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Interaction between amphiphilic antidepressant drug nortryptyline hydrochloride and conventional cationic surfactants: A physicochemical study

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ABSTRACT

The interaction of cationic surfactants, namely dodecyltrimethyl ammonium bromide (DTAB) and cetrimide (CET) with tricyclic antidepressant drug, nortryptyline hydrochloride (NH) (used for depression related illness, nocturnal enuresis, chronic fatigue syndrome, irritable bowel syndrome, chronic pain or neuralgia, and migraine) were studied employing conductometric and tensiometric techniques. From these techniques, various micellar and interfacial parameters such as critical micelle concentration, *cmc*, micellar mole fraction, X_1, micellar interaction parameter, β, activity coefficients f_1 and f_2 in the mixed micelles, excess Gibbs free energy of micellization, ΔG^0_{ex}, standard Gibbs free energy, $\Delta G_m{}^0$, surface excess concentration, Γ_{max}, minimum surface area per molecule, A_{min}, and standard Gibbs free energy of adsorption ΔG^0_{ad} at the interface were evaluated. In addition to this, various other parameters such as, packing parameters of amphiphiles in the micelles, P, volume contribution of the hydrophobic chain, v, and its effective length, l_C have also been calculated for pure and mixed systems. From packing parameters it was confirmed that the micelle/mixed micelles formed have spherical geometry. The ΔG^0_m and ΔG^0_{ad} values for all studied systems were found to be negative and this shows that both micellization as well as adsorption processes are energetically favorable. Furthermore, the values of ΔG^0_{ad} were more negative than their corresponding ΔG^0_m, showing that work is done in transferring the amphiphilic monomers from interface to the micellar stage across the aqueous solution to form micelles. The interaction parameters, β, calculated by using regular solution theory were also observed to be negative suggesting synergistic interaction for the proposed mixed systems.

1. Introduction

The amphiphilic molecules have important property of self-assembly to form micelles, which occurs because of hydrophobic attraction between the hydrocarbon chains balanced by the electrostatic repulsion of head groups [1–10]. The self-assembly of amphiphilic molecules, have various characteristic properties, which includes, critical micelle concentration (*cmc*), aggregation number (N_{agg}), size, and shape, of which micelle formation is very important especially for its use in drug delivery systems. Various drug delivery and targeting systems such as synthetic polymers, microcapsules, cell ghosts, micelles, liposomes, lipid particles, etc., [2,3] have been developed in order to reduce premature drug degradation, prevent harmful side effects onto normal cells, increase drug bioavailability and also increases the content of drug accumulated in the required pathological area. Each of the above mentioned carriers have their own advantages as well as certain shortcomings, so before choosing the drug delivery agents for a particular drug, we should first take into account the disadvantages of that particular drug carrier.

Nortryptyline hydrochloride (NH), is a tricyclic antidepressant drug, and shows amphiphilic nature owing to the presence of hydrophobic ring system and a terminal hydrophilic short chain. The amphiphilic nature of these antidepressant drugs gives them special properties of micelle formation, and interactions with lipid bilayers, surfactants, and biological membranes [7,8]. These antidepressant drugs, as revealed from most of the studies can aggregate to form monomers of 6–12 in number in solution [9,10]. It is very important to study the aggregation and interaction of these drugs with the surfactants so that we can design the most efficient and effective drug carrier systems. Florence and Parfitt [11] have employed various techniques such as NMR, pH, and viscosity in order to study the micellization of phenothiazine drugs,

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