

# Orphenadrine hydrochloride

CAS: 341-69-5

MF: C<sub>18</sub>H<sub>23</sub>NO · HCl

FW: 305.9

Orphenadrine is soluble in water.

## Major uses

Orphenadrine is a diphenhydramine analogue (synthesized and described in 1951), which is used as an antidepressant agent, and for medication of Parkinson's disease. It has some antihistaminic activity and can be used as a skeletal muscle relaxant [1].

## Human toxicity

The range of toxicity is variable and unpredictable. The therapeutic daily dose is up to 300 mg as the hydrochloride or citrate salt.

Among the central nervous system (CNS) symptoms and signs are epileptiform seizures, tremor, mydriasis, nystagmus, shock, and coma. Cardiotoxicity can include disturbance in the cardiac rhythm, tachycardia, and increased blood pressure. The lethal dose is from 2 to 3 g, with respiratory failure and/or cardiac arrest in severe intoxications [2, 3]. At the lethal intoxication, liver degeneration and necrosis were observed [4]. Death usually occurs 3 to 5 h after the ingestion of a lethal dose [5].

The therapeutic serum concentration is in the range of 0.03-0.85 mg/l; the toxic level is approximately 2 mg/l; the lethal level is in the range of 4-8 mg/l [3]. The mean lethal serum concentration, based on the values from several handbooks, is 4.8 mg/l [6].

## Kinetic data

*Absorption:* good.

*Kinetics* is first-order for the therapeutic dose, and possibly biphasic for the overdose situation [6].

*Volume of distribution:* 6 l/kg.

*Accumulation in vital organs:* liver, CNS, and lung [6, 7].

*Blood protein binding:* 20-95% [6].

*Peak plasma level* is reached in 3-4 h.

*Elimination half-life* is about 6 h for the therapeutic dose and 15 h for the overdose situation [6].

*Passage of blood-brain barrier:* free [6].

## Metabolism and excretion

Orphenadrine undergoes rapid biotransformation with only 8% of the administered dose excreted unchanged. Other products found in urine include nororphenadrine

(8%), dinorphenadrine (4%), orphenadrine-N-oxide (5%), conjugated *o*-methylbenzhydroxyacetic acid (13%), and conjugated *o*-methylbenzhydrol (8%). The minor metabolites are *o*-methylbenzhydrol (0.4%) and *o*-methylbenzhydroxyacetic acid (0.2%) [8, 9].

*Excretion:* Approximately 60% of an oral dose is excreted in the urine in 72 h. Up to 30% of a dose may be eliminated unchanged if the urine is maintained at an acidic pH [10, 11].

### **Toxicological mechanism**

Orphenadrine is anticholinergic drug, which competitively antagonize acetylcholine at the neuroreceptor sites. Central nervous system (CNS), cardiac muscle, smooth muscle and exocrine gland (pancreas) are most affected. Reversal of this antagonism is achieved by increasing the available acetylcholine [1, 2, 11].

**Target organs:** CNS, heart, liver (histopathological organ lesions) [6].

### **References**

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