



SOLUBILITY ENHANCEMENT OF FUROSEMIDE IN MICELLAR SOLUTION OF CETYL TRIMETHYLAMMONIUM BROMIDE

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ABSTRACT

The poor aqueous solubility of drugs is a challenging problem of pharmaceutical industries. Objective of present study was to investigate the increasing solubility of furosemide drug in the presence of cetyl trimethylammonium bromide (CTAB) solution. Furosemide is a drug with diuretic properties. Conductivity measurement have been carried out to study the micellar behavior of CTAB in the temperature range of 25°C–40°C. From the measurements, various physicochemical and surface properties Critical micellar concentration (CMC), thermodynamic parameters (ΔG_m° , ΔH_m° , ΔS_m°) have been determined. The negative value of ΔG_m° shows spontaneity of solubilization process. All these parameters have been discussed in terms of drug-drug, drug-solvent and drug-surfactant interactions. This result shows that the solubility of Furosemide drug increases with increasing the concentration of surfactant. This study reveals that use of surfactant in pharmacy is an important tools for finding numerous applications.

KEYWORDS: Micelles; Furosemide; Solubilization; Critical Micellar Concentration.

INTRODUCTION

Furosemide (4-chloro-2-(furan-2-ylmethyl- amino)-5-sulfamoyl benzoic acid is a sulfamoyl anthranilic acid derivative and potent loop diuretic. Furosemide is used in the treatment of hypertension and edema.

Micelle term was introduced by Mc Bain and may be defined as aggregates of long-chain diphilic surfactant molecules or ions formed spontaneously in their solutions at a definite concentration. Micelle formation are important in clinical or pharmaceutical applications. Micelle influence reaction kinetics. Substrate binding and solubilisation in the micelle are the main reasons for influencing reaction kinetics. Micellization characteristics of a surfactant are understood by determining the value of its micellization parameters, such as critical micelle concentration (CMC), aggregation number.

The physico-chemical interactions of drugs with surfactant micelles can be considered as an approximation for their interactions with biological surface. One of the most important aspects associated with this phenomenon is the relative participation of hydrophobic and electrostatic interactions between the drug and surfactant molecule. This may explain the location of drug molecule in the micellar interior. The

combination of intermolecular hydrophobic and hydrophilic interactions between surfactant and drug molecules is considered to affect the self-aggregation of surfactant molecules that leads to the formation of surfactant – drug molecular complexes.

In the present work, we report the interaction of CTAB-Furosemide in aqueous medium using conductivity meter. The drug-surfactant interactions was determined on the basis of conductance of drug when going from an aqueous to more hydrophobic environment at various concentration of surfactant. Micellar solubilization is a widely used alternative for dissolution of poorly soluble drugs. Thus by knowing the structures and properties of micelles the solubility of poorly soluble drugs can be enhanced.

MATERIALS AND METHODS

Chemicals and reagents

Working standards of Furosemide in the form of Lasix tablet were purchased from Sanofi Aventis Pharma, India. Cetyl trimethyl ammonium bromide (CTAB) and potassium chloride was purchased from molychem laboratories (Mumbai, India). Doubly distilled water was used all through the study.

Instrumentation

Digital direct reading systronics type Conductivity meter was used for conductivity measurement. The conductivity meter was calibrated with KCl solution of appropriate concentration range. Thermostat water bath was used for maintaining temperature settings constant throughout the experiments.

Preparation of solutions

A stock solution of CTAB (0.01M) is prepared using double distilled water by direct weighing the chemical in digital electronic balance. From this stock solution a number of solution with desired concentration were prepared. Then these solutions were used for further investigation. The effect of temperature and effect of furosemide drug was found that can be explained through tables and graphs.

Variation of CMC value with increasing temperature

The CMC value is obtained at different temperatures using a digital direct reading conductivity meter. The variation of CMC value of Cetyl trimethyl ammonium bromide (CTAB) with the increasing temperature was found and analyzed for finding suitable temperature required for micellization. The CMC value was measured by plotting a graph between conductivity and concentration of CTAB at various temperature ranging from 25°C- 45°C. Fig. I shows the variation of CMC of CTAB with increasing temperatures.

RESULT AND DISCUSSION

A systematic study on the critical micelle concentration of CTAB was made. Thermal effect and effect of furosemide at different concentration were found. The electrical conductivity is a magnitude that describes the ability of a material or solution to conduct an electric current. The electrical conductivity of a solution depends on the number and mobility of ions and charged particles present in the solution. It was observed that the CMC value of CTAB increases with the increase in temperature. The increases in the CMC value with temperature indicates that the increase in temperature does not favor the formation of micelle. An increase in CMC value with temperature indicates that the CMC value can be reached early at a low temperature i.e. micelle formation can be achieved at a lower temperature and thus solubilization of drugs can also be enhanced in micellar system of CTAB at a low temperature. It was also found that the addition of furosemide decreases the CMC value with increasing the concentration of drug. Thus the oral absorption of hydrophobic drugs can be significantly improved by using this micellar system at low temperature.

Table 1: Variation of CMC of CTAB with the increasing temperature.

S. No.	Temperature (K)	CMC (mM)
1	303	0.9
2	308	1.03
3	313	1.18

Table 2: Variation of CMC of CTAB with increasing concentration of furosemide at different temperature.

Furosemide solution (w/v %)	CMC of CTAB (mM)		
	303K	308K	313K
0	0.9	1.03	1.18
0.01	0.15	0.19	0.23
0.05	0.19	0.22	0.35
0.10	0.25	0.31	0.47

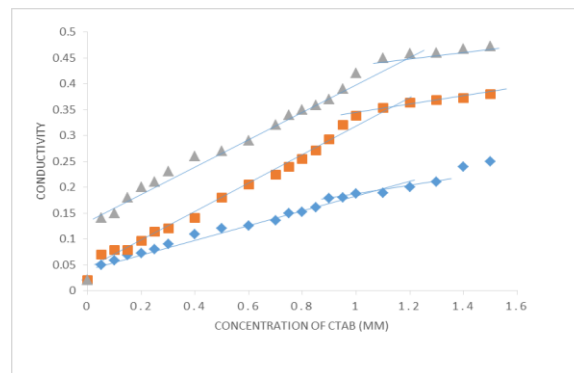


Fig. 1: Conductivity as the function of concentration of CTAB at different temperatures.

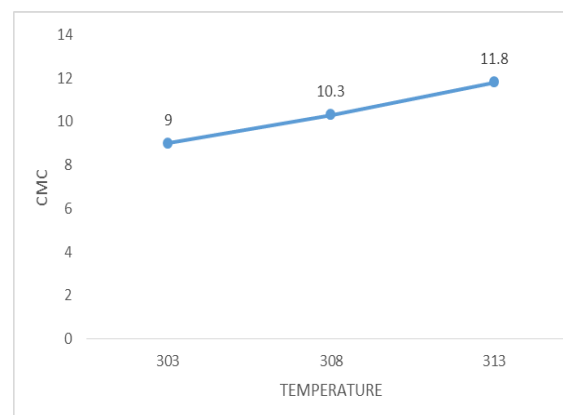


Fig. 2: Variation of CMC of CTAB with increasing temperature.

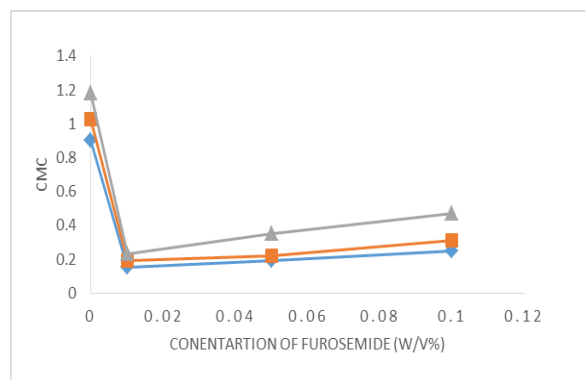


Fig. 3: Variation of CMC of CTAB with increasing concentration of furosemide at different temperature.

CONCLUSION

An increase in the CMC value of CTAB with the increase in temperature suggests that a high temperature retards micellar growth i.e. high temperature does not

favors micellization process. Presence of furosemide in aqueous solutions of CTAB results in a decrease in CMC of these surfactants indicating a good solubility of furosemide in such micellar system. By knowing the suitable values of these parameters, and maintaining these value throughout the experiment, the solubility of poorly soluble drugs in solvent can be enhanced.

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