

## Inhibition of Protein Synthesis by Antibiotics

BioFiles 2006, 1.4, 17.

Protein synthesis is a complex, multi-step process involving many enzymes as well as conformational alignment. However, the majority of antibiotics that block bacterial protein synthesis interfere with the processes at the 30S subunit or 50S subunit of the 70S bacterial ribosome. The aminoacyl-tRNA synthetases that activate each amino acid required for peptide synthesis are not antibiotic targets. Instead, the primary steps in the process that are attacked are (1) the formation of the 30S initiation complex (made up of mRNA, the 30S ribosomal subunit, and formyl-methionyl-transfer RNA), (2) the formation of the 70S ribosome by the 30S initiation complex and the 50S ribosome, and (3) the elongation process of assembling amino acids into a polypeptide.

Tetracyclines, including **doxycycline**, prevent the binding of aminoacyl-tRNA by blocking the A (aminoacyl) site of the 30S ribosome. They are capable of inhibiting protein synthesis in both 70S and 80S (eukaryotic) ribosomes, but they preferentially bind to bacterial ribosomes due to structural differences in RNA subunits. Additionally, tetracyclines are effective against bacteria by exploiting the bacterial transport system and increasing the concentration of the antibiotic within the cell to be significantly higher than the environmental concentration.

Aminoglycoside antibiotics have an affinity for the 30S ribosome subunit. **Streptomycin**, one of the most commonly used aminoglycosides, interferes with the creation of the 30S initiation complex. **Kanamycin** and **tobramycin** also bind to the 30S ribosome and block the formation of the larger 70S initiation complex.

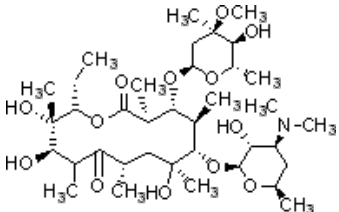
**Erythromycin**, a macrolide, binds to the 23S rRNA component of the 50S ribosome and interferes with the assembly of 50S subunits. Erythromycin, roxithromycin, and clarithromycin all prevent elongation at the transpeptidation step of synthesis by blocking the 50S polypeptide export tunnel. Elongation is prematurely terminated after a small peptide has been formed but cannot move past the macrolide roadblock.

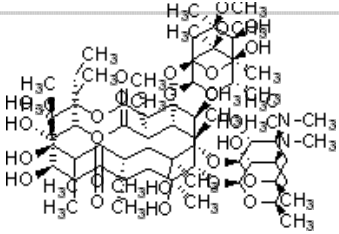
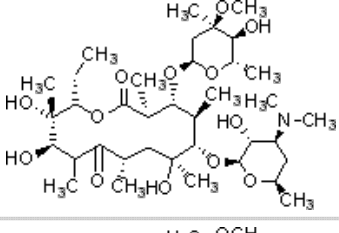
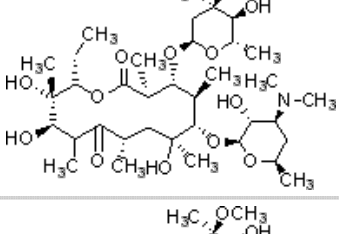
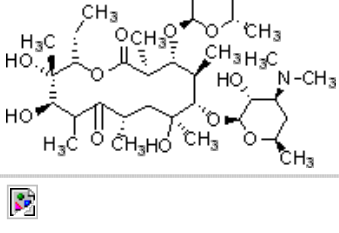







Peptidyl transferase is a key enzyme involved in translocation, the final step in the peptide elongation cycle.

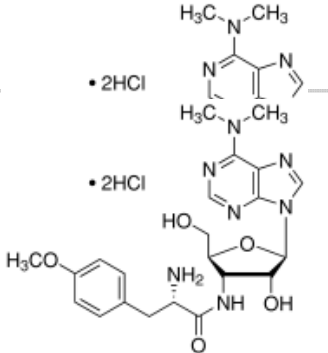
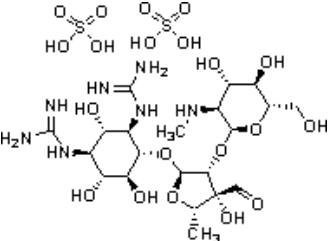
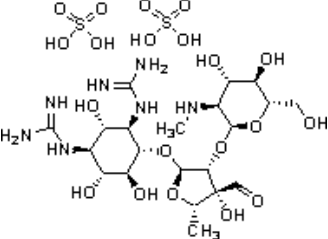
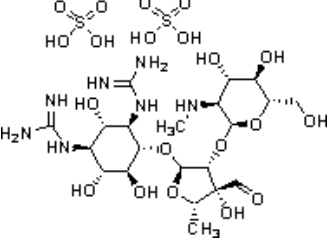
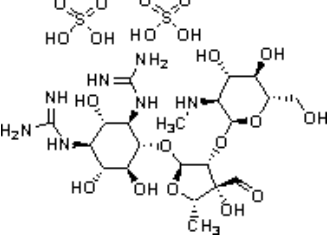
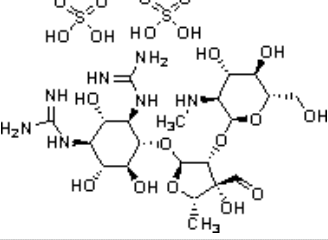
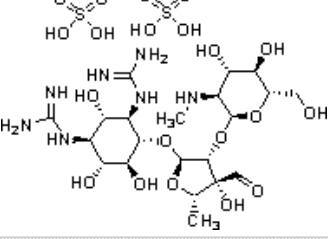
**Lincomycin** and clindamycin are specific inhibitors of peptidyl transferase, while macrolides do not directly inhibit the enzyme. **Puromycin** does not inhibit the enzymatic process, but instead competes by acting as an analog of the 3'-terminal end of aminoacyl-tRNA, disrupting synthesis and causing premature chain termination.

**Hygromycin B** is an aminoglycoside that specifically binds to a single site within the 30S subunit in a region that contains the A, P, and E sites of tRNA. It has been theorized that this binding distorts the ribosomal A site and may be the cause of the ability of hygromycin to induce misreading of aminoacyl-tRNAs as well as prevent the translocation of peptide elongation.

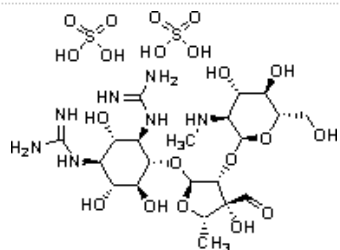
### Materials

Product #	Image	Description	Molecular Formula	Add to Cart
E6376		Erythromycin potency: ≥850 µg per mg	C <sub>37</sub> H <sub>67</sub> NO <sub>13</sub>	pricing
E5389		Erythromycin BioReagent, suitable for cell culture	C <sub>37</sub> H <sub>67</sub> NO <sub>13</sub>	pricing

45674		Erythromycin Ph Eur	$C_{37}H_{67}NO_{13}$	pricing
E0774		Erythromycin meets USP testing specifications	$C_{37}H_{67}NO_{13}$	pricing
E4514		Erythromycin plant cell culture tested, ~98%	$C_{37}H_{67}NO_{13}$	pricing
E7904		Erythromycin Biotechnology Performance Certified	$C_{37}H_{67}NO_{13}$	pricing
H3274		Hygromycin B from <i>Streptomyces hygroscopicus</i> powder, BioReagent, suitable for cell culture, suitable for insect cell culture	$C_{20}H_{37}N_3O_{13}$	pricing
H7772		Hygromycin B from <i>Streptomyces hygroscopicus</i> lyophilized powder	$C_{20}H_{37}N_3O_{13}$	pricing
H9773		Hygromycin B from <i>Streptomyces hygroscopicus</i> plant cell culture tested, BioReagent, $\geq 60\%$ (HPAE), lyophilized powder	$C_{20}H_{37}N_3O_{13}$	pricing
K1876		Kanamycin disulfate salt from <i>Streptomyces kanamyceticus</i>		pricing
L6004		Lincomycin hydrochloride $\geq 90\%$ (TLC)	$C_{18}H_{34}N_2O_6S \cdot HCl$	pricing
L2774		Lincomycin hydrochloride BioReagent, suitable for cell culture	$C_{18}H_{34}N_2O_6S \cdot HCl$	pricing
62143		Lincomycin hydrochloride $\geq 95.0\%$ (TLC)	$C_{18}H_{34}N_2O_6S \cdot HCl$	pricing
P7255		Puromycin dihydrochloride from <i>Streptomyces alboniger</i> $\geq 98\%$ (HPLC), powder	$C_{22}H_{29}N_7O_5 \cdot 2HCl$	pricing

P8833		Puromycin dihydrochloride from <i>Streptomyces alboniger</i> powder, BioReagent, suitable for cell culture	$C_{22}H_{29}N_7O_5 \cdot 2HCl$	pricing
S6501		Streptomycin sulfate salt powder	$C_{21}H_{39}N_7O_{12} \cdot 1.5H_2O_4S$	pricing
S9137		Streptomycin sulfate salt powder, BioReagent, suitable for cell culture	$C_{21}H_{39}N_7O_{12} \cdot 1.5H_2O_4S$	pricing
S1277		Streptomycin sulfate salt powder, BioXtra, suitable for mouse embryo cell culture	$C_{21}H_{39}N_7O_{12} \cdot 1.5H_2O_4S$	pricing
S2522		Streptomycin sulfate salt powder	$C_{21}H_{39}N_7O_{12} \cdot 1.5H_2O_4S$	pricing
S0774		Streptomycin sulfate salt plant cell culture tested	$C_{21}H_{39}N_7O_{12} \cdot 1.5H_2O_4S$	pricing
85884		Streptomycin sulfate salt Ph Eur	$C_{21}H_{39}N_7O_{12} \cdot 1.5H_2O_4S$	pricing

S1567



Streptomycin sulfate salt  
Biotechnology Performance  
Certified, cell culture tested

$C_{21}H_{39}N_7O_{12} \cdot$   
 $1.5H_2O_4S$

pricing

T1783



Tobramycin sulfate salt

$C_{18}H_{37}N_5O_9 \cdot$   
 $xH_2SO_4$

pricing