Colchicine

CAS number: 64-86-8
MF: $C_{22}H_{25}NO_6$
FW: 399.4
Solubility: poorly soluble in water (1:20) and freely soluble in alcohol.

Major use
Colchicine is a naturally occurring alkaloid extracted from the flowers of the Autumn crocus *Colchicum autumnale* and related species. It is an anti-inflammatory drug widely used in the treatment of gouty arthritis as well as a variety of other medical conditions.

Human toxicity
Colchicine is poisoning at very low doses; e.g. as little as 8-11 mg has been associated with death [2]. Systemic poisoning can occur from oral or intravenous exposure. Nausea, vomiting, severe abdominal pain, respiratory distress, renal failure, metabolic acidosis, and cardiovascular collapse are common following overdose. Death within 48 h is generally secondary to rapidly progressive multiorgan failure [1].

The therapeutic daily oral doses for acute gouty arthritis are between 0.5-2 mg [3].

Death has occurred after administration of only 6 mg to an adult [4]. According to Kaye, the minimal lethal dose is 30 mg/70 kg person [5].

The therapeutic blood (its serum or plasma) concentrations are in the range of 0.0003-0.03 mg/l [6]. The fatal blood concentrations of colchicine vary between 0.02 and 0.25 mg/l [4].

Kinetic data
Absorption: In pharmacological doses, colchicine is rapidly absorbed from the gastro-intestinal tract (GIT). After oral administration of a therapeutic dose, bioavailability in healthy subjects was found to be 25% to 40% [2]. Toxic doses are likely to prolong the rate of absorption due to the antimitotic effect on the GIT epithelium.

Colchicine remains in tissue for a prolonged period, up to 10 days. It accumulates in the bone marrow, testicles, lungs, kidneys, liver, spleen, gastro-intestinal wall, and leukocytes [7].

Volume of distribution is 1-2 l/kg [3].

Plasma protein binding for colchicine is about 50%.

Peak plasma levels occur within 0.5 to 2 h [1].

Plasma half-life is in the range of 10-30 h after oral dose [8], and 10-60 min after intravenous dose [3].

Metabolism and excretion
Colchicine is partly deacetylated and partly demethylated in the liver. It is also slowly metabolized in other organs.

About 10-20% of colchicine is excreted unchanged in urine; between 5 and 50% of an intravenous dose is eliminated in the bile within 48 h [3].

Toxicological mechanism
Colchicine is an inhibitor of cell cycle and cell division. It binds to protein tubulin of microtubules and blocks its polymerization, leading to disturbance of the whole microtubule apparatus, followed by a mitosis arrest and cell death. Microtubules are involved in the maintenance of cell shape and structure, as well as in the mitotic spindle formation during mitosis.

Target organ: liver.

References
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