Antibiotics

Are chemical substances produced by microorganism that has the capacity in low concentration to inhibit selectively or even to destroy bacteria by antimetabolite mechanism. Antibiotic is a word derived from the term antibiosis. Anti means against and biosis means life (against life). Antimicrobials are chemical compounds which produced by either chemical synthesis example tripim (methprim) or produce by some medicinal plant. They are not produce by microorganism.
Testing for Antibiotic Production

To test for antibiotic production, overlay the plates with an indicator organism, such as the non-pathogenic bacterium *Staphylococcus epidermidis*. The indicator bacteria will grow and divide until they produce a confluent lawn on the plate.

Screening of antibiotics

The next step in screening procedure is to determine whether the chemical substance that produce the inhibition is a new antibiotic or a known compound. **Bioautography** is the method use to determine this. The assay employ paper chromatography or thin layer chromatography and biological assay.
Because of the different type of chemical structures found in antibiotics there will be no spraying reagent found to detect the spot of the isolated antibiotics, therefore biological method used which is the introduction of agar media over the TLC profile. The antibiotics will diffuse from the plate to the agar. The inhibition zones indicate the activity and location of the spots of antibiotics.

**Classification of antibiotics**

**Actions:** gram negative or gram positive

**In Pharmacognosy** the more important classification is the **biosynthetic pathways**
Biosynthesis of antibiotics

The useful microbial metabolites are produced from amino acid, like penicillin. Tetracyclines and erythromycins are produced via acetate pathway. Carbohydrate is the source of aminoglycoside antibiotics.

Antibiotics derive from amino acid include the penicillin cephalosporin and chloramphinicol

Is a product of Penicillium notatum, The β-lactams essentially comprise of the penicillins, cephalosporins, clavulanic acid, and moxalactam Interestingly, the β-lactam heterocyclic nucleus consists of a 4-membered cyclic ring with a N-atom. There exist a number of structural variants of β-lactam ring whereby the highly-strained β-lactam nucleus is strategically stabilized by means of the fusion of a variety of either 5-membered or 6-membered heterocyclic moieties to give rise to a wide spectrum of newer antibiotics
Antibiotics derived from carbohydrate

Gentamycin, kanamycin, amikacine and streptomycin

The aminoglycosides each contain one or more amino sugars, for instance: neosamine or glucosamine, bridged by glycoside linkages to a basic, either amino or guanidino, six-membered carbon ring, such as: streptamine or streptidine as given below:

![Glucosamine](image1).  

![Streptidine](image2).

9.3.1.2 Gentamicin

**Synonym** Gentamycin.

**Biological Sources** It is an antibiotic complex produced by the fermentation of *Micromonospora purpuraea* and *M. echinospora*; and a number of variants thereof.

**Chemical Structure**

![Chemical structure of Gentamicin](image3)

**Preparation** Gentamycin is normally recovered from a fermentation broth produced when submerged cultures of two subspecies of *Micromonospora purpuraea* are grown in the yeast extract-cereolose medium.

It is currently the most important drug of choice for the treatment of infections caused by most aerobic Gram-negative bacteria.
Preparation Amikacin is obtained by acylation of the C-1 amino function of the 2-deoxystreptamine group of kanamycin with L-(−)-4-amino-2-hydroxy-butyric acid. It is mostly employed in a wide range of infections, such as: septicemia, serious infections due to burns, urinary tract, respiratory tract and various soft tissues, meningitis, peritonitis, osteomyelitis, omphalitis in neonates, and other serious surgical infections.
Neomycin is usually obtained as a mixture of neomycin B (*Framycetin*) and its epimer neomycin C, the latter constitutes 5-15% of the mixture. Interestingly, in contrast to the other clinically useful aminoglycosides, neomycin is observed to comprise essentially of three sugar residues strategically attached to 2-deoxystreptamine as shown above. One of the three sugars present is the D-ribose (a common sugar).

Streptomycin has essentially two sugar components, namely: L-streptose and 2-deoxy-2-methylamino-L-glucose, which are linked to a non-sugar moiety streptidine evidently through two ether-linkages.
Acetate derived antibiotics

The tetracyclines are a conglomerate of broad spectrum orally active actinomycete antibiotics produced by cultures of Streptomyces species, and possessing appreciable therapeutic value. Chlortetracycline was the first true or real member of this group isolated
from *Streptomyces aureofaciens* and discovered by Duggar in 1948. It was immediately followed by **oxy-tetracycline** in 1950 from the cultures of *Streptomyces rimosus*.

![Macrolide antibiotics](image)

**Macrolide antibiotics**

**Erythromycin**

![Erythromycin](image)

**Biological Sources** It is produced by cultures of *Saccharopolyspora erythraea* (formerly known as *Streptomyces erythreus*). Waksman and Henrici were the pioneer in finding this antibiotic in a soil sample collected from the Philippine Archipelago.

**Clarithromycin**

**Biological Source** It is a semi-synthetic derivative of erythromycin which is obtained from *Saccharopolyspora erythraea*.

**Chemical Features** Erythromycin is fairly unstable under acidic environment whereby it undergoes degradation to inactive molecules through the 6-hydroxyl attacking the 9-carbonyl function to form a **hemiketal** (or **hemiacetal**) as shown below:
Biological Source
It is a semi-synthetic derivative of erythromycin which is obtained from Saccharopolyspora erythraea.

Azithromycin

Biological Source
It is a semi-synthetic macrolide antibiotic related to erythromycin A which is obtained from Saccharopolyspora erythraea.

Chemical Structure
Azithromycin is a tailor-made ring-expanded aza-macrolide wherein the carbonyl moiety at C-6 has been subjected to reduction; and this sort of minor alternation means the complex structure has significantly increased the activity when compared to the parent compound.
Doxorubicin

Uses

1. It has one of the broadest spectra of antitumour activity displayed by antitumour drugs.
2. It is extensively employed to treat acute leukemias, lymphomas, and a large number of solid tumours.
3. It has been found to inhibit the synthesis of RNA copies of DNA by virtue of the intercalation of the planar molecule between base pairs on the DNA helix.

Cephalosporins

Is belonging to the three categorized generations are available in the therapeutic armamentarium, besides the cephamycins, which are given as under:

(i) *First generation Cephalosporins*: Cefalotin (Cephalothin); D-Cephalexin (D-Cefalexin); Cephapirin; Cefazolin; D-Cephradine (D-Cefradine); D-Cefadroxil;

(ii) *Second Generation Cephalosporins*: D-Cefactor; D-Cefamandole; Cefuroxime; DCEFonicid; Ceforanide;

(iii) *Third Generation Cephalosporins*: Cefotaxime; Ceftizoxime; D-Cefoperazone;
Ceftazidime; Ceftriaxone; Cefmonoxime, Moxalactam;

<table>
<thead>
<tr>
<th>Class</th>
<th>St. No.</th>
<th>R₁</th>
<th>R₂</th>
<th>Name (Synonym)</th>
<th>Special Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Generation</td>
<td>1</td>
<td>⚫</td>
<td>-CH₃</td>
<td>Cefeleixin</td>
<td>Orally Active</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>⚫</td>
<td>-CH₃</td>
<td>Ceiradine</td>
<td>Orally Active, superseded generally</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>OH</td>
<td>-CH₃</td>
<td>Celadroxil</td>
<td>Orally Active</td>
</tr>
<tr>
<td>Second Generation</td>
<td>4</td>
<td>⚫</td>
<td>-Cl</td>
<td>Celaclor</td>
<td>Orally Active</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-CH=CH₂</td>
<td></td>
<td>Celprozil</td>
<td>Orally Active,</td>
</tr>
</tbody>
</table>

| Third Generation| 6       | ⚫          | -N₃        | Cefamandole [Cefamandole]          | High Resistance to β-Lactamases   |
|                 | 7       | ⚫          |            | Caftazidime                        | Broad-Spectrum                     |
|                 |         |            |            |                                    | Gram-Negative Activity; good      |
|                 |         |            |            |                                    | Activity against                   |
|                 |         |            |            |                                    | Pseudomonas                        |
|                 | 8       | ⚫          | -H₂N        | Ceftriaxone                        | Broad-Spectrum                     |
|                 |         |            |            |                                    | Gram-Negative Activity; Longer    |
|                 |         |            |            |                                    | Half-Life Than Other Cephalosporins|
|                 | 9       | ⚫          | -CH=CH₂    | Cefixime                           | III/III Generation, Orally Active, Long Duration |

Miscellaneous antibiotics

**Ansamycin Antibiotics (or Ansamycins):** These are a class of macrocyclic compounds wherein the non-adjacent positions on an aromatic ring system are usually spanned by the long aliphatic bridge (**Latin**: ansa = handle). The aromatic portion may comprise of either a
substituted benzene ring or a substituted naphthalene or naphthaquinone moiety. The macrocycle present in the ansamycins is normally closed by an amide rather an ester linkage, i.e., ansamycins are ‘Lactams’. Example rifadine

Chloramphenicol

\(\text{Chemical Structure}\)

- **Natural Source**: It may be obtained from the filtrate of a *Streptomyces venezuelae* culture by extraction with ethyl acetate. In case, the charcoal extract is rich in chloramphenicol, the latter may be crystallized from the ethyl acetate by affecting dilution with several volumes of deodourized kerosene oil.

- **Synthetic Route**: Chloramphenicol may be synthesized by many different routes of preparation, but one of the better known starts with para-nitroacetophenone and, after due conversion it into para-nitro-2-amino-acetophenone.

**Sulphonamides and Trimethoprim** Sulphonamides—the first and foremost antimicrobial agents, since discovered in 1930s, still hold the glory and fame of the modern antibiotic era. In general,
sulfanilamide (i.e., para-aminobenzene sulphonamide), obtained as a structural analogue of para-aminobenzoic acid (PABA), is basically the core compound from which hundreds of congeners were synthesized over the years by suitable modifications at N₁ (amide) or N₄ (p-amino function) so as to alter the pharmacological characteristics of the parent compound (sulphanilamide). The following table summarizes some of the approved and clinically useful widespread sulphonamides

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Classification</th>
<th>Drug(s)</th>
<th>R₁</th>
<th>R₂</th>
<th>Brand Name</th>
<th>Therapeutic Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sulphonamides for general Infections</td>
<td>1. Sulphanilamide</td>
<td>H</td>
<td>H</td>
<td>Rhinamid</td>
<td>Obsolete</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Suphapyridine</td>
<td>H</td>
<td>H</td>
<td>M2B 693</td>
<td>Pneumonia; <em>Denmaris herpetitmis.</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Suphazole</td>
<td>H</td>
<td>Cibazol</td>
<td>Bubonic plague staph. infections</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Suphazine</td>
<td>H</td>
<td>Diazyl</td>
<td>Rheumatic fever; Chancroid due to <em>Haemophilus ducreyi.</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Sulphamerazine</td>
<td>H</td>
<td>Solumeidine</td>
<td>General infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6. Sulphamidine (sulphamethazine)</td>
<td>H</td>
<td>Pirmazin</td>
<td>Meningal infections</td>
<td></td>
</tr>
</tbody>
</table>