

Apparent validity of the Washburn equation when applied to compressed tablets

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Recently Carli & Simioni (1979) have drawn attention to some limitations of the Washburn (1921) equation in quantifying liquid penetration rates into beds of hydrophobic drugs. In particular it was suggested that the penetration rate may depend upon the particle size of the constituent particles.

However, we have reason to believe that the Washburn equation in its classical form may be valid when applied to a typical compressed pharmaceutical tablet. Such a system contains hydrophobic as well as hydrophilic particles so that not only does the pore size vary but so also does the nature of the walls constituting the pores.

The Washburn equation is written as

$$L^{1/m} = D \cdot \gamma \cdot \cos \theta \cdot t / (4\eta) \quad \dots \quad (1)$$

where L = length of penetration, D = capillary diameter, θ = solid/liquid contact angle, γ = surface tension and η the viscosity of the penetrating liquid, and t = time. The exponent m is the factor found to vary according to the particle size or pore size distribution by Carli & Simioni (1979) but in the classical form of the equation has a value of 0.5. It will be noted that the term D must be an average value of capillary diameter and does not include a term for the distribution of size which must inevitably occur in any real system.

Using a micro-method of measuring aqueous and non-aqueous liquid penetration rates (Groves & Alkan 1979), we have been able to demonstrate that the controlling factors influencing liquid penetration are the liquid viscosity and surface tension and the apparent contact angle between the liquid and the capillary walls.

The tablets were mixtures of lithium carbonate, starch and lactose granulated with aqueous polyvinyl alcohol and compressed at various pressures (for details see Alkan 1978) to vary the pore size. The average pore size was determined by a low pressure nitrogen permeability method (Groves & Alkan 1978). This method is likely to measure the mean size of those pores which pass through the compact rather than all pores, including those which are blind and would not readily allow fluid to pass through.

The micro-method used consists of recording the time for the liquid under examination to drain from a filled 2 μ l capillary when placed into contact with the tablet

surface. Since the liquid volume is small gravitational effects can be ignored. If liquid penetration is homogeneous and in all directions, the volume of the tablet structure penetrated by the liquid is likely to be in the shape of a hemisphere with a radius corresponding to the depth of penetration L . Thus, the total volume of the penetrated portion of the tablet can be written as

$$v_t = 1/2 \cdot 4/3 \cdot \pi \cdot L^3$$

Liquid may only pass through the voids and the volume will be the same as the void volume v_v of the penetrated space of the tablet.

Now, the tablet porosity $\epsilon = v_v/v_t$ and hence, from equation 1, we may write if $m = 0.5$

$$(3v_v/2\pi\epsilon)^{2/3} = D \cdot \gamma \cdot \cos \theta \cdot t / (4\eta) \quad \dots \quad (2)$$

From this it will be seen that the reciprocal of the penetration time is proportional to the quantity $\epsilon^{2/3} \cdot D$ which is effectively a measure of the pore structure of the compact.

Measurement of the penetration rates of aqueous sucrose solutions (η variable, γ and θ essentially constant) over the range of 0 to 20% w/w showed that a plot of

$\frac{\gamma}{\eta} \cdot \epsilon^{2/3} \cdot D$ vs $1/t$ was linear (correlation coefficient 0.9995),

irrespective of the tablet compression or concentration of the solution. This tends to confirm the validity of the classical form of the Washburn equation in which the exponent $m = 0.5$.

When the same experiment was repeated with a range of aqueous sodium lauryl sulphate solutions (γ variable, η essentially constant) each concentration resulted in similar straight lines but with different slopes. The slope

of the plot $\frac{\gamma}{\eta} \cdot \epsilon^{2/3} \cdot D$ vs $1/t$ is related to the apparent

contact angle θ . The penetration rates increased with increasing surfactant concentration. This indicates that the reduction in surface tension was outweighed by an increase in $\cos \theta$, brought about by a marked reduction in the apparent contact angle θ . This was confirmed in the present system since an increase in the concentration above the critical micelle concentration produced no significant lowering of the measured surface tension but decreased the value of θ as measured by the penetration experiments even further.

It should be pointed out that although the Washburn equation may have some limitations, in practice it has been widely confirmed as being valid for compressed

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tablets (Nogami et al 1967, 1969; Ganderton 1969; Ganderton & Selkirk 1970; Couvreur et al 1975; Dullien et al 1977). The paper of Schicketanz (1974) cited by Carli & Simioni (1979) for the fact that m can vary has been criticized by van Brakel (1975) on the grounds that there were errors in interpretation of the original approach due to Kozeny (1927). In addition, it was noted that the postulated log-log relationship between penetration time and penetration distance was not unique since a direct, non-logarithmic, plot was also linear.

It may well be that the exponent m in equation 1 varies from 1 initially to 0 at infinite time, and is affected by the particle size of the component particles or the pore size and size distribution of the bed in the way suggested by Carli & Simioni. However, in a system designed to mimic a realistic tablet formulation the value of m is effectively 0.5. Since there are probably a range of pore sizes present in any real system the validity of the original Washburn approach in this type of system may be the statistical result of a randomization process due to the distribution of pore sizes.

March 12, 1979

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