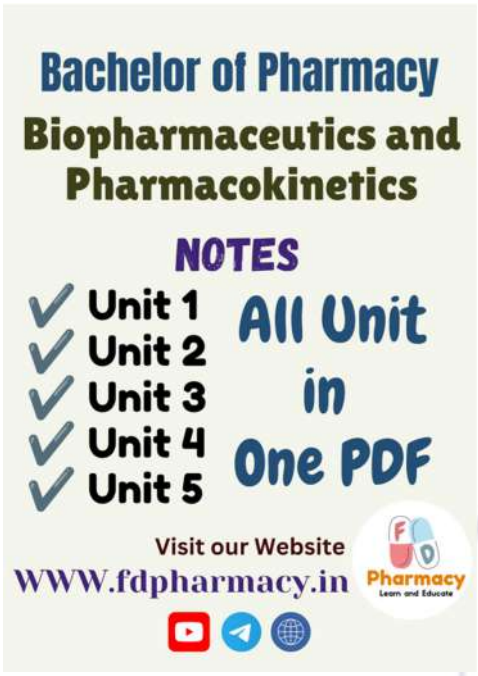
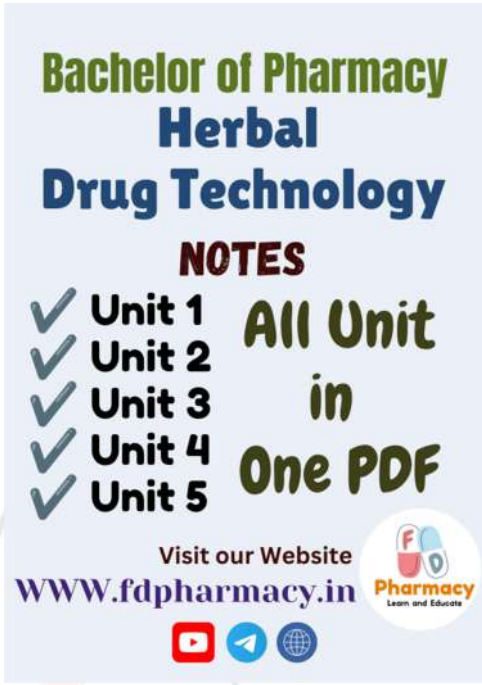
WELCOME

TO


Bachelor of Pharmacy
Biopharmaceutics and Pharmacokinetics
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Herbal Drug Technology
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmaceutical Biotechnology
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Medicinal Chemistry III
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmacology III
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Quality Assurance
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate

MEDICINAL CHEMISTRY - III

UNIT 4

TOPIC :

- **Sulphonamides and Sulfones**

  Historical development, chemistry, classification and SAR of Sulfonamides:

  Sulphamethizole, Sulfisoxazole, Sulphapyridine, Sulphamethizine, Sulfacetamide, *Sulfamethoxaole*, Sulphadiazine, Mefenide acetate, Sulfasalazine

Sulfonamides

→ Sulfonamides are synthetic antibacterial agents that act by inhibiting folic acid synthesis in bacteria.

→ They are bacteriostatic drugs and are structural analogues of para-aminobenzoic acid (PABA).

Classification

A. Systemic Sulfonamides

1. Short-acting

- Sulfamethoxazole
- Sulfisoxazole

2. Intermediate-acting

- Sulfadiazine

3. Long-acting

- Sulfadoxine
- Sulfametomidine

B. Poorly Absorbed (Intestinal) Sulfonamides

- Sulfasalazine
- Phthalylsulfathiazole

C. Topical Sulfonamides

- Silver sulfadiazine
- Mafenide acetate
- Sulfacetamide (ophthalmic)

Mechanism of Action

- Sulfonamides resemble PABA
- They competitively inhibit dihydropteroate synthase
- Folic acid synthesis is blocked
- DNA and RNA synthesis is inhibited
- Bacterial growth is stopped
- Therefore, sulfonamides are bacteriostatic

Spectrum of Activity

- Gram-positive bacteria
- Gram-negative bacteria
- *Chlamydia*
- *Toxoplasma*
- Some protozoa

Therapeutic Uses

- Urinary tract infections
- Respiratory tract infections
- Gastrointestinal infections
- Toxoplasmosis
- Burns (silver sulfadiazine)

Adverse Effects

Common

- Nausea
- Vomiting
- Skin rashes
- Photosensitivity

Serious

- Stevens–Johnson syndrome
- Hemolytic anemia (G6PD deficiency)
- Crystalluria
- Bone marrow suppression
- Kernicterus in newborns

Drug Interactions

- Increase effect of warfarin
- Increase effect of phenytoin
- Increase hypoglycemic effect of sulfonylureas

Resistance

- Increased PABA production
- Altered dihydropteroate synthase
- Decreased drug uptake

Sulfamethizole

→ Sulphamethizole is a synthetic sulfonamide antibiotic.
→ It is primarily used for urinary tract infections (UTIs) caused by Gram-positive and Gram-negative bacteria.
→ Sulfonamides act as competitive inhibitors of dihydropteroate synthase, interfering with folic acid synthesis in bacteria, which is essential for DNA and RNA synthesis.

Classification

Based on Chemical Class

- Sulfonamide derivative (heterocyclic sulfonamide with a methylthiazole group)

Based on Antimicrobial Action

- Bacteriostatic – inhibits bacterial growth by preventing folic acid synthesis

Based on Use

- Oral therapy – tablets or suspension
- Mainly for urinary tract infections

Structure

⇨ Sulfonamide group attached to a heterocyclic methylthiazole ring

Molecular formula: $C_8H_8N_4O_2S_2$

Structural Characteristics

- Water-soluble → well absorbed orally
- Excreted primarily by the kidneys → effective for UTIs
- Formulated as tablets or oral suspension

Nomenclature

- Sulphamethizole → generic name
- Brand names: Thiosulfon, Urodes, Sulphin
- Formulations: oral tablets, oral suspension

Mechanism of Action

- ⇨ Sulphamethizole competitively inhibits bacterial dihydropteroate synthase.
- ⇨ Blocks the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid.
- ⇨ Disrupts folic acid synthesis, which is essential for DNA, RNA, and protein synthesis.
- ⇨ Leads to inhibition of bacterial growth.
- ⇨ Hence, sulphamethizole is bacteriostatic.

Spectrum of Activity

- → Gram-positive bacteria: Staphylococcus spp., Streptococcus spp.
- → Gram-negative bacteria: E. coli, Klebsiella, Proteus spp.
- → Mainly effective for urinary tract infections

Uses

- ⮝ Uncomplicated urinary tract infections
- ⮝ Prophylaxis of recurrent UTIs
- ⮝ Sometimes combined with trimethoprim for synergistic effect (co-trimoxazole)

Adverse Effects

- ⮝ Gastrointestinal: nausea, vomiting, diarrhea
- ⮝ Hypersensitivity reactions: rash, urticaria, photosensitivity
- ⮝ Avoid in patients with G6PD deficiency

Chemical Degradation

- ❖ Sensitive to light and moisture
- ❖ Store in cool, dry place, protected from light
- ❖ Degraded in alkaline or acidic conditions

Structure–Activity Relationship (SAR)

- ➢ Sulfonamide group → essential for inhibition of dihydropteroate synthase
- ➢ Heterocyclic methylthiazole → enhances urinary excretion and activity in UTIs
- ➢ Modifications of the aromatic ring → affect potency and solubility
- ➢ Rapid renal excretion → makes it ideal for urinary tract infections

Sulfamethizole

→ Sulphamethizole is a synthetic sulfonamide antibiotic.
→ It is primarily used for urinary tract infections (UTIs) caused by Gram-positive and Gram-negative bacteria.
→ Sulfonamides act as competitive inhibitors of dihydropteroate synthase, interfering with folic acid synthesis in bacteria, which is essential for DNA and RNA synthesis.

Classification

Based on Chemical Class

- Sulfonamide derivative (heterocyclic sulfonamide with a methylthiazole group)

Based on Antimicrobial Action

- Bacteriostatic – inhibits bacterial growth by preventing folic acid synthesis

Based on Use

- Oral therapy – tablets or suspension
- Mainly for urinary tract infections

Structure

→ Sulfonamide group attached to a heterocyclic methylthiazole ring

Molecular formula: $C_8H_8N_4O_2S_2$

Structural Characteristics

- Water-soluble → well absorbed orally
- Excreted primarily by the kidneys → effective for UTIs
- Formulated as tablets or oral suspension

Nomenclature

- Sulphamethizole → generic name
- Brand names: Thiosulfon, Urodes, Sulphin
- Formulations: oral tablets, oral suspension

Mechanism of Action

→ Sulphamethizole competitively inhibits bacterial dihydropteroate synthase.
→ Blocks the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid.
→ Disrupts folic acid synthesis, which is essential for DNA, RNA, and protein synthesis.
→ Leads to inhibition of bacterial growth.
→ Hence, sulphamethizole is bacteriostatic.

Spectrum of Activity

- Gram-positive bacteria: Staphylococcus spp., Streptococcus spp.
- Gram-negative bacteria: E. coli, Klebsiella, Proteus spp.
- Mainly effective for urinary tract infections

Uses

- Uncomplicated urinary tract infections
- Prophylaxis of recurrent UTIs

Adverse Effects

- Gastrointestinal: nausea, vomiting, diarrhea
- Hypersensitivity reactions: rash, urticaria, photosensitivity
- Rare: crystalluria, hematuria, Stevens-Johnson syndrome, blood dyscrasias
- Avoid in patients with G6PD deficiency

Chemical Degradation

❖ Sensitive to light and moisture
❖ Store in cool, dry place, protected from light
❖ Degraded in alkaline or acidic conditions

Structure–Activity Relationship (SAR)

➢ Sulfonamide group → essential for inhibition of dihydropteroate synthase
➢ Heterocyclic methylthiazole → enhances urinary excretion and activity in UTIs
➢ Modifications of the aromatic ring → affect potency and solubility
➢ Rapid renal excretion → makes it ideal for urinary tract infections

Sulfamethizine

→ Sulphamethizine is a synthetic sulfonamide antibiotic.
→ It is mainly used for urinary tract infections (UTIs) and certain systemic bacterial infections.
→ Sulfonamides act as competitive inhibitors of dihydropteroate synthase, disrupting folic acid synthesis in bacteria, which is essential for DNA, RNA, and protein synthesis.

Classification

Based on Chemical Class

- Sulfonamide derivative (aromatic sulfonamide with a methylthiazole group)

Based on Antimicrobial Action

- Bacteriostatic – inhibits bacterial growth by interfering with folic acid synthesis

Based on Use

- Oral therapy – tablets or suspension

Structure

Sulfonamide group attached to a heterocyclic methylthiazole ring
Molecular formula: $C_{10}H_{12}N_4O_2S$

Structural Characteristics

- Water-soluble → well absorbed orally
- Excreted primarily via renal route → effective for UTIs
- Formulated as tablets or oral suspension

Nomenclature

- Sulphamethizine → generic name
- Brand names: Thiosulphin, Sulphin-S
- Formulations: tablets, oral suspension

Mechanism of Action

- ⇨ Sulphamethizine competitively inhibits bacterial dihydropteroate synthase.
- ⇨ Blocks the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid.
- ⇨ Inhibits folic acid synthesis, essential for DNA, RNA, and protein production.
- ⇨ Results in bacteriostatic effect.
- ⇨ Hence, sulphamethizine is bacteriostatic.

Spectrum of Activity

- → Gram-positive bacteria: Staphylococcus spp., Streptococcus spp.
- → Gram-negative bacteria: E. coli, Klebsiella, Proteus spp.
- → Mainly effective for urinary tract infections

Uses

- Uncomplicated and complicated UTIs
- Systemic bacterial infections (less commonly used)
- Occasionally combined with trimethoprim for enhanced activity

Adverse Effects

- Gastrointestinal: nausea, vomiting, diarrhea
- Hypersensitivity reactions: rash, urticaria, photosensitivity
- Rare: crystalluria, hematuria, blood dyscrasias
- Avoid in patients with G6PD deficiency

Chemical Degradation

- Sensitive to light, moisture, and extreme pH
- Store in cool, dry place, protected from light
- Stability decreases in alkaline or acidic conditions

Structure–Activity Relationship (SAR)

- Sulfonamide group → essential for competitive inhibition of dihydropteroate synthase
- Methylthiazole substitution → improves urinary excretion and UTI activity
- Modifications of the aromatic ring → affect potency, solubility, and spectrum
- Rapid renal excretion → makes it ideal for urinary tract infections

Sulfacetamide

→ Sulfacetamide is a synthetic sulfonamide antibacterial.
→ It is primarily used for ocular infections such as conjunctivitis and sometimes for dermatological conditions like acne vulgaris.
→ Sulfacetamide acts by inhibiting bacterial folic acid synthesis, essential for nucleic acid and protein production.

Classification

Based on Chemical Class

- Sulfonamide derivative
- Synthetic antibacterial

Based on Action

- Bacteriostatic – inhibits bacterial growth
- Mechanism: competitive inhibition of dihydropteroate synthase (DHPS) → blocks folic acid synthesis

Based on Use

- Topical therapy – ophthalmic drops, ointments
- Oral therapy – less commonly used

Structure

➢ Sulfonamide nucleus with acetamide substitution

Molecular formula: $C_8H_{10}N_2O_3S$

Structural Characteristics

- Water-soluble → suitable for ophthalmic preparations
- Acetamide group → improves antibacterial activity and solubility
- Formulated as eye drops, eye ointments, creams

Nomenclature

- Sulfacetamide → generic name
- Brand names: Bleph-10, Sulamyd
- Formulations: ophthalmic solution, ointment, topical creams

Mechanism of Action

- ⇨ Sulfacetamide competes with para-aminobenzoic acid (PABA).
- ⇨ Inhibits dihydropteroate synthase, preventing formation of dihydrofolic acid.
- ⇨ Blocks folic acid metabolism, inhibiting bacterial DNA, RNA, and protein synthesis.
- ⇨ Leads to bacteriostatic effect.

Spectrum of Activity

- → Gram-positive bacteria: Staphylococcus aureus, Streptococcus spp.
- → Gram-negative bacteria: Haemophilus influenzae, Neisseria spp., some E. coli
- → Effective mainly for ocular and topical infections

Uses

- Bacterial conjunctivitis – ophthalmic drops or ointment
- Blepharitis – eyelid infections
- Acne vulgaris – topical creams (alone or in combination with sulfur)
- Minor skin infections

Adverse Effects

- Local irritation: burning, stinging, redness in the eye
- Allergic reactions: rash, urticaria, pruritus
- Rare: systemic absorption → headache, gastrointestinal upset
- Avoid prolonged use in patients with sulfonamide hypersensitivity

Chemical Degradation

- Sensitive to light and alkaline conditions
- Store in a cool, dry place, protected from light
- Ophthalmic solutions often buffered to maintain pH and stability

Structure–Activity Relationship (SAR)

- Sulfonamide group ($-SO_2NH_2$) → essential for DHPS inhibition
- Acetamide substitution → improves water solubility and antibacterial activity
- Topical formulations → minimizes systemic absorption, increases local effect
- Effective mainly against ocular and superficial skin infections

Sulphapyridine

→ Sulphapyridine is a synthetic sulfonamide antibiotic.
→ It was historically used to treat systemic bacterial infections such as rheumatic fever, streptococcal infections, and meningococcal infections.
→ Sulfonamides act as competitive inhibitors of dihydropteroate synthase, interfering with folic acid synthesis in bacteria, essential for DNA, RNA, and protein synthesis.

Classification

Based on Chemical Class

- Sulfonamide derivative (aromatic sulfonamide with pyridine ring)

Based on Antimicrobial Action

- Bacteriostatic – inhibits bacterial growth by blocking folic acid synthesis

Based on Use

- Oral therapy – tablets or suspension
- Historically used for systemic infections

Structure

→ Sulfonamide group attached to a pyridine ring

Molecular formula: $C_{11}H_{11}N_3O_2S$

Structural Characteristics

- Water-soluble → well absorbed orally
- Distributed systemically → effective for blood-borne infections
- Formulated as tablets or oral suspension

Nomenclature

- Sulphapyridine → generic name
- Brand names: Gantrisin (historical), Sulfapyri
- Formulations: oral tablets, oral suspension

Mechanism of Action

- ⇨ Sulphapyridine competitively inhibits bacterial dihydropteroate synthase.
- ⇨ Blocks the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid.
- ⇨ Disrupts folic acid synthesis, which is required for DNA, RNA, and protein synthesis.
- ⇨ Leads to inhibition of bacterial growth.
- ⇨ Hence, sulphapyridine is bacteriostatic.

Spectrum of Activity

- → Gram-positive bacteria: Streptococcus spp., Staphylococcus spp.
- → Gram-negative bacteria: Neisseria spp., E. coli
- → Historically used for meningococcal infections and rheumatic fever prophylaxis

Uses

- Rheumatic fever – prevention and early treatment
- Streptococcal infections
- Meningococcal infections
- Currently largely replaced by newer sulfonamides and antibiotics

Adverse Effects

- Gastrointestinal: nausea, vomiting, diarrhea
- Hypersensitivity: rash, photosensitivity, urticaria
- Rare: hemolytic anemia, crystalluria, blood dyscrasias

Chemical Degradation

- Sensitive to light, moisture, and extreme pH
- Store in cool, dry place, protected from light
- Degradation occurs in alkaline or acidic conditions

Structure–Activity Relationship (SAR)

- ➢ Sulfonamide group → essential for competitive inhibition of dihydropteroate synthase
- ➢ Pyridine substitution → improves systemic absorption and distribution
- ➢ Modifications of the aromatic ring → affect potency and spectrum
- ➢ Systemic distribution → effective for blood-borne infections

Sulfamethoxazole (SMX)

→ Sulfamethoxazole is a synthetic sulfonamide antibacterial commonly used in combination with trimethoprim (as co-trimoxazole).
→ It acts by inhibiting bacterial folic acid synthesis, which is necessary for DNA, RNA, and protein synthesis.
→ The combination with trimethoprim provides synergistic bactericidal activity against a broad spectrum of bacteria.

Classification

Based on Chemical Class

- Sulfonamide derivative
- Synthetic antibacterial

Based on Action

- Bacteriostatic alone
- Bactericidal in combination with trimethoprim
- Mechanism: competitive inhibition of dihydropteroate synthase (DHPS) → blocks folic acid synthesis

Based on Use

- Oral therapy – tablets, suspension
- Often combined with trimethoprim for enhanced effect

Structure

➢ Sulfonamide nucleus with methoxazole substitution

Molecular formula: $C_{10}H_{11}N_3O_3S$

Structural Characteristics

- Poorly water-soluble → absorption enhanced with oral formulations
- Methoxazole ring → improves antibacterial potency and spectrum
- Formulated as tablets, oral suspension, or combination with trimethoprim

Nomenclature

- Sulfamethoxazole → generic name
- Brand names: Gantanol, Bactrim (in combination with trimethoprim)
- Formulations: oral tablets, suspension, combined preparations

Mechanism of Action

- ⇨ Sulfamethoxazole competes with para-aminobenzoic acid (PABA).
- ⇨ Inhibits dihydropteroate synthase, preventing synthesis of dihydrofolic acid.
- ⇨ Combination with trimethoprim inhibits dihydrofolate reductase, producing synergistic bactericidal effect.
- ⇨ Hence, sulfamethoxazole alone is bacteriostatic, but bactericidal with trimethoprim.

Spectrum of Activity

- ⮝ Gram-positive bacteria: Staphylococcus aureus, Streptococcus pneumoniae
- ⮝ Gram-negative bacteria: Escherichia coli, Klebsiella spp., Proteus spp., Haemophilus influenzae
- ⮝ Effective against urinary tract infections, respiratory infections, and some GI infections

Uses

- Urinary tract infections (UTIs)
- Respiratory tract infections – bronchitis, pneumonia
- Gastrointestinal infections – Shigella, Salmonella

Adverse Effects

- Gastrointestinal: nausea, vomiting, diarrhea
- Hypersensitivity: rash, urticaria, photosensitivity
- Rare: Stevens-Johnson syndrome

Chemical Degradation

- ❖ Sensitive to light, moisture, and alkaline conditions
- ❖ Store in cool, dry place, protected from light

Structure–Activity Relationship (SAR)

- ➢ Sulfonamide group (-SO_2NH_2) → essential for DHPS inhibition
- ➢ Methoxazole ring → improves potency and spectrum
- ➢ Combination with trimethoprim → blocks sequential steps in folic acid pathway, enhancing bactericidal effect
- ➢ Effective for systemic and urinary infections due to good oral absorption and tissue penetration

Sulphadiazine

→ Sulphadiazine is a synthetic sulfonamide antibiotic.
→ It is primarily used for systemic bacterial infections and protozoal infections, especially in combination with pyrimethamine for toxoplasmosis.
→ Sulfonamides act as competitive inhibitors of dihydropteroate synthase, interfering with folic acid synthesis in bacteria and protozoa, essential for DNA, RNA, and protein synthesis.

Classification

Based on Chemical Class

- Sulfonamide derivative (heterocyclic sulfonamide with pyrimidine-like substitution)

Based on Antimicrobial Action

- Bacteriostatic – inhibits bacterial growth by blocking folic acid synthesis
- Active against protozoa when combined with dihydrofolate reductase inhibitors

Based on Use

- Oral therapy – tablets or suspension
- Used in combination therapy for toxoplasmosis

Structure

➢ Sulfonamide group attached to a heterocyclic pyrimidine-like ring

Molecular formula: $C_{10}H_{10}N_4O_2S$

Structural Characteristics

- Water-soluble → well absorbed orally
- Systemically distributed → effective for blood-borne infections and protozoal infections
- Formulated as tablets, oral suspension, and injectable forms

Nomenclature

- Sulphadiazine → generic name
- Brand names: Daraprim (in combination), Silvadene (topical for burns)
- Formulations: oral tablets, suspension, topical cream

Mechanism of Action

→ Sulphadiazine competitively inhibits bacterial dihydropteroate synthase.
→ Blocks the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid.
→ Disrupts folic acid synthesis, required for DNA, RNA, and protein synthesis.
→ Results in bacteriostatic effect.
→ When combined with pyrimethamine, it becomes synergistically parasiticidal against Toxoplasma gondii.

Spectrum of Activity

⇨ Gram-positive bacteria: Staphylococcus spp., Streptococcus spp.
⇨ Gram-negative bacteria: E. coli, Salmonella spp., Shigella spp.
⇨ Protozoa: Toxoplasma gondii (in combination with pyrimethamine)
⇨ Used in systemic bacterial and protozoal infections

Uses

- Systemic bacterial infections – UTIs, meningococcal infections
- Toxoplasmosis – in combination with pyrimethamine

Adverse Effects

- Gastrointestinal: nausea, vomiting, diarrhea
- Hypersensitivity: rash, photosensitivity, urticaria
- Monitor renal and hepatic function for prolonged therapy

Chemical Degradation

- Sensitive to light, moisture, and extreme pH
- Store in cool, dry place, protected from light
- Degraded under strongly acidic or alkaline conditions

Structure–Activity Relationship (SAR)

✓ Sulfonamide group → essential for competitive inhibition of dihydropteroate synthase
✓ Heterocyclic pyrimidine substitution → enhances systemic absorption and distribution
✓ Rapid renal excretion → effective for urinary tract infections
✓ Combination with dihydrofolate reductase inhibitors → synergistic anti-protozoal effect

Mefenide Acetate

→ Mefenide acetate is a synthetic sulfonamide antibacterial used primarily as a topical agent in burn wounds.
→ It prevents bacterial infections in second- and third-degree burns and is effective against Gram-positive and Gram-negative organisms.
→ It acts by inhibiting bacterial folic acid synthesis, which is essential for DNA, RNA, and protein synthesis.

Classification

Based on Chemical Class

- Sulfonamide derivative
- Topical antibacterial

Based on Action

- Bacteriostatic – inhibits bacterial growth
- Mechanism: competitive inhibition of dihydropteroate synthase (DHPS) → blocks folic acid synthesis

Based on Use

- Topical therapy – cream for burn wound infections

Structure

➢ Sulfonamide nucleus with acetamide substitution

Molecular formula: $C_{12}H_{14}N_2O_2S$

Structural Characteristics

- Water-soluble → suitable for topical formulations
- Lipophilic properties → penetrates burn eschar
- Formulated as 2% cream

Nomenclature

- Mefenide acetate → generic name
- Brand names: Sulfamylon
- Formulations: topical cream (2%)

Mechanism of Action

- Mefenide acetate competitively inhibits para-aminobenzoic acid (PABA).
- Blocks dihydropteroate synthase (DHPS) → prevents dihydrofolic acid formation.
- Inhibits bacterial DNA, RNA, and protein synthesis.
- Results in bacteriostatic effect in the wound area.
- Hence, mefenide acetate is bacteriostatic.

Spectrum of Activity

- Gram-positive bacteria: Staphylococcus aureus, Streptococcus pyogenes
- Gram-negative bacteria: Pseudomonas aeruginosa, E. coli
- Effective in burn wound infections and prevention of sepsis

Uses

- Topical treatment of burn wounds (2nd and 3rd degree)
- Prevention of infection in extensive burns
- Sometimes used for minor skin infections in sensitive areas

Adverse Effects

- Pain or burning sensation on application
- Allergic reactions: rash, itching
- Metabolic: rare metabolic acidosis when applied to large areas
- Generally well tolerated for topical use

Chemical Degradation

- Sensitive to light and moisture
- Store in cool, dry place, protected from light
- Maintain proper formulation to ensure stability in cream

Structure–Activity Relationship (SAR)

- Sulfonamide group ($-SO_2NH_2$) → essential for DHPS inhibition
- Acetamide substitution → improves lipophilicity and penetration of burn eschar
- Effective topically due to local antibacterial action and limited systemic absorption
- Prevents infection in deep burn wounds without significant systemic toxicity

Sulfasalazine

→ Sulfasalazine is a synthetic sulfonamide derivative with anti-inflammatory and antibacterial properties.
→ It is primarily used in the treatment of inflammatory bowel disease (IBD) such as ulcerative colitis and rheumatoid arthritis.
→ Sulfasalazine acts by inhibiting prostaglandin synthesis and reducing inflammation, while its sulfonamide component provides mild antibacterial activity in the gut.

Classification

Based on Chemical Class

- Sulfonamide derivative linked to 5-aminosalicylic acid (5-ASA)

Based on Pharmacological Action

- Anti-inflammatory – reduces prostaglandin and leukotriene synthesis
- Mild antibacterial – acts locally in the gut
- Metabolized in the colon to 5-ASA (active anti-inflammatory) and sulfapyridine

Based on Use

- Oral therapy – tablets, enteric-coated formulations

Structure

→ Prodrug composed of sulfapyridine linked to 5-aminosalicylic acid via an azo bond (-N=N-)

Molecular formula: $C_{18}H_{14}N_4O_5S$

Structural Characteristics

- Poorly absorbed in the small intestine → reaches colon where bacterial azoreductases cleave it
- Active moiety 5-ASA reduces inflammation locally
- Formulated as tablets or enteric-coated tablets

Nomenclature

◈ Sulfasalazine → generic name
◈ Brand names: Azulfidine, Salazopyrin
◈ Formulations: tablets, enteric-coated tablets

Mechanism of Action

- Sulfasalazine is poorly absorbed in the small intestine.
- In the colon, bacterial azoreductases cleave the azo bond → releases 5-ASA (mesalazine) and sulfapyridine.
- 5-ASA: inhibits prostaglandin and leukotriene synthesis, reducing inflammation.
- Sulfapyridine: mild antibacterial activity in the colon.
- Reduces symptoms of ulcerative colitis and rheumatoid arthritis.
- Hence, sulfasalazine acts as a prodrug with anti-inflammatory and antibacterial action.

Spectrum of Activity

- Anti-inflammatory: colonic mucosa in ulcerative colitis
- Mild antibacterial: acts on intestinal bacteria producing the azo reduction
- Not effective systemically as an antibiotic

Uses

- Ulcerative colitis – induction and maintenance of remission
- Crohn's disease – limited use for colonic involvement
- Off-label: juvenile idiopathic arthritis

Adverse Effects

- Gastrointestinal: nausea, vomiting, abdominal discomfort
- Hypersensitivity: rash, fever, urticaria
- Hematological: rare agranulocytosis, hemolytic anemia, leukopenia

Chemical Degradation

- Sensitive to light and moisture
- Store in cool, dry place, protected from light
- Azo bond is stable in tablet form but cleaved by intestinal bacteria

Structure–Activity Relationship (SAR)

- Azo linkage (-N=N-) → prodrug design allowing colon-specific release
- 5-ASA moiety → responsible for anti-inflammatory activity
- Sulfapyridine moiety → provides local antibacterial effect
- Poor absorption in the small intestine → acts locally in the colon