Tetracycline hydrochloride

CAS: 64-75-5
MF: $C_{22}H_{24}N_2O_8 \cdot HCl$
FW: 480.9
Soluble in water (10.9 mg/ml at 28±4°C, pH 7.0-8.5) and in alcohols (>20 mg/ml).

Major use
Tetracycline is a broad spectrum bacteriostatic antibiotic. It is effective against many gram-positive (e.g. Staphylococcus and Streptococcus) and gram-negative (e.g. Clostridium, Pseudomonas and Haemophilus) bacterial infections, as well as against Rickettsia, Chlamydia, Borrelia, Mycoplasma etc.

Human toxicity
Acute toxicity of tetracycline is relatively low. Severe toxicity following overdose is unlikely [1].

At higher oral doses tetracycline may produce gastrointestinal irritation, with nausea, vomiting, and diarrhea, as well as renal failure. Bone and teeth discoloration are known to occur in humans under clinical treatment with high levels of tetracycline. The drugs of the tetracycline group may produce renal disease and renal impairment [2]. Tetracyclines, particularly demeclocycline, may cause renal medullary toxicity, such as proximal tubular damage with polyuria, glucosuria, and aminoaciduria [3].

The recommended oral daily dosage: 1-2 g/day (therapeutic dose). Oral doses of 250 to 500 mg every 6 h produce plasma concentrations ranging from 1 to 5 mg/l (therapeutic blood concentrations) [1]. The therapeutic blood levels ranged 5-10 mg/l; whereas toxic blood level was estimated to be 30 mg/l [4].

Kinetic data
Absorption: tetracycline is well absorbed (70-80%) from gastro-intestinal tract by oral administration. Tetracycline is widely distributed in the body; the highest levels are present in the liver and kidney.

Volume of distribution: 1 to 2 l/kg [1].

Protein binding: 20-35% [1]; 24-65% (IPCS INCHEM, via Internet).

Peak serum concentration (2-3 mg/l) is reached after 2 to 4 h after an oral therapeutic dose.

The plasma half-life was reported to be about 8-10 h.

Elimination half-life: 6-8 h in adults with normal renal excretory function. In individuals with renal insufficiency – up to 30-79 h [5].

Metabolism and excretion

The knowledge is restricted; the metabolism is negligible. Tetracycline seems to be stable at the neutral pH, however, it is dehydroxylated at the acidic conditions, and some of its stable derivatives are produced.

Excretion: 40-55% of tetracycline is excreted from the body primarily by the kidney, the less part is excreted by the liver followed by reabsorption from the gastrointestinal tract [3]. About 60% is excreted unchanged in the urine during 24 h [1].

Toxicological mechanisms
Tetracycline inhibits protein synthesis (elongation) by preventing binding of aminoacyl-tRNA to the 30S subunit.

There are indications that high doses of tetracycline cause a negative nitrogen balance in the body, with related rise in blood nonprotein nitrogen. Increased urinary excretions of riboflavin and sometimes amino acids (tryptophan, histidine and threonine) have been recorded [5].

Target organs: kidney and liver.

References
1. Poisindex, Thomson Micromedex (2005).
2. Phillips, M.E., Eastwood, J.B., Curtis, J.R., Gower, P.E., de Wardener, H.E. (1974) Tetracycline poisoning in renal failure. Br Med J 2, 149-151.
3. *Casarett and Doull's Toxicology (The Basis Science of Poisons)* (1986) Klaassen, C.D., Amdur, M.O., Doull, J. eds., Macmillan Publishing Company.
4. Uges, D.R.A. (1996) Therapeutic and toxic drug concentrations. The TIAF Bulletin 26, Supplement 1, 1-34.
5. Greenberg, P.A., Sanford, J.P. (1967) Removal and absorption of antibiotics in patients with renal failure undergoing peritoneal dialysis. Ann Int Med 66(3), 465-479.

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