

CLASSIFICATION OF TETRACYCLINES:

Natural tetracyclines :: Eg Tetracycline, Oxytetracycline, chlortetracycline etc.

Semisynthetic tetracyclines:

Eg Doxycycline, Methacycline, Minocycline

Pro tetracyclines:

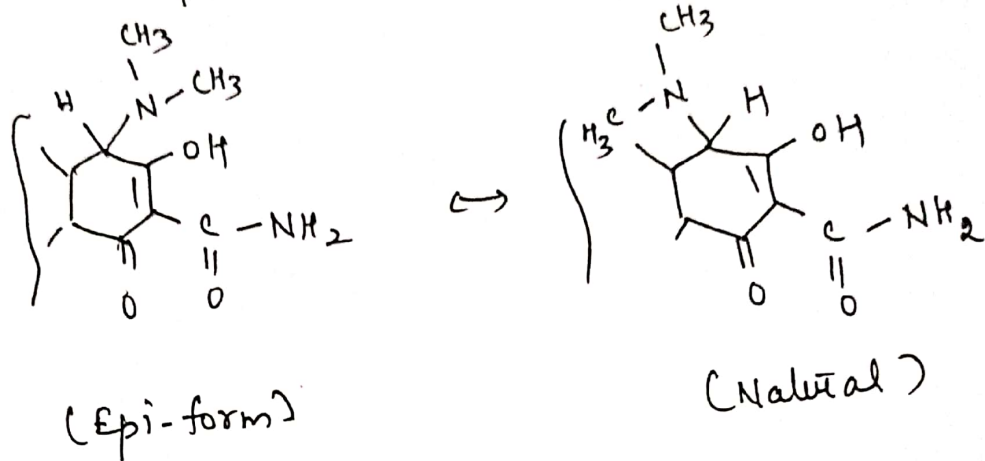
Eg Rolitetracycline, Pipracycline, Clonoxycline

MOA of Tetracyclines

In the Bacterial protein synthesis, the messenger RNA attaches itself to 30S ribosome. Tetracyclines bind to 30S ribosomes and the attachment of aminoacyl tRNA to mRNA ribosome complex is interfered. Protein synthesis is inhibited.

Effect of pH on tetracyclines:

In the Intermediate pH range the tetracyclines have a property of epimerization at C4 position. These isomers are called epitetracyclines.



Effect of metals Ca, Mg & Fe

They form stable chelate complexes with many metals incl. Ca, Mg and Fe. These are chelates and insoluble in water. Hence in the presence of these the impairment of absorption takes place.

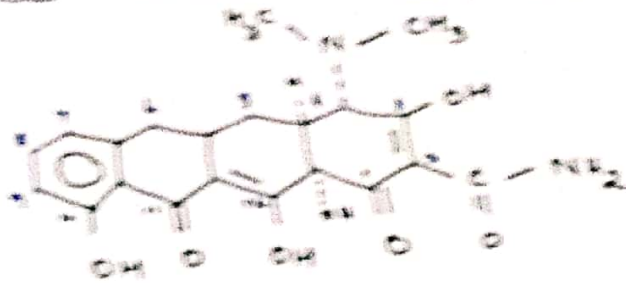
Deposition of these antibiotics in the teeth causes yellow coloration. Hence it should not be taken with milk.

To avoid in children, new born, pregnant women and lactating mothers.

TETRACYCLINES

Q)

CLASSIFICATION, CHEMISTRY, SAR, HDA

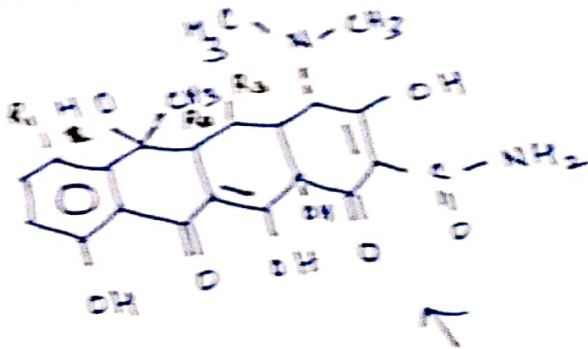


[4 Rings linear]

To remember

Aromatic ring - A between
Double bonds 2 and 3
(2) At 12
[Inside the Rings]
OH groups - 3rd position
10th & 12th position
2 & 12 $\text{C}=\text{NH}_2$ (Amide)
10th $\text{C}=\text{O}$
4th $\text{N}-\text{CH}_3$ (Dimethyl
amino)
10th $\text{C}=\text{O}$ (Ketone)
12th $\text{C}=\text{NH}_2$ (1st & 12th)

TETRACYCLINE :- obtained from Streptomyces spp.

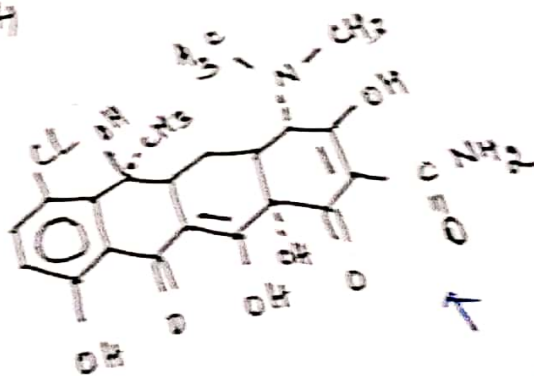


$R_1 - \text{H}$

$R_2 - \text{CH}_3$ (4)

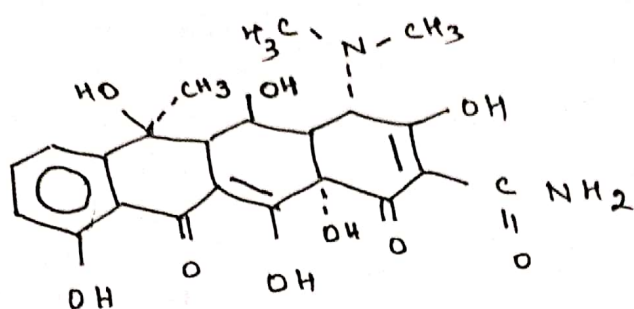
$R_3 - \text{H}$

Tetracycline

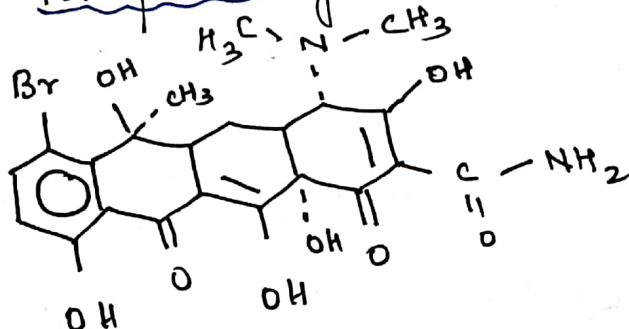
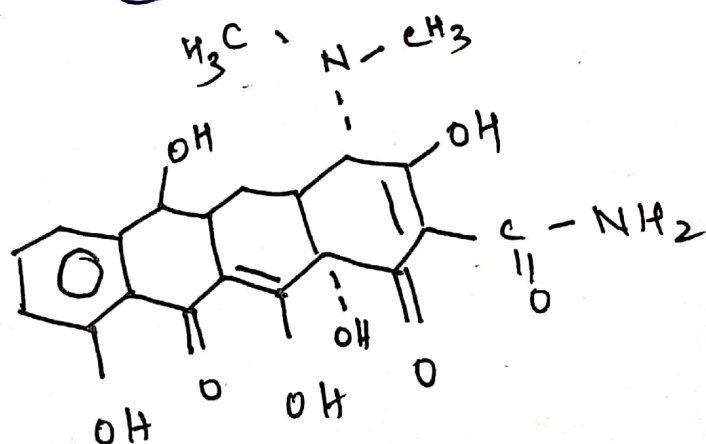


chlorotetracycline

$R_1 - \text{Cl}$
 $R_2 - \text{CH}_3$
 $R_3 - \text{H}$

Oxytetracycline

5th position β -OH gp
 IIIa to tetracycline

BromotetracyclineDexamethyl tetracycline

Chemistry :

Broad spectrum antibiotics
like compounds are known.

- (i) The tetracyclines are amphoteric substances.
forming salts with either acids or bases.
- (ii) The acid salts which are formed through
protonation of the enol group on C-2 exist
as crystalline compounds that are soluble in water.
- (iii) The tetracyclines have an affinity for calcium
salts, hence chelates with many metals
leading to impaired function of tetracyclines.
- ↳ In neutral solutions, Tetracyclines exist
mainly as zwitter ions.
- ↳ Easily available Hydrochloride salts of
tetracyclines are mainly used.
- ↳ With magnesium salts such as (MgCl) hexahy-
drate enhances the rate and height of the
plasma concentration. Increases pharmacokinetic
properties.

- (i) 4 membered linear fused ring is essential.
- (ii) Substituents of the ring can be slightly modified which the ring was known for its antibacterial property.
- (iii) Enolised carbon $C_1 - C_3$ - essential for good activity.
- (iv) Replacement of the amide with other functional groups reduces or abolishes the activity.
- (v) Removal of Dimethyl amino group at 4 decreases the activity.
- (vi) 5-OH group eg Oxytetracycline and doxycycline may influence pharmacokinetic property.
- (vii) Presence of electron withdrawing groups, such as halogens (X, -Cl, Br, I, F) enhances the activity eg chlorotetracycline.
- (viii) 6-OH or 6-CH₃ group is not essential for the activity.
- (ix) Semisynthetic derivatives could be prepared from the suitable modification at 6th position eg Doxycycline and Meltracycline.