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Contact angles and surface free energies of theophylline and salicylic acid powders determined by the Washburn method

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Summary

The Washburn method was used to determine the dynamic contact angles of theophylline and salicylic acid powders. The suitability of the materials for liquid intrusion studies was assessed by packing studies. The liquids used were distilled water, methanol, 1-propanol, 1-butanol, 1-octanol and *n*-hexane. Liquid intrusion was studied with saturated solutions. Despite similarities in the morphology of the particles theophylline presented good packing properties whereas salicylic acid formed a heterogeneous powder bed structure. 1-Propanol was the best wetting liquid for both substances. Water did not penetrate into the salicylic acid powder bed. The contact angle of 1-propanol and the powders was estimated to be 0°. With theophylline the following values for the other liquids were obtained: water, 70.3°; hexane, 28.7°; octanol, 26.6°; methanol, 22.0°; and butanol, 12.3°. With salicylic acid the values obtained were: methanol, 81.7°; hexane, 73.7°; octanol, 71.5°; and butanol, 59.7°. Using the contact angle data obtained, the surface free energy parameters of theophylline, salicylic acid and, with data from a previous study, of lactose, were determined. The parameters were calculated with the geometric mean, harmonic mean and geometric-harmonic mean methods. The validity of the calculated surface free energy parameters is discussed on the basis of spreading coefficients. The dynamic contact angles do not correlate to the calculated surface free energy parameters, whereas the slope of distance squared vs time plots of liquid intrusion showed a relationship with the spreading coefficients.

Introduction

In a previous study the authors used the Washburn method for determining the contact angles of several liquids with lactose powder (Kiesvaara and Yliruusi, 1992). In that study the method was found to be acceptable when using morphologically nodular particles with good packing properties. The main factors affecting the packing are particle shape, density, size and size distribution. Furthermore it is extremely important to ensure constant measuring conditions. The relative humidity and temperature, for instance, affect both the packing of the particles and the advancing of the liquid front in the powder bed.

In pharmaceutical technology wetting has usually been characterized by contact angles (Gissinger and Stamm, 1980; Buckton and Newton,

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1986; Lippold and Ohm, 1986). Often this is adequate, but understanding and utilization of the phenomenon requires measurement of the interfacial energies of the system (Rowe, 1989a, 1990; Buckton, 1992). The interfacial energy is an important parameter because it is a determining factor in the formation and stability of the new interface. The formation of an interface is important in dynamic processes, for example, coating and granulation. Evidently, the stability aspect of the interface is more pronounced in static multiple phase systems, for instance suspensions and emulsions. The conventional method for the determination of the surface free energy of solids is by the sessile drop contact angles.

The studying of the surface free energy (SFE) of solids is increasing in pharmaceutical powder technology (Buckton et al., 1988; Rowe, 1989a,b,c, 1990; Buckton, 1992). Studies have been initiated with polymers (Fox and Zisman, 1950; Wu, 1968, 1969, 1970, 1971, 1973, 1974; Luangtana-alan and Fell, 1987, 1988), and later extended to pharmaceutical raw materials and process intermediates (Ohm and Lippold, 1985, 1986; Rowe, 1989a; Kiesvaara and Yliruusi, 1991b). The SFE of powders is a most interesting parameter considering the extensive use of powders as raw material in pharmaceutical industry. Dynamic contact angles based on liquid intrusion have been used in a few cases to assess surface energetics of pharmaceutical powders (Buckton and Newton, 1985, 1986) by the modified Zisman approach (Fox and Zisman, 1950).

There are several mathematical methods to determine the total surface free energy with dispersion and polar components of a solid surface from equilibrium contact angle data (Fowkes, 1964; Wu, 1971, 1973). The methods are based on different approaches to the nature of the attractive interaction across the interface, and the choice of the mathematical treatment depends on, for example, the degree of polar interaction. This often causes the results to be indicative, rather than absolute.

The purpose of this study was to evaluate the liquid intrusion method with less optimal particle shapes. In addition, the packing of the powders was investigated. Furthermore, the validity of the SFE parameters calculated from dynamic contact angle data were evaluated on the basis of the spreading coefficients and compared with the previously determined values for tablets (Kiesvaara and Yliruusi, 1991b).

Materials and Methods

Materials

The materials used were anhydrous theophylline and salicylic acid (both Ph. Eur. grade). The materials were stored at a constant relative humidity at room temperature (22 ± 2°C, 53 ± 1% RH) for at least 24 h in order to standardize the particle surfaces. The liquids used were distilled water, methanol, 1-propanol, 1-butanol, 1-octanol and *n*-hexane. Liquid intrusion was studied with saturated solutions to maintain the structure of the powder columns during liquid intrusion.

Characterization of the materials

The basic characterization of theophylline and salicylic acid powders was carried out as described earlier (Kiesvaara and Yliruusi, 1992). The main characteristics studied were particle morphology, crystal properties, particle size distribution and specific surface area.

Packing of the powder columns

On the basis of an earlier study (Kiesvaara and Yliruusi, 1992) the packing time of the powders was considered important. The packing of the two materials was studied in order to ensure as similar a pore structure in the powder beds as possible. The packing times studied were 3, 6 and 12 min.

Contact angles and surface free energies

The liquid surface tension components and powder contact angles were calculated as described previously (Kiesvaara and Yliruusi, 1992). The SFEs with dispersion and polar components of the powders were calculated with the geometric-mean, harmonic-mean and geometric-harmonic-mean methods (Wu, 1973) using a computer program described elsewhere (Kiesvaara and Yliruusi, 1991a) and MathCAD (MathSoft

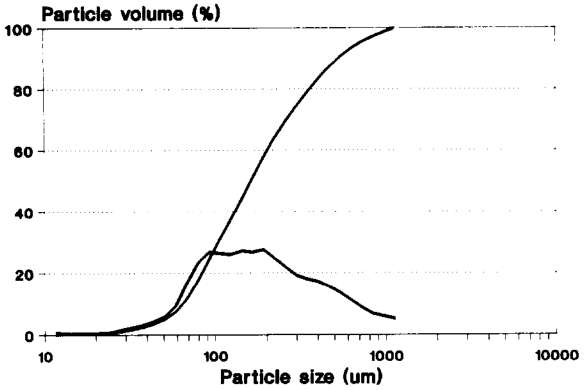

Fig. 1. Particle size distribution of theophylline powder.

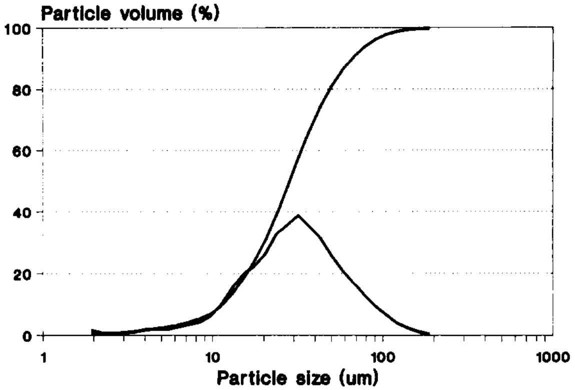

Fig. 2. Particle size distribution of salicylic acid powder.

Inc., U.S.A.) documents. The spreading coefficients were calculated as proposed by Wu (1973).

Results and Discussion

Characterization of the starting materials

The morphology of particles usually explains most of the packing characteristics of a powder, although many other properties such as surface charge and material density affect the rheological behavior. The micrographs obtained by scanning electron microscopy showed that the particle morphology is somewhat similar in both substances. An elongated shape of the particles is typical for the powders. Theophylline particles have an irregular surface structure caused by agglomeration of smaller particles on bigger particles. Salicylic acid particles exhibit more plain crystal faces and a smaller aggregation tendency. According to the X-ray studies both substances are well crystallized. Particle size distributions (Figs 1 and 2) of the powders show that theophylline has a wide size distribution with a median of 200 μm. The size distribution of salicylic acid is narrower and almost log-normal in shape. The median of the distribution is 30 μm. The specific surface area measured by the BET single point method of both powders is quite small: theophylline, 0.21 m^2/g; salicylic acid, 0.28 m^2/g.

The densities and dynamic viscosities of the saturated liquids are presented in Tables 1 and 2. Especially with theophylline the values are close to those in the literature for pure liquids (Weast, 1982), implying low solubility. Salicylic acid is more soluble, yielding greater density and viscosity values for the liquids. Also, the contact angles of the saturated liquids on solid paraffin surface,

TABLE 1

Densities and dynamic viscosities at 21.1 ± 0.5°C, and contact angles (Θ) ($n = 10$) *on solid paraffin surface, surface tensions* (γ_L) *(20 ± 0.2°C) and dispersion* (γ_L^D) *and polar* (γ_L^P) *components of the liquids saturated with theophylline*

Liquid	Density (g/cm^3)	Dynamic viscosity ($mN\ s\ m^{-2}$)	Θ (°)		γ_L (mN/m)	γ_L^D (mN/m)	γ_L^P (mN/m)
			Mean	SE			
Water	1.00	0.90	105.3	1.5	72.2	29.1	43.1
Methanol	0.79	0.59	31.7	1.8	23.1	18.8	4.3
Propanol	0.80	2.08	25.1	1.7	24.1	21.7	2.4
Butanol	0.81	2.82	29.0	0.7	24.8	22.2	2.6
Octanol	0.82	8.73	32.3	1.8	27.8	27.1	0.7
Hexane	0.66	0.31	0	0	18.7	(14.4)	(4.3)

Parentheses indicate an inconsistent result.

TABLE 2

Densities and dynamic viscosities at 21.7 ± 0.2°C, and contact angles (Θ) ($n = 10$) on solid paraffin surface, surface tensions (γ_L^D) (20 ± 0.2°C) and dispersion (γ_L^D) and polar (γ_L^P) components of the liquids saturated with salicylic acid

Liquid	Density (g/cm^3)	Dynamic viscosity ($mN\ s\ m^{-2}$)	Θ (°)		γ_L (mN/m)	γ_L^D (mN/m)	γ_L^P (mN/m)
			Mean	SE			
Water	1.00	0.89	99.4	1.1	64.3	29.8	34.5
Methanol	0.93	1.13	42.1	1.2	27.7	24.0	3.7
Propanol	0.89	2.74	36.5	0.9	26.6	23.7	2.9
Butanol	0.89	3.43	32.4	1.0	27.0	25.5	1.5
Octanol	0.87	9.15	34.0	0.6	28.3	27.6	0.7
Hexane	0.65	0.29	0	0	18.8	(14.5)	(4.3)

Parentheses indicate an inconsistent result.

surface tensions and the calculated dispersion and polar components are summarized in Tables 1 and 2. As in the previous study (Kiesvaara and Yliruusi, 1992), an inconsistency arising from the error included in the numerical values with the liquids of least polarity can be observed in Tables 1 and 2. It is reasonable to presume a similar error in the rest of the numerical values as well.

Water has clearly higher contact angle values than the rest of the liquids. With both substances the contact angle of hexane is 0°, and the surface tensions of the alcohol solutions are also of the same order of magnitude. The surface tension parameters deviate slightly from those presented in the literature (Ohm and Lippold, 1985) for pure liquids because of the dissolved drug.

Packing properties

The packing of theophylline is close to optimal, as estimated from the small variation in liquid penetration data between repetitions (Table 3). The packing of salicylic acid powder was heterogeneous. This could be seen as fluctuating advancement of the sides of the liquid front so that it was not a plane perpendicular to the longitudinal axis of the powder column. In fact, it was practically impossible to obtain a reproducible powder bed structure with any of the packing times used. The difference between the packing properties of the materials is seen in Figs 3 and 4. The theophylline powder column has a reproducible pore structure, whereas salicylic acid actually exhibits two different types of pore structures; in two cases the rate of the liquid intrusion is clearly different. It is possible that the structure of the powder bed has collapsed. Also the paths of the individual data sets are not linear, indicating that the liquid front advancement does not fully obey the Washburn model. This demonstrates that the method is very sensitive to the

TABLE 3

Linear regression parameters of liquid intrusion into theophylline powder bed (k, slope; b, intercept; r, regression coefficient), and the calculated dynamic contact angles of the liquids

Liquid	k (cm^2/s^1)		b (cm^2)		r	Θ (°)		n
	Mean	SE	Mean	SE		Mean	SE	
Water	0.559	0.034	−11.7	9.11	0.994	70.3	1.4	3
Methanol	0.752	0.020	−10.3	1.21	0.999	22.0	2.8	6
Propanol	0.240	0.009	4.50	0.55	0.999	0	3.6	6
Butanol	0.178	0.009	−3.48	1.17	0.999	12.3	4.8	6
Octanol	0.059	0.003	−3.25	1.83	0.999	26.6	3.5	6
Hexane	1.096	0.069	−12.8	1.85	0.999	28.7	4.0	6

The number of data points in regression analysis is 11. Propanol is the best wetting liquid with estimated contact angle of 0°.

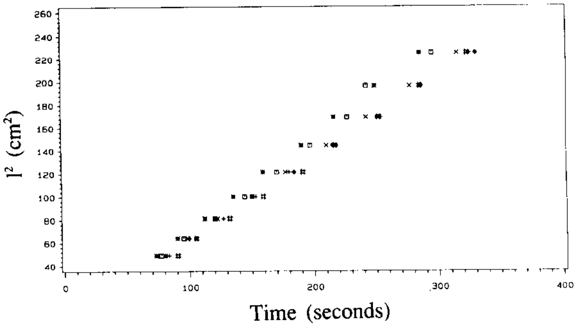

Fig. 3. Methanol intrusion into the theophylline powder bed.

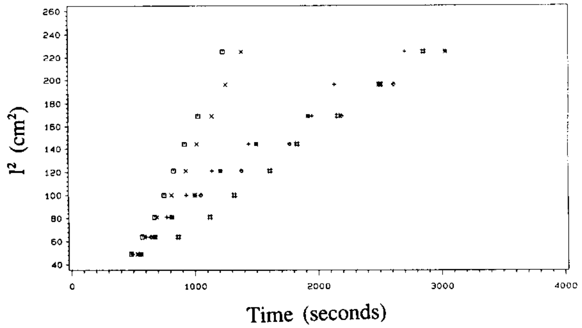

Fig. 4. Methanol intrusion into the salicylic acid powder bed.

particle properties affecting the formation of interparticle spaces. It is evident that an elongated particle shape in connection with the electrostatic charge of the particles restricts packing. The narrow size distribution reduces the degree of packing by increasing the relative size of the interparticle spaces. Theophylline exhibits a better degree of packing because of the wider size distribution enhanced by the small agglomerated particles.

Liquid intrusion

The parameters of the linear least-squares fit of liquid intrusion data, the slope of plots of time vs distance squared, the intercept, the correlation coefficients and the number of data points used in the calculations, are given in Tables 3 and 4. The parameter k is the primary result of the method giving direct information on the dynamic wetting capabilities of the liquids. Thus, it can be considered to be very useful in ranking liquids according to their wettability, for example, for a manufacturing process. It does not, however, relate to the equilibrium state of the system. The intrusion rate into the salicylic acid powder bed is clearly slower than into the theophylline powder bed. This can be explained by both the surface properties and the smaller particle size of salicylic acid. This is in agreement with the previous results from different size fractions of lactose powder (Kiesvaara and Yliruusi, 1992). Hexane intruded fastest with both materials, octanol intrusion being the slowest. Water did not penetrate at all into the salicylic acid powder bed, suggesting a contact angle greater than 90°. The tablet contact angles obtained earlier (Kiesvaara and Yliruusi, 1991b) show an equilibrium contact angle of approx. 40° for water. This implies that compression increases the polar nature of the tablet surface. The alcohols maintain a rank correlation between carbon number and intrusion rate with theophylline, whilst with salicylic acid a discrepancy exists that may be attributed to the poor packing properties of the powder.

TABLE 4

Linear regression parameters of liquid intrusion into salicylic acid powder bed (k, slope; b, intercept; r, regression coefficient), and the calculated dynamic contact angles of the liquids

Liquid	k (cm^2/s^1)		b (cm^2)		r	Θ (°)		n
	Mean	SE	Mean	SE		Mean	SE	
Methanol	0.083	0.003	3.13	3.39	0.991	81.7	2.1	4
Propanol	0.227	0.017	−47.2	3.27	0.988	0	2.4	4
Butanol	0.093	0.006	−36.2	3.86	0.991	59.7	2.3	6
Octanol	0.023	0.005	−9.07	5.13	0.990	71.5	4.3	6
Hexane	0.426	0.019	−10.6	0.88	0.999	73.7	0.8	6

The number of data points in regression analysis is 11. Propanol is the best wetting liquid with estimated contact angle of 0°.

Contact angles

The calculated contact angles are also presented in Tables 3 and 4. With theophylline, water has the highest contact angle value. The alcohols' contact angles are all relatively low, ranging from the estimated 0° for propanol to 26.6° for octanol. The rank correlation that existed with the slope values is not present in the contact angle values due to propanol being the best wetting liquid.

With salicylic acid, all the liquids, apart from propanol, have higher contact angles than with theophylline. The alcohols' contact angles differ from each other significantly. The restriction of the propanol contact angle to 0° has even more drastic effects than with theophylline. Hexane and octanol have more or less similar contact angles.

It should be borne in mind that the results are calculated with respect to the estimated contact angle of the best wetting liquid. Therefore, in most cases, the liquid intrusion method is able to yield dynamic contact angles applicable on a rank correlation level only.

Surface free energies

The SFEs with dispersion and polar components based on the dynamic contact angles of the non-polar hexane and the polar water, methanol, propanol and butanol are presented in Table 5. In addition, the fractional polarities, defined as the portion of polar component of the SFE, are also presented. Lactose data for the SFE calculations were obtained from a previous study (Kiesvaara and Yliruusi, 1992).

Depending on the choice of the polar liquid in the assessment of the SFE, the polar components, and thus the SFEs, vary to some extent. It is evident that water is the best choice for the polar liquid for SFE calculations because of its high polarity. The other liquids were included to provide reference data for the evaluation and comparison of the powders as well as the different SFE calculation methods. The unsuitability of the less polar alcohols to act as polar liquids is manifested as negative values for the parameters in Table 5.

The values obtained from the different calculation methods are of the same order of magni-

TABLE 5

The polar components (γ_S^P), surface free energies (γ_S) and fractional polarities (χ) defined as γ_S^P/γ_S of lactose, theophylline and salicylic acid calculated with different polar liquids

Polar liquid	Geometric-mean			Harmonic-mean				Geometric-harmonic		
	γ_S^P	γ_S	χ	γ_S^D	γ_S^P	γ_S	χ	γ_S^P	γ_S	χ
Lactose										
Water	15.3	34.0	0.45	17.0	18.9	35.9	0.53	18.0	36.7	0.49
Methanol	1.1	19.8	0.06	16.7	2.5	19.2	0.13	1.7	20.4	0.08
Propanol	0.7	19.4	0.03	21.0	0.1	21.1	0.0	0.9	19.6	0.05
Butanol	2.0	20.7	0.10	22.0	0.3	22.3	0.0	2.1	20.8	0.10
Theophylline										
Water	16.1	32.6	0.49	25.7	13.9	39.6	0.35	19.9	36.4	0.55
Methanol	5.0	21.5	0.23	16.6	5.0	21.6	0.23	5.2	21.7	0.24
Propanol	11.2	27.7	0.41	19.2	8.4	27.6	0.30	−22.7	−6.2	3.63
Butanol	11.3	27.8	0.41	19.7	6.3	26.0	0.24	−31.0	−14.5	2.13
Salicylic acid										
Methanol	1.4	9.1	0.15	11.3	0.3	11.6	0.02	4.7	12.4	0.38
Propanol	58.8	66.5	0.88	11.2	−5.9	5.2	−1.14	−4.8	2.9	−1.62
Butanol	26.6	34.3	0.77	12.0	−5.9	6.1	−0.97	−2.3	5.4	−0.42

Dispersion components (γ_S^D) in geometric mean and geometric-harmonic mean methods: lactose, 18.7 mN/m; theophylline, 16.5 mN/m; salicylic acid, 7.7 mN/m.

tude. The harmonic-mean method yields different values for the dispersion component although those of the non-polar liquids remain the same. Considering the origin of the dispersion component (Fowkes, 1964), this should not be the case. As the polar components are calculated on the basis of the dispersion components, among other things, the fractional polarity seems more useful in describing the polar nature of the surface. The constant nature of the dispersion component can be utilized in assessing the general validity of the results.

The salicylic acid SFEs are calculated only with the alcohols as polar liquids. The dispersion component is significantly smaller than with lactose or theophylline due to the large contact angle of hexane. Also, variation in polar component values obtained with different polar liquids can be observed.

The dispersion component of lactose and theophylline calculated by the harmonic mean method differs since hexane was the best wetting liquid, with lactose powder thus having an approximate contact angle of 0° whereas hexane and theophylline have a contact angle of almost 30°. Previously measured tablet surface free energies (Kiesvaara and Yliruusi, 1991b) of the same substances yield dispersion components of roughly 30 mN/m as determined with liquid paraffin having a surface tension of 31.5 mN/m. Considering the difference in the surface tensions of the liquids the dispersion components obtained reflect a similar dispersive attraction in both powder and tablet surfaces.

The magnitude of the numerical values of the polar components are different compared to the tablet polar components of about 42 mN/m (lactose) and 30 mN/m (theophylline) reported earlier (Kiesvaara and Yliruusi, 1991b). The polar component of lactose powder is smaller, whereas that of theophylline powder is greater. The polar components of the powders are closer to each other than the tablet polar components.

Fractional polarities

Comparing the different SFE calculation methods, the fractional polarities (Table 5) calculated with water as the polar liquid show different rank order for the powders. This is mainly because of the variation in the harmonic mean dispersion components. The fractional polarity does not correlate with the chain length of the alcohols when using different polar liquids. Tablet surface fractional polarities are higher with lactose (approx. 0.58 mN/m) but equal with theophylline (approx. 0.50 mN/m) as calculated by the geometric mean method (Kiesvaara and Yliruusi, 1991b).

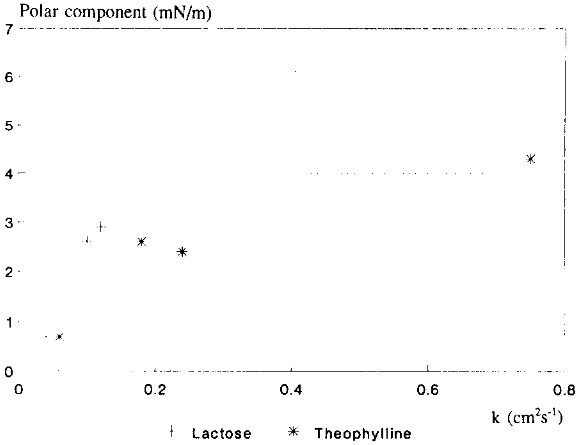

Fig. 5. The scatter plot of liquid intrusion vs liquid polar component for lactose and theophylline.

Correlations between k and the polar component of the alcohols for lactose and theophylline are presented in Fig. 5; the lower the polarity of the liquid, the greater is the intrusion rate. Wu (1973) proposed that optimum wettability is obtained if the polarity of the phases is either similar, or if a great difference exists in the polarity. This implies either a lack of polarity in the powder surface, or that non-polar interaction predominates in dynamic wetting, which was also concluded by Buckton and Newton (1986).

Spreading coefficients

The spreading coefficient (λ) represents the driving force for wetting (Wu, 1973). It is a relative dimensionless index representing the degree of interaction between the phases. It is therefore evident that the liquid spreading coefficients should be able to characterize the intrusion phenomenon. An exponential correlation between k

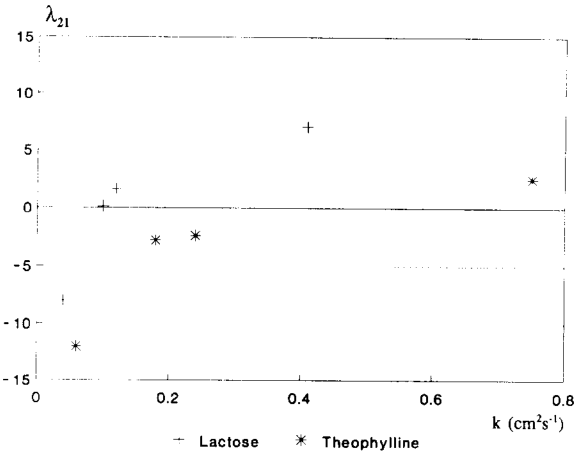

Fig. 6. The scatter plot of liquid intrusion vs spreading coefficient (λ_{21}) for lactose and theophylline.

and λ_{21} of the alcohols can be seen in Fig. 6. The correlation is somewhat similar to that presented in Fig. 5 for k and the polar component of the liquids. Water and hexane data do not show a similar fit. In particular, the λ_{21} of water (-36 for lactose, -48 for theophylline) differs significantly. It should also be noted that the dynamic contact angles do not exhibit a simple correlation with the λ_{21} values.

It is concluded that the packing properties of the powder are important with respect to the validity of the results. The salicylic acid powder studied is not suitable for characterization by the liquid intrusion method. It became evident that one of the major limitations of the Washburn method is the sensitivity to the packing characteristics of the particles. The parameter k directly relates to the dynamic wetting capabilities of the liquids, whereas the calculated dynamic contact angle is valid on a relative basis. The non-polar interaction between the phases is pronounced in liquid intrusion. The surface free energy parameters calculated from dynamic contact angles are different from those evaluated using static contact angles. Therefore, the dynamic contact angles obtained cannot be used to assess surface energetics in the usual meaning. The three SFE calculation methods used yield results differing in nature. The values of the powder dispersion components are of the same order of magnitude as that of the tablet dispersion components. The spreading coefficients obtained characterize with certain restrictions the dynamic wetting of the solid.

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