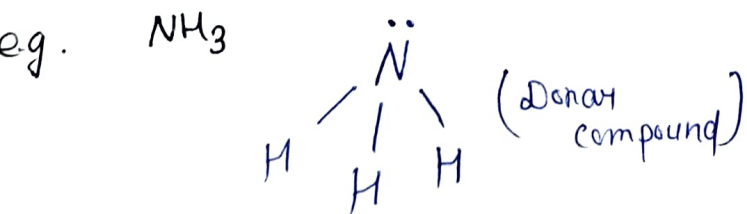


# UNIT - IV Complexation and Protein binding (74)

- Complexes are also called → coordination complex  
or  
Coordination Compounds.
- Complexation may be defined as ⇒ association of two  
or more species to form  
a complex
- A coordination complex is the product of  
↓  
Lewis-acid-base reaction  
or  
Donor-acceptor mechanism  
in which neutral molecules or  
ions → Ligands  
↓  
bond to a central metal atom or ions  
↓  
by coordinate covalent bonds.

Following intermolecular forces are involved in the formation of complexes-

- Covalent bond
- Hydrogen bond
- Vander walls forces
- Ion-dipole
- dipole-dipole.
- dipole-induced dipole





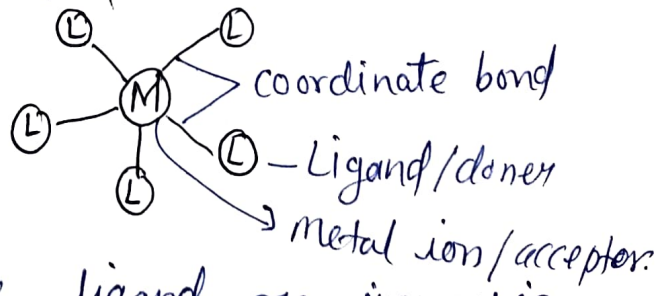
# Applications :-

- ① Physical State :- Physical state of substance can be changed. To convert liquid substances to solid complexes and improve its processing characteristics.
- ② Stability of drug :- Stability of drugs can be enhanced by complexation.
- ③ Solubility :- Enhancement of solubility by using solid complexes.
- ④ Dissolution :- Complexation enhances the solubility, thus, enhancing the dissolution of drugs.
- ⑤ Absorption & Bioavailability :- Complexation helps in increasing the absorption and bioavailability of drug in the body.
- ⑥ Antidote in poisoning :- Also reduced toxicity of poisons by making complex with metal poison. So, work as antidote.

## 1. Metal Ion Complexes → called as

↳ Coordinate Complex.

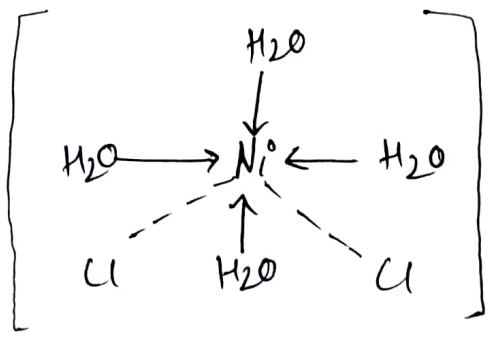
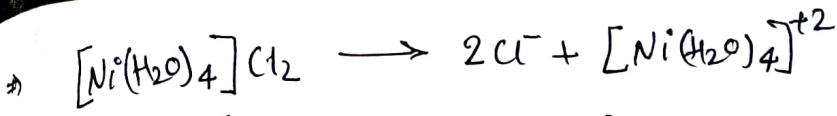
In this type, metal ion constitutes as central atom and interacts with ligands.



### ① Inorganic type :-

In this complex, ligand are inorganic in nature, which attached with metal atom.

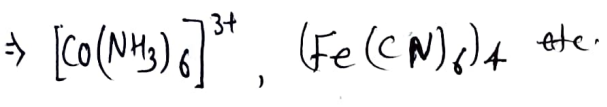
eg. Ligand use →  $\text{NH}_3$ ,  $\text{H}_2\text{O}$ ,  $\text{C}\equiv\text{N}$  (all are inorganic)



1° Valency = Ionic bond = 2  
 2° Valency = Coordinate bond = 4

→ Coordination number = maximum number of atoms binding to the central atom.

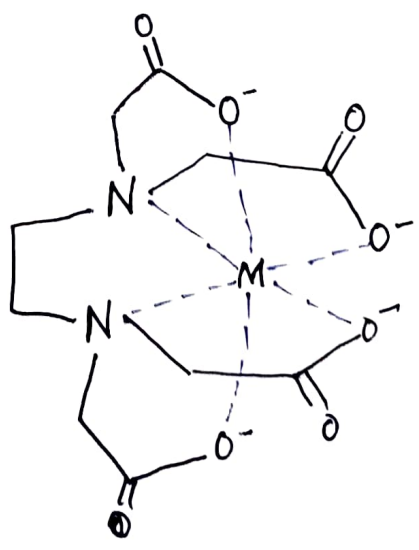
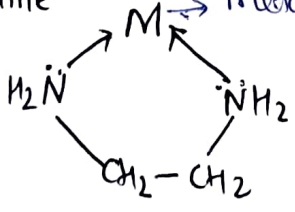
C.N = 2 + 4 = 6



(ii) Chelates :- Substances having two or more donor groups form complex with the metal ion, that complex is known as chelate.

- Bonds involves may be → ionic, primary covalent or co-ordinate covalent bond
- It is only perform in bidentate, tridentate and polydentate.
- when metal ion attached with these ligands, it form cyclic structure.

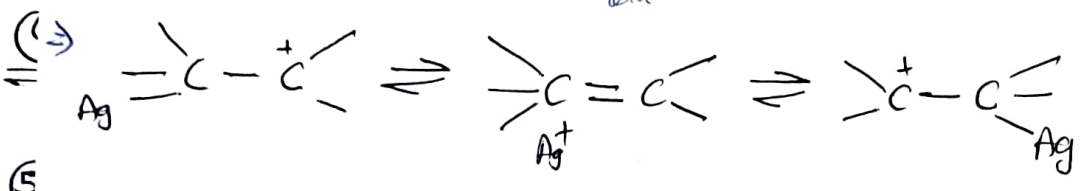
→ Ethylenediamine      metal ion      EDTA.



(iii) Olefin type :-

Aqueous solution of some metal ions like platinum, iron, palladium, mercury, silver absorb olefin such as ethylene to yield water soluble complexes.

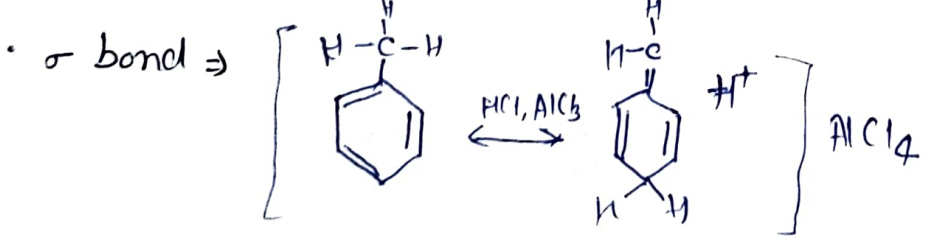
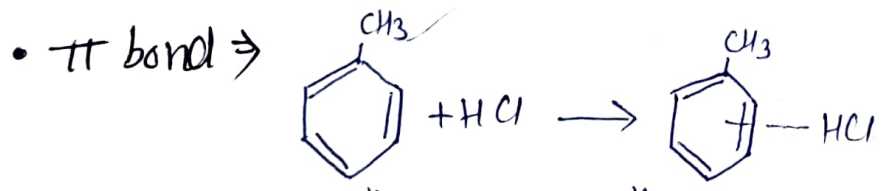
(⇒) A long chain of unsaturated hydrocarbon called oil on the basis of structure.



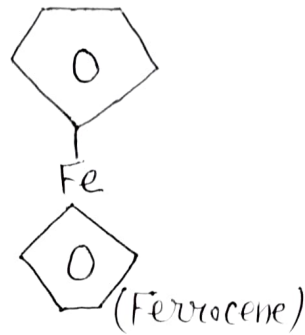
(iv) Aromatic type :-

They are formed by interaction of metal ion as acceptors with aromatic molecules such as benzene, toluene & xylene.

- π bond
- σ bond
- Sandwich compounds



• Sandwich Compound :- Sandwich compounds are relatively (79) stable complexes involving a delocalized covalent bond between the d-orbital of a transition metal and a molecular orbital of aromatic ring.



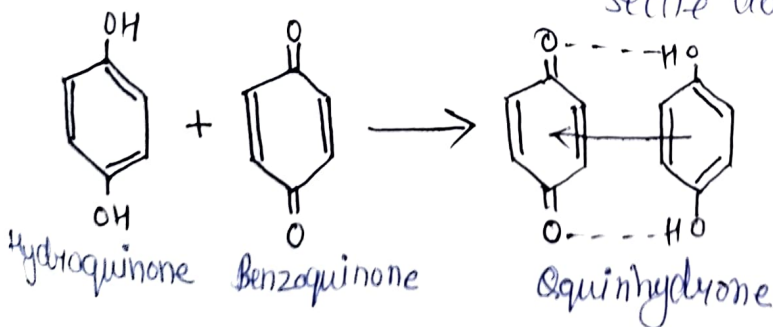
## 2. Organic Molecular Complexes

Organic molecular complexes, also known as addition complexes are formed by union of two organic molecules held together by electrostatic forces, ionic, covalent and also by hydrogen bonded complexes. also known as charge transfer complexes.

### 1) Quinhydrone Complexes :-

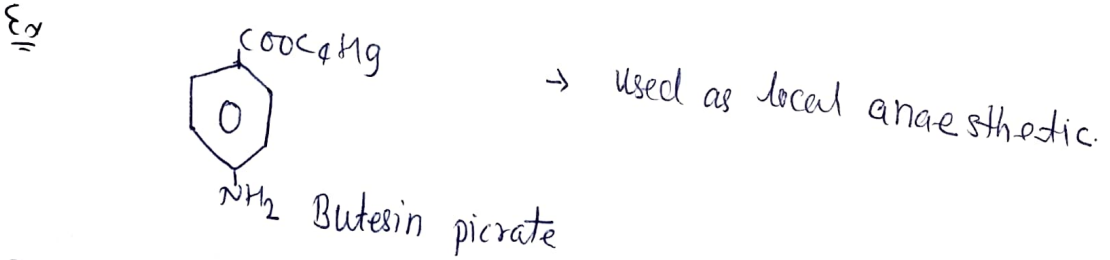
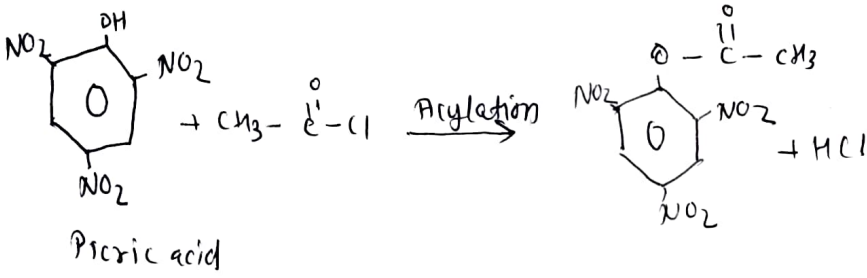
Formed by mixing  $\rightarrow$  equimolar quantity of benzoquinone  
 $\rightarrow$  Hydroquinone<sup>+</sup>

$\downarrow$   
 green crystals of quinhydrone complex settle down.



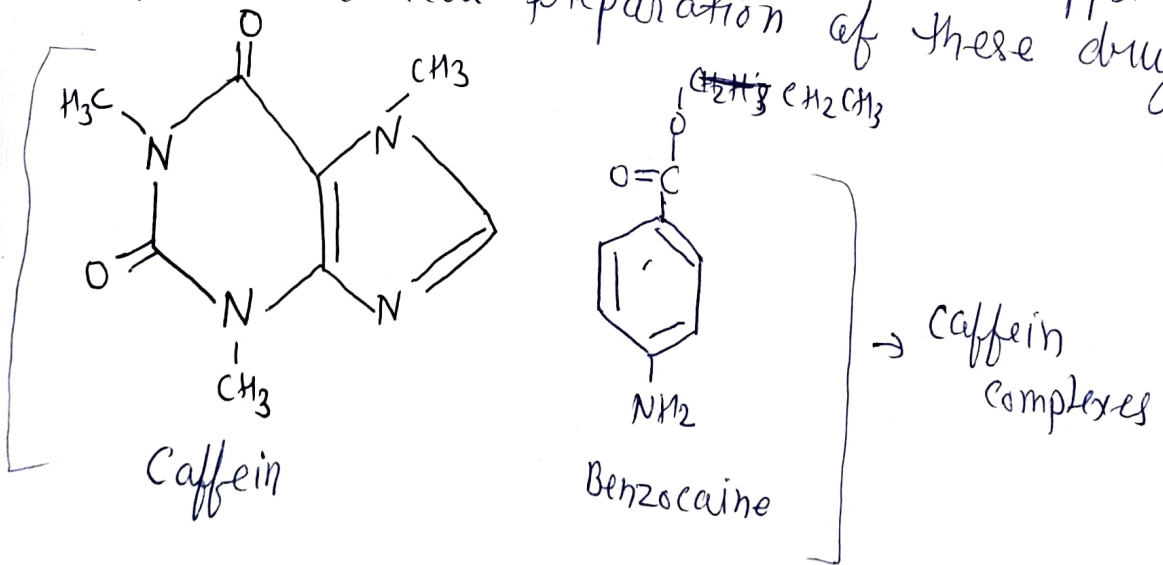
(ii) Picric Acid type

Picric acid (2,4,6-trinitrophenol) being a strong acid, forms organic molecular complexes with weak bases.



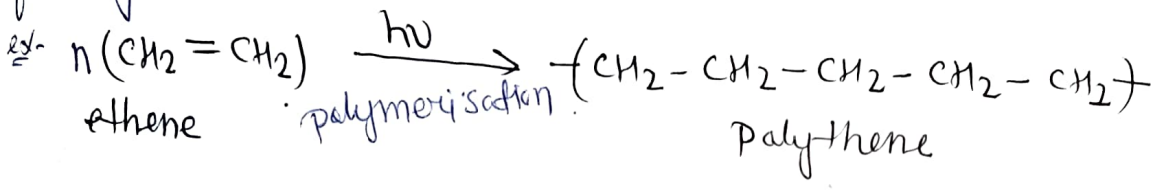
(iii) Caffein and other drug molecules:-

Caffein forms complexes with a number of drug such as benzocaine, tetracaine, or procaine and this enhances the stability and appearance of pharmaceutical preparation of these drugs.



### ① Polymer type :-

Many pharmaceutical additives such as polyethylene glycols (PEGs), Polystyrene, Carboxymethyl cellulose (CMC) etc. can form complexes with a large number of drugs.



### 3. Inclusion Complexes

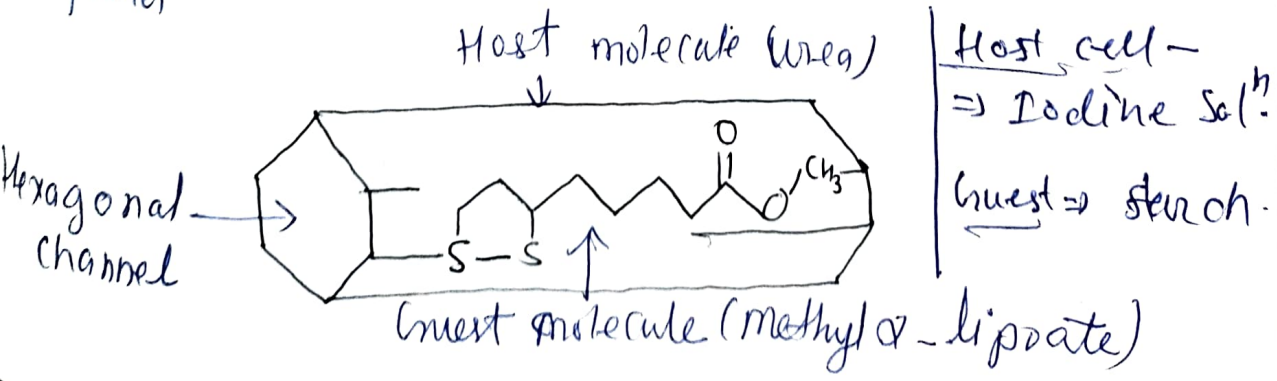
↳ Occulsion compound.

It ~~is~~ can be considered as a host-guest combination in which one compound (host) forms cavity in which other molecule of another compound (guest) fits.

No involvement of any type of bond, so called no-bond complexes.

### ① Channel Lattice type :-

Channels are formed by crystallization of the host molecules in which the guest molecules can fit, the guest component is usually limited to long, unbranched straight chain compound.



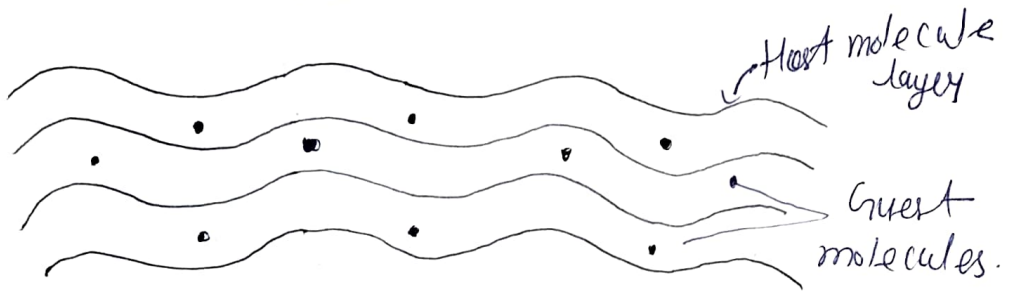


(i) Layer Type:-

In this type, Guest molecules is diffused between the layers of carbon atom, hexagonally oriented to form alternate layer of guest and host molecules.

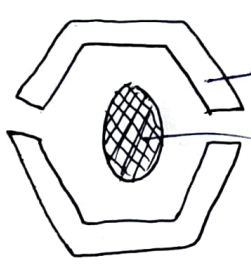
eg Clays, Montmorillonite

⇒ Bentonite intrapped in clays



(ii) Clathrates:-

Clathrates are inclusion compounds in which a molecules of guest compound get entrapped within the cage like structure formed by the association of several molecules of host compounds.



cage shape (host)

Guest (trapped guest)

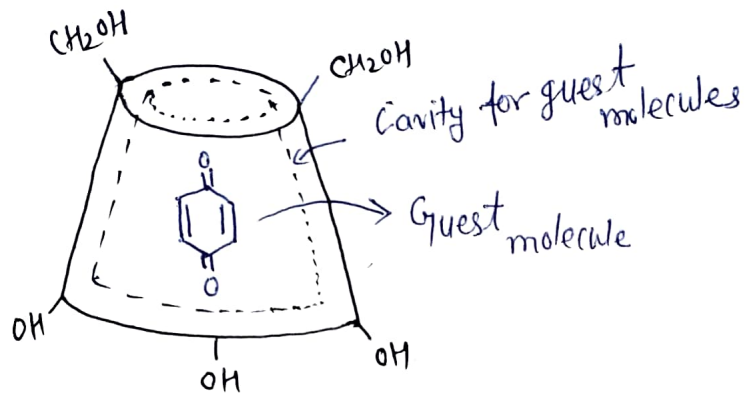
- ⇒ Iso propyl alcohol (guest)
- ⇒ Warfarin (guest)
- Na (host)

Hydroquinone in Benzoquinone

(iv) Monomolecular Compound:-

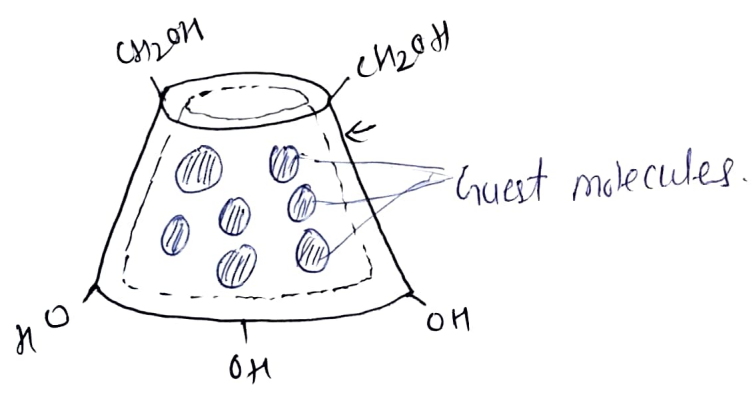
In this complexes, a single guest molecules is entrapped in the cavity of host molecules.

eg cyclodextrins → containing 6 D glucopyranose attached by α-1,4-linkages



① Macromolecular Complexes:

In this complexes, more than one guest molecules are entrapped in the cavity of host molecules. eg. cyclodextrin as a host molecules.



Methods of Analysis of Complexation

After the complexation method, we find out have to know whether the complex is made or not?

for this, we use following method:-

- ① Continuous Variation method
- ② pH titration method.
- ③ Distribution method
- ④ Solubility method
- ⑤ By spectroscopy.