



ANTI BACTERIAL SULPHONAMIDES

Sulfonamide is a functional group (a part of a molecule) that is the basis of several groups of drugs, which are called sulphonamides, sulfa drugs or sulpha drugs. The original antibacterial sulfonamides are synthetic (nonantibiotic) antimicrobial agents that contain the sulfonamide group.

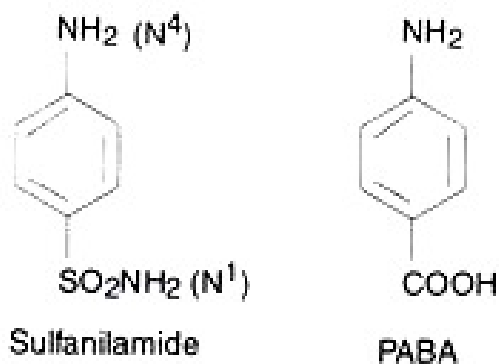
Mechanism of action

Sulfonamides interfere with folic acid synthesis by preventing addition of para-aminobenzoic acid (PABA) into the folic acid molecule through competing for the enzyme dihydropteroate synthetase.

Sulfonamides compete with paraaminobenzoic acid (PABA) for the catalytic site of the enzyme dihydropteroate synthetase thereby inhibiting conversion of PABA to folic acid in bacteria. This action of sulfonamide is selective over bacteria without interfering animal cells.

General Properties

Chemically sulfa drugs are amphoteric. They behave as weak organic acid with pKa 4.79 to 8.56. Though they are weakly soluble in water, their solubility is increased at alkaline pH. Sodium salts are however easily soluble in water. The following are the basic structure of sulfanilamide and PABA.

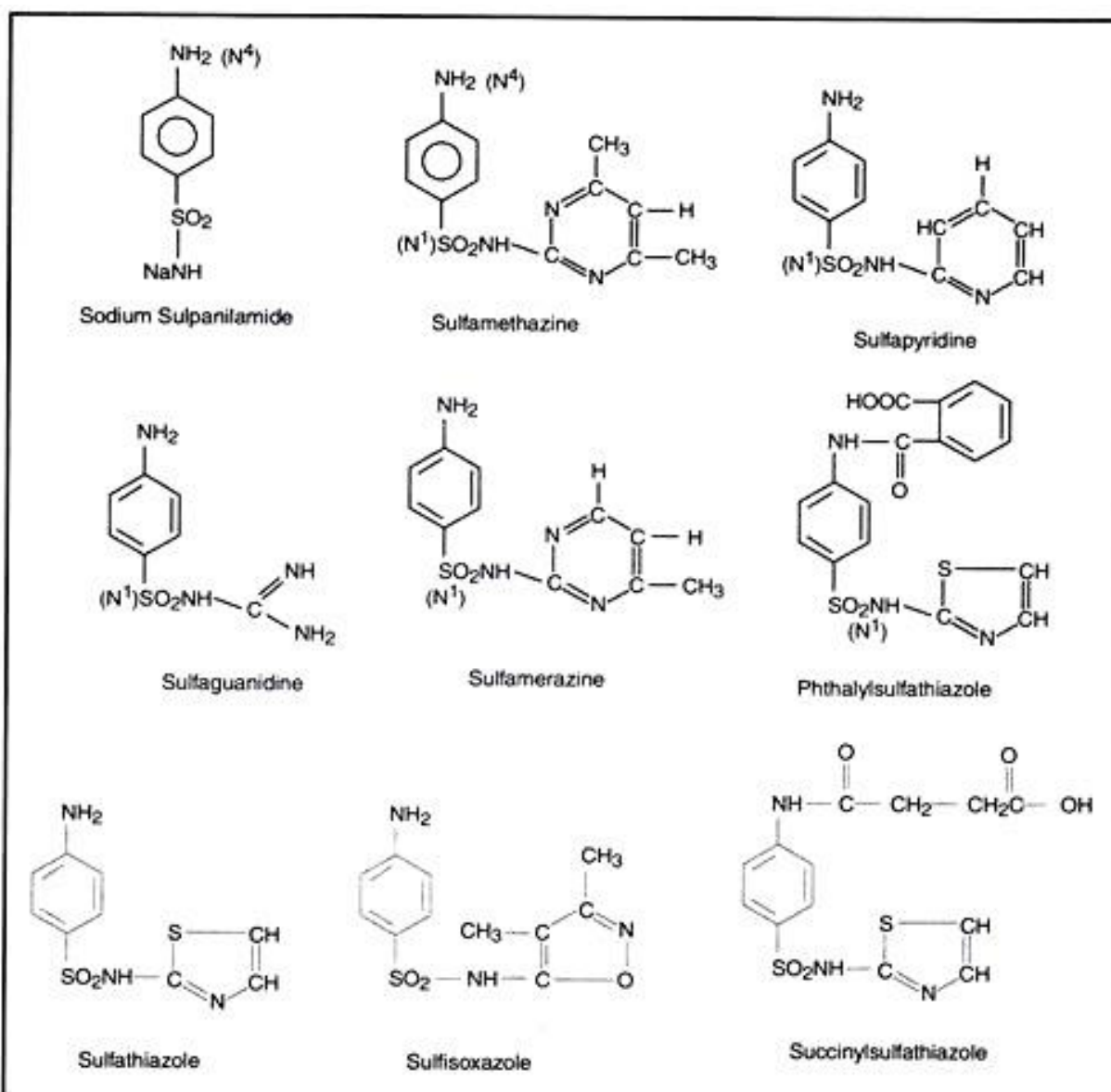


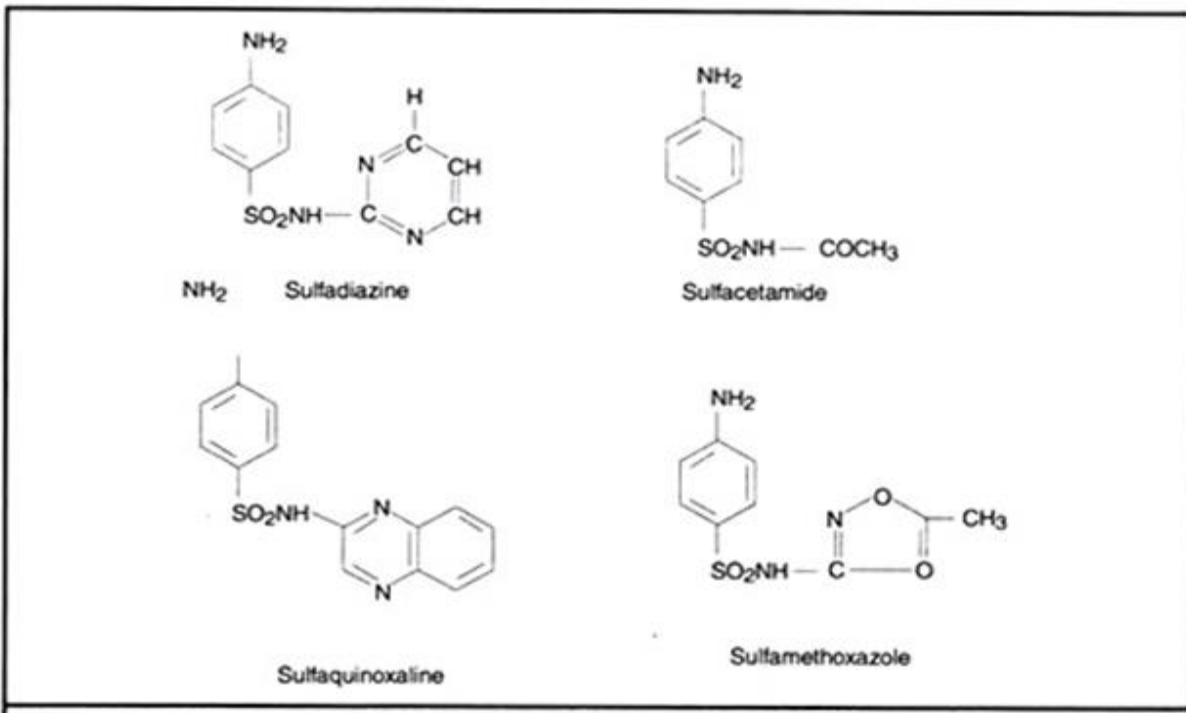
Chemistry

The nitrogen of amino group at para position is designated as N⁴ while nitrogen of SO₂ NH₂ is designated as N¹. Systemic sulfa drugs are evolved by substitution at N¹ position whereas gut active sulfa drugs are produced by substituting N⁴ position (Fig 25.2).

By substitution at N¹ and N⁴ positions about 5000 compounds are synthesized. Among them 30 are of clinical significance. Sulfanilamide and its derivatives are popularly known as sulfonamide or sulfa drug.

Structure Of Common Sulphonamides





Classification of Sulfonamides

1. Based on Chemical Structure:

(i) Both N^1 and N^4 substituted sulfonamides—
Succinyl sulfathiazole, Phthalyl sulfathiazole

(ii) N^1 substituted sulfonamides—
Sulfapyridine, Sulfathiazole, Sulfadimidine (sulfamethazine), Sulfamerazine, Sulfaphenazole, Sulfamethoxazole, Sulfadimethoxine, Sulfacetamide, Sulfamethoxypridazine, Sulfisoxazole (sulfafurazole), Silversulfadiazine, Sulfaguanidine etc.

2. Based on site of action:

(i) Gut acting sulfonamides: Succinylsulfathiazole, Phthalylsulfathiazole and Sulfaguanidine

ii) Systemic sulfonamides – N^1 substituted sulfonamides (except sulfaguanidine and sulfonamides used topically).

(iii) Renal sulfonamides – Sulfisoxazole (sulfafurazole)

(iv) Topical sulfonamides: Silversulfadiazine

(v) Ophthalmic sulfonamide: Sodiamsulfacetamide

3. Based on duration of action:

(i) Long acting – Sulfamethazine

Sulfamerazine , Sulfamethoxypridazine, Sulfaethoxypridazine

(ii) Short acting - Sulfathiazole

(iii) Intermediate acting-Sulfamethoxazole

Antimicrobial Spectrum

Sulfonamides are broad spectrum antimicrobial agents effective against bacteria, chlamydia, toxoplasma and coccidia. Mycobacteria, mycoplasma rickettsias, pseudomonas and spirochaetes are, however, resistant. They are primarily bacteriostatic but in very high concentration, especially in urinary tract, may be bactericidal.

Sulfonamide therapy should be initiated in rapidly multiplying stage of bacteria i.e. in acute disease conditions. They are less effective in chronic diseases. The sulfonamide therapy is continued till complete removal of infection.

If therapy is discontinued before the complete elimination of microorganisms, more resistant strains of bacteria can emerge.

Emergence of drug resistant bacteria is frequent. Resistance may develop due to enzyme adaptation, alternate enzyme pathway, chromosomal mutation or plasmid mediation (R-factor). Cross resistance is commonly observed.

Sulfadiazine

It is an antibiotic. Used together with pyrimethamine, it is the treatment of choice for toxoplasmosis. It is a second-line treatment for otitis media, prevention of rheumatic fever, chancroid, chlamydia, and infections by *Haemophilus influenzae*. It is taken by mouth.

Uses

- It eliminates bacteria that cause infections by stopping the production of folate inside the bacterial cell, and is commonly used to treat urinary tract infections and burns.
- In combination, sulfadiazine and pyrimethamine can be used to treat toxoplasmosis, the disease caused by *Toxoplasma gondii*.

Brand names

This drug is sold branded as Lantrisol, Neotrizine, Sulfa-Triple #2, Sulfadiazine, Sulfaloid, Sulfonamides Duplex, Sulfose, Terfonyl, Triple Sulfa, Triple Sulfas, and Triple Sulfoid.

Sulfacetamide

It is a drug which is used for the treatment of bacterial vaginitis, keratitis, acute conjunctivitis, and blepharitis. Sulfacetamide exists as a solid, slightly soluble (in water), and a weakly acidic compound (based on its pKa). Sulfacetamide has been detected in multiple biofluids, such as urine and blood.

Sulfacetamide as a medicine is available as solution, eye drops, lotion, and powder. It can also be found in the form of the sodium salt, sulfacetamide sodium.

It is available in fixed-dose combinations with prednisolone.

Uses

Sulfacetamide 10% topical lotion, is approved for the treatment of acne and seborrheic dermatitis.

Cotrimoxazole

- Cotrimoxazole is a medicine called an antibiotic. Antibiotics are used to treat or prevent certain types of infections caused by bacteria.
- Cotrimoxazole is made up of 2 medicines, **sulfamethoxazole** and **trimethoprim**.

- Cotrimoxazole called by its brand names, Septra, Bactrim, Apo-Sulfatrim, or Novo-Trimel. Cotrimoxazole comes in tablet and liquid form.

Side effects of cotrimoxazole

- Upset stomach
- Diarrhea (loose, watery stools)
- Vomiting (throwing up)
- Loss of appetite
- Headache
- Dizziness

Uses of cotrimoxazole

- Co-trimoxazole is used to treat certain bacterial infections, such as pneumonia (a lung infection), bronchitis (infection of the tubes leading to the lungs).
- Infections of the urinary tract, ears, and intestines.
- It also is used to treat 'travelers' diarrhea.

The medication could damage the kidneys or lead to kidney stones if too much of it reached the kidney at the same time (e.g., cotrimoxazole, indinavir). So consume more amount of water which helps to "dilute" the extra medication so that too much medication does not go through the kidneys at once.