ASSIGNMENT

SURFACTANTS AND THEIR PHARMACEUTICAL APPLICATIONS

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SUBJECT:

ADVANCE PHARMACEUTICS

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SURFACTANTS AND THEIR PHARMACEUTICAL APPLICATIONS

Surfactants:

"Surfactants are surface active agents/wetting agents that reduce the surface tension or interfacial tension".

The term interface indicates a boundary between any two immiscible phases; the term surface denotes an interface where one phase is a gas, usually air.

Typically they are organic compounds having a hydrophilic head and a hydrophobic tail.

Surface Tension:

Surface tension is a property of the surface of a liquid that allows it to resist an external force, due to the cohesive nature of its molecules.In the liquid state, molecules are surrounded by other molecules in all direction so net effect is zero, but the molecules at surface can only have attractive cohesive forces with the molecules that are situated adjacent and below it. The net effect is that the molecule at the surface of the liquid experience an inward force toward the bulk, such a force pulls the molecules of the surface together, contract the surface, the tension thus created on a surface by this inward pull is called surface tension.Units of surface and interfacial tension are mN m^{-1}.

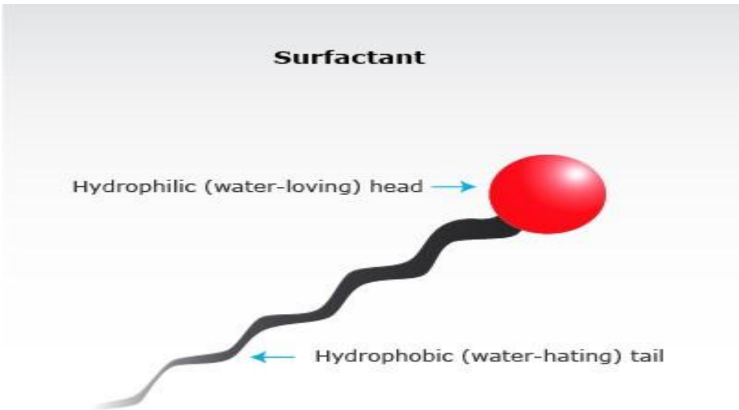
Interfacial Tension:

It is the force per unit area existing at the interfaces between two immiscible liquid phases.

When two immiscible liquid are mixed together an interface is formed between these, this is because the attractive forces between like molecules are stronger than the attractive forces between molecules of immiscible liquids. Therefore they remain immiscible.

Structure of a typical surfactant molecule:

i. Surfactants are usually organic compounds
ii. Surfactants are amphiphilic in nature i.e.; they contain 2 distinct structural units:
    - Tail or hydrophobic group which has little affinity for water
    - Head or hydrophilic group which has strong affinity for water & can be neutral or charged



A Surfactant molecule

Examples

Head Groups	**Tail Groups**
Hydroxyl group (OH) Aldehyde group (CHO) Carboxylic group(COOH) Sulfate group Nitro group (NO2) Amine group (NH2) Halogen (CL or Br)	Lower alkyl group C3 –C8 (CH3-CH2-CH2---) Branching alkyl chains Aromatic ring such as benzene or naphthalene

Hydrophilic-Lipophilic Balance (HLB):

Hydrophilic-Lipophilic Balance (HLB): It is an arbitrary scale from 0 to 20 depicting the Hydrophilic/Lipophilic balance of a surfactant.

- Products with low HLB are more oil soluble.
- High HLB represents good water solubility

RANGE HLB	USES
4-6	W/O emulsifier
7-9	Wetting agents
8-1 8	O/W emulsifiers
13-1 5	Detergents
15-18	Solubilizing

Properties of surfactants:

Surfactants show the following properties:

a. **Emulsifying agent:**
Lowering of interfacial tension between oil and water phases facilitates emulsion formation.

b. **Suspending agent:**
The adsorption of surfactants on insoluble particles enables these particles to be dispersed in form of a suspension.

c. **Wetting agents:**
Their adsorption on solid surfaces enables these surfaces to be more readily wetted.

d. **Solubilizer:**
The incorporation of insoluble compounds within micelles of surfactants can lead to production of clear solution.

e. **Foaming agent:**
A foaming agent is a surfactant which when present in small amounts facilitates the formation of foam, or enhances its colloidal stability by inhibiting the coalescence of bubbles.

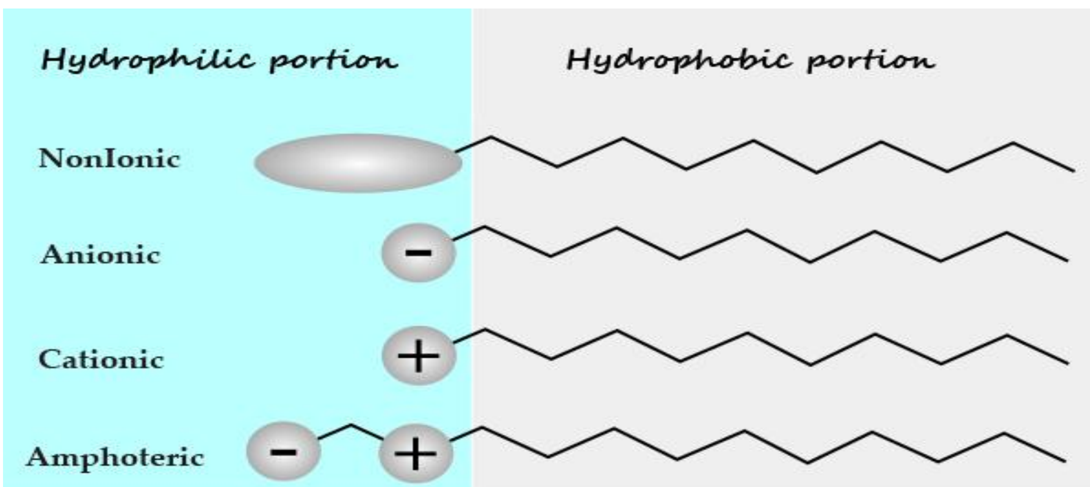
f. **Anti-foaming agents:**
Surfactants also act as anti-foaming agents or defoamers.

g. **Detergent:**
A detergent is a surfactant (or a mixture containing one or more surfactants) having cleaning properties in dilute solution (soaps are surfactants and detergents).
Detergents are also surfactants that reduce the surface tension and aid in wetting the surface and the dirt. The solid will be emulsified and foaming generally occurs and results in washing away of dirt.

CLASSIFICATION OF SURFACTANTS:

1. **On Basis of Composition Of Their Tail:**
Most surfactants' "tails" are fairly similar, consisting of a hydrocarbon chain, which can be branched, linear, or aromatic. Fluorosurfactants have fluorocarbon chains. Siloxane surfactants have siloxane chains.

2. **On Basis Of Composition Of Head:**
There are 4 types of surfactants with a brief review of each as follows. These classifications are based upon the composition of the polarity of the head group: nonionic, anionic, cationic, and amphoteric



The different types of surfactants

a) **Anionic surfactants**:
Anionic surfactants contain anionic functional groups at their head, such as sulfate, sulfonate, phosphate, and carboxylates. They are the most commonly used surfactants that account for 50% of the world production.
They include:

i. **Alkali metal and ammonium soaps:**
Surfactants in this group consist mainly of the sodium, potassium or ammonium salts of long-chain fatty acids, such as: Sodium stearate

ii. **Soaps of divalent and trivalent metals:**
Only the calcium salts are commonly used For example calcium oleate

iii. **Amine soaps:**
Widely used in both pharmaceutical and cosmetic products.
For example: Triethanol amine stearate

iv. **Sulphated and sulphonated compounds:**
An example for Alkyl sulphates is sodium lauryl sulphate.
Sulphonated compounds are much less widely used materials of this class include sodium dioctylsulphosuccinate, and are more often used as wetting agents or for their detergency

b) Cationic surfactants:

They account for only 5-6% of total surfactant production. They are neither good detergents nor foaming agents and they cannot be mixed with formulations which contain anionic surfactants. But they exhibit two very important features:

Cationic surfactants are basically soaps or detergents, in which the hydrophilic, or water-loving, end contains a positively-charged ion, or cation. Cationic surfactants are attracted to negatively-charged sites that occur naturally on most fabrics. They can bind to these sites and provide the fabric with a soft, luxurious feel. For this reason, they are often used as fabric softeners.

Typical examples are trimethylalkylammonium chlorides, and the chlorides or bromides of benzalkonium.

c) Non-ionic surfactants:

They do not produce ions in aqueous solution. They are compatible with other types of surfactants. They are much less sensitive to electrolytes than ionic surfactants and can be used with high salinity or hard water. They are good detergents, wetting agents and emulsifiers. Some of them have good foaming properties.

Many long chain alcohols exhibit some surfactant properties. Prominent among these are the fatty alcohols, cetyl alcohol, stearyl alcohol, and cetostearyl alcohol

d) Zwitter ionic or amphoteric surfactants:

They have two functional groups, one anionic and other cationic. It is the pH which determines which of the groups would dominate; anionic at alkaline pH and cationic at acid pH. Near isoelectric point, these surfactants display both charges and are truly amphoteric, often with a minimum of interfacial activity.

Amphoteric surfactants, particularly the amino acids are quite biocompatible and are used in pharmaceuticals and cosmetics. They include:

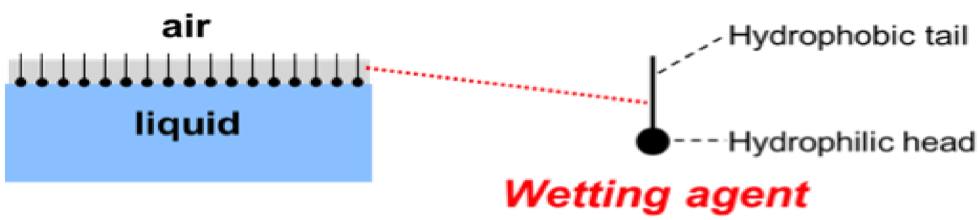
- Aminopropionic acids
- Imidopropionic acids
- Quaternized compounds

3. **On Basis of Composition of Their Counter-Ions:**
   This classification is only for ionic surfactants.
   i. **<u>Monoatomic/Inorganic counter-ions</u>:**
      - Cations: Metals e.g. alkali metals, alkaline earth metals, transition metals.
      - Anions: Halides e.g. chloride, bromide, iodide.
   ii. **<u>Polyatomic/Organic counter-ions</u>:**
      - Cations: e.g. ammonium ions.
      - Anions: Tosyls e.g. methyl sulfates, sulfonat.

4. **<u>Functional Classification</u>**

   i. **<u>As Wetting agent</u>**

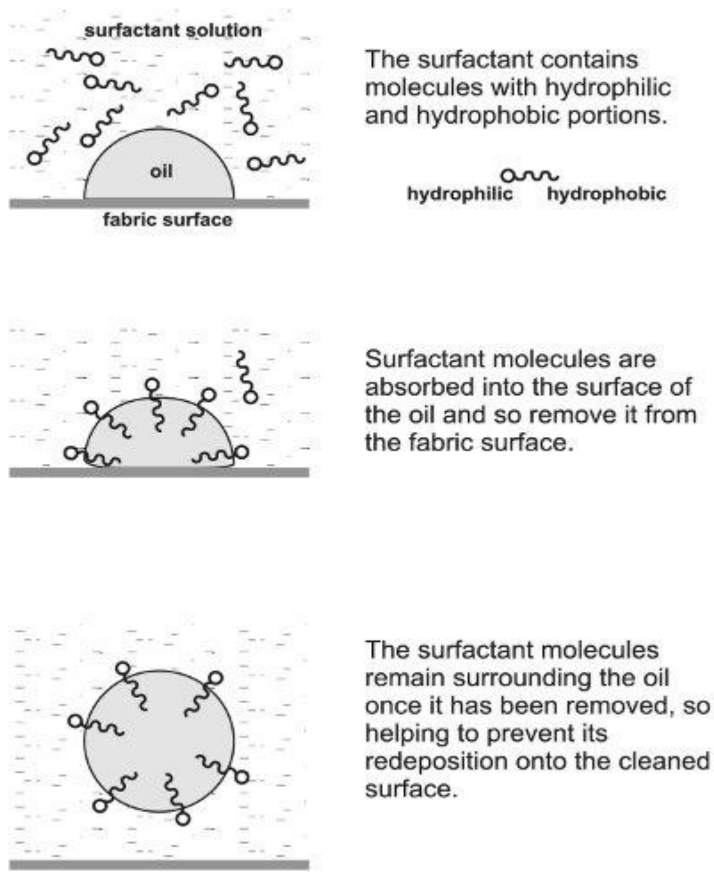
   Wetting is the first step in the dispersion process. The air that surrounds the solid particles in agglomerate must be substituted by liquid. Wetting will not occur when the surface tension of the liquid is too high. A wetting agent does its job because the molecules adsorb and orient on the liquid-air interface.



   Wetting agents increase the spreading and penetrating properties of a liquid by lowering its surface tension. The wettability of a powder may be described in terms of the contact angle, which the powder makes with the surface of the liquid. For a liquid to completely wet a powder, there should be a decrease in the surface free energy as a result of the immersion process. The wetting agent reduce the contact angle by decreasing surface tension and interfacial tension and improve the dispersibility of the powder.
   Examples:
   <u>Benzalkonium Chloride, NF</u>
   <u>Poloxamer 188, NF - P1169</u>

   ii. **<u>As Detergent</u>**

   The dirt/water and solid/water interfacial tensions are lowered and thus the work of adhesion between the dirt and solid is reduced so that the dirt particle may be easily detached. Surfactants function by breaking down the interface between water and oils and/or dirt. They also hold these oils and dirt in suspension, and so allow their removal. They are able to act in this way because they contain both a hydrophilic (water loving) group, such as an acid anion, (-CO_2^- or SO_3^-) and a hydrophobic (water hating) group, such as an alkyl chain.



Examples:

Sodium Lauryl Sulfate, Ultrapure:

Sodium Lauryl Sulfate, Ultrapure, is an organic compound, and anionic surfactant derived from coconut or palm oils, for use as a detergent. As an Organosulfate, this salt has the amphiphilic properties needed in a detergent.

Clorox Healthcare Bleach Germicidal Cleaner:

Clorox Healthcare® Bleach Germicidal Cleaners are unique, stabilized sodium hypochlorite and detergent solutions that kill pathogens fast - with a one-minute contact time for a broad range of microorganisms.

iii. As Emulsifying Agent

Emulsions are stabilized by adding an emulsifier or emulsifying agents. These agents have both a hydrophilic and a lipophilic part in their chemical structure.

All emulsifying agents concentrate at and are adsorbed onto the oil: water interface to provide a protective barrier around the dispersed droplets. In addition to this protective barrier, emulsifiers stabilize the emulsion by reducing the interfacial tension of the system. Some agents enhance stability by imparting a charge on the droplet surface thus reducing the physical contact between the droplets and decreasing the potential for coalescence.

Some commonly used emulsifying agents include tragacanth, sodium lauryl sulfate, sodium dioctyl sulfosuccinate, and polymers known as the Spans and Tweens.

Examples:

Brij(R) C2

Brij(R) C2 is non-ionic surfactant of the polyethylene glycol family. It is used as a solubilizer and emulsifying agent in foods, cosmetics, and pharmaceuticals.

Polysorbate 20, Electrophoresis Grade

Polysorbate 20, Electrophoresis Grade is a frequently used member of the polysorbate family. These have been used as emulsifying agents for the preparation of stable oil in water emulsions

Stearic Acid, Type 50, Powder, NF

Stearic Acid, Type 50, Powder, NF is used as an emulsifying agent, solubilizing agent, tablet and capsule lubricant. The NF grade indicates it is graded suitable for personal care, cosmetic and pharmaceutical applications.

iv. As Dispersing , Suspending And Deflocculating Agent:

Solid particles attract each other. For this reason, energy is needed to separate the particles from each other in the second step of the dispersion process. Also, solid particles must be stabilized after they have been separated from each other. The particles will move to each other and glue together again when particle-particle repulsion is insufficient. The spontaneous process of gluing together of solid particles in a liquid is called **flocculation**. The functionality of a **dispersant** is to prevent flocculation. Dispersants do their job because the molecules adsorb on the solid-liquid interface and assure repulsion between the particles.

The balance of forces appears depend on both the thickness and the concentration of the polymer in the adsorbed layer.

Examples:

Ferrous Chloride, Crystal, Technical

Ferrous Chloride, Crystal, Technical is used in the laboratory synthesis of iron complexes and as a reducing flocculating agent in wastewater treatment,

Agar, Powder, NF

Agar, Powder, NF is used in the pharmaceutical industry for many applications such as a suspending agent, surgical lubricants and in preparations of emulsions, suspensions and capsules

Bentonite, Powder, NF

Bentonite, Powder, NF is used as suspending and emulsifying agent.

v. **As Solubilizing Agent :**

Water insoluble or partly soluble substances are brought into aqueous solution by incorporation into micelles, is termed solublization.

Examples:

Ethyl Oleate, NF

Ethyl Oleate, NF is used as a solubilizing agent in pharmaceutical preparations.

Benzalkonium Chloride, NF

Benzalkonium Chloride, NF is used in the pharmaceutical industry as an antimicrobial preservative, antiseptic, disinfectant, solubilizing agent, and wetting agent.

5. Other Surfactants

i. **FLUORINATED SURFACTANTS**

Hydrogen atoms of the surfactant hydrocarbon tail can be substituted by halogens, particularly F.

Capstone fluorosurfactants enable simplified formulations and higher performance end-products. For applications such as paints and coatings, adhesives, waxes and polishes, and industrial cleaning products, Capstone™ fluorosurfactants enhance the properties of formulations by improving properties, such as wetting and spreading, leveling, penetrating, foaming control, and substantially reducing surface tension.

Examples:

Flexiwet NF:

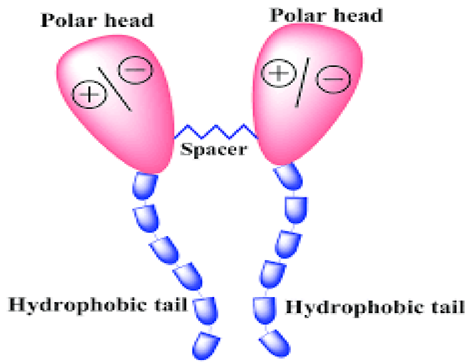
Anionic fluorosurfactant with exceptional wetting properties and excellent chemical and thermal stability

Thetawet FS-8400 is a water-soluble, amphoteric fluorosurfactant in a glycol stabilized aqueous solution. Excellent choice for wetting difficult to wet, low energy surfaces.

ii. **Novel surfactant (Gemini surfactant):**

They are the group of novel surfactants with more than 1 hydrophilic head group and hydrophobic tail group linked by a spacer at or near the head groups.

It has unique properties of Gemini surfactant such as good water solubility, unusual micelle structure and high efficiency in reducing oil/water interfacial tension and low CMC. They are potentially used as cleaning agent, detergent, cosmetic and personal care etc.



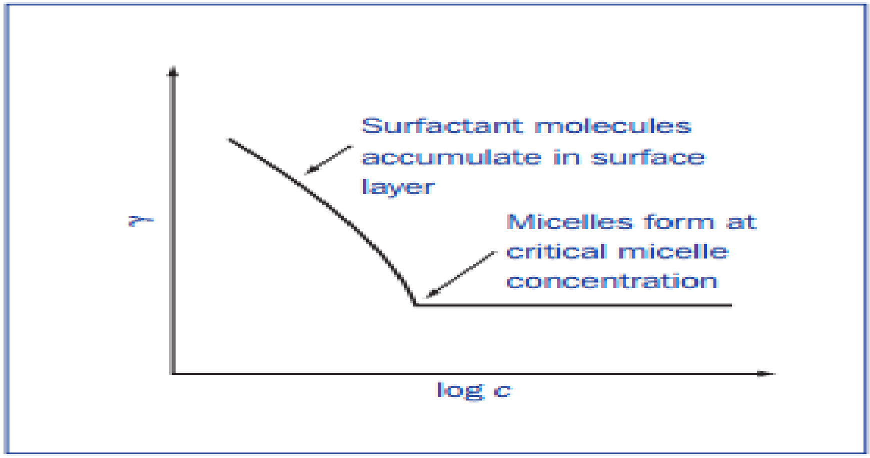
Example:

Siloxane based multifunctional additives

Micellisation

A micelle is an aggregate of surfactant molecules dispersed in a liquid collide. The process of forming micelle is known as Micellisation. The surface tension of a surfactant solution decreases progressively with increase of concentration as more surfactant molecules enter the surface or interfacial layer. However, at a certain condition this layer becomes saturated and an alternative means of shielding the hydrophobic group of the surfactant from the aqueous environment occurs through the formation of aggregates of colloidal dimension called micelles.

Micelles are formed at the critical micelle concentration (CMC), which is detected as an inflection point when physicochemical properties such as surface tension are plotted as a function of concentration (as shown in figure below). The main reason for micelle formation is the attainment of a minimum free energy state. The main driving force for the formation of micelles is the increase of entropy that occurs when the hydrophobic regions of the surfactant are removed from water and the ordered structure of the water molecules around this region of the molecule is lost.

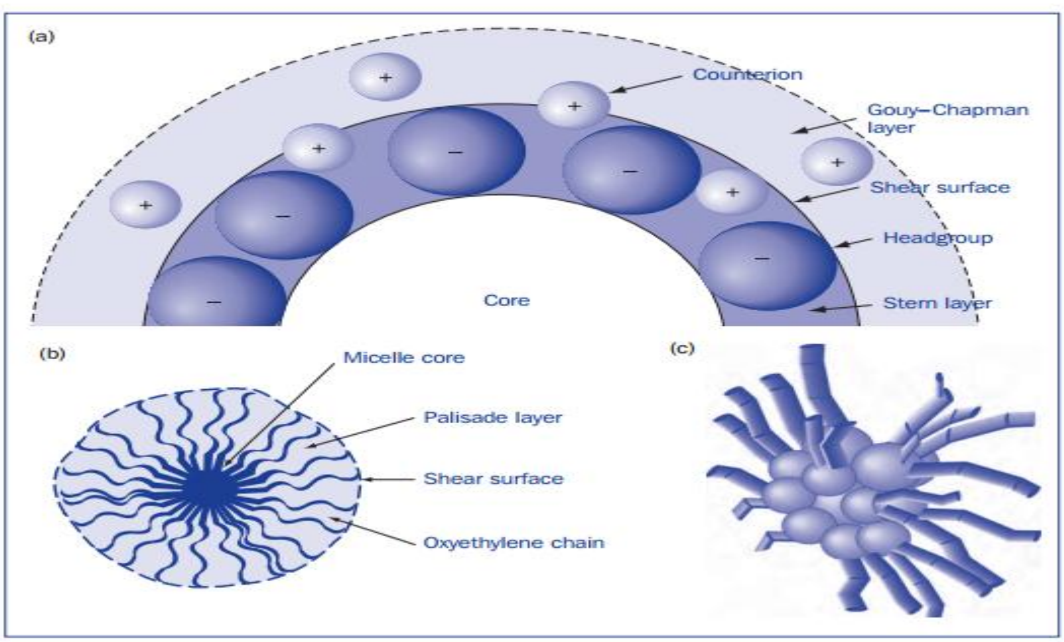


Properties of Micelles

- Most micelles are spherical and contain between 60 and 100 surfactant molecule.
- Micelles are dynamic structures and are continually formed and broken down in solution – they should not be thought of as solid spheres.
- The typical micelle diameter is about 2–3 nm and so they are not visible under the light microscope.
- There is equilibrium between micelles and free surfactant molecules in solution. When the surfactant concentration is increased above the CMC, the number of micelles increases but the free surfactant concentration stays constant at the CMC value.

The structure of the micelles formed by ionic surfactants (as shown in figure below) consists of:

- a hydrophobic core composed of the hydrocarbon chains of the surfactant molecule
- A Stern layer surrounding the core, which is a concentric shell of hydrophilic head groups with (1 –) N counter ions, where is the degree of ionization and N is the aggregation number (number of molecules in the micelle). For most ionic micelles the degree of ionization is between 0.2 and 0.3; that is, 70–80% of the counter ions may be considered to be bound to the micelles
- A Gouy–Chapman electrical double layer surrounding the Stern layer, which is a diffuse layer containing the N counter ions required to neutralize the charge on the kinetic micelle. The thickness of the double layer is dependent on the ionic strength of the solution and is greatly compressed in the presence of electrolyte.



Factors affecting the CMC and micellar size:

i. **Structure of the hydrophobic group**

Increase in length of the hydrocarbon chain results in:

- a decrease in CMC, which for compounds with identical polar head groups is expressed by the linear equation:

$$\text{Log [CMC]} = A - Bm$$

  Where m is the number of carbon atoms in the chain and A and B are constants for a homologous series.
- A corresponding increase in micellar size.

ii. **Nature of the hydrophilic group**
- Non-ionic surfactants generally have very much lower CMC values and higher aggregation numbers than their ionic counterparts with similar hydrocarbon chains.
- An increase in the ethylene oxide chain length of a non-ionic surfactant makes the molecule more hydrophilic and the CMC increases.

iii. **Type of counter ion**
- Micellar size increases for a particular cationic surfactant as the counter ion is changed according to the series $Cl^- < Br^- < I^-$, and for a particular anionic surfactant according to $Na^+ < K^+ < Cs$.
- Ionic surfactants with organic counter ions (e.g. maleates) have lower CMCs and higher aggregation numbers than those with inorganic counter ions.

iv. **Addition of electrolytes**
- Electrolyte addition to solutions of ionic surfactants decreases the CMC and increases the micellar size. This is because the electrolyte reduces the forces of repulsion between the charged head groups at the micelle surface, so allowing the micelle to grow.
- At high electrolyte concentration the micelles of ionic surfactants may become
  non-spherical.

v. **Effect of temperature**
- Aqueous solutions of many non-ionic surfactants become turbid at a characteristic temperature called the cloud point.
- At temperatures up to the cloud point there is an increase in micellar size and a corresponding decrease in CMC.
- Temperature has a comparatively small effect on the micellar properties of ionic surfactants.

Solubilization

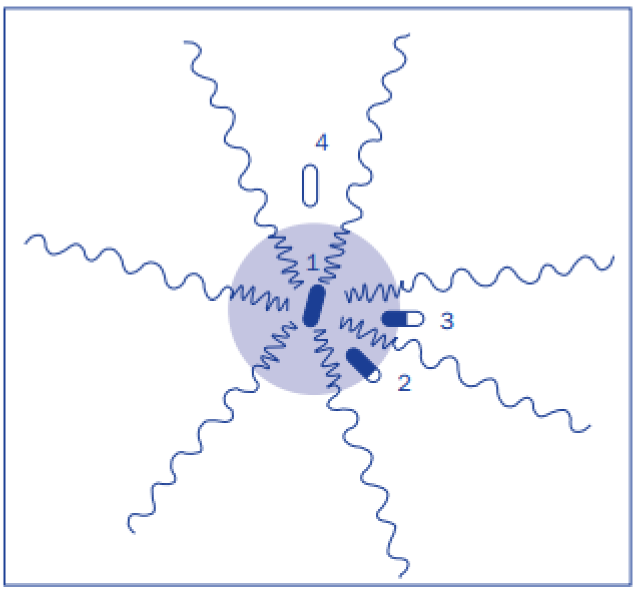
One of the important properties of surfactants that is directly related to micelle formation is solubilization. Solubilization may be defined as the spontaneous dissolving of a substance (solid, liquid, or gas) by reversible interaction with the micelles of a surfactant in a solvent to form a thermodynamically stable isotropic solution with reduced thermodynamic activity of the solubilized material.

Solubilization is distinguished from emulsification by the fact that in solubilization, the solubilized material (the 'solubilizate') is in the same phase as the solubilizing solution and the system is consequently thermodynamically stable.

The maximum amount of solubilisate that can be incorporated into a given system at a fixed concentration is termed the maximum additive concentration (MAC).

The site of solublization within the micelle is closely related to the chemical nature of the solubilisate:

- Non-polar solubilisates (aliphatic hydrocarbons, for example) are dissolved in the hydrocarbon core of ionic and non-ionic micelles (position 1).
- Water-insoluble compounds containing polar groups are orientated with the polar group at the core–surface interface of the micelle, and the hydrophobic group buried inside the hydrocarbon core of the micelle (position 2 and 3).
- In addition to these sites, solublization in non-ionic polyoxyethylated surfactants can also occur in the polyoxyethylene shell (palisade layer) which surrounds the core (position 4).



Factors affecting solublization capacity

i. **Nature of the surfactant**

- When the solubilisate is located within the core or deep within the micelle structure the solublization capacity increases with increase in alkyl chain length up to about C16; further increase has little effect on solublization capacity.
- The effect of an increase in the ethylene oxide chain length of a polyoxyethylated non-ionic surfactant on its solubilizing capacity is

dependent on the location of the solubilisate within the micelle and is complicated by corresponding changes in the micellar size. The aggregation number decreases with increase in the hydrophilic chain length so there are more micelles in a given concentration of surfactant and, although the number of molecules solubilized per micelle decreases, the total amount solubilized per mole of surfactant may actually increase.

ii. **Nature of the solubilisate**

- For a simple homologous series of solubilisates a decrease in solublization occurs when the alkyl chain length is increased.
- A relationship between the lipophilicity of the solubilisate, expressed by the partition coefficient between octanol and water, and its extent of solublization has been noted for several surfactant systems.

iii. **Temperature**

- With most systems the amount solubilized increases as temperature increases.
- This increase is particularly pronounced with some non-ionic surfactants where it is a consequence of an increase in the micellar size with temperature increase.
- In some cases, although the amount of drug that can be taken up by a surfactant solution increases with temperature increase, this may simply reflect an increase in the amount of drug dissolved in the aqueous phase rather than an increased solublization by the micelles.

Pharmaceutical applications of surfactant

1. **Surfactants in Solid Dosage Forms:**
Surface-active agents have been widely shown to enhance drug dissolution rates.This may be due to wetting effects, resulting in increased surface area, effects on solubility and effective diffusion coefficient or a combination of effects. Consequently surfactants have been included in tablet and capsule formulations to improve wetting and deaggregation of drug particles and thus increase the surface area of particles available for dissolution. This wetting effect is found to be operative at concentrations below the CMC.

2. **Surfactants in Semi Solid Systems:**
Surfactants are major constituents of pharmaceutical, cosmetic, and food semisolid formulations, many of which are emulsions, either oil in water (o/w) or water in oil (w/o). They are included for their stabilizing, wetting, solubilizing, detergent and penetration enhancing properties. Emulsion formulation: Water-in-oil emulsions

traditionally contain surfactants of natural origin such as cholesterol, wool fat, wool alcohols, lanolin, divalent salts of fatty acids soaps, calcium oleate and/or synthetic agents of low hydrophilic-lipophilic balance (HLB) (indicating high lipophilicity), such as Spans (fatty acid esters of sorbitan).The water soluble surfactant may be anionic (e.g., sodium lauryl sulphate), cationic (e.g., cetrimide), or non-ionic (e.g., cetomacrogol, Tweens). Mixed emulsifiers control the consistency of a cream by forming a viscoelastic network throughout the continuous phase of the emulsion.

Formulation of Ointments:

Ointments are semisolid preparation meant for external application to skin or mucous membrane; they usually contain medicaments or medicaments in dissolved, suspended or emulsified in an ointment base.

Sometimes in the ointment preparation surfactants are useful for the easy removal from the skin by washing with water & also for the consistency by reduction of surface tension. Surfactants are also used in formulation of cold cream, cleansing cream, vanishing cream, shaving cream or any media.

3. **Surfactants as enhancers for percutaneous absorption:**

   An approach to enhance penetration of drugs through skin is to use the surfactants as penetration enhancers for accelerating drug absorption through stratum corneum. E.g. phospholipids, polysorbate, sorbitan esters. Penetration is enhanced through interaction with skin cells or through changing the physicochemical properties of formulated drug like solubility, diffusion rates etc. Sodium dodecyl Sulphate is a powerful surfactant that denatures and unfolds keratin proteins leading to a porous structure through which drugs can diffuse easily.

4. **Surfactants in mouth washes:**

   Mouthwashes are aqueous solutions often in concentrated form containing one or more active ingredients or excipients. They are used by swirling the liquid in the oral cavity. Mouthwashes can be used for two purposes. They are therapeutic and cosmetic. Therapeutic mouth rinses or washes can be formulated In order to reduce plaque, gingivitis, dental caries, and stomatitis. Cosmetic mouthwashes may be formulated to reduce bad breath through the use of antimicrobial and/or flavoring agents. Surfactants are used because they aid in the solublization of flavors and in the removal of debris by providing foaming action.

5. **Surfactants in respiratory distress therapy:**

   There is a natural lung surfactant produced in our bodies, majorly composed of phospholipids and is gel like, it covers alveolar walls and is constantly renewed. If it is absent there is tension in alveolar walls and lungs can collapse. Neonates do not have this surfactant until birth and often suffer from neonatal respiratory distress syndrome. It is treated by using some exogenous surfactant along with supplemental oxygen and decreases tension of walls. One of the most important pharmaceutical pulmonary surfactant is Survanta.

6. **Surfactants in suppository bases:**
   Several non-ionic surface-active materials have been developed as suppositories vehicles. Many of these bases, known as water-dispersible bases, can be used for the formulation of both water-soluble and oil soluble drugs. The surfactants most commonly used are the polyoxyethylenesorbitan fatty acid esters (Tweens), the polyoxyethylene stearates, and the sorbitan fatty acid esters (Spans). The stainless steel molds are lubricated prior to dipping into the gelatin solution and sodium lauryl sulphate is added to reduce the surface tension of the mix and cause the mold pins to wet more uniformly. Surface-active agents are widely used in combination with other suppository bases. The inclusion of these agents in the formulation may improve the wetting and water-absorption properties of the suppository. In addition, emulsifying surfactants help to keep insoluble substances suspended in a fatty base suppository. The inclusion of a surfactant in the suppository formulation may enhance the rectal absorption of drugs.

7. **Surfactants in suspension aerosols:**
   The addition of surfactants to aerosol suspensions has been most successful. These surfactants exert their activity by coating each of the particles in suspension and orients at the solid-liquid interface. Agglomeration is reduced, thereby increasing stability by providing a physical barrier. Those surfactants having an HLB less than 10, could be utilized for aerosol dispersions.

8. **Surfactants in water based aerosols:**
   Water-based aerosols contain relatively large amount of water. Surfactants have been used to a large extent to produce a satisfactory homogenous dispersion. Surfactants that possess low water solubility and high solubility in nonpolar solvents have been found to be most useful. Long chain fatty acid esters of compounds including glycols, glycerol, and sorbitol exemplify this series.

9. **Surfactants for contact lens cleaning:**
   Surfactants act as cleansers, which emulsify accumulated oils, lipids and inorganic compounds over contact lenses. Surfactant agents are utilized either within a mechanical washing device or by placing several drops of the solution on the lens surface and gently rubbing the lens back and forth with the thumb and fore finger (about 20 to 30 seconds).

10. **Surfactants in hard gelatin capsules:**
    In an experiment benzoic acid as loose powder was filled into a size 00 and a size 1 capsule. The slowest dissolution rate was obtained with the size 1 capsule in which the powder is most tightly packed. They overcome this problem by adding 0.5% of polyol surfactant into the formulation. This greatly improved the dissolution rate which they showed was due to an increase in the deaggregation rate of the material.

11. **Surfactants as cerumen removing solutions:**
    Cerumen is a combination of the secretions of sweat and sebaceous glands of the external auditory canal. The secretions, if allowed to dry, form a sticky semisolid which holds shredded epithelial cells, fallen hair dust and other foreign bodies that make their way into the ear canal. Excessive accumulation of cerumen in the ear may cause itching, pain, impaired hearing and is a deterrent to otologic examination .Through the years, light mineral oil, and hydrogen per oxide have been commonly used agents to soften impacted cerumen for its removal. Recently, solutions of synthetic surfactants have been developed for their cerumenolytic activity in the removal of ear wax. A commercial product utilizes carbamide peroxide in glycerin/propylene glycol. On contact with the cerumen, the carbamide peroxide releases oxygen which disrupts the integrity of the impacted wax, allowing its easy removal.Tri ethanolamine polypeptide oleate- condensate, commercially formulated in propylene glycol, is used to emulsify the cerumen thereby facilitating its removal (Cerumenex drops). Brands in Pakistan ABBOWAX drops, CARBOWAX drops. (Dimmitt P.J Pediatr. Health Care. 2005 Sep-Oct)
12. **Surfactant influencing drug absorption:**
    Surfactants influences drug absorption from the gastrointestinal tract in humans. Surfactant monomers can potentially disrupt the integrity and function of a membrane. Hence, such a membrane disrupting effect would tend to enhance drug penetration and hence absorption across the gastrointestinal barrier.
    The ability of a surfactant to reduce the solid/liquid interfacial tension will permit the gastrointestinal fluids to wet more effectively and to come into more intimate contact with the solid dosage forms.

13. **Surfactants in parenteral dosage forms:**
    Surfactants in parenteral can increase drug solubility through micellization, improve drug wetting, prevent drug precipitation upon injection, improve stability of drug in solution etc. Commonly used surfactant in parenteral is polysorbate 80.

14. **Ophthalmic delivery:**
    Surfactants are sometimes used in topical eye products for dispersing insoluble ingredients or to aid in solubilisation. They are used in smallest concentration since

they can be irritating to sensitive ocular tissues. Non-ionic surfactants are less irritating. Polysorbate 80 is used in preparation of an ophthalmic emulsion.

15. Pulmonary systemic drug delivery:

Pulmonary systemic drug delivery takes advantage of the large surface area of the alveoli, the low enzymatic activity in the lungs, and their rich vascular system to deliver different drugs, especially those of high molecular weight (such as peptides and proteins). To successfully deliver through the lungs, there is a need to use absorption enhancers. Surfactants such as bile salts are used as such enhancers.Surfactants are found in both solution and suspension formulations of metered dose inhalers (MDIs).The most common surfactants found in pressurized aerosol preparations include sorbitantrioleate (Span 85), oleic acid, and Lecithin These agents are non-volatile liquids which dissolve in the propellant blend. Their function in the formulation is to provide lubrication for the metering valves and, in the case of suspension formulations, to maintain the disperse nature of the drug.

16. Buccal and sublingual systemic delivery of drugs:

Buccal and sublingual systemic delivery is a useful alternative administration route through oral mucosa. Penetration enhancing surfactants for example sodium dodecyl sulfate are used to achieve adequate absorption of large molecules. Medicated chewing gum preparations may contain solubilizers, such as lecithin, polysorbates.For example pepsid chewable tablets.

17. Formulation of Shampoo:

Shampoo is a hair care product used for the removal of oils, dirt, skin particles, dandruff, environmental pollutants and other contaminant particles that gradually build up in hair. The goal is to remove the unwanted build-up without stripping out so much as to make hair unmanageable. Shampoo, when lathered with water, is a surfactant, which, while cleaning the hair and scalp, can remove the natural oils (sebum) which lubricate the hair shaft. (Corrigan OI, Healy AM. Surfactants in Pharmaceutical Products and Systems).

Sodium laureth sulfate (SLES) and sodium lauryl sulfate (SLS) are commonly used surfactants (wetting agents) and detergents, often used in diluted form in personal care products like shampoos and body washes. Revlon uses these ingredients in its shampoos. The current science confirms these ingredients are safe for their intended use.

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