COMMUNICATIONS

Interfacial tensions and partition coefficients in water/heptane systems containing 2,6-diisopropylphenol, n-alkylphenols and cycloalkanols

A. RUNYAN, J. H. PERRIN, the late F. A. VILALLONGA, *College of Pharmacy, University of Florida, Gainesville, Florida 32610, USA*

Abstract—The free energies of absorption, dehydration, and transfer in a heptane-water system for a set of phenolic compounds and a series of cycloalkanols have been investigated. The free energy of adsorption depends only upon the molecular surface area of the hydrophobic fraction of the molecule, whereas the free energy of dehydration is independent of this fraction.

The potency of an anaesthetic is largely dominated by Van der Waals' forces and by its proton donor properties (Davies et al 1978). Proton acceptor properties have little effect on the potency but do affect the speed of action, so that reducing the hydrogen bond proton acceptor properties would increase the speed of action by reducing hydrogen bonding in the aqueous phase (Davies et al 1976).

2,6-Diisopropyl phenol has proved to be a useful intravenous (i.v.) anaesthetic agent (Glen 1980). It has been used for maintenance of anaesthesis at interval doses (Major et al 1981) and as an i.v. infusion (Verniquet et al 1981) with good results. 2,6-Dialkyl phenols are a class of compounds that differ in the hydrogen bonding ability of the phenolic group due to the amount of steric hindrance of the 2,6-substituents. Changes in hydrogen bonding will alter the chemical potential of a compound and therefore, the free energies of transfer processes through membranes.

This study was designed to measure the free energies of the processes of absorption (ΔG_{ad}^θ), dehydration (ΔG_{deh}^θ), and transfer (ΔG_{tr}^θ) in a heptane/water system for a set of phenolic compounds and a series of cycloalkanols. The phenolic compounds include phenol, 2,6-dimethylphenol, 2,6-diisopropylphenol, and a series of p-substituted alkylphenols. The relative changes produced by substituents on phenol, and by cyclization of n-alkanols have been examined.

A solute distributes itself between two immiscible solvents so that at equilibrium the molecular chemical potential of the solute (μ_s) at the different regions of the biphasic liquid system (water/heptane) can be written in the following ways (Prigogime et al 1965; Betts & Pethica 1960; Vilallonga et al 1982).

$$\mu_s = \mu_s^{\theta w} + kT \ln x_s^w \gamma_s^{*w} \qquad (1)$$
$$= \mu^{\theta h} + kT \ln x_s^h \gamma_s^{*h}$$
$$= \mu^{\theta i} + kT \ln \pi \gamma_s^{*i}$$

Where the superscripts w, h and i refer to water, heptane and interface, respectively, and x_s to the mole fraction of solute. The surface of zero excess solute mass is chosen as the Gibbs dividing

Correspondence to: J. H. Perrin, College of Pharmacy (Box J-494), University of Florida, Gainesville, Florida 32610, USA.

surface and the surface pressure π is defined as: $\pi = \gamma_0 - \gamma$ where γ_0 is the interfacial tension of the pure solvent/water and γ is the interfacial tension of the solution. The activity coefficient γ^* takes on a value of unity at infinite dilution and $\mu^{\theta i}$ is related to Henry's law constants for the respective phases.

This equation leads to the definition of the free energies of transfer in the Henry's law reference state:

$$(w \rightarrow i):\Delta G_{ad}^\theta = kT \ln\frac{\mu_s^{\theta i}}{\mu_s^{\theta w}} = kT \lim_{x \rightarrow {}_s0} \ln\frac{x_s^w}{\pi} \qquad (2)$$

$$(-\Delta G_{hyd} = \Delta G_{deh})\,(h \rightarrow i):\Delta G_{deh}^\theta = $$
$$kT \ln \frac{\mu_s^{\theta h}}{\mu_s^{\theta i}} = kT \lim_{x \rightarrow {}_s0} \ln \frac{\pi}{x_s^h} \qquad (3)$$

$$(w \rightarrow h):\Delta G_{tr}^\theta = kT \lim_{x \rightarrow {}_s0} \ln \frac{x_s^w}{x_s^h} \qquad (4)$$

Materials and methods

Materials. The analytical grade materials used as supplied were: 1:methanol, 2:ethanol, 3:n-propanol, 4:n-butanol, 5:cyclopentanol, 6:phenol, 7:cyclohexanol, 8:n-pentanol, 9:p-methylphenol, 10:cycloheptanol, 11:n-hexanol, 12:p-ethylphenol, 13:2,6-dimethylphenol, 14:cyclooctanol, 15:n-heptanol, 16:p-propylphenol, 17:n-octanol, 18:p-butylphenol, 19:2,6-diisopropylphenol, 20: n-decanol. 1,2,3,4 were obtained from Baker Philipsburg, N.J. 5,7,8,9, 10, 13, 14, 16, 17, 19 and 20 were obtained from Aldrich Milwaukee, WI. 6, 11, 12 and 18 were obtained from Eastman Kodak, Rochester, N.J. 15 was obtained from Matheson, Coleman and Bell, Norwood, OH, USA.

Interfacial tensions. To calculate the ΔG_{ad}^θ and ΔG_{deh}^θ, respectively, interfacial tensions of the aqueous (0·15 M NaCl) solution/ heptane interface and the heptane solutions/aqueous interface were measured with a Wilhelmy Plate at $20 \pm 1\,^\circ\text{C}$ as described by Vilallonga & Phillips (1980). At least six different concentrations of each solution (aqueous or heptane) were used. Plots of mole fractions against the surface pressure were linear (r > 0·98) and the appropriate slopes (x^w/π, π/x^h) were used in equation 2 and 3 to estimate ΔG_{ad}^θ and ΔG_{deh}^θ

Partition coefficients. At least 5 different concentrations of each compound were equilibrated between 10 mL each of heptane and 0·15 NaCl at $20 \pm 1\,^\circ\text{C}$. Concentrations in the aqueous phase ranged from $1·6 \times 10^{-7}$ to 3×10^{-3} mol fraction. After equilibrium concentrations of the cycloalkanols in the aqueous phase

were determined by gas chromatography. The concentration of phenols in the aqueous phase was determined by UV spectroscopy. The concentration in the heptane phase was obtained by subtracting the measured from the original concentration, then $K^x = (x^w/x^h)$ was calculated. No apparent association of any solute molecules was indicated by the independence of solute concentration at the studied ranges and K^x. The average K^x over a range of different concentrations from at least 2 separate experiments was used to calculate the ΔG_{tr}^θ for each compound.

Results and discussion

A modified MOLAREA computer program was used to calculate the molecular surface area of the compounds. The total molecular surface area (TSA, $\mathring{A}^2$ molecule^{-1}) has been used to describe the effect of functional groups on surface activity (Betts & Pethica 1960; Vilallonga et al 1982). The experimental ΔG^θ values and calculated total surface areas are plotted in Fig. 1 along with values for a series of n-alkanols (Vilallonga & Phillips 1980).
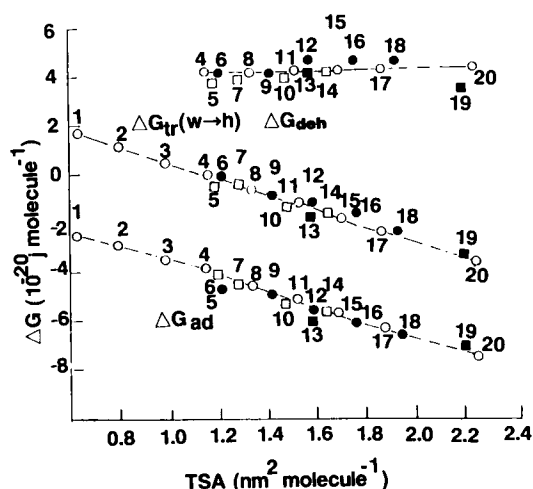

FIG. 1. The plots of free energies (ΔG) of (A) adsorption, (B) dehydration and (C) transfer at water/heptane interfaces against the total molecular surface area (TSA) of molecules listed under Materials and methods.

It has been shown previously that in the case of alkanols (Vilallonga et al 1982) ΔG_{ad}^θ represents the change in free energy

associated with the transfer of a solute molecule from the aqueous solution to the interface where the hydrocarbon moiety of the molecule is a hydrocarbon environment (heptane) and the polar group remains in the aqueous environment.

The points that correspond to the alkylphenols and cycloalkanols fit the straight line defined, within the limits of the experimental error, by the n-alkanols. This seems to indicate that the structure of the hydrophobic moiety (benzene ring or cyclization) does not affect the ΔG_{ad}^θ value which depends only on the molecular surface area of the hydrophobic part.

The plot of ΔG_{deh}^θ against the total molecular area shows independence of the surface area of the hydrophobic moiety of the alkylphenols and cycloalkanols as was shown before (Vilallonga et al 1982) for the n-alkanols, alkylketones, alkylamides and alkylmonocarboxylic acids. This is due to the identical nature of the polar group in all the compounds studied. The average value found, 3.97×10^{-20} J molecule^{-1}, agrees with that of the n-alkanols, 3.88×10^{-20} J molecule^{-1}, (Vilallonga et al 1982) except for the 2,6-diisopropylphenol and suggests that this value can be taken as the OH group contribution to the process of adsorption from the heptane to the water/heptane interface.

The relative free energies of hydrogen bonding interaction in 2,6-dimethyl- and 2,6-diisopropylphenol have been estimated by methods based on CNDO/2 potentials (Davies et al 1978). The overall free energies difference in the interaction with water molecules was found to be 1.2 ± 0.15 kcal mol^{-1} that corresponds to 0.93×10^{-20} J molecule^{-1} or 0.73×10^{-20} J molecule^{-1}. The fact that the difference found between the $\Delta^\circ G_{deh}^\theta$ values of 2,6 dimethyl- and 2,6-diisopropylphenol is 0.72×10^{-20} J molecule^{-1} seems to confirm that the steric hindrance of these isopropyl groups is responsible for the smaller than average value found for all these phenolic compounds.

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