Protein Synthesis Inhibitors

A number of antibiotics exert their antimicrobial effects by targeting bacterial ribosomes and inhibiting bacterial protein synthesis. Most of these agents exhibit bacteriostatic activity.

Bacterial ribosomes differ structurally from mammalian cytoplasmic ribosomes and are composed of 30S and 50S subunits (mammalian ribosomes have 40S and 60S subunits). The high concentrations of drugs such as chloramphenicol or the tetracyclines may cause toxic effects as a result of interaction with mitochondrial mammalian ribosomes, because the structure of mitochondrial ribosomes more closely resembles bacterial ribosomes.

- **Tetracyclines**

Tetracycline, Demeclocycline, Doxycycline, Minocycline.

* **Mechanism of action**

Tetracyclines concentrate intracellularly in susceptible organisms. The drugs bind reversibly to the 30S subunit of the bacterial ribosome.

This action prevents binding of tRNA to the mRNA– ribosome complex, thereby inhibiting bacterial protein synthesis

- **Antibacterial spectrum**

The tetracyclines are bacteriostatic antibiotics effective against a wide variety of organisms,
including gram-positive and gram-negative bacteria, protozoa, spirochetes, mycobacteria, and atypical species.

- They are commonly used in the treatment of acne and Chlamydia infections.

Pharmacokinetis

Tetracyclines are adequately absorbed after oral ingestion . Administration with dairy products or other substances that contain divalent and trivalent cations (for example, magnesium, calcium and aluminum antacids, or iron supplements) decreases absorption, Both doxycycline and minocycline are available as oral and intravenous (IV) preparations.

- The tetracyclines concentrate have site specific concentration , they bind to tissues undergoing calcification (for example, teeth and bones). Only minocycline and doxycycline achieve therapeutic levels in the cerebrospinal fluid (CSF).
- All tetracyclines cross the placental barrier and concentrate in fetal bones and dentition.
- Tetracycline is primarily eliminated unchanged in the urine, whereas minocycline undergoes hepatic metabolism and is eliminated to a lesser extent via the kidney. Doxycycline is preferred in patients with renal dysfunction, as it is primarily eliminated via the bile into the feces.

Adverse effects

1. Gastric discomfort

Epigastric distress commonly results from irritation of the gastric mucosa

2. **Effects on calcified tissues**

Deposition in the bone during the calcification process in growing children result in discoloration and hypoplasia of teeth therefore, the use of tetracyclines is contraindicated in pediatrics.

3. Hepatotoxicity

Rarely hepatotoxicity may occur with high doses, particularly in pregnant women and those with preexisting hepatic dysfunction

4. Phototoxicity

Severe sunburn may occur in patients receiving a tetracycline who are exposed to sun or ultraviolet rays.

5. Vestibular dysfunction

Dizziness, vertigo, and tinnitus may occur particularly with minocycline.

6. Pseudotumor cerebri

Benign, intracranial hypertension characterized by headache and blurred vision may occur rarely in adults.

Contraindications

The tetracyclines should not be used in pregnant or breast-feeding women or in children less than 8 years of age.