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Short Communications

Anisotropy of indium-111 in cetyltrimethylammonium bromide solutions

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The perturbed angular correlation (PAC) technique, which employs the cascading decay of the radionuclide indium-111 (^{111}In), has been used to observe anisotropic changes in various pharmaceutical systems. These include the measurement of tablet dissolution (Beihn and Digenis, 1982), release rate from suppositories (Jay et al., 1983), and drug delivery via liposomes (Hwang and Mauk, 1977). Changes in the tumbling rate (anisotropy) of the ^{111}In nucleus were indicative of changes in the local physical environment of the radionuclide following dissolution or drug release from labelled dosage forms. The present communication reports preliminary data on the effect of a cationic surfactant on the anisotropy of ^{111}In solutions.

Cationic surface-active agents have been used in pharmaceutical systems chiefly as antimicrobial preservatives due to their ability to adsorb to cell membrane structures. Cationic surface-active agents have also been employed as membrane permeability adjuvants to facilitate the rectal absorption of poorly bioavailable drugs. Micellar association of these agents can affect solution properties such as surface tension, osmotic pressure, and electrical conductivity. The effect of colloidal behavior on the anisotropy of ^{111}In has not been previously reported. Cetyltrimethylammonium bromide (CTAB) was chosen for this initial study. Anisotropy of the ^{111}In nucleus, added as 50 μCi of ^{111}InCl$_3$ (carrier free) [1], was measured in CTAB [2] solutions containing 0.1 N HCl. An acidic solution was employed because at higher pH values, indium precipitates as hydroxide complexes. The sample solution was positioned between the three sodium iodide detectors of the PAC apparatus [3].

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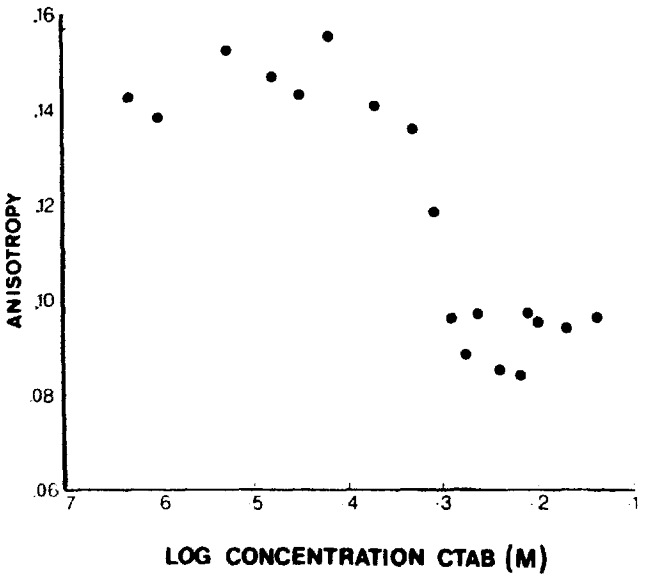

Fig. 1. The effect of cetyltrimethylammonium bromide (CTAB) concentration on the anisotropy of [^{111}In]indium chloride in 0.1 N HCl.

Coincidence count rates were accumulated and anisotropy values calculated as previously described (Beihn and Digenis, 1982). The effect of surfactant concentration on anisotropy of ^{111}In is shown in Fig. 1. For comparison, the surface tension of the surfactant solutions was measured using a DuNuoy ring tensiometer[4] (Fig. 2). As the CTAB concentration approached 10^{-3} M, the anisotropy of the ^{111}In nucleus was markedly depressed. This decrease in anisotropy indicates that the ^{111}In nucleus is existing in a more highly ordered environment (lower tumbling rate) above this concentration. The surface tension measurements indicate that the critical micellar concentration (CMC) for CTAB in water is approximately 1×10^{-3} M which is in good agreement with the literature value of 0.92×10^{-3} M (Mukerjee and Mysels, 1970). However, the CMC of CTAB in 0.1 N HCl is approximately 10-fold lower than that in water. Because anisotropy changes occurred around 10^{-3} M CTAB under conditions where its CMC is 10^{-4} M, it does not appear that the formation of micelles and the decrease in anisotropy of ^{111}In are directly related. However, increasing concentrations of CTAB apparently result in a more highly ordered environment for the $^{111}In^{3+}$ ion.

In order to rule out the effect of bromide ion concentration (which was also increased as more CTAB was introduced into the solution) on anisotropy, solutions of [^{111}In]indium chloride in 0.1 N HCl and 0.1 N HBr were prepared. No difference in the anisotropy values of these solutions was observed. Furthermore, the addition of sodium bromide or concentrated HBr did not alter the anisotropy of the ^{111}In in the 0.1 N HCl solution. Thus, it appears that the anisotropic changes seen in the

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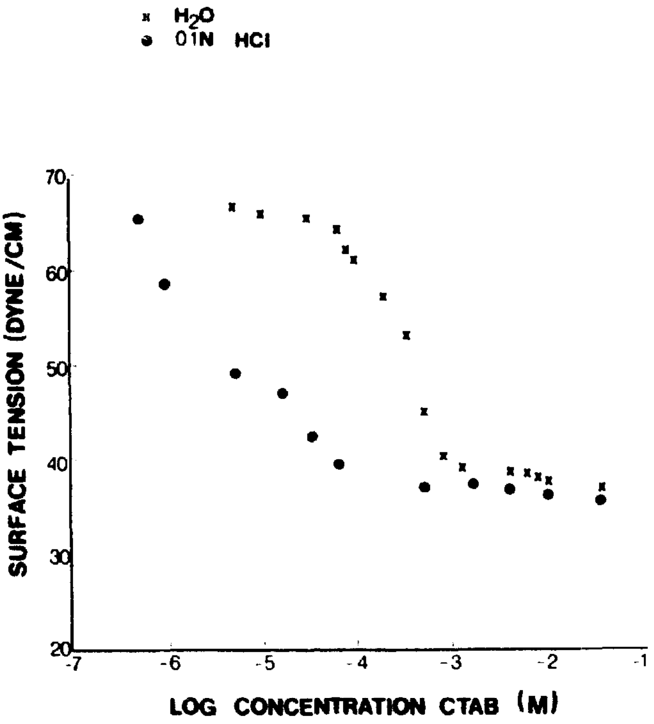

Fig. 2. Surface tension as a function of CTAB concentration in water (×) and 0.1 N HCl (●).

CTAB solutions are due to the presence of the surface-active agent itself and not its counterion. It should be noted here that the concentration of ^{111}In in these solutions is not significant in these studies since 50 μCi of carrier-free ^{111}In amounts to

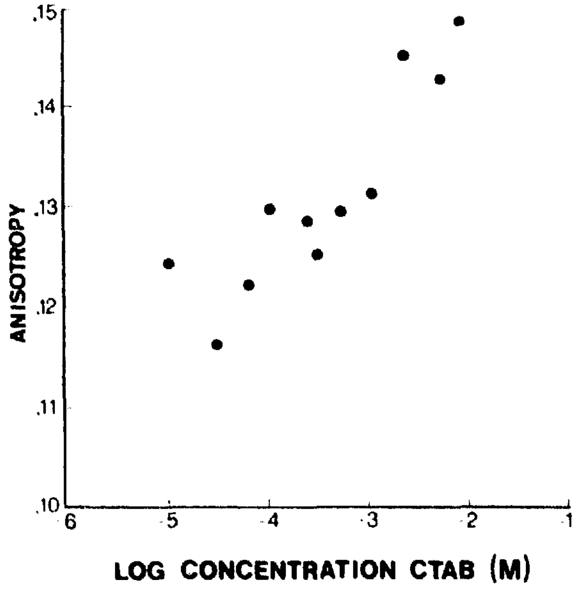

Fig. 3. The effect of CTAB concentration on the anisotropy of [^{111}In]DTPA in water.

1.02×10^{-13} moles of indium. In addition, we have found that anisotropy values are not altered by dilution of [^{111}In]indium chloride solutions.

The studies discussed above involve the interaction of a cationic surfactant with the positively charged trivalent indium ion. Another study was carried out to observe the effect of CTAB on the anisotropy of the negatively charged complex [^{111}In]indium diethylenetriaminepenta-acetic acid ([^{111}In]DTPA). The anisotropy value of [^{111}In]DTPA in water is approximately 0.12. This value is lower than in the indium chloride solutions due to the inherent nature of the coordination complex. Fig. 3 shows that the anisotropy is essentially constant in aqueous CTAB solutions until the surfactant concentration exceeds 10^{-4} M. Above this concentration, the anisotropy value increases until the maximum theoretical value of 0.14–0.15 is obtained. Thus, increasing concentrations of CTAB have the opposite effect on the anisotropy of [^{111}In]DTPA solutions in water compared to [^{111}In]indium chloride solution in 0.1 N HCl. The presence of the cationic surfactant apparently allows the ^{111}In nucleus to exist in a less ordered environment in the former case while creating a more structured environment for the ^{111}In nucleus in the latter.

Although mechanistic interpretations cannot be made rigidly at the present, the results of these studies indicate the sensitivity of the PAC technique on detecting relatively subtle anisotropic changes in the ^{111}In nucleus induced by various pharmaceutically-related phenomena. Studies are continuing on the effect of other cationic and anionic surfactants on the anisotropy of [^{111}In]indium chloride and [^{111}In]DTPA solutions as measured by PAC. In addition, the relationship between the anisotropy change and the CMC of these surfactants is being investigated further.

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