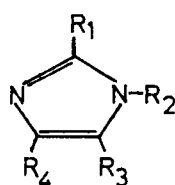


THERMODYNAMICS OF THE AQUEOUS IMMERSION OF A SERIES OF IMIDAZOLES

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The wetting and dispersion of powdered materials in both polar and nonpolar liquids is often an important step not only in their processing but also in their administration as dosage forms such as capsules and aerosols. General techniques used to assess the relative hydrophobicity and dispersibility of powders are the measurement of contact angles, using powder compacts (Kossen and Heertjes, 1965) or liquid penetration (Hansford et al, 1980), or determination of sinking times. All of these techniques only provide limited information and give little or no insight into the underlying energetics of the wetting process. However, if the Gibbs free energy, enthalpy and entropy for immersion of powders were determined these thermodynamic functions could be used to provide a much greater understanding of the factors controlling the wetting and dispersion of powders. The compounds studied were imidazole (I), 2-methylimidazole (II), metronidazole (III), 4-nitroimidazole (IV) and 2-methyl-5-nitroimidazole (V) none of which showed evidence of polymorphism.



	R ₁	R ₂	R ₃	R ₄
I	H	H	H	H
II	CH ₃	H	H	H
III	CH ₃	CH ₂ CH ₂ OH	NO ₂	H
IV	H	H	H	NO ₂
V	CH ₃	H	NO ₂	H

Contact angle measurements were made at 298K using powder compacts. Enthalpies of immersion were also measured at 298K with a Tronac 450 calorimeter by breaking sealed 1cm³ thin-walled glass bulbs containing 0.3 to 0.5g of the vacuum dried powders into 50cm³ of their respective saturated solutions. Specific surface areas of the powders were determined by nitrogen adsorption (Ströhlein areameter). The theory and essential thermodynamic equations for immersion of powders in liquids has been recently published (Schröder, 1984). From the contact angle, θ , and the surface tension of the wetting liquid, γ_{LV} , the Gibbs free energy of immersion, $\Delta_i G$, was calculated using $\Delta_i G = -\gamma_{LV} \cos \theta$.

Table 1. Parameters determined for compounds I to V

Compound	Specific Surface Area (m ² g ⁻¹)	Enthalpy of immersion at 298K (Jm ⁻²)	Contact Angle	Gibbs free energy of immersion at 298K (mJm ⁻²)
I	0.352	44.3	44	-30
II	0.396	33.6	48	-32
III	0.309	4.04	50	-32
IV	0.811	-0.21	59	-22
V	1.28	2.81	64	-18

From the contact angle data above it is only possible to conclude that ease of wetting decreases for compounds I to V in that order, without really understanding why. However, the negative Gibbs free energies indicate that wetting is spontaneous for all these compounds. But only for compound IV is wetting favoured enthalpically, the enthalpy of immersion being negative. For compounds I, II, III and V wetting is entropically driven, most significantly so for compounds I and II, since the enthalpies of immersion are positive.

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Kossen, N.W.F. and Heertjes, P.M. (1965) Chem. Eng. Sci. 20:593-599

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