chapter 4
Surfactants

Overview

In this chapter we will:

- see why certain molecules have the ability to lower the surface and interfacial tension and how the surface activity of a molecule is related to its molecular structure
- look at the properties of some surfactants that are commonly used in pharmacy
- examine the nature and properties of monolayers formed when insoluble surfactants are spread over the surface of a liquid
- look at some of the factors that influence adsorption onto solid surfaces and see how experimental data from adsorption experiments may be analysed to gain information on the process of adsorption
- see why micelles are formed, examine the structure of ionic and non-ionic micelles and look at some of the factors that influence micelle formation
- examine the properties of liquid crystals and surfactant vesicles
- discuss the process of solubilisation of water-insoluble compounds by surfactant micelles and its applications in pharmacy.

Some typical surfactants

Depending on their charge characteristics the surface-active molecules may be anionic, cationic, zwitterionic (ampholytic) or non-ionic. Examples of surfactants that are used in pharmaceutical formulation are as follows:

Anionic surfactants: Sodium Lauryl Sulphate BP

- is a mixture of sodium alkyl sulfates, the chief of which is sodium dodecyl sulfate, $C_{12} H_{25} SO_4^- Na^+$
- is very soluble in water at room temperature, and is used pharmaceutically as a preoperative skin cleaner, having bacteriostatic action against gram-positive bacteria, and also in medicated shampoos
- is a component of emulsifying wax.

Cationic surfactants

- The quaternary ammonium and pyridinium cationic surfactants are important pharmaceutically because of their

> ## KeyPoint
>
> Surfactants have two distinct regions in their chemical structure, one of which is water-liking or *hydrophilic* and the other of which is water-hating or *hydrophobic*. These molecules are referred to as *amphiphilic* or *amphipathic* molecules or simply as *surfactants* or *surface active agents*.

bactericidal activity against a wide range of gram-positive and some gram-negative organisms.

- They may be used on the skin, especially in the cleaning of wounds.
- Their aqueous solutions are used for cleaning contaminated utensils.

Non-ionic surfactants

- *Sorbitan esters* are supplied commercially as *Spans* and are mixtures of the partial esters of sorbitol and its mono- and di-anhydrides with oleic acid. They are generally insoluble in water (low hydrophile–lipophile balance (HLB) value) and are used as water-in-oil emulsifiers and as wetting agents.

- *Polysorbates* are complex mixtures of partial esters of sorbitol and its mono- and di-anhydrides condensed with an approximate number of moles of ethylene oxide. They are supplied commercially as *Tweens*. The polysorbates are miscible with water, as reflected in their higher HLB values, and are used as emulsifying agents for oil-in-water emulsions.
- *Poloxamers* are synthetic block copolymers of hydrophilic poly(oxyethylene) and hydrophobic poly(oxypropylene) with the general formula $E_m P_n E_m$, where E = oxyethylene (OCH_2CH_2) and P = oxypropylene ($OCH_2CH(CH_3)$) and the subscripts m and n denote chain lengths. Properties such as viscosity, HLB and physical state (liquid, paste or solid) are dependent on the relative chain lengths of the hydrophilic and hydrophobic blocks. They are supplied commercially as *Pluronics* and are labelled using the Pluronic grid, for example as F127 or L62, where the letter indicates the physical state (F, P or L, denoting solid, paste or liquid, respectively). The last digit of this number is approximately one-tenth of the weight percentage of poly(oxyethylene); the first one (or two digits in a three-digit number) multiplied by 300 gives a rough estimate of the molecular weight of the hydrophobe.

A wide variety of drugs, including the antihistamines and the tricyclic depressants, are surface-active.

Tip

HLB stands for hydrophile–lipophile balance. Compounds with a high HLB (greater than about 12) are predominantly hydrophilic and water-soluble. Those with very low HLB values are hydrophobic and water-insoluble.

Reduction of surface and interfacial tension

When surfactants are dissolved in water they orientate at the surface so that the hydrophobic regions are removed from the aqueous environment, as shown in Figure 4.1a. The reason for the reduction in the surface tension when surfactant molecules adsorb at the water surface is that the surfactant molecules replace some of the water molecules in the surface and the forces of attraction between surfactant and water molecules are less than those between two water molecules, hence the contraction force is reduced.

Figure 4.1 Orientation of amphiphiles at (a) solution–vapour interface and (b) hydrocarbon–solution interface.
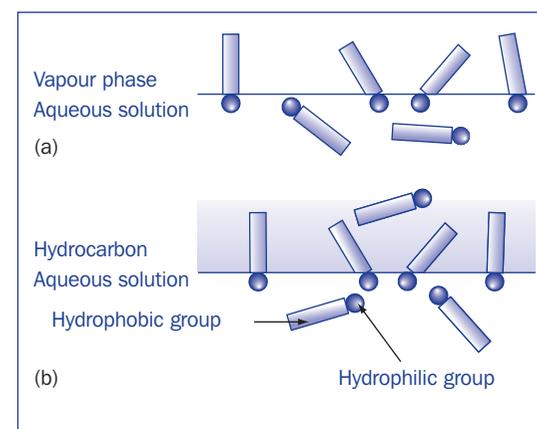
Surfactants will also adsorb at the interface between two immiscible liquids such as oil and water and will orientate themselves as shown in Figure 4.1b, with their hydrophilic group in the water and their hydrophobic group in the oil. The interfacial tension at this interface, which arises because of a similar imbalance of attractive forces as at the water surface, will be reduced by this adsorption.

There is an equilibrium between surfactant molecules at the surface of the solution and those in the bulk of the solution which is expressed by the Gibbs equation:

$$\Gamma_2 = -\frac{1}{xRT}\frac{d\gamma}{2.303\,d\log c}$$

where Γ_2 is the surface excess concentration, R is the gas constant

KeyPoints

- The molecules at the surface of water are not completely surrounded by other molecules as they are in the bulk of the water.
- As a result there is a net inward force of attraction exerted on a molecule at the surface from the molecules in the bulk solution, which results in a tendency for the surface to contract. This contraction is spontaneous and represents a minimum free energy state.
- We express the strength of contraction by the work required to increase the surface area by 1 m²; this is referred to as the *surface tension γ*.
- Units of surface and interfacial tension are mN m⁻¹.

Tip

When substituting values into equations it is important to convert the values into the correct units. In the case of the Gibbs equation it is easy to forget to convert concentration into mol m⁻³ (1 mol l⁻¹ = 1 mol dm⁻³ = 10³ mol m⁻³).

(8.314 J mol^{-1} K^{-1}), T is temperature in kelvins, c is the concentration in mol m^{-3} and x has a value of 1 for ionic surfactants in dilute solution.

The area A occupied by a surfactant molecule at the solution–air interface can be calculated from $A = 1/N_A \Gamma_2$ where N_A is the Avogadro number (6.023×10^{23} molecules mol^{-1}) and dγ/dlog$c$ is the gradient of the plot of surface tension against log$c$ measured at a concentration just below the critical micelle concentration (CMC).

The surface activity of a particular surfactant depends on the balance between its hydrophilic and hydrophobic properties. For a homologous series of surfactants:

- An increase in the length of the hydrocarbon chain (hydrophobic) increases the surface activity. This relationship between hydrocarbon chain length and surface activity is expressed by *Traube's rule*, which states that 'in dilute aqueous solutions of surfactants belonging to any one homologous series, the molar concentrations required to produce equal lowering of the surface tension of water decreases threefold for each additional CH$_2$ group in the hydrocarbon chain of the solute'.
- An increase of the length of the ethylene oxide chain (hydrophilic) of a polyoxyethylated non-ionic surfactant results in a decrease of surface activity.
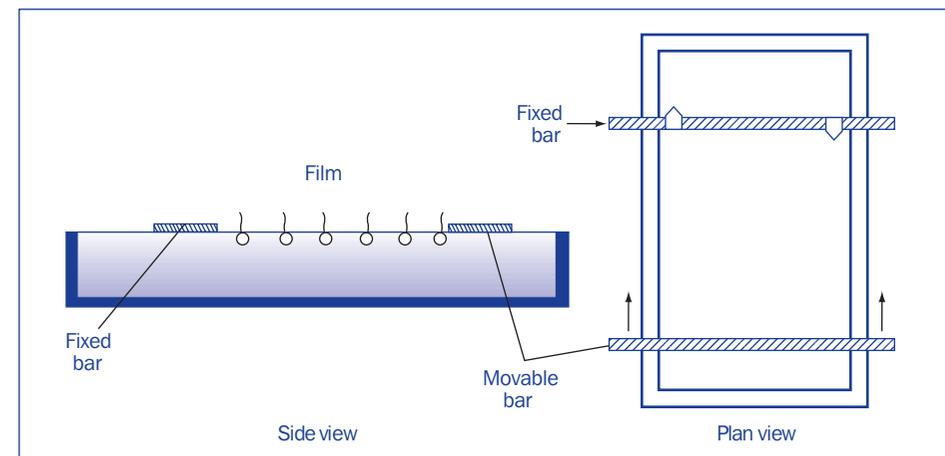
Insoluble monolayers

Insoluble amphiphilic compounds, for example surfactants with very long hydrocarbon chains, will also form films on water surfaces when the amphiphilic compound is dissolved in a volatile solvent and carefully injected onto the surface. Polymers and proteins may also form insoluble monolayers.

The molecules are orientated at the surface in the same way as typical surfactants, i.e. with the hydrophobic group protruding into the air and the polar group acting as an anchor in the surface.

The properties of the film can be studied using a Langmuir trough (Figure 4.2) and the results are presented as plots of surface

> ## Tip
> Remember when using Traube's rule that for every extra CH$_2$ group in the compound you need 3 times less of the compound to produce the same lowering of surface tension. So if you add 2 extra CH$_2$ groups you will require 9 times less of the compound (not 6 times less).

> ## Tip
> Remember that an *increase* in surface activity means a *decrease* in surface tension. Compounds that are most effective in lowering the surface tension are those with a high surface activity.

> ## KeyPoint
> The important difference between the film produced when surfactant molecules accumulate spontaneously at the surface of a surfactant solution and the film formed when insoluble amphiphilic compounds are injected onto a water surface is that in the former the surfactant molecules at the surface are in equilibrium with those in the bulk of the solution and continually move back and forward between the surface and the solution, whereas in insoluble monolayers all the molecules injected on to the surface stay at the surface.

pressure π ($\pi = \gamma_o - \gamma_m$, where γ_o is the surface tension of the clean surface and γ_m is the surface tension of the film-covered surface) against area per molecule.

Figure 4.2 Langmuir trough.

There are three main types of insoluble monolayers (Figure 4.3):

- *Solid or condensed monolayers*, in which the film pressure remains very low at high film areas and rises abruptly when the molecules become tightly packed on compression. The extrapolated limiting surface area is very close to the cross-sectional area of the molecule from molecular models.
- *Expanded monolayers*, in which the π–A plots are quite steeply curved but extrapolation to a limiting surface area yields a value that is usually several times greater than the cross-sectional area from molecular models. Films of this type tend to be formed by molecules in which close packing into condensed films is prohibited by bulky side chains or by a *cis* configuration of the molecule.
- *Gaseous monolayers*, in which there is only a gradual change in the surface pressure as the film is compressed. The molecules in this type of monolayer lie along the surface, often because they possess polar groups that are distributed about the molecule and anchor the molecules to the surface along its length. Monolayers of polymers and proteins are often of this type.

Monolayers are useful models by which the properties of polymers used as packaging materials can be investigated. They may also be used as cell membrane models.

Figure 4.3 Surface pressure, π, versus area per molecule, A, for the three main types of monolayer.
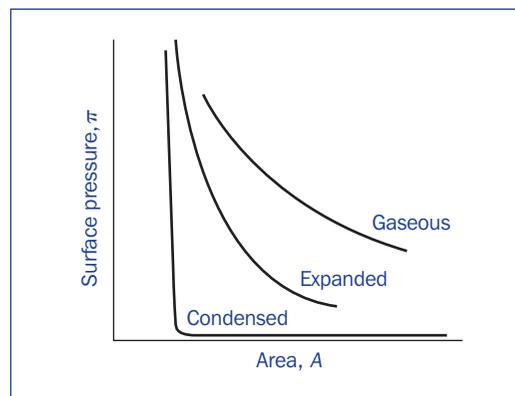
KeyPoint

Note the difference between the term *adsorption*, which is used to describe the process of accumulation at an interface, and *absorption*, which means the penetration of one component throughout the body of a second.

Adsorption at the solid–liquid interface

There are two general types of adsorption:

1. Physical adsorption, in which the adsorbate is bound to the surface through the weak van der Waals forces.
2. Chemical adsorption or chemisorption, which involves the stronger valence forces.

Frequently both physical and chemical adsorption may be involved in a particular adsorption process.

A simple experimental method of studying adsorption is to shake a known mass of the adsorbent material with a solution of known concentration at a fixed temperature until no further change in the concentration of the supernatant is observed, that is, until equilibrium conditions have been established.

Adsorption data may be analysed using the Langmuir and Freundlich equations:

■   The *Langmuir* equation is:

$$x/m = abc/(1 + bc)$$

where x is the amount of solute adsorbed by a weight, m, of adsorbent, c is the concentration of solution at equilibrium, b is a constant related to the enthalpy of adsorption and a is related to the surface area of the solid. For practical usage the Langmuir equation is rearranged into a linear form as:

$$c/(x/m) = 1/ab + c/a$$

Values of a and b may then be determined from the intercept ($1/ab$) and slope ($1/a$) of plots of $c/(x/m)$ against concentration (Figure 4.4).
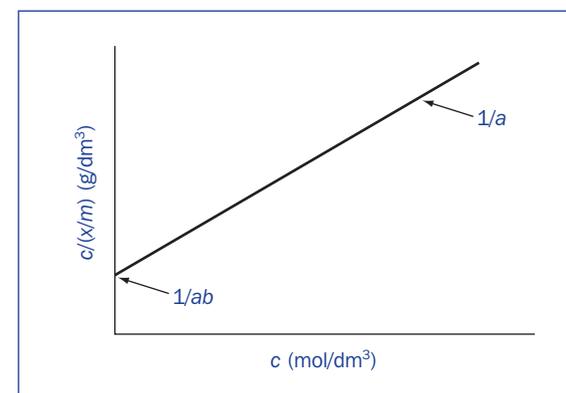
Figure 4.4 A typical Langmuir plot.

■   The *Freundlich* equation is:

$$x/m = ac^{1/n}$$

where a and n are constants, the form $1/n$ being used to emphasise that c is raised to a power less than unity. $1/n$ is a dimensionless parameter and is related to the intensity of drug adsorption. The linear form of this equation is:

$$\log (x/m) = \log a + (1/n) \log c$$

A plot of log (x/m) against log c should be linear, with an intercept of log a and slope of $1/n$ (Figure 4.5). It is generally assumed that, for systems that obey this equation, adsorption results in the formation of multilayers rather than a single monolayer.
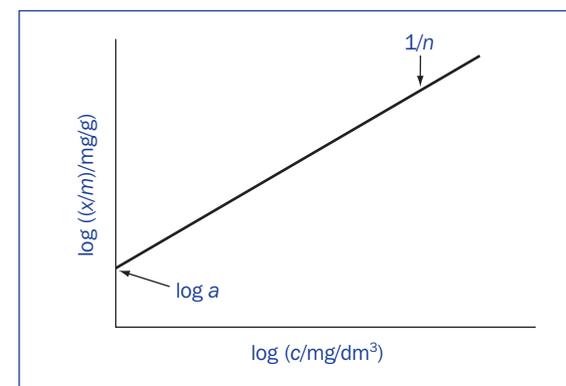
Figure 4.5 A typical Freundlich plot.

Factors affecting adsorption

■   *Solubility of the adsorbate*. In general, the extent of adsorption of a solute is inversely proportional to its solubility in the solvent from which adsorption occurs. This empirical rule is termed *Lundelius' rule*. For homologous series, adsorption from solution increases as the series is ascended and the molecules become more hydrophobic.

■ *pH.* In general, for simple molecules adsorption increases as the ionisation of the drug is suppressed, the extent of adsorption reaching a maximum when the drug is completely unionised (Figure 4.6).

■ *Nature of the adsorbent.* The most important property affecting adsorption is the surface area of the adsorbent; the extent of adsorption is proportional to the specific surface area. Thus, the more finely divided or the more porous the solid, the greater will be its adsorption capacity.

■ *Temperature.* Since adsorption is generally an exothermic process, an increase in temperature normally leads to a decrease in the amount adsorbed.

Figure 4.6 The adsorption onto nylon of a typical weakly basic drug (○) and its percentage in unionised form (●) as a function of pH. Reproduced from N.E. Richards and B.J. Meakin. *J. Pharm. Pharmacol.,* 26, 166 (1974) with permission.
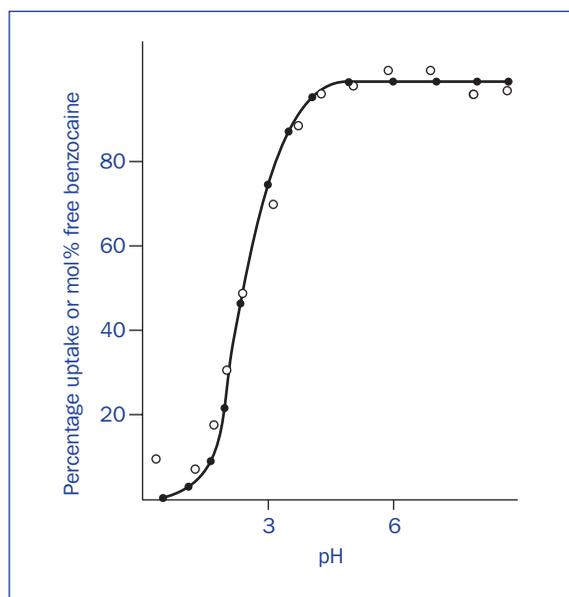
Pharmaceutical applications and consequences of adsorption

■ *Adsorption of poisons/toxins.* The 'universal antidote' for use in reducing the effects of poisoning by the oral route is composed of activated charcoal, magnesium oxide and tannic acid. A more recent use of adsorbents has been in dialysis to reduce toxic concentrations of drugs by passing blood through a haemodialysis membrane over charcoal and other adsorbents.

■ *Taste masking.* Drugs such as diazepam may be adsorbed onto solid substrates to minimise taste problems, but care should be taken to ensure that desorption does not become a rate-limiting step in the absorption process.

■ *Haemoperfusion.* Carbon haemoperfusion is an extracorporeal method of treating cases of severe drug overdoses and originally involved perfusion of the blood directly over charcoal granules. Activated charcoal granules are very effective in adsorbing many toxic materials, but they give off embolising particles and also lead to removal of blood platelets. These problems are removed by microencapsulation of activated charcoal granules by coating with biocompatible membranes such as acrylic hydrogels.

■ *Adsorption in drug formulation.* Beneficial uses include adsorption of surfactants and polymers in the stabilisation of suspensions, and adsorption of surfactants onto poorly soluble solids to increase their dissolution rate through increased wetting. Problems may arise from the adsorption of medicaments by adsorbents such as antacids, which may be taken simultaneously by the patient, or which may be present in the same formulation; and from the adsorption of medicaments on to the container walls, which may affect the potency and possibly the stability of the product.

Micellisation

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 (Figure 4.7).

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.

Most micelles are spherical and contain between 60 and 100 surfactant molecules.
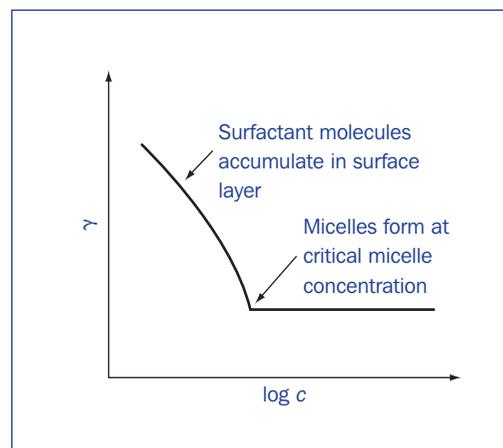
Figure 4.7 Typical plot of the surface tension against logarithm of surfactant concentration, c, showing the critical micelle concentration.

Figure 4.8 (a) Partial cross-section of an anionic micelle showing charged layers; (b) cross-section of a non-ionic micelle; (c) diagrammatic representation of a reverse micelle.

The structure of the micelles formed by *ionic* surfactants (Figure 4.8a) consists of:
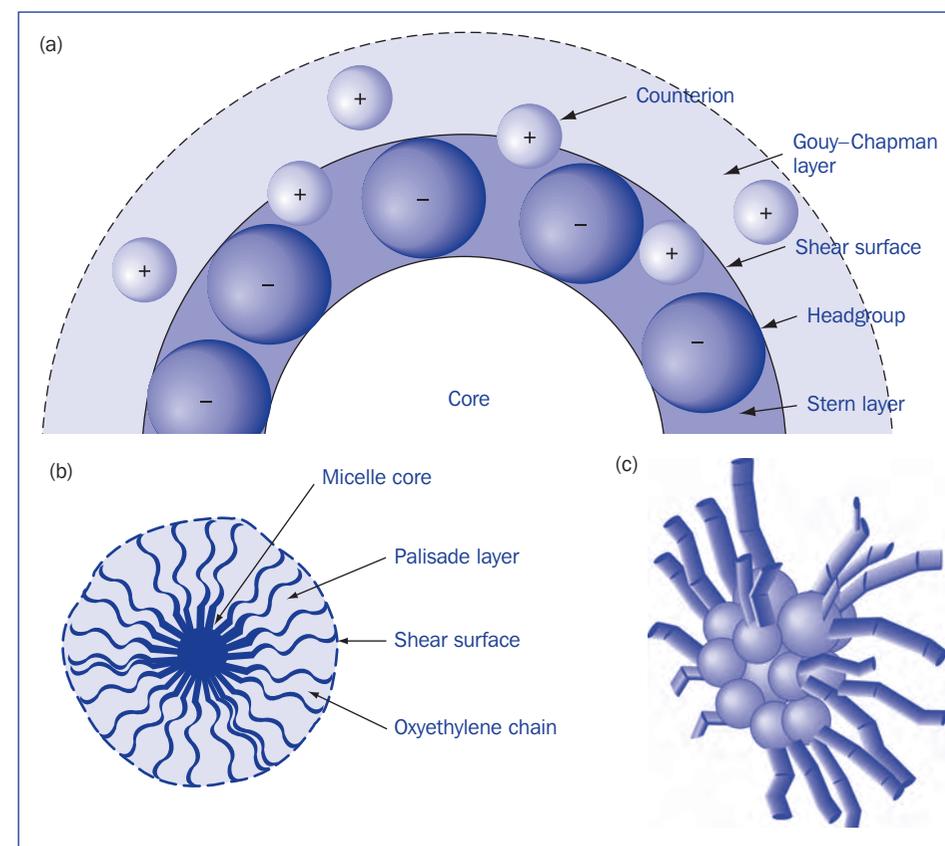
- a hydrophobic *core* composed of the hydrocarbon chains of the surfactant molecule
- a *Stern layer* surrounding the core, which is a concentric shell of hydrophilic head groups with $(1 - \alpha)N$ counterions, where α is the degree of ionisation and N is the aggregation number (number of molecules in the micelle). For most ionic micelles the degree of ionisation α is between 0.2 and 0.3; that is, 70–80% of the counterions 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 αN counterions required to neutralise 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.

Micelles formed by *non-ionic* surfactants:

- are larger than their ionic counterparts and may sometimes be elongated into an ellipsoid or rod-like structure
- have a hydrophobic core formed from the hydrocarbon chains of the surfactant molecules surrounded by a shell (the *palisade layer*) composed of the oxyethylene chains of the surfactant (Figure 4.8b), which is heavily hydrated.

Micelles formed in non-aqueous solution (reverse or inverted micelles) have a core composed of the hydrophilic groups surrounded by a shell of the hydrocarbon chains (Figure 4.8c).

Factors affecting the CMC and micellar size

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:

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

  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.

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.

Type of counterion

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

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.

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.

KeyPoints

- The properties of a surfactant are determined by the balance between the hydrophobic and hydrophilic parts of the molecule.
- If the hydrophobic chain length is increased then the whole molecule becomes more hydrophobic and micelles will form at lower solution concentration, i.e. the CMC decreases.
- If the hydrophilic chain length is increased then the molecule becomes more hydrophilic and the CMC will increase.

## Formation of liquid crystals and vesicles

Lyotropic liquid crystals

The liquid crystalline phases that occur on increasing the concentration of surfactant solutions are referred to as *lyotropic* liquid crystals; their structure is shown diagrammatically in Figure 4.9.

Figure 4.9 Diagrammatic representation of forms of lyotropic liquid crystals.

Hexagonal phase   Cubic phase   Lamellar phase
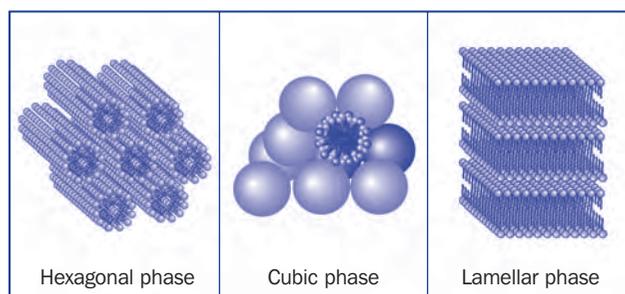
- Increase of concentration of a surfactant solution frequently causes a transition from the typical spherical micellar structure to a more elongated or rod-like micelle.
- Further increase in concentration may cause the orientation and close packing of the elongated micelles into hexagonal arrays; this is a liquid crystalline state termed the *middle phase* or *hexagonal phase*.
- With some surfactants, further increase of concentration results in the separation of a second liquid crystalline state – the *neat phase* or *lamellar phase*.
- In some surfactant systems another liquid crystalline state, the *cubic phase*, occurs between the middle and neat phases (Figure 4.10).
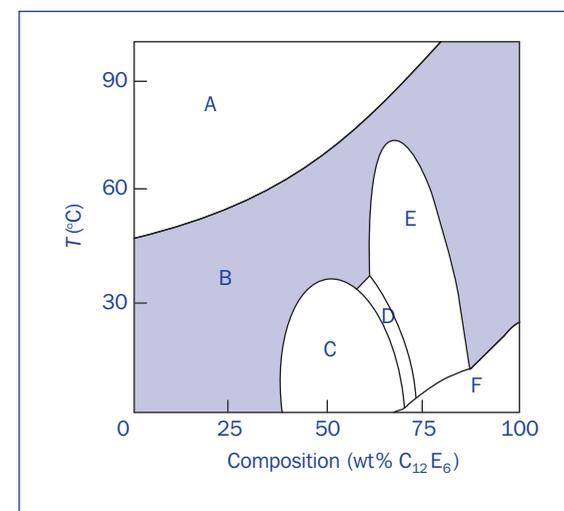
Figure 4.10 Phase diagram of a typical non-ionic surfactant in water. A, two isotropic liquid phases; B, micellar solution; C, middle or hexagonal phase; D, cubic phase; E, neat or lamellar phase; F, solid phase. The boundary between phases A and B is the cloud point. Modified from Clunie J S, Goodman J F, Symons P C. *Trans Farad. Soc.* 1969; 65: 287.

The lyotropic liquid crystals are anisotropic, that is, their physical properties vary with direction of measurement.

- The middle phase, for example, will only flow in a direction parallel to the long axis of the arrays. It is rigid in the other two directions.
- The neat phase is more fluid and behaves as a solid only in the direction perpendicular to that of the layers.
- Plane-polarised light is rotated when travelling along any axis except the long axis in the middle phase and a direction perpendicular to the layers in the neat phase.

KeyPoint

Because of their ability to rotate polarised light, liquid crystals are visible when placed between crossed polarisers and this provides a useful means of detecting the liquid crystalline state.

Thermotropic liquid crystals

Thermotropic liquid crystals are produced when certain substances, for example the esters of cholesterol, are heated. The arrangement of the elongated molecules in thermotropic liquid crystals is generally recognisable as one of three principal types (Figure 4.11):

1. *Nematic liquid crystals*:
   – Groups of molecules orientate spontaneously with their long axes parallel, but they are not ordered into layers.
   – Because the molecules have freedom of rotation about their long axis, the nematic liquid crystals are quite mobile and are readily orientated by electric or magnetic fields.
2. *Smectic liquid crystals*:
   – Groups of molecules are arranged with their long axes parallel, and are also arranged into distinct layers.
   – As a result of their two-dimensional order the smectic liquid crystals are viscous and are not orientated by magnetic fields.
3. *Cholesteric (or chiral nematic) liquid crystals*:
   – Are formed by several cholesteryl esters.
   – Can be visualised as a stack of very thin two-dimensional nematic-like layers in which the elongated molecules lie parallel to each other in the plane of the layer.
   – The orientation of the long axes in each layer is displaced from that in the adjacent layer and this displacement is cumulative through successive layers so that the overall displacement traces out a helical path through the layers.
   – The helical path causes very pronounced rotation of polarised light, which can be as much as 50 rotations per millimeter.
   – The pitch of the helix (the distance required for one complete rotation) is very sensitive to small changes in temperature and pressure and dramatic colour changes can result from variations in these properties.
   – The cholesteric phase has a characteristic iridescent appearance when illuminated by white light due to circular dichroism.

Vesicles

Vesicles are formed by phospholipids and other surfactants having two hydrophobic chains. There are several types:

Liposomes

- Liposomes are formed by naturally occurring phospholipids such as lecithin (phosphatidyl choline).
- They can be multilamellar (composed of several bimolecular lipid lamellae separated by aqueous layers) or unilamellar (formed by sonication of solutions of multilamellar liposomes).

Figure 4.11 Diagrammatic representation of forms of thermotropic liquid crystals. (a) smectic, (b) nematic and (c) cholesteric liquid crystals.
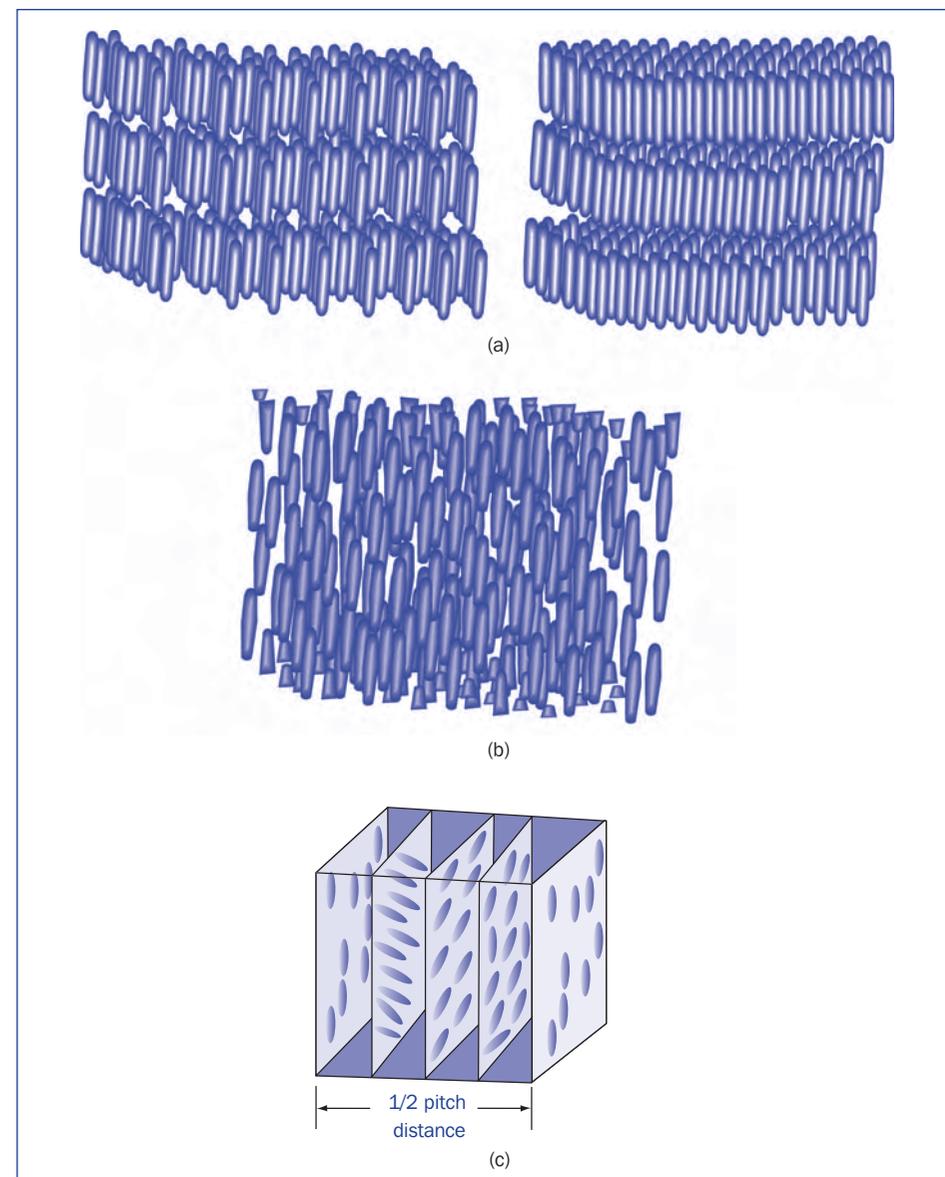
- They may be used as drug carriers; water-soluble drugs can be entrapped in liposomes by intercalation in the aqueous layers, whereas lipid-soluble drugs can be solubilised within the hydrocarbon interiors of the lipid bilayers.

Surfactant vesicles and niosomes

- Formed by surfactants having two alkyl chains.
- Sonication can produce single-compartment vesicles.

KeyPoints

- Solubilisation is the process whereby water-insoluble substances are brought into solution by incorporation into micelles.
- There is a difference between this exact use of the term 'solubilisation' which is used in this chapter and its more general use to mean simply to dissolve in solution.

- Vesicles formed by ionic surfactants are useful as membrane models.
- Vesicles formed from non-ionic surfactants are called niosomes and have potential use in drug delivery.
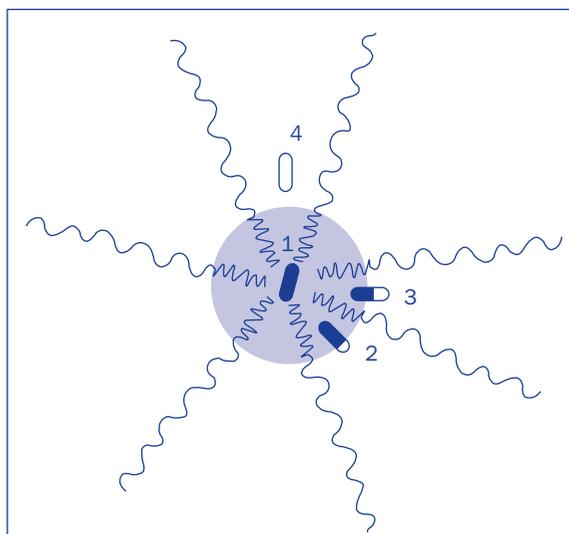
Solubilisation

The *maximum amount of solubilisate* that can be incorporated into a given system at a fixed concentration is termed the *maximum additive concentration* (MAC). Solubility data are expressed as a solubility versus concentration curve or as three-component phase diagrams, which describe the effect of varying all three components of the system (solubilisate, solubiliser and solvent).

The *site of solubilisation* within the micelle is closely related to the chemical nature of the solubilisate (Figure 4.12):

- 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, solubilisation in non-ionic polyoxyethylated surfactants can also occur in the poly–oxyethylene shell (palisade layer) which surrounds the core (position 4).

Figure 4.12 Schematic representation of sites of solubilisation depending on the hydrophobicity of the solubilisate. Redrawn from Torchilin V. *J Control Release* 2001; 73: 137.

Factors affecting solubilisation capacity

Nature of the surfactant

- When the solubilisate is located within the core or deep within the micelle structure the solubilisation capacity increases with increase in alkyl chain length up to about C_{16}; further increase has little effect on solubilisation capacity.
- The effect of an increase in the ethylene oxide chain length of a polyoxyethylated non-ionic surfactant on its solubilising 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 solubilised per micelle decreases, the total amount solubilised per mole of surfactant may actually increase.

Nature of the solubilisate

- For a simple homologous series of solubilisates a decrease in solubilisation 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 solubilisation has been noted for several surfactant systems.

Temperature

- With most systems the amount solubilised 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 solubilisation by the micelles.

Pharmaceutical applications of solubilisation

- the solubilisation of phenolic compounds such as cresol, chlorocresol, chloroxylenol and thymol with soap to form clear solutions for use in disinfection

Tips

- Remember that the micelle core is like a tiny reservoir of hydrocarbon and it is therefore not surprising that there is a close relationship between the distribution of a compound between octanol and water phases in a test tube and its distribution between micelles and water in a micellar solution.
- A very lipophilic solubilisate will mainly reside in the micelles rather than in the aqueous phase surrounding them. This compound will therefore have a high micelle/water partition coefficient and also a high octanol/water partition coefficient.
- On the other hand a hydrophilic compound will be partitioned mainly in the aqueous phase rather than the micelles and will have a low micelle/water and octanol/water partition coefficient.

- solubilised solutions of iodine in non-ionic surfactant micelles (iodophors) for use in instrument sterilisation
- solubilisation of drugs (for example, steroids and water-insoluble vitamins), and essential oils by non-ionic surfactants (usually polysorbates or polyoxyethylene sorbitan esters of fatty acids).

Multiple choice questions

1. **Using Traube's rule, calculate the concentration of a surfactant with a hydrocarbon chain length of 16 carbon atoms that would be required to achieve the same lowering of the surface tension of water as a 8×10^{-4} mol dm⁻³ solution of a surfactant in the same homologous series with a hydrocarbon chain length of 18 carbon atoms:**
   a. 0.89×10^{-4} mol dm⁻³
   b. 7.2×10^{-3} mol dm⁻³
   c. 2.4×10^{-3} mol dm⁻³
   d. 4.8×10^{-3} mol dm⁻³
   e. 1.33×10^{-4} mol dm⁻³

2. **The slope of a plot of surface tension against logarithm of surfactant concentration for an aqueous surfactant solution measured at a concentration just below the CMC at a temperature of 30°C is –0.0115 N m⁻¹. Using the Gibbs equation, calculate the surface excess concentration in mol/m² given that $R = 8.314$ J mol⁻¹ K⁻¹:**
   a. 1.98×10^{-6} mol m⁻²
   b. 2.00×10^{-5} mol m⁻²
   c. 5.04×10^{5} mol m⁻²
   d. 1.64×10^{-5} mol m⁻²
   e. 4.56×10^{-6} mol m⁻²

3. **In relation to the surface tension at the air–water interface, indicate whether each of the following statements is *true* or *false*:**
   a. Surface tension is due to spontaneous expansion of the surface.
   b. Surface tension arises because of the downward pull of molecules in the water.
   c. Surface tension represents a state of maximum free energy.
   d. Surface tension has units of N m⁻¹.
   e. Surface tension is lowered by surface-active agents.

4. **A surfactant has a structure $CH_3(CH_2)_{11}(OCH_2CH_2)_8OH$. Indicate whether each of the following statements is *true* or *false*:**
   a. The surface activity of the surfactant will increase when the alkyl chain length is increased.
   b. The CMC of the surfactant will increase when the alkyl chain length is increased.
   c. The CMC of the surfactant will increase when the ethylene oxide chain length is decreased.

   d. The hydrophobicity of the molecule will increase when the ethylene oxide chain length is increased.
   e. Aqueous solutions of the surfactant will show a cloud point when heated.

5. **Indicate which of the following statements concerning the structure of micelles are correct:**
   a. The core consists of the hydrophobic chains of the surfactant.
   b. The Stern layer of ionic micelles contains the charged head groups.
   c. In ionic micelles most of the counterions are contained in the Gouy–Chapman layer.
   d. Micelles formed by non-ionic surfactants are generally much smaller than those formed by ionic surfactants with identical hydrophobic groups.
   e. The Gouy–Chapman layer of an ionic micelle is compressed in the presence of electrolyte.

6. **In relation to the adsorption of an ionisable drug molecule onto an uncharged solid surface from an aqueous solution, indicate whether each of the following statements is *true* or *false*:**
   a. The amount adsorbed usually increases as the ionisation of the drug decreases.
   b. The amount adsorbed is not affected by change of pH.
   c. The amount adsorbed usually decreases as the ionisation of the drug decreases.
   d. The adsorptive capacity of the solid increases when its surface area is increased.
   e. The adsorptive capacity of the solid is not affected by changes in its surface area.

7. **In relation to insoluble monolayers formed on the surface of water, indicate whether each of the following statements is *true* or *false*:**
   a. Insoluble monolayers are formed by water-soluble surfactants.
   b. The properties of insoluble monolayers are determined by an equilibrium between molecules in the monolayer and those in the bulk solution.
   c. Polymers having several polar groups usually form gaseous films.
   d. Molecules with bulky side chains usually form solid or condensed films.
   e. The area occupied by a molecule in a gaseous film is greater than the cross-sectional area of the molecule.

8. **In relation to liquid crystals, indicate whether each of the following statements is *true* or *false*:**
   a. Thermotropic liquid crystals are formed when concentrated surfactant solutions are heated.
   b. In smectic liquid crystals the long axes of groups of molecules are parallel and organised in layers.
   c. Variation of temperature and pressure of solutions of cholesteric liquid crystals can produce dramatic colour changes.
   d. In the lamellar phase the surfactant molecules are arranged in bilayers.
   e. The hexagonal phase is more fluid than the lamellar phase.

9. **Indicate which** *one* **of the following statements is correct.**
    The main reason why surfactants form micelles is because:
a. There is a decrease of entropy when surfactant molecules are transferred from water to a micelle.
b. There is an increase of entropy when surfactant molecules are transferred from water to a micelle.
c. There is a large decrease of enthalpy when micelles form.
d. There is a large increase of enthalpy when micelles form.
e. The free energy of the system increases when micelles form.

10. **Indicate which** *one* **of the following statements is correct.**
    In the solubilisation of poorly soluble drugs by aqueous surfactant solutions:
a. Non-polar drugs are usually solubilised in the palisade layer of a non-ionic micelle.
b. Polar drugs are usually solubilised in the micelle core.
c. Drugs with a high octanol/water partition coefficient will usually have a high micelle/water partition coefficient.
d. The solubilisation capacity of a non-ionic surfactant usually decreases with increase of temperature.
e. For a homologous series of solubilisates, an increase of solubilisation occurs when the alkyl chain length is increased.