

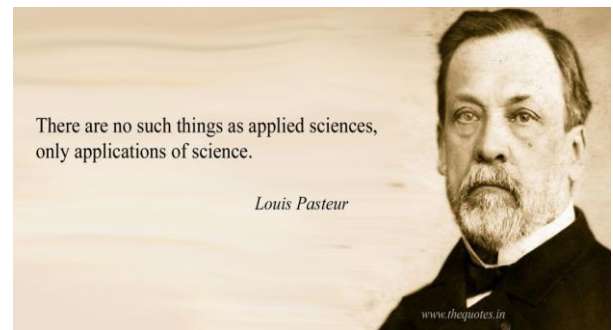
## Antibióticos

1. Histórico
2. Mecanismos de ação
3. Mecanismos de Resistência

## Antibiotics

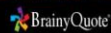
What are antibiotics?  
Who are the main producers?  
Biological functions?  
Resistance  
New developments

**Louis Pasteur (1822-1895):**  
“pasteurization”  
Fermentation: wine  
contamination  
Germ theory: silkworm disease  
Vaccine: anthrax, fowl cholera  
Rabies



Fortune favors the  
prepared mind.

Louis Pasteur



## First antimicrobial drugs

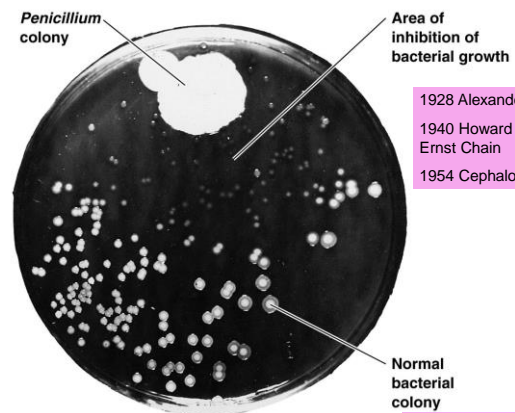
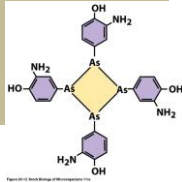
**Paul Ehrlich (1854-1915):**

- Methylene blue: malaria
- Toxin and antitoxin
- Salvarsan: magic bullet against syphilis, *Treponema pallidum*

## First antimicrobial drugs

• **Gerhard Domagk (Nobel Prize 1939)**

Sulfa drugs  
Prontosil  
Sulfanilamide, analog of p-aminobenzoic acid (part of folic acid, precursor of nucleic acids)  
Development of antituberculosis compounds  
thiosemicarbasone and isoniazid



1928 Alexander Fleming  
1940 Howard Florey  
Ernst Chain  
1954 Cephalosporin C

*Staphylococcus aureus*

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Figure 20.1

Salman Waksman, Albert Schatz

1943. Actinomycin

Streptomycin

## Diminishing returns in finding natural products: Genetics to the rescue?

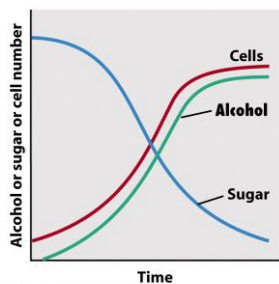
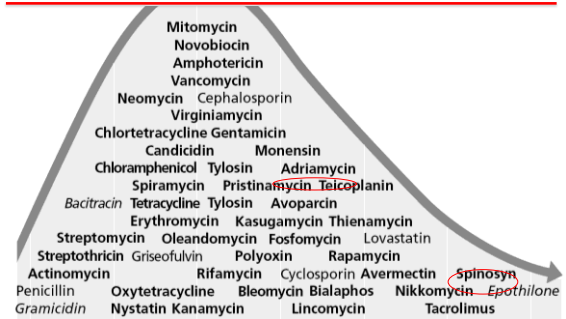


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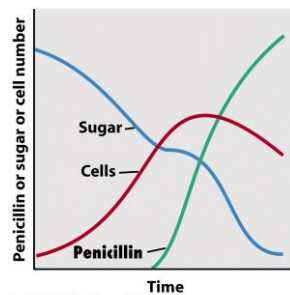


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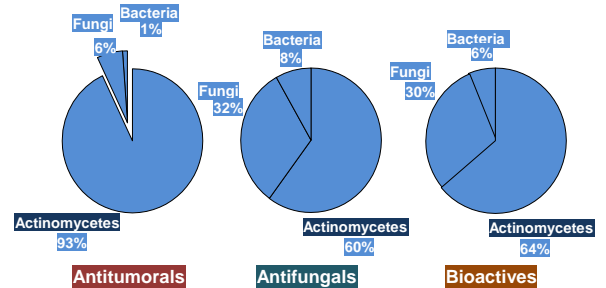
## What are antibiotics?

- Secondary metabolites synthesized by some microorganisms
- Any compound able to cause a damaged in a target cell

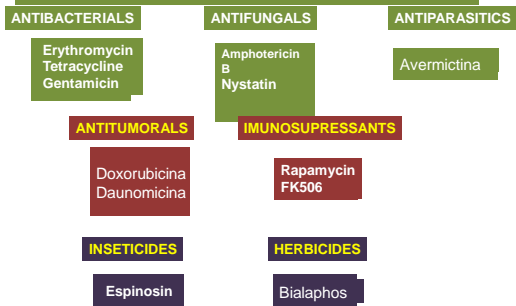
## Who are the main producers

- Bacteria  
Gram positive *Streptomyces*
- Fungi
- Other bacteria

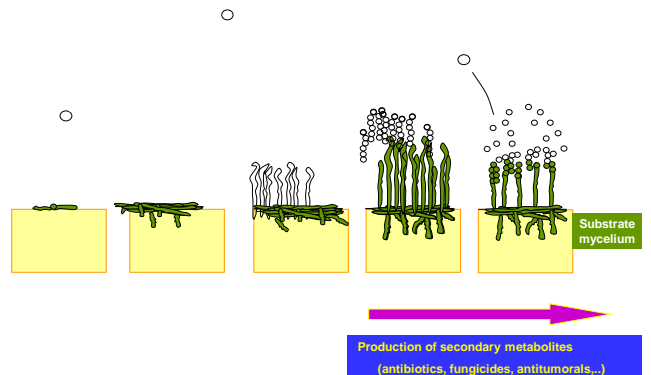
## MICROORGANISMS and BIOACTIVE COMPOUNDS



## BIOACTIVE COMPOUNDS SYNTHESIZED BY ACTINOMYCETES



## LIFE CYCLE OF *Streptomyces*



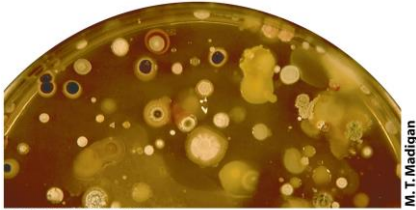


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M. T. Madigan



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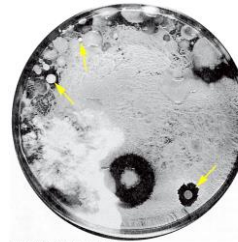


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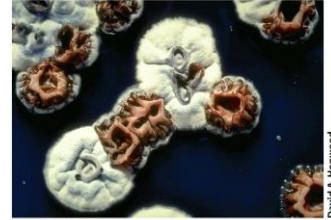


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## Biological functions of antibiotics?

- In the producer:  
Activators of morphological differentiation, UV protector, communication
- In the target microorganism:  
Toxicity

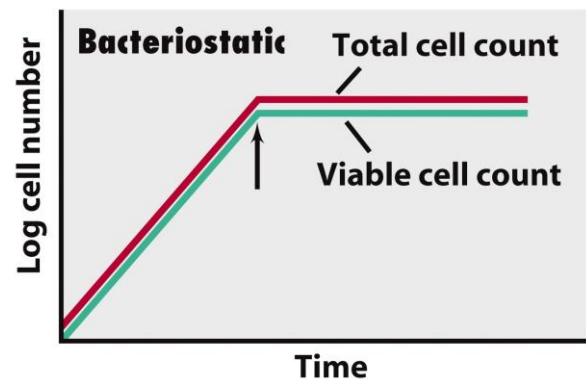


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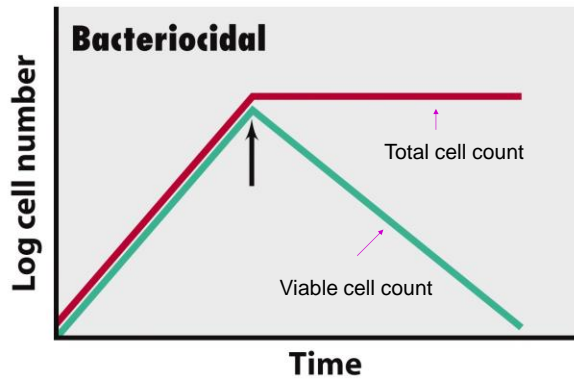


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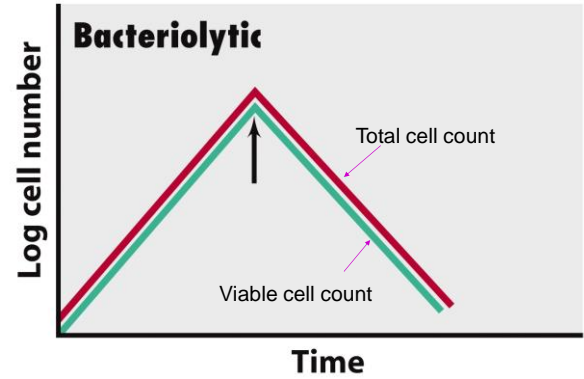


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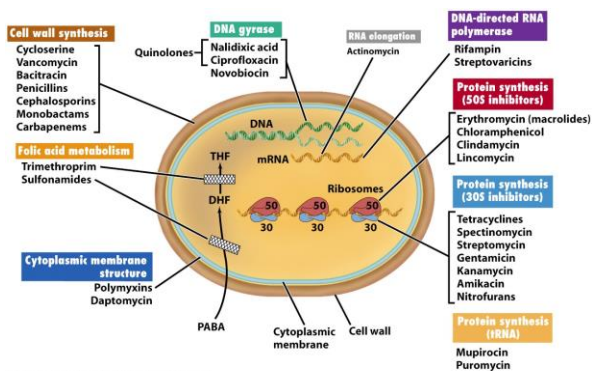


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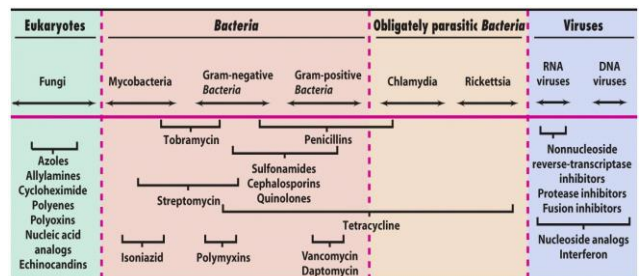


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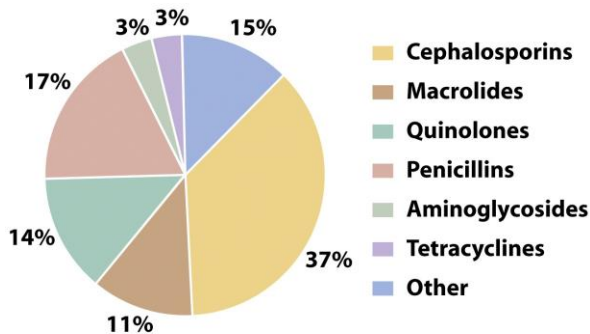


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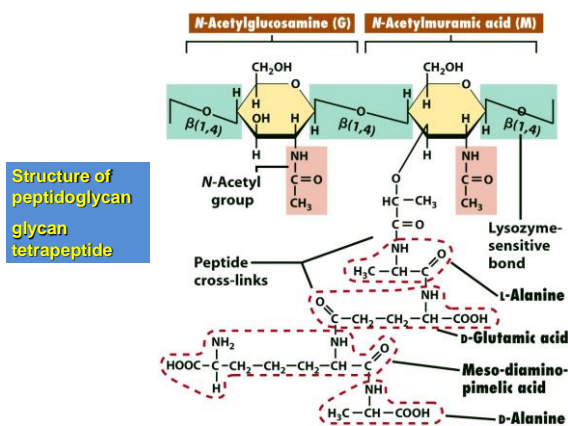
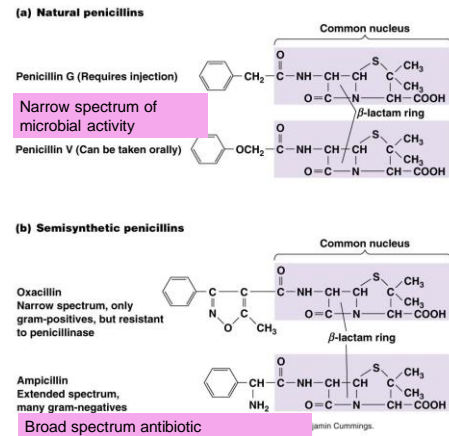


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Peptidoglycan sheet in *Escherichia coli* and *Staphylococcus aureus*

Glycine interbridge in *S. aureus*

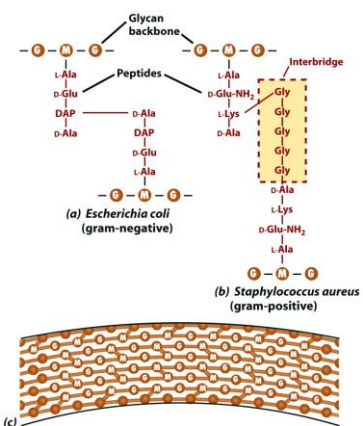


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(a) Rod-shaped bacterium before penicillin.

SEM

1 μm

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Figure 20.3a



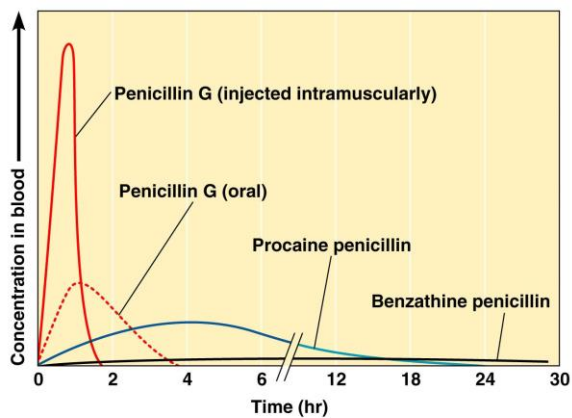
(b) The bacterial cell is lysing as penicillin weakens the cell wall.

SEM

1 μm

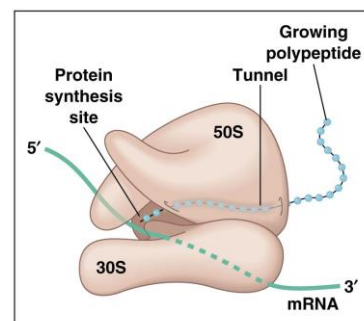
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Figure 20.3b



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Figure 20.7

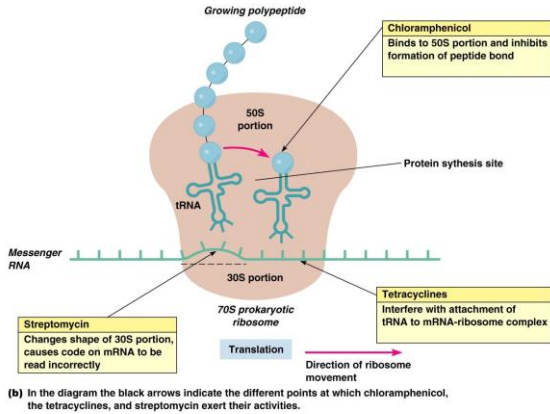


(a) Three-dimensional detail of the protein synthesis site showing the 30S and 50S subunit portions of the 70S prokaryotic ribosome.

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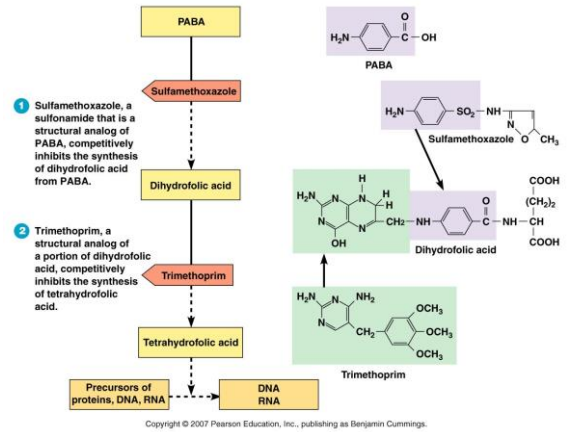
Figure 20.4a





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Figure 20.4b



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Figure 20.13 - Overview

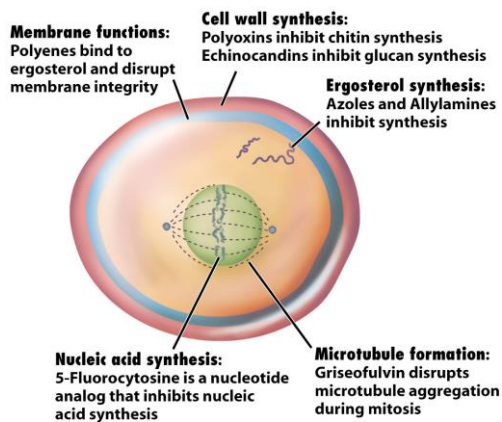
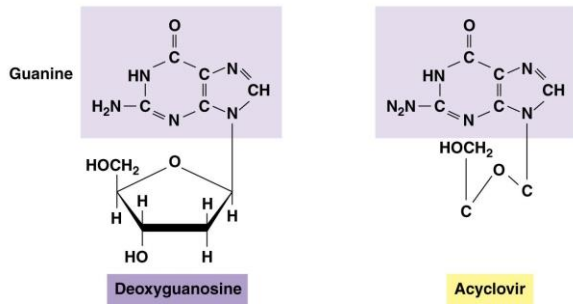


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Injury of plasma membrane of a yeast caused by antifungal drug

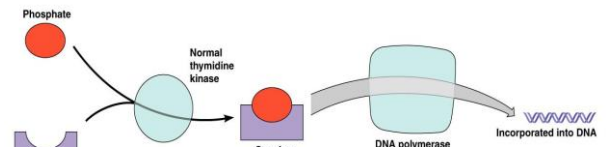
Figure 20.5



**(a) Acyclovir structurally resembles the nucleoside deoxyguanosine.**

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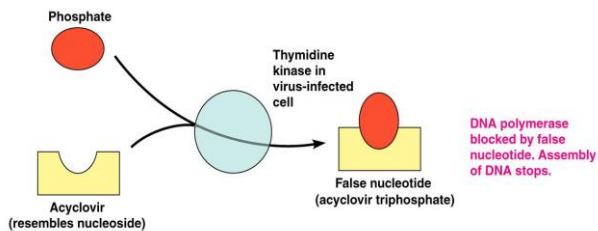
Figure 20.16a



**(b) The enzyme thymidine kinase combines phosphates with nucleosides to form nucleotides, which are then incorporated into DNA.**

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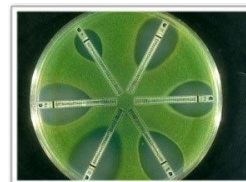
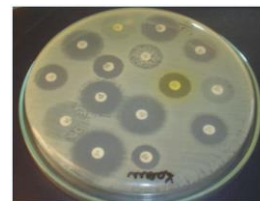
Figure 20.16b

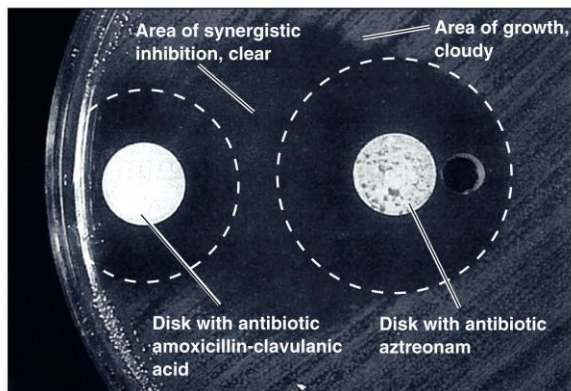


**(c) Acyclovir has no effect on a cell not infected by a virus, that is, with normal thymidine kinase. In a virally infected cell, the thymidine kinase is altered and converts the acyclovir (which resembles the nucleoside deoxyguanosine) into a false nucleotide—which blocks DNA synthesis by DNA polymerase.**

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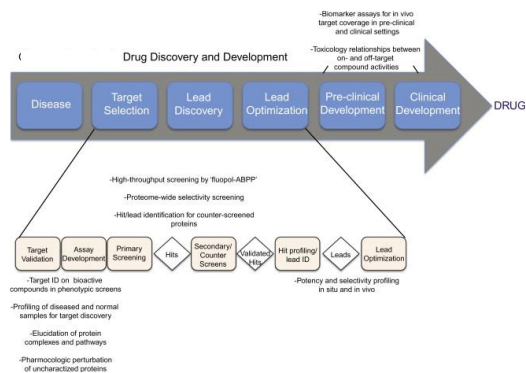
Figure 20.16c





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Figure 20.22



Antibiotic classification	Subclassification	Example
I. Carbohydrate-containing compounds	Pure sugars Aminoglycosides Orthosomycins N-Glycosides C-Glycosides Glycolipids	Nojirimycin Streptomycin Everninomicin Streptothricin Vancomycin Moenomycin
II. Macrocyclic lactones	Macrolide antibiotics Polyene antibiotics Ansamycins Macrotetrolides	Erythromycin Candididin Rifampin Tetractin
III. Quinones and related compounds	Tetracyclines Anthracyclines Naphthoquinones Benzoquinones	Tetracycline Adriamycin Actinorhodin Mitomycin

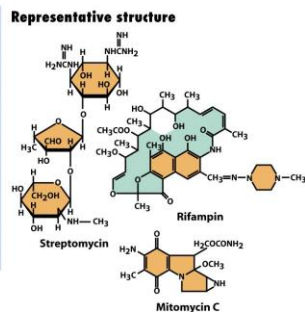


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Antibiotic classification	Subclassification	Example
IV. Amino acid and peptide analogs	Amino acid derivatives β-Lactam antibiotics Peptide antibiotics Chromopeptides Depsipeptides Chelate-forming peptides	Cycloserine Penicillin, ceftriaxone Bacitracin Actinomycin Valinomycin Bleomycin
V. Heterocyclic compounds containing nitrogen	Nucleoside antibiotics	Polyoxins
VI. Heterocyclic compounds containing oxygen	Polyether antibiotics	Monensin

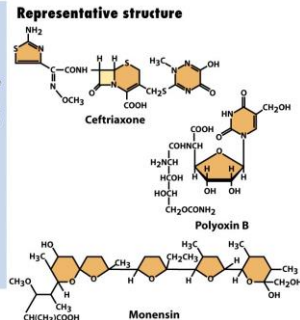


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Antibiotic classification	Subclassification	Example
<b>VII. Alicyclic derivatives</b>	Cycloalkane derivatives Steroid antibiotics	Cycloheximide Fusidic acid
<b>VIII. Aromatic compounds</b>	Benzene derivatives Condensed aromatics Aromatic ether	Chloramphenicol Griseofulvin Novobiocin
<b>IX. Aliphatic compounds</b>	Compounds containing phosphorus	Fosfomycin

#### Representative structure

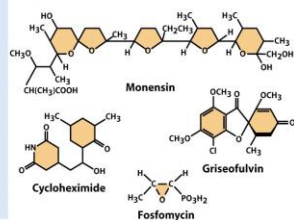


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Antibiotic classification	Subclassification	Example
<b>X. Quinolone compounds</b>	4-Quinolone Fluoro-4-quinolones	Nalidixic acid Ciprofloxacin
<b>XI. Oxazolidinone</b>	Cyclic lactone	2-Oxazolidinone

#### Representative structure

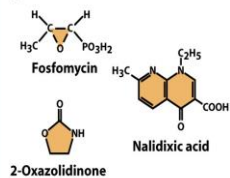


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