ANTI-FUNGAL

Macrorganism
- Prokaryotes → ...
- Eukaryotes → Advanced (superior than prokaryotes) → have Nuclear membrane → pair of chromosomes

fungi:
→ ex. of Eukaryotes
→ They are heteromorphous, surviving/leaving on pre-formed organic matter.

Metabolism of fungi Consist of:
→ Synthesis of Chitin, which is a polymer of N-acetyl-glucosamine → which play role in cell wall Synthesis.
→ Synthesis of ergosteral → participate in formation of plasma cell membrane.

Risk factors:
→ Improper use of broad Spectrum Antibiotics
→ Spread of AIDS → Use of Immunosuppresent
→ Cancer chemotherapy → Older age → Diabetics
→ Pregnant Woman → Burn wound etc.

Transmission:
→ Inhalation of Spores:- Aspergillous, cryptococcus
→ Penetration into mucosa:- Condida albicans
→ Percutaneous Inoculation:- In cutaneous and Sub-cutaneous infection such as
Dexomatophyte and Madura foot.
(dandruff) (infection of limb & feet)
(Itching of fingers)
→ Ingestion of Toxin:- food

Classification:

Drug Acting On Cell Membrane

Polyenes Antibiotics

Amphotericin B,
Nystatin
Natamycin
Hamycin

Allylamines

Terbinafine
Naftifine

Azoles

Imidazole

1. Clotrimazole
2. Econazole
3. Butaconazole
4. Isoconazole
5. Sertaconazole
6. Ketoconazole
7. Miconazole
8. Oxiconazole
9. Sulconazole

Diazoles

1. Fluconazole
2. Itraconazole
3. Isavuconazole
4. Posaconazole
5. Ravuconazole
6. Terconazole
7. Voriconazole

Drug Acting on Cell Wall (Inhibit cell wall S)

Caspofungin — Pneumocandis
Micafungin
Anidulafungin

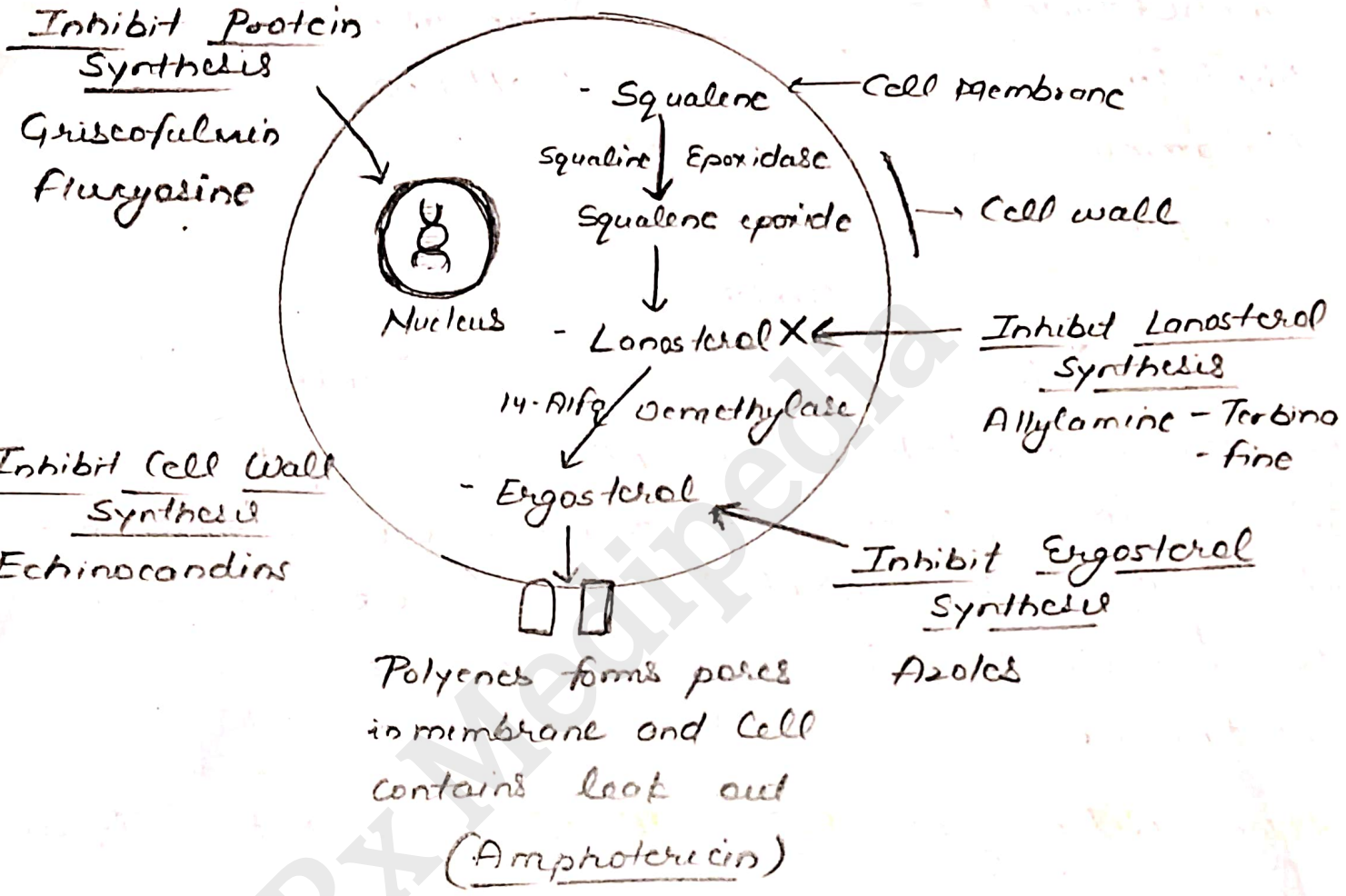
Drug Acting on Nucleus (Inhibit protein Synthesis)

Griseofulvin
Flucytosine

Other topical Agents

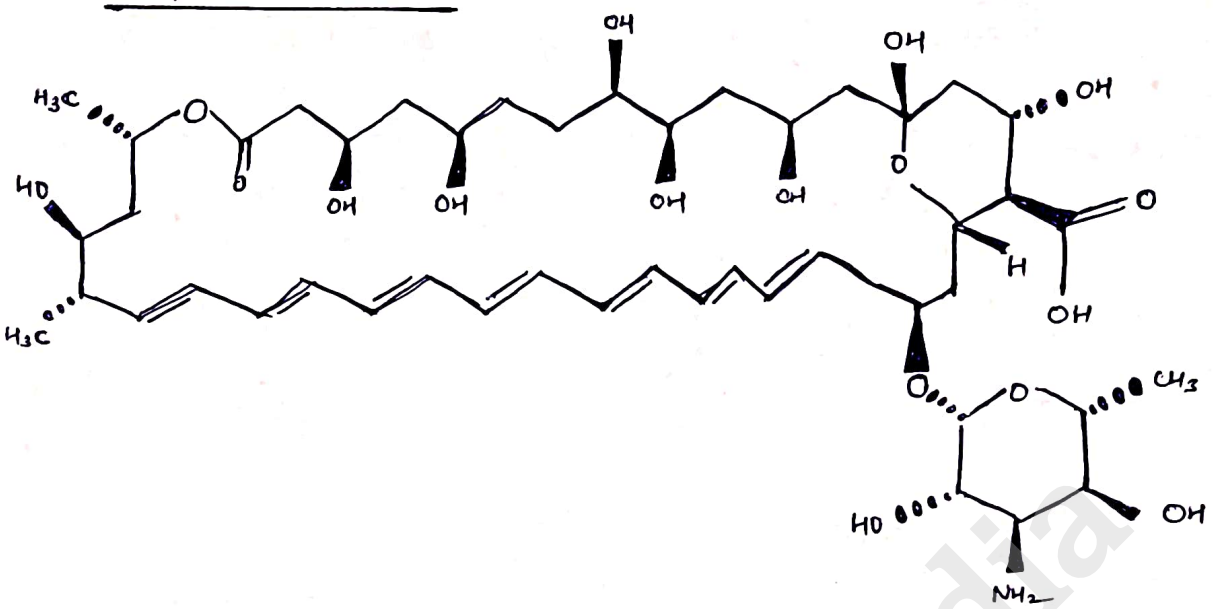
Tolnaflate, Undecylenic Acid, Benzoic Acid, Salicylic Acid, Naftifine, Selenium Sulfide, Ciclopiroxolamine

Mode of Action

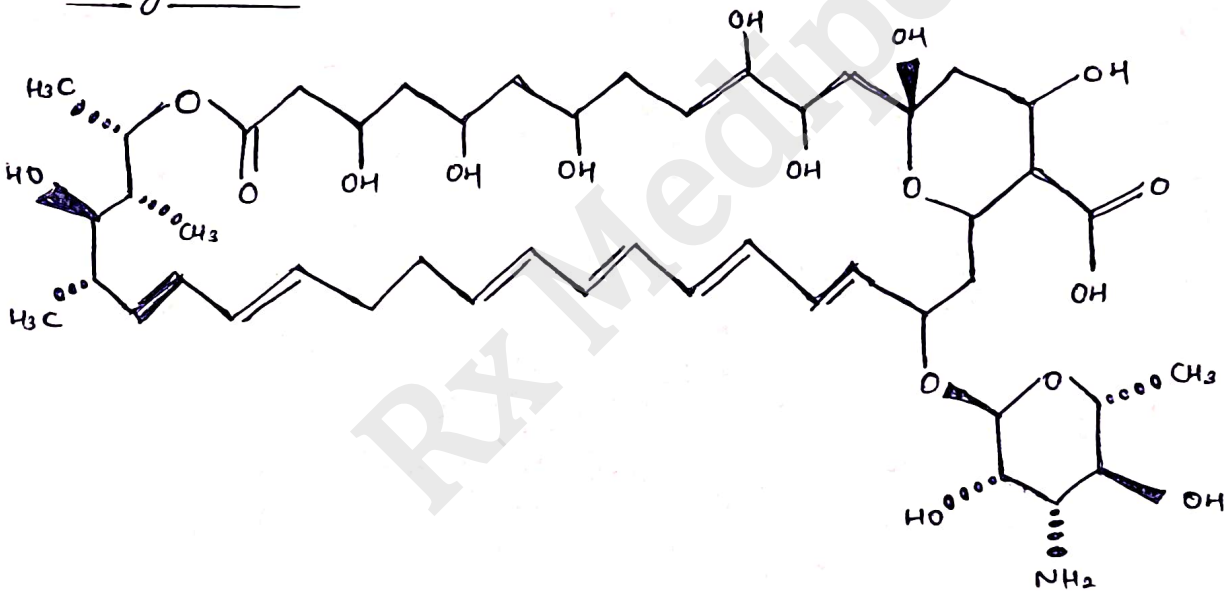


1. Polyenes Antibiotics

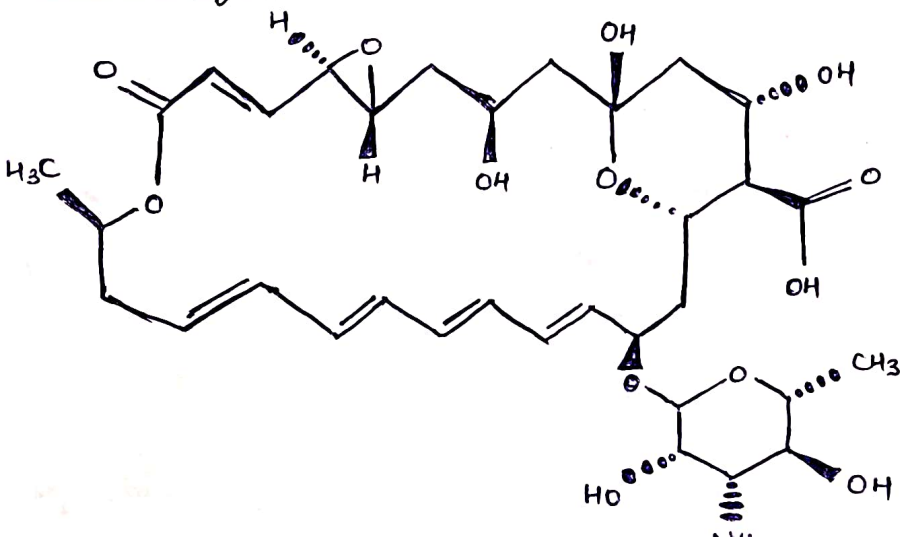
→ Amphotericin – B



→ Nystatin

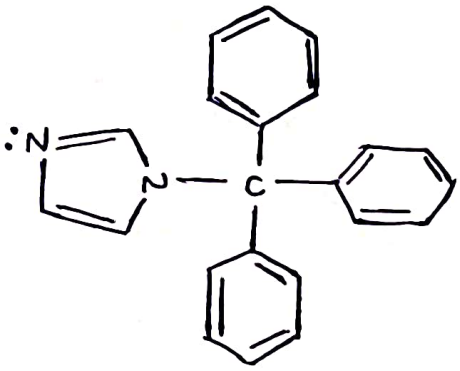


→ Natamycin

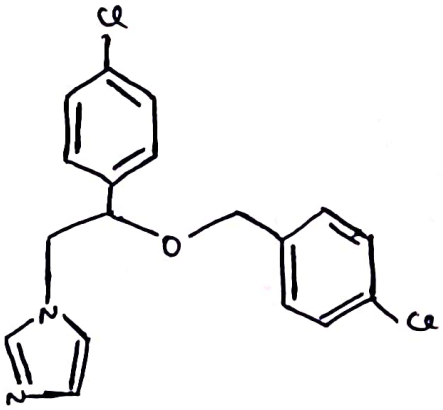


2. Azoles

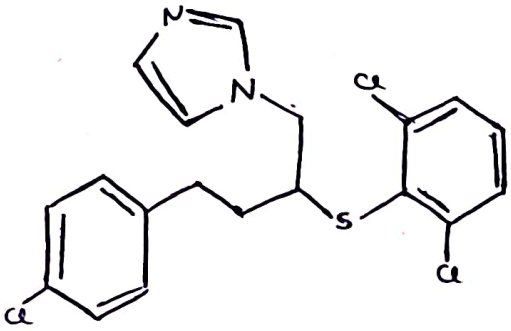
→ **Clotrimazole**



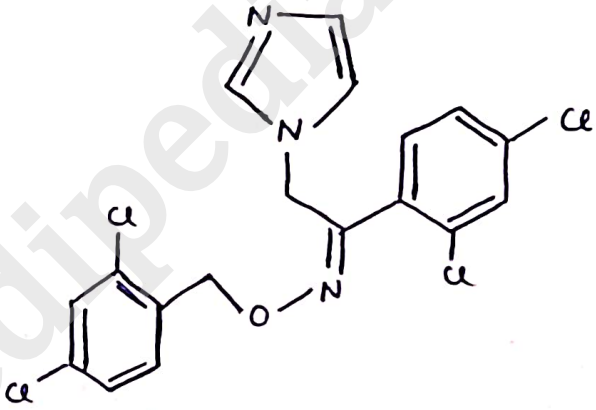
→ **Econazole**



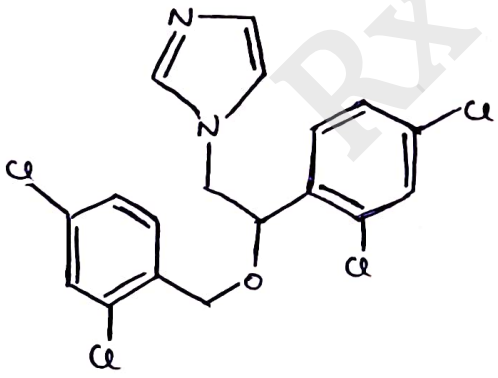
→ **Butaconazole**



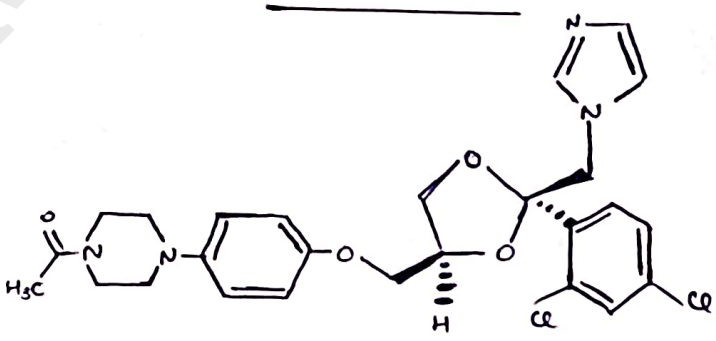
→ **Oxiconazole**



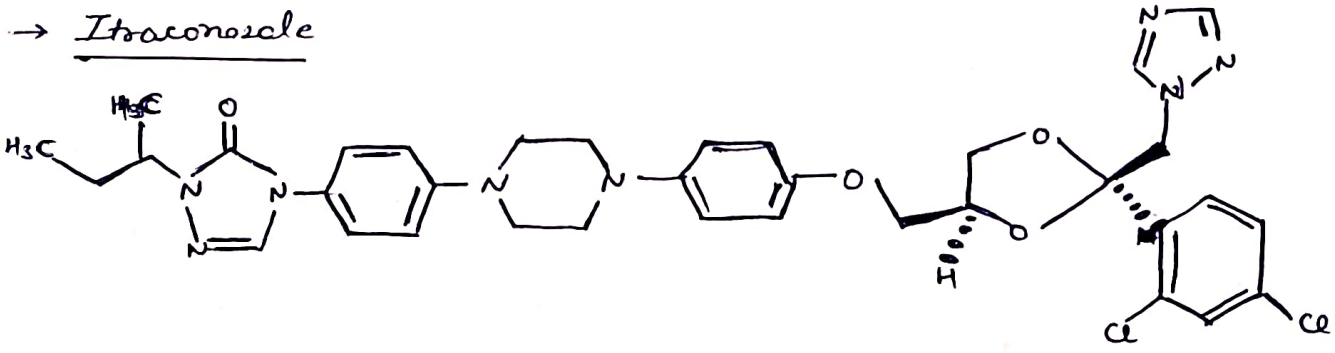
→ **Miconazole**



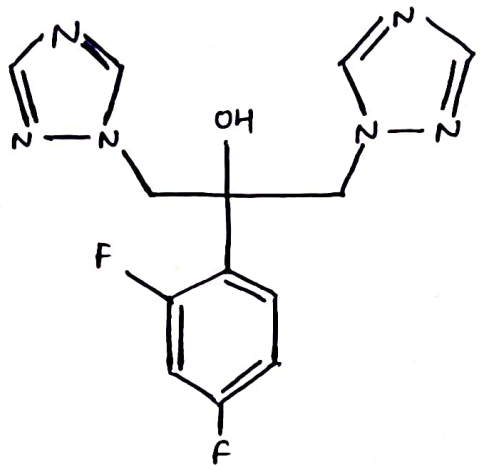
→ **Ketoconazole**



→ **Itraconazole**

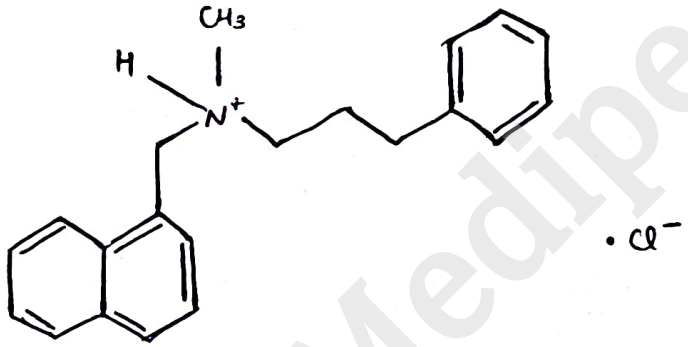


→ Fluconazole



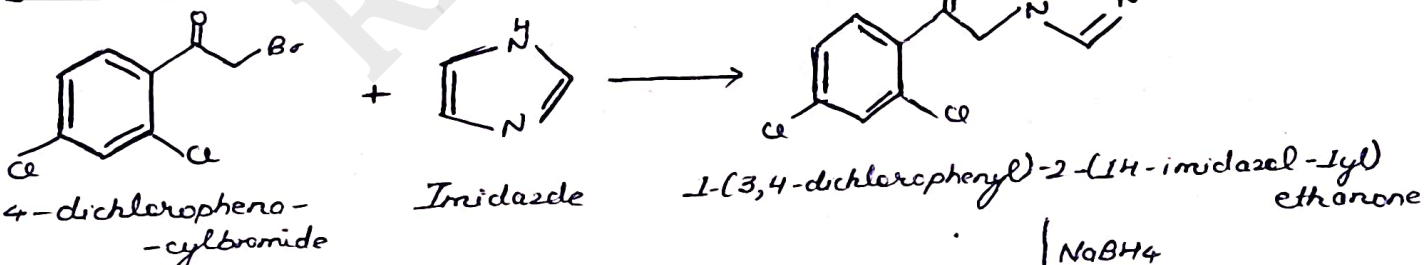
Allylamines

→ Naftifine HCl



SYNTHESIS

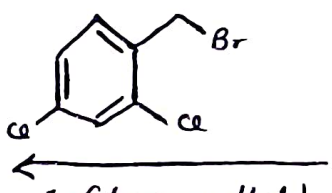
1. Miconazole



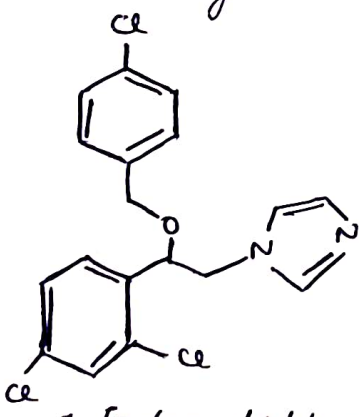
2,4-dichlorophenacylbromide + Imidazole → 1-(3,4-dichlorophenyl)-2-(1H-imidazol-1yl) ethanone

↓ $NaBH_4$

1-(3,4-dichlorophenyl)-2-(1H-imidazol-1yl) ethanone

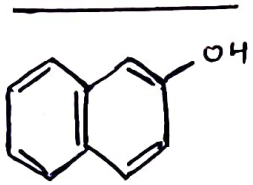


1-(bromomethyl)-2,4-dichlorobenzene

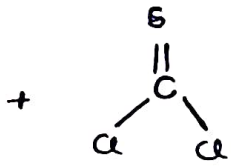


1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methoxy]ethyl] imidazole

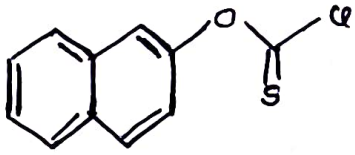
2. Tolnaftate



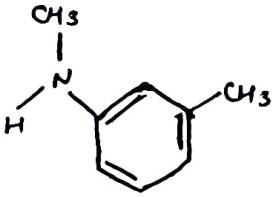
2-Napthol



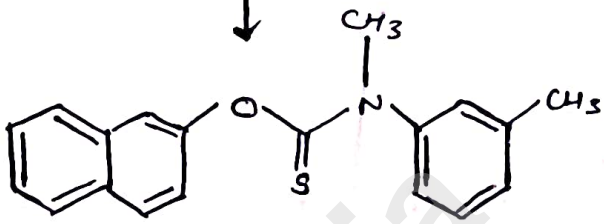
Thiophosgene



[O-napthalen-2yl-carbonochloridothioate]



[N-methyl-3-toludine]



O-napthalene-2yl-methyl(m-tolyl) Carbonothioate

ANTI - PROTOZOAL AGENTS

→ Protozoal diseases are categorized as malaria, Amebiasis.

→ Amebiasis is a disease of large intestine caused by Entamoeba histolytica which affect wall of colon or other parts of body.

It exists in two forms:

i) The motile trophozoite form

ii) The dormant cyst form

Cyst form is responsible for transmission of disease.

→ Anti protozoal agents are used to treat these diseases.

SYMPTOMS OF AMEBIASIS

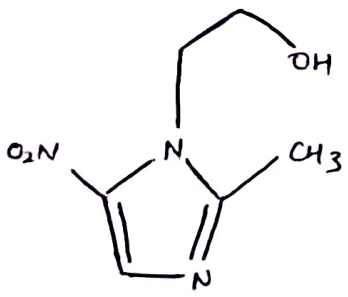
→ Many patients may experience no symptoms

→ Diarrhea

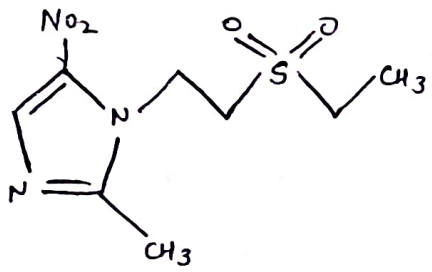
→ Enlargement of liver

DROG PROFILE

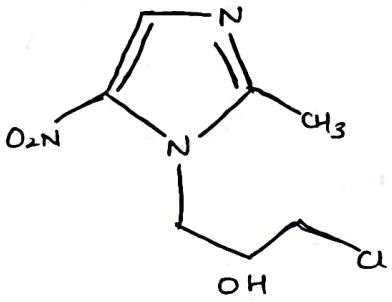
→ Metronidazole



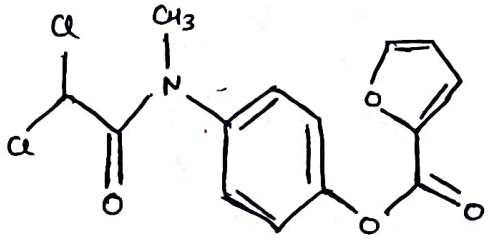
→ Tinidazole



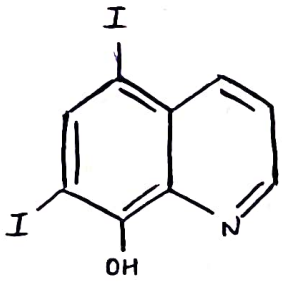
→ Ornidazole



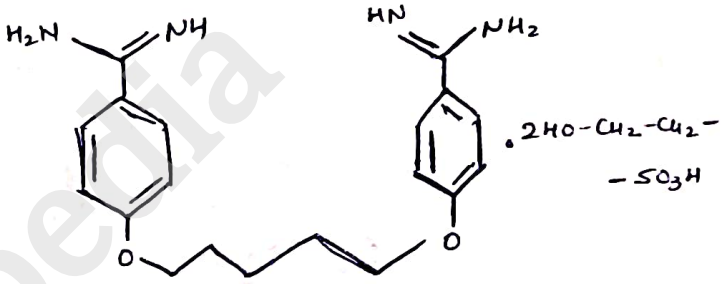
→ Diloxanide



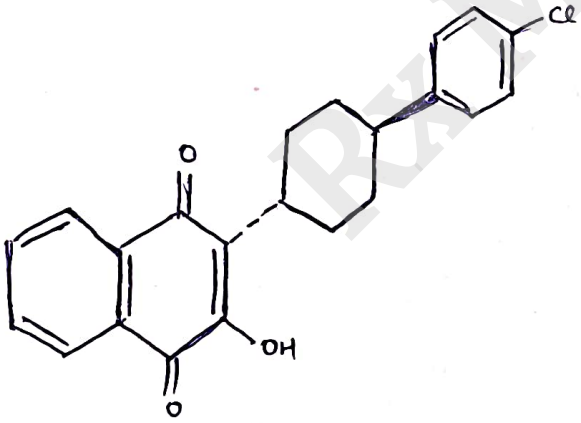
→ Iodoquinol



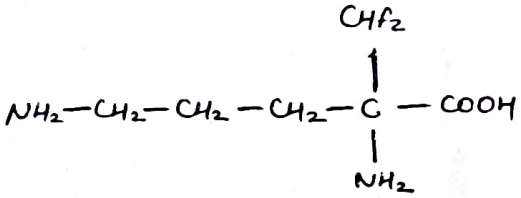
→ Pentamidine Isethionate



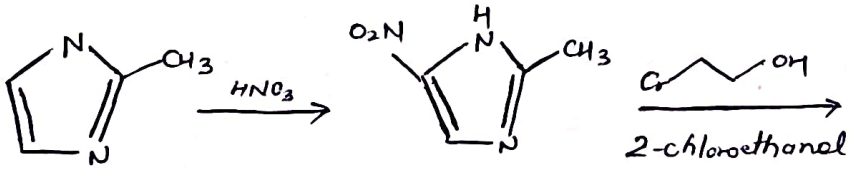
→ Atovaquone



→ Eflornithine



SYNHESIS



2-methyl- Imidazole → 2-methyl 5-nitroimidazole → Metronidazole

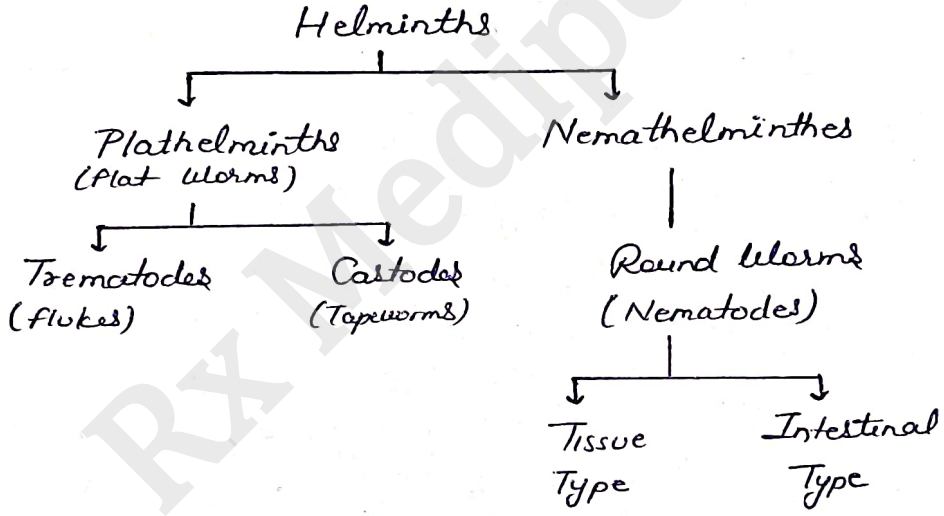
ANTHELMINTICS

→ Anthelmintics or Anti-helmithics are group of anti-parasitic drugs that expel parasitic worms from the body by killing them without causing damage to the host.

→ They are used to treat people who are infected by helminths (parasitic worms), a condition called helminthiasis.

HELMINTHS

→ They are parasitic worms which cause poor nutrient absorption, weakness and disease in the host.



→ Platyhelminths

- They are group of soft bodied flattened invertebrates.
- found in the oceans, fresh water.

a) Cestodes

- flat segmented worms that lives in intestines of some animals.

Types of Cestodes :

i) Beef Tapeworm

ii) Pork Tapeworm

iii) Pork Tapeworm larval stage

iv) Dwarf Tapeworm

v) fish Tapeworm

b) Trematodes [flukes]

types of Trematodes :

i) Schistosoma mansoni

ii) Schistosoma hematobium

iii) Schistosoma japonicum

iv) Paragonimus species

v) fasciolopsis busti

vi) fasciola hepatica

vii) Clonorchis sinensis

→ Nemathelminthes

They are thread or round worm.

a) Nematodes

- Also called roundworms
- Present in every ecosystem like fresh water, soil etc.

Types of Nematodes are:

i) Intestinal Round worms

→ Common Round worm

→ Pinworm

→ Whip worm

→ Threadworm

→ Hookworm

iii) Tissue Round Worms

→ Trichinosis

→ Guineaworm

iii) Other

→ Filariasis

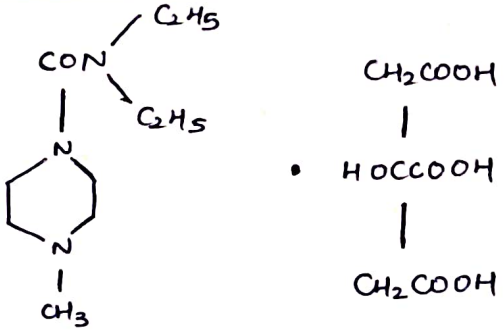
→ Loiasis

CLASSIFICATION

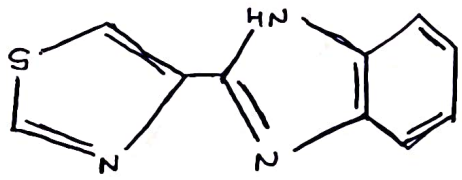
1. Piperazine : Diethylcarbamazine , Piperazine Citrate
2. Dyes : Pyrvinium pamoate
3. Vinyl pyrimidines : Pyrantel pamoate
4. Benzimidazoles : Albendazole, Mebendazole, Thiabendazole
5. Quinolines and Isoquinolines : Oxaminoquine, Praziquantel
6. Natural Products : Ivermectin , Avermectin
7. Phenol derivatives : Niclosamide , Bithional
8. Nitro derivatives : Niridazole
9. Imidazothiazole : Levamisole
10. Antimonial Compounds : Antimony pottasium tartrate
11. Organophosphorus : Metrifonate

DRUG PROFILE

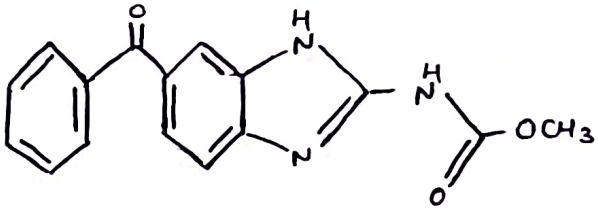
→ Diethyl carbamazine Citrate



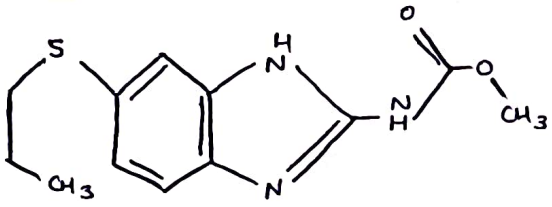
→ Thiabendazole



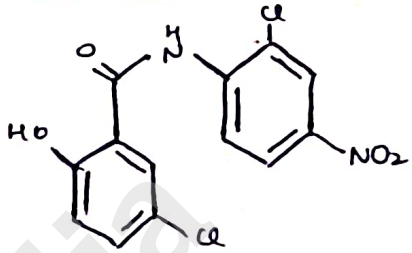
→ Mebendazole



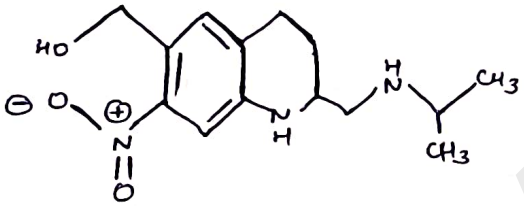
→ Albendazole



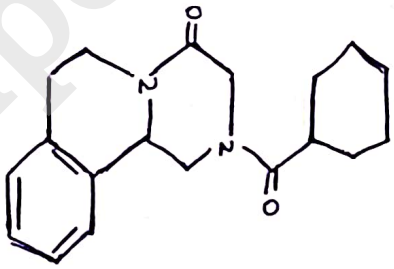
→ Niclosamide



→ Oxamniquine

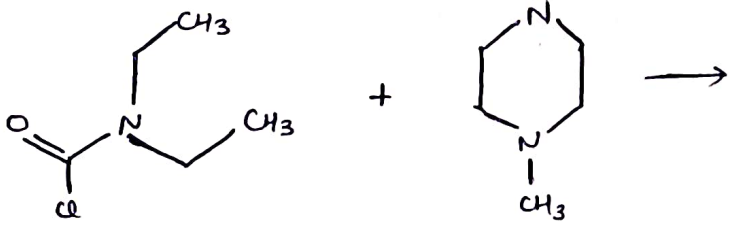


→ Praziquantel



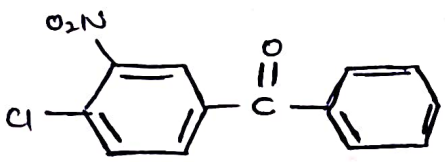
SYNTHESIS

1. Diethylcarbamazine Citrate



Diethylcarbamoyl chloride + 1-methyl-piperazine → Diethyl-Carbamazine

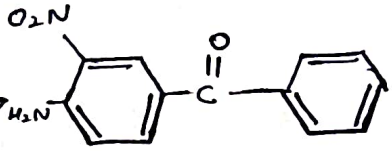
2. Mebendazole



4-Chloro-3-nitro benzophenone

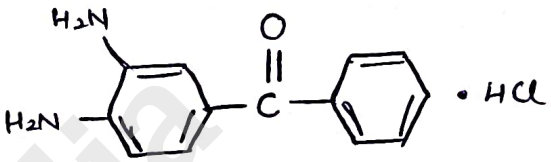
+ NH_4OH

Sulpholane / CH_3OH

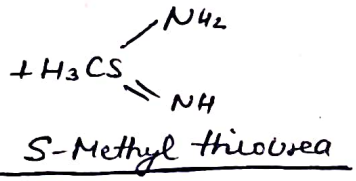


4-Amino-3-nitro benzophenone

+HCl + H_2



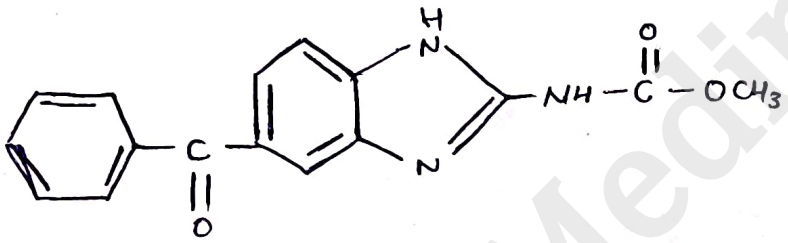
Diamino benzophenone hydrochloride



S-Methyl thiourea

$HClCOOCH_3$

Methyl chloroformate

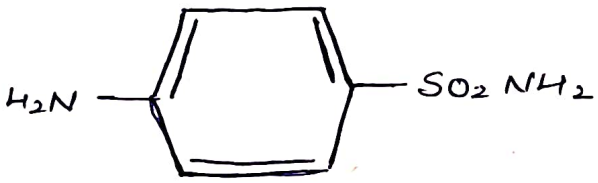


Mebendazole

SULFONAMIDES

→ Derivatives of PABA (Para Amino Benzoic Acid)

→ They are earliest known chemotherapeutics drugs and are commonly used although their place has been taken by other antibiotics like penicillins, cephalosporins, aminoglycosides etc.



[Para Amino benzene Sulfonamide]

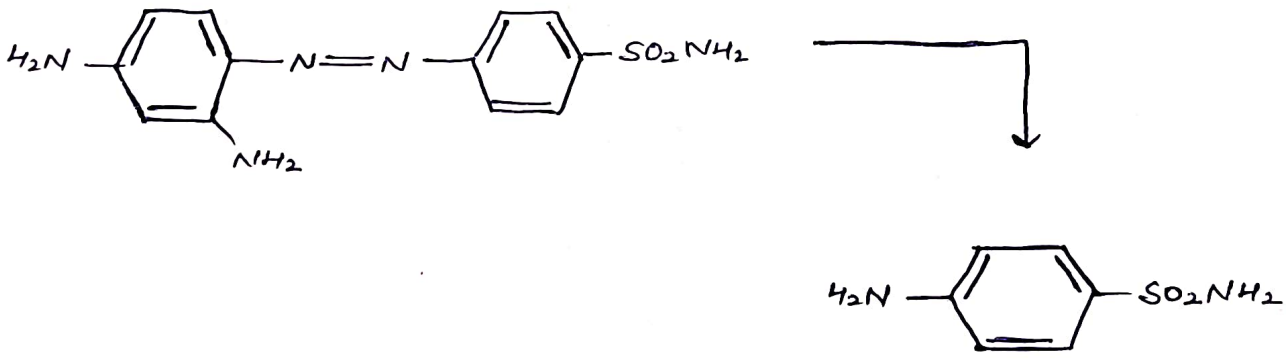
HISTORY

→ First Synthesized in 1908 by Gelmo

→ In 1935, Gerhard Domagk observed number of azo dyes which effective against Streptococci.

→ In 1935, German firm prepared Red dye 4-Sulphonamides-2, 4-diaminobenzene and after 3 years Domagk found curative properties in this compound and named it prontosil.

→ Sulphonamide is metabolic product of prontosil.



Sulfonamide

MECHANISM OF ACTION

Pteridine Precursor [help to growth and
+ make folic acid]

PABA
[Para Amino Benzoic Acid]

Dihydropteorate Synthetase — Sulfonamides

Dihydro folic Acid

Trimethoprim

Dihydrofolate Reductase — 2NADPH-2H → 2NADP

Tetra hydro folic Acid

Amino Acid Synthase | Purine Synthase | Thymidine Synthesis

Responsible for growth and Replication of Microorganism

PABA and precursors are required for growth of bacteria

↓

These bacteria take PABA from surroundings media and prepare folic Acid

↓

When sulfonamides are administered, bacteria can not distinguish between PABA and Para amino benzene sulfonamides.

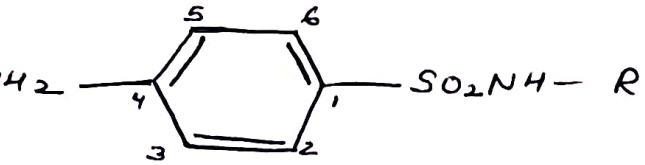
↓

because of their chemical Resemblenes.

↓

They take up sulfonamide in place of Para Amino Benzoic Acid, So they cannot convert into folic Acid.

STRUCTURE ACTIVITY RELATIONSHIP

Amino group [

→ Amino group is essential for the Activity.

→ Sulphonyl group is essential for the Activity.

→ Amino group and sulphonyl group should be 1 and 4 position.

→ The N-4 amino group can be modified to pro-drug.

→ S atom directly linked to benzene Ring.

→ Replacement of benzene Ring by other ring decrease the Activity.

→ Replacement of SO_2NH group by –CONH reduces the Activity.

→ Maximum Anti-bacterial activity is obtained by sulphonamide having pka value between 6.6 to 7.4.

→ Amino group is replaced by group which can be reconverted it back to Amino group.

eg. Acetamido

CLASSIFICATION

[A] On the basis of Site of Action

→ Sulfonamides for general infection : Sulphanilamide , Sulphapyridine , Sulphadiazine , Sulphamethoxazole

→ Sulfonamides for Urinary tract infection : Sulphisoxazole, Sulphathiazole

→ Sulphonamides for intestinal infections : Succinyl sulphathiazole, Sulphasalazine

→ Sulphonamides for Local infections : Sulphacetamide , Mafenide

→ Sulphonamides for dematitis : Dapsone , Solapsone

→ Sulphonamides in Combination : Trimethoprim with Sulphamethoxazole.

[B] On the basis of Pharmacokinetic Properties ;

→ Rapidly absorbed and Rapidly excreted sulfonamides : Sulfamerazine , Sulfadimidine , Sulfadiazine , Sulfonilamide

→ Rapidly absorbed and Slowly excreted Sulfonamides : Sulfamethoxazole , Sulphaphenazole

→ Rapidly absorbed and poorly excreted Sulfonamides : Sulfadimethoxine , Sulfamethoxy pyridiazine

[C] On the basis of Duration of Action

→ Extra long Acting sulfonamides : Sulphasalazine , Sulphaclomide , Sulphalene

→ Long Acting Sulfonamides : Sulphadoxine , Sulphadimethoxine , Sulphamethoxy pyridazine , Sulphaphenazole

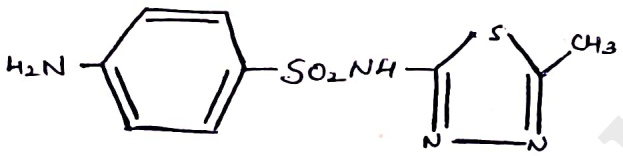
→ Intermediate acting Sulphonamides : Sulphasomizole , Sulpha-methoxazole

→ Short Acting Sulphonamides : Sulphamethiazole , Sulphisoxazole

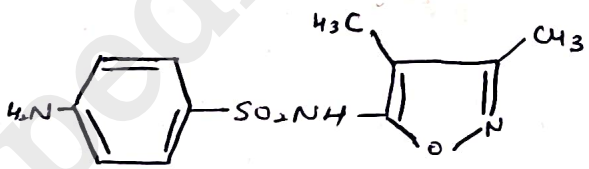
→ Injectables ; Sulphadiazine , Sulphamethoxine

DROG PROFILE

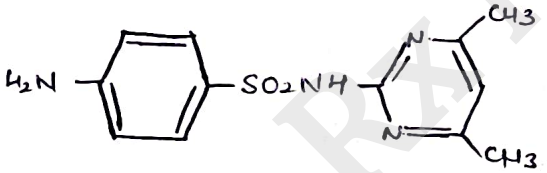
→ Sulphamethizole



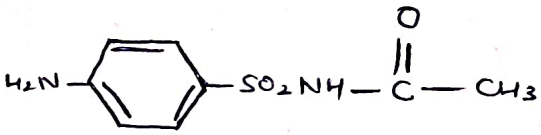
→ Sulphisoxazole



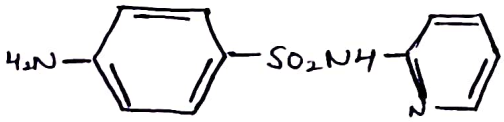
→ Sulphamethazine



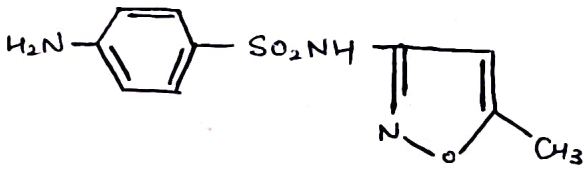
→ Sulphacetamide



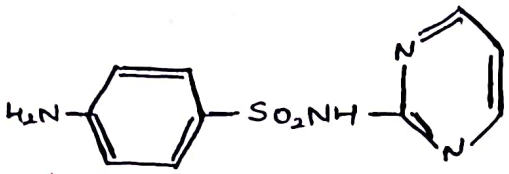
→ Sulphapyridine



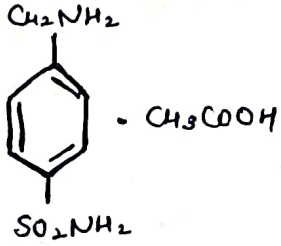
→ Sulphamethoxazole



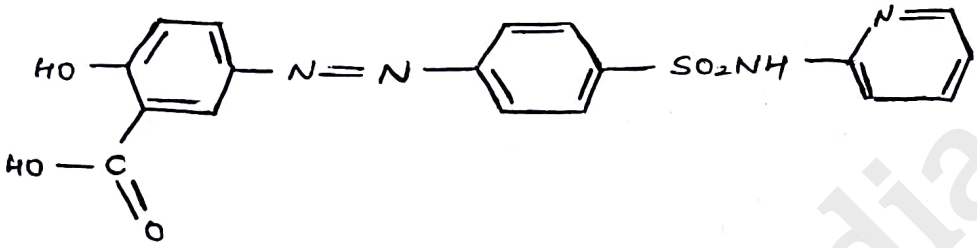
→ Sulphadiazine



→ Mafenide Acetate



→ Sulphasalazine



FOLATE REDUCTASE INHIBITORS

→ They inhibit synthesis of folic Acid by inhibting the function of dihydrofolate Reductase enzyme.

→ Used to treat bacterial, fungal and Protozoal Infection.

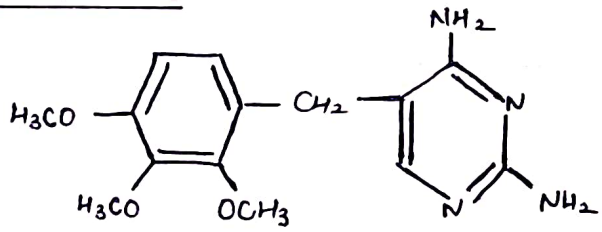
ex. Trimethoprim, Co-trimaxozole

MECHAINISM OF ACTION

→ See Mechonism of Action of Sulfonamides:

DROG PROFILE

1. Trimethoprim



- Used only for treatment of uncomplicated urinary

2. Co-trimoxazole

→ It is a combination of Trimethoprim and Sulphamethoxazole.

→ It is effective against gram +ve and gram -ve bacteria.

→ It consist of 1 part trimethoprim to 5 parts sulphamethoxazole.

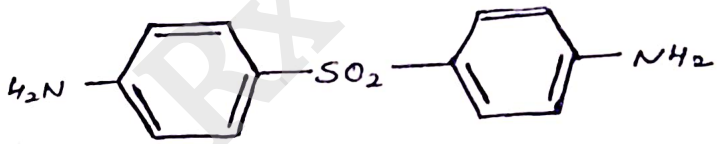
→ Sulphamethoxazole inhibits formation of dihydrofolic Acid from PABA, whereas trimethoprim inhibits dihydrofolate reductase.

→ Used for urinary tract infections.

SULPHONES

→ They are the analogs of PABA [Para Amino Benzoic Acid] that interfere with folic Acid metabolism by inhibiting dyhydropteoroate synthetase.

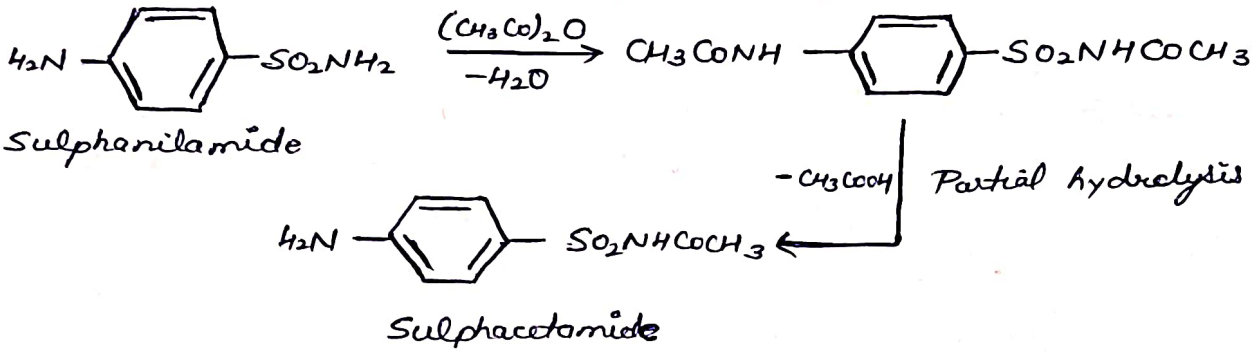
→ Dapsone



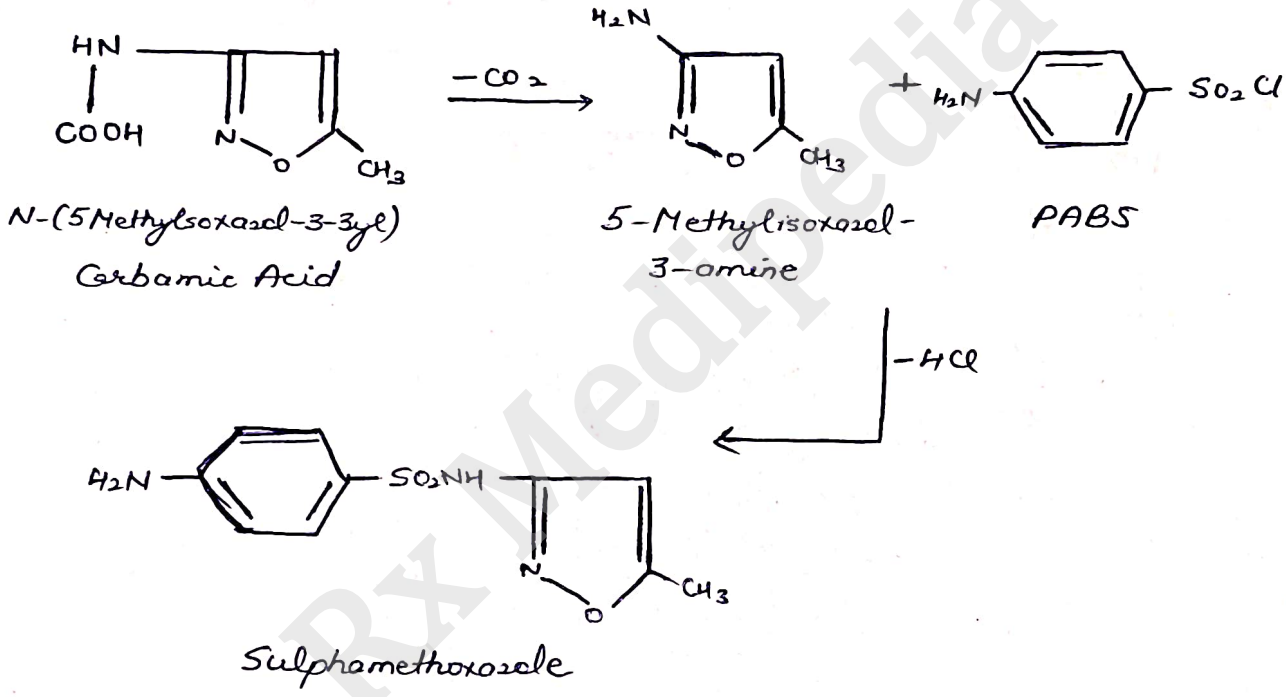
- Used in treatment of leprosy.
- Used as Anti-malarial, anti-infective agent and anti-inflomatory drug.
- It has general properties and Mechanism of Action of Sulphonamides.

SYNTHESIS

1. Sulphacetomide



2. Sulphamethoxazole



3. Dapsone