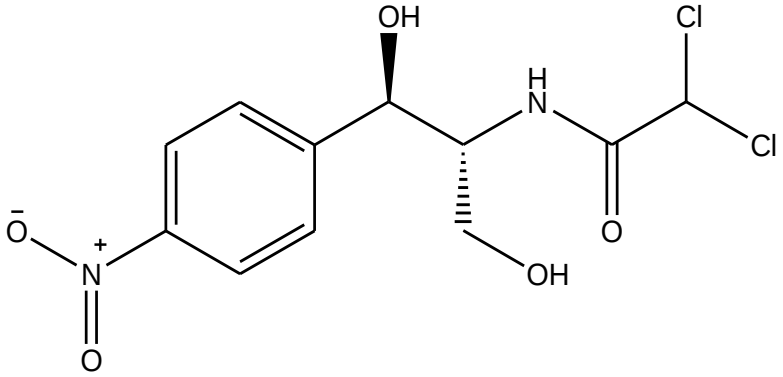
UNCLASSIFIED ANTIBIOTICS

CHLORAMPHENICOL

- It is obtained from *Streptomyces venezuelae*.
- It is broad spectrum antibiotic, like tetracyclines.
- It is available as palmitate and succinate salt.
- The nitrobenzene moiety is supposed to depress the bone marrow and to affect the elements of blood resulting into a fatal outcome.



Chloramphenicol

STRUCTURE ACTIVITY RELATIONSHIP

- **SAR of p-nitro phenyl group**

1. Replacement of the nitro group by other substituents leads to reduction in activity
2. Shifting of nitro group from the Para position also reduces the antibacterial activity
3. Replacement of phenyl group by the alicyclic moieties results in less potent compounds
4. The p-nitro phenyl group may be replaced by other aryl structures without appreciable loss of activity

STRUCTURE ACTIVITY RELATIONSHIP

- **SAR of dichloroacetamido side chain**

1. Other dihaloderivatives of the side chain are less potent though major activities are retained
2. While in case of trihalo derivatives (2-$NHCOCF_3$) would be about 1.7 times as active as chloramphenicol

- **SAR of 1,3-propanediol**

  The primary alcoholic group on C-1 atom if modified, results in a decrease in activity hence the alcoholic group seems to be essential for activity

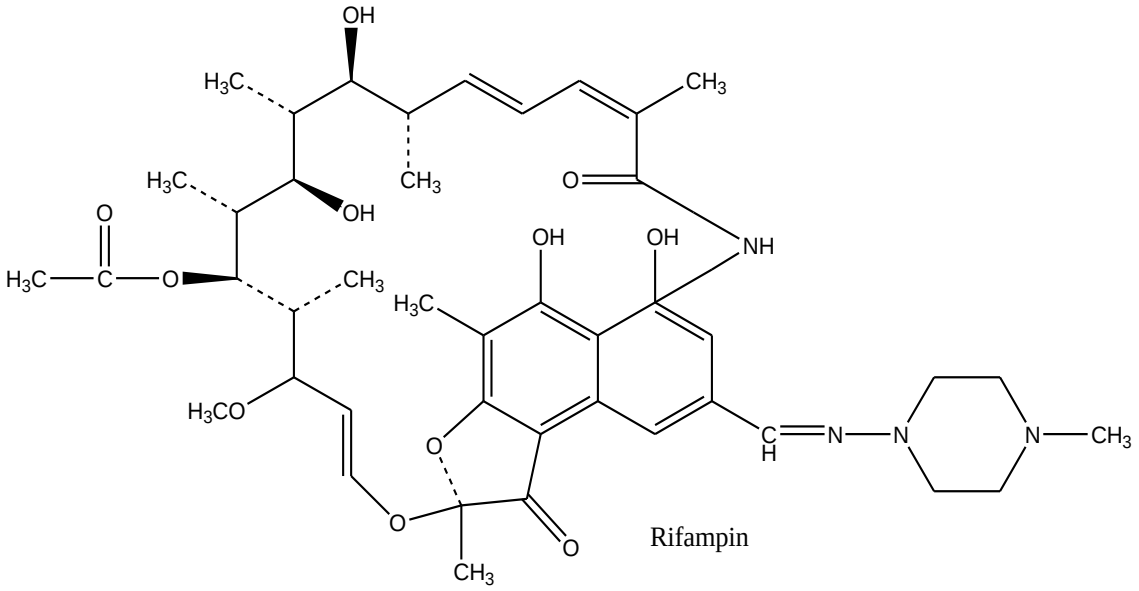
- Of the four stereoisomers of chloramphenicol the antibacterial activity resides in only D-threo compound.

RIFAMPIN

- The rifampin is a group of structurally similar, complex macrocyclic antibiotics obtained from *Streptomyces mediterrani*.
- They belong to ansamycin class which consist of rifamycin A, B, C, D and E.
- It is broad spectrum antibiotic.
- It can penetrate well cerebrospinal fluid and thus is used in the treatment of tuberculous meningitis. It is also used to treat leprosy.
- Rifampin shows hepatotoxicity as side effect.

STRUCTURE ACTIVITY RELATIONSHIP

- Aliphatic modifications do not help to retain the activity.
- In the naphthalene ring position-3 and 4 are bioactive and gives compounds with similar activity.



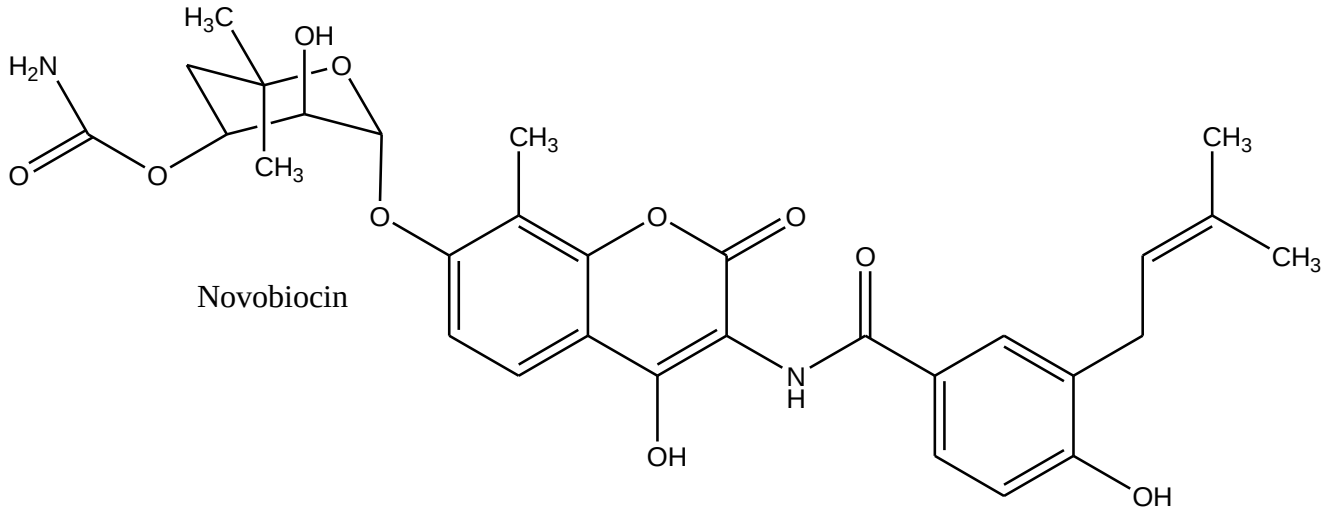
Rifampin

NOVOBIOCIN

- It is obtained from *Streptomyces niveus* and *Streptomyces spheroides*. It is bacteriostatic in action.
- It possesses a glycosidic sugar moiety ‘novobiocin’ and aglycon moiety ‘novobiocic acid’.
- Side effects are urticaria, allergic rashes, hepatotoxicity and blood dyscrasias

MECHANISM OF ACTION

- It inhibits bacterial protein and nucleic acid synthesis. They bind to subunit of DNA gyrase and possibly interfere with DNA supercoiling and energy transduction in bacteria.



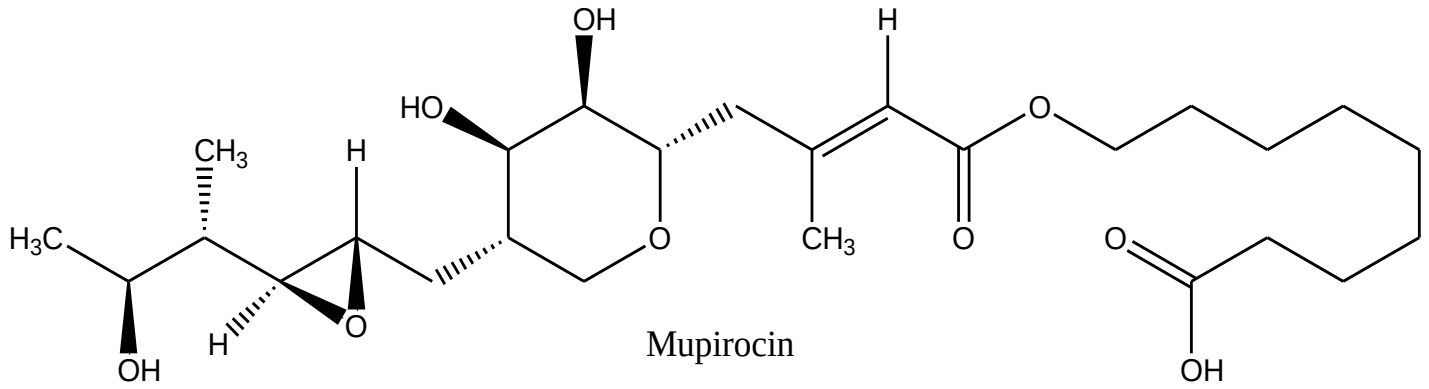
Novobiocin

MUPIROCIN

- It is isolated from *Pseudomonas fluorescens*.
- Systemic administration results in rapid hydrolysis by esterases to mionic acid, which is inactive *in-vivo* because of its inability to penetrate bacteria.
- It is used in the treatment of topical infections.
- Resistance to antibiotic is due to poor cellular penetration of the antibiotic.

MECHANISM OF ACTION

- It specifically and reversibly binds with bacterial isoleucyl transfer-RNA synthase to prevent the incorporation of isoleucine into bacterial proteins.



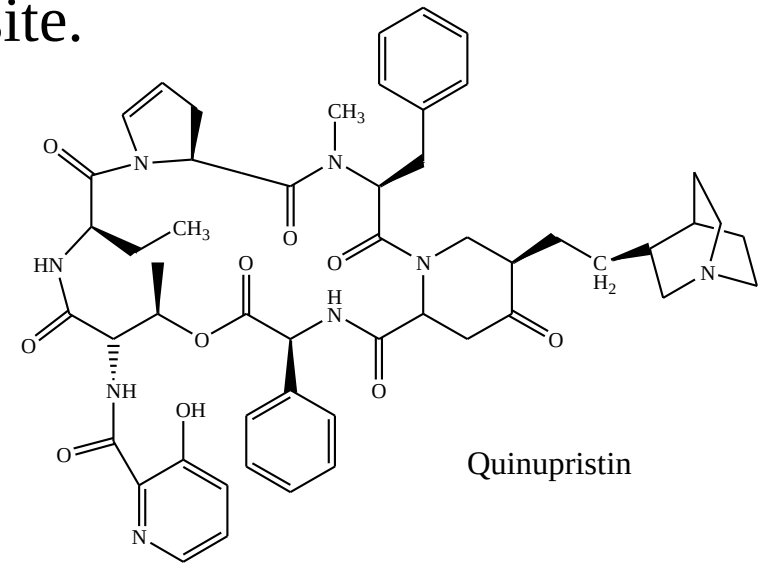
Mupirocin

QUINUPRISTIN/DALFOPRISTIN

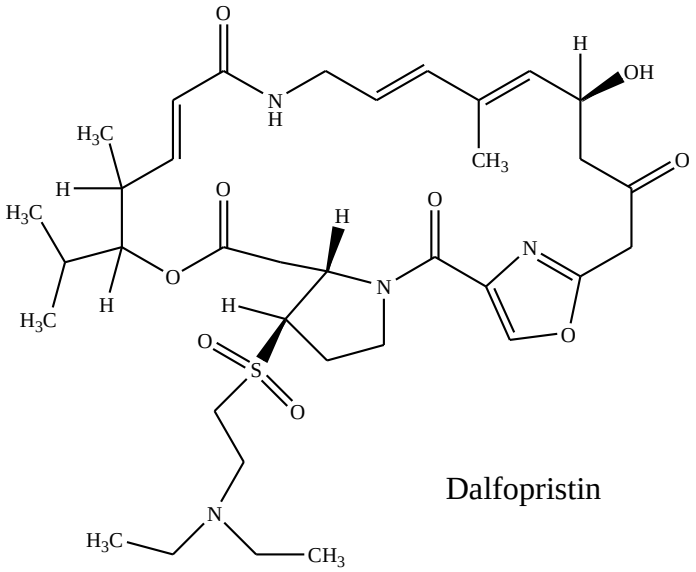
- It is a combination of the streptogramin- B quinupristin with the streptogramin-A dalfopristin in 30:70 ratios.
- Both these compounds are Semisynthetic derivatives of naturally occurring pristinamycins isolated from *streptomyces pristinaspiralis*.
- This combination is active against gram positive organisms only.
- This combination is reserved for the treatment of serious infections caused by multidrug-resistant gram positive organism.

MECHANISM OF ACTION

- These antibiotics bind with 50S ribosomal subunit.
- Quinupristin (like macrolide antibiotic) inhibit polypeptide elongation and early termination of the protein synthesis.
- Dalfopristin causes conformational changes in 50S ribosomal subunit and enhancing the binding of Quinupristin to the target site.



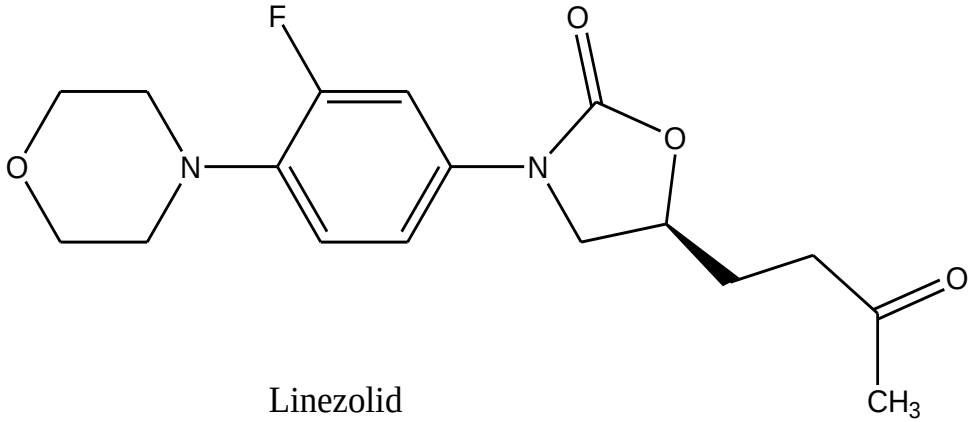
Quinupristin



Dalfopristin

LINEZOLID

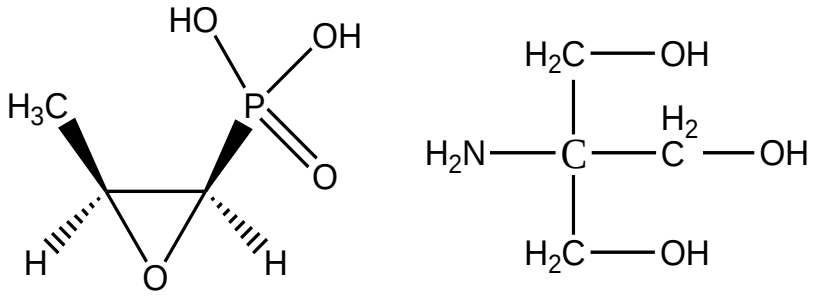
- It is oxazolidinedione type broad spectrum antibiotic.
- It binds to 30S and 50S ribosomal subunits and prevents interaction between the two subunits. It inhibits protein synthesis by preventing the formation of a functional initiation complex.
- It is used in the treatment of skin, soft tissue infection and drug resistant gram positive infections.



Linezolid

FOSFOMYCIN TROMETHAMINE

- Fosfomycin is phosphonic acid epoxide derivative isolated from Streptomyces species. Tromethamine salt formation expands utility by increasing water solubility to allow oral administration.
- It is broad spectrum antibiotic used in the treatment of UTI.
- It inactivates first enzymes in the bacterial cell wall biosynthesis pathway, UDP-N-acetylglycosamine enolpyruvyl transferase (Mur A) by alkylation of the cysteine-115 residue.



Fasfomycin