Polymyxins

Polymyxins are antibiotics that are composed of cationic and basic proteins, which act like detergents. These drugs interact with bacterial membranes via electrostatic interactions, as these cationic polypeptides bind to the anionic lipopolysaccharide (LPS) molecules in the outer membrane of bacteria. Polymyxins then alter the bacterial membrane structure, making it more permeable. This disrupts the osmotic properties of the organism, causing increased water uptake and eventually, cell death. These antibiotics are selectively toxic to gram-negative bacteria because they are composed of cationic polypeptides, which specifically bind to the anionic lipopolysaccharides found on the membranes of gram-negative bacteria. Typical uses for infections include multidrug-resistant Pseudomonas, highly-resistant Enterobacteriaceae, or other drug-resistant, gram-negative bacteria. Keep in mind, polymyxins are relatively neurotoxic and nephrotoxic, and they are used as a last resort option, typically in cases where other classes of antibiotics are ineffective or contraindicated.



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Mechanism of Action

Cationic

Cat-ion positive charge bubble

Polymyxins are antibiotics that are composed of cationic and basic proteins, which act like detergents. These drugs interact with the bacterial membrane via electrostatic interactions, as these cationic polypeptides bind to the anionic lipopolysaccharide (LPS) molecules in the outer membrane of the gram-negative bacteria. Polymyxins then alter the bacterial membrane structure, making it more permeable. This disrupts the osmotic properties of the organism, causing increased water uptake and eventually, cell death.

Act Like Detergents

Cleaning detergent making soap bubbles

Polymyxins are a class of antibiotic that act like detergents, working to disrupt bacterial cell membranes. Because these drugs are composed of a cyclic peptide with a hydrophobic tail, they are able to bind to the cell membranes of bacteria directly by interacting with their phospholipid structure, and make it more permeable. This disrupts the osmotic properties of the organism, causing increased water uptake and eventually, cell death.

Bind to Cell Membranes of Bacteria

Cell Membrane

These drugs interact with the bacterial membrane via electrostatic interactions, as these cationic polypeptides bind to the anionic lipopolysaccharide (LPS) molecules in the outer membrane of the gram-negative bacteria. Once these drugs are able to interact with bacterial membranes, their antibiotic properties come to fruition, as the cells' osmotic properties are disrupted, leading to their eventual death.

Disrupt Their Osmotic Properties

Holes in Membrane causing Water to leak

Polymyxins work to alter the bacterial membrane structure, making it more permeable to water. This disrupts the osmotic properties of the organism, causing increased water uptake and eventually, cell death.

Indications

Resistant Gram-Negative Infections

Resisting Graham-cracker Negative-devil wearing Resistance-bandana

These antibiotics are selectively toxic to gram-negative bacteria because of their cationic and basic properties. Polymyxins are composed of cationic polypeptides which bind to the anionic lipopolysaccharide (LPS) molecules in the outer membrane of gram-negative bacteria. Typical uses for infections include multidrug-resistant Pseudomonas, highly-resistant Enterobacteriaceae, or other drug-resistant gram-negative bacteria. Keep in mind, polymyxins are relatively neurotoxic and nephrotoxic, and are typically only used as a last resort if other classes of antibiotics are ineffective or contraindicated.

Side Effects

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Neurotoxicity

Neuron with Toxic-green-glow

Polymyxins can cause neurotoxicity as a result of the interaction of polymyxins (which bind lipopolysaccharides) with neurons, which have high lipid content. Common symptoms include dizziness, muscle weakness, facial and peripheral paresthesias, partial deafness, visual disturbances, confusion, ataxia, and neuromuscular blockade. Due to neurotoxicity of polymyxins, they are used as a last resort option, typically in cases where other classes of antibiotics are ineffective or contraindicated.

Renal tubular necrosis

Kidney playing Tuba with Necrosis-crow

Nephrotoxicity is a well recognized adverse effect associated with polymyxin use. It has been suggested that the toxicity of polymyxins may be due to increased membrane permeability of renal tubular cells, which cause an increased influx of cations, anions, and water, resulting in cell swelling and lysis. Due to nephrotoxicity of polymyxins, they are used as a last resort option, typically in cases where other classes of antibiotics are ineffective or contraindicated.

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