

D-Amphetamine sulfate

Synonym: Dextroamphetamine sulfate

CAS: 51-63-8 (D-amphetamine sulfate, Sigma)

MF: $C_{18}H_{26}N_2 \cdot H_2SO_4$

FW: 368.49

Solubility: D-amphetamine sulfate is soluble in water and in ethanol.

Major uses

Amphetamine is a synthetic drug (first time synthesized 1887 by German chemist L. Edeleanu) with a broad area of application. It is used as a medicine against obesity (appetite suppressor), as a remedy for treatment of somnolence (sleep disorder), and other related neurological conditions, as an anesthetic, and also for treatment of ADHD (attention-deficient hyperactivity disorder) among children.

At the same time, amphetamine is a commonly abused narcotic drug used mainly by teenagers. It can be ingested orally, intravenously, smoked or snorted.

D-amphetamine sulfate is a d-form of amphetamine. Similar to amphetamine, it may be used for treatment of somnolence and ADHD. It is a central nervous system (CNS) stimulant and sympathomimetic drug, i.e. it excites CNS and heart and affects the diameter of blood vessels. At high doses, it is, like amphetamine, an abusive narcotic drug, with psychoactive and hallucinogenic effects [1, 2].

Human toxicity

Acute overdose of amphetamine may lead to e.g. hyperthermia, respiratory depression, seizures, metabolic acidosis, renal failure, hepatic injury and coma. Among neurological effects, agitation, aggressive behavior, irritability, headache and hallucinations are common. Cardiac symptoms may include arrhythmia, cardiomyopathy, myocardial infarction or ischemic stroke. Among gastrointestinal symptoms, abdominal pain, vomiting, diarrhea, cramps, anorexia and gastrointestinal hemorrhage can be mentioned.

Therapeutic doses are in the range of 5 to 30 mg daily. Therapeutic blood concentrations are in the range of 0.03 to 0.04 mg/l.

Doses over 1-2 g amphetamine or D-amphetamine sulfate can cause severe intoxication. Response is variable and tolerance develops in chronic abusers, who may use as much as 5 to 15 g of amphetamine per day [1].

Blood concentrations of amphetamine in 11 reported fatalities ranged from 0.5 to 41 mg/l, with urine levels of 25 to 700 mg/l [3]. The mean lethal serum concentration, based on the values from several handbooks, was 6.4 mg/l [4].

Kinetic data

Data about D-amphetamine sulfate are restricted; only data about amphetamine are available.

Absorption: if ingested orally, amphetamine is well absorbed from the gastrointestinal tract and buccal mucosa.

Volume of distribution (V_d): 3.2 to 5.6 l/kg [3].

The plasma half-life of amphetamine is dependent on the urine pH. When pH is less than 6.6, the half-life is 7 to 14 h; at pH higher than 6.6, the half-life is 18 to 34 h [1].

Plasma protein binding: 16 to 20% [3, 4].

Passage of blood-brain barrier: free [4].

Metabolism and excretion

Metabolism of amphetamine generally includes aromatic hydroxylation, aliphatic hydroxylation, and n-dealkylation, resulting in inactive and active metabolites. Main metabolites of amphetamine are: hippuric acid (16 to 28%), phenylacetone (0.9%), benzoylglucuronide (4%), norephedrine (2%), conjugated p-hydroxyamphetamine (2-4%) and conjugated p-hydroxynorephedrine (0.3%). One of metabolites, p-hydroxyamphetamine is a potent hallucinogen implicated in the development of amphetamine-induced psychosis [1].

The excretion of unchanged amphetamine is dependent on the urine pH. In an acidic urine (pH less than 6.6) 67 to 73% of an ingested dose is excreted as amphetamine. When pH is higher than 6.7, 17 to 43% is excreted unchanged in the urine [1].

Toxicological mechanisms

Amphetamine and D-amphetamine sulfate has multiple mechanisms of action; only some of them are indicated here: a) Amphetamines stimulate the release of biogenic amines (norepinephrine, dopamine) from stores in adrenergic nerve terminals, as well as directly stimulate α - and β -adrenergic receptors; b) Amphetamines have a stimulating effect on several cortical centers, including the cerebral cortex, medullary respiratory center, and reticular activating system; c) Amphetamines may slow down catecholamine metabolism by inhibiting monoamine oxidase [1].

At an overdose of amphetamine, all these described mechanisms and their effects may have grave neurological, cardiac and other consequences leading at the worst case to coma or even death.

Target organs: CNS, lung, heart, kidney, liver.

References

1. Poisindex, Thomson Micromedex (2005).
2. Casarett and Doull's Toxicology (The Basis Science of Poisons) (1986) Klaassen CD, Amdur MO, Doull J eds., Macmillan Publishing Company.
3. Baselt RC & Cravey RH (1995) Disposition of Toxic Drugs and Chemicals in Man. 4th ed. Year Book Medical Publishers, Chicago, IL.
4. Ekwall, B., Clemedson, C., Crafoord, B., Ekwall, B., Hallander, S., Walum, E. & Bondesson, I. (1998) MEIC Evaluation of Acute Systemic Toxicity: Part V. Rodent and Human Toxicity Data for the 50 Reference Chemicals, ATLA 26, 571-616.

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