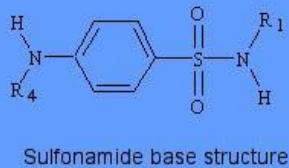
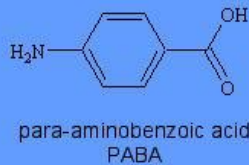
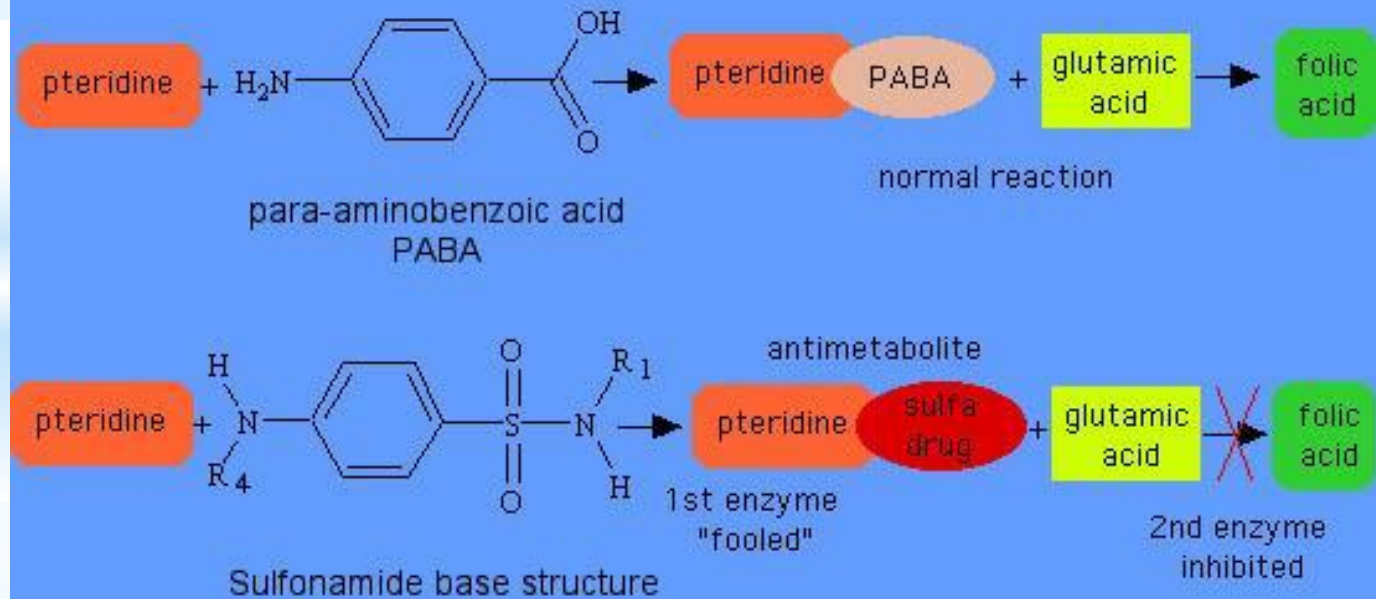


# Sulfonamides, Fluoroquinolones, Oxiquinolines, Nitrofurans, Quinoxalines, Oxazolidinones and Antifungal Drugs

## Sulfa Drugs



## Sulfa Drug - Antimetabolite

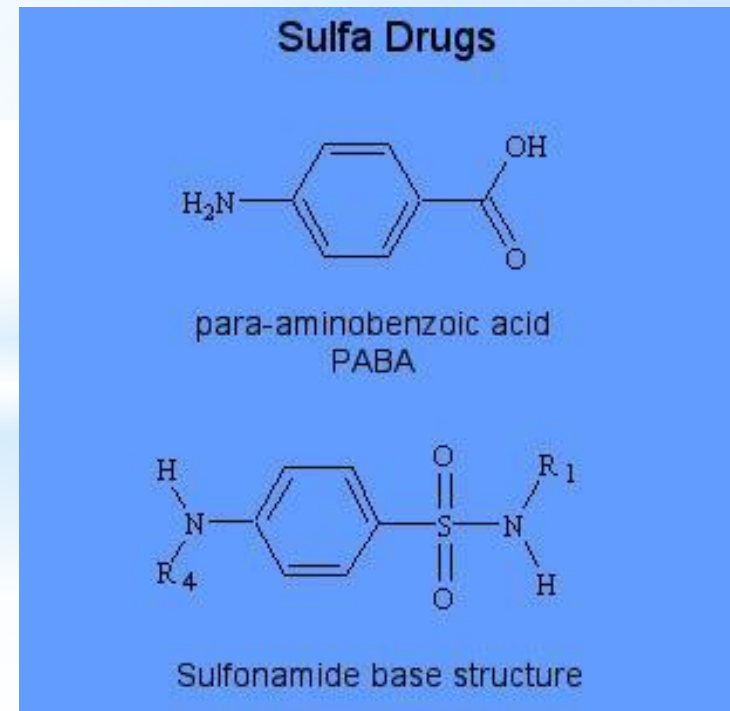


**Sulfonamides** – the synthetic antimicrobial agents, containing a sulfonamido ( $-\text{SO}_2-\text{NH}-$ ) group.

This group is present in other compounds like **antidiabetic sulfonylureas**, **diuretics** like *thiazides*, *furosemide*, and *diacarb*.

The structure of the sulfonamides is similar to Para-Aminobenzoic Acid (PABA).

Sulfonamides tend to be much more soluble at alkaline than at acid pH. Solubility may be decreased in acidic urine, resulting in precipitation of the drug or its acetylated metabolites.



# CLASSIFICATION of SULFONAMIDES

## I. Oral, Absorbable (*Systemic Action*):

### 1. Short-acting (6-9 hours):

*Sulfadimezine, Sulfazine, Ethazol, Urosulfane*

### 2. Long-acting (24 hours) :

*Sulfapyridazine, Sulfadimethoxine*

### 3. Ultra-long acting (72 hours): *Sulfalen*

### 4. Combined preparations with:

- Trimethoprim: *Co-trimoxazole [Biseptol]*

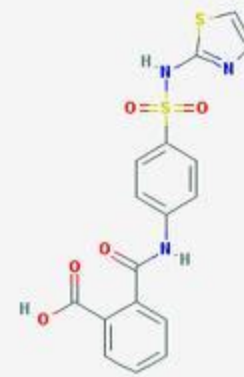
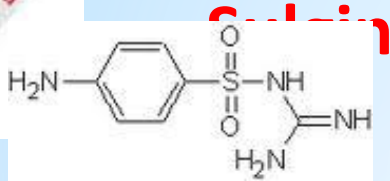
- Aminosalicylic acid: *Salazopyridazine, Sulfasalazine*

*Salazodimethoxine*

## II. Oral, Non-Absorbable

(acting the intestinal flora):

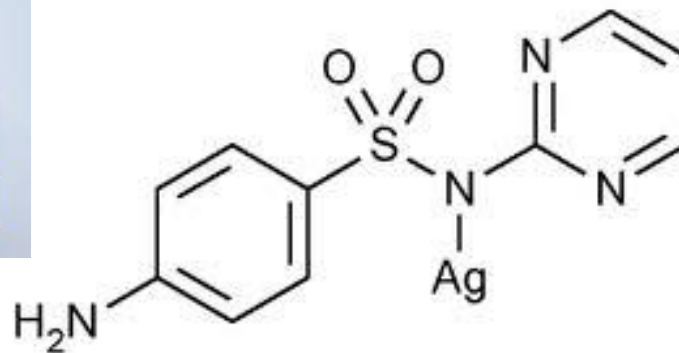
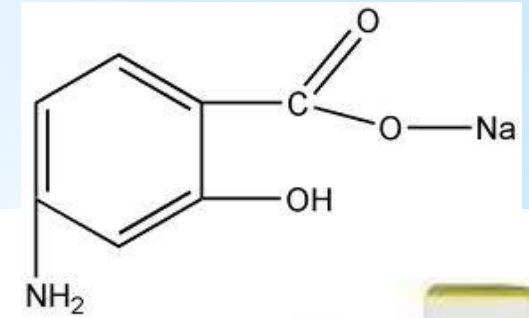
### Phthalazol



## III. For Topical Use:

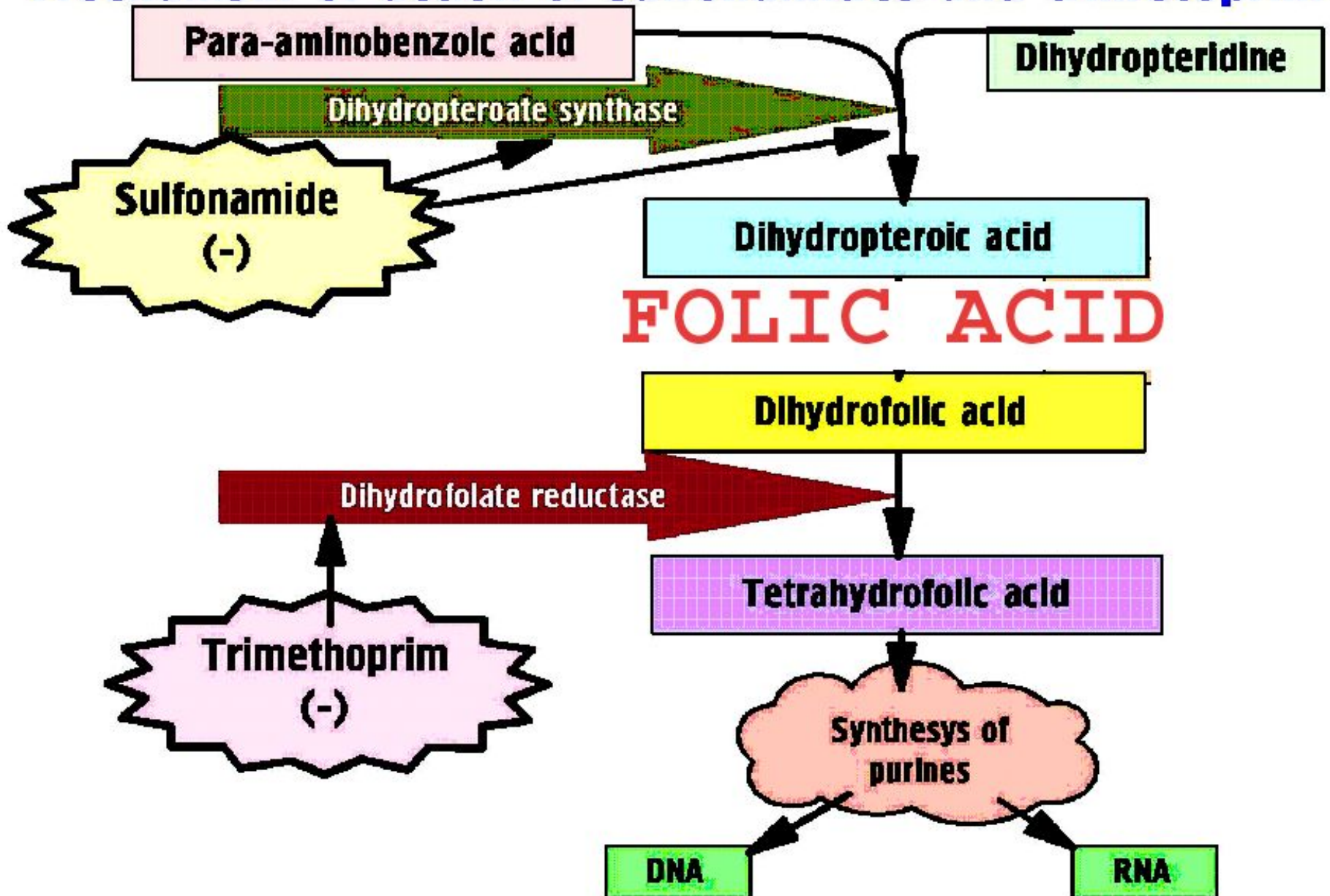
**Sulfacil-natrium (Albucid)**–

**Silver Sulfadiazine (1% cream)**





# Mechanism of action of sulfonamides and trimetoprim



## Clinical Uses of Sulfonamides :

- Respiratory infections
- Acute **urinary tract infection: Urosulfan**
- Combined with **Pyromethamine** –  
for drug-resistant *malaria*, and for *toxoplasmosis*
- Inflammatory bowel disease, non-specific ulcerative colitis  
- **Sulfasalazine** (*Sulfapyridine* + *Aminosalicylate*)
- Some sexually transmitted infections -  
*trachoma, chlamydia*

**Co-trimoxazole:** the combination of

**Sulfamethoxazole** and **Trimethoprim:**

is generally bactericidal

- acts by sequential blockade of **folic acid** enzymes in the synthesis pathway:

**Sulfamethoxazole** inhibits formation of **dihydrofolic acid** from **PABA**,

**Trimethoprim** inhibits **dihydrofolate reductase** responsible for formation of **tetrahydrofolic acid** from **dihydrofolic acid**

**Co-trimoxazole** is effective against :

*Escherichia coli*

*Klebsiella*

*Enterobacter*

*Streptococcus pneumoniae*

*Staphylococcus aureus*

*Salmonella*

*Shigella*

Clinical uses: Chronic Bronchitis,

Urinary tract infections, Otitis media,

*Pneumocystis carini* pneumonitis, Traveller's Diarrhea,  
Pertussis, Cholera.



## Adverse Effects of Sulfonamides:


- **Hypersensitivity Reactions:** rashes, angioedema.

All sulfonamides and their derivatives, including

**Diacarb, Thiazides, Furosemide, Glibenclamide, Diazoxide**  
are **CROSS-ALLERGIC**

- **Nephrotoxicity, Urinary tract disturbances:**

Sulfonamides precipitate in urine, esp. at **neutral** or **acid pH**,  
producing **crystalluria**, **haematuria**, or even **obstruction**.

 **Adequate** **HYDRATION** and **ALKALINIZATION** of **urine**  
**prevent the problem**

- **Haemopoietic disturbances:** hemolytic anemia,  
agranulocytosis, leukopenia, thrombocytopenia
- **CNS:** Depression, aseptic meningitis, seizures

# Acute Poisoning/Overdose with Sulfonamides

**Sulfonamides** are able to:

- form **methemoglobin** and **sulf-methemoglobine**,
- block the **haemopoiesis** and
- produce **hepato-** and **nephrotoxicity**.

**Manifestation:** dizziness, drowsiness, unconsciousness, anorexia, abdominal pain, nausea, vomiting, haemolytic anemia, acidosis, agranulocytosis, sensitivity reactions, jaundice, hepatomegalia

**Treatment:** gastric lavage, forced diuresis

## ANTIDOTES:

\* *Nicotinic acid IV 1% solution 2–5 ml or Nicotinamide*

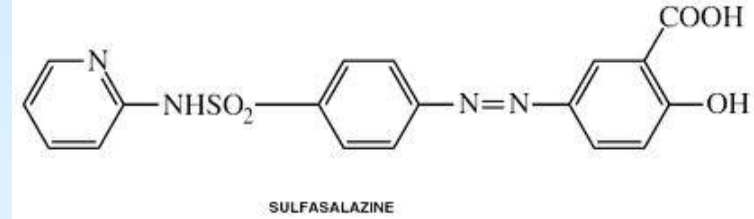
\* *Chromosmon (1% Methylene Blue solution in 25% glucose)  
IV 0.1 ml/kg*

\* *Lipoic acid IV 0.5% solution 60-80 ml*

\* *Folic acid PO 1 mg tid*

**Sulfasalazine** - Tab 0.5 g:

*Sulfapyridine* + *Aminosalicylic Acid* –



is split into its component parts by bacteria in the colon.

### Clinical Uses:

- Ulcerative Colitis, Enteritis, Inflammatory Bowel Diseases
- **Rheumatoid diseases:** acts by scavenging the toxic **oxygen metabolites** produced by **neutrophils**
- ***IgA*** and ***IgM Rheumatoid Factor*** production
- Suppression of **T cell** responses
- Inhibition of **B cell** proliferation
- The absorption of *folic acid* is impaired – this can be countered by giving **Folic Acid** supplements

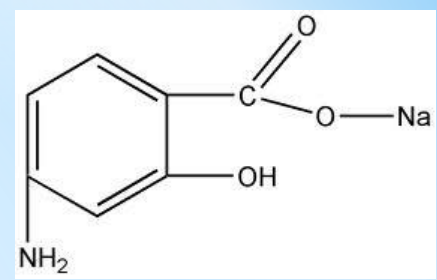


## **Sulfacyl-sodium** (*Albucid*) –

10%, 15%, 30% **ophthalmic solution** or **ointment** - effective for:

- **Bacterial Conjunctivitis** and as **adjunctive therapy** for **Trachoma**.
- **Ocular gonorrhoeal infection** in *newborns* and **adults**.

It acts by **inhibiting the uptake of PABA**, which is required in the synthesis of **Folic Acid** needed for **bacterial growth**.



New Born Baby with  
Gonorrhoea Eye Infection







**Naphthyridine derivatives:** Nalidixic acid  
**Quinolone derivatives:** Oxalinic acid



**Mechanism of action:** inhibition of DNA-gyrase and suppression of protein synthesis and cell division.



**The type of action - bactericidal.**

**The action spectrum - gram(-) bacteria.**

**Side effects: dyspeptic disorders, headache, transitory photodermatoses.**





## Fluorquinolone derivatives:



**First generation** - Ofloxacin, Ciprofloxacin, Pefloxacin, Norfloxacin, Lomefloxacin, Fleroxacin, Enoxacin, Levofloxacin.



**Second generation** - Sparfloxacin, Moxifloxacin,



**Third generation** - Tosufloxacin, Rufloxacin, Sitafloxacin,



**Mechanism of action:** inhibition of DNA-gyrase and suppression of protein synthesis and cell division.



**The type of action** - bactericidal.

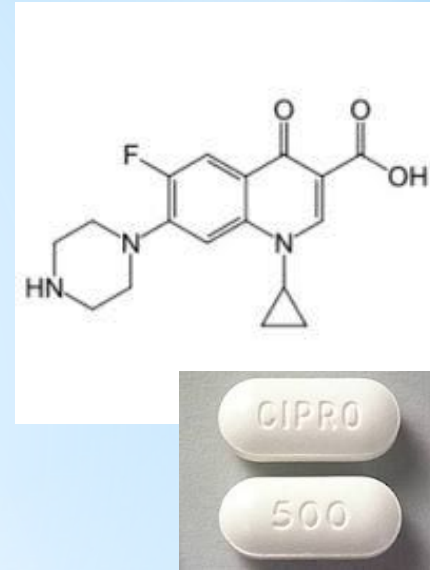
**The action spectrum** - extended: gram(+) and gram(-) bacteria (including Pseudomonas aeruginosa, obligate anaerobes, Chlamidia, Mycoplasma).

**Side effects:** dyspeptic disorders, headache, convulsions

**Ciprofloxacin** (Tab. 0.5 g; amp. 1%-10 ml) – a **synthetic, broad-spectrum, bactericidal antibiotic**, effective against both **Gr(+)** and **Gr(-)** bacteria.

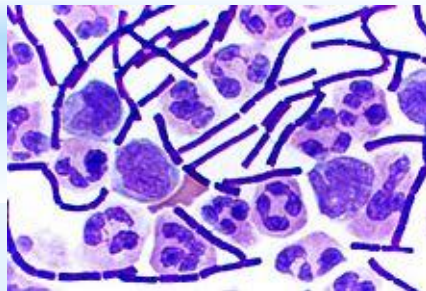
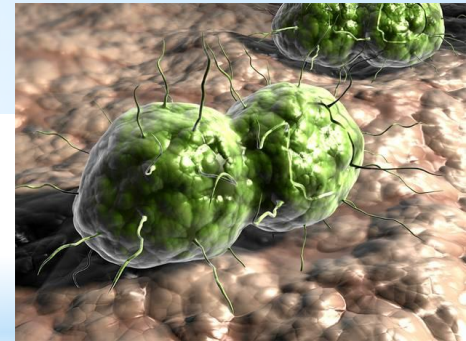
**It has excellent activity against:**

- ***Enterobacteriaceae***
- Enteric **coliform bacilli**, including **resistant to Penicillins, Cephalosporins and Aminoglycosides**
- ***Haemophilus influenzae***,
- Penicillinase-producing ***Neisseria gonorrhoeae***, ***Campylobacter*** and ***Pseudomonads***.
- **Gr(+)** organisms, **streptococci** and **pneumococci** are **only weakly inhibited** and there is high incidence of ***staphylococcal resistance***.



# Clinical uses of Fluoroquinolones

- **Urinary tract infections:** Norfloxacin, Ofloxacin
- **Complicated respiratory tract infections - Gr(-) flora**  
*Pseudomonas aeruginosa* respiratory infection
- **External otitis** caused by *P. aeruginosa*
- **Chronic Gr(-) bacillary osteomyelitis**
- **Eradication of *Salmonella typhi*** in carriers
- **Gonorrhoea:** Norfloxacin, Ofloxacin
- **Anthrax**

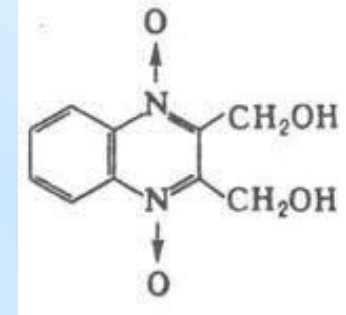
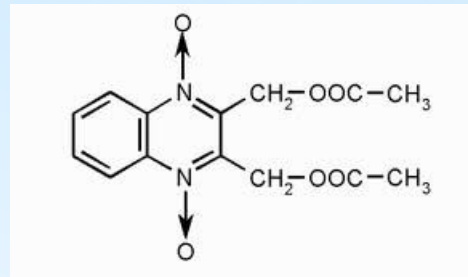




# Quinoxalines

## Chinoxidyn

(*Quinoxidyn* – tab. 0.25 g)



**Dioxydin** (amp. 1%-10 ml for topical use;  
amp. 0.5%-10 ml IV).



- have **broad-spectrum** antibacterial effect including ***Proteus vulgaris*, blue pus bacillus, pathogen anaerobes** and **others**.
- are used in **severe pyoinflammatory processes**.
- are toxic and adverse effects are not infrequent and include GIT upsets, headache, chill, seizures, allergic reactions.





**Nitroxoline** (5-NOK, Nitrox) – Tab. 0.05 g

a **Urinary Antiseptic** -

a **broad-spectrum, bacteriostatic agent.**

- blocks replication of nucleonic acids, forming **chelate complexes** with **microelements** (Fe, Cu) of microbes  
=> enzyme systems inhibition.
- is quickly absorbed from GIT,  
**eliminates in unmodified mode with urine,**  
where it is **accumulated in bacteriostatic concentrations.**



**Clinical uses:** urinary tract infections (Cystitis, Prostatitis, Pyelonephritis, Urethritis), prophylaxis of infections after **kidney and urinary tract surgery.**

**Side effects:** GIT upsets. Urine is discolored **brightly yellow** during administration of drug.



# Nitrofuran derivatives:



**Agents for treatment of the urinary tract infections -**  
**Furaginum [Furazidin], Furadoninum [Nitrofurantoin],**  
**Nifurtoinol, Nifuratel.**



**Agents for treatment of the intestinal infections -**  
**Furazolidone, Nifuroxazide.**



**Agents for local use - Furacillinum.**



**Mechanism of action: inhibition of enzymes of cell membranes of the micro-organisms.**



**The type of action - bacteriostatic, in high dose - bactericidal.**

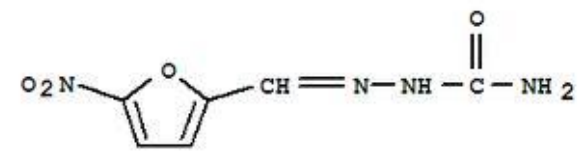


**The action spectrum - extended.**



**Side effects: dyspeptic disorders, fever, allergic reactions.**

# **Furacilin** (*Nitrofurazone, Furacin*)



**0.02% water solution, Tab. 0.02 and 0.1 g**

is a **synthetic, broad-spectrum antibacterial nitrofuran derivative** used mainly for topic application as **ANTISEPTIC**:

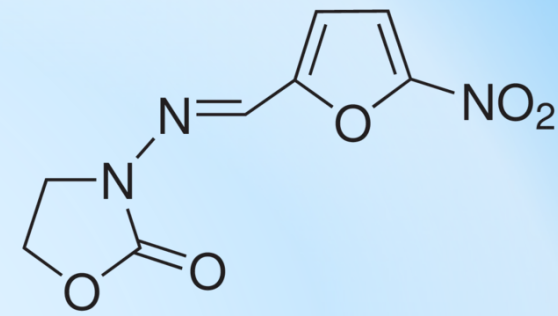
- Externally for the treatment and prevention of pyoinflammatory processes, major burns (esp. when resistance to other antibacterial agents occurs);
- Prevention of skin graft infections.

**0.02% Furacilin Solution** is applied directly to **lesion** or to **dressing** used to **cover** the **affected area daily** or as **indicated**, depending on **severity** of **burn or injury**.



**Furazolidone** (Tab 0.05 g) is a **nitrofuran**

compound active against many Gr(–) bacilli including ***Salmonella***, ***Shigella***, ***Giardia lamblia*** and ***Trichomonas***.



### Clinical Uses:

- For **giardiasis** 100 mg tid for 5–7 days is inferior to **Metronidazole** or **Tinidazole**.
- **Intestinal infections: Bacterial Enteritis**
- **Food poisoning diarrhoeas, Bacillary Dysentery**
- **Trichomonad colpitis**

**Furazolidone** is partly absorbed from intestines and excreted in urine which **turns orange** – patients should be told about it.

It is used **orally, intravaginally** and **rectally**.

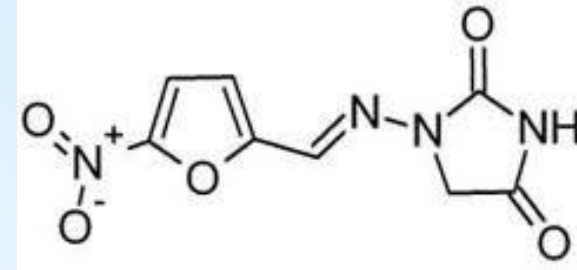
**Adverse effects** are mild and infrequent – nausea, headache, dizziness.

**Furadonin** (*Nitrofurantoin* – Tab. 0.05 g, Caps. 0.1 g) is an effective urinary antiseptic.

- Is a **bacteriostatic** compound, but may be **cidal** at **higher concentrations** and in **acidic urine**:

its **activity** is **enhanced** at **lower pH 5.5** or **below**.

- Inhibits many Gr(+) and Gr(-) bacteria.
- It antagonizes the action of **Nalidixic acid**.



Mechanism of action. Susceptible bacteria appear to **enzymatically reduce furadonin** to generate the **active form**:

it is **highly reactive** and damages **DNA**.

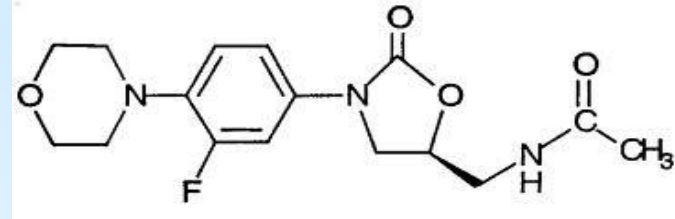
Clinical uses: urinary tract infection.

Adverse reactions: **Interstitial changes** in the lung, **bronchoobstructive syndrome**, **cough**; **neuropathies** and **hemolytic anaemia** occur in **glucose-6-phosphate dehydrogenase** deficiency.

**Rashes**, **pulmonary infiltration** and other **hypersensitivity reactions** (**chills**, **fever**, **anaphylaxis**); **nausea**, **epigastric pain**, **diarrhoea**.



## OXAZOLIDINONES



**Linezolid** (Zyvox) – tab. 0.6 g, amp. 15% - 2 ml

- a synthetic antibiotic for the treatment of resistant Gr(+) coccal (aerobic and anaerobic) and bacillary infections.

**Gr(-) bacteria ARE NOT INHIBITED!**

It is active against *methicillin* resistant and *vancomycin* resistant

*Staph. Aureus* (VRSA), *vancomycin* resistant enterococci (VRE),

penicillin resistant *Strep. pyogenes*, *Str. viridans* and *Str. pneumoniae*, *Corynebacterium*, *Listeria*, *Clostridia* and *Bact. fragilis*.

Linezolid is primarily bacteriostatic, but cidal against some streptococci, pneumococci and *Bact. Fragilis*.

**MOA:** It binds to the **23S fraction** of the **50S ribosomes** and interferes with formation of the ternary **tRNA-ribosome-mRNA** complex and **stops protein synthesis** before it starts.

There is no cross resistance with <sup>23</sup>any other class of antibiotics.



# ANTIFUNGAL DRUGS

I. For the treatment of mycoses caused by **Pathogenic Fungi**:

1. For **subcutaneous** and **systemic mycoses**.



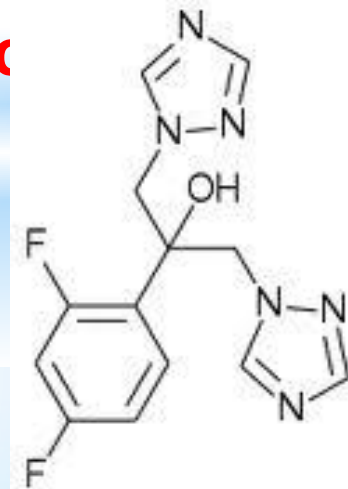
**Antibiotics:**

**Amphotericin**  
**Mycoheptin**



**Azole derivatives:**

- Imidazoles: **Ketoconazole, Miconazole**
- Triazoles: **Itraconazole, Fluconazole**



## 2. Drugs for **Superficial Fungal Infections:**

Antibiotics: **Griseofulvin**

Methylnaftaline derivative:

**Terbinafine** (*Lamizyl* – Tab. 0.25 g; 1% cream)

Imidazole derivatives:

**Miconazole**

**Clotrimazole** (1% cream, Tab. vaginal 0.1 g)

Nitrophenol derivatives:

**Nitrofungin**

Iodine preparations:

**Iodide alcohol solution**

**Potassium iodide solution**

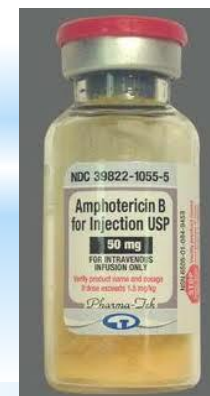
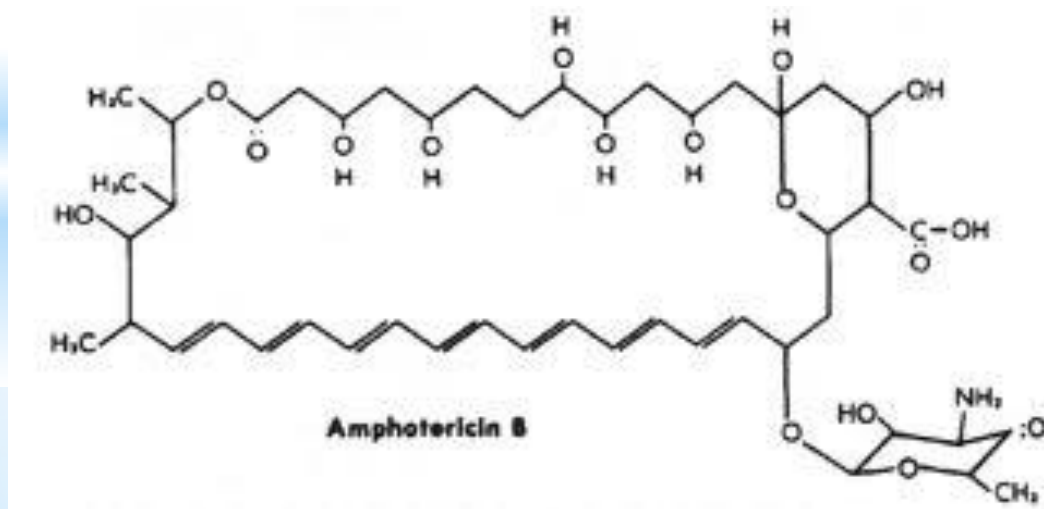




**Amphotericin B** is a macrolide antibiotic, produced by *Streptomyces nodosum*.

the drug of choice in the treatment of the Systemic Mycoses.

**MOA:** Several polyene molecules bind to **ergosterol** in cell membrane of fungal cells to form **pores** disrupting membrane permeability and transport functions, allowing electrolytes (esp. **K+**) and small molecules to leak from the cell, leading to cell death.



# Synthetic Antifungal Agents

Azoles: *Miconazole, Ketoconazole*

Triazoles: *Fluconazole, Itraconazole*

**MOA**: produce inhibition of the fungal **CYP-450 enzyme**,  
**lanosine 14 $\alpha$ -demethylase** which is responsible for  
converting **lanosterol** to **ergosterol**,  
the main sterol in the fungal cell membrane.

The depletion of **ergosterol** =>

=> alters the **fluidity of the membrane**

=> interferes with the action of  
the **membrane-associated enzymes**.

=> Inhibition of Replication.



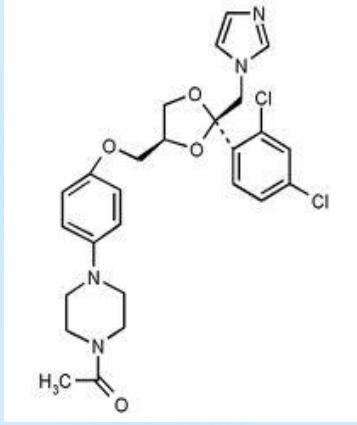
**Ketoconazole** (Nizoral- Tab. 0.2 g, 2% cream, 1% Shampoo)

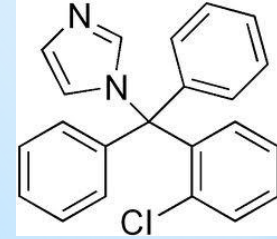
is distinguished from *Fluconazole* and *Itraconazole* by

its greater propensity to **inhibit human CYP-450 enzymes**

Inhibition of human CYP-450 enzymes:

- Interferes with biosynthesis of **adrenal** and **gonadal** steroid hormones, producing significant endocrine effects such as gynecomastia, infertility, and menstrual irregularities.
- ↓↓ Metabolism of other drugs, leading to **enhanced toxicity**





**Clotrimazole** – only for local administration

1% cream, lotion; Tab. vaginal 0.1 g –

a synthetic **imidazole derivative** for **dermatophytic infections**,

including *Tinea corporis*, *Tinea pedis*, *Tinea cruris*;

**Vulvovaginal** and **Oropharyngeal Candidiasis, Keratitis.**

**MOA:** by binding with **phospholipids** in the fungal cell membrane,  
alters cell **membrane permeability**

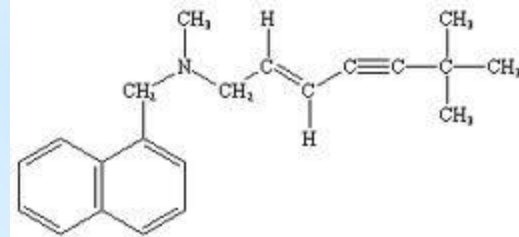
It inhibits or kills many fungi, including **yeast** and **dermatophytes**, and  
also is acting against **some Gr(+)** bacteria.

Pharmacokinetics: Absorption is negligible and adverse effects are rare.



**Terbinafine** (*Lamisil* – Tab 0.25 g; 1% cream) -

**Methylnaftaline derivative for Superficial Fungal Infections –**



a highly lipophilic keratophilic fungicidal compound

- Inhibits the enzyme **squalene epoxidase**, which is involved in the synthesis of **ergosterol** from **squalene** in the fungal cell wall.

**The accumulation of squalene within the cell is toxic to the organism.**

- Given **orally**, it is rapidly absorbed and is taken up by skin, nails and adipose tissue.

- Given **topically**, it penetrates **skin** and **mucous membranes**.

- 1 tab. PO for **12 weeks** achieves a cure rate of up to **90%** for **onychomycosis** (**ringworm of nails**)

Unwanted effects: GIT upsets, rashes, pruritus, joint and muscle pains, hepatitis.





A scenic view of a blue ocean under a clear blue sky with a large, fluffy white cloud formation. The text "Thank You for Attention!" is centered in the lower half of the image.

**Thank You for Attention!**