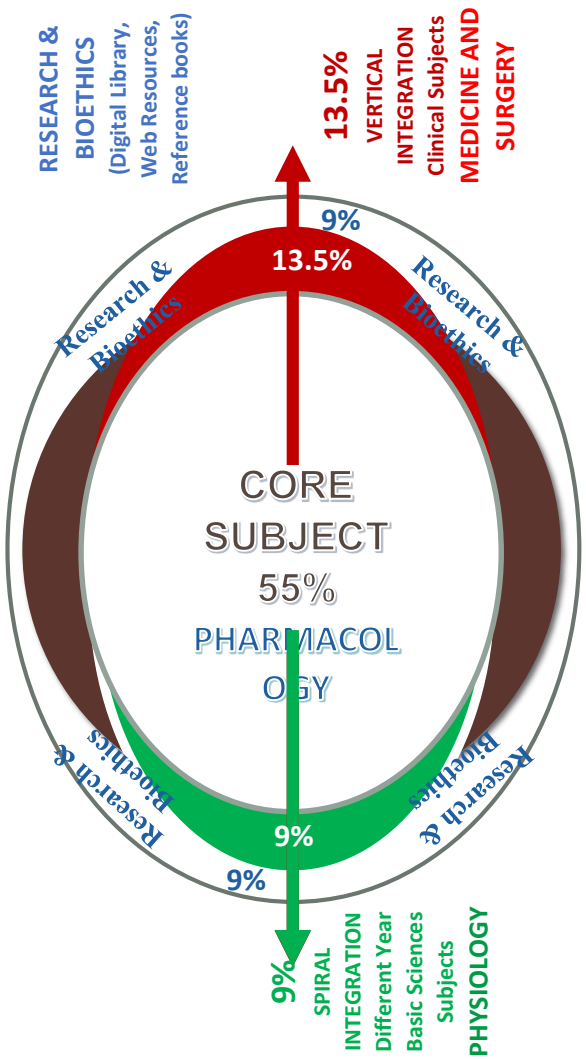

بسم الله الرحمن الرحيم

MOTTO AND VISION

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

Prof. Umar's Clinically Oriented Integration Model
For Basic Sciences Interactive Lectures



Model 3rd Year Pharmacology (33 slides)	
Core Subject – 70%	
Horizontal Integration – 10%	
Vertical integration (Clinical Subjects)	• Medicine (10 %)
Spiral Integration – 15%	
Different Year Basic Sciences Subjects	
Research & Bioethics 5%	

Tetracycline Antibiotics

LEARNING OBJECTIVES

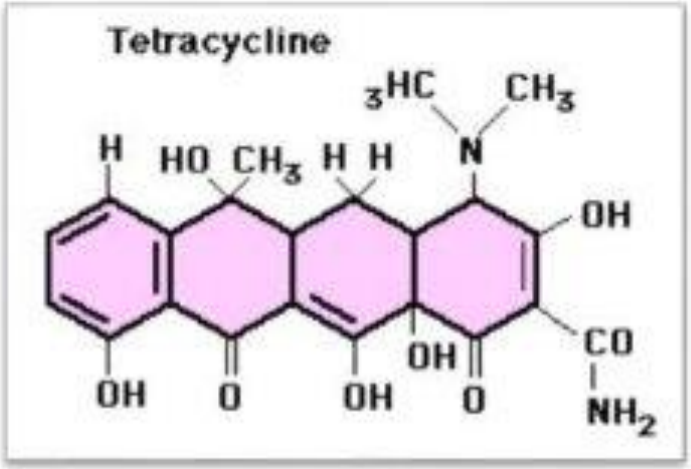
At the end of the lecture, students should know:

- Classification of tetracyclines
- Mechanism of action, clinical uses and adverse effect of tetracyclines
- Antibacterial spectrum and mechanism of resistance of tetracyclines

1) INTRODUCTION & HISTORY

- In the 1940's soil actinomycetes were systematically screened for the elaboration of antimicrobial substances.

TETRACYCLINES



- A class of antibiotics named for their nucleus of four ("tetra-") hydrocarbon rings.
- All are obtained from soil actinomycetes.
- Chlortetracycline (1948).
- Oxytetracycline (1950).
- Tetracycline (1953).

Core subject – Pharmacology

TETRACYCLINES

Are classified in two ways

1. According to source

- Natural
- Semi synthetic

2. According to duration of action

- Short acting(half life is 6-8hrs)
- Intermediate(halflife is 12hrs)
- Long acting(halflife is >16hrs)

PRODUCTS

According to source:

- **Naturally occurring**
  - -Tetracycline
  - -Chlortetracycline
  - -Oxytetracycline
  - -Demeclocycline
- **Semi-synthetic**
  - -Meclocycline
  - -Methacycline
  - -Minocycline
  - -Rolitetracycline

- **GROUP I : (Short Acting)**
  - **C**hlortetracycline
  - **O**xytetracycline
  - **T**etracycline
- **GROUP II : (Intermediate Acting)**
  - **De**meclocycline
  - **Me**thacycline
- **GROUP III : (Long Acting)**
  - **Do**xycycline
  - **Mi**nocycline

COT – DEME - DOMINO

2) CLASSIFICATION

❑ GROUP-I

- Shorter duration ($t_{1/2}$- 6-10 hr)
- Less Potent
- Mildly Absorbed
- QID/TDS
- Renal Excretion

❑ Short Acting

❑ GROUP-II

- Intermediate duration ($t_{1/2}$-12-16 hr)
- Moderately Potent
- Moderately Absorbed
- BD
- Partial Renal

❑ Intermediate Acting

❑ GROUP-III

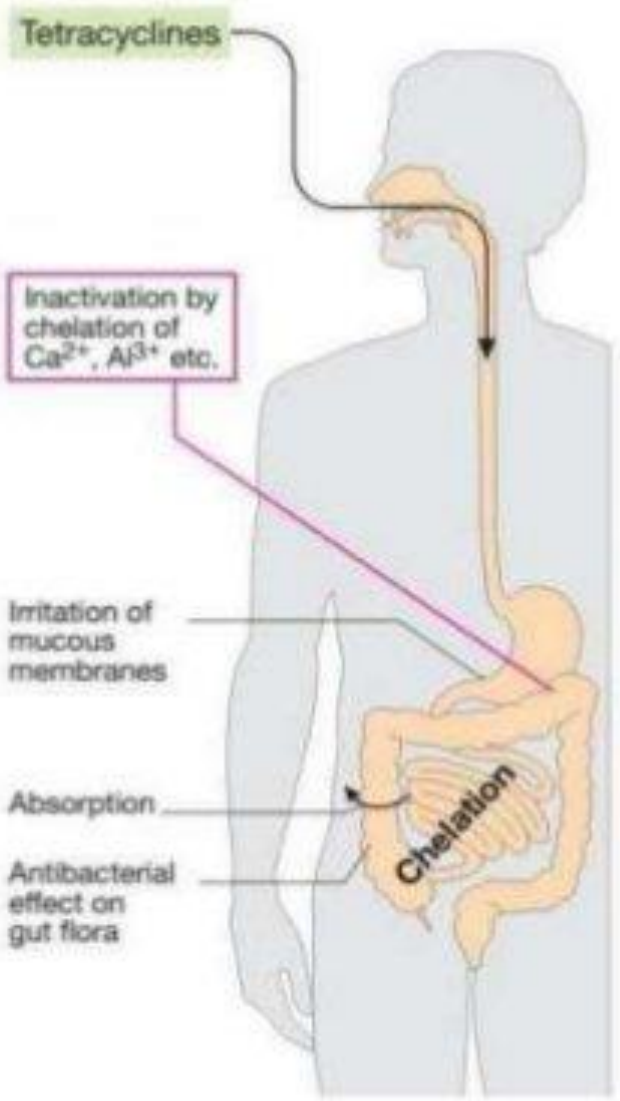
- Longer duration ($t_{1/2}$- 18-24 hr)
- Highly Potent
- Completely Absorbed
- OD
- Excretion Liver

❑ Long Acting

3) PHARMACOKINETICS

GROUP-I	GROUP-II	GROUP-III
Short Acting	Intermediate Acting	Long Acting
Intestinal Absorption		
Moderate	Moderate	Complete
Plasma Protein Binding		
Low	Moderate	High
Elimination		
Rapid renal	Partial Metabolism Slower Renal	Bile & Faeces
Alteration of Intestinal Flora		
High	Moderate	Least
Incidence of Diarrhoea		
High	Moderate	Low

- Chelating Property with dairy product & Al^{+++}, Mg^{++}, Ca^{++}, Fe^{++} & bivalent, trivalent ions.
- Food ⬇ absorption of all TC **except Doxy & Minocyclines**.



❑ DISTRIBUTION :

- Widely distributed to various body tissues & accumulate in **Liver, Spleen, Bone marrow & Teeth**
- Cross BBB,CSF, Placenta, breast milk.

❑ EXCRETION :

- **TC** are partially metabolised & remaining amount is excreted unchanged in **URINE**

  (Minocyclines is exception, considerably metabolized in **LIVER**)

  - ❖ Group I & II – Kidney (70-75%)
  - ❖ Group III – Bile & Faeces - Enterohepatic Circulation (Doxy)

4) Mechanism of Action

BACTERIOSTATIC

Drug enter in bacteria by -

(Gm +ve) - Active Transport

(Cytoplasmic Memb)

(Gm-ve) - Porin channels – Passive diffusion

(Cell Memb)

↓

Binds to 30s ribosome

↓

Inhibits attach of aminoacyl t RNA to "A"site

↓

Inhibition of protein synthesis

5) RESISTANCE

- Decreased AB Influx
- Increased Efflux by Active Transport (Pumping Out of Drug)
- Reduced access of drug to the ribosome (ribosome protection proteins)
- Inactivation of Drug by elaboration of enzymes
- Cross Resistance

Horizontal integration – Microbiology

6) ANTIMICROBIAL SPECTRUM

- **G +ve Cocci :**
  - *Streptococci*
  - *Staphylococci*
- **G –ve Cocci :**
  - *N. gonococci*
  - *N. meningococci*
- **G +ve Bacilli :**
  - *Clostridia*
  - *Corynebacteria*
  - *B. Anthracis*
  - *P. acnes*
- **G –ve Bacilli :**
  - *V. Cholerae*
  - *Brucella*
  - *H. ducryi*
  - *H. pylori*
  - *Y. pestis*
  - *Y. enterocolitica*

ANTIMICROBIAL SPECTRUM Cont.

- Rickettsiae
- Chlamydiae
- Mycoplasma
- Actinomyces
- Spirochetes
- Entamoeba
- Plasmodia

- **VERTICLE INTEGRATION MEDICINE/ SURGERY**

7) Therapeutic Uses

- (A) As First Choice Drug-

- ❑ Rickettsial Infections (Rocky mountain spotted fever, typhus & Q fever.
- ❑ Chlamydial Infections
- ❑ Mycoplasma infection (*M. pneumoniae* – atypical pneumonia)
- ❑ Cholera
- ❑ Plague
- ❑ Relapsing fever

- (B) As Alternative Drug-

- ❑ STD (Gonorrhoea, Syphilis) – Doxy
- ❑ *Streptococcal* Infection (apart from resistance TC can be used if organism is sensitive)

- (C) Resistant-

- ❑ *Staphylococcal & meningococcal*
- ❑ *Salmonella & Shigella infection*
- ❑ UTI

- **Selective Uses:**
- **Tetracycline**
  - Treatment of gastrointestinal ulcers caused by *Helicobacter pylori*
- **Doxycycline**
  - Lyme disease
  - Prevention of malaria
  - Treatment of amebiasis
  - Currently an alternative to macrolides in the initial of community-acquired pneumonia.
- **Minocycline**
  - Meningococcal carrier state
- **Demeclocycline**
  - Inhibits the renal actions of antidiuretic hormone(ADH)
  - Management of patients with ADH-secreting tumors

8) ADVERSE EFFECTS

- GI disturbances
- Effect on teeth & bones – chelating comp
- Superinfection: Disturbances in the normal flora
- Photosenstivity (Demeclo > Doxy > Others)
- Renal (Doxy is safe while Minocycline are moderately safer than other TCs)
- Hepatotoxicity – causes jaundice (Least by Oxy & Tetra)
- Vestibular
- Increased intracranial tension
- Hypersensitivity reactions

Core subject – Pharmacology

Glycylcyclins (TIGECYCLINE)

- It is the first member of a new class of synthetic tetracycline analogues (glycyl-cyclines) which are active against most bacteria that have developed resistance to the classical tetracyclines.
- A derivative of minocycline, and was introduced in 2005
- Poorly absorbed from g.i.t; the only route of administration is by slow i.v. infusion.
- Eliminated mainly in the bile; dose adjustment is not needed in renal insufficiency

- The duration of action is long; elimination t½ is 37–67 hrs
- Not suitable for urinary tract infection, because only low concentrations are attained in urine.
- Dose: 100 mg loading dose, followed by 50 mg 12 hourly by i.v. infusion over 30–60 min, for 5–14 days
- Not recommended for children and during pregnancy.
- The most common side effect is nausea and occasionally vomiting. Others are epigastric distress, diarrhoea, skin reactions, photosensitiviy

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- **Steps to Access HEC Digital Library**

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2. On Home Page, click on the INSTITUTES.
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4. Select your desired Institute.
5. A page will appear showing the resources of the institution
6. Journals and Researches will appear
7. You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.

RESEARCH ARTICLES

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4817740
- https://www.mdpi.com/1999-4923/13/12/2085

MCQs

Q.1 Children younger than eight years should not receive tetracyclines because these agents

- Cause rupture of tendons
- Donot cross into CSF
- Are not bactericidal
- Deposit in tissues undergoing calcification
- Can cause aplastic anemia

- A patient presents with headache, fatigue decreased urine output. He also has hyponatremia and increased urine osmolality. Which of the following tetracyclines is sometimes used in treatment of SIADH (syndrome of inappropriate ADH secretion
- Demeclocycline
- Doxycycline
- Minocycline
- Oxytetracycline
- tetracycline

THANK YOU