

## COMMUNICATIONS

### Extension of Johnson's equation of homogeneity of random mixtures

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The volume-weighted/volume-number mean particle diameter of the ingredient is applied to the equation of Johnson (1972) as a measure of the mean particle size defining the degree of homogeneity of random mixtures. By introducing the volume shape factor, the applications of this equation are extended to ingredients of nonspherical particle shape.

From the Poisson distribution, Johnson (1972) developed equation 1 to define the degree of homogeneity (or heterogeneity) of random mixtures composed of a minor proportion of active ingredient in a large amount of diluent.

$$C_R = 100\{\Sigma(fd^3) \cdot \rho \cdot \pi / 6G\}^{\frac{1}{2}} \quad (1)$$

$C_R$  is the coefficient of variation as a percentage of the mean weight  $G$  of drug content per sample of the random mixture. The term  $\Sigma(fd^3)$  refers to the particle size distribution of the ingredient,  $f$  being the relative weight fractions of particles existing with (almost) uniform particle diameters  $d$ ;  $\rho$  is the density of the ingredient particles.

Equation 1 has been used successfully in predicting the highest degree of homogeneity of pharmaceutical powder mixtures (Egermann 1974; Johnson 1975, 1979; Egermann et al 1985). It does not, however, define the type of mean particle size represented by  $\Sigma(fd^3)$ , and it applies to ingredients of spherical particle shape only.

The 'volume-weighted/volume-number mean diameter'  $\bar{d}_v$ , with the frequency index and the power index both equal to 3 (Edmundson 1967), has been shown to be the type of mean which is representative of mixing quality (Egermann 1982). With a weight frequency distribution exhibiting relative weight proportions  $f_1, f_2, \dots, f_i$  of particles with diameters  $d_1, d_2, \dots, d_i, \bar{d}_v^3$  is derived as  $\Sigma(fd^3)$ :

$$f_1 \cdot d_1^3 + f_2 \cdot d_2^3 \dots + f_i \cdot d_i^3 = \Sigma(fd^3) = \bar{d}_v^3 \quad (2)$$

Numerical examples of calculating  $\bar{d}_v$  from the weight frequency distribution (sieve analysis) and from the number frequency distribution (microscopical analysis) have been given elsewhere (Egermann 1974). To recognize  $\bar{d}_v$  as referring to the degree of mixing may be of practical importance, if  $\bar{d}_v$  is calculated from other

types of mean (Egermann 1982). With  $\bar{d}_v$ , equation 1 becomes:

$$C_R = 100[(\bar{d}_v^3 \cdot \rho \cdot \pi) / 6G]^{\frac{1}{2}} \quad (3)$$

In equation 3, the term

$$(\bar{d}_v^3 \cdot \rho \cdot \pi) / 6 = \bar{m}_s \quad (4)$$

defines  $\bar{m}_s$ , the volume-weighted mean particle weight of spherical particles. With equation 4, equation 3 may be written in the simple form:

$$C_R = 100(\bar{m}_s / G)^{\frac{1}{2}} \quad (5)$$

To allow for non-spherical particle shape, the volume shape factor  $F$  may be introduced:

$$F = v_p / v_s \quad (6)$$

$v_p$  is the volume of particles with dimension  $d$  ( $\bar{d}_v$  respectively), and  $v_s$  the volume  $d^3\pi/6$  of spheres of the same diameter  $d$  ( $\bar{d}_v$ ).

With spheres,  $F$  becomes unity. With non-spheres, the magnitude of  $F$  is dependent both on particle morphology and on which particle dimension is taken as a measure of  $d$ . Providing cubes with the edge length equal  $d$ ,  $v_p$  is  $d^3$  and from equation 6,  $F$  becomes  $6/\pi = 1.91$ . With  $d$  being the diagonal of the cube face,  $v_p$  is  $d^3/2^{1.5}$ , and  $F$  assumes the value  $6/\pi \cdot 2^{1.5} = 0.68$ .

Introducing  $F$  to equation 4, the volume-weighted mean particle weight  $\bar{m}$  of non-spheres (and of spheres) is derived:

$$\bar{m} = \bar{m}_s \cdot F = (\bar{d}_v^3 \cdot \rho \cdot \pi \cdot F) / 6 \quad (7)$$

With  $\bar{m}$  of equation 7, equation 5 approaches:

$$C_R = 100(\bar{m} / G)^{\frac{1}{2}} \quad (8)$$

Equation 8 shows  $C_R$  of the random mixture to be defined by the volume-weighted mean particle weight  $\bar{m}$  and by the sample mean content  $G$  of the ingredient. Substituting equation 7 to equation 8 gives a general form of equation 1, which is not restricted to ingredients of spherical particle shape, and which refers to  $\bar{d}_v$  as being the type of mean particle size representative of  $C_R$ :

$$C_R = 100[(\bar{d}_v^3 \cdot \rho \cdot \pi \cdot F) / 6G]^{\frac{1}{2}} \quad (9)$$

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## Tensile anisotropy of some pigmented tablet film coating systems

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The tensile properties of representative tablet film coating systems, containing hydroxypropyl methylcellulose alone and in combination with either polyvinyl alcohol, polyethylene glycol 400 and polyethylene glycol 1000 and pigmented with either talc or titanium dioxide, have been investigated. Tensile anisotropy was observed between film samples cut parallel to, and perpendicular to, the direction of rotation of the casting substrate and factors accounting for this phenomenon are presented.

It was reported previously (Okhamafe & York 1983) that films consisting of hydroxypropyl methylcellulose and a second polymer additive (cast using the rotating cylinder technique) exhibited some degree of anisotropy with respect to elongation properties, although the tensile strength and Young's modulus data did not show this phenomenon. The main consequence of tensile anisotropy is that the mechanical properties of a film would vary according to the direction of the applied stress. In the present study, this feature is considered for polymer systems pigmented with either talc or titanium dioxide.

### Method

The polymer systems examined were hydroxypropyl methylcellulose (Pharmacoat 606, Shin-Etsu Chem. Co., Japan) alone, and in combination with 20% w/w of either polyvinyl alcohol (Poval PA-5, Shin-Etsu Chem. Co.), polyethylene glycol 400 or polyethylene glycol 1000 (BDH Chem. Ltd). The film formulations were prepared from 10% w/v aqueous solutions of the individual polymers. The main features of the pigment used—designated as talc A (coarse), talc B (fine), TiO<sub>2</sub>A (anatase, untreated) and TiO<sub>2</sub>B (rutile, organically treated)—as well as the methods employed to disperse the pigments in the film formulations, have been described in a recent paper (Okhamafe & York 1984). Free films were cast by the rotating cylinder technique and their tensile properties—tensile strength,

Young's modulus, elongation—determined as previously detailed (Okhamafe & York 1983). For each film type, six samples were cut parallel to, and perpendicular to the direction of rotation of the casting substrate. Mean values of sets of data and associated standard deviations were calculated.

### Results and discussion

As found previously for similar unfilled polymer systems (Okhamafe & York 1983), there was no significant difference (*t*-test at the 95% confidence level) between the tensile strength or Young's modulus of parallel and perpendicular samples for the pigmented films and these data are therefore not listed. However, the results for the mixed polymer systems in Tables 1 and 2 indicate that there was significant difference (95% confidence level) between the elongations of parallel and perpendicular samples at low pigment contents. The gap between these sets of values narrowed with increasing filler concentration.

Two major factors may account for the declining elongation anisotropy of the films with increase in pigment concentration. First, it seems possible that during the drying process the pigments or fillers hindered a uni-directional orientation of the polyvinyl alcohol, and polyethylene glycols 400 and 1000 which consequently became more randomly arranged, thus leading to a decrease in elongation anisotropy. This could have been achieved either as a result of the physical presence of the pigments or pigment-polymer interaction. Second, even if it is assumed that the alignment of the polymer additives in the films is not influenced by the presence of the pigments, the effect of molecular orientation of the polymer additives on film elongation is likely to decrease with increase in pigment levels. This is because the stress associated with the pigment particles as well as the effect of any pigment-polymer interaction would make the films more brittle. The direction of applied stress would therefore be increasingly less important as pigment concentration rises because the pigment particles are presumably

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