PHARM.D • YEAR 3

Medicinal Chemistry

CHAPTER 5

Antibiotics

PPT CHAPTER COVER



Antibiotics: the big picture

1. What are antibiotics?

Antibiotics are antibacterial agents originally obtained from microorganisms or developed as semisynthetic derivatives; everyday usage often also includes fully synthetic antibacterials.



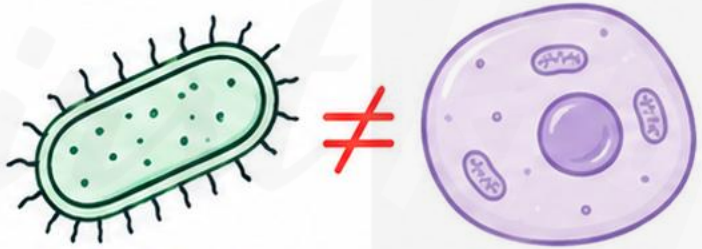
Microorganisms



Semisynthetic and synthetic derivatives

2. How do they work and what do they target?

Selective toxicity exploits differences between bacterial and human cells.



Bacterial cell (target) ≠ Human cell (not targeted)

Bactericidal

Kill susceptible bacteria.

Bacteriostatic

Inhibit growth under defined conditions.

3. Clinical considerations



Spectrum, tissue penetration and resistance influence clinical usefulness.



Antibiotics do not treat ordinary viral infections.



Stewardship means using a justified agent, route and duration, guided by diagnosis and susceptibility rather than relying on a long brand list.

Antibacterial targets and resistance

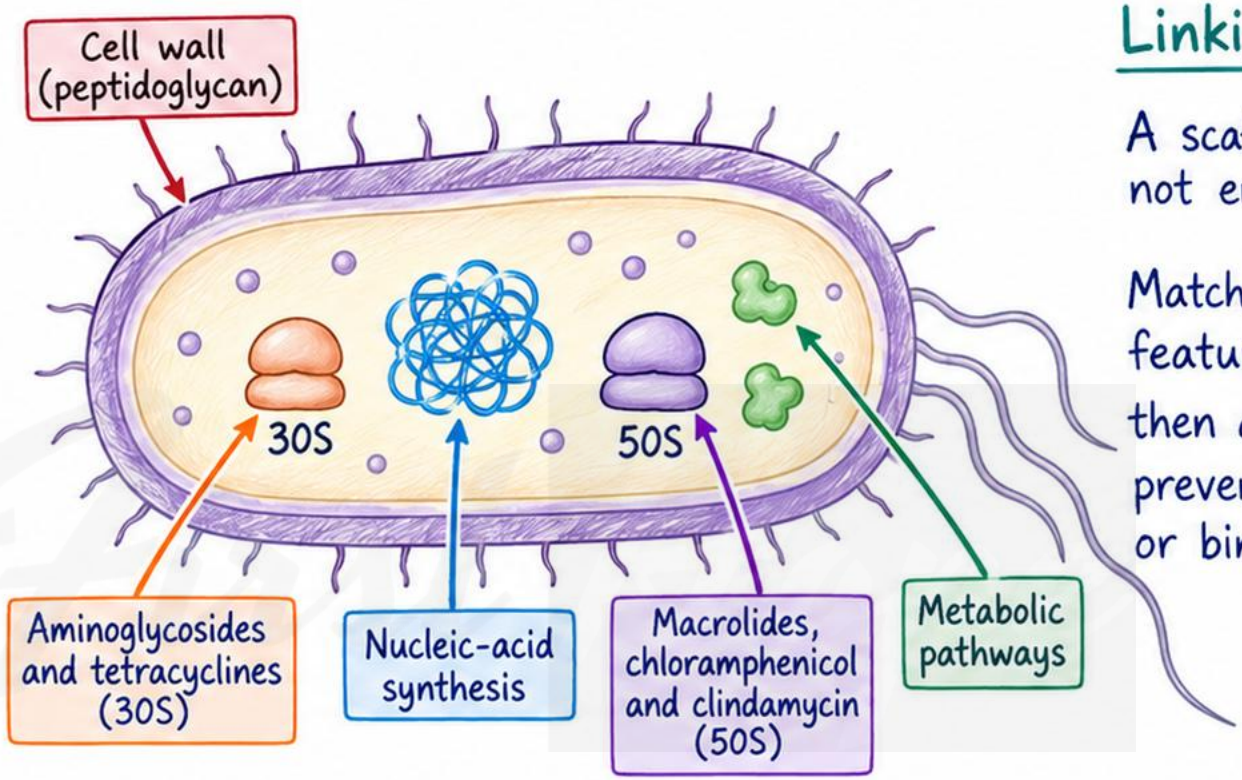
Key antibacterial targets

Cell-wall agents inhibit peptidoglycan synthesis.

Aminoglycosides and tetracyclines act at the 30S ribosomal subunit.

Macrolides, chloramphenicol and clindamycin act at 50S.

Other antibacterial classes target nucleic-acid synthesis or metabolic pathways.



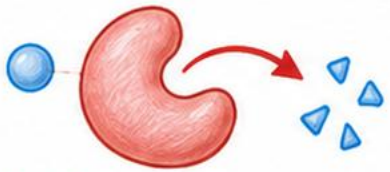
Linking chemistry to activity

A scaffold's presence alone does not ensure susceptibility.

Match a medicinal-chemistry feature to the bacterial target, then ask how the organism can prevent effective exposure or binding.

Resistance mechanisms

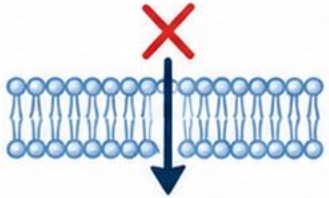
Resistance can arise through drug destruction, target alteration, reduced entry, efflux or metabolic bypass. These mechanisms may coexist.



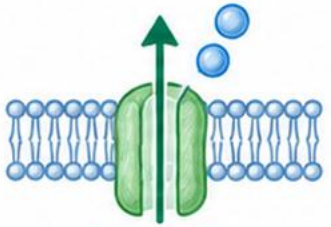
1. Drug destruction



2. Target alteration



3. Reduced entry



4. Efflux



5. Metabolic bypass

Beta-lactams: ring families

Penicillins

Combine the four-membered beta-lactam ring with a five-membered thiazolidine ring.

Carbapenems

Replace the penicillin sulfur-containing ring arrangement with an unsaturated carbon-containing ring.

Four-membered cyclic amide

Cephalosporins

Have a six-membered dihydrothiazine partner ring.

Monobactams

Such as aztreonam have a monocyclic beta-lactam system.

These structural differences influence target binding, spectrum, chemical stability and beta-lactamase susceptibility.

Beta-lactams: mechanism and SAR

Mechanism of action

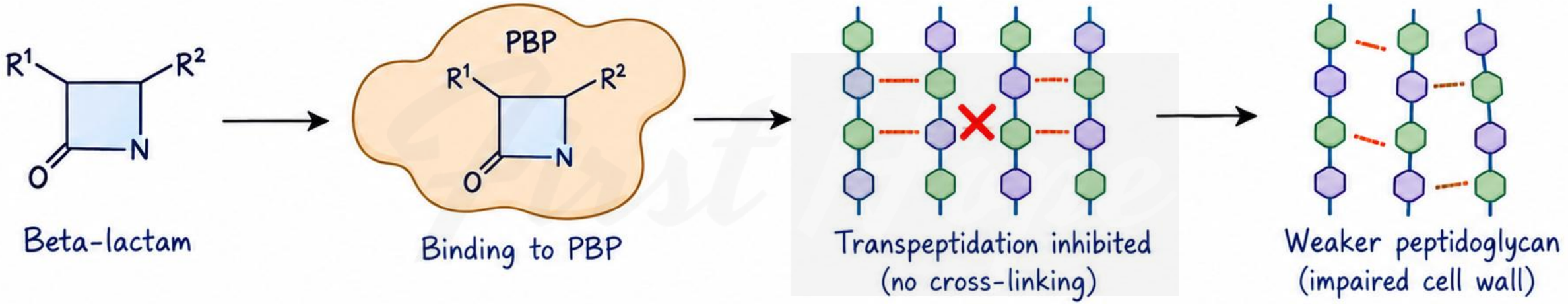
Beta-lactams bind penicillin-binding proteins and inhibit transpeptidation during peptidoglycan cross-linking.

Reactive pharmacophore

The strained beta-lactam ring supplies the reactive pharmacophore.

Enzymatic inactivation

Ring opening by beta-lactamases usually destroys antibacterial activity.



Side chains (SAR)

Side chains alter acid stability, target affinity, penetration and resistance to selected enzymes.

Carboxylate and stereochemistry

The carboxylate region and correct stereochemistry help position the molecule at its target.

Pharmacodynamic requirement

Activity usually depends on adequate time above the organism's inhibitory concentration.

Beta-lactamase diversity

Different beta-lactamases have different substrate and inhibitor profiles; one inhibitor cannot neutralize them all.

First Hope

FREE PREVIEW

Click here to visit our website

PHARMACY PREMIUM NOTES

Complete subject and semesters are available on FirstHope app only.

Scan or click here

Click here to get the app >

Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram >

Scan or click here

@FirstHopeNotes

Instagram

@firsthope.official

Click here to follow >

YouTube channel

FirstHope-Pharmacy / Live streams

Click here to watch >

WhatsApp channel

Follow FirstHope on WhatsApp

Click here to join >

FirstHope website

firsthope.co.in

Click here to visit >

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.