MEDICINAL CHEMISTRY-I

B. PHARM IV TH SEMESTER

UNIT-V CNS

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* GENERAL ANAESTHETICS:-

* General anaesthics are CNS depressants which cause partial or complete loss of consciousness, sense or pain. The effect is reversible and generally used to produce unconsciousness during painful surgeries.
* General anaesthetics bring about descending depression of CNS, starting with the cerebral cortex, the basal ganglia, the cerebellum and finally the spinal cord.

Stages of General anaesthesia :-

* **Stage-I (Stage of Analgesia) :-** This is period from the begining of anaesthetic administration to the loss of consciousness. The patient progressively loses pain.
* **Stage-II (Stage of delirium) :-** This period extends from the loss of consciousness through a stage of irregular and specific breathing to the re-establishment of regular breathing. Respiration is normal and regular. The patient may laugh, vomit or struggle and for this reason it is called the stage of excitment.

* Stage-III (Stage of surgical anaesthesia) ⇒
* In this stage excitment is lost and skeletal muscle relaxation is produced. Most types of surgeries are done in this stage.
* Stage-IV - (Stage of medullary depression):-
Overdose of the anaesthetic may bring the patient to this stage. Respiratory & circulatory failure occur in this stage.

* Classification General Anaesthetics :-

(1) Inhalation Anaesthetics.
- Halothane*
- Methoxyflurane
- Enflurane
- Sevoflurane
- Isoflurane
- Desflurane

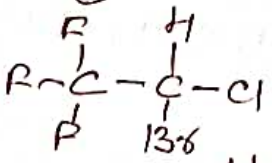
(2) Ultra short acting barbiturate
- Methohexital sod.*
- Thiamylal sod.
- Thiopental sod.

(3) Dissociative Anaesthetics
- Ketamine HCl

(1) Halothane ⇒

$Cl_2C^1=CH^2-Cl \xrightarrow[130°C]{HF_2/SbCl_3} CF_3^1CH^2Cl \xrightarrow[450°C]{Br_2}$ [illegible]

Trichloroethylene — 2-Chloro-1,1,1-trifluoroethane



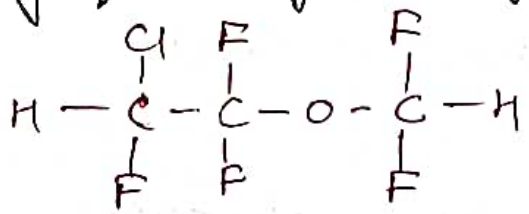
Halothane.

MOA ⇒ Halothane causes anaesthesia due to its action on multiple ion channels, which ultimately depresses nerve condution, breathing, cardiac contractility.

⇒ Halothane's effect are also likely due to binding to NMDA (n-methyl-D-aspartate) receptor and calcium channels causing hyperpolarization

Uses ⇒ In halation anaesthetics
- both long and short lasting surgical operation
- It act very quickly & very safe.

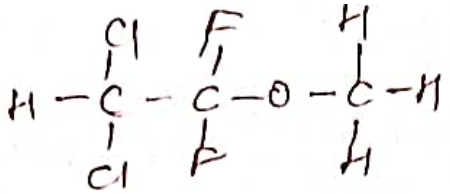
(2) Enflurane :-



MOA ⇒ Enflurane acts as a positive allosteric modulator of the GABA$_A$ receptor. It is also inhibits the receptor activity in the NMDA glutamate receptor subtypes. These yield to sed depolarization and therefore, tissue excitability which results in anaesthesia

Uses ⇒ Used for induction and maintenance of general anaesthesia during surgery and as analgesia during child delivery

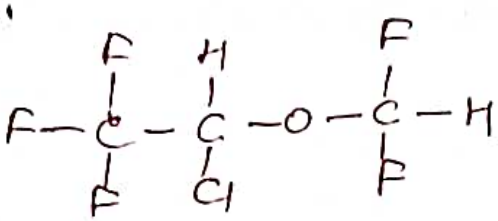
③ Methoxy flurane :-



MOA & Use ⇒ same as enflurane.

Uses

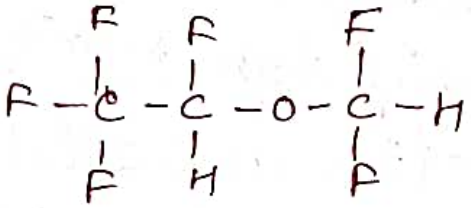
④ Isoflurane :-



MOA ⇒ Similar to enflurane

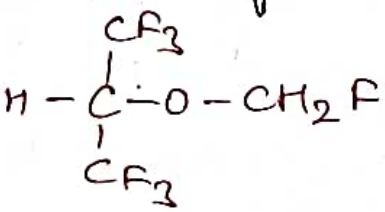
Uses ⇒ Used for the induction and maintenance of general anaesthesia during surgery and cesarean section and also used for analgesia during child delivery.

⑤ Desflurane :-



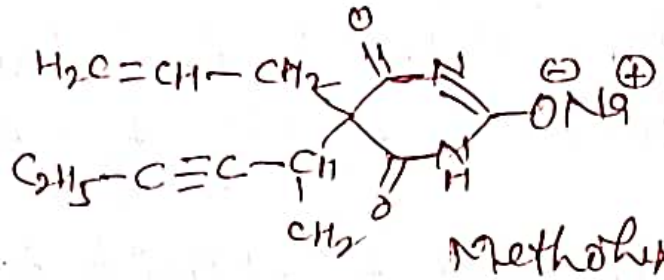
MOA & Uses ⇒ Similar to enflurane

⑥ Sevoflurane :-



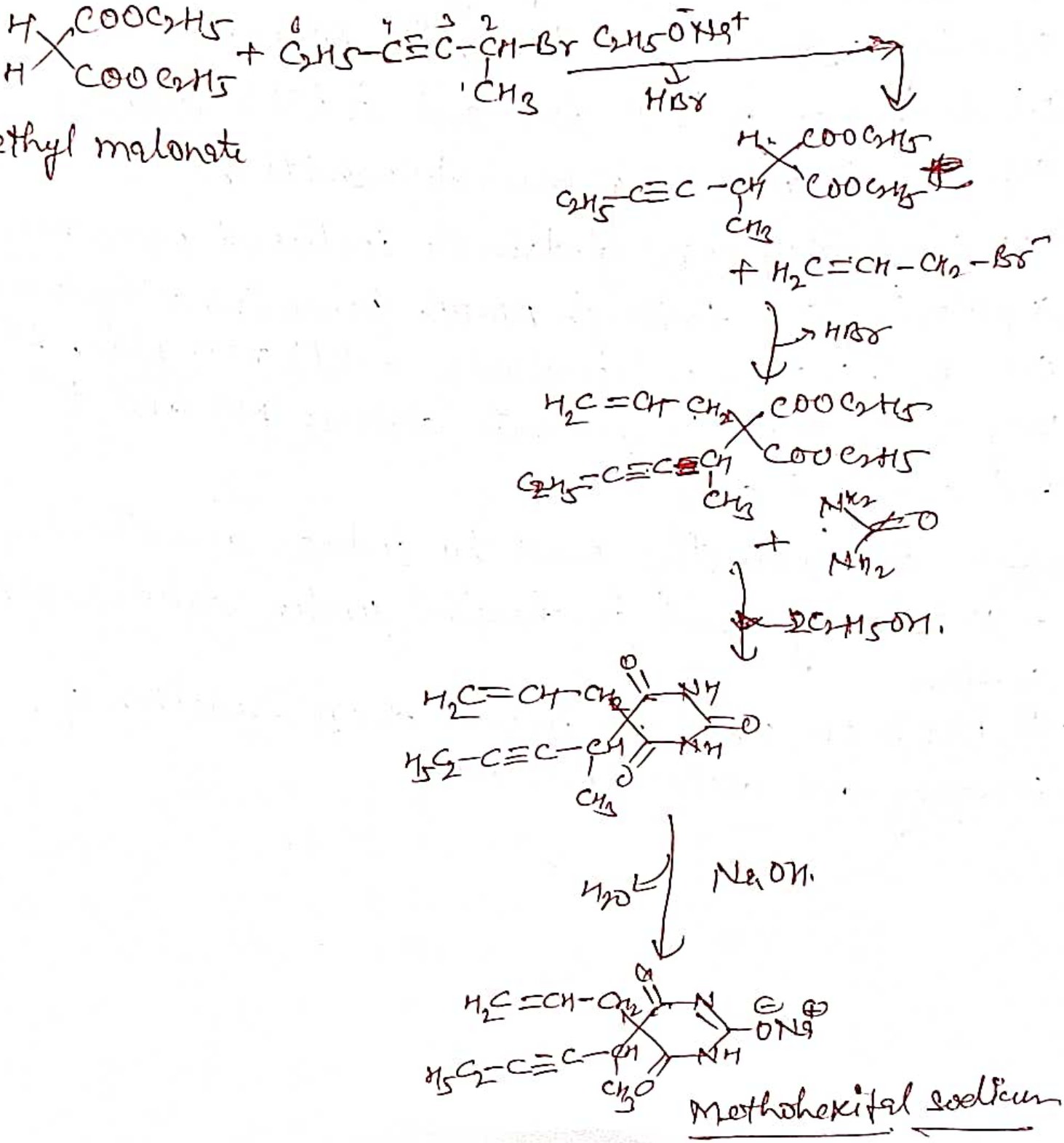
* MOA & Uses :- Similar to enflurane.

* Methohexital Sodium ⇒



Methohexital sodium

Synthesis ⇒



Methohexital sodium

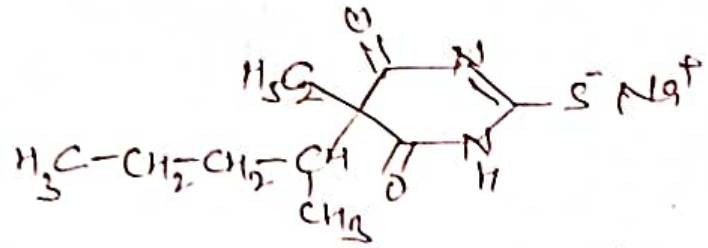
* MOA ⇒ Methohexital bind to GABA-B2D receptor-chloride ion channel complex. This binding increases affinity of GABA for the GABA, receptor.

⇒ It leads to increase in chloride ion conductance via rise in the frequency of the chloride channel opening. At higher dose, it directly increase conductance of Cl^- ion and inhibit calcium dependent release of neurotransmitter

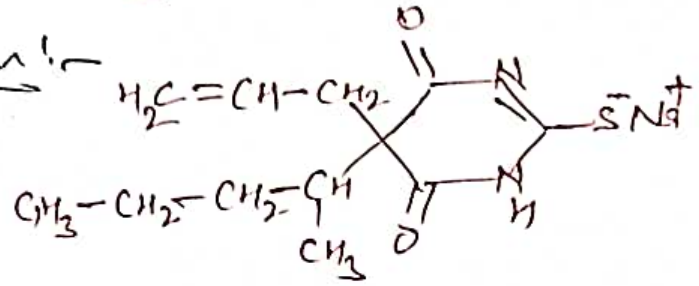
⇒ It also depress glutamate induced neuronal depolarization through AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptor. At very high dose barbiturate depress Na^+ and K^+ ion channel also.

* Use:- It is primarily used to induce anaesthesia.
- It is only used in hospital under strict supervision.
- It has been used to induce deep sedation for surgery and dental procedure.

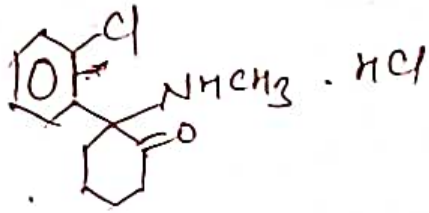
3) Thiopental Sodium :-



3) Thiamylal sodium :-



* Ketamine HCl ⇛



A Mode of Action :- Ketamine ~~acts~~ show multiple therapeutic properties like analgesic anaesthetic and sympathomimetic effect by acting on different sites.

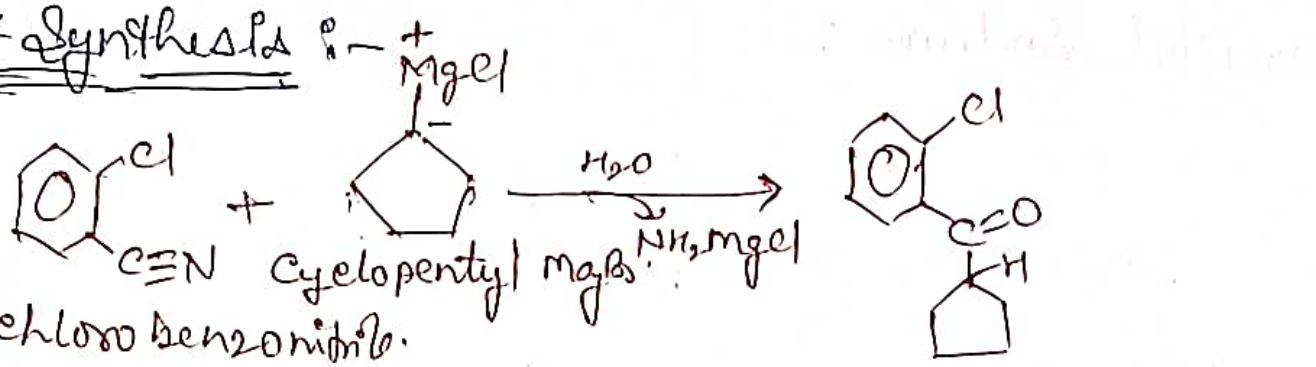
⇒ NMDA ~~receptor~~ antagonism is the most important neuropharmacological mechanism for the analgesic effect of Ketamine.

⇒ Sympathomimetic properties are mediated by enhanced central and peripheral monoaminergic transmission

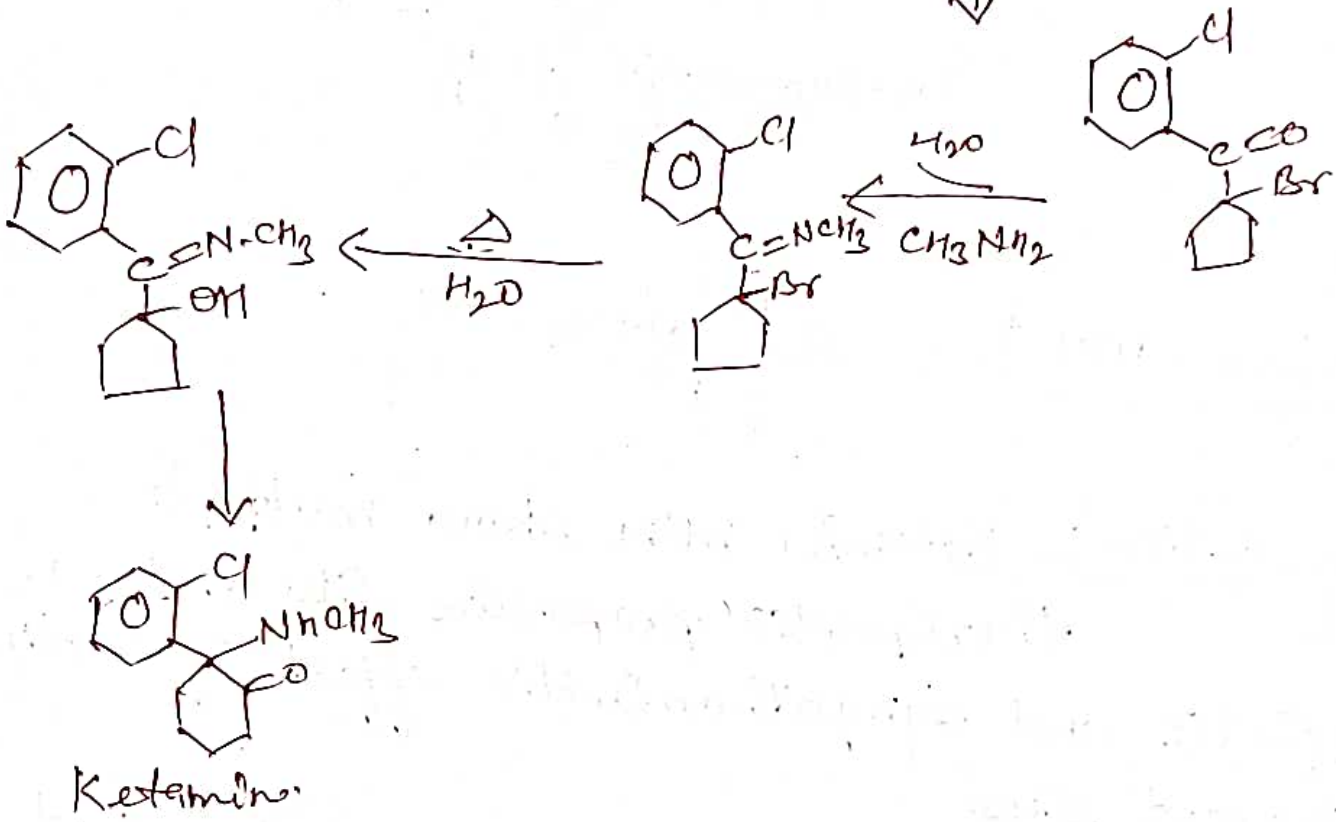
⇒ Inhibition of central and peripheral cholinergic transmission may contribute to the induction of anaesthetic state and hallucinations.

Uses Ketamine is a specific drug for non-inhalation anaesthesia. It is used in brief surgical procedure

* Synthesis :-



2-chloro Benzonitrile. Cyclopentyl MgBr



Ketamine.