Nuclear magnetic resonance studies of interactions between cetomacrogol and phenol

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Phenol solubilized in cetomacrogol micelles appears to accumulate principally in the polyoxyethylene region and appears not to be randomly distributed along the polyoxyethylene chains. When concentrations of phenol are sufficiently high, a phenol–cetomacrogol-rich phase separates. This phase contains relatively little water and the phenol molecules may be randomly distributed along the polyoxyethylene chains. Transfer of molecules between the phases of these cloudy systems is relatively slow.

Nuclear magnetic resonance (nmr) spectroscopy may conveniently be used to follow the change of environment of a molecule upon solubilization by a surfactant, because the proton chemical shift depends (among other factors) on its physical environment. The total shielding which a proton experiences can be expressed as

$$\sigma = \sigma_d^L + \sigma_p^L + \sigma_p^N + \sigma_d^N + \sigma_s \qquad (1)$$

where the terms on the right hand side represent, in order, local diamagnetic, local paramagnetic, neighbouring paramagnetic, interatomic diamagnetic and solvent shielding contributions. The solvent shielding can be further expressed as a function of five separate effects:

$$\sigma_s = \sigma_B + \sigma_w + \sigma_a + \sigma_E + \sigma_c \qquad (2)$$

where the terms on the right hand side of the equation are associated respectively with bulk susceptibility, van der Waals interactions, diamagnetic anisotropy of the solvent, electric polarization and polarizability of the solvent, and interactions such as hydrogen bonding and charge transfer (Jackman & Sternhell, 1969a). Only the last two terms of equation (2) may differ significantly for different non-polar solutes in a particular solvent. It is generally found that if a molecule is transferred from a more polar to a less polar environment it experiences a high-field shift if the change in σ_c and σ_a is small (Buckingham, Schaeffer & Schneider, 1960; Eriksonn & Gillberg, 1966).

Thus the signals of the ring protons of phenol shift to higher field on addition of sodium dodecyl sulphate as increasing proportions of the phenol molecules are solubilized in the less-polar micellar environment (Jacobs, Anderson & Watson, 1971). Water protons also show a high-field shift on addition of sodium dodecyl sulphate due to disruption of water structure (Clifford & Pethica, 1964.)

Donbrow & Rhodes (1966) noted that the signals of the alkyl protons and the polyethylene oxide protons of cetomacrogol shift upfield when benzoic acid is solubilized in the surfactant solution. The change of chemical shift for the alkyl protons was the larger and this was interpreted as supporting other evidence that solubilized benzoic acid is located at the junction of the hydrocarbon nucleus and the polyoxyethylene region.

In the present study the chemical shifts observed in series of phenol–cetomacrogol–water systems are interpreted in terms of interactions between the components.

MATERIALS AND METHODS

Materials

Cetomacrogol 1000, B.P.C.; phenol, reagent grade; deuterium oxide (99·9 % D_2O) was obtained from the Australian Atomic Energy Commission, Lucas Heights, Sydney; water was freshly distilled from an all-glass still.

Instrumental techniques

Spectra were obtained in water (unless otherwise specified) using a Perkin-Elmer R-12 high resolution spectrometer equipped with double resonance accessory, and locking to the signal of tetramethylsilane (TMS) used as an external standard. The operating temperature of the probe was 35° and all samples were allowed to equilibrate for at least 10 min before spectra were recorded.

Small chemical shifts were measured by expanding the field to 50 or 100 Hz per chart width. All shifts are quoted as changes with respect to the position of the peak concerned under some standard condition. The precision varies from 0·2 Hz for narrow peaks to 0·5 Hz for broad peaks such as that for polyethylene oxide protons in the presence of relatively high concentrations of phenol.

Each spectrum was run at least five times and the average change of signal position is reported. Corrections for bulk susceptibility have been applied where necessary.

Susceptibility corrections

When comparing chemical shifts of solutes at different concentrations or in different solvents, corrections for changes in volume diamagnetic susceptibility of the systems should be made, especially where the change in chemical shift is small.

The volume diamagnetic susceptibility of a mixture is given by

$$\chi_v^{1,2} = x_1 \chi_v^1 + x_2 \chi_v^2 \tag{3}$$

where x_1 and x_2 are the volume fractions of the components and $\chi_v^{1,2}$, χ_v^1 and χ_v^2 are the volume susceptibilities of the mixtures and the pure components respectively (Pople, Schneider & Bernstein, 1959a).

The corrections were made using the relation

$$\sigma = \sigma_{obs} + \tfrac{2\pi}{3}(\chi_{v,ref} - \chi_v) \tag{4}$$

where σ and σ_{obs} are the true and observed chemical shifts and $\chi_{v,\,ref}$ and χ_v are the volume susceptibilities of the reference system and the system under consideration (Pople, Schneider & Bernstein, 1959b).

Using volume susceptibility values of $0·675 \times 10^{-6}$ and $0·721 \times 10^{-6}$ for phenol and water respectively (*Handbook of Chemistry & Physics*, 1966) in equations (3) and (4) it may be calculated that the chemical shift in a 1 % phenol–water solution requires a correction of $-0·063$ Hz when compared with that in pure water. Using Pascal constants, the volume susceptibility of cetomacrogol was estimated to be $-0·730 \times 10^{-6}$; a 10 % solution in water would therefore require a correction of $+0·125$ Hz. For the concentrations used in this study the necessary corrections are very small and of about the same magnitude as the experimental error.

RESULTS AND DISCUSSION

Solubilization of phenol by cetomacrogol leads to a change of environment for both phenol and cetomacrogol molecules, with subsequent changes in the chemical shifts shown in nmr spectra. (The peak positions observed are the weighted means of the positions of the free and solubilized species, as transfer is relatively rapid).

The signals of the phenolic ring protons shift upfield with increasing cetomacrogol concentration (Fig. 1), indicating a change to a less-polar environment as a greater proportion of the phenol molecules is solubilized in the cetomacrogol micelles.
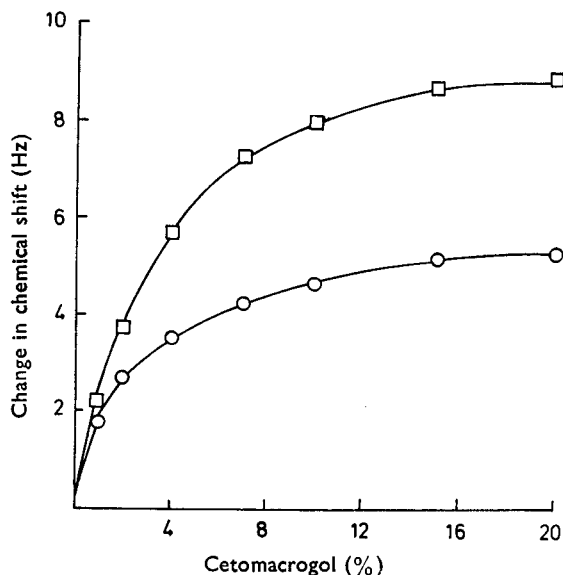

FIG. 1. Changes in chemical shift of ring protons of phenol (1%) in the presence of varying concentrations of cetomacrogol (measured with respect to the peak positions of 1% phenol in water): □ meta and para protons, ○ ortho protons.

An upfield shift could also be due to increased diamagnetic shielding of the aromatic rings, if the rings are randomly arranged. However, the changes of shift of the phenol ring protons in 10% cetomacrogol, with respect to the peaks in the corresponding phenol-water solutions, become smaller as the phenol concentrations increase from 0·5 to 3% (Fig. 2). Since the distribution coefficient favours solution in the micellar environment, increasing the overall phenol concentration will result in a greater increase in concentration in the micelles than in the true aqueous phase. Consequently the observed reduction in shift with increasing phenol concentration suggests a small degree of order in the arrangement of the aromatic rings which would lead to decreased diamagnetic shielding. Hence the high-field shift of the phenol ring protons with increasing cetomacrogol concentration (Fig. 1) must be due to the less polarizable environment of the micelles rather than increased diamagnetic shielding.

The phenol molecules may be solubilized in one or more of three regions of the micelles; (a) in the lipophilic centres of the micelles, (b) in the outer polyoxyethylene region and (c) at the junction of these two regions. The solubilized phenol molecules would be expected to cause a change in the chemical shift of cetomacrogol protons
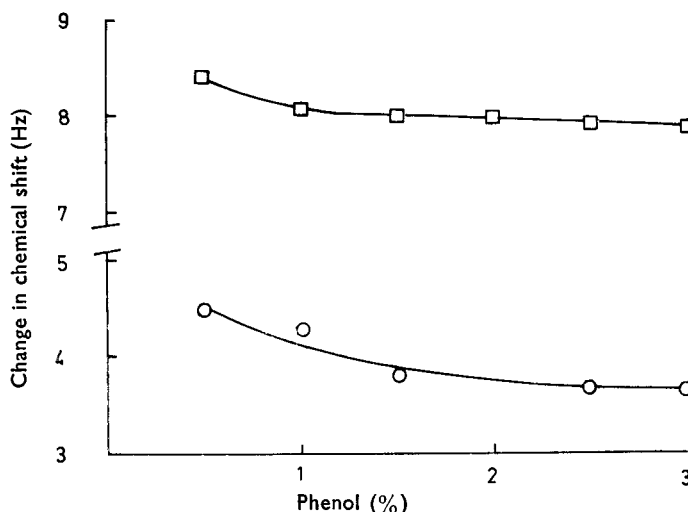
FIG. 2. Changes in chemical shift of ring protons of phenol with varying concentrations of phenol in the presence of 10% cetomacrogol (measured with respect to the peak positions of corresponding concentrations of phenol in water): □ *meta* and *para* protons, ○ *ortho* protons.

in the region or regions of solubilization, and nmr spectra may provide data to help determine where the solubilizate is concentrated in cetomacrogol micelles (Donbrow & Rhodes, 1966).

Fig. 3 shows the change in chemical shifts for both the polyethylene oxide protons and the alkyl methylene protons in the presence of increasing phenol concentrations. The greater total shift for the polyethylene oxide protons suggests that the phenol accumulates mainly in this region. This conclusion, however, is only valid if, when phenol is introduced, the changes in σ_E and σ_c of equation (2) are relatively small or about the same for both alkyl and polyethylene oxide protons. In this case, it is assumed that the diamagnetic anisotropic shielding contribution (σ_a) would outweigh
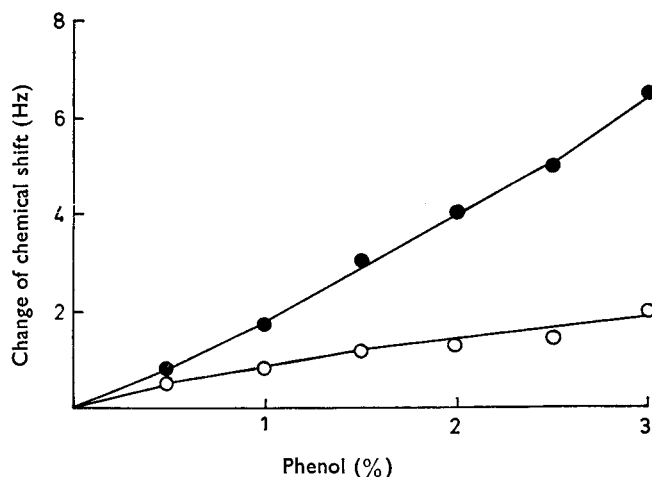

FIG. 3. Changes in chemical shift of protons of cetomacrogol (10%) in the presence of varying concentrations of phenol (measured with respect to the peak positions of 10% cetomacrogol in water): ● polyethylene oxide protons (major peak), ○ alkyl protons.

any other contributions.   Since it is likely that σ_a is about the same for both alkyl and polyethylene oxide protons, a greater shielding would represent either a greater concentration of phenol or a specific orientation of the aromatic rings (σ_c).   However, much orientation of the aromatic rings seems unlikely and the greater shielding of the polyethylene oxide protons may be attributed to a greater concentration of phenol in this region.

This conclusion is supported by the greater relative broadening of the polyethylene oxide peak compared with the alkyl peak.   The presence of phenol would be expected to hinder the rotational freedom of the polyoxyethylene chains, leading to shorter transverse relaxation times and consequently to broader peaks.   This evidence does not preclude solubilization at the junction between the lipophilic micelle centre and the polyoxyethylene region (where the solute molecules will have some association with each region) as well as solubilization of some phenol molecules in the lipophilic centre with most of the phenol being associated with the polyoxyethylene shell.

It is noteworthy that the protons in the polyoxyethylene chains have identical chemical shifts in aqueous solution.   However, on the addition of phenol, this equivalence no longer exists and as the phenol concentration is increased, the apparent singlet at about $\delta\,4\cdot2$ separates into three peaks as shown in Fig. 4.   This may be
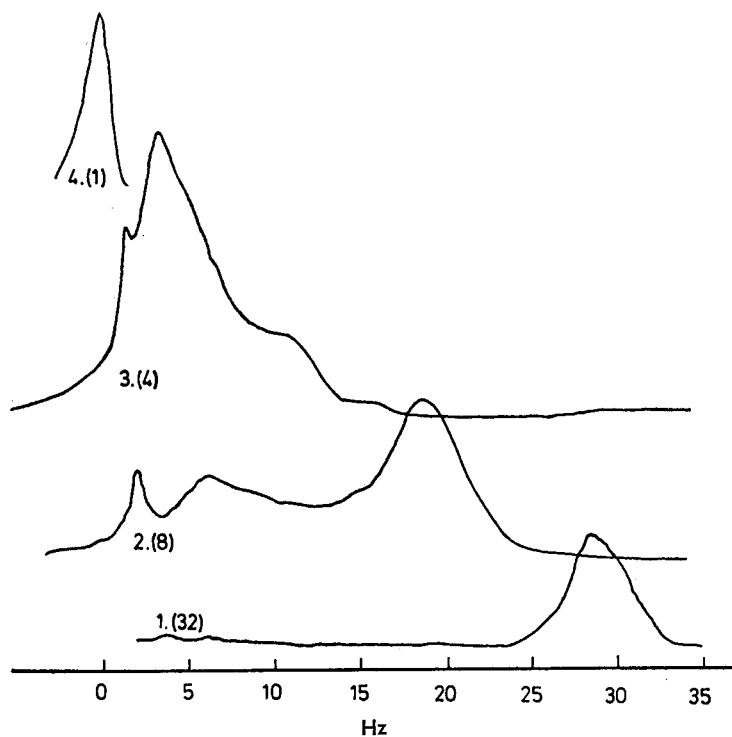

FIG. 4.   Polyethylene oxide proton peaks of phenol–cetomacrogol–water systems.

Curve	Composition
1	3 % phenol, 1 % cetomacrogol
2	3 % „ , 6 % „
3	3 % „ , 15 % „
4	— „ , 10 % „

Numbers in brackets refer to the relative instrumental sensitivity.

caused by a non-homogeneous distribution of phenol in the polyoxyethylene region of the micelles.

As the phenol concentration is increased further, the system becomes cloudy owing to the formation of a phenol–cetomacrogol-rich phase, and a fourth peak appears. This peak has been assigned to the polyethylene oxide protons of the disperse phase. This is confirmed by the spectrum of the separated phenol–cetomacrogol-rich phase (Fig. 5). In contrast with the corresponding absorption in the aqueous system, this peak appears as a broad apparent singlet, indicating that in this system all polyethylene oxide protons are approximately equivalent.
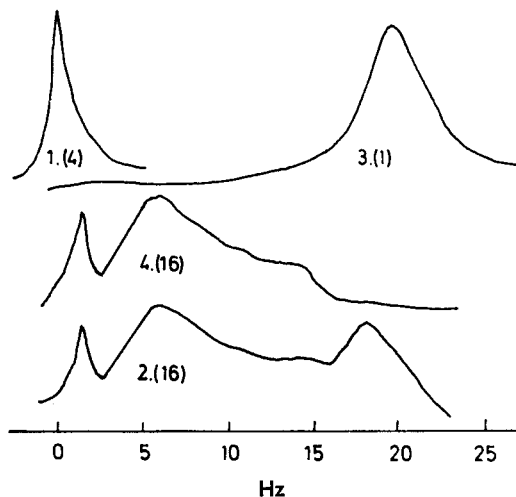

FIG. 5. Polyethylene oxide proton peaks of phenol–cetomacrogol–water systems.
    Curve: 1. Cetomacrogol 7% in water. 2. Cloudy system before separation of phases (ceto-macrogol 7%, phenol 3%). 3. Lower (cetomacrogol-rich phase) of system 2 after separation. 4. Upper (aqueous) phase of system 2 after separation. Numbers in brackets refer to the relative instrumental sensitivity.

The two separate absorptions which occur for the polyethylene oxide protons in the aqueous and phenol–cetomacrogol-rich phases of the cloudy systems indicate that transfer of molecules between the two phases is relatively slow, with residence times of at least 30 ms (Jackman & Sternhell, 1969b).

The changes in chemical shift of the polyethylene oxide protons with varying concentration of surfactant in the presence of 3% phenol are shown in Fig. 6. At low concentrations of cetomacrogol, and hence relatively high ratios of phenol to surfactant, the small amount of disperse phase contains most of the cetomacrogol along with high concentrations of phenol and the upfield changes of chemical shift of the polyethylene oxide protons are large. This phase contains relatively little water (see later) and the large upfield shift reflects the great change in environment of the polyethylene oxide protons. Little or no cetomacrogol is present in the aqueous phase and no signal from polyethylene oxide protons in the aqueous phase is apparent until the surfactant concentration reaches about 6%. As the overall surfactant concentration is increased to about 5%, the amount of the disperse phase increases, the phenol to cetomacrogol ratio in it falls and the upfield change of the signal from the polyethylene oxide protons becomes smaller.
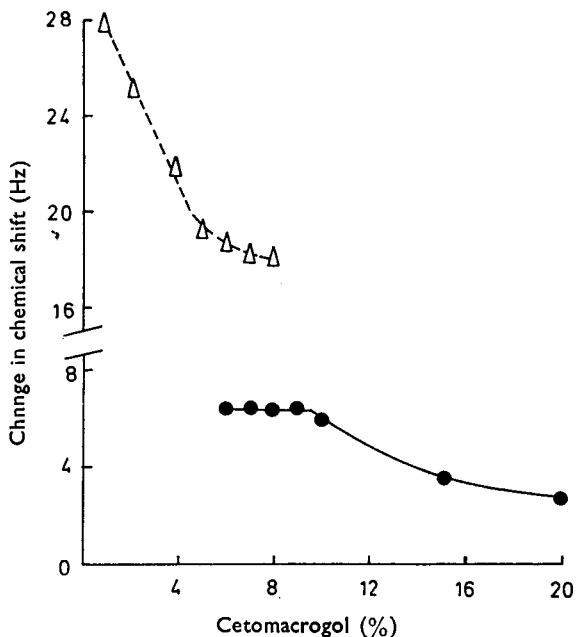
FIG. 6. Changes in chemical shift of polyethylene oxide protons of cetomacrogol in the presence of 3% phenol (measured with respect to the corresponding concentration of cetomacrogol in water): △ signal from protons in phenol–cetomacrogol-rich phase (in turbid systems), ○ signal from protons in aqueous phase (systems turbid up to 10% cetomacrogol, clear above 10% cetomacrogol).

When the cetomacrogol concentration is between 6 and 8%, sufficient surfactant is present in each phase to give two measurable signals. Both are upfield from the reference peak of the polyethylene oxide protons in water, but the signals from the protons in the disperse phase are shifted much more than that from the aqueous phase. The relative amount of the disperse phase changes over this concentration range; at 10% cetomacrogol the system has become transparent and further addition of cetomacrogol causes shifts to lower fields as the phenol in the micelles undergoes more and more dilution.

Over the range of 6 to 9% cetomacrogol, the intensities of the signals from the polyethylene oxide protons alter, reflecting changes in the relative amounts of surfactant present in each phase but there is no change in the chemical shifts observed, and the compositions of the phases would seem to be unchanged. This is supported by an estimation, from integrated spectra, of the composition of the phenol–cetomacrogol-rich phases separated from cloudy systems containing 6% and 7% cetomacrogol and 3% phenol. The molar ratio of phenol:ethylene oxide units:water was found to be the same in each sample (about 3:10:12·5). The number of water molecules per ethylene oxide unit is thus much less than for cetomacrogol in the form of micelles, where about six water molecules are incorporated per ethylene oxide unit (Elworthy, 1960).

It is generally believed that about two water molecules are associated with each ether oxygen of the polyoxyethylene chains, the remainder being trapped inside cone-shaped cavities formed by the ethylene oxide chains. It is likely then, that all the water molecules in the phenol–cetomacrogol-rich phase are associated with

the ether oxygens, and that little or no water is trapped in cavities in polyoxyethylene cones. A possible arrangement would be a lamellar structure, with the cetomacrogol molecules arranged side by side; the phenol would be concentrated in the polyoxy-ethylene region of this phase.

The water peak in water–cetomacrogol systems shifts to higher field with increasing concentration of cetomacrogol (Fig. 7). The addition of a solute to water generally has two opposing effects. Solutes may break up the water structure and give rise to high-field shifts; on the other hand possible hydrogen bonding between water and the solute would lead to downfield shifts. It may be assumed that the hydrogen bonding between water and the ether oxygens is less effective overall than inter-water hydrogen bonds.
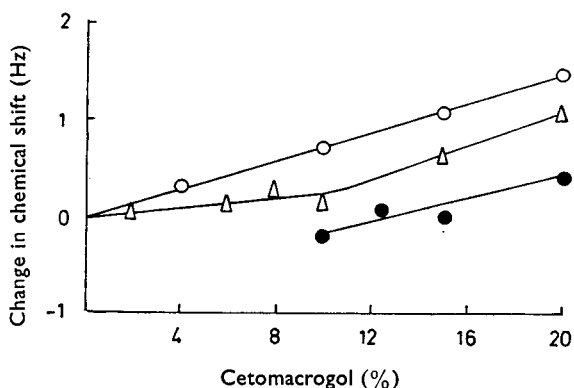

FIG. 7. Changes in the chemical shifts of water protons in the presence of: ○ varying concentrations of cetomacrogol (measured with respect to water), △ 1% phenol and varying concentrations of cetomacrogol (measured with respect to water containing 1% phenol), ● 3% phenol and varying concentrations of cetomacrogol (measured with respect to water containing 3% phenol).

When phenol is present along with cetomacrogol and water, the water shifts, with respect to the corresponding phenol–water solutions, are reduced. Phenol also disrupts water structure causing shifts to higher field (Jacobs & others, 1971), so the downward displacements shown in Fig. 7 for phenol-containing systems are due to removal of phenol from the bulk water by the cetomacrogol.

Acknowledgement

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