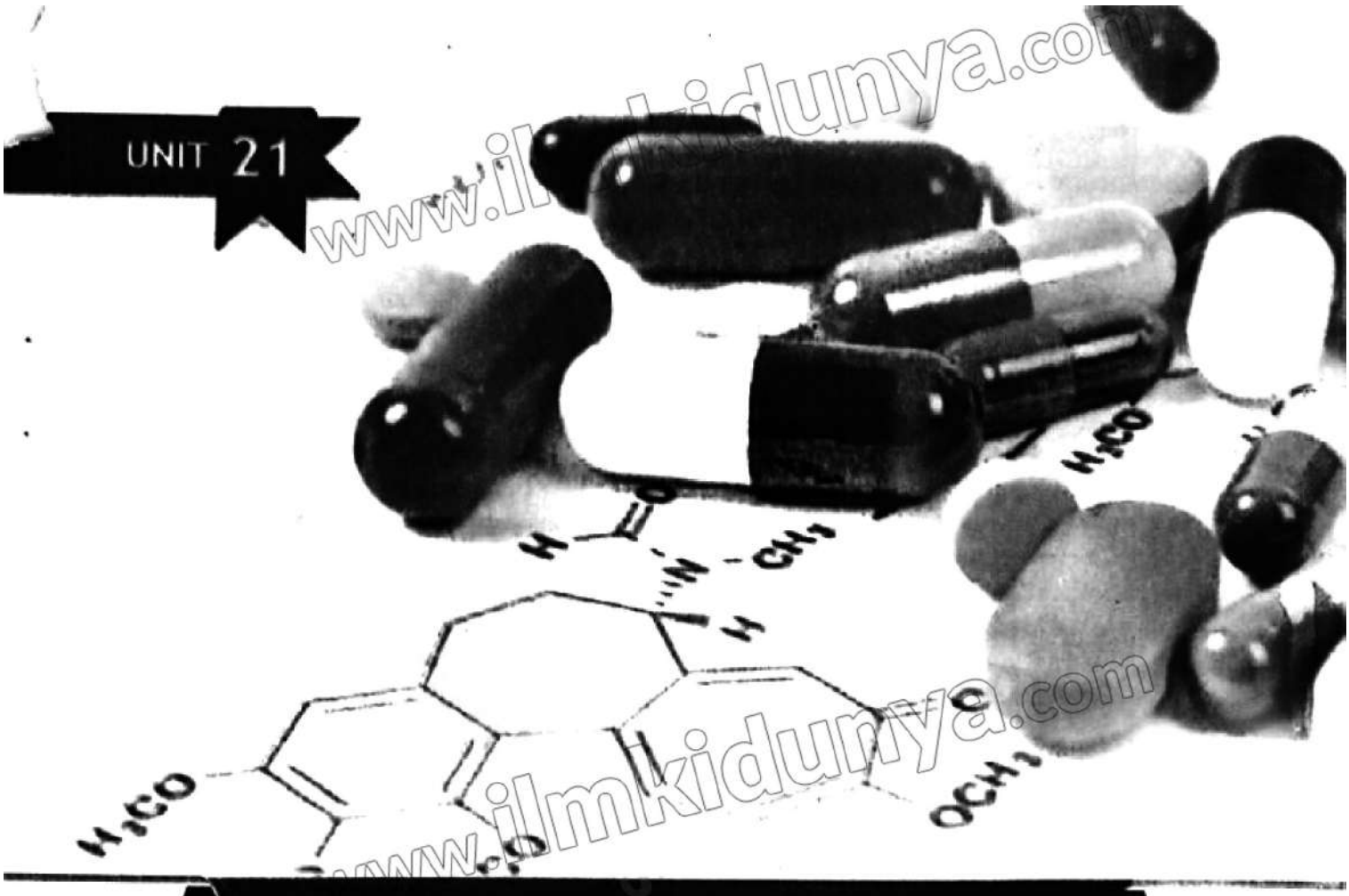
UNIT 21



MEDICINE

Student Learning Outcomes (SLOs)

- Recognise the concept of therapeutic index and therapeutic window in relation to drug administration.
- Explain the mechanism of action and uses aspirin and penicillin and explain the chemical structure of the same.
- Describe the mechanism of action of opiates and the concept of opioid receptors in the brain.
- Describe the pH regulation of stomach and its relation to the concept of non-specific reactions and active metabolites.
- Recognised the challenges in treating viral infections with drugs and the concept of antiviral medications.

21.1 Therapeutic Index

The therapeutic window, also known as the therapeutic range or therapeutic index, indicates the range of drug amounts in the body that bring about the desired therapeutic effects with minimum adverse effects. This means, it expresses the dosage range in which a medication can be both effective and safe.

21.1.1 Key Components of therapeutic index

1. **Minimum Effective Concentration (MEC):**
   This is the lowest amount of a drug in the bloodstream that triggers the desired therapeutic effect. Below this concentration, the drug may not be effective.
2. **Maximum Tolerated Concentration (MTC):**
   This signifies the highest amount of a drug in the bloodstream that a patient can bear without experiencing severe side effects or toxicity.
   The therapeutic window acts as a safety zone for drug administration, ensuring that the drug is potent enough to be effective while staying within safe limits to prevent harm to the patient. Falling below the MEC may result in inadequate treatment, while surpassing the MTC can lead to toxicity.

21.1.2 Factors Influencing the Therapeutic Window:

a. **Individual Variability:** People may metabolize drugs differently due to genetic factors, age, or overall health.
b. **Drug Interactions:** The simultaneous use of multiple medications can modify the concentrations of each drug.
c. **Patient Characteristics:** Factors like age, weight, and pre-existing medical conditions can affect how a drug is absorbed, distributed, metabolized, and eliminated.

21.2 Mechanism of Drug Action

Drug action refers to certain biochemical or physiological effects that the drug produces in the body to produce a therapeutic response. A drug's mechanism of action is the molecular or cellular process by which a drug exerts its pharmacological effects.

Aspirin and penicillin are two fundamental medications in medicine, each with unique mechanisms of action, applications, and chemical compositions. Let's explore each one in detail.

21.2.1 Aspirin

Mechanism of Action:

The primary mode of action of aspirin involves the inhibition of the enzyme cyclooxygenase (COX). This enzyme plays a vital role in the synthesis of prostaglandins. Prostaglandins contribute to the development of inflammation, pain, and fever, while thromboxanes are involved in platelet aggregation, and are essential for blood clotting. By blocking COX, aspirin reduces inflammation, pain, and fever, and also inhibits blood clot formation by preventing thromboxane production.

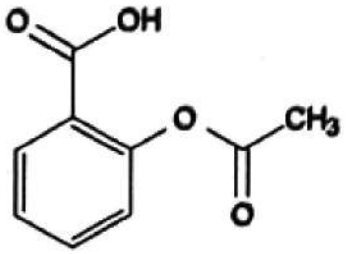
Uses:

Aspirin is utilized for various purposes, including:

1. Pain relief: for headaches, muscle pain, and mild arthritis.
2. Anti-inflammatory effects: to alleviate inflammation.
3. Antipyretic properties: to reduce fever.
4. Anticoagulant effects: in low doses, it prevents heart attacks and strokes by inhibiting blood clot formation.

Chemical Structure:

The chemical name of aspirin is acetylsalicylic acid. It consists of an aromatic ring (benzene ring) linked to a carboxylic acid group (–COOH) and an ester group ($-COOCH_3$). The structure can be simplified as:



Aspirin

21.2.2 Penicillin

Mechanism of Action:

Penicillin binds to the β-lactam ring on the transpeptid enzyme, preventing it from cross-linking and preventing new cell walls from forming. By inhibiting these enzymes, penicillin disrupts the formation of a normal cell wall in bacteria. This leads to a weakened cell wall that eventually ruptures, causing the bacteria to die due to osmotic pressure.

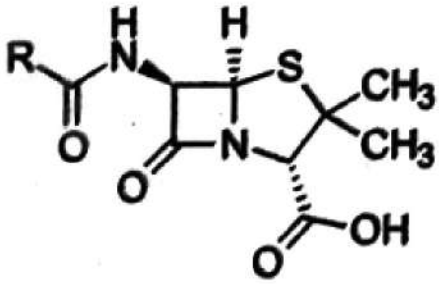
Uses:

Penicillin antibiotics are employed in the treatment of various bacterial infections, such as:

1. Pneumonia and other respiratory tract infections.
2. Meningitis.
3. Skin infections.
4. Syphilis.
5. Throat infections

Chemical Structure:

The key structural feature of the penicillins is the four-membered β-lactam ring; this structural moiety is essential for penicillin's antibacterial activity. The β-lactam ring is itself fused to a five-membered thiazolidine ring.



Penicillin

21.2 .3 OPIATES

Opiates, also called opioids are a class of drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and legal prescription pain relievers such as oxycodone, hydrocodone, codeine, morphine, and many others.

They are known for their strong pain-relieving effects. They induce euphoria and, unfortunately, addiction. The mechanism of action of opiates involves their interaction with opioid receptors located in the brain and throughout the central nervous system.

21.2.4 Opioid receptors:

Three main types of opioid receptors include:

1. Mu (μ) receptors: These are mainly responsible for the analgesic effects of opiates and are the main targets of most clinically used opioids. Activation of mu receptors can also cause respiratory depression, euphoria, and physical dependence.
2. Delta (δ) receptors: Their function is not fully understood, but they are thought to affect pain-relieving mechanisms and may play a role in mood regulation.
3. Kappa (κ) receptors: Activation of kappa receptors can cause pain and relief, but in some cases, they are also associated with dysphoria and hallucinations.

Mechanism of Action:

Opiates bind to opioid receptors located on certain cells in the brain, spinal cord, and other body areas. These receptors are part of the body's natural pain relief system and are often activated by endorphins which are naturally occurring hormones. Opiates, when bound, stimulate the endorphins, producing powerful analgesic effects to blunt the pain sensation.

Research indicates that commonly used drugs, such as opiates, alcohol, nicotine, amphetamines, and cocaine, trigger a neurochemical reaction that significantly boosts dopamine release by brain neurons in the reward centre. This results in feelings of euphoria and well-being.

Therapeutic Uses of Opioids

1. **Pain Management:**
   Opioids are used to treat moderate to severe pain, especially when other pain relievers are ineffective.
2. **Cough Suppression:**
   Some opiates have antitussive (cough suppressant) effects.
3. **Diarrhea Treatment:**
   Opioids can decrease bowel motility, relieving diarrhoea.

Risks and Considerations:

While opiates are effective for pain relief and have legitimate medical uses, their potential for abuse, addiction, and overdose is a serious issue. The euphoric effect can lead to abuse, and long-term use can result in tolerance (requiring higher doses for the same effect) and physical dependence and addiction. Abrupt discontinuation of the drug can cause withdrawal symptoms. Overdose, especially with potent synthetic opioids like fentanyl, can lead to death.

21.3 pH Regulation in the Stomach

The stomach's pH regulation is a dynamic process for proper digestion and enzyme activation. Parietal cells in the gastric glands release hydrochloric acid into the stomach lumen. This acid maintains an acidic environment in the stomach. This tightly controlled process is essential for breaking down ingested food. This acidification aids in activating digestive enzymes, denaturing proteins, and eliminating harmful microorganisms in food.

pH Level in the Stomach:

The stomach's pH typically ranges from 1.5 to 3.5, creating an acidic environment necessary for optimal enzyme function, especially pepsin for protein breakdown.

Control Mechanisms:

Various factors, such as food presence, hormonal signals (gastrin), and neural signals, regulate HCl release.

21.4 Non-Specific Reactions and Active Metabolites

1. Non-Specific Reactions:

The reactions that occur without specificity to a particular substrate are called non-specific reactions. For instance, the low pH of the stomach lumen helps kill pathogens in the food and break down complex food molecules like proteins, lipids, and carbohydrates. The stomach`s HCl unfolds proteins, making them more accessible for enzymatic digestion by pepsin.

2. Active Metabolites:

What is a metabolite? A metabolite is a biologically active form of a drug or substance produced by the body's metabolic processes. The stomach's pH can affect the formation of metabolically active drugs. Some medications undergo significant metabolism in the stomach due to the acidic environment and enzyme activity. These metabolites can metabolize the drug or render it inactive.

21.5 Viral Infections and Their Treatment

Unlike bacteria, viruses lack many cellular structures and metabolic pathways, making it difficult to target them without affecting the host cells. Therefore, treating viral infections with pharmaceuticals presents unique challenges.

Antiviral drugs are developed to disrupt the viral life cycle by targeting different stages of replication. This can include preventing the virus from entering host cells, inhibiting the replication of the viral genome, or stopping the release of new virus particles.

Enzyme inhibition is a common mechanism of action for numerous antiviral drugs, as they focus on viral enzymes essential for replication. Protease inhibitors, reverse transcriptase inhibitors, and polymerase inhibitors are examples of medications that break the viral life cycle.

In addition to enzyme inhibition, some antiviral drugs enhance the host's immune response to viral infections. For instance, interferons are proteins that can boost the immune system's ability to combat viruses. Viral protease inhibitors specifically target the activity of viral proteases, which are enzymes essential for processing viral proteins. These inhibitors are frequently used in the treatment of HIV and hepatitis C virus infections.

To combat drug resistance and viral diversity, combination therapy involving multiple antiviral agents with different mechanisms of action is commonly used. This strategy aims to reduce the risk of resistance development and improve treatment effectiveness.

21.5.1 Challenges in Treating Viral Infections

Virus and bacteria possess different structures. Viruses can develop a protective covering around themselves. Unlike bacteria viruses do not have cell walls which can be attacked by antibiotics.

Therefore, the treatment of viral infections poses many challenges. For instance;

1. Viruses multiply inside host cells, using the host's ribosomes. Therefore treating viral infection without harming the host cell requires specific antiviral agents.
2. Viruses can mutate rapidly, producing new strains. This quick mutation rate can cause resistance to antiviral medications, complicating ongoing treatment.
3. Viruses lack cellular structures like a cell wall or metabolic pathways, which are common targets for antibacterial drugs. This limits the potential targets for antiviral medications.
4. Some viruses develop protective covering and can remain dormant in the body for a longer period.
5. Medications for viral infection may affect host cell functions, leading to toxic side effects. Balancing the selectivity of antiviral drugs is essential to minimize harm to the host.

21.6 Concept of Antiviral Drugs

Antiviral drugs are a class of medicines particularly used to treat viral infections. Drugs that combat viral infections are called antiviral drugs. Viruses are among the major pathogenic agents that cause several serious diseases in humans, animals, and plants. Antiviral medications disrupt the viral life cycle by inhibiting specific stages of replication, such as blocking virus entry into host cells.

KEY POINTS

- The therapeutic window, also known as the therapeutic range or therapeutic index, indicates the range of drug concentrations in the body that bring about the desired therapeutic effects with minimum adverse effects.
- The simultaneous use of multiple medications can modify the concentrations of each drug.
- Drug action refers to certain biochemical or physiological effects that the drug produces in the body to produce a therapeutic response.
- The primary mode of action of aspirin involves the inhibition of the enzyme cyclooxygenase (COX).
- The chemical name of aspirin is acetylsalicylic acid.
- The key structural feature of the penicillins is the four-membered β-lactam ring; this structural moiety is essential for penicillin's antibacterial activity.
- Opiates are compounds that have strong pain-relieving effects.
- Opioids are used to treat moderate to severe pain, especially when other pain relievers are ineffective.
- The stomach's pH regulation is a dynamic process for proper digestion and enzyme activation.

- The stomach's pH typically ranges from 1.5 to 3.5
- The reactions that occur without specificity to a particular substrate are called non-specific reactions.
- A metabolite is a biologically active form of a drug or substance produced by the body's metabolic processes.
- Virus and bacteria possess different structures. Viruses can develop a protective covering around themselves.
- Unlike bacteria viruses do not have cell walls which can be attacked by antibiotics.
- Antiviral drugs are a class of medicines particularly used to treat viral infections.

EXERCISE

1. Multiple Choice Questions (MCQs)

i. What is the significance of maintaining an acidic pH in the stomach for digestion?

a) Enhances the absorption of lipids

b) Facilitates the activation of digestive enzymes

c) Promotes the breakdown of carbohydrates

d) Increases the secretion of bile

ii. Which opioid receptor is primarily responsible for the analgesic effects of opiates?

a) Delta (δ) receptors

b) Kappa (κ) receptors

c) Mu (μ) receptors

d) Sigma (σ) receptors

iii. What is a major challenge in developing broad-spectrum antiviral drugs?

a) High mutation rate of viruses

b) Lack of selectivity

c) Limited understanding of viral replication

d) Inability to target host cells

iv. Why is understanding the mechanism of action of a drug essential for healthcare professionals?

a) To identify potential side effects

b) To determine the optimal dosage

c) To assess drug interactions

d) All of the above

v. Which of the following best describes the therapeutic window?

a) The range of drug concentrations that is toxic

b) The range of drug concentrations that produces therapeutic effects without causing significant adverse effects

c) The range of drug concentrations that is ineffective

d) The range of drug concentrations that causes adverse effects

vi. If a drug's concentration in the bloodstream falls below the MEC, what is the most likely outcome?

a) The patient will experience toxicity

b) The drug will have no therapeutic effect

c) The patient will experience severe side effects

d) The drug will be at its maximum effectiveness

vii. What is the primary therapeutic use of aspirin?

a) Antibacterial b) Analgesic and anti-inflammatory

c) Antiviral d) Antifungal

viii. Penicillin is most effective against which type of organisms?

a) Viruses b) Fungi c) Gram-positive bacteria d) Protozoa

ix. How does penicillin inhibit bacterial growth?

a) By disrupting bacterial DNA synthesis

b) By inhibiting the enzyme responsible for cell wall synthesis

c) By disrupting bacterial protein synthesis

D. By inhibiting bacterial RNA synthesis

x. Which of the following is a common therapeutic use of opiates?

a) Treating bacterial infections b) Reducing inflammation

c) Relieving severe pain d) Lowering blood pressure

xi. Why can long-term use of opiates lead to addiction?

a) Because they inhibit serotonin reuptake

b) Because they cause irreversible binding to receptors

c) Because they increase dopamine release in the brain

d) Because they decrease the production of natural endorphins

2. Short Answer Questions

i. Explain the role of hydrochloric acid in the stomach and its impact on the activation of digestive enzymes.

ii. Briefly describe how opioids activate mu receptors and how this activation leads to pain relief.

iii. Discuss two challenges in developing antiviral drugs and provide potential strategies to overcome them.

iv. How does the secretion of hydrochloric acid influence the digestion?

3. Long Answer Questions

i. Discuss the link between the mechanism of action of opioids and the potential for drug addiction.

ii. Analyse the challenges involved in developing antiviral drugs.

iii. Explain the relationship between the Minimum Effective Concentration (MEC) and the Maximum Tolerated Concentration (MTC). How do these parameters define the therapeutic window?

iv. Describe the chemical structure of aspirin and penicillin, highlighting the functional groups that are critical for their mechanisms of action. Explain how these structures relate to their respective therapeutic uses.

v. A patient presents with symptoms of a bacterial infection. The doctor prescribes penicillin. Explain how penicillin works to treat the infection. Discuss potential resistance mechanisms that bacteria might employ against penicillin and how these mechanisms can be overcome.

vi. Identify and describe the main types of opioid receptors in the brain. Discuss their roles in pain modulation and the physiological effects of their activation by opiates.

vii. Analyse the impact of long-term opiate use on brain chemistry and function. Discuss the changes in receptor density and neurotransmitter levels that occur with prolonged exposure to opiates. Evaluate the implications of these changes for treatment options and recovery strategies for opiate addiction.