

## **SULFONAMIDES**

### **Mechanism of action.**

Sulfonamides competitively inhibit dihydropteroate synthase, the enzyme which catalyzes the incorporation of PABA into dihydrofolic acid. Folic acid is required for purine and DNA synthesis and thus bacterial growth is inhibited. Mammalian cells and bacteria that use preformed folic acid are not affected.

Sulfonamides are broad spectrum (including protozoa) and bacteriostatic.

**Therapeutic uses. Sulfonamides were widely used in the prevention and treatment of local and systemic infections in all species but now resistance is common**

**Example of Sulfonamides used in veterinary medicine include the following:**

- 1-Sulfamethazine:-** is used in cattle, sheep, and swine.
- 2. Sulfadimethoxine:-** is a long-acting sulfonamide. It is more soluble and less toxic than sulfamethazine.
- 3. Sulfachlorpyridazine :-**is a rapidly absorbed and rapidly excreted sulfonamide used orally in calves under 1 month of age and in swine for the treatment of respiratory and enteric infections, especially colibacillosis.
- 4. Sulfamethoxazole** is used to treat urinary tract infections in small animals.

Thus high concentrations may be attained in urine with minimal danger of renal crystalluria

- 5. Sulfacetamide** is the only sulfonamide that can be prepared as the sodium salt at neutral pH and thus can be used in ophthalmic preparations.

**6. Sulfasalazine** is an “enteric” sulfonamide employed in the therapy of colitis and inflammatory bowel disease in dogs and cats.

7. Other sulfonamides used in veterinary medicine are **sulfathiazole** and **sulfaquinoxaline**. Potentiated sulfonamides are fixed combinations of a **sulfonamide** with **trimethoprim** or **ormetoprim**.

Note ;Trimethoprim and ormetoprim inhibit dihydrofolate reductase in bacteria (but not mammalian cells) and thus block the formation of tetrahydrofolic acid essential for purine and DNA synthesis.

#### **Adverse effects:-**

1. Renal crystalluria due to precipitation of sulfonamides in neutral or acidic urine may occur with large or prolonged doses or inadequate water intake, especially with the order ,less soluble sulfonamides such as sulfathiazole .
2. Keratoconjunctivitis sicca (KCS) may be observed in dogs treated with sulfonamides, such as sulfadiazine, which contain the pyrimidine nucleus.
3. Hypoprothrombinemia, thrombocytopenia, and anemia occur rarely and are probably immune-mediated reactions. Sulfonamides should not be used in animals with preexisting bleeding disorders.

#### **FLUOROQUINOLONES.**

Mechanism of action. The fluoroquinolones inhibit bacterial DNA gyrase, an enzyme which controls DNA supercoiling as the replicating strands separate. Inhibition of gyrase results in degradation of chromosomal DNA at the replicating fork. Fluoroquinolones are broad spectrum and bactericidal.

#### **Therapeutic uses.**

1. **Enrofloxacin** is used in the treatment of dermal, respiratory, and urinary tract infections(including prostatitis) in dogs, cats, and birds and in respiratory infections in cattle .
2. **Danofloxacin** is used for the treatment of bovine respiratory infections

3. **Difloxacin** is used for treatment of dermal, respiratory, and urinary tract infections in dogs .

4. **Orbifloxacin** and Marbofloxacin are used for the treatment of dermal, respiratory, and urinary tract infections of dogs and cats. Orbifloxacin is used for susceptible Gram(–) infections in horses.

#### **Adverse effects.**

Toxicity associated with fluoroquinolones is erosion of articular cartilage in young dogs and foals, particularly, if they are used at high doses for longer than 14 days in rapid growth phase.

Retinal degeneration has been reported due to acute and diffuse retinal damage in cats .

#### **Metronidazole.**

##### **Mechanism of action.**

Metronidazole is taken up by anaerobic bacteria and protozoa are reduced to a cytotoxic metabolite, which disrupts DNA.

It is bactericidal against most anaerobes and is active against protozoa, including Giardia and Trichomonas spp.

##### **Therapeutic uses.**

#### **Metronidazole**

Treatment of severe infections caused by anaerobic pathogens, especially brain abscesses and pelvic, genitourinary tract, and respiratory infections, used in dogs, cats, and horses .

Metronidazole is also used to treat protozoal infections such as giardiasis and trichomoniasis in dogs and cats.

#### **Rifampin .**

##### **Mechanism of action.**

Rifampin inhibits DNA-dependent RNA polymerase, which prevents initiation of RNA synthesis. It is bactericidal for mycobacteria and Gram(+) pathogens. It is effective against intracellular infections.

#### **Therapeutic uses.**

Rifampin is combined with erythromycin in the treatment of R. equi infections in foals. Rifampin is also used in combination with other antifungal agents to treat fungal infections such as aspergillosis or histoplasmosis in dogs and cats when infection involves the CNS.

#### **Adverse effects.**

Side effects are rare. Hepatotoxicity may occur in animals with preexisting liver disease. Rifampin may produce red-orange colored urine, sweat, and saliva but this is not harmful.

### **Nitrofurans**

#### **Mechanism of action.**

The nitrofurans are reduced by bacteria to reactive intermediates that inhibit nucleic acid synthesis. They produce DNA fragmentation and may also block mRNA translation. They are broad spectrum and bacteriostatic.

#### **Therapeutic uses.**

Nitrofurantoin is occasionally used in the treatment of lower urinary tract infections in dogs and cats.

Nitrofurazone is used topically as an antibacterial ointment, powder, and water-soluble wound dressings in all species.

**Adverse effects.**

Side effects are rare. Nausea, vomiting, and diarrhea may occur in dogs and cats following oral administration. Nitrofurans may not be used in food-producing animals (include topically) because they have been shown to be potential carcinogens in laboratory animals.