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Center for Drug Information and Pharmacy Practice<sup>1</sup>, ABDA – Federal Union of German Associations of Pharmacists, Berlin, and Institute of Legal Medicine<sup>2</sup>, University of Hamburg, Germany

## **Therapeutic and toxic blood concentrations of more than 800 drugs and other xenobiotics**

M. SCHULZ<sup>1</sup>, A. SCHMOLDT<sup>2</sup>

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*Dr. Martin Schulz, Zentrum für Arzneimittelinformation und Pharmazeutische Praxis (ZAPP), ABDA, Jaegerstrasse 49/50, 10117 Berlin, Germany  
M.Schulz@abda.aponet.de*

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In order to assess the significance of drug levels measured in clinical and forensic toxicology as well as for Therapeutic Drug Monitoring (TDM) it is essential that good collections of data are readily available. For more than 800 substances, therapeutic ('normal') and, if data was available, toxic, and fatal plasma concentrations as well as elimination half-lives were compiled in a table. The compilation includes data for hypnotics, benzodiazepines, neuroleptics, antidepressants, sedatives, analgesics, anti-inflammatory agents (e.g., NSAIDs), antihistamines, antiepileptics, betaadrenergic antagonists, antibiotics (penicillins, cephalosporins, aminoglycosides, gyrase inhibitors), diuretics, calcium-channel blockers, cardiac glycosides, antiarrhythmics, antiasthmatics, ACE-inhibitors, opiate agonists, and local anesthetics, among others. In addition, toxicologically relevant xenobiotics were listed. Data have been abstracted from published information, both compilations and primary sources and have been completed with data collected in our own forensic and clinical toxicology laboratories. Wherever possible, ranges for therapeutic plasma concentrations are expressed as trough concentration at steady state. The half-life values given for each drug are chosen to represent the terminal log-linear phase at most. It is the purpose to rapidly assess the significance of drug levels for the therapeutic monitoring of patients, and to facilitate the diagnostic and clinical assessment in case of intoxications.

### **1. Introduction**

It has been common for several years that plasma concentrations of drugs having a narrow therapeutic range have to be measured. This accounts, among others, for antiepileptics, cardiac glycosides, aminoglycosides, antiarrhythmics, theophylline, immunosuppressants, and few cytostatics. It is indicated to draw blood samples for the following reasons: if doses are high and borderline, if signs of overdosage occur although the dose is within normal range (e.g. genetic polymorphism), if there is no effect although the dose is correct or if non-compliance can be expected. In general, plasma concentrations at steady state are retrievable from dosage and pharmacokinetic data. However, sufficient pharmacokinetic data are often not available. Therefore, it makes sense to offer a compilation of therapeutic and toxic plasma concentration ranges for quick information. A list [469] published in 1997 has been completely revised and updated. In particular, data for drugs recently introduced to the market have been added. Reviews, compilations of other authors [e.g., 28, 99, 100, 109, 111, 112, 114, 155, 268, 269, 340, 354, 395, 423, 426–429, 495, 528, 534] and publications concerning individual drugs/xenobiotics and case reports have been used to set up the database. Experience

gained over several years from working in the clinical and forensic toxicological field also contributed to the following list.

### **2. Selection and criteria for evaluation**

The substances have been selected by clinical and toxicological aspects, by frequency of prescribing and other matters in the area of internal intensive care medicine as well as clinical and forensic toxicology. There is an increase in determining antibiotic concentrations using analytical and chemical methods and there are special cases which are closely monitored although therapeutic concentrations depend on the susceptibility of the microorganisms and tissue concentrations are often more reliable.

Screening the data in daily practice, it became obvious that for many well known drugs there is only insufficient pharmacokinetic data available. However, for current substances little documented data is published about intoxications and their plasma/blood concentrations.

In general, therapeutic plasma concentration ranges or concentrations found after therapeutic dosing refer to trough levels at steady state. Inter-individual deviation is high. Therefore, any data listed can only be taken as orientation.

Often, it is not possible to find the threshold between the therapeutic and toxic concentration for the specific patient. This is the case if tolerance develops and if drug interactions or additional diseases are involved. In order to keep the overall context clear, we preferred not to go into further details.

Data about fatal plasma concentrations consciously orient on life threatening or lethal intoxications who occurred at low plasma concentrations so that actual and potential dangers in clinical cases are not being underestimated. Many intoxicated patients survived even with significantly higher concentrations. It is also difficult to relate the concentrations to the clinical picture because the interval between intake of the drug and drawing a blood sample is

generally unknown. In any case, it is more relevant to have the correct concentration measured rather than how much drug has been – presumably – taken. Statements about case histories are often not reliable. And often, it is not known how much drug has been absorbed after intake of charcoal, due to vomiting and/or irrigation of the stomach. Elimination half-lives are statistically more reliable than data gathered in case of intoxications. Yet even with this data, substantial deviation can be expected. In addition, most pharmacokinetic parameters are retrieved from healthy subjects after application of relatively low doses. The data indicated generally deals with the terminal elimination half-life which most of the time is higher than the half-life of the intended biological effect (see annotations).

**Table: Therapeutic ('normal'), toxic, and comatose-fatal blood-plasma/serum concentrations (µg/mL) in man**

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Acamprosate	appr. 0.37–0.65 <sup>231</sup>			13–20 <sup>232</sup>	[155, 444]
Acebutolol	0.2–2 (0.5–1.255)			15–20	[440, 466]
N-Acetylacetolol <sup>1</sup>	1–2.5			90–150	[466]
Accainide	see (N-Acetyl-) Procainamide				
Acecarbromal(um)	10–20 (sum)	25–30		?	
Acemetacin	see Indomet(h)acin				
Acenocoumarol	0.03–0.1 <sup>197</sup>	0.1–0.15		3–11	[155, 340, 527, 528]
Acetaldehyde	0–30	100–125			[527, 528]
Acetaminophen	see Paracetamol				
Acetazolamide	(4–)10–20 <sup>267</sup>	25–30		2–6	[155, 468, 469, 528]
Acetohexamide	20–70	500		1.3	[423]
Acetone	(2–)5–20	100–400; 2000 <sup>8</sup>	550	(6–)8–31	[528, 545, 573]
Acetonitrile			0.77		[528]
Acetyldigoxin <sup>3</sup>	0.0005–0.0008	0.0025–0.003	0.005	40–70	[420, 516]
Acetylsalicylic acid (ASS, ASA) <sup>2</sup>	20–200	300–350	(400–)500	3–20 <sup>37</sup>	[77, 207, 234, 329, 334, 409, 548]
Acitretin	appr. 0.01–0.05 <sup>112</sup>			2–4 <sup>6</sup>	[291, 488]
Acyclovir	(0.4–0.63) 0.5–1.5 <sup>203</sup>			2–5 <sup>83</sup>	[148, 155, 358, 476, 527]
Adipidone-Meglumine	850–1200			0.5	[489]
Äthanol	see Ethanol			– <sup>139</sup>	
Ajmaline	(0.1–) 0.53–2.21 (?)			5.5 <sup>8</sup>	[155, 426]
Albendazole	0.5–1.5 <sup>92</sup>			8–9 <sup>92</sup>	[104, 333, 348, 572]
Albuterol	see Salbutamol				
Alcuronium	0.3–3			3.3±1.3	
Aldrin	–0.0015	0.0035			[528]
Alendronate	<0.005			– <sup>6</sup>	[411]
Alfentanil	0.03–0.6 <sup>4</sup>			0.6–2.3 <sup>96</sup>	[299, 327, 462, 541]
Alfuzosine	0.003–0.06			3–9	[423]
Alimemazine (Trimeprazine)	0.05–0.4	0.5	1–3.2	8	[114, 428]
Alizapride	0.1–2			2–3	[423]
Allobarbitol	2–5	10	20	40–48	
Allopurinol	2–19			0.5–3	[133, 528]
Alphaprodine	0.87–1			1.6–2.6	[528]
Alprazolam	0.005–0.05 (–0.08) <sup>65</sup>	0.1–0.4	252	6–20	[114, 155, 272, 286, 293, 301, 341]
Alprenolol <sup>48</sup>	0.025–0.14	1–2	40–48	2–7	[466]
Aluminium	<0.005 <sup>234</sup>	0.05–0.15	4.4 <sup>8</sup>	appr. 0.5	[133, 371, 429, 528]
Amantadine	0.2–0.6 (–1)	1; 2.4 <sup>8</sup>	21 <sup>8</sup>	9–15	
Amfebutamone	see Bupropion				
Amikacin <sup>76</sup>	10–25	30		2–3	[71]
Aminobenzoic acid	300–600	600			[429]
Aminoglutethimide	0.5–25			13.3 ± 2.65	[133, 155, 528]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Aminophenazone	10–20			appr. 2–4	[423]
4-Aminopyridine (Fampridine)	0.025–0.075	0.14 <sup>8</sup> ; 0.2		3–3.5	[503, 527, 528]
5-Aminosalicylic acid (5-AS, 5-ASA)	see Mesalazine				
Amiodarone <sup>261</sup>	(0.5–) 1–2 (–2.5)	2.5–3		30–120 <sup>6</sup>	[54, 133, 155, 449]
Amisulpride	–0.4			12–18	[423]
Amitriptyline <sup>7, 48</sup>	0.05–0.3	0.5–0.6	1.5–2	30–50	[45, 57, 114, 121, 151, 181, 304, 305, 345, 415]
Amlodipine	0.005–0.015 (0.003–0.011)	0.088 <sup>8, 165</sup>	0.1–0.2 <sup>8, 166</sup>	34–50	[268, 275, 492]
Ammonia	0.5–1.7				[528]
Amobarbital	1–5	5–6	10	15–30	
Amodiaquine	–0.05 <sup>270</sup>			– <sup>270</sup>	[133, 510]
Amoxapine	0.18–0.6 <sup>151</sup>	3	5	8	[340]
Amoxicillin	0.5–1 (5–15)			1–2	[423]
Amphetamine	0.02–0.1	0.2	0.5–1	4–8	[201, 429]
Amphotericin B	(0.1–) 0.2–3	(3–) 5–10		24–48 <sup>110</sup>	[79, 192, 310]
Ampicillin	0.02–2 (2–20)			1	[71]
Amrinone	1–2(–4)			3–12	[155, 200, 269]
Amsacrine	0.1–0.5 (0.15–5.5)			5–7	
Anileridine	<0.5		0.9 <sup>8</sup>	?	[528]
Aniline	appr. –1 (urine)		6		[133, 528]
Antimony	–0.01	0.2			[133]
Antipyrine	see Phenazone				
Apomorphine	0.002–0.02 <sup>204</sup>			appr. 0.75	[155, 527]
Aprindine <sup>48</sup>	1–2	2–3		13–50	
Aprobarbital	4–20	30–40	50	14–34	
Arsenic	0.002–0.07	0.05–0.25	9–15		[133, 528]
Articaine	<1.5–2 (?)			0.3 (–1)	[379]
Ascorbic acid (Vitamin C)	4–15	?		– <sup>6</sup>	[39, 155, 241, 321, 546]
Astemizole	0.002–0.05 <sup>43</sup>	14 <sup>8</sup>		appr. 20 <sup>6, 42, 43</sup>	[28, 155, 487a]
Atenolol	0.1–1 (–2) <sup>77</sup>	2–3	27 <sup>8</sup>	4–14 <sup>9</sup>	[155, 426, 466, 504]
Atovaquone	13.9 ± 6.9 (>15)			2–3 <sup>6</sup>	[490]
Atracurium(besylate)	0.1–0.5 (–5)			appr. 0.5	
Atropine	0.002–0.025 <sup>155</sup>	0.03–0.1	0.2	2–6.5, 13–38	[429, 524, 528]
Azapropazone (Apazone)	40–80			8–24	
Azathioprine <sup>10</sup>	–2			1–4 <sup>11</sup>	
Azelastine	0.002–0.003(–0.01)			22–25	[423]
Azithromycin	appr. 0.04–1			50–60 (2–4 <sup>6</sup> )	[17, 312, 402, 436, 470]
Aztreonam	1–10 (50–250)			1.5–2	[528]
Baclofen	0.08–0.4(–0.6)	1.1–3.5	6–9.6	6.8 ± 0.7	[28, 340, 528]
Bambuterol	see Terbutaline			10	
Barbital	2–20	20–50	50	57–120	
Barium	–0.001				[133]
Bendrofluazide	0.05–0.1			appr. 3	[426]
Benoxapofen	–50			19–39	[133, 155]
Benperidol	appr. –0.002			4–8	[423]
Benzbromarone	2–10			2–4	
Benzene	–0.0002 <sup>271</sup>		0.95		[528]
Benzphetamine	0.025–0.5	0.5	14 <sup>8</sup>	?	[28, 528]
Benztropine	0.01–0.18	0.05	0.2–0.7	?	[423, 528]
Benzyl alcohol	?	18 <sup>8, 194</sup>		– <sup>195</sup>	[155, 210, 314]
Benzylpenicillin	1.2–12			1	[71, 489]
Bepidil	0.6–2.5			33–42	[178]
Beryllium	–0.0003				[133]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Betacarotene	4–6 <sup>196</sup>	?			[155, 168]
Betaxolol	0.005–0.05		36 <sup>8</sup>	14–22	[28, 34a, 466]
Bethanidine	0.02–0.5			9–10	[155, 528]
Bevantolol	0.2–2			2	[423]
Bezafibrate	–15			2	[133, 155]
Bicalutamide	1.5–17.5 (–25) <sup>163</sup>			(3–) 7–10 <sup>6</sup>	[325]
Biperiden	0.05–0.1		0.25 <sup>8</sup>	18–24	[114]
Bismut(h)	<0.05 (–0.1)	0.05–0.1		– <sup>6</sup>	
Bisoprolol	0.01–0.1			10–12	[466]
Bopindolol	0.001–0.015 <sup>54</sup>			4–8 <sup>54</sup>	[466]
Borate	0–7	20	200		[429]
Boron	0.8–6	20–50	50–150		[528]
Brallobarbital (Brallobarbitone)	4–8	8–10	15	20–40	
Bretylium	0.8–2.4			6–11	[155]
Brodifacoum		0.02	0.03–0.17; acute: 3.9 <sup>8</sup>	20–60 <sup>6</sup>	[391a, 528]
Bromadiolon		0.02			[528]
Bromazepam	(0.05–) 0.08–0.2	0.3–0.4	(1–) 2	8–22	[272]
Bromide	10–50	500–1500; 3000 <sup>8, 242</sup>	2000	12–13 <sup>6</sup>	[186, 213, 497, 528]
Bromisoval	10–20	30–40		appr. 4 <sup>28, 105</sup>	
Bromoxynil		20			[133]
Bromperidol	0.001–0.02			20–36	
Brompheniramine	0.005–0.015	0.2 <sup>8</sup>		2–10 (–20)	[423]
Brotizolam	0.001–0.02		10 <sup>8</sup>	4–10	[28, 443a]
Budipine	appr. 0.1–0.3			30	[423]
Buflomedil	appr. 0.2–0.5 (–1.0)	15–25	25–50; 275 <sup>8</sup>	2–4	[426, 528]
Bunitrolol	0.001–0.015			2–6	[466]
Bupivacaine	(0.25–) 0.5–1.5 (–2)	2–4		0.5–3	[155, 202, 260, 300]
Bupranolol	– <sup>44</sup>			2–4	[466]
Buprenorphine	0.0005–0.005 (–0.01)	0.2 (?)	1.1 <sup>8</sup> ; 4–13	3–5	[28, 133, 155, 520a, 544]
Bupropion (Amfebutamone)	0.01–0.02; 0.05–0.1 <sup>152</sup>	1.2 <sup>246</sup>	7.3	10–20	[28, 132, 148a, 214, 222, 287, 305, 412, 509]
Buspirone	0.001–0.004 (–0.01)			2–3	[528]
Butabarbital	see Secbutabarbital				
Butalbital	1–5	10–15	15–30	30–40	
Butanone	–10	500			[133]
Butaperazine	0.02–0.3(–0.7)			12	[423]
Butorphanol	0.0006–0.002			4–9	[423]
Butriptyline	0.07–0.15	0.4–0.5		?	[423]
Cadmium	–0.0065	0.015–0.05			[133, 528]
Caffeine (Coffein)	(2–) 4–10	15–20	180	2–10	[28, 82, 155, 350, 433]
Calcifediol	0.01–0.05				[429]
Camazepam	0.1–0.6	2		20–24	[272]
Camphor		0.3–0.4	1.7	?	[423]
Candesartan	0.08–0.18			5–7	[423]
Canrenone	see Spironolactone				
Captopril	0.05–0.5 (–1)	5–6	60	1–2	[4, 268, 426]
Carazolol <sup>23</sup>	–0.015			9	[466]
Carbamazepine <sup>12</sup>	2–8 (4–12)	10	20	12–60 (7–35) <sup>140</sup>	[60, 81, 114, 124, 145, 258, 311]
Carbaryl		5	6		[28, 114a]
Carbenoxolone	appr. 5–30			8–20	[429]
Carbimazole <sup>95</sup>	0.5–3.4 <sup>95</sup>			3–5 <sup>95</sup>	
Carbinoxamine	appr. 0.02–0.04			appr. 10–15	[502]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Carboc(h)romene	0.8–2.4			0.2–1.5	
Carbon monoxide	– <sup>200</sup>	25–30%	50–60%		[155, 527, 528]
Carbon tetrachloride	–0.07	7.1 <sup>8</sup> , 269 ; 20–50	100–200		[458, 528]
Carboplatin	max. 10–25			2.5–6 <sup>106</sup>	
Carbromal(um) <sup>13</sup>	2–10	15–20	40	7–15	
Carisoprodol	10–30	40	50 <sup>8</sup> , 104	8	[114, 528]
β-Carotene	see Betacarotene				
Carteolol	0.01–0.1			3–7	[466]
Carvedilol	appr. 0.02–0.15 (–0.3)			6–10	[155, 269]
Cefaclor	13–35 (i.v. –900)			0.5–1	[155, 528]
Cefalexin	–65			1–1.5	[489]
Cefaloridine	20–80			1.5	[489]
Cefamandole	1–5 (10–40–150)			0.5–1.2	[489, 528]
Cefazolin	–150			1.5–2	[71, 489]
Cefoperazone	–250			1–2 (–5)	[88]
Cefotaxime	0.5–2 (10–50, i.v. –225)			1–1.5	[71]
Cefotetan	65–90			3.5	[489]
Cefotiam	–150 <sup>71</sup>			0.7–1.5 (–2)	[464, 489]
Cefoxitin	–150			0.7–1	[489]
Cefsulodin	20–100			1.6–1.9	[155, 528]
Ceftazidime	20–40 (50–200)			1.6–2	[155, 528]
Ceftibuten	appr. 3–20			2–4	
Ceftizoxime	40–160			6–9	[489]
Ceftriaxone	15–75			6.5–8.5	[71]
Cefuroxime	0.5–1 (–180) ; 7–59 <sup>243</sup>			1.1–1.3	[155, 315, 392, 527, 528]
Celiprolol	0.05–0.5			3–6	
Cephalothin (Cefalotin)	–30			0.5–0.6	[155, 489]
Cerivastatin	0.002–0.04			1.5–3	[423]
Cetirizine	appr. 0.02–0.3	2–5		7–9	[28, 423]
Chinidine	see Quinidine				
Chinine	see Quinine				
Chloralhydrate <sup>14</sup>	1.5–15	40–50	60–100	8–30	
Chlorambucil	0.15–0.3 (–1.0)			1.5–3	[423]
Chloramphenicol	5–10 (–15) <sup>59</sup>	25		2–6	[277, 528]
Chlordane	–0.001	0.0025	1–7		[133, 528]
Chlordecone		0.5			[133]
Chlordiazepoxide <sup>15</sup>	0.4–3	3.5–10	20	6–24	[18, 28, 114, 528]
Chlormethiazole	see Clomethiazole				
Chlormezanone	(3–) 5–9 (–14)	appr. 20	18 <sup>8</sup> ; 53 <sup>8</sup>	20–30	[104, 114, 279]
Chlorobutanol	?	75			[429]
Chloroform	20–50	70–250	390		[528]
Chlorophacinone		0.1			[133]
Chloroquine	0.02–0.5	1	3	dose-dependent <sup>6</sup>	[83, 114, 234]
Chlorothiazide	appr. 6			0.5–2	[155, 528]
Chlorphen(ir)amine	0.003–0.017		1.1 <sup>8</sup>	15–25	[28, 133, 155, 528]
Chlorpromazine <sup>66</sup>	0.03–0.1 (–0.5)	1–2	3–4	10–30	[114, 155, 245, 346]
Chlorpropamide	30–150	200–750		25–60	[429, 528]
Chlorprothixene	0.02–0.2	0.4	0.8	10–30	
Chlorpyrifos		0.2		27	[28, 133]
Chlortalidone	0.15–0.3 (–1.4)	appr. 2		44–48 (35–70)	
Chlortetracycline	1–5 (–10)	30		5–6	[340, 468, 469]
Chromium	–0.00035		32 <sup>8</sup>		[28, 133]
Cibenzoline	0.2–0.4 (–0.9)	(0.5–) 1		7–8 <sup>83</sup>	[155, 537]
Cicletanine	appr. 1–2			5–23	[155, 423]
Ciclosporine	see Cyclosporine				
Cidofovir	appr. 7–43			2.5	[155, 423]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Cilazapril(-)at	0.003–0.09			30–50	[423]
Cimetidine	0.25–3 (0.75–4)	30–50	110 <sup>8</sup>	1.5–4	[172, 477]
Cinoxacin	appr. 15			1.5–4	
Ciprofloxacin	2.5–4	11.5 <sup>8</sup>		3–6	[80, 93, 454, 494]
Cisaprid	0.04–0.08			6–12	[423]
Citalopram	appr. 0.01–0.2 (– 0.1?)		5–6 <sup>160</sup>	appr. 33 <sup>170</sup>	[173, 188, 242, 380, 386–388, 423]
Cladribine	appr. 0.006			0.1–0.2 (6.4–19.7)	[36, 248, 261]
Clarithromycin	appr. 0.2–2			3–7 <sup>217</sup>	[17, 53, 423, 436, 437, 463]
Clemastine	appr. 0.001–0.002 (?)			appr. 8	[56, 423]
Clenbuterol	0.0003–0.0006	0.003 <sup>8</sup>		34–35	[28]
Clindamycin	appr. 0.5			2–3	
Clobazam <sup>17</sup>	0.1–0.4			10–32	[272, 274]
Clobutinol	appr. 0.05–0.2			23–34	[155, 423]
Clofibrate	50–250			10–18	
Clomethiazole (Chlormethiazole)	0.7–2	(2.8–) 4–15	50	3–7	[155, 273, 340, 468, 532]
Clomipramine <sup>48, 85</sup>	(0.02–) 0.09–0.25 (–0.4) <sup>226</sup>	0.4–0.6	1–2	20–26 <sup>86</sup>	[20, 87, 131, 151, 156, 285, 305]
Clonazepam	(0.004–) 0.01–0.08 <sup>150</sup>	0.1		20–60	[60, 286, 431]
Clonidine	0.001–0.002 (–0.004)	0.025–0.05 (0.009 <sup>8</sup> )	0.23 <sup>8</sup>	8–25	[28, 127, 367, 417]
Clopenthixol	0.002–0.015	0.05–0.1		15–25	[423, 528]
Clorazepate <sup>15</sup>	see Nordazepam			1–2	[145]
Clotiazepam	0.1–0.7			3–15	
Cloxacillin	5–30 (–85)			0.5–1 (0.3–2)	
Clozapine <sup>136</sup>	(0.1–) 0.3–0.6 (>0.35 ?)	0.6–1 (9.5 <sup>8</sup> )	1.2 <sup>8</sup> ; 2 <sup>8</sup> ; 5.2 <sup>8</sup>	6–14	[85, 134, 174, 326, 571]
Cobalt	0.0001–0.0022				[133, 528]
Cocaine	0.05–0.3	0.5–1	4	0.5–1 <sup>18</sup>	[28, 65, 133, 397, 468, 469, 528]
Codeine <sup>48</sup>	0.03–0.25	0.5–1	1.8	3–4	[155, 484]
Coffein(e)	see Caffeine				
Colchicine	0.0003–0.0025	0.005	0.024 <sup>8</sup>	11–32 <sup>143</sup>	[29, 435, 527]
Colistin	1–5			2–5	
Copper	0.6–1.5	2	5		[133, 429]
Cotrimoxazole	see Sulfamethoxazole and Trimethoprim				
Cresol (Methylphenols)		appr. 50	120		[133, 528]
Cromolyn (Cromoglycate)	appr. –0.01			1–1.5	[133, 155]
Cyanide	– <sup>177</sup>	0.5	1–3	appr. 19 <sup>184</sup>	[30, 155, 179, 220, 434, 446, 497, 505]
Cyclizine	0.1–0.25	0.75–1	15	24	[133, 528]
Cyclobarbitol	2–6	10	20	8–17	
Cyclobenzaprine	appr. 0.003–0.04	0.4		18 (9–40) <sup>253</sup>	[133, 528, 565]
Cyclohexane	–0.4				[133]
Cyclophosphamide	10–25			4–8 (1.3–16)	[155, 423]
Cyclopropane	80–180				[133, 528]
Cyclosporine A (CsA)	<0.1–0.15–0.25	0.3–0.4 <sup>16</sup>		10–27 <sup>169</sup>	[116, 219, 306, 307, 377, 520]
Cyproheptadine	appr. –0.05		0.47 <sup>8</sup>	appr. 16	[28, 133, 155]
Cyproterone acetate	?			30–40	[325]
Cytarabine	0.05–0.5			0.1–0.2 (1.9–2.5)	[248, 340]
2,4-D	see 2,4-Dichloro-phenoxyacetic acid				
Danazol	appr. –0.2			4.5	[133, 155]
Dantrolene	(0.1–) 0.4–1.5 (–3)			4–12	[155, 340, 534]

**REVIEW**

**Table (continued)**

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Dapsone <sup>48</sup>	0.5–2	10	18 <sup>8</sup>	25–31	[280, 406]
Deferoxamine (Desferrioxamine)	3–15			4–6	
Demoxepam	0.5–0.74	1	2.7		[429]
Desipramine <sup>48, 69</sup>	0.01–0.5 (0.12–0.25)	0.5–1	3	15–25 <sup>70</sup>	[57, 69, 304, 305, 356]
Desmethyldiazepam	see Nordazepam			40–80	[272]
Dexamethasone	appr. 0.05–0.265 <sup>247</sup>			2.5–9.5	[155, 432]
Dexfenfluramine	appr. 0.03–0.06	0.15–0.25		appr. 18	[429, 528]
Dextromethorphan <sup>48</sup>	0.01–0.04	0.1	3	2–4	[195, 427]
Dextromoramide	0.075–0.15	0.2	0.9	0.1–1.5 (?)	[28, 266a, 423, 526, 528]
Dextropropoxyphene	0.05–0.3 (–0.5)	1	1–2	10–30	[234]
3,4-Diaminopyridin (DAP)	<0.04 <sup>213</sup>	0.1 (?)		0.3–2 <sup>214</sup>	[37]
Diazepam <sup>19</sup>	0.2–2 (–2.5)	3–5		24–48	[65, 107, 155, 272, 431, 468, 469, 521]
Diazinon		0.05–0.1 (–0.5)			[133, 528]
Diazoxide	10–20 (–50)	50 (–100)		20–36 (–48)	[155, 268, 426, 527, 528]
Dibenzepine	0.025–0.15 (0.1–0.5)	3	18	3.5–5	[133, 528]
Dichloromethane		200	280		[133]
2,4-Dichlorophenoxyacetic acid (2,4-D)	–	appr. 100	200; 392 <sup>8</sup> ; 720 <sup>8</sup>	appr. 18 <sup>182</sup>	[155, 528]
Dichlorvos			29	0.16	[28]
Diclofenac	0.5–3	50; 60 <sup>8</sup>		1–2	[92, 133, 141, 142]
Dicoumarol	8–30	50–70		1–4 <sup>6</sup>	[133, 528]
Dicyclomine (Dicycloverin)	–0.1	appr. 0.2	0.5	1.8–2	[133, 423]
Didanosine	appr. 1–30 µmol/l			1	[66, 67, 155, 358]
Dieldrin	–0.0015	0.15–0.3			[28, 133, 528]
Diethylcarbamazine	>0.8–1.0			4–15	[47]
Diethylpentenamide (Valdetamide)	2–10	20	45	6–7	
Diethylpropion	0.003–0.007 (–0.2)	2	5.4 <sup>8</sup>	4–8 <sup>23</sup>	[133, 155, 423, 528]
Difenacoum		0.5			[133]
Diflunisal	40–100 (–200)	300–500	600	5–12 <sup>83</sup>	[133, 155, 340, 528, 556]
Digitoxin	0.01–0.025	0.03	0.04	140–200	[109, 171]
Digoxin	0.0005–0.0008 (–0.002)	0.0025–0.003	0.005	40–70	[108, 120, 217, 251, 357, 420, 516, 529, 550]
Dihydralazine	see Hydralazine				
Dihydrocodeine	0.03–0.25	0.5–1	2	3–4	[133, 469, 528]
Dihydroergotamine	0.001–0.01			7–9	[133, 155]
Diltiazem	0.03–0.13 (–0.25) <sup>157</sup>	0.8–1	2–6; 7 <sup>8</sup> ; 8 <sup>8</sup>	2–6 (4–9)	[133, 155, 268, 528]
Dimenhydrinate	see Diphenhydramine				
Dimethadione	700–1000	1000		?	[133, 155, 528]
Dimethindene	0.01–0.05			appr. 6	[155, 423]
N,N-Dimethyltryptamine	0.001–0.1				[528]
4,6-Dinitro–2-methylphenol		40			[133]
Dinitro-o-cresol (DNOC)	1–5	30–60	75		[528]
Diphenhydramine	0.05–0.1 (–1)	1–2 (–4)	5–10	4–10, 20–60	[86, 235, 524, 528]
Diphenoxylate	appr. 0.01			2–3	
Dipipanone	appr. –0.05	0.2		?	[133]
Diprophylline	see Dyphylline				
Dipyridamole	0.1–1.5	4		11–13	[340, 468, 469]
Dipyron	see Metamizole				
Diquat		0.1–0.4			[133, 528]
Disopyramide	2–7 <sup>78</sup>	8		5–8	[133, 528]
Disulfiram	0.05–0.4	5	8	appr. 5–7	
Dixyrazine	appr. 0.3 <sup>249</sup>		5.5 <sup>8</sup> ; 9.4 <sup>8</sup>		[383]



**REVIEW**

**Table (continued)**

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Domperidone	appr. 0.01–0.1			12–16	[24, 155, 208, 223, 343]
Donepezil <sup>207</sup>	appr. 0.03–0.075			70–100	[230, 438]
Dothiepin (Dosulepin) <sup>20</sup>	0.02–0.1	0.8	1	11–40	[265, 467]
Doxacurium	0.01–0.3			1–2 <sup>83</sup>	
Doxapram	(1.5–) 2–5	9 <sup>268</sup>		2.4–9.9	[22, 133, 155, 528]
Doxazosin	0.01–0.15			10–22	[269]
Doxepin <sup>21</sup>	0.01–0.2 (0.03–0.1)	0.5–1	2–4	8–25	[8, 45, 126, 181, 282, 305, 356]
Doxorubicin (Adriamycin)	0.006–0.02			20–48	[133, 155, 528]
Doxycycline	1–5 (–10)	30		7–20	
Doxylamine	0.05–0.2	1–2	5	9–11	
Dronabinol (Delta-9-tetrahydrocannabinol, THC)	0.005–0.01 (–0.05) <sup>137</sup>			50–100	[65, 246, 382]
Droperidol	appr. –0.05			1.5–2.5 <sup>237</sup>	[133, 155, 450]
Dyphylline	6.5–14 (–20)	40		2	[133, 528]
Edrophonium	–0.15	appr. 0.15		1.3–2.4	[9, 155, 528]
Emetine	appr. –0.1	0.5		?	[133]
Enalapril <sup>52</sup>	0.01–0.05 (–0.1)			8–11	[4, 268]
Encainide <sup>48</sup>	– <sup>175</sup>			1.5–3.5 <sup>176</sup>	[155]
Endrin	–0.003	0.01–0.03			[133, 528]
Enoxacin	1–4			3–6	[93]
Enoximone	≥0.2			4–7	[155, 269]
Entacapone	0.4–1.0 (–7.0)			1.5–3.5	[155, 423]
Ephedrine	0.02–0.2	1	5 <sup>8</sup>	3–11	[133, 428, 528]
Epirubicin	0.01–0.05			24–52	
Eprosartan	0.4–1.0 (–1.85)			5–9	[155, 423]
Erythromycin	2–6 (–8)	12–15		1–3	[133, 528]
Esmolol	0.15–2			4–16 min	[466]
Estazolam	0.055–0.2			10–24	[133, 155, 528]
Et(h)amsylate	15–20			2.5–4	
Ethacrynic acid	0.05–0.1			1–4	[155, 340]
Ethambutol	0.5–6	10		2.5–3.5	[236, 528]
Ethanol		1000–2000	3500–4000	– <sup>139</sup>	
Ethchlorvynol	0.5–8	20	50	10–25 (–35)	[133, 155, 528]
Ethinamate	1.5–10	50–100	200 <sup>8</sup>	appr. 2	
Ethosuximide	30–100 (40–60)	150–200	250	30–60	[60, 145]
Ethylene glycol		200–500	2000		[429]
Etidocaine	0.5–1.5	1.6–2		2–3	[557]
Etilefrine	appr. 0.06			2–3.5	
Etodolac	>14 <sup>229</sup>			6–8	[51, 155, 423]
Etomidate	0.1–0.5 (–1)			3.9 ± 1.1 (2–11)	[155, 340]
Etoposide	1–6			4–11	[133, 155, 528]
Ezetimibe	>0.015			appr. 30	[129, 130]
Famotidine	0.02–0.2	0.42 <sup>8</sup>		2–4.5	[13, 155, 570]
Fampridine	see 4-Aminopyridine				
Felbamate	50–110 <sup>164</sup>	200 (?)		20–24	[167, 522, 542]
Felbinac	appr. 0.4–1 (topical)			10–17	[48, 155]
Felodipine	0.001–0.012	0.01		22–27 <sup>88</sup>	[43, 268, 423]
Fenbufen	appr. –60			10–12	[133, 155]
Fendiline	0.02–0.15			appr. 20	
Fenfluramine	0.04–0.3	0.5–0.7	6	1–2, 18–25	
Fenitrothion			1.1		[28]
Fenofibrate	5–30 <sup>241</sup>			20–22	[155, 313]
Fenoldopam	0.003–0.06			0.1	[423]
Fenopropfen	(25–) 30–60			2–3	[206]
Fenoterol	(0.001–) 0.01–0.04			appr. 7	

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Fentanyl	0.003–0.3 <sup>4</sup>		0.003–0.02 <sup>8,103</sup>	1–3.5 (transdermal patch: appr. 17)	[13, 28, 226, 297, 299, 403, 462, 482, 486, 493, 569]
Fexofenadine	appr. –0.3 <sup>191</sup>			14–18	[423, 478]
Finasteride	0.008–0.01			5–7	[499]
Flecainide <sup>48</sup>	(0.2–) 0.4–0.8	1–2	2.6 <sup>8</sup> ; 13 <sup>8</sup>	10–20	[128]
Fleroxacin	1–4			8–13	
Flucloxacillin	3–30			0.7–1.5	
Fluconazole	appr. 1–5 (–15)	20; 95 <sup>8</sup>		22–31 <sup>83</sup>	[98, 430, 461, 528]
Flucytosine	35–70 (20–50)	100		3–5	[192]
Flumazenil <sup>22</sup>	(0.01–) 0.02–0.1	0.5		1–2	
Flunarizine	0.025–0.2	0.3		– <sup>6</sup>	[426]
Flunitrazepam <sup>23</sup>	0.005–0.015	0.05		10–20	[49, 114, 272]
Fluoride	0.095–0.190 (–0.285) <sup>39</sup>	2	3	short	[155, 391, 407, 497, 527, 528, 552]
5-Fluorouracil	0.05–0.3	0.4–0.6		<0.5	[133, 155, 528]
Fluoxetine	appr. 0.16–0.5	1	6 <sup>8</sup>	2–4 <sup>6, 130</sup>	[69, 121, 188, 204, 356, 425]
Flupentixol	0.0005–0.002			19–39	
Fluphenazine	0.0002–0.004	0.05–0.1		10–18 <sup>45</sup>	
Flupirtine	0.5–1.5	appr. 3–4		7–11	[368]
Flurazepam <sup>24</sup>	0.02–0.1	0.2–0.5	0.8; 24 <sup>8</sup>	appr. 2 <sup>24</sup>	
Flurbiprofen	5–15			3–4	[138]
Flutamide <sup>60</sup>	0.4–1.5 <sup>60</sup>			7–20 <sup>60</sup>	[104, 465]
Fluvoxamine	appr. (0.05–) 0.15–0.25	0.65	2.8 <sup>8</sup>	15–22	[28, 170, 188]
Furosemide (Frusemide)	1–6	25–30		1–3	[133, 155, 528]
Fusidinic acid	30–200			4–6	
Gabapentin	5.9–21 <sup>185</sup>	85 <sup>8</sup>		5–8 <sup>186</sup>	[28, 44, 64, 400, 483, 500, 519, 562]
Galant(h)amine	appr. 0.03–0.14 (?)			6–8	[38, 474]
Gallopamil	0.02–0.1		8 <sup>8</sup>	3–8	[146, 268]
Gamma-hydroxybutyric acid (gamma-hydroxybutyrate, gamma-butyrolactone, GHB, liquid ecstasy)	see 4-Hydroxybutyrate				
Ganciclovir	(0.29–0.51) 0.5–5 <sup>107</sup>	3–5		2–4 <sup>83</sup>	[252, 358, 476]
Gemcitabine	15–20 µmol/l <sup>146</sup>	– <sup>192</sup>		0.05 (0.18–0.43)	[248]
Gemfibrozil	appr. –25			1.5	[133, 155]
Gentamicin	(2–) 4–10 <sup>233</sup>	12		1.5–6	[58, 71, 119, 120, 231, 278, 353, 547]
Glibenclamide (Glyburide)	0.05–0.2	0.6		10	
Glipizide	0.1–1.0 (–1.5)	2		3–7	[429]
Glutethimide	0.2–5	10–30	20–50	5–20	[234]
Glyburide	see Glibenclamide				
Glyceryl trinitrate	see Nitroglycerin				
Gold	3–8	10–15			[528]
Granisetron	0.009–0.017 (?)			3–14	[155, 423]
Griseofulvin	0.3–1.3			22	
Guaifenesin	appr. 0.3–1.4			appr. 1	[155, 423]
Guanethidine	0.01			5–10 <sup>6</sup>	[133, 155, 528]
Halazepam <sup>15</sup>	see Nordazepam			30–40	
Haloperidol	0.005–0.017 (0.001–0.02)	0.05–0.5	0.5; 0.18 <sup>8, 74</sup>	10–35 <sup>153</sup>	[104, 288, 346, 413, 520, 530, 531, 571]
Hematin	50–100			?	
Hemin	see Hematin				
Heptabarb(ital)	0.5–4	8–15	20	6–11	
Heptaminol	appr. 0.2–1 (–1.5)			2–3	
Hexachlorophene	0.003–0.65 (–1)		35	6–44	[133, 528]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
n-Hexane	-0.01				[133]
Hexapropymate	2-5	10-20		?	[528]
Hexobarbital	1-5	10-20	50	4-6	
Hirudin-rec	- <sup>171</sup>	- <sup>171</sup>		(1-) 2.5-3	[76, 104, 155]
Hydralazine <sup>5</sup>	0.05-0.5 (-1.5)			2-6	[268]
Hydrochlorothiazide	appr. 0.04-2			10-12	[155, 426]
Hydrocodone	0.01-0.05	0.1	0.2	appr. 4	[423]
Hydromorphone	appr. 0.005-0.015	0.1	0.2	2-3	[176, 340, 423, 427]
4-Hydroxybutyrate (GHB)	appr. 50-120 <sup>4</sup>	80 (abuse)	250-280 (abuse)	0.3-0.5 (-1)	[28, 133, 155, 335a, 423]
Hydroxychloroquine	-0.1 (-0.4)	0.5-0.8	4	dose-dependent <sup>6</sup>	[133, 155, 284, 468, 469]
Hydroxyzine	0.05-0.1	0.1	39 <sup>8</sup>	7-20	[114, 528]
Ibuprofen	15-30	200		2-3	[28, 140, 206, 556]
Idebenone	0.05-0.2			16-22	[155, 405]
Iloprost	appr. 0.0001			appr. 0.5	
Imatinib	0.72 <sup>258</sup>			appr. 18	[113, 320]
Imipenem	0.5-5 (20-75)			1	[513]
Imipramine <sup>48, 125</sup>	0.05-0.35	0.5-1	1.5-2	6-20 <sup>26</sup>	[8, 57, 126, 151, 181, 249, 304, 305]
Indinavir	- <sup>260</sup>	0.5		1.5-2	[53, 155, 421]
Indomet(h)acin	0.3-1 (-3)	4-5		3-11	[157]
Indoramin	appr. 0.025-0.1			12 (3.5-15)	[269]
Iproniazid	appr. -5 ( ?)			?	[133]
Iridium	-0.02				[133]
Iron	0.5-2	6	17		[133, 426, 528]
Isoniazid (INH)	5-10	20	(30-) 100	1-3	[155, 236, 423]
Isopropanol		200-400	1000		[28, 528]
Isosorbid mononitrate (ISMN)	0.1-1			2-5	[269]
Isotretinoin	appr. 0.001-0.002 (topical) <sup>224</sup>			10-20	[155, 349, 375]
Isoxicam	5-15			20-50	
Isradipine	0.0005-0.002 (-0.01)	0.01	0.26 <sup>8, 259</sup>	5-10	[78, 155, 268, 439, 523]
Itraconazole	appr. 0.4-2 <sup>111</sup>			24-36	[25, 309, 366, 485]
Ivermectin	appr. 0.05 <sup>51</sup>			16-28	[155, 384]
Kanamycin	1-4 (10-25)	25-30		0.5-3	
Ketamine	1-6	7 (abuse)	7 (abuse)	1-3	[28, 50a, 114, 191, 499a]
Ketanserin	0.05-0.5			10-22	
Ketazolam <sup>15</sup>	0.001-0.02			1-3	[272]
Ketobemidone	appr. 0.3		0.6	2-2.5	[28, 50a, 155, 499a]
Ketoconazole	1-3 (-6)			6-10	[423]
Ketoprofen	1-6 (-20)		1100 <sup>8</sup>	1.5-2 (-4)	[21, 28, 106, 206, 237, 302, 364]
Ketorolac	0.5-3	5		4-10	[155, 423]
Ketotifen	0.001-0.004	0.02	1.2 <sup>8</sup>	21	[428]
Labetalol	0.03-0.18 (-0.65) <sup>50</sup>	1		3-10	[155, 269, 466]
Lacidipine	0.003-0.006			12-19	[423]
Lamivudine	- <sup>230</sup>			(3-) 5-7	[155, 247]
Lamotrigine	(1-5) 3-14	15-30	50 <sup>8</sup>	24-36 <sup>109</sup>	[28, 64, 419, 453, 519]
Lead	-0.16 (-0.3)	0.4-0.6	3	- <sup>6, 180</sup>	[28, 133, 155, 452, 456]
Leflunomide <sup>255</sup>	8.8 ± 2.9, 18 ± 9.6, 63 ± 36 <sup>256</sup>			11 (4-28) <sup>6</sup>	[32, 155, 163, 316]
Levetiracetam	10-37	400 <sup>8, 264</sup>		5-8	[27]
Levocabastine	<0.001-0.01 <sup>147</sup>			33-40	[209]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Levodopa (L-Dopa)	0.3–1.6		650 <sup>8</sup>	1–3 <sup>215</sup>	[15, 182–184, 507]
Levomepromazine <sup>27</sup>	0.005–0.025 (–0.2)	0.4	0.5	15–30 <sup>28</sup>	
Levomethadone	0.04–0.3	1	0.2	10–40	[155, 451]
Levorphanol	0.007–0.02	0.1	2.7 <sup>8</sup>	11–30	[423]
Levothyroxine	0.045–0.14 <sup>47</sup>			6–8 <sup>6</sup>	[143]
Lidocaine (Lignocaine)	(1–) 1.5–5 <sup>113</sup>	6–7	10	1–4 <sup>113</sup>	[95, 189, 231, 557, 567]
Lisinopril	(0.005–) 0.02–0.07	0.5		12	[268]
Lithium	4–8 <sup>79</sup>	13	14	8–50 <sup>28</sup>	[5, 161, 305, 356, 361]
Lofepamine	0.003–0.01			10–20	
Loperamide	– <sup>84</sup>			7–15	
Loprazolam	0.003–0.01			11–20	[272]
Loratadine	0.001–0.02 <sup>138</sup>			8–14	[418, 575]
Lorazepam	(0.02–) 0.08–0.25	0.3–0.5		10–40	[203, 272, 424, 431]
Lorcainide	(0.04–) 0.1–0.4 (–0.9)			5–10	
Lormetazepam	0.005–0.025 (–0.1)			10–15	[272]
Losartan	<0.2 <sup>227</sup>			1.5–2	[155]
Loxapine	0.01–0.03 (–0.1)	1	7.7	4 (1–14)	[133, 528]
Lysergide (lysergic acid diethyl amide, LSD)	0.0005–0.005	0.001	0.002–0.005	appr. 2–5	[317, 423, 528]
Magnesium	55–75 <sup>121</sup>	120–140	150–180		[155, 558]
Malathione		0.5	175 <sup>8</sup>		[28, 133]
Manganese	0.0005–0.0015				[133]
Maprotiline	0.1–0.6 (0.1–0.25)	0.5–1	1–5	20–60	
MCPA	see 2-Methyl–4-chloro-phenoxyacetic acid				
MCPP	see 2-Methyl–4-chloro-phenoxypropionic acid				
Mebendazole	≥0.1 <sup>67</sup>	appr. 0.6		2.8–9	[104]
Medazepam <sup>30</sup>	0.1–0.5 (–1)			2–5	
Mefenamic acid	2–10 (–20)	25		2–4	[340, 468, 469]
Mefloquine	0.4–1 <sup>108</sup>	1.5–2 <sup>8</sup>		appr. 21 <sup>6</sup>	[68, 199]
Melitracen	0.01–0.1			12–23	
Meloxicam	0.4–2			17–22	[373, 423]
Melperone	<0.2 <sup>19</sup>		17.1 <sup>8</sup>	4–8	[228, 423, 496a]
Melphalan	–1.5			1.5–2	
Meperidine	see Pethidine				
Mephesisin	3–10 (?)			appr. 2–4	[423]
Mepindolol	0.007–0.07			3–6	[466]
Mepivacaine	appr. 0.4 (–4)	5–6 (–10)	50	1–3	[423]
Meprobamate	5–10	10–25	30	6–17	[114]
Meptazinol	0.025–0.25			2–3	
Mercury	appr. 0.0015–0.002 (<0.005) <sup>178</sup>	0.05–0.2	0.5	appr. 3 <sup>6</sup>	[133, 155, 372, 429, 481]
Mesalazine (Mesalamine)	–appr. 1 <sup>119</sup>			0.5–2.4 <sup>120</sup>	[271]
Mesoridazine	0.15–1	3–5	3 <sup>8</sup> ; 4 <sup>8</sup> ; 16 <sup>8</sup>	20	[423]
Mesuximide	see Methsuximide			1–2	[155]
Metaclazepam	0.05–0.2			7–23	[272]
Metamizole (Dipyrone) <sup>5</sup>	10 <sup>32</sup>	20 <sup>32</sup>		6–8	[423]
Metformin	0.1–1 (0.6–1.3)	5–10	64 <sup>8</sup> ; 85 <sup>8</sup> ; 91 <sup>8</sup> ; 166 <sup>8</sup>	2–4 (–10)	[101, 422]
Methadone <sup>135</sup>	(0.05–) 0.1–0.5 (–0.75)	0.2	0.4	23–25 (13–55)	[218, 232, 233, 457, 525]
Methamphetamine	0.01–0.05	0.2–1	10–40	6–9	[423]
Methanol	appr. –2	200	900		[133, 423, 528]
Methapyrilene	appr. 0.1	4			[133]
Methaqualone	1–3	3–5	5–10	10–40	

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Methemoglobin	— <sup>199</sup>	25–30%	60–70%		[155, 527, 528]
Methimazole	0.5–2			2–28	[317, 423]
Methocarbamol	25–40 (–50)	250		0.9–2	[133, 155, 528]
Methohexital	(0.5–) 1–6 <sup>55</sup>			1–3	
Methomyl			28 (8–57)		[28]
Methotrexate	0.04-?	0.4		2–10	
Methotrimeprazine	see Levomepromazine				
Methoxsalen (8-Methoxy-psoralene)	0.025–0.1 (–0.2)	1			[155, 527]
Methsuximide (Mesuximide) <sup>223</sup>	10–40	40–50		20–40	[155, 496, 528]
D-Methylamphetamine	–0.1	1			[133]
2-Methyl-4-chlorophenoxy- acetic acid (MCPA)	—	appr. 100	appr. 180	— <sup>187</sup>	[155, 459]
2-Methyl-4-chlorophenoxy- propionic acid (MCPA)	—	appr. 100	669 <sup>8</sup> ; 715 <sup>8, 181</sup>	17 <sup>183</sup>	[155]
Methyl-dopa	1–5	9 <sup>8</sup>		1.5–3	[340, 468, 469]
Methylenedioxyamphetamine (MDA)	–0.4	1.5	2		[317, 423, 528]
Methylenedioxyethyl- amphetamine (MDEA)	0.2		1		[28]
3,4-Methylenedioxymethyl- amphetamine (XTC, MDMA)	0.1–0.35 <sup>236</sup>	0.35–0.5	0.4	9–10	[75, 317, 423, 528]
Methylphenidate	0.01–0.06	0.5; 1 <sup>8</sup>	2.3	2–7	[427]
4-Methylthioamphetamine (4-MTA, p-MTA)			2 <sup>8</sup> ; 4.2 <sup>8</sup> ; 7.4 <sup>8</sup>		[46, 123, 410, 512, 549]
Methyprylon(e)	<10–20	12–75	50 (–100)	3–6, 9–11	
Metiamide	0.01–0.06			?	[528]
Metildigoxin <sup>3</sup>	0.0005–0.0008	0.0025–0.003	0.005	40–70	[420, 516]
Metipranolol <sup>33</sup>	0.02–0.08			2–3.5	
Metoclopramide	0.05–0.15	0.2	4.4 <sup>8</sup>	3–6	[429]
Metocurine	appr. –0.4			?	[133]
Metoprolol <sup>48</sup>	0.035–0.5	0.65 <sup>8</sup> ; 12–18	4.7 <sup>8</sup> ; 12 <sup>8</sup> ; 63 <sup>8</sup>	3–6	[28, 155, 466]
Metrifonate	appr. 1.4–3.6			2–5	[423]
Metronidazole	3–10 (–20)	200 <sup>8</sup>		6–10 (–14)	[423]
Mexiletine	(0.5–) 0.7–2	2.5	35 <sup>8</sup>	5–26	[338]
Mianserin	0.01–0.15	0.5–5		8–19	[114]
Miconazole	appr. 1			24	
Midazolam	0.04–0.1 (–0.25) <sup>134</sup>	1–1.5		1.5–3 <sup>46</sup>	[16, 42, 227, 293, 431]
Mifepristone	— <sup>216</sup>			24–48 (20–54)	[196]
Milrinone	0.15–0.25	0.3		1–2	[155, 269, 426]
Minaprine	appr. –0.1			?	[133]
Minoxidil <sup>149</sup>	appr. 0.02–0.25	1.4 <sup>8</sup> ; 3.1 <sup>8</sup>	2.7 <sup>8</sup>	2.8–4.2	[28, 155, 268]
Mirtazapine	–0.3	1–2		20–40 <sup>188</sup>	[155, 501]
Mizolastine	appr. 0.2–0.8			8–17	[155, 423]
Moclobemide <sup>141</sup>	appr. 0.5–1.5 (–3)	11 <sup>162</sup> ; 25–60		1–3	[150, 175, 239, 336, 363, 365]
Modafinil	appr. 2–3 <sup>257</sup>			12–15	[201, 352]
Molindone	appr. –0.5			?	[133]
Molsidomine	0.002–0.01			1–2.5	[269]
Molybdenum	–0.005				[133]
Montelukast	appr. 0.05–0.3			3–6	[155, 423, 574]
Moricicine	appr. 0.12–1.27			6–13	[317, 423]
Morphine	0.01–0.1	0.1	0.1–4	1–4	[1, 65, 159, 253]
Moxonidine	0.001–0.002 (–0.004)			2–3	[155, 269]
Muromonab-CD3 (OKT 3)	appr. 0.7–1.3			appr. 18	
Mycophenolate mofetil	— <sup>211</sup>			16–18 <sup>212</sup>	[33, 149, 225, 448]
Nabumetone	— <sup>206</sup>			— <sup>206</sup>	[155, 560]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Nadolol	0.01–0.25		1,3 <sup>8</sup>	14–24	
Naftidrofuryl (Nafrolyl)	<0.5			1–2	[133]
Nalbuphine	0.02–0.2			2.5–7	
Nalidixic acid	10–30	40–50		1 (–7)	[155, 340, 423]
Nalmefene	–0.1			8.5–11	[133, 155]
Naloxone	0.01–0.03			1–2	
Naltrexone	–0.05 <sup>99</sup>			4–10	
Naproxen	20–50 (–100)	200–400; 414 <sup>8</sup>		10–20	[90, 206, 335, 556]
Naratriptan	appr. 0.01–0.05			5–6	[155, 423]
Nebivolol	<0.02 (–0.2)	0.48 <sup>8</sup>		10 (8–27)	[155, 197, 211, 337]
Nedocromil	<0.025			1.5–3.3	[133, 155]
Nefazodone	appr. 0.01–0.3 (?) <sup>220</sup>	5.5 <sup>8</sup> , 221		2–7 <sup>222</sup>	[23, 94, 153, 155, 169, 262, 445]
Nefopam	0.01–0.1	4 <sup>8</sup>	12 <sup>8</sup>	3–8	
Neostigmine	appr. 0.001–0.01 <sup>127</sup>			0.4–1.3	[9, 74]
Netilmicin	1–12			2–3 <sup>80</sup>	
Nicardipine	0.07–0.1			7–12	[268]
Nickel	–0.003	0.005			[133, 528]
Nicotine <sup>123</sup>	0.005–0.02 (–0.03)	0.4 (–1)	5; 13.6 <sup>8</sup>	1–4 <sup>124</sup>	[155, 255, 426]
Nicotinic acid	4–18			0.3–1	
Nifedipine	0.025–0.1	appr. 0.15–0.2	5.4 <sup>8</sup>	2–5	[28, 268]
Niflumic acid	2–35			2–3	[423]
Nilvadipine	<0.01			11–20	[268]
Nimesulide	appr. 1–3 <sup>235</sup>			2–7	[34, 155, 423]
Nimodipine	0.01–0.05			1–2 (8–9)	[268]
Nimustine	0.0002–0.0005			?	[528]
Nisoldipine	0.0003–0.001			7–12	[155, 268]
Nitrazepam	0.03–0.1	0.2–3	5 (?)	20–30	
Nitrendipine	0.01–0.05			8–12	[268]
Nitrofurantoin	1–3	3–4		1 ± 0.3	
Nitroglycerin (Glyceryl trinitrate)	appr. –0.015			20–30 min	[355]
Nitroprusside	see Thiocyanate	see also Cyanide			
Nizatidine	0.05–0.5 (–1.0)			0.7–2.1	
Nomifensine	0.01–0.1	8–10		2–5	
Nordazepam	0.02–0.2 (–0.8)	1.5–2		40–80	
Norephedrine	see Phenylpropanol-amine				
Norfenefrine	–0.4			2–3	
Norfloxacin	0.5–5			3–4	[155, 528]
Normesuximide <sup>31</sup>	10–30	40		38	
Nortriptyline <sup>48</sup>	0.02–0.2 (0.05–0.15)	0.5	1–3	18–56 <sup>68</sup>	[151, 305, 345, 415]
Obidoxime	1–10 (appr. 10–15 µmol/l)				[133, 518, 528]
Ofloxacin	appr. 2.5–5.5	(30–) 40 <sup>8</sup>		(3–) 5–8	[155, 289]
OKT 3	see Muromonab-CD3				
Olanzapine	appr. 0.02–0.03 (–0.05)	0.2	1 <sup>8</sup> ; 4.9 <sup>8</sup>	33 (21–54)	[28, 73, 121a, 423, 477a, 528]
Omeprazole <sup>48</sup>	– <sup>98</sup>			0.5–1 (–1.5)	
Ondansetron	0.03–0.3			3–5.5	[429]
Opipramol	0.1–0.5	2–3	7–10	6–12 <sup>262</sup>	[104, 264]
Orphenadrine	0.1–0.2 (–0.6)	1.7	3.6 <sup>8</sup> ; 5–7	14–18	[86, 114, 340]
Oxatamide	0.02–0.1			14–30	[133, 155]
Oxazepam	0.2–1.5	2	3–5	6–20	[107, 155, 272, 468]
Oxazolam <sup>15</sup>	see Nordazepam			1–2	
Oxcarbazepine	12–24 <sup>172</sup>			1–2.5 <sup>172</sup>	[155, 517, 519]
Oxpentifylline	see Pentoxifylline				
Oxprenolol	0.05–0.3 (–1.0)	2–3	10	1–4	[466]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Oxycodone	(0.005–) 0.02–0.05	0.2	0.6; 5 <sup>8</sup>	2–5 <sup>53</sup>	[340, 426, 528]
Oxyfedrine	appr. 0.06			4.2	[269]
Oxypurinol <sup>61</sup>	5–15	20		18–30	[528]
Oxytocin	appr. –0.0002			3–5 min	[133, 155]
Paclitaxel	0.085–1 (?) <sup>122</sup>			4–8 (–13)	
Pamidronate	appr. 0.5–1			appr. 2.5	
Pancuronium	0.1–0.6	0.4 <sup>8</sup> ; 1 <sup>98</sup>	1.6	1.5–2.5	[536]
Pantoprazole	appr. –4.6			1–2	[155, 423]
Papaverine	(0.2–) 0.6–1 (–2)			1–2, 6–7	[428]
Paracetamol	(5–)10–25	100–150	200–300	2–4	[50, 166, 260, 331, 369, 442, 455, 484, 487, 535]
Paraldehyde	10–100	200	400–500	4–10	
Paraoxon	–	0.005			[528]
Paraquat	–	0.05	1–2 <sup>201</sup>		[155, 187, 528]
Parathion	–	0.01–0.05	0.05–0.08		[155, 527, 528]
Paroxetine <sup>48</sup>	<0.01–0.05 (–0.1)	0.35–0.4		16–24 <sup>93</sup>	[69, 170, 188, 283, 479, 480]
Pefloxacin	1–10 (3–6)	25		8–15	
Pemoline	appr. 1–7			7–13	
Penbutolol	0.01–0.3 (–1.0)			20–26	[466]
Penfluridol	0.004–0.025			70	[155, 528]
(D–)Penicillamine	1.7–5.6 (–11)			1–3	
Pentachlorophenol	–0.2	30	45		[133, 528]
Pentamidine	appr. 0.3–0.5			6–9	[155, 423]
Pentazocine	0.01–0.2	1–2	3	2–5	
Pentobarbital	1–10	10–19	15–25	20–40	
Pentoxifylline <sup>72</sup>	appr. 0.5–2			0.5–2 (4–6)	
Perazine	0.02–0.35	0.5 (6.1 <sup>8</sup> )		8–16 (–35)	[164, 423]
Perici(y)azine	0.005–0.03	0.1		?	[340]
Perindopril	0.08–0.15			0.8–1.5 <sup>265</sup>	[155, 423]
Perphenazine	0.001–0.02 (0.0008–0.0024) <sup>161</sup>	0.05		8–12 (–21)	[308]
Pethidine <sup>115</sup>	0.1–0.8	1–2	2 (–3)	3–6 (–10)	[10, 31, 177, 215, 257]
Phenacetin <sup>62</sup>	5–10 (–20)	50		appr. 1	[340, 468]
Phenazone (Antipyrine)	5–25	50–100		10–12	
Phencyclidine (PCP)		0.007–0.24	1–5	1–12	[317, 423, 528]
Phendimetrazine	0.02–0.24 (–0.3)			2–4	[133]
Phenelzine	0.001–0.002 (–0.04)	0.5	1.5	6–8	[155, 528]
Phenformin	0.03–0.1	0.6	3	4–13	[155, 423]
Pheniramine	0.01–0.27		2 (?)	16–19	[155, 423]
Phenmetrazine	0.02–0.25	0.5	4	ca. 8	
Phenobarbital	10–30 (15–40)	30–40	50–60	60–130	[60, 145, 157]
Phenol		50	90		[133, 528]
Phenprocoumon	0.16–3.6 (1–5)	appr. 5		100–160 <sup>35</sup>	[528]
Phensuximide	4–10 (–20)	80		4–12	[423, 528]
Phentermine	0.03–0.1	0.9	1	appr. 20	[423, 528]
Phenylbutazone <sup>36</sup>	50–100	120–200	400	30–175 <sup>37</sup>	[340, 468]
Phenylephrine	0.04–0.1			2–3	[423]
Phenylpropanolamine (Norephedrine)	0.1–0.5	2	48	3–7	[155, 340]
Phenytol	5–15 (10–20) <sup>81</sup>	20–25	43 <sup>8</sup> ; 50	10–60 <sup>37</sup>	[6, 55, 145, 147, 193, 221, 351, 362, 416]
Pholcodine	appr. –0.2			?	[133]
Physostigmine	<0.001–0.005			0.4–1	[9, 14, 230]
Pimozide	appr. 0.004–0.01 (–0.02)			24–55	

**REVIEW**

**Table (continued)**

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Pinazepam <sup>15</sup>	0.01–0.05			16	[272]
Pindolol	0.02–0.15	0.7–1.5		2–5	[466]
Pipamperone	0.1–0.4	0.5–0.6		<4	
Piperacilline	1–5 (20–70)			1–2	[423, 528]
Piperazine	0.02–0.1	0.5			[426, 429, 528]
Pipotiazine	0.001–0.06	0.1		8–11	[155, 340, 423, 528]
Piracetam	appr. 20–50			4.5–7	
Pirenzepine	0.03–0.45			8–20	
Piritramide	0.0088 ± 0.0053 <sup>128</sup>			4–10	[266]
Pirmenol	1–4			6–18	[155, 528]
Piroxicam	2–6	14 <sup>8</sup>		30–70	
Pizotifen	0.007–0.009			26	
Prajmalium <sup>48</sup>	0.06–0.44			5–7	
Pramipexole	appr. 0.0002–0.007			8–14	[317, 423]
Pranlukast	appr. 0.2–1.2			appr. 2–9	[155, 423]
Prazepam <sup>15</sup>	0.2–0.7	1		1–3	
Praziquantel	appr. 0.2			1–2.5	
Prazosin	0.001–0.02	0.9		2.9 ± 0.8	[269, 426]
Prednisolone	0.5–1			2–6	
Prilocaine	0.5–1.5 (–2) <sup>126</sup>	5–6	appr. 20	1–2	[162, 557]
Primaquine	appr. 0.1–0.2			4–7	[423]
Primidone <sup>63</sup>	4–12 (8–15)	20–50	65	4–12, 9–22	[60, 145]
Probenecid	100–200 (20–150)			3–17 <sup>37</sup>	
Procaine	0.2–2.5 (–10)	15–20	20	–0.5	[423, 528]
Procainamide <sup>5</sup>	4–10 (3–9)	10–15	20	2–5	
N-Acetylprocainamide <sup>38</sup>	5–30 (10–35, 15–40)			3–7	
Prochlorperazine	0.01–0.05	0.2–0.3	5	7–9 (–18)	[155, 340, 528]
Procyclidine	0.08–0.63	1–2	7.8 <sup>8</sup>	7–16	[423, 528]
Proguanil <sup>48</sup>	appr. 0.04–0.15 <sup>114</sup>			13–24 <sup>114</sup>	[117]
Promazine	0.01–0.05 (–0.4)	1	5	5–41 (8 ± 7)	
Promethazine	0.05–0.2 (–0.4)	1–2	2.4 <sup>8</sup> ; 1.8–5.4 <sup>250</sup>	8–15 (–20)	[114, 506]
Propafenone <sup>48</sup>	0.4–3 (0.06–1)	2–3	7.7 <sup>8</sup>	5–8, 2–32 <sup>48</sup>	[244, 426]
Propallylonal	0.3–10	>10		appr. 3	
2-Propanol	see Isopropanol				
Propantheline	appr. –0.02			1–3	[133, 155]
Propiomazine	<0.3 (?)			8–10	[114, 190]
Propofol	appr. 2–8			3–8 <sup>91</sup>	[11, 299]
Propoxyphene	see Dextropropoxyphen				
Propranolol	0.02–0.3	(0.5–) 1–3	4–10	2–6	[466, 504]
Propylene glycol	0.05–0.5	1000–2000; 4700 <sup>8</sup>			[62, 528]
Propylhexedrine	0.01	0.5	2–3	?	[133, 528]
Propyphenazone	3–12			1–1.5 (–3)	[340, 468, 469]
Prothipendyl	appr. 0.05–0.2	appr. 0.5 (–1)		2–3	
Protriptyline	0.05–0.3	0.5	1	50–200	
Pseudoephedrine	0.5–0.8		19–20	9–16	[423, 528]
Pyrazinamide	30–75			9–10 (–25)	[110, 155, 340]
Pyridostigmine	<0.05–0.2			1–2.5	[9, 554, 559]
Pyridoxine	0.003–0.018			3–6	[429]
Pyrimethamine	appr. –1.5			80–96	[133, 155]
Pyrithyldione	1–10			11–20	[340, 468, 469]
Quazepam <sup>131</sup>	0.01–0.05 (–0.15)			39 (25–41)	[272, 423, 528]
Quetiapine	<1 <sup>239</sup>	1.8 <sup>8</sup>	12.7 <sup>8</sup>	appr. 5–7 <sup>240</sup>	[12, 102, 185, 374, 408]
Quinidine <sup>48</sup>	1–5	6–10	10–15	4–12	[357]
Quinine	1–7	10		4–15	[115, 390]



**REVIEW**

**Table (continued)**

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Rabeprazole	appr. -0.6			1-2	[423]
Ramipril	appr. 0.001-0.01 <sup>228</sup>			1-5	[155]
Ranitidine	0.05-1			2-4	[344]
Reboxetine	C <sub>max</sub> < 0.3			12-14	[135, 155]
Recainam	1.3-5.7			5-7	[7]
Remoxipride	2.15 ± 0.59 <sup>132</sup>		41-150	5-10	[114, 250, 290]
Retinol (Vitamin A)	0.2-0.8 (0.7-2.8 µmol/l)				[342, 429]
Ricin		0.0005			[276a]
Rifabutin	0.05-0.15			45 (?)	[155]
Rifampicin (Rifampin)	0.1-10 <sup>101</sup>		55 <sup>8</sup>	2.3-5	[28, 110, 236, 407a]
Rifapentine	?			13.2	[110]
Riluzole	appr. 0.05-0.5 (-1.5)			9-15	[317, 423]
Risperidone <sup>48</sup>	appr. 0.006 <sup>158</sup>		1.8 <sup>8</sup>	2-4 <sup>159</sup>	[28, 401]
Ritonavir	appr. 5-11 (-20)			3-5	[155, 224]
Rivastigmine	?			1-2	[230, 423]
Rizatriptan	appr. -0.1			2-3	[155, 423]
Ropinirole	0.0004-0.006 <sup>254</sup>			6 (2-10)	[263]
Ropivacaine		(1-) 2 <sup>173</sup>		2 <sup>168</sup>	[125, 332, 473]
Roxatidine	0.1-0.8			5-6	
Roxithromycin	4-12			12	[17, 155]
Salbutamol (Albuterol)	<0.01-0.02	0.1-0.15 <sup>116</sup>	0.16	3-6	[303, 528]
Salicylamide	5-40			appr. 1	
Salicylic acid	20-200	300-350	(400-) 500	3-20	[77, 155, 207, 234, 329, 334, 409]
Scopolamine	0.0001-0.0003 (-0.001)			appr. 3	[423, 528]
Secbutabarbital	5-10 (-15)	20	30	34-42	
Secobarbital	1.5-5	7-10	10-15	15-30	
Selegiline	see Amphetamine and Methamphetamine			1.2	[155]
Selenium	0.045-0.13	0.4			[133, 155, 359]
Sertraline	0.05-0.25 (-0.5)	0.29 <sup>8</sup>	1.6 <sup>8</sup> ; 3 <sup>8</sup>	24-28	[28, 317, 345a, 423, 528]
Sildenafil	appr. 0.05-0.5			3-5	[155, 423]
Silver	-0.005	0.06-0.6			[528]
Sirolimus	0.005-0.015 <sup>244</sup>	0.015 (-0.06)		57-63	[155, 256, 322, 324, 576]
Sodium nitroprusside	see Thiocyanate			0.1	
Sodium oxybate (GHB)	see 4-Hydroxybutyrate				
Sodium valproate	see Valproic acid				
Sotalol <sup>167</sup>	0.5-3 (-4)	7.5-16 <sup>8</sup>	40 <sup>8</sup> ; 43 <sup>8</sup>	5-13 (-17)	[118, 466, 498]
Sparteine <sup>48</sup>	0.5-1			2.6	
Spiramycin	appr. -3			5-8	[61, 155]
Spirolactone	(0.05-) 0.1-0.25 (-0.5) <sup>73</sup>			13-24 <sup>73</sup>	[423, 528]
Stiripentol	appr. 4-22	20		13	[133, 155]
Streptomycin	1-5 (15-40)	40-50		2-4	[317, 423, 528]
Strontium	-0.03				[133]
Strychnine		0.075-0.1	0.2-2	appr. 10-15	[423, 528]
Sufentanil	0.0005-0.01 <sup>4</sup>		0.001-0.007 <sup>8</sup>	2-5, 22	[19, 28, 52, 194, 226, 403, 460, 462]
Sulbactam	-80			1-2 <sup>70</sup>	[88, 155]
Sulfamethoxazole	30-60 <sup>56</sup>	200-400		9-12	[155, 389]
Sulfasalazine <sup>34</sup>	5-30 (-70)			4-10	
Sulfinpyrazone	6-17			3-5	
Sulindac	1-5 <sup>102</sup>			appr. 7	[91]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Sulpiride	0.05–0.4 (–0.6) <sup>225</sup>		3.8 <sup>8</sup> ; 38 <sup>8</sup>	4–7	[28, 104, 155, 528]
Sultiam (Sulthiame)	0.5–12.5 (6–10)	12–15	20–25	3–30	[496]
Sumatriptan	0.018–0.06			2	[423]
Suramin	>100 <sup>117</sup>	300 <sup>118</sup>		44–54	[281]
2,4,5-T	see 2,4,5-Trichloro-phenoxyacetic acid				
Tacrine	appr. 0.01			2–4	[230]
Tacrolimus (FK–506)	0.005–0.015 (–0.02)	(0.015–) 0.02–0.025		9–16	[216, 254, 306, 360, 511, 528, 533, 538–540, 543, 564]
Talinolol	0.04–0.15		5 <sup>8</sup> , 12 <sup>9</sup> ; 20 <sup>8</sup>	10–14	[466, 514, 515]
Talipexole	appr. 0.0001–0.001			5–9	[423]
Tamoxifen	0.05–0.5			5–7 <sup>6</sup>	[133, 155]
Taxol	see Paclitaxel				
Teicoplanin	(10–) 15–20 (–40)	200		10–15; 83–168 <sup>83</sup>	[243, 561]
Temazepam	0.02–0.15 (–0.9)	1	8.2 <sup>8</sup> ; 14 <sup>8</sup>	6–25	[139, 272, 423, 528]
Tenoxicam <sup>174</sup>	appr. 5–10			(50–) 70–90	[198, 370]
Terazosin	appr. 0.02–0.08			8–12	[423]
Terbinafine	0.01–0.03 <sup>205</sup>			22–26	[155, 527, 528]
Terbutaline	0.001–0.006 (–0.01)		0.04	16–20 <sup>89</sup>	[423, 528]
Terfenadine	<0.01	0.06 <sup>148</sup>	0.4 <sup>8</sup>	15–22 <sup>64</sup>	[28, 155, 566]
Tetrachloroethylene			4–5		[528]
Tetracycline	1–5 (5–10)	30		6–10	[155, 423, 528]
Tetrazepam <sup>40</sup>	0.05–0.6 (–1)			10–26	[272]
Thalidomide	0.5–1.5 (–8)			5–9	[155, 423]
Thallium		0.1–0.5 <sup>179</sup> ; 5.6 <sup>8</sup>	0.5–11	– <sup>6</sup>	[59, 155, 528]
Theobromine	10–15	20		6–10	[528]
Theophylline	(5–) 8–15 (–20) <sup>82</sup>	20	50	6–9 <sup>41</sup>	[84, 103, 120, 122, 157, 180, 217, 267, 404, 447, 475, 508, 553]
Thiamphenicol	0.5–3–10 (–15)	20		2–7	[423]
Thiazinamium	0.05–0.15	0.3			[317, 423, 528]
Thiocyanate	1–12 <sup>144</sup>	35–50	200	3–4 <sup>6</sup>	[3, 155, 446, 528]
from Nitroprusside	5–30	50–100			
Thiopental <sup>57</sup>	1–5		10–15 <sup>58</sup>	3–8	
Thiopropazine	appr. 0.001–0.02	0.1			[423]
Thioridazine <sup>133</sup>	0.1–2 (0.2–0.8–1.25) <sup>133</sup>	2.5–5	3–10	7–13 (–36)	[114]
Thiothixene	see Tiotixene				
Thyroxine	see Levothyroxine				
Tiagabine	0.05–0.2 (?)	0.5–0.6; 3.1 <sup>8</sup> , 24 <sup>5</sup>		7–9 (4–13)	[2, 155, 294, 295, 318, 399, 423, 519]
Tiaprude	max. 1–2			appr. 3–4	[423]
Tiaprofenic acid	appr. 15–40 <sup>193</sup>			1.5–3	[89, 155, 414]
Ticlopidine	<1–2 (?)			0.8 <sup>100</sup>	
Tilidine <sup>25</sup>	0.05–0.12		1.7 <sup>8</sup>	appr. 3	
Tiludronate	0.2–1.5			65–78 (–150)	[472]
Timolol	0.005–0.05 (–0.1)			2–6	
Tin	0.03–0.14				[133, 528]
Tinidazol	max. –60			11–15	[133, 155]
Tiopronin	appr. 2–5			23 ± 11	[158]
Tiotixene	0.001–0.03 (0.002–0.014)	0.1		34–36	[346]
Tizanidine	appr. 0.015			appr. 2.5	[155]
Tobramycin	4–10 <sup>154</sup>	12–15		2–3	[71, 155, 454, 489]
Tocainide	4–12 (6–10)	13–15; 20 <sup>8</sup>	74 <sup>8</sup> ; 140 <sup>8</sup>	8–25	[23a, 28, 155, 292]
Tofenacine	0.025–0.1	0.5–1			[340, 528]
Tolbutamide	50–100	400–500	640 <sup>8</sup>	4–12	[26, 528]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Tolmetin	10–80	60 (?)		2–4	[528]
Toluene			10		[528]
Topiramate	3.4–5.2 (–10?) <sup>218</sup>			20–30	[399, 423, 519]
Topotecan	appr. 0.001–0.01 <sup>190</sup>			2–3	[152, 155, 205]
Tramadol <sup>48</sup>	0.1–1 (>0.3) <sup>87</sup>	1	2 <sup>8, 49</sup> ; 13 <sup>8</sup> ; 38.3 <sup>8, 252</sup>	5–10	[35, 298, 341, 528]
Tranexamic acid	10–50			10	
Tranlycypromine	–0.2 (?)	0.5 <sup>8, 202</sup>	0.7 <sup>8</sup> ; 5 <sup>8</sup>	1.5–3.5	[238]
Trapidil	(4–) 6–10			2–6, 12	[155, 269, 339]
Trazodone <sup>145</sup>	(0.5–) 0.8–1.6	4	12–15 <sup>8</sup>	4–8 (6–13)	[104, 381]
Triamterene	0.01–0.1			1.5–4	[155, 426]
Triazolam	0.002–0.02	0.04		2–5	[229, 272, 366]
2,2,2-Tribromoethanol		50	90		[133, 528]
Trichloroethane			100–1000		[528]
2,2,2-Trichloroethanol	5–15	40–70	60–100		[28, 133, 528]
2,4,5-Trichlorophenoxyacetic acid (2,4,5-T)	–	appr. 100	200	23–33	[155, 528]
Trifluoperazine	0.001–0.01 (0.05)	0.1–0.2		7–18	
Triflupromazine	0.03–0.1	0.3–0.5		appr. 6	
Trihexyphenidyl	– <sup>75</sup>	0.5		3–5	[340, 524]
Trimeprazine	see Alimemazine				
Trimethadione	20–40			?	[528]
Trimethobenzamide	1–2			?	[133, 528]
Trimethoprim	1.5–2.5 <sup>56</sup>	20		8–11	[155, 389]
Trimipramine	0.01–0.25	0.5	1.7–8.2 <sup>251</sup>	10–20 (–40)	[114]
Tripelennamine	0.02–0.06		10	5–8	[423, 428, 528]
Triprolidine	0.004–0.045			2–5	[428]
Tropisetron	appr. 0.02–0.05			5.6–8.6	[429]
Tubocurarine	(0.6–) 1–3 (–6)			2–4	
Tungsten	–0.035				[133]
Urapidil	appr. 0.1–0.2			2.7–7	[155, 269]
Valdetamide	see Diethylpentenamide				
Valnoctamide	5	40		?	[528]
Valproic acid	40–100 (50–150)	150–200	720 <sup>8</sup>	10–20 (7–17)	[28, 60, 145]
Vanadium	–0.05				[133]
Vancomycin	≤5–10 (–12) <sup>142</sup>	30		4–11 <sup>83</sup>	[28, 71, 119, 144, 296, 323, 330, 394, 551]
Vecuronium	appr. 0.2–0.37 (–0.5)			1–1.5	[133, 155, 340]
Venlafaxine	appr. 0.2–0.4 <sup>189</sup>	1–1.5 <sup>266</sup>	6.6 <sup>8</sup>	3–5	[28, 270, 528]
Verapamil <sup>90</sup>	(0.01–) 0.02–0.25 (–0.4)	1	2.5; 3.9 <sup>8</sup>	6–14 <sup>42</sup>	[114, 268, 292, 319, 471]
Vigabatrin	2–9 (–15) <sup>94</sup>			5–8	[28, 519]
Viloxazine	–6.0–8.0 (?)			2–5	[104, 155, 423]
Vincamine	<0.25 (?)			1–2 (8–17)	
Vinylbital	1–3	5	8	18–33	
Viquidil	appr. 0.15–0.25			6–12	
Vitamin A	see Retinol				
Vitamin C	see Ascorbic acid				
Vitamin D	>50 nmol/l <sup>263</sup>			appr. 30 <sup>6</sup>	[328]
Warfarin	1–3 (–7)	10–12	100	37–50 <sup>97</sup>	[155, 426, 469, 555]
Wismut	see Bismut(h)				
Xamoterol	appr. 0.02–0.04 (–0.1)			7–8	[133, 155]
Xipamide	–20			5–8	[133, 155]
Xylene			3–40		[528]
Yohimbine	appr. 0.05–0.3			1–3	[133, 423]
Zafirlukast	0.005–0.03			10	[155, 423]

Table (continued)

Substance	Blood-plasma/serum concentration (µg/ml)			t <sub>1/2</sub> (h)	Ref.
	Therapeutic ('normal')	toxic (from)	comatose-fatal (from)		
Zalcitabine	appr. 0.1 (0.5 µmol/l)			1–3 <sup>83</sup>	[66, 358]
Zanoterone	0.1–0.5				[568]
Zidovudine <sup>51</sup>	0.1–0.3 (–1)	2–3		1–1.5	[66, 136, 137, 155, 212, 358]
Zinc	0.6–1.3	2	4 <sup>28</sup>		[429]
Zipeprol	0.1–0.7		5.8 <sup>8</sup> ; 10.6 <sup>8</sup>	?	[133, 428]
Ziprasidone	0.02–0.06			2–7	[155, 423]
Zolmitriptan	appr. 0.007–0.01			2.5–3	[423]
Zolpidem	0.08–0.15 (–0.2)	0.5	2–4	2–5	[96, 114, 154, 155, 160, 282, 423, 528, 563]
Zonisamide	(15–) 20–30 (–40)	(30–) 40–70	100 <sup>208</sup>	50–70 <sup>209</sup>	[276, 347, 399, 519]
Zopiclone	<0.1	0.15	0.6–1.8	3.5–8	[114, 155, 423, 528]
Zotepine	0.01–0.15	0.15–0.2		14–16	[155]
Zuclopenthixol <sup>48</sup>	0.005–0.1	0.15–0.3		appr. 20	[423, 469]

Clinical categories used for grouping analytical data:

Therapeutic: blood-plasma/serum concentrations (in general, trough at steady state) observed following therapeutically effective doses; no, or only minimal, side-effects (drugs); 'normal': concentrations associated with no, or only minimal, toxic effects (other xenobiotics).

Toxic: blood-plasma/serum concentrations which produce toxicity.

Comatose-fatal: blood-plasma/serum (comatose) concentrations and whole blood (fatal) concentrations reported to have caused coma and death, respectively.

t<sub>1/2</sub>: in general, terminal elimination half-life.

Ref.: if not specifically referenced, data was taken from review articles [13, 28, 40, 41, 57, 63, 72, 99, 100, 104, 105, 109, 111, 112, 114, 133, 155, 165, 240, 272, 317, 340, 354, 376, 378, 393, 395, 423, 426–429, 441, 443, 466, 468, 469, 489, 491, 495, 510, 527, 528, 534] and/or supplemented with our clinical and forensic analytical results.

Annotations

- <sup>1</sup> active metabolite of acebutolol
- <sup>2</sup> as salicylic acid (for analgesic and antipyretic effect)
- <sup>3</sup> as digoxin
- <sup>4</sup> during mechanical ventilation
- <sup>5</sup> slow (poor) and rapid (extensive) acetylators (metabolizers)
- <sup>6</sup> days
- <sup>7</sup> active metabolites nortriptyline (see Table) and amitriptyline oxide (t<sub>1/2</sub>: 1.5–3 h)
- <sup>8</sup> case report
- <sup>9</sup> in patients with impaired renal function in some cases up to 100 h
- <sup>10</sup> active metabolite 6-mercaptopurine (t<sub>1/2</sub>: 1–1.5 h)
- <sup>11</sup> appr. 0.2 h for azathioprine
- <sup>12</sup> active metabolite carbamazepine-10,11-epoxide (t<sub>1/2</sub>: 5–16 h; usual plasma concentration range 0.2–2 µg/ml) should be considered in case of intoxication
- <sup>13</sup> each sum carbromal(um) + carbamide (t<sub>1/2</sub>: 12–15 days)
- <sup>14</sup> each as trichloroethanol
- <sup>15</sup> active metabolite desmethyldiazepam = nordazepam (see Table)
- <sup>16</sup> nephrotoxic
- <sup>17</sup> active metabolite desmethylclobazam
- <sup>18</sup> duration of pharmacological effects: 0.3–0.4 h; major metabolite: benzoyllecgonine (t<sub>1/2</sub>: 5–6 h)
- <sup>19</sup> active metabolites nordazepam and oxazepam (see Table)
- <sup>20</sup> active metabolite nordothiepin (t<sub>1/2</sub>: 20–60 h)
- <sup>21</sup> active metabolite desmethyldoxepin (nordoxepin, t<sub>1/2</sub>: 33–80 h) should be considered in case of intoxication
- <sup>22</sup> benzodiazepineantagonist
- <sup>23</sup> active metabolites
- <sup>24</sup> active metabolite desalkylflurazepam (t<sub>1/2</sub>: 74 ± 24 h)
- <sup>25</sup> active metabolite nortilidine (t<sub>1/2</sub>: 6 h), comatose-fatal plasma concentration: 4.4 µg/ml<sup>8</sup>
- <sup>26</sup> in some cases up to 80 h
- <sup>27</sup> active metabolite levomepromazine sulfoxide (t<sub>1/2</sub>: 5–10 h)
- <sup>28</sup> t<sub>1/2</sub> for biological effects
- <sup>29</sup> active metabolite desipramine (see Table)
- <sup>30</sup> active metabolites diazepam, nordazepam plus oxazepam (see Table)
- <sup>31</sup> active metabolite of mesuximide
- <sup>32</sup> sum of active metabolites
- <sup>33</sup> each as desacetylmepipranolol
- <sup>34</sup> active metabolite 5-aminosalicylic acid (mesalazine, see Table); rapid/slow acetylators of the primary metabolite sulfapyridine
- <sup>35</sup> in some cases longer
- <sup>36</sup> active metabolite oxyphenbutazone (t<sub>1/2</sub>: 27–64 h)
- <sup>37</sup> dose dependent
- <sup>38</sup> active metabolite of procainamide
- <sup>39</sup> for the management of osteoporosis

- <sup>40</sup> active metabolite nortetrazepam (t<sub>1/2</sub>: 25–51 h)
- <sup>41</sup> smokers: 3–6 h
- <sup>42</sup> during steady state
- <sup>43</sup> astemizole plus desmethylastemizole
- <sup>44</sup> blood drug concentrations following therapeutically effective doses below detection limit
- <sup>45</sup> as decanoate (t<sub>1/2</sub>: 5–12 days)
- <sup>46</sup> in intensive care patients in some cases 8–22 h
- <sup>47</sup> physiologic
- <sup>48</sup> rapid (extensive) and slow (poor) metabolizers (genetic polymorphism)
- <sup>49</sup> 6 month-old-child, appr. 15 h after 100 mg rectally tramadol
- <sup>50</sup> total labelalol: 0.7–5.0 µg/ml
- <sup>51</sup> C<sub>max</sub> 0.038 ± 0.006 µg/ml after a single oral dose of 150 µg/kg in nine persons with onchocerciasis (t<sub>1/2</sub>: 56 ± 7 h)
- <sup>52</sup> as enalaprilat
- <sup>53</sup> duration of clinical effect: 3–5 h
- <sup>54</sup> product after hydrolysis
- <sup>55</sup> narcotic; analyzed during distribution phase
- <sup>56</sup> for pneumocystis carinii pneumonia (PcP) treatment: sulfamethoxazole 100–200 µg/ml, trimethoprim 5–10 µg/ml
- <sup>57</sup> metabolite: pentobarbital (see Table)
- <sup>58</sup> "narcotic"
- <sup>59</sup> higher with meningism (–25 µg/ml); decreased protein binding in neonates results in increased unbound drug
- <sup>60</sup> each as 2-hydroxyflutamide (active and major metabolite)
- <sup>61</sup> active metabolite of allopurinol
- <sup>62</sup> active metabolite paracetamol (acetaminophen, see Table)
- <sup>63</sup> active metabolite phenobarbital (see Table)
- <sup>64</sup> as active carboxylic acid metabolite = fexofenadine (t<sub>1/2</sub>: mean 15 h)
- <sup>65</sup> 1 mg oral alprazolam/day equals appr. a plasma concentration of 10 ng alprazolam/ml during steady state. Usually higher doses/plasma concentrations are recommended for the treatment of phobias when compared to panic disorder/attacks
- <sup>66</sup> highly inter- and intraindividual variable kinetics; for children (therapeutically): 0.04–0.1 µg/ml; active metabolite desmethylchlorpromazine
- <sup>67</sup> ≥0.25 µmol/l desirable for echinococcosis
- <sup>68</sup> mean: 27 h; for geriatric patients (>65 years) in some cases increased to more than 90 h
- <sup>69</sup> active metabolite 2-hydroxydesipramine (t<sub>1/2</sub>: mean 18 h; in patients with impaired renal function several fold increased)
- <sup>70</sup> in patients with impaired renal function several fold increased
- <sup>71</sup> in colon tissue 0.8–1.8 h after 1 × 2 g i.v.: 94.0–7.4 µg/g
- <sup>72</sup> active metabolites 1-(5-hydroxyhexyl)-3,7-dimethylxanthine and 1-(3-carboxypropyl)-3,7-dimethylxanthine (t<sub>1/2</sub>: 1–1.6 h), among others, with 5 and 8 times, respectively, higher plasma levels than pentoxifylline
- <sup>73</sup> as canrenone (one of the active metabolites of spironolactone, t<sub>1/2</sub>: 1.31.4 h)

- 74 appr. 8 h after ingestion of probably 210 mg haloperidol and 1400 mg orphenadrine-HCl with life-threatening arrhythmias
- 75 data on effective plasma concentrations for Parkinson's disease not available
- 76 peak: 20–30 µg/ml, trough: <7 µg/ml
- 77 for hypertension: 0.2–0.45 µg/ml; for angina/CHD, arrhythmias: 0.3–0.8 µg/ml
- 78 therapeutic concentration of the unbound fraction: appr. 0.5–2 µg/ml
- 79 in mmol/l (mEq/l, mval/l): 0.4–1.2 (0.6–1.4), toxic from 1.5
- 80 terminal elimination  $t_{1/2}$ : 37 ± 6 h; increased in case of renal dysfunction
- 81 therapeutic concentration of the unbound fraction: 1–2.2 µg/ml
- 82 for (sleep) apnea: 5–10 µg/ml
- 83 increased in patients with impaired renal function
- 84  $C_{max}$  3–5 h after 4 mg oral loperamide hydrochloride: 1–3 ng/ml
- 85 active metabolite N-desmethylclomipramine ( $t_{1/2}$ : 21–65 h, mean: 40 h) 12–36 h
- 86 post-operative (on-demand; i.v.): 0.02–1–2 µg/ml (median: 0.29–0.92 µg/ml) as minimal (analgesic) effective concentration; O-desmethyltramadol: 0.03–0.04 µg/ml (median: 0.036 µg/ml)
- 88 10–36 h
- 89 11–26 h
- 90 stereoselective metabolism (therapeutic concentration after oral application higher than after intravenous administration)
- 91  $t_{1/2}$  for β-phase: 0.5–1 h
- 92 as albendazole sulfoxide (active metabolite)
- 93  $t_{1/2}$  in slow (poor) metabolizers appr. 40 h
- 94 through plasma concentration at steady state during 2 g twice daily p.o. appr. 9 µg/ml;  $C_{max}$  0.8 h after 1 g orally: appr. 45 µg/ml
- 95 as active metabolite methimazole
- 96 mean 80 min
- 97 15–85 h
- 98 plasma concentrations does not correspond with pharmacological effects
- 99 plasma concentrations of the less potent major metabolite 6-β-naltrexol ( $t_{1/2}$ : 11–13 h) are usually 1.5–10 times higher
- 100 appr. 25–30 h for the metabolites
- 101 sum rifampicin plus metabolites
- 102 sum sulindac plus metabolites (sulindac sulfide,  $t_{1/2}$ : 15–18 h;  $t_{1/2}$  sulfone: 17–20 h)
- 103 abuse
- 104 sum carisoprodol plus meprobamate
- 105 12–15 days for the metabolites
- 106  $t_{1/2}$  for total platinum plasma concentrations: 20–40 h (up to 6–7 days) 2–20 µmol/l
- 108 carboxylic acid metabolite ( $t_{1/2}$ : appr. 20 days): 1.5–5.5 µg/ml
- 109 during concomitant therapy with carbamazepine or phenytoin 8–33 h (mean: 15 h), during concomitant therapy with valproic acid 31–89 h (mean: 60 h)
- 110 in infants and after intoxications in some cases dramatically increased
- 111 during steady state 3–4 h after oral doses of 100–400 mg; prophylaxis of candidiasis: >0.2 µg/ml and of aspergillosis: >1.0 µg/ml in patients with acute myeloid leukemia (AML)
- 112 plasma concentrations of the major metabolite 13-cis-acitretin are usually higher
- 113 higher and increased, respectively, in patients with impaired hepatic function; for tinnitus aurium: therapeutic plasma concentration appr. 1–2 µg/ml
- 114 biologically active/major metabolite cycloguanil ( $t_{1/2}$ : 8–17 h): plasma concentration level after daily oral doses of 100–200 mg proguanil appr. 0.02–0.06 µg/ml
- 115 active metabolite norpethidine ( $t_{1/2}$ : 14–24 (–48) h): toxic from appr. 0.5 µg/ml
- 116 tremor, hypokalemia
- 117 as cytostatic drug: >200 µg/ml
- 118 neurotoxic
- 119 in terminal renal insufficiency appr. 0.5–2 µg/ml, cumulation of the inactive metabolite N-acetyl-5-aminosalicylic acid (Ac-5-ASA) up to 20 µg/ml without adverse effects
- 120  $t_{1/2}$  of the inactive major metabolite N-acetyl-5-aminosalicylic acid (Ac-5-ASA) appr. 6–9 h
- 121 tocolytic (4.5–6.25 mval(mEq)/l, 2.25–3.125 mmol/l). Approximate normal range: 18–25 µg Mg<sup>2+</sup>/ml (0.74–1.03 mmol/l); conversion factor: mg/dl × 0.4113 = mmol/l
- 122  $C_{max}$  appr. 2–8 µmol/l (i.e. 1.7–6.8 µg/ml, after 170–275 mg/m<sup>2</sup> intravenously for 6 h); much lower after intraperitoneal injection
- 123 as transdermal system (patch); plasma concentrations of the major metabolite cotinine ( $t_{1/2}$ : mean 16–20 h) appr. 10 times higher
- 124 mean 2 h; after application of the transdermal system possibly longer
- 125 active metabolites desipramine (see Table), 2-hydroxyimipramine ( $t_{1/2}$ : 6–18 h), and 2-hydroxydesipramine<sup>69</sup>
- 126 3–7 min after retrobulbar blockade: 0.5–1.1 µg/ml
- 127 for myasthenia gravis
- 128 EC<sub>50</sub> analgesia; EC<sub>50</sub> respiratory depression: 0.035 ± 0.022 µg/ml
- 129 appr. 14 h after oral ingestion of 1.5 g
- 130  $t_{1/2}$  of the active metabolite norfluoxetine: 7–9 days (mean)
- 131 active metabolites 2-oxoquazepam ( $t_{1/2}$ : 39 (28–43) h) and N-desalkyl-2-oxoquazepam (N-desalkylflurazepam,  $t_{1/2}$ : 74 ± 24 h)
- 132 peak plasma concentration during steady state ( $C_{max}^{ss}$ )
- 133 range of plasma concentrations after therapeutically effective doses of thioridazine for the active metabolites mesoridazine (thioridazine-2-sulfoxide): 0.2–1.6 µg/ml ( $t_{1/2}$ : 10–14 h) and sulforidazine (thioridazine-2-sulfone): up to 0.6 µg/ml ( $t_{1/2}$ : 10–16 h) and for the inactive metabolite thioridazine-5(ring)-sulfoxide: 0.06–4 µg/ml; probably, the best correlation exists between the plasma concentration of mesoridazine and the clinical response
- 134 usually sleep occurred with ≥0.1 µg/ml; in infants and children (<13 years): in some cases during mechanical ventilation up to 3 µg/ml; α-hydroxymidazolam-glucuronide likely contributes in case of impaired renal function to prolonged sedation
- 135 plasma concentration range of the primary metabolite 1,5-dimethyl-3,3-diphenyl-2-ethylidene-pyrrolidine during steady state: 0.005–0.055 µg/ml (daily oral methadone dose: 10–225 mg, mean 60 mg)
- 136 ratio clozapine/active metabolite N-desmethylclozapine (norclozapine,  $t_{1/2}$ : 19.2 ± 10.2 h) usually 1.0 to 2.5
- 137 maximum antiemetic effect at >0.01 µg/ml
- 138 active metabolite descarboethoxyloratadine ( $t_{1/2}$ : 17–24 h): appr. 0.005–0.02 µg/ml
- 139 0.15 ± 0.05% per h
- 140 during chronic administration appr. 10–20 h (induction of own metabolism)
- 141 caution is warranted in case of concomitant use or intoxication with serotonin reuptake inhibitors (SSRI) as citalopram, clomipramine (fluoxetine, paroxetine): possible serotonin syndrome
- 142 trough concentration; peak concentration: <40 µg/ml
- 143 distribution half-life: 0.3–0.5 (–1) h
- 144 non-smoker: 1–4 µg/ml (17–69 µmol/l); smoker: 3–12 µg/ml (52–206 µmol/l)
- 145 major active metabolite 1-m-chlorophenylpiperazine; plasma concentration appr. 1/10 compared to trazodone
- 146 plasma concentration for maximal cellular accumulation of the active form gemcitabine-5'-triphosphate
- 147 after topical nasal or ocular administration
- 148 Torsade de pointes, usually due to cytochrome P450 3A4 inhibition (e.g., ketoconazole, erythromycin) and/or impaired hepatic function
- 149 after oral administration; after topical application: plasma concentration < 0.03 µg/ml and  $t_{1/2}$  appr. 22 h
- 150 for each added 1 mg/day dose of clonazepam, there is appr. an increase of 12 ng/ml in the plasma (patients with panic disorder)
- 151 sum amoxapine and major metabolite 8-hydroxyamoxapine ( $t_{1/2}$ : appr. 30 h;  $t_{1/2}$  7-hydroxyamoxapine: 4–6.5 h)
- 152 sum bupropion (amfebutamone) and morpholinole metabolite ( $t_{1/2}$ : 19–22 h)
- 153 after i.m.-application as decanoate appr. 3 weeks
- 154  $C_{min}$  <1–2 µg/ml at best (especially in patients with renal dysfunction)
- 155 appr. 0.02 µg/ml in organophosphorous ester poisoning depending on the clinical symptoms
- 156 in case of organophosphorous ester (e.g. parathion) intoxication; 250 mg intravenously as bolus followed by an infusion of 750 mg/24 h if used as an antiarrhythmic appr. 0.1–0.4 µg/ml
- 157 using daily oral doses of ≤25 mg 0.00046 µg risperidone/ml per mg dose and 0.0064 µg/ml per mg dose for risperidone plus 9-hydroxyrisperidone (the clinical effects likely results from the combined concentrations)
- 159 extensive metabolizers;  $t_{1/2}$  for risperidone plus 9-hydroxyrisperidone: 22–24 h
- 160 6 case reports: post-mortem 5.2–49 µg citalopram/g blood and 0.3–1.4 µg desmethylcitalopram/g blood
- 161 concentration/dose-values for extensive metabolizers: 0.025–0.55 (median 0.098) nmol/l per mg oral perphenazine, and 0.096–0.75 (median 0.195) nmol/l per mg oral perphenazine (mol wt 506.07) for poor metabolizers, respectively
- 162 two cases after ingestion of appr. 4 g moclobemide in combination with clomipramine (plasma concentration: 0.3–0.5 µg/ml, i.e. toxic)
- 163 as R-enantiomer, mean: 9 µg/ml
- 164 dosage: 50–55 mg/kg per day
- 165 appr. 2.5 h after ingestion of 50–100 mg amlodipine besylate with alcohol (263 mmol ethanol/l)
- 166 101 ng/ml 4 h after ingestion of 70 mg and 185 ng/ml at 10.5 h, complicated by oxazepam ingestion
- 167 data for d,l-sotalol
- 168 after i.v.-application;  $t_{1/2}$ : 4–7 h following epidural administration (appr. 4–5 h following intercostal block and appr. 8 h following brachial plexus blockade, respectively)
- 169 mean 19 h;  $t_{1/2}$  of oral cyclosporine microemulsion is appr. 8 h
- 170 a longer  $t_{1/2}$  has been reported in elderly patients, up to 3.8 days
- 171 target range of activated partial thromboplastin time (aPTT) is prolongation of 50–70 sec, aPTT prolongation of more than 100 sec has been associated with an increased risk of hemorrhagic events

- 172 as 10-hydroxycarbazepine for seizures; in patients with trigeminal neuralgia, therapeutic serum concentrations of the active metabolite 10-hydroxycarbazepine ( $t_{1/2}$ : 8–11 h): 50–110  $\mu\text{mol/l}$
- 173 mild CNS symptoms (limited data)
- 174 pharmacologically inactive metabolites 5' and 6'-hydroxytenoxicam
- 175 effective plasma concentrations for the 2 active metabolites: O-desmethylencaimide (0.05–0.3; toxic from 0.3  $\mu\text{g/ml}$ ,  $t_{1/2}$ : 11 h) and 3-methoxy-o-desmethylencaimide (0.06–0.28  $\mu\text{g/ml}$ ;  $t_{1/2}$ : >24 h) during long-term therapy
- 176 in poor metabolizers 9–11 h
- 177 "normal": 0.001–0.006; smoker: 0.005–0.012 (–0.15)  $\mu\text{g/ml}$ ;  $\mu\text{mol/l} \times 0.026 = \mu\text{g/ml}$
- 178 reference value; 0.001  $\mu\text{g/g}$  creatinine or 0.0014  $\mu\text{g/ml}$  urine; <30  $\mu\text{g/24 h}$  urine ("normal"); "toxic" from appr. 0.05–0.3  $\mu\text{g/ml}$  urine
- 179 >0.04  $\mu\text{g/ml}$  urine
- 180 up to years in chronically exposed workers
- 181 combination with 2,4-D and chlorpyrifos
- 182 in case of intoxication/overdose: 70–90 h
- 183 overdose
- 184 one case of toxicokinetic estimation in acute KCN poisoning
- 185 tentative target range;  $C_{\text{max}}^{\text{ss}}$  appr. 4.6  $\mu\text{g/ml}$  (300 mg tid) and appr. 8.4  $\mu\text{g/ml}$  (600 mg tid)
- 186 prolonged in case of impaired renal function to 16–43 h; >100 h in dialysis dependent patients
- 187 dependent of urine pH, if alkaline appr. 8–10 h
- 188 females showed significantly longer elimination half-lives (35.4  $\pm$  13.7 h) than males (mean 21–26 h); the  $t_{1/2}$  of the R(–)-enantiomer is twice that of the S(+)-enantiomer
- 189 after doses of 25, 75, and 150 mg every 8 h for 3 days, mean peak serum levels were 0.053, 0.167, and 0.393  $\mu\text{g/ml}$ ; corresponding levels of the major active metabolite O-desmethylvenlafaxine ( $t_{1/2}$ : 10–11 h) were 0.148, 0.397, and 0.686  $\mu\text{g/ml}$
- 190 at least 10 nmol of the lactone (mol wt 421.46) $\text{l}$  (?); decreases in absolute neutrophil counts of 50–90% were observed with steady state plasma concentrations of total topotecan (lactone + hydroxy acid) of 20–60 nmol/l, respectively
- 191 a mean steady state peak plasma concentration of 0.286  $\mu\text{g/ml}$  was observed in healthy volunteers after 60 mg (oral solution) every 12 hours for 10 doses
- 192 the metabolite 2',2'-difluoro-deoxyuridine (dFdU) has minimal antitumor activity but may contribute to the toxicity of gemcitabine
- 193  $C_{\text{max}}$  after 200 mg tid
- 194 serum concentration of benzoic acid following high dose diazepam i.v.-infusion and severe metabolic acidosis (5-year-old girl; urine concentration: 1200  $\mu\text{g/ml}$ )
- 195 1.5 h in dogs after i.v.-administration
- 196 for erythropoietic protoporphyria (EPP)
- 197 trough; peak: 0.1–0.5  $\mu\text{g/ml}$
- 198 +0.4  $\mu\text{g}$  of its metabolite 3-deacetylpancuronium/ml
- 199 "normal":  $\leq$ 2–3% of total Hb; from 15–20%: cyanosis, headache, dizziness
- 200 "normal":  $\leq$ 5% (elderly: –15%); smoker: 8–10%
- 201 2 h after ingestion
- 202 3 h after ingestion of 400 mg with no severe symptoms
- 203 mean steady state trough concentration; peak: 5–15  $\mu\text{g/ml}$
- 204 for Parkinson's disease (appr. 15–50 pmol/ml)
- 205 peak: 0.5–3  $\mu\text{g/ml}$
- 206 plasma concentrations below detection limit; plasma concentrations of the active metabolite 6-methoxy-2-naphthylacetic acid ( $t_{1/2}$ : appr. 24 h), which appears to be responsible for the effects, were 10–37  $\mu\text{g/ml}$  3–6 h after single oral doses of 250, 500, and 1000 mg
- 207 active metabolite 6-O-desmethyldonepezil
- 208 coma in a patient overdosing zonisamide, carbamazepine, and clonazepam
- 209 25–30 h in patients co-medicated with enzyme-inducing anticonvulsants
- 210 2–4 h in patients co-medicated with enzyme-inducing anticonvulsants
- 211 long-term (2–3 years) treated renal-transplant patients had significantly lower trough plasma concentrations of mycophenolic acid (1.94  $\pm$  0.24  $\mu\text{g/ml}$ ), the active metabolite, compared with patients taking mycophenolate mofetil (1 g twice daily) short-term (2–10 months; 3.53  $\pm$  0.45  $\mu\text{g/ml}$ ). Proposed mycophenolic acid pre-dose target concentration: 1–3.5  $\mu\text{g/ml}$
- 212 as mycophenolic acid
- 213 ten men with multiple sclerosis, 10–20 mg p.o. every 6 h 30 min before the next dose; peak levels <0.1  $\mu\text{g/ml}$  30 min after a dose
- 214 nine patients, maximum tolerated oral dose 50–100 mg
- 215  $t_{1/2}$  metabolite 3-O-methyldopa: 15 h
- 216 appr. 2.5  $\mu\text{mol/l}$  (1  $\mu\text{g/ml}$ ) 24 h after single doses of 100–800 mg and during daily treatment with 200 mg
- 217 active metabolite 14-hydroxyclarithromycin ( $t_{1/2}$ : 5–7 h)
- 218  $C_{\text{max}}$  following oral administration of 200, 400, 800, and 1200 mg, respectively: 3.7, 8, 18, and 29  $\mu\text{g/ml}$
- 219 at a daily dosage of 60, 120, and 240 mg the mean  $\pm$  SD concentration in patients with symptomatic ventricular tachyarrhythmias (n = 9–18) was 75  $\pm$  46, 144  $\pm$  105, and 324  $\pm$  180 nmol/l, respectively
- 220 nonlinear kinetics
- 221 appr. 5 h after ingestion of 3 g, not associated with severe toxicity to a 27-year-old woman
- 222 slightly increased (8–12 h) in patients with impaired hepatic function; active metabolites hydroxynefazodone ( $t_{1/2}$ : 2–5 h), m-chlorophenyl-piperazine ( $t_{1/2}$ : 4–10 h), and triazolidione ( $t_{1/2}$ : 10–12 h)
- 223 each as N-desmethyloximide; appr. methsuximide ( $t_{1/2}$ : 1–2 h) steady state concentration: 0.04–0.08  $\mu\text{g/ml}$
- 224 mean steady state trough concentration in 15 young adults receiving a daily dose of 0.47–1.71 mg isotretinoin/kg: 0.05–0.34  $\mu\text{g/ml}$  ( $t_{1/2}$ : 29  $\pm$  40 h), and for the 4-oxo metabolite ( $t_{1/2}$ : 22  $\pm$  10 h): 0.16–0.68  $\mu\text{g/ml}$
- 225 for depression; higher in case of schizophrenia (2–3  $\mu\text{g/ml}$ ?)
- 226 suggested threshold for the sum of clomipramine (0.05–0.06  $\mu\text{g/ml}$ ) and N-desmethylclomipramine (0.16–0.18  $\mu\text{g/ml}$ ): 0.2–0.24  $\mu\text{g/ml}$
- 227 for the active metabolite E-3174 ( $t_{1/2}$ : 4–9 h); plasma concentration of losartan producing 50% of maximal blood pressure response to exogenous angiotensin-II: 0.032  $\mu\text{g/ml}$
- 228 as ramiprilat ( $t_{1/2}$ : 13–17 (50–110) h)
- 229  $\text{IC}_{50}$  level for analgesic effect after oral surgery
- 230 the inhibitory concentration to reduce the level of extracellular hepatitis B DNA by 50% varied from 2.3 ng/ml to 1.3  $\mu\text{g/ml}$
- 231  $C_{\text{max}}$  at steady state (666 mg tid p.o.)
- 232 after oral administration of the enteric-coated tablet
- 233 trough <2 plus peak 6–10 (5–12)  $\mu\text{g/ml}$
- 234 reference value; <0.015  $\mu\text{g/ml}$  urine
- 235 active metabolite 4'-hydroxynimesulide ( $t_{1/2}$ : 3–9 h)
- 236  $C_{\text{max}}$  126.5 and 226.3 ng/ml (at 2 h) after 75 and 125 mg p.o.
- 237 in patients >60 years prolonged up to 10 h
- 238 adjuvant in methadone maintenance therapy
- 239 means of the 'average' steady state plasma concentration for the relatively high dose of 250 mg q8 h appr. 0.4–0.6  $\mu\text{g/ml}$
- 240 combination of distribution and elimination processes
- 241 as active metabolite fenofibric acid
- 242 appr. 37.5 mmol/l (mval/l, mEq/l)
- 243 steady state concentration 21.6  $\pm$  14.2  $\mu\text{g/ml}$  (mean  $\pm$  SD) during continuous infusion of 3 g (1.1–2.2 mg/kg h) every 24 hours in 44 patients undergoing coronary artery bypass graft surgery
- 244 target trough concentration if cyclosporin (CsA) is being used at trough concentrations of 0.075–0.15  $\mu\text{g/ml}$ ; without CsA: appr. 0.03  $\mu\text{g/ml}$  (LC/UV assay)
- 245 4 hours after ingestion of 30–40 tiagabine HCl 8 mg tablets (coma)
- 246 bupropion plus 10-hydroxybupropion
- 247 calculated steady state concentration in children (4 months to 16 years) receiving 0.3 mg/kg b.w. i.v.
- 248 femoral blood concentration of the metabolite desmethylalimemazine after fatal intoxication: 0.2–1.3  $\mu\text{g/g}$
- 249 40–50 min after 0.15 mg/kg i.v.
- 250 femoral blood concentration of the metabolite desmethylpromethazine after fatal intoxication (n = 3): 0.3–1.8  $\mu\text{g/g}$
- 251 femoral blood concentration of the metabolite desmethyltrimipramine after fatal intoxication (n = 10): 0.3–2.5  $\mu\text{g/g}$
- 252 fatal overdose with tramadol, alprazolam (0.21  $\mu\text{g/ml}$ ), and alcohol (1.29 g/kg) in a 30-year-old woman
- 253 enterohepatic circulation; prolonged in elderly subjects to 33.4 hours (range: 20.0–53.4 h)
- 254  $C_{\text{min}}/\text{D}$  [(ng/ml)/mg], i.e. dose-normalised trough plasma drug concentration, dosage interval 8 h
- 255 all data refer to the active metabolite A771726
- 256 steady state concentrations at 5, 10, and 25 mg/d, respectively
- 257 steady state trough concentrations after 400 mg/d orally; two major metabolites modafinil acid (appr. 0.5–0.8  $\mu\text{g/ml}$ ,  $t_{1/2}$ : 7.3  $\pm$  1.1 h) and modafinil sulfone (appr. 4.5–5.3  $\mu\text{g/ml}$ ), but neither appears to contribute to the wake-promoting properties of modafinil
- 258 mean plasma trough concentration at steady state obtained from 400 mg imatinib/day in 83 adult patients with chronic phase CML; peak: 2.3  $\mu\text{g/ml}$
- 259 in a 5-year-old girl
- 260 at this time (March 2003), there is insufficient evidence to recommend a general therapeutic range
- 261 active metabolite N-desethylamiodarone ( $t_{1/2}$ : 57–64 days), which achieves plasma concentrations similar to the parent compound
- 262 inactive metabolites deshydroxyethyl opipramol ( $t_{1/2}$ : 97  $\pm$  24 h) and opipramol N-oxide ( $t_{1/2}$ : 10.7  $\pm$  3.2 h)
- 263 as 25-hydroxyvitamin D for adults >49 years
- 264 6 h after reportedly ingestion of 30 g in a 38-year-old woman
- 265 metabolite perindoprilat, 3 to 10 hours, with a prolonged terminal half-life between 25 to 120 h
- 266 sum venlafaxine and O-desmethylvenlafaxine
- 267 for glaucoma 4–5  $\mu\text{g/ml}$
- 268 doxapram + keto-doxapram
- 269 24 h after ingestion of appr. 20 ml
- 270 active metabolite desethylamodiaquine ( $t_{1/2}$ : 1–10 days)
- 271 smokers: –0.0006  $\mu\text{g/ml}$

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