Sodium pentobarbital

CAS: 57-33-0
MF: $C_{11}H_{17}N_2O_3Na$
MW: 248.3
Solubility: Very slightly soluble in water, carbon tetrachloride, acetone and methyl alcohol [1].

Pentobarbital (free acid; active substance)
MF: $C_{11}H_{18}N_2O_3$
MW: 226.3

Major uses
Pentobarbital and its sodium salt are short-acting barbiturates (first prepared in 1930). They are the central nervous system (CNS) depressants and are prescribed for severe intractable insomnia. It has also been used orally and parenteral as pre-medication prior to surgery [2].

Human toxicity
CNS depression with and without respiratory depression, hypotension, and hypothermia are the most consistent findings. Pentobarbital overdose may be complicated by the development of renal tubular necrosis, muscle necrosis, hypothermia, bullous skin lesions, pneumonia, and hypoglycemia. Also cardiovascular collapse, cardiac arrest and respiratory arrest may occur following severe intoxication [2, 3].

The fatal dose in non-addicted adults is estimated at 3 to 6 g [3].

Coma in non-addicted adults may occur with blood concentration levels of 18 mg/l. A severe intoxication resulting in respiratory depression and hypotension may occur at levels of 24 mg/l and greater [3]. Potentially lethal blood concentration of pentobarbital is approximately 30 mg/l; however, some patients have survived much higher blood concentrations [1].

Kinetic data
Absorption: ≈ 100%. Rapid absorption, with apparent action in 15 to 30 min [2, 3].

Volume of distribution: 0.5-1 l/kg [2, 3]

The plasma half-life: 20-30 h, mean: 27 h [2].

Time to peak: 1 h [2].

Protein binding: 45% to 70% [3].

Metabolism and excretion
Pentobarbital is almost completely eliminated by metabolic processes. Three major metabolites have been recognized, and they are 3'-hydroxypentobarbital (7% as the (d) isomer and 30% as the (l) isomer), 3'-oxypentobarbital (7-14%), and a 3'-carboxy-pentobarbital (10-15%). In addition, N-glycoside conjugate (13%) has been identified [2].

Metabolites more toxic than pentobarbital: none.

Excretion: The major route of elimination is via the kidneys with approximately 80% of the dose excreted in the urine over 5 days, with only 1% of the dose as unchanged drug [2, 3].

Pharmacological and toxicological mechanisms
Pentobarbital depresses the CNS. Part of this action may relate to interference with synaptic transmission and multi-neuronal connections. A direct local anesthetic effect has also been demonstrated. Barbiturates have multiple actions including enhancement of GABAergic excitations, reduction of glutaminergic and cholinergic excitations, reduction in pre-synaptic calcium entry and non-synaptic sodium and potassium conductance and blockage of repetitive firing. Brain function depression is associated with parallel dose-dependent reduction in cerebral metabolic rate and blood flow [2].

Target organ: CNS [3].

References

1. HSDB, TOXNET (2006).
2. *Therapeutic drugs*, ed. C. Dollery, Vols. 1 & 2, London: Churchill Livingstone (1993).
3. Poisindex, Thomson Micromedex (2006).

Written by Cecilia Clemedson, April 2006; revised March 2007
Cecilia@Stifud.se