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Aqueous Solubility Enhancement of Spironolactone: Effect of Surfactant

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Abstract: ***Here we present experimental surface tension variation of two different categories of surfactant, sodium dodecyl sulphate (SDS) and cetyl trimethylammonium bromide (CTAB) in the presence and absence of spironolactone drug at room temperature. Spironolactone, a potassium sparing diuretic drug has poor aqueous solubility (0.022mg/ml) which possess antihypertensive and antiandrogen activities. From experiments, it was observed that in the presence of drug, the surface tension of surfactant decreases with increasing concentration. From the measurement the decrease value of critical micellar concentration (CMC) was explained on the basis of reduction of free energy. This result shows that the solubility of spironolactone increases in the presence of surfactant. This study will help pharmaceutical industries for drug discovery.***

I. INTRODUCTION

The most common challenges faced by pharmaceutical industry to develop a drug with good aqueous solubility. The poor solubility and permeability through bio-membrane leads poor bio availability of drugs which affect the drug delivery system. 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.

Surfactants widely used in almost every sector of modern industry. They are used in a wide variety of pharmaceutical applications such as in the solubilization of hydrophobic drugs, and as additives in formulations including creams, emulsions, micro emulsions, and suspensions. Surfactants are amphiphilic compounds, which dissolve completely at low concentrations, at least partially water soluble. Because surfactants are absorbed mainly on the surface of the solution, creating a thin monolayer, they are called surface active agents.

Spironolactone is a potassium-sparing diuretic drug with brand name- Lactone. It help to restore a healthy balance of sodium and potassium in body. It is used in the treatment of hypertension, edema, hypokalemia and severe heart failure. The solubility of spironolactone in water is 0.022mg/ml at 25°C.

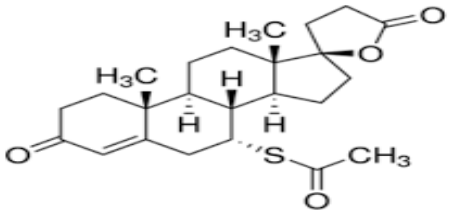


Fig 1: - Chemical structure of spironolactone

In the present work, we report the interaction between different surfactant and spironolactone in aqueous medium using Du nouy tensiometer. The drug-surfactant interactions was determined on the basis of surface tension 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.

II. MATERIAL AND METHOD

A. Chemicals and Apparatus

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Sodium dodecyl sulphate (SDS), cetyl tyrimethylammonium sulphate (CTAB) are purchased from molychem industries, Mumbai (India). All the chemicals are analytical grade. Spironolactone 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.

B. Surface Tensiometer

The surface tension of aqueous solution at various concentration of surfactants were measured on the surface tensiometer (Jencon India) using platinum ring detachment method. The value of surface tension was the average of the three separate measurement. The platinum ring was cleaned with distilled water for 20-25 times. The cleanliness of the glassware and plate were tested by checking the surface tension of pure water. All the measurements were taken at room temperature. Surface tension of solution was measured by vertically hung ring.

C. Preparation Of Solutions

A stock solution of surfactant 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. The working solution of drug (0.005%, 0.01%, and 0.05%) was prepared by 1% w/v solution. The effect of spironolactone drug was found that can be explained through tables and graphs.

III. RESULT AND DISCUSSION

The effect of SDS and CTAB on the solubility of spironolactone was investigated. A linear decrease in surface tension was observed with increase in SDS concentration up to CMC. The CMC of the surfactant decreased in the presence of drug, the decrease being depended upon the concentration of spironolactone. When an increasing amount of the surfactant is added then the concentration of surfactant on water interface increases. In tensiometry, the CMC were obtained from the sharp breaks in the curve of surface tension (γ) versus surfactant concentration. 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 thermodynamic point of view, all the solubilization behavior of the studied system can be measured by the standard free energy of solubilization (ΔG°_m) given by the following equation –

$$\Delta G^\circ_m = -RT \ln CMC$$

Table 1: variation of CMC value of SDS and CTAB with increasing molar concentration of spironolactone

Molar concentration of spironolactone	CMC value of SDS	CMC value of CTAB
0	8.9	0.09
0.005	3.1	0.035
0.01	2.6	0.03
0.05	2.3	0.024

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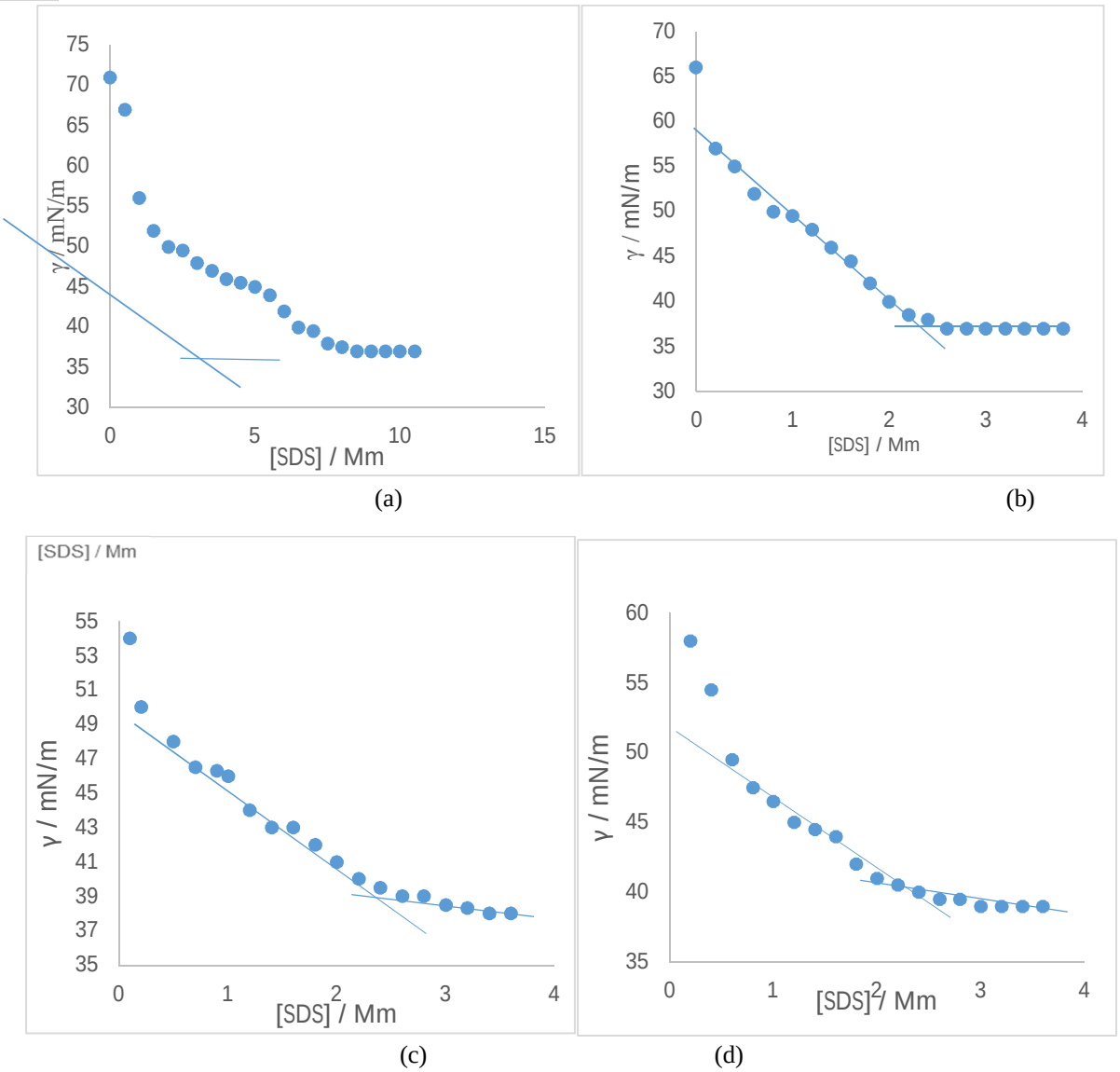
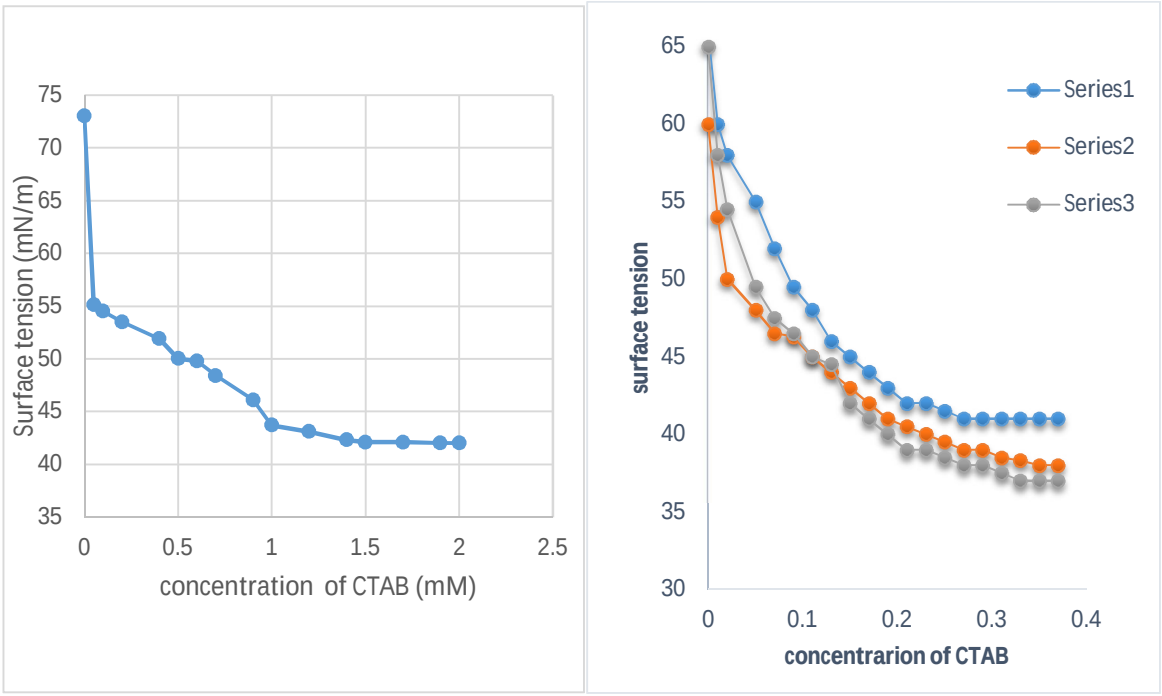


Fig 2: - Surface tension verses concentration of SDS at various concentration of spironolactone (a) zero (b) 0.005 % (c) 0.01 % and (d) 0.05 % at room temperature.

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(A) (B)

Fig 3: - Surface tension verses concentration of CTAB at (A) zero concentration of spironolactone (B) various concentration (0.005, 0.01 and 0.05 W/v %) of spironolactone at room temperature.

IV. CONCLUSION

Presence of spironolactone in aqueous solutions of SDS and CTAB results in a decrease in CMC of these surfactants indicating a good solubility of spironolactone in such micellar system. Various parameters i.e., molar solubilization ratio, critical micellar concentration and Gibb's free energy of solubilization ($\Delta G°_m$) for spironolactone has been calculated in micellar solution. The negative value of ($\Delta G°_m$) shows the spontaneity of solubilization process. 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.

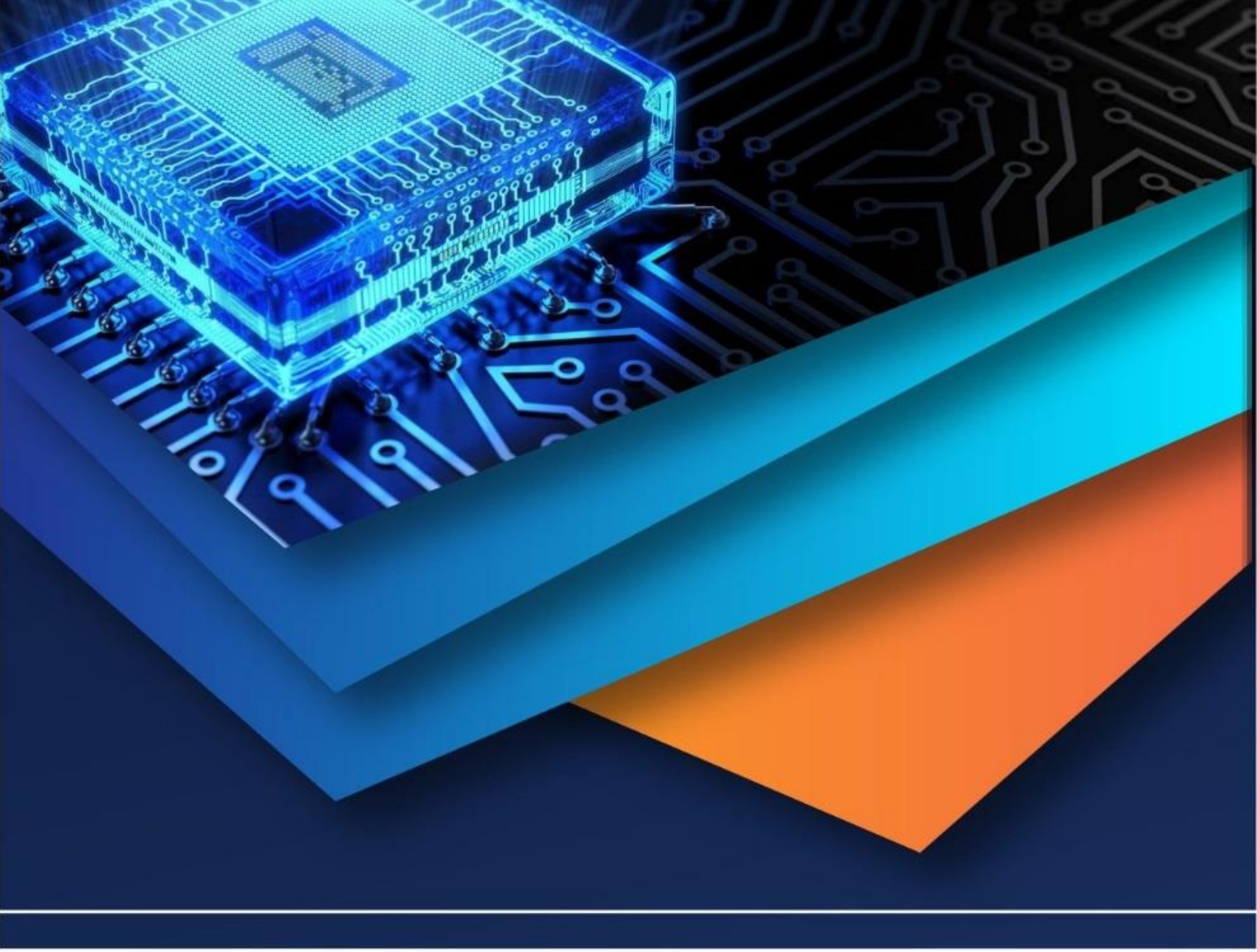
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