Microenvironment Effect on the Location Distribution of Phenothiazine in Cetyltrimethylammonium Bromide/n-Pentanol/H_2O W/O and Bi-continuous Microemulsions

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Abstract In cetyltrimethylammonium/n-pentanol/H_2O W/O (W/O = water in oil microemulsion) mixtures and bi-continuous microemulsions, phenothiazine (PTZ) molecules exist in the membrane phase of the dispersion either with the N atom or with the S atom pointed toward the polar head of cetyltrimethylammonium (CTAB). Cyclic voltammetry has been used to investigate the effects of the compositions and structures of the microemulsions, pH, and the salt on the location distribution of PTZ in the membrane phase of the dispersion in CTAB/n-C_5H_11OH/H_2O W/O and bi-continuous microemulsions. The results show that the location distribution of PTZ in the membrane phase of the dispersion in microemulsions is mainly dependent on the hydrogen bond between PTZ and n-C_5H_11OH (or the counterion), and on the electrostatic attractive interaction between the N atom in PTZ and the polar head of CTAB.

Keywords Phenothiazine · Microemulsion · Cetyltrimethylammonium bromide · Cyclic voltammetry · Location distribution

1 Introduction

Many biological processes occur at the surface of biological membranes or within their hydrophobic moiety. Physicochemical aspects of the binding of nitrogen-containing heterocyclic drugs to model and natural membranes have been the subjects of extensive studies involving a great variety of drugs from different therapeutic categories [1, 2]. Microemulsions provide an attractive model system for biomembranes because they mimic several important and essential features of biological membranes. The three-component microemulsion system, composed of surfactant, cosurfactant and water, is often used as the basic system of microemulsions [3]. In practice, a molecular-level understanding of the conditions and factors
that influence the drug-microemulsion interactions is desirable. An important step to understand such interactions is to characterize in detail the drug interaction sites, as well as the effect of the microenvironment on the drug interaction sites. Various techniques have been applied to the study of solute distribution in such heterogeneous systems, including NMR spectroscopy, small-angle X-ray and neutron scattering, fluorescence and various other photophysical methods [4–7].

Phenothiazines with two or more polar moieties exhibit a great variety of biological, medical, and chemical properties, and are commonly used in clinics as antidepressant, antihistamines and antipsychotic drugs [8, 9]. Some studies have been focused on the location distribution of phenothiazines in micelles [10, 11]. These studies have only focused on the location sites of the guest molecule in the heterogeneous system, but not on the location distribution of the polar moieties in phenothiazines. Usually, the sensitive group of the organic drug molecules is the polar group in the molecules. Therefore, the interaction between the polar head of the surfactant and the polar group of the organic molecule, as well as the micropolarity change around the polar group of the molecule can lead to a variation of the properties of organic molecules in the heterogeneous system. Recently, many studies have shown that the activity and the photochemical electron transfer depends strongly on the exact location of the sensitive group (usually being the polar group) of the organic molecules in the heterogeneous system [12, 13], which has also been confirmed by our recent studies [14, 15].

The parent of the phenothiazines, phenothiazine (PTZ), is a typical and useful organic compound with an N atom that easily looses one electron to form the cation radical [16]. In our previous work, some significant results concerning the effect of the microenvironment on the location of PTZ in the membrane phase of microdroplets in sodium dodecyl sulfate/n-\text{C}_5\text{H}_{11}\text{OH}/water microemulsions have been found by using cyclic voltammetry [15]. To better understand the location of PTZ in the microemulsion comprised of a cation surfactant, the effects of the microenvironment on the location distribution of PTZ in the membrane phase of the dispersion in the CTAB/n-\text{C}_5\text{H}_{11}\text{OH}/\text{H}_2\text{O} bi-continuous and W/O microemulsions have been investigated by cyclic voltammetry in the present study. It has been found, interestingly, that the compositions and structures of the microemulsions, pH, and the salts play different roles in determining the location distribution of PTZ in the membrane phase of dispersions in CTAB/n-\text{C}_5\text{H}_{11}\text{OH}/\text{H}_2\text{O} bi-continuous and W/O microemulsions, compared with those in sodium dodecyl sulfate/n-\text{C}_5\text{H}_{11}\text{OH}/water microemulsions. Our results show again that cyclic voltammetry is a powerful method for probing electroactive substances and microemulsion interactions.