www.sphinxsai.com

PharmTech

International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.1, No.4, pp 1354-1365, Oct-Dec 2009

Basics and Potential Applications of Surfactants - A Review

Manisha mishra[1], P.Muthuprasanna[2*], K.Surya prabha[2], P.Sobhita rani[2], I . A.Satish babu[3] , I. Sarath Chandiran[4],G.Arunachalam[5] and S.Shalini[6].

[1]Department of biotechnology,Amity university,Lucknow,India.
[2]Hindu College of Pharmacy, Amaravathi road, Guntur, Andhra Pradesh,India.
[3] Raos College of Pharmacy , Nellore, Andrapradesh, India.
[4]Gokulakrishna College of Pharmacy , Sullurpet , Andrapradesh , India.
[5]PGP College of Pharmacy , Nammakal, Tamilnadu ,India.
[6]Vidyanikethan College of Pharmacy ,Thirupathi,Andrapradesh,India.

Corresponding author: p_ra2000@yahoo.com

ABSTRACT: Surfactants plays a vital role in various drug delivery. To formulate compounds sparingly soluble in water, pharmaceutically acceptable cosolvents or surfactants are typically employed to increase solubility. Polymeric micelles made by surfactants have a whole set of unique characteristics, which make them a very promising drug carriers for a wide range of drugs. The low solubility in biological fluids displayed by about 50% of the drugs still remains the main limitation in oral, parenteral, and transdermal administration. Among the existing strategies to overcome these drawbacks, inclusion of hydrophobic drugs into polymeric micelles which composed of surfactants are one of the most attractive alternatives. This article reviews about the surfactants, their basics explaining the mechanism to form micelles and its applications related to various site of action.

KEYWORDS: Solubility, Surfactants, Polymeric Micelles, Hydrophobic Drugs.

INTRODUCTION

Surface chemistry deals with the behavior of matter where such behavior is determined largely by forces acting on the surfaces. When phases exist together, the boundary between two of them is termed as interface. Several types of interface can exist depending on whether the adjacent phases are in the solid, liquid or gaseous state. The term surface is customarily used when referring to either a gas-solid or a gas-liquid interface. Every surface is an interface. Interfacial phenomena in pharmacy and medicine are significant factors that affect absorption of drugs onto solid adjuncts in dosage forms, penetration of molecules through biologic membranes, emulsion formation and stability, and the dispersion of insoluble particles in liquid media to form suspensions. The interfacial properties of a surface active agent found lining the alveoli of the lung are responsible for the efficient operation of the organ[1].This surface tension in the surface is defined as the force per unit length that must be applied parallel to the surface so as to counterbalance the net inward pull. This surface tension, has units of dyne/cm in the cgs system. Interfacial tension is the force per unit length existing at the interface between two immiscible liquid phases and, like surface tension, the units are dyne/cm. Interfacial tensions are less than surface tensions because the adhesive forces between two liquid phases forming an interface are greater than when a liquid and gas phase exist together. It follows that if two liquids are completely miscible, no interfacial tension exists between them[2]. The formation of a liquid surface involves a surface free energy change. The surface free energy, which is defined as the work or energy required to increase the surface area by one unit. The units for surface free energy are milli jouls/ m^2 [3].

Surfactants, are wetting agents that lowers the surface tension of a liquid, allowing easier spreading, and can also lower the interfacial tension between two liquids. . The term surfactant was coined by Antara Products in 1950. Surfactants are usually organic compounds that are amphipathic, as they contain both

hydrophobic groups ("tails") and hydrophilic groups ("heads"). Therefore, they are soluble in both organic solvents and water. Surfactants are indicated by the presence of both polar and non polar region.

A surfactant molecule are formed by two parts with different affinities for the solvents. One of them has affinity for water (polar solvents) and the other for oil (non-polar solvents). A little quantity of surfactant molecules rests upon the water-air interface and decreases the water surface tension value (the force per unit area needed to make available surface).

When water, oil and a surfactant are mixed, the surfactant rests at the water-oil interface. These systems depending on their stability are called emulsions or microemulsions (thermodynamically stable). Although, the properties for an emulsion and a micro emulsion are different, both obey the same principle. They try to form enough interface for preventing the polar non-polar solvent contact.

In the field of pharmaceutical sciences , the surfactants are used as emulsifiers , wetting agents solubilizers etc. Those surfactants are mostly derived from petroleum but some may be from natural fats or sugars .

Micro emulsion

Microemulsions are very interesting systems, because the oil-surfactant-water interface forms a wide variety of structures to avoid the direct oil/water contact[4]. The sizes of these structures are in the range of a few hundreds of nanometers, so the solutions are transparent. Micelles are the simplest structures: spherical or cylindrical objects formed by surfactant molecules, separating oil and water molecules. Micelles are like drops of oil in water and reverse micelles are like drops of water in oil.

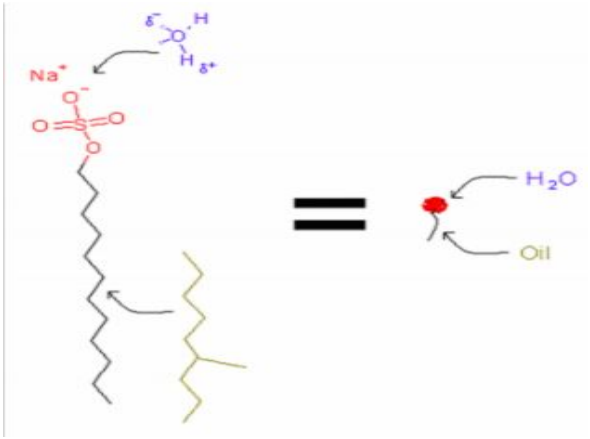

Figure 1 Sodium dodecyl sulphate .The polar "head" has affinity for water and the "tail" has affinity for oil[66]

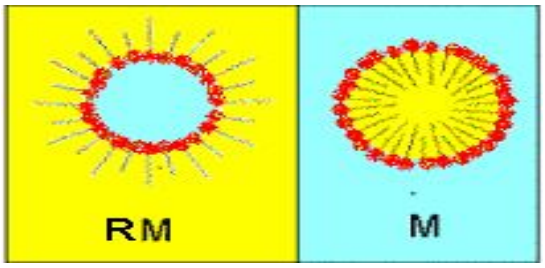

Figure 2 Spherical micelle (M) and reverse micelle (RM)[66]

Another micro emulsion structure are the lamellae where water and oil consecutive layers are separated by surfactant layers oriented conveniently. It presents birefringence and maintains the order even at diluted concentrations. These structures are related with the spherulite structure (onion structure). It is possible that spherulites are only out-of-equilibrium transient lamellar phases induced by mechanical work (yet to be proved) or by other stimulus. The thermodynamic stability of spherulites is still under study[5].

Surfactants, being surface-active agents, adsorb at the oil/water interfaces. The patterns in which they adsorb are well defined due to the properties of each end of the molecule. The hydrophilic heads favours water, while the hydrophobic tails favours oil. It is said that surfactants form oriented, stabilizing films.

In the case of an anionic surfactant, each of the droplets will be negatively charged and a cationic surfactant would give positively charged droplets. Since like charges repel, the surfactant helps to slow the rate of droplet coalescence. This is known as electrostatic stabilisation.

Nonionic surfactants are a little bit more complicated. Rather than forming a charged film, nonionic surfactant heads are polymeric chains dissolved in water. These polymeric chains can be thought of as little springs that push off other droplets, stopping them from coalescing. This is known as steric stabilisation. The surfactant is crucial to creating and maintaining the emulsion. For this reason surfactants are often called emulsifying agents or emulsifiers[6].

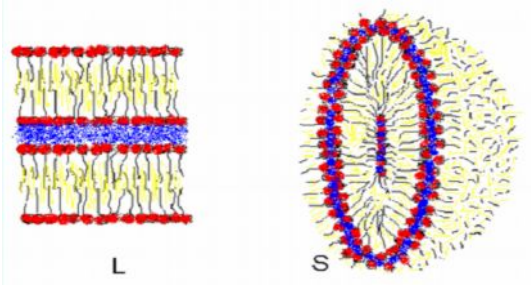

Figure 3 The lamellae (L) and the spherulite (S) structures. The surfactant molecules in the spherulite are arranged as onion like layers[66]

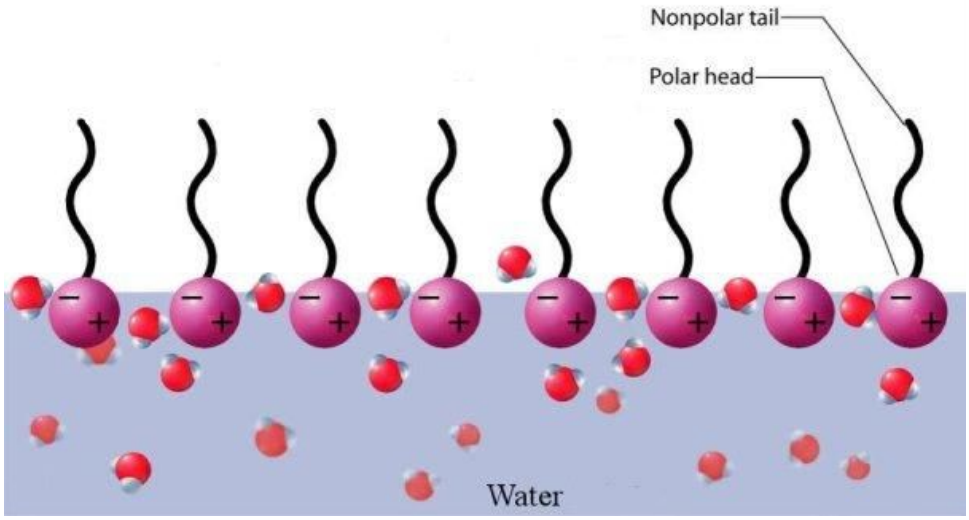

Figure 4 Head and tail orientation of surfactants[67]

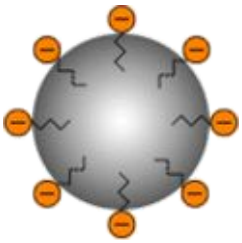

Figure 5 An anionic surfactant gives the emulsion droplets a negative Charge[68]

Mechanism of Action

Surfactants can work in three different ways: Roll-up, Emulsification and Solubilization.

(a) Roll-up mechanism: The surfactant lowers the oil/solution and fabric/solution interfacial tensions and in this way lifts the stain of the fabric.

(b)Emulsification: The surfactant lowers the oil-solution interfacial tension and makes easy emulsification of the oil.

(c)Solubilization: Through interaction with the micelles of a surfactant in a solvent (water), a substance spontaneously dissolves to form a stable and clear solution.

Surfactants are also referred as wetting agents and foam formers. Surfactants not only used for preparing emulsion but also helps in removing dirt/stains from the fabric .Surfactants lower the surface tension of the medium in which it is dissolved. By lowering this interfacial tension between two media or interfaces (e.g. air/water, water/stain, stain/fabric) the surfactant plays a key role in entrapping oil phase. The lower surface tension of the water makes it easier to lift oil which would be the basis of cleaning dirt and grease off dirty dishes, clothes and other surfaces, and help to keep those oily dirt or grease suspended in the water thus forming emulsions. The water-loving or hydrophilic head remains in the water and it pulls the oil towards the water.

Contact angle:

The contact angle is the angle at which a liquid/vapor interface meets the solid surface. The contact angle is specific for any given system and are determined by the interactions across the three interfaces. Most often the concept is illustrated with a small liquid droplet resting on a flat horizontal solid surface. The shape of the droplet is determined by the Young-Laplace equation[7]. The contact angle plays the role of a boundary condition and measured using "Goniometer" [7]. The contact angle is not limited to a liquid/vapour interface; it is equally applicable to the interface of two liquids or two vapour[8].

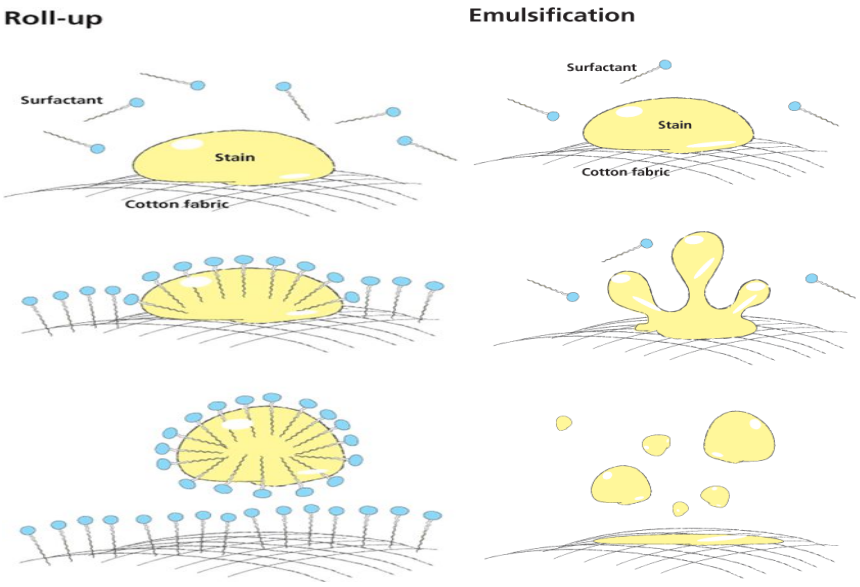

Figure 6 Surfactant mechanism of action in stain removal from fabric[69]

Figure 7 Waterdroplet on a glass slide [70]

Figure 8 Contact angle [71]

Classification of surfactants:

Surfactant can be classified based on charged groups present in their head. A nonionic surfactant do not have any charge groups over its head. The head of an ionic surfactant carries a net charge. If the charge is negative, the surfactant is more specifically called anionic and if the charge is positive, it is called cationic. If a surfactant contains a head with two oppositely charged groups, it is termed zwitterion.

(a)Anionic surfactants:

In solution, the head is negatively charged. These surfactants are the most widely used type of surfactant for preparing shampoos because of its excellent cleaning properties and high hair conditioning effects. Anionic surfactants are particularly effective at oily cleaning and oil/clay suspension. Still, they can react in the wash water with the positively charged water hardness ions (calcium and magnesium), which can lead to partial deactivation. The more calcium and magnesium molecules in the water, the more the anionic surfactant system suffers from deactivation. To prevent this, the anionic surfactants need help from other ingredients such as builders (Ca/Mg sequestrants) and more detergent should be dosed in hard water. The most commonly used anionic surfactants are alkyl sulphates, alkyl ethoxylate sulphates and soaps[7]. Most of the anionic surfactants arre carboxylate ,sulfate and sulfonate ions [72] . The straight chain is a saturated /unsaturated C12-C18 aliphatic group. The water solubility potential of the surfactant is determined by the presence of double bonds [73].

There are five subgroups of anionic surfactants. They are Alkali metal and ammonium soaps , Divalent and trivalent metal soaps, Amine soaps , Alkyl sulphates and alkyl phosphate anionic surfactants. Alkali metal soaps are sodium ,potassium or ammonium salts of long chain fatty acids such as oleic ,stearic and ricinoleic acid and they produce oil in water emulsion. They are stable above pH 10 but are very sensitive to acids and the emulsion to break. Divalent and trivalent surfactants are water in oil emulsifying surfactant. They are less alkaline and less sensitive to acids. In the case of amine surfactants triethanolamine surfactant is preferentially used for pharmaceutical applications. They form oil in water emulsion. Alkyl sulphate anionic surfactants are the esters of fatty alcohols and sulphuric acids. Most widely used surfactants are sodium lauryl sulphate. They are oil in water emulsifying agents .Alkyl phosphates are similar to that of alkyl sulphates but they have their alcohols phosphate instead of sulphated.They are mostly sued to prepare oil in water emulsion creams.

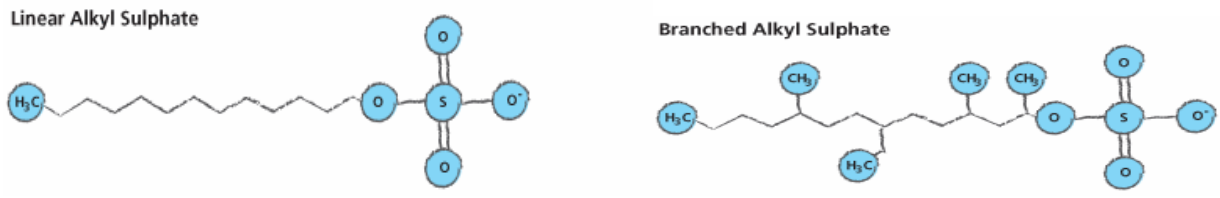

Figure 9 Linear and branched alkyl sulphates(Anionic surfactant)[74]

(b) Cationic Surfactants:

In solution, the head of the cationic surfactant is positively charged.Cationic surfactants are quartenary ammonium compounds and they are mostly used for their disinfectant and preservative properties as they have good bactericidal properties.They are used on skin for cleansing wounds or burns. Mostly used cationic surfactants are cetrimide which has tetradecyl trimethyl ammonium bromide with minimum amount of dodecyl and hexadecyl compounds [75] . Other cationic surfactants are benzalkonium chloride,cetylpyridinium chloride etc.

(c) Non-Ionic Surfactants:

Those surfactants do not have any electrical charge, which makes them resistant to water hardness deactivation. They are less irritant than other anionic or cationic surfactants. The hydrophilic part contains the polyoxyethylene ,polyoxypropylene or polyol derivatives. The hydrophobic part contains saturated or unsaturated fatty acids or fatty alcohols They are excellent grease/oil removers and emulsifiers. Non-ionic surfactants contribute to making the surfactant system less hardness sensitive.The non ionic surfactant can be classified as Polyol esters ,polyoxyethylene esters , poloxamers . The polyol esters includes glycol and glycerol esters and sorbitan derivatives.Polyoxyethylene esters includes polyethylene glycol (PEG 40,PEG -50 ,PEG- 55). The most commonly used non-ionic surfactants are ethers of fatty Alcohols[7].

(d) Amphoteric/Zwitterionic Surfactants:

These surfactants are very mild, making them particularly suited for use in personal care preparations over sensitive skins. They can be anionic (negatively charged), cationic (positively charged) or non-ionic (no charge) in solution, depending on the acidity or pH of the water. Those surfactants may contain two charged groups of different sign. Whereas the positive charge is almost always ammonium but the source of the negative charge may vary (carboxylate, sulphate, sulphonate). These surfactants have excellent dermatological properties. They are frequently used in shampoos and other cosmetic products, and also in hand dishwashing liquids because of their high foaming properties[7].

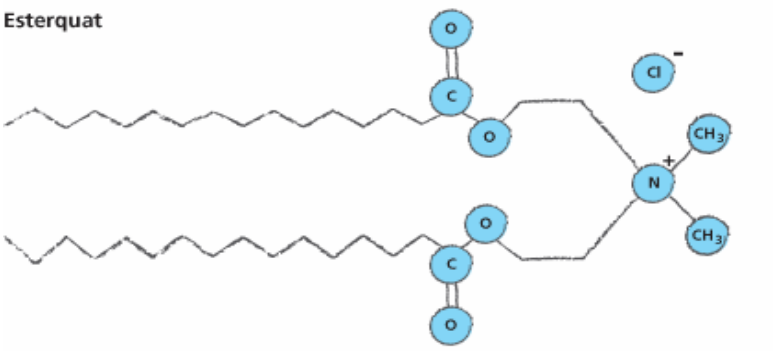

Figure 10 Esterquat cationic surfactant[76]

Figure 11 Esters of fatty alcohols [76]

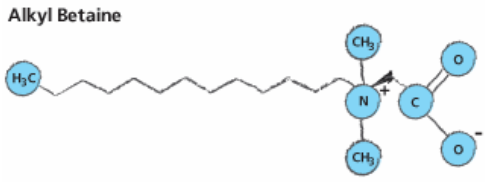

Figure 12 Alkyl betaine [76]

Pharmaceutical Application of surfactants

(a) Surfactants as enhancers for percutaneous absorption:

The transport of molecules through the skin can be increased by the use of certain adjuvant known as enhancers. Ionic surfactants enhance transdermal absorption by disordering the lipid layer of the stratum corneum and by denaturation of keratin. Enhancers may increase drud penetration by causing the stratum corneum to swell and/or leach out some of the structural components, thus reducing the diffusional resistance and increasing the permeability of the skin[8].

Nishihata et al proposed a mechanism for the enhancing the effect of reducing agents such as ascorbate and dithiothreitol[10]. The poor permeability of the skin is due to the ordered layer of intercellular lipids and to low water content. Proteins in keratinized tissue are rich in cysteine residues, and the strong disulfide bonds may be the reason for the insoluble nature of this protein. The reducing agents causes a decrease in the number of disulfide bridges, thus increasing the hydration of the proteins, which results in increased skin permeability.

Azone is one of the most efficient enhancers of percutaneous absorption[11]. It greatly improves the penetration of hydrophilic and hydrophobic compounds, the latter to a small degree. A possible mechanism of azone is its fluidization of the intercellular lipid lamellar region of the stratum corneum. Azone is a very nonpolar molecule which enters the lipid bilayers and disrupts their structure. In contrast, a strongly dipolar solvent, dimethyl sulfoxide (DMSO), enters the aqueous region and interacts with the lipid polar heads to form a large solvation shell and expands the hydrophilic region between the polar heads. As a result, both azone and DMSO increases the lipid fluidity, thus reducing the resistance of lipid barrier to the diffusion of drugs. Alcohol derivatives of N, N disubstituted amino acids and hexamethylene lauramine also enhance the permeability of drugs[12].

(b) Surfactants as flocculating agents:

A suspending agent is frequently added to retard sedimentation of the floccules. Such agents are carboxy methyl cellulose, carbopol 934, veegum, tragacanth, or bentonite which are employed either alone or in combination. This may lead to incompatibilities, depending on the initial particle charge and the charge carried by the flocculating agent and the suspending agent. Flocculating a positively charged particles are done by the addition an anionic electrolyte such as monobasic potassium phosphate[13].

(c) 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 inorder to reduce plaque, gingivitis, dental caries, and stomatitis. Cosmetic mouthwashes may be formulated to reduce bad breath through the use of antimicrobial and/or flavouring agents. Surfactants are used because they aid in the solubilization of flavours and in the removal of debris by providing foaming action[14].

(d) Surfactants in respiratory distress therapy:

Surfactant preparations are used as replacement therapy for the treatment of premature infants suffering from neonatal respiratory distress syndrome (also known as hyaline membrane disease). This pulmonary condition occurs in approximately 20% of the 250,000 premature babies born in the US each year and accounts 5000 deaths annually. A substantial deficiency in the endogenous lung surfactant is the principal factor contributing to the pathology of respiratory distress syndrome. The lung surfactant preparations are used in combination with supplemental oxygen and mechanical ventilation to facilitate gas exchange for either prophylactic or rescue treatment of neonatal respiratory distress syndrome. The exogenous surfactants are either derived from animals or synthesized[15].

(e) Surfatants in suppository bases:

Several nonionic surface active agents, closely related chemically to the polyethylene glycols, have been developed as suppository vehicles[16]. Many of these bases can be used for formulating both water soluble and oil soluble drugs. The surfactants most commonly used in suppository formulations are the polyoxyethylene sorbitan fatty acid esters (tween), polyoxyethylene stearates (Myrj), and the sorbitan fatty acid esters (Span and Arlacel). Caution must be exercised in the use of surfactants with drugs. There are reports indicating increased rate of drug absorption[17-20], and other reports showing interaction of these surface active agents with drugs and consequent decrease in therapeutic activity[21-24]. Each formulation must be tested in vivo to evaluate its medicinal effectiveness, as well as safety. Gross and Becker recommended a water dispersible, high melting point (50^0 C) suppository base consisting of polyoxyethylene 30 stearate (Myrj 51), water, white wax, and dioctyl sodium sulfosuccinate (Aerosol OT)[25].The use of aerosol OT in the formula was claimed to lend synergism to the surfactant and thus aid in rapid disintegration of suppository. The drugs studied were Phenobarbital, quinine hydrochloride, tannic acid, and chloramphenicol. Ward reports on several polyoxyethylene sorbitan derivatives (Tweens), which are designed to melt at body temperature into liquids that disperse readily in the body fluids[26,27].

(f) 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, there by increasing stability

by providing a physical barrier. According to the investigations carried out by Young, Thiel, and Laursen[29] nonionic surfactants were found to be most effective than the other type of surfactants. Those surfactants having an HLB less than 10, such as sorbiton trioleate, could be utilized for aerosol dispersions. Other agents that were found to be useful are sorbiton monolaurate, sorbiton monooleate, and sorbiton sesqioleate[28].

(g) Surfactants in water based aerosols:

Relatively large amounts of water can be used to replace all or part of the nonaqueous solvents used in aerosols. These products are generally referred to as water-based aerosols and depending on the formulation they are emitted as a spray or foam. To produce a spray, the formulation must consist of a dispersion of active ingredients and other solvents in an emulsion system in which the propellant is in the external phase. In this way, when the product is dispensed, the propellant vaporizes and disperses the active ingredients into minute particles. Since propellant and water are not miscible, a three phase aerosol forms (propellent phase, water phase and vapor phase).

Surfactants have been used to a large extent to produce a satisfactory homogeneous 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 polyhydroxylic compounds including glycols, glycerol, and sorbitol esters of oleic, stearic, palmitic, and lauric acid exemplify this series. In general, about 0.5% to 2.0% of surfactant is used. The propellent content varies from 25to60%, but can be as low as 5%, depending on the nature of the product[28].

(h) 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 with in 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 or by placing the lens in the palm of the hand and rubbing gently with a finger tip (about 20 to 30 seconds). The ingredients in these cleansers usually include a nonionic detergent, wetting agent, buffers, and preservatives[28].

(i) Surfactants in hard gelatin capsules:

Aguiar et al measured the dissolution of poorly soluble benzoic acid presented as a loose powder, and the same powder 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. If hydrophobic compounds have to be included in formulations because of filling machine requirements, their deleterious effect on drug release can be overcome by the addition of wetting agents, surfactants at levels of 0.1-0.5%[31].

(j) Surfactants as emulsifying agents:

In surfactants, the lipophilic protein of the molecule generally accounting for the surface activity of the molecule. Owing to their opposing ionic charges, anionic and cationic agents tend to neutralize each other if present in the same system and are thus considered incompatible with one another. Depending upon their individual nature certain members of these groups form o/w emulsions and others w/o emulsions. Anionic emulsifiers include various monovalent, poplyvalent, and organic soaps such as triethanolamine oleate and sulfonate such as sodium lauryl sulfate, benzalkonium type of emulsifier. Agents of the nonionic type include sorbiton esters and the polyoxtetylene derivatives. The ionic nature of the surfactant is of prime consideration in the selection of a surfactant to utilize in forming an emulsion. Non ionic surfactants are effective over pH range 3 to 10, cationic surfactants are effective over pH range 3 to 7, and anionic surfactants require a pH of greater than 8.

A hydrophilic Tween can be combined with a lipophilic Span surfactant at varying proportions so as to produce the desired o/w or w/o emulsion[32] .Boyd et al discussed the molecular association of Tween 40 and Span 80 in stabilizing the emulsions[33]. If the hydrocarbon portion of the Span 80 (sorbiton mono oleate) molecule lies in the oil globule , the sorbiton radical lies in the aqueous phase. The bulky sorbiton heads of the Span molecule prevent the hydrocarbon tails from associating closely in the oil phase. When Tween 40 (polyoxyethylene sorbiton monopalmitate) is added, it orients at the interface such that part of its hydrocarbon tail is in the oil phase, and the reminder of the chain, together with the sorbiton ring and the polyoxyethylene chains, is located in the water phase. It is observed that the hydrocarbon chain of the Tween 40 molecule is situated in the oil globule between the Span 80 chains, and this orientation results in effective van der waals attraction. In this manner the interfacial film is strengthened and the stability of the o/w emulsion is increased against particle coalescence[34].

(k) 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 peroxide 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. One of these agents are tri ethanolamine polypeptide oleate-condensate, commercially formulated in propylene glycol, is used to emulsify the cerumen thereby facilitating its removal (Cerumenex drops). Another commercial product utilizes carbamide peroxide in glycerin/propylene glycol (Debrox drops). On contact with the cerumen, the carbamide peroxide releases oxygen which disrupts the integrity of the impacted wax, allowing its easy removal[35].

(l) Surfactant influencing drug absorption:

Surfactants in general cannot be assumed to be inert excipients since they have been shown to be capable of increasing, decreasing or exerting no effect on the transfer of drugs across biological membranes. In addition, surfactants might also produce significant changes in the biological activity of drugs by exerting an influence on drug metabolizing enzymes or on the binding of drugs to receptor proteins.

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. Inhibition of drug absorption may occur as a consequence of a drug being incorporated into surfactant micelles. If such surfactant micelles are not absorbed, which appears to be usually the case, and then solubilisation of drug may result in a reduction of the concentration of free drug in solution in the gastro intestinal fluids which is available for absorption. Inhibition of drug absorption in the presence of micellar concentrations of surfactant would be expected to occur in the case of drugs which are normally soluble in the gastrointestinal fluid , in the absence of surfactant. However, in the case of poorly soluble drugs whose absorption is dissolution rate limited, the increase in saturation solubility of the drug by solubilization in surfactant micelles could result in more rapid rates of drug dissolution and hence absorption. Very high concentrations of surfactant in excess of that required to solubilize the drug could decrease drug absorption by decreasing the chemical potential of the drug. Release of poorly soluble drugs from tablets and hard gelatin capsules may be increased by the inclusion of surfactants in their formulations.

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. This wetting effect may thus aid the penetration of gastrointestinal fluids into the mass of capsule contents which often remains when the hard gelatin shell has dissolved and/or reduce the tendency of poorly soluble drug particles to aggregate in the gastrointestinal fluids. In each case the resulting increase in total effective surface area of the drug in contact with gastrointestinal fluids would tend to increase the dissolution and absorption rates of the drugs[36].

(m) Surfactant in drug absorption from rectal suppositories:

Riegalman and Crowell have shown that the rate at which the drug diffuses to the surface of the suppository depends on the particle size of suspended drug, and the presence of surface active agents are factors that affect drug release from suppositories[37]. Surfactants can both increase and decrease drug absorption rate. For instance, in the case of sodium iodide, absorption is accelerated in the presence of surfactants and appears to be proportional to the relative surface tension lowering of the vehicle. In addition, Riegelman and Crowell stated that the acceleration of sodium iodide absorption might also be attributed to the mucus peptizing action of the vehicle. The rectal membrane is covered by a continuous blanket, which may be more readily washed away by colonic fluids that have reduced surface tension. The cleansing action caused by the surfactant-containing vehicle may make additional pore spaces available for drug absorption, thus facilitating drug movement across the rectal membrane barrier. In case of phenol-type drugs, absorption rate is decreased in the presence of surfactant, probably because of the formation of a drug-surfactant complex[38].

(n) Surfactants used in transdermal penetration of drugs:

The permeability of a drug depends on the hydration of the stratum corneum. The higher the hydration, greater the permeability. The dermal tissue is fully hydrated, while the concentration of water in the stratum corneum is much lower, depending on ambient conditions. Hydration may promote the passage of drugs in the following way. Water associate through hydrogen bonding with the polar head groups of the lipid bilayers present in the intercellular spaces. The formation of a hydrogen shell loosens the lipid packing so that the bilayer region becomes more fluid[39]. This facilitates the migration of drugs across the stratum corneum. From the rate of transpiration (passage of water from inner layers to the stratum corneum) and diffusivity of water in the stratum corneum, the amount of water in the tissue can be obtained[40].

Surfactants can affect penetration of drugs through the skin. Sarpotdar and zatz[41] studied the penetration of lidocaine through hairless mouse skin invitro from vehicles containing various proportions of propylene glycol and polysorbate20. Propylene glycol is a good solvent for lidocaine and reduces its partitioning into the stratum corneum, lowering the penetration rate. In this study the effect of the surfactants depend on the

concentration of propylene glycol in the vehicle. The decrease of flux for 40% w/w propylene glycol concentration may be explained by micellar solubilisation of lidocaine. It is generally assumed that only the free form of drug is able to penetrate the skin. Thus the micellar solubilisation of lidocaine reduces the thermodynamic activity of the vehicle and retards its penetration. At higher propylene glycol concentration(60% and 80%), an increase in flux was observed, possibly owing to an interaction of the surfactant with propylene glycol[42].

(o) Surfactants in microbiology:

A surfactant may affect the activity of a drug or may itself exert drug action. As an example of the first case, the penetration of hexyl resorcinol into the pinworm Ascaris is increased by the presence of a low concentration of surfactant. This potentiation of activity is due to a reduction of interfacial tension between the liquid phase and the cell wall of the organism. As a result, the adsorption and spreading of hexyl resorcinol over the surface of the organism is facilitated. When the concentration of surface active agent exceeds that required to form micelles, however, the rate of penetration of the anthelmentic decreases nearly to zero. This is because the drug is now partitioned between the micelles and the aqueous phase, resulting in the reduction in the effective concentration.

Quaternary ammonium compounds are examples of surface active agents that in themselves posses antibacterial activity. The agents are adsorbed on the cell surface and supposedly bring about destruction by increasing the permeability or leakiness of the lipid cell membrane. Death then occurs through a loss of essential materials from the cell. Both gram negative and gram positive organisms are susceptible to the action of the cationic quaternary compounds, where as gram positive organisms are attacked more easily by anionic agents than are gram negative bacteria. Nonionic surfactants are least effective as antibacterial agents. In fact they, often aid rather than inhibit the growth of bacteria; presumably by providing long chain fatty acids in a form that is easily metabolized by the organism[43].

(P) Other potential uses of surfactants:

(a) In biochemistry, the practical as well as theoretical importance of surfactants may be illustrated with the following examples: Surfactants have allowed the investigation of molecular properties of membrane proteins and lipoproteins, acting as solubilizing agents and as probes for hydrophobic binding sites[56]. The properties of surfactants, as well as further facts relevant to the particular experiments, must be carefully considered[44]. Surfactants have successfully contributed to the purification of receptors in their active forms[60], such as the neuropeptide receptors[45] and opiate receptors[46]. All holoreceptor- complex and reaction- center isolations require the use of a surfactant in order to separate the integral protein systems from the rest of the membrane[47].

(b) Surfactants have been used in the investigation of the denaturation of bacteriorhodopsin[48] and in thermal stability experiments of rhodopsin[49].

(c) The operations of exchange[50] and removal[51] of surfactants bound to membrane proteins are crucial and have been successfully applied to a wide variety of these proteins.

(d) The effects of surfactants on the function of membrane-bound enzymes such as cytochrome P-450[68] and $(Na^+ + K^+)$-ATPase[52] have also been determined.

(e) Integral membrane proteins can be separated from hydrophilic proteins and identified as such in crude surfactant extracts of membrane or cells[53].

(f) Methods for the solubilization of low-density lipoproteins have advanced the understanding of the assembly, interconversion and molecular exchange processes with plasma lipoproteins[54].

(g) In electrophoresis, various techniques require the use of surfactants. The popular techniques of SDS-PAGE for the identification and subunit molecular weight estimation of proteins is based on a specific type of surfactant-protein interaction[55]. 2D-PAGE uses SDS in one direction and Triton X-100 in the other. This technique has been used to identify proteins containing long hydrophobic regions [56] and relies on the different binding ability of non-ionic surfactants to water-soluble and intrinsic membrane proteins. Isoelectric focusing[57], native electrophoresis and blotting[58] are other electrophoretic techniques which may need surfactants for the solubilization or transfer of membrane proteins.

(h) In high performance liquid chromatography, common techniques such as ion-exchange HPLC, reversed-phase HPLC and sizeexclusion-HPLC may require surfactants to solubilize membrane proteins[59]. Ionpair HPLC requires surfactants as reagents in order to achieve the separation conditions (ionpairing)[60].

(i) Affinity surfactants have been used as reversibly bound ligands in high performance affinity chromatography[61].

(j) Crystallization of membrane proteins was achieved using short chain surfactants, which are believed to shield the hydrophobic intermembrane part of the molecule. Thus the polar interactions between individual molecules come into play, providing the stabilizing force in crystallization[62].

(k) Surfactants are also employed to promote the dissociation of proteins from nucleic acids on extraction from biological material.

(l) Further applications of surfactants in biochemistry are the solubilization of enzymes in apolar solvents via reversed micelles[63] and the isolation of hydrophobic proteins[64].

(m) In analytical chemistry, surfactants have been recognized as being very useful for improving analytical methodology, e.g. in chromatography and luminiescence spectroscopy [65]. For applications requiring highest

quality products, a range of BioUltra standard precipitation reagents were offered[65].

CONCLUSION

Surfactant plays a vital role either in pharma and non pharma field. An exhaustive study of its role and mechanism towards medical field would reveal a wide range of its potential in therapeutic usage. Narrowing the research on each and every surfactant would certainly benefit the field of medical science towards a better cure for various ailments.

REFERENCES

1. Nkadi PO, Merritt TA, Pillers DA.Mol Genet Metab. 2009 Jun; 97(2):95-101.
2. Douillard JM.J Colloid Interface Sci. 2009 Sep 1;337(1):307-10.
3. The Science Of Dosage Form Design. Edited by AE Aulton,2nd edn. Page No:50.
4. Eslamian M, Shekarriz M.Recent Pat Nanotechnol. 2009;3(2):99-115.
5. Striolo A. Small molecules. 2007 Apr;3(4):628-35.
6. Tadros T. Adv Colloid Interface Sci. 2009 Mar-Jun;147-148:281-99
7. Zhang W, Dai X, Zhao Y, Lu X, Gao P.Langmuir. 2009 Feb 17;25(4):2363-8.
8. Choi EC, Choi WS, Hong B.J Nanosci Nanotechnol. 2009 Jun;9(6):3805-9
9. Nokhodchi A, Shokri J, Dashbolaghi A, Hassan-Zadeh D, Ghafourian T, Barzegar-Jalali M.Int J Pharm. 2003 Jan 16;250(2):359-69.
10. .Nishihata T, Rytting JH, Takahashi K, Sakai K.Pharm Res. 1988 Nov;5(11):738-40.
11. L ZP, Liu Q, Lu XW.Di Yi Jun Yi Da Xue Xue Bao. 2002 Nov;22(11):1003-4.
12. Wong O, Huntington J, Nishihata T, Rytting JH.Pharm Res. 1989 Apr;6(4):286-95.
13. Li X, Gu L, Xu Y, Wang Y.Drug Dev Ind Pharm. 2009 Jul;35(7):827-33.
14. Reshad M, Nesbit M, Petrie A, Setchell D.Eur J Prosthodont Restor Dent. 2009 Mar;17(1):2-8.
15. Logan JW, Moya FR.Ther Clin Risk Manag. 2009 Feb;5(1):251-60.
16. Realdon N, Dal Zotto M, Morpurgo M, Franceschinis E.Pharmazie. 2008 Jun;63(6):459-63.
17. Eckert, V., and Muhlemann, H.:Pharmaceutical Acta Hewetiae, 33: 649, 1958:21-24.
18. Whitworth C.W., and Larococa, J.P.: J.Am. pharm. Assoc., Sci. Ed., 48: 353,1959: 576-579.
19. Tardos, L., Ello, I., Magda, K., and Jobba gyi, L.: Acta Pharm. Hung., 29:22, 1959:32-36.
20. Tardos, L.,Weisman, L.J., and Ello, I.: pharmazie 14: 526; 1960:44-47
21. Riegelman, S., and Crowell, W.J: J.Am. pharm. Assoc., Sci. Ed., 47: 127, 1958:433-438.
22. Allawala, N.A., and Riegalman S.: J. Am. Pharm. Assoc., Sci, Ed., 42: 267, 1953:42-48.
23. Eckert, V., and Muhlemann, H.:Pharmaceutical Acta Hewetiae, 33: 649, 1958:65-68.
24. Hennig, W, Uber die Rektale Resorption Von Medicamenten, Zurich, JUris verlag.21(3). 1959:67-73.
25. Gross, H.M., and Becker, C.H.: J.Am.Pharm Assoc., Sci. Ed., 42: 498, 1953:53-58.
26. Ward, W.C. J. Am. Pharm. Assoc., Sci. Ed., 39: 265, 1950:73-76.
27. The Theory And Practice Of Industrial Pharmacy. Leon Lachman, Herbert A. Lieberman, Joseph L.Kanig. 3rd Edition, Page No: 578, 579.
28. The Theory And Practice Of Industrial Pharmacy. Leon Lachman, Herbert A. Lieberman, Joseph L.Kanig. 3rd Edition, Page No: 578, 579.
29. Chokshi U, Selvam P, Porcar L, da Rocha SR.Int J Pharm. 2009 Mar 18;369(1-2):176-84.
30. Subbaraman LN, Bayer S, Glasier MA, Lorentz H, Senchyna M, Jones L.Optom Vis Sci. 2006 Mar;83(3):143-51.
31. Pennings FH, Kwee BL, Vromans H.Drug Dev Ind Pharm. 2006 Jan;32(1):33-7
32. Giménez-Arnau A, Gilaberte M, Conde D, Espona M, Pujol RM.Contact Dermatitis. 2007 Jul;57(1):61-2.
33. J. Boyd, C. Parkinton and P. Sherman, J. Coll. Interface Sci. 41, 359, 1972. 490.
34. Jiao J, Burgess DJ.AAPS PharmSci. 2003;5(1):E7.
35. Cerumen removal products.Dimmitt P.J Pediatr Health Care. 2005 Sep-Oct;19(5):332-6.
36. Li H, Zhao X, Ma Y, Zhai G, Li L, Lou H.J Control Release. 2009 Feb 10;133(3):238-44.
37. Riegelman, S., and Crowell, W.J: J.Am. pharm. Assoc., Sci. Ed., 47: 115, 123, 127, 1958..
38. The Theory And Practice Of Industrial Pharmacy. Leon Lachman, Herbert A. Lieberman, Joseph L.Kanig. 3rd Edition, Page No: 578, 579.
39. B.W. Barry, Int.J.Cosmet. Sci, 10,281, 1988. Through Physical Pharmacy, Alfred Martin, 4th Edition, Page No: 540.
40. Ward, W.C.: J. Am. Pharm. Assoc., Sci. Ed., 39: 265, 1950:32-35.
41. P.P. Sarpotdar and J.L. Zatz, J.Pharm. Sci. 75, 176, 1986:46-48.
42. Physical Pharmacy, Alfred Martin, 4th Edition, Page No: 541: 542.
43. E.Miyamoto, A. Tsuji and T.Yamana, J. Pharm. Sci. 72, 651, 1983:366-368.

44. A. Helenius et al., Methods Enzymol. 56, 1979:734.
45. M. H. Perrin, Methods Enzymol. 124, 164.1986.431:437.
46. R.S. Zukin, R. Maneckjee, Methods Enzymol. 124.1986:53-58.
47. P..A. Loach, Methods Enzymol. 69, 155 1980:36-39.
48. W.J. de Grip, Methods Enzymol. 81, 256.1982:62-69.
49. W.C. Robinson et al., Biochemistry 23, 6121:1984:41-47.
50. S.E. Laursen et al., Anal. Biochem. 153, 387 (1986); B. Kaplan, M. Ras, J. Chromatogr. 423, 376 .1987:421-428.
51. L.S. Kaminsky et al., Biochemistry 26, 1276 .1987:61-64.
52. C. Bordier, J. Biol. Chem. 256, 1604.1981.69-74.
53. M.T. Walsh, D. Atkinson, Methods Enzymol. 128, 582 .1986:58-59.
54. T. B. Nielsen, J. A. Reynolds, MethoUs Enzymol. 48(3).1978:67-69.
55. A. Helenius, K. Simons, Proc. Natl. Acad. Sci. 74, 529 .1977:52-57.
56. P.G. Righetti, Isoelectric Focusing, Elsevier, Amsterdam (1983).
57. Electrophoresis ,O.J. Bjerrum B.J. Radola, ebs. 2nd edn Vol. 9 .1987:51-59.
58. J.P. Andersen. Biochemistry 25, 6439.1986:32-36.
59. lon-Pair Chromatography (M.T. Hearn, ed.), M. Dekker, New York .1985:42-46.
60. L.J. Delucas, C.E. Bugg,Trends in Biotechnology 7, 188 .1987:78-79.
61. P. L. Luisi, C. Laane Trends in Biotechnology 6, 153.1986:52-54.
62. R. Hensch; Biotech. Forum 3, L.J. Cline Love et al., Anal. Chem. 56, 1132A 1984:42-47.
63. H. Hoffmann, G. Ebert, Angew. Chem. 100, 933.1988:59-64.
64. Accessed internet via http://www.sigmaaldrich.com/Area_of_Interest/ Biochemicals/BioUltra/ Detergents_Surfactants.html dated 21-6-2009.
65. Accessed internet via http://www.ficci.com/media-room/speeches-presentations/2000/oct/J__ficci_surfactants.pdf. dated 21-6-2009
66. Accessed internet via http://www.fisica.unam.mx/ grupos/liquids/ tutorials/ microemulsions.htm. dated 21-6-2009
67. Accessed internet via http://www.answers.com/topic/langmuir-blodgett-film. dated 21-6-2009
68. Accessed internet via http://surface.akzonobelusa.com/ asphalt_russian/ chemicals/be/ morebe.htm. dated 21-6-2009.
69. Accessed internet via http://www.scienceinthebox.com/ en_UK/glossary/ surfactants_en.html. dated 21-6-2009
70. Accessed internet via http://www.answers.com/topic/surface-energy. dated 21-6-2009
71. Accessed internet via http://windowoutdoors.com/ WindowOutdoors/ Waterproof%20Breathable%20Fabrics%20-%20Outdoor%20Guide.html. dated 21-6-2009
72. ARG Remington ,The science and practice of pharmacy ,19th edn ,Vol 1 , Easton PA publishing , 1995 ,250 – 251.
73. G.Zagrafti .The science and practice of pharmacy ,19th edn.Vol 1.Easton ,PA , Mack publishing ,1995.pp 241-251.
74. Accessed internet via http://www.scienceinthebox.com/ en_UK/glossary/ surfactants_en.html. dated 21-6-2009
75. S.J.Carter.Dispensing for pharmaceutical students, CBS publisher , PP 128.
76. Accessed internet via http://www.scienceinthebox.com/ en_UK/glossary/ surfactants_en.html. dated 21-6-2009

*****