Q Write a note on Sulphonamides

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Sulphonamide is a class of organic compounds that are amides of sulphonic acids, some of which are ~~drugs~~ Sulpha drugs and act as powerful inhibitors of bacterial activity

Building on Ehrlich's early work, Gerhard Domagk, a medical doctor employed by a German dye manufacturer made a breakthrough discovery by finding that a dye known as prontosil, dosed orally, was effective in curing life threatening streptococci infections in humans

In 1935, it was discovered that a red dye called prontosil had antibacterial properties in vivo

But no antibacterial effect was observed in vitro. In other words, prontosil could not kill bacteria growth on the test-tube.

Later it was discovered that prontosil was metabolized by bacteria present in the small intestine of the test ~~ani~~ animal to give a product called sulphanilamide

It was this compound ~~s~~ was the true antibacterial agent. Thus, prontosil was an early example of a prodrug

Chemically, sulphonamide is a molecule containing sulfonamide functional group attached to an aniline. Structurally related to p-amino benzoic acid

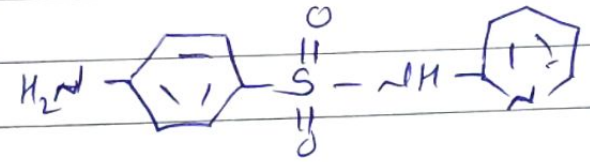
Sulfonamide drugs were the first anti-microbial drugs. The first sulfonamide was trade named Prontasil

✡ Classification:

I Based on site of action

a) Sulphonamides for general infection
Eg: Sulphapyridine ✡
Sulphanilamide
Sulphamethoxazole

✡ Sulphapyridine

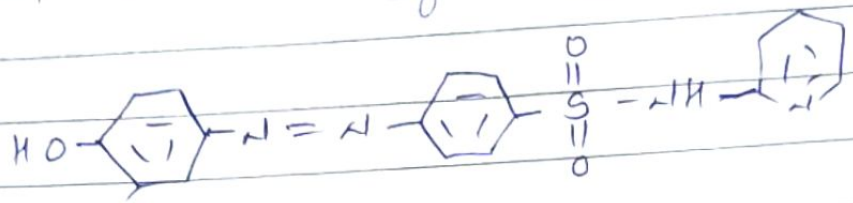


(4-pyridin-2-yl)-4-amino benzene sulphonamide

b) Sulphonamides for UTI
Eg: Sulphathiazole
Sulphaisoxazole

c) Sulphonamides for intestinal infections. ✡
Eg: Sulfasalazine
Succinyl sulphathiazole
Phthalylsulphathiazole

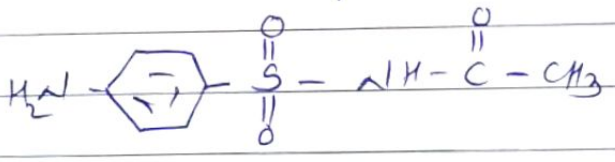
Sulfasalazine



2-hydroxy-5-[4-(pyridin-2-yl) sulphamoyl] phenyl diazen-1-yl benzoic acid

d) Sulphonamides for local infections
Eg: Sulphacetamide
Mafenamide
Silver Sulphadiazine

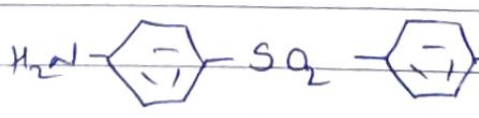
Sulphacetamide



N-Sulphanilyl acetamide

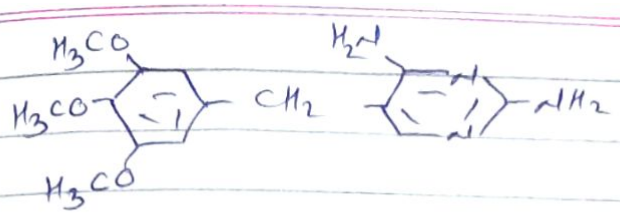
e) Sulphonamides for dermatitis
Eg: Dapsone
Solapsone

Dapsone

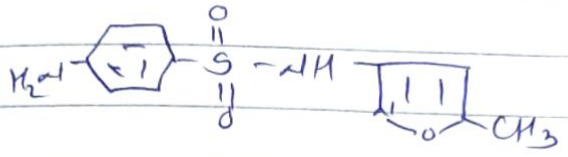


4, 4'-diamino diphenyl sulphone

f) Sulphonamides in combination
Eg Trimethoprim & sulphamethoxazole



Trimethoprim



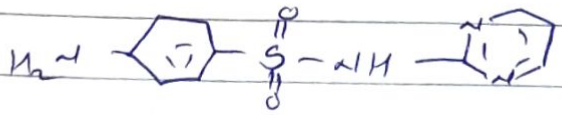
Sulphamethoxazole

II Based on pharmacokinetic properties

a) Poorly absorbed sulphonamides (locally acting sulphonamides)
Eg: Sulphasalazine
Phthalylsulphathiazole
Sulphaguanidine

b) Rapidly absorbed & rapidly excreted (systemic sulphonamides)
Eg: Sulphadiazine
Sulphamethoxazole
Sulphaisoxazole

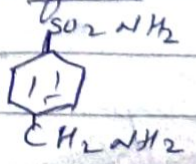
Sulphadiazine



N¹-(pyrimidine-2-yl) Sulphanilamide

c) Topically used sulphonamides
Eg: Mefenide
Sulphacetamide
Sulphathiazole

Mefenide

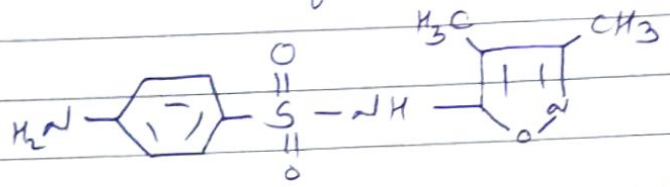


4-(Aminomethyl) benzene sulphonamide

III Based on pharmacological activity.

a) Antibacterial agents
Eg: Sulfisoxazole ☆
Sulphadiazine

☆ Sulfisoxazole



N-(3,4-dimethyl isoxazol-5-yl) Sulphanilamide

b) Drugs used in dermatitis
Eg: Dapsone ☆

IV Based on duration of action.

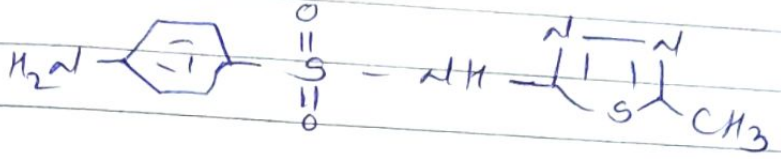
a) Extra long acting Sulphonamides (half life > than 50)
Eg: Sulphasalazine ☆
Sulphadomide
Sulphalene

b) Long acting Sulphonamides (half life > 24 hrs)
Eg: Sulphadoxine
Sulphadimethoxine
Sulphamethoxine

c) Intermediate acting Sulphonamides (half life b/w 10-24 hrs)
Eg: Sulphamethoxazole ☆
Sulphasomizole

d) Short acting Sulphonamides (half life < 20 hrs)
Eg: Sulphamethizole ★
Sulphaisoxazole

★ Sulphamethizole



4- amino - N (5-methyl -1, 3, 4- thiadiazol -2-yl) benzene sulphonamide

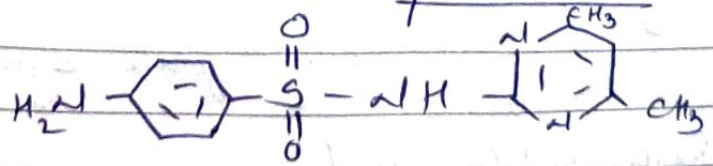
N- (5- methyl -1, 3, 4- thiadiazol -2-yl) sulphanilamide

e) Injectable (soluble sulpha drugs)
Eg: Sulphadiazine ★
Sulphafurazole
Sulphamethoxine

IV Based on chemical structure

a) N-1 substituted sulphonamide
Eg: Sulphadimidine / Sulphamethazine ★
Sulphadiazine
Sulpha cetamide

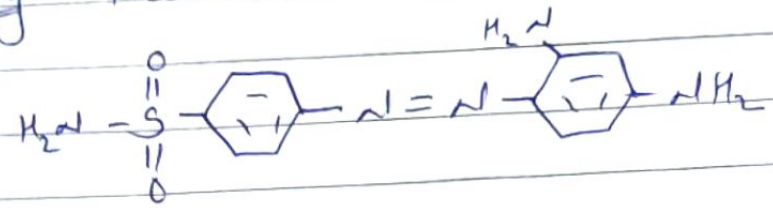
★ Sulphadimidine



(N -4,6- dimethyl pyrimidin- 2-yl) 4- amino benzene Sulphonamide

b) N-4 substituted sulphonamides (prodrugs)

Eg: Prontosil



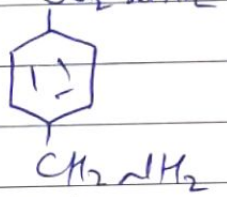
c) Both N-1 & N-4 substituted sulphonamides.

Eg: Succinyl sulphathiazole
Phthalyl sulphathiazole

d) Miscellaneous.

Eg: Mefenide acetate

✡ Mafenide acetate



4-(aminomethyl) benzene sulphonamide

✡ Mechanism of action :

p-aminobenzoic à + Pteridine

Sulfonamides ⊣ Pteridine synthase

Dihydropteroic acid

↓ Dihydrofolate synthase

Dihydrofolic acid

Trimethoprim ⊣ Dihydrofolate reductase

Tetrahydrofolic acid

Thymidine ← ↓ → Methionine

Purines

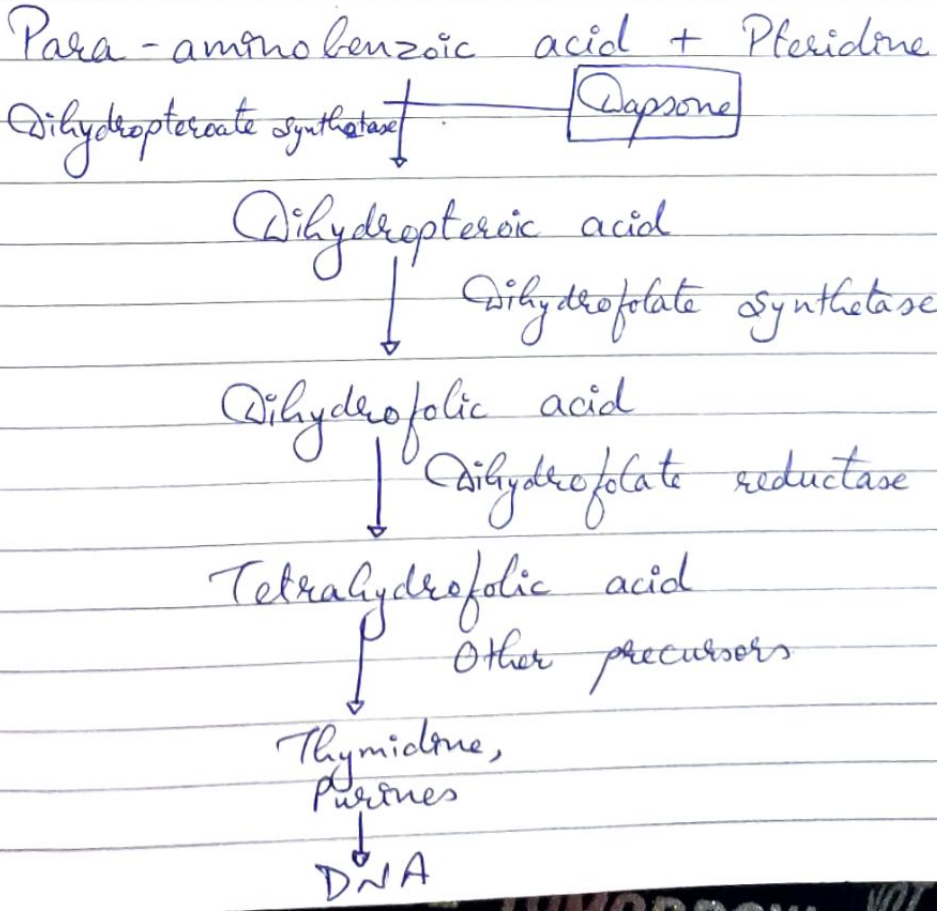
Side effects:

- Nausea, vomiting, headache & mental depression.
- Hypersensitivity reactions (rashes, fever, eosinophilia).
- Rarely - Stevens - Johnson syndrome, erythema multiforme
- Kernicterus (bilirubin induced brain dysfunction) in neonates
- Hepatitis, bone marrow depression & crystalluria

Therapeutic uses:

- UTIs
- Upper respiratory tract infections
- Nocardiosis
- Sulfasalazine in IBD
- Sulfacetamide in bacterial conjunctivitis & trachoma
- Silver sulfadiazine for prevention of infection of burn wounds

MOA of Dapsone



ADR of Dapsone

- Haemolytic anaemia
- Nausea, anorexia
- Methaemoglobinaemia, Headache, paresthesias, drug fever
- Allergic rashes, hypermelanosis, phototoxicity, dermatitis
- Hepatitis & agranulocytosis

Therapeutic uses

- Mycobacterium leprae infections (leprosy)/Hansen's disease
- Acne
- Pneumocystis pneumonia
- Dermatitis Herpetiformis
- Toxoplasmosis - Prophylaxis