17/MHS06/067

PHARMACOLOGY 302

A NAMED BACTERIAL PROTEIN SYSNTHESIS INHIBITOR:

**TETRACYCLINES**

The tetracyclines are a large group of drugs with a common basic structure and activity.

All tetracyclines have a nucleus of four cyclic rings.They are called broad spectrum antiboitics.

All tetracyclines are slightly bitter solids, weak water soluble, however their hydrochlorides are **Tetracyclines** are classified as :short acting (chlortetracycline, tetracycline, oxytetracycline),

intermediate acting (demeclocycline and methacycline), or long-acting (doxycycline and minocycline) based on serum half-livesmore soluble.

 **MECHANISM OF ACTION**

They inhibit protein synthesis by binding to 30S ribosomal subunit at a site that blocks binding of charged tRNA to the 30S site of the ribosome. They are bacteriostatic.

Tetracyclines can inhibit mammalian protein synthesis, but because they are "pumped" out of most mammalian cells do not usually reach concentrations needed to significantly reduce mammalian protein synthesis. The main mechanisms of resistance to tetracycline, is decreased intracellular accumulation due to either impaired influx or increased efflux by an active transport protein pump.

**INDICATION OF USE**

 A tetracycline is the drug of choice in infections with Mycoplasma pneumoniae, chlamydiae, rickettsiae, and some spirochetes, cholera, Brucellosis, Plague, relapsing fever due to Borrelia recurrentia, Venereal diseases.

They are used in combination regimens to treat gastric and duodenal ulcer disease caused by Helicobacter pylori.

They may be employed in various gram-positive and gram-negative bacterial infections, including Vibrio infections.

A tetracycline in combination with an aminoglycoside is indicated for plague, tularemia, and brucellosis.

Tetracyclines are sometimes employed in the treatment of E. histolytica or P. falciparum .Other situations where tetracyclines can be used:

Urinary tract infections, amoebiasis, as an adjuvant to quinine or sulfadoxine-pyrimethamine for chloroquine resistant strains of malaria, acne, chronic obstructive lung disease.

ADVERSE EFFECTS:

Gastrointestinal adverse effects:

Nausea, vomiting, and diarrhea are the most common and these effects are attributable to direct local irritation of the intestinal tract.

Tetracyclines suppress susceptible coliform organisms and causes overgrowth of Pseudomonas, Proteus, staphylococci, resistant coliforms, clostridia, and Candida.

 This can result in intestinal functional disturbances, anal pruritus, vaginal or oral candidiasis, or enterocolitis (associated with

Clostridium difficile) with shock and death.

 Pseudomembranous enterocolitis should be treated with metronidazole.

Bony structures and teeth:

Tetracyclines are readily bound to calcium deposited in newly formed bone or teeth in young children. It causes discoloration, and enamel dysplasia;

they can also be deposited in bone, where it may cause deformity or growth inhibition.

If the drug is given to children under 8 years of age for long periods, similar changes can result.

They are hepato and nephrotoxic drug, they also induce sensitivity to sunlight (demeclocycine) and vestibular reactions (doxycycline, and minocycline].

**TOXICITY:**

- Liver damage. Tetracyclines can cause acute hepatic necrosis in pregnant woman.

- Kidney damage. All tetracyclines except doxycyclines accumulate and enhance kidney damage.

Phototoxicity. Distortion of nails, sun burn like reaction on exposed parts is seen in some individuals.

Increased intracranial pressure

Diabetes insipidus

Antianabolic effect eg tetracyclines.

Vestibular toxicity eg ataxia, vertigo mostly with the minocyclines.