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REVIEW ARTICLE

Drug Solubilization by Surfactants: Experimental Methods and Theoretical Perspectives

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Abstract: This mini review will give an insight into the need and usefulness of investigating the solubilization of poorly soluble drugs. Commonly used experimental and theoretical models are outlined to study the efficacy of the carrier or excipient for the poorly soluble drugs. Furthermore, the use of surface active agents for drug solubilization is discussed in correlation with the mathematical models suggested from time to time. A few experimental techniques are also discussed which would be very helpful in elucidating the interactions prevailing in the mixed systems of poorly soluble drugs and surface active agents.

Keywords: Solubilization, drug + surfactant, physiochemical properties, theoretical models, thermodynamic parameters, poorly soluble drugs.

1. INTRODUCTION

A lot of pharmaceutical preparations use surface active molecules as dispersal agents. Their use as dispersal or solubilizing media has been widely endorsed in suspensions, emulsions, aerosols, and gels. The various challenges faced in drug release rate, drug solubilization capacity, minimization of drug degradation, and reduction of drug toxicity are being thoroughly investigated. The micelles are thermodynamically stable and possess the property of providing a suitable environment not only for the poorly soluble drugs for their solubilization but also for unstable drugs which get protected from degradation. An understanding of the physicochemical properties and performance of drug + surfactant, both in solution and at interfaces, has become a vital topic for research at academic and industrial levels.

Various thermodynamic and kinetic interpretations of drug solubilization into the micelles have been reported. A few well-established ones are given below:

1.1. Micellar-Drug Solubilization

Solubilization is expressed as the process of dissolution of solubilizate (drug or any other additive) into the micelle to prepare an isotropic solution which is thermodynamically stable. It is already well established that the solubilization of poorly soluble drugs increases after the surfactants have reached a critical minimum concentration, above which micelles are formed (Fig. **1**). The maximum concentration or partitioning of drug which can be solubilized are being investigated using the phase-separation model of micellisation (micelles are considered to be a separate phase in equilibrium with monomers) [1, 2].

Molar solubilization capacity, χ, and the micelle water partition coefficient, *P*, are the parameters which are used to study the drug solubilization in a micellar system. The values of χ are calculated using the equation [13]:

$$\chi = \frac{(S_{tot} - S_w)}{(C_{surf} - cmc)} \quad (1)$$

The significance of χ value lies in the fact that it determines how much one mole of surfactant system solubilizes the moles of drug into the micelle. Here,

S_{tot} = total drug solubility,

$S_{W=}$ water drug solubility,

C_{surf} = molar concentration of surfactant in solution,

CMC = critical micelle concentration and

($C_{surf} - CMC$) ≈ Surfactant concentration in the micellar form as above the *CMC*, the monomer concentration of surfactant becomes approximately equal to the *CMC*.

$$\chi = \frac{\text{drug concentration in the micelles}}{\text{surfactant concentration in the micellar form}}$$

The micelle-water partition coefficient (*P*) is given by the equation:

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