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# Micellar and interfacial properties of amphiphilic drug–non-ionic surfactants mixed systems: Surface tension, fluorescence and UV–vis studies



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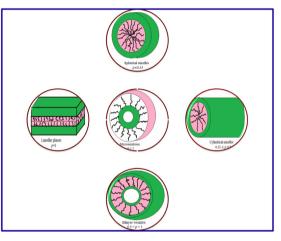
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## HIGHLIGHTS

# GRAPHICAL ABSTRACT

- Interactions of CPZ with non-ionic surfactants have been studied.
- It has many side effects therefore; need a carrier for safe drug delivery.
- The negative β values show attractive interactions between drug and surfactants.
- The results have been applicability in the model drug delivery systems.

The aggregates structures of amphiphiles, predicted from packing parameter.



## ARTICLE INFO

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# ABSTRACT

This study reports the influence of non-ionic surfactants (TX-100 and TX-114) on the CPZ by surface tension, fluorescence and UV-vis spectra to explore their applications as drug delivery vehicles. The synergism is indicated by the values of the interaction parameters and activity coefficients, which are negative and less than unity, respectively. The ideal micellar mole fraction values of CPZ are less than the experimental values, confirming the high contribution of CPZ in mixed systems. The stability of these mixed systems is demonstrated by negative free energies of mixing.

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## 1. Introduction

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http://dx.doi.org/10.1016/j.colsurfa.2017.02.093 0927-7757/© 2017 Elsevier B.V. All rights reserved. Amphiphiles or surfactants, being amphiphilic in nature, have an important place in the scientific world and find multiple applications in industry and laboratories. The two main fundamental

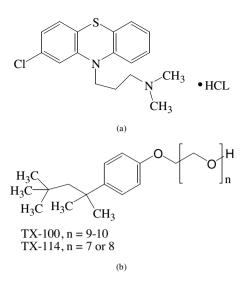


Fig. 1. Chemical structure of (a) Chlorpromazine hydrochloride (CPZ), (b) Triton X.

properties of amphiphiles are the ability to adsorb at interfaces in an oriented fashion and to form micelles [1–3]. The dynamic behaviors of many systems (stability of foams, the droplet size in jets and sprays, the spreading of drops on solid surfaces, and the smooth coating of multiple layers) are controlled by the adsorption of surfactants at the air–water interface [4–6]. Many micelles have catalytic properties and are structurally similar to that of globular proteins and biological membranes [7–9]. Amphiphiles are employed by organic chemists and biochemists in different industrial processes, such as laundry [10], emulsion formation [11], corrosion prevention [12] and firefighting [13].

However, mixed amphiphilic systems are experienced in almost all applications of amphiphiles and the mixed systems behave better than single amphiphiles [14–18]. The amphiphilic systems used in industry are typically mixtures of different chemical species, such as ionic and non-ionic amphiphiles, electrolytes, dyes and fillers. The ionic strength, pH, viscosity and other beneficial physicochemical properties are acquired by mixed systems. Mixed systems of different amphiphiles often show synergism. The physical properties like surface tension reduction efficiency and effectiveness, foaming, wetting, solubilizing, detergency, are also associated with synergism [2]. It can be ascribed to non-ideal mixing effects in the amphiphile films and in the micellar aggregates, which result in interfacial tensions and in critical micellization concentrations (cmc) which is substantially lower, than it for the used surfactants. The ionic-non-ionic mixed systems are more interesting from the fundamental point of view because they often exhibit highly non-ideal behavior. The addition of a non-ionic surfactant to an ionic amphiphile can reduce the electrostatic repulsions between the charged surfactant heads and greatly facilitate mixed micelle formation. Among the amphiphiles, non-ionic amphiphiles having ethylene oxide chains (hydrophilic group) are important class of amphiphiles (Fig. 1). Because of their fascinating properties, non-ionic amphiphiles are used in industrial and pharmaceutical formulations. Similar to other amphiphiles, non-ionic amphiphiles also form thermodynamically stable nano-scale assemblies called 'micelles' but at lower concentration. If we use an amphiphilic drug with a carrier (surfactants), then the drug efficiency increases with fewer side effects. The superior behavior of the drug+carrier systems is due to the interaction between the components.

Chlorpromazine hydrochloride (CPZ) is an amphiphilic phenothiazine drug having great chemical, medical and a variety of biological properties [19]. It is employed to treat schizophrenia, disorders with psychosis, and mania. Other important uses of CPZ are to prevent and treat nausea and vomiting. The chemical balance in the brain can be controlled by CPZ. It is an amphiphilic cationic compound, under current physiological conditions, which consist of hydrophobic nitrogen containing a charged amino group (Fig. 1). The study of phenothiazine aggregates has attracted much attention because of their photosensitizing effects in patients under therapy. The phenothiazine compounds have interesting physicochemical behavior associated with their capacity to change the properties of natural and model bio-membranes. CPZ is a tricyclic antipsychotic drug having drowsiness, dizziness, dry mouth, blurred vision, and tiredness side effects [20]. In addition to this, CPZ induces phospholipidosis, which is the excessive intracellular accumulation of phospholipids [21]. The interaction occurs between the negative phosphate oxygen of the lipids found in the body and the protonated amine group of CPZ. To reduce these side effects, CPZ is preferentially used with a carrier.

Thus, the purpose of our study is to investigate the adsorption and micellization of cationic amphiphilic drug (CPZ) mixed with non-ionic surfactants (TX-100 and TX-114). Such explorations are a guide to depicting the involvement of the individual components in the mixed aggregates and mixed adsorbed monolayer. The applicability of a thermodynamic model for binary systems is also considered. The analysis of data has been made in the light of various theoretical models, including those of Rubing, Clint, and Maeda.

### 2. Experimental methods and materials

#### 2.1. Materials

All the chemicals were employed as obtained without further purification throughout the study. Chlorpromazine hydrochloride (CPZ), Triton X-100 (TX-100), and Triton X-114 (TX-114) were the product of Sigma (USA) with a purity >98%. De-ionized and double distilled water was when preparing stock solutions of single and mixed amphilies solutions. Pure amphiphiles (CPZ, TX-100 and TX-114) solution were prepared by diluting concentrated stock solutions (accurately weigh the compounds according to the requirement). The mixer of solutions in different mole fractions (0.1, 0.3, 0.5, 0.7 and 0.9) were prepared by mixing pure solutions (CPZ, TX-100 and TX-114) and kept at least for 12 h to equilibrate. The surface tension at each mole fraction was measured by successive additions of a concentrated solution of amphiphile mixture in pure water by using a Hamilton syringe. All experiments were carried out at 298.15 K.

#### 2.2. Surface tension measurements

The surface tension of CPZ, TX-100, TX-114 and their binary mixtures were obtained by using Attension tensiometer (Sigma 701, Germany) at 298.15 K in the ring detachment method. The temperature of the studied solution was kept constant within  $\pm 0.1$  K by regularly circulating thermostated water through a jacketed vessel. Attension tensiometer work on Du Nouy principle. Accordingly the force to lift the ring from the surface of a liquid is related to the surface tension of that liquid by the relation:

$$F = 2\pi (r_1 + r_2)\gamma \tag{1}$$

where  $r_1$  and  $r_2$  are the radius of the inner ring and outer ring of the liquid film respectively. The concentration of a solution was varied by the aliquot addition of stock surfactant solution of known concentration to a known volume of solvent in the vessel. For each set of experiments, the ring was cleaned by heating it in an ethanol flame. The measured surface tension values were plotted as a function of

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