Macrolide Antibiotics and Lincosamides

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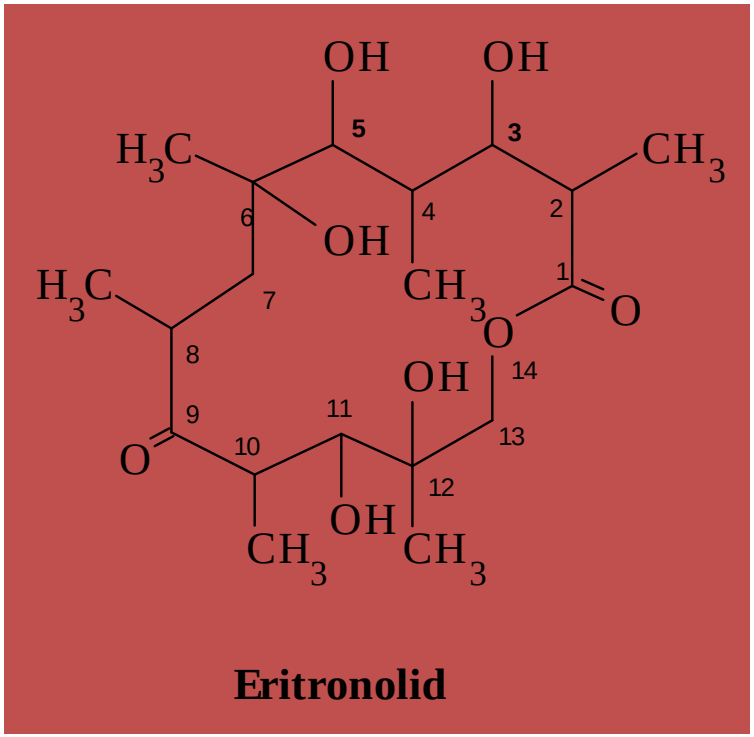
-Antibiotics obtained from Actinomycetes → **Macrolide**

-Erythromycin, Oleandomycin, Troleandomycin, Roxithromycin, Spiramycin are currently used antibiotics.

-Also called erythromycin group antibiotics.

Common features

They carry 12, 14 or 16 atoms of lactone ring.



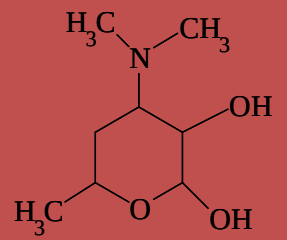
Eritronolid

They carry 2 or 3 oz molecules, at least one bearing an amine group.

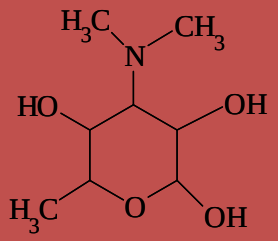
Amine groups provide molecular basic properties.

Bazı Ozlar

Bazik yapıda olanlar

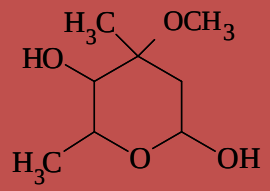


D-Desozamin (Eritromisin A, B, C ve Oleandomisin)

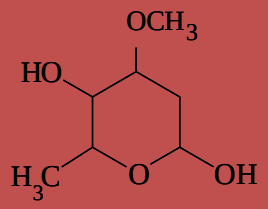


D-Mikamikoz (Spiramisin)

Nötr yapıda olanlar



L-Kladinoz Eritromisin



L-Oleandroz (Oleandomisin)

The lactone ring and the sugars are linked by ether bonds.

Antibacterial spectrum

-In particular, they are effective against to Gr (+) bactera, some Gr (-) bacteria (such as diphtheria, brucella) and rickettsiales.

-They are effective against especially staphylococci.

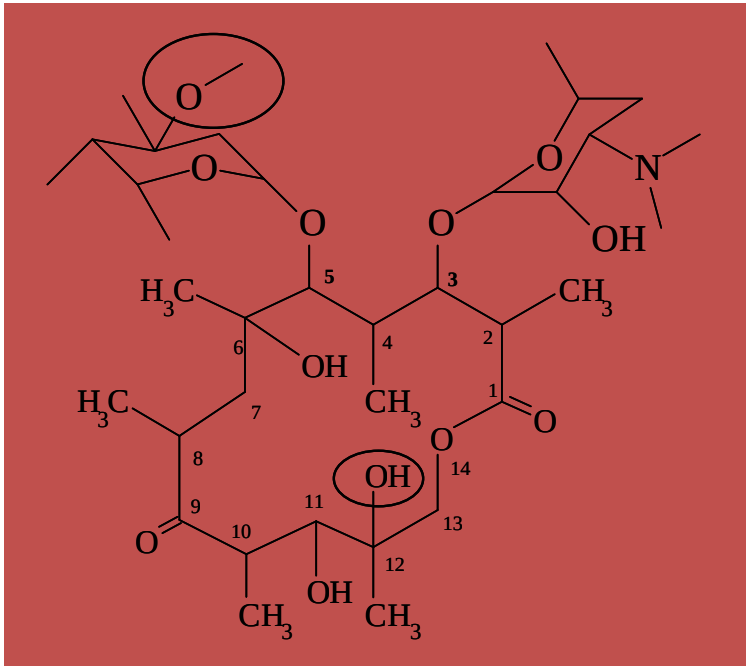
-bind to the 50S subunits of the ribosomes in bacteria, preventing the t-RNA molecule from binding at the same time, thereby inhibiting protein synthesis.

-bacteriostatic

Erythromycin (ErytrocinR)

They are isolated from Streptomyces erythreus (Erythromycin A, B and C)

Bileşik		12. konum
Eritromisin-A		OH
Eritromisin-B		H
Eritromisin-C	Kladinoz $OCH_3 \longrightarrow$	H OH

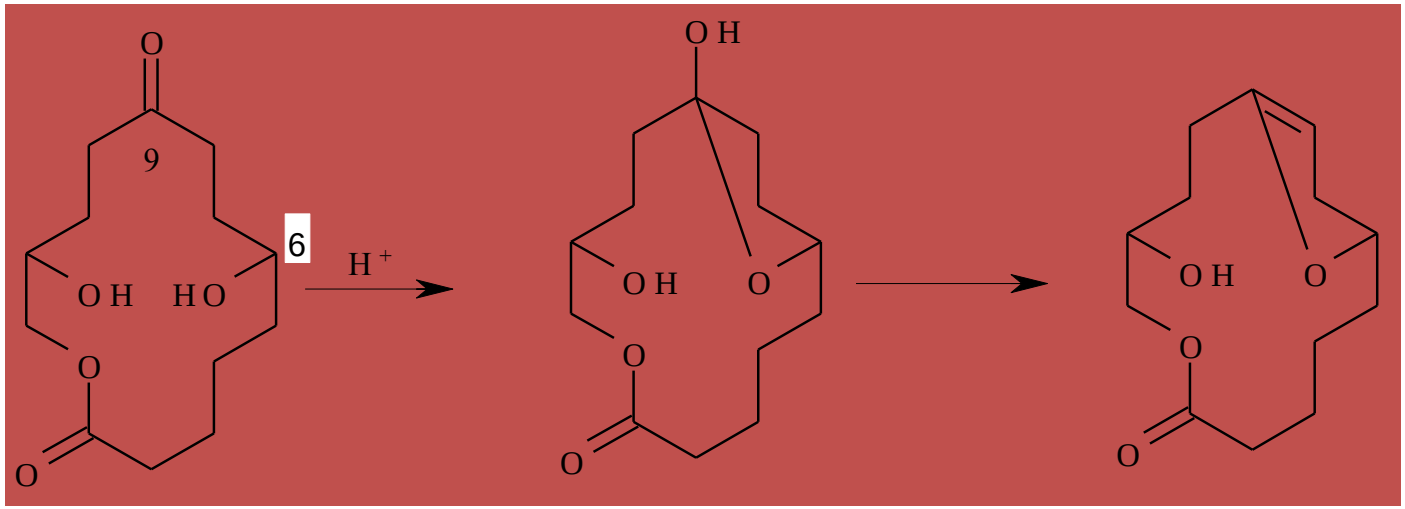


-slightly soluble in water.

-Soluble in organic solvents.

-The aqueous solutions are basic.

-It is unstable under pH = 4 (acidic environment) (ketone in the 9th position returns to the enol, ketalized with -OH at 6th position ⟶ becomes inactive



Oral use, acid-resistant pharmaceutical forms are used to prevent degradation in gastric acid .

Derivatives are prepared to increase acid stability and water solubility.

1- Acid salts (e.g. stearate) to increase water solubility

2 - Esters (e.g. ethyl succinate, propionate) are prepared to increase acid resistance.

Erythromycin propionate + lauryl sulphate

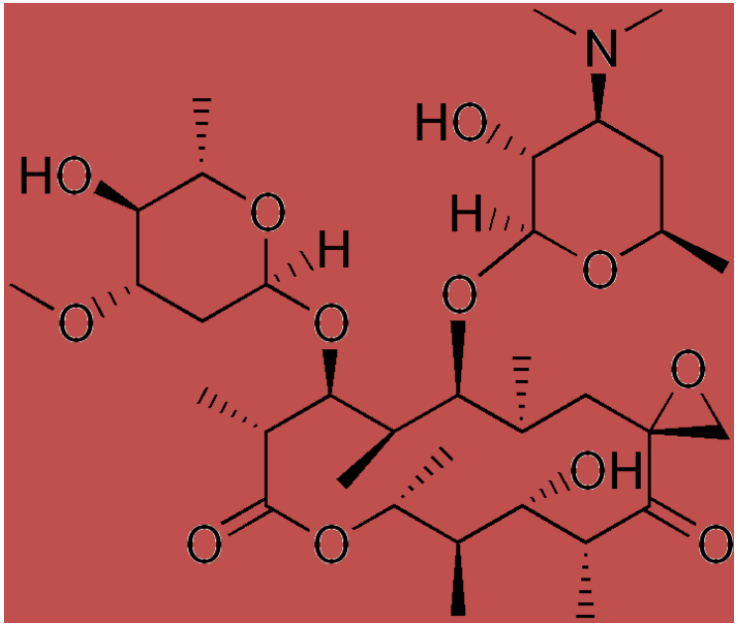
Erythromycin estolate

(water-soluble, acid-resistant)

Oleandomycin

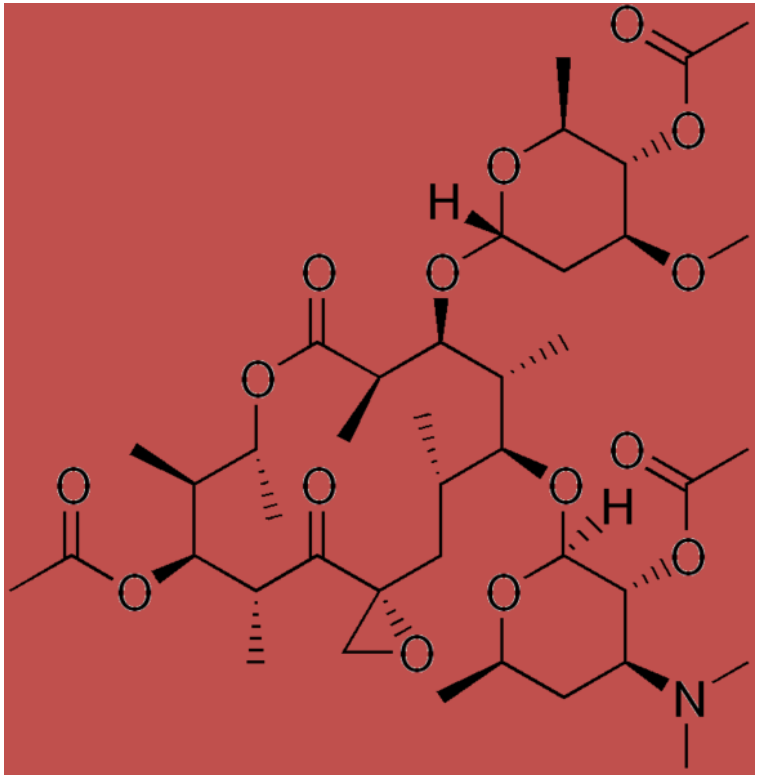
isolated from Streptomyces antibioticus.

14-membered lactone oleandolite, Desozamine (amino sugar), L-Oleandroz (neutral sugar).



Troleandomycin (Triacetyloleandomycin)

It is the triacetate ester of the tri -OH group of oleandomycin. According to erythromycin, more stable to the acid and absorbs better. It is used for upper respiratory tract infections.



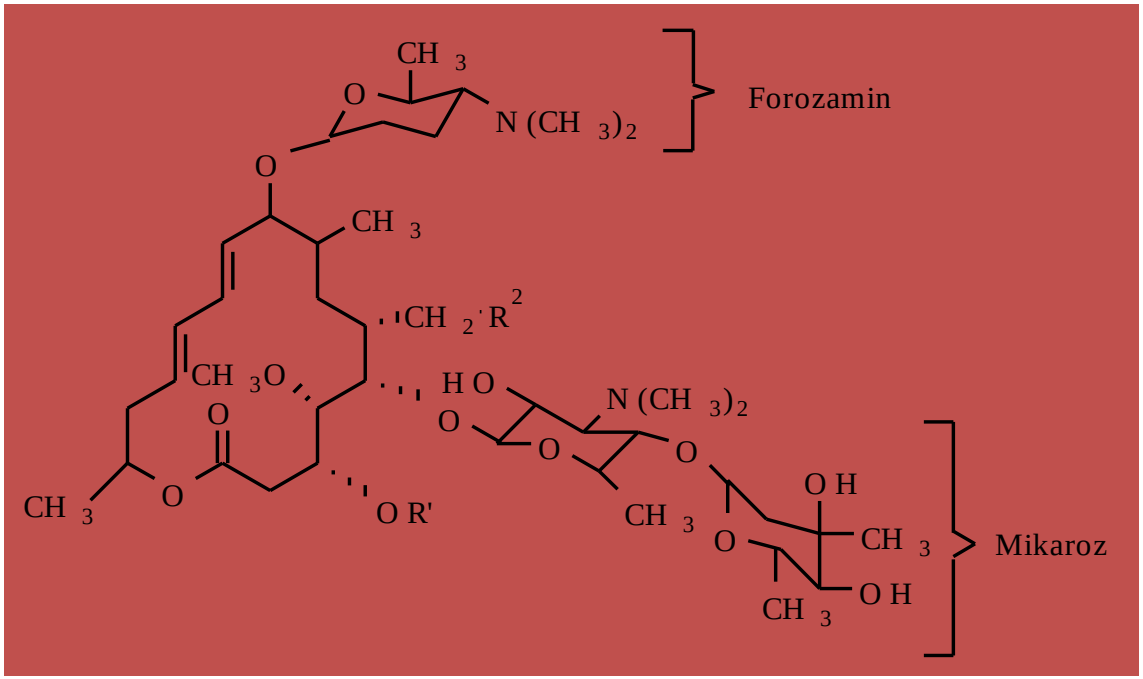
Spiramycin (RovamycineR)

It was isolated from streptomyces ambofaciens.

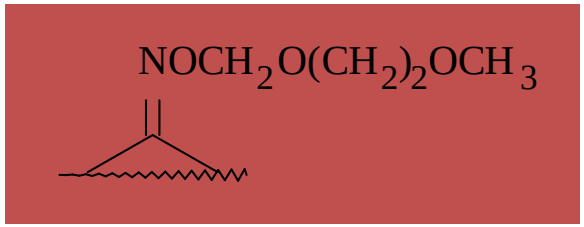
It is a mixture of Spiramycin A, B and C.

Less active than erythromycin.

Spiramycin A: R '= H,
Spiramycin B: R '= COCH3,
Spiramycin C: R '= COCH2CH3



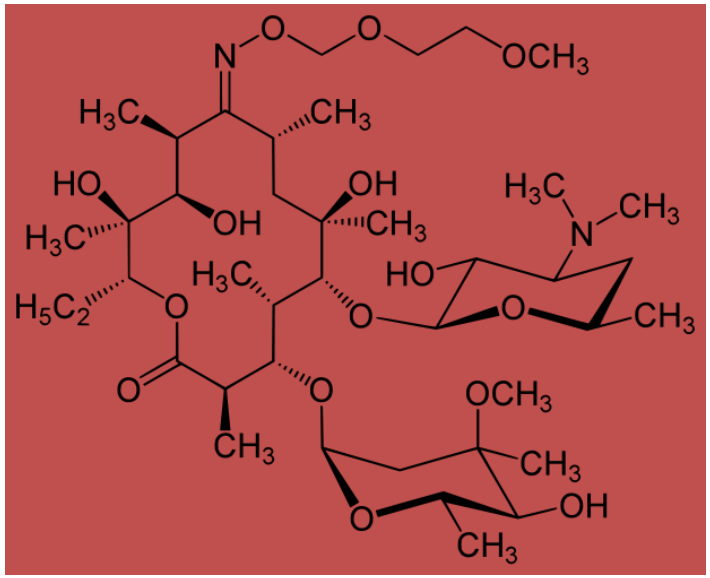
Roksitromycin (RulidR)



It is 9- [O - [(2-methoxyethoxy) methyl] oxime] derivative of Erythromycin.

Z isomer is more active.

The antibacterial spectrum is similar to erythromycin, more resistant to the acid .



Clarithromycin (KlacidR)

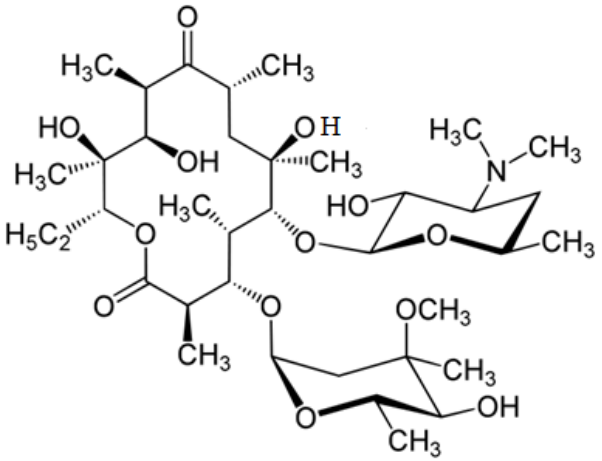
6-O-methyl erythromycin

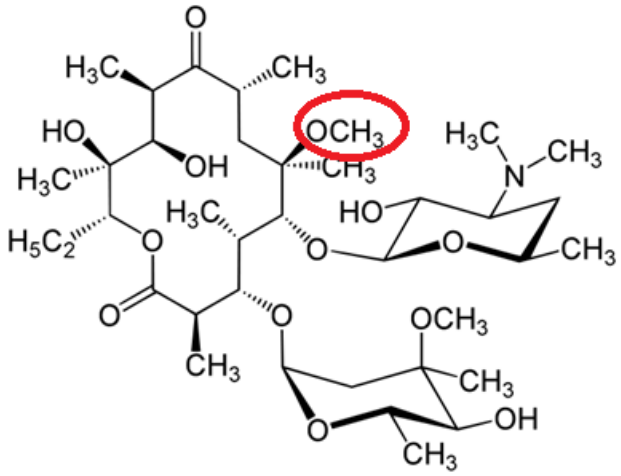
-Stable to acid and long acting.

Tissue penetration is very good.

It is used in upper and lower respiratory tract infections and recently in the treatment of pneumonia.

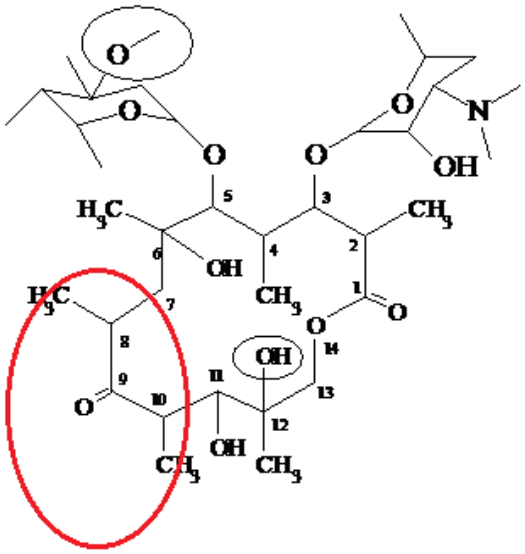
Used in ulcers caused by Helicobacter pylori.

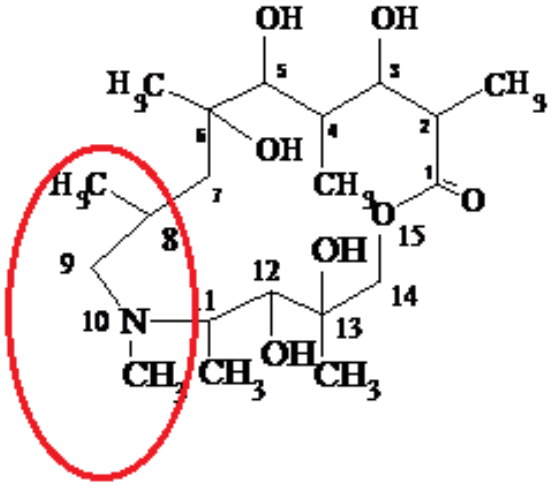


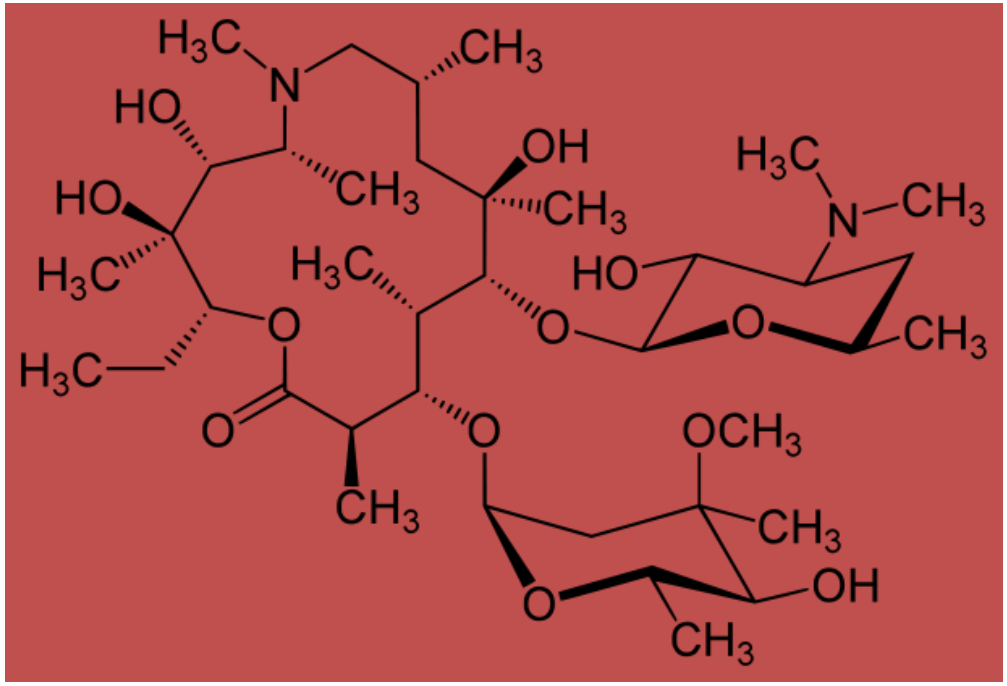


Azithromycin (AzitroR)

It is a methylated nitrogen-bearing derivative in the lactone ring of Erythromycin.







10-aza-9-deoxy homoerythromycin

- The antibacterial spectrum is similar to erythromycin, more resistant to stomach acid.

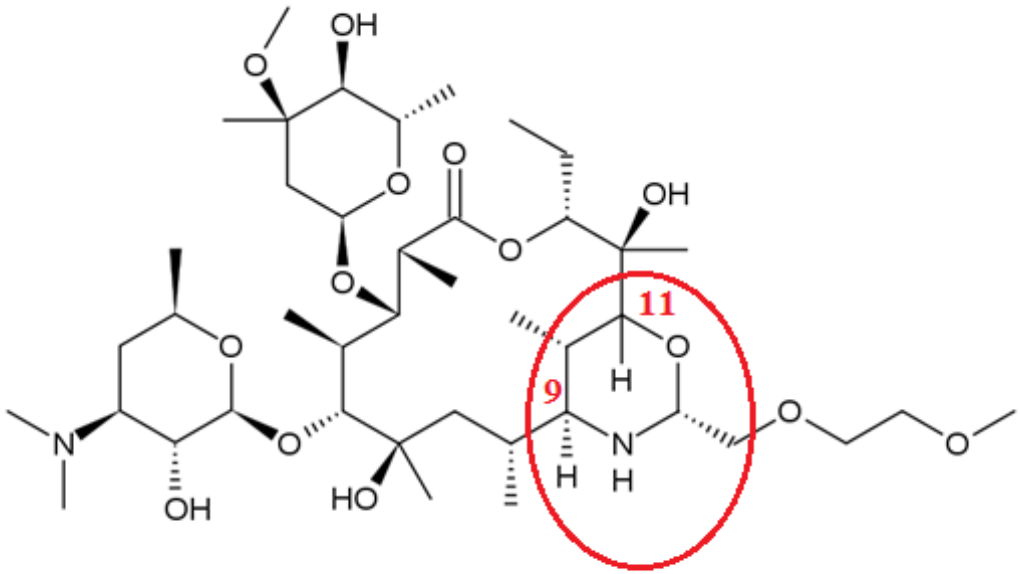
- Another advantage over erythromycin is that the duration of action is long.

Diritromycin (DynabacR)

The spectrum of antibacterial activity is similar to that of erythromycin, more active than erythromycin *in in vivo* .

It is effective in secondary bacterial infections due to chronic and acute bronchitis, pneumonia, pharyngitis and tonsillitis.

It is also effective in H. pylori.



9-N-11-O-oxazine-erythromycin

Ketolides

Ketolides are derived from erythromycin by substituting the cladinose sugar with a keto-group and attaching a cyclic carbamate group in the lactone ring.

These modifications give **ketolides** much broader spectrum than other macrolides.

It is a new group compound especially effective against macrolides-resistant upper and lower respiratory tract pathogens.

Semi-synthetic derivatives of erythromycin A (Telithromycin, Setiromycin)

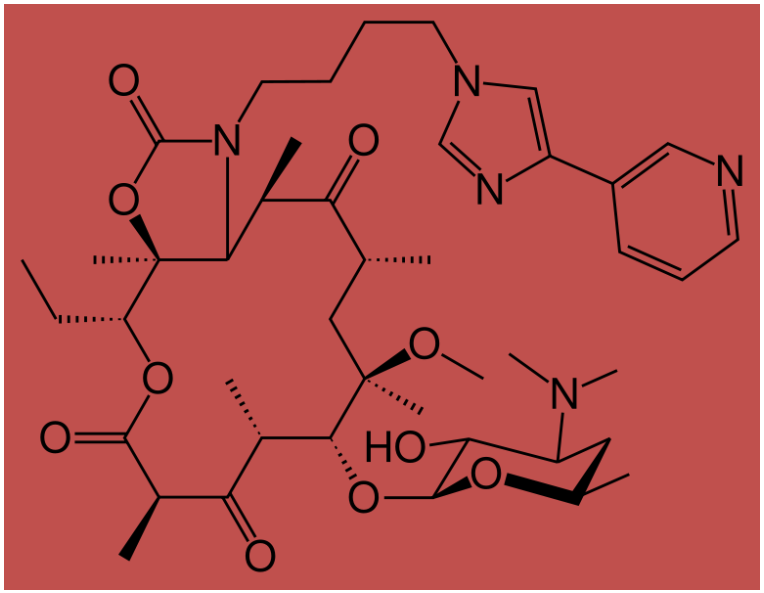
Telithromycin (KetekR)

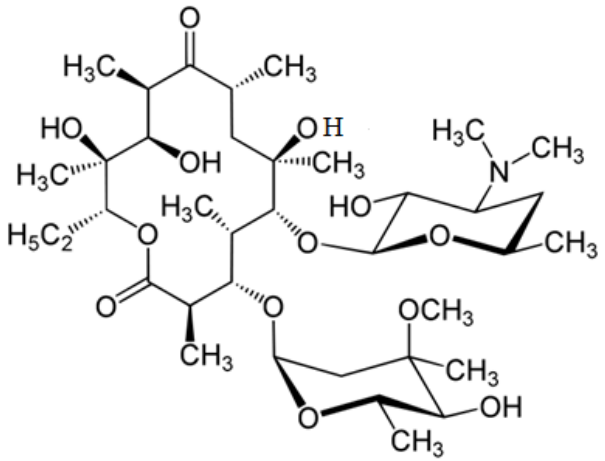
-Macrolactone of erythromycin and Desozamine at the 5th position is constant.

-The 3-position L-Cladinose is removed and the -OH group is oxidized to the =O group,

-Cyclic carbamates were prepared via the -OH groups at positions 11 and 12.

-These chemical changes increase acid tolerance, ribosome binding and antimicrobial power.





It is particularly effective against to Streptococcus pneumoniae resistant to Beta lactam and macrolides

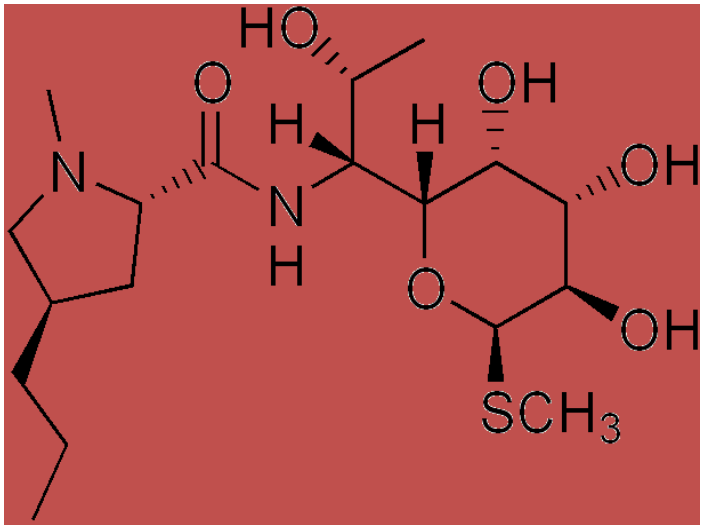
Lincosamides

linkomycin

-obtained from Streptomyces lincolnensis

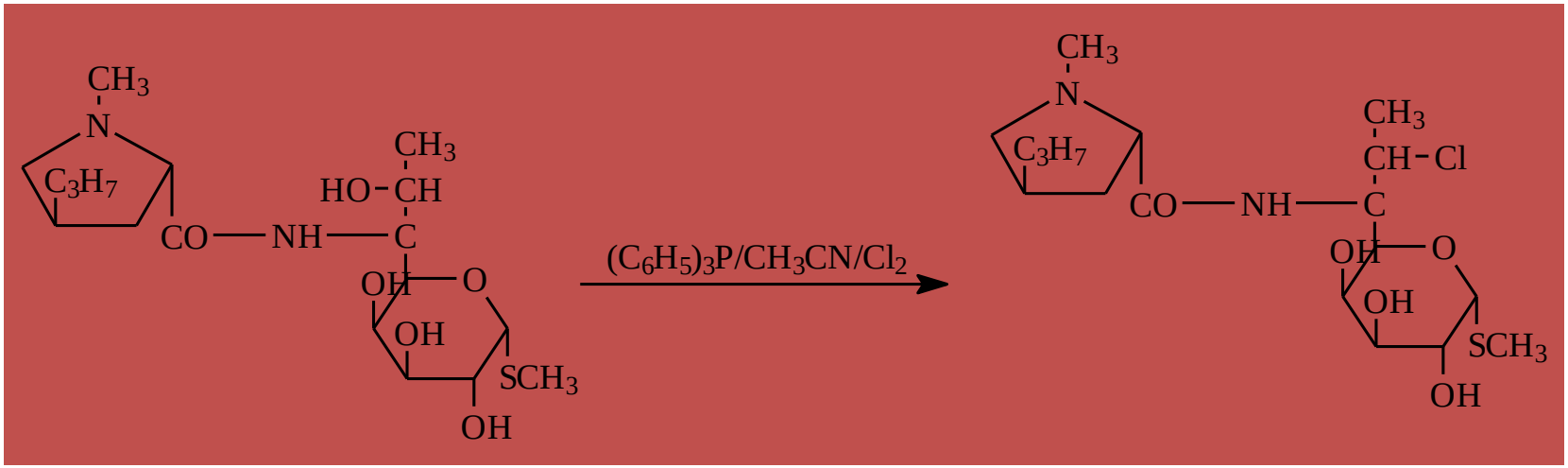
-effective against the majority of Gram (+) bacteria.

-*In vitro* cross resistance with macrolides and clindamycin.



Clindamycin (7-Cl-Linkomycin) CleocinR

it is superior to the linkomycin due to its easy absorption from the intestines and the strong antibacterial activity,.



It binds to 50S subunits in ribosomes and inhibits protein synthesis.

It has bacteriostatic and bactericidal action according to the concentration reached to the effect region and the sensitivity of the applied organism.

Steroidal Antibiotic

Fusidic Acid (Fusidine R)

-It is obtained from *Fusidium coccineum.*

- It is used locally.

-It inhibits the synthesis of steroids.