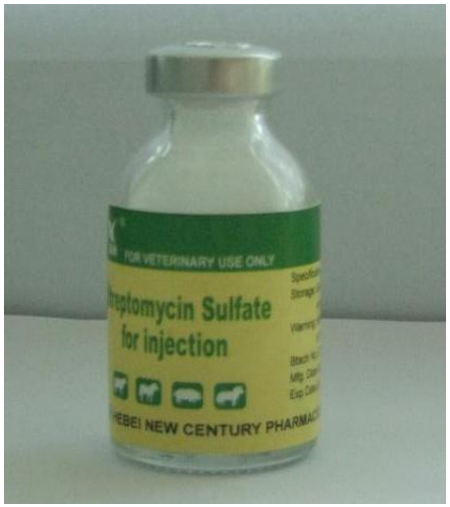
Aminoglycosides



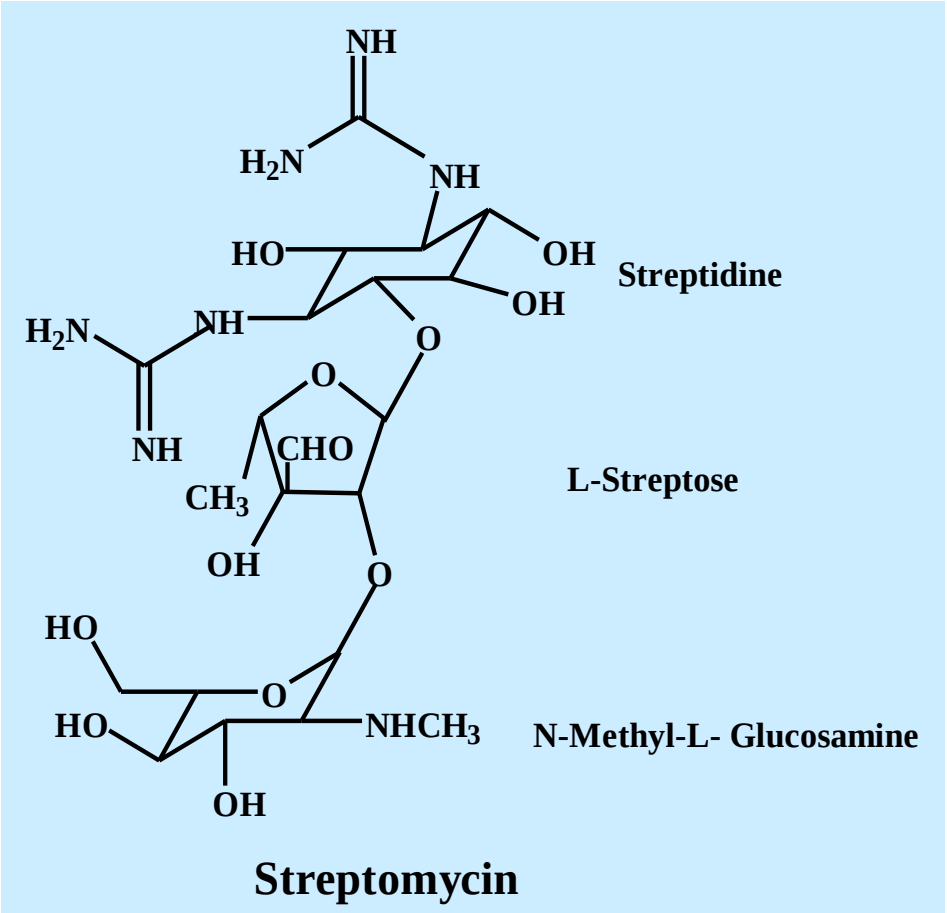
1. Aminoglycosides are group of natural and semi -synthetic antibiotics. They have polybasic amino groups linked glycosidically to two or more aminosugar like: sterptidine, 2-deoxy streptamine, glucosamine

2. Aminoglycosides which are derived from: Streptomyces genus are named with the suffix –**mycin.** While those which are derived from Micromonospora are named with the suffix –**micin.**

Classification of Aminoglycosides

1. **Systemic aminogycosides**
   - Streptomycin (*Streptomyces griseus)*
   - Gentamicin *(Micromonospora purpurea)*
   - Kanamycin *(S. kanamyceticus)*
   - Tobramycin *(S. tenebrarius)*
   - Amikacin (Semisynthetic derivative of Kanamycin)
   - Sisomicin *(Micromonospora inyoensis)*
   - Netilmicin (Semisynthetic derivative of Sisomicin)
2. **Topical aminoglycosides**
   - Neomycin *(S. fradiae)*
   - Framycetin *(S. lavendulae)*

Pharmacology of Streptomycin



Streptomycin

Biological Source

It is a oldest aminoglycoside antibiotic obtained from *Streptomyces griseus*.

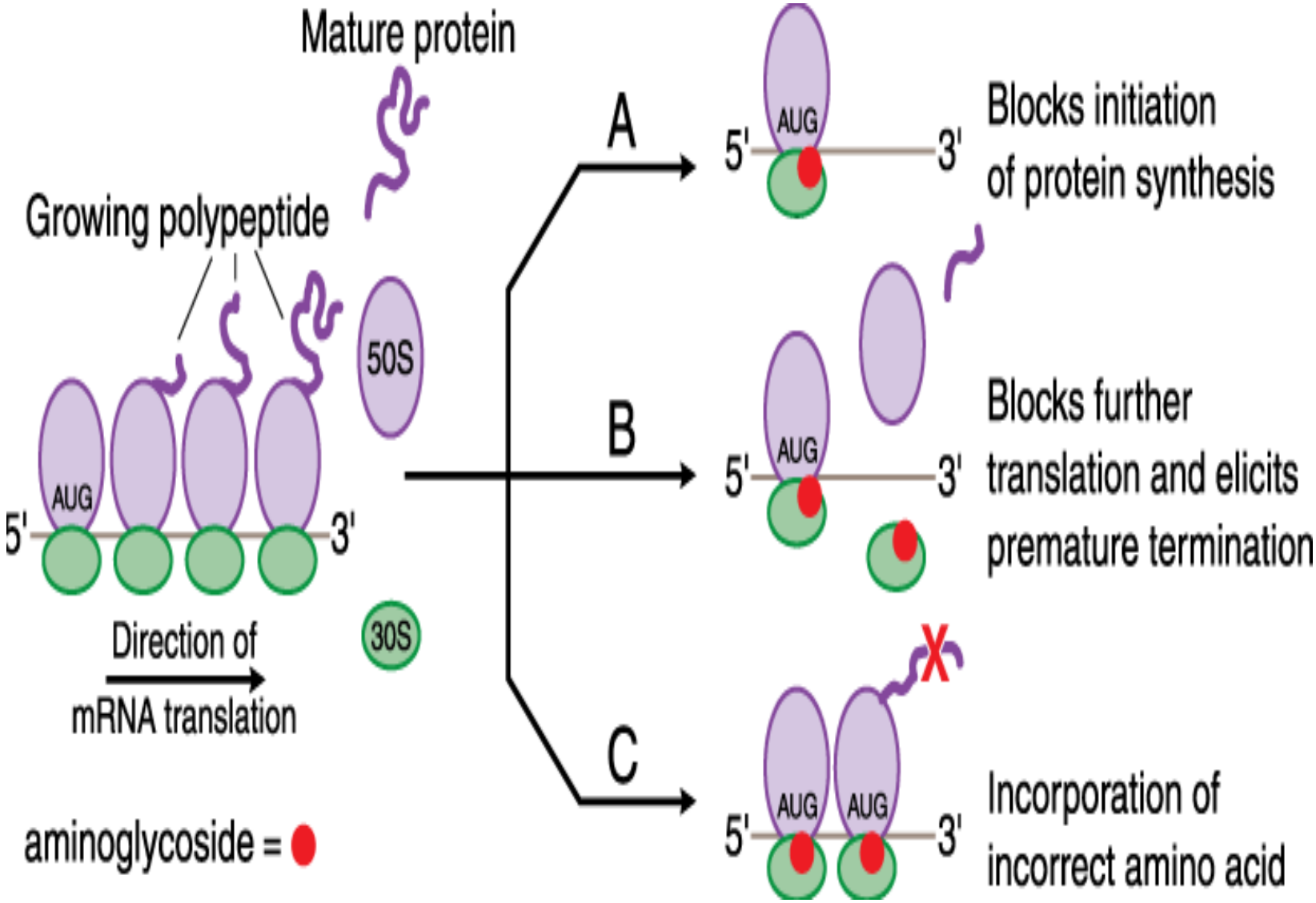
Antibacterial spectrum

1. It is mostly active against gram negative bacteria like *H. ducreyi*, *Brucella*, *Yersinia pestis*, *Francisella tularensis*, *Nocardia*,etc.
2. It is also used against *M.tuberculosis*
3. Few strains of *E.coli*, *V. cholerae*, *H. influenzae* , *Enterococci* etc. are sensitive at higher concentration.

Mechanism of action

Aminoglycosides bind to the 16S rRNA of the 30S subunit and inhibit protein synthesis.

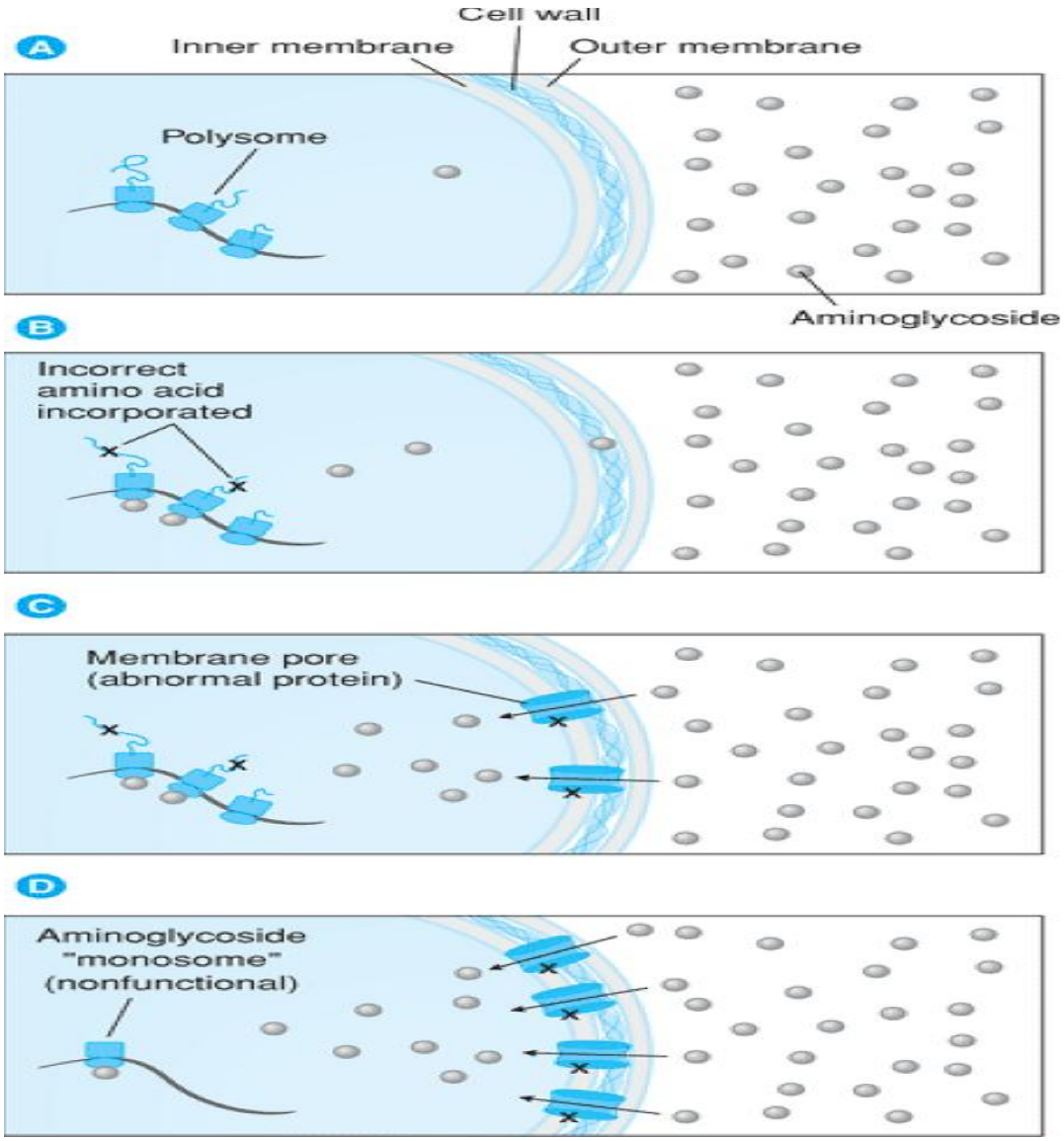
1. **Transport of aminoglycoside through cell wall and cytoplasmic membrane.**
   a) Diffuse across cell wall of gram negative bacteria by porin channels.
   b) Transport across cell membrane by carrier mediated process liked with electron transport chain
2. **Binding to ribosome resulting in inhibition of protein synthesis**


Mature protein
Growing polypeptide
AUG
5'
3'
50S
30S
Direction of
mRNA translation
aminoglycoside =
A
B
C
AUG
5'
3'
Blocks initiation
of protein synthesis
AUG
5'
3'
Blocks further
translation and elicits
premature termination
X
AUG
AUG
5'
3'
Incorporation of
incorrect amino acid

A. Aminoglycoside (represented by red circles) binds to the 30S ribosomal subunit and interferes with initiation of protein synthesis by fixing the 30S–50S ribosomal complex at the start codon (AUG) of mRNA. As 30S–50S complexes downstream complete translation of mRNA and detach, the abnormal initiation complexes, so-called streptomycin monosomes, accumulate, blocking further translation of the message. Aminoglycoside binding to the 30S subunit also causes misreading of mRNA, leading to

B. premature termination of translation with detachment of the ribosomal complex and incompletely synthesized protein or

C. incorporation of incorrect amino acids (indicated by the red X), resulting in the production of abnormal or nonfunctional proteins.



The Davis model for bactericidal activity of aminoglycosides.

Mechanism of resistance

1. Acquisition of cell membrane bound inactivating enzymes which phosphorylate/adenylate/acetylate the antibiotic
2. Decrease in affinity of antibiotic for ribosome due to mutation.
3. Decrease efficiency of aminoglycoside transporting mechanism.

Cross resistance: Only partial and unidirectional between streptomycin and other aminoglycosides

Pharmacokinetics

Absorption: Streptomycin is highly ionized. It is neither absorbed nor destroyed in GIT. However, absorption from injection site is rapid.

Distribution: Distributed on extracellularly. Vd is 0.3L/kg.

Low concentration in synovial, pleural, peritoneal, serous fluids.

Plasma $t_{1/2}$ is 2-4 hr.

Metabolism: It is not metabolized.

Excretion: It is excreted unchanged in urine by glomerular filtration.

Adverse effects

A) Toxicity

Ototoxicity

a) Cochlear damage

b) Vistibular damge

Nephrotoxicity

Neuromuscular Blockade

B) Skin reaction

Uses

Aerobic gram negative bacteria, *H influenzae*, *M catarrhalis*, *and Shigella* species; often used in combinations with beta-lactams Gonorrhea (spectinomycin, IM); tuberculosis (streptomycin, IM).

Brands

AMBISTRYN-S 0.75-1g powder per vial for inj.