Shree H. N. Shukla Institute of Pharmaceutical Education and Research, Rajkot

B. Pharm

Semester-VI

Subject Name: Medicinal Chemistry

Subject Code: BP601TP

Prepared by:-Ms. Foram J. Vagadia

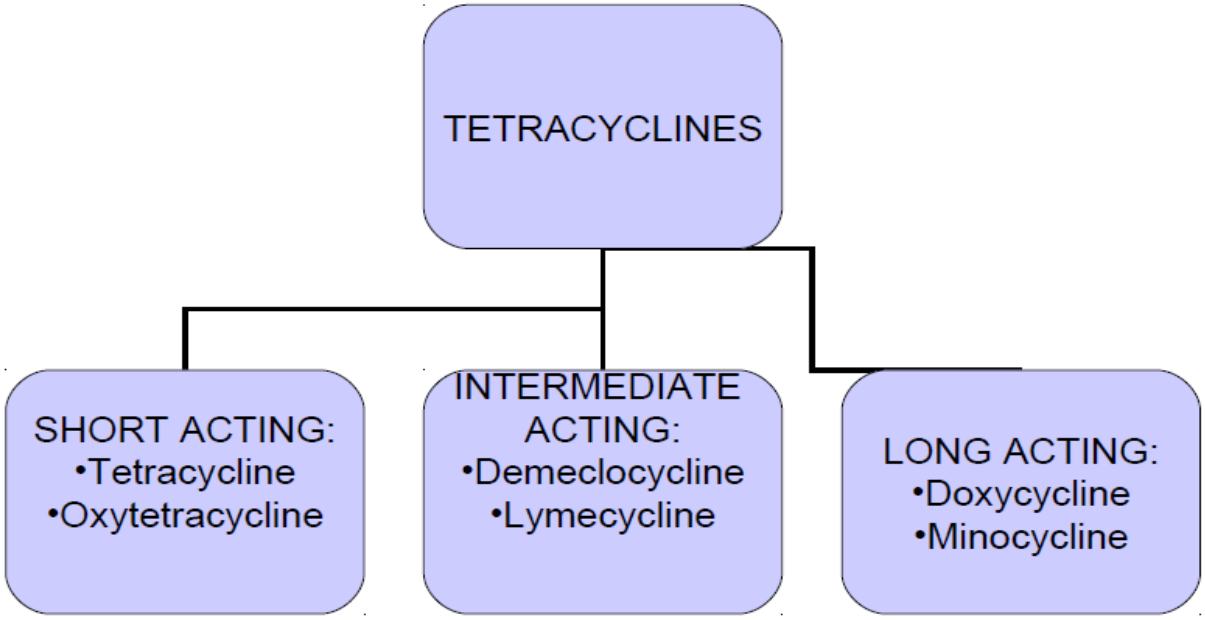
Tetracycline

Tetracyclines is a group of antibotic that include tetracycline.

Tetracyclines are obtained by fermentation from Streptomyces spp. Or by chemical transformation of natural products.

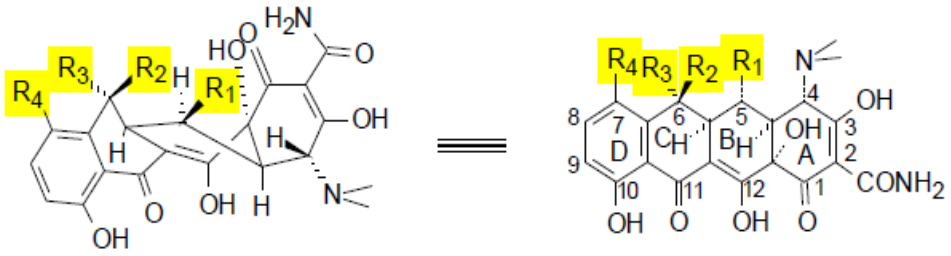
They are derivatives of an octahydro- naphthacene,a hydrocarbon system that comprises four annulated six membre rings.

CLASSIFICATION



Structure of Tetracycline

- The stereochemistry of the tetracycline is very complex. carbon atom 4,4a,5,5a,6 and 12a, are potentially chiral depending on substitution.
- Oxytetracycline and Doxycycline posses 5alpha-hydroxy substituent have six chiral carbon and others have five chiral carbon.
- These are amphoteric compounds, forming salts with either acids or bases.
- It exists mainly as zwitter ions in neutral solutions .
- They are yellow in colour , The HCL salts are used for oral adminstration and usually given in the form of capsule to mask the bitter taste.



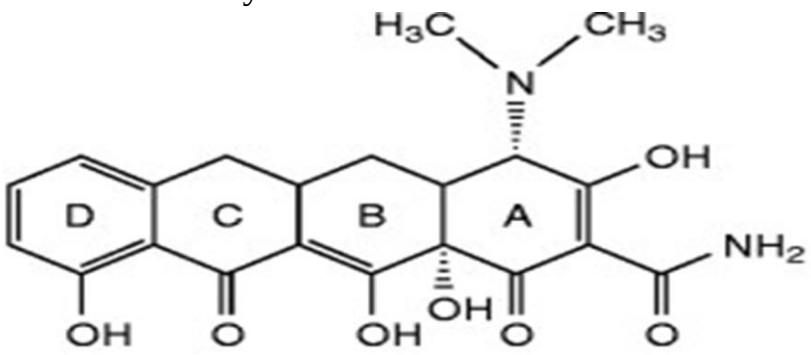
¨Oxytetracycline£© R_1 = -OH R_2 = -OH R_3 = -CH_3 R_4 = -H

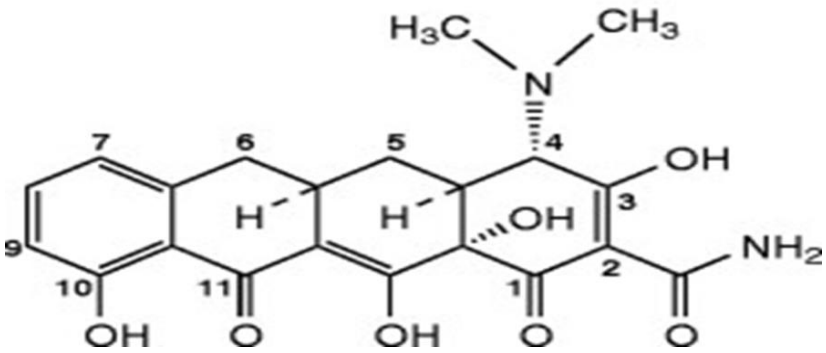
¨Chlotetracycline£© R_1 = -H R_2 = -OH R_3 = -CH_3 R_4 = -Cl

¨Tetracycline£© R_1 = -H R_2 = -OH R_3 = -CH_3 R_4 = -H

Tetracycline pharmacophore and numbering

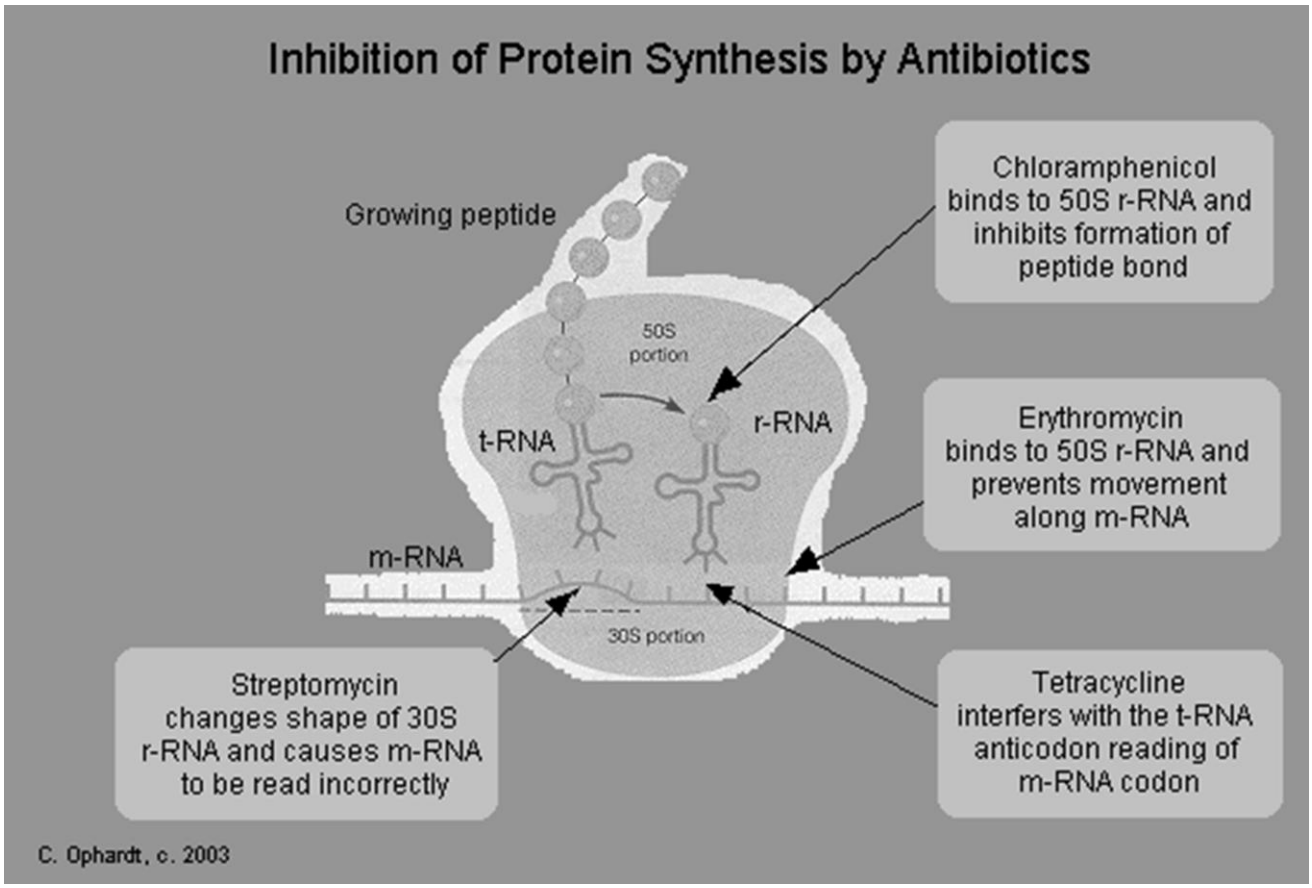
Positions at the "bottom" of the molecule (10, 11, 1) and most of ring A (positions 2, 3, and 4) represent the invariant pharmacophore region of the molecule, where modifications are not tolerated without loss of antibiotic activity.



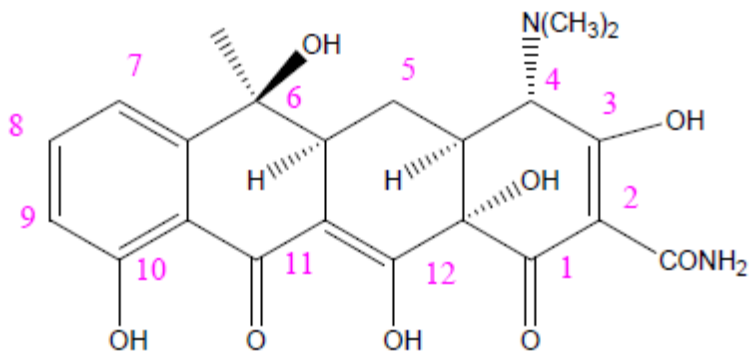


Mechanism of Action

- Tetracyclines are specific inhibitors of bacterial protein synthesis. They bind to the 30S ribosomal subunit and thereby prevent the binding of aminoacyl tRNA to the mRNA ribosome complex.
- Tetracyclines also inhibit protein synthesis in the host,but are less likely to reach the concentration required because eukaryotic cells do not have a tetracycline uptake mechanism.

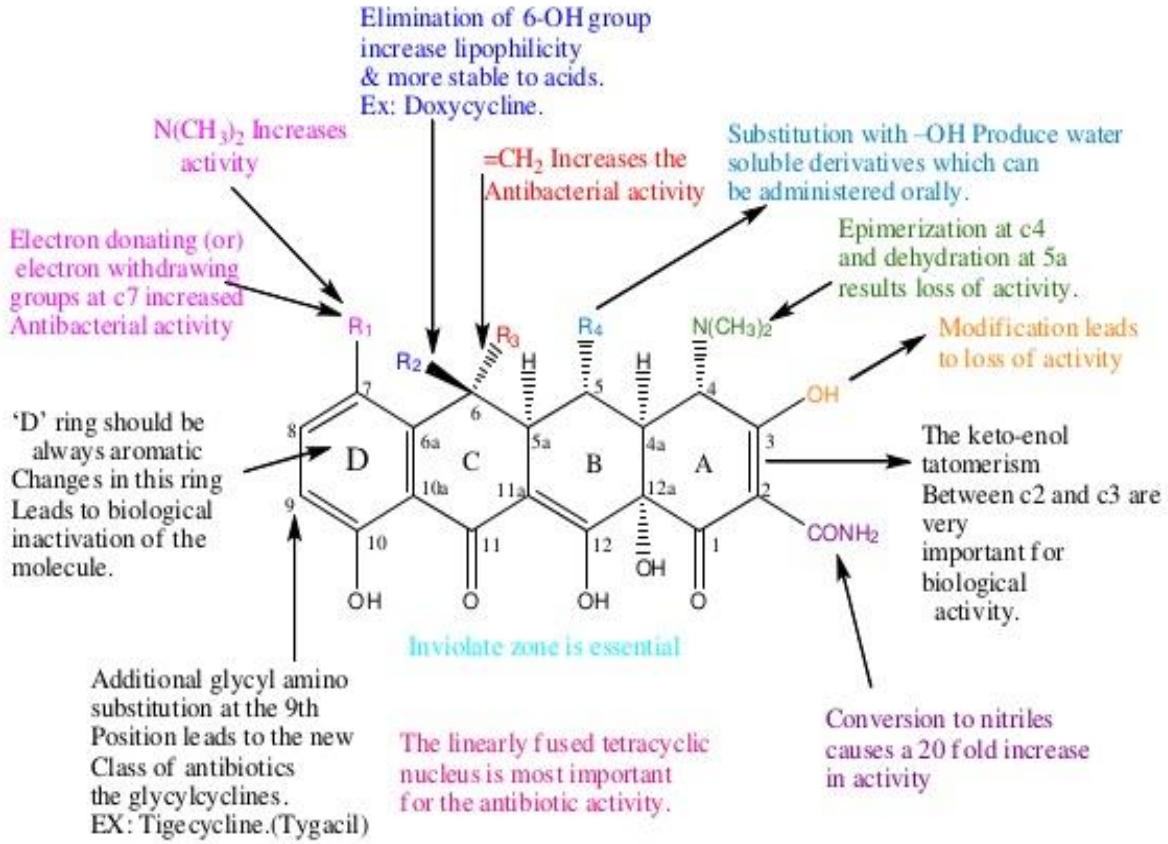


SAR of tetracyclines



6-methyl-4-(dimethylamino)-3,6,10,12,12a pentahydroxy-1,4,4a,5,5a,6,11,12a-octahydro- 2- naphthacenecarboxamide.

Structural Activity Relationship:



SAR OF TETRACYCLINES