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Surface Free Energy Data to Predict the Surface Modification Ability of force Control Agents

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ABSTRACT

In this study, the efficiency of using force control agents (FCAs) namely Polyethylenglycol 6000 (PEG) and polyvinylpyrrolidone (povidone k-30) (PVP) and Sodium lauryl sulfate (SLS) in modifying the surface of lactose were invisitigated. Lactose surface was modified by sinking within aqueous solution containing one of each mentioned FCAs. The surface free energies of FCAs unprocessed lactose and processed lactose powders were measured using contact angle measurements. Results showed high negative spreading coefficient (λ_{12}) of SLS over lactose which expalins the disability of SLS to adhere to the surfaces of lactose. On other hand, a positive λ_{12} value of PVP enabled its adherence to lactose surfaces and so to modify the surface energy to a significant extent. These changes were furthermore observed in case of PEG which had the highest λ_{12} compared to others. It is concluded that the more positive the spreading coefficient of a FCA over lactose, the higher the ability of the FCA to modify the surface of lactose is. Also the cohesion works of the powders were directly correlated to the Carr's index and Hausner ratio which are used as indictors of the flow ability. It was also found that all the modified surface lactose powders had surface free energy and cohesion work less than the original lactose. Therefore, surface free energy data can be used as a predict tool to screen for the suitable FCA for each carrier. DSC and FT-IR confirmed the absence of any significant interaction between FCAs and lactose.

Keywords: Lactose, Surface energy, Work of cohesion, Spreading coefficient, Force control agents.

1. INTRODUCTION

Dry powder inhalation is a convenient, reproducible, and non-invasive method for drug delivery to the lung tissue and/or the systemic circulation. Carriers, which include mainly sugars, enhance the performance of inhaled drug powders. The carrier surface contains sites with diffferent free energy. The sites that bind to drug particles with a high energy relative to other sites are generally considered to be active sites. In addition, during mixing pseudo-active sites with high binding energy are generated due to a high susceptibility of the drug particles to press-on forces of mixing. This implies that 'inactive sites' also exist. However, all sites are active to some extent, and none are truly inactive(1). Surface free energy represents the average of these sites. Surface free energies affect the inhalation formulations' performance, as they control drug powder aggregation process, the ease of powder dispersibility, adhesion and removal of drugs to/from containers and carriers, and the dispersion of particles in liquefied propellants(2).

Lactose is the most widely used excipient(3). It is pharmacologically safe and FDA-approved for inhalation. Therefore, lactose is the predominant carrier in dry powder inhalation(4). Surface morphology and surface free energy of lactose are the main paramters which have been modified to alter cohesion and adhesion work

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between inhaled drugs and carreir particles(5).

Fluid-bed spray coating used to coat lactose particles with force control agents (FCAs) dissolved within suitable solvents(6). However, several practical constraints limit the use of this technique. These constraints are mainly due to the tendencyof lactose to agglomerate or granulate in the fluid bed due to its particle sizes which are usually smaller than 100 μm(7). Another simple solvent based coating method includes wetting of lactose surface with ethanol/water solutions containing safe additives such as magnesium stearate (MgSt) or amino acids. The wetted particles are then dried under vacuum during high speed mixing(8). Solvent-less coating processes called mechanical dry coating approaches are a preferred alternative for the surface modification of lactose carrier.Mechanical dry coating techniques such as MechanoFusion® processors, the Hybridizer®, the Magnetically Assisted Impaction Coater (MAIC) ® and the Theta-composer® use intensive mechanical forces to coat the surface of carriers(e.g., lactose) with smaller guest particles(9). More details about each technique are recently reviewed(5).

The ability of FCAs to modify the surface components of pharmaceutical powders has not been studied yet. Here, we will try to find a numerical tool to predict this ability. Polyethylene glycol 6000 (PEG), polyvinylpyrrolidone (povidone k-30) (PVP) and Sodium lauryl sulfate (SLS) are chosen as solid FCAs. Lactose powders will be sinking within the aqueous solutions of these FCAs. Then, the surface free energies of FCAs, unprocessed lactose and processed lactose powders, will be measured using contact angle measurements. The measured numbers will be used to correlate the surface free energies to the ability of FCAs to modify the surface of lactose. Although PEG and PVP are FDA-approved to be used in inhalation formulations(10, 11), SLS is lung irritant agent causing severe coughs(12). However, in this study, SLS was used as a model of solid surfactant.

2. Material and methods

2.1 Materials:

Lactose monohydrate (Kerry-USA) Polyethylene glycol 6000 (PEG) (Brenntag Export), Polyvinylpyrrolidone (povidone k-30, nominal molecular weight of 50000 Dalton) (PVP) (Ashland, USA), Sodium lauryl sulfate (SLS) (Zhengzhou Sino Chemical Co., Ltd., China) and Diiodomethane (CH_2I_2) (Aldrich, USA) were generously gifted by Pharma International Company, Jordan.

2.2 Sinking method to modify surface lactose powders

Lactose (600g) was dissolved in deionized water (1000g) at 60°C. The resulting supersaturated lactose solution was cooled down to room temperature, and then it was gravity filtered to get saturated clear lactose solution. The amount of α-lactose, which is enough to saturate water at 60°C, was calculated by a model developed by Visser(13).

For each 100 ml of the filtered saturated lactose solution, a force control agent was added and dissolved. Hence, 1, 3, and 5 g of PVP, PEG and SLS were separately used to prepare nine different sinking solutions, in which 10 g of α-lactose was suspended under continuous stirring (magnetic stirrer, 400 rpm) at room temperature for 10 min.

The precipitated powders were collected by filtration (Whatman Filter Paper, 0.7 μm) and dried at 60 °C. The dried powders were screened through sieves (63-90 μm) (Retsch GmbH, Haan, Germany) to break up aggregates and to give approximately uniform particle sizes. The produced powders were labeled as Lactose in PVP 1%, Lactose in PVP 3%, Lactose in PVP 5%, Lactose in PEG 1%, Lactose in PEG 3%, Lactose in PEG 5%, Lactose in SLS 1%, Lactose in SLS 3% and Lactose in SLS 5%.

2.3 Flowability evaluation

Flow ability of unprocessed and processed lactose samples was assessed from Carr's Index (CI) and Hausner Ratio (HR). The CI and HR were calculated from the bulk and tapped densities.

Bulk density was measured into a dry graduated 25 mL cylinder, where 5 g of the powder was introduced without compacting. The apparent volume of the introduced powder was taken by leveling the powder without compacting, or reading the unsettled apparent volume to the nearest graduated unit, and then the bulk density was calculated in g/mL by formula (mass/ apparent volume).

Tapped density was determined by tapping the samples (5g) into a 25 ml measuring cylinder using a tapping machine. The equations to calculate CI and HR are:

$$\mathrm{CI} = [(\text{Tapped density}-\text{Bulk density})/\text{Tapped density}] \times 100. \quad (1)$$

$$\mathrm{HR} = \text{Tapped density}/\text{Bulk density}. \quad (2)$$

2.4 Contact Angle Measurements On flat-surfaces

The sessile drop technique was used to measure the equilibrium contact angles of two different liquids (Water for HPLC and Diiodomethane). In this technique, flat and smooth surfaces of each powder were prepared by compressing the 500 mg using a flat punch. However, in case of lactose and SLS, the flat surfaces were prepared by moulding sufficient amount of their powder in a plastic mould. This is because both materials cannot be compressed into tablets. A smooth surface of powder is essential to obtain reliable results(14). A small drop of each liquid (10 µl) was then placed on the flat surfaces of each material using a micropipet. Images of the surfaces were taken using G7 Canon camera (10 mega pixels) and the contact angles were then measured by AutoCAD software used to analyze images of the liquid drops and surfaces. All contact angle measurements were performed at room temperature. Three contact angle measurements were performed for each powder and their average was used to do further calculations.

To measure the surface free energy of a solid, contact angles with several liquids must be measured. Usually two liquids of known surface components (dispersive γ_L^d and specific γ_L^{sp}) are enough for measurement(15). The dispersive free energy γ_S^d and specific free energy γ_S^{sp} of the solids, in addition to their interaction works can be assessed according to Fowfes's (1964) following equations(16).

$$(1+\cos\theta)\gamma_L = 2(\sqrt{\gamma_S^d\gamma_L^d} + \sqrt{\gamma_S^{sp}\gamma_L^{sp}}) \quad (3)$$

Where γ_L is the total surface free energy of the liquids and θ is the contact angle. The total surface free energy (γ^{total}) of both liquids and solids can be expressed according to the following equation(4).

$$\gamma^{total} = \gamma^{sp} + \gamma^d \quad (4)$$

Both the work of adhesion W_a (between particles of different materials) and work of cohesion W_c (between particles of same material) can be determined from the surface energy of mixtures using equations 5 and 6;

$$W_c = 2\gamma^{total} \quad (5)$$

$$W_a = 4\left[\frac{\gamma_1^d \cdot \gamma_2^d}{\gamma_1^d + \gamma_2^d} + \frac{\gamma_1^{sp} \cdot \gamma_2^{sp}}{\gamma_1^{sp} + \gamma_2^{sp}}\right] \quad (6)$$

Moreover the spreading coefficient of a material over another one can be determined from the cohesion and adhesion work using equations 7, 8 and 9.

$$\lambda_{12} = W_a - W_{c1} \quad (7)$$

$$\lambda_{12} = 4\left[\frac{\gamma_1^d \cdot \gamma_2^d}{\gamma_1^d + \gamma_2^d} + \frac{\gamma_1^{sp} \cdot \gamma_2^{sp}}{\gamma_1^{sp} + \gamma_2^{sp}} - \frac{\gamma_1^{total}}{2}\right] \quad (8)$$

where λ_{12} is the spreading coefficient of phase one over phase and two.

2.5 Fourier transformation infrared (FT-IR) studies

The FT-IR spectra (range 450–4000 cm^{-1}) of the samples were recorded using attenuated total reflection ATR technique with a FT-IR spectrophotometer (PerkinElmer Spectrum Version 10.03.06, UK). A few particles of the sample were placed on the middle of the sample stage using a microspatula and force was applied by twisting the top of the arm of the sample stage. After obtaining sharp peaks with reasonable intensity, the spectra were recorded by averaging 4 scans at 1 cm^{-1} resolution.

2.6 DSC measurements

Differential scanning calorimetry (DSC) thermograms were obtained using a DSC 204 F1 phoenix instrument (Netzsch-Gerätebau GmbH, Postfach, Germany).Samples (4-7 mg) were weighed in aluminium pans on an analytical balance. The escape of water was facilitated by placing a pinhole in the lid prior to sealing. The samples were equilibrated at 25°C and heated to 300°C at a heating rate of 10°C/min under a dry nitrogen flow of 20 ml/min. The temperature axis and cell constant of the DSC cell were calibrated with indium (10 mg, 99.999% pure, melting point 156.60°C, heat of fusion 28.40 J/g).

3 Results and discussion

3.1 Surface free energy components

The contact angles of water and Diiodomethane on the flat surfaces of all powders were measured by AutoCAD software (e.g., Fig. 1).

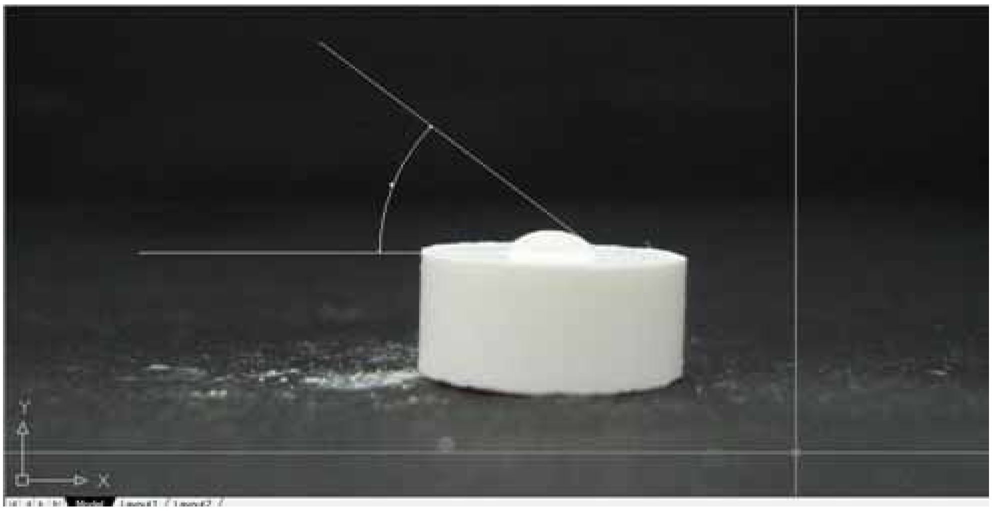

Fig. 1: AutoCAD software windows showing the picture of Diiodomethane drop (10 µl) on the flat surface of Lactose in SLS 3%

The surface energy components of water and diiodomethane (Table 1) and the measured contact angles were used in Eq.3 to calculate dispersive component of surface free energy (γ_s^d) and specific component of surface free energy (γ_s^{sp}) for all powders.

Table 1. Reported surface energy components of water and diiodomethane (17, 18)

Liquid	Total surface energy mJ/m^2	Dispersive surface energy Component mJ/m^2	Specific surface energy Component mJ/m^2
Water	72.8	21.8	51.0
Diiodomethane	50.4	50.4	0.0

The total surface free energy (γ_s^{total}) and work of cohesion (W_c) for all the powders were then calculated according to Eqs.4 and 5, and the results weretabulated in Table 2.

It was found that the calcualted surface free energy of the used materials (stated in Table 2) were comparable to published values (19, 20, 21). However, there are little differences which could be due to the different molecular arrangements.

Table 2. The surface parameters (mean ± SD) of unprocessed lactose powder, the force control agents (SLS, PVP, and PEG), and the surface modified lactose powders

Sample description	CH_2I_2	H_2O	γ_s^d	γ_s^{sp}	γ_s^{total}	W_c
	θ°	θ°	mJ/m^2	mJ/m^2	mJ/m^2	mJ/m^2
Lactose	33.5 ±1.3	13.7 ±1.8	42.4 ±0.6	33.6 ±0.5	75.9 ±0.6	151.9 ±1.1
PVP	8.8 ±1.0	44.7 ±1.8	49.8 ±0.1	16.9 ±0.9	66.7 ±0.9	133.4 ±1.8
Lactose in PVP 1%	25.3 ±1.5	30.7 ±2.1	45.7 ±0.6	25.6 ±0.8	71.3 ±1.2	142.6 ±2.4
Lactose in PVP 3%	27.3 ±2.5	30.2 ±2.6	44.9 ±1.0	26.2 ±1.2	71.1 ±1.3	142.3 ±2.7
Lactose in PVP 5%	24.3 ±2.3	26.8 ±2.0	46.0 ±0.8	27.1 ±1.2	73.1 ±0.6	146.3 ±1.2
PEG	20.0 ±1.3	59.8 ±1.9	47.4 ±0.4	10.0 ±1.0	57.4 ±0.7	114.8 ±1.3
Lactose in PEG 1%	30.7 ±1.8	52.7 ±2.5	43.6 ±0.7	15.0 ±1.7	58.6 ±0.9	117.2 ±1.9
Lactose in PEG 3%	30.8 ±1.3	52.5 ±1.3	43.5 ±0.5	15.1 ±0.5	58.6 ±1.0	117.3 ±2.1
Lactose in PEG 5%	28.0 ±1.0	53.8 ±1.0	44.7 ±0.4	14.0 ±0.5	58.6 ±0.8	117.2 ±1.5
SLS	88.7 ±1.5	0.0 ±0.0	13.2 ±0.7	61.1 ±1.0	74.3 ±0.3	148.7 ±0.6
Lactose in SLS 1%	39.0 ±1.8	12.8 ±2.0	39.8 ±0.9	35.3 ±0.7	75.1 ±0.6	150.2 ±1.2
Lactose in SLS 3%	41.5 ±2.3	11.8 ±1.3	38.5 ±1.2	36.3 ±1.0	74.9 ±0.3	149.7 ±0.6
Lactose in SLS 5%	42.7 ±1.3	11.2 ±2.3	37.9 ±0.7	36.8 ±0.5	74.8 ±0.6	149.5 ±1.2

± Standard deviation; n= 3·

Table 2 shows that all the force control agents significantly changed (ANOVA: $P < 0.05$) the surface free energies (γ_s^d , γ_s^{sp} and γ_s^{total}) of lactose and hence its cohesion energy. The extent of changes in the surface free energy of lactose is related to the nature of the force control agents.

In general, All surface modified lactose powders have surface free energy and cohesion work less than the original lactose. However, in case of SLS, the reduction in γ_s^d was significant (T-test: $P < 0.05$), but minor ~2%. At the same time γ_s^{sp} increased in similar manner. Therefore, no significant change in γ_s^{total} (T-test: $P > 0.05$) occurred. And hence, no change in W_c was detected. Regarding PVP, although γ_s^d significantly increased (T-test: $P < 0.05$) by about 6%, γ_s^{sp} dramatically decreased by about 21%. This caused a noticeable reduction in γ_s^{total} and W_c by about 4% and 6%, respectively. On the other hand, an enormous significant decrease (T-test: $P < 0.05$) in both γ_s^{total} and W_c were detected, in case of PEG. PEG induced a reduction in γ_s^{total} and W_c by about 24%. This reduction was due to the massive reduction in γ_s^{sp}, while γ_s^d did not significantly change (T-test: $P > 0.05$). Moreover, in all cases (PVP, PEG and SLS), the changes in the surface modified lactose powders did not vary by increasing the concentration of the force control agents in the saturated solutions of lactose (Table 2).

Table 3. Spreading coefficients of PVP, PEG, And SLS over lactose

	λ_{12} mJ/m^2
PVP	3.1
PEG	5.5
SLS	-21.7

Spreading coefficients (λ_{12}) can be used to account for the ability of the force control agents to spread over the lactose suspended particles in their saturated solution. Many published papers proved the strong correlation between spreading coefficients and the ability of a material to cover the surface of another material. For example, Positive spreading coefficient values of binders over the model substance correlates well with the ability of the binder to cover the substance and hence to enhance its mechanical properties such as friability and tensile strength$^{(22)}$. The positive values of the spreading coefficients are essential to enable the coating agent to adhere to substrate. The adhesion of the coating agents to the substrate directly relates to the positive λ_{12}, while the negative values prevent adhesion (23, 24, 25).

Therefore, we calculated the adhesion work between each force control agent and lactose according to Eq.6. We then calculated λ_{12} for each force control agent over lactose particles according to Eq.7.The results were tabulated in Table 3.

Table 3 shows a high negative spreading cofficient (λ_{12}) of SLS over lactose. Hence, this expalins the disability of SLS to adhere to the surfaces of lactose and consequently to modify its surface energy. On the other hand, the positive λ_{12} value of PVP enabled its adherence to the lactose surfaces and so to modify the surface energy to a significant extent. These changes were furthermore observed in case of PEG which had the highest λ_{12} compared to others. These values of λ_{12} interpret the above changes in the surface modified lactose powders compared to the unprocessed lactose powders. In other words, it can be concluded that the more positive the spreading coefficient of a FCA over lactose, the higher the ability of the FCA to modify the surface of lactose.

3.2 Flow ability evaluation of lactose powders

Carr's index and Hausner ratio were used as indirect measures of the interparticulate forces within each modified lactose, and hence their flow ability. Both of them were calculated using the bulk and tap densities of the lactose batches according to Eqs1 and 2. The results were tabulated in Table 4.

Table 4 shows that there was no significant difference in the Carr's index of the different modified lactose samples prepared using different concentration of PVP (ANOVA, $p > 0.05$), indicating similar flow properties of all tested samples. This was also confirmed by the similarity in Hausner ratios for all samples. The same similarity was also found in the case of both SLS and PEG samples. Although changing the concentration of the force control agents did not change the flow ability, each force control agent induced significant decrease in both Carr's index and Hausner ratios compared to unprocessed lactose. The extent of the decrease was dependent on the nature of the force control agent. We then classified the flow ability of each sample according to scale of flow ability of Pharmacopeia USP 34 NF 29 2011 (Table 5).

Table 4. The bulk and tap densities, Carr's index (CI%) and Hausner ratio (HR) of the unprocessed and modified lactose powders

Sample	Bulk density g/cm^3	Tapped density g/cm^3	CI %	HR
Unprocessed Lactose	0.63 ±0.01	0.77 ±0.01	18.18 ±1.00	1.22 ±0.04
Lactose in PVP 1%	0.67 ±0.02	0.76 ±0.03	11.84 ±1.60	1.13 ±0.02
Lactose in PVP 3%	0.68 ±0.01	0.78 ±0.02	12.82 ±1.80	1.15 ±0.03
Lactose in PVP 5%	0.68 ±0.01	0.77 ±0.01	11.69 ±1.70	1.13 ±0.03
Lactose in PEG 1%	0.72 ±0.03	0.78 ±0.02	7.69 ±2.00	1.08 ±0.03
Lactose in PEG 3%	0.71 ±0.02	0.77 ±0.01	7.79 ±1.50	1.08 ±0.03
Lactose in PEG 5%	0.70 ±0.04	0.76 ±0.01	7.89 ±1.40	1.09 ±0.02
Lactose in SLS 1%	0.66 ±0.01	0.78 ±0.03	15.38 ±1.10	1.18 ±0.04
Lactose in SLS 3%	0.65 ±0.02	0.76 ±0.02	14.47 ±1.20	1.17 ±0.03
Lactose in SLS 5%	0.66 ±0.01	0.77 ±0.04	14.29 ±1.70	1.17 ±0.04

± Standard deviation; n= 3.

Table 5. Scale of lactose samples' flow ability according to Pharmacopeia USP 34 NF 29 2011

Sample	Scale of Flow ability according to Pharmacopeia USP 34 NF 29 2011
Unprocessed Lactose	Fair
Lactose in PVP	Good
Lactose in PEG	Excellent
Lactose in SLS	Good

Table 5 shows that all modified powders had improved flow ability compared to unprocessed lactose. Moreover, if the data in Table 2 was matched with those of Table 5, a good inverse correlation between the flow ability of the powders and their cohesion work can be deduced. This is a logic correlation, as cohesion work expresses the inter-particulate frictions, and these frictions control powders' flow. It is clear that the powder with lowest cohesion work (Lactose in PEG) had the lowest CI% and HR, hence, the highest flow ability, and vice versa in case of unprocessed lactose and Lactose in SLS.

Furthermore, Table 4 shows that there was no significant difference in the tapped densities of the different lactose samples (ANOVA, $p>0.05$), indicating similar micromeritics properties of all tested samples. This would indicate that the sinking process did not affect the particle size and shape of the original particles, irrespective of the force control agents.

Nonetheless, the changes in both CI% and HR were caused by the changing in the bulk densities, as significant differences (ANOVA, $p<0.05$) were detected (Table 4). These differences in bulk densities were due to the differences in surface free energy of the different powders, which affected the powder flow ability and hence their bulk densities. The powder flow ability depends on the surface free energy values(26).

Both Fig.2 shows a strong direct correlation between the cohesion works of the powders and their CI% and HR, respectively.

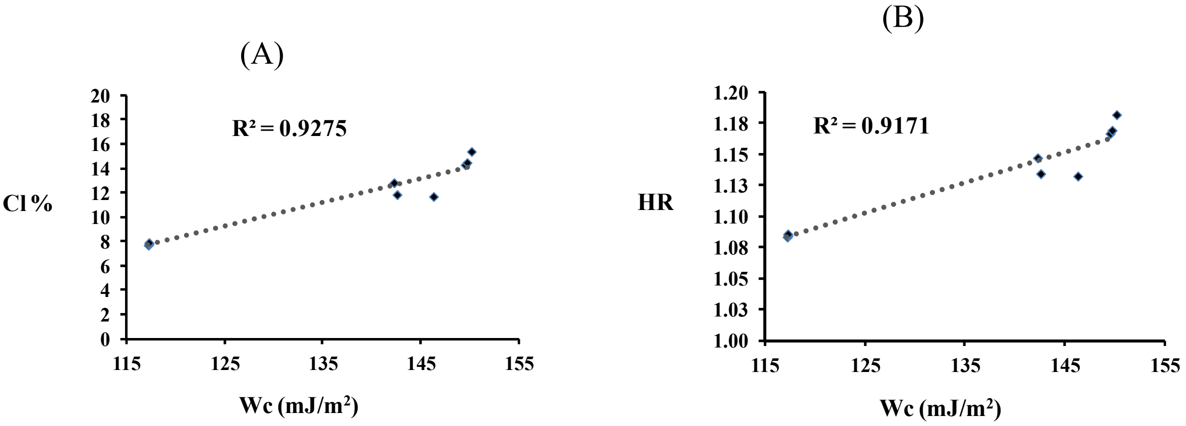

Fig. 2: (A) Correlation between cohesion work and Carr Index (taken from Table 4). (B) Correlation between cohesion work and Hausner Ratio (taken from Table 4).

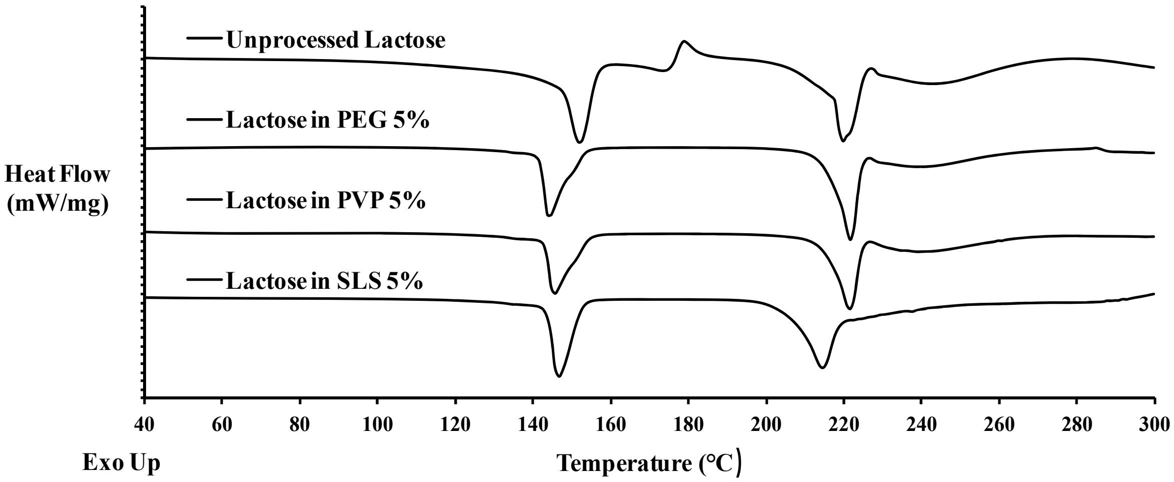

Fig. 3: DSC thermograms showing the thermal profiles of unprocessed lactose and Lactose in PEG 5%, Lactose in PVP 5% and Lactose in SLS 5%

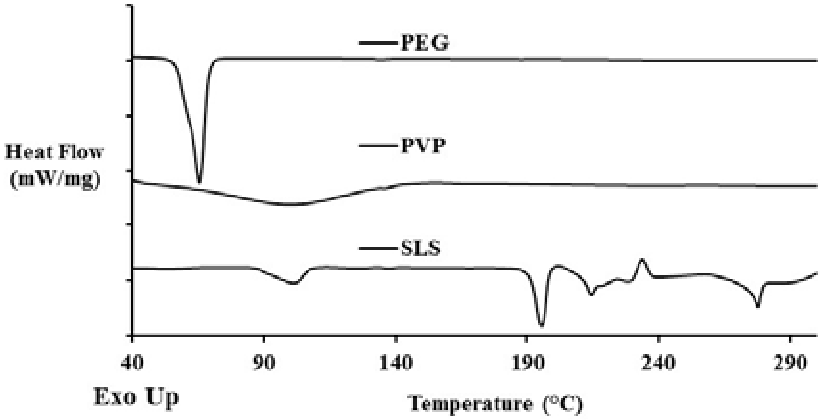

Fig. 4: DSC thermograms showing the thermal profiles of PVP, PEG and SLS

3.3 Differential scanning calorimetry of lactose samples

Figure 4 shows the thermal profiles of unprocessed lactose and dried sunk lactose samples (at highest concentration of the force control agents)

The DSC thermogram of unprocessed lactose showed two distinctive endothermic peaks at about 149°C and 218°C, which correspond to the dehydration of crystalline hydrate water and the melting of anhydrous α-lactose, respectively(27). These two endothermic peaks appeared in the DSC thermographs of all surface modified samples.

The DSC thermogram of unprocessed lactose also showed a small exothermic peak at about 173°C, which corresponds to the crystallization of amorphous lactose to mostly α-lactose as reported by several researchers(28). However, this exothermic peak disappeared in all surface modified lactose powders relevant thermograms. This indicates that sinking process in aqueous media induced amorphous-crystalline transformation of the amorphous regions observed in the unprocessed lactose thermogram.

The endothermic peak at about 240°C did not appear in the thermograms obtained for all of the lactose samples, which corresponds to the temperature of the melting of β-lactose(29). This confirms the absence of β-lactose in all samples.

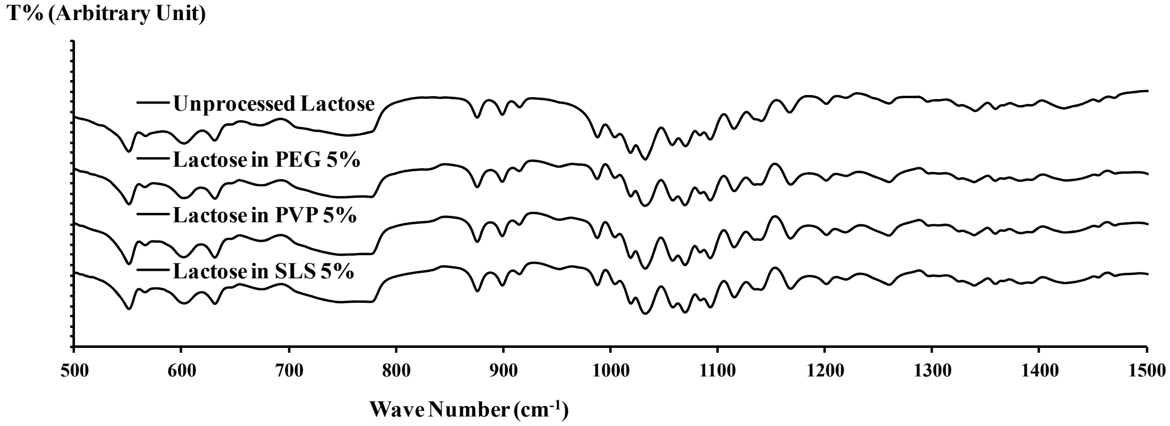

Fig. 5: Finger print regions of FT-IR spectra of unprocessed lactose, Lactose in PVP 5%, Lactose in PEG 5%, and Lactose in SLS 5%

Fig. 5 shows that the DSC thermograms of Lactose in PVP 5%, Lactose in PEG 5% and Lactose in SLS 5% did not contain any thermal transition event of PVP glass transition, PEG melting or SLS melting, respectively. This indicates that the amount of the force control agents, which would adhere to the surface of lactose during the sinking process, were negligible to minor limits which cannot be detected by DSC.

3.4 Fourier Transform Infrared Spectroscopy

Fourier transform infrared (FT-IR) spectra of unprocessed lactose and modified surface lactose powders (only with highest concentration of the force control agents, i.e., Lactose in PVP 5%, Lactose in PEG 5% and Lactose in SLS 5%) were registered to investigate any changes in lactose powders on the molecular level during the sinking process.

The FT-IR spectrum of all the surface modified samples (Fig. 6) showed a band at 920 cm^{-1},which is a specific diagnostic band for α-lactose anomer(30). This band is apparent in unprocessed lactose and all the surface modified lactose samples. However, the band at 950 cm^{-1} which is a specific diagnostic band for β-lactose anomer is absent from the spectra of the entirelactose sample. These results support those from the DSC experiments, which confirmed the melting point of α-lactose anomer in all the samples, and confirmed the absence of the melting point of β-lactose.

This indicates that surface modification of lactose by the three FCAs did not induce any change on the inner or intramolecular level of lactose

4 CONCLUSION

All the modified surface lactose powders had surface free energy and cohesion work less than the original lactose. The extent of changes in the surface free energy of lactose was related to the nature of the force control agents. However, we found that the changes in the surface modified lactose powders did not change further by increasing the concentration of the force control agents in the saturated solutions of lactose. Positive spreading coefficient values of the agents over the model substance is essential to enable the agents to cover the lactose powder and hence to modify its surface free energy. Therefore, the negative spreading coefficient (λ_{12}) of SLS over lactose expalined its disability to adhere to lactose surfaceand to modify its surface energy. Conversely, the positive λ_{12} of PVP indicates the ability of its adherence to the lactose surface, and so to modify the surface energy to significant extents. These changes were further obvious in the case of PEG which had the highest λ_{12} compared to others. This work guides for future further researches to understand the effect of surface energy on the performance of inhalable powders, and then to optimize the surface free energy the performance of these powders. For future work we can obtain some information on the aerodynamics of the processed particles to find a correlation with the surface energy data.

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استخدام طاقة السطوح الحرة كأداة للتنبؤ بقدرة عوامل التحكم بالقوة على تعديل السطح

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ملخص

تم في هذه الدراسة فحص كفاءة استخدام عوامل التحكم بالقوة (FCAs) وهي بولي إيتلين غليكول (PEG) 6000 والبولي فنيل بيروليدين (بوفيدون 30ك) (PVP) وكبريتات لوريل الصوديوم (SLS) في تعديل سطح اللاكتوز FCAs. تم التعديل من خلال إدخال اللاكتوز في داخل محلول مائي يحتوي على واحد من كل العوامل المذكورة FCAs. تم قياس طاقة السطوح الحرة لمساحيق اللاكتوز غير المعالج واللاكتوز المعالج باستخدام قياسات زاوية التماس. أظهرت النتائج قيمة سالبة عالية لمعامل التوزع (λ_{12})للSLS على اللاكتوز الذي يفسر إعاقة التصاق SLS على سطح اللاكتوز. من جهة أخرى مكنت القيمة الموجبة للPVP من التصاقها على سطح اللاكتوز وذلك لتعديل الطاقة السطحية إلى حد كبير.هذه التغييرات لوحظت في حالة PEGالتي كانت أعلى مقارنة معا لآخرين. ويستنتج من ذلك أنه كلما كانت قيمة معامل الانتشار أكثر إيجابية للFCAs على اللاكتوز كلما ارتفعت قدرة FCA لتعديل سطح اللاكتوز. كذلك سطح مسحوق اللاكتوز المعالج يملك طاقة حرة وقدرة على الالتصاق أقل من اللاكتوز غير المعالج. لذلك يمكن أن نستخدم قيمة الطاقة الحرة للسطح كأداة لاختيار ال FCA المناسب لكل عامل حامل.

الكلمات الدالة: لاكتوز، طاقة السطح، جهد الالتصاق، معامل الانتشار، عوامل التحكم بالسطح.

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