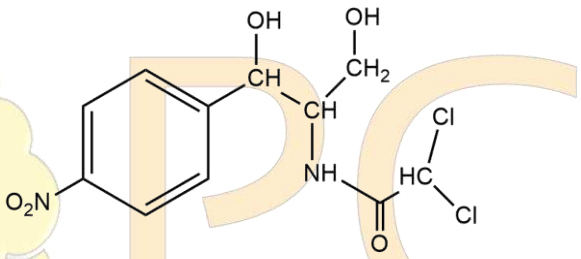
Chapter 6: Others Antibiotics

Miscellaneous: Chloramphenicol*, Clindamycin

A) **Chloramphenicol**

- ✓ It is **broad spectrum** antibiotic obtained from *Streptomyces venezuelae*. D-threo form of chloramphenicol is active
- ✓ Chloramphenicol inhibits bacterial protein synthesis by act as same site of the 50s ribosomal subunit as erythromycin and clindamycin.
- ✓ Bacterial resistence occurs due to production of *acetyltransferase enzyme.*
- ✓ **Chloramphenicol causes serious adverse drug reaction like bone merrow depression, aplastic anemia and **gray baby syndrome** in new born child.*



2,2-dichloro-*N*-(1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)acetamide

A) Modification of *p*-nitrophenyl group: The *p*-nitrophenyl group may be modified through the following ways:

a. Replacement of the nitro group by other substituents leads to a reduction in activity.

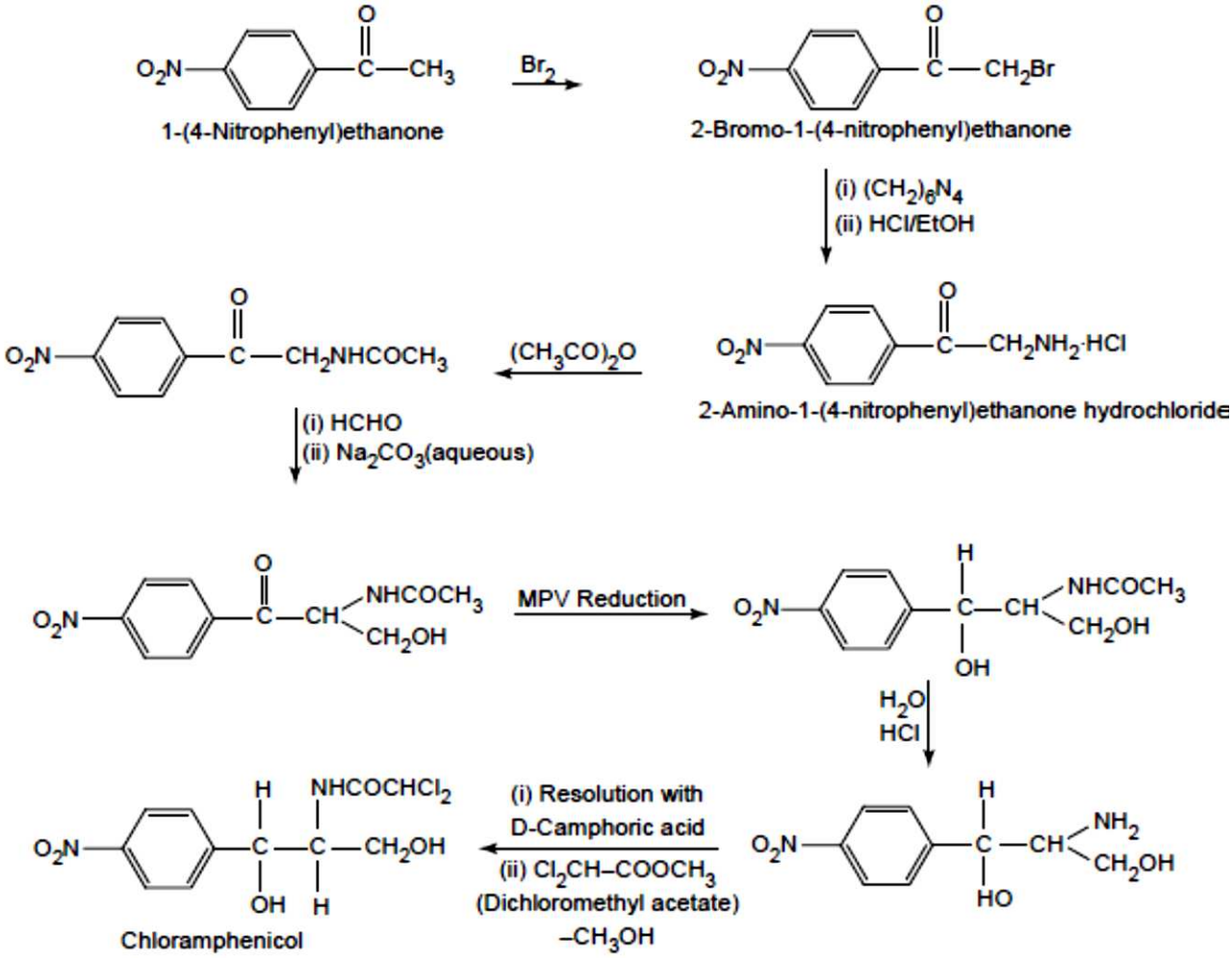
b. Shifting of the nitro group from the para position also reduces the antibacterial activity.

c. Replacement of phenyl group by the alicyclic moieties results in less potent compounds.

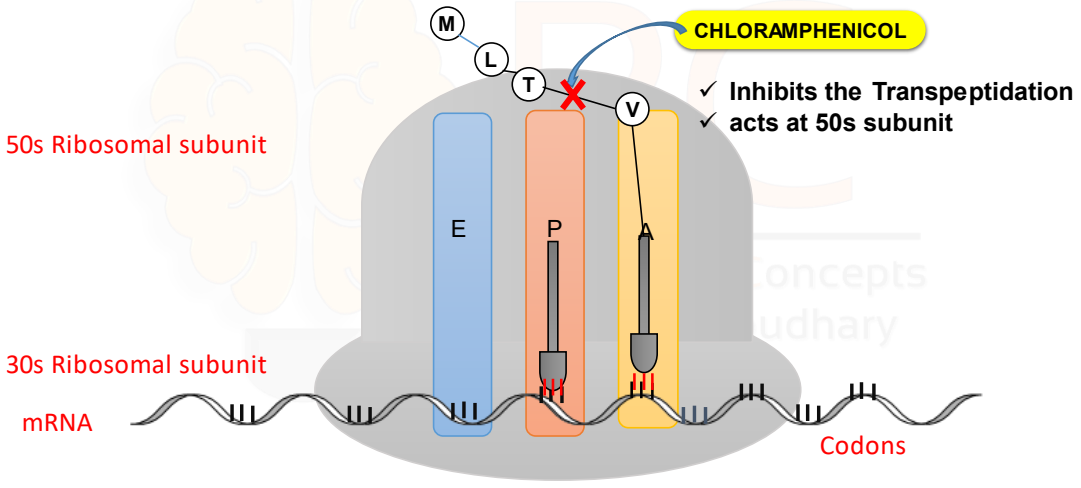
B) Modification of dichloroacetamide side chain: Other dihalo derivatives of the side chain are less potent although major activities are retained.

C) Modification of 1,3-propanediol: If the primary alcoholic group on C-1 atom is modifi ed, it results in a decrease in activity; hence, the alcoholic group seems to be essential for activity.

Synthesis



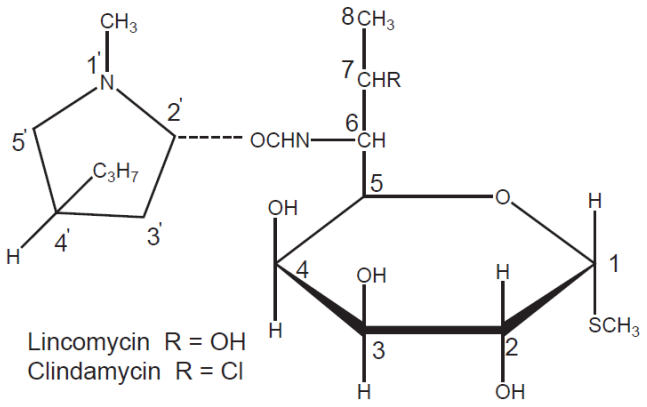
MOA:



Uses:

- ✓ Chloramphenicol is sensitive on both Gram positive and Gram-negative bacteria. It acts as bacteriostetics on most of the microorganism, but bacteriocidal action on *H. influenzae.*
- ✓ Used in treatment of serious infections caused by bacteria and Rickettsia
- ✓ Effective against N. meningitidis, H. influenzae, and S. pneumoniae.
- ✓ Alternative to penicillin and cephalosporin for N. meningitis

B) **Clindamycin and Lincomycin**



- ✓ **Lincomycin** are sulphur containing antibiotics obtained from *Streptomyces lincolensis* and **Clindamycin** was first isolated form *Streptomyces venezuelae* in 1947 and 1949 by Parke-Davis and Mildred Rebstock.
- ✓ They bind specifically to 50 S subunit of bacterial ribosome and arrest protein synthesis by inhibition of peptide-chain elongation. It blocks the A site of ribosome and prevent the attachment of oligosaccharide side chains to glycoproteins.

Lincomycin: It is bacteriostatic and spectrum of activity is similar to penicillin and erythromycin. It is active against anaerobes such as fragilis, penicillin resistant *Staphylococci*. Gram negative aerobic bacteria are resistant to lincomycin.

Clindamycin: It is semisynthetic derivative of lincomycin. Its actions are similar to lincomycin. It is bacteriostatic at lower concentration and bactericidal at higher concentration.

Uses:

- ✓ It is chiefly used against *Staphylococcal*, *Pneumococcal* and *Streptococcal* infections not responding to penicillin and erythromycin. It is also used in chronic osteomyelitis.
- ✓ Effective against bone and joint infection caused by *Staphylococcus aureus*
- ✓ It is used for treatment of Pharyngitis and Tonsillitis caused by *S. pyogenes.*
- ✓ Used combination with primaquine for the treatment of mild to moderately sever pneumonia.

****Lincomycins should not be combined with erythromycin (since erythromycin binds to same site 50S ribosomal subumit) to prevent competition for binding site.**