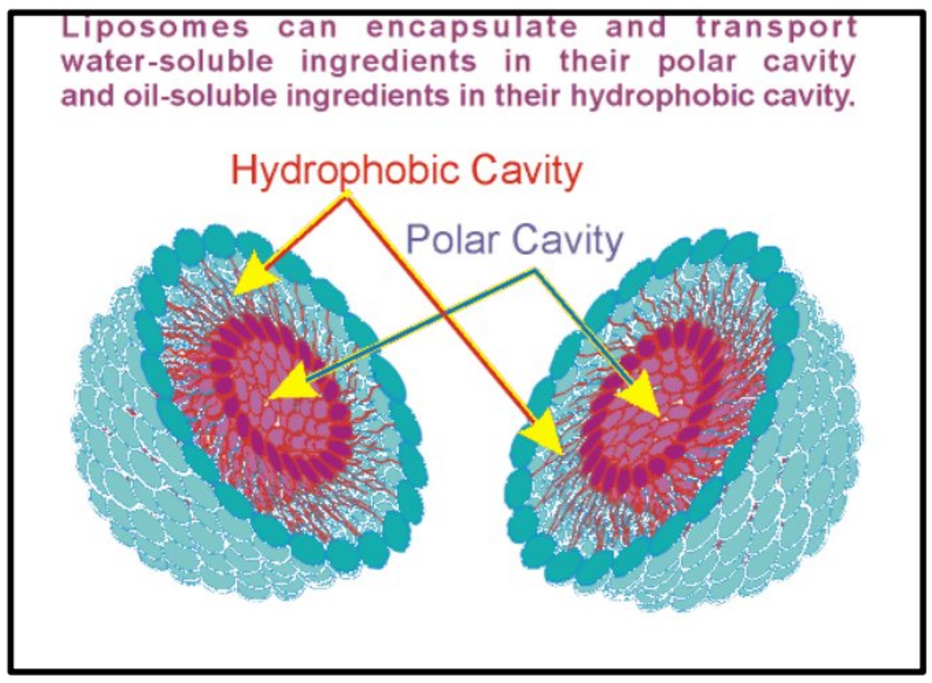
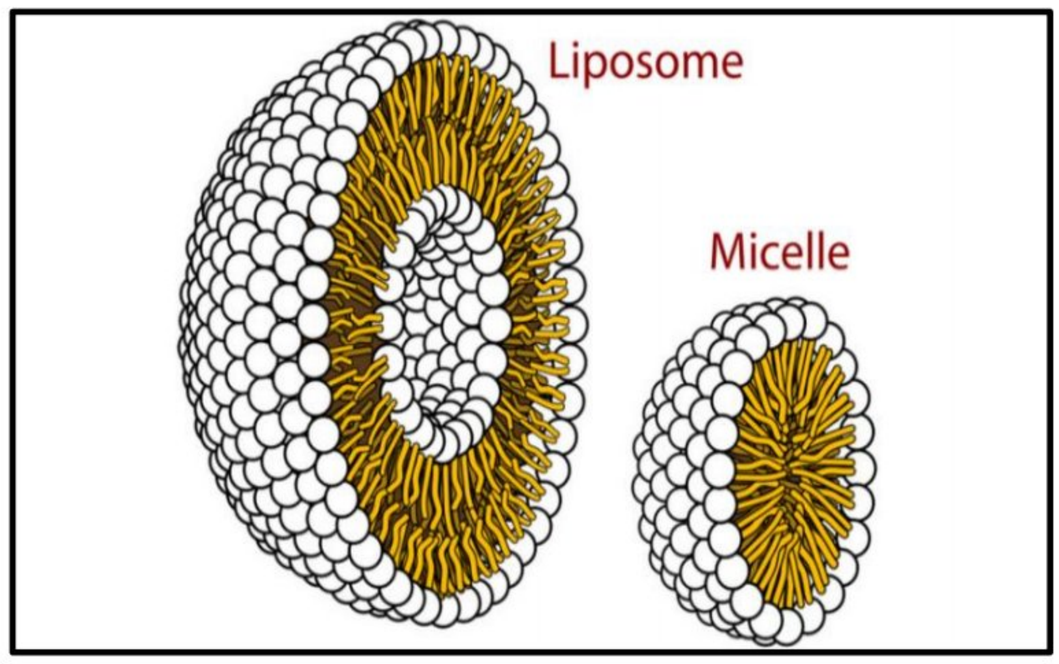
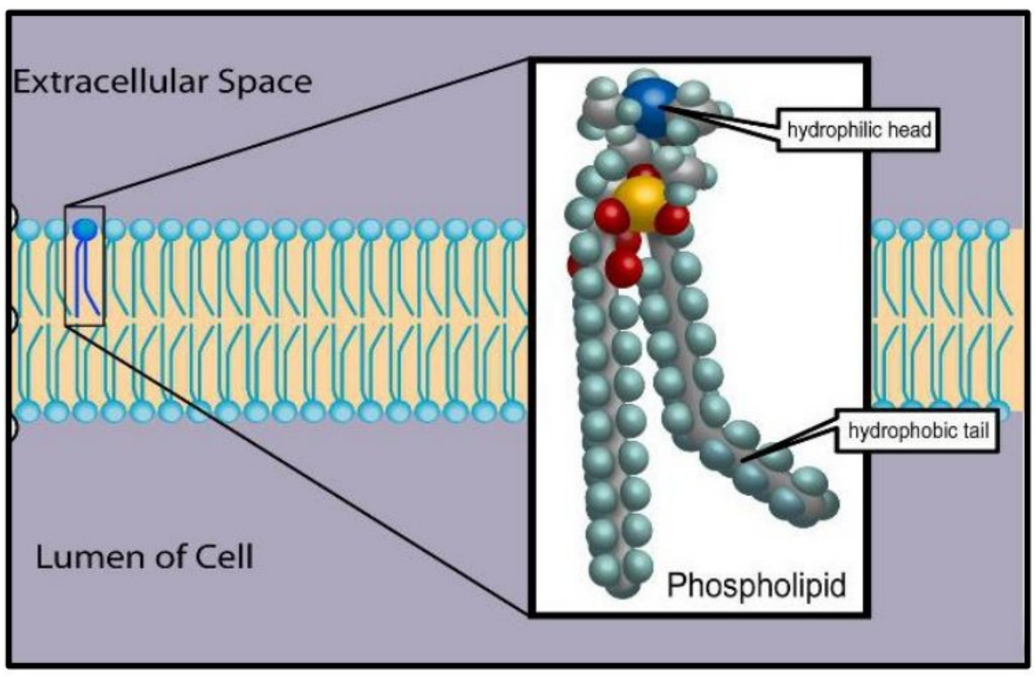
•LIPOSOMES

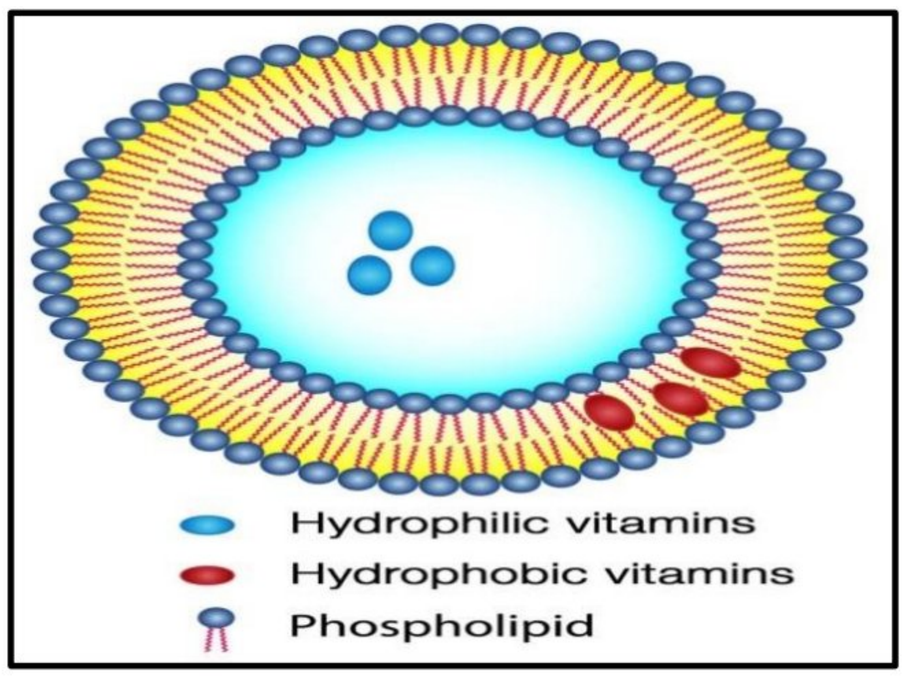
-Liposomes are **microscopic spheres made from fatty materials**, predominantly phospholipids.

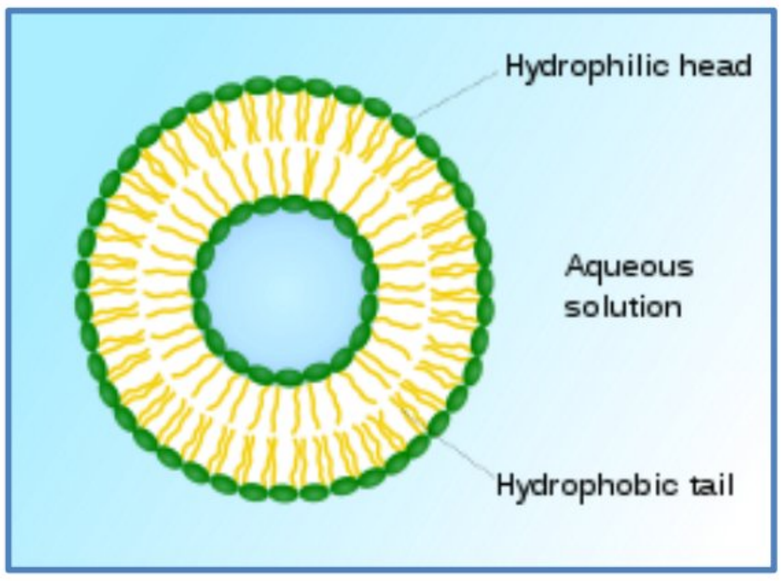
-Liposomes are made of molecules with hydrophilic and hydrophobic ends that form hollow spheres which can encapsulate water-soluble ingredients (drugs) in their inner water space and oil-soluble ingredients (drugs) in their phospholipid membranes that are made up of one or more concentric lipid bilayers, and range in size from 50 nanometers to several micrometers in diameter.











Diagrams and images to understand Liposomes

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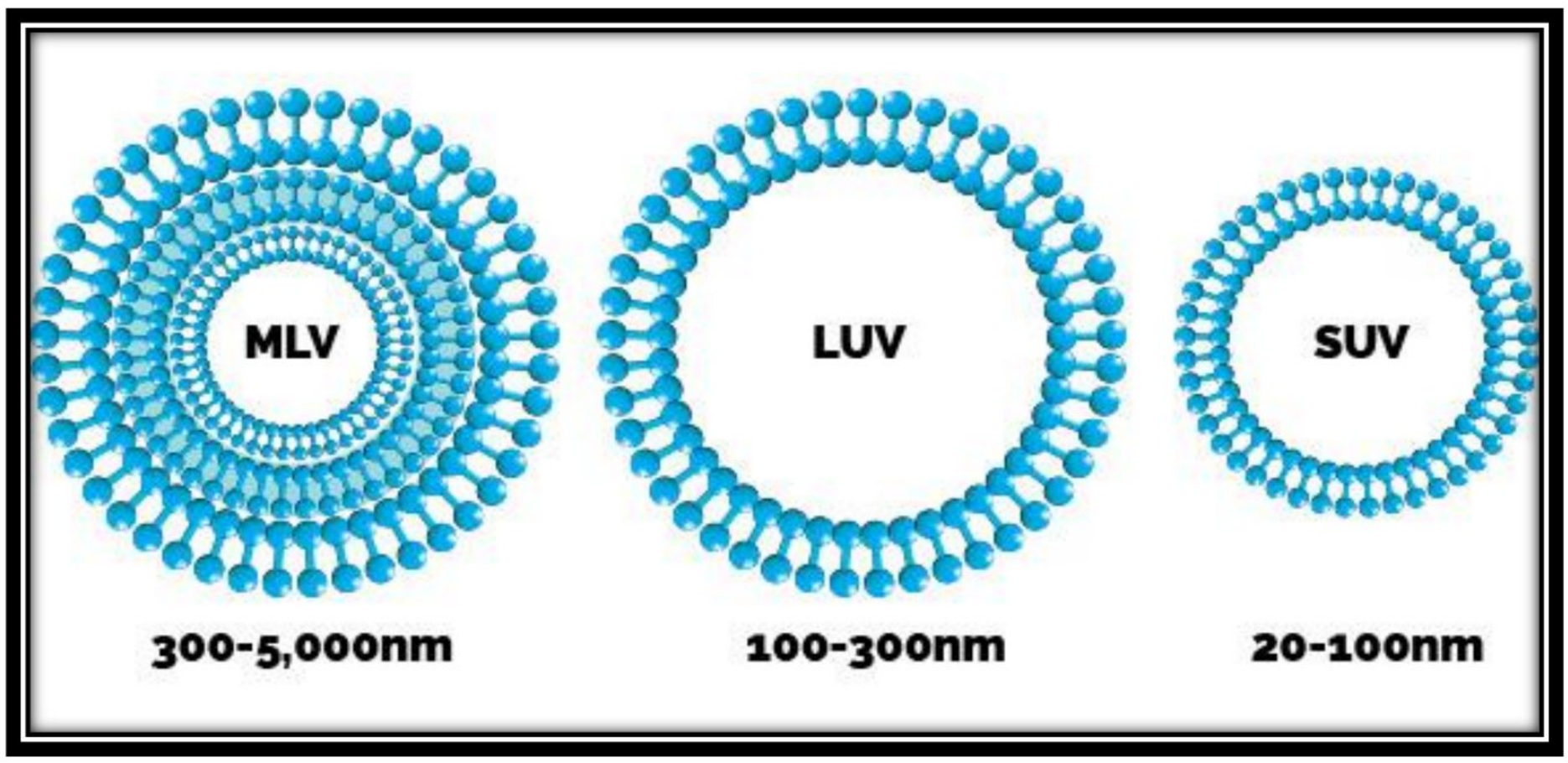
→ Based on their size and number of bilayers liposomes are classified into three basic types:-

1) Multilamellar Vesicles (MLVs)
2) Large Unilamellar Vesicles (SUVs)
3) Small Unilamellar Vesicles (LUVs)

-**Multilamellar Vesicles (MLVs)** are of several lipid bilayers separated one another by aqueous spaces.
-They are heterogenous in size, often ranging from a few hundred to thousands of nanometer in diameter.

-Both **Small Unilamellar Vesicles (SUVs)** and **Large Unilamellar Vesicles (LUVs)** consist of single bilayer surrounding the entrapped aqueous space.

-SUVs are less than 100nm in size whereas LUVs have diameter larger than 100nm.



→ In terms of composition and mechanism of intracellular delivery liposomes are classified into five types:-

(i) Conventional liposomes
(ii) pH sensitive liposomes
(iii)Cationic liposomes
(iv)Immuno liposomes
(v) Long circulating liposomes

➢ Formulation/ Composition of Liposomes-

-Material used in the liposomes formulation depends upon the drug nature.
-The commonly used material includes phospholipids, glycosphingolipids, sterols, cationic lipid, a variety of other lipids and surfactants.

-There are number of structural and nonstructural components of liposomes, major structural components of liposomes are-

1) Phospholipid- It is the major component of the biological membrane; two types of phospholipids are used natural and synthetic phospholipids.
-The most common natural phospholipid is the Phosphatidylcholine (PC).
-It is amphipathic molecule and also known as **lecithin**.
-It is originated from animal (hen egg) and vegetable (soya bean).

2) Cholesterol- Incorporation of cholesterol in liposome bilayer can bring about big changes in the preparation of these membranes.
-It can be incorporated into phospholipids membrane in very high concentration up to 1:1 or 2:1 molar ratios of cholesterol to Phosphatidylcholine.
-Being an amphipathic Molecule, cholesterol insert into the membrane with its hydroxyl group of Cholesterol oriented towards the aqueous surface and aliphatic chain aligned parallel to acyl chains in the centre of the bilayers.

Method of preparation of of liposomes:-

1) Mechanical Dispersion Method
2) Solvent Dispersion Methods
3) Detergent Removal Methods

1) Mechanical dispersion methods- Lipid is solubilized in organic solvent, drug to be entrapped is solubilized in aqueous solvent, the lipid phase is hydrated at high speed stirring.
- Due to affinity of aqueous phase to polar head, it is entrapped in lipid vesicles.

-for example- Lipid film hydration, Micro-emulsification, Sonication, Dried reconstituted vesicle.

2) Solvent dispersion methods- In this method, lipids are first dissolved in organic solvent, which is then brought in to contact with aqueous phase containing material which is to be entrapped in liposome under rapid dilution at rapid evaporation of organic solvent.

-for example- Ethanol injection, Ether injection, De-emulsification.

3) Detergent removal method- In this method, phospholipids are brought into intimate contact with the aqueous phase via detergent which associate with phospholipids molecule and serve to screen the hydrophobic portions of the molecules from water.

➢ Evaluation of Liposomes-

-The characterization parameters for the purpose of evaluation could be classified into three broad categories, which include-

1) Physical Characterization parameter-

- Physical characterization evaluates various parameters, including size, shape, surface features, lamellarity and phase behavior and drug release profile.

2) Chemical characterization parameter-

-This parameter includes those studies which establish the purity and potency of various liposomal constituents.

3) Biological characterization parameter-

- These are helpful in establishing the safety and suitability of the formulations for the *in-vivo* use or the therapeutic application.

4) Drug Entrapment Efficiency-

-It is the measure of % drug entrapped to how much drug was added in the bulk for entrapment.

$$\%\ \boldsymbol{Entrapment\ Efficinecy} = \frac{\boldsymbol{Entrapped\ Drug}}{\boldsymbol{Total\ Drug\ Added}} \times \mathbf{100}$$

5) *In Vitro* Drug release study-

- *In Vitro* diffusion studies are carried out using **Franz diffusion cell.**

Advantages of Liposomes-

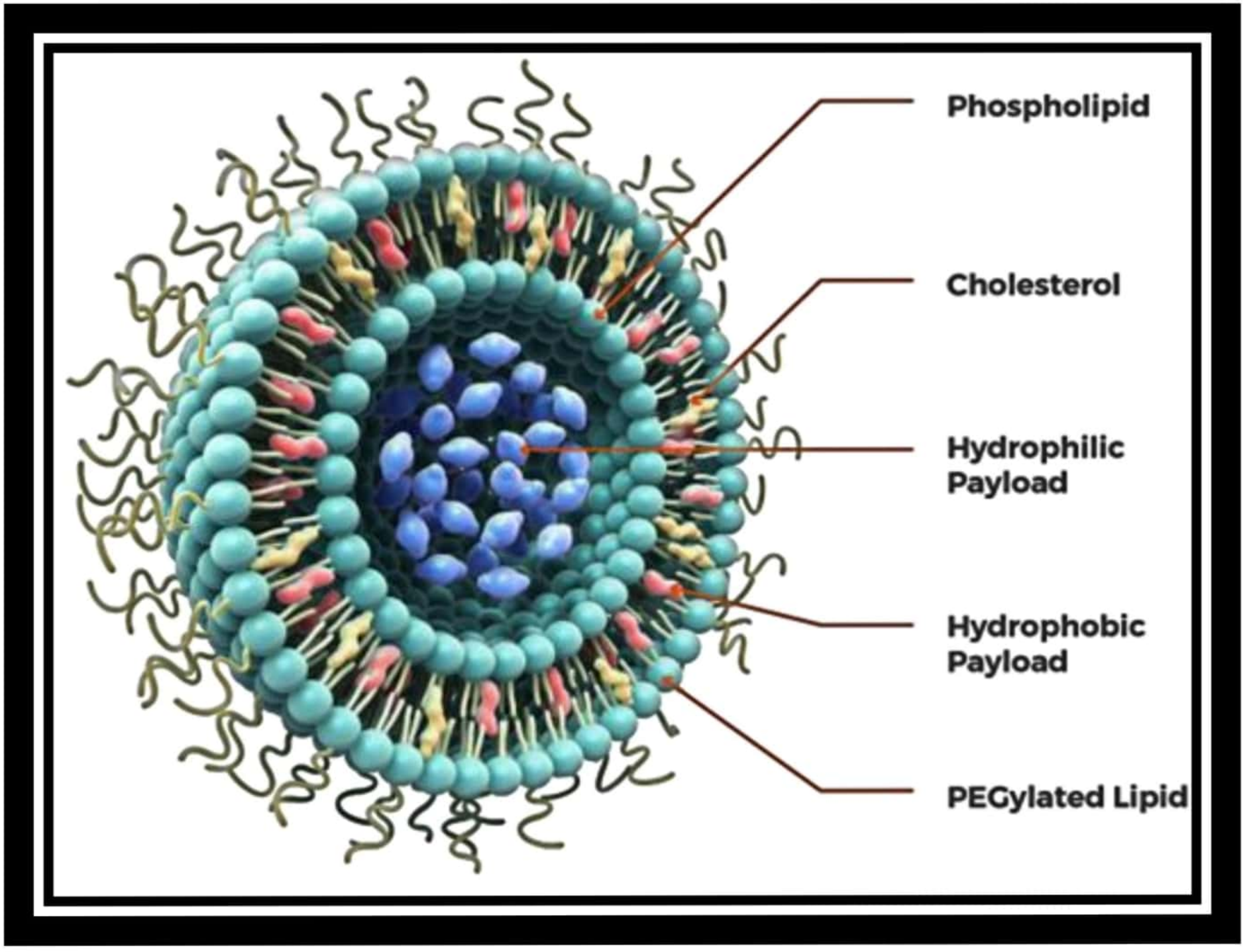
-Liposomes are biocompatible, completely biodegradable, non-toxic, flexible and non-immunogenic for systemic and non-systemic administration.
-Liposomes supply both a lipophilic environment and aqueous in one system and are therefore suitable for delivery of hydrophobic, amphipathic, and hydrophilic drugs and agents.
-Liposomes have ability to protect their encapsulated drug from the external environment and to act as sustained release depots.
-Liposomes can be formulated as a suspension, as an aerosol, or in a semisolid form such as gel, cream and lotion, as a dry vesicular powder (proliposome) for reconstitution or they can be administered through most routes of administration including ocular, pulmonary, nasal, oral, intramuscular, subcutaneous, topical and intravenous.
-Liposomes are increased efficacy and therapeutic index of drug (Actinomycin D)
-Liposomes help to reduce exposure of sensitive tissues to toxic drugs.

Disadvantages of Liposomes-

-Production cost is high.
-Leakage and fusion of encapsulated drug.
-Sometimes phospholipid undergoes oxidation and hydrolysis like reaction.
-Short half-life.
-Low solubility.

Applications of Liposomes-

-Liposomes can target a drug to the intended site of action in the body, thus enhancing its therapeutic efficacy (drug targeting, site-specific delivery).
-Liposomes may also direct a drug away from those body sites that are particularly sensitive to the toxic action of it (site-avoidance delivery).
-Liposomes can act as a depot from which the entrapped compound is slowly released over time. Such a sustained release process can be exploited to maintain therapeutic (but nontoxic) drug levels in the bloodstream or at the local administration site for prolonged periods of time. Thus, an increased duration of action and a decreased frequency of administration are beneficial consequences.
-Drugs incorporated in liposomes, in particular those entrapped in the aqueous interior, are protected against the action of detrimental factors (e.g. degradative enzymes) present in the host. Conversely, the patient can be protected against detrimental toxic effects of drugs.
-Liposomes can interact with target cells in various ways and are therefore able to promote the intracellular delivery of drug molecules that in their 'free' form (i.e. non-encapsulated) would not be able to enter the cellular interior due to unfavorable physicochemical characteristics (e.g. DNA molecules).
-If the drug is an antigen, liposomes can act as immunological adjuvant in vaccine formulations.



3-D image of a Liposome