

Pharmacology

① Anti-Epileptics

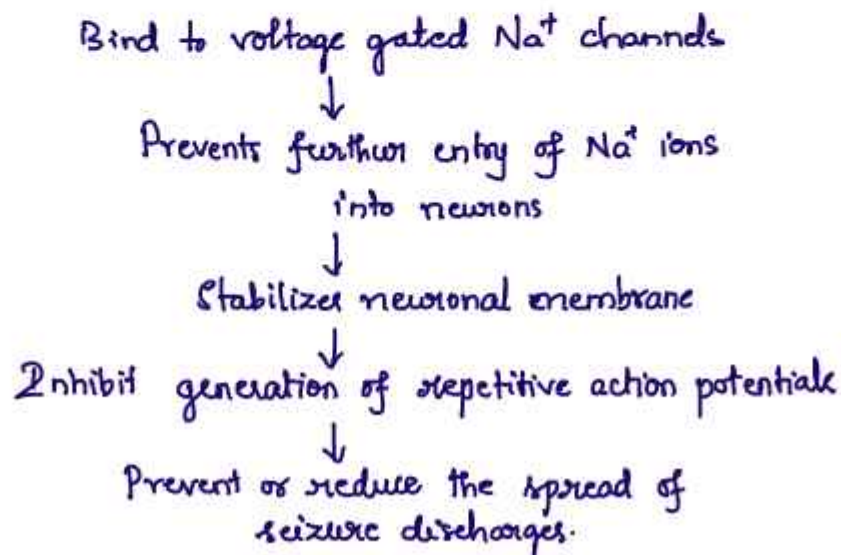
Classification :-

Anti-epileptic drugs are classified on the basis of their mechanism of action or chemical structure.

- i. Sodium channel blockers → Phenytoin ← Barbiturate
Carbamazepine } Imidostilbene
Oxcarbazepine }
Valproate ← Carboxylic acid
Lamotrigine
Lacosamide
- ii. Calcium channel blockers → Ethosuximide ← succinimide
Gabapentin } Cyclic GABA analogues
Pregabalin }
- iii. GABA enhancers → Phenobarbital
Benzodiazepines (Diazepam, Clonazepam)
Tiagabine }
Vigabatrin }
Zonisamide
- iv. Glutamate receptor blockers → Topiramate
Felbamate
- v. Other drugs → Levetiracetam
Zonisamide

Mechanism of Action :-

Phenytoin :-



Therapeutic uses :

- i. Generalized tonic-clonic seizures
- ii. Focal seizures
- iii. Status epilepticus
- iv. Seizure prophylaxis after neurosurgery or head trauma.
- v. Trigeminal neuralgia as second line of treatment.

Adverse effects :-

i. Dose related (Acute) :

- CNS effects → Dizziness, ataxia, nystagmus, sedation
- Ocular → Diplopia and blurred vision.
- GI → Epigastric pain, nausea & vomiting
- CVS → Bradycardia, cardiac arrhythmias, local vascular injury.

ii. At therapeutic levels (Chronic use) :

- Gingival Hyperplasia
- Hirsutism
- Peripheral neuropathy
- Osteomalacia
- Folate deficiency
- Teratogenicity - fetal hydantoin syndrome

iii. Idiosyncratic reactions :-

- Hypersensitivity reactions - skin rashes, Stevens Johnson syndrome, Toxic epidermal necrolysis.
- Hepatotoxicity
- Leukopenia & thrombocytopenia.

Contraindications :

- i. Hypersensitivity to phenytoin or its derivatives.
- ii. Sinus bradycardia or other heart block.
- iii. Pregnancy - teratogenic effects
- iv. Liver dysfunction.

Drug interactions :

- a) Enzyme induction → Phenytoin is a strong inducer of cytochrome P450 enzymes, it reduces the effectiveness of drugs like warfarin, oral contraceptives, corticosteroids, & cyclosporins.

- b) Displacement rxn $\rightarrow$ Phenytoin is highly protein bound & can displace other drugs (warfarin) leading to altered levels.
- c) Increased toxicity $\rightarrow$ When combined with alcohol or sedatives, phenytoin can cause excessive CNS depression.

Management of Status Epilepticus $\div$

Status epilepticus is a life threatening condition characterized by prolonged or recurrent seizures lasting more than 5 min without recovery of consciousness b/w them.

i) Initial stabilization $\div$

- Airway - ensure airway patency & provide O_2 .
- Obtain IV access.
- Monitor blood glucose.

ii) 1st line of treatment $\rightarrow$ Benzodiazepines $\left\{ \begin{array}{l} \text{Lorazepam } 4\text{mg IV} \\ \text{Diazepam } 10\text{mg IV} \end{array} \right.$

iii) 2nd " " $\rightarrow$ Phenytoin - IV / 15-20 mg/kg at a rate of 50 mg/min

Fosphenytoin - IV / 15-20 mg PE/kg

Valproate - IV / 20-40 mg/kg

Phenobarbitone sod - IV / 50-100 mg/min

iv) 3rd line of treatment $\rightarrow$ Propofol

Thiopental

Midazolam infusion.

Valproic acid / Sodium Valproate $\div$

Mof $\div$

Bind to voltage gated Na^+ channels



Prevent further entry of Na^+ ions into neuronal membrane



Stabilizes neuronal membrane



Inhibits generation of repetitive action potentials



Prevent or reduce the spread of seizure discharge.

It is a broad spectrum antiepileptic drug.

- It blocks T-type Ca^{2+} current in thalamic neurons.
- It increases activity of GABA by increasing GABA synthesis by stimulating GAD enzyme & decreased degradation of GABA by inhibiting GABA-T enzyme.

Therapeutic uses :-

- Generalized tonic clonic seizures
- Focal (partial) seizures & myoclonic seizures.
- In bipolar disorder
- In migraine prophylaxis.
- Mania.

Adverse effects :-

- GIT effects → Nausea, Vomiting, Anorexia & abdominal discomfort.
- CNS → Sedation, ataxia & tremor.
- Fulminant hepatitis
- Teratogenicity
- Skin rashes, Aplopleria & curling of hair.
- CVS → Thrombocytopenia & leukopenia.

Contraindications :-

- Liver disease
- Contraindicated in pregnancy due to a high risk of teratogenicity.
- Contraindicated in patients with mitochondrial disorders.
- Hypersensitivity to sodium valproate.

Drug interactions +

- Enzyme inhibition → Valproate inhibits Cyt P-450 enzymes, which can ↑ the levels of other drugs like lamotrigine, warfarin & phenobarbital.
- Protein binding → Valproate is highly protein bound & may displace other highly protein bound drugs such as phenytoin.
- Antiepileptics → Carbamazepine & phenytoin induce hepatic enzymes that can decrease valproate levels.
Valproate can ↑ the toxicity of phenobarbital & lamotrigine.
- Valproate interferes with clotting mechanisms
- Combining alcohol with valproate increases risk of CNS depression & hepatotoxicity.

Divalproex Sodium :-

It is a compound form of valproic acid, consisting of sodium valproate & valproic acid in a 1:1 ratio. It is available in delayed release & extended release formulations.

Advantages → GI tolerability
Better compliance
Similar mechanism like sodium valproate.

Uses → for generalized tonic clonic seizures, absence seizures & focal seizures.

Treatment of Bipolar disorder
In migraine prophylaxis.

Anti-psychotic drugs :-

Classification :-

1. Phenothiazines → Chlorpromazine
Trifluoperazine
Trifluoperazine
Thioridazine
Fluphenazine
2. Thioxanthenes → Thiothixene
3. Butyrophenones → Haloperidol, Trifluoperidol
4. Atypical anti-psychotics → Risperidone, clozapine, olanzapine, quetiapine, ziprasidone, aripiprazole.
5. Others → Lozapine
Pimozide.

Chlorpromazine and Olanzapine :-

MOA :-

- Dopamine D_2 receptor antagonist in the mesolimbic & mesocortical pathways reducing dopamine-mediated neurotransmission.
- Also antagonizes histamine (H_1), adrenergic (α_1), muscarinic (M_1) & serotonin ($5-HT_2$) receptors.

Pharmacological actions :-

- i. Antipsychotic → Controls hallucinations, delusions by blocking D_2 receptors.
- ii. Sedation → Due to H_1 receptor blockade.

- iii. Antiemetic $\rightarrow$ Via D_2 receptor blockade in the chemoreceptor trigger zone.
- iv. Hypotension $\rightarrow$ from α_1 adrenergic receptor blockade.
- vi. Anticholinergic effects $\rightarrow$ due to M_1 receptor blockade, causing dry mouth, blurred vision, etc.

Therapeutic uses $\vdash$

- i. Schizophrenia
- ii. Bipolar disorder
- iii. Nausea & Vomiting
- iv. Intractable hiccups
- v. Sedation

Adverse effects $\vdash$

- i. Extrapyramidal symptoms — Dystonia, Akathisia, Parkinsonism, Dyskinesia
- ii. Neuroleptic Malignant syndrome
- iii. Hyperprolactinemia
- iv. Sedation, Hypotension
- v. Anti-cholinergic effects $\rightarrow$ dry mouth, constipation, urinary retention, blurred vision.
- vi. Weight gain
- vii. Arrhythmias.

Contraindications $\vdash$

- i. Coma or severe CNS depression.
- ii. Bone marrow suppression.
- iii. Severe liver disease
- iv. Hypersensitivity to phenothiazines & olanzapines.
- v. Pheochromocytoma.

Drug interactions $\vdash$

- i. CNS depressants (Opioids, alcohols, benzodiazepines) — $\uparrow$ risk of sedation and respiratory depression.
- ii. Antihypertensives — Potentiation of hypotensive effects.
- iii. Anti-cholinergic drugs — additive anti-cholinergic $\vdash$
- iv. Levodopa — antagonizes its effect due to dopamine blockade
- v. QT prolonging drugs — increased risk of arrhythmias.

Antidepressants :-

Classification :-

- i. Tricyclic antidepressants → Amitriptyline Doxepine, Desipramine
Nortriptyline
Trimipramine Protriptyline
Imipramine Clomipramine
- ii. Selective serotonin (5-HT) reuptake inhibitors (SSRIs) → Fluoxetine
Fluvoxamine
Citalopram
Escitalopram
Sertraline
- iii. Serotonin & noradrenaline reuptake inhibitors (SNRIs) → Duloxetine
Venlafaxine
- iv. Atypical antidepressants → Trazodone
Bupropion
Mirtazapine
mianserin.
- v. MAO-A inhibitors → Moclobemide
Clorgyline

Selective Serotonin Reuptake Inhibitors :-

MOA :-

- SSRI inhibit the reuptake of serotonin (5-HT) into the presynaptic neuron by blocking the serotonin transporter (SERT)
- This increases serotonin levels in the synaptic cleft, enhancing serotonergic neurotransmission in the brain, which is believed to improve mood & reduce symptoms of depression.

Pharmacological actions :-

- i. Antidepressant effect → By enhancing serotonergic activity, SSRIs help alleviate symptoms of major depressive disorder
- ii. Anxiolytic effect → Effective in reducing symptoms of anxiety disorders such as generalized anxiety disorder & panic disorders.
- iii. Obsessive Compulsive disorder (OCD) → SSRIs reduce the frequency & severity of obsessions & compulsions.

- i. Other effects → SSRIs may have a role in treating other conditions like PTSD, social anxiety disorder & premenstrual dysphoric disorder (PMDD).

Therapeutic uses :-

- i. Major depressive disorder (MDD)
- ii. Generalized anxiety disorder (GAD) & Panic disorder.
- iii. Obsessive Compulsive disorder (OCD)
- iv. Post-Traumatic Stress disorder (PTSD)
- v. Premenstrual dysphoric disorder (PMDD)
- vi. Social anxiety disorder
- vii. Bulimia Nervosa.

Adverse effects +

- GI effects → Nausea, Vomiting, Diarrhoea & loss of appetite
- Sexual dysfunction → decreased libido, erectile dysfunction, delayed ejaculation anorgasmia.
- Weight gain & Weight loss
- Insomnia or sedation
- Serotonin syndrome
- Withdrawal symptoms → Abrupt discontinuation can cause dizziness, anxiety, irritability
- Increased risk of suicide.

Contraindications :-

- i. Concurrent use of MAOIs can lead to serotonin syndrome.
- ii. Hypersensitivity to SSRIs.
- iii. Patients with bipolar disorder → risk of inducing manic episodes.
- iv. Liver diseases.

Drug interactions +

- i. Monoamine oxidase inhibitors (MAOIs) — Coadministration can cause serotonin syndrome.
- ii. Triptans — used for migraines, can increase risk of serotonin syndrome.
- iii. Antiplatelet drugs & NSAIDs — increased risk of bleeding.
- iv. Warfarin — increased risk of bleeding.
- v. CYP enzyme inhibitors → Drugs like fluoxetine & fluvoxamine inhibit CYP450 enzymes, increasing risk of co-administered drugs metabolized by these enzymes.

Opioid Analgesics :-

Classification :-

- i) Natural opium alkaloids - Morphine
Codeine
Thebaine
Papaverine
Noscapine
- ii) Semisynthetic opiates → Heroin
Pholcodine
Hydromorphone
Oxycodone
- iii) Synthetic opioids → Pethidine, f
Tramadol
Methadone
Fentanyl
Alfentanil
Sufentanil
Remifentanyl
2. Opioid agonist-antagonists → Pentazocine
Butorphanol
3. Partial μ -receptor agonist & κ -receptor antagonist - Buprenorphine

Morphine :-

MOA :-

- Morphine binds to opioid receptors primarily μ receptors in CNS & GI tract.



Pharmacological actions :-

- i- Analgesia → provides relief from both acute & chronic pain by reducing the perception & emotional response to pain
Mediated mainly through μ -receptors at spinal & supraspinal sites

- ii. Euphoria → Activates brain reward system, causing a sense of well-being.
- iii. Sedation → Causes drowsiness & impairs cognitive function.
- iv. Respiratory depression → Inhibits the brainstem's response to CO_2 , reducing respiratory drive.
- v. Cough suppression → inhibits cough reflex in medulla.
- vi. Hypothermia.
- vii. Reduces GI motility, leading to constipation.
- viii. CVS effects - cause hypotension due to histamine release & vasodilation.

Therapeutic Uses:

- i. Management of pain
 { in acute pain (post operative pain)
 in chronic pain (cancer or palliative care)
- ii. Management of MI - reduce pain & anxiety & decreases O_2 demand on the heart.
- iii. Cough suppression
- iv. Pulmonary oedema

Adverse effects:

- i. Respiratory depression
- ii. Constipation
- iii. Nausea & Vomiting
- iv. Urinary retention
- v. Sedation
- vi. Tolerance
- vii. Physical dependence, withdrawal & addiction
- viii. Pruritus.

Contraindications:

- a. Conditions like asthma or COPD may be exacerbated by morphine's respiratory depressant effects.
- b. Head injury - morphine increases intra cranial pressure.
- c. Hypotension - due to morphine's potential vasodilation & histamine release, it may worsen hypotension.
- d. Liver or kidney impairment
- e. Concurrent use of other CNS depressants - enhanced sedation & respiratory depression.

Drug interactions:

- CNS depressants - benzodiazepines, alcohol - increased risk of severe respiratory depression, sedation & coma.
- MAO inhibitors - can lead to serotonin syndrome or hypotension.
- Anticholinergic drugs - additive effects, increased risk of severe constipation, urinary retention or paralytic ileus.
- SSRIs & SNRIs - Can enhance risk of serotonin syndrome.

Morphine poisoning:

Clinical features → Respiratory depression - Bradypnea, hypoxia, cyanosis
Coma
Pinpoint pupils
Hypotension & bradycardia
Cold & clammy skin
Pulmonary edema
Death - in severe cases.

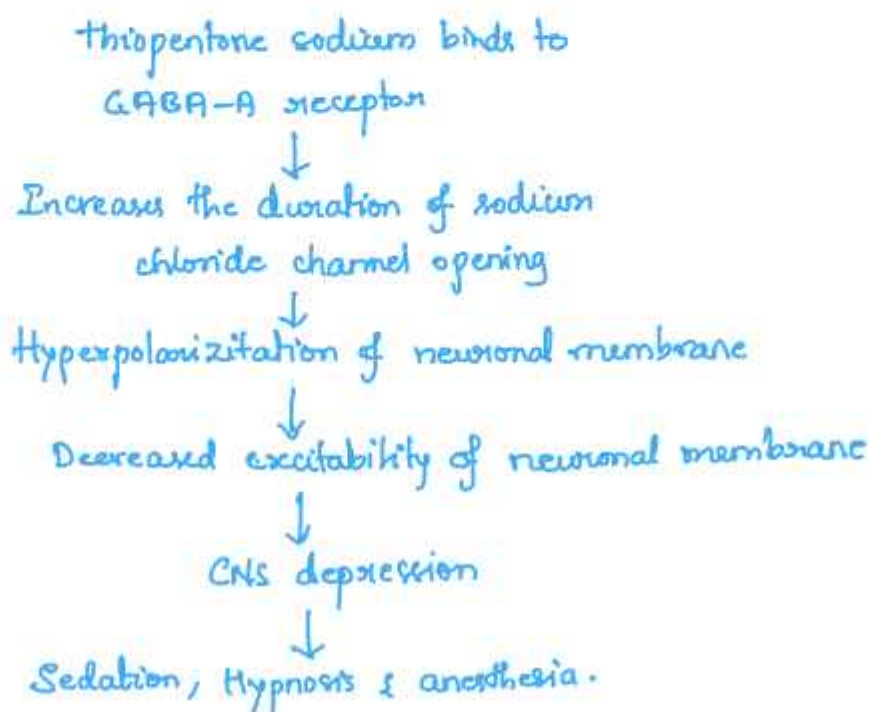
Treatment:

- Supportive care - maintain a clear airway & provide assisted ventilation if necessary. Monitor vitals.
- Naloxone (Opioid antagonist) - Administer naloxone, an opioid antagonist, to reverse the effects of morphine overdose.
Routes - IV, IM or Intranasal
Repeated dosing is required as naloxone has shorter half life than morphine.
- Activated charcoal - used if the overdose is recent to reduce further absorption of morphine from the GI tract.
- Oxygen therapy to counteract respiratory depression.
- 24-hr observation to see any rebound respiratory depression.

⊕ Thiopentone Sodium :-

MOA :-

- Thiopentone sodium is a short acting barbiturate. Its mechanism of action involves enhancing the activity of inhibitory neurotransmitter GABA at the GABA-A receptor.



Pharmacological actions :-

- CNS depressant → induces sedation, hypnosis & anaesthesia
- Anticonvulsant → at subanaesthetic doses, it can reduce neuronal excitability & used in managing seizures.
- Decreases intracranial pressure → it reduces cerebral metabolism & O_2 consumption, which in turn ↓ ICP.
- Causes peripheral vasodilation → that leads to hypotension.
- Respiratory depression.

Therapeutic uses :-

- i) Induction of Anaesthesia.
- ii) In short surgical procedures.
- iii) In status epilepticus.
- iv) Reduction of ICP & to maintain cerebral perfusion during certain brain surgeries.

Adverse effects :-

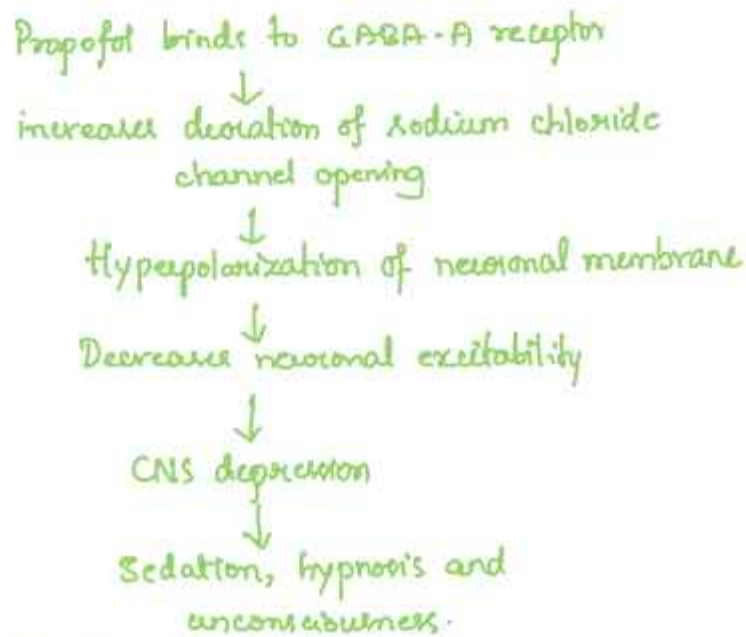
- i) Respiratory depression
- ii) Hypotension & Myocardial depression
- iii) Allergic rxns.
- iv) Laryngospasm & Bronchospasm
- v) Thrombophlebitis
- vi) Hangover effect.

② Propofol +

MOA +

Its mechanism of action is similar to that of thiopentone sodium.

Propofol increases activity of inhibitory neurotransmitter GABA at the GABA-A receptor.



Pharmacological actions :-

- i. Sedation & Hypnosis → Propofol produces rapid & profound sedation & hypnosis due to its action on the GABA-A receptor.
Rapid onset of action
short duration of action.
- ii. Anxiolytic & Amnesic effects → Causes amnesia & anxiolysis (reduce anxiety)
- iii. Antiemetic properties → Reduce post operative nausea & vomiting.
- iv. Anticonvulsant action → at higher doses, propofol shows anticonvulsant action.
- v. Vasodilation & Myocardial depression
- vi. Respiratory depression.

Therapeutic uses :-

- i. Induction of anaesthesia.

- ii. Maintenance of anaesthesia.
- iii. Conscious sedation — during colonoscopy, laryngoscopy, bronchoscopy.
- iv. Anti-nausea
- v. Sedation in ICU.

Adverse effects :-

- i. Cardiovascular depression
 ← hypotension
 bradycardia
 Reduced cardiac output.
- ii. Respiratory depression.
- iii. Propofol infusion syndrome
- iv. Pain on injection.
- v. Hypertriglyceridaemia
- vi. Allergic reactions.

Ketamine :-

MOA :-

Ketamine primarily acts as an N-methyl-D-aspartate (NMDA) receptor antagonist.

Ketamine inhibits NMDA
receptor

↓
Reduces excitatory neurotransmitter
glutamate's action in brain

↓
Altered sensory perception, pain relief & dissociation

⇒ Ketamine modulates various neurotransmitters such as dopamine & serotonin, contributing to its mood enhancing effects.

Pharmacological actions :-

- i) Dissociative anaesthesia → disconnects brain from sensory input, producing unconsciousness, amnesia & analgesia.
- ii) Acts as analgesic
- iii) Acts as antidepressant
- iv) Sympathomimetic effects — increasing heart rate & BP.

Therapeutic uses :-

- i) Anaesthesia — induction & maintenance of anaesthesia
- ii) Pain management — pain during trauma, chronic pain
- iii) Sedation in ICU
- iv) Status asthmaticus & Bronchospasm

v) Treatment resistant depression.

Adverse effects :-

i) CVS $\rightarrow$ increase in heart rate, BP & cardiac output.

ii) Psychologic effects $\rightarrow$ Hallucinations, vivid dreams, delirium

iii) Cognitive impairment

iv) Respiratory depression

v) Renal effects $\rightarrow$ Ketamine induced cystitis, urinary frequency, urgency & bladder pain

Isoflurane :-

MOA :-



Pharmacological actions :-

- i. CNS effects $\rightarrow$ dose dependent depression of CVS, leading to unconsciousness & analgesia
it also causes amnesia, & inhibits motor reflexes.
- ii. Respiratory system $\rightarrow$ Depresses respiratory drive
Reduction in tidal volume
& increase in respiratory rate.
- iii. Cardiovascular system $\rightarrow$ Decreases blood pressure.
- iv. Skeletal muscle relaxant.

Therapeutic uses :-

- i. Maintenance of general anesthesia
- ii. Inhalation anesthesia in various procedures.
- iii. In neurosurgical procedures - has minimal effect on cerebral blood flow at lower doses.

Adverse effects:

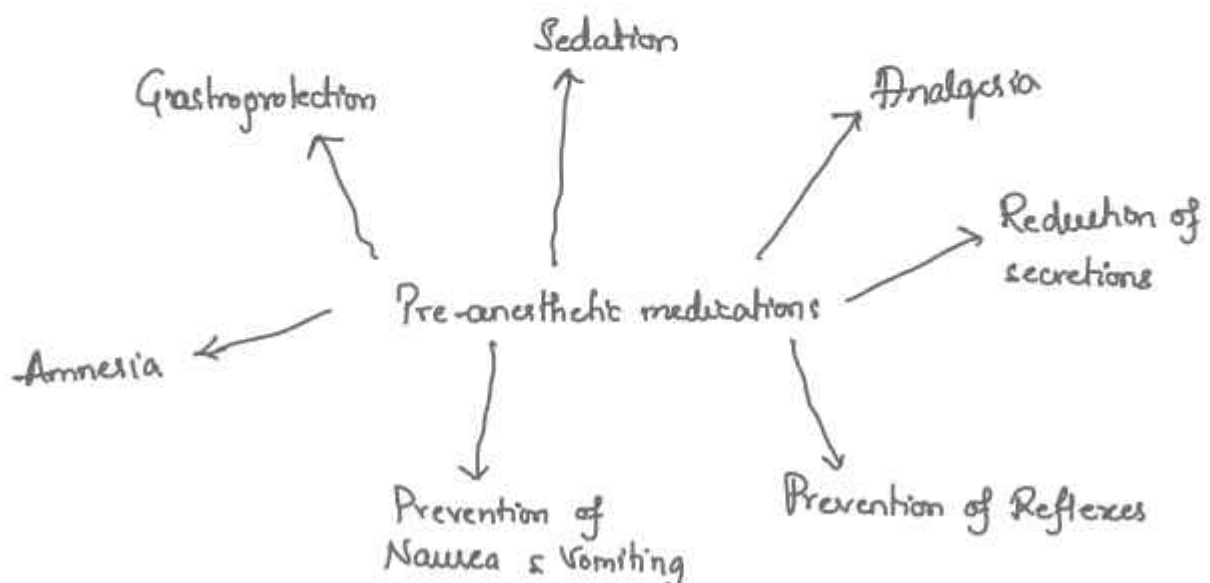
- i. Respiratory depression — hypoventilation.
- ii. Hypotension
- iii. Malignant hyperthermia.
- iv. Nephrotoxicity
- v. Post operative nausea & vomiting.

Pre-anesthetic medications:

MOA:

- Sedatives (Benzodiazepines, Barbiturates) → Enhances the effect of GABA at the GABA-A receptors, leading to CNS depression & sedation.
- Opioids (Morphine, Fentanyl) → Bind to opioid receptors in the CNS & peripheral tissues, producing sedation & analgesia by inhibiting neurotransmitter release.
- Anticholinergics (Atropine, Glycopyrrolate) → Blocks muscarinic acetylcholine receptors, reducing secretions in respiratory tract & GI tract & prevents vagal induced bradycardia.
- Antiemetics (Ondansetron, Metoclopramide) → Blocks 5HT₃ & serotonin receptors or dopamine (D₂) receptors, reducing nausea & vomiting by acting on CTZ & vomiting centre.
- Antihistamines (Diphenhydramine, Promethazine) → Blocks Histamine H₁ receptors, providing sedation & reducing allergic signs.

Pharmacological actions:



Therapeutic uses :-

- i) Anxiolysis
- ii) Post-operative pain relief
- iii) Prevention of Bradycardia
- iv) Reduction of secretions.
- v) Nausea & Vomiting prophylaxis
- vi) Sedation & Amnesia
- vii) Prevention of Aspiration.

Adverse effects :-

- i) Sedation & drowsiness
- ii) Respiratory depression
- iii) Cognitive impairment
- iv) Nausea & Vomiting
- v) Constipation
- vi) Hypotension
- vii) Dry mouth, blurred vision, tachycardia, urinary retention
- viii) Headache & Dizziness
- ix) GI irritation & ulceration
- x) Hepatotoxicity.

Disulfiram :-

MOA :-

- Disulfiram, inhibits aldehyde dehydrogenase (ALDH), an enzyme responsible for metabolizing acetaldehyde, a toxic metabolite of alcohol.
- When alcohol is consumed, ethanol is 1st metabolized by ADH into acetaldehyde, which is normally further broken down by ALDH into acetate, a non-toxic substance.
- By inhibiting ALDH, disulfiram leads to the accumulation of acetaldehyde in the bloodstream, causing unpleasant effects.

Pharmacological actions :-

- i. Inhibition of ALDH — causing symptoms like flushing, nausea, vomiting, & palpitations.
- ii. Aversion therapy — disulfiram helps in behaviour modification by conditioning the patient to avoid alcohol.

Therapeutic uses :-

- i. Alcohol use disorder (AUD) → Disulfiram is used as an adjunct in long term treatment of alcoholism.
- ii. In cocaine dependence

Adverse effects :-

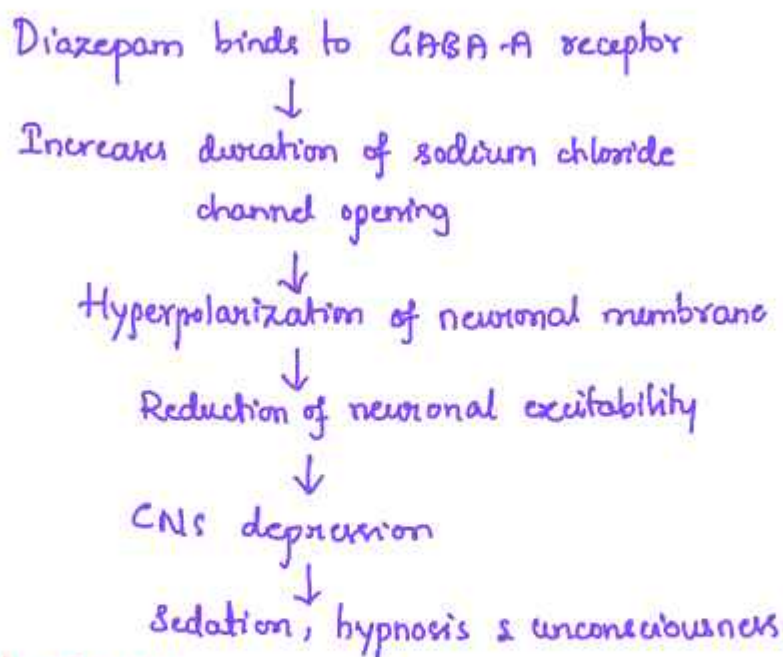
- i. Drowsiness and fatigue
 - ii. Head ache
 - iii. Metallic or garlic like taste
 - iv. Skin rash
- } Common adverse effects

- i. Flushing, throbbing head ache
 - ii. Nausea & Vomiting
 - iii. Hypotension, palpitations, tachycardia
 - iv. Blurred vision & dizziness
- } Disulfiram-alcohol rxn.

- i. Hepatotoxicity
 - ii. peripheral neuropathy
 - iii. Depression & psychosis
 - iv. Dermatitis
- } severe adverse effects.

Diazepam :-

MOA :-



Pharmacological actions :-

- Anxiolytic → Reduces anxiety
- Sedative / Hypnotic → induces sedation & sleep
- Acts as anticonvulsant
- Acts as muscle relaxant - reduces muscle spasm.

- Cause retrograde amnesia.

Therapeutic uses :

- Anxiety disorders
- Seizures
- Muscle spasm
- Alcohol withdrawal syndrome
- Induce sedation or anesthesia.

Adverse effects :

- CNS depression — drowsiness, dizziness, fatigue & ataxia
- Cognitive impairment
- Dependence and Withdrawal
- Respiratory depression.
- Paradoxical reactions.

Advantages of Diazepam over Phenobarbitone :

- Faster onset of action
- Less sedation
- Lower risk of respiratory depression
- Wide therapeutic index.
- Less tolerance & dependence

Phenobarbitone :

MOA :

Phenobarbitone binds to GABA-A receptors

↓
Increases duration of sodium channel opening

↓
Hyperpolarization of neuronal membrane

↓
Reduces neuronal excitability

↓
CNS depression.

Pharmacological actions :

- CNS depression — produces dose dependent depression of CNS activity, from sedation & hypnosis at low doses to anesthesia & coma at high doses.

- ii. Acts as anticonvulsant
- iii. Sedative-Hypnotic
- iv. Inducer of Cytochrome P450 enzymes.

Therapeutic uses:

- i) Treatment of generalized tonic clonic seizures & partial seizures.
- ii) Status Epilepticus.
- iii) Sedation & Preoperative Anesthesia.
- iv) Management of Hyperbilirubinemia in Neonates.

Adverse effects:

- i) CNS depression — causes drowsiness, lethargy & impaired cognitive function.
- ii) Respiratory depression.
- iii) Dependence & withdrawal.
- iv) Paradoxical excitement
- v) Hepatic enzyme induction
- vi) Tolerance.

Zopiclone :-

MOA :-

- ⇒ Zopiclone binds to the benzodiazepine site of the GABA-A receptor, but it is chemically different from benzodiazepines.
- ⇒ By modulating the GABA-A receptor, it increases the inhibitory effects of GABA, leading to sedation, muscle relaxation, & anxiolysis.
- ⇒ Zopiclone is more selective for receptors involved in sleep regulation, leading to fewer anxiolytic & muscle relaxant effects than benzodiazepines like diazepam.

Pharmacological actions :-

- Hypnotic effect → promotes sleep by increasing the action of GABA, helping to shorten the time to fall asleep & increase total sleep duration.
- Sedative effect
- Anxiolytic → reduces anxiety
- Muscle relaxant → relaxes muscle spasms.

Therapeutic uses:

- Treatment of Insomnia

- Sleep disorders.

Adverse effects :-

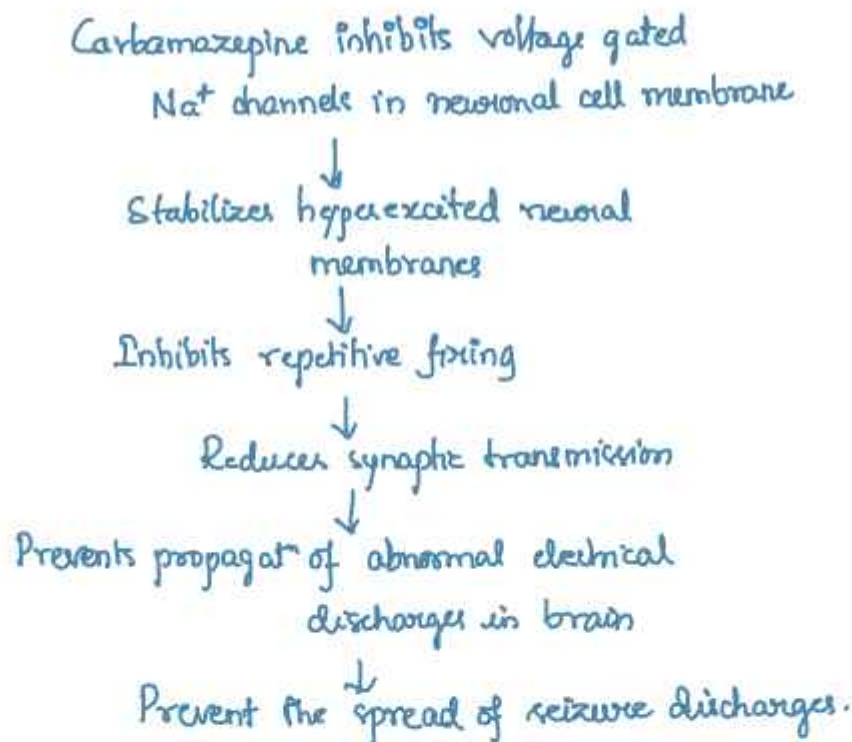
- Drowsiness, dry mouth, dizziness, bitter or metallic taste → more common.
- Headache, nausea, vomiting, memory impairment → less common
- Respiratory depression & parasomnias (Rare but severe)

Advantages of Zopiclone over Diazepam :-

- i) Lower risk of dependence and tolerance
- ii) Selective sedative effect.
- iii) Shorter half life
- iv) Fewer drug interactions
- v) Better tolerance in elderly patients

Carbamazepine +

MOA :-



Pharmacological actions :-

- i) Anticonvulsant → prevents the spread of seizure activity by stabilizing neuronal membrane.
More effective in generalized tonic clonic seizures & partial seizures
- ii) Mood stabilizer → Management of bipolar disorder, particularly in controlling manic episodes.

iii) Analgesic for neuropathic pain.

Therapeutic uses

- i) Epilepsy — partial seizures
generalized tonic clonic seizures
Mixed seizures
- ii) Bipolar disorder
- iii) Trigeminal Neuralgia
- iv) Neuropathic pain.

Adverse effects

- i. CNS effects → drowsiness, dizziness, vertigo, ataxia
Cognitive impairment, blurred vision.
- ii. GIT effects → Nausea, vomiting, constipation
- iii. CVS → aplastic anemia, thrombocytopenia, arrhythmias
- iv. Skin rashes
- v. Hepatotoxicity
- vi. Hyponatremia.
- vii. Teratogenicity.

Newer antiepileptic drugs:

Lamotrigine
Levetiracetam
Topiramate
Zonisamide
Lacosamide
Rufinamide
Perampanel
Brivaracetam

MOA — Blocks voltage gated sodium channels and T-type calcium channels, inhibiting the release of excitatory neurotransmitters like glutamate.

Pharmacological action

Reduces seizure propagation
Anticonvulsant action
Mood stabilization.

Therapeutic uses

- i. Generalized tonic clonic seizures
- ii. Partial seizures.
- iii. Migraine prophylaxis
- iv. Lennox-Gastaut syndrome.

Adverse effects

Drowsiness, dizziness, nausea, vomiting, kidney stones, anorexia, arrhythmias, headache, weight gain -- etc

Seligiline :

MOA :

- ⇒ Seligiline is a selective & irreversible inhibitor of monoamine oxidase type B (MAO-B), an enzyme responsible for the breakdown of dopamine in the brain.
- ⇒ By inhibiting MAO-B, seligiline increases dopamine availability, especially in basal ganglia.
- ⇒ At high doses, seligiline also inhibits MAO-A, which breaks down serotonin & noradrenaline.

Pharmacological actions :

- Increases dopamine levels — reduces motor symptoms of Parkinson's disease such as bradykinesia & rigidity.
- Neuroprotective effects → seligiline has antioxidant properties, hence it protects dopaminergic neurons from oxidative stress.
- Antidepressant effects → seligiline can increase serotonin & norepinephrine levels, leading to antidepressant effects.

Therapeutic uses :

- Parkinson's disease — seligiline is used as adjunct therapy to levodopa / carbidopa in the treatment of Parkinson's disease.
- Transdermal seligiline patch used for treating depression.
- Off label use — occasionally used for Alzheimer's disease or cognitive disorders.

Adverse effects :

- Nausea
- Insomnia
- Orthostatic hypotension
- Hallucinations & confusion
- Serotonin syndrome
- Dry mouth
- Hypertensive crisis

Drug induced Parkinsonism and its management :

Drug induced parkinsonism refers to development of Parkinson's like symptoms (tremor, rigidity, bradykinesia) as a side effect of certain drugs.

It is caused by irreversible blockage of depletion of dopamine in the brain, mainly in basal ganglia.

Cause +

Antipsychotic drugs $\left\{ \begin{array}{l} \text{typical} - \text{Chlorpromazine, haloperidol} \\ \text{atypical} - \text{olanzapine, risperidone} \end{array} \right.$

Antiemetic drugs — Metoclopramide, Prochlorperazine

Mood stabilizers — Lithium

Antiepileptic drugs — Sodium valproate

Antidepressant a — SSRIs & SNRIs

Symptoms +

- i. Bradykinesia
- ii. Rigidity — lead pipe rigidity
- iii. Tremor — resting tremor.
- iv. Postural instability
- v. Facial masking — reduced facial expressions.

Management +

a) Discontinuation or dose reduction of the causative drug

first line treatment is stopping the offending drug or reducing its dose, which often leads to gradual improvement of symptoms.

b) Switching to an atypical antipsychotic $\rightarrow$ like clozapine or quetiapine have a lower risk of causing parkinsonism.

c) Dopaminergic agents $\rightarrow$ Amantadine $\rightarrow$ dopamine agonist
Levodopa $\rightarrow$ avoided in DIP

d) Anticholinergic drugs $\rightarrow$ Benztropine
Trihexyphenidyl $\left. \vphantom{\begin{array}{l} \text{Benztropine} \\ \text{Trihexyphenidyl} \end{array}} \right\} \text{Manage tremor \& rigidity}$

e) Monitoring & supportive care $\rightarrow$ physical therapy & patient education.

Importance of centrally acting anti cholinergics in Parkinsonism :-

$\Rightarrow$ In Parkinson's disease, there is a deficiency of dopamine in the nigrostriatal pathway of the brain.

$\Rightarrow$ This leads to imbalance b/w dopamine & acetylcholine activity.

$\Rightarrow$ Normally dopamine inhibits Ach release in this region, so when dopamine

levels are reduced, the activity of ACh becomes excessive.

This cholinergic overactivity contributes to several Parkinson's symptoms.

- Tremors - resting tremors.
- Rigidity & Bradykinesia.

MOA:

Centrally acting anticholinergics, such as benztropine, & trihexyphenidyl, work by blocking α muscarinic acetylcholine receptors in the brain, mainly in basal ganglia.

By reducing ACh activity, they help to restore the balance b/w dopamine & ACh, improving motor symptoms.

Therapeutic uses:

- i) Reduction of Tremors
- ii) Improvement of Rigidity & Bradykinesia
- iii) Adjunctive therapy

Adverse effects:

- i) Cognitive impairment
- ii) Dry mouth, constipation & urinary retention
- iii) Blurred vision
- iv) Exacerbation of glaucoma
- v) Sedation & drowsiness.

Atypical antipsychotics:

MOA:

Olanzapine, Aripiprazole, Ziprasidone.
Clozapine
Quetiapine
Risperidone

- i) Dopamine D_2 Receptor Antagonism $\rightarrow$ Atypical antipsychotics block D_2 dopamine receptors, which helps reduce positive symptoms of schizophrenia (hallucinations, delusions).
- ii) 5-HT $_2A$ Receptor Antagonism $\rightarrow$ They also block 5HT $_2A$ receptors. This action modulates dopamine release in diff regions of the brain, reducing -ve symptoms of schizophrenia (blunted effect, social withdrawal), improving cognition.
- iii) 5HT $1A$ Agonism - partially activate 5HT $1A$ receptors, improving mood & cognitive effects.

Pharmacological actions:

- Antipsychotic effects → reduce +ve symptoms of Schizophrenia (delusions & hallucinations)
- Mood stabilization → atypical antipsychotics like quetiapine, olanzapine, aripiprazole are used for mood stabilization in bipolar disorder & adjunctive therapy for depression.
- Sedation → Useful for agitation & insomnia.

Therapeutic uses:

- First line treatment for Schizophrenia
- Treatment of Bipolar disorder.
- In adjunct therapy of major depressive disorder (MDD)
- To control agitation & aggression in psychiatric emergencies.

Adverse effects:

- Weight gain
- Dyslipidemia
- Insulin resistance
- Sedation — drowsiness & fatigue.
- Increased prolactin levels — galactorrhea, gynaecomastia & menstrual irregularities.
- Prolongation of QT interval (arrhythmias), Orthostatic hypotension.
- Neuroleptic Malignant syndrome
- Agranulocytosis.

Lithium:

MOA:

- Modulation of neurotransmitter activity — Lithium affects the balance of excitatory (glutamate) & inhibitory (GABA) neurotransmitters helping to stabilize mood.
- Lithium inhibits enzymes involved in the phosphoinositide pathway, such as inositol monophosphatase, this results in decreased cellular responses.
- Neuroprotection & Neuroplasticity — Lithium promotes neurogenesis & protects neurons from damage by increasing levels of brain derived neurotrophic factor (BDNF)

d) Lithium inhibits glycogen synthase kinase-3, which may influence circadian rhythm, synaptic plasticity & cellular survival.

Pharmacological actions:

- a) Mood stabilization
- b) Antisuiicidal effect
- c) Neuroprotective effects.

Therapeutic uses:

- a) Bipolar disorder
- b) Major depressive disorder
- c) Cluster headaches
- d) Schizoaffective disorder.
- e) Augmentation therapy.

Adverse effects:

- a) Nausea, vomiting & diarrhoea
- b) Tremors
- c) Nephrogenic diabetes insipidus
- d) Hypothyroidism & Wt gain
- e) Confusion, ataxia, slurred speech & seizures.
- f) Arrhythmias
- g) Teratogenic effects.

Haloperidol : typical antipsychotic drug, dopamine D₂ receptor antagonist

MOA:

Haloperidol blocks dopamine D₂ receptors in brain



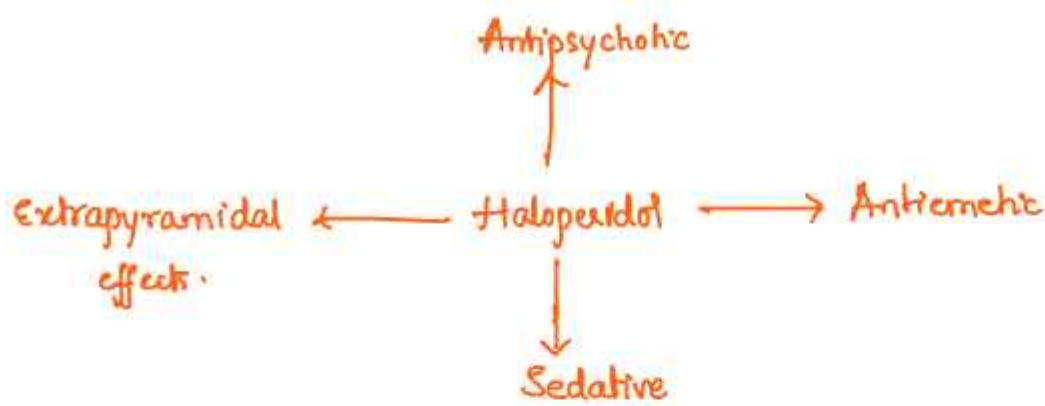
Reduce dopaminergic transmission



Alleviate symptoms of psychosis, such as delusions & hallucinations.

⇒ It also has effects on other receptors such as α -adrenergic, histaminergic (CH₁) and muscarinic receptors to a lesser extent.

Pharmacological actions:



Therapeutic uses:

- i) Schizophrenia
- ii) Acute psychosis & Bipolar disorder.
- iii) Delirium
- iv) Tourette syndrome
- v) Agitation in Dementia
- vi) Nausea & vomiting - management.

Adverse effects:

- i) Extrapyramidal symptoms — acute dystonia
Akathisia
Parkinsonism
Tardive dyskinesia.
- ii) Neuroleptic malignant syndrome
- iii) Sedation
- iv) Orthostatic hypotension
- v) Prolonged QT interval
- vi) Dry mouth, constipation, urinary retention & blurred vision.
- vii) Hyperprolactinemia
- viii) Seizures

Tricyclic Antidepressants:

MOA:

TCA's inhibit the reuptake of 2 neurotransmitters i) serotonin (5HT) and ii) norepinephrine (NE) at the presynaptic nerve terminals

↓
Increased conc of these neurotransmitters in the synaptic cleft

↓
Enhancing effect on mood regulation.

Also blocks histamine H_1 receptors, $\alpha-1$ adrenergic receptors, muscarinic ACh receptors.

Pharmacological actions +

- i) Antidepressant effect $\rightarrow$ TCA increases levels of norepinephrine & serotonin in the brain, improving mood and anxiety.
- ii) Sedative effects $\rightarrow$ due to histamine receptor antagonism, some TCA are useful for their sedative properties.
- iii) Anticholinergic effects $\rightarrow$ due to muscarinic receptor antagonism
- iv) Antihypertensive " $\rightarrow$ by blocking α_1 adrenergic receptors.

Therapeutic uses :-

- i) Major depressive disorder (MDD)
- ii) Generalized anxiety disorder (GAD) & Obsessive compulsive disorder (OCD).
- iii) Neuropathic pain
- iv) Migraine prophylaxis.
- v) Insomnia.

Adverse effects :-

- i) Dry mouth, blurred vision, constipation, urinary retention, tachycardia.
- ii) Sedation — drowsiness & fatigue
- iii) Orthostatic hypotension, QT prolongation or arrhythmias.
- iv) Weight gain
- v) Reduced libido, erectile dysfunction & delayed orgasm
- vi) Seizures.

Serotonin - Norepinephrine reuptake inhibitors (SNRIs) :-

Ex:- Venlafaxine, Duloxetine, Desvenlafaxine, Levomilnacipran.

MOA :-

SNRIs inhibits transporters SERT & NET at presynaptic neurons.



SNRIs block the reuptake of both serotonin (5-HT) and norepinephrine (NE)



Increased synaptic conc of serotonin (5-HT) & norepinephrine (NE)



Increased neurotransmission

↓
Improves mood, reducing anxiety
& alleviates pain

Pharmacological actions:

- i) Increase in serotonin & norepinephrine levels — that enhances mood, focus & energy levels.
- ii) Mood stabilization — SNRIs reduce depressive symptoms by regulating neurotransmitter balance.
- iii) Analgesic effects — in treating chronic pain conditions like fibromyalgia & neuropathic pain.

Therapeutic uses:

- i) Major depressive disorder and Generalized anxiety disorder (GAD)
- ii) Panic disorder & social anxiety disorder.
- iii) Treatment of fibromyalgia, neuropathic pain & musculoskeletal pain.
- iv) Attention deficit Hyperactivity disorder.

Adverse effects:

- i) Nausea & Vomiting
- ii) Headache, Dizziness & Dry mouth.
- iii) Insomnia.
- iv) Sexual dysfunction
- v) HTN
- vi) Sweating
- vii) Withdrawal symptoms — dizziness, irritability, fatigue or brain zaps.

Atypical antidepressants:

MOA:

- Bupropion → inhibits the reuptake of norepinephrine & dopamine (NDRI). It increases availability of these neurotransmitters in the brain, improving mood and energy levels.
- Mirtazapine → acts as an antagonist at α_2 -adrenergic receptors & serotonin receptors ($5HT_2$ & $5HT_3$), that enhances noradrenergic & serotonergic transmission.
- Trazodone → blocks serotonin $5HT_2$ receptors & inhibits serotonin reuptake.

Pharmacological actions:

Bupropion → improves mood and energy without sexual dysfunction or wt gain.
Mirtazapine → it has potent sedative & appetite stimulating effects.
Trazodone → provides antidepressant & anxiolytic effects

Therapeutic uses :-

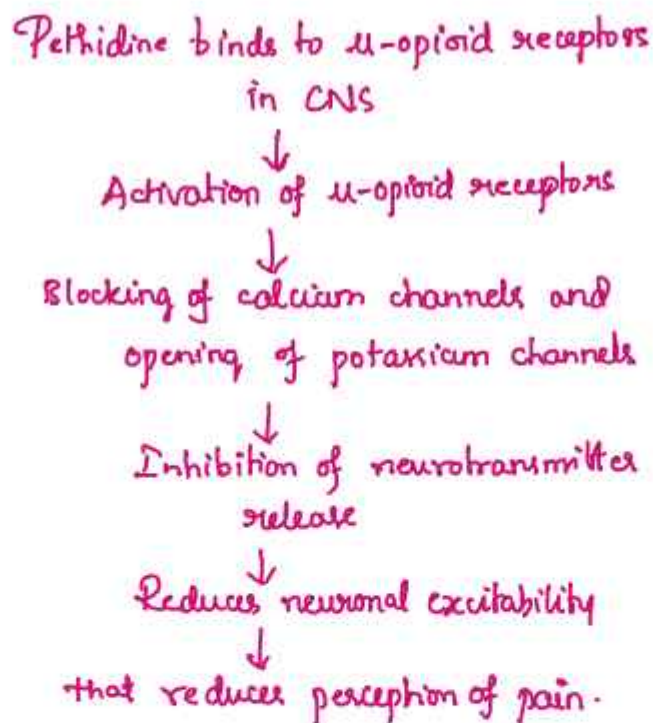
- i) Major depressive disorder (MDD) & smoking cessation.
- ii) Insomnia
- iii) In sexual dysfunction.

Adverse effects :-

- i) Dry mouth, insomnia, increased sweating, agitation
- ii) Seizures, sedation & HTN
- iii) Dizziness & priapism
- iv) Nausea, vomiting & diarrhoea.
- v) Headache & orthostatic hypotension.

Pethidine :-

MOA :-



Pharmacological actions :-

- i) Analgesia → it is effective in relieving moderate to severe pain by altering the perception and emotional response to pain.
- ii) Sedation → Pethidine induces drowsiness or sedation.
- iii) Euphoria → Pethidine produces sense of well being.

iv) Antispasmodic → due to structural similarity to atropine, pethidine has antispasmodic effect i.e. it relaxes smooth muscles in GI tract & biliary tract.

Therapeutic uses:-

i) Acute pain → short term relief of moderate to severe pain, such as post-surgical pain or during labour.

ii) Obstetric pain

iii) Pre-anesthesia

iv) Biliary colic — due to its antispasmodic effects.

Adverse effects:-

CNS → sedation, confusion, delirium and seizures.

GI → Nausea, vomiting and constipation.

CVS → Tachycardia & Hypotension.

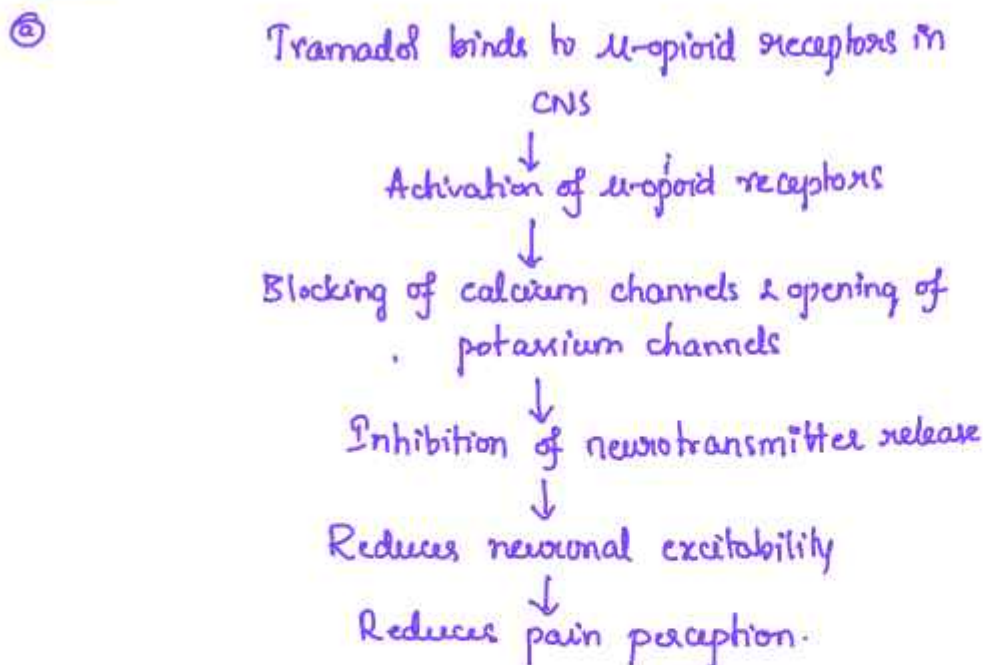
RI → Respiratory depression

Serotonin syndrome

Renal & hepatic toxicity.

Tramadol:-

MOA:-



② Tramadol also inhibits the reuptake of serotonin & norepinephrine, neurotransmitters involved in the descending modulation of pain.

This dual mechanisms enhances its analgesic effect.

Pharmacological actions:-

- Analgesia → tramadol provides pain relief by reducing pain signal transmission through opioid receptor activation & by modulating pain pathways via its effects on serotonin & norepinephrine reuptake.
- Mood elevation → mild antidepressant effects.

Therapeutic uses:

- Moderate to moderately severe pain — tramadol used in
 - post surgical pain
 - osteoarthritis
 - chronic pain
- Neuropathic pain
- Fibromyalgia

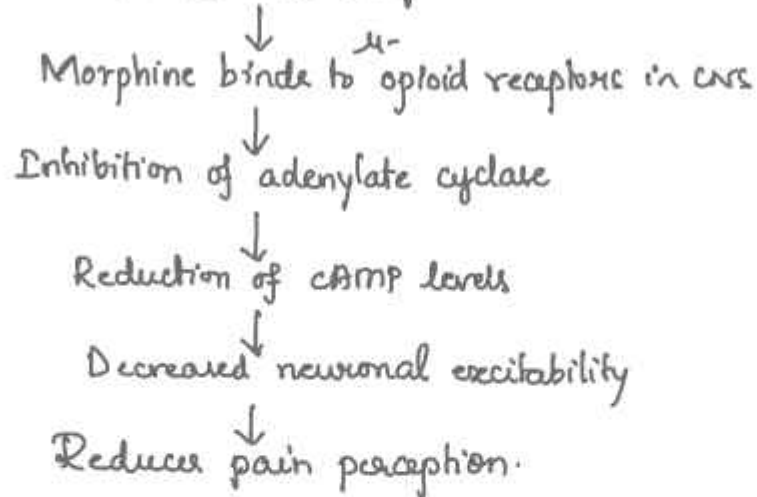
Adverse effects:

- Nausea & Constipation
- Headache & dizziness
- Drowsiness
- Seizures and serotonin syndrome
- Respiratory depression.

Codeine

MOA:

Codeine metabolized in the liver by the enzyme CYP2D6 into morphine



Pharmacological actions:

- Analgesic → Codeine has mild to moderate analgesic effects due to its opioid's action.
- Antitussive effect → cough suppression by suppressing the cough reflex.
- Sedative → mild sedative effect due to CNS depression.

Therapeutic uses:

- Management of pain
- Cough suppression — particularly in conditions like bronchitis.

ii) Treatment of diarrhoea $\rightarrow$ codeine reduces GI motility

Adverse effects:-

- i) Sedation, dizziness, confusion & euphoria.
- ii) Nausea, vomiting & constipation
- iii) Allergic rxns
- iv) Respiratory depression
- v) Hypotension & bradycardia

Opioid antagonists:-

MOA:-

Opioid antagonists have a high affinity for opioid receptors (μ , κ , & δ receptors) in CNS & peripheral tissues.

Opioid antagonists competitively inhibits opioid agonists, such as morphine or heroin by binding to these receptors without activating them.

This prevents opioid induced effects like euphoria, analgesia & respiratory depression.

Ex: Naloxone & Naltrexone.

Pharmacological actions:-

- i) Reversal of opioid effects like respiratory depression, sedation & hypotension.
- ii) Blocking euphoria & analgesia.
- iii) Activation of withdrawal symptoms.

Therapeutic uses:-

- i) Treatment of opioid overdose — naloxone is used
- ii) Prevention of opioid relapse — naltrexone is used.
- iii) Alcohol use disorder.

Adverse effects:-

- i) Nausea, vomiting & constipation
- ii) Anxiety, agitation, sweating, muscle cramps & tachycardia.
- iii) HTN, tachycardia & arrhythmias
- iv) Liver toxicity.
- v) Swelling or pain at injected site.

① Name the drugs used for Mania?

Drugs used for mania

- mood stabilizers
- antipsychotics
- benzodiazepines (occasionally)

Mood stabilizers

- Lithium — gold standard — acute mania.
- Valproate — acute mania
- Carbamazepine — anticonvulsant used as mood stabilizer
- Lamotrigine

Atypical antipsychotics →

- Olanzapine
- Risperidone
- Quetiapine
- Ziprasidone
- Aripiprazole

Typical antipsychotics → Haloperidol.

Benzodiazepines → Lorazepam, clonazepam

② Cognitive enhancers :-

Cholinesterase inhibitors →

- Donepezil
- Rivastigmine
- Galantamine

NMDA receptor antagonists → Memantine

Methylphenidate

Amphetamines

Nutraceuticals → Piracetam

Omega-3 fatty acids

Caffeine

Dopaminergic agents →

- d-dopa
- Seligiline.

③ CNS stimulants :-

class of drugs that enhance the activity of the CNS, leading to increased alertness, attention, energy & in some cases euphoria.

CNS stimulants increase the activity of neurotransmitters like dopamine, norepinephrine & serotonin.

i) Amphetamines → Amphetamine, Methamphetamine, Lisdexamphetamine

ii) Methylphenidate & Dexamethylphenidate

iii) Modafinil & Armodafinil

iv) Caffeine

v) Nicotine

vi) Xanthines $\begin{cases} \text{Theophylline} \\ \text{Theobromine} \end{cases}$

vii) Cocaine

viii) Phentermine

④ Dissociative Anesthesia :-

Dissociative anesthesia is mediated by NMDA receptor antagonism. The drug used for dissociative anesthesia block the NMDA receptor in the brain, which is involved in pain transmission, memory & consciousness.

By inhibiting these receptors, dissociative anesthesia lead to sensory isolation & detachment.

Drugs used for dissociative anesthesia $\begin{cases} \text{ketamine} \\ \text{Phencyclidine} \\ \text{Tiletamine} \end{cases}$

Features of dissociative anesthesia — Analgesia
Amnesia
Cardiovascular stability
Immobilization
Consciousness preservation

Adverse effects $\rightarrow$ Psychological rxn's — hallucinations, delirium, vivid dreams
Increased ICP
HTN & increased heart rate
Nausea & Vomiting
Hypersalivation.

⑤ Second gas effect :-

Second gas effect is a phenomenon seen during administration of certain inhalational anesthetics, mainly nitrous oxide (N_2O), in addⁿ with other volatile anesthetics.

Second gas effect enhances the uptake of primary anesthetic agent that leads to more rapid induction of anesthesia.

Mechanism :-

i) Increased alveolar conc $\leftarrow$ When N_2O is administered along with other volatile anesthetics, N_2O diffuses rapidly into the bloodstream & tissues

due to its low solubility.

this rapid uptake creates conc gradient that helps to draw the other anesthetic from alveoli into bloodstream and increasing partial pressure in the alveoli.

ii) Conc effect → As N_2O is absorbed, it decreases the volume of gas in the alveoli effectively concentrating remaining volatile anesthetic. this conc leads to faster conduction & rapid onset of action.

⑥ Advantages of atypical antipsychotics over chlorpromazine :-

- Lower incidence of extrapyramidal symptoms (tremor, rigidity, bradykinesia)
- Improved efficacy in negative symptoms of schizophrenia
- Better cognitive functioning
- Broader mechanism of action.
- Lower risk of hypoprolactinemia
- Rapid onset of action.
- Lower sedation levels
- Increased tolerability.

⑦ Rationale the basis for combining halothane & nitrous oxide?

Combining halothane (a volatile anesthetic) with nitrous oxide (N_2O) has specific rationales and benefits.

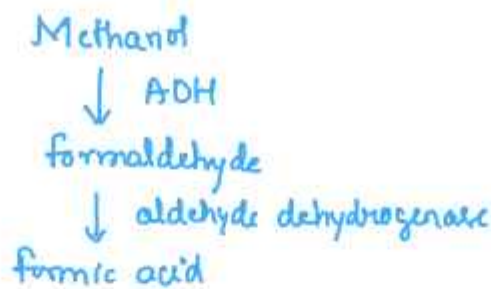
- Enhanced anesthetic effect → due to synergistic action of halothane and N_2O
- Reduced dosage requirements → By using N_2O , the required conc of halothane can be reduced.

this is useful becoz higher concs of halothane can lead to increased side effects & complications.

- Improved anesthetic induction → due to rapid onset & offset action of N_2O .
- Maintaining cardiovascular stability
- Pain control due to analgesic prop of N_2O .
- Disociative anesthesia → second gas effect.

⑧ Methanol poisoning :-

Methanol poisoning is a serious & life threatening condition that occurs due to ingestion, inhalation or absorption of methanol.



Formaldehyde causes damages to cellular structures & is a potent irritant.

Formic acid causes metabolic acidosis, inhibits mitochondrial respiration & can lead to retinal damage & blindness.

Symptoms :- Headache, dizziness
 Nausea & Vomiting
 Abdominal pain
 Flushing or skin irritation
 blurred vision
 Confusion, agitation or coma
 Respiratory distress
 seizures
 Metabolic acidosis

Treatment :- Ethanol } ADH inhibitors
 Fomepizole }
 Sodium bicarbonate - metabolic acidosis.
 Folic acid - to enhance formic acid metabolism.

⑨ Management of benzodiazepine poisoning :-

- i) Get the history, including the type of benzodiazepine involved, the amount ingested & the time of ingestion.
- ii) Physical examination, monitoring vital signs, neurological status & respiratory function.
- iii) Ensure the airway is patent. Administer supplemental O_2 if needed.
- iv) Decontamination by activated charcoal - it reduces absorption of benzodiazepines.
- v) Administration of Flumazenil - benzodiazepine antagonist that competitively inhibits the binding of benzodiazepines at the GABA-A receptor.
- vi) IV fluid administration
- vii) Symptomatic treatment is done.
- viii) Monitoring and follow up.

⑩ Management of acute barbiturate poisoning:

i) Immediate stabilization

⇒ Airway: ensure the airway is patent, use intubation if necessary.

⇒ Breathing: provide supplemental O_2 & artificial ventilation.

⇒ Circulation: Treat hypotension with IV fluids or vasopressors.

ii) GI decontamination — activated charcoal administration reduce further absorption by adsorbing barbiturates in GI tract.
Gastric lavage is done if patient takes high doses.

iii) Increased elimination — by urinary alkalinization by sodium bicarbonate
Hemodialysis or Hemoperfusion is done.

iv) Supportive care — monitoring, temp control, hydration, seizure control.

⑪ Classify drugs used in bipolar disorder:

Mood stabilizers — Lithium
anticonvulsants — sodium valproate, carbamazepine, lamotrigine

Atypical antipsychotics — Olanzapine
Risperidone
Quetiapine
Aripiprazole
Ziprasidone

Typical antipsychotics — Haloperidol
Chlorpromazine

Antidepressants — SSRIs — Fluoxetine, sertraline, Escitalopram
SNRIs — Venlafaxine, Duloxetine.

Benzodiazepines — Lorazepam
Clonazepam.

⑫ Rationale behind combining carbidopa with levodopa:

i. Increased Levodopa availability in the brain +

By inhibiting dopa decarboxylase in the periphery, carbidopa ensures that more levodopa reaches the brain.

ii. Reduction of peripheral side effects → Carbidopa reduces side effects such as nausea, vomiting, cardiovascular issues by preventing the peripheral conversion of levodopa to dopamine.

- iii. Lower doses of levodopa required $\rightarrow$ more levodopa reaches the brain when combined with carbidopa, so lower doses of levodopa are needed to achieve same therapeutic effect.
- iv. Improved Tolerability & compliance.

⑫ Difference b/w morphine and pethidine

Properties	Morphine	Pethidine
Analgesic	More	Less
Onset of action	slow	Rapid
Duration of action	more	Less
Action on smooth muscle	more	less
Cough centre	Depresses	No effect.
Effect on CVS	Bradycardia	Tachycardia
" on CNS	Same	same
" on Asthma	Contraindicated	Can be given
" on biliary spasm	More	less.

⑭ Treatment of chronic alcoholism and acute alcohol intoxication :-

Treatment of chronic alcoholism $\rightarrow$

- Detoxification & management of alcohol withdrawal — Benzodiazepines $\left\{ \begin{array}{l} \text{diazepam} \\ \text{lorazepam} \\ \text{clonazepam} \end{array} \right.$
 IV or IM Thiamine
 IV fluids & electrolytes.
 Anticonvulsants $\left\{ \begin{array}{l} \text{Valproate} \\ \text{carbamazepine} \end{array} \right.$
- long term management $\rightarrow$ psychosocial therapy — cognitive behavioural therapy
 Counselling.
 pharmacological therapy — disulfiram, naltrexone, topiramate, gabapentin.
- Nutritional support $\rightarrow$ vitamins — thiamine, folate

Acute alcohol intoxication :-

It occurs when a person consumes a large amount of alcohol in a short period, leading to impaired cognitive, motor & physiological functions.

⑤ Monitoring of Lithium therapy & its advantages:-

Lithium is a mood stabilizer mainly used in the treatment of bipolar disorder to manage both manic and depressive episodes.

Serum lithium levels $\rightarrow$ therapeutic range - for acute mania - 0.8 - 1.2 mEq/L
for maintenance therapy - 0.6 - 1.0 mEq/L

Renal function $\rightarrow$ lithium is primarily excreted by the kidneys & long term use can cause renal impairment.

tests $\rightarrow$ serum creatinine
GFR.

Thyroid function $\rightarrow$ Lithium can cause hypothyroidism by interfering with thyroid hormone synthesis

tests $\rightarrow$ Serum TSH

Electrolytes $\rightarrow$ Serum Na^+ , K^+ , Cl^-

Advantages:-

- i) High efficacy - mood stabilization
prevention of recurrence
- ii) Anti-suicidal effect.
- iii) Neuroprotective effects.
- iv) Cost effectiveness.
- v) Long term efficacy.

⑥ MAO-A inhibitors:-

Monoamine oxidase inhibitors (MAOIs) are class of antidepressants used to treat mood disorders, mainly depression.

They work by inhibiting the activity of the enzyme MAO, which breaks down neurotransmitters like serotonin, norepinephrine, & dopamine.

By preventing this breakdown, MAOIs increase the levels of these neurotransmitters, which helps to alleviate depressive symptoms.

Pharmacological actions $\rightarrow$ antidepressant effect
anti-anxiety effect.

Therapeutic effect $\rightarrow$ Depression
Anxiety disorders

Social anxiety disorder

OCD

Parkinson's disease.

Commonly used MAOIs → Phenelzine
Tranylcypromine
Isocarboxazid.
Selegiline

⑪ Cheese reaction and its management :-

⇒ Cheese reaction refers to a hypotensive crisis caused by consuming tyramine rich foods while taking MAOIs.

⇒ This reaction occurs because MAOIs block the enzyme MAO, which normally breaks down tyramine in the gut and liver.

⇒ When tyramine is not broken down, it enters the bloodstream in excessive amounts, leading to the release of norepinephrine, which causes vasoconstriction & sudden increase in blood pressure.

Symptoms → Severe headache, HTN, palpitations, chest pain, sweating, nausea & vomiting, sore neck, visual disturbances.

In severe cases - intracranial hemorrhage

Management → Dietary restrictions — Aged cheeses, cured meats, red wine, beer, overripe fruits, fermented or pickled foods.

Stop the MAOI

IV administration of phentolamine / 2.5-5mg — α -adrenergic antagonist

IV nifedipine / 10-20mg — calcium channel blocker.

IV nitroprusside.

⑫ Compare & contrast the effect of halothane & nitrous oxide :-

	Propofol	Nitrous oxide	Halothane
i) Nature		the only inorganic gas in G.A	Volatile anesthetic
ii) Induction		Rapid & pleasant	Rapid & smooth, but slower.
iii) Analgesic		Strong	Very strong
iv) Effect on muscle relaxation		Poor	Good
v) CNS effect		minimal effects on ICP	↑ ICP.

v) CVS & respiratory system	No effect	↓ HR & BP, depress respiration.
vi) Characteristics	Non-inflammable Not explosive Colorless, odorless	Non inflammable sweet odour

⑱ Rationale behind morphine contraindicated in head injury?

Morphine, an opioid analgesic, is contraindicated in patients with head injury due to several reasons.

- i) Respiratory depression → In patients with head trauma, maintaining required ventilation is critical. respiratory depression can lead to hypoxia, exacerbating brain injury & increasing the risk of secondary brain damage.
- ii) Risk of increased ICP → In patients with head injuries, maintaining stable ICP is vital. Opioids can cause vasodilation & alter cerebral perfusion pressure, further complicating the management of head injuries.
- iii) Altered consciousness & neurological assessment.
- iv) Risk of seizures.

⑳ Rationale behind Levodopa Therapy Failure in Drug induced Parkinsonism?

- Receptor blockade → In drug induced parkinsonism, the dopamine receptors are often blocked by the offending drug, meaning that even if levodopa increases dopamine levels, there may be inefficient functional receptors to respond.
- Dopamine receptor changes → The prolonged exposure to dopamine antagonists can lead to changes in receptor density or sensitivity, which can further diminish the effectiveness of levodopa therapy.