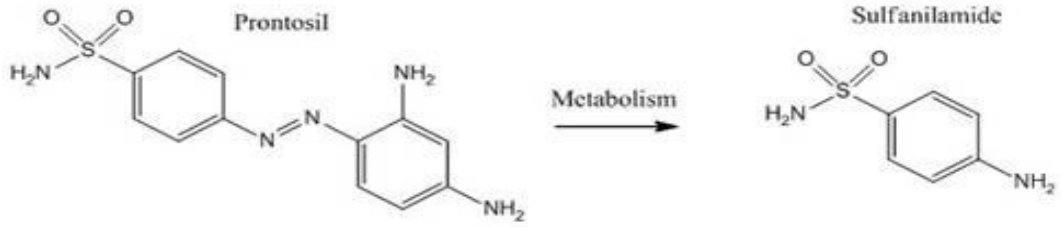
LECTURE#1

SULPHONAMIDES

The term sulphonamides are employed as a generic name for the derivatives of <u>para amino benzene sulphonamide (sulphanilamide).</u>

Sulfanilamide was the first sulfonamide developed in 1906, although it was not used as an antimicrobial agent until the late 1930s. The sulphonamides are bacteriostatic antibiotics with a wide spectrum action against most gram-positive bacteria and many gram-negative organisms..Actually, is was found to be metabolic product of prontosil, which is responsible for antibacterial activity.



Sulphonamides are total synthetic substances that are produced by relatively simple chemical synthesis. The advent of penicillin and other antibiotics has diminished the usefulness of sulphonamides. This group is also present in other compounds, such as antidiabetic agents (e.g. Tolubutamide), diuretics (e.g. chlorthiazide and its congeners, furosemide, and acetazolamide), and anticonvulsants such as sulthiame.

MECHANISM OF ACTION:

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

GENERAL CHARACTERISTICS OF SULPHONAMIDES:

- white powder
- mildly acidic in character
- form water soluble salts with bases

CLASSIFICATION OF SULPHONAMIDES:

Sulphonamides can be classified in various ways on the basis of indications and chemical structure is described below

On the basis of the indication

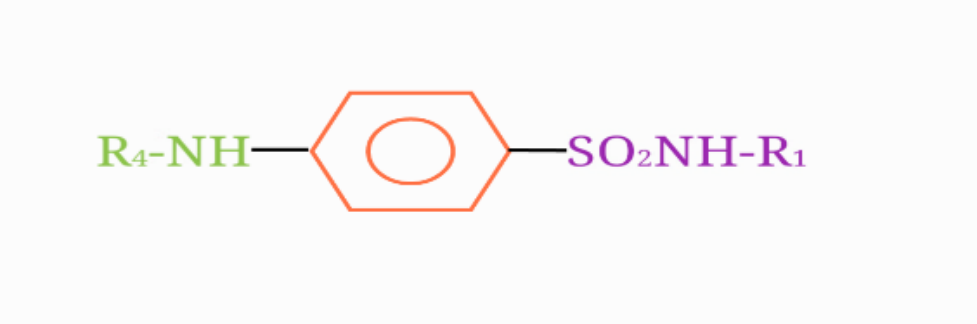
- Antibacterial agents:Sulphadiazine, Sulfisoxazole.
- Drugs used in dermatitis: Dapsone.
- Meningitis:sulphadiazine
- Leprosy:dapsone,sotaprone
- UTI: Sulphaisoxazole, Sulphathiazole
- dermatitis: Dapsone, Solapsone
- intestinal infections: Phthalylsulphathiazole, Succinyl sulphathiazole, Sulphasalazine.
- local infections: Sulpahacetamide, Mafenamide, Silver sulphadiazine.

On the basis of the chemical structure

- N-substituted sulphonamide:Sulphadiazine, Sulphacetamide, Sulphadimidine.
- N-4 substituted sulphonamides (prodrugs): Prontosil.
- Both N-1 and N-4 substituted sulphonamides: Succinyl sulphathiazole, Phthalylsulphathiazole.
- Miscellaneous: Mefenide sodium.

LECTURE #2

SAR OF SULPHONAMIDES:

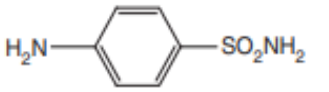


(i) Free para amino group is essential for antibacterial activity.

(ii) Substitution of heterocyclic aromatic components at N^4 position produces more potent sulpha drugs.
(iii) Any substitution in benzene ring causes loss of activity.

(iv) So_2 NH_2 group is not essential as such however, sulphur atom is directly linked with benzene ring.
(v) The more negative So_2 group at N^1 exhibits greater antibacterial activity.
(vi) Substitutions made in the amide NH_2 (N^1) have variable antibacterial activity.
(vii) The para NH_2 group (N^4) can be replaced or substituted by such chemical groups that can be converted into free NH_2 group in the body

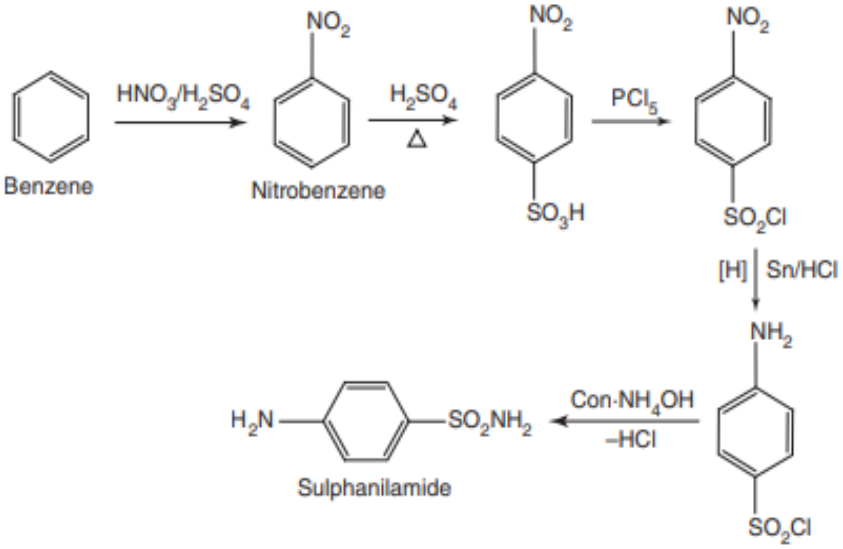
1. SULPHANILAMIDE:



4-Aminobenzene sulphonamide

Synthesis

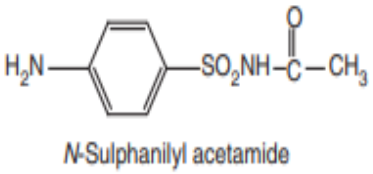
Route-I. From: Benzene



Benzene — Nitrobenzene — Sulphanilamide

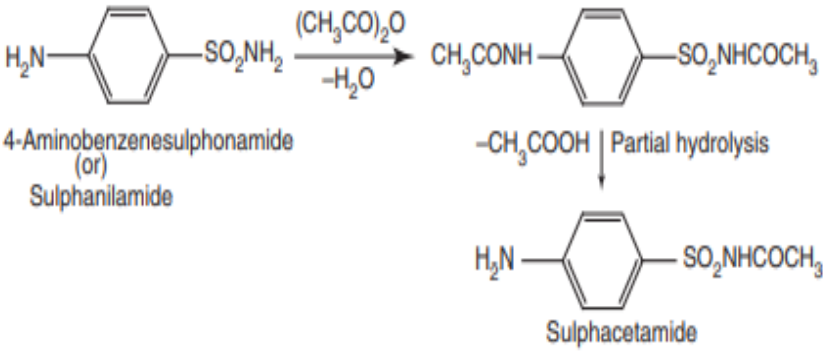
USES: It is used in veterinary medicine as an antibacterial agent.

2. SULPHACETAMIDE:



N-Sulphanilyl acetamide

Synthesis



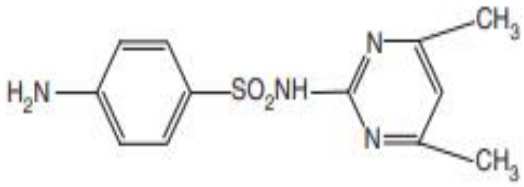
4-Aminobenzenesulphonamide (or) Sulphanilamide

Sulphacetamide

USES: Used in treatment of

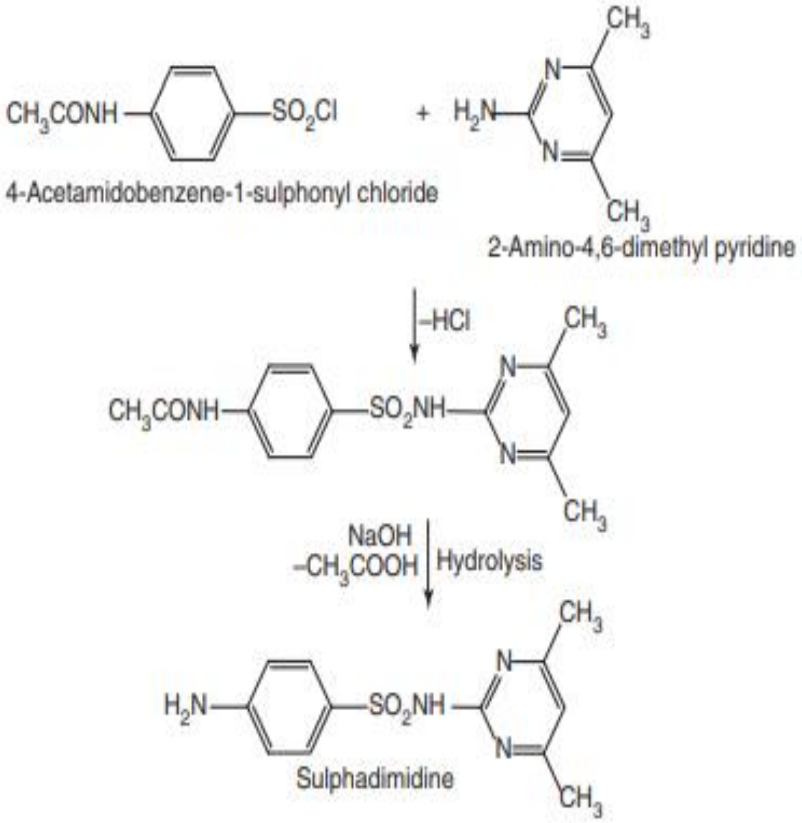
- bacterial infections of urinary tract.
- Eye infections

3.SULPHADIMIDINE:



N' (4, 6- Dimethyl -2- pyrimidinyl) Sulphanilamide

Synthesis

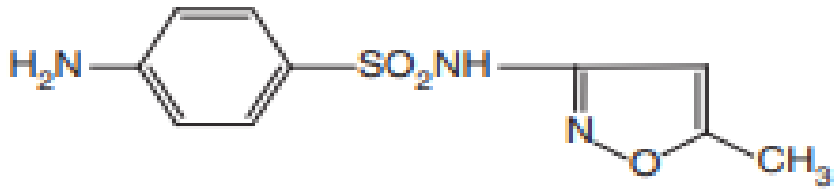


USES:

sulphadimidine is used for the treatment and control of diseases like coccidia, chlamydia and toxoplasma etc.

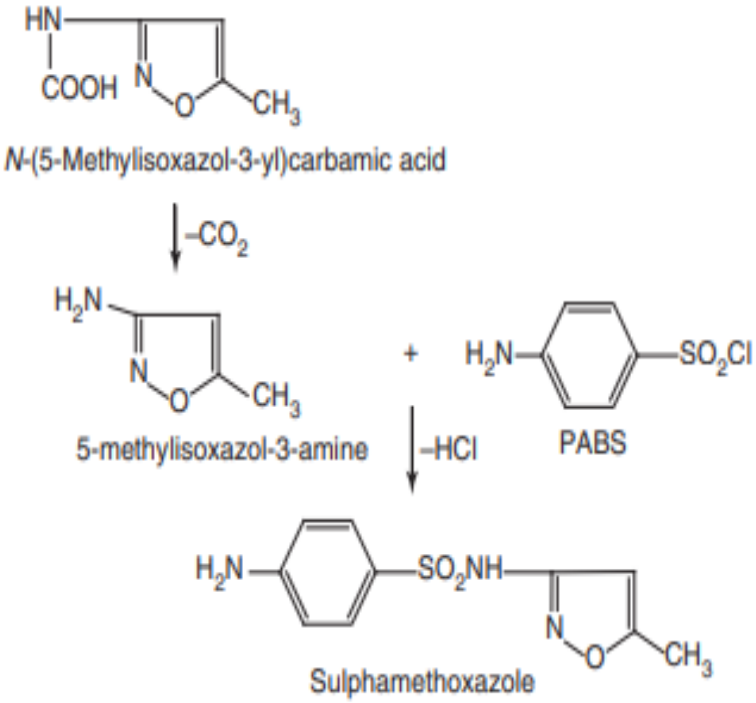
LECTURE#3

4.SULPHAMETHOXAZOLE:



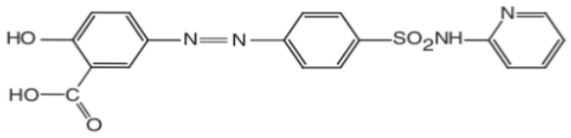
3-(4-Amino benzene sulphamido)-5-methyl isoxazole

Synthesis

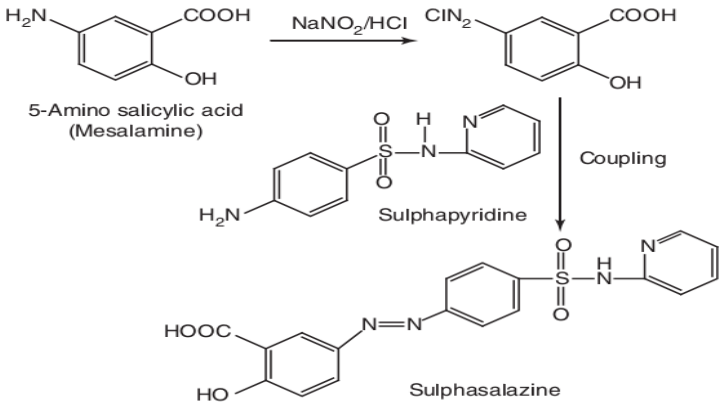


USES: It is used in treatment of wide variety of bacterial infections such as middle ear, respiratory and intestinal infections.

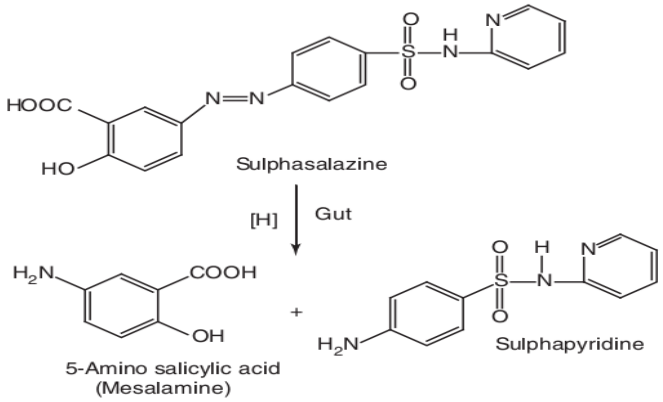
5.SULFADIAZINE



Synthesis



Metabolism: It undergoes reductive metabolism by gut bacteria, converting the drug into sulfapyridine and 5-amino salicylic acid, which are active components.



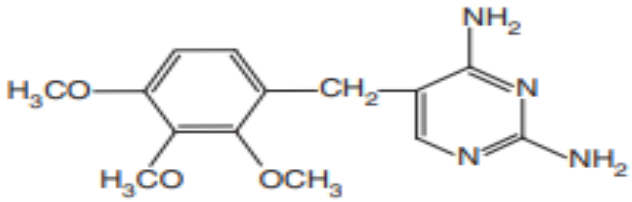
Properties and uses: Sulphasalazine is a bright yellow or brownish-yellow fine powder, very slightly soluble in alcohol, practically insoluble in methylene chloride. It dissolves in dilute solutions of alkali hydroxides. It is used in the treatment of ulcerative colitis.

Assay: Dissolve and dilute the sample in 0.1 M sodium hydroxide and add 0.1 M acetic acid and measure the absorbance at the maxima of 359 nm using ultraviolet spectrophotometer.

Dosage forms: Sulphasalazine tablets B.P.

6.DRUGS USED IN COMBINATION OF SULPHONAMIDES:

TRIMETHOPRIM:



5-(2,3,4-Trimethoxybenzyl)pyrimidine-2,4-diamine

USES: Sulfamethoxazole and trimethoprim is a combination antibiotic used to treat ear infections, urinary tract infections, bronchitis, traveler's diarrhea, shigellosis, and Pneumocystis jiroveci pneumonia.