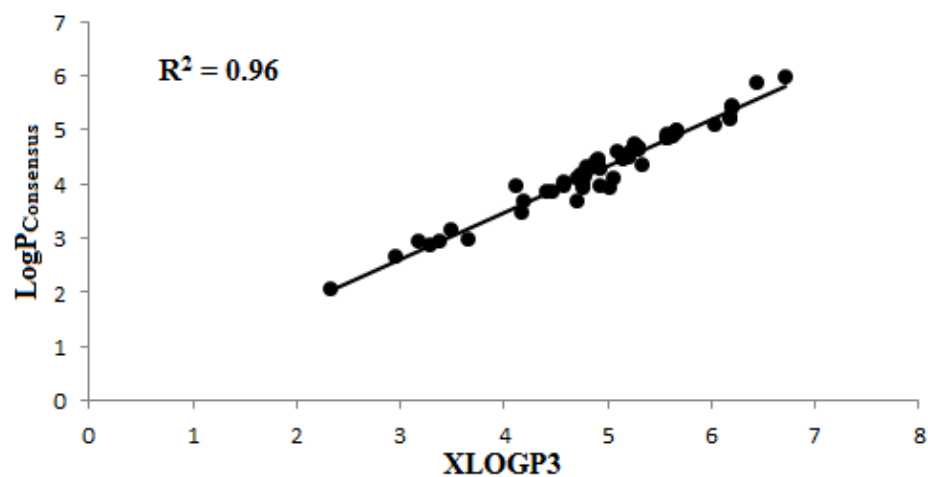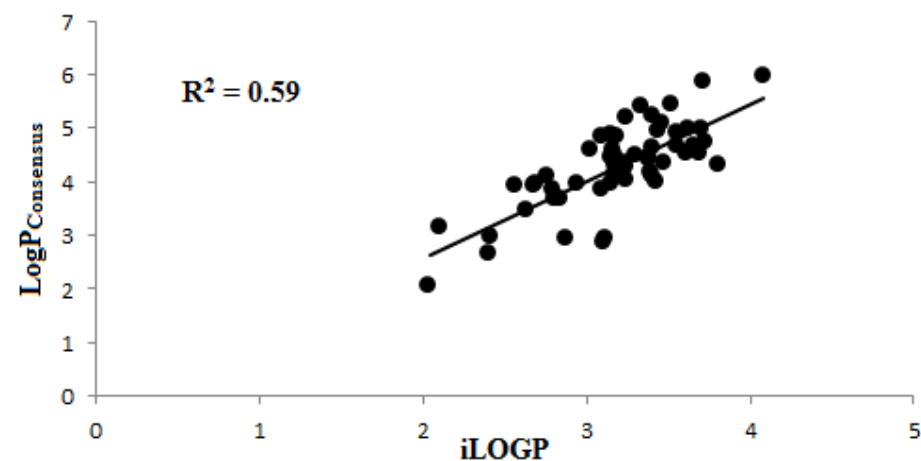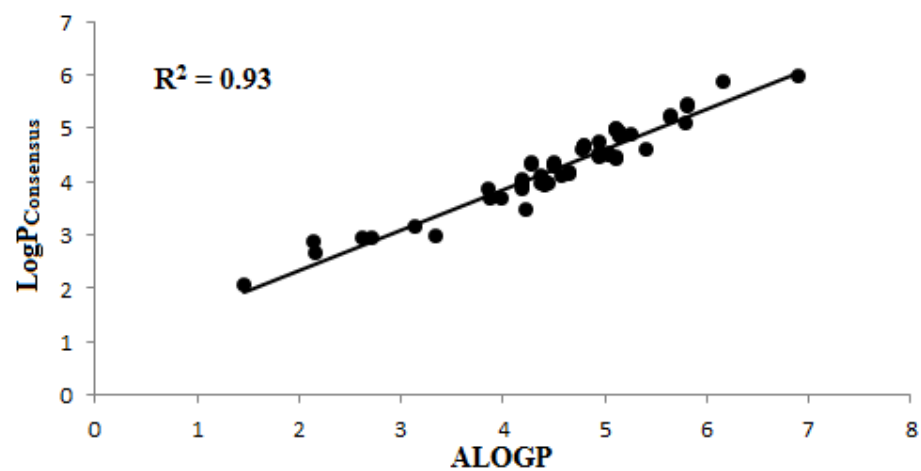
Figure S2. Correlation of the LogP values for Salubrinal and its analogues calculated by different methods with LogP$_{Consensus}$ (continued follows below).
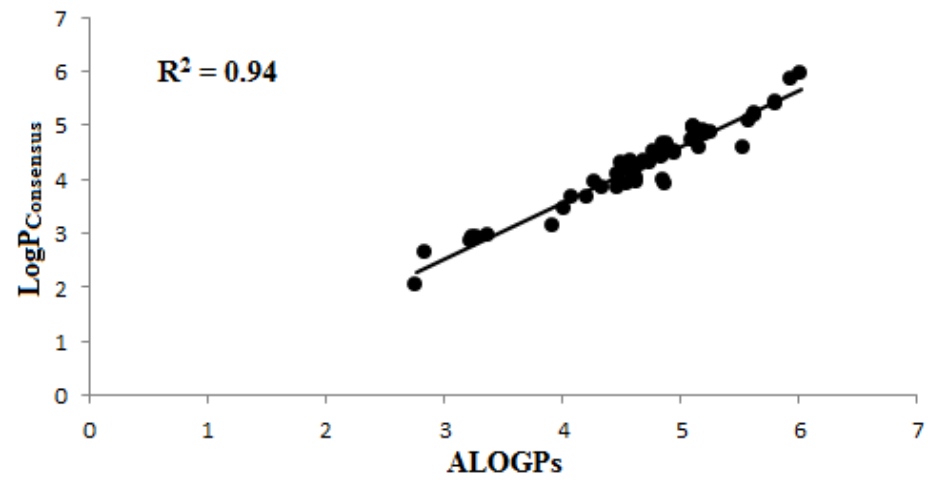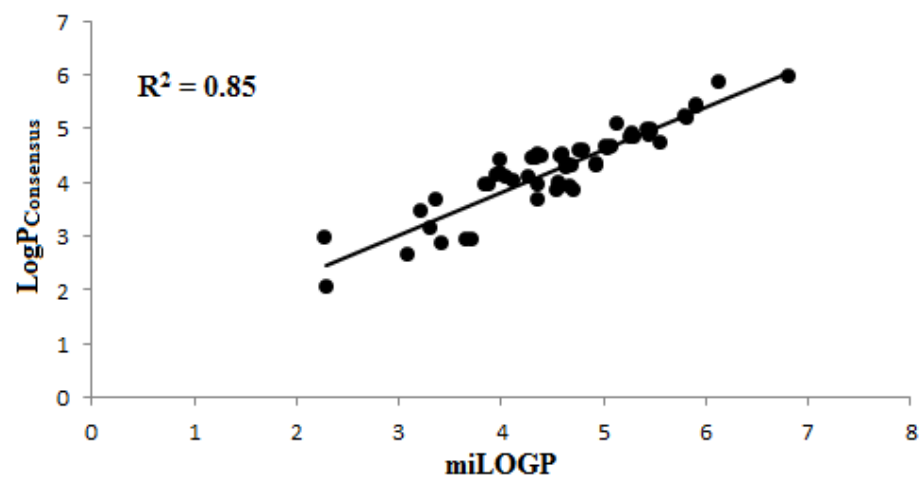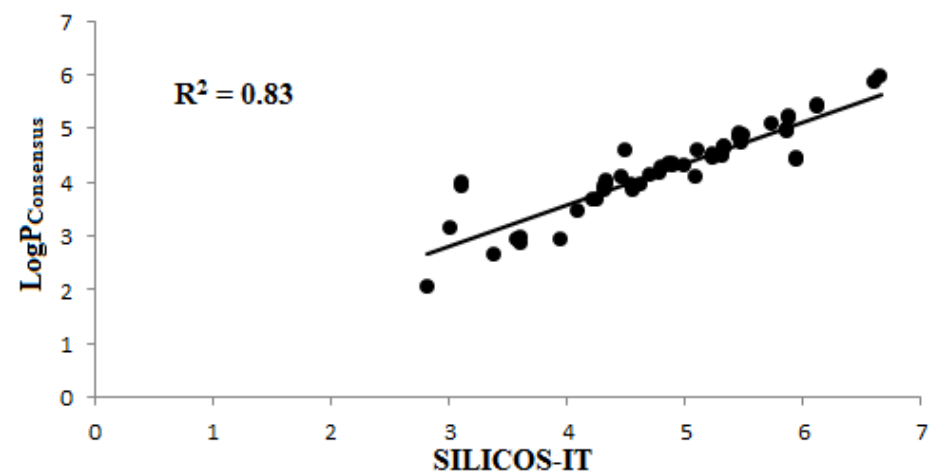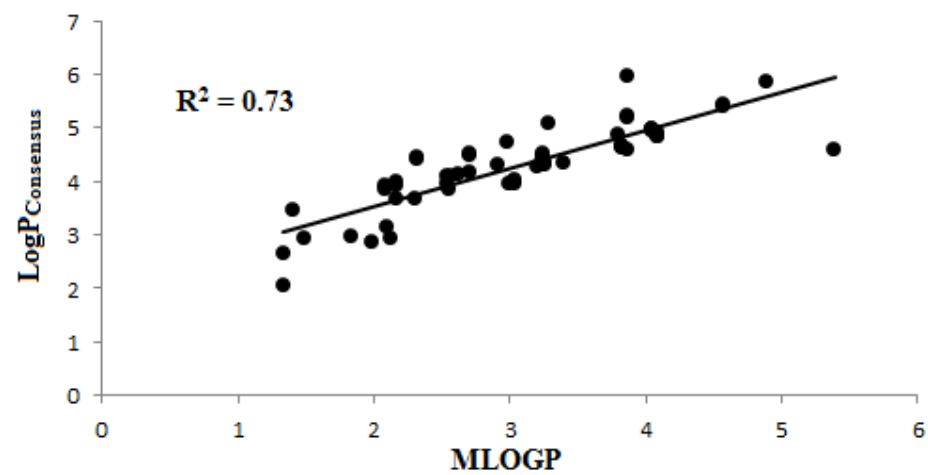
Figure S2. Cont.

Table S6. Calculation results of 2D PSA and 3D PSA by different methods.

Comp.	2D PSA (TPSA), Å²		3D PSA, Å²		
	Molinspiration, N+O	SwissADME, N+O+S	PyMol, N+O *	PyMol, N+O+S **	PyMol, Total
S1	66.04	98.14	40.15	69.78	454.76
S2	66.04	98.14	41.38	72.02	461.29
S3	53.15	85.25	30.46	60.17	463.64
S4	53.15	85.25	29.55	60.74	466.96
S5	96.25	128.34	56.67	84.08	392.14
S6	79.46	111.55	58.05	85.72	405.76
S7	91.48	123.58	61.44	89.34	550.49
S8	53.15	85.25	28.84	56.65	411.63
S9	53.15	85.25	29.25	57.56	430.94
S10	53.15	85.25	28.91	57.58	426.97
S11	53.15	85.25	28.56	57.27	431.02
S12	53.15	85.25	28.81	56.96	451.16
S13	53.15	85.25	28.46	56.60	454.71
S14	53.15	85.25	29.66	58.61	453.74
S15	73.38	105.48	41.96	70.63	423.24
S16	73.38	105.48	43.01	71.70	426.06
S17	53.15	124.05	28.81	83.09	435.62
S18	62.39	94.48	39.73	68.41	446.38
S19	62.39	94.48	39.95	68.78	442.33
S20	90.45	122.55	57.49	85.86	441.50
S21	90.45	122.55	59.53	88.08	442.54
S22	79.46	111.55	51.65	80.13	461.60
S23	98.98	131.07	72.03	101.18	440.33
S24	98.98	131.07	71.73	100.34	441.74
S25	53.15	85.25	29.15	57.58	427.18
S26	53.15	85.25	29.12	57.51	429.53
S27	53.15	85.25	28.68	57.34	428.63
S28	53.15	85.25	29.25	57.61	429.84
S29	53.15	85.25	28.72	57.17	443.03
S30	53.15	85.25	28.81	57.40	436.74

Comp.	2D PSA (TPSA), Å²		3D PSA, Å²		
	Molinspiration, N+O	SwissADME, N+O+S	PyMol, N+O *	PyMol, N+O+S **	PyMol, Total
S31	53.15	85.25	28.69	56.87	469.19
S32	82.25	114.35	52.22	80.83	467.46
S33	77.88	109.97	50.82	79.21	523.10
S34	113.32	153.79	75.56	110.44	475.67
S35	66.04	98.14	40.41	69.08	404.84
S36	66.04	98.14	39.90	68.30	443.89
S37	87.29	127.77	68.08	102.54	436.96
S38	44.36	76.46	28.22	58.87	416.23
S39	53.60	85.69	38.36	68.78	409.86
S40	47.60	79.70	32.24	62.40	432.94
S41	66.04	98.14	41.05	69.92	361.18
S42	66.04	98.14	39.17	69.36	402.87
S43	66.04	98.14	41.27	69.65	422.64
S44	66.04	98.14	38.67	68.58	421.36
S45	66.04	98.14	39.11	70.02	444.94
S46	66.04	98.14	43.06	72.74	425.00
S47	66.04	98.14	42.90	71.77	445.23
S48	66.04	98.14	44.33	72.69	444.57
S49	66.04	98.14	42.92	71.57	441.58
S50	66.04	98.14	43.98	73.17	447.34
S51	75.28	107.37	53.79	83.18	453.79
S52	66.04	98.14	43.52	72.41	470.87
S53	79.18	111.28	51.83	81.98	411.56
S54	66.04	126.38	39.60	91.55	452.03
S55	66.04	126.38	40.21	93.48	450.56

* For the calculation, we used the following commands:

set dot_density, 4

set dot_solvent, off

get_area elem N+O;

** For the calculation, we used the following commands:

set dot_density,

set dot_solvent, off

get_area elem N+O+S;

Table S7. Prediction results of the inhibitory and substrate activity of Salubrinal and its analogues concerning the transmembrane transporter P−gp.

Comp.	ADMETLab				admetSAR 2.0 *				Vienna LiverTox				AutoDock Vina, ΔG (kcal/mol)
	inhibitor		substrate		inhibitor		substrate		inhibitor		substrate		
	result	prob.	result	prob.	result	prob.	result	prob.	result	score	result	score	
S1	++	0.763	――	0.098	–	0.471	–	0.742	+	0.560	–	0.030	−9.3
S2	++	0.795	――	0.097	–	0.515	–	0.701	–	0.460	–	0.120	−9.0
S3	++	0.772	――	0.158	–	0.500	–	0.805	–	0.420	–	0.220	−10.2
S4	++	0.874	――	0.055	–	0.531	–	0.874	–	0.410	–	0.220	−10.2
S5	+	0.644	–	0.341	–	0.805	–	0.733	–	0.120	–	0.430	−8.7
S6	++	0.754	――	0.130	–	0.704	–	0.778	–	0.210	–	0.120	−8.3
S7	++	0.850	――	0.195	–	0.453	+	0.527	–	0.400	–	0.410	−8.0
S8	++	0.761	――	0.076	–	0.707	–	0.906	–	0.200	–	0.030	−8.9
S9	++	0.757	――	0.185	–	0.601	–	0.794	–	0.360	–	0.030	−9.0
S10	++	0.851	――	0.175	–	0.578	–	0.769	–	0.250	–	0.030	−9.4
S11	++	0.847	――	0.144	–	0.605	–	0.867	–	0.390	–	0.030	−9.3
S12	++	0.784	–	0.339	–	0.506	–	0.720	–	0.430	–	0.120	−9.3
S13	++	0.840	――	0.180	–	0.562	–	0.764	–	0.460	–	0.120	−9.2
S14	++	0.777	――	0.177	–	0.491	–	0.790	–	0.430	–	0.120	−9.1
S15	+	0.578	――	0.207	–	0.702	–	0.822	–	0.210	–	0.320	−9.1
S16	+	0.651	――	0.123	–	0.669	–	0.742	–	0.140	–	0.320	−9.3
S17	++	0.809	――	0.069	–	0.659	–	0.822	–	0.350	–	0.130	−8.7
S18	++	0.844	――	0.137	–	0.533	–	0.751	–	0.480	–	0.030	−8.7
S19	+++	0.900	――	0.034	–	0.573	–	0.858	–	0.300	–	0.120	−9.1
S20	++	0.733	――	0.158	–	0.627	–	0.839	–	0.420	–	0.240	−9.9
S21	++	0.766	――	0.108	–	0.660	–	0.851	–	0.290	–	0.240	−9.3
S22	+++	0.908	――	0.125	–	0.478	–	0.787	+	0.650	–	0.120	−8.7
S23	++	0.783	――	0.080	–	0.633	–	0.751	–	0.410	–	0.120	−9.7
S24	++	0.792	――	0.052	–	0.642	–	0.863	–	0.350	–	0.020	−9.5
S25	++	0.753	――	0.089	–	0.633	–	0.862	–	0.340	–	0.010	−8.8
S26	++	0.818	――	0.115	–	0.625	–	0.789	–	0.290	–	0.100	−9.4
S27	++	0.855	――	0.052	–	0.630	–	0.910	–	0.310	–	0.100	−9.0
S28	++	0.851	――	0.060	–	0.649	–	0.891	–	0.240	–	0.120	−9.1

Comp.	ADMETLab				admetSAR 2.0 *				Vienna LiverTox				AutoDock Vina, ΔG (kcal/mol)
	inhibitor		substrate		inhibitor		substrate		inhibitor		substrate		
	result	prob.	result	prob.	result	prob.	result	prob.	result	score	result	score	
S29	++	0.849	――	0.071	–	0.606	–	0.854	–	0.470	–	0.100	−9.4
S30	++	0.871	――	0.076	–	0.600	–	0.835	–	0.430	–	0.100	−9.2
S31	+++	0.913	――	0.088	–	0.500	–	0.749	+	0.580	–	0.280	−9.2
S32	++	0.784	――	0.191	–	0.493	–	0.785	–	0.210	–	0.220	−9.0
S33	++	0.801	――	0.081	+	0.634	–	0.867	–	0.270	–	0.120	−9.2
S34	+	0.644	――	0.060	–	0.569	–	0.838	–	0.360	–	0.330	−9.3
S35	+	0.601	――	0.154	–	0.728	–	0.811	–	0.210	–	0.020	−9.0
S36	+++	0.921	――	0.105	–	0.640	–	0.727	+	0.570	–	0.020	−9.1
S37	++	0.787	――	0.209	–	0.725	–	0.681	–	0.330	–	0.220	−9.0
S38	++	0.785	――	0.166	–	0.666	–	0.795	–	0.260	–	0.010	−8.5
S39	++	0.785	–	0.307	–	0.640	–	0.762	–	0.160	–	0.010	−8.4
S40	++	0.842	+	0.521	–	0.630	–	0.618	–	0.220	–	0.110	−8.5
S41	+	0.506	――	0.069	–	0.806	–	0.660	–	0.290	–	0.010	−8.2
S42	+	0.553	――	0.075	–	0.713	–	0.663	–	0.430	–	0.010	−7.9
S43	+	0.545	――	0.086	–	0.683	–	0.560	–	0.410	–	0.010	−7.9
S44	+	0.508	――	0.083	–	0.727	–	0.664	–	0.320	–	0.010	−8.3
S45	+	0.647	――	0.076	–	0.450	–	0.727	+	0.750	–	0.030	−9.5
S46	+	0.553	――	0.067	–	0.528	–	0.736	–	0.440	–	0.010	−8.9
S47	++	0.724	――	0.104	–	0.507	–	0.607	+	0.530	–	0.010	−9.2
S48	++	0.769	――	0.062	–	0.481	–	0.588	+	0.630	–	0.010	−9.5
S49	++	0.760	――	0.113	–	0.434	–	0.623	+	0.730	–	0.010	−9.3
S50	++	0.759	――	0.049	–	0.453	–	0.681	+	0.580	–	0.030	−9.0
S51	++	0.822	――	0.032	+	0.597	–	0.572	+	0.660	–	0.010	−9.4
S52	++	0.759	――	0.049	+	0.624	–	0.650	+	0.700	–	0.400	−10.6
S53	+	0.623	――	0.074	–	0.595	–	0.655	+	0.570	–	0.000	−8.4
S54	++	0.725	――	0.041	–	0.500	–	0.691	+	0.560	–	0.020	−9.0
S55	++	0.811	――	0.077	–	0.515	–	0.647	+	0.570	–	0.020	−8.8

* The obtained values of the probability for the unification of the results were rounded to thousandths.
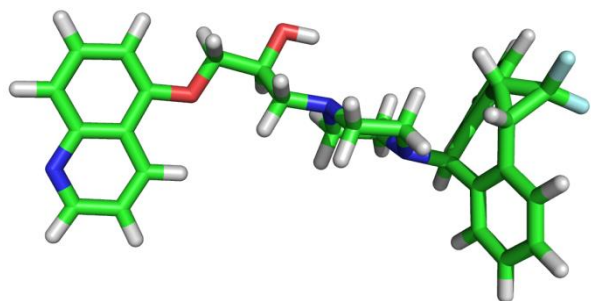
Zosuquidar
ΔG = −143467.0 kcal/mol
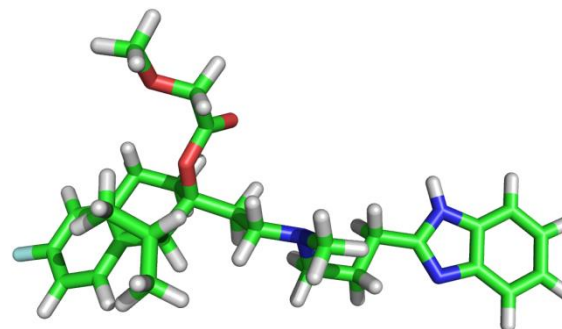
Mibefradil
ΔG = −−134440.7 kcal/mol
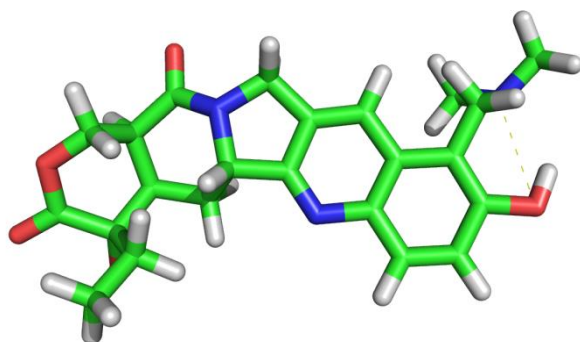
Topotecan
ΔG = −117544.3 kcal/mol
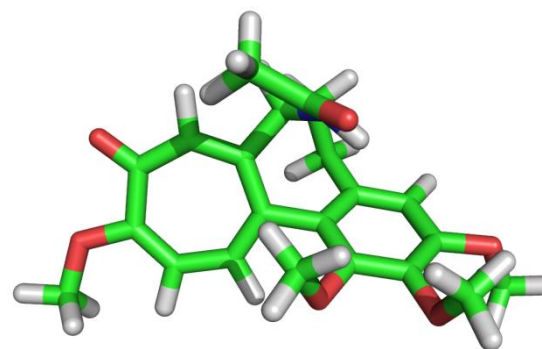
Colchicin
ΔG = −113309.8 kcal/mol

Figure S3. Zosuquidar, Mibefradil, Topotecan and Colchicin structures optimized using the semi−empirical PM3 method in the ArgusLab 4.0.1 software package.

Table S8. Results of *in silico* analysis of the distribution of Salubrinal and its analogues in the body.

Comp.	Volume Distribution (V$_{dss}$)				PPB (Plasma Protein Binding), %		AutoDock Vina, ΔG (kcal/mol)				BBB (Blood–Brain Barrier)				
	ADMETLab		pkCSM		ADMETLab	admetSAR 2.0	HAS *		AGP **		ADMETLab		admetSAR2.0 ***		pkCSM, Log BB
	Log V$_d$	L/kg	Log V$_d$	L/kg			Site 1	Site 2	A	F1*S	result	prob.	result	prob.	
S1	−0.379	0.418	0.123	1.327	94.830	1.184	−9.8	−9.9	−9.9	−9.5	++	0.843	+	0.973	−0.063
S2	−0.342	0.455	0.130	1.349	94.946	1.143	−9.4	−10.2	−8.9	−9.8	++	0.863	+	0.974	0.028
S3	−0.279	0.526	0.003	1.007	93.248	1.126	−9.9	−10.1	−8.9	−9.8	+++	0.962	+	0.975	0.086
S4	−0.302	0.499	0.008	1.019	94.064	1.178	−10.2	−10.6	−9.1	−9.9	+++	0.961	+	0.975	0.033
S5	−0.746	0.179	−0.517	0.304	73.802	1.043	−7.5	−8.2	−7.5	−8.6	+++	0.984	+	0.976	−1.095
S6	−0.884	0.131	−0.530	0.295	78.081	0.967	−7.6	−7.9	−7.9	−7.8	+++	0.992	+	0.975	−1.160
S7	−0.970	0.107	−0.518	0.303	83.535	1.215	−8.1	−8.8	−8.6	−8.1	+++	0.982	+	0.975	0.004
S8	−0.315	0.484	0.033	1.079	91.112	1.104	−8.5	−9.1	−8.7	−8.8	+++	0.985	+	0.976	0.036
S9	−0.327	0.471	0.220	1.660	91.936	1.122	−8.7	−9.5	−8.6	−9.1	+++	0.964	+	0.974	0.096
S10	−0.326	0.472	0.030	1.072	91.609	1.041	−8.8	−9.6	−8.5	−9.1	+++	0.962	+	0.975	0.001
S11	−0.336	0.461	−0.004	0.991	91.771	1.044	−8.4	−9.3	−8.5	−9.0	+++	0.972	+	0.975	0.027
S12	−0.237	0.579	0.132	1.355	92.003	1.213	−9.0	−9.9	−8.8	−9.6	+++	0.960	+	0.974	−0.015
S13	−0.253	0.558	0.092	1.236	91.785	1.063	−8.9	−9.8	−8.7	−9.4	+++	0.929	+	0.974	−0.013
S14	−0.253	0.558	0.105	1.274	91.509	1.071	−9.0	−9.7	−8.9	−9.6	+++	0.929	+	0.974	0.005
S15	−1.099	0.080	−0.017	0.962	90.919	1.169	−8.3	−9.3	−8.2	−8.8	++	0.833	+	0.973	−1.241
S16	−0.907	0.124	−0.217	0.607	91.411	1.100	−9.0	−9.2	−8.3	−8.8	++	0.858	+	0.976	−1.238
S17	−0.476	0.334	0.189	1.545	90.705	1.121	−8.5	−9.0	−8.0	−8.4	+++	0.943	+	0.974	0.079
S18	−0.516	0.305	0.069	1.172	90.894	1.001	−8.8	−9.3	−8.2	−8.9	+++	0.943	+	0.974	−0.028
S19	−0.511	0.308	−0.150	0.708	90.536	0.983	−8.7	−9.2	−8.1	−8.8	+++	0.961	+	0.976	−0.109
S20	−1.382	0.042	−0.592	0.256	91.421	1.253	−9.1	−9.4	−8.7	−9.0	++	0.725	+	0.969	−1.364
S21	−1.301	0.050	−0.723	0.189	91.148	1.167	−8.7	−9.6	−8.5	−9.5	++	0.841	+	0.972	−1.424
S22	−0.961	0.109	−0.234	0.583	91.812	1.021	−8.3	−9.3	−8.8	−8.7	+++	0.937	+	0.972	−1.297
S23	−0.916	0.121	−0.172	0.673	91.501	1.083	−8.9	−9.5	−8.6	−9.4	+++	0.931	+	0.974	−1.141
S24	−0.917	0.121	−0.184	0.655	91.593	1.123	−8.7	−9.7	−8.5	−8.8	+++	0.949	+	0.974	−1.145
S25	−0.456	0.350	0.167	1.469	90.811	1.200	−8.7	−9.4	−8.5	−8.8	+++	0.955	+	0.974	0.083
S26	−0.450	0.355	−0.025	0.944	91.166	1.177	−8.7	−9.4	−8.3	−9.1	+++	0.971	+	0.975	−0.012

| Comp. | Volume Distribution (V_dss) | | | | PPB (Plasma Protein Binding), % | | AutoDock Vina, ΔG (kcal/mol) | | | | BBB (Blood–Brain Barrier) | | | | |
| | ADMETLab | | pkCSM | | | | HAS * | | AGP ** | | ADMETLab | | admetSAR2.0 *** | | pkCSM, Log BB |
	Log V_d	L/kg	Log V_d	L/kg	ADMETLab	admetSAR 2.0	Site 1	Site 2	A	F1*S	result	prob.	result	prob.	
S27	−0.436	0.366	−0.059	0.873	91.215	1.164	−8.4	−9.3	−8.3	−9.0	+++	0.976	+	0.975	0.014
S28	−0.467	0.341	0.101	1.262	91.009	1.119	−8.4	−9.2	−9.1	−8.8	+++	0.972	+	0.975	0.040
S29	−0.610	0.245	−0.019	0.957	90.462	1.120	−9.0	−9.6	−8.4	−9.1	+++	0.946	+	0.974	−0.039
S30	−0.681	0.208	−0.007	0.984	90.511	1.118	−8.8	−9.5	−9.0	−9.3	+++	0.946	+	0.974	−0.021
S31	−0.841	0.144	−0.084	0.824	90.414	1.128	−9.2	−9.8	−9.0	−9.7	+++	0.946	+	0.974	−0.029
S32	−0.728	0.187	−0.223	0.598	88.448	1.087	−8.7	−9.6	−8.5	−8.8	+++	0.985	+	0.976	−1.269
S33	−0.499	0.317	−0.064	0.863	92.921	1.088	−9.7	−10.6	−9.5	−9.3	++	0.893	+	0.975	−1.243
S34	−1.044	0.090	−0.493	0.321	87.658	1.219	−8.7	−9.4	−8.6	−8.8	+++	0.901	+	0.969	−1.471
S35	−0.514	0.306	−0.077	0.838	90.790	1.019	−8.4	−9.0	−8.7	−8.9	+++	0.950	+	0.974	−0.105
S36	−0.646	0.226	−0.204	0.625	90.554	1.140	−8.7	−9.5	−8.4	−8.8	++	0.884	+	0.974	−0.263
S37	−0.859	0.138	−0.186	0.652	82.880	1.267	−8.7	−9.3	−8.3	−8.8	++	0.774	+	0.974	−1.234
S38	−0.148	0.711	0.399	2.506	91.422	1.066	−8.2	−9.0	−8.8	−8.8	+++	0.975	+	0.980	0.107
S39	−0.264	0.545	0.122	1.324	83.181	1.128	−8.2	−8.5	−8.4	−8.3	+++	0.969	+	0.978	−0.142
S40	−0.073	0.845	0.497	3.141	81.589	1.036	−8.4	−8.9	−8.2	−8.6	+++	0.944	+	0.981	−0.025
S41	−0.448	0.356	−0.254	0.557	87.140	1.073	−8.1	−8.6	−9.0	−8.4	++	0.884	+	0.973	−0.106
S42	−0.420	0.380	−0.147	0.713	89.128	1.126	−8.0	−8.6	−9.2	−8.4	++	0.868	+	0.974	−0.109
S43	−0.368	0.429	−0.063	0.865	89.494	1.073	−8.2	−8.4	−9.6	−8.4	+++	0.909	+	0.975	−0.119
S44	−0.303	0.498	−0.140	0.724	89.041	1.223	−7.9	−8.7	−9.5	−8.7	++	0.826	+	0.974	−0.064
S45	−0.270	0.537	0.190	1.549	93.744	1.141	−9.5	−9.5	−9.9	−9.5	++	0.795	+	0.975	−0.027
S46	−0.247	0.566	0.128	1.343	93.806	1.124	−8.7	−9.0	−10.2	−9.1	++	0.879	+	0.972	−0.003
S47	−0.308	0.492	−0.096	0.802	93.723	1.031	−9.1	−9.1	−10.6	−9.5	++	0.816	+	0.973	0.070
S48	−0.303	0.498	−0.079	0.834	93.685	1.083	−9.1	−9.4	−10.8	−9.6	+	0.692	+	0.973	0.067
S49	−0.305	0.495	−0.091	0.811	93.657	1.098	−8.9	−9.0	−10.6	−9.9	++	0.760	+	0.973	0.070
S50	−0.407	0.392	0.191	1.552	93.873	1.144	−8.9	−9.9	−9.6	−9.3	++	0.821	+	0.973	−0.035
S51	−0.586	0.259	−0.171	0.675	94.508	1.072	−8.6	−9.4	−10.2	−9.6	++	0.719	+	0.975	−1.427
S52	−0.316	0.483	0.102	1.265	96.183	1.110	−10.0	−10.7	−10.0	−10.3	++	0.837	+	0.972	0.045
S53	−0.571	0.269	0.106	1.276	91.192	0.995	−8.6	−9.1	−10.1	−8.6	+++	0.918	+	0.973	−1.395
S54	−0.470	0.339	0.048	1.117	94.315	1.118	−8.9	−9.2	−9.8	−9.0	++	0.860	+	0.970	−0.082

Comp.	Volume Distribution (V_{dss})				PPB (Plasma Protein Binding), %		AutoDock Vina, ΔG (kcal/mol)				BBB (Blood–Brain Barrier)				
	ADMETLab		pkCSM		ADMETLab	admetSAR 2.0	HAS *		AGP **		ADMETLab		admetSAR2.0 ***		pkCSM, Log BB
	Log V_d	L/kg	Log V_d	L/kg			Site 1	Site 2	A	F1*S	result	prob.	result	prob.	
S55	−0.471	0.338	0.048	1.117	94.298	1.089	−8.9	−9.4	−9.9	−8.6	++	0.756	+	0.970	−0.082

* Molecular docking results with the first (site 1) and second (site 2) active site of human serum albumin (HSA); ** Molecular docking results with the AGP A variant and F1*S variant; *** The obtained values of the probability for the unification of the results were rounded to thousandths.
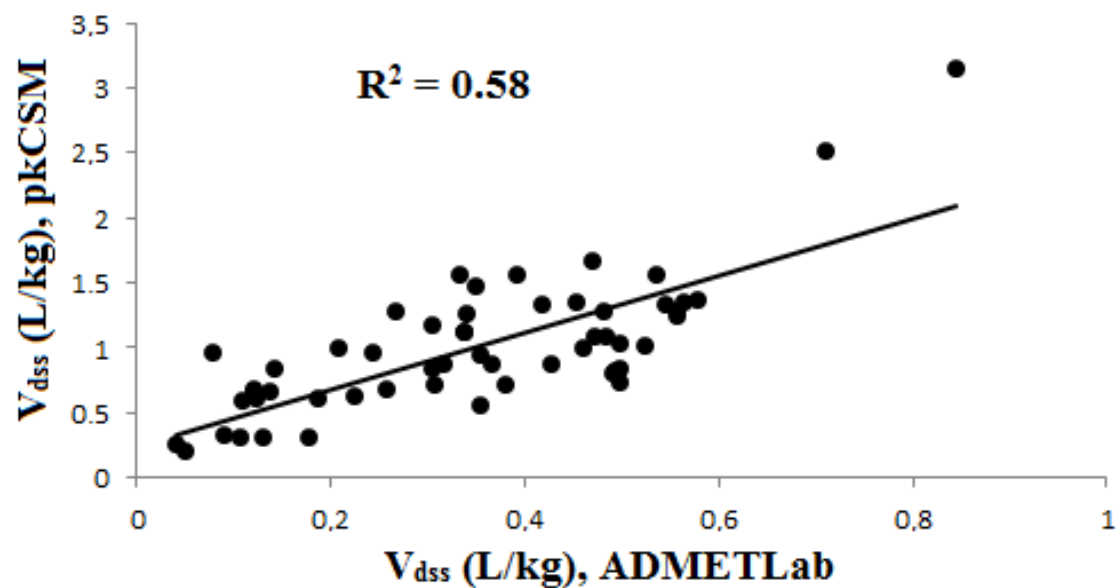
Figure S4. Correlation of the V_{dss} values for Salubrinal and its analogues calculated using online servers pkCSM and ADMETLab.
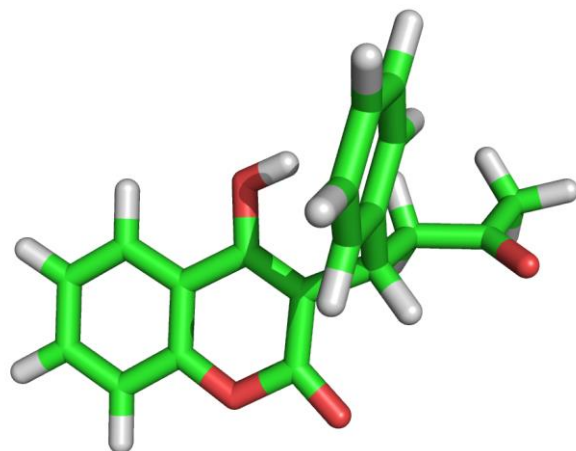
Figure S5. Warfarin structure optimized using the semi−empirical PM3 method in the ArgusLab 4.0.1 software package.

Table S9. Prediction results of the inhibitory and substrate activity of Salubrinal and its analogues concerning the metabolic enzyme CYP1A2.

Comp.	Inhibitory activity														Substrate activity	
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab	
							MACCS		Morgan					
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.
S1	++	0.879	+	0.887	+	−	−	0.636	−	0.623	−5.9	3.0	+	0.524
S2	++	0.839	+	0.911	+	−	−	0.632	−	0.604	−6.7	3.5	+	0.524
S3	+++	0.928	+	0.929	+	+	−	0.571	−	0.572	−6.5	3.4	−	0.465
S4	+++	0.924	+	0.929	+	+	−	0.571	−	0.617	−7.1	3.7	−	0.488
S5	+	0.656	−	0.542	−	−	−	0.868	−	0.720	−8.4	4.5	−	0.326
S6	++	0.835	+	0.548	−	−	−	0.838	−	0.567	−8.3	4.4	−	0.419
S7	+	0.636	+	0.537	−	−	−	0.910	−	0.778	−4.5	2.2	−	0.386
S8	+++	0.962	+	0.912	+	+	−	0.593	+	0.554	−8.5	4.5	+	0.506
S9	++	0.809	+	0.901	+	+	−	0.586	−	0.570	−8.1	4.3	+	0.606
S10	+++	0.967	+	0.924	−	+	−	0.585	+	0.621	−8.5	4.5	+	0.556
S11	+++	0.912	+	0.905	−	+	−	0.585	−	0.630	−8.0	4.2	+	0.572
S12	++	0.826	+	0.895	−	+	−	0.607	−	0.595	−7.3	3.8	+	0.584
S13	++	0.753	+	0.895	−	+	−	0.607	+	0.534	−6.3	3.3	+	0.562
S14	++	0.848	+	0.895	−	+	−	0.607	+	0.539	−8.0	4.2	+	0.588

Comp.	Inhibitory activity												Substrate activity	
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab	
							MACCS		Morgan					
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.
S15	+++	0.902	+	0.604	+	−	+	0.615	−	0.553	−7.2	3.8	−	0.458
S16	+++	0.906	−	0.500	+	−	−	0.578	+	0.526	−8.5	4.5	−	0.486
S17	++	0.838	+	0.774	+	+	−	0.650	−	0.509	−7.3	3.8	+	0.520
S18	+++	0.904	+	0.730	−	+	−	0.578	−	0.517	−7.6	4.0	+	0.616
S19	+++	0.925	+	0.646	−	+	−	0.564	−	0.562	−7.8	4.1	+	0.646
S20	+	0.524	−	0.612	−	−	−	0.699	−	0.563	−8.0	4.2	+	0.522
S21	+	0.690	−	0.554	−	−	−	0.719	−	0.620	−7.4	3.9	−	0.472
S22	++	0.810	+	0.608	−	−	−	0.683	+	0.595	−6.7	3.5	+	0.604
S23	++	0.863	+	0.682	+	−	−	0.645	+	0.608	−6.9	3.6	−	0.450
S24	+	0.661	+	0.682	+	−	−	0.645	−	0.526	−7.5	3.9	−	0.480
S25	+++	0.917	+	0.877	+	+	−	0.584	−	0.522	−8.9	4.2	+	0.558
S26	+++	0.978	+	0.911	−	+	−	0.589	+	0.589	−9.2	4.5	+	0.546
S27	+++	0.968	+	0.911	−	+	−	0.589	−	0.537	−9.8	5.2	+	0.546
S28	+++	0.914	+	0.908	+	+	−	0.586	−	0.530	−9.2	3.9	+	0.500
S29	+++	0.916	+	0.877	−	+	−	0.584	+	0.528	−6.3	3.3	+	0.562
S30	+++	0.932	+	0.877	−	+	−	0.584	+	0.554	−7.8	4.1	+	0.558
S31	++	0.881	+	0.873	−	+	−	0.572	+	0.615	−6.8	3.5	+	0.586
S32	++	0.726	+	0.782	−	−	−	0.665	−	0.556	−5.7	2.9	+	0.612
S33	++	0.772	+	0.840	−	−	−	0.598	−	0.576	−4.5	2.2	−	0.488
S34	+	0.596	−	0.792	−	−	−	0.938	−	0.832	−4.5	2.2	−	0.446
S35	++	0.825	+	0.891	−	−	−	0.712	−	0.795	−8.2	4.3	+	0.510
S36	++	0.842	+	0.905	−	−	−	0.713	−	0.549	−5.9	3.0	−	0.480
S37	−	0.316	−	0.723	−	+	−	0.889	−	0.803	−7.5	3.9	−	0.442
S38	+	0.669	−	0.711	−	−	−	0.902	−	0.823	−7.6	4.0	−	0.496
S39	−−−	0.282	−	0.850	−	+	−	0.906	−	0.819	−7.4	3.9	−	0.430
S40	−−−	0.291	−	0.815	−	+	−	0.902	−	0.818	−6.1	3.1	+	0.596
S41	++	0.842	+	0.915	+	+	−	0.613	−	0.577	−8.9	4.7	+	0.622
S42	++	0.852	+	0.869	+	+	−	0.631	−	0.613	−9.6	4.8	+	0.680
S43	++	0.791	+	0.771	−	+	−	0.736	−	0.641	−9.8	5.2	+	0.656

Comp.	Inhibitory activity												Substrate activity	
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab	
							MACCS		Morgan					
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.
S44	++	0.895	+	0.808	−	+	−	0.724	−	0.671	−7.8	4.1	+	0.560
S45	++	0.848	+	0.817	+	+	−	0.735	−	0.678	−8.9	4.7	−	0.462
S46	++	0.839	+	0.899	+	+	−	0.623	−	0.648	−8.6	4.6	+	0.503
S47	++	0.818	+	0.897	+	+	−	0.640	−	0.594	−5.4	2.7	+	0.689
S48	++	0.779	+	0.915	+	+	−	0.613	−	0.524	−9.6	4.8	+	0.619
S49	++	0.798	+	0.915	+	+	−	0.613	−	0.656	−5.9	3.0	+	0.619
S50	++	0.841	+	0.915	+	+	−	0.629	−	0.613	−7.3	3.8	+	0.553
S51	++	0.833	+	0.718	+	+	−	0.582	−	0.616	−7.3	3.8	+	0.690
S52	+++	0.902	+	0.899	+	−	−	0.623	−	0.542	−5.4	2.7	+	0.573
S53	++	0.860	+	0.852	+	+	−	0.581	−	0.605	−8.6	4.6	+	0.563
S54	++	0.800	+	0.824	+	+	−	0.615	−	0.619	−6.2	3.2	+	0.635
S55	++	0.739	+	0.824	+	+	−	0.615	−	0.584	−5.4	2.7	+	0.534

* The obtained values of the probability for the unification of the results were rounded to thousandths; ** When forecasting online, the SuperCYPsPred server allows you to select the fingerprints, MACCS, or Morgan, in the form of which the molecule will be presented. We used both fingerprints in our work; *** pAC$_{50}$ was determined by solving the equation $y = -0.5687x - 0.329$; where y is pAC$_{50}$; x − ΔG.

Table S10. Prediction results of the inhibitory and substrate activity of Salubrinal and its analogues concerning the metabolic enzyme CYP2C9.

Comp.	Inhibitory activity												Substrate activity			
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *	
							MACCS		Morgan							
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.	result	prob.
S1	++	0.888	+	0.893	+	+	+	0.585	−	0.686	−10.1	6.5	+	0.564	−	0.791
S2	++	0.840	+	0.901	+	+	+	0.600	−	0.685	−10.0	6.5	−	0.486	−	0.595
S3	+++	0.922	+	0.880	+	+	+	0.634	−	0.689	−10.6	6.8	+	0.643	−	0.786
S4	++	0.899	+	0.880	+	+	+	0.634	−	0.556	−10.3	6.6	+	0.555	−	0.786
S5	+	0.551	+	0.509	−	+	−	0.756	−	0.825	−7.6	5.0	−	0.349	−	0.798
S6	+	0.690	+	0.537	−	+	−	0.604	−	0.610	−7.3	4.8	+	0.545	−	0.602

| Comp. | ADMETLab | | admetSAR 2.0 * | | pkCSM | SwissADME | SuperCYPsPred ** MACCS | | Morgan | | AutoDock Vina | | ADMETLab | | admetSAR 2.0 * | |
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.	result	prob.
S7	+	0.693	+	0.539	−	+	−	0.527	−	0.745	−7.9	5.2	−	0.428	−	0.809
S8	+++	0.945	+	0.921	+	+	+	0.618	−	0.625	−8.1	5.3	−	0.423	−	0.602
S9	+++	0.945	+	0.924	+	+	+	0.690	−	0.610	−9.0	5.8	−	0.499	−	0.606
S10	+++	0.917	+	0.928	+	+	+	0.630	−	0.672	−8.3	5.4	−	0.474	−	0.606
S11	+++	0.968	+	0.928	+	+	+	0.630	−	0.643	−9.3	6.0	+	0.527	−	0.606
S12	+++	0.953	+	0.889	+	+	+	0.677	−	0.574	−8.7	5.7	+	0.608	−	0.606
S13	+++	0.912	+	0.889	+	+	+	0.677	−	0.631	−8.5	5.5	+	0.553	−	0.606
S14	+++	0.924	+	0.889	+	+	+	0.677	−	0.707	−8.9	5.8	+	0.519	−	0.606
S15	+++	0.953	+	0.744	+	+	+	0.614	−	0.632	−8.8	5.7	−	0.494	−	0.602
S16	+++	0.938	+	0.797	+	+	+	0.640	−	0.634	−8.9	5.8	−	0.495	−	0.602
S17	+++	0.910	+	0.877	+	+	+	0.598	−	0.615	−8.1	5.3	+	0.528	−	0.602
S18	++	0.881	+	0.870	+	+	+	0.673	−	0.603	−8.7	5.7	+	0.623	−	0.598
S19	+++	0.943	+	0.888	+	+	+	0.667	−	0.681	−8.1	5.3	+	0.684	−	0.598
S20	+++	0.916	+	0.788	+	+	+	0.638	−	0.594	−8.4	5.5	+	0.543	−	0.598
S21	+++	0.900	+	0.779	+	+	+	0.560	−	0.726	−8.7	5.7	−	0.451	−	0.798
S22	++	0.889	+	0.901	+	+	+	0.661	−	0.556	−8.5	5.5	+	0.559	−	0.805
S23	+++	0.945	+	0.751	+	+	+	0.551	−	0.571	−8.4	5.5	−	0.405	−	1.000
S24	+++	0.920	+	0.751	+	+	+	0.551	−	0.605	−8.4	5.5	−	0.477	−	1.000
S25	+++	0.930	+	0.907	+	+	+	0.687	−	0.611	−8.4	5.5	+	0.530	−	0.803
S26	+++	0.936	+	0.905	+	+	+	0.633	−	0.629	−8.7	5.7	−	0.475	−	0.803
S27	+++	0.957	+	0.905	+	+	+	0.633	−	0.678	−9.8	6.3	+	0.528	−	0.803
S28	+++	0.969	+	0.878	+	+	+	0.639	−	0.670	−8.3	5.4	−	0.462	−	0.602
S29	+++	0.925	+	0.907	+	+	+	0.687	−	0.607	−8.6	5.6	+	0.546	−	0.803
S30	+++	0.932	+	0.907	+	+	+	0.687	−	0.618	−8.8	5.7	+	0.537	−	0.803
S31	++	0.890	+	0.883	+	+	+	0.682	−	0.669	−8.9	5.8	+	0.503	−	0.807
S32	++	0.872	+	0.933	+	+	+	0.615	−	0.755	−9.0	5.8	−	0.497	−	0.606
S33	++	0.887	+	0.849	+	+	+	0.568	−	0.782	−9.2	6.0	−	0.425	−	0.602
S34	++	0.883	−	0.714	+	+	−	0.513	−	0.783	−8.9	5.8	−	0.481	−	0.798
S35	++	0.786	+	0.925	−	+	+	0.588	−	0.695	−8.4	5.5	+	0.541	+	0.596

Comp.	Inhibitory activity												Substrate activity			
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *	
							MACCS		Morgan							
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.	result	prob.
S36	++	0.885	+	0.869	−	+	+	0.632	−	0.649	−8.6	5.6	−	0.412	+	0.602
S37	−	0.463	−	0.649	−	+	−	0.634	−	0.790	−8.4	5.5	−	0.468	−	0.611
S38	++	0.779	−	0.555	−	+	−	0.525	−	0.699	−8.2	5.4	+	0.519	−	0.604
S39	+	0.670	−	0.602	−	+	−	0.588	−	0.731	−8.3	5.4	+	0.553	−	0.592
S40	+	0.591	−	0.617	−	+	−	0.578	−	0.784	−8.4	5.5	+	0.550	+	0.600
S41	+	0.582	+	0.890	−	+	+	0.545	−	0.703	−7.9	5.2	+	0.613	+	0.603
S42	+	0.693	+	0.848	−	+	+	0.541	−	0.651	−8.3	5.4	+	0.628	+	0.605
S43	++	0.730	+	0.755	+	+	+	0.521	−	0.681	−8.1	5.3	+	0.543	+	0.809
S44	++	0.781	+	0.899	+	+	+	0.549	−	0.647	−8.4	5.5	+	0.509	−	0.600
S45	+++	0.914	+	0.813	+	+	+	0.503	−	0.646	−9.0	5.8	+	0.524	−	0.584
S46	+++	0.912	+	0.888	+	+	+	0.548	−	0.659	−9.5	6.2	+	0.505	−	0.806
S47	+++	0.900	+	0.869	+	+	+	0.586	−	0.662	−9.2	6.0	+	0.558	−	0.800
S48	++	0.850	+	0.890	+	+	+	0.545	−	0.691	−9.2	6.0	+	0.519	−	0.588
S49	++	0.891	+	0.890	+	+	+	0.545	−	0.662	−9.5	6.2	+	0.532	−	0.588
S50	++	0.869	+	0.866	+	+	+	0.580	−	0.656	−9.3	6.0	−	0.443	−	1.000
S51	++	0.854	+	0.836	+	+	+	0.563	−	0.656	−9.0	5.8	+	0.623	−	1.000
S52	++	0.866	+	0.888	+	+	+	0.548	−	0.611	−9.4	6.1	−	0.485	−	0.806
S53	+++	0.908	+	0.833	−	+	+	0.551	−	0.607	−8.6	5.6	+	0.517	−	0.805
S54	++	0.854	+	0.873	+	+	+	0.571	−	0.645	−9.2	6.0	+	0.622	−	0.590
S55	++	0.788	+	0.873	+	+	+	0.571	−	0.708	−9.3	6.0	+	0.552	−	0.590

* The obtained values of the probability for the unification of the results were rounded to thousandths; ** When forecasting online, the SuperCYPsPred server allows you to select the fingerprints, MACCS, or Morgan, in the form of which the molecule will be presented. We used both fingerprints in our work; *** pAC$_{50}$ was determined by solving the equation $y = -0.6155x + 0.305$; where y is pAC$_{50}$; $x - \Delta G$.

Table S11. Prediction results of the inhibitory and substrate activity of Salubrinal and its analogues concerning the metabolic enzyme CYP2C19.

Comp.	Inhibitory activity												Substrate activity	
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab	
							MACCS		Morgan					
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.
S1	++	0.810	+	0.840	+	+	−	0.706	−	0.663	−10.0	6.7	−	0.340
S2	++	0.740	+	0.892	+	+	−	0.702	−	0.623	−9.8	6.5	−	0.322
S3	++	0.876	+	0.872	+	+	−	0.629	−	0.680	−10.1	6.7	−	0.364
S4	++	0.817	+	0.872	+	+	−	0.629	−	0.603	−8.8	5.9	⎯⎯⎯	0.250
S5	+	0.556	−	0.527	−	+	−	0.861	−	0.825	−8.1	5.5	−	0.304
S6	++	0.862	+	0.621	−	+	−	0.745	−	0.784	−8.1	5.5	−	0.337
S7	++	0.757	+	0.671	−	+	−	0.672	−	0.766	−8.8	5.9	−	0.304
S8	++	0.809	+	0.886	+	+	−	0.663	−	0.755	−9.2	6.2	−	0.342
S9	++	0.823	+	0.913	+	+	−	0.647	−	0.782	−9.5	6.4	−	0.459
S10	+++	0.915	+	0.905	+	+	−	0.652	−	0.707	−9.7	6.5	−	0.434
S11	+++	0.921	+	0.905	+	+	−	0.652	−	0.703	−9.0	6.0	−	0.473
S12	++	0.828	+	0.898	+	+	−	0.632	−	0.765	−9.8	6.5	−	0.445
S13	++	0.872	+	0.898	+	+	−	0.632	−	0.654	−9.8	6.5	−	0.477
S14	++	0.872	+	0.898	+	+	−	0.632	−	0.716	−9.7	6.5	−	0.493
S15	++	0.742	+	0.674	+	+	−	0.729	−	0.771	−9.4	6.3	−	0.354
S16	++	0.759	+	0.679	+	+	−	0.679	−	0.763	−9.1	6.1	−	0.342
S17	++	0.787	+	0.830	+	+	−	0.681	−	0.757	−9.1	6.1	−	0.338
S18	++	0.843	+	0.878	+	+	−	0.653	−	0.719	−9.1	6.1	−	0.419
S19	+++	0.905	+	0.866	+	+	−	0.580	+	0.666	−9.0	6.0	−	0.563
S20	⎯⎯⎯	0.265	−	0.573	−	+	−	0.868	−	0.783	−9.5	6.4	−	0.310
S21	−	0.375	−	0.538	−	+	−	0.863	−	0.748	−9.1	6.1	−	0.330
S22	++	0.853	+	0.766	+	+	−	0.713	−	0.683	−9.4	6.3	−	0.377
S23	++	0.812	+	0.682	+	+	−	0.653	−	0.648	−9.3	6.2	−	0.314
S24	++	0.791	+	0.682	+	+	−	0.653	−	0.641	−9.0	6.0	−	0.366
S25	++	0.847	+	0.905	+	+	−	0.654	−	0.709	−9.4	6.3	−	0.476
S26	++	0.882	+	0.899	+	+	−	0.664	−	0.738	−9.5	6.4	−	0.384
S27	++	0.894	+	0.899	+	+	−	0.664	−	0.706	−8.2	5.6	−	0.432
S28	+++	0.925	+	0.884	+	+	−	0.664	−	0.717	−8.7	5.9	−	0.372

Comp.	Inhibitory activity												Substrate activity	
	ADMETLab		admetSAR 2.0 *		pkCSM	SwissADME	SuperCYPsPred **				AutoDock Vina		ADMETLab	
							MACCS		Morgan					
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	result	prob.
S29	++	0.870	+	0.905	+	+	−	0.654	−	0.662	−9.3	6.2	−	0.434
S30	++	0.870	+	0.905	+	+	−	0.654	−	0.658	−9.5	6.4	−	0.438
S31	++	0.826	+	0.877	+	+	−	0.659	−	0.685	−10.3	6.9	−	0.408
S32	+	0.647	+	0.862	+	+	−	0.703	−	0.762	−9.2	6.2	−	0.449
S33	+	0.691	+	0.785	+	+	−	0.682	−	0.738	−8.5	5.7	−	0.304
S34	+	0.541	−	0.827	−	−	−	0.870	−	0.786	−9.3	6.2	−	0.338
S35	++	0.706	+	0.903	+	+	−	0.734	−	0.791	−8.8	5.9	−	0.381
S36	++	0.886	+	0.899	+	+	−	0.743	−	0.686	−9.6	6.4	−	0.457
S37	−	0.428	−	0.609	−	+	−	0.799	−	0.853	−8.9	6.0	−	0.388
S38	++	0.850	+	0.764	+	+	−	0.754	−	0.757	−8.9	6.0	−	0.451
S39	++	0.806	+	0.530	−	+	−	0.813	−	0.776	−8.6	5.8	−	0.424
S40	++	0.704	−	0.541	+	+	−	0.763	−	0.795	−8.7	5.9	+	0.627
S41	++	0.726	+	0.910	+	+	−	0.729	−	0.746	−8.6	5.8	−	0.429
S42	+++	0.921	+	0.891	+	+	−	0.717	−	0.729	−9.1	6.1	−	0.477
S43	+++	0.911	+	0.821	+	+	−	0.740	−	0.755	−9.0	6.0	−	0.441
S44	+++	0.904	+	0.900	+	+	−	0.690	−	0.743	−8.8	5.9	−	0.365
S45	+++	0.928	+	0.789	+	+	−	0.740	−	0.609	−10.2	6.8	−	0.368
S46	+++	0.912	+	0.859	+	+	−	0.730	−	0.636	−10.3	6.9	−	0.304
S47	+++	0.925	+	0.890	+	+	−	0.750	−	0.637	−9.7	6.5	−	0.431
S48	+++	0.951	+	0.910	+	+	−	0.729	−	0.685	−10.6	7.0	−	0.408
S49	+++	0.954	+	0.910	+	+	−	0.729	−	0.697	−9.9	6.6	−	0.387
S50	+++	0.961	+	0.865	+	+	−	0.733	−	0.662	−9.5	6.4	−	0.316
S51	+++	0.952	+	0.819	+	+	−	0.709	−	0.593	−9.4	6.3	−	0.481
S52	+++	0.903	+	0.859	+	+	−	0.730	−	0.574	−11.0	7.3	–––	0.282
S53	++	0.888	+	0.851	+	+	−	0.698	−	0.631	−9.4	6.3	−	0.370
S54	++	0.867	+	0.843	+	+	−	0.661	−	0.726	−9.1	6.1	−	0.440
S55	++	0.821	+	0.843	+	+	−	0.661	−	0.695	−8.9	6.0	−	0.422

* The obtained values of the probability for the unification of the results were rounded to thousandths; ** When forecasting online, the SuperCYPsPred server allows you to select the fingerprints, MACCS, or Morgan, in the form of which the molecule will be presented. We used both fingerprints in our work; *** pAC$_{50}$ was determined by solving the equation $y = −0.6192x + 0.4734$; where y is pAC$_{50}$; x − ΔG.

Table S12. Prediction results of the inhibitory and substrate activity of Salubrinal and its analogues concerning the metabolic enzyme CYP2D6.

Comp.	Inhibitory activity														Substrate activity				
	ADMETLab		admetSAR 2.0 *		pkCSM	Swis-sADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *		pkCSM
							MACCS		Morgan								
	result	prob.	result	prob.			result	prob.	result	prob.	ΔG, kcal/mol	pAC_{50} ***	result	prob.	result	prob.	
S1	−	0.401	−	0.719	−	+	−	0.590	−	0.649	−11.8	7.2	−	0.394	−	0.858	+
S2	−	0.488	−	0.647	−	+	−	0.587	−	0.592	−11.1	6.4	−	0.391	−	0.874	+
S3	−	0.388	+	0.635	−	−	−	0.583	−	0.581	−11.5	6.8	−	0.401	−	0.840	+
S4	+	0.500	+	0.635	−	−	−	0.583	−	0.606	−10.6	5.9	−	0.374	−	0.840	+
S5	−	0.406	−	0.815	−	−	−	0.638	−	0.601	−9.4	4.6	−	0.307	−	0.849	−
S6	−	0.359	−	0.827	−	−	−	0.602	−	0.650	−9.3	4.5	−	0.340	−	0.855	−
S7	+	0.516	−	0.814	−	−	−	0.551	−	0.565	−9.5	4.7	−	0.372	−	0.852	−
S8	+	0.507	+	0.784	−	−	−	0.623	−	0.733	−10.7	6.0	----	0.290	−	0.847	+
S9	−	0.398	+	0.529	−	−	−	0.585	−	0.642	−10.8	6.1	−	0.339	−	0.862	+
S10	+	0.516	+	0.653	+	−	−	0.606	−	0.730	−10.6	5.9	−	0.330	−	0.862	+
S11	−	0.445	+	0.653	+	−	−	0.606	−	0.679	−10.5	5.8	−	0.378	−	0.862	+
S12	−	0.437	−	0.541	−	−	−	0.575	−	0.670	−10.8	6.1	−	0.307	−	0.862	+
S13	−	0.440	−	0.541	+	−	−	0.575	−	0.646	−10.0	5.2	−	0.386	−	0.862	+
S14	+	0.510	−	0.541	+	−	−	0.575	−	0.641	−11.1	6.4	−	0.406	−	0.862	+
S15	−	0.409	−	0.813	−	−	−	0.731	−	0.658	−10.4	5.7	−	0.338	−	0.842	+
S16	+	0.529	−	0.733	+	−	−	0.723	−	0.741	−10.6	5.9	−	0.332	−	0.842	+
S17	−	0.395	+	0.552	−	−	−	0.610	−	0.660	−10.2	5.4	−	0.335	−	0.848	+
S18	−	0.388	−	0.836	−	−	−	0.682	−	0.621	−10.4	5.7	+	0.507	−	0.833	+
S19	−	0.484	−	0.762	−	−	−	0.674	−	0.639	−9.6	4.8	+	0.568	−	0.833	+
S20	−	0.309	−	0.763	−	−	−	0.794	−	0.767	−11.2	6.5	----	0.257	−	0.878	−
S21	−	0.473	−	0.686	−	−	−	0.806	−	0.757	−10.2	5.4	−	0.339	−	0.862	−
S22	−	0.371	−	0.777	−	−	−	0.711	−	0.669	−10.7	6.0	−	0.333	−	0.872	−
S23	+	0.542	−	0.762	−	−	−	0.721	−	0.757	−10.8	6.1	----	0.287	−	0.865	−
S24	−	0.490	−	0.762	−	−	−	0.721	−	0.723	−9.8	5.0	−	0.310	−	0.865	−
S25	−	0.431	+	0.789	−	−	−	0.577	−	0.646	−10.7	6.0	−	0.309	−	0.854	+
S26	+	0.660	+	0.893	+	−	−	0.594	−	0.706	−10.5	5.8	−	0.304	−	0.854	+

Comp.	Inhibitory activity												Substrate activity				
	ADMETLab		admetSAR 2.0 *		pkCSM	Swis-sADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *		pkCSM
							MACCS		Morgan								
	re-sult	prob.	result	prob.			re-sult	prob.	re-sult	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	re-sult	prob.	result	prob.	
S27	+	0.559	+	0.893	+	−	−	0.594	−	0.648	−10.0	5.2	−	0.323	−	0.854	+
S28	+	0.510	+	0.875	−	−	−	0.583	−	0.674	−9.5	4.7	−	0.339	−	0.846	+
S29	+	0.567	+	0.789	+	−	−	0.577	−	0.623	−9.8	5.0	−	0.337	−	0.854	+
S30	+	0.623	+	0.789	+	−	−	0.577	−	0.617	−10.9	6.2	−	0.344	−	0.854	+
S31	+	0.614	+	0.624	−	−	−	0.572	−	0.607	−11.1	6.4	−	0.348	−	0.848	+
S32	−	0.468	−	0.589	−	−	−	0.674	−	0.654	−9.6	4.8	−	0.375	−	0.862	+
S33	−	0.457	−	0.530	−	−	−	0.602	−	0.653	−9.7	4.9	−	0.344	−	0.847	+
S34	+	0.533	−	0.823	−	+	−	0.775	−	0.720	−9.0	4.1	−	0.337	−	0.853	−
S35	−	0.402	+	0.519	−	−	−	0.618	−	0.666	−10.1	5.3	−	0.309	−	0.866	−
S36	−	0.450	+	0.510	−	−	−	0.545	−	0.646	−10.3	5.5	−	0.357	−	0.872	+
S37	−	0.461	−	0.864	−	−	−	0.737	−	0.655	−10.2	5.4	−	0.365	−	0.837	−
S38	−	0.415	−	0.813	−	−	+	0.563	+	0.535	−10.6	5.9	−	0.423	−	0.834	−
S39	−	0.350	−	0.910	−	−	−	0.507	−	0.548	−10.3	5.5	−	0.401	−	0.850	−
S40	−	0.451	−	0.834	−	−	+	0.556	+	0.552	−10.6	5.9	−	0.417	−	0.758	+
S41	−	0.372	−	0.835	−	−	−	0.576	−	0.711	−9.5	4.7	−	0.364	−	0.848	−
S42	−	0.449	−	0.867	−	−	−	0.558	−	0.647	−9.8	5.0	−	0.399	−	0.846	−
S43	−	0.415	−	0.810	−	−	+	0.525	−	0.693	−9.8	5.0	−	0.378	−	0.823	−
S44	−	0.389	−	0.883	−	−	−	0.567	−	0.732	−9.7	4.9	−	0.381	−	0.854	−
S45	−	0.493	−	0.698	−	+	+	0.505	−	0.604	−11.0	6.3	−	0.366	−	0.799	+
S46	−	0.443	−	0.784	−	+	−	0.592	−	0.708	−11.1	6.4	−	0.310	−	0.853	+
S47	−	0.372	−	0.814	−	+	−	0.576	−	0.681	−11.0	6.3	−	0.362	−	0.888	+
S48	−	0.443	−	0.835	−	+	−	0.576	−	0.695	−11.5	6.8	−	0.394	−	0.868	+
S49	−	0.423	−	0.835	−	+	−	0.576	−	0.733	−10.5	5.8	−	0.406	−	0.868	+
S50	−	0.479	−	0.663	−	+	−	0.547	−	0.696	−10.7	6.0	−	0.357	−	0.852	+
S51	−	0.449	−	0.890	−	+	−	0.657	−	0.706	−10.3	5.5	+	0.584	−	0.833	−
S52	−	0.465	−	0.784	−	+	−	0.592	−	0.618	−11.8	7.2	−	0.387	−	0.853	+
S53	−	0.487	−	0.781	−	+	+	0.529	−	0.642	−10.3	5.5	−	0.393	−	0.854	−
S54	−	0.477	−	0.832	−	−	−	0.572	−	0.623	−10.9	6.2	−	0.430	−	0.859	+

Comp.	Inhibitory activity												Substrate activity				
	ADMETLab		admetSAR 2.0 *		pkCSM	Swis-sADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *		pkCSM
							MACCS		Morgan								
	re-sult	prob.	result	prob.			re-sult	prob.	re-sult	prob.	ΔG, kcal/mol	pAC_{50} ***	re-sult	prob.	result	prob.	
S55	−	0.413	−	0.832	−	−	−	0.572	−	0.683	−10.7	6.0	−	0.398	−	0.859	+

* The obtained values of the probability for the unification of the results were rounded to thousandths; ** When forecasting online, the SuperCYPsPred server allows you to select the fingerprints, MACCS, or Morgan, in the form of which the molecule will be presented. We used both fingerprints in our work; *** pAC_{50} was determined by solving the equation y = −1.0875x − 5.6588; where y is pAC_{50}; x − ΔG.

Table S13. Prediction results of the inhibitory and substrate activity of Salubrinal and its analogues concerning the metabolic enzyme CYP3A4.
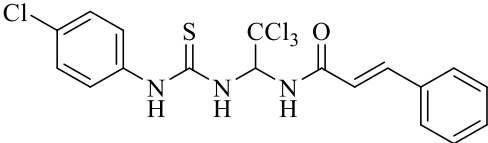
Comp.	Inhibitory activity												Substrate activity				
	ADMETLab		admetSAR 2.0 *		pkCSM	Swis-sADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *		pkCSM
							MACCS		Morgan								
	re-sult	prob.	re-sult	prob.			re-sult	prob.	re-sult	prob.	ΔG, kcal/mol	pAC_{50} ***	re-sult	prob.	re-sult	prob.	
S1	++	0.749	+	0.836	+	+	−	0.776	−	0.571	−10.4	5.5	−	0.372	+	0.551	+
S2	++	0.852	+	0.898	+	+	−	0.776	−	0.504	−9.5	5.3	−	0.380	+	0.559	+
S3	++	0.831	+	0.896	+	+	−	0.799	−	0.531	−10.8	5.6	−	0.362	+	0.554	+
S4	++	0.877	+	0.896	+	+	−	0.799	+	0.556	−9.5	5.3	−	0.346	+	0.535	+
S5	+	0.500	+	0.730	−	−	−	0.855	−	0.592	−8.4	4.9	----	0.282	−	0.535	+
S6	−	0.483	+	0.559	−	−	−	0.775	−	0.523	−7.7	4.7	−	0.452	+	0.520	+
S7	+	0.604	+	0.750	+	+	−	0.685	+	0.527	−8.7	5.0	+	0.504	+	0.603	+
S8	++	0.837	+	0.829	+	+	−	0.821	−	0.618	−9.3	5.2	−	0.344	−	0.521	+
S9	++	0.880	+	0.821	+	+	−	0.780	−	0.612	−9.8	5.3	+	0.594	+	0.527	+
S10	+++	0.947	+	0.851	+	+	−	0.817	−	0.544	−9.8	5.3	+	0.535	+	0.552	+
S11	+++	0.944	+	0.851	+	+	−	0.817	−	0.551	−9.8	5.3	+	0.568	+	0.547	+
S12	++	0.896	+	0.734	+	+	−	0.768	−	0.585	−10.1	5.4	+	0.564	+	0.548	+
S13	++	0.894	+	0.734	+	+	−	0.768	−	0.534	−10.1	5.4	+	0.558	+	0.547	+
S14	++	0.832	+	0.734	+	+	−	0.768	−	0.540	−10.2	5.5	+	0.598	+	0.529	+
S15	++	0.891	+	0.632	+	+	−	0.824	−	0.580	−9.4	5.2	−	0.364	+	0.512	+
S16	+++	0.955	+	0.827	+	+	−	0.799	−	0.512	−9.4	5.2	−	0.360	+	0.545	+
S17	++	0.779	+	0.870	+	+	−	0.749	−	0.593	−9.4	5.2	−	0.328	+	0.510	+
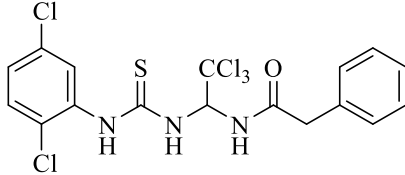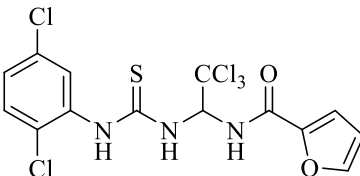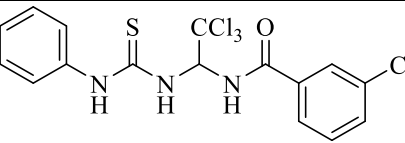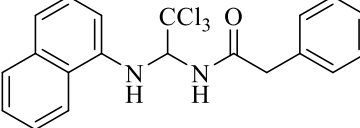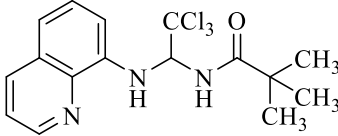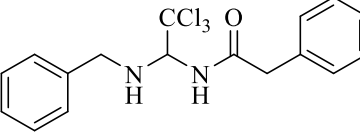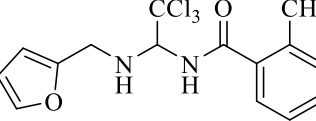
Comp.	Inhibitory activity													Substrate activity				
	ADMETLab		admetSAR 2.0 *		pkCSM	Swiss-sADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *		pkCSM
							MACCS		Morgan								
	re-sult	prob.	re-sult	prob.			re-sult	prob.	re-sult	prob.	ΔG, kcal/mol	pAC_{50} ***	re-sult	prob.	re-sult	prob.	
S18	+++	0.923	+	0.714	+	+	−	0.786	−	0.575	−9.5	5.3	+	0.576	+	0.573	+
S19	+++	0.945	+	0.823	+	+	−	0.824	−	0.631	−9.3	5.2	+	0.574	+	0.601	+
S20	+	0.682	+	0.665	−	−	−	0.886	−	0.659	−8.8	5.0	−	0.310	−	0.557	+
S21	+	0.671	+	0.742	−	−	−	0.902	−	0.688	−10.1	5.4	−	0.354	−	0.500	+
S22	++	0.854	+	0.748	+	+	−	0.784	−	0.632	−8.7	5.0	+	0.562	+	0.568	+
S23	++	0.894	+	0.814	+	+	−	0.689	−	0.514	−9.9	5.4	−	0.430	+	0.612	+
S24	++	0.848	+	0.814	+	+	−	0.689	−	0.580	−9.9	5.4	−	0.414	+	0.611	+
S25	++	0.865	+	0.757	+	+	−	0.777	−	0.594	−9.7	5.3	−	0.454	+	0.521	+
S26	+++	0.909	+	0.796	+	+	−	0.818	−	0.554	−9.6	5.3	−	0.438	+	0.578	+
S27	+++	0.931	+	0.796	+	+	−	0.818	−	0.607	−9.7	5.3	−	0.444	+	0.570	+
S28	++	0.871	+	0.715	+	+	−	0.816	−	0.560	−9.6	5.3	−	0.386	+	0.535	+
S29	+++	0.910	+	0.757	+	+	−	0.777	−	0.511	−9.8	5.3	−	0.448	+	0.577	+
S30	+++	0.923	+	0.757	+	+	−	0.777	−	0.548	−10.0	5.4	−	0.458	+	0.592	+
S31	++	0.797	+	0.615	+	+	−	0.769	−	0.544	−10.5	5.6	−	0.438	+	0.582	+
S32	++	0.794	+	0.901	+	+	−	0.827	−	0.610	−9.8	5.3	+	0.588	+	0.559	+
S33	++	0.720	−	0.527	+	+	−	0.793	−	0.597	−10.0	5.4	−	0.390	+	0.533	+
S34	++	0.820	+	0.533	−	+	−	0.931	−	0.628	−9.8	5.3	−	0.420	+	0.516	+
S35	+	0.611	+	0.853	−	+	−	0.788	−	0.625	−9.1	5.1	−	0.380	+	0.517	+
S36	++	0.885	+	0.738	+	+	−	0.757	+	0.531	−9.6	5.3	+	0.582	+	0.602	+
S37	+	0.544	+	0.634	−	+	−	0.848	−	0.619	−9.1	5.1	−	0.460	+	0.570	+
S38	++	0.819	+	0.550	−	+	−	0.757	−	0.563	−8.8	5.0	−	0.424	+	0.500	+
S39	+	0.631	−	0.760	−	+	−	0.777	−	0.552	−8.6	5.0	−	0.352	+	0.508	+
S40	+	0.589	−	0.807	−	+	−	0.789	−	0.586	−8.8	5.0	++	0.732	+	0.552	+
S41	−	0.462	+	0.824	−	+	−	0.794	−	0.645	−8.0	4.8	+	0.522	+	0.544	+
S42	+	0.696	+	0.668	−	+	−	0.791	−	0.623	−8.4	4.9	+	0.572	+	0.533	+
S43	+	0.710	+	0.799	+	+	−	0.725	−	0.598	−8.3	4.9	+	0.570	+	0.562	+
S44	++	0.769	+	0.817	−	+	−	0.744	−	0.633	−8.7	5.0	+	0.578	+	0.555	+
S45	++	0.867	+	0.890	+	+	−	0.748	−	0.537	−9.9	5.4	−	0.354	+	0.564	+
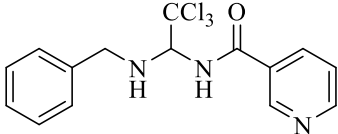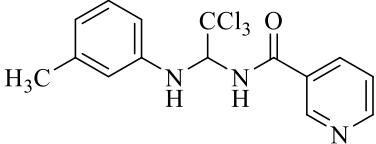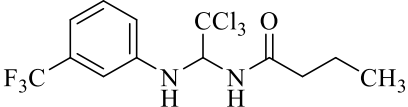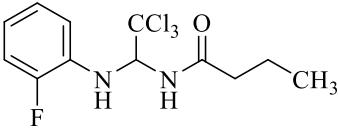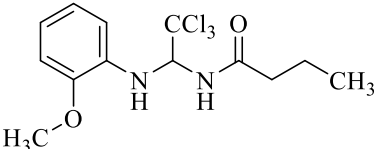
Comp.	Inhibitory activity												Substrate activity				
	ADMETLab		admetSAR 2.0 *		pkCSM	Swis-sADME	SuperCYPsPred **				AutoDock Vina		ADMETLab		admetSAR 2.0 *		pkCSM
							MACCS		Morgan								
	re-sult	prob.	re-sult	prob.			re-sult	prob.	re-sult	prob.	ΔG, kcal/mol	pAC$_{50}$ ***	re-sult	prob.	re-sult	prob.	
S46	++	0.797	+	0.802	+	+	−	0.791	−	0.567	−9.8	5.3	−	0.328	+	0.530	+
S47	++	0.857	+	0.824	+	+	−	0.765	−	0.596	−10.6	5.6	+	0.610	+	0.584	+
S48	++	0.856	+	0.824	+	+	−	0.794	−	0.550	−10.3	5.5	+	0.570	+	0.583	+
S49	++	0.878	+	0.824	+	+	−	0.794	−	0.573	−9.1	5.1	+	0.534	+	0.582	+
S50	++	0.804	+	0.711	+	+	−	0.794	−	0.541	−9.8	5.3	−	0.346	+	0.578	+
S51	+++	0.935	+	0.522	+	+	−	0.835	−	0.508	−9.8	5.3	+	0.560	+	0.623	+
S52	++	0.826	+	0.802	+	+	−	0.791	−	0.554	−10.5	5.6	−	0.368	+	0.570	+
S53	++	0.785	+	0.901	−	+	−	0.745	−	0.597	−9.0	5.1	−	0.340	+	0.586	+
S54	++	0.895	+	0.921	+	+	−	0.693	+	0.508	−9.6	5.3	−	0.436	+	0.592	+
S55	++	0.825	+	0.921	+	+	−	0.693	−	0.561	−9.7	5.3	−	0.436	+	0.605	+

* The obtained values of the probability for the unification of the results were rounded to thousandths; ** When forecasting online, the SuperCYPsPred server allows you to select the fingerprints, MACCS, or Morgan, in the form of which the molecule will be presented. We used both fingerprints in our work; *** pAC$_{50}$ was determined by solving the equation $y = -0.2997x + 2.4041$; where y is pAC$_{50}$; x − ΔG.

Table S14. Molecular docking results for reference compounds **E1−E13** with enzymes of the P450 family.

Entry	Structure	CYP1A2		CYP2C9		CYP2C19		CYP2D6		CYP3A4	
		pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol
E1	Sal 003 (**S27**)	5.40	−9.8	6.25	−9.8	5.45	−8.2	5.10	−10.0	5.35	−9.7

Entry	Structure	CYP1A2		CYP2C9		CYP2C19		CYP2D6		CYP3A4	
		pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol	pAC$_{50}$	ΔG, kcal/mol
E2		*	–	6.25	−9.8	6.95	−10.4	5.50	−10.1	5.35	−9.6
E3		4.90	−9.2	**	–	5.80	−8.3	4.95	−9.9	5.20	−9.4
E4		4.80	−9.2	5.90	−9.0	5.90	−8.9	4.85	−9.7	5.30	−9.5
E5		5.15	−9.6	5.15	−8.6	6.15	−9.2	*	–	4.95	−9.0
E6		4.70	−9.0	5.90	−9.2	6.10	−9.1	4.80	−9.6	5.15	−9.4
E7		4.60	−9.0	5.95	−8.6	6.10	−9.0	4.85	−9.6	4.85	−8.2
E8		4.85	−9.2	7.40	−11.2	4.90	−7.4	*	–	4.60	−7.8

Entry	Structure	CYP1A2		CYP2C9		CYP2C19		CYP2D6		CYP3A4	
		pAC50	ΔG, kcal/mol	pAC50	ΔG, kcal/mol	pAC50	ΔG, kcal/mol	pAC50	ΔG, kcal/mol	pAC50	ΔG, kcal/mol
E9		*	–	4.85	−8.4	5.35	−8.2	*	–	4.90	−8.1
E10		4.65	−8.6	6.65	−10.4	5.55	−8.4	*	–	5.00	−8.6
E11		4.70	−8.9	5.85	−8.4	6.15	−9.1	5.05	−9.8	4.80	−7.8
E12		4.65	−8.5	5.05	−7.3	5.55	−7.8	*	–	4.85	−8.0
E13		4.85	−9.0	6.10	−9.2	5.25	−7.5	*	–	4.85	−8.0

* Substance does not exhibit inhibitory activity or AC50 > 10μ; ** No data on the inhibitory activity of this substance.
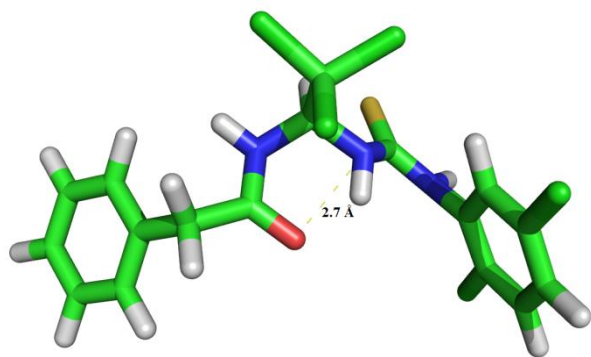
E2, ΔG = −110176.6 kcal/mol
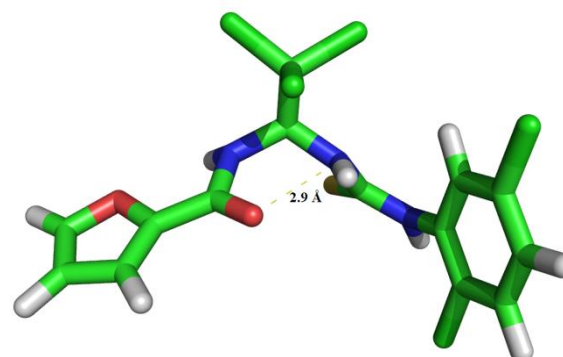
E3, ΔG = −107309.9 kcal/mol
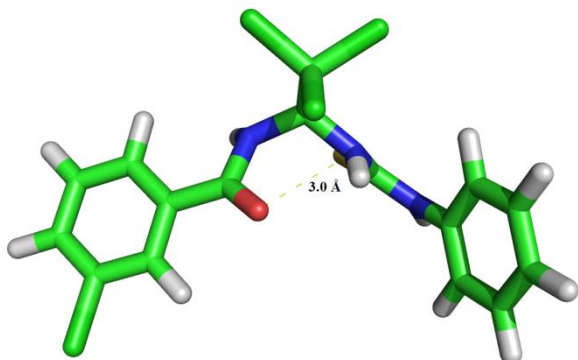
E4, ΔG = −99785.6 kcal/mol
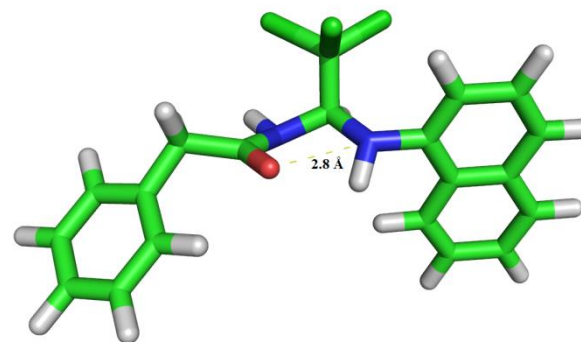
E5, ΔG = −96809.0 kcal/mol
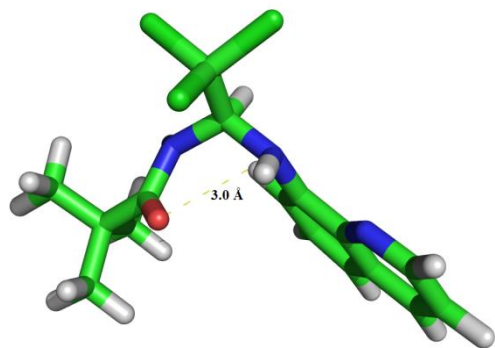
E6, ΔG = −90013.1 kcal/mol
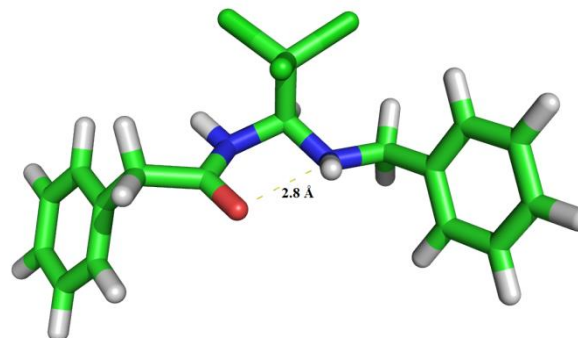
E7, ΔG = −88627.7 kcal/mol
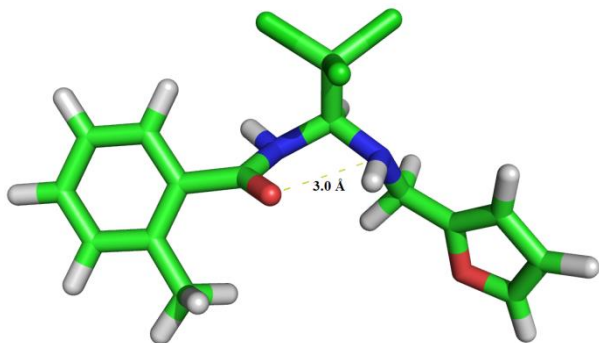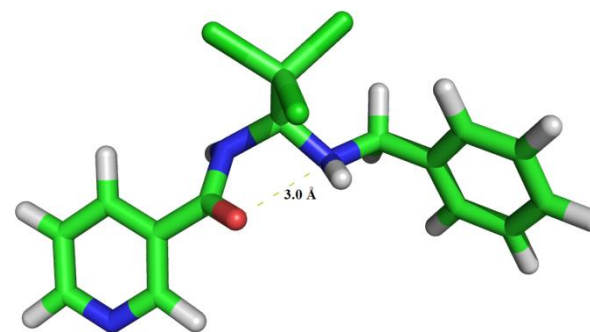
**E8, ΔG = −89215.4 kcal/mol**   **E9, ΔG = −85835.2 kcal/mol**

Figure S6. Structures of compounds **E2**–**E13** optimized by the PM3 method in the ArgusLab 4.0.1 software package (continued follows below).
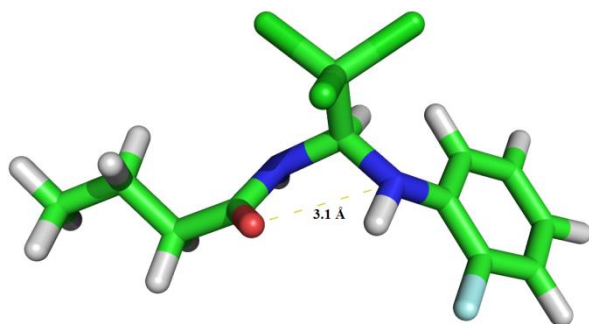
* Geometry optimization of **E1** (Sal 003, **S27**) was carried out earlier in the work: Zadorozhnii et al. Molecular docking studies of salubrinal and its analogs as inhibitors of the GADD34:PP1 enzyme, ADMET DMPK 7 (2019) 140–150. http://dx.doi.org/10.5599/admet.632.
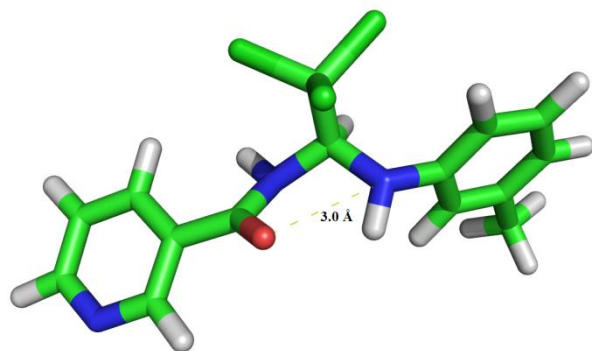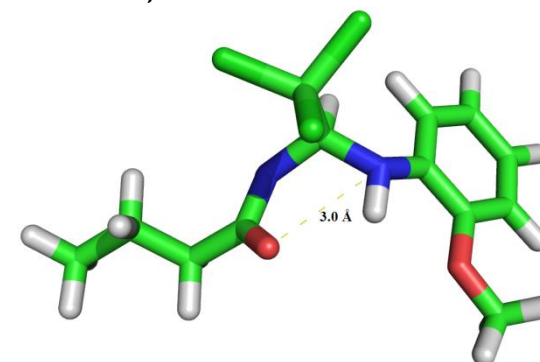
E10, ΔG = −85837.5 kcal/mol
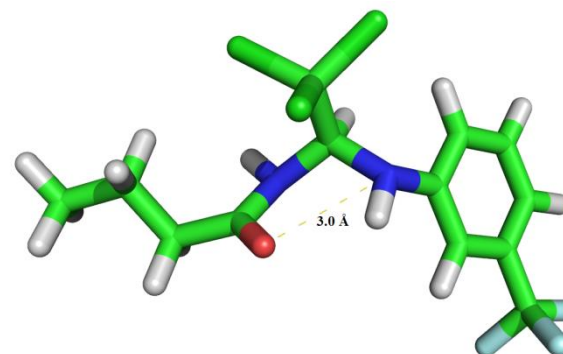
E11, ΔG = −107148.8 kcal/mol

E12, ΔG = −84079.4 kcal/mol

E13, ΔG = −84493.8 kcal/mol

Figure S6. Cont.

Table S15. Predicted results of the total clearance ($CL_{tot.}$) and half−life time ($T_{1/2}$) for Salubrinal and its analogues.

Comp.	Total clearance ($CL_{tot.}$), mL/min/kg			Half−life ($T_{1/2}$), h
	ADMETLab	**pkCSM ***		
		log $CL_{tot.}$	**$CL_{tot.}$**	
S1	0.780	−0.166	0.682	1.928
S2	0.660	−0.306	0.494	1.948
S3	0.709	−0.289	0.514	1.980
S4	0.609	−0.403	0.395	1.954
S5	1.092	−0.256	0.555	1.073
S6	1.108	−0.088	0.817	0.862
S7	0.860	−0.437	0.366	1.571
S8	0.773	−0.343	0.454	1.819
S9	0.802	−0.385	0.412	1.794
S10	0.792	−0.450	0.355	1.731
S11	0.764	−0.402	0.396	1.795
S12	0.819	−0.487	0.326	1.778
S13	0.793	−0.443	0.361	1.780
S14	0.834	−0.495	0.320	1.784
S15	0.921	−0.260	0.550	1.238
S16	0.893	−0.341	0.456	1.317
S17	0.780	−0.288	0.515	1.628
S18	0.901	−0.112	0.773	1.387
S19	0.865	−0.314	0.485	1.393
S20	0.825	−0.216	0.608	1.275
S21	0.790	−0.420	0.380	1.292
S22	0.862	−0.096	0.802	1.458
S23	0.793	−0.261	0.548	1.531
S24	0.745	−0.325	0.473	1.589
S25	0.811	−0.206	0.622	1.635
S26	0.872	−0.416	0.384	1.638
S27	0.781	−0.478	0.333	1.624
S28	0.739	−0.498	0.318	1.696
S29	0.798	−0.284	0.520	1.663

| Comp. | Total clearance (CL$_{tot.}$), mL/min/kg | | | Half–life (T$_{1/2}$), h |
| | ADMETLab | pkCSM * | | |
		log CL$_{tot.}$	CL$_{tot.}$	
S30	0.830	−0.282	0.522	1.663
S31	0.775	−0.225	0.600	1.562
S32	0.753	−0.553	0.280	1.694
S33	0.571	−0.394	0.404	1.792
S34	0.495	−0.592	0.256	1.704
S35	0.828	−0.360	0.440	1.605
S36	0.870	−0.540	0.288	1.605
S37	0.818	−0.122	0.755	1.785
S38	0.981	−0.193	0.641	1.475
S39	1.062	0.202	1.592	1.328
S40	0.992	0.154	1.426	1.478
S41	0.961	−0.051	0.889	1.724
S42	0.944	−0.037	0.918	1.648
S43	1.019	−0.071	0.849	1.611
S44	1.041	−0.065	0.861	1.708
S45	0.770	−0.039	0.914	1.929
S46	0.942	−0.166	0.682	1.902
S47	0.920	−0.214	0.611	1.862
S48	0.918	−0.224	0.597	1.849
S49	0.947	−0.229	0.590	1.866
S50	0.922	−0.319	0.480	1.832
S51	0.994	−0.143	0.719	1.583
S52	0.975	−0.223	0.598	1.845
S53	0.985	−0.086	0.820	1.630
S54	0.725	−0.221	0.601	1.863
S55	0.759	−0.351	0.446	1.833

* pkCSM provides the forecast result as the logCL$_{tot.}$ value. For the unification of the results, the obtained values were converted to CL$_{tot.}$