Characteristic of Surfactant and Block Copolymer in Controlled Drug Delivery

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Abstract—*Block copolymers have found application in the areas of biomaterials, protein separation, drug delivery and cardiovascular therapeutics and as industrially important surfactants. Supramolcular assemblies of block copolymers and polymeric micelles are useful nano carriers for systematic delivery of drugs. Recently, there has been a strong encouragement to build up polymeric micelles with smart functions. Such smart polymeric micelles are assumed to enhance the effectiveness of the loaded drugs as well as to reduce side effects beyond current drug delivery formulations. Synergistic behaviors of mixed surfactant systems may be exploited to diminish the total amount of surfactant used in particular applications resulting in reduction of cost and environment impact. In recent years, the study of the physicochemical properties of solutions formed by mixtures of surfactants has become a topic of interest in the area of self-assembly of surfactants.*

1. INTRODUCTION

- Surfactants

Surfactants, or surface active agents, are very interesting molecules due to their amphiphilic behavior. Surfactant contains both a hydrophobic part and a hydrophilic part. The non-polar hydrophobic part is typically referred to as tail (composed by one or more hydrocarbon chains, although fluorocarbon and dimethylsiloxane chains can be used) and the polar hydrophilic part is referred to as head group which might be either charged or uncharged. Surfactants exist in many different forms in nature [1–2]

Surfactant finds applications in almost every aspects of our daily life directly or otherwise in household detergents and personal care products, in industrial process as in pharmaceuticals, food processing, oil recovery and in nanotechnologies, etc. [3-6].

Surfactant systems play an important role in modern drug delivery since they allow, for instance, the control of drug uptake and release rate and minimization of drug degradation and toxicity. An effective synergism between surfactant systems and drugs is nowadays recognized as a key issue to assure remedial competence. Thus, it becomes key to understand the physicochemical properties and behavior of surfactants in formulations. [7]
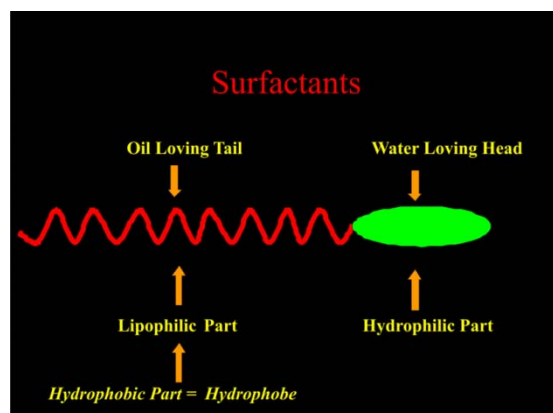

Fig. 1

Some of the surfactant applications are: Surfactants as enhancers for percutaneous absorption, as flocculating agents, surfactants in mouth washes, in respiratory distress therapy, for contact lens cleaning, for influencing drug absorption, used in transdermal penetration of drugs, in microbiology and many more. [8-16]

Surfactant system having structures such as micellar solutions (micelles), liquid crystalline phases or microemulsions, vesicles often play vital role in drug delivery [17].
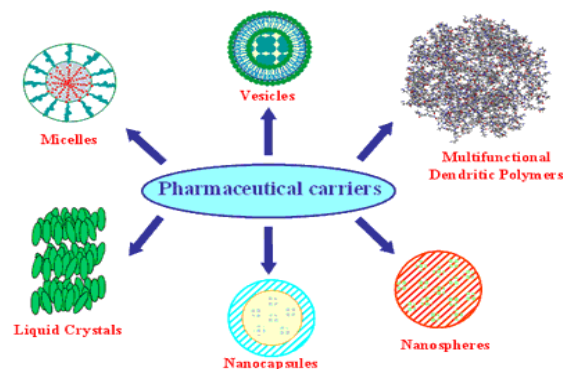

Fig. 2

The goal is to optimized drug loading and release properties and having low toxicity and that can be achieved by using these systems in pharmaceutical formulations.

- Block copolymers

Polymers are large molecules composed of small chemical repeating units called monomers, covalently bound together. Polymers are common plastics, synthetic fibers, as well as cellulose and proteins. They are universally and can show different responses. Many applications require natural occurring polymers, which may be chemically modified to reach a specific function. Chemical and physical versatility, and the potential for a broad range of applications, are good reasons to continue the research on the polymer field.

Natural polymers often possess good biocompatibility, making them popular choices for many bio-applications such as tissue engineering scaffolding. There is a lot of research on the drug delivery systems using polymers but there is still a lot to explore and to improve. [7, 18]

Polymers can show a variety of forms. They can be linear, branched or crosslinked. Also may be composed by monomers of the same type or of different types. The latter can be designated as heteropolymer or copolymer. Copolymer can be further classified by the arrangement of the different monomers along the chain. Therefore, copolymers can be random, block or graft copolymers.

Polyethylene oxide-polypropylene oxide-polyethylene oxide (PEO-PPO-PEO) also known as EPE block copolymers are nonionic surfactants with following structure
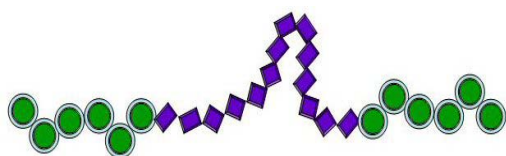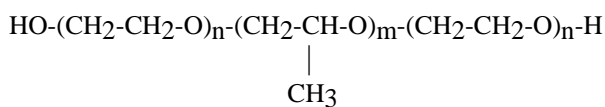
$$HO-(CH_2-CH_2-O)_n-(CH_2-CH-O)_m-(CH_2-CH_2-O)_n-H$$
$$|$$
$$CH_3$$

Fig. 3

Water soluble block copolymers have been found to form nanoaggregates with potential applications. Block copolymers in solvent free systems form spherical, cylindrical and lamellar morphologies. Temperature induced sphere-rod transitions have also been reported in block copolymers.

Self-assembled nanoaggregates of amphiphilic block copolymers depict strong research interest due to the large number of gifted and potential applications. These include smart nanocontainers for encapsulation, delivery and controlled release of biologically active molecules in nanomedicine, food and personal care products.

"Smart" polymers can be constituted by different "smart" blocks, covalently linked together. This type of multi-responsive systems used for multi-drug release at various specific conditions or for diagnosis, is recently attracting researchers. These systems can be simultaneously sensitive to temperature, pH, UV radiation and magnetic fields.

Table 1: Advantages and disadvantages of different structures in drug delivery

| System: Micelles	
Advantages	**Disadvantages**
Low surfactant concentrations required	Sensitive to dilution
Small droplet size	Low solubilization
Easy preparation, Low viscosity	Potential toxicity of surfactant
System: Liquid crystalline phases	
Generally viscous	Generally viscous
Superior solubilization	Short release period
Solubilization of both kind of hydrophilic and hydrophobic drugs	In few cases complicated to prepare, sensitive to dilution
System: Vesicles	
Responsive compound	High viscosity
Superior solubilization capacity	In few cases, difficult to prepare
System: Microemulsions	
Long-term stability, simple preparation	Potential toxicity of surfactant
Superior solubilization capacity, tiny droplet size	Requires high surfactant concentrations
System: polymer-surfactant	
Superior stability	Very stable
Solubilization of both kind of hydrophilic and hydrophobic drugs	Hard to degrade or dissolve
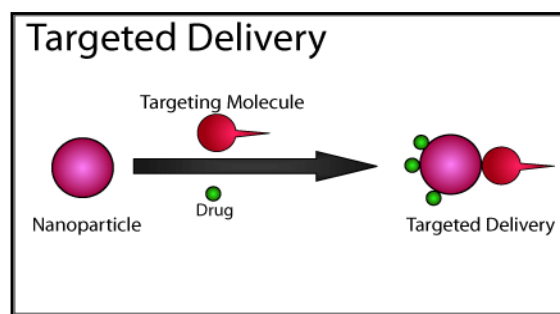
Fig. 4

Due to the widespread use of mixtures of polymers and surfactants in drug delivery formulations, it is very important to control and to understand the phase behavior of such mixtures. The entire concept of having a drug delivery system which allows the body to use the administered drug in the suitable amount and site is constantly spreading attention in the scientific society [19-21]

Similar to block copolymers, low molecular weight amphiphiles are well known to form micelles that solubilize hydrophobic drugs. For the purpose of drug delivery clear advantages may exist for polymeric micelles, mainly due to the polymeric nature of these systems (Fig. 5).

The tendency for micellization is overall much higher in block copolymers in comparison to surfactants since the exposure of a long hydrophobic block to water is adverse to a greater extent
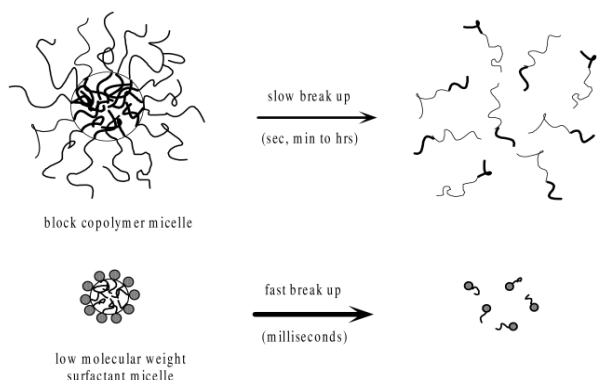

Fig. 5: Break up of polymeric micelles versus low molecular weight surfactant micelles

Efforts have led for the preparations of micellar carriers that can be safely administered to humans and adequately solubilize drugs. The hydrophilic block in these systems is usually PEO with a molecular weight ranging from 1000 to 20,000 g mol. PEO has been used safely in humans and is approved by regulatory agencies for administration. The use of other hydrophilic polymers as shell-forming blocks has been reported for bioadhesive. [22]

Most of the studies on block copolymers have been conducted on Pluronics. Like low molecular weight surfactants; Pluronics demonstrate solubilizing effects for parenteral drug administration. Overall, many Pluronics used for drug solubilization have high ratios of PEO to PPO and are non-toxic relative to many low molecular weight surfactants, e.g. Tween 80 [23-24]

2. FUTURE SCENARIO

Trends now focus to substitute the nonbiodegradable detergents by ecofriendly substitutes and biosurfactants are a step forward in this field. Though the biosurfactants may not as powerful as the existing detergents, their functional properties can be greatly modified when present as mixture with EO-PO block copolymers**.** Since the block copolymers being ecofriendly and finds large biomedical applications, their mixed micelle systems will be exploited to tune their best performance in controlled drug release, two-phase protein extraction and their interaction with biosurfactant. Thus we

can say that amphiphilic moieties are versatile as far as their application is concerned.

3. CONCLUSIONS

A wide range of self assembling surfactant structures in the size ranging from few nanometers to many micrometers have been reported. Of these, some structures like liposomes, micelles, vesicles, Pluronics have conventionally been used for drug delivery. Polymeric micelles have a great potential for selective drug delivery in a passive or active manner. [25] Supramolcular assemblies of block copolymers and polymeric micelles are useful nanocarriers for systematic delivery of drugs. Recently, there has been a strong incentive to develop polymeric micelles with smart functions. Such smart polymeric micelles are assumed to enhance the efficiency of the loaded drugs as well as to minimize side effects beyond current drug delivery formulations.

4. ACKNOWLEDGEMENTS

REFERENCES

[1] Schramm LL (2000) Surfactants: fundamentals and applications in the petroleum industry, University Press, Cambridge

[2] Goodwin J (2004) Colloids and interfaces with surfactants and polymers-an introduction, Wiley, Chichester

[3] Y. Moroi, Micelle, Theoretical and Applied Aspects, Plenum Press, New York and London, 7, 1992

[4] L. L. Schramm, Surfactants: Fundamentals and Applications in Petroleum Industry, Cambridge University Press, Cambridge, 2000

[5] K. Holmberg, B. Jonsson, B. Kronberg, B. Lindman, Surfactants and Polymers in Aqueous Solution, 2nd Ed., John Wiley and Sons, New York, 2002

[6] L. L. Schramm, E. N. Stasiuk, D. Gerrard Marangoni, Annu. Rep. Prog. Chem., Sect. C, 99, 3, 2003

[7] Salomé dos Santos, Bruno Medronho, Tiago dos Santos, and Filipe E. Antunes, Amphiphilic Molecules in Drug Delivery Systems, Springer Science, 2013

[8] Li X, Gu L, Xu Y, Wang Y.Drug Dev Ind Pharm. 2009 Jul;35(7):827-33.

[9] Reshad M, Nesbit M, Petrie A, Setchell D.Eur J Prosthodont Restor Dent. 2009 Mar; 17(1):2-8.

[10] Logan JW, Moya FR.Ther Clin Risk Manag. 2009 Feb;5(1):251-60.

[11] Realdon N, Dal Zotto M, Morpurgo M, Franceschinis E.Pharmazie. 2008 Jun; 63(6):459-63

[12] Leon Lachman, Herbert A. Lieberman, Joseph L.Kanig, The Theory And Practice Of Industrial Pharmacy. 3rd Edition, Page No: 578, 579

[13] Chokshi U, Selvam P, Porcar L, da Rocha SR.Int J Pharm. 2009 Mar 18; 369(1-2):176-84

[14] Li H, Zhao X, Ma Y, Zhai G, Li L, Lou H.J Control Release. 2009 Feb 10; 133(3):238-44.

[15] Ward, W.C.: J. Am. Pharm. Assoc., Sci. Ed., 39: 265, 1950:32-35

[16] Alfred Martin, Physical Pharmacy, 4th Edition, Page No: 541: 542

[17] Malmsten M (2002) Surfactants and polymers in drug delivery. Marcel Dekker, Inc, New York

[18] Lawrence MJ, Rees GD (2000) Microemulsion-based media as novel drug delivery systems, Adv Drug Deliv Rev 45:89–121

[19] Youan BB (2008) Impact of nanoscience and nanotechnology on controlled drug delivery. Nanomedicine (Lond) 3:401–406

[20] Silva GA (2009) Nanotechnology applications and approaches for neuroregeneration and drug delivery to the central nervous system. Ann N Y Acad Sci 1199:221–230

[21] Ferrari M (2005) Cancer nanotechnology: opportunities and challenges. Nat Rev Cancer 5: 161–171

[22] T. Inoue, G. Chen, K. Nakamae, A.S. Hoffman, An AB block copolymer of oligo(methyl methacrylate) and poly (acrylic acid) for micellar delivery of hydrophobic drugs, J. Control. Release 51 (1998) 221–229

[23] I.R. Schmolka, in: P.J. Tarcha (Ed.), Polymers for Controlled, Drug Delivery, CRC Press, Boca Raton, 1991

[24] T.P. Johnston, S.C. Miller, Toxicological evaluation of poloxamer vehicles for intramuscular use, J. Parenter. Sci., Technol. 39 (1985) 83–89.

[25] A.V. Kabanov, V.A. Kabanov, Interpolyelectrolyte and block ionomer complexes for gene delivery: physico-chemical aspects, Adv. Drug Deliv. Rev. 30 (1998) 49–60