- Analgesic Drugs
  - Types of Analgesic Drugs
    - Narcotic analgesics (opioid drugs) relieve pain centrally but can cause drowsiness in large doses. Prolonged use can lead to tolerance and dependence.
    - Non-steroidal anti-inflammatory drugs (NSAIDs) are another class of analgesics that reduce inflammation and pain.
    - Analgesic-antipyretics are used to relieve pain and reduce fever.
    - Drugs for neuropathic pain and migraine are specialized treatments targeting specific types of pain.
- Classification of Narcotic Analgesics
  - Types of Opioid Receptors
    - Mu (μ) Receptors: Responsible for supra-spinal and spinal analgesia, sedation, inhibition of respiration, constipation, and modulation of hormone and neurotransmitter release.
    - Kappa (κ) Receptors: Involved in supraspinal and spinal analgesia, psychotomimetic effects, and constipation.
    - Delta (δ) Receptors: Contribute to supraspinal and spinal analgesia and modulation of hormone and neurotransmitter release.
  - Pharmacokinetics of Opioids
    - The half-life (t½) of opioids is typically 2-3 hours, with a duration of action of 6-8 hours.
    - Opioids are well absorbed orally, subcutaneously (S.C.), and intramuscularly (I.M.), but have low oral bioavailability (30%).
    - Routes of administration include intravenous (I.V.) for shock, transdermal patches, and nasal insufflation to bypass first-pass metabolism.
- Morphine: A Key Opioid
  - Distribution and Metabolism
    - Morphine is distributed throughout the body and crosses the placental barrier, posing risks during pregnancy and labor.
    - It is metabolized into morphine-6-glucuronide (more active) and morphine-3-glucuronide (neuro-excitatory), with metabolites excreted by the kidneys.
  - Pharmacodynamics and Mechanism of Action
    - Morphine stimulates opiate receptors in the central nervous system (C.N.S.) and periphery, inhibiting adenyl cyclase and decreasing cAMP levels.
    - Presynaptically, it blocks calcium channels, reducing the release of excitatory neurotransmitters like glutamate and substance P.
    - Postsynaptically, it opens potassium channels, leading to hyperpolarization and inhibitory postsynaptic potential (IPSP).
- Pharmacological Actions of Morphine
  - Central Nervous System Effects
    - Depressant Actions: Effective analgesic for deep visceral pain, narcosis, and depression of respiratory and vasomotor centers.
    - Stimulant Effects: Induces euphoria, miosis (pinpoint pupils), bradycardia, and stimulates the chemoreceptor trigger zone (CTZ) leading to vomiting.
  - Autonomic Nervous System Effects
    - Enhances parasympathetic activity (bradycardia) while depressing sympathetic activity (hypotension).
  - Gastrointestinal and Renal Effects
    - Morphine decreases gastrointestinal secretions, causes constipation, and can lead to urine retention due to ureteric spasm.
- Therapeutic Uses of Morphine
  - Indications for Morphine Use
    - Pain Management: Effective for severe visceral pain, including cardiac pain, cancer pain, and postoperative pain.
    - Preanesthetic Medication: Provides analgesia and sedation but may delay awakening and cause respiratory depression.
    - Pulmonary Edema: Reduces anxiety and preload in acute left ventricular failure.
    - Neurogenic Shock: Administered via slow I.V. route to manage shock.
  - Side Effects and Contraindications
    - Common side effects include CNS depression, respiratory issues, constipation, urinary retention, and potential for dependence.
    - Contraindications include age extremes, head injuries, increased intracranial pressure, and impaired pulmonary function.
- Morphine Toxicity
  - Acute and Chronic Toxicity
    - Acute Toxicity: Symptoms include coma, pinpoint pupils, and respiratory failure. Treatment involves artificial respiration and administration of naloxone.
    - Chronic Toxicity: Characterized by tolerance, dependence, and withdrawal symptoms upon cessation, including pain, muscle spasms, and gastrointestinal disturbances.
  - Treatment of Morphine Addiction
    - Treatment strategies include gradual withdrawal, replacement with methadone, and use of buprenorphine for maintenance therapy.
- Other Opioids and Their Characteristics
  - Codeine and Its Uses
    - Codeine is a phenanthrene opium alkaloid with better oral bioavailability and is used as an analgesic and antitussive.
  - Semi-Synthetic and Synthetic Opioids
    - Heroin: Highly lipid-soluble, addictive, and not used for medical purposes.
    - Meperidine: Less potent than morphine, used for severe pain and preanesthetic medication.
    - Fentanyl: A potent synthetic opioid used in anesthesia and pain management, with a rapid onset and short duration.
  - Mixed Agonist-Antagonists
    - Drugs like pentazocine and buprenorphine act as partial agonists at mu receptors and are used in pain management and addiction treatment.
  - Narcotic Antagonists
    - Naloxone: Used for acute morphine poisoning and neonatal asphyxia, with a short half-life.
    - Naltrexone: An oral antagonist used in addiction treatment with a longer duration of action.