SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES
Sathy Main Road, SNS Kalvi Nagar,
Saravanampatti Post, Coimbatore - 641 035,
Tamil Nadu.

AMINOGLYCOSIDES

Aminoglycoside antibiotics had been the mainstays for treatment of serious infections due to aerobic gram-negative bacilli. However, because their use is associated with serious toxicities, they have been replaced to some extent by safer antibiotics, such as the third- and fourth-generation cephalosporins, the fluoroquinolones, and the carbapenems. Aminoglycosides that are derived from Streptomyces have -mycin suffixes, whereas those derived from Micromonospora end in -micin. The terms oeaminoglycosid stem from their

Structure two amino sugars joined by a glycosidic linkage to a central hexose (aminocyclitol) nucleus. Their polycationic nature precludes their easy passage across tissue membranes. All members of this family are believed to inhibit bacterial protein synthesis by the mechanism determined for *streptomycin* as described below.

A. Mechanism of action

Susceptible gram-negative organisms allow aminoglycosides to diffuse through porin channels in their outer membranes. These organisms also have an oxygen-dependent system that transports the drug across the cytoplasmic membrane. The antibiotic then binds to the 30S ribosomal subunit prior to ribosome formation. There, it interferes with assembly of the functional ribosomal apparatus and/or can cause the 30S subunit of the completed ribosome to misread the genetic code. Polysomes become depleted, because the aminoglycosides interrupt the process of polysome disaggregation and assembly.

B. Antibacterial spectrum

The aminoglycosides are effective in the empirical treatment of infections suspected of being due to aerobic gram-negative bacilli, including Pseudomonas aeruginosa. To achieve an additive or synergistic effect, aminoglycosides are often combined with a Î²-lactam antibiotic, or*vancomycin*, or a drug active against anaerobic bacteria. All aminoglycosides are bactericidal. The exact mechanism of their lethality is unknown because other antibiotics that affect protein synthesis are generally bacteriostatic. [Note: The aminoglycosides are effective only against aerobic organisms because strict anaerobes lack the oxygen-requiring drug transport system.]

C. Resistance

Resistance can be caused by 1) decreased uptake of drug when the oxygen-dependent transport system for aminoglycosides or porin channels are absent and 2) plasmid-associated synthesis of enzymes (for example, acetyl transferases, nucleotidyltransferases, and phosphotransferases) that modify and inactivate aminoglycoside antibiotics.

D. Pharmacokinetics

Administration: The highly polar, polycationic structure of the aminoglycosides prevents adequate absorption after oral administration. Therefore, all aminoglycosides (except *neomycin* must be given parenterally to achieve adequate serum levels

E. Adverse effects

Ototoxicity: Ototoxicity (vestibular and cochlear) is directly related to high peak plasma levels and the duration of treatment. The antibiotic accumulates in the endolymph and perilymph of the inner ear, and toxicity correlates with the number of destroyed hair cells in the organ of Corti.

Nephrotoxicity: Retention of the aminoglycosides by the proximal tubular cells disrupts calcium-mediated transport processes, and this results in kidney damage ranging from mild, reversible renal impairment to severe, acute tubular necrosis, which can be irreversible.

Neuromuscular paralysis: This side effect most often occurs after direct intraperitoneal or intrapleural application of large doses of aminoglycosides. The mechanism responsible is a decrease in both the release of acetylcholine from prejunctional nerve endings and the sensitivity of the postsynaptic site. Patients with myasthenia gravis are particularly at risk. Prompt administration of *calcium gluconate* or *neostigmine* can reverse the block.

Allergic reactions: Contact dermatitis is a common reaction to topically applied *neomycin*.