Use of SPM to Measure Adhesion Forces: Some Pharmaceutical Applications

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Particle Adhesion in Pharmaceutical Science

- Particle adhesion important to a number of areas of interest.
- Adhesion science has received relatively little attention by pharmaceutical scientists.
- Particle adhesion related to:
  - Powder flow
  - Powder mixing
  - Powder dispersion in Dry Powder aerosol devices
  - Tablet hardness

Powder Dispersion in Dry Powder Inhalation Devices

- Problem:

  Dry powders can inhaled directly for pulmonary delivery of drugs.

  A constant amount of particles in the range of 2-5μm must be delivered to the lung.

  Variable adhesion between components results in variable drug delivery.

Principles of Adhesion

$$W_a = \gamma_1 + \gamma_2 - \gamma_{12}$$

$$W_a = W_a^{LW} + W_a^{AB}$$

vOGC

$$W_a^{AB} = 2\left(\gamma_1^{+}\gamma_2^{-}\right)^{1/2} + 2\left(\gamma_1^{-}\gamma_2^{+}\right)^{1/2}$$

Fowkes

$$W_a^{AB} = -f \cdot N \cdot \Delta H_a^{AB}$$

$$f = \left[1 - \frac{\partial \ln W_a^{AB}}{\partial \ln T}\right]^{-1}$$

$$\Delta H^{AB} = K_a DN + K_d AN^{*}$$

Particle Size and Adhesion

For sphere-sphere and sphere-plane interactions:

London - van der Waals Forces: $F(r) \propto r$

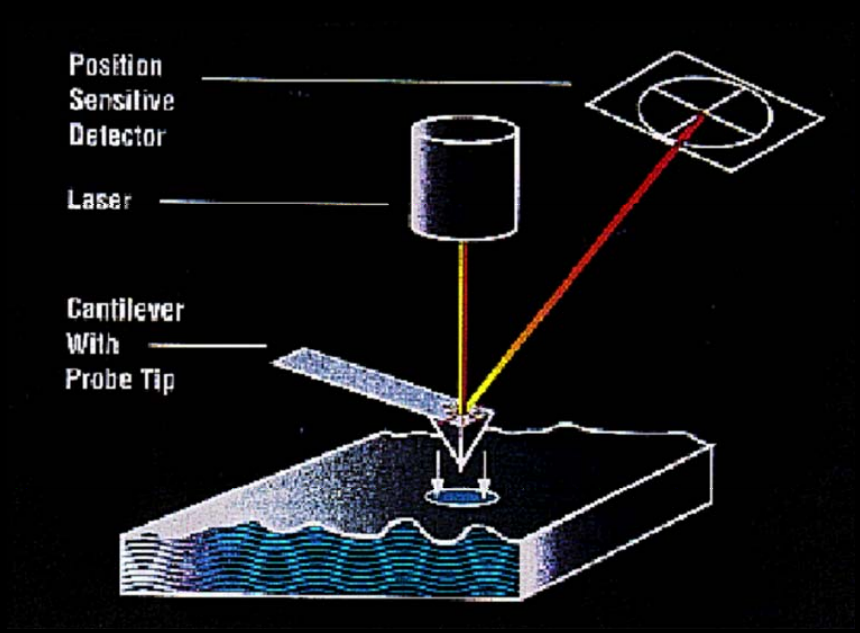
Electrical: $F(r) \propto r^{\frac{2}{3}}$

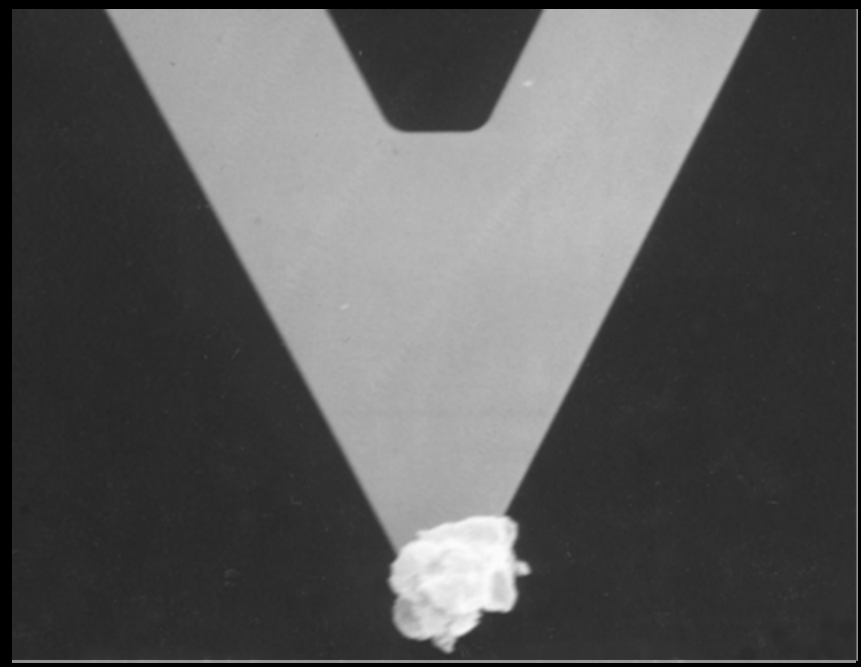
Coulomb: $F(r) \propto \frac{1}{r^2}$

Capillary: $F(r) \propto r(1-r^x) \qquad x > 1$

Zimon, A.D. *Adhesion of Dust and Powder*, 2nd ed. 1982.

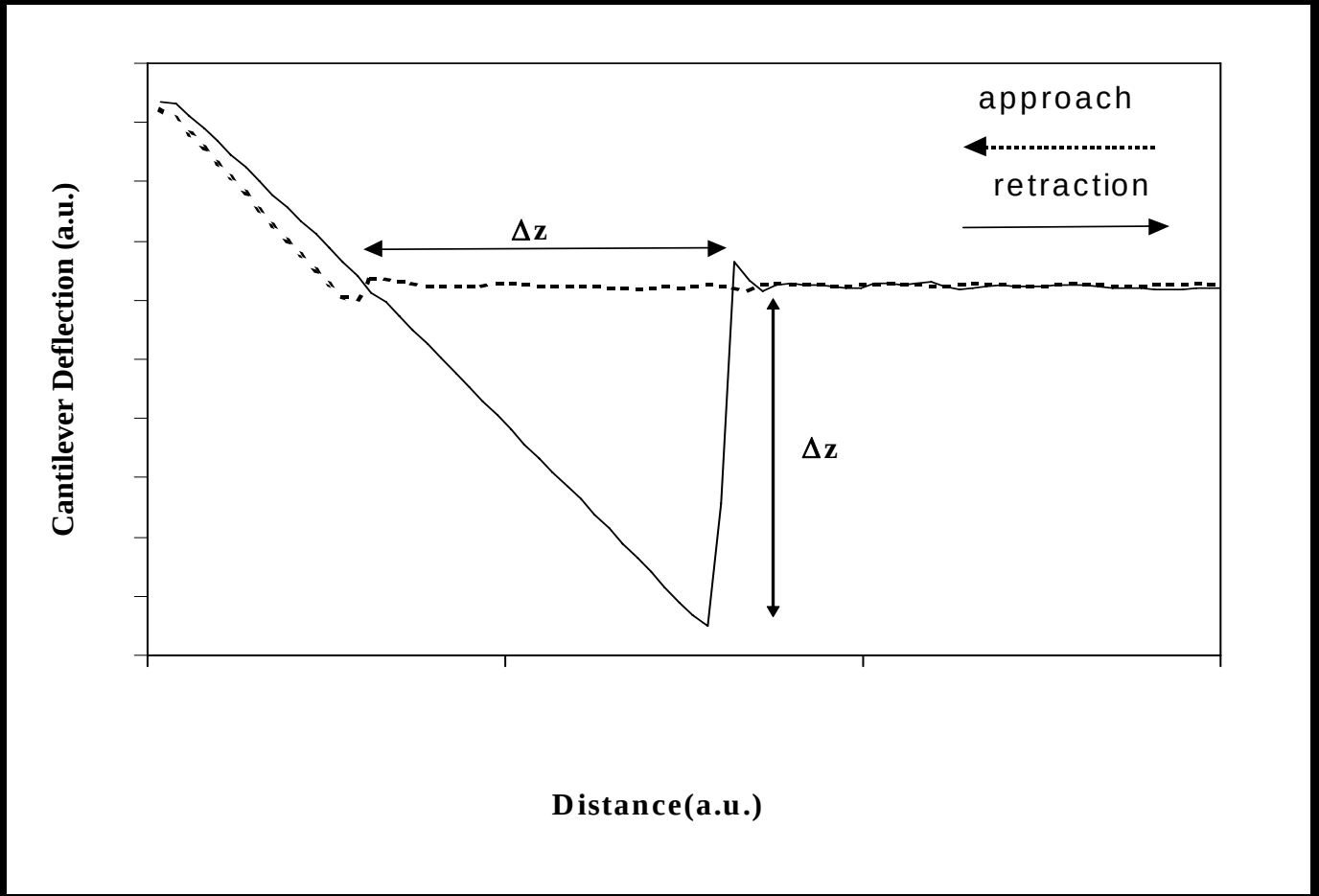
SPM to Measure Adhesion Forces



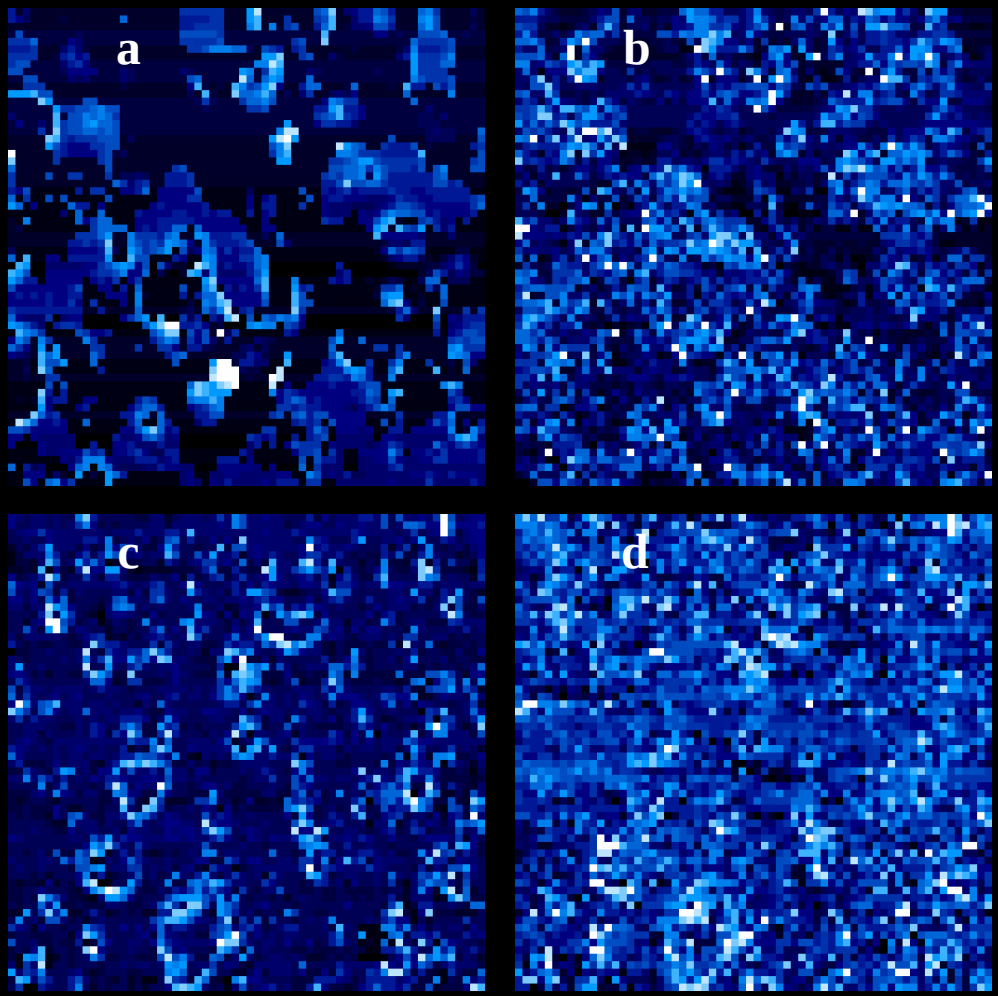


Colloidal Probe

Adhesion Force Curve



Adhesion Mapping
Gelatin Capsules

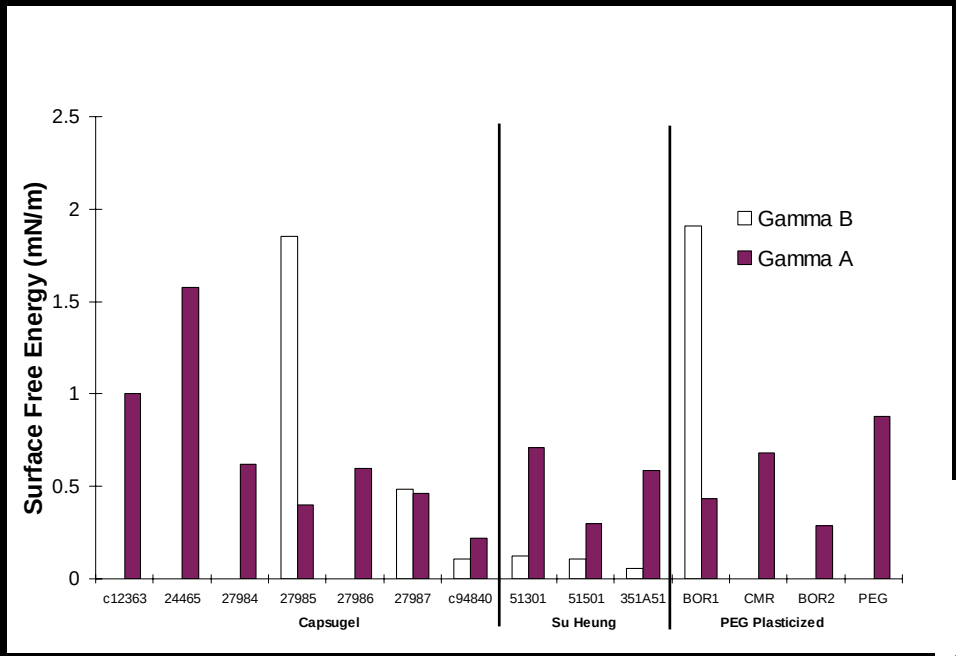


Adhesion maps
(10 x 10 μm scan):

(a) adhesion and (b) adhesion area map of a capsule.

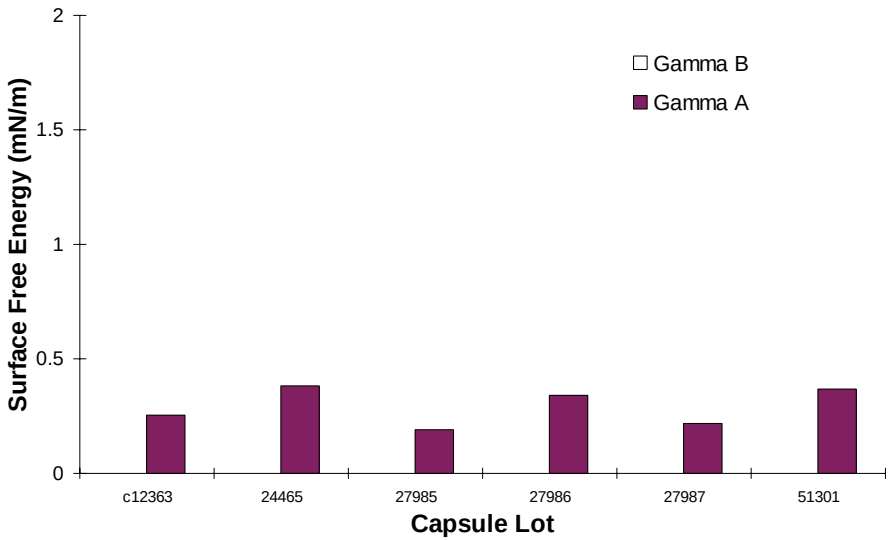
(c) adhesion and (d) adhesion area map of capsule after extraction process.

vOCG Acid Base Parameters of Gelatin Capsules

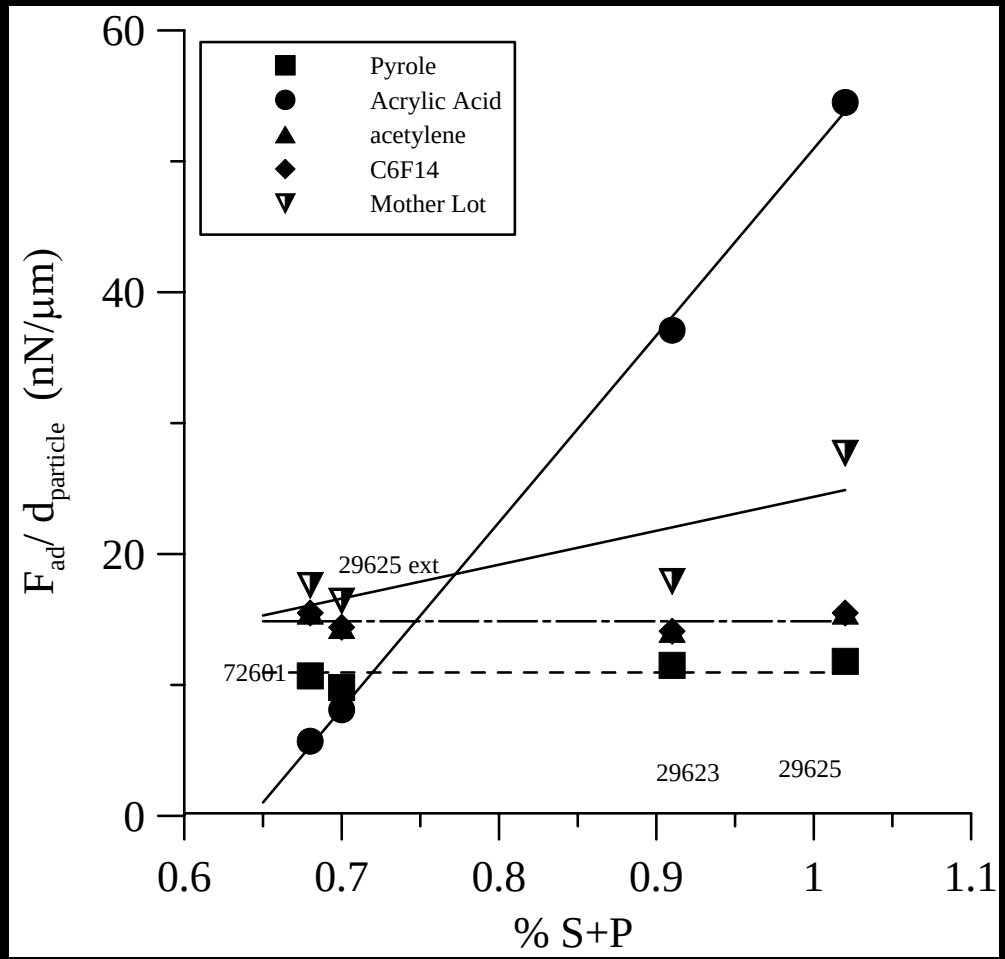


Extracted

Normal



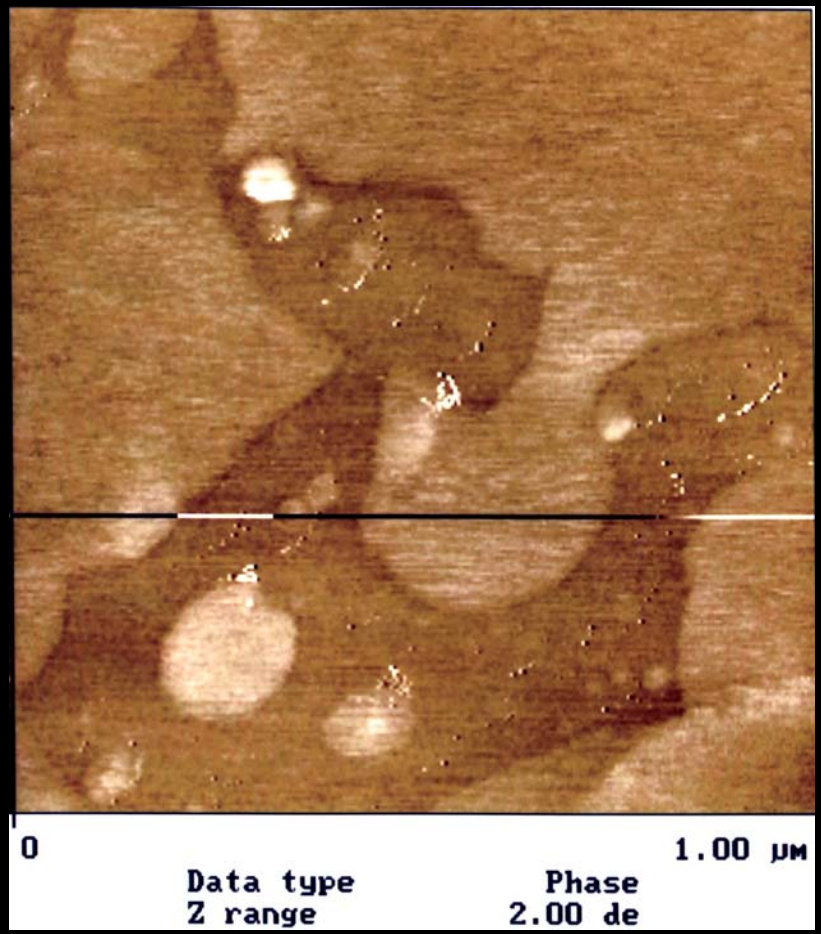
Contamination of Capsule Affects Adhesion



TOF-SIMS shows surface contamination of capsules with SDS.

Some mold release components are unextractable

Lactose Surface Imaging

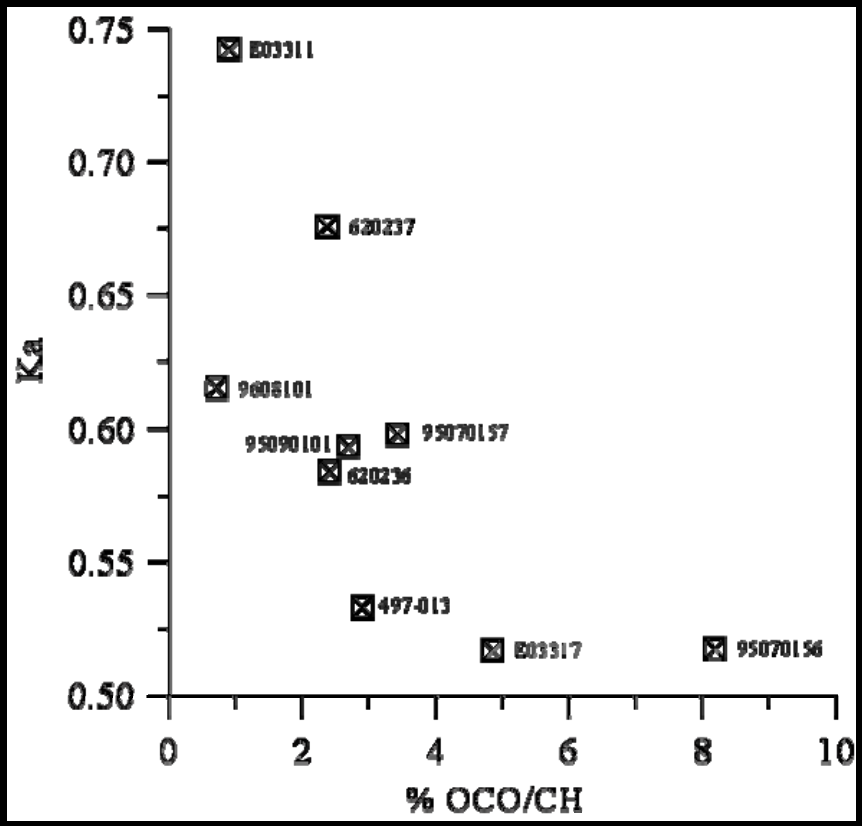


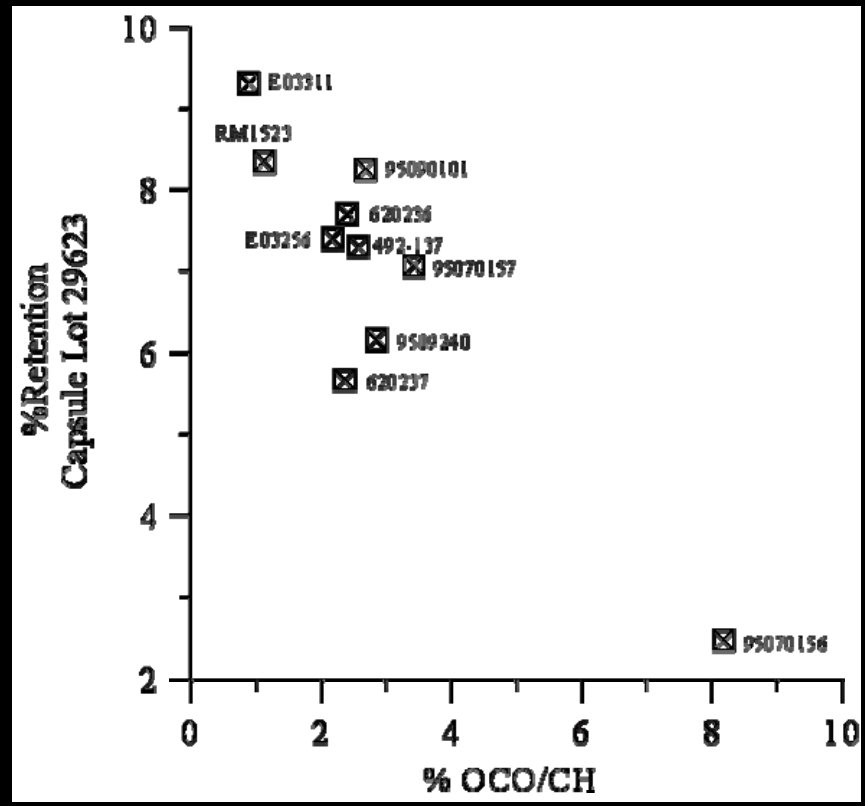
SPM phase image of a surface of a single particle of lactose (1x1µm).

Dark area represents a thin layer of contaminating material.

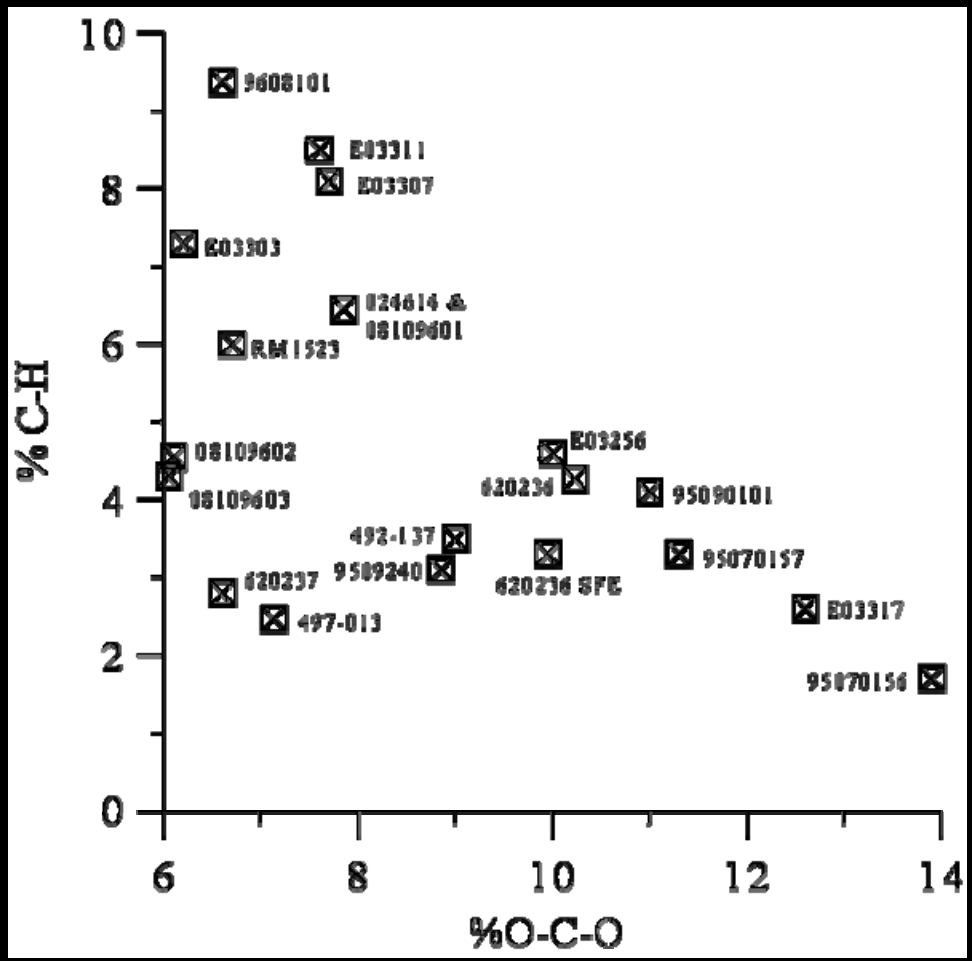
White specks are another surface contaminant.

Lactose Surface Chemistry and Capsule Adhesion





Surface Contamination of Lactose



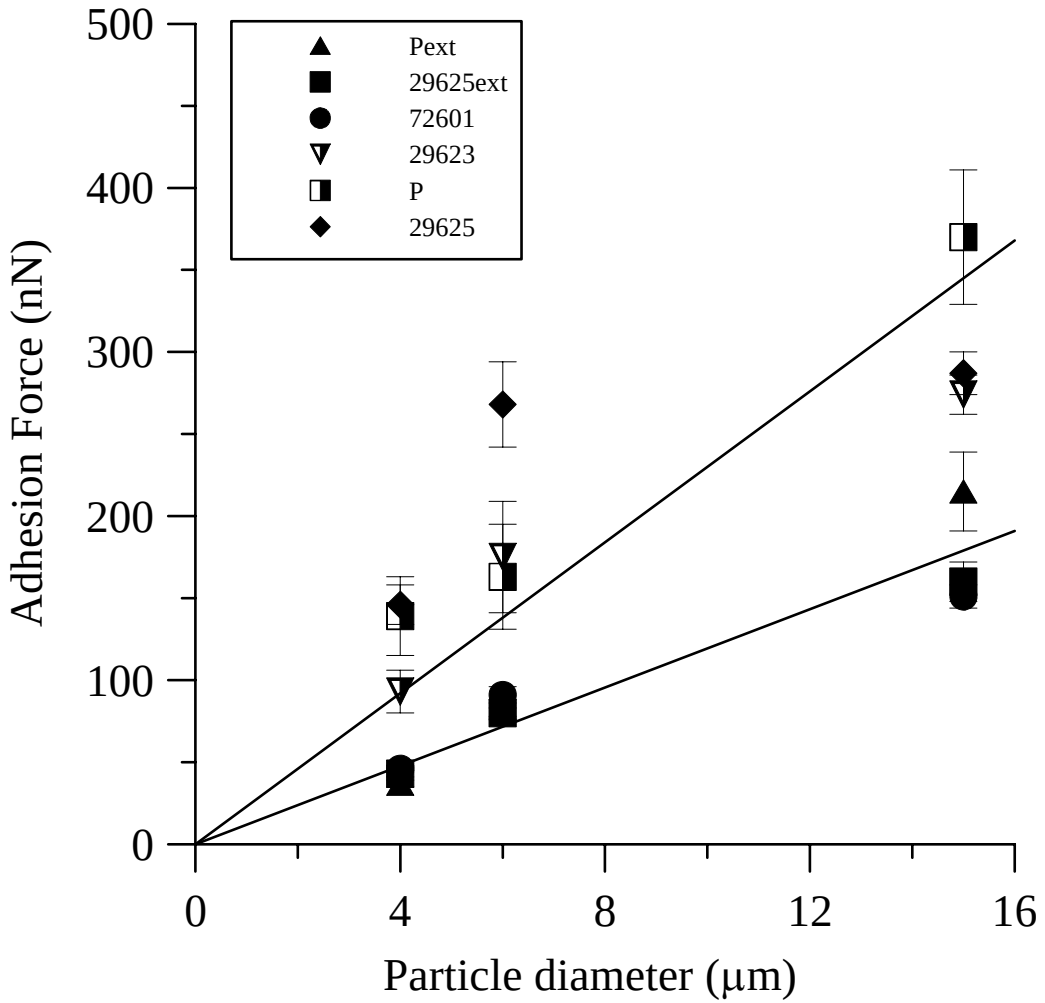
CH vs OCO

ESCA suggests partial coverage of lactose with aliphatic containing materials.

SIMS confirms ESCA results.

Acidic surfaces are more contaminated

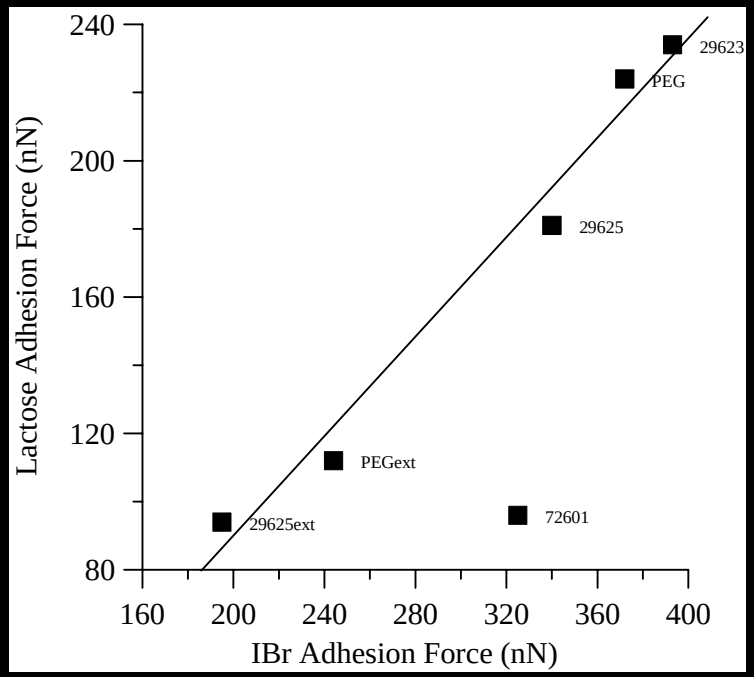
Lactose –Gelatin Adhesion

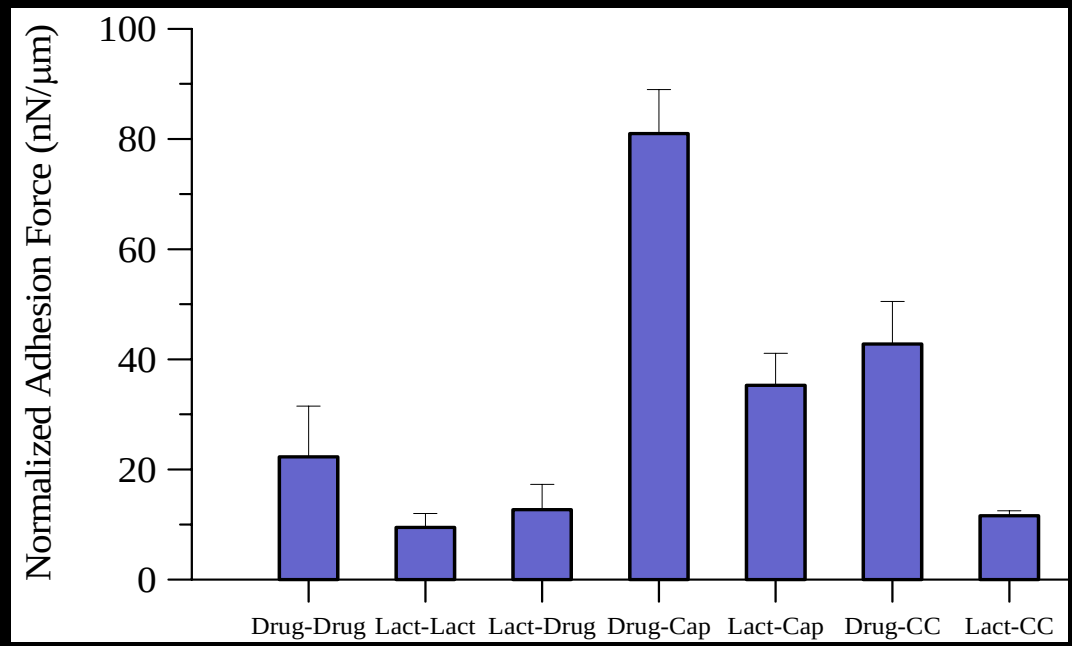


Adhesion force of Pharmatose 200M vs colloidal probe diameter.

Linear relation indicates that interaction is primarily via London - van der Waals forces.

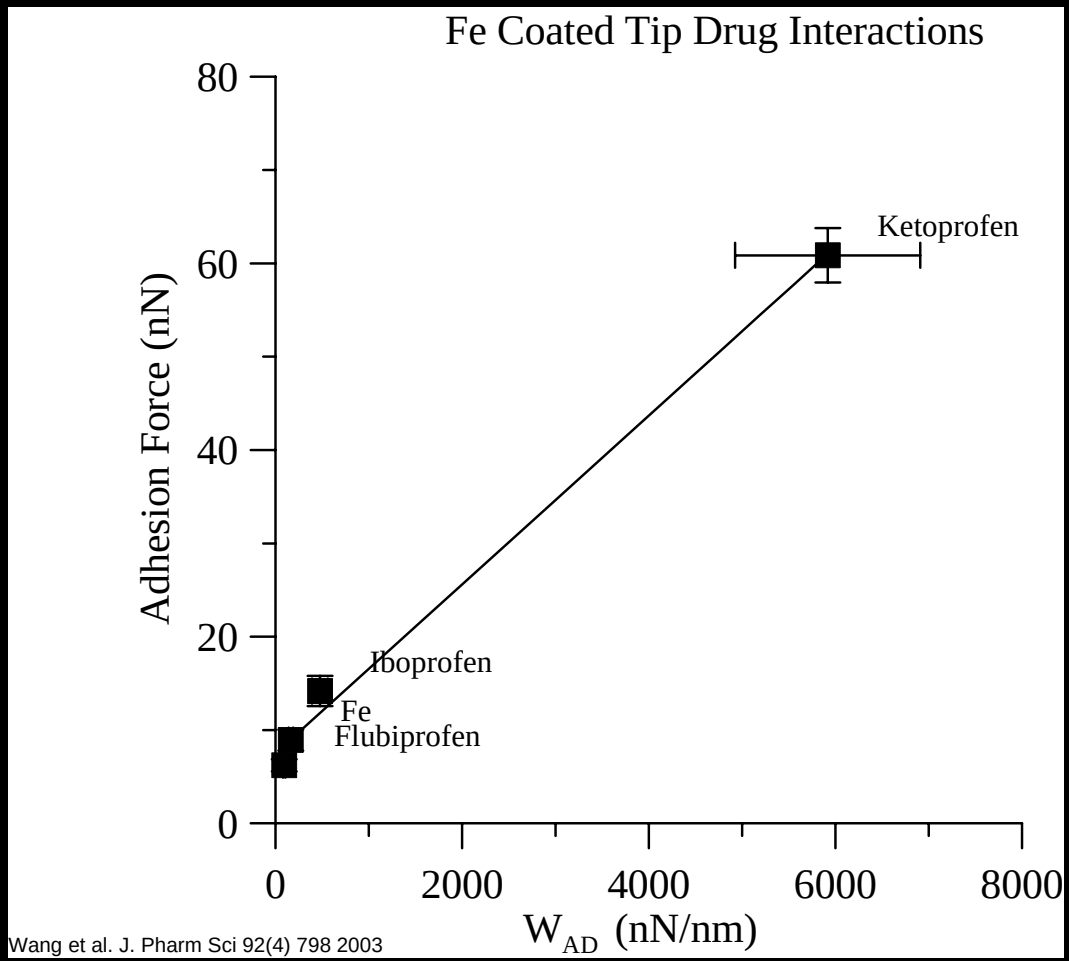
Relative Adhesion of Drug and Lactose on Capsules





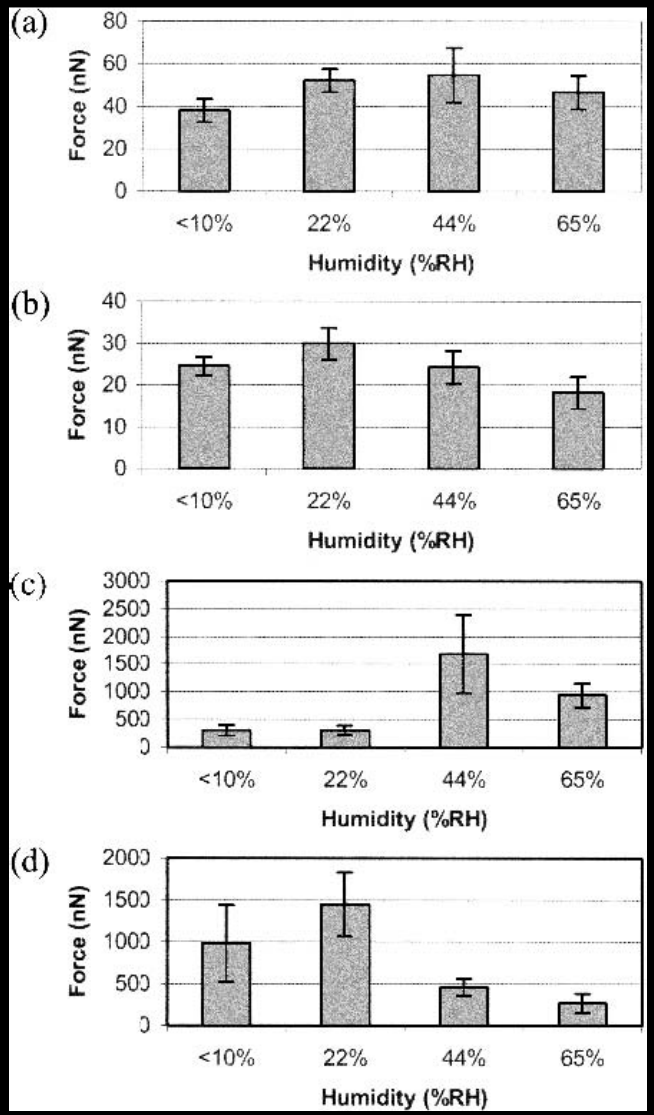
$$F_N = \frac{F_{\text{exp}}}{d}$$

SPM in Tablet Making
Punch Sticking



Wang et al. J. Pharm Sci. 92(4),798 (2003)

Effect of Humidity on Particle Adhesion



Force measurements taken using blank AFM tips against compressed disks of SEDS and micronized salbutamol.

(a) Flexible contact tip against micronised salbutamol

(b) Flexible contact tip against SEDS salbutamol

(c) Stiffer tapping tip against micronized salbutamol

(d) Stiffer tapping tip against SEDS salbutamol

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Friction on Steel

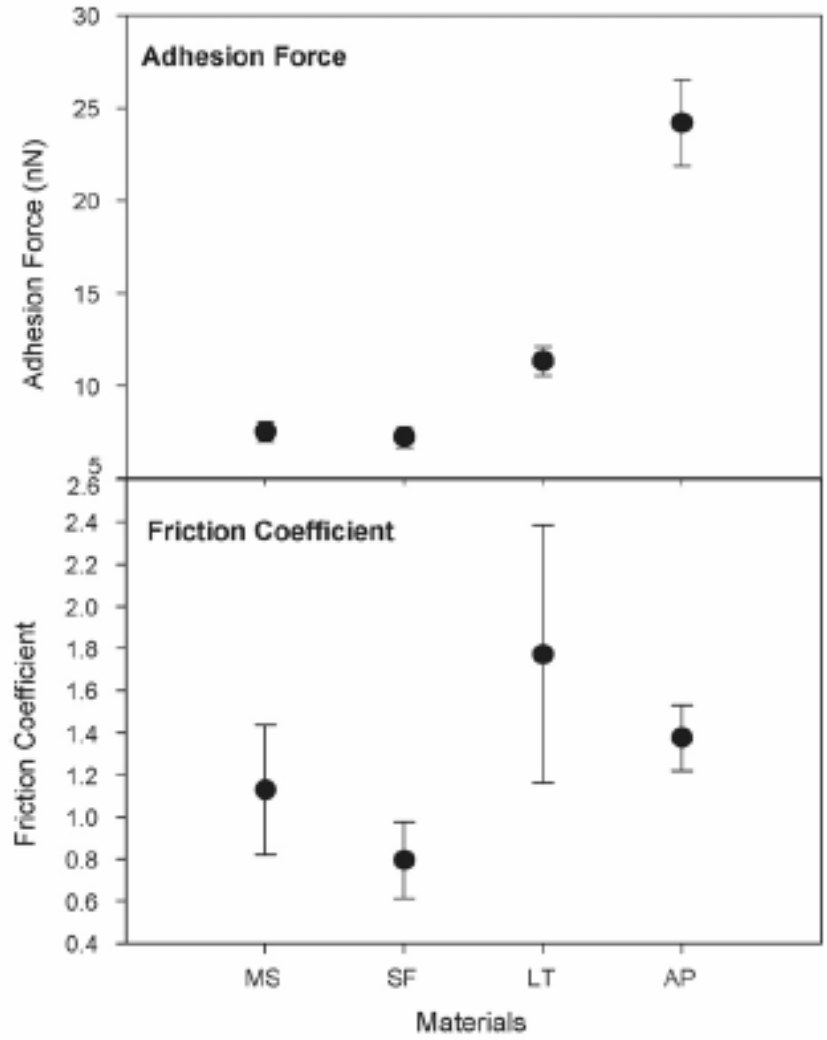

Fig. 5. Comparison between friction coefficients and adhesion forces of various pharmaceutical materials with stainless steel. The adhesion force data are taken from the previous report (Lee, 2004) for comparison.

J. Lee / International Journal of Pharmaceutics 340 (2007) 191–197

Take Home Message

- SPM can be a useful tool in pharmaceutical applications.
- Several applications to inhalation formulations have been published.
- SPM can help determine the surface chemical purity of surfaces.
- SPM can be used to understand the relative adhesion between materials.
- Other surface chemical methods (e.g. IGC) can be used successfully with SPM to enhance understanding.
- Further application to pharmaceutical science appears to be promising.