Effect of Sitagliptin on the Micellization of CetylTrimethylammonium Bromide

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ABSTRACT *Here we determine the specific conductivity of aqueous solution of sitagliptin, an anti-diabetic drug in the presence of cationic surfactant cetyl trimethylammonium bromide (CTAB) at different temperature range. It was interested to enhance the solubility of sitagliptin in the micellar solution. The critical micellar concentration (CMC), degree of ionization and thermodynamic parameters such as Gibb's free energy, enthalpy and entropy were estimated by conductivity measurements. The results confirms that CTAB micelles can solubilizes sitagliptin significantly and increases its solubility in aqueous medium.*

Keywords: *Schedulingmicellization, sitagliptin, cetyltrimethylammonium bromide, solubility.*

INTRODUCTION

Micellar solubilization is an area of investigation for improvement of poorly soluble compounds having pharmaceutical properties. Surfactants are the ampiphilic organic compound having hydrophobic non-polar tail and hydrophilic polar head in a single molecule. In aqueous solution, molecules of surfactant clumps and form an aggregate called micelle. Solubilization of drugs by surfactant system has been reviewed and discussed by a number of researchers. The advantages of micellar solubilization of drugs for drug delivery purpose, solubility of poorly soluble drug, reducing toxicity, improving bioavailability and other side effects.

Sitagliptin is an oral dipeptidyl peptidase IV drug usually used in the treatment of type II diabetes mellitus. They increases the level of insulin and decrease the glycogen in pancreas with the help of alpha cells.

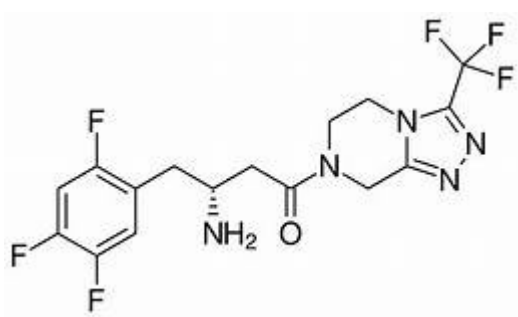


Fig 1: - Chemical structure of sitagliptin

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 comparison between the interactions of CTAB- sitagliptin 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.

EXPERIMENTAL

Surfactant and chemicals are purchased from molychem laboratories, Mumbai and these are AR grade. Januvia (sitagliptin) drug tablets are purchased from authentic distributor. Micropipette (10-100µL)

was used for preparing various working solutions. All the glass wares used are sterilized and cleaned with double distilled water. Double distilled water was used in all solution preparations.

Conductivity measurement were performed with digital conductivity meter supplied by systronic direct reading (type 306). The conductivity cell constant was calibrated with KCl (0.001 and 0.01M) solution in appropriate concentration range. The surfactant solution was progressively added with the help of micro pipette taken in a small beaker and the conductance was measured after thorough at temperature equilibrium. The break point in the plot of specific conductivity versus the total surfactant concentration was taken as the CMC at the mole fraction.

RESULT AND DISCUSSION

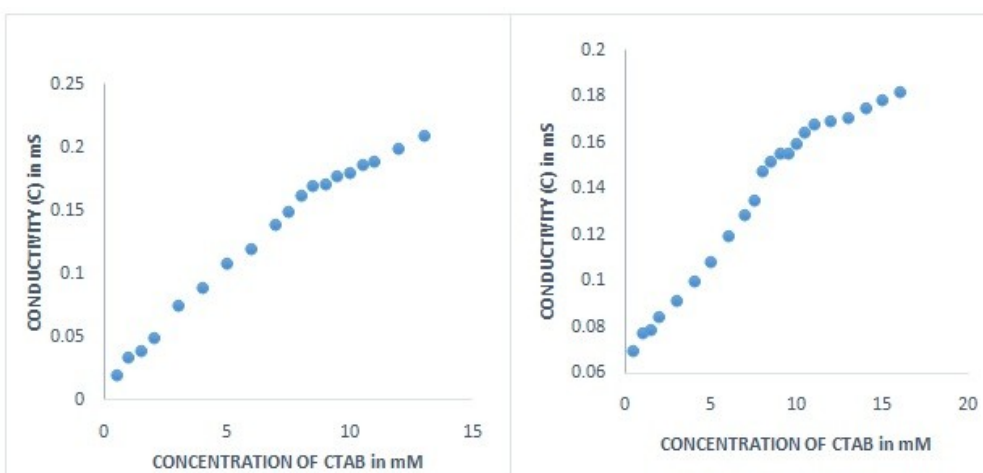
The CMC value of CTAB is obtained at different temperatures using a digital direct reading conductivity meter. The variation of CMC value of Cetyltrimethyl ammonium bromide (CTAB) with the increasing temperature was found and analyzed for finding suitable temperature required for micellization. The CMC value was measured by plotting a graph between equivalent conductivity Vs. $C^{1/2}$ at various temperature ranging from 25°C- 45°C. Fig. II shows the variation of CMC of CTAB with increasing temperatures.

Table 1: VARIATION OF CMC OF CTAB WITH THE INCREASING TEMPERATURE

TEMPERATURE	CMC OF CTAB X 10^{-3}
303 K	9
308 K	11
313 K	14

Table 2: VARIATION OF CMC VALUE OF CTAB WITH INCREASING MOLAR CONCENTRATION OF SITAGLIPTIN AT DIFFERENT TEMPERATURES

MOLAR CONC. OF SITAGLIPTIN	CMC at 303K	CMC at 308K	CMC at 313K
2 x 10^{-3}	8.2 x 10^{-4}	9 x 10^{-4}	10 x 10^{-4}
4 x 10^{-3}	7.4 x 10^{-4}	8.3 x 10^{-4}	9.0 x 10^{-4}
6 x 10^{-3}	7.35 x 10^{-4}	7.9 x 10^{-4}	8.7 x 10^{-4}



[A] [B]

Fig 2: - Conductivity as the function of concentration of CTAB at different temperatures [A] at 303K [B] at 308K.

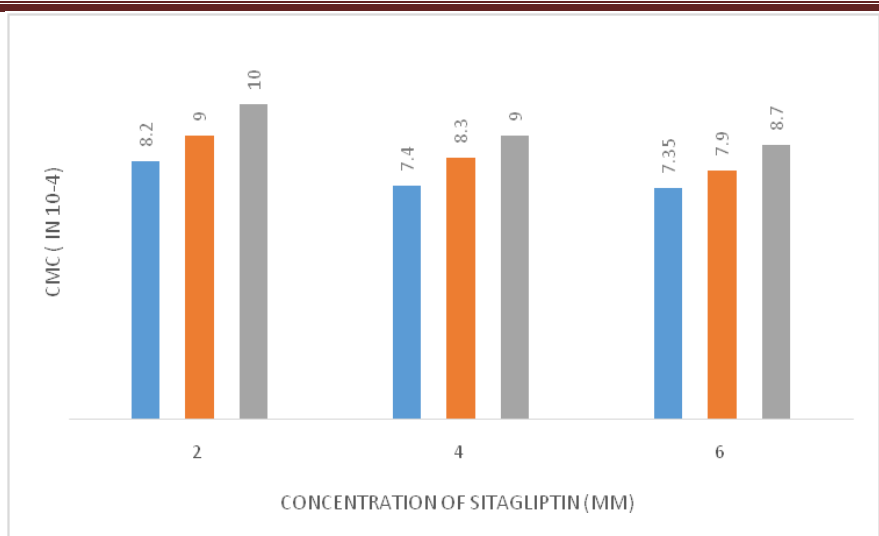


Fig 3: - Variation of CMC value of CTAB with increasing molar concentration of sitagliptin at different temperatures.

The solubility of spironolactone was found to increase with increasing concentration of both the surfactants. Solubilization of drug in surfactant solution can be given by two descriptors such as molar solubilization ratio and micelle-partition coefficient.

From the value of CMC, thermodynamic parameters Gibb's free energy, enthalpy and entropy were estimated as a function of temperature and concentration of drug. From the thermodynamic point of view, all the solubilization behavior of the studied system can be measured by the standard free energy of solubilization ($\Delta G°_m$) given by the following equation –

$$\Delta G°_m = -RT \ln CMC$$

CONCLUSION

Anincrease in the CMC value of SDS with the increase in temperature suggests that a high temperature retards micellar growth i.e. high temperature does not favors micellization process. Presence of spironolactone in aqueous solutions of SDS results in a decrease in CMC of these surfactants indicating a good solubility of spironolactone 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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