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The potential value of dielectric response measurements in the assessment of the wettability of powders

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Summary

The wettability of powders is important in formulation, preparation and dissolution of solid pharmaceutical dosage forms. Conventional methods of assessing the wettability of powders, by use of indirect assessment of contact angles, all have practical and/or theoretical limitations. Alternative techniques may, therefore, be of value in assessing the wettability of powders. In this study two samples, one hydrophobic (amylobarbitone) and one relatively hydrophilic (barbitone) have been studied by the novel application of dielectric spectroscopy at various controlled humidities and temperatures. The results obtained demonstrate that the technique can differentiate between samples of a powder with very similar water content, and furthermore appears to aid the understanding of the mechanism of the wetting process. As such, the technique may be of value in assessing the wettability of powders.

Introduction

Assessment of the wettability of powders has generally been undertaken by one of three approaches.

(i) Liquid penetration. The most frequently cited liquid penetration method is the adaptation of the Washburn (1921) approach, proposed by Studebaker and Snow (1955). This method has been critically assessed (Buckton and Newton, 1985a, 1986a) and ascribed as a pseudo-theoretical method with empirical results. Liquid penetration results do, however, provide a good practical assessment of wettability.

(ii) Sessile drops on compressed powder discs (Kossen and Heertjes, 1965; Heertjes and Kossen, 1967; Zografi and Tam, 1976). These methods have recently been criticised (Buckton and Newton, 1985b, 1986b) for the process of forming the powder compacts alters the surface energy of the powder, such that it is not representative of the bulk of the sample.

(iii) Enthalpies of immersion. Hydrophobic powders, such as amylobarbitone, will not immerse in water, and thus wetting by water cannot be directly assessed by this method (Buckton, 1985). Some workers have measured immersion in a series of alcohol/water mixtures, and then ex-

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trapolated to the limiting value for water (Hansford et al., 1980); however, the use of such extrapolations has been questioned (Buckton, 1985; Buckton and Newton, 1986a).

The inadequacies that exist, by way of practical and/or theoretical limitations, in each of the existing techniques, makes it desirable that alternative methods should be sought to study this important process (Buckton et al., 1986). Investigation of dielectric response has been used as a method of observing water vapour adsorption onto materials, two such examples are a ceramic catalyst (Ramdeen et al., 1984) and compressed powder pellets of bovine serum albumin (Shablakh et al., 1984). There is then the possibility that this technique could be used to assess the interaction between pharmaceutical powders and water, and hence lead to an assessment of their relative wettability. A preliminary investigation was undertaken into the plausability of the application of dielectric measurements in this manner.

Introduction to Dielectric Theory

A dielectric is a material which possesses charged dipoles which, on the application of an electric field can be aligned in the field direction. As the charges are bound in the structure and not free to move they contribute to the electric polarisation and not the conductivity. For small electrical fields the resultant change in polarisation, P, is proportional to the electric field, E, with the constant of proportionality being defined as the permittivity of the material, i.e.

$$\frac{\mathrm{d}P}{\mathrm{d}E} = \varepsilon_0 \cdot \varepsilon \tag{1}$$

where ε_0 is the absolute permittivity of free space, $8.85 \times 10^{-12}\ \mathrm{F \cdot m^{-1}}$, and ε, the relative permittivity, is characteristic of the number of dipoles and the strength of the dipole moment $q \cdot d$, where q is the magnitude of one dipole charge and d the separation between individual charges. Hence a measurement of the relative permittivity gives a measure of the strength of the dipolar response. Water forms a particularly strong dipole, liquid water having a very high permittivity of 80, so the measurement of the dielectric properties of a powder into which water has been introduced should, in principle, give a means of observing the water/powder interaction.

In practice the most convenient method of measuring the permittivity is to apply a small AC signal to the sample and observe the out of phase, capacitative, response. The capacitance, C, being given by

$$C = \varepsilon_0 \varepsilon A/s \tag{2}$$

where A is the area of the plane parallel electrodes and s their spacing.

In general more than one type of dipolar response occurs in materials, these are usually characterised by their rates of response, ω_p. For any one particular process:

$$\varepsilon(\omega) = \chi(\omega) + \varepsilon(\infty) \tag{3}$$

where the frequency range of interest is in the region of ω_p for this process. All the processes that occur at higher frequencies have been added together into the so-called infinite frequency permittivity $\varepsilon(\infty)$. $\chi(\omega)$ is the frequency-dependent susceptibility and can be written, with complete generality, in the form:

$$\chi(\omega) = \chi(0) \cdot F(\omega/\omega_\mathrm{p}) \tag{4}$$

where $\chi(0)$ is the magnitude of the response and

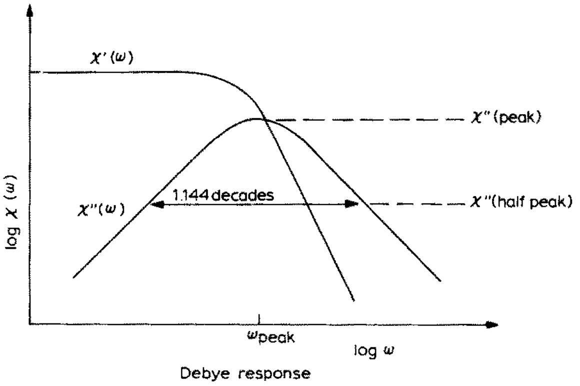

Fig. 1. Frequency-dependent susceptibilities predicted by Debye (1945).

$F(\omega/\omega_p)$ the spectral shape function. For a single dipole interacting with its surroundings only through a frictional force the Debye (1945) model of response (Fig. 1) gives:

$$F(\omega/\omega_p) = (1 + i \cdot \omega/\omega_p)^{-1} \tag{5}$$

in which $i = (-1)^{1/2}$ so that the susceptibility (and capacitance) have real and imaginary components representing the out-of-phase and in-phase responses to the applied AC signal

$$C(\omega) = C^{1}(\omega) - i \cdot C^{11}(\omega) \tag{6}$$

and from Eqns. 2, 3 and 6:

$$C(\omega) = \varepsilon_0 \cdot A \cdot s^{-1}\{\chi^{1}(\omega) - i \cdot \chi^{11}(\omega) + \varepsilon(\infty)\} \tag{7}$$

A number of empirical functions have been proposed for the spectral shape function $F(\omega/\omega_p)$ (see Cole and Cole, 1941; Davidson and Cole, 1951; Jonscher, 1977; Hill, 1978). The function that will be used here is that derived by two of the authors on the basis of a cooperative, many body, response of the dipoles and the medium in which they are embedded (Dissado and Hill, 1979, 1983, 1984). The Dissado-Hill function is capable of giving a complete description of dielectric susceptibility, furthermore, both Hill's empirical relationship (Hill, 1978) and Jonscher's Universal Law of dielectric response (Jonscher, 1977) can be obtained as limiting behaviour from this particular function. The theory behind the Dissado-Hill function is essentially that the relaxation of a single dipole forces cooperative configurational changes in the surrounding medium to form a single cluster of response. The individual clusters interact with each other through cluster exchange processes. Neither the inter-cluster development nor the intra-cluster exchanges are perfectly efficient, letting these fractional efficiencies be n and m, respectively, with $0 \leqslant m, n \leqslant 1$, the spectral shape function takes the form

$$F(\omega/\omega_p) = F_0^{-1}(l + ix)^{n-1} \cdot {}_2F_1\left(l - n,\, l - m;\, 2 - n;\, \frac{l}{l\text{-}ix}\right) \tag{8}$$

in which ${}_2F_1(,;;)$ is the gaussian hypergeometric function, x is the reduced frequency ω/ω_p, F_0 is a normalising frequency which can be expressed in terms of gamma functions of m and n. The cooperative parameters m and n are available from the experimentally observed behaviour of the capacitance as a function of frequency, should their numerical value be required to quantify the process.

Materials and Methods

Measurements of capacitance and conductivity were made on a precision capacitance measuring transformer radio arm bridge (General Radio, 1612) with a frequency range of 10^1 to 10^5 Hz. The powdered sample was placed in a stainless steel sample-holder (Fig. 2) which acted as one electrode, and a concentrically mounted stainless

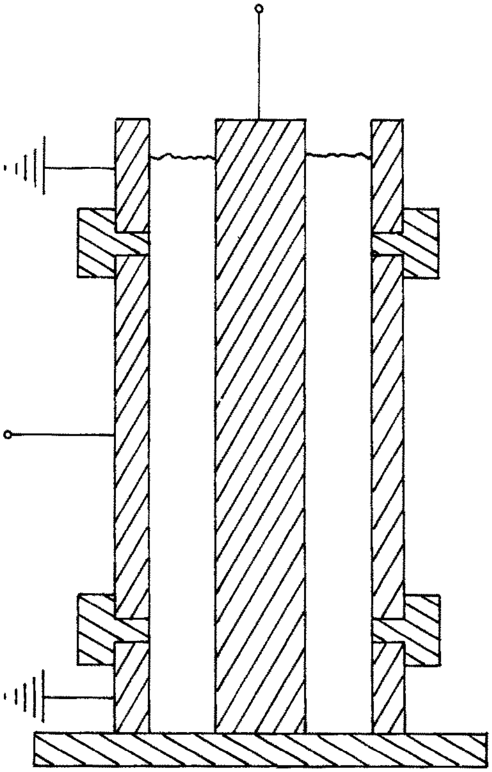

Fig. 2. Diagrammatic representation of the dielectric cell. ▨, conductor; ▧, insulator.

steel rod acted as the other electrode of the measuring cell. Experiments were undertaken on two powders, amylobarbitone and barbitone, which were chosen as examples of hydrophobic and hydrophilic powders, respectively, as assessed by liquid penetration experiments (Buckton and Newton, 1986a). The powders were equilibrated in the cell prior to testing at a range of humidities from 0 to 100% R.H. and at 5 temperatures: 10, 15, 20, 26 and 32°C; these variables were controlled in an Angelatoni Central Sud environment chamber. By measuring capacitance and conductance, in situ, each hour it was found that after 6–8 h consecutive readings became constant and thus equilibrium had been achieved, consequently readings were taken 12 h after introducing the sample thus ensuring equilibrium conditions.

Effect of powder pretreatment

Three samples of barbitone were studied, one of which had no pretreatment, one had been dried at 100°C for 1 h and one had been dried for 24 h under a vacuum of 10^{-3} mbar at 20°C. Measurements were made at an environmental chamber setting of 20°C, 0% R.H.

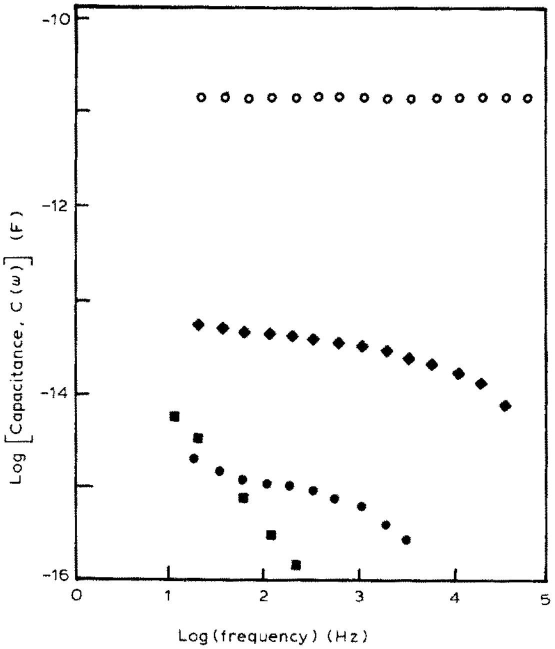

Fig. 3. Frequency–response curve for barbitone at 20°C. ◆, untreated (as received); ●, heated at 100°C for 1 h; ■, vacuum-dried; ○, constant capacitance response for all three samples.

The results in Fig. 3 show the measured data for a sample of barbitone powder in the untreated, that is as received, form, after heating the powder to 100°C for 1 h and after vacuum-drying. In the upper part of the plot the data for the magnitude of the real part of the capacitance, $C^1(\omega)$, did not change with treatments but the loss characteristics, in the lower part of the diagram, are clearly sensitive to the moisture content, with a decrease in loss of almost two orders of magnitude between the untreated and vacuum-dried sample. This can be interpreted on the basis that adsorbed water influences the relaxation process. The technique appears to offer a sensitive method of assessing the quantity of adsorbed water on the powder surface. The vacuum-dried sample seems to be drier than the heated sample; consequently all other experiments were undertaken on powders which had been dried for 24 h at 10^{-3} mbar.

Frequency–response curves

Due to the operating limits of the measuring bridge, the frequency range available is from 10^1 to 10^5 Hz, giving an effective frequency window on the overall process of 4 decades. By observing the frequency shift in particular peaks after reaching equilibrium at different humidities and temperatures it was possible to re-scale the frequency. No shift in amplitude was observed. The re-scaling technique is commonly referred to as frequency normalisation (Hill, 1978) and effectively widens the frequency window over which the relaxation process can be observed.

Frequency–response curve for barbitone

Figs. 4 and 5 show the effects of varying both the humidity and temperature on the dielectric properties of the barbitone powder. The large loss peak observed under dry and relatively low humidity conditions (Fig. 4) leads to a dispersion in the real part of the capacitance whilst at higher temperatures and relatively low humidities a second loss peak process is seen but, as in Fig. 3, the magnitude of the peak is too small to give a significant dispersion in the capacitive component.

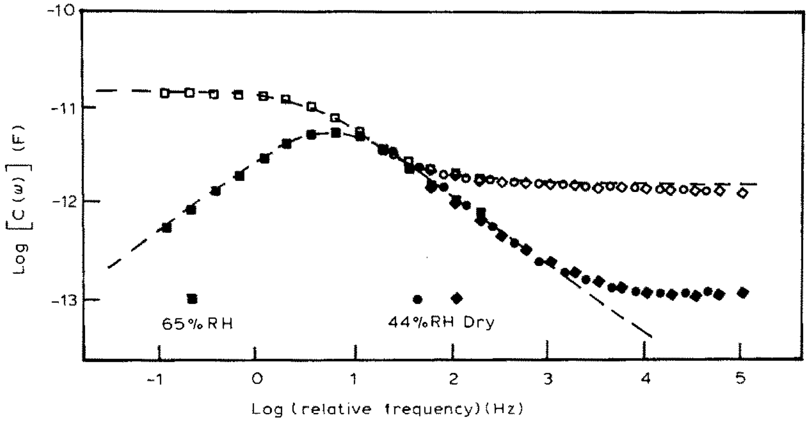

Fig. 4. Normalised frequency-response curve for barbitone at low relative humidities and temperatures. All measurements at 10 ° C, scaled at dry.

Frequency-response curves for amylobarbitone

It was observed (Figs. 6–8) that neither temperature nor humidity had as significant an effect on amylobarbitone as they had on barbitone. The plots exhibit the humidity-normalised data for 10, 20 and 32 ° C, respectively. In all cases the low magnitude of the loss peak has resulted in an almost non-dispersive real capacitance. The data at 20 and 32 ° C could be re-normalised with respect to temperature by dividing the lower temperature frequency scale by a factor of 5. It is, therefore, likely that the same loss peak is being observed at these temperatures. The loss peak observed at 10 ° C over a range of humidities appears to be sharper although it is very much of the same magnitude as the peak observed at 20 and 32 ° C.

Discussion

A peak on the frequency-response curve of capacitance corresponds to the relaxation of a dipole. In a study of the dielectric response of

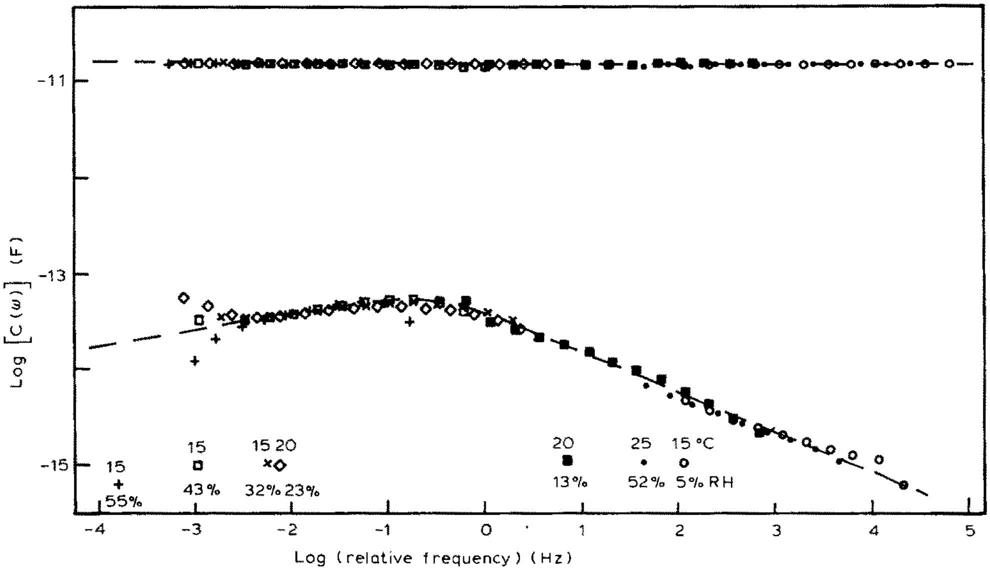

Fig. 5. Normalised frequency-response curve for barbitone at higher temperatures, scaled at 15 ° C, 5% R.H.

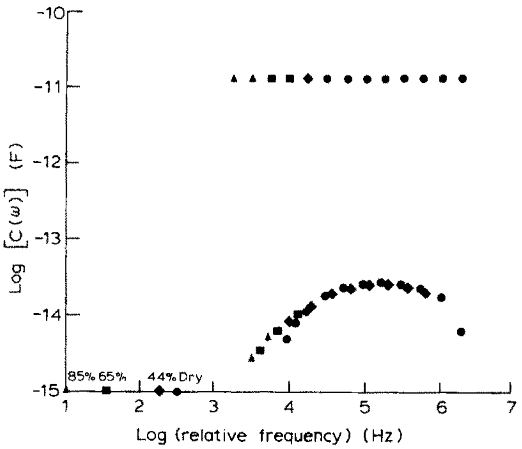

Fig. 6. Normalised frequency-response curve for amylobarbitone at 10 °C, scaled at 85% R.H.

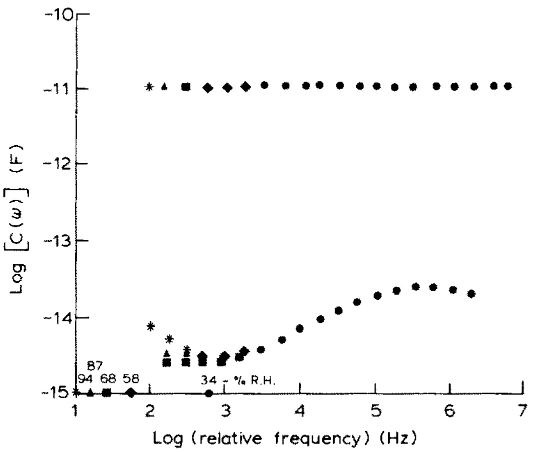

Fig. 8. Normalised frequency-response curve for amylobarbitone at 32 °C, scaled at 94% R.H.

cyclohexanol, for example, it could be expected that two possible relaxation processes and hence two peaks would be observed. One would be due to the orientation of the hydroxy group and the other due to boat–chair transformation of the ring. It is likely that the rotation of the hydroxy group would be a rapid process giving rise to high relaxation frequencies, whilst the boat–chair transformation would be a slower process giving a lower frequency peak. The frequency–response curve for the vapour phase interaction of water with barbitone which is reported here consists of two peaks, one broad peak (Fig. 5) and one large peak at high relative frequencies (Fig. 4). This suggests that the ring structure of barbitone is being hydrated in two stages. The large peak at the lowest relative humidity is a typical response for a rapid easy process (e.g. relaxation of the hydroxyl group of cyclohexanol), and can be regarded as an easily accessible hydration site. This is followed by a second peak, which is a less readily undertaken hydration. The large peak observed in Fig. 4 indicates a major hydration process, and this is not observed with amylobarbitone, where only one clear peak is observed similar in shape and magnitude to the major peak in Fig. 5. There is a possibility that amylobarbitone has a further peak at lower relative frequencies; however, the results indicate that as the humidity increases this peak appears to increase in magnitude rather than shift in frequency. This implies that the process is associated with multilayer formation rather than the hydration of a different centre. The results indicate that the process by which amylobarbitone is hydrated also occurs with barbitone, as the peak in Fig. 5 can be superimposed on Fig. 7 which suggests that this part of the response is identical. However, barbitone also has a second process which is large and easily accessible. This suggests that the hydration of the ring structure is severely reduced due to steric hindrance of amylobarbitone's extended side chain.

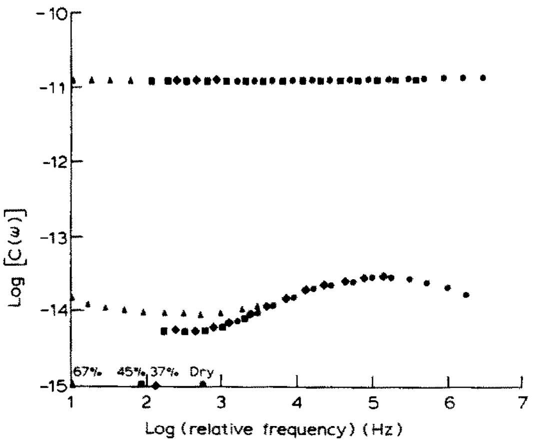

Fig. 7. Normalised frequency-response curve for amylobarbitone at 20 °C, scaled at 67% R.H.

It should be noted that the term 'hydration site' may refer to different physical sites on the powder surface, or to different strengths or types of bonding at the same site.

Conclusions

Dielectric measurements, under controlled environmental conditions, on powders clearly provide a method for showing differences between powders containing only very slightly different quantities of water.

This technique adequately demonstrates that barbitone is more readily wetted than amylobarbitone. Furthermore, the mechanism of the interaction between the powders and water is indicated. It would appear that the main value of this application of dielectric spectroscopy, is the study, on a molecular level, of the nature of the interaction. In conjunction with dielectric measurements, such techniques as infra-red spectroscopy, X-ray crystallography, and nuclear magnetic resonance, could yield valuable information on the hydration process at powder surfaces.

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