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Theoretical Consideration of Micellar Soubilization

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Abstract

Delivery of poorly water soluble drugs is a major challenge for pharmaceutical formulation scientist. Hydrophobic drugs due to its low bioavailability exhibits unpredictable absorption patterns. Surfactants which upon self assembly results into formation of colloidal sized structures called as micelles are excellent solubilizing agents. This review illustrates the theoretical concepts of Micellar soubilization like solubilization capacity (χ), micelle water partition coefficient (K) and thermodynamics of Micellar solubilization.

Introduction

One the major challenge today in front of formulation scientist is delivering the poorly water soluble drugs effectively. Last two decades have witnessed number of newly discovered drug molecules with poor aqueous solubility. This leads to low bioavailability and erratic absorption patterns. It has been reported that 70% of the new drugs are poorly water soluble (1, 2). The drugs with solubility less than 100µg/ml are considered poorly water soluble and 40% of the currently marketed drugs are practically water insoluble (3). The low solubility of the drugs leads to poor dissolution rate which limits the bioavailability of the orally administered drugs (3). The common strategies for improving the aqueous solubility of the drugs are particle size reduction (4, 5), use of co-solvents (6, 7), cyclodextrin inclusion complexation (8, 9), nono emulsions (10). Surfactants which are amphiphilic molecules have both hydrophilic and hydrophobic portions and regions. By the virtue of this property of surfactants they form colloidal-sized clusters in solutions called as micelles at the concentration threshold called as critical Micellar

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concentration (CMC) (11). It is because of this property of surfactants that they solubilize the hydrophobic drugs (12). Micelles structure has anisotropic distribution i.e. the concentration of water decreases from the surface of the micelles to its core. The core is completely devoid of water and is a complete hydrophobic region of the micelles and it is this region of the micelle which is responsible for solubilizing the hydrophobic drugs. The core is considered to be formed by the association of hydrophobic segment of the surfactant where as the shell of the micelle which is the interface (corona) between the aqueous phase and the core is formed by the hydrophilic segment of the surfactant. The position of the drug getting solubilized in the micelle will depend on the polarity of the drug. The non-polar or hydrophobic drugs gets completely portioned into the core of the micelles where as the drugs with intermediate polarity gets distributed in the palisade layer or on the surface of the micelle (11).

It is highly desirable to estimate the solubilization efficiency of the surfactant so as to comment upon its further utilization in developing a delivery system for a particular drug. The two most common descriptors used for this purpose are molar solubilization capacity (χ) and micelle water partition coefficient (K). These parameters characterize the solubilization efficiency of the surfactant for a particular drug in question. This review also discuss in brief about the micellization process and thermodynamics of micellization and solubilization.

Micellization process

Surfactants are amphiphilic molecules composed of hydrophilic 'head' and hydrophobic 'tail'. Due to this amphiphilic nature when surfactants are added in low concentration to an aqueous solution they adsorb at the air-water interface this results in significant change in the surface or interfacial energy, usually in reduction of interfacial energy. The surfactants form a Micellar structure in the solution at or above the concentration threshold called as critical micelle concentration (12). At CMC both interface and the bulk of the solution are saturated and any further addition of surfactants monomers results in the formation of Micellar aggregates. During the process of micellization the hydrophobic portion of the surfactant molecules associate to form the core of the micelle and the hydrophilic portion positions itself between the core and the external aqueous environment. The core is stabilized by the shell formed by the hydrophilic

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portion of the surfactant. Shell also serves as an interface between the core and the aqueous solution (13). The standard change in the free energy of micellization is given by the following expression:

$$\Delta G = RT\ In\ (CMC) \quad (1)$$

Where ΔG is the change in the Gibbs free energy of micellization, R is the universal gas constant, T is the absolute temperature and CMC is the critical micelle concentration.

The CMC of the surfactant can be determined by sharp deviation in the physical properties of the solution like surface tension, conductivity, osmotic pressure etc. The most commonly used method for determination of CMC of surfactant is surface tension measurement. When the surface tension is plotted as the function of logarithm of surfactant concentration, it is observed that initially the surface tension is dependent on the concentration of the surfactant but when the CMC is reached a sharp break in the curve is observed which indicates the formation of micelles.

Solubility descriptors

The most widely used solubility descriptors of surfactant are (1) molar solubilization capacity (χ) and (2) micelle water partition coefficient (*K*) (15). These descriptors are used to estimate the efficiency of a particular surfactant to solubilize a drug molecule and to compare the solubilization efficiency of various surfactants.

The solubilization capacity (χ) is defined as the number of moles of solute (drug) that can be solubilized by one mole of Micellar surfactant. Solubilization capacity characterizes the capacity or ability of the surfactant to solubilize the solute. It can be calculated by the equation (2) which is the general equation for Micellar solubilization.

$$\chi = \frac{(S_{tot} - S_W)}{(C_{surf} - CMC)} \quad (2)$$

In the above equation S_{tot} is the total drug solubility, S_W is the water solubility of the drug in absence of surfactant, C_{surf} is the molar concentration of the surfactant in the solution, CMC is the critical Micelle concentration.

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The above equation may be rewritten as

$$S_{tot} = S_w + \chi(C_{surf} - CMC) \quad (3)$$

As above the CMC the surfactant monomer concentration is approximately equal to the CMC, hence the term $(C_{surf} - CMC)$ in equation 2 & 3 is equal to the surfactant concentration in miceller form. Hence the equation 3 may be written as:

$$S_{tot} = S_w + \chi C_{surf} \quad (4)$$

Equation 4 may be compared to the equation of straight line. When S_{tot} is plotted against C_{surf} it will result in a straight line with the slope equal to χ i.e. solubilization capacity of the surfactant. In other words the solubilization capacity of the surfactant can be defined as the ratio of the drug concentration in the micelles to the surfactant concentration in the Micellar form (16).

Micelle water partition coefficient (K) is defined as the ratio of drug concentration in the micelle to the concentration of the drug in the water i.e. the solubility of the drug in water S_{tot}. The can be expressed in the mathematical form as equation (5).

$$K = \frac{(S_{tot} - S_W)}{S_W} \quad (5)$$

The micelle water partition coefficient (K) and solubilization capacity (χ) can be related by combining the equation (2) and (5).

$$K_M = \frac{\chi(C_{surf} - CMC)}{S_W} \quad (6)$$

It can now obvious that the above equations that the solubilization capacity (χ) of the surfactant is not related to the water solubility of the drug molecule (equation 2). Whereas the micelle water partition coefficient (K) is related to water solubility of the drug molecule as is evident from equation 6.

From the thermodynamic point of view the Micellar solubilization of the drug molecule is considered as the partitioning of the drug molecule between the two phases i.e. the micelle and

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the aqueous phase (17). The standard free energy of solubilization ΔG can be given by the following expression:

$$\Delta G = -RT\ InK_M \quad (7)$$

Where R is the universal gas constant, T is the absolute temperature and K_M is the molar partition coefficient between the micelle and the aqueous phase. Molar partition coefficient is the partition coefficient when the C_{surf} = 1M. The equation (6) can then be written as $K_M = \frac{\chi(1-CMC)}{S_W}$, so as to eliminate the dependence of micelle water partition coefficient K on the surfactant concentration. The negative value of ΔG indicates spontaneous solubilization. The low value of CMC indicates that the micelles formed are stable for a particular surfactant and the micelles formed by such surfactant will exist even on high dilution with a large volume of blood.

References

1. Lipinski C. Drug-like properties and the causes of poor solubility and poor permeability. J Pharmacol Toxicol Methods. 2000; 44(1): 235–249. doi:10.1016/S1056-8719(00)00107-6
2. Merisko-Liversidge EM, Liversidge GG. Drug nanoparticles: formulating poorly water-soluble compounds. Toxicol Pathol. 2008; 36(1): 43–48. doi: 10.1177/0192623307310946.
3. Horter D, Dressman JB. Influence of physicochemical properties on dissolution of drugs in the gastrointestinal tract. Adv Drug Deliv Rev. 2001; 46(1-3): 75–87. doi:10.1016/S0169-409X(00)00130-7
4. Che E, Zheng X, Sun C, Chang D, Jiang T, Wang S. Drug nanocrystals: a state of art formulation strategy for preparing the poorly water-soluble drugs. Asian J Pharm Sci, 2012; 7(2): 85-95.
5. Elamin AA, Ahlneck C, Alderborn G, Nyström C. Increased metastable solubility of milled griseofulvin, depending on the formation of a disordered surface structure. Int J Pharm, 1994; 111(2): 159-170. doi:10.1016/0378-5173(94)00132-4

ISSN: 2320-3714
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6. Etman MA, Salama RO, Shamsedeen MA, El-Kamel A. Solubilization of etodolac for parenteral administration. Indian J Pharm Sci. 2001; 63(6):459–467.
7. Li P, Zhao L, Yalkowsky SH. Combined effect of cosolvent and cyclodextrin on solubilization of nonpolar drugs. J Pharm Sci. 1999; 88(11):967–969. doi:10.1021/js990159d
8. Kumar NK, Murali MBGV, Prasad CDS, Himasankar K, Seshasayana HA, Murthy VR. Comparative studies on the effect of some hydrophilic polymers on the dissolution rate of a poorly water-soluble drug meloxicam. Indian Drugs. 2002; 39(6): 323–329.
9. Corvi MP, Cirri M, Allolio B. Enhancement of solubility and bioavailability by ternary complexation with β-cyclodextrin and glycine. J Pharm Sci. 2003, 92(11):2177–2184. doi: 10.1002/jps.10485
10. Yen CC, Chen YC, Wu MT, Wang CC, Wu YT. Nanoemulsion as a strategy for improving the oral bioavailability and anti-inflammatory activity of andrographolide. Int J Nanomedicine. 2018; 13: 669–680. doi:10.2147/IJN.S154824
11. Rangel-Yagui CO, Pessoa A Jr, Tavares LC, Micellar solubilization of drugs. J Pharm Pharmaceut Sci.2005; 8(2):147-163, 2005. PMID: 16124926
12. Mall S, Buckton G, Rawlins DA. Dissolution behaviour of sulphonamides into sodium dodecyl sulphate micelles: A thermodynamic approach. J Pharm Sci. 1996: 85(1):75-78. doi: 10.1021/js950225l
13. Jiao J. Polyoxyethylated nonionic surfactants and their applications in topical ocular drug delivery. Adv Drug Deliv Reviews. 2008; 60(15):1663–1673. doi:10.1016/j.addr.2008.09.002
14. Shireen B, Sulthanaa SGT, Bhatb AK, Rakshita. Thermodynamics of micellization of a non-ionic surfactant Myrj 45: effect of additives Colloids and Surfaces A: Physicochemical and Engineering Aspects. 1996; 111(1-2): 57-65. doi:10.1016/0927-7757(95)03491-9
15. Atwood D, Florence AT. Physicochemical principles of pharmacy. 3rd ed. London, The MacMillan Press; 2003.

ISSN: 2320-3714
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September 2021
Impact Factor: 5.2
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16. Alvarez-núñez FA, Yalkowsky SH. Relationship between polysorbate 80 solubilizationdescriptors and octanol-water partition coefficient of drugs. Int J. Pharm. 2000; 200(2): 217-222. doi:10.1016/S0378-5173(00)00386-0

17. Torchilin VP. Structure and design of polymeric surfactant-base drug delivery systems. J Control Rel. 2001; 73:137-172. doi:10.1016/S0168-3659(01)00299-1

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