**Effects of enzyme on cell wall**

The bacterial cell wall, a structural unit of peptidoglycan polymer comprised of glycan strands consisting of a repeating disaccharide motif [N‐acetylglucosamine (NAG) and N‐acetylmuramylpentapeptide (NAM pentapeptide)], linked by β‐(1,4) bonds. It encases bacteria and provides structural integrity and protection. Lysozymes are enzymes that break down the bacterial cell wall and disrupt the bacterial life cycle by cleaving the linkage between the NAG and NAM carbohydrates, catalyzing the hydrolysis of β‐(1,4) linkages between the NAM and NAG saccharides.



**Effects of antibiotics on cell wall**

* Peptidoglycan construction begins in the cytoplasm with the synthesis of a muramyl pentapeptide precursor containing a terminal D-Ala-D-Ala. Some antibiotics interfere with the synthesis of the basic peptidoglycan building block. For example, **D-cycloserine** inhibits two enzymes involved in the precursor synthesis, preventing both conversion of L-alanine to D-alanine by racemase, and the construction of D-alanyl-D-alanine by D-Ala-D-Ala ligase. In the cytoplasm, muramyl pentapeptide is anchored via a water-soluble UDP-glucosamine moiety.
* In the second phase of peptidoglycan construction, muramyl pentapeptide N-acetylglucosamine is transferred to a C55undecaprenyl phosphate with the release of UMP to form a Lipid I intermediate. **Tunicamycin** inhibits the enzymatic conversion of the undecaprenyl phosphate to the lipid I intermediate, stopping the completion of the peptidoglycan structure.
* An additional glycosylation step completes the peptidoglycan unit, following which it is transported via its C55 lipid tail to the external periplasmic surface of the membrane where its peptidoglycan unit becomes integrated into the cell wall matrix. **Bacitracin** inhibits lipid phosphatase, preventing the release of the finished peptidoglycan from its C55lipid carrier.
* Several transpeptidases and transglycosylases connect the newly formed peptidoglycan structures to the cell wall peptidoglycan matrix. The specificity of β-lactam antibacterials is due to their ability to inhibit transpeptidase enzymes and prevent the assembly of the peptidoglycan layer in both Gram-positive and Gram-negative bacteria. β-Lactam molecules, with their structural similarity to the D-alanyl-D-alanine group within the peptidoglycan structure, compete for the binding sites of transpeptidases. When it was first commercialized, **penicillin**, a β-lactam antibiotic, was considered a “magic bullet” because of its specificity for bacterial infections without harming the patient.
* **Vancomycin**, a glycopeptide antibiotic with a significantly larger structure, also prevents cell wall construction by interfering with transglycosylases. Its effectiveness is limited to Gram-positive bacteria because it is unable to penetrate the outer cytoplasmic membrane of Gram-negative bacteria due to its large size as compared to penicillin.