

PHARMACOLOGY-III
UNIT-II
TOPIC: TETRACYCLINES



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*Shaping Lives...
Empowering Communities...*

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TETRACYCLINES

INTRODUCTION • Obtained from soil actinomycetes.

- Introduced in 1948 by Benjamin Minge Duggar (chlortetracycline, aureomycin).
- Tetracyclines is broad spectrum antibiotic having four cyclic ring nucleus.
- All tetracyclines are slightly bitter solids, weakly water soluble, their hydrochlorides are more soluble.
- Aqueous solutions are unstable. Tetracyclines available in India for clinical use:- Tetracycline, Oxytetracycline, Demeclocycline, Doxycycline, Minocycline.

MECHANISM OF ACTION

- Tetracyclines are primarily bacteriostatic.
- Inhibit protein

synthesis by binding to 30s ribosome in susceptible organism.

- Inhibit binding of aminoacyl tRNA to the acceptor site of mRNA peptide chain fails to grow
- Entry of these agents into susceptible organisms is mediated both by passive diffusion and by an energy-dependent transport protein mechanism unique to the bacterial inner cytoplasmic membrane.

D. Pharmacokinetics

Absorption: All tetracyclines are adequately but incompletely absorbed after oral ingestion.

However, taking these drugs concomitantly with dairy foods in the diet decreases absorption due to the formation of nonabsorbable chelates of the tetracyclines with calcium ions. Nonabsorbable chelates are also formed with other divalent and trivalent cations (for example, those found in magnesium and aluminum antacids and in iron preparations). [Note: This presents a problem if a patient self-treats the epigastric upsets caused by tetracycline ingestion with antacids

Doxycycline and minocycline are almost totally absorbed on oral administration. Currently, doxycycline is the preferred tetracycline for parenteral administration.

Typical therapeutic applications of tetracyclines.

Distribution: The tetracyclines concentrate in the liver, kidney, spleen, and skin, and they bind to tissues undergoing calcification (for example, teeth and bones) or to tumors that have a high calcium content (for example, gastric carcinoma). Penetration into most body fluids is adequate.

Although all tetracyclines enter the cerebrospinal fluid (CSF), levels are insufficient for therapeutic efficacy, except for minocycline. Minocycline enters the brain in the absence of inflammation and also appears in tears and saliva. Although useful in eradicating the meningococcal carrier state, minocycline is not effective for central nervous system infections.

All tetracyclines cross the placental barrier and concentrate in fetal bones and dentition.

Fate: All the tetracyclines concentrate in the liver, where they are, in part, metabolized and conjugated to form soluble glucuronides. The parent drug and/or its metabolites are secreted into the bile. Most tetracyclines are reabsorbed in the intestine via the enterohepatic circulation and enter the urine by glomerular filtration. Obstruction of the bile duct and hepatic or renal dysfunction can increase their half-lives. Unlike other tetracyclines, doxycycline can be employed for treating infections in renally compromised patients, because it is preferentially **excreted via the bile into the feces.**

E. Adverse effects

Effect of antacids and milk on the absorption of tetracyclines.

Gastric discomfort: Epigastric distress commonly results from irritation of the gastric mucosa and is often responsible for noncompliance in patients treated with these drugs. The discomfort can be controlled if the drug is taken with foods other than dairy products.

1. Effects on calcified tissues: Deposition in the bone and primary dentition occurs during calcification in growing children. This causes discoloration and hypoplasia of the teeth and a temporary stunting of growth.
2. Fatal hepatotoxicity: This side effect has been known to occur in pregnant women who received high doses of tetracyclines, especially if they were experiencing pyelonephritis.
3. Phototoxicity: Phototoxicity, such as severe sunburn, occurs when a patient receiving a tetracycline is exposed to sun or ultraviolet rays. This toxicity is encountered most frequently with tetracycline.
4. Vestibular problems: These side effects (for example, dizziness, nausea, and vomiting) occur particularly with minocycline, which concentrates in the endolymph of the ear and affects function. Doxycycline may also cause vestibular effects.
5. Pseudotumor cerebri: Benign, intracranial hypertension characterized by headache and blurred vision may occur rarely in adults. Although discontinuation of the drug reverses this condition, it is not clear whether permanent sequelae may occur.
6. Superinfections: Overgrowths of *Candida* (for example, in the vagina) or of resistant staphylococci (in the intestine) may occur. Pseudomembranous colitis due to an overgrowth of *Clostridium difficile* has also been reported.