MEDICINAL CHEMISTRY-I

UNIT 5 NOTES

DRUGS ACTING ON CNS

- GENERAL ANAESTHETICS
- NARCOTIC & NON NARCOTIC ANALGESICS
- NARCOTIC ANTAGONIST

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General Anesthetics

- General Anesthesia is a type of drugs used during surgery to make person unconcious and unable to feel pain.
- It effects the whole body and the person doesn't wake up until the surgery is over.
- They are depressant drugs that produce a partial or total loss of the sensation.

General Mechanism Of Action

- The mechanism of action of general anesthesia involves multiple effects on the central nervous system that result in loss of conciousness, amnesia, analgesia and immobility.
- The exact mechanisms are complex and not completely understood, but the general principles includes :

1. Enhancement of Inhibitory Pathways

Most of general anesthetics enhance the action of inhibitory neurotransmitters, especially Gamma - aminobutyric Acid (GABA) at the GABA - A receptor. This leads to :-

- Hyperpolarization of neurons
- Reduced neuronal excitability
- Sedation, amnesia and unconciousness

② Inbition of Excitotary Pathways

Some anesthetics inhibit excitotary neurotransmitters such as glutamate, particularly at the NMDA (N-methyl-D-Aspartate) receptors.

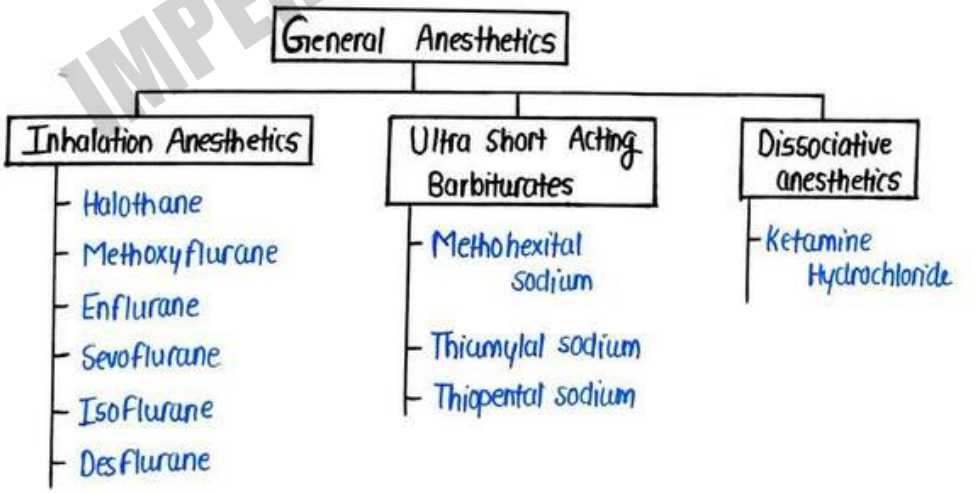
Example: Ketamine blocks NMDA receptors, contributing to its dissociative anesthetic effect.

③ Modulation of Ion Channels

General anesthetics also acts on potassium (K^+) and sodium (Na^+) channels:

Promotes K^+ reflux – hyperpolarization
Inhibit Na^+ reflux – reduced action potential generation.

CLASSIFICATION



INHALATION ANESTHESIA

- They are gases as volatile liquid which are mixed with oxygen & administered through inhalation.
- They cause CNS depression & anesthesia by rapidly reaching the blood & brain in sufficient concentration.

Mechanism of Action

- Inhalation anesthetics induce anesthesia by modulating synaptic transmission in the central nervous system, leading to unconciousness, amnesia and immobility.

① Most inhalation anesthetics enhance the GABA at GABA-A receptors, increasing chloride (Cl^-) reflux, which hyperpolarizes neurons and reduces neuronal activity.

- Some (e.g. isoflurane) may also activate glycine receptors, enhancing inhibitory neurotransmission in the spinal cord.

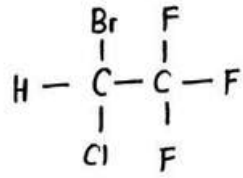
② They inhibit excitatory neurotransmitters like glutamate, especially at NMDA receptors (notably nitrous oxide and xenon).

- This reduces neuronal excitation and contributes to the anesthetic effect.

DRUGS

- Halothane *
- Methoxyflurane
- Enflurane
- Sevoflurane
- Isoflurane
- Desflurane

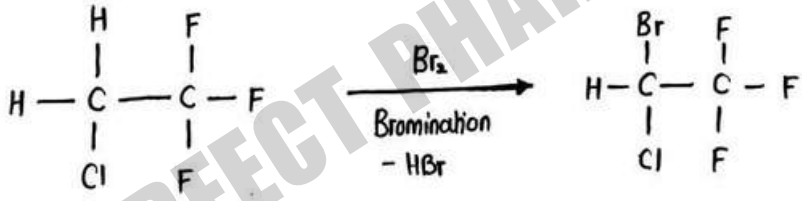
① HALOTHANE *



MOA

- Same as mentioned in General Anaesthetics & Inhalation Anaesthesia

SYNTHESIS



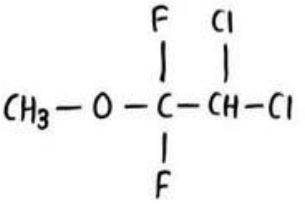
2 - Chloro - 1,1,1 - trifluoroethane

Halothane

Uses

- Anaesthetic Agent
- Skeletal Muscle Relaxation

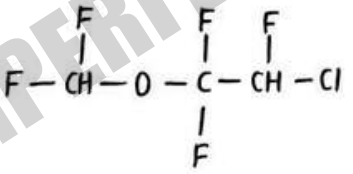
② METHOXYFLURANE



Uses

- It's produce light anesthesia with deep analgesic and muscle relaxation.
- It is rarely used in dental surgery.

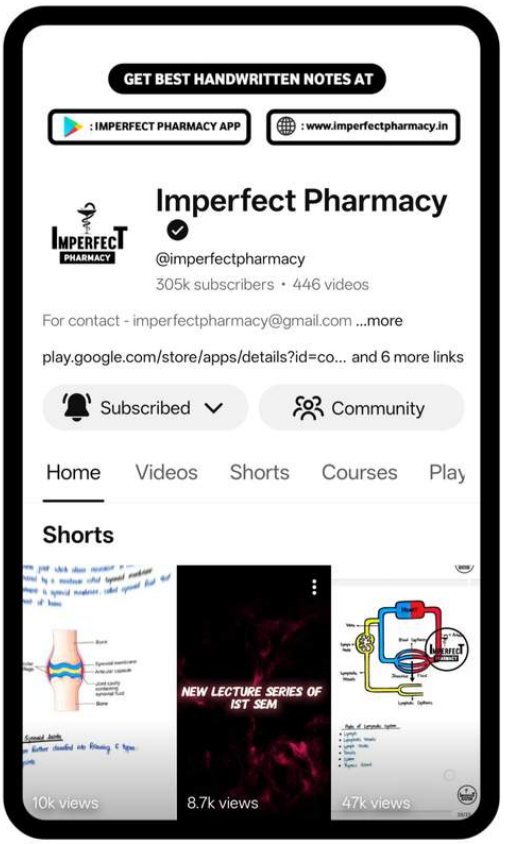
③ ENFLURANE

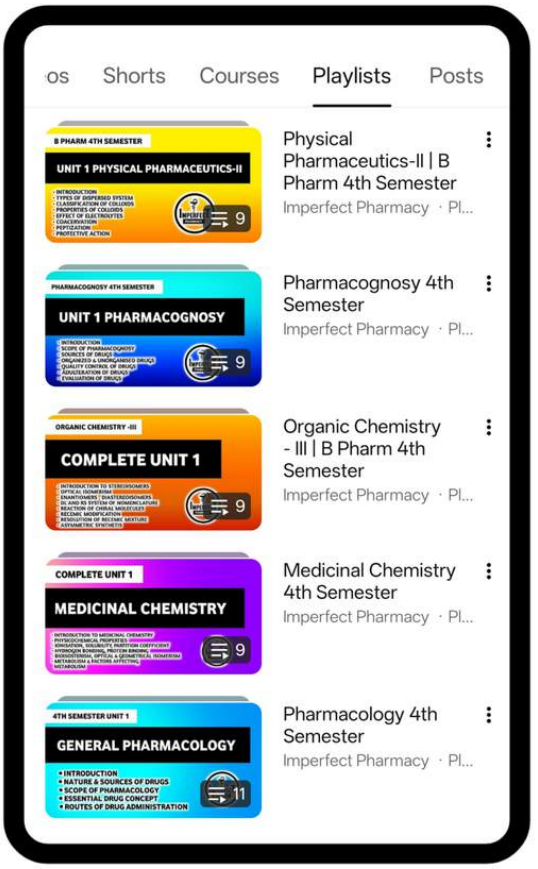


Uses

- Used to produce general anesthesia, during surgery especially on vaginal delivery.

FOR LECTURE VIDEOS VISIT OUR CHANNEL





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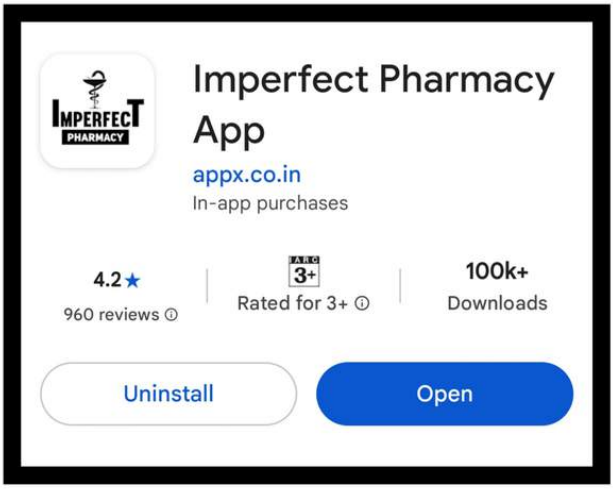
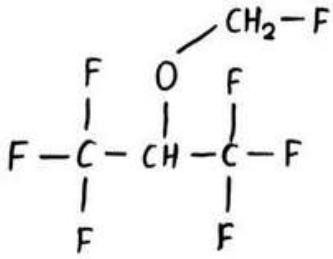


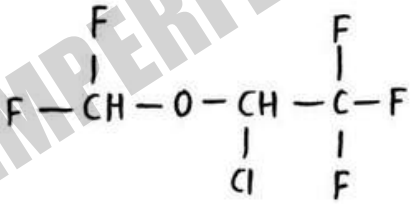
④ SEVOFLURANE



Uses

- Commonly used as volatile anesthetics.
- It also used to put children on sleep for surgery by inhalation.

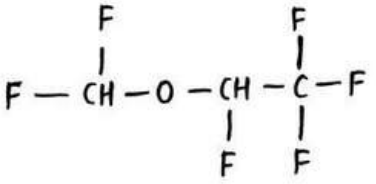
⑤ ISOFLURANE



Uses

- It is used for induction and maintenance of general anesthesia.

⑥ DESFLURANE



Uses

- It has the most rapid onset and offset of all the volatile anesthetic drugs.

ULTRA SHORT ACTING BARBITURATES

- They are intravenously administered for producing rapid unconciousness in surgical & Basal anesthesia.

Mechanism of Action

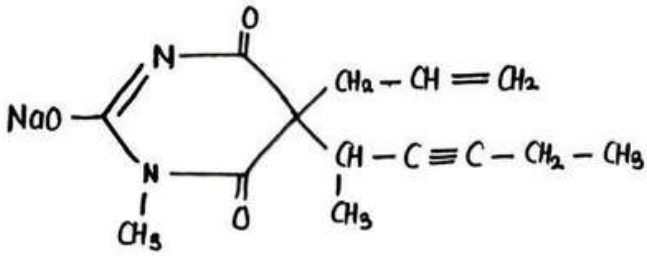
- Ultra-short acting barbiturates act primarily by acting on GABA by enhancing the activity of GABA, the main inhibitory neurotransmitter in CNS.

- They binds with GABA-A receptors in CNS and this increases the duration of chloride channel opening when GABA is present and this increased chloride reflux hyperpolarizes neurons, making them less excitable and leading to CNS depression.

DRUGS

- Methohexital sodium *
- Thiamylal sodium
- Thiopental sodium

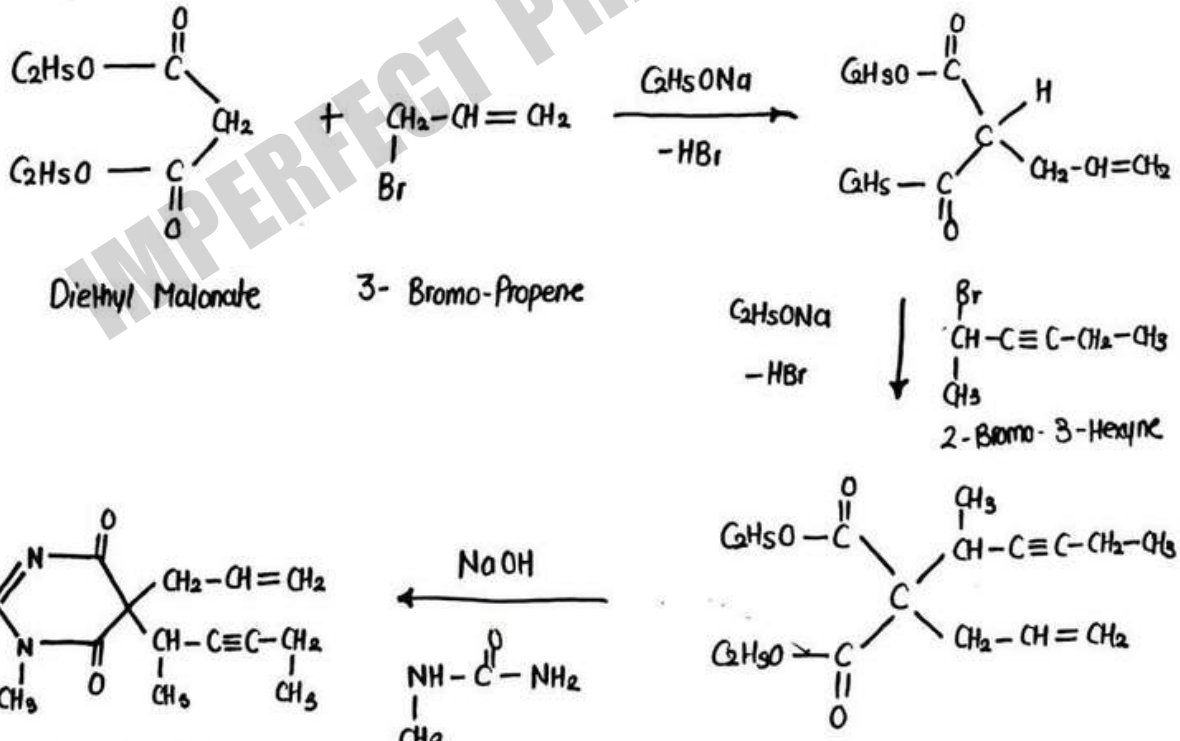
① METHOHEXITAL SODIUM *



MOA

Same as mentioned in Ultra Short Acting Barbiturates

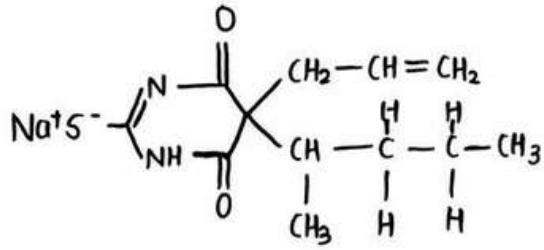
SYNTHESIS



Uses

- Anaesthetic Agent
- Electroconvulsive Therapy

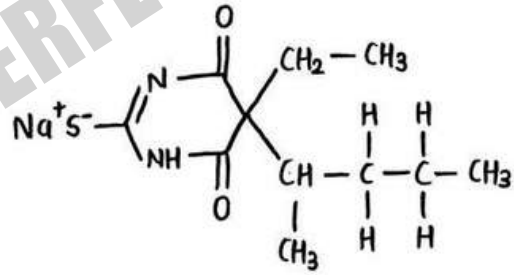
② THIAMYLAL SODIUM



Uses

- Used as intravenous anesthetic drug used to induce drowsiness or sleep or psychological excitement.

③ THIOPENTAL SODIUM



Uses

- Used in caesarean delivery for producing anesthesia.
- Used as a sedative, hypnotic and anticonvulsant.

DISSOCIATIVE ANESTHETICS

- They are class of drugs that reduce or block signals to the concious mind from other parts of the brain, leading to sense of detachment from the environment and self.
- They produce analgesia, amnesia and causing complete unconciousness.

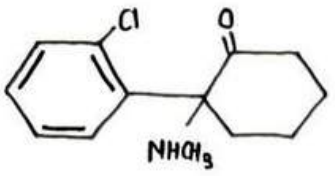
Mechanism of action

- They block the NMDA (N-methyl-D-Aspartate) receptor, a subtype of glutamate receptor, which is responsible for excitatory neurotransmission in the CNS.
- This noncompetetive antagonism prevents calcium reflex and distrupts synaptic transmission, particularly in the cortex and limbic system, leading to sensory dissociation.

DRUGS

Ketamine Hydrochloride.

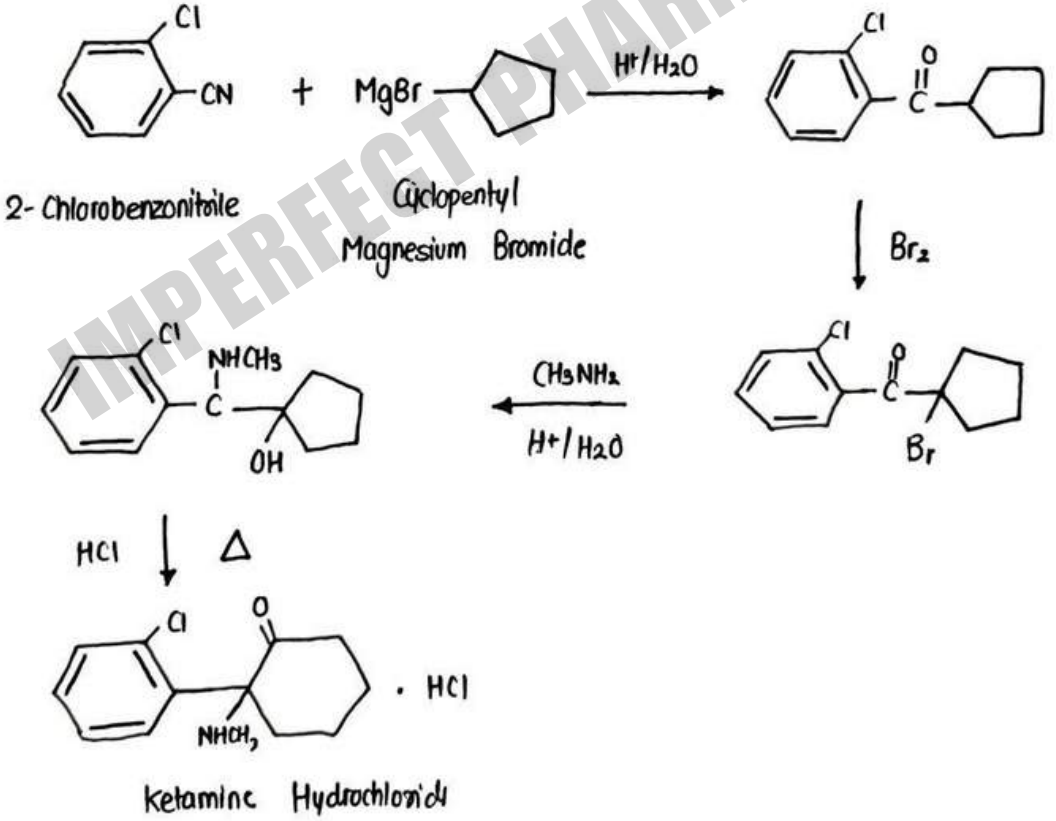
① KETAMINE HYDROCHLORIDE *



MOA

Same as mentioned in Dissociative Anaesthetics.

SYNTHESIS



Uses

- General Anaesthetic
- Skeletal Muscle Relaxant

Narcotics And Non-narcotics Analgesics

Narcotic Analgesics

- These are strong painkillers that can make you feel sleepy or drowsy.
- They are often used for severe pain.

Examples: Morphine, Codiene etc.

Non-Narcotic Analgesics

- These are milder painkillers that don't cause sleepiness.
- They are used for mild to moderate pain, like headaches or muscle pain.

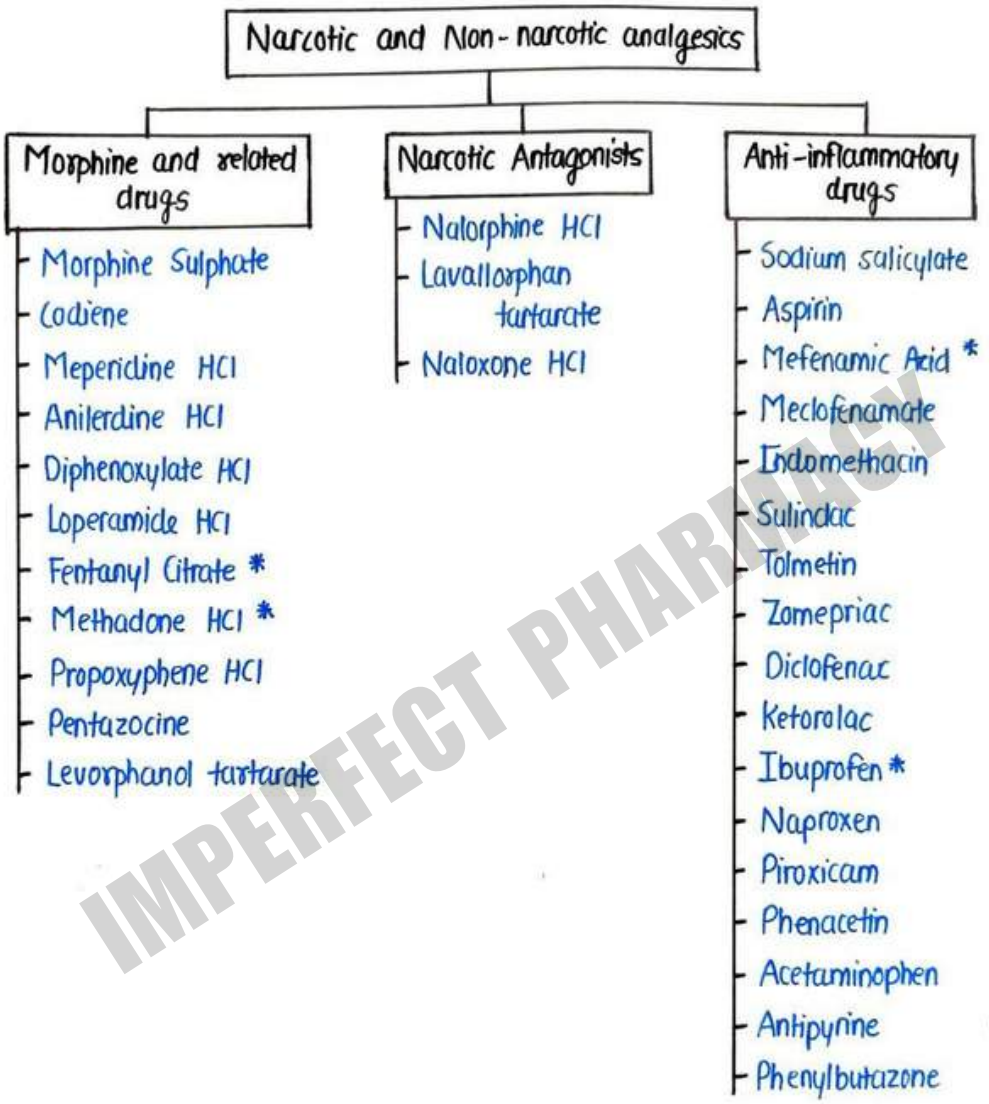
Examples: Paracetamol (Acetaminophen), Ibuprofen etc.

Mechanism of Action

① Narotic Analgesics: They work by binding to opioid receptors in the brain and spinal cord, blocking pain signals and changing how your body feels pain.

② Non-narcotic Analgesics: They work by blocking enzymes COX that produce prostaglandins, which are chemicals that cause pain and swelling.

CLASSIFICATION



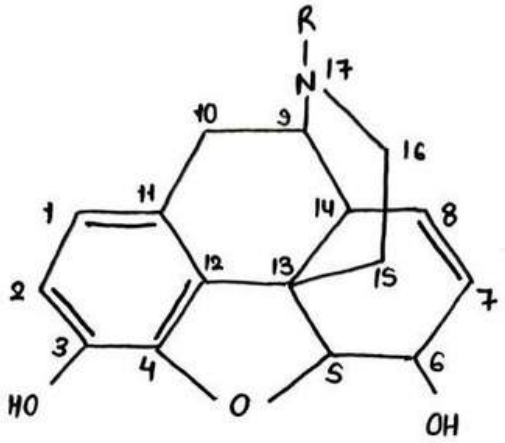
MORPHINE AND RELATED DRUGS

- Morphine is a naturally occuring Alkaloid obtained from the Opium Poppy (Papaver Somniferum)
- It is the prototypical nargotic analgesic, meaning it serves as the standard against which other opoid (narcotic) analgesics are compared.

MOA

- Morphine binds to mu- opoid receptors in the brain & spinal cord.
- This leads to:
- Inhibition of Adenylate Cyclase → ↓ cAMP
- Closes Ca^{2+} Channels → ↓ neurotransmitter release
- Opens K^{+} Channels → Hyperpolarization
- Result: Pain signals are blocked → Pain relief (analgesia) + sedation, respiratory depression.

SAR OF MORPHINE ANALOGUES



① Aromatic Ring

- The phenolic -OH at position 3 is crucial for hydrogen bonding with receptor.
- Modific or removal leads to severe loss of activity.

② Alcohol at Position 6

- It is hydrophilic group contributes in receptor binding
- Oxidation of this -OH into ketone increases potency.

③ Double Bond B/w $C_7 = C_8$

- Saturation of this double bond tends to increase potency & reduce toxicity

④ Tertiary Amines (Position 17)

- Small Alkyl Substitution : Good Agonist
- Cyclic Substitution : Can lead to Antagonist.

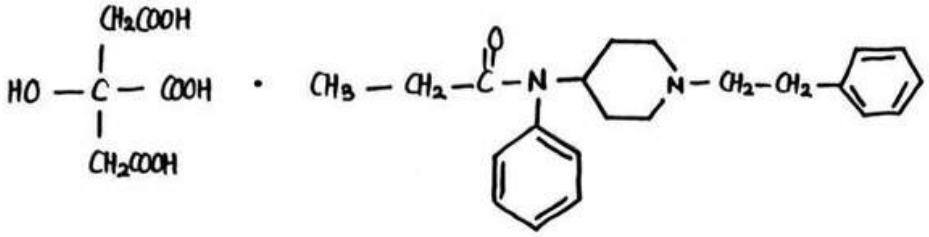
⑤ Ether Bridge (C_4-C_5)

- Essential for maintaining rigid 3 - dimensional conformation.

⑥ Hydroxylation at C-14

- Introduction of an OH group at position 14 significantly increases potency.

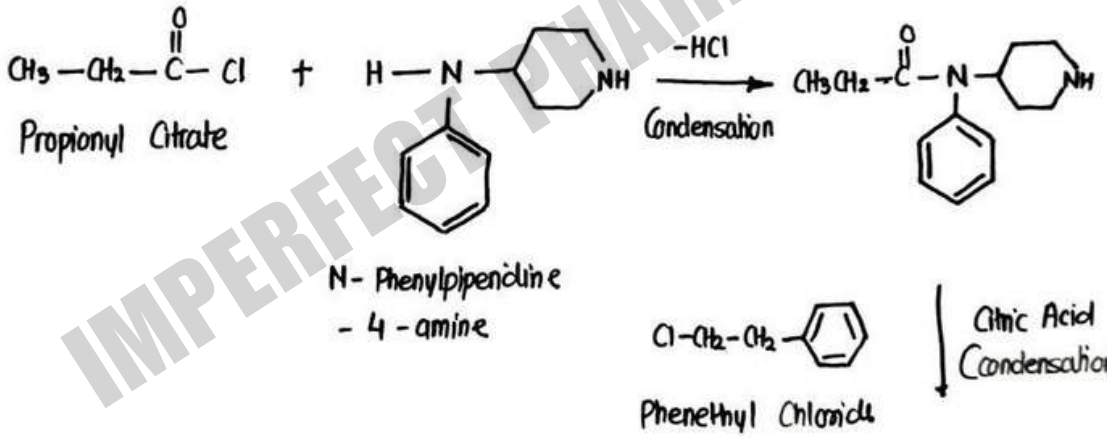
① FENTANYL CITRATE *

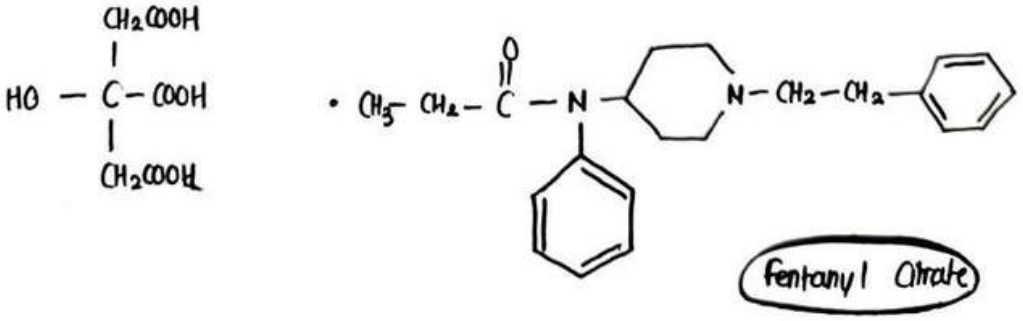


MOA

Mentioned in Morphine Analogues

SYNTHESIS

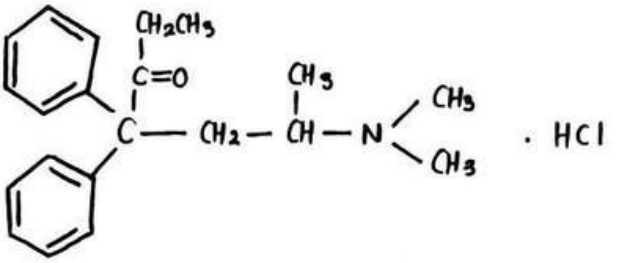




Uses

- Narcotic therapy for cancer patients.

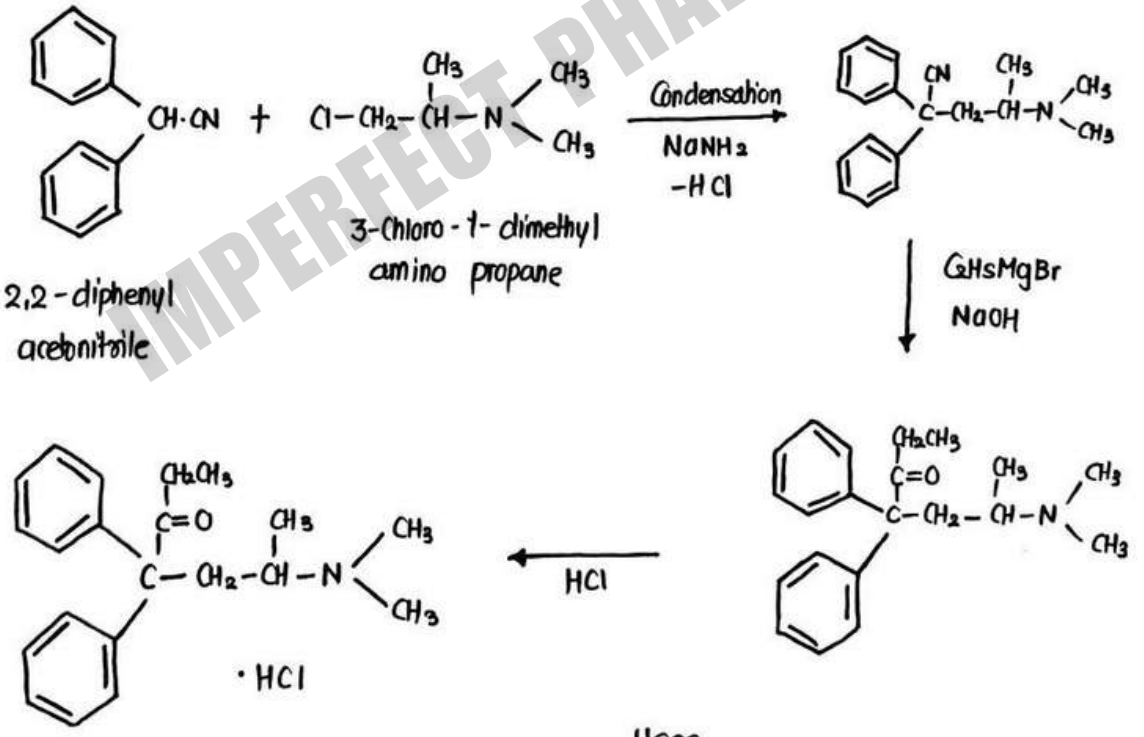
② METHADONE HYDROCHLORIDE *



MOA

- Mentioned in Morphine Analogues

SYNTHESIS



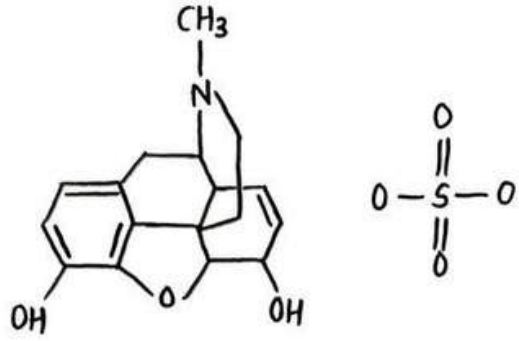
2,2-diphenyl acetonitrile

Methadone Hydrochloride

Uses

- Treatment of Opioid Dependence
- Pain Management.

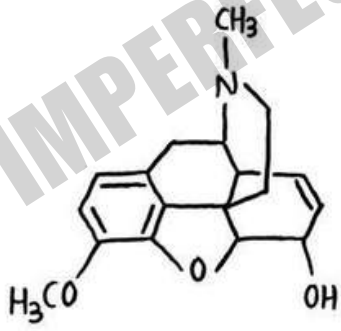
③ Morphine Sulphate



Uses

- It is used for treating & relieving severe pain.

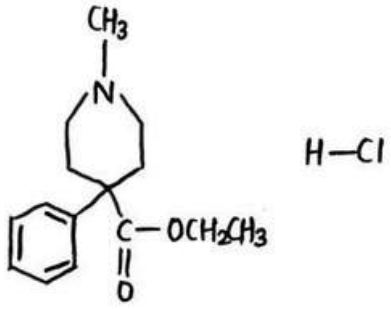
④ Codeine



Uses

- It is used for treating and relieving severe pain.
- Antidiarrheal and cough suppressant.

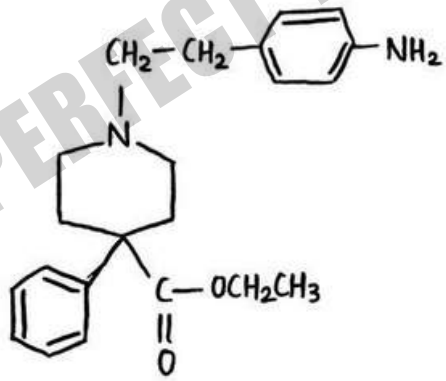
⑤ Meperidine Hydrochloride



Uses

- Used for controlling moderate to severe pain.

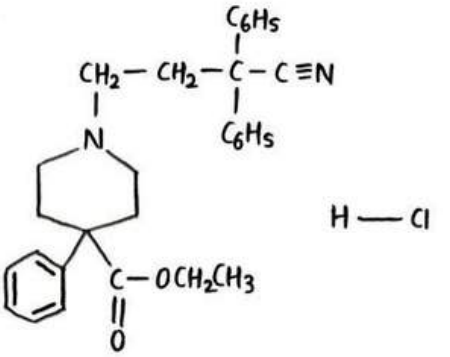
⑥ Anilerdine Hydrochloride



Uses

- It is used for treating & relieving severe pain.
- Also used as an adjunct in anesthesia.

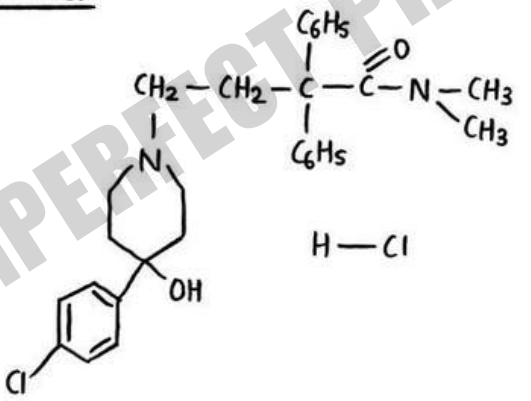
⑦ DIPHENOXYLATE HCl



Uses

- Used in adjunctive therapy in managing diarrhoea.

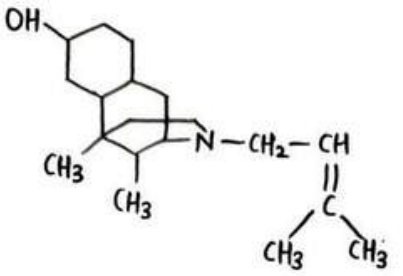
⑧ LOPERAMIDE HCl



Uses

- Used to treat acute non-specific diarrhoea & chronic diarrhoea related to inflammatory bowel disease & gastroenteritis.

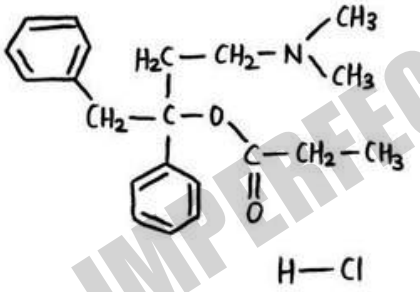
⑨ PENTAZOCINE



Uses

- Used to relieve moderate pain by activating receptors in the spinal cord.

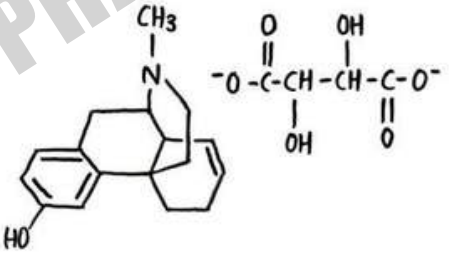
⑩ PROPOXYPHENE HCl



Uses

- Used to reliving mild to moderate pain.

⑪ LEVORPHENOL TARTARATE



Uses

- Used to relieving mild to moderate pain.

NARCOTIC ANTAGONIST

- Narcotic antagonist are medicines that block the effect of narcotic (opioid) drugs.
- It stops or reverses the effects of narcotics, especially in cases of overdose.

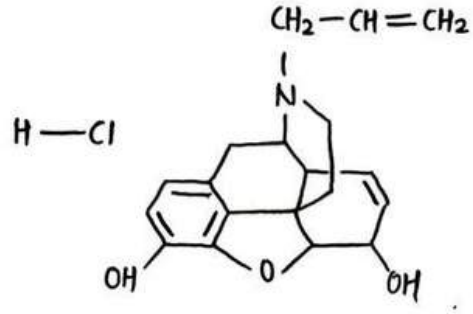
Mechanism of Action

- It works by attaching to opioid receptors in the brain and blocking them, so opioid drugs can't work.
- This stops or reverse the effects of narcotics like pain relief, drowsiness or slowed breathing.

Drugs

- Nalorphine Hydrochloride
- Levallorphan tartarate
- Naloxone hydrochloride

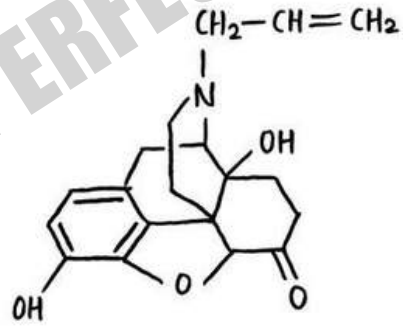
① NALORPHINE HYDROCHLORIDE



Uses

- Used for reversing opioid overdosing.

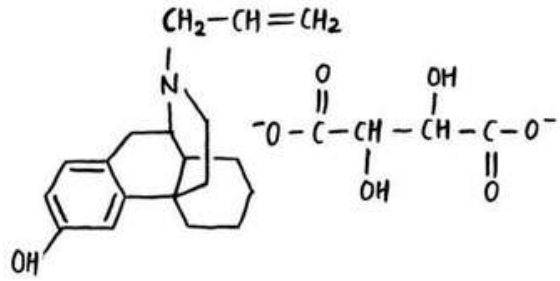
② NALOXONE HYDROCHLORIDE



Uses

- It is used for diagnosing acute opioid overdose.
- Used as completely or partially reversing respiratory depression by opioids.

③ LEVALLORPHAN TARTARATE



Uses

- Used for completely a partially reversing narcotic depression such as Respiratory depression by opioids.

ANTI - INFLAMMATORY AGENTS

- They are medicines that reduce pain, swelling and fever without making you sleepy.
- They are also known as NSAIDs, that are widely used for the treatment of minor pain and for the management of edema and tissue damage resulting from inflammatory joint disease.

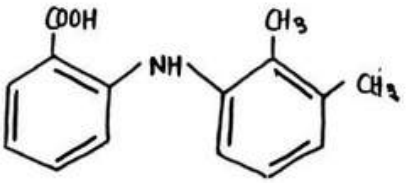
Mechanism of Action

- They blocks cyclooxygenase (COX) enzymes responsible for production of prostaglandins, which promotes inflammation, pain and fever reduced by it.

Drugs

- Sodium salicyclate
- Aspirin
- Mefenamic Acid *
- Meclofenamate
- Indomethacin
- Sulindac
- Tolmetin
- Zomepriac
- Diclofenac
- Ketorolac
- Ibuprofen *
- Naproxen
- Piroxicam
- Phenacetin
- Acetaminophen
- Antipyrine
- Phenylbutazone

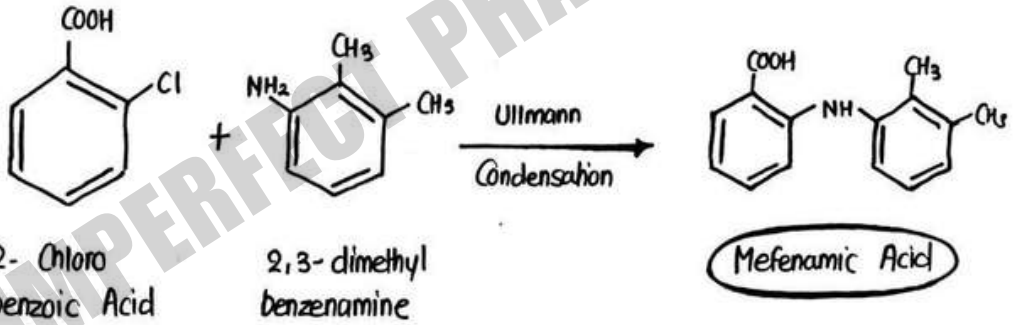
① MEFENAMIC ACID *



MOA

As mentioned in Anti- inflammatory agents.

SYNTHESIS



2- Chloro benzoic Acid

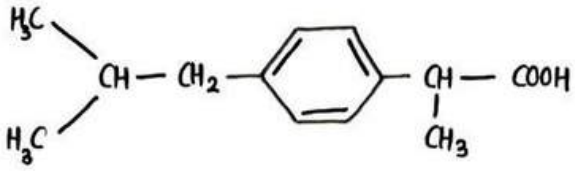
2,3- dimethyl benzenamine

Mefenamic Acid

Uses

- Used mainly in muscle & back pain

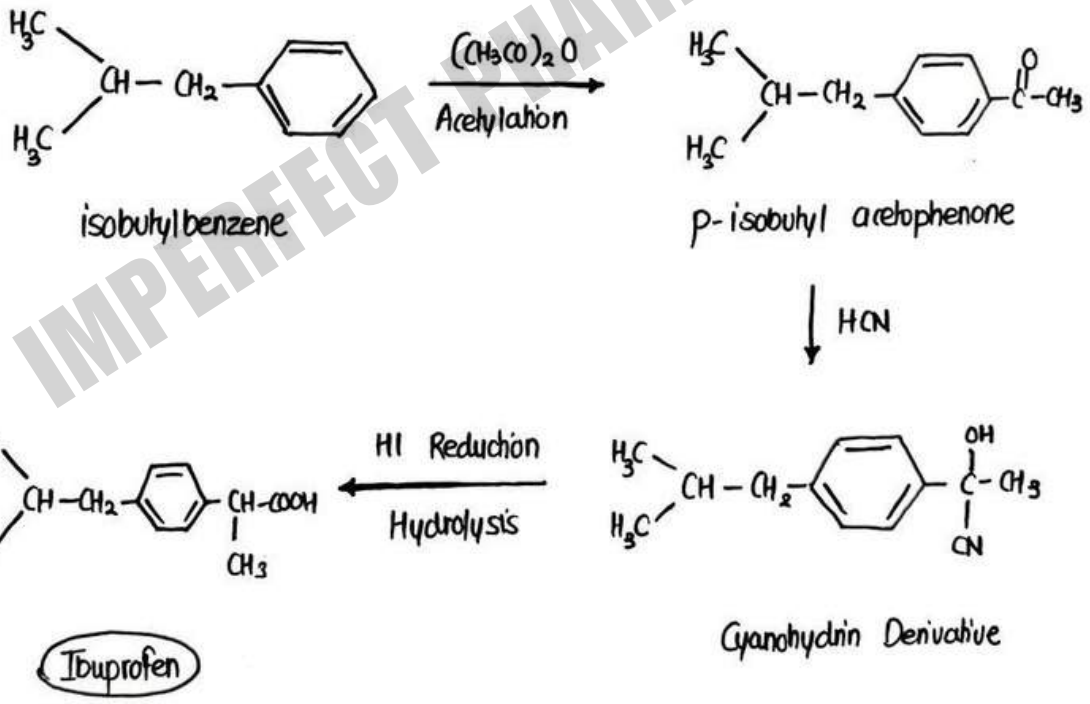
② IBUPROFEN *



MOA

Mentioned in Anti-inflammatory Agents.

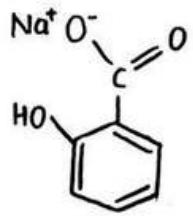
SYNTHESIS



Uses

- Reduce Fever, Pain, Inflammation

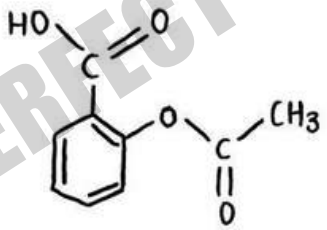
③ Sodium Salicyclate



Uses

- It is used as an analgesic & antipyretic.
- It induces apoptosis in cancer cell & necrosis.

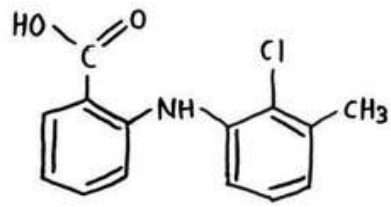
④ Aspirin



Uses

- It can be used for relieving pain & swelling in arthiritis.

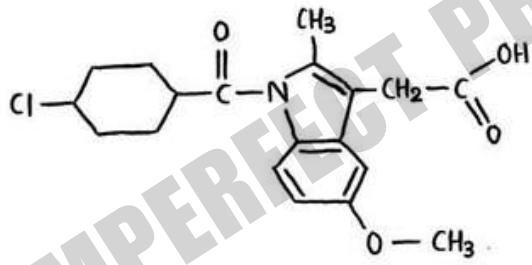
⑤ MECLOFENAMATE



Uses

- Used in rheumatoid arthritis & osteoarthritis.
- To stop excessive bleeding at mensuration time.

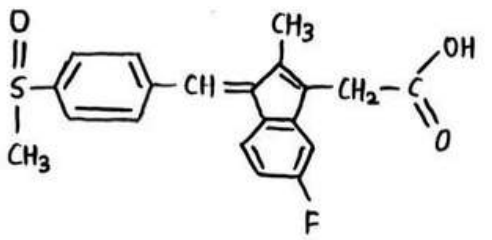
⑥ INDOMETHACIN



Uses

- Treat moderate to severe osteoarthritis, rheumatoid arthritis, gouty arthritis or ankylosing spondylitis (rare type of arthritis that causes pain and stiffness in spine).

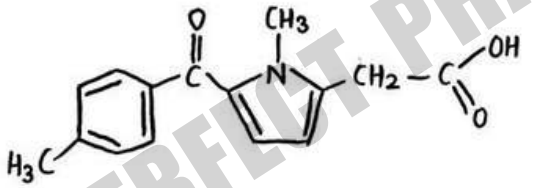
⑦ SULINDAC



Uses

- Treat pain or inflammation caused by arthiritis, ankylosing spondylitis, tendinitis, bursitis or gout.

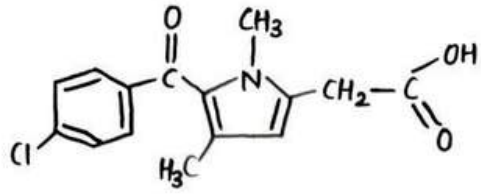
⑧ TOLMETIN



Uses

- Relieve pain, swelling, tenderness and stiffness in conditions such as osteoarthiritis and rheumatoid arthinitis, including juvenile rheumatoid arthinitis.

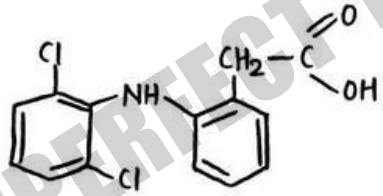
⑨ ZOMEPRIAC



Uses

- Managing mild to severe pain.
- More effective than aspirin & codiene alone.

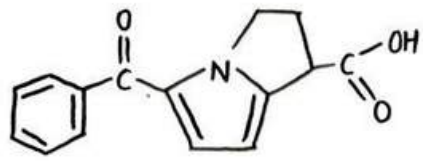
⑩ DICLOFENAC



Uses

- Used to treat pain and inflammatory disease such as gout or ankylosing spondylitis.

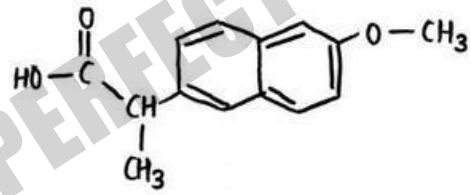
⑪ KETOROLAC



Uses

- Effective when administered with paracetamol to control pain in newborns because it does not depress respiration as do opioids.

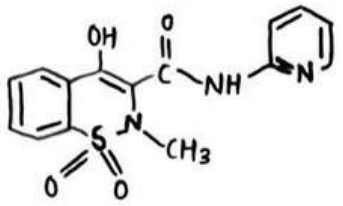
⑫ NAPROXEN



Uses

- Used for relieving mild to moderate pain & for treating primary dysmennorrhea.
- Used in rheumatoid arthiritis, osteoarthintis ankylosing spondylitis acute gout.

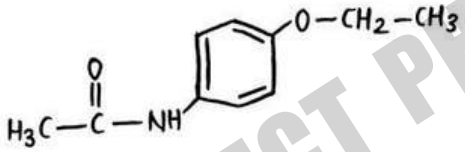
(13) PIROXICAM



Uses

- Used for treating osteoarthritis & rheumatoid arthritis.

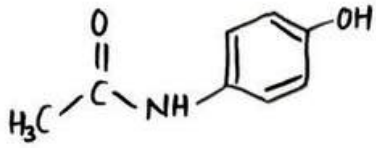
(14) PHENACETIN



Uses

- Mainly used as an analgesic.
- One of the first non-opioid analgesic.

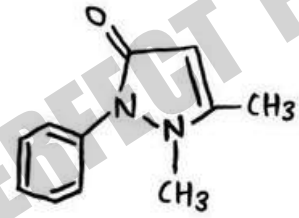
(15) ACETAMINOPHEN



Uses

- Used as first choice of drug for fever.
- It is used for temporary relief from fever, minor aches & pain.

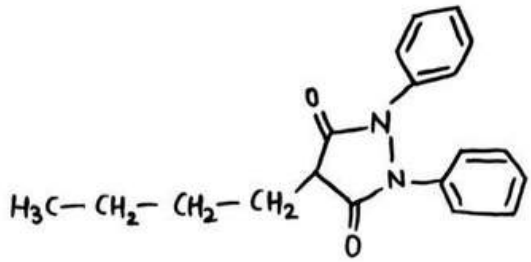
(16) ANTIPYRINE



Uses

- It is used as an analgesic & for testing the effects of drugs on lice enzymes.

⑰ PHENYLBUTAZONE



Uses

- It is used for treating backache, ankylosing spondylitis, rheumatoid arthiritis & Rieter's Syndrome.

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

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