

5ml

**Chloramphenicol**

Eye Drops BP

**CHLORAMPHENICOL**

**BY ADMUND**

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# CHLORAMPHENICOL (chloromycetin)

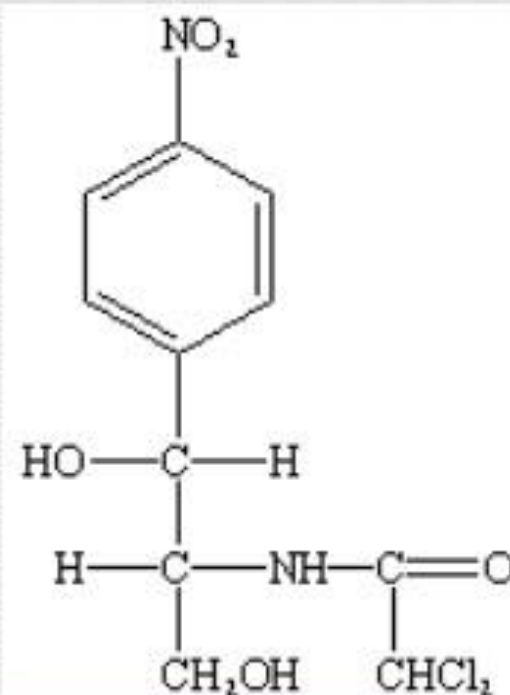
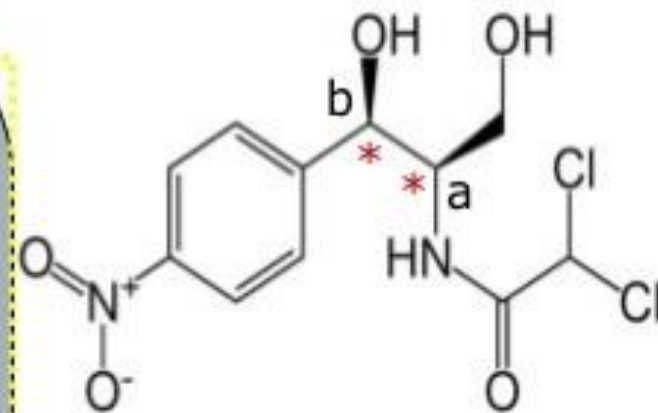
- Chloramphenicol was originally derived from the bacterium *Streptomyces venezuelae*, isolated by David Gottlieb, and introduced into clinical practice in 1949, under the trade name Chloromycetin.
- ~~It was the first antibiotic to be manufactured synthetically on a large scale.~~
- Chloramphenicol is a broad-spectrum antibiotic that acts as a bacteriostatic, but at higher concentrations can act as a bactericidal.
- A broad spectrum antibiotic which is a nitrobenzine derivative derived from dichloro acetic acid.

## □ Structure and chemical characteristics

- Chloramphenicol contains a **nitrobenzene ring, an amide bond, and an alcohol function.**
- The presence of chlorides in biologically produced organic molecules is unusual. The nitrobenzene is relevant because it leads to the formation of aromatic amines which may be carcinogenic.
- The amide is hydrolyzed by some resistant bacteria leading to inactivation.
- The **alcohol serves as a functional group facilitating the formation of esters that improve chloramphenicol's water solubility.** Chloramphenicol base has low water solubility and high lipid (in organic alcohols) solubility. Its palmitate ester is similar, but the succinate ester has high water solubility.



1. molecular formula is  $C_{11}H_{12}Cl_2N_2O_5$
2. Basic nucleus is P-nitrobenzene contains a side chain at p-position to  $-NO_2$  group.
3. Side chain contains one  $-OH$  group at "b" and one **hydroxymethyl** group at "a".
4. on the "a" carbon presence of 2,2-dichloroacetamide moiety hence the side chain can also be named as acyl amido propanediol.
5. Stereochemistry of chloramphenicol exists in 2 pairs of enantiomers(optically active compounds which are mirror images.
6. It contains 2 chiral carbons .
7. **4 enantiomers are possible.**  
 one is *D and L threo*– (2 identical groups are *opposite sides* of chiral carbons)  
*Erythro* ( 2 identical groups are on *same side* of chiral carbon atom.  
 out of 4 enantiomers *D- Threo form shows biological activity..*



# Mechanism of action:

- ❑ Chloramphenicol is bacteriostatic (that is, it stops bacterial growth).
- ❑ It is a protein synthesis inhibitor
- ❑ Chloramphenicol binds to the 50S subunit of ribosomes and appears to act by inhibiting the movement of ribosomes along mRNA, probably inhibiting the peptidyl transferase reaction by which the peptide chain is extended.

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Since it binds to the same region as macrolides, lincosamides these drugs can't be used in combination.

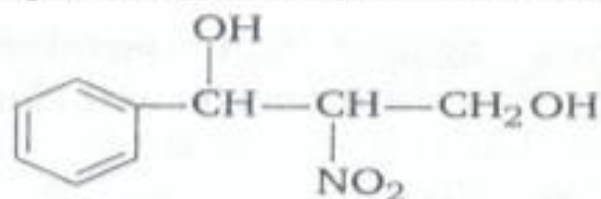
The nitro group and both alcohol groups are also important but can be replaced by other electronegative groups.

**Bacteria with resistance to the drug contain an enzyme called Chloramphenicol acetyltransferase, which catalyses the acylation of the hydroxyl groups.**

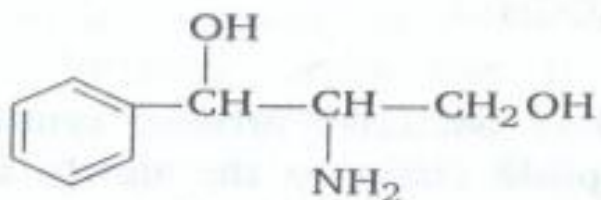
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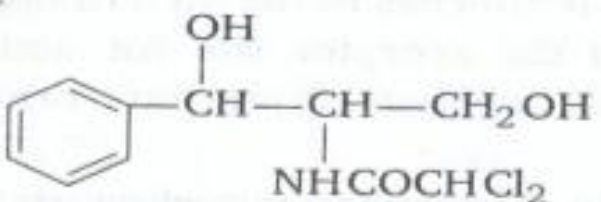
# Synthesis of chloramphenicol



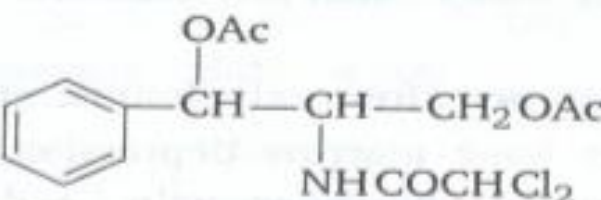
(1)  $\text{H}_2$  (reduction)  
(2) Separate  
(3) Resolve



(1)  $\text{Cl}_2\text{CHCOCl}$  (dichloro acetyl chloride)  
(2)  $\text{OH}^-$

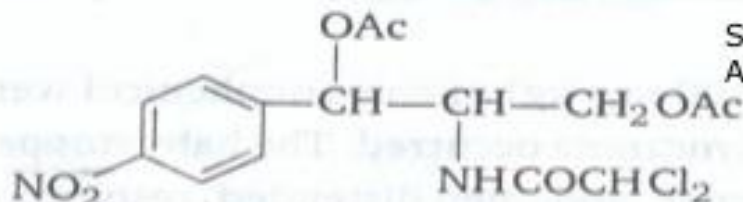


$\text{Ac}_2\text{O}$



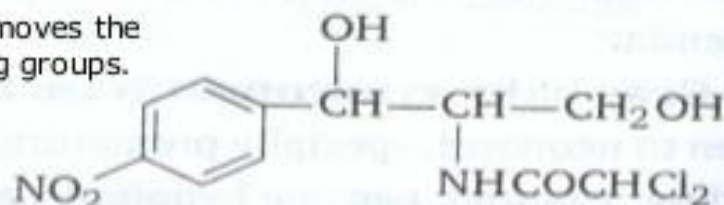
(nitrated with nitric-sulfuric acid mixture)

$\text{HNO}_3$   
 $\text{H}_2\text{SO}_4$



Saponification removes the Acetate protecting groups.

$\text{OH}^-$



Chloramphenicol

# Side effects of chloramphenicol

- ☐ Abdominal pain; Bloating; Blood disorders which may be serious; Diarrhoea; Fatigue; Fever; Headache; Nausea and vomiting; **Newborn babies with immature liver function can get a serious side effect where the skin develops a grey colour and there is circulatory collapse (grey syndrome)**  
Pins and needles (paraesthesia);  
Rash  
Sore throat  
Stomach upset  
Tingling of the hands or feet  
Unusual bleeding or bruising  
Vision changes or eye pain  
Visual disturbances
  - ☐ Vomiting;
  - ☐ This drug is quite toxic to bone marrow (suppression of bonemarrow).The nitro group is suspected to be responsible for this, although intestinal bacteria are capable of reducing this group to an amino group.
  - ☐ **aplastic anaemia**
  - ☐ Anorexia
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# Uses of chloramphenicol

- ❑ Chloramphenicol is an antibiotic used to treat a variety of bacterial infections
- ❑ In some regions in the world chloramphenicol is the drug of the choice
- ❑ ~~for the treatment of typhoid when more expensive drugs cannot be afforded.~~
- ❑ It is also widely used against eye and ear infections.
- ❑ ***Meningitis, Anthrax, Brucellosis***
- ❑ ***Burkholderia Infections*** (in cystic fibrosis patients, immunocompromised patients )
- ❑ ***Chlamydial Infections***
- ❑ Clostridium Infections
- ❑ ***Vibrio*** (*Infections Treatment of cholera caused by Vibrio cholerae*)
- ❑ ***Ehrlichiosis, Plague, Rat-bite Fever***
- ❑ ***Rickettsial Infections, Haemophilus influenzae infection***
- ❑ Chloramphenicol treats only bacterial eye infections. Chloramphenicol will not work for other types of eye infections
- ❑ anti-infective ear preparations.
- ❑ ~~Those bacteria sensitive to this drug include clostridium, chlamydia,, salmonella.~~
- ❑ Chloramphenicol has also shown activity against Mycoplasma.