Sulphonamides

Sulfonamides and Sulfones

Introduction

- Sulfonamides and sulfones are antimicrobial agents that inhibit bacterial growth by targeting folic acid synthesis, a crucial pathway for bacterial survival.

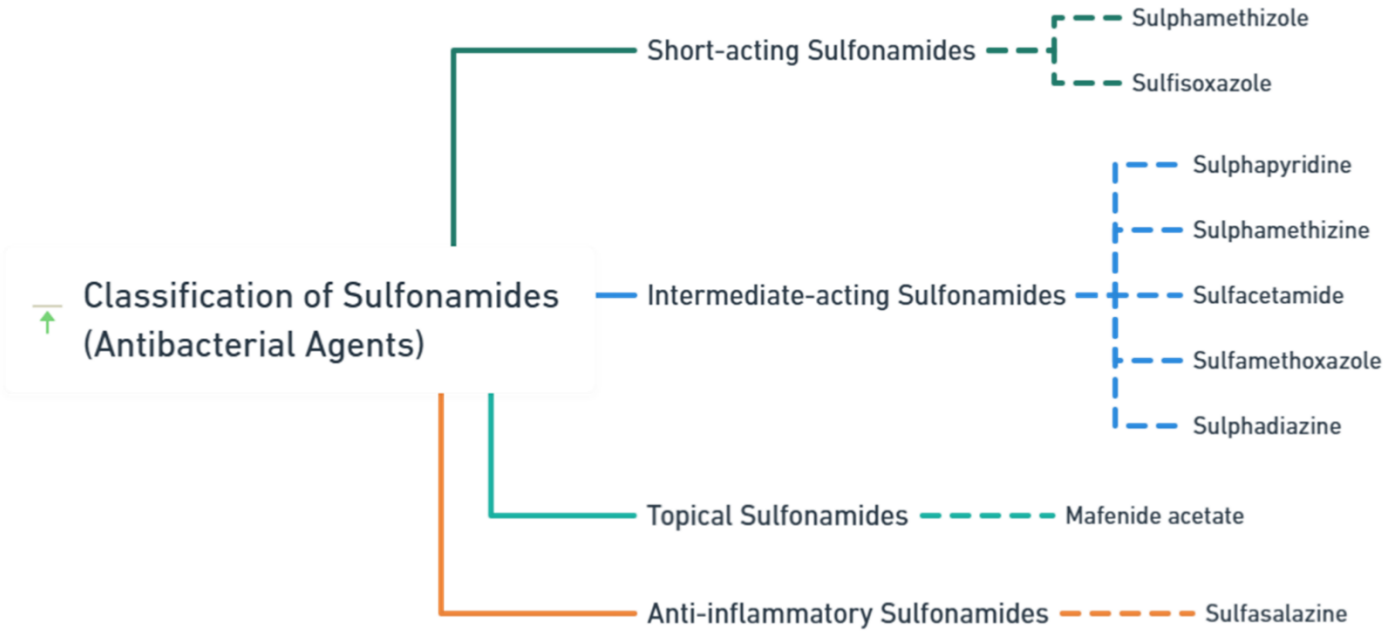
Historical Development

- Sulfonamides were the first synthetic antibacterial agents, discovered in the 1930s.
- Sulfones, like Dapsone, emerged later and became essential for treating leprosy and other bacterial infections.

Chemistry & Structure-Activity Relationship (SAR)

- Sulfonamides contain a sulfonyl functional group ($-SO_2NH_2$) attached to an aromatic ring, crucial for antibacterial activity.
- Modifications in the R-groups affect solubility, potency, and spectrum of activity.
- They act as competitive inhibitors of dihydropteroate synthase, blocking folic acid synthesis.

Classification of Sulfonamides (Antibacterial Agents)



1. **Short-acting Sulfonamides**
   - **Sulphamethizole**
   - **Sulfisoxazole**
2. **Intermediate-acting Sulfonamides**
   - **Sulphapyridine**

- **Sulphamethizine**
- **Sulfacetamide**
- **Sulfamethoxazole**
- **Sulphadiazine**

3. **Topical Sulfonamides**
   - **Mafenide acetate**
4. **Anti-inflammatory Sulfonamides**
   - **Sulfasalazine** *(used for inflammatory bowel disease and rheumatoid arthritis)*

SAR of Sulfonamides *(Generalized class overview)*

Structural Feature	SAR Insight
p-Amino group	Essential for PABA mimicry and enzyme binding. Acetylation/inactivation reduces activity.
Sulfonamide (-SO_2NH_2) group	Key for competitive inhibition of **dihydropteroate synthase**.
Aromatic ring	Required for optimal fit; substitutions can affect potency.
N^1-substitution (alkyl, aryl)	Modifies absorption, protein binding, and half-life.
Electron-withdrawing groups	May increase activity by stabilizing molecule/enzyme complex.

Classification of Folate Reductase Inhibitors (Potentiators of Sulfonamides)

- These inhibit dihydrofolate reductase (DHFR), preventing bacterial DNA synthesis.
  - Trimethoprim
  - Cotrimoxazole *(Combination of Sulfamethoxazole + Trimethoprim)*

Classification of Sulfones (Antileprotic and Antibacterial Agents)

- Dapsone *(Used in leprosy, Pneumocystis pneumonia, and dermatitis herpetiformis)*

Mechanism of Action

- Sulfonamides act as competitive inhibitors of dihydropteroate synthase, preventing folic acid synthesis.
- Folate reductase inhibitors (Trimethoprim, Cotrimoxazole) block dihydrofolate reductase, enhancing the antibacterial effect.
- Sulfones, like Dapsone, have a similar mechanism but are primarily used for leprosy and certain bacterial infections.

Brand Names Of Important Marketed Products

- These are synthetic antimicrobial agents. **Sulphonamides** inhibit bacterial folic acid synthesis. **Sulphones** are structurally related and used mainly in leprosy.

Sulphonamides

Drug	Brand Name	Formulation	Uses
Sulfamethoxazole + Trimethoprim	**Bactrim, Septran, Co-trimoxazole**	Tablets, Suspension	UTIs, respiratory infections, PCP pneumonia
Sulfadiazine	**Silvadene (with silver)**	Tablet	Toxoplasmosis, meningitis
Sulfasalazine	**Salazopyrin, Sazo**	Tablets	Ulcerative colitis, rheumatoid arthritis
Sulfacetamide	**Bleph-10, Sulfacyl Sodium**	Eye drops	Bacterial eye infections
Sulfadoxine + Pyrimethamine	**Fansidar, Malinil**	Tablets	Malaria (with artesunate), intermittent preventive therapy

Sulphones

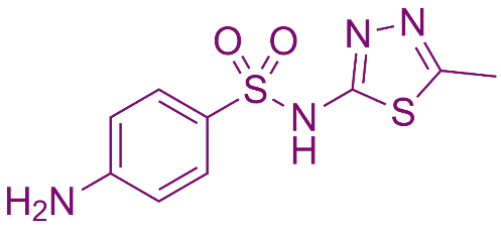
Drug	Brand Name	Formulation	Uses
Dapsone	**Aczone, Avlosulfon**	Tablets	Leprosy, dermatitis herpetiformis, acne
Clofazimine	**Lamprene, Hanclox**	Capsules	Multibacillary leprosy
Acedapsone	**DADDS** (long-acting)	Injection	Long-term leprosy management

Various Sulfonamides

1. Sulfamethizole

Chemical Structure / Formula

- **Formula:** C9H10N4O2S2
- **Structure:** A **thiazole-containing sulfonamide**.



Mechanism of Action

- Inhibits dihydropteroate synthase, blocking folic acid synthesis in bacteria.
- **Bacteriostatic**: prevents bacterial growth.

Uses

- Urinary tract infections (UTIs).
- Respiratory infections.

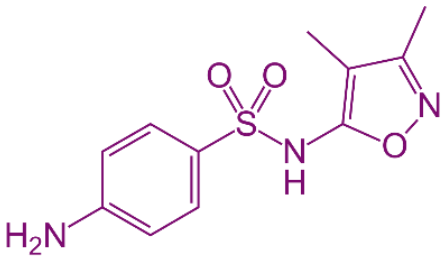
Side Effects

- Hypersensitivity reactions (rash, Stevens-Johnson syndrome).
- Crystalluria, nephrotoxicity.

2. Sulfisoxazole

Chemical Structure / Formula

- **Formula:** C11H13N3O3S
- **Structure:** Isoxazole-containing sulfonamide.



Mechanism of Action

- Inhibits folic acid synthesis by competing with para-aminobenzoic acid (PABA) for dihydropteroate synthase.

Uses

- UTIs, otitis media (often in combination with erythromycin).

Side Effects

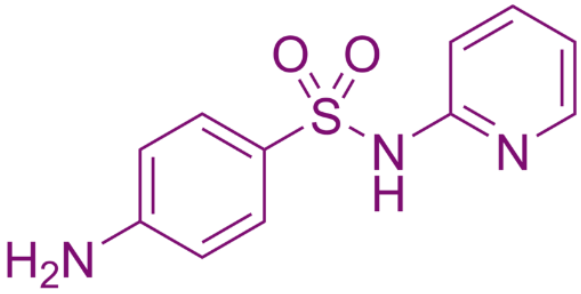
- GI upset, allergic reactions, crystalluria.

3. Sulfapyridine

Chemical Structure / Formula

- **Formula:** C11H11N3O2S

- **Structure:** Pyridine-containing sulfonamide.



Mechanism of Action

- Inhibits dihydropteroate synthase, blocking folate metabolism.

Uses

- Used in combination (as sulfasalazine) for inflammatory bowel diseases (IBD, ulcerative colitis, Crohn's disease).

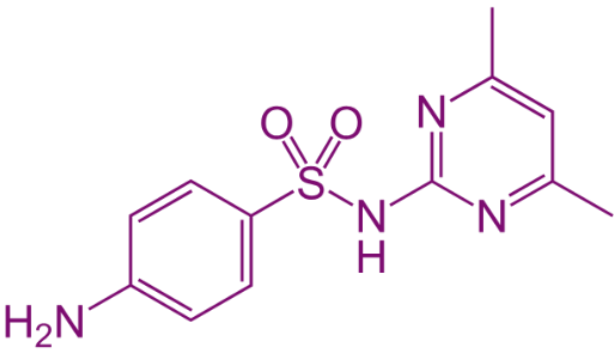
Side Effects

- Hypersensitivity, GI upset, hemolysis in G6PD-deficient patients.

4. Sulfamethizine

Chemical Structure / Formula

- **Formula:** C12H14N4O2S
- **Structure:** Thiazole-containing sulfonamide.



Mechanism of Action

- **Inhibits folic acid synthesis**, preventing bacterial DNA replication.

Uses

- Respiratory and urinary tract infections.

Side Effects

- Hypersensitivity reactions, nephrotoxicity, anemia.

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