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Effect of quercetin on micellization behaviour of Tween-20 in hydro-ethanolic solvent system: An electrolyte induced thermodynamic study

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Abstract. The thermodynamic studies for non-ionic surfactant Tween-20 has been performed in presence of a well known flavonoid quercetin. The conductivity studies have been carried out with different concentrations of quercetin in 30% v/v ethanolic solution at five different temperatures (20 °C to 40 °C with difference of 5 °C). Since Tween-20 is non-ionic in nature, 1% w/v sodium chloride solution has been added as an electrolyte. Critical micelle concentration (CMC) and X_{CMC} values as a function of temperature have been determined from conductance studies. Furthermore, various thermodynamic parameters *viz.* change in enthalpy (ΔH_m°), entropy (ΔS_m°) and Gibb's free energy (ΔG_m°) of micellization have been calculated. Overall, the changes in micellization process of Tween-20 in presence of quercetin has been studied and reported.

1. Introduction

The study of thermodynamics is very essential in determining physico-chemical properties of various compounds and materials. Apart from its importance in fields of chemistry and physics, thermodynamics is widely been used in fields of engineering, pharmacy and biotechnology. In engineering, the principles of thermodynamics are used in heat conversion processes. Various engines, ventilation systems, power plants, insulators, radiators etc. are designed by using the knowledge of thermo-science [1,2]. In biotechnology, applications of chemical thermodynamics vary from processing of new biochemical products to separation of aqueous proteins and in understanding diseases like Alzheimer's, cataracts and sickle cell anaemia through various thermodynamic models [3,4]. In pharmaceutical and cosmetic industry, thermodynamics helps in determining the concentration of active ingredients in formulation development studies. It also helps in overcoming the problems of poor aqueous solubility, low bioavailability and skin penetration associated with active pharmaceutical ingredients by providing proper choice of solvents [5–7].

Micellization is a process of formation of molecular aggregates that constitutes a colloidal particle. In micellization, monomers in the solution aggregates themselves by intermolecular interaction so as to form a micellar structure [8]. These micelles are widely used in fermentation and detergent industries as well as for analytical purposes *i.e.* in chromatography and electrophoresis [9,10]. Quercetin is a well known lipophilic antioxidant that belongs to flavonoid group of polyphenols. It possess wide number of biological activities such as antimicrobial, anti-cancer, cardiovascular agent and anti-inflammatory properties [11,12]. Despite wide range of biological activities and potential, the problems of poor water solubility and low bioavailability are a matter of concern [13]. Thus, incorporation of quercetin into micellar structure of surfactants is a topic of high interest and is known to help in overcoming these problems. Tween-20 is a non-ionic surfactant that belongs to polysorbate family. Its hydrophilic nature is due to presence of ethylene oxide subunits in its structure while hydrocarbon chains are responsible for hydrophobicity [14]. The structures of quercetin and Tween 20 are shown in Figure 1 [14,15].



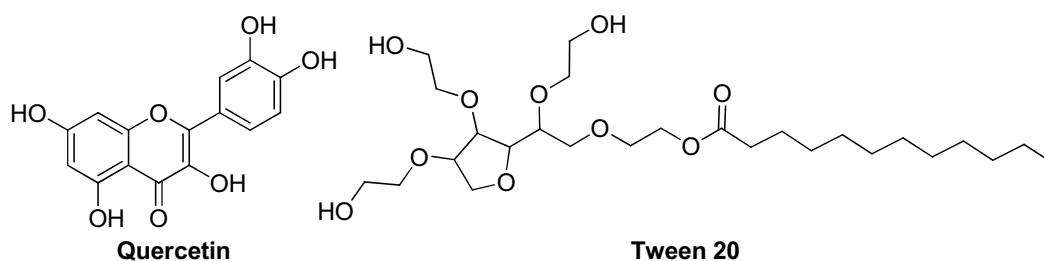


Figure 1. Chemical structures of Quercetin and Tween-20.

In this present work, the electrolyte induced micellar interaction of quercetin and Tween-20 in 30% v/v ethanolic solution have been presented. The study has been performed in three different concentrations of quercetin (1 mM, 2 mM and 3 mM) and five different temperatures (20 °C, 25 °C, 30 °C, 35 °C and 40 °C). Although quercetin is widely used as additive in food industry, the specific Acceptable Daily Intake (ADI) dose has not been recommended by World Health Organization. For this reason, minimum concentrations of quercetin were selected for the study. Further, the thermodynamic parameters have been studied so as to understand the nature of reactions and types of interactions occurring within the system.

2. Experimental section

2.1. Chemicals

Quercetin and Tween-20 have been purchased from Sigma-Aldrich (Purity more than 99%). Absolute ethanol has been purchased from Merck Chemicals. Sodium chloride has been obtained from HiMedia Laboratories Pvt. Ltd., India. Millipore Elix distillation assembly has been used to prepare fresh distilled water. The specific conductance of water has been found within range of $(1-3) \times 10^{-7}$ S.cm⁻¹ at 25 °C. The pH value was well within range of 6.5-7.0.

2.2. Equipments and methods

The specific conductance has been measured with Cyber Scan CON-510 conductivity meter. The equipment was calibrated with 0.01 mol dm⁻³ standard KCl solution prior to its use. The temperature was maintained by using circulating water thermostat with digital temperature controller. The water thermostat was supplied by Harsh & Co., Ambala, India. A stock solution of Tween-20 has been prepared in 30% v/v ethanol solution. From the stock, different concentrations of Tween-20 (0.01-0.14 mmol) have been prepared. Quercetin of different concentrations (1-3 mM) has been prepared in hydro-ethanolic solvent system. All the samples were prepared almost a day before experimental work so as to settle time dependent effects. Critical micelle concentration (CMC) has been calculated from specific conductance values. CMC has been obtained by plotting the graph between specific conductance and Tween 20 concentration. The pre-micellar and post-micellar regions were identified from the graph and tangents were drawn from these points. The intersection point of the two tangents has been considered as CMC value. These values have been further utilized to calculate various thermodynamic parameters i.e. change in enthalpy (ΔH_m°), change in entropy (ΔS_m°) and change in Gibb's free energy (ΔG_m°) of micellization.

3. Results and Discussion

3.1. Specific conductance and micellization

With increasing surfactant concentration, an increase in specific conductance values was observed at all temperatures and quercetin concentration. The graphical data between specific conductance vs.

Tween 20 concentration is shown in Figure 2. With increase in surfactant concentration, the ionization process also increases as the amount of solute becomes more in same volume of solvent. This leads to enhancement of ions in the solution aiding in conducting electricity [16]. These plots were used to determine CMC values that are given in Table 1.

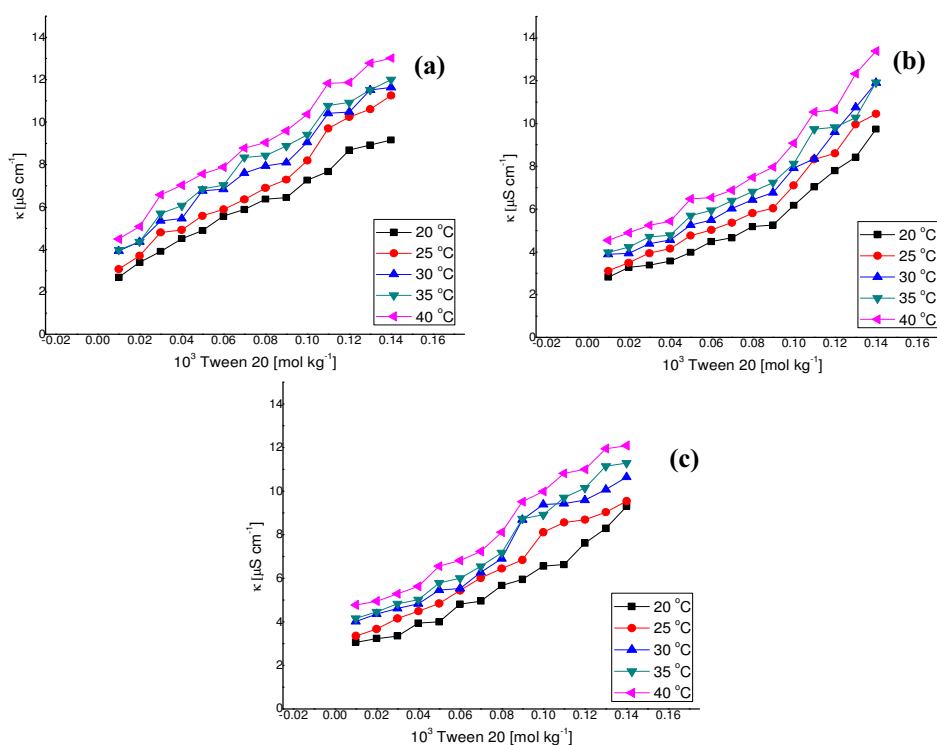


Figure 2. Specific conductance vs. Tween 20 concentration in 30% v/v ethanol solution containing Quercetin [(a) 1 mM; (b) 2 mM and (c) 3 mM] at different temperatures.

Table 1. CMC data obtained by interaction of Quercetin with Tween 20 at five different temperatures.

T (°C)	Quercetin concentration		
	1 mM	2mM	3 mM
20	0.08	0.088	0.069
25	0.09	0.09	0.09
30	0.098	0.098	0.089
35	0.088	0.097	0.085
40	0.085	0.094	0.084

It was observed that with increase in temperature, the CMC values initially increased and then decreased at all concentrations of quercetin. Moreover, these values were found to be more than the reported CMC value of Tween 20 at all temperatures (the CMC value at 25 °C is 0.06 mmol) [17]. The increase in CMC values can be accounted to the fact that when organic additives such as quercetin are introduced into the system, a decrease in micellization process is observed [18]. The presence of hydrophilic oxyethylene group in structure of Tween 20 is responsible for the decrease in CMC values

after initial increase. With small increase in temperature, the hydrophilic nature of oxyethylene group dominates which causes early micellization. However, when temperature is further increased, the effect of this group decreases due to weak intermolecular forces at high temperatures, thus resulting in increased CMC values [19].

3.2. Thermodynamic parameters

From the obtained CMC values, their mole fraction units i.e. X_{CMC} was determined and used to calculate various thermodynamic parameters. The following equations were used to calculate change in enthalpy (ΔH_m°), change in entropy (ΔS_m°) and change in Gibb's free energy (ΔG_m°) of micellization [20]:

$$\Delta H_m^{\circ} = -RT^2(2 - \alpha) [d(\ln X_{CMC}) / dT] \quad (1)$$

$$\Delta G_m^{\circ} = (2 - \alpha) RT (\ln X_{CMC}) \quad (2)$$

$$\Delta S_m^{\circ} = (\Delta H_m^{\circ} - \Delta G_m^{\circ}) / T \quad (3)$$

In these equations, $d(\ln X_{CMC})$ represents the slope of straight line obtained by plotting $\ln X_{CMC}$ against temperature. The degree of ion dissociation (α) is calculated from relation, $\alpha = S_2/S_1$. The symbols S_1 and S_2 represent slopes in the pre micellar and post micellar region. The values obtained for X_{CMC} and thermodynamic parameters are given in Table 2.

Table 2. Thermodynamic parameters for different concentrations of Quercetin (1-3 mM) with Tween 20 in 30% v/v ethanol solution.

Que. Conc.	T (°C)	X_{CMC} (10^3)	ΔH_m° (kJ mol^{-1})	ΔG_m° (kJ mol^{-1})	ΔS_m° ($\text{J mol}^{-1} \text{K}^{-1}$)
1mM	20	0.00144	-1.92712	-22.98	0.071853
	25	0.00162	-1.99345	-23.0803	0.070761
	30	0.00176	-2.06091	-23.253	0.069941
	35	0.00158	-2.12949	-23.9124	0.070724
	40	0.00153	-2.19919	-24.3908	0.0709
2mM	20	0.00158	-2.85499	-22.7478	0.067894
	25	0.00162	-2.95327	-23.0803	0.06754
	30	0.00176	-3.0532	-23.253	0.066666
	35	0.00175	-3.1548	-23.663	0.066585
	40	0.00169	-3.25806	-24.1289	0.06668
3mM	20	0.00124	-4.99624	-23.3403	0.062608
	25	0.00162	-5.16822	-23.0803	0.060108
	30	0.0016	-5.3431	-23.4957	0.05991
	35	0.00153	-5.5209	-24.0012	0.060001
	40	0.00151	-5.7016	-24.4216	0.059808

The data revealed that values for ΔH_m° and ΔG_m° were negative whereas the values for ΔS_m° were positive. The negative values of ΔH_m° indicate exothermic nature of reactions within the system while the values of ΔG_m° suggest that the micellization process is entropically controlled. The positive

ΔG_m^0 values reveal the spontaneity of reaction within the system indicating that the reaction is moving in forward direction. The results obtained from all thermodynamic parameters suggests that the interactions between quercetin and Tween 20 are favourable and is suitable for performing other physico-chemical properties that might further aid in formulation development studies. The plots for ΔH_m^0 , ΔG_m^0 and ΔS_m^0 at different temperatures have been represented in Figure 3.

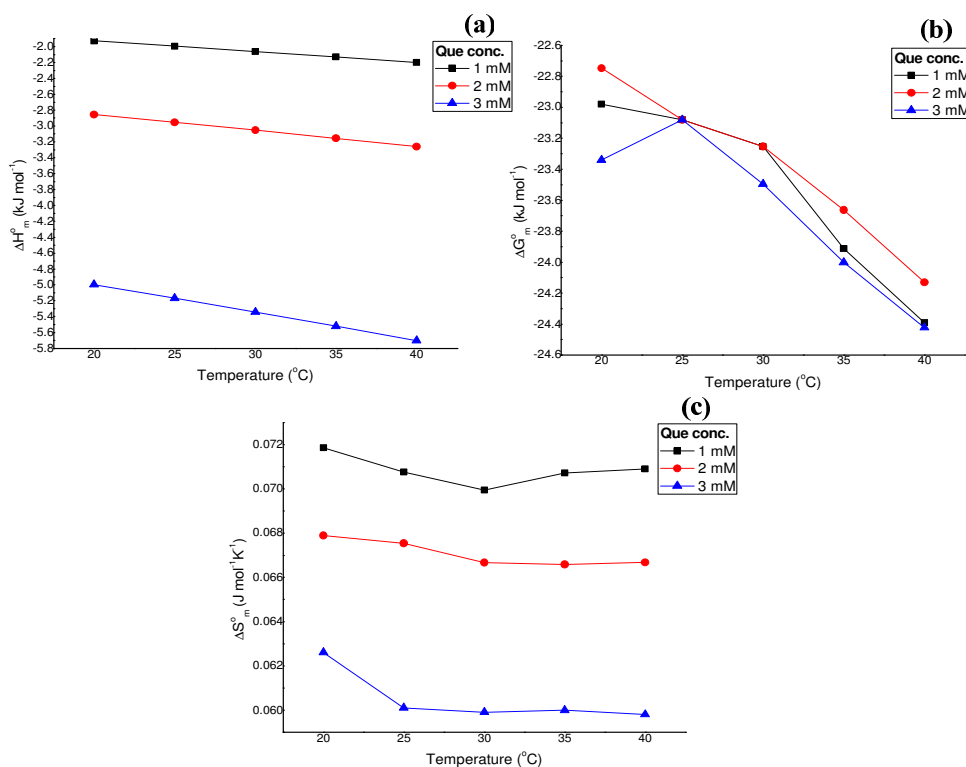


Figure 3. Plots for (a) ΔH_m^0 , (b) ΔG_m^0 and (c) ΔS_m^0 vs. temperature for different concentrations of Quercetin-Tween 20 system.

On comparing the values at different concentrations of quercetin, it was observed that when concentration of quercetin is increased from 1 mM to 3 mM, the values of ΔH_m^0 became more negative. It signifies that the introduction and further addition of quercetin makes London dispersion forces more dominant, thus making the values more negative [21]. The values of ΔG_m^0 have also been found to decrease with increase in quercetin concentration. This behaviour suggests that addition of quercetin aids in increasing the solubility resulting in conversion of quercetin-surfactant system from dispersed to micellar phase at a faster rate. The similar trend in values of ΔH_m^0 and ΔG_m^0 has been observed when compared with respect to change in temperature.

4. Conclusion

The physico-chemical studies were performed on flavonoid-surfactant system in order to identify the effect of quercetin on micellization process of Tween 20. It was observed that micelle formation is delayed in presence of quercetin due to presence of organic aromatic rings in its structure. The CMC values exhibited parabolic behaviour with respect to temperature as the values initially increased and then decreased with increase in temperature. It was noticed from thermodynamic studies that the solute-solvent interactions were exothermic, spontaneous and entropically driven, signifying the

feasibility of our selected system. Overall, the results were found to be favourable and will be utilized in formulation development studies in our ongoing project work.

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