

MEDICINAL CHEMISTRY - III

UNIT 4 NOTES

- ANTIFUNGAL AGENTS
- ANTIPROTOZOAL AGENTS
- ANTHELMINTICS
- SULFONAMIDES & SULFONES



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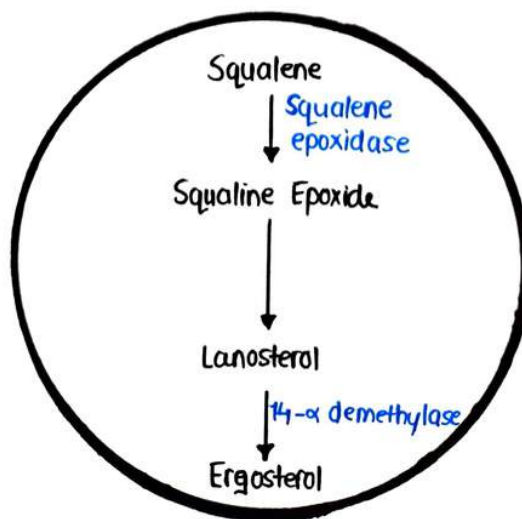
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ANTIFUNGAL AGENTS

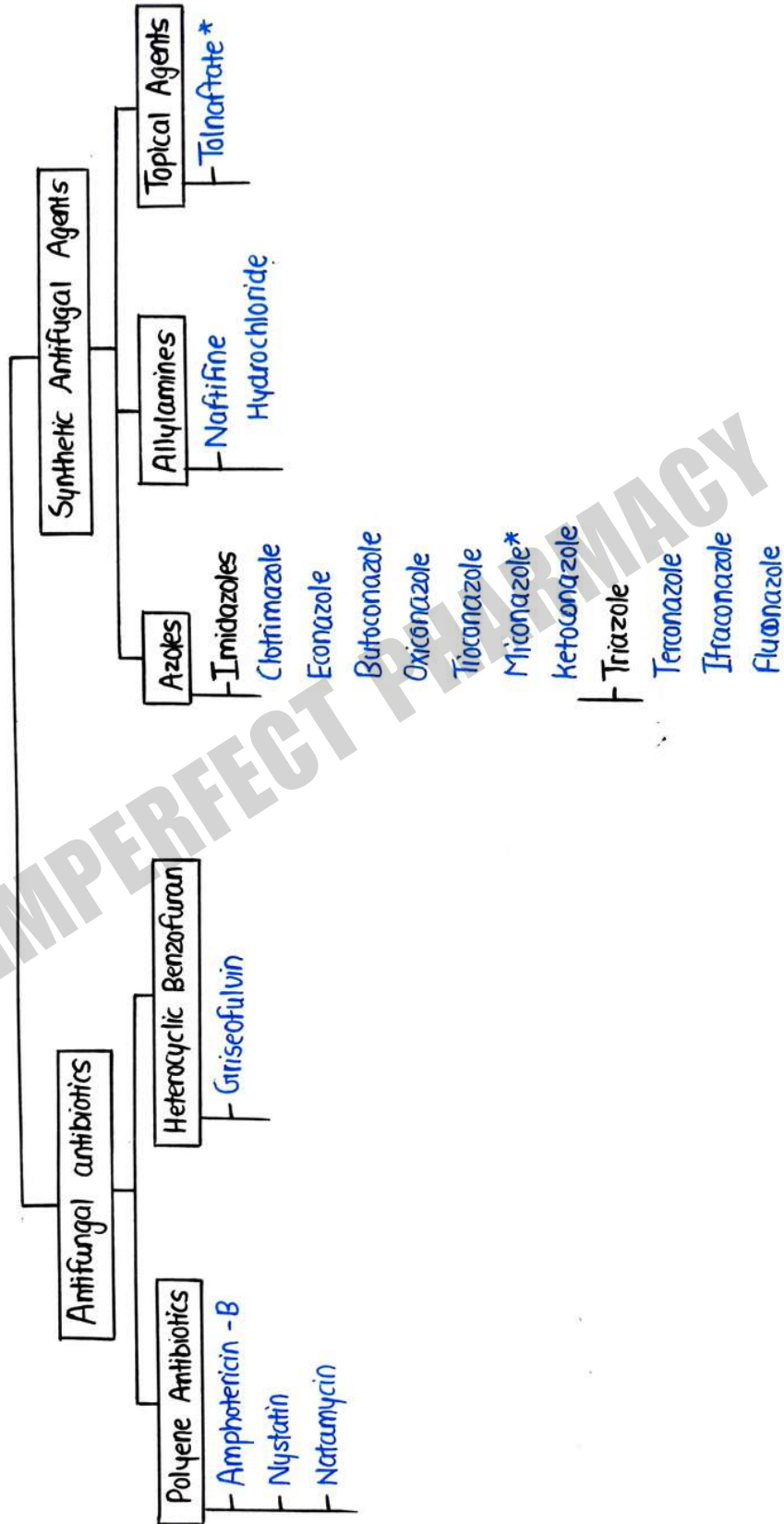
- Antifungal agents are drugs or substances used to prevent or treat fungal infections by inhibiting the growth or killing fungal cells.
- A fungal infection also known as a mycosis, is a disease caused by fungi invading & growing on or inside the human body.
- There are mainly two types of fungal infections :
 - ① Superficial: Ringworm, Candidiasis
 - ② Systemic: Candida albicans

FUNGI

- Fungi are eukaryotic micro-organisms.
- They possess mitochondria, nuclei, cell membrane & cell wall.
- Their cell wall contains chitin (Polymer of N-acetylglucosamine) as well as polysaccharides.
- Ergosterol is the major component of fungal cell membrane.



CLASSIFICATION OF ANTIFUNGAL AGENTS



ANTIFUNGAL ANTIBIOTICS

- These are class of antimicrobial drugs specifically used to treat & prevent fungal infections.
- In our syllabus, we have to study two types of Antibiotics :
 - ① Polyene Antibiotics
 - ② Heterocyclic Benzofuran

① POLYENE ANTIBIOTICS

Polyene antibiotics, such as Amphotericin-B & Nystatin exert their antifungal effect by targeting ergosterol, a key component of fungal cell membranes.

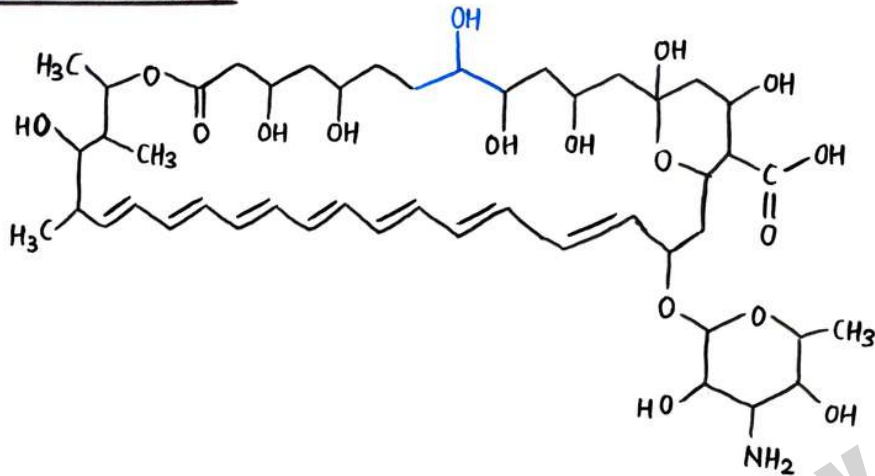
MOA

- Polyenes binds to ergosterol, present in fungal cell membranes.
- After binding to ergosterol, polyenes form pores or channels in the fungal cell membranes.
- These pores cause leakage of essential intracellular ions & molecules.
- This disruption leads to loss of membrane potential osmotic imbalance & ultimately fungal cell death.

Drugs

- Amphotericin B
- Nystatin
- Natamycin

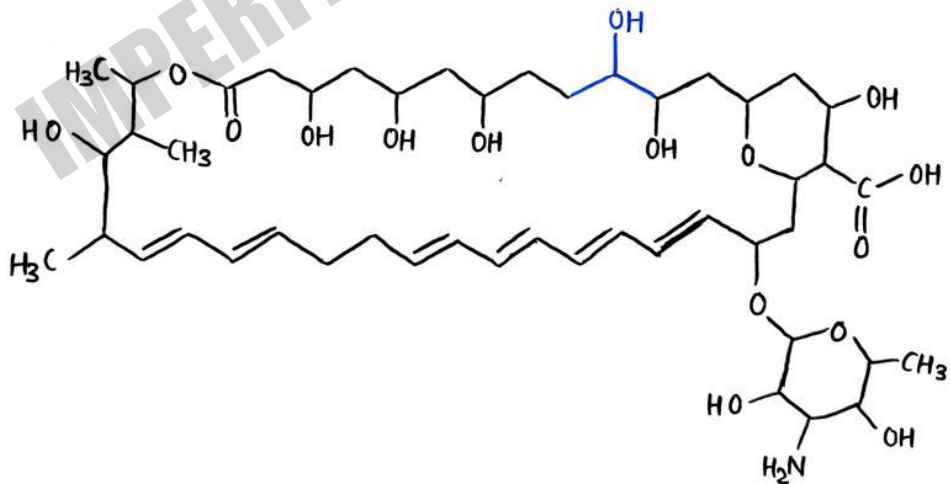
① AMPHOTERICIN B



Uses

- Candidiasis
- Cryptococcosis

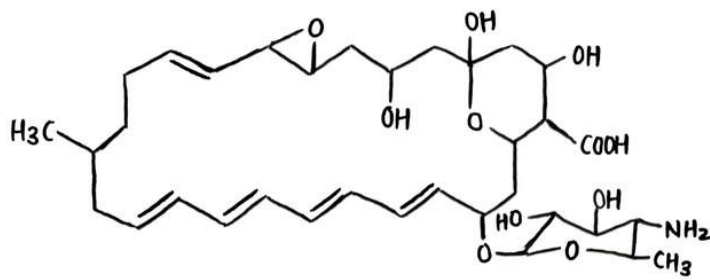
② NYSTATIN



Uses

- Dermatitis
- Candidiasis
- Esophagitis

③ NATAMYCIN

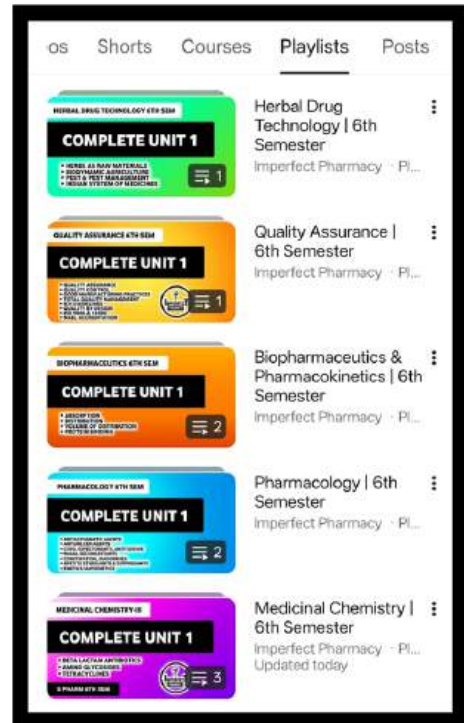
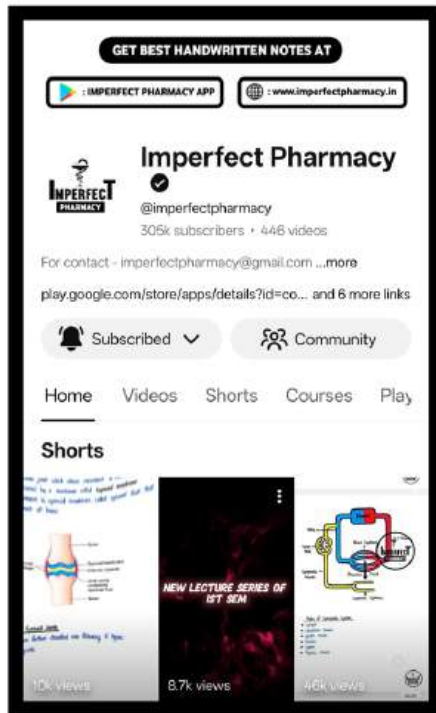


Uses

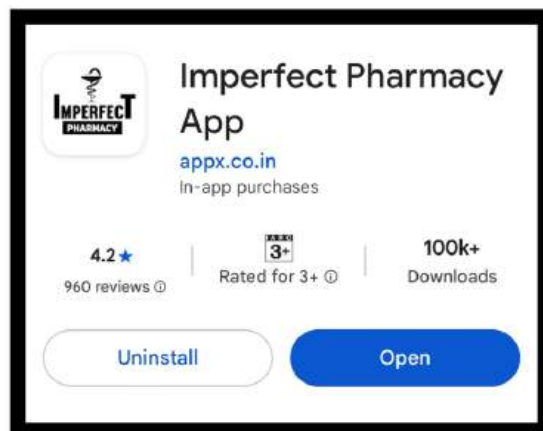
- Candidiasis
- Mycoses
- Conjunctivitis

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FOR MORE CONTENT : VISIT OUR  APP



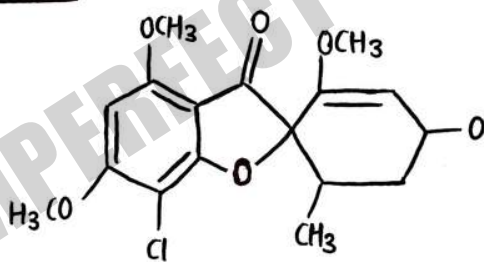
② HETEROCYCLIC BENZOFURAN

Heterocyclic Benzofuran such as Griseofulvin are antifungal agents primarily used to treat dermatophytic infections (e.g. ringworm, athlete's foot).

MOA

- They binds to fungal microtubule proteins, disrupting the function of mitotic spindle.
- This binding interferes with mitosis, particularly during metaphase, inhibiting fungal cell division.

④ GRISEOFULVIN



Uses

- Ringworm
- Athlete's foot
- Nail fungus

SYNTHETIC ANTIFUNGAL AGENTS

- These are the drugs that are chemically synthesized in laboratories to treat fungal infections by targeting specific components of fungal cells.
- It includes :
 - ① Azoles
 - ② Allylamines
 - ③ Topical agents

① AZOLES

- Azoles are major class of synthetic antifungal agents used to treat a wide range of fungal infections.
- They are characterized by the presence of Azole ring (either imidazole or triazole) in their chemical structure.

MOA

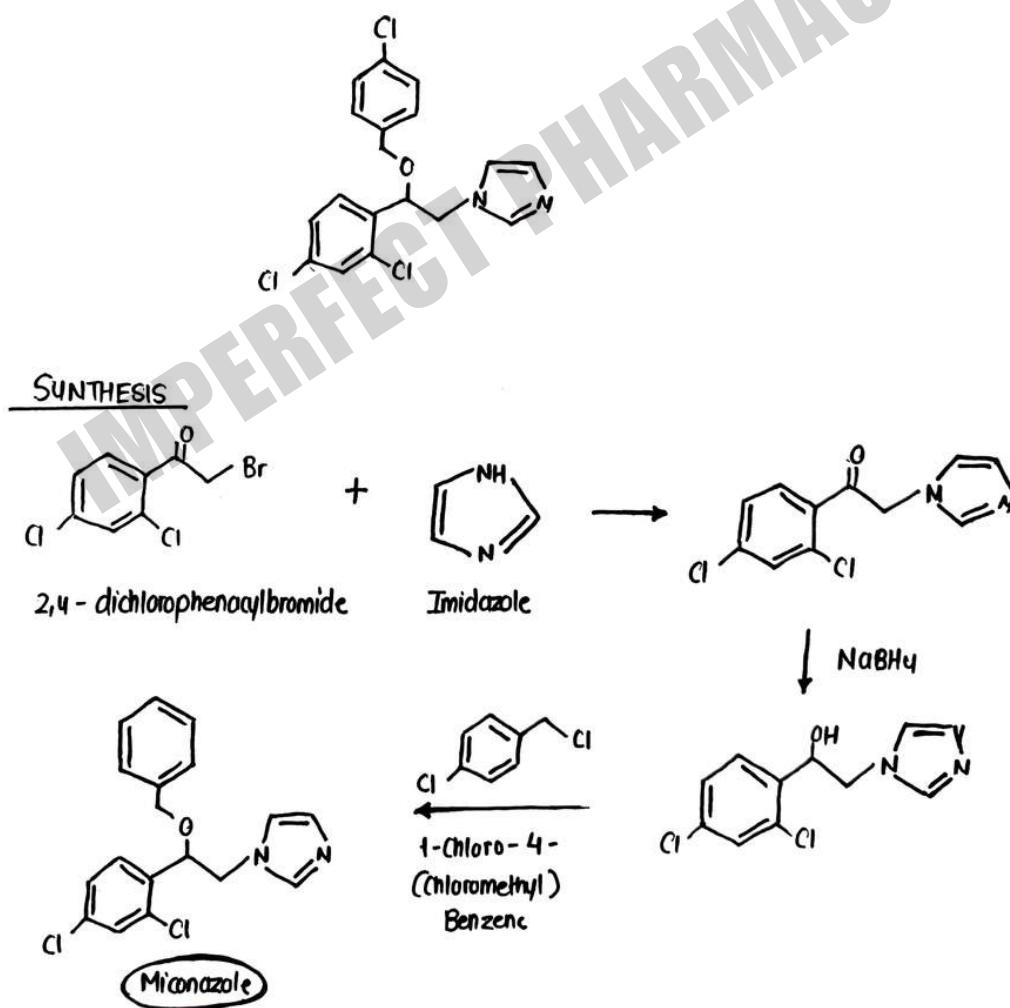
- Azoles inhibit the enzymes 14 α -demethylase, a cytochrome P450 enzyme required for ergosterol synthesis (a vital component of fungal cell membrane)
- This leads to disruption of membrane integrity, increased permeability & inhibition of fungal growth.

Drugs

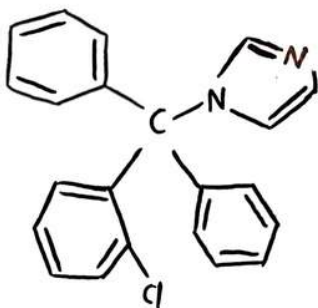
- ① Clotrimazole
- ② Econazole
- ③ Butoconazole
- ④ Oxiconazole

- Ⓔ Tioconazole
- Ⓕ Miconazole *
- Ⓖ Ketoconazole
- Ⓗ Terconazole
- Ⓘ Itraconazole
- ⓫ Fluconazole

Ⓐ MICONAZOLE *



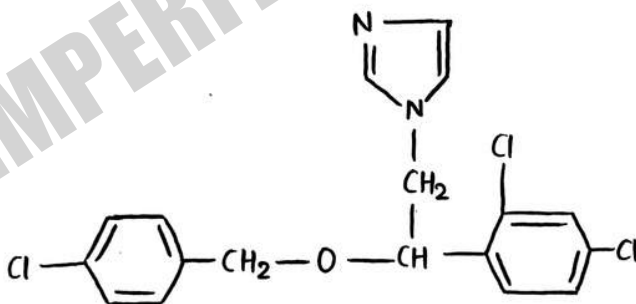
⑥ CLOTRIMAZOLE



Uses

- Ringworm
- Candidiasis

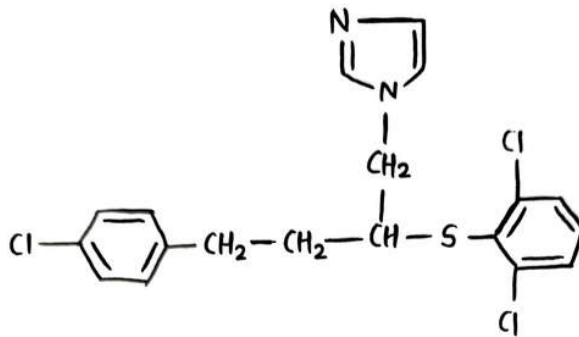
⑦ ECONAZOLE



Uses

- Tinea
- Dermatitis

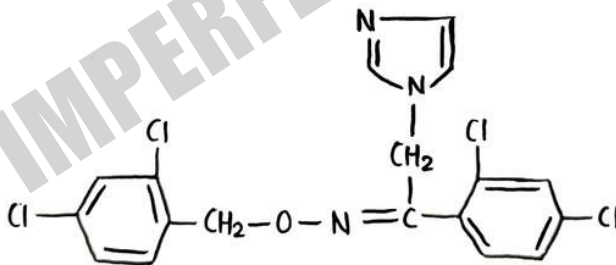
④ BUTACONAZOLE



Uses

- Mycosis
- Vaginitis

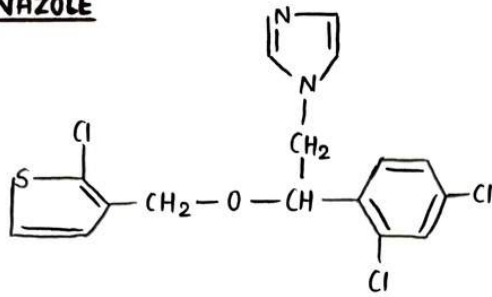
⑤ OXICONAZOLE



Uses

- Athlete's foot
- Ringworm

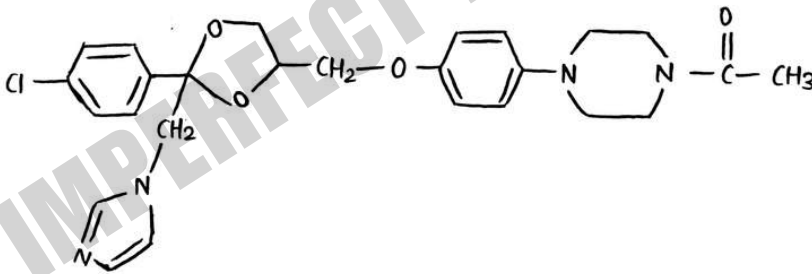
⑧ TIOCONAZOLE



Uses

- Jock itch
- Ringworm

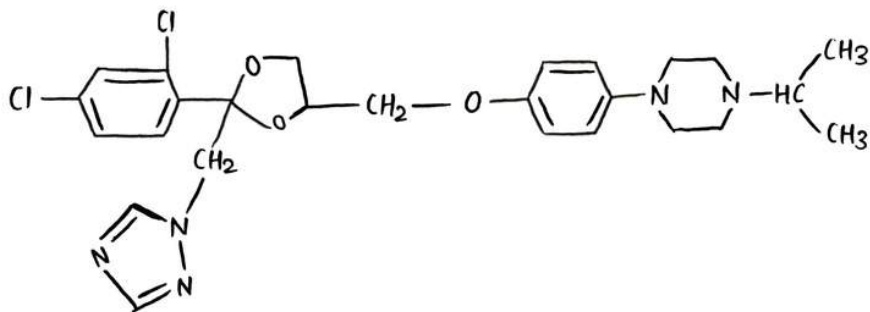
⑨ KETOCONAZOLE



Uses

- Tinea
- Dermatitis

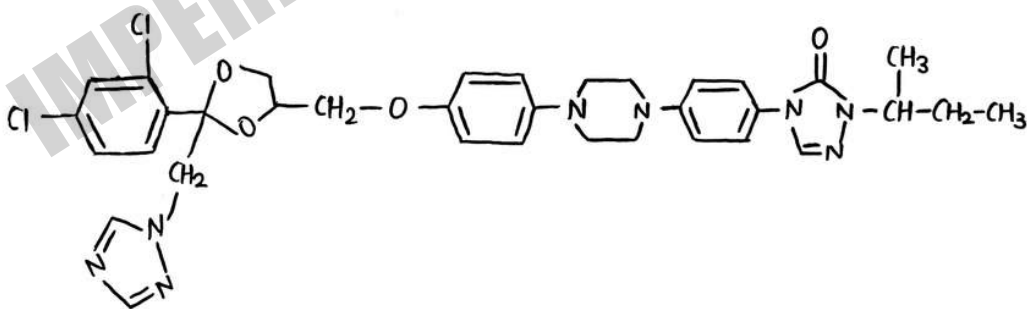
h) TERCONAZOLE



Uses

- Candidiasis
- Mycosis
- Vaginitis

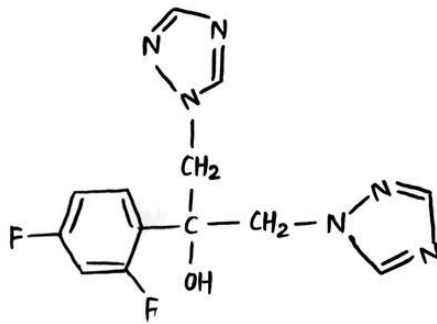
i) ITRACONAZOLE



Uses

- Aspergilliosis
- Dermatophytosis

④ FLUCONAZOLE



Uses

- Meningitis
- Candidiasis
- Tinea

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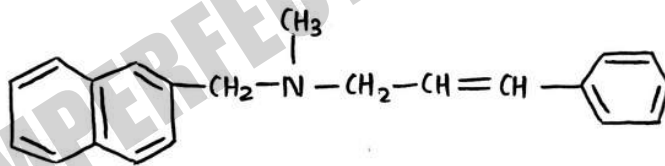
ALLYLAMINE

Allylamine are class of synthetic antifungal agents that interferes with cell membrane of Fungi.

MOA

- Allylamine inhibits the enzyme squalene epoxidase, which is essential in the ergosterol biosynthesis pathway.
- This leads to decreased ergosterol synthesis & accumulation of squalene, which is toxic to Fungal cells.
- The dual effect of ergosterol depletion & toxic squalene buildup results in fungal cell death.

NAFTIFINE HYDROCHLORIDE



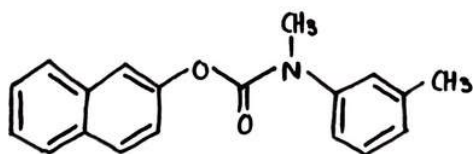
Uses

- Jock itch
- Ringworm
- Athlete's foot

TOPICAL AGENTS

Topical antifungal agents are medications applied directly to the skin, nails or mucous membrane to the superficial fungal infections.

① TOLNAFTATE *



MOA

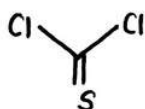
Same as Allylamine

SYNTHESIS

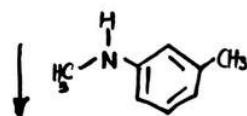
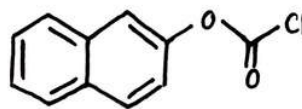


2- Naphthol

+



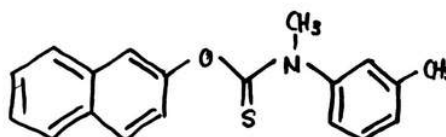
Thiophosgene



N-methyl - 3 - toluidine

Uses

- Ringworm
- Athlete's foot etc.



Tolnaftate

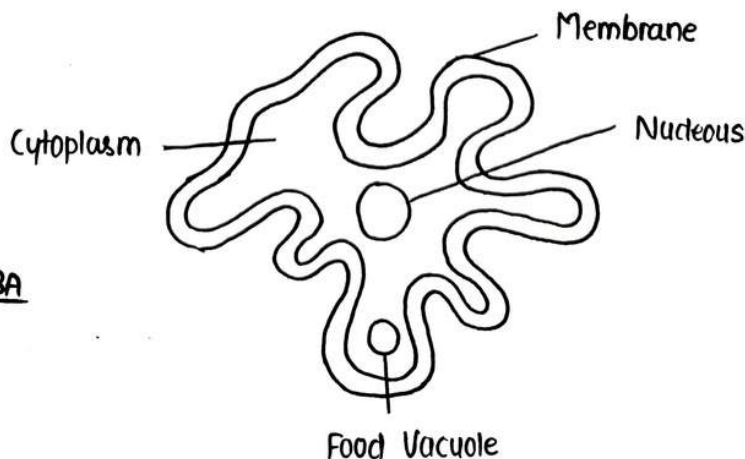
ANTIPROTOZOAL AGENTS

- Antiprotozoal agents are medications used to treat infection caused by Protozoa - unicellular micro-organisms.
- These agents work by inhibiting the growth & reproduction of protozoa or by directly killing them.

PROTOZOA

- Protozoa are single celled, microscopic organisms that belong to the Protista Kingdom.
- They are Eukaryotic micro-organisms.
- The infections caused by protozoa referred to Protozoan infections.
- These infections occur when protozoa invade the body often through contaminated water, food, insect bites or direct contact & multiply within host.
- Some common infections caused by protozoa are:
 - Amoebiasis
 - Giardiasis
 - Trichomoniasis
 - Toxoplasmosis etc

AMOEBA



AMOEBIASIS

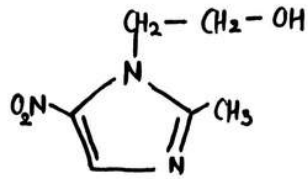
- Amoebiasis is one of the most common protozoan infection caused by *Entamoeba Histolytica*.
- It primarily affects the large intestine but in some cases, it can spread to other organs such as liver.
- It mainly transmitted through:
 - Drinking or eating contaminated water or food.
 - Having poor sanitation or hygiene
- Symptoms includes:
 - Mild to severe diarrhea
 - Stomach cramps or pain
 - fever
 - fatigue
 - Nausea
 - Bloody stools

DRUGS IN OUR SYLLABUS

- Metronidazole*
- Tinidazole
- Ornidazole
- Diloxanide
- Idoquinol
- Pentamidine Isethionate
- Atovaquone
- Efflornithine

① METRONIDAZOLE

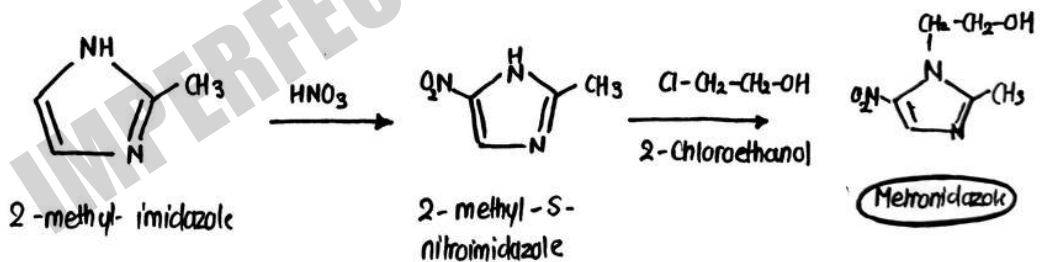
Metronidazole is a nitroimidazole class antimicrobial drug used against anaerobic bacteria & protozoa.



MOA

It is a prodrug that gets reduced inside anaerobic microorganisms. The reduced form interacts with DNA, causing strand breakage and inhibition of nucleic acid synthesis, leading to cell death.

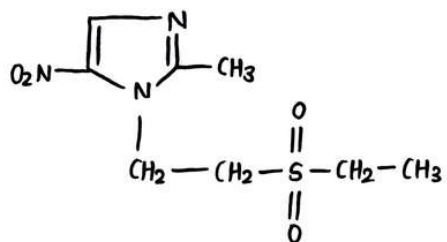
SYNTHESIS



Uses

- Amoebiasis
- Giardiasis
- Anaerobic Bacterial Infections

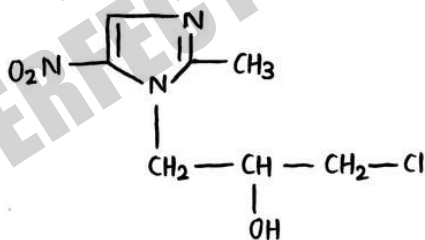
② TINIDAZOLE



Uses

- Amoebiasis
- Giardiasis
- H. pylori infections

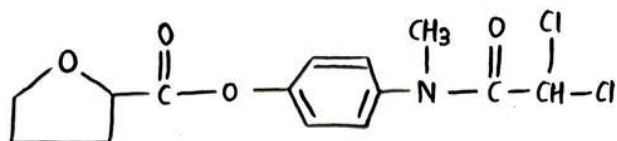
③ ORNIDAZOLE



Uses

- Dysentery
- H. pylori Infections

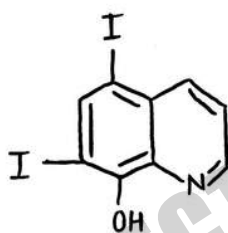
④ DIOXANIDE



Uses

- Amoebiasis
- Dysentery

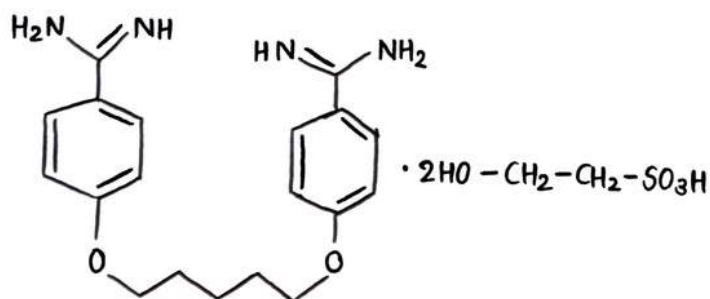
⑤ IODOQUINOL



Uses

- Diarrhea
- Giardiasis

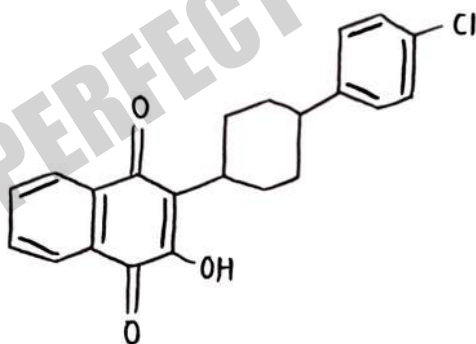
⑥ PENTAMIDINE ISETHIONATE



Uses

- Pneumocystosis
- Blastomycosis

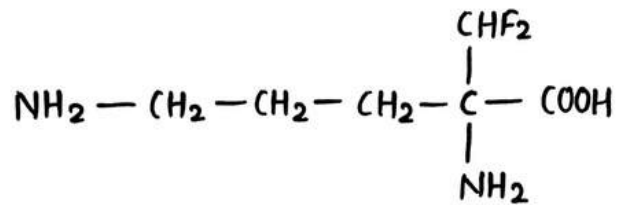
⑦ ATOVAQUONE



Uses

- Toxoplasmosis
- Malaria

⑧ EFLORNITHINE



Uses

- Psoriasis
- Trypanosomiasis
- Cancer

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ANTHELMINTICS

- Anthelmintics are drugs that expel parasitic worms (helminths) from the body, either by stunning (vermifuge) or killing (vermicidal) them without causing significant damage to the host.
- The diseases caused by helminths are known since ancient times & still constitutes a major public health hazard worldwide.

CLASSIFICATION OF HELMINTHS

Helminths are broadly classified into :

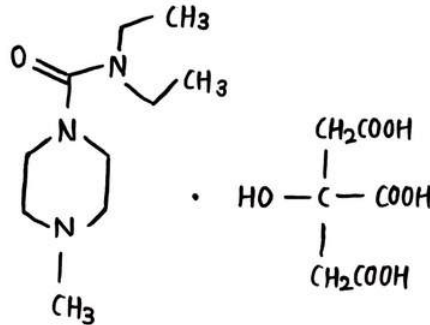
- ① Nematodes (Roundworms)
- ② Cestodes (Tapeworms)
- ③ Trematodes (Flukes)

DRUGS IN OUR SYLLABUS

- Diethylcarbamazine citrate*
- Thiabendazole
- Mebendazole*
- Albendazole
- Niclosamide
- Oxamniquine
- Praziquantel
- Ivermectin

① DIETHYLCARBAMAZINE CITRATE

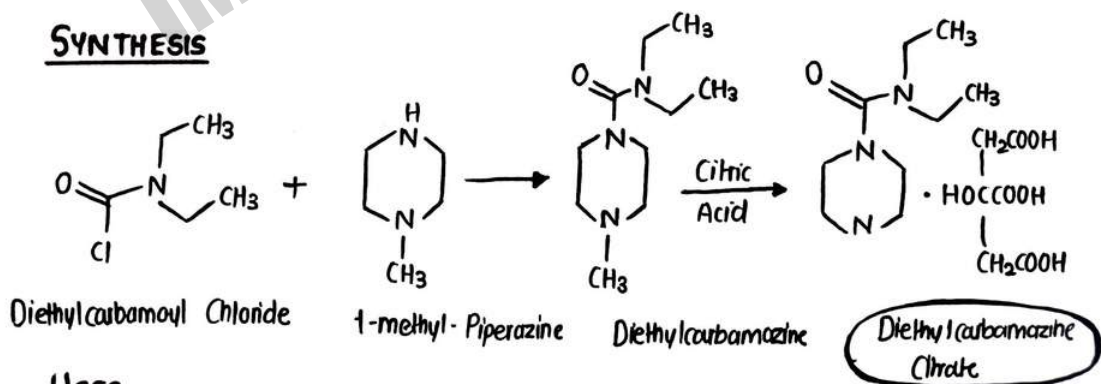
It is synthetic anthelmintic drug primarily used for treatment and prevention of filariasis a parasitic disease caused by filarial worms.



MOA

- DEC doesn't kill adult worms directly but is effective against microfilariae (larval worms).
- It alters the surface structure of microfilariae, making them more susceptible to phagocytosis by host's immune system.
- It also interferes with arachidonic acid metabolism in the parasite leading to immobilization & destruction by host defences.

SYNTHESIS

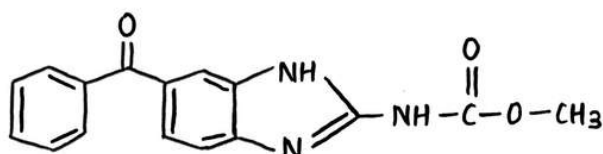


Uses

- Lymphatic Filariasis

② MEBENDAZOLE

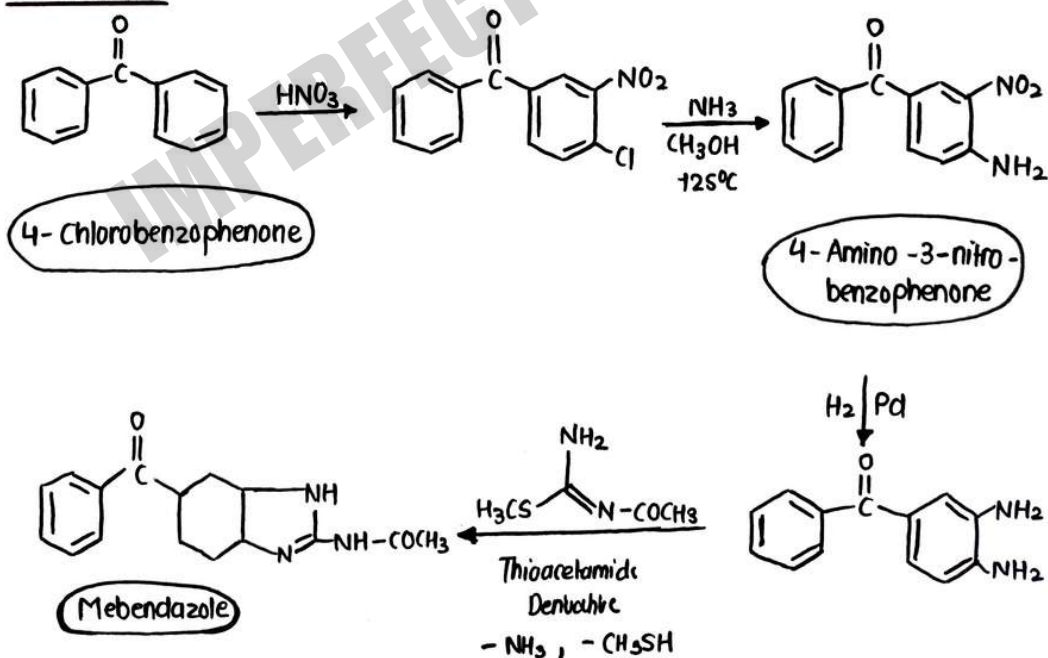
Mebendazole is a broad spectrum anthelmintic drug used to treat various intestinal worm infections caused by nematodes.



MOA

- Mebendazole binds to β -tubulin of parasitic worms.
- This inhibits microtubule formation - microtubule are needed for glucose transport inside the worm.
- Without glucose, the worm loses energy (ATP) & dies.

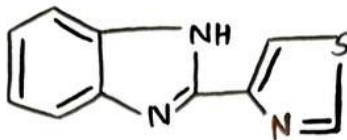
SYNTHESIS



USES

- Ascariasis, Hookworm Infections.

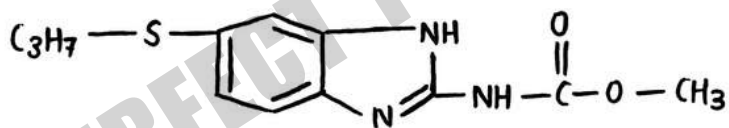
③ THIABENDAZOLE



Uses

- Pin worms
- Hook worms

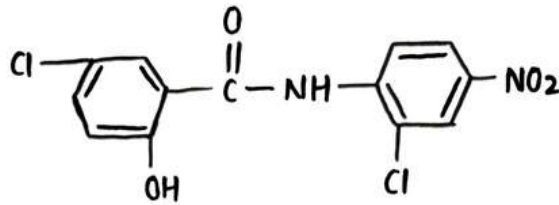
④ ALBENDAZOLE



Uses

- Ascariasis
- Giardiasis

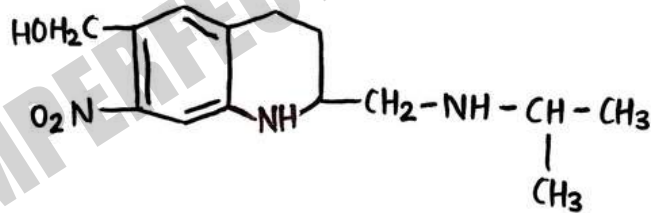
⑤ NICLOSAMIDE



Uses

- Tapeworms
- COVID -19

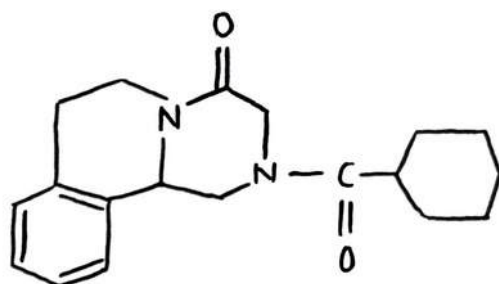
⑥ OXAMNIQUINE



Uses

- Trematodiasis
- Manson

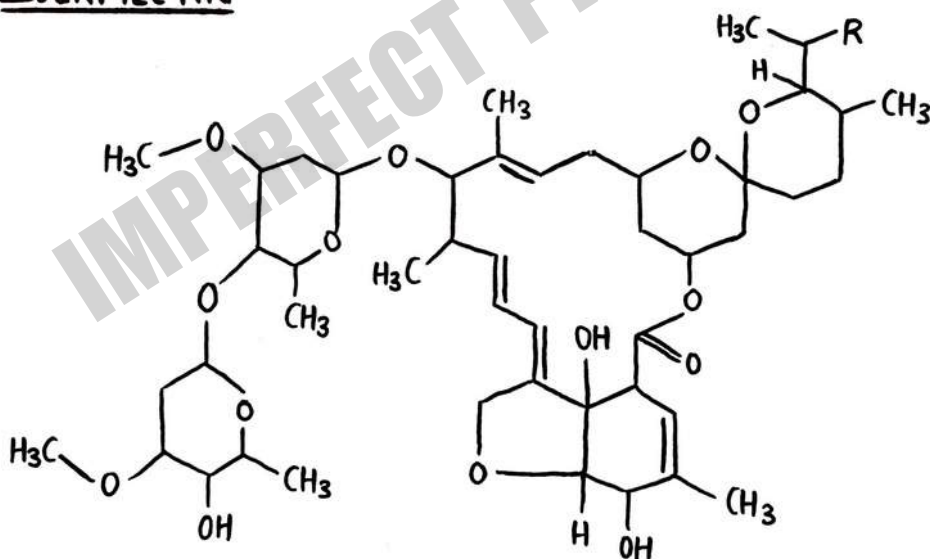
⑦ PRAZIQUANTEL



Uses

- Teniasis
- Schistosomiasis

⑧ IVERMECTIN



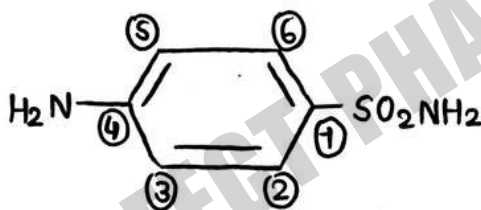
Uses

- Ascariasis
- Scabies

SULPHONAMIDES

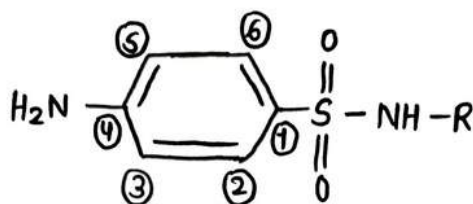
- Sulfonamides was firstly noted as anti-bacterial in 1900's by Gerhard Domagk, a nobel prize winner in 1939.
- They contain a sulfonamide ($-SO_2NH_2$) functional group.
- NC(=O)c1ccc(S(=O)(=O)N)cc1 was the first discovered sulfonamide, which was a prodrug of sulphonilamide.

GENERAL STRUCTURE



- Most antibacterial sulphonamides are para-amino benzene sulphonamides.
- NH_2 at para position is essential for Antibacterial activity.
- They are acidic in nature.
- They are insoluble in water.

SAR OF SULPHONAMIDES



① Para- Amino Group

- It's essential for activity.
- It helps the drug bind to the bacterial enzyme (dihydropteroate synthase).
- It should not be substituted
- Interference will decrease or abolishes activity.

② Sulphonamide Group

- This is the key group that resembles PABA.
- It is very necessary for antibacterial activity.

③ N₁ Substitution

Different types of groups can be substituted here,

- Simple Alkyl group (e.g. Methyl, Ethyl) → less lipophilic
- Heterocyclic ring (e.g. Thiazole, Pyrimidine) → Improves lipid solubility, enhances protein binding
- Aryl Groups (e.g. Sulfadoxine) → Long Half life, ↑ DOA
- Electronegative Groups (-Cl, -NO₂) → Increases acidity & binding affinity.

MECHANISM OF ACTION

- Bacteria need folic acid to grow & multiply, they make it themselves from a compound called PABA (Paraaminobenzoic Acid).
- Sulfonamides are structurally similar to PABA.
- So they compete with PABA for the bacterial enzyme dihydropteroate synthase.
- When sulfonamides bind to the enzyme instead of PABA.
- The enzyme is blocked.
- Dihydrofolic acid is not formed.
- Folic acid synthesis stops.
- Without folic acids, bacteria can't make DNA or proteins, so they stop growing.

CLASSIFICATION

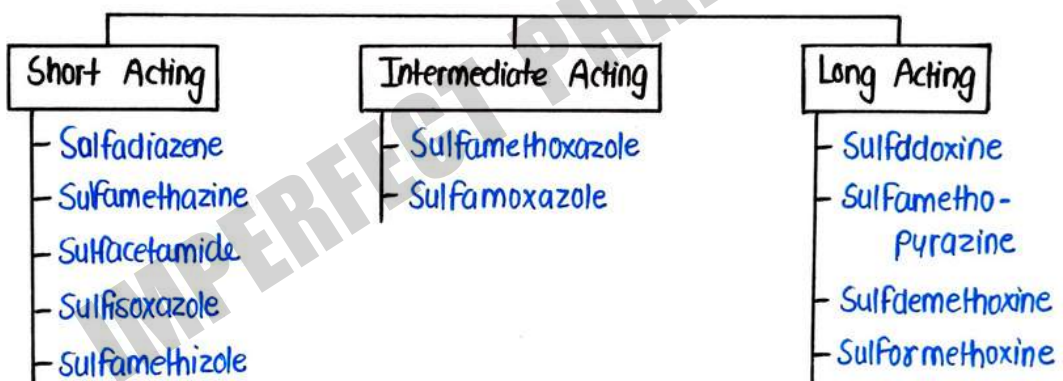
Sulfonamides can be classified as 3 types :

- ① On the basis of site of action
- ② On the basis of DOA
- ③ On the basis of chemical structure.

① ON THE BASIS OF SITE OF ACTION

- For general infections : Sulphanilamide , Sulfamethoxazole
- For Urinary Tract infections : Sulphisoxazole
- For Intestinal infections : Sulphasalazine
- For Local infections : Sulphacetamide
- For Dermatitis : Dapsone
- In Combination : Trimethoprim with Sulphamethoxazole (Cotrimoxazole)
- Injectables : Sulphafurazole (soluble sulph drugs)

② ON THE BASIS OF DOA



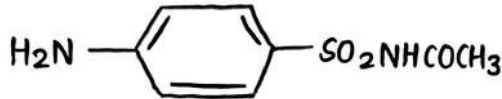
③ ON THE BASIS OF CHEMICAL STRUCTURE

- N- Substituted sulphonamide : Sulphadiazene , Sulphacetamide , Sulphadimidine .
- N₄ Substituted sulphonamides (Prodrugs) : Prontosil
- Both N-1 & N-4 substituted sulphonamides : Succinyl sulphathiazole, Phthalylsulphathiazole
- Miscellaneous : Mefenide sodium

DRUGS IN OUR SYLLABUS

① SULFACETAMIDE

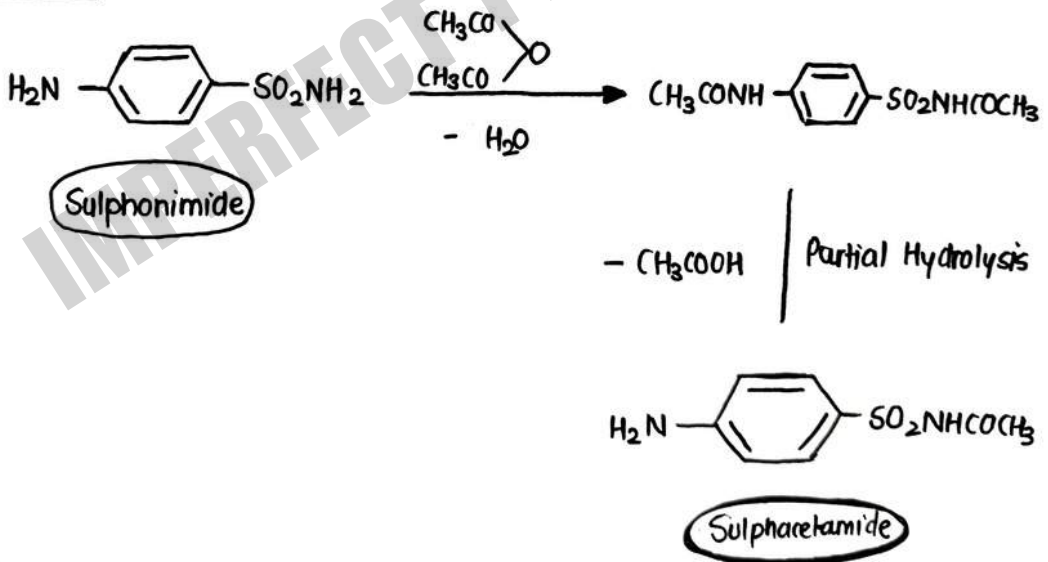
Sulfacetamide is a synthetic sulfonamide antibiotic used primarily in ophthalmic & dermatological preparations.



MOA

Same as mentioned in sulphonamide.

SYNTHESIS

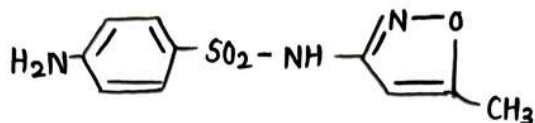


Uses

- Bacterial Conjunctivitis
- Vaginitis

② SULPHAMETHOXAZOLE

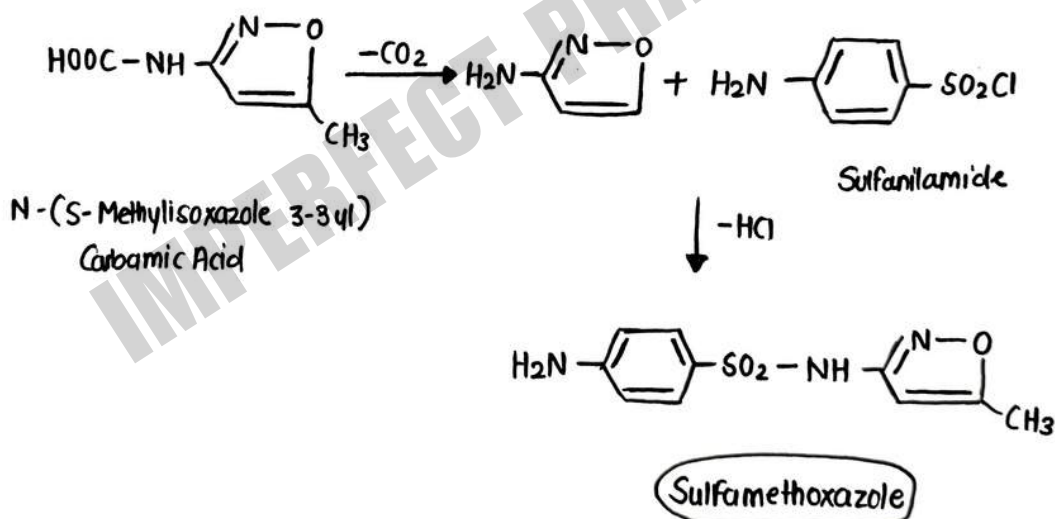
Sulphamethoxazole is a sulfonamide antibiotic often used in combination with trimethoprim for enhanced antibacterial action.



MOA

Same as mentioned in sulfonamides.

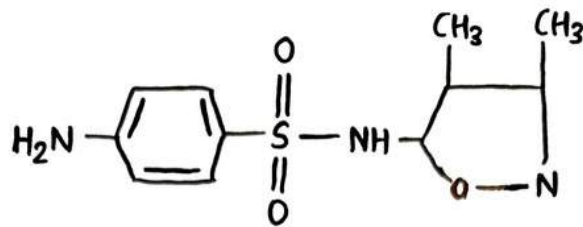
SYNTHESIS



Uses

- Bronchitis
- Urinary Tract Infections

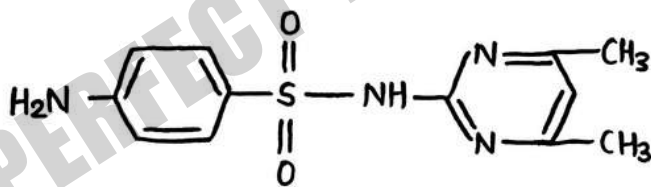
③ SULFISOXAZOLE



Uses

- Trachoma
- Meningitis
- Conjunctivitis

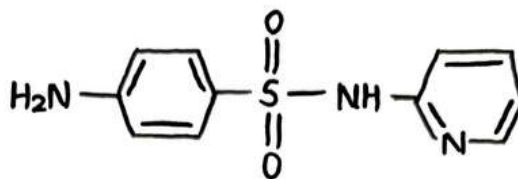
④ SULFAMETHAZINE



Uses

- Bronchitis
- Trachoma
- UTIs.

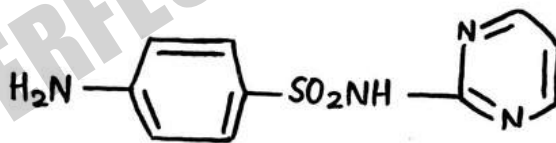
⑤ SULFAPYRIDINE



Uses

- Dermatitis
- Arthritis

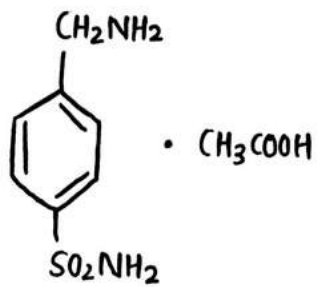
⑥ SULFADIAZENE



Uses

- Rheumatic fever
- Congenital infections

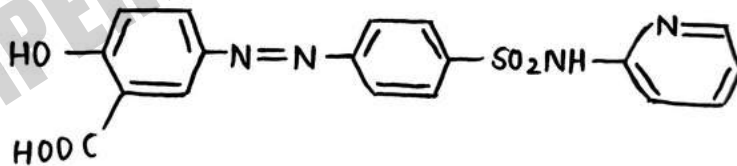
⑦ MEFENIDE ACETATE



Uses

- Burns
- Wounds
- Necrosis

⑧ SULPHASALAZINE



Uses

- Inflammatory Bowel Disease
- Ulcerative colitis
- Crohn's disease

FOLATE REDUCTASE INHIBITORS

Folate reductase inhibitors are class of drugs that block the activity of enzyme dihydrofolate reductase (DHFR).

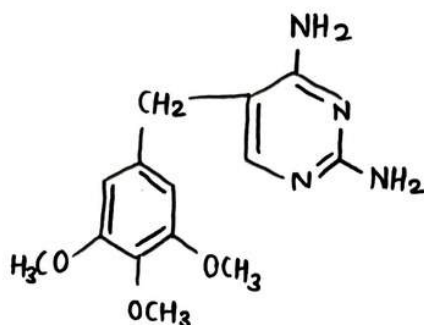
MOA

- Dihydrofolate Reductase (DHFR) normally reduces Dihydrofolate (DHF) to Tetrahydrofolate (THF).
- Folate reductase inhibitors bind to the active site of DHFR, which leads to inhibition of THF production.
- Since THF is essential for nucleotide (DNA, RNA) synthesis, inhibition leads to impaired DNA replication & cell division.

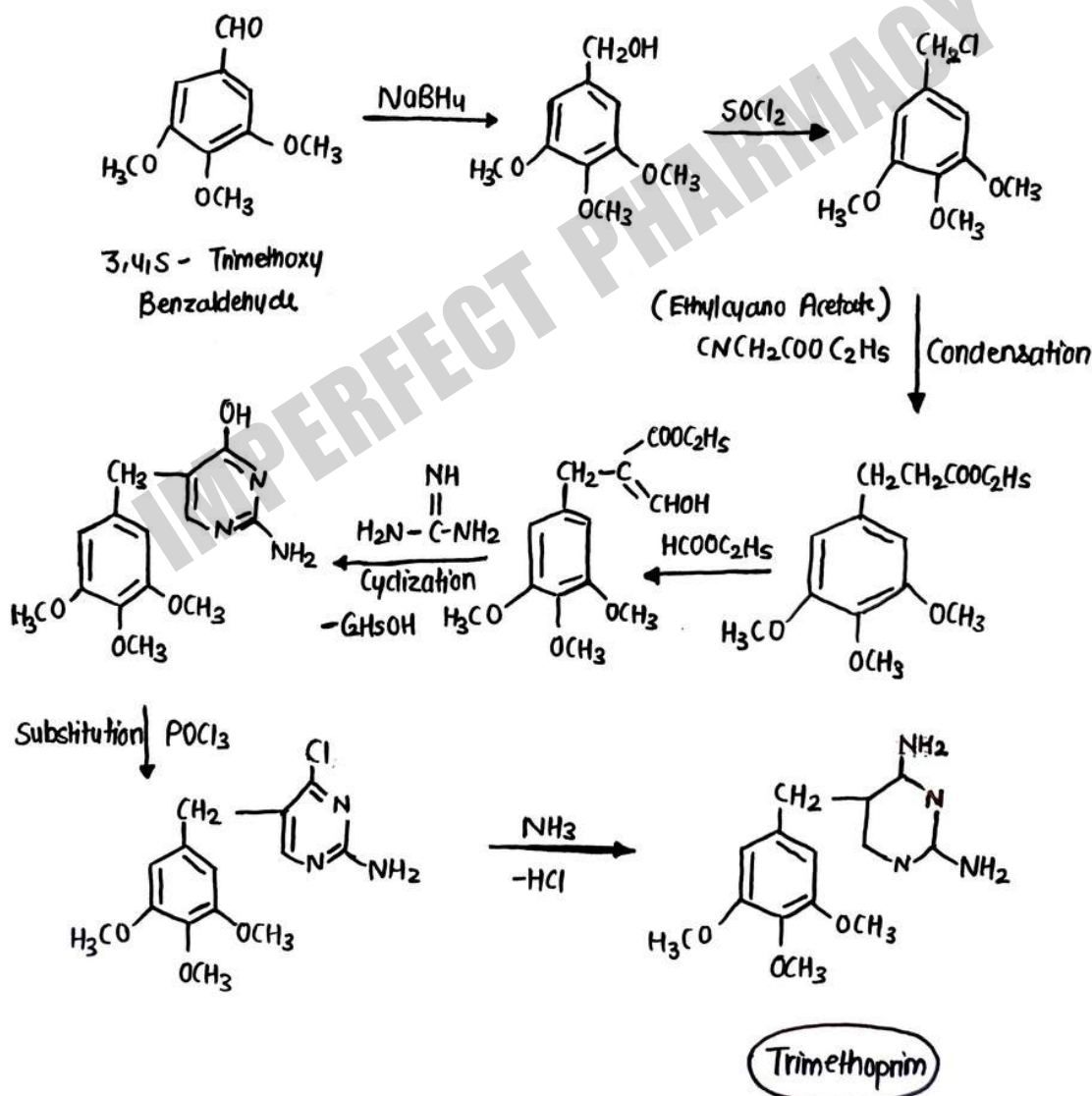
DRUGS

- Trimethoprim*
- Cotrimoxazole

④ TRIMETHOPRIM



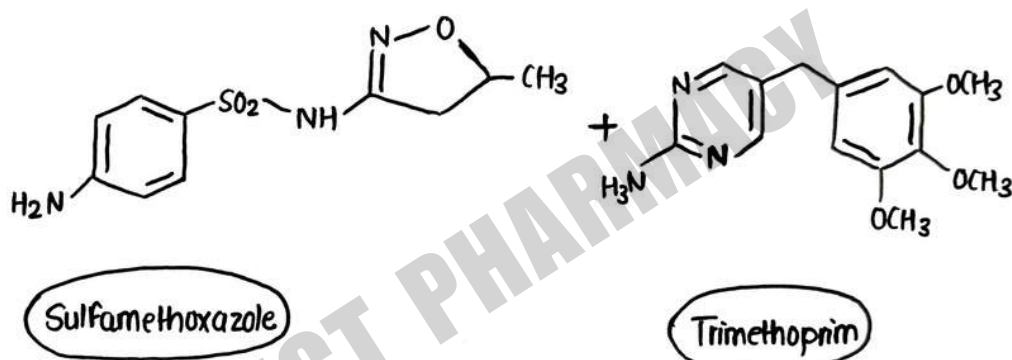
SYNTHESIS



Uses

- Uncomplicated pyelonephritis
- Mild acute prostatitis
- Respiratory Tract Infections
- Pneumonia

② COTRIMOXAZOLE



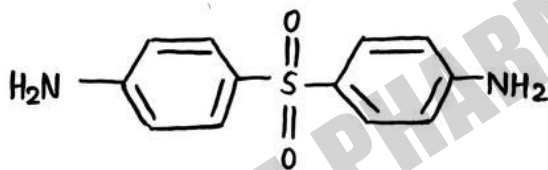
Uses

- E. coli
- Streptococcus pneumoniae
- Staphylococcus Aureus
- Salmonella

SULPHONES

- Sulphones are organic compounds that contain a sulfonyl group ($-SO_2-$) bonded to two carbon atoms.
- These carbon atoms can belong to either alkyl or aryl groups.

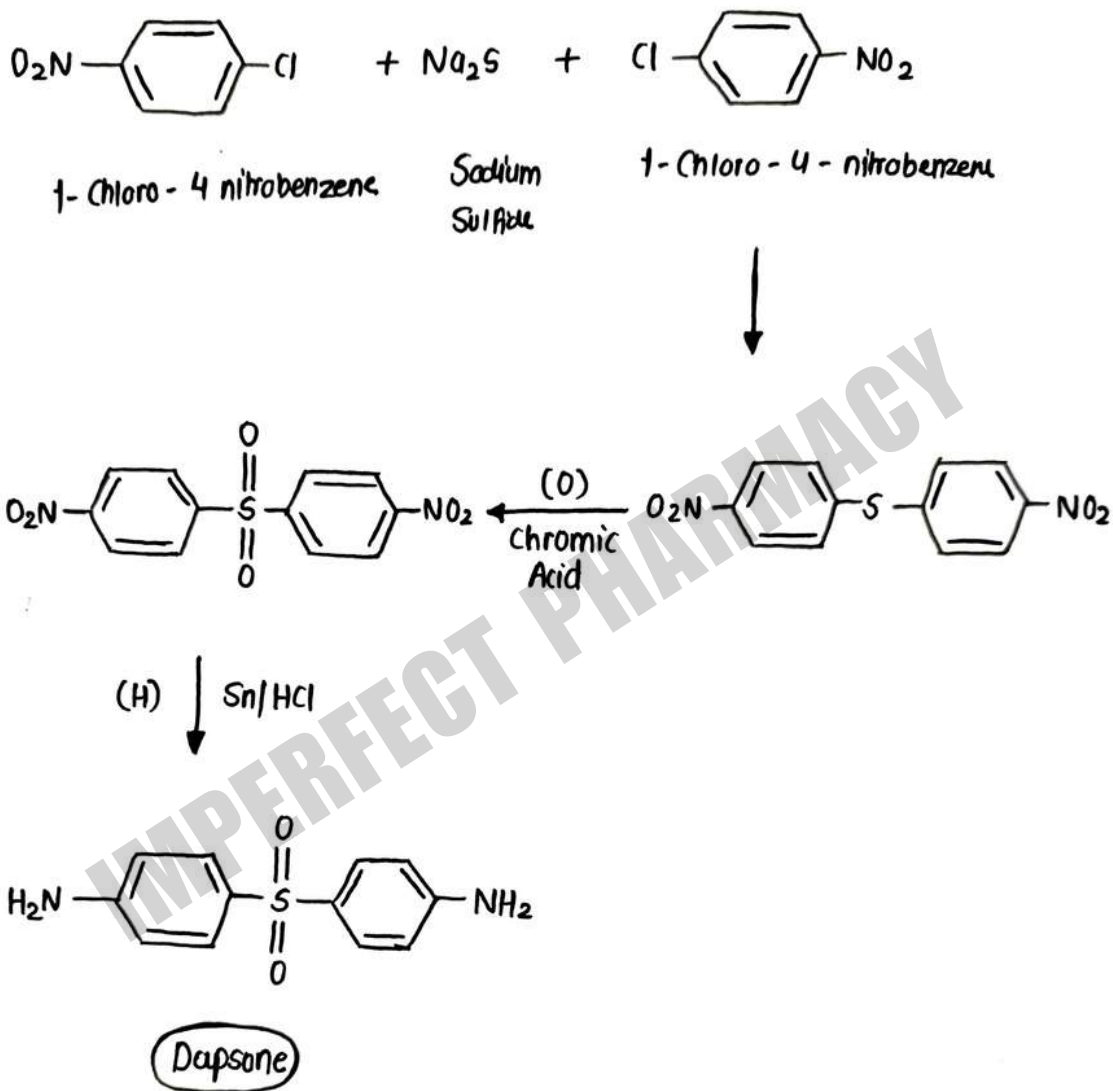
DAPSONE



MOA

Same as Sulfonamides.

SYNTHESIS



Uses

- Anti-inflammatory Agent
- Treatment for leprosy.

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER



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