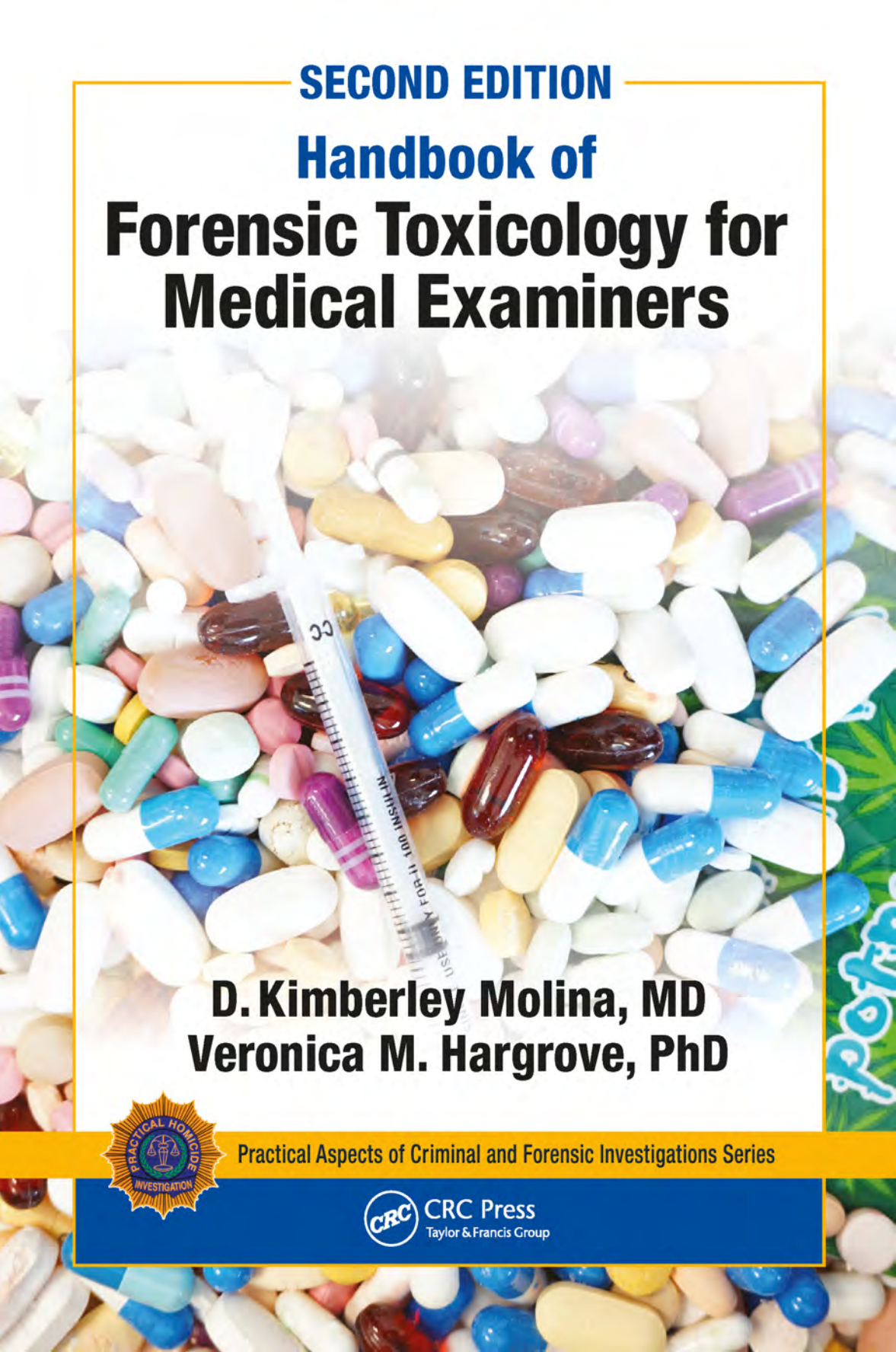
SECOND EDITION

Handbook of Forensic Toxicology for Medical Examiners



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Practical Aspects of Criminal and Forensic Investigations Series

CRC Press
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Handbook of Forensic Toxicology for Medical Examiners

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Handbook of FORENSIC TOXICOLOGY for MEDICAL EXAMINERS

Second Edition

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Editor's Note

This textbook is part of a series titled "Practical Aspects of Criminal and Forensic Investigations." This series was created by Vernon J. Geberth, a retired New York City Police Department lieutenant commander who is an author, educator, and consultant on homicide and forensic investigations.

This series has been designed to provide contemporary, comprehensive, and pragmatic information to the practitioner involved in criminal and forensic investigations by authors who are nationally recognized experts in their respective fields.

Contents

Series Editor

The Series Editor for *Practical Aspects of Criminal and Forensic Investigations* is Lieutenant Commander (retired) Vernon J. Geberth, New York City Police Department, who was the commanding officer of the Bronx Homicide Task Force, which handled more than 400 homicides a year. Commander Geberth has been president of P.H.I. Investigative Consultants, Inc., Marco Island, FL, since 1987. He has more than 47 years of law enforcement experience and has conducted homicide investigation seminars for more than 74,000 attendees from more than 8,000 law enforcement agencies.

Commander Geberth holds dual master's degrees in Clinical Psychology and Criminal Justice. He is a fellow in the American Academy of Forensic Sciences, Colorado Springs, CO, a graduate of the FBI National Academy, Quantico, VA, and the recipient of the Lifetime Achievement Award from the Vidocq Society.

He is an author, educator, and consultant on homicide and forensic investigations. He has published three best-selling books in this series, *Practical Homicide Investigation, Fifth Edition; Sex-Related Homicide and Death Investigation: Practical and Clinical Perspectives, Second Edition;* and *Practical Homicide Investigation: Checklist and Field Guide, Second Edition*.

He created, edited, and designed this series of more than 65 publications to provide contemporary, comprehensive, and pragmatic information to the practitioner involved in criminal and forensic investigations by authors who are nationally recognized experts in their respective fields.

He welcomes the opportunity to review new proposals for books covering any area of criminal and forensic investigation and may be reached through his email: vernongeberth@practicalhomicide.com.

List of Abbreviations

ABFT	American Board of Forensic Toxicology
aceta	acetaminophen
ACh	acetylcholinesterase
ASA	aspirin
BAC	blood alcohol (ethanol) content
bid	twice a day
CNS	central nervous system
CV	cardiovascular
d	day
g	gram
gtts	drops
h	hour
im	intramuscular
iv	intravenous
kg	kilogram
L	liter
mEq	milliequivalent
mg	milligram
min	minute
mL	milliliter
mo	month
NAME	National Association of Medical Examiners
ng	nanogram
NRI	norepinephrine reuptake inhibitor
NSAID	non-steroidal anti-inflammatory drug
OTC	over the counter
ppm	parts per million
po	by mouth (per os)
pr	per rectum
prn	as needed
q	every
qam	in the morning
qd	once a day
qHS	at bedtime
qid	four times a day

SC	subcutaneous
SNRI	serotonin and norepinephrine reuptake inhibitor
SSRI	selective serotonin reuptake inhibitor
supp	suppository
susp	suspension
TCA	tricyclic antidepressant
THC	delta-9-tetrahydrocannabinol
tid	three times a day
$\mathbf{V_d}$	volume of distribution
w/	with
wk	week
yr	year
λ	half-life
µg	microgram

How to Use This Book 1

For postmortem toxicology, the two most important concepts for any death investigator are:

1. **Drug concentrations should never be interpreted in a vacuum.**
2. **There is no such thing as a "lethal drug concentration."**

The purpose of this book is to assist forensic pathologists in the interpretation of common toxicology results. *This book is in no way meant as a substitute for a thorough death investigation and complete autopsy.*

Important points to consider are listed in the following:

- The concentrations given in this book are a compilation of the data from the literature.
  - The therapeutic/nontoxic concentrations given were determined either in serum during pharmacokinetic studies or were from whole blood samples taken from postmortem data from individuals dying of unrelated causes — who died with the drug present but without it contributing to death;
  - The toxic concentrations are serum concentrations obtained from individuals who suffered toxicities due to the drug listed but survived;
  - The lethal concentrations listed are for whole blood unless otherwise noted;
  - The lethal and toxic cases listed represent pure, single-drug intoxications unless otherwise noted.
- Consider the source.
  - Peripheral blood is preferable
    - Understand postmortem redistribution and the variables involved;
    - Some drugs are not as affected as others.
    - Not all peripheral blood is created equally — femoral is preferred.
  - Antemortem specimens may be serum and could affect interpretation.
  - Liver, urine, bile, and stomach contents do not necessarily indicate acute toxicity, only exposure.

- Consider the test.
  - Immunoassays may have cross reactivity giving false positive or false negative results.
  - Make certain to direct the testing for the drugs of interest.
    - Know which drugs are on the testing panels ordered and which drugs are found on which panels.
    - Some drugs may require specialized testing or sample collection.
- Consider the time.
  - Time elapsed since death may affect concentrations.
    - Some drugs may be metabolized after death or during the agonal period.
    - Postmortem redistribution may occur.
- Consider the circumstances.
  - When was the decedent last seen? What was the decedent doing? How was the deceased acting?
  - Are the terminal events consistent with a drug toxicity?
- Consider the decedent.
  - Are there other disease processes present?
  - How do the drugs and the diseases interact?
- Consider tolerance.
  - How long has the deceased been on the drug? At what dose? On what regimen?
    - Specifically consider in deaths with opiates/opioids, benzodiazepines, barbiturates, and ethanol.
  - Could withdrawal be possible?
    - Specifically consider with ethanol and benzodiazepines.
- Consider the presence of other drugs.
  - The presence of multiple drugs with similar effects can result in death or other adverse effects, such as serotonin syndrome.
- Consider intrinsic drug properties.
  - QT interval
    - Certain prescription and illicit drugs can prolong the QT interval.
    - Can be associated with sudden death, especially in the presence of underlying rhythm disturbances.
  - Metabolism
    - Approximately 30% of all drugs are affected by a drug metabolizing enzyme, the majority are part of the CYP450 system
    - Drug concentrations can vary by a factor of 600 between two individuals given the same dosage.
    - Genetic factors may play a role in how an individual absorbs, distributes, and metabolizes a drug.
      - A mutation in a drug metabolizing enzyme can lead to accumulation of a drug and toxicity.

Special Drug Groups 2

Acetylcholinesterase Inhibitors

While acetylcholinesterase inhibitors were historically used as pesticides and herbicides, in recent years they have been used to develop medications to treat Alzheimer's disease and myasthenia gravis. Commonly, their toxicity is measured by the percentage of acetylcholinesterase (ACh) activity with toxicity beginning 20% below the level of normal activity (or 80% activity level) and becoming pronounced by 50% activity level. Severe toxicity and death occur at 90% suppression (measured activity level = 10%). Postmortem testing should utilize the red blood cell (RBC), ACh as it better reflects neural ACh activity.

Table 2.1 is a non-comprehensive list of common drugs, nerve agents, and insecticide/pesticides that are acetylcholinesterase inhibitors.

Table 2.1 Acetylcholinesterase Inhibitors

Drugs—Alzheimer's disease	*Drugs—myasthenia gravis*	*Drugs—glaucoma*	*Poisons—nerve agents*
Donepezil (Aricept)	Ambenonium (Mytelase)	Demecarium (Humorsol)	Cyclosarin
Galantamine (Razadyne, Reminyl, Nivalin)	Edrophonium (Tensilon, Enlon, Reversol)	Echothiophate (Phospholine iodide)	Sarin
Huperzine A	Neostigmine (Prostigmin)		Soman
Ladostigil	Physostigmine (Antilirium)		Tabun
Metrifonate	Pyridostigmine (Mestinon, Regonol)		VX
Rivastigmine (Exelon)			VE
Tacrine (Cognex)			VG
			VM
Insecticides or pesticides			
Acephate (Orthene)	Dichlorvos (DDVP, Vapona)	Formetanate (Carzol)	Oxydemeton-methyl (Meta systox-R)
Aldicarb (Temik)	Dicrotophos (Bidrin)	Fenthion (Baytex, Tiguvon, Entex)	Parathion (Niran, Phoskil)
Azinphos-methyl (Guthion)	Diisopropyl fluorophosphate (Dyflos)	Fonofos (Dyfonate)	Phorate (Thimet)
Bendiocarb (Ficam)	Dimethoate (Cygon, De-Fend)	Isofenphos (Oftanol, Amaze)	Phosalone (Zolonc)
Bufencarb	Dioxathion (Delnav)	Malathion (Cythion)	Phosmet (Imidan, Prolate)
Carbaryl (Sevin)	Disulfoton (Di-Syston)	Methamidophos (Monitor)	Phosphamidon (Dimecron)
Carbofuran (Furadan)	EPN	Methidathion (Supracide)	Pirimicarb (Pirimor)
Carbophenothion (Trithion)	Ethiofencarb	Methiocarb (Mesurol)	Propoxur (Baygon)
Chlorfenvinphos (Birlane)	Ethion	Methomyl (Lannate, Nudrin)	Temephos (Abate)
Chlorpyrifos (Dursban, Lorsban)	Ethoprop (Mocap)	Methyl parathion (Penncap-M)	TEPP
Coumaphos (Co-Ral)	Famphur	Mevinphos (Phosdrin)	Terbufos (Counter)
Crotoxyphos (Ciodrin, Ciovap)	Fenamiphos (Nemacur)	Monocrotophos	Tetrachlorvinphos (Rabon, Gardona)
Crufomate (Ruelene)	Fenitrothion (Sumithion)	Naled (Dibrom)	Trichlorfon (Dylox, Neguvon)
Demeton (Systox)	Fensulfothion (Dasanit)	Oxamyl (Vydate)	
Diazinon (Spectracide)			

Anesthetic Agents

General Anesthetics

General anesthetic agents are commonly used in the clinical setting to induce or maintain anesthesia. When used for this purpose, in a monitored clinical setting and in ventilated patients, the risk of death due to overdose is minimal. Some anesthetic agents are associated with other toxic effects, such as malignant hyperthermia, liver toxicities, and prolonged QT, but a discussion of these effects is beyond the scope of this book. However, when such agents are abused outside of the monitored clinical setting, **even therapeutic concentrations can be lethal**. Table 2.2 summarizes lethal concentrations of these medications, which have been reported in the literature.

Ketamine and propofol deserve special mention and are described in more detail below.

- Ketamine
  - In addition to being a widely used anesthetic agent, ketamine has become a drug of abuse known as Jet, Special K, Vitamin K, and Special K lube when combined with ethanol and gamma hydroxybutyric acid (GHB).
  - As ketamine is also used as a recreational drug, its presence alone may not indicate a lethal intoxication. The following nontoxic concentrations have been reported:

Blood (mg/L)	Liver (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Cardiac Muscle (mg/kg)	Skeletal Muscle (mg/kg)
0.5–9	0.8	0.6	4	3.5	1.2

Table 2.2 Lethal Concentrations of General Anesthetic Agents

Anesthetic Agent	Blood (mg/L)	Vitreous (mg/L)	Liver (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Lung (mg/kg)	Muscle (mg/kg)
Etomidate	0.4	0.3					
Halothane	3.4–720		1.7–880	12–14	104–1560	500	
Isoflurane	1.8–48		31–1000	27–53	29–307	9–34	9 (skeletal)
Ketamine	1.5–38		4.9–6.6	3.2–3.6	3.2–4.3		2.4 (cardiac)
Nitrous oxide	11–2030				47–2200	370–2420	
Propofol	0.03–5.5		1.4–27	1.8–5.5	2.9–17		222 (skeletal)
Sevoflurane	8–26	87	31–269	13–29			

- Propofol
  - With high volume of distribution and lipophilicity, it can be found several days following a surgical procedure at low tissue and blood concentrations and may not indicate an acute intoxication.
  - Can cause propofol infusion syndrome—characterized by metabolic acidosis, bradyarrhythmias, rhabdomyolysis, hypotension, and cardiac failure.
  - Therapeutic/nontoxic concentrations of propofol have been reported from 0.4 to 6.8 mg/L in blood.

Local Anesthetics

Local anesthetics usually result in toxicity and death by central nervous system excitation and seizure activity. They can also be cardiotoxic, resulting in arrhythmias and ventricular fibrillation.

Tables 2.3 and 2.4 summarize the pharmacokinetic properties and nonlethal and lethal concentrations of several local anesthetic agents.

Table 2.3 Pharmacokinetic Parameters and Toxic and Lethal Concentrations of Local Anesthetic Agents

Anesthetic Agent	ʎ (h)	Vd (L/kg)	Nontoxic Blood (mg/L)	Nontoxic Liver (mg/kg)	Toxic Blood (mg/L)	Lethal Blood (mg/L)	Lethal Liver (mg/kg)
Benzocaine	Unknown	Unknown	0.05–0.5		1.0–5.2[a]	3.5[a]	
Bupivacaine	1–3	0.4–1	0.2–3.5		0.3–20	3.8	
Lidocaine	0.7–5	1–4	0.3–5	0.01–4	8–12	12–44	10–96
Mepivacaine	1.5–2	0.5–4	0.1–5		4–9	16[b]–50	75
Prilocaine	0.5–2.5	0.7–4	0.9–5		0.3–2.8	13–15	14[a]–49
Procaine	7–8 min	0.3–1	4–43		18–96		
Ropivacaine	2–4	0.5–1	0.4–3		1.5–6	2	4.4

[a] Children.
[b] Mixed with lidocaine 4.9 mg/L.

Table 2.4 Additional Tissue Concentrations for Lidocaine and Mepivacaine

	Nontoxic Concentrations				Lethal Concentrations			
Anesthetic Agent	Kidney (mg/kg)	Brain (mg/kg)	Cardiac Muscle (mg/kg)	Skeletal Muscle (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Cardiac Muscle (mg/kg)	Skeletal Muscle (mg/kg)
Lidocaine	0.01–15	0.01–5.9	0.8	0.9–2.9	12–204	6.6–135	9–13	20
Mepivacaine	51–59	51–83			51	51		

Lidocaine, benzocaine, and prilocaine deserve special mention and are described in additional detail below.

- Benzocaine and prilocaine toxicity can result in methemoglobinemia.
- Lidocaine is metabolized by CYP 1A2 and 3A4 to the active metabolite, monoethylglycinexylidide (MEGX) and has been used as an adulterant in illicit drugs.

Neuromuscular Blocking Agents

Neuromuscular blocking agents block neuromuscular transmission at the neuromuscular junction, resulting in paralysis. These are most often used in anesthesia to assist in intubation. The use of these agents in the clinical setting, while the patient is being artificially ventilated, should not result in death. **The presence of these agents outside of a clinical setting, in a non-ventilated patient, can result in death at any concentration**.

Common neuromuscular blocking agents include: atracurium, cisatracurium, doxacurium, gallamine, mivacurium, pancuronium, pipecuronium, rapacurium, rocuronium, succinylcholine, tubocurarine, and vecuronium.

Succinylcholine deserves an additional note, because it

- Can be difficult to find in postmortem cases due to short half-life.
- Absorbs onto glassware during storage.
- Is rapidly hydrolyzed to succinylmonocholine, choline, and succinic acid, all of which are found endogenously.

Metals and Metalloids

Humans are exposed to metals and elements through the environment, food and water, smoking, and certain occupations or hobbies. Some metals have also been used not only medicinally but also as poisons, including being components of insecticides or pesticides. The concentrations of metals seen in blood and tissues are often extremely variable due to diet, environment, and occupation, making interpretation of postmortem metal concentrations extremely difficult; it is recommended that such interpretation be done with great skepticism and reflection.

Metals tend to be eliminated by and accumulate in the kidneys, so renal tissue is often the preferred tissue when testing for an acute overdose. Chronic exposure can often be delineated by testing of the hair and/or fingernails. Tables 2.5 and 2.6 outline reported metal concentrations.

Numerous procedures can be utilized to test for metals, including inductively coupled plasma mass spectrophotometry (ICP), atomic absorption spectroscopy (AAS), atomic emission spectrophotometry (AES), and x-ray defraction. Be certain to contact the testing laboratory for any specific requirements.

The following metals deserve special consideration:

Aluminum

- Classic exposure was through dialysis; no longer common.
- Blocks incorporation of calcium into bone.
- Associated with elevated calcium concentrations.

Arsenic

- Is a metalloid. Used medicinally for years.
- A known carcinogen.
- Elemental arsenic (As^{o}) is not toxic; can be found in shellfish and seafood.
- Arsenate (As^{+5}), arsenite (As^{+3}), and arsine gas (AsH_3) are toxic—$As^{+5} < As^{+3} < AsH_3$.
- Can cause white lines across the nails, known as Mees lines or leukonychia striata.

Barium

- Often used in medical procedures as 40%–80% suspension (e.g., Entero-H and Barotrast).
- Overdose can cause hypokalemia.

Cadmium

- Most common exposure is from smoking and fish consumption.
- Inhalation of cadmium fumes can cause fatal pneumonitis.

Table 2.5 Nontoxic Concentrations of Common Metals

Metal	λ	Blood (mg/L)	Liver (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Cardiac Muscle (mg/kg)	Skeletal Muscle (mg/kg)	Lung (mg/kg)	Other (mg/kg)
Aluminum	8 h–8 yr	0.004–0.4	0.6–2	0.07–0.4	0.2–0.9		0.07–0.9		Bone 1–12
Antimony	Unknown	0.002–0.06	0.01–0.07	0.01–0.1	0.01–0.1	0.01–0.1	0.01–0.1	0.03–0.2	Hair 0.1–2 Nail 0.2–2
Arsenic	10–30 h	0.003–0.3	0.02–0.09	0.02–0.1	0.02–0.1	0.02–0.06	0.04–0.1	0.05–0.1	Bone 0.05–0.2 Nail 0.9 Hair 0.02–8
Barium	10–80 h	0.001–0.1	0.003	0.01–0.09	0.004	0.009		0.16	
Bismuth	5–11 d	0.003–0.5	0.01–7	3	0.6			0.9	
Cadmium	10–30 yr	0.001–0.1	0.7–23	1–166	0.02–0.2	0.06–0.3	0.07–1	0.2–2	Bone 0.02–0.1 Hair 527–967
Copper	15–25 d	0.7–1.8	2–23	1–13	2–8	2–12	0.4–3	0.8–2	Spleen 4 Bone 3
Iron	3–6 h	0.3–1.5	29–479	7–160	8–96	6–73	11–59	112–280	Spleen 57–600
Lead	Blood 1–2 mo Bone >20 yr	0.003–0.5	0.2–4	0.1–2	0.02–0.8	0.01–1	0.02–0.5	0.05–2	Bone 0.2–4 Hair 0.1–20 Nail 0.06–1.5
Lithium	**See page 124**								
Mercury	14–50 d	0.002–0.2	0.002–1	0.2–3	0.04–0.2	0.001–0.1	0.02–0.2	0.02–0.3	Bone 0.05–0.07 Hair 1–15 Nail 0.06–0.8
Thallium	3–30 d	0.002–0.08	0.1–0.9	0.001–0.08	0.001–0.02				Hair 0.005–0.01

Table 2.6 Toxic and Lethal Concentrations of Common Metals

Metal	Toxic Blood (mg/L)	Blood (mg/L)	Liver (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Spleen (mg/kg)	Lung (mg/kg)	Hair (mg/kg)	Other (mg/kg)
Aluminum	0.02–0.2	0.4–24	5–90	3–32	1–5				Bone 1–30
Antimony	0.05–210	4.6	45	32	6	6	6		Cardiac muscle 4
Arsenic	0.02–3	0.1–10	2–400	0.2–100	0.2–20	0.5–200		10–200	Nail 50–67 Skeletal muscle 12
Barium	0.3–27	0.2–23	2–141	7–162	0.4–31	23–26	15–24		Vitreous 26–50 Cardiac muscle 17–22
Bismuth	0.05–2	1–100			3–25				
Cadmium	0.01–0.05	0.1–1	11–200	70–5980	0.5–3		1–4		Heart 8–12
Copper	1–13	2–74	8–1410	9–61	1–11				
Iron	3–26	2–50[a]	1504	982	483				
Lead	0.1–6	1–5	8–34	8–24	7–74				Bone 2–2680
Lithium	**See page 124**								
Mercury	0.05–6	0.2–12	1–217	2–284	1–35	1–100	3–23	400–1600	Cardiac muscle 1–17
Thallium	0.05–8	0.2–11	1–54	1–37	2–55		0.5–1	10–14	Skeletal muscle 6–13 Cardiac muscle 2–13

[a] Serum concentrations.

Lead

- Associated with blood smear basophilic stippling.
- Can cause Burton's lines (thin blue lines along the gums at the dental margin).
- Causes hypochromic microcytic anemia.

Mercury

- Previously used medicinally and as dental amalgam fillings.
- Component of cinnabar pigment.
- In fish, may be found in elevated concentrations.
- Associated with acrodynia.
- Is found in three forms: elemental, inorganic, and organic. Inorganic forms of mercury are the most toxic.

Thallium

- May also cause Mees line and alopecia.
- Toxicity may be misdiagnosed as Guillain Barre syndrome.

Novel Psychoactive Substances

A novel psychoactive substance is a new term used to describe a large group of drugs that are meant to mimic the effects of more commonly known drugs such as amphtemaines, cocaine, opiates, or delta-9-tetrahydrocannabinol (THC). With many new identifications appearing monthly, the number of these drugs has grown significantly in recent years. Therapeutic, toxic, and/or lethal concentrations overlap, and drug interactions are not well known. Caution should be used when interpreting their potential role in deaths, taking into account the circumstances surrounding death.

Novel psychoactive substances can be sedating, stimulating, or hallucinogenic compounds. The main classes of these drugs can be separated into synthetic cannabinoids, synthetic stimulants and hallucinogens, and synthetic opioids.

Synthetic Cannabinoids

Synthetic cannabinoids are a class of drugs manufactured to mimic the effects of delta-9-tetrahydrocannabinol, the active ingredient in marijuana. Similar to THC, synthetic cannabinoids bind to cannabinoid receptors. However, it is important to note that THC is a weak partial agonist at these receptors, while synthetic cannabinoids are full agonists. In addition, their affinity for the receptors is greatly increased allowing them to have increased adverse effects. Some adverse effects can include seizures, agitation, irritation, anxiety, confusion, paranoia, tachycardia, hypertension, chest pain, hypokalemia, hallucinations, tremors, delusions, nausea, and vomiting.

In vitro stability of some synthetic cannabinoids has been shown to be short; therefore, it is best to keep samples frozen and test as soon as possible. There are hundreds of synthetic cannabinoids, and new drugs are developed regularly. Table 2.7 is a non-comprehensive list of some common synthetic cannabinoids that have been implicated in causing toxicities.

Synthetic Opioids

Synthetic opioids are a class of drugs that bind to opioid receptors, much like opiates (codeine, morphine) and semi-synthetic opioids (hydrocodone, oxycodone) and as such, they cause pain relief and anesthesia. In addition to pain relief and anesthesia, much like other opiates and opioids, these drugs can cause sedation, respiratory depression, and drowsiness, which can lead to coma and death.

Table 2.8 is a non-comprehensive list of synthetic opioids that have been implicated in causing toxicities.

Table 2.7 Synthetic Cannabinoids Implicated in Causing Toxicities

5F-AB-001	ADBICA	CUMYL-THPINACA	JWH-122	MO-CHMINACA
5F-ADB	ADB-PINACA	EG-2201	JWH-133	NM-2201
5F-ADBICA	AF-AMB	FUB-144	JWH-200	NNE1
5F-ADB-PINACA	AM-1248	FUB-AKB-48	JWH-210	PB-22
5F-AMB	AM-2201	FUB-AMB	JWH-250	PX1/PX-1
5F-APICA	AM-2233	FUBIMINA	JWH-251	PX2/PX-2
5F-APINACA	AM-679	FUB-JWH-018	JWH-260	RCS-4
5F-MN-A8	AM-694	FUB-PB-22	MAB-CHMINACA	RCS-4-C4
5F-PB-22	AMB	HU-210	MDMB-CHMCZCA	RCS-8
A-796260	AMB-FUBINACA	JWH-015	MDMB-CHMINACA	THJ-018
AB-CHMINACA	APICA	JWH-018	MDMB-FUBINACA	THJ-2201
ABDICA	APINACA	JWH-018-5-Chloropentyl	MDMB-CHMICA	UR-144
AB-FUBINACA	APP-CHMINACA	JWH-019	MMB-CHMICA	WIN 55-212
AB-PINACA	BB-22	JWH-022	MMB-CHMINACA	XLR-11
ADB-CHMINACA	CP 47-,497	JWH-073	MN-18	
ADB-FUBINACA	CP-55,940	JWH-081	MN-25	

Table 2.8 Synthetic Opioids Implicated in Causing Toxicities

3-Methylfentanyl	p-Fluorobutyrylfentanyl
4-ANPP	p-Fluorofentanyl
4-Fluorobutyrfentanyl	Furanylfentanyl
4-Methoxy-butyryl fentanyl	Isobutyryl fentanyl
4-Methylphenethyl acetylfentanyl	Methoxyacetyl fentanyl
α-ME fentanyl	MT 45 (1-cyclohexyl-4-(1,2-diphenylethyl)piperazine)
Acetylfentanyl	Ocfentanyl
Acrylfentanyl	Ortho-fluorofentanyl
Acryloylfentanyl	Para-fluorofentanyl
AH7921	Sufentanil
Alfentanyl	Tetrahydrofuranyl fentanyl
Alpha-methylfentanyl	Thiafentanil
Beta-hydroxythiofentanyl	U-47700 (3,4-dichloro-*N*-[2-(dimethylamino) cyclohexyl]-*N*-methylbenzamide)
Butyrylfentanyl	U-48800
Carfentanil	U-49900 (trans-3,4-dichloro-*N*-[2-(diethylamino) cyclohexyl]-*N*-methyl-benzamide)
Cyclopropylfentanyl	U-50488 (*rel*-3,4-dichloro-*N*-methyl-*N*-[(1R,2R)-2-(1-pyrrolidinyl)cyclohexyl]-benzeneacetamide)
Despropionyl fentanyl	Valerylfentanyl
FIBF (Para-Fluoro-Isobutyryl Fentanyl)	

Synthetic Stimulants and Hallucinogens

Synthetic stimulants and hallucinogens mimic other more commonly known stimulants and hallucinogens such as methamphetamine, cocaine, and lysergic acid diethylamide (LSD). Similarly, they act on monoamines by inhibiting their transport and/or inducing their release. Synthetic stimulants are generally amphetamines, cathinones, tryptamines, phenethylamines, piperazines, piperidines, or related substances. Some adverse effects can include tachycardia, restlessness, anxiety, agitation, hypertension, nausea, vomiting, and diarrhea among others.

In vitro stability of some synthetic drugs has been shown to be short, therefore, it is best to keep samples frozen and test as soon as possible. Table 2.9 includes non-comprehensive lists of some common synthetic stimulants and hallucinogens that have been implicated in causing toxicities.

Volatiles

Volatiles as a class of drugs are considered forensically when they are intentionally inhaled with the intent of obtaining psychoactive effects; they are also referred to as *inhalants*. Volatiles are commonly constituents of fuel gases, propellants, solvents, anesthetics, automotive fuels, refrigerants, paint thinner, glues, and dry-cleaning agents. These compounds most commonly include aromatic and halogenated hydrocarbons and fluorocarbons. They are known to be cardiotoxic and are associated with lethal arrhythmias; they can also cause death by oxygen exclusion.

Common volatile compounds include benzene, butane, carbon tetrachloride, chloroform, diethyl ether, enflurane, ether, ethyl ether, fluothane, freon, gasoline, helium, isoflurane, methyl ether, nitrous oxide, oxybismethane, perchloroethylene, propane, tetrachloroethene, tetrafluoroethane, toluene, trichloroethylene, trichloroethane, trichloromethane, trifluoroethane, and xylene.

Volatiles are highly lipophilic, so in addition to blood, the brain is often a good secondary source. In fact, 1,1-difluoroethane has been detected in cerebral material approximately 50 hours after exposure and prolonged hospitalization.

Diagnosis of volatile or inhalant toxicity usually depends upon the circumstances of death and the presence of such a substance in the blood or tissue samples, regardless of concentration of the substance. However, concentrations in fatal cases have been reported and are described in Table 2.10.

Table 2.9 Synthetic Stimulants and Hallucinogens Implicated in Causing Toxicities

2 AI (2-Aminoindane)
2 DPMP (2-Diphenylmethylpiperidine)
2 MAPB (1-(benzofuran-2-yl)-*N*-methylpropan-2-amine)
2 Methoxydiphenidine
2 Methyl PPP (2-methyl-alpha-pyrrolidinopropiophenone)
2 MMC (2-Methylmethcathinone)
25 B NBOMe
25 C NBOMe
25 H NBOMe
25 I NBOMe
2C B (4-Bromo-2,5-dimethoxyphenethylamine)
2C B FLY (8-Bromo-2,3,6,7-tetrahydrobenzo[1,2-b:4,5-b′]difuran-4-ethanamine)
2C C (2,5-Dimethoxy-4-chlorophenethylamine)
2C E (2,5-Dimethoxy-4-iodophenethylamine)
2C H (2,5-Dimethoxyphenethylamine)
2C I (2,5-Dimethoxy-4-iodophenethylamine)
2C N (2,5-Dimethoxy-4-nitrophenethylamine)
2C P (2,5-Dimethoxy-4-propylphenethylamine)
2C T (2,5-Dimethoxy-4-methylthiophenethylamine)
2C T2 (2,5-Dimethoxy-4-ethylthiophenethylamine)
2C T4 (2,5-Dimethoxy-4-isopropylthiophenethylamine)
2C T7 (2,5-Dimethoxy-4-propylthiophenethylamine)
3 FMC (3 Fluoromethcathinone)
3 MeO PCP (3-Methoxy-phencyclidine)
3 MMC (3 Methylmethcathinone)
3,4 DMMC (3,4 Dimethylmethcathinone)
3,4 MDPBP (3,4 Methylenedioxy-alpha-pyrrolidinobutiophenone)
3,4 MDPV (3,4-Methylenedioxypyrovalerone)
4 CAB (4-Chlorophenylisobutylamine)
4 Fluoroamphetamine
4 MBC (4-Methylbenzylidene camphor)
4 MEC (4-Methylethcathinone)
4 MeO PCP (4-Methoxyphencyclidine)
4 Methylamphetamine
4 Methylthioamphetamine
4 MPBP (4-Methyl-2-pyrrolidinoburyrophenone)
4 MTA (4-Methylthioampheatmine)
4 OH DET (4-Hydroxy diethyltryptamine)
5 APDI (5-(2-Aminopropyl)-2,3-dihydro-1H-indene
5 APB (5-(2-Aminopropyl)benzofuran)
5 APDB (5-(2-Aminopropyl)-2,3-dihydrobenzofuran)
5 IAI (5-Iodo-2-aminoindane)
5 IT (5-(2-Aminopropyl)indole)
5 MAPB (5-(2-Methylaminopropyl)benzofuran)
5 MeO AMT (5-Methoxy-alpha-methyltryptamine)
5 MeO DALT (*N*,*N*-Diallyl-5-Methoxytryptamine)
5 MeO DiPT (5-Methoxy-*N*,*N*-diisopropyltryptamine)
5 MeO DMT (5-Methoxy-*N*,*N*-dimethyltriptamine)
5 MeO MiPT (5-Methoxy-*N*-methyl-*N*-isopropyltryptamine)
6 APB (6-(2-Aminopropyl)benzofuran)
6 IT (6-(2-Aminopropyl)indole)

(*Continued*)

Table 2.9 (*Continued*) Synthetic Stimulants and Hallucinogens Implicated in Causing Toxicities

Alpha PBP (alpha-Pyrrolidinobutiophenone)
Alpha PHP (2-(1-pyrrolidinyl)-hexanophenone)
Alpha-PHPP (alpha-Pyrrolidinopentiophenone)
Alpha PPP (alpha-pyrrolidinopropiophenone)
Alpha PVP (alpha Pyrrolodinopentiophenone)
Alpha PVT (alpha-pyrrolidinopentiothiophenone)
AMT (alpha methyltryptamine)
BCP (Benocyclidine)
BDB (Benzodioxole-5-butanamine)
Brephedrone
Brolamfetamine
Bromo dragon FLY
Buphedrone
Butylone
BZP (Benzylpiperazine)
CathinoneD2PM (Diphenyl-2-pyrrolidinemethanol)
DBZP (1,4-Dibenzylpiperazine)
DET (*N*,*N*-Diethyltryptamine)
Dibutylone
Dimethylcathinone
Dimethylone
DiPT (*N*, *N*-diisopropyltryptamine)
DMA (2,5 Dimethoxyamphetamine)
DMAA (Methylhexanamine)
DMT (*N*, *N*-Dimethyltryptamine)
DOB (4 Bromo 2,5 dimethoxyamphetamine)
DOC (4 Chloro 2,5 dimethoxyamphetamine)
DOET (2,5 Dimethoxy 4 ethylamphetamine)
DOI (4 Iodo 2,5-dimethoxyamphetamine)
DOM (2,5 Dimethoxy 4 methylamphetamine)
DPT (Dipropyltryptamine)
EEC (Ethylethcathinone)
Escaline
Ethcathinone
Ethylamphetamine
Ethylcathinone
Ethylethcathinone
Ethylone
Ethylphenidate
Eutylone
Fenethylline
Flephedone
Fluoromethamphetamine
FMC (Fluoromethcathinone)

(*Continued*)

Table 2.9 (*Continued*) Synthetic Stimulants and Hallucinogens Implicated in Causing Toxicities

MBDB (*N*-Methyl-1,3-Benzodioxolylbutanamine)	Methylone
MBZP (Methylbenzylpiperazine)mCPP (1-(3-Chlorophenyl)piperazine)	MMC (Methylmethcathinone)
MDAI (5,6-Methylenedioxy2-aminoindane)	MPHP (Methyl-alpha-pyrrolidinohexanophenone)
MDEA (Methylenedioxyethylamphetamine)	MXE (Methoxetamine)
MDPPP (Methylenedioxy-alpha-pyrrolidinopropiophenone)	MXP (Methoxphenidine)
MeOPP (1-(4-Methoxyphenyl)piperazine)	*N*-Ethylpentylone
MeOPPP (4-Methoxy-alpha-pyrrolidinopropiophenone)	Naphyrone
Mephedrone	NEB (N-Ethylbuphedone)
Mephentermine	Pentedrone
Methcathinone	Pentylone
Methcopropamine	PMA (Phorbol 12-myristate 13-acetate) PMMA (para-Methoxymethamphetamine)
Methedrone	
Methiopropamine	Pyrovalerone
Methoxetamine	TFMPP (1-(m-Trifluoromethylphenyl)piperazine)
Methoxyamphetamine	TMA (Trimethoxyamphetamine)
Methoxymethamphetamine	WIN 35428 (beta-Carbomethoxy-3-beta-(4-fluorophenyl)tropane)

Table 2.10 Lethal Concentrations of Selected Volatile Substances

Volatile	Blood (mg/L)	Vitreous (mg/L)	Liver (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Lung (mg/kg)	Adipose Tissue (mg/kg)	Skeletal Muscle (mg/kg)	Cardiac Muscle (mg/kg)
Benzene	0.9–120		2.6–379	5.5–75	14–179	22	22–120		
Butane	0.05–129		0.5–147	0.4–78	0.4–288	0.03–128	1.8–234	5.4–112	
Carbon tetrachloride	57–260	170	59–142	150	175–243	39–127		71	78–188
Chloroform	29–834		26–298	38–124	21–133	14–92	79–128		
Difluoroethane (Freon 152a)	3.2–380	2.6–200	88		118	60	236		
Trichloro-fluoromethane (Freon 11)	0.6–63		45–74	50	61–109	32–149			407
Chlorodifluoro-methane (Freon 22)	26–560	0.7–1	4.4–381	33–75	2.8–414	1.6–80			
Trichloro-trifluoroethane (Freon 113)	0.4–32		2.9–81	476	0.5–1370	0.05–3.5	5.4	8.8	
Propane	0.2–69		0.3–33	0.2–75	1–128	0.2–55	0.9–1276	0.3–213	1.7–34
Toluene (methyl-benzene)	1–114		3.6–433	39	19–740	6.6–100	12		63
Trichloro-ethane	0.1–720		4.9–220	2.6–120	3.2–1230	1.8–22		2.6–49	
Trichloro-ethylene	1.1–210		2.5–747	12–78	32–809	9.3–21			
Xylene (dimethyl-benzene)	4.9–110		3.6–29		6.1–19		7.1		12

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Alphabetical Listing of Drugs

3

Acetaminophen

Brand names: Tylenol and Paracetamol
Classification: Analgesic
λ: 1–3 h
V_d: 0.8–1 L/kg
Usual dosage: 325–1000 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	5–26 mg/L	30–981 mg/L	160–1280 mg/L
Vitreous			779–878 mg/L
Liver			220–3260 mg/kg
Kidney			93–188 mg/kg
Brain			220 mg/kg
Skeletal muscle	18–55 mg/kg		179–220 mg/kg

Comments

- Metabolized by CYP 1A2 and 2E1
- Overdoses treated with *N*-acetylcysteine
- Causes hepatic necrosis; death usually occurs 3–5 days after ingestion

- Concentration is interpreted based on time since ingestion
  - Concentrations above the line are indicative of probable hepatotoxicity
  - Concentrations below the line indicate a low risk for hepatotoxicity

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Acetone

Brand names: Component of nail polish remover and industrial solvents
Classification: Solvent
λ: 17–27 h
V_d: 0.4–0.6 L/kg
Usual dosage: Not applicable

Source	Nontoxic	Toxic	Lethal
Blood	8–460 mg/L	1000–4000 mg/L	2570–5500 mg/L
Vitreous	80–500 mg/L		
Skeletal muscle	300–900 mg/kg		

Comments

- Metabolite of isopropanol
- Can be used as an inhalant
- Can be detected/present in diabetic/fasting states, ranging from:
  - 120–1950 mg/L blood
  - 180–2100 mg/L vitreous

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Acetylsalicylic Acid

Brand names: Aspirin (Bayer and Ecotrin)
Classification: Non-steroidal anti-inflammatory (NSAID)
λ: 15–20 min
V_d: 0.1–0.2 L/kg
Usual dosage: 325–650 mg q 4–6 h

Source	Therapeutic/Nontoxic[a]	Toxic[a]	Lethal[a]
Blood	45–300 mg/L	300–1100 mg/L	400–7320 mg/L
Vitreous	93–228 mg/L		228 mg/L
Liver			258–1000 mg/kg
Kidney			300–1200 mg/kg
Brain			131–700 mg/kg
Skeletal muscle	28–400 mg/kg		440–1175 mg/kg

[a] All concentrations given are for salicylic acid.

Comments

- Rapidly metabolized to salicylic acid (λ 2–19 h; V_d 0.1–0.2 L/kg)
- May cause sudden death in asthmatics, regardless of concentration
- May cause Reye's syndrome in children

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Albuterol

Brand names: Proventil and Ventolin
Alternate name: Salbutamol
Classification: β agonist
λ: 2–6 h
V_d: 1–3 L/kg
Usual dosage:
Inhaled: two inhalations q 4–6 h
oral: 2–4 mg t/qid
0.1–0.2 mg/kg/dose3

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.06 mg/L	0.02–0.45 mg/L	See comments

Comments

- Fatalities usually attributed to asthma rather than drug overdose

Selected Sources

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Alprazolam

Brand name: Xanax
Classification: Benzodiazepine
λ: 6–27 h
V_d: 1–1.5 L/kg
Usual dosage: 0.25–0.5 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.7 mg/L	0.04–0.6 mg/L	0.2–2.1 mg/L
Vitreous			0.6 mg/L
Liver			2.4–9.2 mg/kg
Kidney			3.8 mg/kg
Brain	0.007–0.1 mg/kg		
Skeletal muscle	0.05–0.2 mg/kg		

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations
- Sudden withdrawal can cause seizures and death
- Metabolized by CYP 3A

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Wright CE, Sisson TL, Fleishaker JC, Antal EJ. (1997). Pharmacokinetics and psychomotor performance of alprazolam: Concentration-effect relationship, *J Clin Pharmacol*, 37(4): 321–329.

Amanitin

Brand name: Not applicable
Classification: Poison
λ: Unknown
V_d: ~1 L/kg
Usual dosage: Not applicable

Source	Nontoxic	Toxic	Lethal
Blood	No data available		0.008–0.19 mg/L

Comments

- Found in *Amanita*, *Galerina*, and *Conocyte* ("death cap") mushrooms
- Generally found in blood for 1–1.5 days, 4 days in urine, and 5 days in the liver or kidney
- Symptoms or signs of toxicity include nausea/vomiting/diarrhea, renal failure, and hepatic necrosis
- Symptoms start 5–15 hours after ingestion

Selected Sources

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Vesconi S, Langer M, Iapichino G, Costantino D, Busi C, Fiume L. (1985). Therapy of cytotoxic mushroom intoxication, *Crit Care Med*, 13(5): 402–406.

Amantadine

Brand name: Symmetrel
Classification: Antiviral/anti-Parkinson's
λ: 9–31 h
V_d: 3–11 L/kg
Usual dosage: 100–200 mg bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.06–1 mg/L	1.5–13 mg/L	4–48 mg/L
Liver			135 mg/kg

Comments

- May prolong QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Fahn S, Craddock G, Kumin G. (1971). Acute toxic psychosis from suicidal overdosage of amantadine, *Arch Neurol*, 25(1): 45–48.
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Schwartz M, Schwartz MD, Patel MM, Kazzi ZN, Morgan BW. (2008). Cardiotoxicity after massive amantadine overdose, *J Med Toxicol*, 4(3): 173–179.

Amisulpride

Brand names: Socian and Solian
Classification: Antipsychotic
λ: 11–27 h
V_d: 5–6 L/kg
Usual dosage: 50–400 mg/d

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–0.4 mg/L	9.6–4671 mg/L	13–140 mg/L

Comments

- Not available in the United States

Selected Sources

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Isbister GK. (2006). Amisulpride deliberate self-poisoning causing severe cardiac toxicity including QT prolongation and torsades de pointes, *Med J Aust*, 184(7): 354–356.

Kratzsch C, Peters FT, Kraemer T, Weber AA, Maurer HH. (2003). Screening, library-assisted identification and validated quantification of fifteen neuroleptics and three of their metabolites in plasma by liquid chromatography/mass spectrometry with atmospheric pressure chemical ionization, *J Mass Spectrum*, 38(3): 283–295.

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Tracqui A, Mutter-Schmidt C, Kintz P, Berton C, Mangin P. (1995). Amisulpride poisoning: A report on two cases, *Hum Exp Tox*, 14(3): 294–298.

Amitriptyline

Brand names: Elavil, Vanatrip, and Endep
Classification: Antidepressant (TCA)
λ: 8–50 h
V_d: 12–18 L/kg
Usual dosage: 75–150 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.24 mg/L	0.5–2.2 mg/L	1.8–86 mg/L
Vitreous			0.8–6 mg/L
Liver	3.2–10 mg/kg	>50 mg/kg	26–518 mg/kg
Kidney			5–98 mg/kg
Brain			4.8–22 mg/kg
Skeletal muscle	0.08–1 mg/kg		1.2–11 mg/kg

Comments

- Active metabolite: Nortriptyline
- Metabolized by CYP 2D6, 3A, 1A2, and 2C19
- May prolong QT interval; associated with cardiac arrhythmias

Selected Sources

Apple FS. (1989). Postmortem tricyclic antidepressant concentrations: Assessing cause of death using parent drug to metabolite ratio, *J Anal Toxicol*, 13(4): 197–198.

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Margalho C. (2007). Massive intoxication involving unusual high concentration of amitriptyline, *Hum Exp Toxicol*, 26(8): 667–670.

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Vasiliades J, Bush KC. (1976). Gas liquid chromatographic determination of therapeutic and toxic levels of amitriptyline in human serum with a nitrogen-sensitive detector, *Anal Chem*, 48(12): 1708–1714.

Amlodipine

Brand name: Norvasc
Classification: Calcium channel blocker
λ: 32–44 h
V_d: 17–25 L/kg
Usual dosage: 2.5–10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.4 mg/L	0.07–0.14 mg/L	0.2–2.7 mg/L
Liver			8.7–91 mg/kg
Kidney			40 mg/kg
Brain			5.4 mg/kg
Skeletal muscle			2.9 mg/kg

Selected Sources

Adams BD, Browne WT. (1998). Amlodipine overdose causes prolonged calcium channel blocker toxicity, *Am J Emer Med*, 16(5): 527–528.

Bexar County Medical Examiner's Office data 1996–2015.

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Poggenborg RP, Videbaek L, Jacobsen IA. (2006). A case of amlodipine overdose, *Basic Clin Pharm Tox*, 99(3): 209–212.

Sklerov JH, Levine B, Ingwersen KM, Aronica-Pollack PA, Fowler D. (2006). Two cases of fatal amlodipine overdose, *J Anal Toxicol*, 30(5): 346–351.

Stanek EJ, Nelson CE, DeNofrio D. (1997). Amlodipine overdose, *Ann Pharmacotherapy*, 31(7–8): 853–856.

Amoxapine

Brand name: Asendin
Classification: Antidepressant (TCA)
λ: 8 h
V_d: Unknown
Usual dosage: 150–400 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.4 mg/L	0.3–2 mg/L	0.8–18 mg/L
Vitreous			0.2 mg/L
Liver			17–150 mg/kg
Brain			2.5–52 mg/kg

Comments

- Active metabolites: 8-hydroxyamoxapine (λ 30 h) and 7-hydroxy-amoxapine
- Metabolite of loxapine
- May prolong QT interval

Selected Sources

Beierle FA, Hubbard RW. (1983). Liquid chromatographic separation of antidepressant drugs: II. Amoxapine and maprotiline, *Ther Drug Monit*, 5(3): 293–301.
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Kinney JL, Evans RK Jr. (1982). Evaluation of amoxapine, *Clin Pharm*, 1(5): 417–424.
Sedgwick P, Spiehler VR, Lowe DR. (1982). Toxicological findings in amoxapine overdose, *J Anal Toxicol*, 6(2): 82–84.
Taylor RL, Crooks CR, Caplan YH. (1982). The determination of amoxapine in human fatal overdoses, *J Anal Toxicol*, 6(6): 309–311.
Winek CL, Wahba WW, Rozin L. (1984). Amoxapine fatalities: Three case studies, *Forensic Sci Intl*, 26(1): 33–38.

Amphetamine

Brand names: Adderall, Dexedrine, Dextrostat, and Vyvanase (prodrug)
Street names: Bennies, Uppers, Speed, Pep Pills, and Co-pilots
Classification: Stimulant
λ: 9–12 h
V_d: 3–6 L/kg
Usual dosage: 2.5–20 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.7 mg/L	0.2–3 mg/L	0.5–41 mg/L
Liver			4.3–45 mg/kg
Kidney			3.8–48 mg/kg
Brain			2.8–41 mg/kg
Skeletal muscle			4 mg/kg

Comments

- Deaths are due to cardiovascular and central nervous system effects
  - Minimal concentration for central nervous system effects = 0.005 mg/L
  - Minimal concentration for cardiovascular effect = 0.02 mg/L
- Metabolized by CYP 2D6
- Metabolite of benzphetamine, clobenzorex, famprofazone, fenethylline, fenproporex, mefenorex, mesocarb, prenylamine, and lisdexamfetamine

Selected Sources

Adjutantis G, Coutselinis A, Dimopoulos G. (1975). Fatal intoxication with amphetamines, *Med Sci and Law*, 15(1): 62–63.

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Meyer E, Van Bocxlaer JF, Dirinck IM, Lambert WE, Thienpont L, De Leenheer AP. (1997). Tissue distribution of amphetamine isomers in a fatal overdose, *J Anal Toxicol*, 21(3): 236–239.

Aripiprazole

Brand name: Abilify
Classification: Antipsychotic
λ: 47–75 h
V_d: 5 L/kg
Usual dosage: 10–30 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.9 mg/L	0.72–1.4 mg/L	1.9[a]–2.1[b] mg/L

[a] Co-intoxicant methadone 1.5 mg/L.
[b] Co-intoxicant not listed.

Comments

- Active metabolite: Dehydro-aripiprazole
- Metabolized by CYP 2D6 and 3A

Selected Sources

Carstairs SD, Williams SR. (2005). Overdose of aripiprazole, a new type of antipsychotic, *J Emerg Med*, 28(3): 311–313.

Mallikaarjun S, Salazar DE, Bramer SL. (2004). Pharmacokinetics, tolerability, and safety of aripiprazole following multiple oral dosing in normal healthy volunteers, *J Clin Pharmacol*, 44(2): 179–187.

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Skov L, Johansen SS, Linnet K. (2015). Postmortem femoral blood reference concentrations of aripiprazole, chlorprothixene and quetiapine, *J Anal Toxicol*, 39(1): 41–44.

Asenapine

Brand name: Saphris
Classification: Antipsychotic
λ: 24 h
V_d: 20–25 L/kg
Usual dosage: 5–10 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.02 mg/L	No data available	0.04[a]–0.7[b] mg/L
Liver			0.4[a]–42[b] mg/kg

[a] Co-intoxicants ethanol 0.16 g/dL, fluoxetine 2.6 mg/L, quetiapine 1.4 mg/L, hydrocodone 0.11 mg/L.
[b] Suffocation due to plastic bag and co-intoxicants quetiapine 2.9 mg/L, alprazolam 0.16 mg/L.

Comments

- Metabolized by CYP1A2

Selected Sources

Miller C, Pleitez O, Anderson D, Mertens-Maxham D, Wade N. (2013). Asenapine (Saphris®): GC-MS method validation and the postmortem distribution of a new atypical antipsychotic medication, *J Anal Toxicol*, 37(8): 559–564.

Taylor JE, Chandrasena RD. (2013). A case of intentional asenapine overdose, *Prim Care Companion CNS Disord*, 15(6).

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Atenolol

Brand name: Tenormin
Classification: β-blocker
λ: 5–8 h
V_d: 0.7–0.8 L/kg
Usual dosage: 50–200 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.7 mg/L	2.5–9.4 mg/L	No data available

Selected Sources

Amery A, De Plaen JF, Lijnen P, McAinsh J, Reybrouck T. (1977). Relationship between blood level of atenolol and pharmacologic effect, *Clin Pharm Thera*, 21(6): 691–699.

Czendlik CH, Sioufi A, Preiswerk G, Howald H. (1997). Pharmacokinetic and pharmacodynamic interaction of single doses of valsartan and atenolol, *Eur J Clin Pharm*, 52(6): 451–459.

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Gerkin R, Curry S. (1987). Signigicant bradycardia following acute self-poisoning with atenolol, *Vet Hum Tox*, 29: 479.

Montgomery AB, Stager MA, Schoene RB. (1985). Marked suppression of ventilation while awake following massive ingestion of atenolol, *Chest*, 88(6): 920–921.

Saitz R, Williams BW, Farber HW. (1991). Atenolol-induced cardiovascular collapse treated with hemodialysis, *Crit Care Med*, 19(1): 116–118.

Atomoxetine

Brand name: Strattera
Classification: Norepinephrine reuptake inhibitor
λ: 5 h
V_d: 1–2 L/kg
Usual dosage: 0.3–1.2 mg/kg bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.9 mg/L	No data available	5.4–8.3 mg/L[a]
Vitreous			0.96 mg/L[a]
Liver			29 mg/kg[a]

[a] Co-intoxicant venlafaxine 100 mg/L.

Comments

- Metabolized by CYP 2D6
- May prolong QT interval

Selected Sources

Garside D, Ropero-Miller JD, Riemer EC. (2006). Postmortem tissue distribution of atomoxetine following fatal and nonfatal doses—Three case reports, *J Forensic Sci*, 51(1): 179–182.

Sauer JM, Ring BJ, Witcher JW. (2005). Clinical Pharmacokinetics of Atomoxetine, *Clin Pharmacokinet*, 44(6): 571–590.

Atropine

Brand names: AtroPen and Sal-Tropine
Classification: Antimuscarinic
λ: 2–3 h
V_d: 1–3 L/kg
Usual dosage: 0.4–0.6 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.006–0.3 mg/L	0.02–0.2 mg/L	0.2–3.1 mg/L
Liver			0.7 mg/kg

Comments

- Used to treat organophosphate poisoning
- Physostigmine is antidote to atropine poisoning

Selected Sources

Berghem L, Bergman U, Schildt B, Sorbo B. (1980). Plasma atropine concentrations determined by radioimmunoassay after single-dose i.v. and i.m. administration, *Br J Anaesth*, 52(6): 597–601.

Bogan R, Zimmermann T, Zilker T, Eyer F, Thiermann H. (2009). Plasma level of atropine after accidental ingestion of *Atropa belladonna*, *Clin Toxicol* (*Phila*), 47(6): 602–604.

Hayden PW, Larson SM, Lakshminarayanan S. (1979). Atropine clearance from human plasma, *J Nucl Med*, 20(4): 366–367.

Kehe CR, Lasseter KC, Miller NC, Wick KA, Shamblen EC, Ekholm BP, Sandahl JH, Chang SF, Goldlust MB, Kvam DC. (1992). Comparative absorption of atropine from a metered-dose inhaler and an intramuscular injection, *Ther Drug Monit*, 14(2): 132–134.

Matsuda K, Morinaga M, Okamoto M, Miyazaki S, Isimaru T, Suzuki K, Tohyama K. (2006). Toxicological analysis of a case of *Datura stramonium* poisoning, *Rinsho Byori*, 54(10): 1003–1007.

Schneider F, Lutun P, Kintz P, Astruc D, Flesch F, Tempe JD. (1996). Plasma and urine concentrations of atropine after the ingestion of cooked deadly nightshade berries, *J Tox Clin Tox*, 34(1): 113–117.

Baclofen

Brand names: Lioresal and Kemstro
Classification: Muscle relaxant
λ: 2–8 h
V_d: 0.7–0.9 L/kg
Usual dosage: 5–15 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–0.6 mg/L	0.4–6 mg/L	17–106 mg/L

Selected Sources

Chapple D, Johnson D, Connors R. (2001). Baclofen overdose in two siblings, *Ped Emer Care*, 17(2): 110–112.

De Giovanni N, d'Aloja E. (2001). Death due to baclofen and dipyrone ingestion, *Forensic Sci Intl*, 123(1): 26–32.

Fraser AD, MacNeil D, Isner AF. (1991). Toxicological analysis of a fatal baclofen (Lioresal®) ingestion, *J Forensic Sci*, 36: 1596–1602.

Perry HE, Wright RO, Shannon MW, Woolf AD. (1998). Baclofen overdose: Drug experimentation in a group of adolescents, *Pediatrics*, 1(6): 1045–1048.

Wall GC, Wasiak W, Hicklin GA. (2006). An initially unsuspected case of baclofen overdose (Clinical Report), *Am J Crit Care*, 15(6): 611–613.

Wiersma HE, van Boxtel CJ, Butter JJ, van Aalderen WM, Omari T, Benninga MA. (2003). Pharmacokinetics of a single oral dose of baclofen in pediatric patients with gastroesophageal reflux disease, *Thera Drug Monitoring*, 25(1): 93–98.

Wu VC, Lin SL, Lin SM, Fang CC. (2005). Treatment of baclofen overdose by haemodialysis: A pharmacokinetic study, *Nephrol Dial Transplant*, 20(2): 441–443.

Benzphetamine

Brand name: Didrex
Classification: Stimulant/anorectic
λ: Unknown
V_d: Unknown
Usual dosage: 25–50 mg tid/bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.5 mg/L	No data available	14 mg/L
Vitreous			21 mg/L
Liver			106 mg/kg
Kidney			38 mg/kg
Brain			31 mg/kg

Comments

- Metabolized to d-amphetamine and d-methamphetamine

Selected Sources

Brooks JP, Phillips M, Stafford DT, Bell JS. (1982). A case of benzphetamine poisoning, *Am J Forensic Med Path*, 3(3): 245–257.

Cody JT, Valtier S. (1998). Detection of amphetamine and methamphetamine following administration of benzphetamine, *J Anal Toxicol*, 22(4): 299–309.

Kraemer T, Maurer HH. (2002). Toxicokinetics of amphetamines: metabolism and toxicokinetic data of designer drugs, amphetamine, methamphetamine, and their N-alkyl derivatives, *Ther Drug Monit*, 24(2): 277–289.

Benztropine

Brand name: Cogentin
Classification: Anti-Parkinson's agent
λ: Unknown
V_d: Unknown
Usual dosage: 1–2 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.004–0.4 mg/L	0.05–0.1 mg/L	0.2–1.1 mg/L
Vitreous			0.3 mg/L
Liver			1.6–9.6 mg/kg

Comments

- Metabolized by CYP 2D6

Selected Sources

Fahy P, Arnold P, Curry SC, Bond R. (1989). Serial serum drug concentrations and prolonged anticholinergic toxicity after benztropine (cogentin) overdose, *Am J Emer Med*, 7(2): 199–202.

Jindal SP, Lutz T, Hallstrom C, Vestergaard P. (1981), A stable isotope dilution assay for the antiparkinsonian drug benztropine in biological fluids, *Clin Chim Acta*, 112(3): 267–273.

Lynch MJ, Kotsos A. (2001). Fatal benztropine toxicity, *Med Sci Law*, 41(2): 155–158.

McIntyre IM, Mallett P, Burton CG, Morhaime J. (2014). Acute benztropine intoxication and fatality, *J Forensic Sci*, 59(6): 1675–1678.

Rosano TG, Meola JM, Wolf BC, Guisti LW, Jindal SP. (1994). Benztropine identification and quantitation in a suicidal overdose, *J Anal Toxicol*, 18(6): 348–353.

Bromazepam

Brand names: Compendium and Lectopam
Classification: Benzodiazepine
λ: 18–65 h
V_d: 1–1.5 L/kg
Usual dosage: 1.5–3 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.5 mg/L	0.3–0.4 mg/L	0.8–7.7 mg/L
Brain	0.003–0.49 mg/kg		

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Escande M, Monjanel-Mouterde S, Diadema B, Coassolo P, Orluc A, Aubert C, Durand A, Cano JP. (1989). Determination of the optimal dose of bromazepam in the elderly, *Therapie*, 44(3): 219–222.

Fujii J, Inotsume N, Nakano M. (1990). Effect of food on the bioavailability of bromazepam following oral administration in healthy volunteers, *J Pharm Dyn*, 13(5): 269–271.

Laurito TL, Mendes GD, Santagada V, Caliendo G, de Moraes ME, De Nucci G. (2004). Bromazepam determination in human plasma by high-performance liquid chromatography coupled to tandem mass spectrometry: A highly sensitive and specific tool for bioequivalence studies, *J Mass Spect*, 39(2): 168–176.

Marrache F, Megarbane B, Pirnay S, Rhaoui A, Thuong M. (2004). Difficulties in assessing brain death in a case of benzodiazepine poisoning with persistent cerebral blood flow, *Hum Exp Tox*, 23(10): 503–505.

Michaud K, Romain N, Giroud C, Brandt C, Mangin P. (2001). Hypothermia and undressing associated with non-fatal bromazepam intoxication, *Forensic Sci Intl*, 124(2–3): 112–114.

Skov L, Dollerup Holm KM, Johansen SS, Linnet K. (2016). Postmortem brain and blood reference concentrations of alprazolam, bromazepam, chlordiazepoxide, diazepam and their metabolites and a review of the literature, *J Anal Toxicol*, 40(7): 529–536.

Brompheniramine

Brand names: Component of BroveX, Dallergy, Lodrane, Dimetapp, and Bromfed
Classification: Antihistamine
λ: 12–35 h
V_d: 9–15 L/kg
Usual dosage: 4 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.004–0.3 mg/L	No data available	0.4–1 mg/L[a]
Liver			4.2 mg/kg[a]
Skeletal muscle			2.3 mg/kg[a]

[a] Co-intoxicant phenylpropanolamine 6.3 mg/L blood.

Selected Sources

Bruce RB, Pitts JE, Pinchbeck FM. (1968). Determination of brompheniramine in blood and urine by gas–liquid chromatography, *Anal Chem*, 40(8): 1246–1250.

Jumbelic MI, Hanzlick R, Cohle S. (1997). Alkylamine antihistamine toxicity and review of pediatric toxicology registry of the National Association of Medical Examiners, Report 4: Alkylamines, *Am J Forensic Med Path*, 18(1): 65–69.

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Buprenorphine

Brand names: Buprenex, Subutex, Sublocade, and Suboxone (with naloxone)
Classification: Opiate agonist–antagonist
λ: 3–44 h
V_d: 1–1.5 L/kg
Usual dosage: 2–16 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.02 mg/L	0.02–0.2 mg/L	0.14–100 mg/L
Brain			6.4 mg/kg

Comments

- Interacts with HIV protease inhibitors and antifungals (azoles) resulting in increased buprenorphine concentrations
- Metabolized by CYP 3A4

Selected Sources

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Elkader A, Sproule B. (2005). Buprenorphine: Clinical pharmacokinetics in the treatment of opioid dependence, *Clin Pharmacokinet*, 44(7): 661–680.

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Bupropion

Brand names: Wellbutrin and Zyban
Classification: Antidepressant
λ: 12–30 h
V_d: 17–20 L/kg
Usual dosage: 100 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.6 mg/L	0.28–1.4 mg/L	1.5–21 mg/L
Vitreous			1.6 mg/L
Liver			12–14 mg/kg
Kidney			1.2 mg/kg
Skeletal muscle	0.08–0.2 mg/kg		

Comments

- Has multiple active metabolites
- Metabolized by CYP 2B6

Selected Sources

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Buspirone

Brand name: Buspar
Classification: Anxiolytic
λ: 2–6 h
V_d: 3–8 L/kg
Usual dosage: 15–30 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0002–0.01 mg/L	No data available	2–7.3 mg/L

Comments

- Active metabolite: 6-hydroxybuspirone

Selected Sources

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Butalbital

Brand names: Bupap, Esgic, Floricet (w/ acetaminophen, caffeine), and Fiorinal (w/ caffeine)
Classification: Barbiturate
λ: 30–40 h
V_d: Unknown
Usual dosage: 50–100 mg per dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–11 mg/L	7.0–40 mg/L	13–50 mg/L
Liver	0.5–24 mg/kg		50 mg/kg
Kidney	0.2–11 mg/kg		
Brain	0.2–0.6 mg/kg		
Skeletal muscle	0.1–7.1 mg/kg		
Cardiac muscle	0.2–8.7 mg/kg		

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Butorphanol

Brand name: Stadol
Classification: Opiate agonist–antagonist
λ: 2–8 h
V_d: 7–11 L/kg
Usual dosage: 1 mg iv; 2 mg im; 1–2 mg intranasal q3–4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0009–0.004 mg/L	No data available	4–9 mg/L

Selected Sources

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Caffeine

Brand name: Cafcit
Classification: Methylxanthine (stimulant)
λ: 2–10 h
V_d: 0.5–0.9 L/kg
Usual dosage: 5 mg/kg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	2–34 mg/L	15–80 mg/L	33–1040 mg/L
Vitreous			100–159 mg/L
Liver			58–670 mg/kg
Kidney			13–352 mg/kg
Brain			75–188 mg/kg

Comments

- Metabolized by CYP 1A2
- Common sources of caffeine: 12 oz soda, ~40 mg; cup of coffee, ~150 mg; and energy drink, ~50–200 mg

Selected Sources

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Carbamazepine

Brand names: Tegretol, Carbatrol, Equetro, and Epitol
Classification: Anticonvulsant
λ: 12–65 h
V_d: 0.8–1.4 L/kg
Usual dosage: 200–800 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1.9–19 mg/L	10–55 mg/L	20–73 mg/L
Liver	2.2 mg/kg		123 mg/kg
Kidney			72 mg/kg
Brain			78–86 mg/kg
Cardiac muscle			64 mg/kg
Skeletal muscle	6.9–9.7 mg/kg		

Comments

- Metabolized by CYP 3A

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.
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Carbinoxamine

Brand names: Palgic and Pediox
Classification: Antihistamine
λ: 10–20 h
V_d: Unknown
Usual dosage: 4–24 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.2 mg/L	No data available	0.25[a]–15 mg/L
Liver	2.5 mg/kg		

[a] Infant.

Comments

- Elevated concentrations may be associated with SIDS in infants

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Stockis A, Lebacq E, Deroubaix X, Allemon AM, Laufen H. (1992). Relative bioavailability of carbinoxamine and phenylpropanolamine from a retard suspension after single dose administration in healthy subjects, *Arzneimittelforschung*, 42(12): 1478–1481.

Carbon Monoxide

Brand name: Not applicable
Classification: Gas (combustion product of organic material)
λ: 5–6 h (21% O_2); 30–90 min (100% O_2)
V_d: Unknown
Usual dosage: Not applicable

Source	Nontoxic	Toxic	Lethal
Blood	0%–3% nonsmoker 3%–8% smoker 0.5%–4.7% infant 10% hemolytic anemia	10% SOB, headache 15%–30% impaired judgment 40%–50% confusion 60%–70% unconsciousness	33%–72%
Spleen	<10%	30%–50%	29%–72%

Environmental CO Concentration	Symptoms
100–200 ppm	Headache and dizziness after 2–3 h exposure; decreased judgment
400 ppm	Headache and dizziness after 1–2 h exposure
800 ppm	Dizziness and nausea after 45 min exposure; unconscious after 2 h exposure
1600 ppm	Headache, tachycardia, dizziness after 20 min exposure; death <2 h exposure
3200 ppm	Headache, tachycardia, dizziness after 5–10 min exposure; death 30 min exposure
6400 ppm	Headache, tachycardia, dizziness after 1–2 min exposure; death <20 min exposure
12800 ppm	Unconsciousness after 2–3 breaths; death in minutes

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Carisoprodol

Brand name: Soma and Vanadom
Classification: Muscle relaxant
λ: 1–8 h
V_d: Unknown
Usual dosage: 350 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	10–40 mg/L	30–50 mg/L	39–110 mg/L
Liver	21–45 mg/kg		127 mg/kg
Kidney			110 mg/kg
Skeletal muscle	8.9–50 mg/kg		103 mg/kg

Comments

- Active metabolite: Meprobamate
- Metabolized by CYP 2C19
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Backer RC, Zumwalt R, McFeeley P, Veasey S, Wohlenberg N. (1990). Carisoprodol concentrations from different anatomical sites: Three overdose cases, *J Anal Toxicol*, 14(5): 332–334.

Bexar County Medical Examiner's Office data 1996–2015.

Davis GG, Alexander CB. (1998). A review of carisoprodol deaths in Jefferson County, Alabama, *South Med J*, 91(8): 726–730.

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Olsen H, Koppang E, Alvan G, Mørland J. (1994). Carisoprodol elimination in humans, *Ther Drug Monit*, 16(4): 337–340.

Cetirizine

Brand name: Zyrtec
Classification: Antihistamine
λ: 5.5–9 h
V_d: 0.4–0.6 L/kg
Usual dosage: 2.5–10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–1 mg/L	2.4[a] mg/L	No data available

[a] Child (18 months).

Comments

- Xyzal (levocetirizine) is R-enantiomer of cetirizine and *laboratories usually do not differentiate between cetirizine and levocetirizine*

Selected Sources

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Ridout SM, Tariq SM. (1997). Cetirizine overdose in a young child, *J Allergy Clin Immunol*, 99(6 Pt 1): 860–861.

Wood SG, John BA, Chasseaud LF, Yeh J, Chung M. (1987). The metabolism and pharmacokinetics of 14C-cetirizine in humans, *Ann Allergy*, 59(6 Pt 2): 31–34.

Chloral Hydrate

Brand names: Somnote, Aquachloral, and Noctec
Classification: Sedative/hypnotic
λ: 3–4 min
V_d: 0.3–1 L/kg
Usual dosage: 500–2000 mg tid/qid

Source	Therapeutic/Nontoxic[a]	Toxic[a]	Lethal[a]
Blood	1.5–15 mg/L	40–50 mg/L	60–1700 mg/L
Vitreous			73 mg/L

[a] All concentrations are for trichloroethanol.

Comments

- Active metabolite: Trichloroethanol (λ 8–30 h)

Selected Sources

Benson R. (2000). *Concise International Chemical Assessment Document No, 25: Choral Hydrate International Programme on Chemical Safety*. World Health Organization, Geneva, Switzerland.

Benson R. (2000). *Toxicological Review of Chloral Hydrate* (*CAS No.302–17-0*). U.S. EPA, Washington, DC.

Bexar County Medical Examiner's Office data 1996–2015.

Gaulier JM, Merle G, Lacassie E, Courtiade B, Haglund P, Marquet P, Lachâtre GJ. (2001). Fatal intoxications with chloral hydrate, *Forensic Sci*, 46(6): 1507–1509.

Heller PF, Goldberger BA, Caplan YH. (1992). Chloral hydrate overdose: Trichloroethanol detection by gas chromatography/mass spectrometry, *Forensic Sci Intl*, 52(2): 231–234.

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Chlordiazepoxide

Brand names: Librium and Librax (with Clidinium)
Street name: Lib
Classification: Benzodiazepine
λ: 24–48 h
V_d: 0.3–0.6 L/kg
Usual dosage: 5–10 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1–10 mg/L	3–60 mg/L	7.7[a]–20 mg/L
Liver			10 mg/kg
Brain	0.003–1.85 mg/kg		
Skeletal muscle	0.9–1.5 mg/kg		

[a] Ethanol was co-intoxicant 0.19 g/dL.

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations
- Active metabolite: Nordiazepam (λ 38–135 h) and temazepam (λ 7–18 h)

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Chloroquine

Brand name: Aralen
Classification: Antimalarial/antiarthritic
λ: 72–300 h
V_d: 116–285 L/kg
Usual dosage: 150–600 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–2.3 mg/L	0.5–1.0 mg/L	3–460 mg/L
Vitreous			5.3 mg/L
Liver	2.9–58 mg/kg		16–1307 mg/kg
Kidney	0.6–5.8 mg/kg		11–1690 mg/kg
Brain	0.7–7.3 mg/kg		1–100 mg/kg
Skeletal muscle			10–132 mg/kg
Cardiac muscle			23–24 mg/kg

Comments

- Prolongs QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Noirfalise A. (1978). Chloroquine intoxication: Two case reports, *J Forensic Sci*, 11(3): 177–179.

Chlorpheniramine

Brand names: Component of over-the-counter (OTC) cold medications including: Tylenol Cold, Vicks 44, Tussionex, Chlor-trimeton
Classification: Antihistamine
λ: 12–43 h
V_d: 2.5–3.8 L/kg
Usual dosage: 4 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal[a]
Blood	0.01–0.3 mg/L	0.5 mg/L	1.1 mg/L
Liver	0.5–2.5 mg/kg		6.6 mg/kg
Kidney			1.4 mg/kg
Brain			2.5 mg/kg
Lung			5.2 mg/kg
Skeletal muscle	0.07–0.08 mg/kg		5.0 mg/kg

[a] Co-intoxicant ethanol 0.12 g/dL and diazepam/nordiazepam combined concentration 0.2 mg/L.

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Chlorpromazine

Brand names: Thorazine, Largactil, and Ormazine
Classification: Antipsychotic
λ: 23–37 h
V_d: 10–35 L/kg
Usual dosage: 300–800 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–5 mg/L	0.5–3 mg/L	3–43 mg/L
Liver	3.5–17 mg/kg		45–2110 mg/kg
Kidney			4–740 mg/kg
Brain			125–200 mg/kg
Skeletal muscle	1 mg/kg		12 mg/kg

Comments

- Prolongs QT interval
- Metabolized by CYP 2D6

Selected Sources

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Citalopram

Brand names: Celexa and Lexapro (escitalopram)
Classification: Antidepressant (SSRI)
λ: 12–37 h
V_d: 10–18 L/kg
Usual dosage: 20–60 mg qd (escitalopram 10–20 mg qd)

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–1.7 mg/L	0.48–5.9 mg/L	3.2–49 mg/L
Vitreous	0.1–0.2 mg/L		0.3 mg/L
Liver	0.4–21 mg/kg		12–55 mg/kg
Kidney			13 mg/kg
Brain			2–22 mg/kg
Skeletal muscle	0.06–1.1 mg/kg		

Comments

- Prolongs QT interval
- Metabolized by CYP 2C19, 2D6, and 3A
- Escitalopram is the s-enantiomer of citalopram and *laboratories usually do not differentiate between escitalopram and citalopram*

Selected Sources

Anastos N, McIntyre IM, Lynch MJ, Drummer OH. (2002). Postmortem concentrations of citalopram, *J Forensic Sci*, 47(4): 882–884.

Bexar County Medical Examiner's Office data 1996–2015.

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Clobazam

Brand names: Frisium and Urbanyl
Classification: Benzodiazepine
λ: 10–40 h
V_d: 1 L/kg
Usual dosage: 5–15 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.14–0.41 mg/L	No data available	3.9 mg/L
Liver			2.4 mg/kg
Kidney			5.3 mg/kg

Comments

- Active metabolite: Desmethylclobazam
- Not available in the United States
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Monjanel-Mouterde S, Antoni M, Bun H, Botta-Frindlund D, Gauthier A, Durand A, Cano JP. (1994). Pharmacokinetics of a single oral dose of clobazam in patients with liver disease, *Pharmacol Toxicol*, 74(6): 345–350.

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Rouini M, Ardakani YH, Hakemi L, Mokhberi M, Badri G. (2005). Simultaneous determination of clobazam and its major metabolite in human plasma by a rapid HPLC method, *J Chromatogr B Analyt Technol Biomed Life Sci*, 823(2): 167–171.

Clomipramine

Brand name: Anafranil
Classification: Antidepressant (TCA)
λ: 19–37 h
V_d: 9–25 L/kg
Usual dosage: 25 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–0.4 mg/L	0.6–1.6 mg/L	1.7–3.3 mg/L
Liver	7–20 mg/kg		12–320 mg/kg
Brain			4.9–8 mg/kg

Comments

- Can cause serotonin syndrome
- Active metabolite: *N*-desmethylclomipramine
- Metabolized by CYP 1A2, 2D6, 3A, and 2C19
- May prolong QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.

Gex-Fabry M, Haffen E, Paintaud G, Bizouard P, Sechter D, Bechtel PR, Balant LP. (2000). Population pharmacokinetics of clomipramine, desmethylclomipramine and hydroxylated metabolites in patients with depression receiving chronic treatment: Model evaluation, *Ther Drug Monit*, 22(6): 701–711.

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Meatherall RC, Guay DR, Chalmers JL, Keenan JR. (1983). A fatal overdose with clomipramine, *J Anal Toxicol*, 7(4): 168–171.

Stolk LM, van der Geest S. (1998). Plasma concentrations after a clomipramine intoxication, *J Anal Toxicol*, 22(7): 612–613.

Clonazepam

Brand name: Klonopin
Classification: Benzodiazepine
λ: 19–60 h
V_d: 1.5–4.4 L/kg
Usual dosage: 0.25–5 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.004–0.2 mg/L	0.1–0.6 mg/L	0.7–1.4 mg/L

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Berlin A, Dahlström H. (1975). Pharmacokinetics of the anticonvulsant drug clonazepam evaluated from single oral and intravenous doses and by repeated oral administration, *Eur J Clin Pharmacol*, 9(2–3): 155–159.

Bexar County Medical Examiner's Office data 1996–2015.

Burrows DL, Hagardorn AN, Harlan GC, Wallen ED, Ferslew KE. (2003). A fatal drug interaction between oxycodone and clonazepam, *J Forensic Sci*, 48(3): 683–686.

Greenblatt DJ, Blaskovich PD, Nuwayser ES, Harmatz JS, Chen G, Zinny MA. (2005). Clonazepam pharmacokinetics: Comparison of subcutaneous microsphere injection with multiple-dose oral administration, *J Clin Pharmacol*, 45(11): 1288–1293.

Welch TR, Rumack BH, Hammond K. (1977). Clonazepam overdose resulting in cyclic coma, *Clin Tox*, 10(4): 433–436.

Clozapine

Brand names: Clozaril and FazaClo
Classification: Antipsychotic
λ: 4–66 h
V_d: 4.6–5 L/kg
Usual dosage: 300–450 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–1.7 mg/L	0.9–7.0 mg/L	1.3–13 mg/L
Vitreous			1.3 mg/L
Liver	0.8–1.5 mg/kg	5.9–17 mg/kg	6.5–85 mg/kg
Skeletal muscle	1.7 mg/kg		

Comments

- Prolongs QT interval
- Metabolized by CYP 1A2, 3A4, and 2D6
- Active metabolite: Desmethylclozapine

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.
Flanagan RJ, Spencer EP, Morgan PE, Barnes TR, Dunk L. (2005). Suspected clozapine poisoning in the UK/Eire, 1992–2003, *Forensic Sci Intl*, 155(2–3): 91–99.
Ishii A, Mizoguchi K, Kageoka M, Seno H, Kumazawa T, Suzuki O. (1997). Nonfatal suicidal intoxication by clozapine, *J Tox Clin Tox*, 35(2): 195–197.
Keller T, Miki A, Binda S, Dirnhofer R. (1997). Fatal overdose of clozapine, *Forensic Sci Intl*, 86(1–2): 119–125.
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Medical Economics. (2007). *Physicians' Desk Reference*, (61st ed.), Thomson PDR, Montvale, NJ, pp. 2184–2189.
Worm K, Kringsholm B, Steentoft A. (1993). Clozapine cases with fatal, toxic or therapeutic concentrations, *Int J Legal Med*, 106(3): 115–118.

Cocaine

Brand name: Cocaine hydrochloride
Street names: Coke, Snow, and Crack; w/ heroin: Dynamite and Belushi, Eightball, Moonrock, and Speedball; w/ PCP: Jim Jones, Parachute, and Spaceball
Classification: Local anesthetic (ENT)/stimulant
λ: 0.7–1.5 h
V_d: 1.7–2.7 L/kg
Usual dosage: 1%–10% solutions used topically; 1–2 mg/kg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–15 mg/L	0.1–5 mg/L	0.1–330 mg/L
Vitreous			0.8–13 mg/L
Liver			0.2–393 mg/kg
Kidney			3.8–28 mg/kg
Brain			0.04–74 mg/kg
Skeletal muscle	0.1 mg/kg		0.1–48 mg/kg

Comments

- Can be metabolized *in vitro* (and *in vitro*) to ecgonine methyl ester and benzoylecgonine
- Active metabolites: Cocaethylene, and norcocaine
- Metabolized by CYP 3A

Selected Sources

Amon CA, Tate LG, Wright RK, Matusiak W. (1986). Sudden death due to ingestion of cocaine, *J Anal Toxicol*, 10(5): 217–218.

Bexar County Medical Examiner's Office data 1996–2015.

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Jenkins AJ, Levine B, Titus J, Smialek JE. (1999). The interpretation of cocaine and benzoylecgonine concentrations in postmortem cases, *Forensic Sci Intl*, 101(1): 17–25.

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Winek CL, Wahba WW, Rozin L, Janssen JK. (1987). An unusually high blood cocaine concentration in a fatal case, *J Anal Toxicol*, 11(1): 43–46.

Codeine

Brand names: Often combined with acetaminophen or aspirin (ASA) (Tylenol w/ codeine, Empirin w/ codeine)
Classification: Opiate
λ: 1.1–4 h
V_d: 2.2–4.7 L/kg
Usual dosage: 15–60 mg q 4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.4 mg/L	0.5–1 mg/L	1–48 mg/L
Vitreous	0.02–0.4 mg/L		0.6–1.2 mg/L
Liver	0.6 mg/kg		13–128 mg/kg
Kidney			2.3–36 mg/kg
Brain			2–33 mg/kg
Skeletal muscle	0.06–1 mg/kg		1.9 mg/kg
Adipose tissue			2.1 mg/kg

Comments

- Metabolized to morphine by CYP 2D6
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Pearson MA, Poklis A, Morrison RR. (1979). A fatality due to the ingestion of (methyl morphine) codeine, *Clin Tox*, 15(3): 267–271.
Peat MA, Sengupta A. (1977). Toxicological investigations of cases of death involving codeine and dihydrocodeine, *J Forensic Sci*, 9(1): 21–32.

Cyanide

Brand names: Component of some insecticides
Classification: Poison
λ: 1 h
V_d: 0.4 L/kg
Usual dosage: Not applicable

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	<0.25 mg/L	0.25–5 mg/L	1–249 mg/L
Vitreous			0.5–1.4 mg/L
Liver			0.1–43 mg/kg
Kidney			0.5–55 mg/kg
Brain			0.6–30 mg/kg

Comments

- Associated with bright red lividity and musculature at autopsy
- Distinct bitter almond smell
- Can be created by microorganisms; best to test blood immediately
- Can be found in fire deaths: 0.2–2 mg/L survivors; 1–5 mg/L fatalities

CN concentration	Symptoms
<0.2 mg/L	Usually none
0.5–1.0 mg/L	Flushing, tachycardia
1–2.5 mg/L	Stupor and agitation
>2.5 mg/L	Coma

Selected Sources

Adelson L. (1974). Chapter XIII murder by poison, in *The Pathology of Homicide*, Charles C Thomas (Ed.), Springfield, IL, pp. 725–875.

Bexar County Medical Examiner's Office data 1996–2015.

Hall AH, Doutre WH, Ludden T, Kulig KW, Rumack BH. (1987). Nitrite/thiosulfate treated acute cyanide poisoning: estimated kinetics after antidote, *J Tox Clin Tox*, 25(1–2): 121–133.

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Stoll S, Roider G, Keil W. (2017). Concentrations of cyanide in blood smaples of corpses after smoke inhlataion of varying origin, *Int J Legal Med*, 131: 123–129.

Cyclizine

Brand name: Marezine
Classification: Antihistamine
λ: 7–24 h
V_d: 13–21 L/kg
Usual dosage: 50 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.3 mg/L	0.75–1 mg/L	15–80 mg/L
Liver			37 mg/kg
Brain			3 mg/kg

Selected Sources

Backer RC, McFeeley P, Wohlenberg N. (1989). Fatality resulting from cyclizine overdose, *J Anal Toxicol*, 13(5): 308–309.

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Schulz M, Schmoldt A. (2003). Therapeutic and toxic blood concentrations of more than 800 drugs and other xenobiotics, *Pharmazie*, 58(7): 447–474.

Cyclobenzaprine

Brand names: Flexeril, Amrix, and Fexmid
Classification: Muscle relaxant
λ: 8.3–47 h
V_d: Unknown
Usual dosage: 5 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.5 mg/L	No data available	0.7–1.8 mg/L
Liver			3.1–120 mg/kg
Skeletal muscle	0.16–0.5 mg/kg		0.6 mg/kg

Comments

- Metabolized by CYP 1A2

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Spiller HA, Cutino L. (2003). Fatal cyclobenzaprine overdose with postmortem values, *J Forensic Sci*, 48(4): 883–884.
Winchell GA, King JD, Chavez-Eng CM, Constanzer ML, Korn SH. (2002). Cyclobenzaprine pharmacokinetics, including the effects of age, gender and hepatic insufficiency, *J Clin Pharmacol*, 42(1): 61–69.

Cyproheptadine

Brand name: Periactin
Classification: Antihistamine
λ: 8.6 h
V_d: Unknown
Usual dosage: 4 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.03 mg/L	No data available	0.5[a]–0.6[b] mg/L
Liver			7.6[b] mg/kg
Kidney			1.8[b] mg/kg

[a] Co-intoxicant citalopram 2.3 mg/L.
[b] Blood ethanol 0.09 g/dL.

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Gunja N, Collins M, Graudins A. (2004). A comparison of the pharmacokinetics of oral and sublingual cyproheptadine, *J Tox Clin Tox*, 42(1): 79–83.
Levine B, Green-Johnson D, Hogan S, Smialek JE. (1998). A cyproheptadine fatality, *J Anal Toxicol*, 22(1): 72–74.

Desipramine

Brand name: Norpramin
Classification: Antidepressant (TCA)
λ: 12–28 h
V_d: 24–60 L/kg
Usual dosage: 75–150 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.6 mg/L	0.4–1.8 mg/L	3–36 mg/L
Vitreous	0.04 mg/L		
Liver			50–140 mg/kg
Skeletal muscle	0.08 mg/kg		10 mg/kg

Comments

- Metabolite of imipramine
- Prolongs QT interval
- Metabolized by CYP 2D6

Selected Sources

Amitai Y, Frischer H. (2004). Excess fatality from desipramine and dosage recommendations, *Ther Drug Monit*, 26(5): 468–473.

Bexar County Medical Examiner's Office data 1996–2015.

Burke MJ, Harvey AT, Preskorn SK. (1996). Pharmacokinetics of the newer antidepressants, *Am J Med*, 100(1): 119–121.

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Linder MW, Keck PE. (1998). Standards of laboratory practice: Antidepressant drug monitoring, National Academy of Clinical Biochemistry, *Clin Chem*, 44(5): 1073–1084.

Sawyer WT, Caudill JL, Ellison MJ. (1984). A case of severe acute desipramine overdose, *Am J Psychiatry*, 141(1): 122–123.

Desloratadine

Brand name: Clarinex
Classification: Antihistamine
λ: 27–36 h
V_d: 49 L/kg
Usual dosage: 2.5–10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.006 mg/L	No data available	

Comments

- May prolong QT interval
- Active metabolite: 3-hydroxydesloratadine

Selected Sources

Affrime M, Banfield C, Gupta S, Cohen A, Boutros T, Thonoor M, Cayen M. (2002). Comparison of pharmacokinetics and metabolism of desloratadine, fexofenadine, levocetirizine and mizolastine in humans, *Clin Pharmacokinet*, 41(Suppl 1): 21–28.

Devillier P, Roche N, Faisy C. (2008). Clinical pharmacokinetics and pharmacodynamics of desloratadine, fexofenadine and levocetirizine: A comparative review, *Clin Pharmacokinet*, 47(4): 217–230.

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Desvenlafaxine

Brand name: Pristiq
Classification: Antidepressant (SNRI)
λ: 8–14 h
V_d: 3–4 L/kg
Usual dosage: 50–100 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.06–0.3 mg/L	No data available	

Comments

- Metabolite of venlafaxine

Selected Sources

Baird-Bellaire S, Behrle JA, Parker VD, Patat A, Paul J, Nichols AI. (2013). An open-label, single-dose, parallel-group study of the effects of chronic hepatic impairment on the safety and pharmacokinetics of desvenlafaxine, *Clin Ther*, 35(6): 782–794.

Nichols AI, Focht K, Jiang Q, Preskorn SH, Kane CP. (2011). Pharmacokinetics of venlafaxine extended release 75 mg and desvenlafaxine 50 mg in healthy CYP2D6 extensive and poor metabolizers: A randomized, open-label, two-period, parallel-group, crossover study, *Clin Drug Investig*, 31(3): 155–167.

Dexfenfluramine

Brand name: Redux
Classification: Anorectic
λ: 13–20 h
V_d: 10–14 L/kg
Usual dosage: 15 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.013–0.05 mg/L	0.15–0.8 mg/L	3.3 mg/L[a]

[a] Postmortem sample in suicide case; exact cause of death not given.

Comments

- No longer available in the United States
- Associated with pulmonary hypertension and cardiac valve disease
- Active metabolite: Nordexfenfluramine
- Metabolized by CYP 2D6 and 1A2

Selected Sources

Cheymol G, Weissenburger J, Poirier JM, Gellee C. (1995). The pharmacokinetics of dexfenfluramine in obese and non-obese subjects, *Br J Clin Pharm*, 39(6): 684–7.

LoVecchio F, Curry SC. (1998). Dexfenfluramine overdose, *Ann Emer Med*, 32(1): 102–103.

Redux™ package insert (1996). Wyeth-Ayerst Laboratories.

Dextromethorphan

Brand names: Common component of OTC cough medicines including Balamine, Tylenol Cold, and Vicks
Classification: Antitussive
λ: 3–4 h
V_d: 5–6 L/kg
Usual dosage: 10–30 mg q 4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–0.8 mg/L	0.1–2.8 mg/L	1.3–18 mg/L
Vitreous			0.7 mg/L
Liver			19–230 mg/kg
Skeletal muscle	0.07–0.5 mg/kg		

Comments

- Metabolized by CYP 2D6 and 3A4

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Ganetsky M, Babu KM, Boyer EW. (2007). Serotonin syndrome in dextromethorphan ingestion responsive to propofol therapy, *Pediatr Emerg Care*, 23(11): 829–831.
Logan BK, Goldfogel G, Hamilton R, Kuhlman J. (2009). Five deaths resulting from abuse of dextromethorphan sold over the internet, *J Anal Toxicol*, 33(2): 99–103.
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Rammer L, Holmgren P, Sandler H. (1988). Fatal intoxication by dextromethorphan: A report on two cases, *Forensic Sci Intl*, 37(4): 233–236.
Schadel M, Wu D, Otton SV, Kalow W, Sellers EM. (1995). Pharmacokinetics of dextromethorphan and metabolites in humans: Influence of the CYP2D6 phenotype and quinidine inhibition, *J Clin Psychopharmacol*, 15(4): 263–269.
Schwartz AR, Pizon AF, Brooks DE. (2008) Dextromethorphan-induced serotonin syndrome, *Clin Toxicol* (*Phila*), 46(8): 771–773.
Vetticaden SJ, Cabana BE, Prasad VK, Purich ED, Jonkman JH, de Zeeuw R. (1989). Phenotypic differences in dextromethorphan metabolism, *Pharm Res*, 6(1): 13–19.
Yoo Y, Chung H, Kim E, Kim M. (1996). Fatal zipeprol and dextromethorphan poisonings in Korea, *J Anal Toxicol*, 20(3): 155–158.

Diazepam

Brand names: Valium and Valrelease
Street name: V
Classification: Benzodiazepine
λ: 30–66 h
V_d: 1–2 L/kg
Usual dosage: 2–20 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–4 mg/L	3–20 mg/L	1.2–30 mg/L
Liver			16 mg/kg
Brain	0.002–0.6 mg/kg		
Skeletal muscle	0.1–1 mg/kg		

Comments

- Sudden withdrawal can lead to anxiety, seizures, and death
- Tolerance can develop and should be considered when interpreting drug concentrations
- Metabolized by CYP 2C19 and 3A4
- Active metabolite: Nordiazepam (λ 38–135 h) and temazepam (λ 7–18 h)

Selected Sources

Cardauns H, Iffland R. (1973). Fatal intoxication of a young drug addict with diazepam, *Archiv für Toxikologie*, 31(2): 147–151.

Finkle BS, McCloskey KL, Goodman LS. (1979). Diazepam and drug-associated deaths. A survey in the United States and Canada, *JAMA*, 242(5): 429–434.

Greenblatt DJ, Harmatz JS, Friedman H, Locniskar A, Shader RI. (1989). A large-sample study of diazepam pharmacokinetics, *Ther Drug Mon*, 11(6): 652–657.

Jönsson AK, Söderberg C, Espnes KA, Ahlner J, Eriksson A, Reis M, Druid H. (2014). Sedative and hypnotic drugs—fatal and non-fatal reference blood concentrations, *Forensic Sci Int*, 236: 138–145.

Tada K, Moroji T, Sekiguchi R, Motomura H, Noguchi T. (1985). Liquid-chromatographic assay of diazepam and its major metabolites in serum, and application to pharmacokinetic study of high doses of diazepam in schizophrenics, *Clin Chem*, 31(10): 1712–1715.

Vukcević NP, Ercegović GV, Segrt Z, Djordjević S, Stosić JJ. (2016). Benzodiazepine poisoning in elderly, *Vojnosanit Pregl*, 73(3): 234–238.

Dicyclomine

Brand names: Bentyl, Byclomine, and Dibent
Classification: Antimuscarinic/antispasmotic
λ: 1.8 h
V_d: 3.6 L/kg
Usual dosage: 10–20 mg qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.6 mg/L	0.2 mg/L	0.2–0.5 mg/L[a]
Vitreous			0.1 mg/L[a]

[a] Infant deaths.

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Garriott JC, Rodriquez R, Norton LE. (1984). Two cases of death involving dicyclomine in infants. Measurement of therapeutic and toxic concentrations in blood, *J Tox Clin Tox*, 22(5): 455–462.
Medical Economics. (2006). *Physicians' Desk Reference*, (60th ed.), Thomson PDR, Montvale, NJ, pp. 724–726.

Digitoxin

Brand name: Digitaline
Classification: Cardiac glycoside
λ: 6–12 d
V_d: 0.5–0.8 L/kg
Usual dosage: 0.05–0.2 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.006–0.03 mg/L	0.03–0.6 mg/L	0.2–0.8 mg/L

Comments

- Usually measured by immunoassays that may cross-react with oleander and digoxin
- Treated with digibind (digoxin immune fab)
- Found in several plant species including foxglove (*digitalis purpurea*)

Selected Sources

Kanji S, MacLean RD. (2012). Cardiac glycoside toxicity: More than 200 years and counting, *Crit Care Clin*, 28(4): 527–535.

Krappweis J, Petereit G, Justus J, Altmann E, Kirch W. (1996). Digitoxin intoxication with lethal outcome, *Eur J Med Res*, 1(12): 551–553.

MacFarland RT, Marcus FI, Fenster PE, Graves PE, Perrier D. (1984). Pharmacokinetics and bioavailability of digitoxin by a specific assay, *Eur J Clin Pharm*, 27(1): 85–89.

Ochs HR, Grube E, Greenblatt DJ, Arendt R, Bodem G. (1981). Pharmacokinetics and pharmacodynamics of intravenous digoxin and digitoxin, *Wien Klin Wochenschr*, 59(16): 889–897.

Schmitt K, Tulzer G, Häckel F, Sommer R, Tulzer W. (1994). Massive digitoxin intoxication treated with digoxin-specific antibodies in a child, *Ped Card*, 15(1): 48–49.

Woolf AD, Wenger T, Smith TW, Lovejoy FH. (1992). The use of digoxin-specific Fab fragments for severe digitalis intoxication in children, *NEJM*, 326(26): 1739–1744.

Digoxin

Brand names: Lanoxin, Lanoxicaps, and Digitalis
Classification: Cardiac glycoside
λ: 1.5–2 d
V_d: 4–8 L/kg
Usual dosage: 0.125–3 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0008–0.01 mg/L	0.002–0.04 mg/L	0.003–1.3 mg/L
Vitreous	0.002–0.007 mg/L		0.003–0.05 mg/L
Liver	0.03–0.2 mg/kg		0.03–0.73 mg/kg
Kidney	0.05–0.4 mg/kg		0.1–1.7 mg/kg
Brain	0.003–0.3 mg/kg		0.009–0.05 mg/kg
Skeletal muscle	0.008–0.06 mg/kg		0.01–0.4 mg/kg
Cardiac muscle	0.03–0.5 mg/kg		0.04–1.2 mg/kg

Comments

- Causes increased potassium
- Usually measured by immunassays that may cross-react with oleander and digitoxin
- Treated with digibind (digoxin immune fab)

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Dihydrocodeine

Brand names: Codicontin, Synalgos (w/ ASA and caffeine), Novahistine (w/ phenylephrine), and HydroTussin (w/ pseudoephedrine and chlorpheniramine)
Classification: Opioid
λ: 3–4.5 h
V_d: 1–1.5 L/kg
Usual dosage: 16–32 mg q 4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.3 mg/L	0.5–1 mg/L	0.4–166 mg/L
Liver			1.3 mg/kg
Kidney			11 mg/kg
Brain			0.8 mg/kg

Comments

- Metabolite of hydrocodone
- Active metabolite: Dihydromorphine
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Diltiazem

Brand names: Cardizem and Tiazac
Classification: Calcium channel blocker
λ: 2–13 h; 28–40 h for ER
V_d: 3–11 L/kg
Usual dosage: 60–120 mg bid; 120–420 mg qd for ER

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–1.4 mg/L	0.6–6.1 mg/L	3–42 mg/L
Vitreous	0.1 mg/L		3.5–5.5 mg/L
Liver	0.3–3 mg/kg		41–182 mg/kg
Kidney	0.8–1 mg/kg		49 mg/kg
Brain	0.5–0.8 mg/kg		33–76 mg/kg
Skeletal muscle	0.1–1.7 mg/kg		

Selected Sources

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Diphenhydramine

Brand names: Benadryl, Nytol, Simply Sleep, Sominex, and Compoz
Classification: Antihistamine
λ: 2–13 h
V_d: 2–5 L/kg
Usual dosage: 25–50 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.004–3.8 mg/L	1–19 mg/L	5–39 mg/L
Vitreous			6–15 mg/L
Liver	0.5–4 mg/kg		34–260 mg/kg
Kidney			50–114 mg/kg
Brain			8–32 mg/kg
Skeletal muscle	0.5–2 mg/kg		7–22 mg/kg

Comments

- May prolong QT interval
- Metabolized by CYP 2D6

Selected Sources

Abdelmalek D, Schwarz ES, Sampson C, Halcomb SE, McCammon C, Arroyo-Plasencia A, Stenger A, Krehbiel N, Mullins ME. (2014). Life-threatening diphenhydramine toxicity presenting with seizures and a wide complex tachycardia improved with intravenous fat emulsion, *Am J Ther*, 21(6): 542–544.

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Dipyrone

Brand names: Analgin, Conmel, Novalgin, and Metamizole
Classification: NSAID
λ: 2–4 h
V_d: 1 L/kg
Usual dosage: 500–1000 mg tid

Source	Therapeutic/Nontoxic[a]	Toxic[a]	Lethal[a]
Blood	4–11 mg/L	20 mg/L	669 mg/L[b]

[a] Concentrations are of active metabolite, 4-methyl-amino-antipyrine (MAA).
[b] Co-intoxicant baclofen 106 mg/L.

Comments

- Not available in the United States
- May cause agranulocytosis or renal insufficiency
- Active metabolite: 4-methyl-amino-antipyrine (MAA)

Selected Sources

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Donepezil

Brand name: Aricept
Classification: Acetylcholinesterase inhibitor (Alzheimer treatment)
λ: 50–80 h
V_d: 10–12 L/kg
Usual dosage: 5–10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.5 mg/L	0.55 mg/L	No data available
Liver	1.2–9.2 mg/kg		
Skeletal muscle	1–1.5 mg/kg		

Comments

- Toxicities treated with atropine
- Metabolized by CYP 2D6 and 3A4

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Dothiepin

Brand names: Dosulepin and Prothiaden
Classification: Antidepressant (TCA)
λ: 11–24 h
V_d: 19–195 L/kg
Usual dosage: 75–300 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.1 mg/L	0.8–5.5 mg/L	2.3–62 mg/L
Vitreous			0.3–0.9 mg/L
Liver			2–52 mg/kg
Kidney			3.1–10 mg/kg
Brain			2.8 mg/kg
Skeletal muscle			0.4–18 mg/kg
Cardiac muscle			2.9–17 mg/kg

Comments

- Active metabolite: Desmethyldothiepin

Selected Sources

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Doxepin

Brand names: Sinequan, Adapin, and Silenor
Classification: Antidepressant (TCA)
λ: 6–23 h
V_d: 17–31 L/kg
Usual dosage: 30–150 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.009–0.7 mg/L	0.2–6.7 mg/L	1–150 mg/L
Vitreous			3 mg/L
Liver			6–500 mg/kg
Kidney			3–70 mg/kg
Brain			2–42 mg/kg
Skeletal muscle			1–38 mg/kg
Cardiac muscle			3–16 mg/kg

Comments

- Metabolized by CYP 2D6 and 2C19
- May prolong QT interval
- Active metabolite: Desmethyldoxepin (nordoxepin)

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Doxylamine

Brand names: Bendectin and Unisom
Classification: Antihistamine
λ: 10–12 h
V_d: 2–3 L/kg
Usual dosage: 25–50 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–4 mg/L	1–7.5 mg/L	1–165 mg/L
Liver	17–40 mg/kg		5–500 mg/kg
Kidney			22 mg/kg
Skeletal muscle			6.3 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Duloxetine

Brand name: Cymbalta
Classification: Antidepressant (SNRI)
λ: 8–17 h
V_d: 16–23 L/kg
Usual dosage: 20–60 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.4 mg/L	0.4–2 mg/L	0.9–6 mg/L
Vitreous			0.6 mg/L
Liver	0.3–22 mg/kg		360 mg/kg

Comments

- Metabolized by CYP 2D6 and 1A2
- May cause liver failure

Selected Sources

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Bexar County Medical Examiner's Office data 2003–2015.

Hanje AJ, Pell LJ, Votolato NA, Frankel WL, Kirkpatrick RB. (2006). Case report: Fulminant hepatic failure involving duloxetine hydrochloride, *Clin Gastroenterol Hepatol*, 4(7): 912–917.

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Ephedrine

Brand names: Primatene and Rynatuss (w/ chlorpheniramine, phenylephrine, and carbetapentane)
Street names: Ma Huang, Herbal Ecstasy
Classification: Stimulant/decongestant
λ: 3–11 h
V_d: 2–4 L/kg
Usual dosage: 10–20 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–0.14 mg/L	0.11–23 mg/L	3.5–20 mg/L
Liver			15[a]–24 mg/kg
Kidney			14 mg/kg
Brain	<0.2 mg/kg		8.9 mg/kg

[a] Co-intoxicant caffeine 86 mg/L.

Comments

- Found in *Ephedra* species of plants
- No longer available in the United States

Selected Sources

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Ryall JE. (2008). Caffeine and ephedrine fatality, *Bull Assoc Forensic Tox*, 17(3): 13.

Ethanol

Brand names: Drinking alcohol; ethyl alcohol
Classification: CNS depressant
λ: zero-order kinetics; 0.01–0.03 g/dL per hour
V_d: 0.4–0.6 L/kg
Usual dosage: Approximately 14 g of ethanol per beverage

Blood Ethanol Content	Findings
0.05 g/dL	Less alert with impaired coordination
0.08–0.1 g/dL	Impaired coordination and judgment, decreased reaction time, loss of concentration, emotional instability
0.1–0.2 g/dL	Disorientation, decreased balance and gait functioning, slurred speech, poor sensory perception, confusion
0.2–0.3 g/dL	Stupor, lack of response to stimuli, vomiting
0.3–0.45 g/dL	Unconsciousness, depressed reflexes, coma
>0.45 g/dL	Death

Lethal Concentrations

Blood	0.3–1.8 g/dL	Liver	0.2–1.2 g/100 g
Kidney	0.3–1.0 g/100 g	Brain	0.3–0.9 g/100 g

Comments

- Metabolized by CYP 2E1
- Can develop tolerance
- Specimen to whole blood ratios at equilibrium:
  - Serum, 1.1–1.35; saliva 1.1; vitreous 1.2; bile 1.0; CSF 1.1
  - Liver 0.6; kidney 0.7; brain 0.8
- Ethanol production is possible with decomposition (0.07–0.22 g/dL), especially in the setting of diabetes (up to 0.5 g/dL)

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Ethylene Glycol

Brand name: Component of antifreeze
Classification: Alcohol
λ: 2–5 h
V_d: 0.5–0.8 L/kg
Usual dosage: Not applicable

Source	Nontoxic	Toxic	Lethal
Blood	94–182 mg/L	50–3860 mg/L	100–23400 mg/L
Vitreous			454–10280 mg/L
Liver			300–15120 mg/kg
Kidney			225–3900 mg/kg
Brain			135–1960 mg/kg
Skeletal muscle			643–3600 mg/kg
Cardiac muscle			58 mg/kg

Comments

- Associated with calcium oxalate crystal deposition in kidneys, brain, and blood vessels

Selected Sources

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Viinamaki J, Sajantila A, Ojanpera I. (2015). Ethylene glycol and metabolite concentrations in fatal ethylene glycol poisonings, *J Anal Toxicol*, 39(6): 481–485.

Felbamate

Brand name: Felbatol
Classification: Anticonvulsant
λ: 18–23 h
V_d: 0.7–0.9 L/kg
Usual dosage: 300–600 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	35–157 mg/L	111–200 mg/L	No data available
Brain	13–74 mg/kg		

Comments

- Associated with hepatic necrosis and aplastic anemia
- May prolong QT interval
- Metabolized by CYP 2E1 and 3A4

Selected Sources

Adusumalli VE, Wichmann JK, Kucharczyk N, Kamin M, Sofia RD, French J. (1994). Drug concentrations in human brain tissue samples from epileptic patients treated with felbamate, *Drug Metab Dispos*, 22(1): 168–170.

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Fenfluramine

Brand name: Pondimin
Classification: Anorectic
λ: 13–30 h
V_d: 12–16 L/kg
Usual dosage: 20 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.3 mg/L	0.5–2.5 mg/L	6–16 mg/L
Liver			31–136 mg/kg
Kidney			27 mg/kg
Brain			42 mg/kg
Skeletal muscle			16 mg/kg
Cardiac muscle			20 mg/kg

Comments

- Not available in the United States
- Associated with pulmonary hypertension and cardiac toxicity

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Fentanyl

Brand names: Duragesic, Actiq, Ionsys, Sublimaze, and Fentora
Street names: China Girl, King Ivory, Goodfellas
Classification: Opioid
λ: 3–12 h
V_d: 3–8 L/kg
Usual dosage: 12.5–100 μg/h transdermal; 200–1600 μg self-titrated oral transmucosal

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0002–0.07 mg/L	0.003–0.02 mg/L	0.003–0.2 mg/L
Liver	0.008–0.2 mg/kg		0.004–0.4 mg/kg
Kidney			0.01–0.09 mg/kg
Brain	0.003–0.01 mg/kg		0.01–0.1 mg/kg
Cardiac muscle			0.1–0.2 mg/kg
Skeletal muscle	0.004–0.05 mg/kg		0.2–0.5 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations
- Has shown tremendous variation in postmortem concentrations with significant postmortem redistribution
- Metabolized by CYP 3A4

Selected Sources

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Fexofenadine

Brand name: Allegra
Classification: Antihistamine
λ: 8–18 h
V_d: 5–6.5 L/kg
Usual dosage: 30–180 mg q d/bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–1.5 mg/L	No data available	

Selected Sources

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Flecainide

Brand name: Tambocor
Classification: Antiarrhythmic
λ: 11–27 h
V_d: 5–9 L/kg
Usual dosage: 50–150 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–4.0 mg/L	1.0–11 mg/L	7–100 mg/L
Vitreous	1.4 mg/L		8–15 mg/L
Liver			18–550 mg/kg
Kidney			28–74 mg/kg

Comments

- Concentrations may increase postmortem

Selected Sources

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Flunitrazepam

Brand name: Rohypnol
Street names: Forget Me Not, Mexican Valium, Roofies, Rope
Classification: Benzodiazepine
λ: 9–24 h
V_d: 3–5.5 L/kg
Usual dosage: 1–2 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.15 mg/L 0.02–0.05 mg/L 7-AF	0.05 mg/L	0.06–0.8 mg/L 0.1–1.6 mg/L 7-AF
Kidney			0.2–0.5 mg/kg
Brain			0.3 mg/kg
Cardiac muscle			0.04 mg/kg
Skeletal muscle			0.1 mg/kg

Comments

- Active metabolite: 7-aminoflunitrazepam (7-AF)
- Often not detected on routine (immunoassay) benzodiazepine screens

Selected Sources

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Fluoride

Brand name: Component of some insecticides or rodenticides
Classification: Element
λ: 2–9 h
V_d: 0.5–0.7 L/kg
Usual dosage: Not applicable

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.6 mg/L	0.3–38 mg/L	3–300 mg/L
Vitreous			2.5–12 mg/L
Liver	0.7 mg/kg		1.6–81 mg/kg
Kidney	0.8 mg/kg		2–68 mg/kg
Brain	0.6 mg/kg		2.5–20 mg/kg
Lung			17.5–19 mg/kg
Cardiac muscle	0.6 mg/kg		14 mg/kg
Skeletal muscle			4.5–18 mg/kg

Comments

- Chronic exposure can lead to skeletal fluorosis
- A toxic component of sulfuryl fluoride, which is a colorless, odorless gas used as fumigant

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Fluoxetine

Brand names: Prozac and Sarafem
Classification: Antidepressant (SSRI)
λ: 1–3 d
V_d: 20–45 L/kg
Usual dosage: 20–80 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–1 mg/L	0.9–2 mg/L	1.3–33 mg/L
Vitreous			5.2 mg/L
Liver	0.7–29 mg/kg		54–400 mg/kg
Kidney	0.2–9 mg/kg		
Brain	0.3–12 mg/kg		
Skeletal muscle	0.6–3 mg/kg		
Cardiac muscle	0.2–8 mg/kg		

Comments

- Metabolized by CYP 2D6, 3A4, 2C9, and 2C19
- Active metabolite: Norfluoxetine
- Prolongs QT interval

Selected Sources

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Fluphenazine

Brand names: Prolixin
Classification: Antipsychotic
λ: 11–28 h (HCl); 7–14 d (decanoate)
V_d: 11 L/kg
Usual dosage: 2.5–10 mg bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.02 mg/L	0.05–0.1 mg/L	See comments

Comments

- Fatalities have been reported due to neuroleptic malignant syndrome
- May prolong QT interval

Selected Sources

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Flurazepam

Brand names: Dalmane and Dalmadorm
Classification: Benzodiazepine
λ: 1–3 h
V_d: 3–5 L/kg
Usual dosage: 15–30 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0005–0.16 mg/L	0.15–0.2 mg/L	0.5–5.5 mg/L
Vitreous			1.3 mg/L
Liver			2.7–130 mg/kg
Kidney			0.9 mg/kg
Brain			0.8 mg/kg

Comments

- Active metabolite: *N*-desalkylflurazepam (therapeutic: 0.03–0.15 mg/L; toxic > 0.05 mg/L)
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Fluvoxamine

Brand names: Luvox, Faverin, and Dumyrox
Classification: Antidepressant (SSRI)
λ: 9–28 h
V_d: 25 L/kg
Usual dosage: 50–100 mg qd/bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.5 mg/L	0.65–1.9 mg/L	2.2–11 mg/L
Vitreous	0.16–0.28 mg/L		1.9 mg/L

Comments

- Metabolized by CYP 2D6; minor pathway CYP 1A2

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Gabapentin

Brand names: Neurontin and Gabarone
Classification: Anticonvulsant
λ: 5–7 h
V_d: 0.5–0.9 L/kg
Usual dosage: 100–1800 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	2–20 mg/L	23–104 mg/L	32–180 mg/L
Vitreous	3–8 mg/L		32 mg/L
Liver	1–10 kg/kg		26–42 mg/kg
Skeletal muscle	1.6 mg/kg		

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Gamma-hydroxybutyrate (GHB)

Brand name: Xyrem
Street names: Liquid Ecstasy, Georgia Home Boy, Grievous Bodily Harm, Max (w/ amphetamine), Special K-lube (w/ ketamine and ETOH)
Classification: Sedative/hypnotic
λ: 0.5–1 h
V_d: 0.4–1 L/kg
Usual dosage: 2–6 g/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.08–197 mg/L	100–340 mg/L	220–4400 mg/L
Vitreous	0.2–39 mg/L		48–2856 mg/L
Liver			52–1080 mg/kg
Brain	10–50 mg/kg		102–711 mg/kg

Comments

- Endogeneous concentrations in postmortem blood measured to be <50 mg/L in the absence of decomposition
- Concentrations increase with decomposition

Selected Sources

Andresen-Streichert H, Jensen P, Kietzerow J, Schrot M, Wilke N, Vettorazzi E, Mueller A, Iwersen-Bergmann S. (2015). Endogenous gamma-hydroxybutyric acid (GHB) concentrations in post-mortem specimens and further recommendation for interpretative cut-offs, *Int J Legal Med*, 129(1): 57–68.

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Mazarr-Proo S, Kerrigan S. (2005). Distribution of GHB in tissues and fluids following a fatal overdose, *J Anal Toxicol*, 29(5): 398–400.

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Zvosec DL, Smith SW, Porrata T, Strobl AQ, Dyer JE. (2011). Case series of 226 γ-hydroxybutyrate-associated deaths: Lethal toxicity and trauma, *Am J Emerg Med*, 29(3): 319–332.

Guaifenesin

Brand names: Hytuss, Organidin, Humibid, and Mucinex
Classification: Expectorant
λ: 1–5 h
V_d: 1 L/kg
Usual dosage: 200–400 mg q 4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–1.4 mg/L	No data available	25[a]–27[b] mg/L
Vitreous			7[b]–9[a] mg/L
Liver			25[a] mg/kg
Brain			17[a] mg/kg

[a] Co-intoxicant: Ethanol 0.12 g/dL.
[b] Co-intoxicant: Diphenhydramine 8.8 mg/L and chlorpheniramine 0.2 mg/L.

Selected Sources

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Haloperidol

Brand name: Haldol
Classification: Antipsychotic
λ: 13–23 h
V_d: 11–25 L/kg
Usual dosage: 0.5–10 mg bid/tid po; 2–5 mg/dose im

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–0.1 mg/L	0.05–0.5 mg/L[a]	0.2–1.9 mg/L
Liver	5.0 mg/kg		44 mg/kg
Kidney	0.7 mg/kg		

[a] Children.

Comments

- Associated with malignant neuroleptic syndrome
- Prolongs QT interval particularly at higher doses
- Metabolized by CYP 3A4

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

Froemming JS, Lam YW, Jann MW, Davis CM. (1989). Pharmacokinetics of haloperidol, *Clin Pharmacokinet*, 17(6): 396–423.

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Heroin

Brand name: Not applicable; diacetylmorphine
Street names: Brown Sugar, H, Horse, Junk, Smack; w/ cocaine: Belushi, Dynamite, Eightball, Speedball, and Moonrock; w/ cocaine & LSD: Frisco
Classification: Opioid
λ: 2–6 min (MAM 10–40 min)
V_d: 0.5–1.5 L/kg
Usual dosage: Not applicable

	Chronic Use/Nontoxic		Lethal	
Source	Morphine	MAM	Morphine	MAM
Blood	0.01–0.2 mg/L	0.001–0.02 mg/L	0.01–1.7 mg/L	0.001–0.5 mg/L
Vitreous			0.01–0.2 mg/L	0.004–0.2 mg/L
Liver			0.04–10 mg/kg	
Kidney			0.7–1.9 mg/kg	
Brain			0.02–0.7 mg/kg	
Skeletal muscle	0.01–0.2 mg/kg	0.001–0.06 mg/kg	0.14–1 mg/kg	0.01–0.35 mg/kg

Comments

- Metabolized to morphine and 6-monoacetylmorphine (MAM); the latter is considered specific for heroin
- Codeine and papaverine, components of the poppy seed, may also be present in small amounts in heroin deaths

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Wyman J, Bultman S. (2004). Postmortem distribution of heroin metabolites in femoral blood, liver, cerebrospinal fluid, and vitreous humor, *J Anal Toxicol*, 28(4): 260–263.

Hydrocodone

Brand names: Zohydro and Hysingla; component of Vicodin, Hycodan, Lortab, Norco, and Hycotuss
Classification: Opioid
λ: 3.5–6 h
V_d: 3–5 L/kg
Usual dosage: 5–10 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.3 mg/L	0.1–0.2 mg/L	0.2–1.6 mg/L
Vitreous	0.02–0.4 mg/L		0.5–0.9 mg/L
Skeletal muscle	0.1–0.6 mg/kg		0.3–0.9 mg/kg

Comments

- Main active metabolite: Hydromorphone
- Metabolized by CYP 2D6
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Hydrogen Sulfide

Brand name: Not applicable
Classification: Gas
λ: Unknown
V_d: Unknown
Usual dosage: Not applicable

	Nontoxic		Lethal	
Source	Sulfide	Thiosufate	Sulfide	Thiosufate
Blood	0–0.05 mg/L	0–0.3 mg/L	0.1–32 mg/L	0.01–137 mg/L
Liver	0.02–3 mg/kg		0.4 mg/kg	
Kidney	0.02–3.6 mg/kg		0.3 mg/kg	
Lung	0.02–0.7 mg/kg		0.4 mg/kg	9.3 mg/kg
Brain	0.1–0.5 mg/kg		1–2.7 mg/kg	5 mg/kg
Skeletal muscle	0.2–0.3 mg/kg		0.16 mg/kg	

Environmental H_2S concentration	Symptoms
0.02–0.1 ppm	Notice odor; headache, nausea
5–100 ppm	Irritation of mucous membranes; offensive odor
100–500 ppm	Olfactory fatigue/paralysis; pulmonary edema
500 ppm	Unconscious within 30–60 min of exposure
700–900 ppm	Rapidly unconscious; coma
>1000 ppm	Collapse of CNS; death

Comments

- A naturally occurring gas formed by the breakdown of organic material in the absence of oxygen; it smells like rotten eggs
- Exposure can cause black discoloration of coins in pockets and green discoloration of mucus membranes
- Can be produced during decomposition
  sulfide = 2–33 mg/L blood; 1.4–3.8 mg/kg lung; 0.9 mg/kg brain; 4–6 mg/kg skeletal muscle; 2–7 mg/kg liver; and 4–5 mg/kg kidney

Selected Sources

Barbera N, Montana A, Indorato F, Arbouche N, Romano G. (2017). Evaluation of the role of toxicological data in discriminating between H_2S femoral blood concentration secondary to lethal poisoning and endogenous H_2S putrefactive production, *J Forensic Sci*, 62(2): 390–394.

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Hydromorphone

Brand names: Dilaudid and Palladone
Classification: Opioid
λ: 2–3.5 h
V_d: 1–3 L/kg
Usual dosage: 1–4 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.1 mg/L	0.1 mg/L	0.06–2.9 mg/L
Vitreous	0.02–0.04 mg/L		0.06–0.2 mg/L
Liver			0.07–0.8 mg/kg
Kidney			0.1–0.7 mg/kg
Brain			0.5 mg/kg

Comments

- Metabolite of hydrocodone and morphine
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Hydroxychloroquine

Brand names: Plaquenil and Quineprox
Classification: Aminoquinolone (antimalarial)
λ: 16–56 d
V_d: 580–815 L/kg
Usual dosage: 200–600 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–39 mg/L	3–26 mg/L	36–104 mg/L
Vitreous	1.4–1.5 mg/L		3.3 mg/L
Liver			71–500 mg/kg
Skeletal muscle	3.5–4.4 mg/kg		5–60.5 mg/kg

Comments

- It can be used chronically in high doses to treat autoimmune diseases

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Hydroxyzine

Brand names: Vistaril, Atarax, and Rezine
Classification: Antihistamine/anxiolytic
λ: 5–24 h
V_d: 13–28 L/kg
Usual dosage: 25–100 mg qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.07–0.4 mg/L	0.1–1.4 mg/L	0.7–39 mg/L
Liver	0.9–4.9 mg/kg		15–414 mg/kg
Brain			0.5–163 mg/kg

Comments

- Active metabolite: Cetirizine
- May prolong QT interval

Selected Sources

Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.

Johnson GR. (1982). A fatal case involving hydroxyzine, *J Anal Toxicol*, 6(2): 69–70.

Kintz P, Godelar B, Mangin P. (1990). Gas chromatographic identification and quantification of hydroxyzine: Application in a fatal self-poisoning, *Forensic Sci Intl*, 48(2): 139–143.

McIntyre IM, Mallett P, Trochta A, Morhaime J. (2013). Hydroxyzine distribution in postmortem cases and potential for redistribution, *Forensic Sci Int*, 231(1–3): 28–33.

Péhourcq F. (2004). A simple high-performance liquid chromatographic method for detection of hydroxyzine in human plasma after overdose, *J Pharm Tox Methods*, 50(1): 41–44.

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Ibogaine

Brand name: Not applicable
Classification: Hallucinogen/stimulant
λ: 4–7 h
V_d: 13 L/kg
Usual dosage: 500–1000 mg/dose

	Nontoxic		Lethal	
Source	Ibogaine	Noribogaine	Ibogaine	Noribogaine
Blood	0.03–1.3 mg/L	0.02–1.2 mg/L	0.2–11 mg/L	11–22 mg/L
Liver			0.2–40 mg/kg	6–50 mg/kg
Kidney			0.3–7 mg/kg	4–5 mg/kg
Brain			12–19 mg/kg	19 mg/kg
Skeletal muscle			7.7 mg/kg	3.4 mg/kg

Comments

- It is an alkaloid from *Tabernanthe iboga* used to treat opiate withdrawal
- Active metabolite: Noribogaine
- Metabolized by CYP 2D6 as well as CYP 2C9 and 3A4
- Associated with cardiac arryhthymias

Selected Sources

Alper KR, Stajić M, Gill JR. (2012). Fatalities temporally associated with the ingestion of ibogaine, *J Forensic Sci*, 57(2): 398–412.

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Papadodima SA, Dona A, Evaggelakos CI, Goutas N, Athanaselis SA. (2013). Ibogaine related sudden death: A case report, *J Forensic Leg Med*, 20(7): 809–811.

Ibuprofen

Brand names: Advil and Motrin
Classification: NSAID
λ: 1.5–2.5 h
V_d: 0.1–0.2 L/kg
Usual dosage: 200–800 mg q 4–6 h

Source	Therapeutic/Nontoxic[a]	Toxic[a]	Lethal
Blood	10–60 mg/L	100–740 mg/L	81–1050 mg/L
Liver			74–942 mg/kg
Brain			284 mg/kg
Skeletal muscle	1–14 mg/kg		232 mg/kg

[a] Renal toxicity can occur in the therapeutic range.

Comments

- Metabolized by CYP 2C9 as well as 2C8, 2C19 and 3A4
- May cause renal failure

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Holubek W, Stolbach A, Nurok S, Lopez O, Wetter A, Nelson L. (2007). A report of two deaths from massive ibuprofen ingestion, *J Med Toxicol*, 3(2): 52–55.
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Imipramine

Brand name: Tofranil
Classification: Antidepressant (TCA)
λ: 7–18 h
V_d: 10–25 L/kg
Usual dosage: 75–300 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–0.4 mg/L	0.5–6 mg/L	1.2–28 mg/L
Vitreous			1.9 mg/L
Liver	9.7–17 mg/kg		24–293 mg/kg
Kidney			37–55 mg/kg
Brain			28–67 mg/kg
Skeletal muscle	0.1–0.4 mg/kg		9.6–24 mg/kg
Cardiac muscle			19–65 mg/kg

Comments

- Active metabolite: Desipramine
- May prolong QT interval
- Metabolized by CYP 2D6, 1A2, 2C19, and 3A4

Selected Sources

Apple FS. (1989). Postmortem tricyclic antidepressant concentrations: Assessing cause of death using parent drug to metabolite ratio, *J Anal Toxicol*, 13(4): 197–198.

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Sandeman DJ, Alahakoon TI, Bentley SC. (1997). Tricyclic poisoning—successful management of ventricular fibrillation following massive overdose of imipramine, *Anaesth Intensive Care*, 25(5): 542–545.

Insulin

Brand names: Novolog, Humalog, Lantus, Novolin, and Humulin
Classification: Hormone
λ: 0.5–24 h (depending upon formulation)
V_d: 0.2–0.4 L/kg
Usual dosage: 0.3–1.5 units/kg/d SC in divided doses

Source	Therapeutic/Nontoxic[a]	Toxic[a]	Lethal[a]
Blood	6–70 μunit/mL[b] 50–1100 μunit/mL[c]	300–7390 μunit/mL	297–7500 μunit/mL
Vitreous			29–103 μunit/mL
Kidney	See comments		384 μunit/g
Skeletal muscle			373 μunit/g
Adipose tissue	10–75 μunit/g		581–74000 μunit/g

[a] All concentrations are for free insulin.
[b] Nondiabetics.
[c] Insulin-dependent diabetics.

Comments

- Insulin is not found in significant concentrations in tissue (liver, brain, or kidney)
- Testing may be performed by immunoassay, but immunoassay cannot differentiate endogeneous vs exogeneous insulin
  - Not all immunoassays crossreact with all synthetic insulins
  - It can get interference from anti-insulin antibodies
- It can test for c-peptide to differentiate endogeneous and exogeneous insulin
  - Normal insulin:c-peptide ratio, <1 (0.1–0.5); exogeneous insulin ratio, >1
- Insulin concentrations may decrease postmortem due to degradation, particularly in hemolyzed samples

Selected Sources

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Isopropanol

Brand name: Rubbing alcohol
Classification: Solvent/disinfectant
λ: 3–4 h
V_d: 0.6 L/kg
Usual dosage: 60%–70% aqueous solution applied topically

Source	Nontoxic	Toxic	Lethal
Blood	8–390 mg/L	150–5600 mg/L	1000–4780 mg/L
Vitreous	8–500 mg/L		1300–2440 mg/L
Liver			53[a]–2660 mg/kg

[a] 30 h after ingestion.

Comments

- Metabolized to and from acetone
- Can be created antemortem and postmortem
- Often a component of embalming fluid in which acetone is absent
- Concentrations <1000 mg/L usually do NOT indicate exposure/intoxication
- Concentrations >1000 mg/L and isopropanol: Acetone ratio > 1 usually indicative of intoxication

Selected Sources

Alexander CB, McBay AJ, Hudson RP. (1982). Isopropanol and isopropanol deaths-ten years' experience, *J Forensic Sci*, 27(3): 541–548.

Bexar County Medical Examiner's Office data 1996–2015.

Gaulier JM, Lamballais F, Yazdani F, Lachâtre G. (2011). Isopropyl alcohol concentrations in postmortem tissues to document fatal intoxication, *J Anal Toxicol*, 35(4): 254–255.

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Pappas AA, Ackerman BH, Olsen KM, Taylor EH. (1991). Isopropanol ingestion: A report of six episodes with isopropanol and acetone serum concentration time data, *J Tox Clin Tox*, 29(1): 11–21.

Lamotrigine

Brand name: Lamictal
Classification: Anticonvulsant
λ: 12–74 h
V_d: 0.9–1 L/kg
Usual dosage: 25–200 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.9–14 mg/L	16–78 mg/L	36[a]–85 mg/L
Vitreous	0.3–1.8 mg/L		
Liver	16–36 mg/kg		220 mg/kg
Kidney			110 mg/kg
Skeletal muscle			324 mg/kg

[a] 19 h post ingestion.

Comments

- Can cause hepatic necrosis

Selected Sources

Algahtani HA, Aldarmahi AA, Al-Rabia MW, Almalki WH, Bryan Young G. (2014). Generalized myoclonus and spasticity induced by lamotrigine toxicity: A case report and literature review. *Clin Neuropharmacol*, 37(2): 52–54.

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O'Donnell J, Bateman DN. (2000). Lamotrigine overdose in an adult, *J Toxicol Clin Toxicol*, 38(6): 659–660.

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Schwartz MD, Geller RJ. (2007). Seizures and altered mental status after lamotrigine overdose, *Ther Drug Monit*, 29(6): 843–844.

Levetiracetam

Brand name: Keppra
Classification: Anticonvulsant
λ: 5–11 h
V_d: 0.5–0.7 L/kg
Usual dosage: 500–1500 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	3–70 mg/L	72–463 mg/L	190–230 mg/L[a]
Liver	14 mg/kg		
Kidney	1.8 mg/kg		
Skeletal muscle	76 mg/kg		

[a] Suicide with tape over mouth in presence of heart disease and benzoylecgonine.

Selected Sources

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Levine B, Phipps RJ, Naso C, Fahie K, Fowler D. (2010). Tissue distribution of newer anticonvulsant drugs in postmortem cases, *J Anal Toxicol*, 34(8): 506–509.

Page CB, Mostafa A, Saiao A, Grice JE, Roberts MS, Isbister GK. (2016). Cardiovascular toxicity with levetiracetam overdose, *Clin Toxicol*, 54(2): 152–154.

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Medical Economics. (2007). *Physicians' Desk Reference*, (61st ed.), Thomson PDR, Montvale, NJ, pp. 3314–3320.

Levorphanol

Brand name: Levo-Dromoran
Classification: Opioid
λ: 11–16 h
V_d: 10–13 L/kg
Usual dosage: 1–3 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–0.1 mg/L	0.1 mg/L	0.8–2.7 mg/L
Liver			5.4–11 mg/kg
Kidney			1–3.4 mg/kg
Brain			1.8 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Dixon R, Crews T, Inturrisi C, Foley K. (1983). Levorphanol: pharmacokinetics and steady-state plasma concentrations in patients with pain, *Res Comm Chem Path Pharm*, 41(1): 3–17.
Turner JE, Richards RG. (1977). A fatal case involving levorphanol, *J Anal Toxicol*, 1: 103–104.

Lisdexamfetamine

Brand name: Vyvanse
Classification: Stimulant
λ: 0.4–0.6 h
V_d: Unknown
Usual dosage: 30–70 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.05 mg/L LDA 0.02–0.15 mg/L amphet	See amphetamine	

Comments

- Prodrug of d-amphetamine
- Rapidly converted to amphetamine in the gastrointestinal tract

Selected Sources

Krishnan SM, Stark JG. (2008). Multiple daily-dose pharmacokinetics of lisdexamfetamine dimesylate in healthy adult volunteers, *Curr Med Res Opin*, 24(1): 33–40.

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Protiti Sarker P, Baker G, Hwang R. (2010). Case notes: Pharmacokinetic and pharmacodynamic distribution of lisdexamfetamine (A prodrug of dextroamphetamine) in a postmortem sample, *ToxTalk*, 34(4): 9.

Lithium

Brand names: Lithate, Lithobid, and Eskalith
Classification: Mood stabilizer (antimanic)
λ: 20–50 h
V_d: 0.3–1 L/kg
Usual dosage: 600–1800 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.6–1.2 mEq/L	1.5–8.2 mEq/L	1.9–14 mEq/L
Liver			0.2–9.4 mEq/kg
Kidney			0.6–9.3 mEq/kg
Brain			0.4–6.5 mEq/kg
Skeletal muscle			0.4–2.2 mEq/kg
Cardiac muscle			0.4 mEq/kg

Comments

- To convert mEq/L to mg/L, multiply by 6.94; mEq/L = mmol/L for lithium

Selected Sources

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Loperamide

Brand name: Imodium
Classification: Antidiarrheal and synthetic opioid
λ: 9–40 h
V_d: Unknown
Usual dosage: 2–4 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0002–0.07 mg/L	0.02–0.2 mg/L	0.08–2.6 mg/L
Liver	0.15–0.6 mg/kg		0.5–30 mg/kg
Kidney			8.5 mg/kg

Comments

- Abused for opiate effects
- Metabolized by CYP2C8 and CYP3A4 as well as CYP2B6 and CYP2D6
- May prolong QT interval

Selected References

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Loratadine

Brand names: Claritin and Tavist
Classification: Antihistamine
λ: 4–15 h
V_d: 119 L/kg
Usual dosage: 5–10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.007–0.03 mg/L	0.3 mg/L[a]	No data available

[a] 3 y/o pediatric patient.

Comments

- Active metabolite: Desloratadine
- Metabolized by CYP 3A4 and 2D6
- May cause tachycardia and increased blood pressure; may be hepatotoxic

Selected Sources

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Lorazepam

Brand name: Ativan
Classification: Benzodiazepine
λ: 9–40 h
V_d: 1–1.5 L/kg
Usual dosage: 0.5–5 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.2 mg/L	0.3–0.6 mg/L	See below[a]
Liver	0.1 mg/kg		
Skeletal muscle	0.05–0.2 mg/kg		

[a] All fatalities are mixed with other drugs; no pure fatalities reported.

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Loxapine

Brand names: Loxitane and Loxapac
Classification: Antipsychotic
λ: 1–14 h
V_d: Unknown
Usual dosage: 10–50 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.2 mg/L	0.2–0.7 mg/L	1.2–9.5 mg/L
Vitreous			1.5 mg/L
Liver	0.7 mg/kg		12–150 mg/kg
Brain	0.3 mg/kg		4.5 mg/kg

Comments

- Active metabolites: Amoxapine and 8-hydroxyloxapine
- Can cause seizures

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Lurasidone

Brand name: Latuda
Classification: Atypical antipsychotic
λ: 18–37 h
V_d: 80–90 L/kg
Usual dosage: 20–160 mg/d

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–0.2 mg/L	No data available	

Comments

- May cause neuroleptic malignant syndrome
- Metabolized by CYP 3A4
- Active metabolite: ID-14283

Selected Sources

Bexar County Medical Examiner's Office data 1996–2016.

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Lysergic Acid Diethylamide

Brand name: Not applicable
Street names: LSD, Acid; w/ heroin: Frisco Special and Frisco Speedball
Classification: Hallucinogen
λ: 1–5 h
V_d: 0.2–1 L/kg
Usual dosage: 100–500 mg/dose

Source	Nontoxic	Toxic	Lethal
Blood	0.001–0.007 mg/L	0.001–0.03 mg/L	0.005–0.01 mg/L

Comments

- Fatalities are usually due to the injuries sustained while intoxicated rather than due to the drug itself

Selected Sources

Dolder PC, Schmid Y, Steuer AE, Kraemer T, Rentsch KM, Hammann F, Liechti ME. (2017). Pharmacokinetics and pharmacodynamics of lysergic acid diethylamide in healthy subjects, *Clin Paharmacokinet*, 56(10): 1219–1230.

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Meclizine

Brand names: Antivert and Vertin-32
Classification: Antihistamine
λ: 5–6 h
V_d: Unknown
Usual dosage: 25–50 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–2.2 mg/L	No data available	

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Fouda HG, Falkner FC, Hobbs DC, Luther EW. (1978). Selected ion monitoring assay for meclizine in human plasma, *Biomed Mass Spectrometry*, 5(8): 491–494.

Melperone

Brand names: Buronil, Burnil, and Eunerpan
Classification: Antipsychotic
λ: 2–6 h
V_d: 7–10 L/kg
Usual dosage: 100–300 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.4 mg/L	1.8 mg/L	1–23 mg/L

Selected Sources

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Memantine

Brand name: Namenda
Classification: Anti-Alzheimer's agent
λ: 60–100 h
V_d: 9–11 L/kg
Usual dosage: 5–20 mg/d

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–4 mg/L	12 mg/L	No data available
Vitreous	0.39 mg/L		
Liver	3–25.5 mg/kg		
Skeletal muscle	1.2 mg/kg		

Selected Sources

Bexar County Medical Examiner's Office data 2004–2015.
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Meperidine

Brand names: Demerol and Pethidine
Classification: Opioid
λ: 3–8 h
V_d: 3–6 L/kg
Usual dosage: 50–150 mg q 3–4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–2 mg/L	0.5–6.5 mg/L	6–21 mg/L
Liver	0.8–5 mg/kg		2–30 mg/kg
Brain			9.5–17 mg/kg
Skeletal muscle			19 mg/kg

Comments

- Active metabolite: Normeperidine
- Tolerance can develop and should be considered when interpreting drug concentrations
- Metabolized by CYP 2B6

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Meprobamate

Brand name: Miltown
Classification: Sedative/anxiolytic
λ: 6–16 h
V_d: 0.7 L/kg
Usual dosage: 200–600 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	7–25 mg/L	30–208 mg/L	73–346 mg/L
Vitreous	8–20 mg/L		
Liver			58–600 mg/kg
Kidney			285–550 mg/kg
Brain			118–140 mg/kg
Skeletal muscle	4–20 mg/kg		93 mg/kg

Comments

- Metabolite of carisoprodol
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Maddock RK, Bloomer HA. (1967). Meprobamate overdosage. Evaluation of its severity and methods of treatment, *JAMA*, 201(13): 999–1003.

Mescaline

Brand name: Not applicable
Alternate names: Mescalito and peyote
Classification: Psychodelic
λ: 6 h
V_d: Unknown
Usual dosage: 100–500 mg/dose

Source	Intoxicated	Lethal
Blood	0.48–15 mg/L	See comments
Vitreous	2.4 mg/L	
Liver	8–71 mg/kg	
Brain	2.2 mg/kg	

Comments

- Fatalities usually secondary to trauma while intoxicated
- From *Lophophora williamsii* (cactus)

Selected Sources

Henry JL, Epley J, Rohrig TP. (2003). The analysis and distribution of mescaline in postmortem tissues, *J Anal Toxicol*, 27(6): 381–382.

Nolte KB, Zumwalt RE. (1999). Fatal peyote ingestion associated with mallory-weiss lacerations, *Western J Med*, 170(6): 328.

Metaxalone

Brand name: Skelaxin
Classification: Muscle relaxant
λ: 1–15 h
V_d: Unknown
Usual dosage: 800 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.7–9 mg/L	20 mg/L	14–63 mg/L
Vitreous			3–12 mg/L
Liver	9–14 mg/kg		45–195 mg/kg
Brain			74–163 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Bishop-Freeman SC, Miller A, Hensel EM, Winecker RE. (2015). Postmortem metaxalone (Skelaxin®) data from North Carolina, *J Anal Toxicol*, 39(8): 629–636.
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Stephenson J. (2009). Case Notes #1: Driving under the influence of a possibly lethal level of metaxalone, *ToxTalk*, 33(3): 8.

Methadone

Brand names: Dolophine and Methadose
Street name: Frizzies
Classification: Opioid
λ: 8–59 h
V_d: 3–5 L/kg
Usual dosage: 30–120 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–1.8 mg/L	0.2–1 mg/L	0.2–6.1 mg/L
Vitreous			0.03–0.08 mg/L
Liver	0.3–8.4 mg/kg		0.8–50 mg/kg
Kidney			1–8 mg/kg
Brain	0.1–0.5 mg/kg		0.4–3.7 mg/kg
Skeletal muscle	0.4–1.3 mg/kg		0.5–1.7 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations
- Metabolized by CYP 3A4, 2B6, 1A2, and 2D6
- Prolongs QT interval, especially dangerous at initiation of treatment

Selected Sources

Bastos ML, Galante L. (1976). Toxicological findings in victims of traumatic deaths, *J Forensic Sci*, 21(1): 176–186.

Bexar County Medical Examiner's Office data 1996–2015.

Li L, Levine B, Smialek JE. (2000). Fatal methadone poisoning in children: Maryland 1992–1996, *Subst Use Misuse*, 35(9): 1141–1148.

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Ziminski KR, Wemyss CT, Bidanset JH, Manning TJ, Lukash L. (1984). Comparative study of postmortem barbiturates, methadone, and morphine in vitreous humor, blood, and tissue, *J Forensic Sci*, 29(3): 903–909.

Methamphetamine

Brand names: Desoxyn (d-isomer); Vicks inhaler (l-isomer)
Street names: Chalk, Crystal, Ice, Meth, Speed, and Crank
Classification: Stimulant
λ: 6–15 h
V_d: 3–7 L/kg
Usual dosage: 2–5 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–7.8 mg/L	0.15–9.5 mg/L	0.1–69 mg/L
Liver			0.2–206 mg/kg
Kidney			0.2–87 mg/kg
Brain			0.2–144 mg/kg
Skeletal muscle	0.2–2.8 mg/kg		0.5–48 mg/kg

Comments

- Most laboratories do not differentiate between l- and d-isomers
  - D-methamphetamine illicit; also metabolite of benzphetamine and famprofazone
  - L-methaphetamine; metabolite of selegiline and famprofazone
- Active metabolite: Amphetamine
- Deaths are due to cardiovascular and CNS effects

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Fukunaga T, Mizoi Y, Adachi J, Tatsuno Y, Fujiwara S, Ueno Y. (1987). Methamphetamine concentrations in blood, urine, and organs of fatal cases after abuse, *Nihon Hoigaku Zasshi*, 41(4): 328–334.

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Logan BK, Fligner CL, Haddix T. (1998). Cause and manner of death in fatalities involving methamphetamine, *J Forensic Sci*, 43(1): 28–34.

Methanol

Brand name: Wood alcohol
Alternate name: Methyl alcohol
Classification: Solvent
λ: 2–24 h
V_d: 0.4–0.7 L/kg
Usual dosage: Not applicable

Source	Nontoxic	Toxic	Lethal
Blood	1.5–30 mg/L	200–1300 mg/L	230–7400 mg/L
Vitreous			120–3960 mg/L
Liver			56–4490 mg/kg
Kidney			67–5130 mg/kg
Brain			450–1811 mg/kg
Skeletal muscle			1120 mg/kg
Cardiac muscle			3450 mg/kg

Comments

- The presence of methanol and formaldehyde indicates embalming solution
- Formaldehyde is not part of methanol metabolism

Selected Sources

Andresen H, Schmoldt H, Matschke J, Flachskampf FA, Turk EE. (2008). Fatal methanol intoxication with different survival times—Morphological findings and postmortem methanol distribution, *Forensic Sci Int*, 179(2–3): 206–210.

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Methocarbamol

Brand name: Robaxin
Classification: Muscle relaxant
λ: 1–2 h
V_d: Unknown
Usual dosage: 1500 mg qid

Source	Therapeutic/Nontoxic	Toxic	Lethal[a]
Blood	16–40 mg/L	250 mg/L	257–525[a] mg/L
Liver			459 mg/kg
Kidney			83 mg/kg

[a] Co-intoxiant: ethanol, 0.13 g/dL.

Selected Sources

Ferslew KE, Hagardorn AN, McCormick WF. (1990). A fatal interaction of methocarbamol and ethanol in an accidental poisoning, *J Forensic Sci*, 35(2): 477–482.

Kemal M, Imami R, Poklis A. (1982). A fatal methocarbamol intoxication, *J Forensic Sci*, 27(1): 217–222.

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Sica DA, Comstock TJ, Davis J, Manning L, Powell R, Melikian A. (1990). Pharmacokinetics and protein binding of methocarbamol in renal insufficiency and normals, *Eur J Clin Pharm*, 39(2): 193–194.

Methylenedioxymethamphetamine

Brand name: Not applicable
Street names: MDMA, XTC, Ecstasy, and Adam
Classification: Hallucinogenic stimulant
λ: 6–9 h
V_d: 5.5–8.5 L/kg
Usual dosage: 50–150 mg/dose

Source	Nontoxic	Toxic	Lethal
Blood	0.1–2.4 mg/L	0.3–1.8 mg/L	0.5–54 mg/L
Vitreous			1.9–3.4 mg/L
Liver			5.1–34 mg/kg
Kidney			12–14 mg/kg
Brain			8.4–17 mg/kg
Skeletal muscle			4.5 mg/kg
Cardiac muscle			14 mg/kg

Comments

- Active metabolite: MDA (methylenedioxyamphetamine; λ 6–10 h)
- Metabolized by CYP 2D6

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Methylphenidate

Brand names: Ritalin, Methylin, and Concerta
Street names: Uppers and West Coast
Classification: Stimulant
λ: 2–4 h
V_d: 11–33 L/kg
Usual dosage: 5–20 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.2 mg/L	0.1–18 mg/L	1–3 mg/L
Vitreous			0.8 mg/L
Liver			0.3–3.6 mg/kg
Kidney			3.0 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Metoclopramide

Brand name: Reglan
Classification: Gastrointestinal motility agent; dopaminergic antagonist
λ: 3–9 h
V_d: 2–5 L/kg
Usual dosage: 5–15 mg q 6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–3 mg/L	No data available	4.4[a]–46[b] mg/L
Liver	0.8 mg/kg		

[a] Co-intoxicant: Diltiazem, 8.5 mg/L.
[b] Co-intoxicants: Propranolol, 60 mg/L; doxepin, 72 mg/L.

Comments

- Associated with dystonias and neuroleptic malignant syndrome

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Metoprolol

Brand names: Toprol and Lopressor
Classification: β-blocker
λ: 3–9 h
V_d: 2.5–6 L/kg
Usual dosage: 25–400 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.07–2.6 mg/L	7.8–18 mg/L	3.5–75 mg/L
Vitreous			3.3–42 mg/L
Liver	0.01–1.6 mg/kg		6.3–230 mg/kg
Kidney	0.01–0.5 mg/kg		7.1 mg/kg
Brain	0.04–0.2 mg/kg		
Skeletal muscle	0.2–2.3 mg/kg		

Comments

- Metabolized by CYP 2D6

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Wallin CJ, Hulting J. (1983). Massive metoprolol poisoning treated with prenalterol, *Acta Med Scand*, 214(3): 253–255.

Mexiletine

Brand name: Mexitil
Classification: Antiarrhythmic
λ: 8–16 h
V_d: 5–7 L/kg
Usual dosage: 100–300 tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.4–5.7 mg/L	2–20 mg/L	10–45 mg/L
Vitreous			9–17 mg/L
Liver			55–433 mg/kg
Kidney			170 mg/kg
Brain			84 mg/kg

Comments

- Metabolized by CYP2D6 and CYP1A2

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Rohrig TP, Harty LE. (1994). Postmortem distribution of mexiletine in a fatal overdose, *J Anal Toxicol*, 18(6): 354–356.

Midazolam

Brand name: Versed
Classification: Benzodiazepine
λ: 1–4 h
V_d: 1–6 L/kg
Usual dosage: 1–5 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–1.4 mg/L	0.2–2 mg/L	2.4–62 mg/L
Liver	0.02–1.7 mg/kg		
Kidney	0.01–1.1 mg/kg		
Brain	0.1–4.4 mg/kg		
Skeletal muscle	0.3 mg/kg		

Comments

- Metabolized by CYP 3A

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Oertel R, Pietsch J, Arenz N, Zeitz SG, Goltz L, Kirch W. (2011). Distribution of metoprolol, tramadol, and midazolam in human autopsy material, *J Chromatogr A*, 1218(30): 4988–4994.

Milnacipran

Brand name: Ixel
Classification: Antidepressant (SNRI)
λ: 7–8 h
V_d: 3–8 L/kg
Usual dosage: 50–100 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–0.4 mg/L	3–8 mg/L	20–22 mg/L

Selected Sources

Fanton L, Bevalot F, Grait H, Le Meur C, Gaillard Y, Malicier D. (2008). Fatal intoxication with milnacipran, *J Forensic Legal Med*, 15: 388–390.

Levine M, Truitt CA, O'Connor AD. (2011). Cardiotoxicity and serotonin syndrome complicating a milnacipran overdose, *J Med Toxicol*, 7(4): 312–316.

Puozzo C, Panconi E, Deprez D. (2002). Pharmacology and pharmacokinetics of milnacipran, *Intl Clin Psychopharmacology*, 17(1): S25–S35.

Rop PP, Sournac MH, Burle J, Fornaris M, Coiffait PE. (2002). Blood concentration of milnacipran in a case of a fatal automobile accident, *J Anal Toxicol*, 26(2): 123–126.

Mirtazapine

Brand name: Remeron
Classification: Antidepressant (tetracyclic)
λ: 12–20 h
V_d: 9–15 L/kg
Usual dosage: 15–45 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.3 mg/L	0.2–2.3 mg/L	2.6–9.3 mg/L
Vitreous	0.01–0.04 mg/L		
Liver	0.2–0.5 mg/kg		1.7–15 mg/kg
Kidney			1.8 mg/kg
Brain			0.6 mg/kg
Skeletal muscle	0.3 mg/kg		0.3 mg/kg

Comments

- Metabolized by CYP 1A2 and 2D6

Selected Sources

Bexar County Medical Examiner's Office data 2003–2015.
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Holzbach R, Jahn H, Pajonk FG, Mähne C. (1998). Suicide attempts with mirtazapine overdose without complications, *Biol Psychiatry*, 44(9): 925–926.
Kirkton C, McIntyre IM. (2006). Therapeutic and toxic concentrations of mirtazapine, *J Anal Toxicol*, 30(9): 687–691.
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Retz W, Maier S, Maris F, Rösler M. (1998). Non-fatal mirtazapine overdose, *Intl Clin Psychopharmacology*, 13(6): 277–279.
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Mitragynine

Brand names: Kratom and Biak-Biak
Classification: Alkaloid
λ: 23 h
V_d: 38 L/kg
Usual dosage: 5–45 mg per dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.5 mg/L		0.2–1.1 mg/L
Vitreous			0.05–0.15 mg/L
Liver			0.1–0.4 mg/kg
Kidney			0.2 mg/kg[a]
Spleen			0.2 mg/kg[a]
Lung			0.01 mg/kg[a]

[a] Co-intoxicants present.

Comments

- From *Mitragyna speciosa*; leaves often chewed, smoked or brewed into a tea; also sold in capsule and liquid form
- Low to moderate doses can cause mild stimulant effects; higher doses produce opioid-like effects

Selected Sources

Bexar County Medical Examiner's Office data 2003–2015.

Holler JM, Vorce SP, McDonough-Bender PC, Magluilo J, Solomon CJ, Levine B. (2011). A drug toxicity death involving propylhexadrine and mitragynine, *J Anal Toxicol*, 35: 54–59.

Karinen R, Fosen JT, Rogde S, Vindenes V. (2014). An accidental poisoning with mitragynine, *Forensic Sci Intl*, 24: e29–e32.

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Trakulsrichai S, Sathirakul K, Auparakkitanon S, Krongvorakul J, Sueajai J, Noumjad N, Sukasem C, Wananukul W. (2015). Pharmacokinetics of mitragynine in man, *Drug Des Devel Ther*, 9: 2421–2429.

Mizolastine

Brand names: Mizollen and Mistamine
Classification: Antihistamine
λ: 6–17 h
V_d: 1–1.5 L/kg
Usual dosage: 10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–2.5 mg/L	No data available	

Selected Sources

Lebrun-Vignes B, Diquet B, Chosidow O. (2001). Clinical pharmacokinetics of mizolastine, *Clin Pharmacokinetics*, 40(7): 501–507.

Rosenzweig P, Thebault JJ, Caplain H, Dubruc C, Bianchetti G, Fuseau E. (1992). Pharmacodynamics and pharmacokinetics of mizolastine (SL 85.0324), a new nonsedative H1 antihistamine, *Ann Allergy*, 69(2): 135–139.

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Moclobemide

Brand names: Aurorix and Manerix
Classification: Antidepressant (MAOI)
λ: 1–4 h
V_d: 0.8–1 L/kg
Usual dosage: 100–200 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–2 mg/L	3–61 mg/L	15–498 mg/L
Liver			45–432 mg/kg
Kidney			57 mg/kg
Cardiac muscle			21 mg/kg

Comments

- Not available in the United States
- Metabolized by CYP 2C18, CYP 2D6, and CYP 1A2

Selected Sources

Bleumink GS, van Vliet AC, van der Tholen A, Stricker BH. (2003). Fatal combination of moclobemide overdose and whisky, *Neth J Med*, 61(3): 88–90.

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Camaris C, Little D. (1997). A fatality due to moclobemide, *J Forensic Sci*, 42(5): 954–955.

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Giroud C, Horisberger B, Eap C, Augsburger M, Ménétrey A, Baumann P. (2004). Death following acute poisoning by moclobemide, *Forensic Sci Intl*, 140(1): 101–107.

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Raaflaub J, Haefelfinger P, Trautmann KH. (1984). Single-dose pharmacokinetics of the MAO-inhibitor moclobemide in man, *Drug Res/Arzneimittel-Forschung*, 34(1): 80–82.

Rogde S, Hilberg T, Teige B. (1999). Fatal combined intoxication with New Antidepressants. Human cases and an experimental study of postmortem moclobemide redistribution, *Forensic Sci Intl*, 100(1–2): 109–116.

Modafinil

Brand name: Provigil
Classification: Stimulant
λ: 10–17 h
V_d: 0.8 L/kg
Usual dosage: 200–400 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	3–17 mg/L	13[a]–18[b] mg/L	No data available

[a] 18 h after intial presentation.
[b] Co-intoxicant: escitolopram.

Comments

- Armodafinil (Nuvigil) is R-enantiomer of modafinil; most laboratories cannot differentiate between the two

Selected Sources

Gresham C, Wallace KL. (2008). Challenges in detection and confirmation of modafinil use, *Clin Toxicol*, 46: 642.
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Johnson-Arbor K, Christ M. (2008). Prolonged delirium in a pediatric patient after modafinil and escitalopram ingestion, *Clin Toxicol*, 46: 623.
Robertson P, Hellriegel ET. (2003). Clinical pharmacokinetic profile of modafinil, *Clin Pharmacokinetics*, 42(2): 123–137.

Molindone

Brand name: Moban
Classification: Antipsychotic
λ: 2 h
V_d: 3–6 L/kg
Usual dosage: 5–50 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–0.4 mg/L	0.15 mg/L	6–19 mg/L
Liver			26–69 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Flammia DD, Bateman HR, Saady JJ, Christensen ED. (2004). Tissue distribution of molidone in a multidrug overdose, *J Anal Toxicol*, 28(6): 533–536.
Johnson SB, Alvarez WA, Freinhar JP. (1986). A case of massive rhabdomyolysis following molindone administration, *J Clin Psychiatry*, 47(12): 607–608.
Zetin M, Cramer M, Garber D, Plon L, Paulshock M, Hoffman HE. (1985). Bioavailability of oral and intramuscular molindone hydrochloride in schizophrenic patients, *Clin Therapeutics*, 7(2): 169–175.

Morphine

Brand names: MS Contin, Roxanol, Kadian, Avinza, and Oramorph
Street names: Dreamer, Hows, M, and Miss Emma
Classification: Opiate
λ: 1.3–6.7 h
V_d: 2–5 L/kg
Usual dosage: 5–30 mg q 4–8 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.6 mg/L	0.3–2.5 mg/L	0.2–7.2 mg/L
Vitreous			0.03–0.8 mg/L
Liver			0.05–18 mg/kg
Kidney			0.05–7 mg/kg
Brain			0.05–1 mg/kg
Skeletal muscle			0.1–2 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations
- Metabolite of heroin
- Active metabolites: Morphine-6-glucuronide and normorphine
- Above concentrations are not differentiated between free or total morphine as not all references specified what was measured

Selected Sources

Chan SC, Chan EM, Kaliciak HA. (1986). Distribution of morphine in body fluids and tissues in fatal overdose, *J Forensic Sci*, 31(4): 1487–1491.

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Stanski DR, Greenblatt DJ, Lappas DG, Koch-Weser J, Lowenstein E. (1976). Kinetics of high-dose intravenous morphine in cardiac surgery patients, *Clin Pharm Therapeutics*, 19(6): 752–756.

Wallace JE, Blum K, Singh JM. (1974). Determination of drugs in biological specimens—A review, *J Tox Clin Toxicol*, 7(5): 477–495.

Ziminski KR, Wemyss CT, Bidanset JH, Manning TJ, Lukash L. (1984). Comparative study of postmortem barbiturates, methadone, and morphine in vitreous humor, blood, and tissue, *J Forensic Sci*, 29(3): 903–909.

Naloxone

Brand name: Narcan
Classification: Opioid antagonist
λ: 30–80 min
V_d: 0.8–3 L/kg
Usual dosage: 0.4–2 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.004–0.1 mg/L	No data available	

Comments

- Used to treat opiate and opioid overdoses

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

Ngai SH, Berkowitz BA, Yang JC, Hempstead J, Spector S. (1976). Pharmacokinetics of naloxone in rats and in man: Basis for its potency and short duration of action, *Anesthesiology*, 44(5): 398–401.

Reid RW, Deakin A, Leehey DJ. (1993). Measurement of naloxone in plasma using high-performance liquid chromatography with electrochemical detection, *J Chromatography A*, 614(1): 117–122.

Naltrexone

Brand names: Depade and Revia
Classification: Opioid antagonist
λ: 1–10 h
V_d: 14–16 L/kg
Usual dosage: 25–50 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.05 mg/L	No data available	

Selected Sources

Verebey K, Mulé SJ. (1979). Naltrexone, 6 beta-naltrexol and 2-hydroxy-3-methoxy-6 beta-naltrexol plasma levels in schizophrenic patients after large oral doses of naltrexone, *NIDA Res Monograph*, 27: 296–301.

Verebey K, Volavka J, Mulé SJ, Resnick RB. (1976). Naltrexone: Disposition, metabolism, and effects after acute and chronic dosing, *Clin Pharm Therapeutics*, 20(3): 315–328.

Naproxen

Brand names: Naprosyn, Aleve, and Anaprox
Classification: NSAID
λ: 10–18 h
V_d: 0.1–0.2 L/kg
Usual dosage: 250–500 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	20–125 mg/L	414–1580 mg/L	760–1040 mg/L
Liver			520 mg/kg

Comments

- Metabolized by CYP 1A2 and 2C9

Selected Sources

Anttila M, Haataja M, Kasanen A. (1980). Pharmacokinetics of naproxen in subjects with normal and impaired renal function, *Eur J Clin Pharm*, 18(3): 263–268.
Bexar County Medical Examiner's Office data 1996–2015.
Fredell EW, Strand LJ. (1977). Naproxen overdose, *JAMA*, 238(9): 938.
Mullen WM, Meier KM, Hagar SM, Olson KR. (2003). Severe naproxen overdose with elevated serum levels, *J Tox Clin Toxicol*, 41(5): 655.
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Nefazodone

Brand name: Serzone
Classification: Antidepressant
λ: 2–4 h
V_d: 0.2–0.9 L/kg
Usual dosage: 100–300 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–3.9 mg/L	5.5–7.5 mg/L	No data available

Comments

- Active metabolites: Hydroxynefazodone, triazolodione, and meta-chlorophenylpiperazine
- Metabolized by CYP 3A

Selected Sources

Barbhaiya RH, Buch AB, Greene DS. (1996). A study of the effect of age and gender on the pharmacokinetics of nefazodone after single and multiple doses, *J Clin Psychopharmacology*, 16(1): 19–25.

Gaffney PN, Schuckman HA, Beeson MS. (1998). Nefazodone overdose, *Ann Pharmacotherapy*, 32(11): 1249–1250.

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Nicotine

Brand names: Nicorette, Nicotrol, Nicoderm, Habitrol, and Prostep
Classification: Alkaloid
λ: 24–84 min
V_d: 1–3 L/kg
Usual dosage: 0.2–4 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.2 mg/L	0.05–1 mg/L	3.7–5800 mg/L
Liver	0.01–0.3 mg/kg		4–2270 mg/kg
Kidney	0.007–0.2 mg/kg		10–1128 mg/kg
Brain	0.001–0.09 mg/kg		8–1910 mg/kg
Skeletal muscle	0.003–0.05 mg/kg		12 mg/kg

Comments

- Metabolized by CYP 2A6
- 1 cigarette = 0.1–2 mg nicotine; e-cigarette = 6–18 mg nicotine
- Concentrations in nonsmokers 0–0.006 mg/L; with passive inhalation, 0.001–0.003 mg/L; and in adult smokers, 0.01–0.05 mg/L

Selected Sources

Bartschat S, Mercer-Chalmers-Bender K, Beike J, Rothschild MA, Jübner M. (2015). Not only smoking is deadly: Fatal ingestion of e-juice-a case report, *Int J Legal Med*, 129(3): 481–486.

Davies P, Levy S, Pahari A, Martinez D. (2001). Acute nicotine poisoning associated with a traditional remedy for eczema, *Arc Disease in Childhood*, 85(6): 500–502.

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Nifedipine

Brand names: Adalat, Nifediac, and Afeditab
Classification: Calcium channel blocker
λ: 2–8 h
V_d: 1–1.5 L/kg
Usual dosage: 30–120 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.1 mg/L	0.1–0.6 mg/L	0.2–0.5 mg/L
Liver			1.1 mg/kg

Comments

- Metabolized by CYP 3A

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Nitrazepam

Brand name: Mogadon
Classification: Benzodiazepine
λ: 17–48 h
V_d: 2–5 L/kg
Usual dosage: 2.5–10 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.5 mg/L	0.2 mg/L	0.4–9 mg/L
Liver			0.7–4 mg/kg
Kidney			0.7 mg/kg
Brain			2–6 mg/kg
Skeletal muscle			2.1 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

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Nortriptyline

Brand names: Pamelor and Aventyl
Classification: Antidepressant (TCA)
λ: 15–90 h
V_d: 20–57 L/kg
Usual dosage: 20–50 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.4 mg/L	0.5–2.3 mg/L	0.8–86 mg/L
Vitreous			1.4 mg/L
Liver			11–664 mg/kg
Kidney			9–904 mg/kg
Brain			97–202 mg/kg
Skeletal muscle	0.2–1 mg/kg		2.5–4 mg/kg

Comments

- Metabolite of amitriptyline
- Metabolized by CYP 2D6
- May prolong QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Olanzapine

Brand name: Zyprexa
Classification: Antipsychotic
λ: 21–54 h
V_d: 10–26 L/kg
Usual dosage: 5–20 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.009–0.5 mg/L	0.05–1 mg/L	1–21 mg/L
Vitreous	0.4–1 mg/L		1–2 mg/L
Liver	0.4–9 mg/kg		6–52 mg/kg
Kidney			2–6.5 mg/kg
Brain			0.2–2 mg/kg

Comments

- Metabolized by CYP 1A2

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Vance C, McIntyre IM. (2009). Postmortem tissue concentrations of olanzapine, *J Anal Toxicol*, 33(1): 15–26.

Oleandrin

Brand name: Anvirzel (oleandrin extract)
Classification: Cardiac glycoside
λ: Unknown
V_d: Unknown
Usual dosage: 15 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.001–0.007 mg/L	0.001–0.03 mg/L	0.01–12 mg/L
Liver			30 mg/kg
Kidney			39 mg/kg
Brain			10 mg/kg
Cardiac muscle			1–23 mg/kg

Comments

- From *Nerium oleander*
- Cross reacts with digoxin RIA

Selected Sources

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Ondansetron

Brand name: Zofran
Classification: Antiemetic
λ: 2–6 h
V_d: 1–3 L/kg
Usual dosage: 8 mg q 8 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.14 mg/L	No data available	

Comments

- Metabolized by CYP 1A2, 2D6, 3A
- May prolong QT interval

Selected Sources

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Orphenadrine

Brand names: Norflex and Norgesic (w/acetaminophen and caffeine)
Classification: Anti-Parkinson/muscle relaxant
λ: 13–20 h
V_d: 4–8 L/kg
Usual dosage: 25–100 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–0.85 mg/L	2–3.6 mg/L	5–368 mg/L
Liver			7–410 mg/kg
Kidney			10–105 mg/kg
Brain			3–20 mg/kg

Selected Sources

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Wilkinson LF, Thomson BM, Pannell LK. (1983). A report on the analysis of orphenadrine in post mortem specimens, *J Anal Toxicol*, 7(2): 72–75.

Oxazepam

Brand name: Serax
Classification: Benzodiazepine
λ: 5–15 h
V_d: 0.6–2 L/kg
Usual dosage: 15–30 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–1.6 mg/L	0.5[a]–4 mg/L	2–6.3 mg/L
Brain	0.002–1.5 mg/kg		

[a] Child.

Comments

- Metabolite of temazepam and nordiazepam
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.

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Shimkin PM, Shaivitz SA. (1966). Oxazepam poisoning in a child, *JAMA*, 196(7): 662–663.

Oxcarbazepine

Brand name: Trileptal
Classification: Anticonvulsant
λ: 1–5 h
V_d: 3–12 L/kg
Usual dosage: 300–1200 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–5 mg/L OX 8–52 mg/L 10-OHC	8–12 mg/L OX 32–65 mg/L 10-OHC	16–99 mg/L OX 3–199 mg/L 10-OHC
Liver	7–29 mg/kg		19–219 mg/kg OX 4–428 mg/kg OHC
Kidney	11–43 mg/kg		4–41 mg/kg OX 1–74 mg/kg OHC
Skeletal muscle			1.8 mg/kg OX 40 mg/kg OHC

OX = oxcarbazepine; 10-OHC = 10-hydroxycarbazepine.

Comments

- Active metabolite: 10-hydroxycarbazepine (λ 7–20 h; V_d 0.75 L/kg)
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Jolliff HA, Fehrenbacher N, Dart RC. (2001). Bradycardia, hypotension and tinnitus after accidental oxcarbazepine overdose, *J Tox Clin Tox*, 39(3): 316–317.
Klys M, Bystrowska B, Bujak-Gizycka B. (2003). Postmortem toxicology of carbamazepine, *J Anal Toxicol*, 27(4): 243–248.
Levine B, Phipps RJ, Naso C, Fahie K, Fowler D. (2010). Tissue distribution of newer anticonvulsant drugs in postmortem cases, *J Anal Toxicol*, 34(8): 506–509.
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van Opstal JM, Janknegt R, Cilissen J, L'Ortije WHM, Nel JE, De Heer F. (2004). Severe overdosage with the antiepileptic drug oxcarbazepine, *Br J Clin Pharm*, 58(3): 329–331.

Oxycodone

Brand names: Roxicodone and Oxycontin; Percocet, Endocet, and Roxicet (w/acetaminophen); Percodan (w/ ASA)
Classification: Opioid
λ: 3–8 h
V_d: 2–4 L/kg
Usual dosage: 5–30 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.9 mg/L	0.2–2.4 mg/L	0.1–53 mg/L
Vitreous	0.03–0.4 mg/L		0.25–1 mg/L
Liver	0.06–2.3 mg/kg		0.2–6.6 mg/kg
Brain	0.06–1.9 mg/kg		1–2 mg/kg
Skeletal muscle	0.1–0.6 mg/kg		

Comments

- Active metabolite: Oxymorphone
- Tolerance can develop and should be considered when interpreting drug concentrations
- May prolong QT interval at high doses

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

Darke S, Duflou J, Torok M. (2011). Toxicology and characteristics of fatal oxycodone toxicity cases in New South Wales, Australia 1999–2008, *J Forensic Sci*, 56(3): 690–693.

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Spiller HA. (2003). Postmortem oxycodone and hydrocodone blood concentrations, *J Forensic Sci*, 48(2): 429–431.

Oxymorphone

Brand names: Opana and Numorphan
Classification: Opioid
λ: 7–11 h
V_d: 2–4 L/kg
Usual dosage: 5–20 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0003–0.01 mg/L	No data available	0.03–0.8 mg/L
Vitreous			0.05 mg/L
Liver			0.1–2 mg/kg

Comments

- Metabolite of oxycodone
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Adams MP, Ahdieh H. (2005). Single- and multiple-dose pharmacokinetic and dose-proportionality study of oxymorphone immediate-release tablets, *Drugs in R D*, 6(2): 91–99.

Bexar County Medical Examiner's Office data 2003–2015.

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Guay DRP. (2007). Use of oral oxymorphone in the elderly, *Consult Pharm*, 22(5): 417–430.

Papaverine

Brand name: Para-Time
Classification: Vasodilator
λ: 1–1.5 h
V_d: 0.5–1.5 L/kg
Usual dosage: 150–300 mg bid

Source	Therapeutic/Nontoxic	Postmortem Procurement	Toxic	Lethal
Blood	0.2–4 mg/L	0.04–42 mg/L	No data available	

Comments

- Often used postmortem to dilate veins for procurement procedures
- Overdose may result in hepatotoxicity or lactic acidosis
- Can be found as a component in heroin

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Ronnov-Jessen V, Tjernlund A. (1969). Hepatotoxicity due to treatment with papaverine. Report of four cases, *NEJM*, 281(24): 1333–1335.
Vaziri ND, Stokes J, Treadwell TR. (1981). Lactic acidosis, a complication of papaverine overdose, *Clin Tox*, 18(4): 417–423.

Paroxetine

Brand names: Paxil and Pexeva
Classification: Antidepressant (SSRI)
λ: 7–65 h
V_d: 3–28 L/kg
Usual dosage: 20–40 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.9 mg/L	0.35–1.8 mg/L	1–16 mg/L
Vitreous	0.003–0.03 mg/L		
Liver	0.1–5.2 mg/kg		110–113 mg/kg
Lung	0.3–10 mg/kg		
Kidney	0.02–1.6 mg/kg		
Spleen	0.06–2.6 mg/kg		
Skeletal muscle	0.001–0.1 mg/kg		
Brain	0.1–2.2 mg/kg		
Cardiac muscle	0.03–0.6 mg/kg		

Comments

- Prolongs QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
DeVane CL. (2003). Pharmacokinetics, drug interactions, and tolerability of paroxetine and paroxetine CR, *Psychopharmacol Bull*, 37(Suppl 1): 29–41.
Goeringer KE, Raymon L, Christian GD, Logan BK. (2000). Postmortem forensic toxicology of selective serotonin reuptake inhibitors: A review of pharmacology and report of 168 cases, *J Forensic Sci*, 45(3): 633–648.
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Vermeulen T. (1998). Distribution of paroxetine in three postmortem cases, *J Anal Toxicol*, 22(6): 541–544.
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Pentazocine

Brand names: Talwin and Talacen (w/acetaminophen)
Classification: Opioid
λ: 2–3.5 h
V_d: 4–8 L/kg
Usual dosage: 50–100 mg q 3–4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–0.24 mg/L	0.5–2 mg/L	1–9 mg/L
Liver			34–87 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Berkowitz BA, Asling JH, Shnider SM, Way EL. (1969). Relationship of pentazocine plasma levels to pharmacological activity in man, *Clin Pharm Thera*, 10(3): 320–328.

Bexar County Medical Examiner's Office data 1996–2015.

Finkle B. (1974). Pentazocine, *Bull Intl Assoc Forensic Tox*, 10(3): 7.

Poklis A, Mackell MA. (1982). Toxicological findings in deaths due to ingestion of pentazocine: A report of two cases, *Forensic Sci Intl*, 20(1): 89–95.

Stahl SM, Kasser IS. (1983). Pentazocine overdose, *Ann Emer Med*, 12(1): 28–31.

Pentobarbital

Brand name: Nembutal
Classification: Barbiturate
λ: 15–50 h
V_d: 0.5–1 L/kg
Usual dosage: 50–200 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1–5 mg/L	8–24 mg/L	15–241 mg/L
Vitreous			7–27 mg/L
Liver			8–980 mg/kg
Kidney			7–72 mg/kg
Brain			4–48 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Phencyclidine

Brand name: Not applicable
Street names: PCP, Angel Dust, Peter Pan, Wack, Ozone, Elephant, Super Kools w/ Cocaine: Spaceball, Parachute, Space Base, Tragic Magic, Lovelies, Beam Em Up w/ MJ: Happy Stick, Love Boat, Supergrass, Donk, Killer Joints, Wacky Weed
Classification: Hallucinogen
λ: 7–46 h
V_d: 5–7.5 L/kg
Usual dosage: 3–10 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–1.1 mg/L	0.09–0.5 mg/L	0.3–25 mg/L
Vitreous	0.01–0.5 mg/L		
Liver	0.3–3.4 mg/kg		0.9–170 mg/kg
Brain	0.09–0.9 mg/kg		0.1–32 mg/kg
Lung			0.4–7.6 mg/kg
Kidney			0.1 mg/kg
Spleen			20 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Phenelzine

Brand name: Nardil
Classification: Antidepressant (MAOI)
λ: 9–12 h
V_d: Unknown
Usual dosage: 15 mg tid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.2 mg/L	0.5 mg/L	1–2 mg/L

Selected Sources

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Waring WS, Wallace WAH. (2007). Acute myocarditis after massive phenelzine overdose, *Eur J Clin Pharm*, 63(11): 1007–1009.

Pheniramine

Brand name: Avil; ingredient in many OTC cold medicines
Classification: Antihistamine
λ: 8–19 h
V_d: 1.5–3 L/kg
Usual dosage: 25–50 mg q 8 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.2–0.9 mg/L	No data available	2–30 mg/L
Liver			6.6–115 mg/kg
Kidney			4 mg/kg
Brain			5.3 mg/kg

Selected Sources

Queree EA, Dickson SJ, Missen AW. (1979). Therapeutic and toxic levels of pheniramine in biological specimens, *J Anal Toxicol*, 3: 253–255.

Witte PU, Irmisch R, Hajdú P. (1985). Pharmacokinetics of pheniramine (Avil) and metabolites in healthy subjects after oral and intravenous administration, *Intl J Clin Pharm Ther Tox*, 23(1): 59–62.

Phenobarbital

Brand names: Luminal and Solfoton
Classification: Barbiturate anticonvulsant
λ: 2–6 d
V_d: 0.5–0.7 L/kg
Usual dosage: 30–100 mg qd/bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	4–40 mg/L	35–253 mg/L	48–348 mg/L
Vitreous			2–22 mg/L
Liver	2.4–5.2 mg/kg		17–275 mg/kg
Kidney	1.7–4.9 mg/kg		12–84 mg/kg
Brain	0.01–3.6 mg/kg		5–75 mg/kg
Skeletal muscle			35–86 mg/kg

Comments

- Metabolized by CYP 2C9 and 2C19

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Ziminski KR, Wemyss CT, Bidanset JH, Manning TJ, Lukash L. (1984). Comparative study of postmortem barbiturates, methadone, and morphine in vitreous humor, blood, and tissue, *J Forensic Sci*, 29(3): 903–909.

Phentermine

Brand names: Pro-Fast and Adipex
Classification: Stimulant/anorectic
λ: 19–24 h
V_d: 3–4 L/kg
Usual dosage: 37.5 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.07–0.9 mg/L	0.2–0.9 mg/L	1.5–7.6 mg/L
Liver	4 mg/kg		14–15 mg/kg
Kidney			12–16 mg/kg

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Groenewoud G, Schall R, Hundt HK, Müller FO, van Dyk M. (1993). Steady-state pharmacokinetics of phentermine extended-release capsules, *Intl J Clin Pharm Ther Tox*, 31(8): 368–372.
Levine B, Caplan YH, Dixon AM. (1984). A fatality involving phentermine, *J Forensic Sci*, 29(4): 1242–1245.
Price K. (1974). Phenteramine, *Bull Intl Assoc Forensic Tox*, 10(1): 12.

Phenylephrine

Brand names: Sudafed PE and Neo-Synephrine; ingredient in OTC cold medicines
Classification: α-adrenergic agonist
λ: 0.5–3 h
V_d: 3.5–5 L/kg
Usual dosage: 10 mg q 4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.04 mg/L	No data available	

Selected Sources

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Hengstmann JH, Goronzy J. (1982). Pharmacokinetics of 3H-phenylephrine in man, *Eur J Clin Pharm*, 21(4): 335–341.

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Phenylpropanolamine (PPA)

Brand names: Accutrim and Dexatrim
Classification: α-adrenergic agonist
λ: 3–4.5 h
V_d: 4.5 L/kg
Usual dosage: 25–75 mg q 6–8 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–0.3 mg/L	2 mg/L	0.63–48 mg/L

Comments

- Associated with arrhythmias and hemorrhagic cerebrovascular accidents
- No longer available in the United States

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.

Lake CR, Gallant S, Masson E, Miller P. (1990). Adverse drug effects attributed to phenylpropanolamine: A review of 142 case reports, *Am J Med*, 89(2): 195–208.

Scherzinger SS, Dowse R, Kanfer I. (1990). Steady state pharmacokinetics and dose-proportionality of phenylpropanolamine in healthy subjects, *J Clin Pharm*, 30(4): 372–377.

Phenytoin

Brand name: Dilantin
Classification: Anticonvulsant
λ: 7–60 h
V_d: 0.6–0.7 L/kg
Usual dosage: 100–200 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	2–25 mg/L	20–101 mg/L	45–242 mg/L
Liver			14–272 mg/kg
Kidney			5.2–112 mg/kg
Brain			15–78 mg/kg

Comments

- Metabolized by CYP 2C9, 2C8, and 2C19

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Jenkins A. (2006). A case of phenytoin toxicity in a patient with advanced lung cancer, *Palliative Med*, 20(4): 479–480.
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Thimmisetty RK, Gorthi JR, Abu Hazeem M. (2014). Oral phenytoin toxicity causing sinus arrest: A case report, *Case Reports Cardiol*, 2014: 851767.

Pimozide

Brand name: Orap
Classification: Antipsychotic
λ: 55–111 h
V_d: 13–37 L/kg
Usual dosage: 1–5 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.01 mg/L	0.02 mg/L	0.09[a]–0.5 mg/L

[a] Co-intoxicants present.

Comments

- Prolongs QT interval
- Metabolized by CYP 3A4 as well as 1A2 and 2D6

Selected Sources

Harrison D, Elliot S. (2001). A novel case of fatal pimozide poisoning, *Bull Intl Assoc Forensic Tox*, 31(2): 11–12.

Krähenbühl S, Sauter B, Kupferschmidt H, Krause M, Wyss PA, Meier PJ. (1995). Case report: Reversible QT prolongation with torsades de pointes in a patient with pimozide intoxication, *Am J Med Sci*, 309(6): 315–316.

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Salness RA, Goetz CM, Gorman RL. (1992). Two cases of pimozide ingestion, *Vet Hum Tox*, 34: 4.

Söderberg C, Wernvik E, Tillmar A, Spigset O, Kronstrand R, Reis M, Jönsson AK, Druid H. (2016). Antipsychotics—Postmortem fatal and non-fatal reference concentrations, *Forensic Sci Int*, 266: 91–101.

Prazepam

Brand names: Centrax, Lysanxia, and Demetrin
Classification: Benzodiazepine
λ: 1–2 h
V_d: 12–14 L/kg
Usual dosage: 30–60 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.008–0.3 mg/L	1–5 mg/L	No data available

Comments

- Active metabolite: Nordiazepam (λ 38–135 h)
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Repetto MR, Repetto M. (1997). Habitual, toxic, and lethal concentrations of 103 drugs of abuse in humans, *J Tox Clin Tox*, 35(1): 1–9.

Schulz M, Schmoldt A. (2003). Therapeutic and toxic blood concentrations of more than 800 drugs and other xenobiotics, *Pharmazie*, 58(7): 447–474.

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Pregabalin

Brand name: Lyrica
Classification: Anticonvulsant
λ: 5–7 h
V_d: 0.5 L/kg
Usual dosage: 150–600 mg divided b/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1.4–14 mg/L	7.7–112 mg/L	36–207 mg/L[a]
Kidney	14 mg/kg		
Liver	3 mg/kg		

[a] All fatalities have either co-intoxicants or significant natural disease present.

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Häkkinen M, Vuori E, Kalso E, Gergov M, Ojanperä I. (2014). Profiles of pregabalin and gabapentin abuse by postmortem toxicology, *Forensic Sci Int*, 241: 1–6.

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Olaizola I, Ellger T, Young P, Bösebeck F, Evers S, Kellinghaus C. (2006). Pregabalin-associated acute psychosis and epileptiform EEG-changes, *Seizure*, 15(3): 208–210.

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Primidone

Brand names: Mysoline, Myidone, and Sertan
Classification: Anticonvulsant
λ: 5–20 h
V_d: 0.6–1 L/kg
Usual dosage: 100–250 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	5–19 mg/L	80–209 mg/L	65 mg/L

Comments

- Active metabolite: Phenobarbital

Selected Sources

Bailey DN, Jatlow PI. (1972). Chemical analysis of massive crystalluria following primidone overdose, *Am J Clin Path*, 58(5): 583–589.

Baselt RC, Cravey RH. (1977). A compendium of therapeutic and toxic concentrations of toxicologically significant drugs in human biofluids, *J Anal Toxicol*, 1: 81–103.

Bexar County Medical Examiner's Office data 1996–2015.

Cate JC, Tenser R. (1975). Acute primidone overdosage with massive crystalluria, *Clin Tox*, 8(4): 385–389.

Lehmann DF. (1987). Primidone crystalluria following overdose. A report of a case and an analysis of the literature, *Med Tox*, 2(5): 383–387.

van Heijst AN, de Jong W, Seldenrijk R, van Dijk A. (1983). Coma and crystalluria: A massive primidone intoxication treated with haemoperfusion, *J Tox Clin Tox*, 20(4): 307–318.

Procainamide

Brand names: Pronestyl and Procanbid
Classification: Antidysrhythmic
λ: 2.5–5 h
V_d: 1.5–2.5 L/kg
Usual dosage: 250–1250 mg q 6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	4–16 mg/L	8–63 mg/L	30–114 mg/L
Liver			283 mg/kg

Comments

- Concentations can range from 25–75 mg/L when given during resuscitation
- Active metabolite: *N*-acetylprocainamide (NAPA)
- Prolongs QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

Bizjak ED, Nolan PE, Brody EA, Galloway JM. (1999). Procainamide-induced psychosis: A case report and review of the literature, *Ann Pharmacotherapy*, 33(9): 948–951.

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White SR, Dy G, Wilson JM. (2002). The case of the slandered halloween cupcake: Survival after massive pediatric procainamide overdose, *Pediatric Emerg Care*, 18(3): 185–188.

Promazine

Brand names: Sparine and Protactyl
Classification: Antipsychotic
λ: 10–40 h
V_d: 23–43 L/kg
Usual dosage: 50–150 mg im q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.14 mg/L	1–1.8 mg/L	5 mg/L

Selected Sources

Hu OY, Tang HS, Sheeng TY, Chen SC, Lee SK, Chung PH. (1990). Pharmacokinetics of promazine: I. Disposition in patients with acute viral hepatitis B, *Biopharm Drug Dispos*, 11(7): 557–568.

Larsimont V, Meins J, Fieger-Büschges H, Blume H. (1998). Validated high-performance liquid chromatographic assay for the determination of promazine in human plasma. Application to pharmacokinetic studies, *J Chromatography—B*, 719(1–2): 222–226.

Schulz M, Schmoldt A. (2003). Therapeutic and toxic blood concentrations of more than 800 drugs and other xenobiotics, *Pharmazie*, 58(7): 447–474.

Promethazine

Brand name: Phenergan
Classification: Antiemetic
λ: 9–16 h
V_d: 9–20 L/kg
Usual dosage: 12.5–50 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.004–0.5 mg/L	0.14[a]–2 mg/L	2–64 mg/L
Liver	9–12 mg/kg		23–180 mg/kg
Kidney	7 mg/kg		26–92 mg/kg
Skeletal muscle	0.5 mg/kg		

[a] Concentration obtained 5 h post exposure.

Selected Sources

Allender WJ, Archer AW. (1984). Liquid chromatographic analysis of promethazine and its major metabolites in human postmortem material, *J Forensic Sci*, 29(2): 515–526.

Bexar County Medical Examiner's Office data 1996–2015.

Bonnichsen R, Geertinger P, Maehly AC. (1970). Toxicological data on phenothiazine drugs in autopsy cases, *Zeitschrift für Rechtsmedizin*, 67(3): 158–169.

Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.

Pan CV, Quintela AG, Anuncibay PG, Vic JM. (1989). Topical promethazine intoxication, *DICP: Ann Pharmacother*, 23(1): 89.

Propoxyphene

Brand names: Darvon; Wygesic, Darvocet, and Propacet (w/ acetaminophen)
Classification: Opioid
λ: 6–12 h
V_d: 10–18 L/kg
Usual dosage: 50–100 mg q 4 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–1 mg/L	0.8–2 mg/L	1–60 mg/L
Liver	0.05–0.16 mg/kg		2–550 mg/kg
Kidney			3–58 mg/kg
Brain			20 mg/kg
Skeletal muscle	0.2–2 mg/kg		2–20 mg/kg

Comments

- Withdrawn from the U.S. market in 2010
- Active metabolite: Norpropoxyphene
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Baselt RC, Wright JA. (1975). Propoxyphene and norpropoxyphene tissue concentrations in fatalities associated with propoxyphene hydrochloride and propoxyphene napsylate, *Arch Tox*, 34(2): 145–152.

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Christensen H. (1977). Dextropropoxyphene and norpropoxyphene in blood, muscle, liver and urine in fatal poisoning, *Acta Pharmacologica et Toxicologica*, 40(2): 298–309.

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Garriott JC. (1991). Skeletal muscle as an alternative specimen for alcohol and drug analysis, *J Forensic Sci*, 36(1): 60–69.

Koski A, Vuori E, Ojanperä I. (2005). Relation of postmortem blood alcohol and drug concentrations in fatal poisonings involving amitriptyline, propoxyphene and promazine, *Hum Exp Toxicol*, 24(8): 389–396.

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Wetli CV, Bednarczyk LR. (1980). Deaths related to propoxyphene overdose: A ten-year assessment, *Southern Med J*, 73(9): 1205–1209.

Propranolol

Brand name: Inderal
Classification: β-blocker
λ: 2–6 h
V_d: 3–5 L/kg
Usual dosage: 40–180 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–1 mg/L	2–12 mg/L	4–167 mg/L
Liver	0.2 mg/kg		10–170 mg/kg
Kidney	0.025 mg/kg		26–119 mg/kg
Brain			6–67 mg/kg
Skeletal muscle	0.003 mg/kg		

Comments

- Metabolized by CYP 1A2, 2D6, and 2C19

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Fucci N, Offidani C. (2000). An unusual death by propranolol ingestion, *Am J Forensic Med Path*, 21(1): 56–58.
Gault R, Monforte JR, Khasnabis S. (1977). A death involving propranolol (Inderal), *Clin Tox*, 11(3): 295–299.
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McVey FK, Corke CF. (1991). Extracorporeal circulation in the management of massive propranolol overdose, *Anaesthesia*, 46(9): 744–746.
Paterson SC. (1985). Drug levels found in cases of fatal self-poisoning, *Forensic Sci Intl*, 27(2): 129–133.
Suarez RV, Greenwald MS, Geraghty E. (1988). Intentional overdosage with propranolol. A report of two cases, *Am J Forensic Med Path*, 9(1): 45–47.

Pseudoephedrine

Brand name: Sudafed; component of many OTC cold medicines
Classification: α and β adrenergic agonist
λ: 3–16 h
V_d: 2–3.5 L/kg
Usual dosage: 30–60 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.3–1 mg/L	1.4 mg/L	6[a]–33 mg/L
Liver	5 mg/kg		16 mg/kg[a]

[a] Infant.

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Boland DM, Rein J, Lew EO, Hearn WL. (2003). Fatal cold medication intoxication in an infant, *J Anal Toxicol*, 27(7): 523–526.
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Sica DA, Comstock TJ. (1989). Pseudoephedrine accumulation inrRenal failure, *Am J Med Sci*, 298(4): 261–263.

Psilocin/Psilocybin

Brand name: Not applicable
Street names: Magic Mushroom and Shrooms
Classification: Hallucinogen
λ: 1.5–4.5 h
V_d: 2.5–5 L/kg
Usual dosage: 5–20 mg/dose

Source	Nontoxic[a]	Toxic[a]	Lethal[a]
Blood	0.005–0.02 mg/L	0.05 mg/L	0.03[b]–4 mg/L

[a] All concentrations are for psilocin.
[b] Heart transplant patient.

Comments

- Psilocybin (λ 0.5–2 h) rapidly metabolized to active metabolite, psilocin
- Component in certain species of *Psilocybe, Conocybe, Copelandia, Panaeolus, Gymnopilus, Pluteus*, and *Stropharia* mushrooms

Selected Sources

Hasler F, Bourquin D, Brenneisen R, Bär T, Vollenweider FX. (1997). Determination of psilocin and 4-Hydroxyindole-3-Acetic acid in plasma by HPLC-ECD and pharmacokinetic profiles of oral and intravenous psilocybin in man, *Pharmaceutica Acta Helvetiae*, 72(3): 175–184.

Lim TH, Wasywich CA, Ruygrok PN. (2012). A fatal case of "magic mushroom" ingestion in a heart transplant recipient. *Intern Med J*, 42(11): 1268–1269.

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Quetiapine

Brand name: Seroquel
Classification: Antipsychotic
λ: 5–7 h
V_d: 6–14 L/kg
Usual dosage: 25–300 mg bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–1 mg/L	1.8–20 mg/L	4–50 mg/L
Vitreous			0.9–5 mg/L
Liver			1.1–120 mg/kg
Kidney			4.2 mg/kg
Brain	0.01–5.3 mg/kg		1.2–26 mg/kg
Skeletal muscle			5.9 mg/kg
Cardiac muscle			5.3 mg/kg

Comments

- Metabolized by CYP 3A4
- Prolongs QT interval

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Quinidine

Brand names: Cardioquin, Duraquin, Quinalan, and Quinidex
Classification: Antiarrhythmic/antimalarial
λ: 6–8 h
V_d: 1.5–4 L/kg
Usual dosage: 200–648 mg bid/tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	2–5 mg/L	8.5–28 mg/L	19–45 mg/L
Liver	8.8 mg/kg		220 mg/kg
Brain	0.29 mg/kg		

Comments

- Metabolized by CYP 3A
- Prolongs QT interval

Selected Sources

Baselt RC, Cravey RH. (1977). A compendium of therapeutic and toxic concentrations of toxicologically significant drugs in human biofluids, *J Anal Toxicol*, 1: 81–103.

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Quinine

Brand names: Qualaquin, Quinerva, and Quinite
Classification: Antimalarial
λ: 9–18 h
V_d: 1–2 L/kg
Usual dosage: 542–648 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	3–10 mg/L	6–16 mg/L	11–58 mg/L
Liver			52–350 mg/kg
Kidney			72–370 mg/kg
Brain			63–72 mg/kg

Comments

- Metabolized by CYP 3A4 and 2C19
- Active metabolite: 3-hydroxyquinine
- Prolongs QT interval

Selected Sources

Bodenhamer JE, Smilkstein MJ. (1993). Delayed cardiotoxicity following quinine overdose: A case report, *J Emer Med*, 11(3): 279–285.

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Winek CL, Davis ER, Collom WD, Shanor SP. (1974). Quinine fatality—Case report, *Clin Tox*, 7(2): 129–132.

Reboxetine

Brand names: Edronax and Vestra
Classification: Antidepressant (NRI)
λ: 12–15 h
V_d: 0.5–2 L/kg
Usual dosage: 2–4 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.7 mg/L	No data available	

Selected Sources

Hendershot PE, Fleishaker JC, Lin KM, Nuccio ID, Poland RE. (2001). Pharmacokinetics of reboxetine in healthy volunteers with different ethnic descents, *Psychopharmacology*, 155(2): 148–153.

Pellizzoni C, Poggesi I, Jørgensen NP, Edwards DM, Paus E, Benedetti MS. (1996). Pharmacokinetics of reboxetine in healthy volunteers. single against repeated oral doses and lack of enzymatic alterations, *Biopharm Drug Dispos*, 17(7): 623–633.

Poggesi I, Pellizzoni C, Fleishaker JC. (2000). Pharmacokinetics of reboxetine in elderly patients with depressive disorders, *Int J Clin Pharmacol Ther*, 38(5): 254–259.

Ricin

Brand name: Not applicable
Classification: Plant lectin
λ: Unknown
V_d: Unknown
Usual dosage: Not applicable

Source	Nontoxic[a]	Toxic[a]	Lethal[a]
Blood	0.25–10 ng/mL	0.3–1.5 ng/mL ricin 46 ng/mL ricinine [b]	2.3–33 ng/mL ricinine [b]
Urine	None detected ricin 0.2–4.2 ricinine [b]	0.06–0.3 ng/mL ricin 20–8540 ng/mL ricinine [b]	0.3 ng/mL ricin 0.08–58 ng/mL ricinine [b]

[a] Note units are in ng/mL.
[b] Ricinine is a marker for ricin exposure.

Comments

- From *Ricinus communis* (castor bean)
- Inhibits protein synthesis
- Death usually occurs 48–72 h post exposure

Selected Sources

Audi J, Belson M, Patel M, Schier J, Osterloh J. (2005). Ricin poisoning: A comprehensive review, *JAMA*, 294(18): 2342–2351.

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Godal A, Olsnes S, Pihl A. (1981). Radioimmunoassays of abrin and ricin in blood, *J Tox Environ Health*, 8(3): 409–417.

Johnson RC, Lemire SW, Woolfitt AR, Ospina M, Preston KP, Olson CT. (2005). Quantification of ricinine in rat and human urine: A biomarker for ricin exposure, *J Anal Toxicol*, 29(3): 149–155.

Kopferschmitt J, Flesch F, Lugnier A, Sauder P, Jaeger A, Mantz JM. (1983). Acute voluntary intoxication by ricin, *Hum Tox*, 2(2): 239–242.

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Røen BT, Opstad AM, Haavind A, Tønsager J. (2013). Serial ricinine levels in serum and urine after ricin intoxication, *J Anal Toxicol*, 37(5): 313–317.

Risperidone

Brand name: Risperdal
Classification: Antipsychotic
λ: 2.5–20 h
V_d: 1–2 L/kg
Usual dosage: 0.5–8 mg bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.009–0.1 mg/L	0.3–1.1 mg/L	0.5–1.8 mg/L

Comments

- Active metabolite: 9-hydroxyrisperdone (paliperidone)
- Metabolized by CYP 2D6
- Prolongs QT interval

Selected Sources

Brown K, Levy H, Brenner C, Leffler S, Hamburg EL. (1993). Overdose of risperidone, *Ann Emer Med*, 22(12): 1908–1910.

Hitosugi M, Tsukada C, Yamauchi S, Nagai T. (2014). A case of fatal risperidone poisoning alerts physicians, *J Clin Psychopharmacol*, 34(2): 268–269.

Lee HS, Tan CH, Au LS, Khoo YM. (1997). Serum and urine risperidone concentrations in an acute overdose, *J Clin Psychopharm*, 17(4): 325–326.

Linnet K, Johansen SS. (2014). Postmortem femoral blood concentrations of risperidone, *J Anal Toxicol*, 38(1): 57–60.

Springfield AC, Bodiford E. (1996). An overdose of risperidone, *J Anal Toxicol*, 20(3): 202–203.

Scopolamine

Brand names: Scopace, Scopoderm, and Hyoscine (ophthalmologic gtts)
Classification: Anticholinergic/antiemetic
λ: 2–9.5 h
V_d: 1.5–5 L/kg
Usual dosage: 0.4–0.8 mg q 8 h; 1 mg q 3 d (transdermal)

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.0002–0.02 mg/L	0.0005–0.01 mg/L	0.005–0.3 mg/L[a]

[a] Co-intoxicant: Citalopram, 0.5–0.7 mg/L.

Comments

- Metabolized by CYP 3A

Selected Sources

Balíková M. (2002). Collective poisoning with hallucinogenous herbal tea, 128(1–2): 50–52.

Lusthof KJ, Bosman IJ, Kubat B, Vincenten-van Maanen MJ. (2017). Toxicological results in a fatal and two non-fatal cases of scopolamine-facilitated robberies, *Forensic Sci Intl*, 274: 79–82.

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Secobarbital

Brand name: Seconal
Classification: Barbiturate
λ: 15–40 h
V_d: 1.5–2 L/kg
Usual dosage: 100–300 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.48–2.2 mg/L	3.2–22 mg/L	4–40 mg/L
Vitreous			2–10 mg/L
Liver	3.1–3.2 mg/kg		3–213 mg/kg
Kidney	1.8–2.8 mg/kg		3–30 mg/kg
Brain	0.6–1.8 mg/kg		1–25 mg/kg

Comments

- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Finkle BS. (1971). Ubiquitous reds: A local perspective on secobarbital abuse, *Clin Tox*, 4(2): 253–264.
Sunshine I, Hackett E. (1957). Chemical findings in cases of fatal barbiturate intoxications, *J Forensic Sci*, 2(2): 149–158.

Selegiline

Brand names: Eldepryl, Zelapar, Emsam, Deprenyl, and Anipryl
Classification: Anti-Parkinson's (MAOI)
λ: 1–3 h
V_d: 4–25 L/kg
Usual dosage: 5 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.005 mg/L selegiline 0.04–0.08 mg/L l-meth 0.02–0.05 mg/L l-amphet	No data available	0.2–0.3 mg/L l-meth 0.07–0.08 mg/L l-amphet
Liver			0.7 mg/kg l-meth 0.4 mg/kg l-amphet

Comments

- Active metabolites: l-methamphetamine, l-amphetamine, and l-desmethylselegiline

Selected Sources

Kupiec TC, Chaturvedi AK. (1999). Stereochemical determination of selegiline metabolites in postmortem biological specimens, *J Forensic Sci*, 44(1): 222–226.

Meeker JE, Reynolds PC. (1990). Postmortem tissue methamphetamine concentrations following selegiline administration, *J Anal Toxicol*, 4(5): 330–331.

Sertraline

Brand name: Zoloft
Classification: Antidepressant (SSRI)
λ: 13–45 h
V_d: 20–76 L/kg
Usual dosage: 50–200 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–0.9 mg/L	1–2.9 mg/L	5.6–26 mg/L
Vitreous	0.001–0.03 mg/L		
Liver	0.2–36 mg/kg		
Kidney	0.1–8.7 mg/kg		
Skeletal muscle	0.07–2.4 mg/kg		8.3 mg/kg
Lung	0.8–13 mg/kg		
Spleen	0.1–21 mg/kg		
Brain	0.08–5.2 mg/kg		
Cardiac muscle	0.02–2.2 mg/kg		

Comments

- Active metabolite: Desmethylsertraline
- Prolongs QT interval
- Metabolized by CYP 2B6, 2C9, and 2C19

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Sildenafil

Brand names: Revatio and Viagra
Classification: Phosphodiesterase inhibitor
λ: 3–5 h
V_d: 1.5–3.5 L/kg
Usual dosage: 25–100 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal[a]
Blood	0.04–0.9 mg/L	3.9–22 mg/L	6.3 mg/L[b]
Vitreous	0.09 mg/L		
Liver	0.2–5.5 mg/kg		
Kidney	0.02–4.3 mg/kg		
Brain	0.01–6.4 mg/kg		
Skeletal muscle	0.002–0.04 mg/kg		
Cardiac muscle	0.03–6.1 mg/kg		
Lung	0.3–5.4 mg/kg		
Spleen	0.09–1.4 mg/kg		

[a] Multiple fatalities reported without concentrations due to heart disease.
[b] Concomitant heart disease.

Comments

- Metabolized by CYP 3A4 and 2C9
- Active metabolite: *N*-desmethylsildenafil

Selected Sources

Lewis RJ, Johnson RD, Blank CL. (2006). Quantitative determination of sildenafil (Viagra) and its metabolite (UK-103,320) in fluid and tissue specimens obtained from six aviation fatalities, *J Anal Toxicol*, 30(1): 14–20.

Matheeussen V, Maudens KE, Anseeuw K, Neels H. (2015). A non-fatal self-poisoning attempt with sildenafil, *J Anal Toxicol*, 39(7): 572–576.

Pagani S, Mirtella D, Mencarelli R, Rodriguez D, Cingolani M. (2005). Postmortem distribution of sildenafil in histological material, *J Anal Toxicol*, 29(4): 254–257.

Tracqui A, Miras A, Tabib A, Raul JS, Ludes B, Malicier D. (2002). Fatal overdosage with sildenafil citrate (Viagra): First report and review of the literature, *Hum Exp Tox*, 21(11): 623–629.

Strychnine

Brand names: Component of pesticides
Classification: Alkaloid
λ: 10–11 h
V_d: 13 L/kg
Usual dosage: Not applicable

Source	Nontoxic	Toxic	Lethal
Blood	Negative	0.1–4.7 mg/L	0.2–61 mg/L
Vitreous			0.4 mg/L
Liver			0.3–175 mg/kg
Kidney			0.5–70 mg/kg
Brain			0.9–2.4 mg/kg
Skeletal muscle			2.3 mg/kg
Cardiac muscle			16 mg/kg

Comments

- From *Strychnos nux vomica*
- Causes muscular convulsions

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

Duverneuil C, de la Grandmaison GL, de Mazancourt P, Alvarez J-C. (2004). Liquid chromatography/photodiode array detection for determination of strychnine in blood: A fatal case report, *Forensic Sci Intl*, 141(1): 17–21.

Heiser JM, Daya MR, Magnussen AR, Norton RL, Spyker DA, Allen DW. (1992). Massive strychnine intoxication: Serial blood levels in a fatal case, *J Tox Clin Tox*, 30(2): 269–283.

Lindsey T, O'Hara J, Irvine R, Kerrigan S. (2004). Strychnine overdose following ingestion of gopher bait, *J Anal Toxicol*, 28(2): 135–137.

Marques EP, Gil F, Proenca P, Monsanto P, Oliveira MF, Castanheira A. (2000). Analytical method for the determination of strychnine in tissues by gas chromatography/mass spectrometry: Two case reports, *Forensic Sci Intl*, 110(2): 145–152.

Palatnick W, Meatherall R, Sitar D, Tenenbein M. (1997). Toxicokinetics of acute strychnine poisoning, *J Tox Clin Tox*, 35(6): 617–620.

Rosano TG, Hubbard JD, Meola JM, Swift TA. (2000). Fatal strychnine poisoning: Application of gas chromatography and tandem mass spectrometry, *J Anal Toxicol*, 24(7): 642–647.

Wood D, Webster E, Martinez D, Dargan P, Jones A. (2002). Case report: Survival after deliberate strychnine self-poisoning, with toxicokinetic data, *Critical Care*, 6(5): 456–459.

Suvorexant

Brand name: Belsomra
Classification: Hypnotic
λ: 8–15 h
V_d: 0.7 L/kg
Usual dosage: 5–20 mg qHS

Source	Nontoxic	Toxic	Lethal
Blood	0.1–1.5 mg/L	No data available	

Comments

- Metabolized by CYP 3A

Selected Sources

Belsomra Prescribing Information (package insert) Merck & Co, Inc. 2014.
Sun H, Yee KL, Gill S et al. (2015). Psychomotor effects, pharmacokinetics and safety of the orexin receptor antagonist suvorexant administered in combination with alcohol in healthy subjects, *J Psychopharmacol*, 29(11): 1159–1169.
Sutton EL. (2015). Profile of suvorexant in the management of insomnia, *Drug Des Devel Ther*, 9: 6035–6042.
Uemura N, McCrea J, Sun H et al. (2015). Effects of the orexin receptor antagonist suvorexant on respiration during sleep in healthy subjects, *J Clin Pharmacol*, 55(10): 1093–1100.

Tadalafil

Brand name: Cialis
Classification: Phosphodiesterase inhibitor
λ: 16–22 h
V_d: 0.5–1 L/kg
Usual dosage: 5–20 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.4 mg/L	No data available	

Selected Sources

Forgue ST, Phillips DL, Bedding AW, Payne CD, Jewell H, Patterson BE. (2007). Effects of gender, age, diabetes mellitus and renal and hepatic impairment on tadalafil pharmacokinetics, *Br J Clin Pharm*, 63(1): 24–35.

Mehrotra N, Gupta M, Kovar A, Meibohm B. (2007). The role of pharmacokinetics and pharmacodynamics in phosphodiesterase-5 inhibitor therapy, *Intl J Impotence Res*, 19(3): 253–264.

Proença P, Mustra C, Marcos M, Franco JM, Corte-Real F, Vieira DN. (2013). Validated UPLC-MS/MS assay for the determination of synthetic phosphodiesterase type-5 inhibitors in postmortem blood samples. *J Forensic Leg Med*, 20(6): 655–658.

Trocóniz IF, Tillmann C, Staab A, Rapado J, Forgue ST. (2007). Tadalafil population pharmacokinetics in patients with erectile dysfunction, *Eur J Clin Pharm*, 63(6): 583–590.

Tapentadol

Brand name: Nucynta
Classification: Opioid
λ: 4–5 h
V_d: 6–9 L/kg
Usual dosage: 50–100 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.4 mg/L	No data available	0.8[a]–6.6 mg/L
Vitreous			0.9 mg/L[a]
Liver	0.5 mg/kg		1.7–9.9 mg/kg[a]
Brain	0.4 mg/kg		1.6 mg/kg[a]

[a] Co-intoxicants: Blood tapentadol, 0.8–1.1 mg/L.

Comments

- Metabolized by CYP2C9 and CYP2C19
- Can contribute to serotonin system if combined with other serotonergic drugs

Selected Sources

Anderson D, deQintana S, Valencia KH. (2010). New drug: Tapentadol (Nucynta), *Toxtalk*, 34(3): 22–23.

Bexar County Medical Examiner's Office data 1996–2015.

Cantrell FL, Mallett P, Aldridge L, Verilhac K, McIntyre IM. (2016). A tapentadol related fatality: Case report with postmortem concentrations, *Forensic Sci Int*, 266: e1–e3.

Franco DM, Ali Z, Levine B, Middleberg RA, Fowler DR. (2014). Case report of a fatal intoxication by nucynta, *Am J Forensic Med Pathol*, 35(4): 234–236.

Kemp W, Schlueter S, Smalley E. (2013). Death due to apparent intravenous injection of tapentadol, *J Forensic Sci*, 58(1): 288–291.

Larson SJ, Pestaner J, Prashar SK, Bayard C, Zarwell LW, Pierre-Louis M. (2012). Postmortem distribution of Tapentadol and N-desmethyltapentadol, *J Anal Toxicol* 36: 440–443.

Temazepam

Brand names: Restoril and Normison
Classification: Benzodiazepine
λ: 7–18 h (biphasic)
V_d: 1–1.5 L/kg
Usual dosage: 7.5–30 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–1 mg/L	1 mg/L	2.9–10 mg/L
Liver			39–107 mg/kg
Brain	0.003–0.2 mg/kg		
Skeletal muscle	0.5–0.6 mg/kg		3–8.8 mg/kg

Comments

- Active metabolite: Oxazepam
- Metabolite of diazepam
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

Forrest AR, Marsh I, Bradshaw C, Braich SK. (1986). Fatal temazepam overdoses, *Lancet*, 2: 226.

Langford AM, Taylor KK, Pounder DJ. (1998). Drug concentration in selected skeletal muscles, *J Forensic Sci*, 43(1): 22–27.

Martin CD, Chan SC. (1986). Distribution of temazepam in body fluids and tissues in lethal overdose, *J Anal Toxicol*, 10(2): 77–78.

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Williams KR, Pounder DJ. (1997). Site-to-site variability of drug concentrations in skeletal muscle, *Am J Forensic Med Path*, 18(3): 246–250.

Terbutaline

Brand names: Brethine and Bricanyl
Classification: β-agonist
λ: 2.5–4.5 h
V_d: 1–2 L/kg
Usual dosage: 2.5–5 mg q 6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.01 mg/L	0.04–0.2 mg/L	0.04 mg/L[a]
Liver	0.009–0.05 mg/kg		
Kidney	0.05 mg/kg		
Skeletal muscle	0.06 mg/kg		
Cardiac muscle	0.004–0.04 mg/kg		

[a] Concomitant natural disease.

Selected Sources

Couper FJ, Drummer OH. (1996). Gas chromatographic-mass spectrometric determination of beta 2-agonists in postmortem blood: Application in forensic medicine, *J Chromatogr B Biomed Appl*, 685(2): 265–272.

Heath A, Hultén BA. (1987). Terbutaline concentrations in self-poisoning: A case report, *Hum Tox*, 6(6): 525–526.

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Tetrahydrocannabinol

Brand names: Marinol, Cesamet, and Sativex (dronabinol, nabilone)
Alternate name: delta-9-tetrahydrocannabinol (Δ^9THC, THC)
Street names: Pot, Weed, Grass, Mary Jane, Dope, Doobie, Hashish, and Hash
Classification: Cannabinoid/psychoactive
λ: 2–57 h
V_d: 1–10 L/kg
Usual dosage: 10–30 mg/dose

	Therapeutic/Nontoxic		Toxic	
Source	THC	11-OH-THC	THC	Lethal
Blood	0.001–0.20 mg/L	0.02–0.1 mg/L	0.2 mg/L	See below[a]
Serum/plasma	0.005–0.04 mg/L	0.006–0.04 mg/L		
Liver	0.02–0.05 mg/kg	0.001–0.07 mg/kg		
Lung	0.002–0.15 mg/kg	0.001–0.01 mg/kg		
Kidney	0.001–0.45 mg/kg	0.002–0.02 mg/kg		
Spleen	0.001–0.02 mg/kg	0.01–0.02 mg/kg		
Muscle	0.001–0.4 mg/kg	0.01 mg/kg		
Brain	0.001–0.04 mg/kg	0.001–0.04 mg/kg		
Heart	0.002–0.5 mg/kg	0.002–0.2 mg/kg		

[a] May be associated with sudden cardiac death in the presence of severe coronary artery diease.

Comments

- Active ingredient in *Cannabis*
- Metabolized to 11-OH-THC (λ 12–36 h) (active) and THC-COOH (λ 1–6 d)
- Metabolized by CYP 2C9, CYP 3A4
- PM concentrations should be interpreted with caution as cannabinoids exhibit moderate PMR and have been detected 30 days after sustained abstinence in live chronic users
- Distribution of cannabinoids between plasma and whole blood is not equal
- Second hand smoke
  - In high-intensity environment (whole blood)—THC 0.0–0.006 mg/L; COOH-THC 0.0–0.005 mg/L
  - In coffee shop (serum)—THC 0.0–0.0007 mg/L; COOH-THC 0.0–0.002 mg/L

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Theophylline

Brand names: Quibron-T, Slo-phyllin, Senophylline, Theo-24, Theodur, and Slo-bid
Classification: Bronchodilator
λ: 3–8 h
V_d: 0.3–0.7 L/kg
Usual dosage: 5–20 mg/kg/d divided q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1–20 mg/L	31–170 mg/L	63–290 mg/L
Liver			108–275 mg/kg
Kidney			212 mg/kg
Brain			120–231 mg/kg

Comments

- Metabolized by CYP 1A2 and 2E1

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.
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Winek CL, Bricker JD, Collom WD, Fochtman FW. (1980). Theophylline fatalities, *Forensic Sci Intl*, 15(3): 233–236.

Thiopental

Brand name: Pentothal
Classification: Barbiturate
λ: 3–28 h
V_d: 0.4–4 L/kg
Usual dosage: 25–250 mg/dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	3–50 mg/L[a]	8–10 mg/L	11–279 mg/L
Liver			32–114 mg/kg
Kidney			16–41 mg/kg
Brain			3.3–22 mg/kg
Skeletal muscle			5.4–55 mg/kg
Cardiac muscle			5–64 mg/kg

[a] Therapeutic concentrations during surgical anesthesia.

Comments

- Active metabolite: Pentobarbital
- Therapeutic concentrations can be fatal if drug not administered in a monitored, medical setting

Selected Sources

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Thioridazine

Brand name: Mellaril
Classification: Antipsychotic
λ: 7–36 h
V_d: 18 L/kg
Usual dosage: 20–200 mg bid/tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–0.7 mg/L	2.4–12 mg/L	1.8–28 mg/L
Liver	3–7 mg/kg		25–513 mg/kg
Kidney			18–135 mg/kg
Brain			6.4 mg/kg
Skeletal muscle	0.3–1.4 mg/kg		

Comments

- Active metabolite: Mesoridazine
- Metabolized by CYP 2D6
- Prolongs QT interval
- Causes agranulocytosis and hepatitis

Selected Sources

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Bexar County Medical Examiner's Office data 1996–2015.

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Tiagabine

Brand name: Gabitril
Classification: Anticonvulsant
λ: 4–9 h
V_d: 0.5–2 L/kg
Usual dosage: 2–16 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.5 mg/L	0.4–4.6 mg/L	7–9 mg/L

Comments

- Metabolized by CYP 3A

Selected Sources

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Topiramate

Brand name: Topamax
Classification: Anticonvulsant
λ: 19–25 h
V_d: 0.6–0.8 L/kg
Usual dosage: 50–400 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1.7–20 mg/L	4.2[a]–10 mg/L	36–170 mg/L
Vitreous			65–118 mg/L
Liver	12–14 mg/kg		140–234 mg/kg
Kidney	9–10 mg/kg		55 mg/kg
Brain			157 mg/kg

[a] Pediatric patient.

Selected Sources

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Tramadol

Brand names: Ultram and Ultracet (w/acetaminophen)
Classification: Opioid
λ: 5–7 h
V_d: 3–5 L/kg
Usual dosage: 50–100 mg q 4–6 h

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.1–3.0 mg/L	1–24 mg/L	1.3–89 mg/L
Liver	0.3 mg/kg		6.2–69 mg/kg
Kidney	0.4 mg/kg		3–37 mg/kg
Skeletal muscle			1.1 mg/kg
Brain			44 mg/kg
Lung			106 mg/kg

Comments

- Metabolized by CYP 2D6 and CYP 3A4
- Active metabolite: O-desmethyltramadol, 200x more active than parent drug
- Tolerance may develop and should be considered when interpreting drug concentrations
- Can contribute to serotonin system if combined with other serotonergic drugs

Selected Sources

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Trazodone

Brand name: Desyrel
Classification: Antidepressant
λ: 3–9 h
V_d: 0.9–1.5 L/kg
Usual dosage: 50–400 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.5–2.0 mg/L	1.5–26 mg/L	5–25 mg/L
Liver	0.6–2.2 mg/kg		26–82 mg/kg
Kidney			40 mg/kg
Brain			21 mg/kg
Skeletal muscle			6.6–9 mg/kg

Comments

- Active metabolite: m-chlorophenylpiperzine
- Metabolized by CYP 3A4
- May prolong QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
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Root I, Ohlson GB. (1984). Trazodone overdose: Report of two cases, *J Anal Toxicol*, 8(2): 91–94.

Triazolam

Brand name: Halcion
Classification: Benzodiazepine
λ: 1–5 h
V_d: 1–3 L/kg
Usual dosage: 0.125–0.5 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.002–0.02 mg/L	0.004–0.04 mg/L	0.01–0.4 mg/L
Liver			0.09–0.5 mg/kg
Kidney			0.07–0.3 mg/kg
Brain			0.1 mg/kg
Skeletal muscle			0.1 mg/kg

Comments

- Metabolized by CYP 3A4
- Tolerance can develop and should be considered when interpreting drug concentrations

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.

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Trihexylphenidyl

Brand names: Artane, Trihexane, and Benzhexal
Classification: Anti-Parkinson's agent
λ: 3–10 h
V_d: Unknown
Usual dosage: 1–20 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–0.06 mg/L	No data available	0.1–1.8 mg/L[a]
Liver			0.5 mg/kg[a]

[a] All fatalities have either co-intoxicants or significant natural disease present.

Comments

- Toxicities associated with torsade de pointes

Selected Sources

Bexar County Medical Examiner's Office data 2003–2015.

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Trimipramine

Brand name: Surmontil
Classification: Antidepressant (TCA)
λ: 16–39 h
V_d: 17–48 L/kg
Usual dosage: 50–100 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.4 mg/L	0.4–2 mg/L	1.8–12 mg/L
Liver			51–544 mg/kg

Comments

- Active metabolite: Desmethyl-trimipramine
- May prolong QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Druid H, Holmgren P. (1991). Fatal seizures associated with trimipramine poisoning, *Forensic Sci Intl*, 49(1): 75–79.
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Hucker RS. (1983). A fatal clomipramine and trimipramine poisoning, *Bull Intl Assoc Forensic Tox*, 17(2): 20–22.

Valproic Acid

Brand names: Depakene, Depacon, and Depakote
Alternate names: Valproate, divalproex, and dipropylacetic acid
Classification: Anticonvulsant
λ: 5–20 h
V_d: 0.1–0.4 L/kg
Usual dosage: 250–500 mg tid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	17–100 mg/L	200–1440 mg/L	556–2204 mg/L
Vitreous			516–821 mg/L
Liver			104–985 mg/kg
Kidney			69–1580 mg/kg
Brain			510–545 mg/kg
Skeletal muscle	30–124 mg/kg		482 mg/kg
Cardiac muscle			670 mg/kg

Comments

- Metabolized by CYP 2C9 and 2C19

Selected Sources

Andersen GO, Ritland S. (1995). Life threatening intoxication with sodium valproate, *J Tox Clin Tox*, 33(3): 279–284.

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Vardenafil

Brand name: Levitra
Classification: Phosphodiesterase inhibitor
λ: 4–5 h
V_d: 2–3 L/kg
Usual dosage: 5–20 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.003–0.3 mg/L	No data available	
Liver	0.09 mg/kg		
Kidney	0.02 mg/kg		
Skeletal muscle	0.008 mg/kg		
Cardiac muscle	0.03 mg/kg		
Lung	0.2 mg/kg		

Comments

- May prolong QT interval
- Metabolized by CYP3A4; also CYP3A5 and CYP2C

Selected Sources

Johnson RD, Lewis RJ, Angier MK. (2007). The postmortem distribution of vardenafil (Levitra) in an aviation accident victim with an unusually high blood concentration, *J Anal Toxicol*, 31(6): 328–333.

Ku HY, Shon JH, Liu KH, Shin JG, Bae SK. (2009). Liquid chromatography/tandem mass spectrometry method for the simultaneous determination of vardenafil and its major metabolite, N-desethylvardenafil, in human plasma: Application to a pharmacokinetic study, *J Chromatogr B Analyt Technol Biomed Life Sci*, 877(1–2): 95–100.

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Venlafaxine

Brand name: Effexor
Classification: Antidepressant (SNRI)
λ: 2.5–8 h
V_d: 4–12 L/kg
Usual dosage: 37.5–225 mg qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–2.1 mg/L	1.8–15 mg/L	6.5–130 mg/L
Vitreous			6.7–58 mg/L
Liver			81–425 mg/kg
Kidney			420 mg/kg
Brain			543 mg/kg
Skeletal muscle	0.5–1.9 mg/kg		

Comments

- Active metabolite: O-desmethylvenlafaxine (Pristiq)
- Metabolized by CYP 2D6
- Prolongs QT interval

Selected Sources

Bexar County Medical Examiner's Office data 1996–2015.
Jaffe PD, Batziris HP, van der Hoeven P, DeSilva D, McIntyre IM. (1999). A study involving venlafaxine overdoses: Comparison of fatal and therapeutic concentrations in postmortem specimens, *J Forensic Sci*, 44(1): 193–196.
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Verapamil

Brand name: Calan
Classification: Calcium channel blocker
λ: 4–14 h
V_d: 2.5–6.5 L/kg
Usual dosage: 40–120 mg tid/qid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.03–1 mg/L	1.5–4 mg/L	1.5–85 mg/L
Liver			2.4–258 mg/kg
Kidney			1.5–33 mg/kg
Skeletal muscle	0.2–0.5 mg/kg		

Comments

- Active metabolite: Norverapamil
- Metabolized by CYP 1A2 and 3A

Selected Sources

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Vigabatrin

Brand names: Sabril and Sabrilex
Classification: Anticonvulsant
λ: 5–8 h
V_d: 0.8 L/kg
Usual dosage: 500–3000 mg/d divided bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	1–43 mg/L	No data available	40–49 mg/L[a]

[a] Fatality was due to hepatotoxicity in a child.

Selected Sources

Deeb S, McKeown DA, Torrance HJ, Wylie FM, Logan BK, Scott KS. (2014). Simultaneous analysis of 22 antiepileptic drugs in postmortem blood, serum and plasma using LC-MS-MS with a focus on their role in forensic cases, *J Anal Toxicol*, 38(8): 485–494.

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Vilazodone

Brand name: Viibryd
Classification: Antidepressant (SSRI)
λ: 25–37 h
V_d: 13–17 L/kg
Usual dosage: 20–40 mg/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.2 mg/L	No data available	

Comments

- Metabolized by CYP 3A4 as well as 2C19 and 2D6

Selected Sources

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Warfarin

Brand name: Coumadin
Classification: Anticoagulant
λ: 20–60 h
V_d: 0.1–0.2 L/kg
Usual dosage: 1–10 mg qd

Source	Therapeutic/Nontoxic	Toxic[a]	Lethal[a]
Blood	0.7–9 mg/L	>10 mg/L	

[a] Toxicity/lethality results from bleeding diatheses.

Comments

- Metabolized by CYP 2C9, 2C19, 2C8, 2C18, 1A2, and 3A4
- Toxicity can be diagnosed by prothrombin time

Selected Sources

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Yohimbine

Brand names: Aphrodyne, Yocon, Viritab, and Yohimex
Classification: α-adrenergic blocker
λ: 0.5–1 h
V_d: 0.3–2 L/kg
Usual dosage: 5–15 mg per dose

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.04–0.4 mg/L	5–5.2 mg/L	5.4–7.4 mg/L

Comments

- Active metabolite: 11-OH-yohimbine

Selected Sources

Anderson C, Anderson D, Harre N, Wade N. (2013). Case study: Two fatal case reports of acute yohimbine intoxication, *J Anal Toxicol*, 37(8): 611–614.

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Zaleplon

Brand name: Sonata
Classification: Sedative/hypnotic
λ: 1–1.5 h
V_d: 1–1.5 L/kg
Usual dosage: 5–20 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.01–0.4 mg/L	No data available	2.2 mg/L[a]

[a] Co-intoxicants: Promethazine and butalbital.

Comments

- Metabolized by CYP 3A

Selected Sources

Drover D, Lemmens H, Naidu S, Cevallos W, Darwish M, Stanski D. (2000). Pharmacokinetics, pharmacodynamics, and relative pharmacokinetic/pharmacodynamic profiles of zaleplon and zolpidem, *Clin Therapeutics*, 22(12): 1443–1461.

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Ziprasidone

Brand name: Geodon
Classification: Antipsychotic
λ: 3–7 h
V_d: 1–1.5 L/kg
Usual dosage: 20–80 mg bid

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–0.1 mg/L	0.3–2.0 mg/L[a]	5.7 mg/L[b]

[a] Toddler.
[b] Co-intoxicants: Ethanol, 0.16 g/dL; venlafaxine, 120 mg/L; and zolpidem, 0.08 mg/L.

Comments

- Prolongs QT interval; may develop Torsades de Pointes in overdose
- Metabolized by CYP 3A4

Selected Sources

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Roman M, Kronstrand R, Lindstedt D, Josefsson M. (2008). Quantitation of seven low-dosage antipsychotic drugs in human postmortem blood using LC-MS-MS, *J Anal Toxicol*, 32(2): 147–155.

Zolpidem

Brand name: Ambien
Classification: Sedative/hypnotic
λ: 1.5–5 h
V_d: 0.5–1 L/kg
Usual dosage: 5–10 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.05–2.2 mg/L	0.1–1.4 mg/L	0.6–7.9 mg/L
Vitreous			0.5–1.6 mg/L
Liver	0.4–1.3 mg/kg		12–23 mg/kg
Skeletal muscle	0.2–0.5 mg/kg		

Comments

- Metabolized by CYP 3A4

Selected Sources

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Druid H, Holmgren P. (1997). A compilation of fatal and control concentrations of drugs in postmortem femoral blood, *J Forensic Sci*, 42(1): 79–87.
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Jönsson AK, Söderberg C, Espnes KA, Ahlner J, Eriksson A, Reis M, Druid H. (2014). Sedative and hypnotic drugs—Fatal and non-fatal reference blood concentrations, *Forensic Sci Int*, 236: 138–145.
Keller T, Schneider A, Tutsch-Bauer E. (1999). GC/MS determination of zolpidem in postmortem specimens ina voluntary intoxication, *Forensic Sci Intl*, 106(2): 103–108.
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Winek CL, Wahba WW, Janssen JK, Rozin L, Rafizadeh V. (1996). Acute overdose of zolpidem, *Forensic Sci Intl*, 78(3): 165–168.

Zonisamide

Brand name: Zonegran
Classification: Anticonvulsant
λ: 27–105 h (~63 h)
V_d: 1–2 L/kg
Usual dosage: 25–200 mg bid/qd

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	2.3–40 mg/L	40–202 mg/L	44 mg/L[a]

[a] Other confounding variables present; not definitive zonisamide intoxication.

Comments

- Metabolized by CYP 3A4

Selected Sources

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Hofer KE, Trachsel C, Rauber-Lüthy C, Kupferschmidt H, Kullak-Ublick GA, Ceschi A. (2011). Moderate toxic effects following acute zonisamide overdose, *Epilepsy Behav*, 21(1): 91–93.

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Zopiclone

Brand names: Imovane, Zimovane; Lunesta (eszopiclone)
Classification: Sedative/hypnotic
λ: 3–8 h
V_d: 1–2 L/kg
Usual dosage: 3.75–7.5 mg qHS

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.02–1.3 mg/L	0.25–1.6 mg/L	0.4–4.1 mg/L
Vitreous			94 mg/L
Liver			4.9–8.7 mg/kg
Kidney			1.7 mg/kg
Spleen			5.8 mg/kg
Brain			2.8 mg/kg
Skeletal muscle			1.9–3.3 mg/kg
Cardiac muscle			1.6 mg/kg

Comments

- Eszopiclone is the s-enantiomer of zopiclone and *laboratories usually do not differentiate between zopiclone and eszopiclone*

Selected Sources

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Zuclopenthixol

Brand names: Clopixol, Cisordinol, and Ciatyl-Z
Classification: Antipsychotic
λ: 12–30 h
V_d: 15–20 L/kg
Usual dosage: 10–20 mg po bid; 50–150 mg im qod

Source	Therapeutic/Nontoxic	Toxic	Lethal
Blood	0.005–0.1 mg/L	0.15–0.3 mg/L	0.3–0.9 mg/L
Liver			0.75 mg/kg
Lung			5.2 mg/kg
Kidney			1.4 mg/kg
Brain			0.1 mg/kg

Comments

- Metabolized by CYP 2D6

Selected Sources

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Roman M, Kronstrand R, Lindstedt D, Josefsson M. (2008). Quantitation of seven low-dosage antipsychotic drugs in human postmortem blood using LC-MS-MS, *J Anal Toxicol*, 32(2): 147–155.

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Appendix A

Specimen Types and Collection

- **Blood**
  - Most common and preferable sample.
  - Peripheral blood is more desirable than central blood because it is less affected by postmortem redistribution.
    - Femoral blood, followed by subclavian, heart, and cavity blood are recommended.
  - Used for screening and confirmatory testing.
  - Should be collected into glass tubes because drugs can bind to polymers of plastic tubes.
    - Collect at least 20 mL into glass tube with appropriate preservative for testing, such as sodium fluoride/potassium oxalate or EDTA.
    - For volatile testing, collect a full Teflon-lined screw top tube.
    - Additional tubes can be used for serology and/or genetic testing.
- **Urine**
  - Relatively easy to obtain and store.
  - Good screening sample.
  - Drug concentrations in urine do not accurately reflect the corresponding blood concentrations or indicate acute toxicity.
  - May reflect a drug that was ingested many hours, and sometimes days, prior to testing.
  - Can be used as a confirmatory sample.
  - Collect 5–10 mL into glass red top tube (no preservative).
- **Vitreous**
  - Excellent specimen with good stability.
  - Only available in a limited quantity.
  - Most often used for electrolyte testing.
  - Good for detection of short-lived metabolites like 6-MAM.
  - Collected into glass, red top tubes (no preservative); usually 2–4 mL.

- **Bile**
  - Not recommended to detect drug toxicity deaths.
  - Certain drugs are concentrated in the bile making interpretation of elevated levels difficult.
  - Collect into glass, red top tubes (no preservative); usually 2–10 mL.
- **Synovial Fluid**
  - Available in limited quantities.
  - Can be used to confirm drug presence.
- **Tissue**
  - Usually readily available in large quantities.
  - Interpretation of drug concentration can be difficult as concentrations may be elevated in chronically administered drugs.
  - Collect at least 50 g into clean, unused specimen containers.
  - Collect at least 50 g into clean, unused specimen containers.
    - Muscle speciments should be collected from quadriceps.
    - Liver from the deep right lobe.
    - Lung from the apex.
  - Specific issues to be considered:
    - Liver may concentrate drugs.
    - Kidney is good for heavy metal testing.
    - Brain is good for lipophilic drugs, including volatiles.
    - Lung is good for inhaled toxins, such as volatile compounds.
    - Spleen can be used as an alternative sample for carbon monoxide testing.
    - Adipose tissue can be used for pesticide and volatile analysis.
- **Stomach/Gastric Contents**
  - The presence of a drug in gastric contents, even at elevated concentrations may not indicate drug toxicity.
  - May be useful in directing blood testing.
- **Hair**
  - Not routinely used in the postmortem setting.
  - Yields information about drug intake over a period of months to years, depending on the length of hair sampled.
  - Often used as screening source for arsenic poisoning.
  - To collect, shave 100–200 mg, usually of scalp hair, tie the root end to mark direction, and place into a new, unused, dry specimen container.

- **Labeling and Storage**
  - Samples should be labeled with the following: the type of specimen, case number, date of collection, name of deceased, and the names of medical examiner and person securing the sample (if they are different).
  - Blood samples should be labeled with the exact site of collection rather than simply "peripheral" or "central."
  - Samples should be immediately refrigerated or frozen until ready for transport to the toxicology laboratory.

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Appendix B

Common Methodologies

Screening Tests

- **Immunoassay**
  - *Theory*: An antibody reacts against a particular drug or drug class.
  - *Types*: Radioimmunoassay (RIA), enzyme multiplied immunoassay technique (EMIT), fluorescent polarization immunoassays (FPIA), kinetic interaction of microparticles in solution (KIMS), and enzyme linked immunosorbent assay (ELISA).
  - *Advantages*: Relatively easy to use and to perform, good sensitivity, and requires small amount of sample.
  - *Disadvantages*: Limited specificity; interfering substances may result is false positive or false negative results.
- **Spectrophotometry**
  - *Theory*: Measures the changes in the wavelength of light passing through a substance.
  - *Types*: Ultraviolet (UV), visible spectra, and infrared (IR).
  - *Advantages*: Ease of use.
  - *Disadvantages*: Lack of sensitivity and specificity.
- **Chromatography**
  - *Theory*: Drugs are identified based upon the time it takes to transverse the stationary phase.
  - *Types:* Can be gas (GC) or liquid (LC).
  - *Advantages*: Sensitive; specific when paired with a mass spectrometer.
  - *Disadvantages*: Time consuming; requires significant sample preparation; expensive.

Confirmatory Tests

- Usually more specific than screening tests.
- Performed by a different methodology than the screening test and on a different sample, if possible.
- Preferred methods are GC or LC paired with mass spectrometry.
- Confirmation of an immunoassay by another immunoassay is not acceptable.

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Appendix C

Normal Laboratory Values

Blood

Cell Counts

WBC	4.1–10.9 × 10^3/μL
Hb	13.2–17.2 g/dL Male 12.0–15.2 g/dL Female
Hct	40%–52% Male 37%–48% Female
Plt	140–450 × 10^3/μL
PT/PTT	12–14/18–28 s

Electrolytes

Ca	8.5–10.5 mg/dL
Cl	98–108 mEq/L
K	3.5–5 mEq/L
Na	135–145 mEq/L

Liver Function

NH_4	12–55 μmol/L
Bilirubin (total)	0.2–1.3 mg/dL
AST/ALT	5–35/7–56 U/L
GGT	8–78 U/L

Renal Function

BUN	7–21 mg/dL
Cr	0.6–1.5 mg/dL
Glucose	65–110 mg/dL

Blood Gases

pH	7.35–7.45
pCO_2	35–45 mmHg
pO_2	75–100 mmHg

Cardiac

CPK (total)	38–120 ng/mL
Troponin	<0.4 ng/mL

Enzymes

Amylase	30–110 U/L
Lipase	7–60 U/L
Alk phos	38–126 U/L

Vitreous

K	3.5–10 mEq/L (levels > 15 mEq/L indicate decomposition)[a]
Na	130–155 mEq/L[a]
Cl	105–135 mEq/L[a]
Ca	6–8.4 mg/dL
Urea nitrogen	7–30 mg/dL
Cr	<1.5 mg/dL
Glucose	<60 mg/dL (or ½ serum level)

[a] After death, potassium increases while sodium and chloride decrease.

Average Blood Volume

Neonates	85–95 mL/kg
Infants	80 mL/kg
Adults	75 mL/kg Male 65 mL/kg Female

Appendix D

Conversion Charts

Metric Units

k = kilo = 10^3
d = deci = 10^{-1}
c = centi = 10^{-2}
m = milli = 10^{-3}
μ = micro = 10^{-6}
n = nano = 10^{-9}
p = pico = 10^{-12}

Volume

1 L = 1000 mL = 1000 cc
30 mL ~ 1 fluid ounce

Weight

65 mg = 1 grain
437.5 grain = 1 oz
28.35 g = 1 oz
1 kg = 2.2 lbs
1 g = 0.035 oz

Length

1 cm = 0.4 inch
2.54 cm = 1 inch
1 meter = 39.37 inches

Temperature

$°C = (°F - 32) \times 0.555$
$°F = (°C \times 1.8) + 32$

Concentration

µg/mL = mg/L
µg/g = mg/kg
µg/L = ng/mL
µg/µL = mg/mL
mmol/L * molecular weight (g/mol) = mg/L

Density

blood = 1.055 g/mL
1 mL blood = 1.055 g

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