Tetracyclines

Introduction

- Tetracyclines are a group of broad-spectrum, bacteriostatic antibiotics that inhibit protein synthesis in bacteria.
- Discovered in the 1940s, they are effective against a wide variety of gram-positive, gram-negative, intracellular organisms, and atypical pathogens (e.g. *Mycoplasma*, *Chlamydia*, *Rickettsia*).
- They are named for their characteristic four-ring structure. Resistance to tetracyclines has become common, but some derivatives (like doxycycline and minocycline) remain widely used.

Classification



1. Short-acting Tetracyclines

- Tetracycline
- Oxytetracycline
- **Half-life:** 6–8 hours

2. Intermediate-acting Tetracyclines

- Demeclocycline
- **Half-life:** 12 hours

3. Long-acting Tetracyclines

- Doxycycline
- Minocycline
- **Half-life:** 16–20 hours

4. Glycylcyclines (Tetracycline Derivatives)

- Tigecycline
- Broader spectrum, effective against some resistant bacteria

Mechanism of Action

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- **Tetracyclines:**
  - Bind reversibly to the 30S subunit of bacterial ribosomes
  - Inhibit the binding of aminoacyl-tRNA to the mRNA-ribosome complex
  - This prevents the addition of amino acids to the growing peptide chain
    - **Inhibits protein synthesis**
- **Bacteriostatic** effect

Pharmacokinetics (ADME)

Absorption:

- Oral absorption varies:
  - Good: **Doxycycline**, **Minocycline**
  - Poorer: **Tetracycline**, especially with food
- Absorption is reduced by divalent and trivalent cations (Ca^{2+}, Mg^{2+}, Fe^{3+}, Al^{3+}) found in antacids, dairy, and iron supplements

Distribution:

- Widely distributed, including lungs, prostate, intracellularly
- Cross placenta, found in teeth and bones
- Enter CNS in low concentrations (Minocycline achieves better levels)

Metabolism and Excretion:

- **Tetracycline:** Excreted renally (dose adjustment in renal failure)
- **Doxycycline and Minocycline:** Mainly excreted in bile and feces (safe in renal failure)

Pharmacodynamics

- Bacteriostatic
- Time-dependent activity
- Inhibits growth, allowing host immune system to eliminate infection
- Effective against both extracellular and intracellular pathogens

Antimicrobial Spectrum

Gram-positive bacteria

- *Streptococcus*, *Staphylococcus* (including some MRSA strains)

Gram-negative bacteria

- *Haemophilus influenzae*, *Brucella*, *Vibrio cholerae*

Atypical organisms

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- *Mycoplasma pneumoniae*
- *Chlamydia trachomatis*, *C. pneumoniae*
- *Rickettsia* (typhus, Rocky Mountain spotted fever)
- *Coxiella burnetii* (Q fever)

Other organisms

- *Borrelia burgdorferi* (Lyme disease)
- *Treponema pallidum* (alternative to penicillin in syphilis)
- *Helicobacter pylori* (part of combination regimens)
- *Plasmodium* spp. (adjunct in malaria treatment)

Therapeutic Uses

1. **Respiratory tract infections**
    - Atypical pneumonia (*Mycoplasma*, *Chlamydia*)
2. **Sexually transmitted infections**
    - Chlamydia, syphilis (penicillin allergy), pelvic inflammatory disease
3. **Rickettsial infections**
    - Typhus, Rocky Mountain spotted fever
4. **Lyme disease** – *Borrelia burgdorferi*
5. **Acne vulgaris** – especially long-term doxycycline or minocycline
6. **Malaria prophylaxis and treatment** – doxycycline
7. **Periodontal infections**
8. **H. pylori eradication regimens**
9. **Plague, tularemia**, and **brucellosis** (with other agents)

Adverse Effects

1. Gastrointestinal Distress

- Nausea, vomiting, epigastric pain
- Esophageal irritation (doxycycline) – advise taking with water and staying upright

2. Photosensitivity

- Skin rash and sunburn with sun exposure (especially doxycycline)

3. Teeth and Bone Effects

- Permanent yellow-brown discoloration of teeth
- Inhibition of bone growth in fetuses and children

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- Contraindicated in children <8 years and pregnancy

4. Superinfections

- Overgrowth of non-susceptible organisms (*Candida*, *Clostridioides difficile*)

5. Hepatotoxicity

- Especially in high doses or pregnancy

6. Nephrotoxicity

- Mostly with outdated tetracycline → **Fanconi syndrome** (renal tubular dysfunction)

7. Vestibular Toxicity

- With **minocycline**: dizziness, vertigo

Contraindications

- **Pregnancy** (risk to fetus: teeth staining, bone growth suppression)
- **Children <8 years old**
- **Renal failure**: avoid tetracycline (but doxycycline is safe)
- Hypersensitivity to tetracyclines

Drug Interactions

- **Antacids, iron, dairy products**: reduce absorption (chelation)
- **Oral contraceptives**: may reduce effectiveness
- **Warfarin**: may enhance anticoagulant effect (inhibits vitamin K synthesis)
- **Retinoids** (e.g., isotretinoin): increased risk of intracranial hypertension

Dose and Route of Administration

Tetracycline

- 250–500 mg orally every 6 hours
- Taken on an **empty stomach**, 1 hour before or 2 hours after meals

Doxycycline

- 100 mg orally or IV every 12 hours
- Used widely due to once or twice daily dosing, good GI tolerance

Minocycline

- 100 mg orally every 12 hours

Note: Always advise patients to take tetracyclines with a full glass of water and remain upright for 30 minutes to prevent esophageal irritation.

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