Supplementary Material

Modeling Chemical Interaction Profiles: I. Spectral Data-Activity Relationship and Structure-Activity Relationship Models for Inhibitors and Non-inhibitors of Cytochrome P450 CYP3A4 and CYP2D6 Isozymes

Table 1. Tentative substrates and inhibitors of CYP3A4 isozyme. The calculations were carried out for hazardous waste chemicals recorded in the ATSDR EH Portfolio using the P450 substrate and P450 inhibitor modules of the ACD/ADME suite from Advanced Chemistry Development, Inc. (Toronto, ON, Canada). A probability (*p*) cutoff of 0.5 and reliability index (*RI*) cutoff of 0.4 were applied. Several compounds, whose activity was confirmed by screening the literature, are shown in **bold** (but an extensive systematic search for all compounds was not performed at this time).

3A4		
CAS	**Substrates**	**Inhibitors**
3218-36-8	(1,1a-biphenyl)-4-carboxaldehyde	
39001-02-0	1,2,3,4,6,7,8,9-octachlorodibenzofuran	
67562-39-4	1,2,3,4,6,7,8-heptachlorodibenzofuran	
35822-46-9	1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin	
70648-25-8	1,2,3,4,6,7,9-heptachlorodibenzofuran	
58200-70-7	1,2,3,4,6,7,9-heptachlorodibenzo-p-dioxin	
69698-58-4	1,2,3,4,6,8,9-heptachlorodibenzofuran	
55673-89-7	1,2,3,4,7,8,9-heptachlorodibenzofuran	
38178-99-3	1,2,4,5,7,8-hexachoro-(9H)-xanthene	
470-82-6	1,8-cineole	
28548-08-5	12-ketoendrin	12-ketoendrin
132861-79-1	15-tetracosynoic acid, methyl ester	15-tetracosynoic acid, methyl ester
2597-11-7		1-hydroxychlordene
832-69-9	1-methylphenanthrene	
2381-21-7	1-methylpyrene	
5566-34-7	Gamma-chlordane	Gamma-chlordane
2051-24-3	decachlorobiphenyl	
40186-72-9	2,2′,3,3′,4,4′,5,5′,6-nonachlorobiphenyl	
35694-08-7	2,2′,3,3′,4,4′,5,5′-octachlorobiphenyl	
52663-79-3	2,2′,3,3′,4,4′,5,6,6′-nonachlorobiphenyl	
42740-50-1	2,2′,3,3′,4,4′,5,6′-octachlorobiphenyl	
35065-30-6	2,2′,3,3′,4,4′,5-heptachlorobiphenyl	
33091-17-7	2,2′,3,3′,4,4′,6,6′-octachlorobiphenyl	
52663-71-5	2,2′,3,3′,4,4′,6-heptachlorobiphenyl	
52663-77-1	2,2′,3,3′,4,5,5′,6,6′-nonachlorobiphenyl	
52663-75-9	2,2′,3,3′,4,5,5′,6′-octachlorobiphenyl	
68194-17-2	2,2′,3,3′,4,5,5a6-octachlorobiphenyl	
52663-74-8	2,2′,3,3′,4,5,5′-heptachlorobiphenyl	

Table 1. *Cont.*

3A4		
CAS	**Substrates**	**Inhibitors**
52663-73-7	2,2′,3,3′,4,5,6,6′-octachlorobiphenyl	
38411-25-5	2,2′,3,3′,4,5,6′-heptachlorobiphenyl	
68194-16-1	2,2′,3,3′,4,5,6-heptachlorobiphenyl	
40186-71-8	2,2′,3,3′,4,5′,6,6′-octachlorobiphenyl	
52663-70-4	2,2′,3,3′,4,5′,6′-heptachlorobiphenyl	
40186-70-7	2,2′,3,3′,4,5′,6-heptachlorobiphenyl	
55215-18-4	2,2′,3,3′,4,5-hexachlorobiphenyl	
52663-65-7	2,2′,3,3′,4,6,6′-heptachlorobiphenyl	
61798-70-7	2,2′,3,3′,4,6-hexachlorobiphenyl	
2136-99-4	2,2′,3,3′,5,5′,6,6′-octachlorobiphenyl	
52663-67-9	2,2′,3,3′,5,5′,6-heptachlorobiphenyl	
52663-64-6	2,2′,3,3′,5,6,6′-heptachlorobiphenyl	
52704-70-8	2,2′,3,3′,5,6-hexachlorobiphenyl	
38411-22-2	2,2′,3,3′,6,6′-hexachlorobiphenyl	
52663-76-0	2,2′,3,4,4′,5,5′,6-octachlorobiphenyl	
35065-29-3	2,2′,3,4,4′,5,5′-heptachlorobiphenyl	
74472-52-9	2,2′,3,4,4′,5,6,6′-octachlorobiphenyl	
60145-23-5	2,2′,3,4,4′,5,6′-heptachlorobiphenyl	
74472-47-2	2,2′,3,4,4′,5,6-heptachlorobiphenyl	
52663-69-1	2,2′,3,4,4′,5′,6-heptachlorobiphenyl	
74472-48-3	2,2′,3,4,4′,6,6′-heptachlorobiphenyl	
52712-05-7	2,2′,3,4,5,5′,6-heptachlorobiphenyl	
74472-49-4	2,2′,3,4,5,6,6′-heptachlorobiphenyl	
68194-15-0	2,2′,3,4,5,6′-hexachlorobiphenyl	
68194-14-9	2,2′,3,4,5′,6-hexachlorobiphenyl	
52663-68-0	2,2′,3,4′,5,5′,6-heptachlorobiphenyl	
74487-85-7	2,2′,3,4′,5,6,6′-heptachlorobiphenyl	
68194-08-1	2,2′,3,4′,6,6′-hexachlorobiphenyl	
68194-09-2	2,2′,3,5′,6,6′-hexachlorobiphenyl	
33979-03-2	2,2′,4,4′,6,6′-hexachlorobiphenyl	
74472-53-0	2,3,3′,4,4′,5,5′,6-octachlorobiphenyl	
39635-31-9	2,3,3′,4,4′,5,5′-heptachlorobiphenyl	
41411-64-7	2,3,3′,4,4′,5,6-heptachlorobiphenyl	
74472-50-7	2,3,3′,4,4′,5′,6-heptachlorobiphenyl	
74472-51-8	2,3,3′,4,5,5′,6-heptachlorobiphenyl	
39635-35-3	2,3,3′,4,5,5′-hexachlorobiphenyl	
74472-43-8	2,3,3′,4,5′,6-hexachlorobiphenyl	
74472-46-1	2,3,3′,5,5′,6-hexachlorobiphenyl	
129-79-3		2,4,7-trinitrofluorenone
3674-66-6	2,5-dimethyl-phenanthrene	
54964-82-8	2,6,10,14-tetramethyloctadecane	
31551-45-8		2,7-dinitrofluorenone
117-79-3		2-aminoanthraquinone
2698-41-1		2-chlorobenzylidene malononitrile
31081-17-1	2-methyl-5-propylnonane	

Table 1. *Cont.*

3A4		
CAS	**Substrates**	**Inhibitors**
1560-97-0	2-methyldodecane	
2531-84-2	2-methyl-phenanthrene	
91-94-1		3,3´-dichlorobenzidine
119-90-4		3,3´-dimethoxybenzidine
33954-06-2	3-5-dimethylphenanthrene	
56-49-5	3-methylcholanthrene	
17312-57-1	3-methyldodecane	
101-14-4		4,4´-methylenebis(2-chloroaniline)
92-67-1		4-aminobiphenyl
832-64-4	4-methylphenanthrene	
4736-56-5	5alpha-stigmast-22-en-3beta-ol	
3697-24-3	5-methylchrysene	
57-97-6	7,12-dimethylbenz(a)anthracene	
20302-14-1		9,9-diphenylfluorene
779-02-2	9-methylanthracene	
34256-82-1	Acetochlor	
1757-18-2	Akton	
15972-60-8	Alachlor	
309-00-2	Aldrin	Aldrin
56534-02-2		Alpha-chlordene
834-12-8	Ametryn	
92-87-5		Benzidine
30777-19-6	Benzo(b)fluorene	
61089-87-0	Benzofluorene	
205-39-0	Benzonaphthofuran	
53-89-4		Benzpiperylon
56534-03-3		Beta-chlordene
33399-00-7	Bromfenvinphos	
128-37-0		Butylated hydroxytoluene
133-06-2		Captan
786-19-6	Carbophenothion	Carbophenothion
143-50-0	Chlordecone	Chlordecone
3734-48-3		Chlordene
470-90-6	Chlorfenvinphos	
24934-91-6	Chlormephos	
26264-07-3		Chloroanthraquinone
2921-88-2	**Chlorpyrifos**	
57-88-5	Cholest-5-en-3beta-ol	
14982-53-7	Cholestane	
80-99-9	Cholestene-3-ol	
218-01-9	Chrysene	
5103-71-9	Cis-chlordane	Cis-chlordane
360-68-9	Coprosterol	
56-72-4		Coumaphos
26444-49-5		Cresyl diphenyl phosphate

Table 1. *Cont.*

3A4		
CAS	**Substrates**	**Inhibitors**
7700-17-6	Crotoxyphos	Crotoxyphos
21725-46-2	Cyanazine	
2636-26-2	Cyanophos	Cyanophos
68359-37-5		Cyfluthrin
68085-85-8		Cyhalothrin
52315-07-8		Cypermethrin
950-10-7	Cytrolane	
789-02-6	DDT, O,P′-	
50-29-3	DDT, P,P′-	
52918-63-5		Deltamethrin
13684-56-5		Desmedipham
333-41-5	Diazinon	Diazinon
1770-80-5	Dibutyl chlorendate	Dibutyl chlorendate
2528-36-1	Dibutyl phenyl phosphate	
115-32-2	Dicofol	
60-57-1	Dieldrin	Dieldrin
60-51-5	Dimethoate	
29062-98-4	Dimethyl phenanthrene	
78-34-2	Dioxathion	
298-04-4	**Disulfoton**	
13560-92-4	Dechlorane 603	Dechlorane 603
68937-40-6		Tris(isobutylphenyl) phosphate
68937-41-7		Isopropylphenyl phosphate
115-29-7	Endosulfan	Endosulfan
959-98-8	Alpha-endosulfan	Alpha-endosulfan
33213-65-9	Beta-endosulfan	Beta-endosulfan
1031-07-8	Endosulfan sulfate	Endosulfan sulfate
72-20-8	Endrin	Endrin
7421-93-4	Endrin aldehyde	Endrin aldehyde
53494-70-5	Endrin ketone	Endrin ketone
2104-64-5		EPN
4651-51-8	(3beta)-ergost-5-en-3-ol	
563-12-2	Ethion	Ethion
13194-48-4	Ethoprop	
91-53-2		Ethoxyquin
22224-92-6	Fenamiphos	
122-14-5	Fenitrothion	Fenitrothion
64257-84-7		Fenpropathrin
115-90-2	Fensulfothion	Fensulfothion
55-38-9	Fenthion	Fenthion
69770-45-2		Flumethrin
85509-19-9		Flusilazole
944-22-9	Fonophos	Fonophos
56641-38-4		Gamma-chlordene
86-50-0		Guthion

Table 1. *Cont.*

3A4		
CAS	**Substrates**	**Inhibitors**
76-44-8	Heptachlor	Heptachlor
1024-57-3	Heptachlor epoxide	Heptachlor epoxide
2440-02-0		Heptachloronorbornene
70-30-4	Hexachlorophene	Hexachlorophene
16958-85-3	Hexadecanoic acid, octyl ester	
630-06-8	Hexatriacontane	
2899-02-7	1,3-dichloro-1,3-bis(2,4,6-trichlorophenyl)urea	
42509-80-8	Isazophos	
465-73-6	Isodrin	Isodrin
1617-70-5	Lupenone	
121-75-5	Malathion	Malathion
57837-19-1	Metalaxyl	
301-12-2	Metasystox R	
950-37-8	Methidathion	
2032-65-7	Methiocarb	
41637-90-5	Methylchrysene	
29253-36-9	Methylethylnaphthalene	
298-00-0	Methyl parathion	Methyl parathion
953-17-3	Methyl trithion	Methyl trithion
51218-45-2	Metolachlor	
2385-85-5	Mirex	Mirex
5103-73-1	Cis-nonachlor	Cis-nonachlor
39765-80-5	Trans-nonachlor	Trans-nonachlor
18181-70-9	Iodofenphos	Iodofenphos
2524-09-6	o,o,s-triethyl-dithiophosphate	
32536-52-0	Octabromodiphenyl-ether	
31472-83-0	Octachlorobiphenyl	
706-78-5		Octachlorocyclopentene
3268-87-9	Octachlorodibenzo-*p*-dioxin	
112516-18-4	Octahydrotrimethyl-(1-methylethyl)-phenanthrene	Octahydrotrimethyl-(1-methylethyl)-phenanthrene
511-15-9	Octahydrotrimethyl(methylethyl)-phenanthrenol	
27304-13-8	Oxychlordane	Oxychlordane
56-38-2	Parathion	Parathion
630-07-9	Pentatriacontane	
86508-42-1	Perfluoro compounds, c5–18	
77-09-8		Phenolphthalein
298-02-2	**Phorate**	
13366-73-9		Photodieldrin
39801-14-4	Photomirex	Photomirex
150-86-7	Phytol	
51-03-6		**Piperonyl butoxide**
311-45-5	**Paraoxon**	**Paraoxon**

Table 1. *Cont.*

3A4		
CAS	**Substrates**	**Inhibitors**
1610-18-0	Prometon	
7287-19-6	Prometryn	
2312-35-8	Propargite	
139-40-2	Propazine	
34643-46-4	Prothiophos	
299-84-3	Ronnel	
83-79-4		Rotenone
78-48-8	**Tribufos**	
94-59-7		Safrole
85-60-9	4,4´-butylidenebis(6-tert-butyl-3-methylphenol)	
515-03-7	Sclareol	Sclareol
1014-70-6	Simetryn	
601-58-1	Stigmastane	
8001-50-1	Strobane	Strobane
57-24-9	Strychnine	
3689-24-5	Sulfotep	
35400-43-2	**Sulprofos**	Sulprofos
88671-89-0	Systhane	Systhane
1401-55-4		Tannin
514-07-8	Taraxerone	
56803-37-3		t-butylphenyl diphenyl phosphate
79538-32-2	Telfluthrin	
3383-96-8	Temephos	Temephos
13071-79-9	Terbufos	
33693-04-8	Terbumeton	
886-50-0	Terbutryn	
4181-95-7	Tetracontane	
116-29-0	Tetradifon	
107-49-3	Tetraethyl pyrophosphate	
3590-84-9		Tetraoctylstannane
8001-35-2	Toxaphene	Toxaphene
5103-74-2	Trans-chlordane	Trans-chlordane
2303-17-5	Triallate	
126-73-8	Tributylphosphate	
688-73-3	Tributyltin	
1330-78-5		Tricresyl phosphate
78-30-8		Tri-o-cresyl phosphate
869-59-0		Trioctylstannane
603-34-9	Triphenyl amine	
217-59-4	Triphenylene	
639-58-7	Triphenyltin chloride	
126-72-7	Tris(2,3-dibromopropyl) phosphate	
6145-73-9	Tris(2-chloropropyl) phosphate	
25155-23-1		Trixylyl phosphate
81-81-2	Warfarin	

Table 2. Tentative substrates and inhibitors of CYP2D6 isozyme. The calculations were carried out for hazardous waste chemicals recorded in the ATSDR EH Portfolio using the P450 substrate and P450 inhibitor modules of the ACD/ADME suite from the Advance Chemistry Development, Inc. (Toronto, ON). A probability (*p*) cutoff of 0.5 and reliability index (*RI*) cutoff of 0.4 were applied. Several compounds, whose activity was confirmed by screening the literature, are shown in **bold** (but an extensive systematic search for all compounds was not performed at this time).

2D6		
CAS	**Substrates**	**Inhibitors**
538-74-9		Dibenzyl sulphide
1165-57-7		1-phenyl-2-(3-phenylphenyl)benzene
95-73-8		2,4-dichlorotoluene
612-94-2		2-phenylnaphthalene
1165-14-6		1,2,3-tri(phenyl)benzene
203-64-5		4H-cyclopenta(def)phenanthrene
486-60-2		5-hydroxy-6,7-furanocoumarin
260-94-6	Acridine	
30777-19-6		Benzo(b)fluorene
207-08-9		Benzo(k)fluoranthene
61089-87-0		Benzofluorene
53-89-4		Benzpiperylon
786-19-6	Carbophenothion	
298-04-4	**Disulfoton**	
563-12-2	Ethion	
91-53-2		Ethoxyquin
55-38-9	Fenthion	
944-22-9	Fonophos	
58-27-5		Menadione
537-46-2	**Methamphetamine**	Methamphetamine
27323-29-1	Methylcarbazole	
953-17-3	Methyl trithion	
298-02-2	**Phorate**	
78-48-8	S,S,S-tributyl phosphorotrithioate	
35400-43-2	**Sulprofos**	
13071-79-9	Terbufos	
869-59-0		Trioctylstannane