UNIT – 2

Antibiotics

Historical Background:

- The discovery of antibiotics in the early 20th century revolutionized medicine.
- Paul Ehrlich coined the term "magic bullet" and developed Salvarsan, an arsenic-based drug.
- Alexander Fleming's discovery of penicillin in 1928 marked the beginning of the antibiotic era.

Nomenclature:

- Antibiotics are named based on chemical structure, source, or function.
- The suffix "-mycin" is common for macrolides, "-cillin" for penicillins, etc.

Stereochemistry:

- Stereochemistry plays a role in antibiotic activity, affecting interactions with biological targets.
- For example, the macrolide ring structure in macrolide antibiotics has specific stereochemical requirements.

Structure-Activity Relationship (SAR):

- SAR studies aid in understanding how the structure of antibiotics influences their pharmacological activity.
- In macrolides, the macrocyclic lactone ring is crucial for activity against Gram-positive bacteria.

Chemical Degradation:

- Antibiotics may degrade due to environmental factors like temperature, light, or pH.
- Proper storage is crucial to maintain their stability.

Classification and Important Products:

Macrolides:

1. **Erythromycin:**
    - **Structure:** Macrocycle with cladinose and desosamine sugar moieties.
    - **Activity:** Broad-spectrum against Gram-positive bacteria.
2. **Clarithromycin:**
    - **Semi-synthetic derivative of erythromycin.**
    - **Advantages:** Improved acid stability and broader spectrum.

3. **Azithromycin:**
    - **Structure:** Azalide subclass of macrolides.
    - **Features:** Longer half-life, once-daily dosing.

Miscellaneous Antibiotics:

1. **Chloramphenicol:**
    - **Activity:** Broad-spectrum against Gram-positive and Gram-negative bacteria.
    - **Concerns:** Associated with serious side effects, limiting its use.
2. **Clindamycin:**
    - **Structure:** Lincosamide antibiotic.
    - **Application:** Effective against anaerobic bacteria.

Prodrugs:

- **Basic Concepts:**
    - Prodrugs are inactive drug precursors that undergo transformation in the body to release the active drug.
    - Used to improve absorption, stability, or reduce side effects.
- **Application of Prodrugs:**
    - Examples include enalapril (converted to enalaprilat for hypertension) and oseltamivir (converted to oseltamivir carboxylate for influenza).

Antimalarials:

1. **Quinolines:**
    - **Structure-Activity Relationship (SAR):**
        - Quinine and chloroquine have a quinoline structure.
        - Resistance issues have led to the development of newer agents.
    - **Important Products:**
        - **Quinine Sulphate:** Used historically for malaria.
        - **Chloroquine:** Effective against Plasmodium species.
        - **Amodiaquine, Primaquine Phosphate, Pamaquine:** Varied uses in malaria treatment and prevention.
        - **Quinacrine Hydrochloride:** Historically used for malaria, now mainly for other conditions.
        - **Mefloquine:** Used for both treatment and prevention.
2. **Biguanides and Dihydrotriazines:**

- **Products:**
    - **Cycloguanil Pamoate, Proguanil:** Antifolate antimalarials.

3. **Miscellaneous Antimalarials:**
    - **Pyrimethamine:** Antifolate used in combination therapies.
    - **Artesunate, Artemether:** Derived from artemisinin, effective against multidrug-resistant malaria.
    - **Atovaquone:** Inhibits mitochondrial electron transport in the parasite.

This overview provides a comprehensive understanding of antibiotics, including historical context, nomenclature, stereochemistry, structure-activity relationships, chemical degradation, and important products within the specified classes.