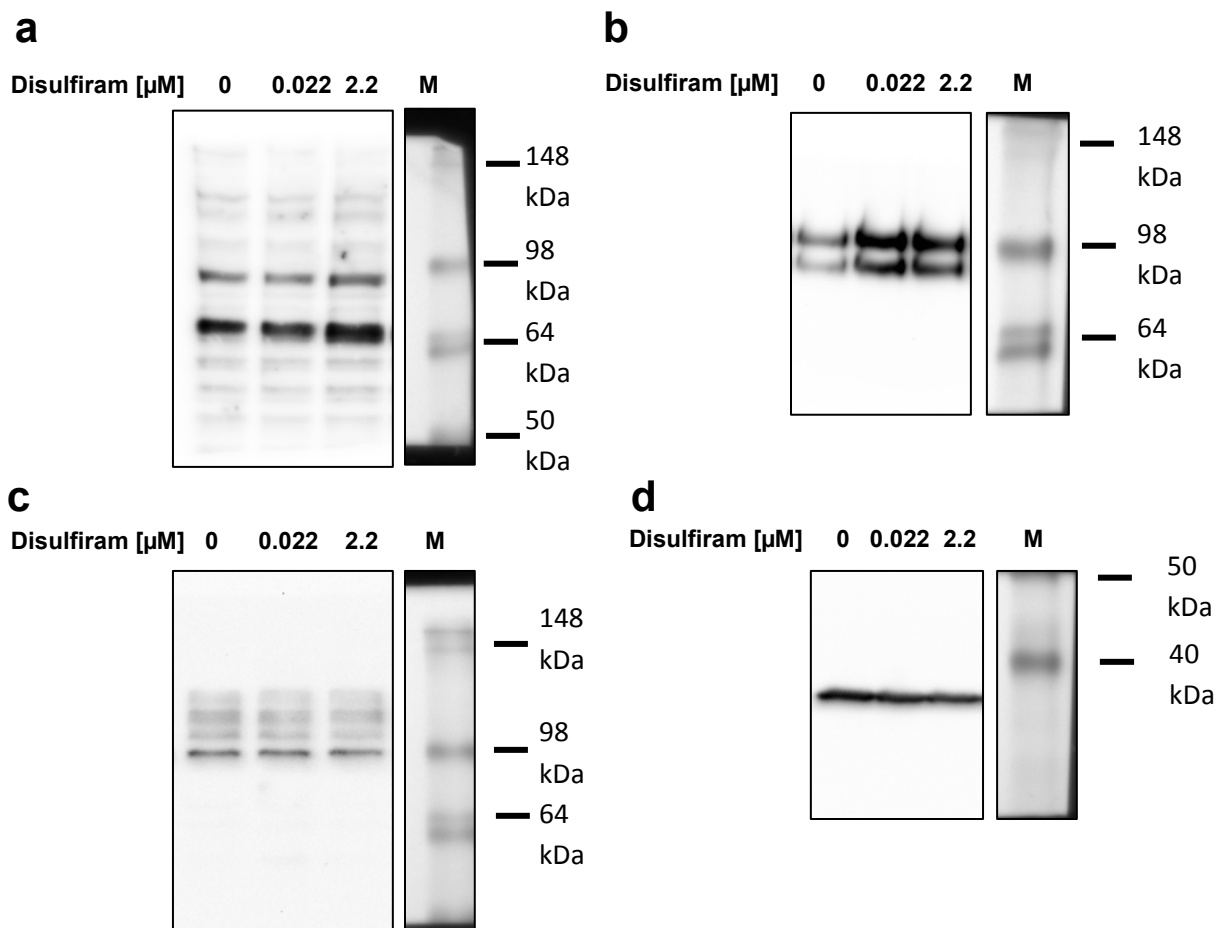


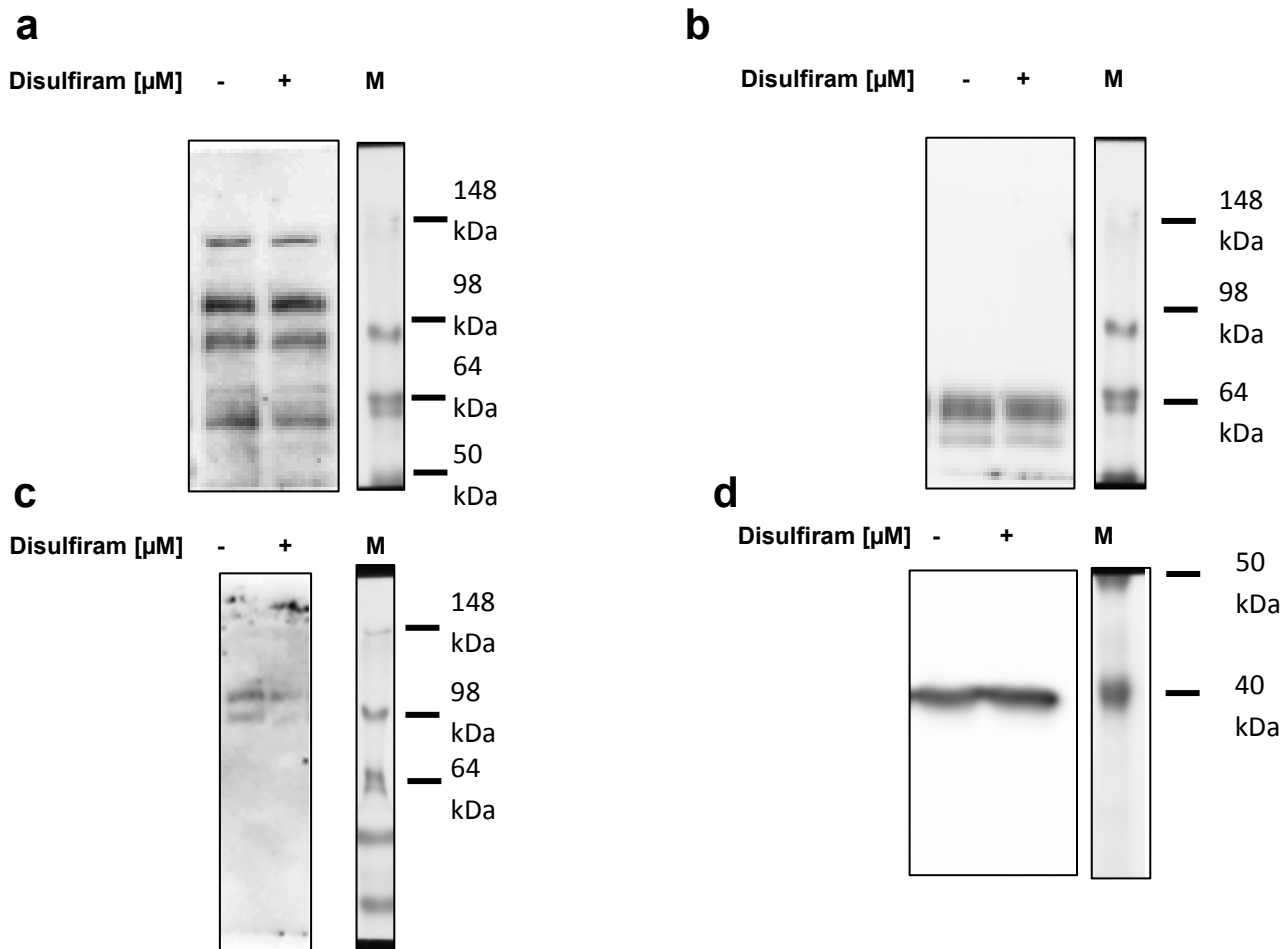
Identification of disulfiram as a secretase-modulating compound with beneficial effects on Alzheimer's disease hallmarks

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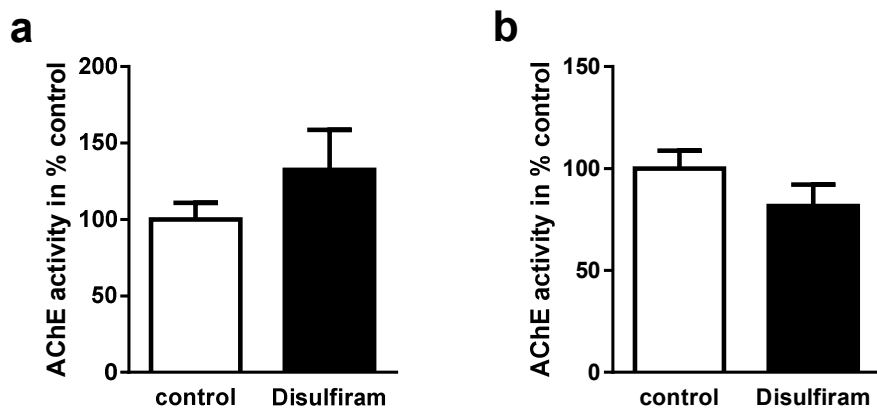
Suppl. Fig. 1 Examples of full-length blots from Fig. 2 C

Western Blot pictures in Fig. 2 C have been cropped for being able to combine several blots in one picture. Here, examples of full-length blots for each protein-detection are given where possible. Blots with cell lysates were cut at a height between 50 and 40 kDa to use the upper blot part for detection of ADAM10 or full-length APP and the lower blot part for detection of GAPDH. a) ADAM10; b) sAPP-alpha; c) APP; d) GAPDH. The lane with the marker (M) has been added to indicate molecular weights.



Suppl. Fig. 2 Examples of full-length blots from Fig. 3

Western Blot pictures in Fig. 3 have been cropped for presentation. Exemplary pictures of full-length blots for each protein-detection are given where possible. Blots with cell lysates (BACE1, TACE) were cut at a height between 50 and 40 kDa to use the upper blot part for detection of the proteinases and the lower blot part for detection of GAPDH. a) TACE; b) BACE1; c) sAPP-beta; d) GAPDH. The lane with the marker (M) has been added to indicate molecular weights.



Suppl. Fig. 3 Acetylcholine esterase activity in brain and ileum of disulfiram-treated AD model mice

Tissue from mice treated for two days with disulfiram or DMSO as control were sacrificed and brain and ileum tissue collected (ileum tissue was mechanically purified and washed with PBS). Homogenates of tissue samples were prepared in potassium phosphate buffer and diluted aliquots used for measuring AChE activity with Ellman's reaction (a: brain; b: ileum; $n \geq 9$ per group). Values are given as mean + SEM, statistical analysis was conducted by unpaired Student's t-test (Welsh correction for analysis of data from brain; ns, $p > 0.05$).

Suppl. Table 1 FDA-approved drugs tested for ADAM10 and BACE-1 promoter regulatory effect

Substances were initially tested for potential toxic/ proliferative effects in SH-SY5Y cells and subsequently diluted to obtain the final concentration in the dual promoter assay. 13 drugs were excluded because of remaining toxic effects and are therefore not included in the list.

Nr.	Drug	final conc. [µM]	Nr.	Drug	final conc. [µM]	Nr.	Drug	final conc. [µM]
1	Moroxydine HCl	3,15	101	Sulpiride s(-)	1,91	201	Denbutylline	2,04
2	Clindamycin HCl	1,54	102	Diphenhydramine HCl	2,56	202	Miltefosine	1,60
3	Felbamate	2,74	103	Promethazine HCl	2,30	203	Latanoprost	1,51
4	Cyclosporin a	0,54	104	Ranitidine HCl	2,08	204	Ouabain	0,02
5	Donepezil HCl	1,57	105	Naltrindole HCl	1,58	205	Clopidamide	1,89
6	Lincomycin	1,61	106	Idazoxan	3,20	206	Molsidomine	2,70
7	Lomofungin	2,08	107	Spiperone	1,65	207	Pravadoline	1,73
8	Mycophenolic acid	0,08	108	Epinephrine-(+)-tartrate l(-)	3,86	208	Tranilast	2,00
9	Novobiocin Na	1,07	109	Xylazine HCl	2,97	209	Alfuzosin	1,68
10	Rapamycin	0,71	110	Norepinephrine-(+)-tartrate (-)	2,05	210	Bromocriptine mesylate	1,00
11	Spectinomycin	1,97	111	Quetiapine fumarate	0,74	211	Clozapine	2,00
12	Bepiridil	1,58	112	Alprenolol HCl	2,62	212	Clothiapine	1,90
13	Amlodarone	1,01	113	Imipramine HCl	2,33	213	Actretin	2,00
14	Nicardipine	1,27	114	Amoxapine	2,08	214	Remoxipride	1,76
15	Pimozide	1,42	115	Mesulegine HCl	1,80	215	Calcifediol	1,63
16	Loperamide	1,27	116	Amfebutamone	2,73	216	Calcitriol	1,57
17	Fluspirilene	1,37	117	Metoclopramide HCl	2,18	217	Ketoconazole	1,23
18	Tolbutamide	2,42	118	Naltriben methanesulfonate hydrate	1,28	218	Oxatomide	1,53
19	Pinacidil	2,66	119	Vitamin a (acetate)	1,99	219	Disodium cromoglycate	1,28
20	Glipizide	1,47	120	Levallorphan tartrate	2,31	220	Capsaicin	2,14
21	PhentolamineHCl	2,06	121	Nalbuphine HCl	1,83	221	Dexamethasone	1,67
22	Quinine	1,81	122	Carbamylcholine Cl	4,44	222	Dipyridamole	1,30
23	Flufenamic acid	2,32	123	Carbamyl-beta-methylcholine Cl	4,05	223	Ethacrynic acid	2,16
24	Propafenone	1,91	124	Butyrylcholine Cl	3,75	224	Indomethacin	1,83
25	Phenytoin	2,59	125	Famotidine	1,94	225	Naproxen	2,84
26	Procainamide	2,40	126	Terfenadine	1,39	226	Clofibrate	2,69
27	Lidocaine	2,41	127	Isoniazid	4,77	227	Ibuprofen	3,17
28	Flecainide	1,38	128	Ticlopidine HCl	2,48	228	Benserazide HCl	2,54
29	Rosiglitazone maleate	1,38	129	Amorolfine	2,06	229	Debrisoquin sulfate	3,73
30	Amantadine HCl	3,48	130	Clemastine fumarate	1,90	230	Actarit	3,38
31	Oxymetazoline HCl	2,51	131	Vardenafil	1,34	231	Bumetanide	1,79
32	Ifenprodil	2,01	132	Linezolid	1,94	232	Neomycin sulfate	1,06
33	Naftopidil 2HCl	1,67	133	Docetaxil	0,01	233	Auranofin	0,02
34	Prazosin HCl	1,56	134	Olopatadine	1,94	234	Captopril	3,01
35	Clonidine HCl	2,45	135	Manidipine	1,07	235	Docebenone	2,00
36	Guanabenz acetate	2,83	136	Tolcapone	2,39	236	Tranlycypromine	4,91
37	Rilmenidine hemifumarate	3,63	137	Gestrinone	2,12	237	Piroxicam	1,97
38	Buphenine	1,95	138	Olmesartan	1,17	238	Moxifloxacin HCl	1,49
39	Yohimbine HCl	1,67	139	Nisoldipine	1,68	239	Troleandomycin	0,01
40	Dihydroergotamine mesylate	1,12	140	Lacidipine	1,43	240	Carbidopa	2,89
41	Nicefingolone	1,35	141	Olanzapine	2,09	241	Nimesulide	2,12
42	Emtricitabine	2,64	142	Lovastatin	1,62	242	Ketoprofen	2,57
43	Betaxolol HCl	2,13	143	Lamotrigine	2,55	243	Meloxicam	1,86
44	Pioglitazone	2,45	144	Azathioprine	2,36	244	Terbinafine HCl	2,24
45	Timolol maleate (s)	2,07	145	Sildenafil	1,38	245	Sodium phenylbutyrate	3,51
46	Xamoterol hemifumarate	1,93	146	Atovaquone	1,78	246	Ergothioneine	2,85
47	Clenbuterol	2,36	147	Sertaconazole	1,49	247	Ambroxol	1,73
48	Procaterol HCl	2,25	148	Butenafine	2,06	248	Idobenone	1,93
49	Salbutamol sulfate	2,73	149	Dorzolamide	2,01	249	Mevastatin	1,67
50	Pindolol	2,63	150	Escitalopram	2,01	250	Sinvastatin	1,56
51	Cimetrol HCl	2,98	151	Eprosartan	1,54	251	Suramin sodium	0,51
52	Dobutamine HCl	2,17	152	Sodium phenylacetate	4,13	252	Goserelin acetate	0,51
53	Pronethalol HCl	0,11	153	Ozagrel	2,86	253	Guaiacol	5,26
54	Sotalol HCl	2,40	154	Entacapone	2,14	254	Retinoic acid	2,18
55	Maprotiline HCl	2,36	155	Bopindolol malonate	1,72	255	Troglitazone	1,48
56	Nisoxetine HCl	2,41	156	Guanfacine HCl	2,31	256	Bezafibrate	1,81
57	Canthaxanthin	1,16	157	Tizanidine HCl	2,58	257	Raloxifene HCl	0,06
58	Pilocarpine HCl	3,14	158	Meglumine	3,35	258	Etoposide	0,04
59	Ipratropium Br	1,97	159	Propranolol HCl s(-)	2,21	259	Mitomycin c	0,08
60	Pirenzepine 2HCl	1,86	160	Carvedilol	1,61	260	Puromycin 2HCl	1,20
61	Telenzepine 2HCl	1,76	161	Cerivastatin	0,06	261	Delavirdine mesylate	0,06
62	Tropicamide	2,30	162	Aclarubicin	0,02	262	10-hydroxycamptothecin	0,04
63	Pancuronium Br	1,14	163	Flumazenil	2,15	263	Doxorubicin HCl	0,05
64	Ivermectin	0,75	164	Fenretinide	1,67	264	Cetirizine 2HCl	1,42
65	Physostigmine sulfate	2,37	165	Gefitinib	1,46	265	Lapatinib	0,04
66	Nialamide	2,19	166	Ibudilast	2,84	266	Methyl salicylate	0,17
67	Haloperidol HCl	1,74	167	Imatinib	1,32	267	Pioglitazone	1,83
68	Piribedil HCl	2,19	168	Montelukast	1,11	268	Pranlukast	1,36
69	Mepyramine maleate	2,29	169	Deprenyl	2,92	269	Rivastigmine	2,61
70	Trans-triprolidine HCl	0,05	170	Vatalanib	1,88	270	Rofecoxib	2,08
71	Cimetidine	2,59	171	Fumagillin	1,43	271	Ergotamine D-tartrate	1,12
72	Tiotidine	2,09	172	Exemestane	2,21	272	Sulindac	1,83
73	Zonisamide	3,08	173	Dinoprostone	1,85	273	Valproic acid	0,18
74	Zoledronic acid	2,40	174	Metformin	5,06	274	Calcipotriene	1,58
75	Naltrexone HCl	1,91	175	Anagrelide	2,55	275	Zafirlukast	0,01
76	zolmitriptan	2,15	176	Dofetilide	1,48	276	Zileuton	0,11
77	Memantine HCl	3,65	177	Erlotinib	1,66	277	Pentamidine	1,92
78	Aniracetam	2,98	178	Lobeline	1,94	278	Bambuterol	1,78
79	Riluzole HCl	2,79	179	Melatonin	2,81	279	Fentiazac	1,98
80	Propofol	3,67	180	Dinoprost	1,84	280	Mephenytoin	2,99
81	Mianserin HCl	2,47	181	HA1077	1,79	281	Diazoxide	2,83
82	Aminophylline	3,63	182	Hydroxytacrine maleate	3,05	282	Glyburide	1,32
83	Furafylline	2,51	183	Oxotremorine sesquifumarate	3,17	283	Minoxidil	3,12
84	nateglinide	2,06	184	Tacrine HCl	3,30	284	Tolazamide	2,10
85	Isoproterenol	3,09	185	Gallamine triethiodide	1,28	285	Nicorandil	0,12
86	AcetyldiholoneCl	4,47	186	Galanthamine HBr	2,27	286	Bexarotene	0,08
87	Atropine sulfate	2,26	187	Amiloride	2,46	287	Tranexamic acid	4,16
88	Decamethonium 2Br	2,53	188	Amlodipine	1,60	288	Celecoxib	1,71
89	Mecamylamine HCl	3,91	189	Nifedipine	1,45	289	Levetiracetam	3,84
90	Neostigmine Br	2,93	190	Diltiazem	1,89	290	Letrozole	2,29
91	Strychnine HCl	1,95	191	Nimodipine	1,56	291	Abamectin	0,75
92	Tubocurarine Cl (+)	1,07	192	Nitrendipine	1,81	292	Alfalcaldol	1,63
93	Butaciamol (+)	1,81	193	Verapamil	1,33	293	Anethole-trithione (anetholtrithion)	2,72
94	Apomorphine r (-)	2,44	194	Niguldipine HCl	1,01	294	Anastrozole	0,04
95	Chlorpromazine HCl	2,05	195	Flunarizine-2HCl	1,37	295	Bicalutamide	1,52
96	Domperidone	1,53	196	Gabapentin	3,82	296	Clodronate disodium	2,67
97	Fluphenazine 2HCl	1,49	197	Felodipine	1,70	297	Clindamycin palmitate	1,54
98	Pergolide mesylate	2,08	198	Clinidipine	1,33	298	Vorinostat	0,10
99	Raclopride l-tartrate s(-)	1,88	199	Phenoxybenzamine HCl	1,92	299	Didanosine	2,77
100	Risperidone	1,59	200	Trifluoperazine 2HCl	1,36	300	Dolasetron	2,01

Nr.	Drug	final conc. [µM]	Nr.	Drug	final conc. [µM]	Nr.	Drug	final conc. [µM]
301	Enalaprilat	1,88	401	Dehydroepiandrosterone	2,27	501	Pantoprazole	1,70
302	Fluvastatin Na	1,59	402	Desloratadine	2,10	502	Paroxetine HCl	1,98
303	Fosinopril	1,16	403	Dextromethorphan HBr	2,41	503	Pazufloxacin	2,05
304	Gemcitabine HCl	2,48	404	Diclofenac, Na	2,21	504	Pefloxacin mesylate	1,96
305	Ginkgolide a	0,06	405	2',3'-dideoxycytidine	3,09	505	Penciclovir	2,58
306	Granisetron	2,09	406	Diethylstilbestrol	2,44	506	Pentoxifylline	2,35
307	Nedaplatin	2,16	407	Diflunisal	2,61	507	Pencilin v potassium	1,87
308	Oxaliplatin	1,65	408	Disulfiram	2,20	508	Phenylbutazone	2,12
309	Anethole, trans-	4,41	409	Doxazosin mesylate	1,45	509	Piperacillin	1,26
310	Atazanavir	0,93	410	Doxifluridine	2,65	510	Pravastatin lactone	1,61
311	Mycophenolate mofetil	0,06	411	Doxofylline	2,45	511	Pranoprofen	2,56
312	Etoricoxib	1,82	412	Doxycycline HCl	1,47	512	Prednisolone	1,81
313	Clofarabine	2,15	413	Enalapril	1,74	513	Progesterone	2,08
314	Cabergoline	1,45	414	Enoxacin	2,04	514	Procarbazine HCl	2,95
315	Dilazep	1,08	415	Enrofloxacin	1,82	515	Prothionamide	3,63
316	Ibandronate	2,05	416	Ethisterone	2,09	516	Prednisone	1,82
317	Imipenem	2,18	417	Esomeprazole potassium	1,89	517	Pregnenolone	2,07
318	Lomustine	2,80	418	Estradiol	2,40	518	Primaquine phosphate	2,52
319	Iloprost	1,81	419	Estrinol	2,27	519	Praziquantel	2,09
320	Lomerizidine HCl	1,39	420	Estrone	2,42	520	Pyrantel pamoate	1,10
321	Lofexidine	2,52	421	Etilonate 2Na	3,20	521	Quinacrine 2HCl dihydrate	0,07
322	Meropenem	1,70	422	Etretinate	1,84	522	Quinapril HCl	1,49
323	Nifekalant HCl	1,61	423	Trichloromethiazide	1,72	523	Racecadotril	1,70
324	Octreotide	0,64	424	Famciclovir	2,03	524	Ranolazine 2HCl	1,53
325	Oseltamivir	2,09	425	Fenbendazole	0,09	525	Ramipril	1,57
326	Pamidronic acid	2,78	426	Fenbufen	2,57	526	Rebamipide	1,76
327	Pramipexole	3,09	427	Fenoldopam mesylate	2,14	527	Ribavirin	2,68
328	Triptorelin	0,50	428	Fenoprofen	2,70	528	Nelfinavir mesylate	0,98
329	Rifamycin sv	0,94	429	Fenofibrate	1,81	529	Rimantadine HCl	3,65
330	Risedronic acid	2,31	430	Finasteride	1,75	530	Propranolol	2,52
331	Rocuronium bromide	1,23	431	5-fluorouracil	5,02	531	Roxatidine acetate HCl	1,88
332	Ricobendazole	2,32	432	Flurbiprofen	2,68	532	Roxithromydin	0,78
333	Sulbactam	2,80	433	Fleroxacin	1,77	533	Rufloxacin	1,80
334	Thiamphenicol glydinate	1,58	434	Amitriptyline HCl	2,08	534	Sarafloxacin HCl	1,70
335	Tulobuterol	2,87	435	Floxuridine	2,65	535	Scopolamine n-butylbromide	1,81
336	Vinorelbine	0,03	436	Fluocinonide acetamide	1,44	536	Scopolamine HBr	2,15
337	Vindesine	0,03	437	Flubendazole	0,08	537	Secnidazole	3,53
338	Salmeterol	1,57	438	Flutamide	2,37	538	Sibutramine HCl	2,34
339	Vincristine sulfate	0,03	439	Fluconazole	2,13	539	Sparfloxacin	1,67
340	Acemetacin	1,57	440	Formestane	2,16	540	Spironolactone	1,57
341	Acetylsalicylic acid	3,63	441	Tofarur	3,27	541	Stanozolol	1,99
342	Acipimox	4,24	442	Furosemide	1,98	542	Streptomycin sulfate	0,04
343	Acetofenac	1,85	443	Ganciclovir	2,56	543	Sulfadoxine	2,11
344	Acycloguanosine	2,90	444	Gatifloxacin	1,74	544	Sulfadiazine	2,61
345	3'-azido-3'-deoxythymidine	2,45	445	Gentamycin sulfate	1,37	545	Sulfadimethoxine	2,11
346	Allopurinol	4,80	446	Gemfibrozil	2,61	546	Tamsulosin HCl	1,64
347	Alendronate	2,63	447	Gliclazide	2,02	547	Tamsulosin HCl	1,64
348	Altretamine	3,11	448	Glimepirid	1,33	548	Telmisartan	1,27
349	Albendazole	0,10	449	Guaifenesin	3,30	549	Tenoxicam	1,94
350	Sumatriptan succinate	1,58	450	Hexestrol	2,42	550	Terazosin HCl	1,69
351	Amifostine	3,05	451	Hydrocortisone	1,80	551	Tetracycline	1,47
352	Di-aminoglutethimide	2,81	452	Hydrocortisone 21-acetate	1,62	552	Tenatoprazole	1,89
353	4-aminosalicylic acid	4,27	453	17-hydroxyprogesterone	1,98	553	Temozolomide	3,37
354	5-aminosalicylic acid	4,27	454	Iodoxuridine	1,85	554	Tibolone	2,09
355	Ampicillin trihydrate	1,87	455	Ifosfamide	2,50	555	Tioconazole	1,69
356	Ampiroxycam	1,46	456	Imiquimod	2,72	556	Tinidazole	2,64
357	Apramycin	1,21	457	Indapamide	1,79	557	Tobramycin (free base)	1,40
358	Artemisinin	2,31	458	Ilopride HCl	1,82	558	Tosufloxacin	1,62
359	Atenolol	2,45	459	Itraconazole	0,93	559	Topotecan	0,06
360	Atracurium besylate	0,70	460	Ketoprofen+D153	2,57	560	Toremifene	1,61
361	Azaperone	2,00	461	Levamisole HCl	3,20	561	Tofenamic acid	2,50
362	Vinblastine sulfate	0,03	462	Levonorgestrel	2,09	562	Tolmetin Na	0,10
363	Azithromycin	0,87	463	Levodopa	3,31	563	Amoxicillin	1,79
364	Aztreonam	1,50	464	Levofloxacin HCl	1,81	564	Tramadol HCl	0,10
365	Betamethasone	1,30	465	Leflunomide	2,42	565	Triamcinolone	1,66
366	Bifonazole	2,11	466	Lisinopril	1,61	566	Trimethoprim	2,25
367	Bisacodyl	1,81	467	Lomefloxacin HCl	1,86	567	Tropisetron HCl	0,09
368	Bromhexine HCl	1,74	468	Loratadine	1,71	568	Tylosin tartrate	0,03
369	Buspirone HCl	1,70	469	Lorglumide	1,42	569	Valaciclovir	2,02
370	Canrenone	1,92	470	Losartan potassium	1,42	570	Vecuronium Br	0,05
371	Carbadox	2,49	471	Mebendazol	0,09	571	Venlafaxine HCl	2,36
372	Carboplatin	1,94	472	Medroxyprogesterone-17 acetate	1,69	572	Vidarabine	0,02
373	Carbamazepine	2,77	473	Mefenamic acid	2,71	573	Iproniazid	3,65
374	Cefoperazone acid	1,01	474	Melphalan	0,09	574	Benzamil HCl	1,83
375	Cefotaxime acid	1,43	475	Methyldopa	3,09	575	Bupivacaine HCl	2,27
376	Ceftazidime	1,20	476	Methylprednisolone	1,75	576	Astemizole	0,06
377	Chloramphenicol	2,02	477	Metoprolol tartrate	2,44	577	Ketotifen fumarate	2,11
378	Chlormadinone acetate	1,46	478	Methimazole	5,72	578	Levocastine HCl	0,03
379	Chlorambucil	2,15	479	Metronidazole	3,82	579	Naloxone HCl	2,00
380	Chlorpheniramine maleate	2,38	480	Miconazole	1,57	580	Naloxonazine 2HCl	0,04
381	Chloroquine phosphate	2,04	481	Minocycline HCl	1,43	581	Harmine	3,08
382	Thalidomide	2,53	482	Mitoxantrone 2 HCl	0,06	582	Cinaserin	1,92
383	Ciprofloxacin	1,97	483	Taxol	0,03	583	Dibenzepine HCl	2,21
384	Citalopram	2,01	484	Myclobutanil	2,26	584	Dihydroergocristine mesylate	1,07
385	Clarithromycin	0,87	485	Nadifloxacin	1,81	585	Fluperlapine	2,11
386	Climbazole	2,23	486	Nabumetone	2,86	586	Fluoxetine HCl	2,11
387	Clinafloxacin HCl	1,79	487	Naphazoline HCl	3,11	587	Ondansetron	0,04
388	Clomiphene citrate	1,61	488	Nefazodone	1,39	588	Ketanserin tartrate	1,65
389	Amisulprid	1,77	489	Niflumic acid	2,32	589	Tiotropium Br	1,38
390	Clopidogrel sulfate	2,03	490	Norethindrone	2,19	590	Mesoridazine besylate	0,07
391	Clobetasol propionate	1,40	491	Norfloxacin	2,05	591	Thioridazine HCl	1,76
392	Orphenadrine citrate	1,42	492	Nystatin	0,71	592	Cilostamide	0,08
393	Corticosterone	1,89	493	Ofloxacin	1,81	593	Etazolate	0,09
394	Crotamiton	3,22	494	Oflupraz	2,89	594	Amrinone	0,14
395	Cyclophosphamide monohydrate	2,50	495	Omeprazole	1,89	595	Irsogladine maleate	2,55
396	Cyproterone acetate	1,57	496	Oxcarbazepine	2,59	596	Mirinone	0,12
397	Cycloctidine HCl	0,12	497	Oxiconazole nitrate	1,52	597	Rolipram	2,37
398	Cytarabine	0,11	498	Oxaliillin sodium monohydrate	1,63	598	Siguazodan	0,09
399	Dacarbazine	3,59	499	Oxfendazole	2,07	599	Trequisin HCl	1,48
400	Danazol	1,94	500	Oxibendazole	0,10	600	Vinpocetine	1,86

Nr.	Drug	final conc. [µM]
601	Zaprinast	2,41
602	Zardaverine	0,10
603	Alprostadil	1,84
604	Misoprostol	0,07
605	Artesunate	1,70
606	Picotamide	1,74
607	Butoconazole nitrate	1,38
608	Mifepristone	0,03
609	Megestrol acetate	1,70
610	Melengestrol acetate	0,07
611	Tamoxifen citrate	0,07
612	Amprenavir	1,29
613	Aprepitant	1,22
614	Bosentan	1,18
615	Efavirenz	2,07
616	Taurocholic acid, sodium salt hydrate	1,27
617	Miglustat	2,98
618	Fulvestrant	1,08
619	Methysergide	0,02
620	Esmolol	2,21
621	Pantothenic acid	2,98
622	Capecitabine	1,82
623	Phenylpropanolamine	4,32
624	Succinylcholine	2,25
625	L-thyroxine[[3-[4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diidophenyl]-l-alanine]	0,84
626	Cyproheptadine	2,27
627	Benzylamine	2,11