

## Characterisation of the surface physico-chemical stability of materials directly applicable to inhalation therapy

The power of atomic force microscopy (AFM)

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## Synopsis

- Introduction
- Atomic Force Microscopy (AFM) Studies
  - Characterisation of model and processed Salbutamol Sulphate Crystals
- Conclusions
- Acknowledgments

## Why is surface characterisation important?

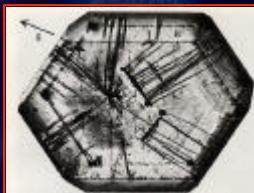
- Pharmaceutical processes involve interfacial contact.
- A change in surface nature will affect interfacial interactions.
- The success or failure of an inhalation formulation is dependant on the nature of the surfaces.

## What influences the surface properties of powders?

- Presence of different crystal habits
- A change in polymorphic form
- **Presence of amorphous material**

## Amorphous Generation

- Uncontrolled crystallisation conditions
- Rapid drying
- Milling
- Any other processing!



Highly processed materials most at risk!

## Is a few % amorphous content important?

If all at the surface!

- Altered interfacial interactions
- Change in product properties
- Batch-to-batch variation

How do we measure the nature of processed powder surfaces?

# Characterisation and Quantification

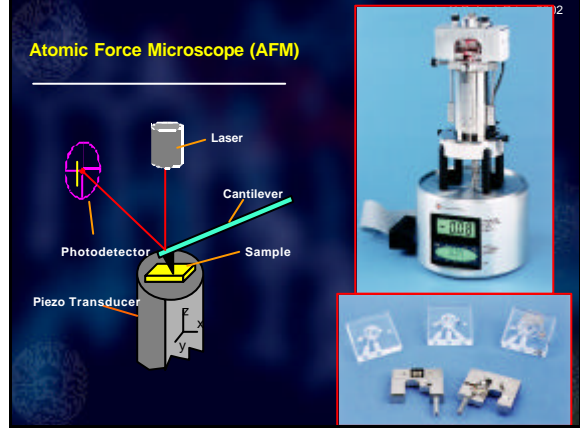
## Bulk Analysis

- X-ray Powder Diffraction
- Differential Scanning Calorimetry
- Isothermal Microcalorimetric Techniques

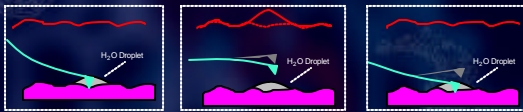
## Individual Particle

### Atomic Force Microscopy

- Phase Imaging (Qualitative)
- Scanning Thermal Microscopy (Quantitative?)
- Scanning Raman Microscopy (Quantitative?)



## Modes of operation



Contact Mode

Non-Contact Mode

Tapping Mode

Height  
Deflection

Height  
Amplitude  
Frequency

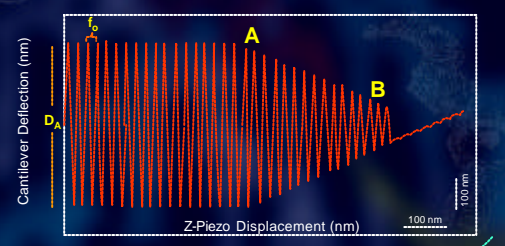
Height  
Amplitude  
Frequency

Lateral Force Microscopy (LFM)

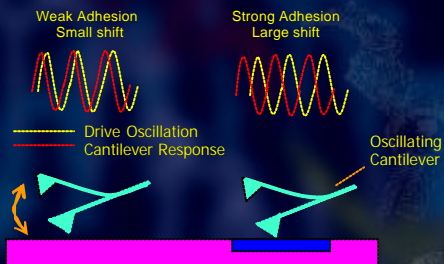
Phase

Phase Imaging  
Electrical Force Microscopy (EFM)  
Magnetic Force Microscopy (MFM)

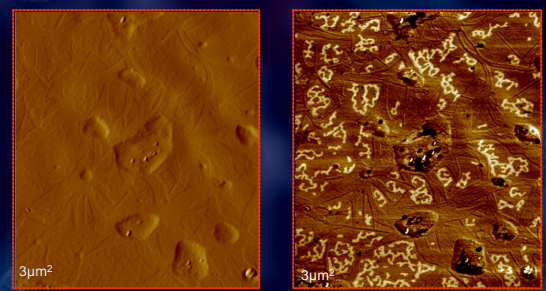
## Tapping Mode™ Operation



## Phase Imaging

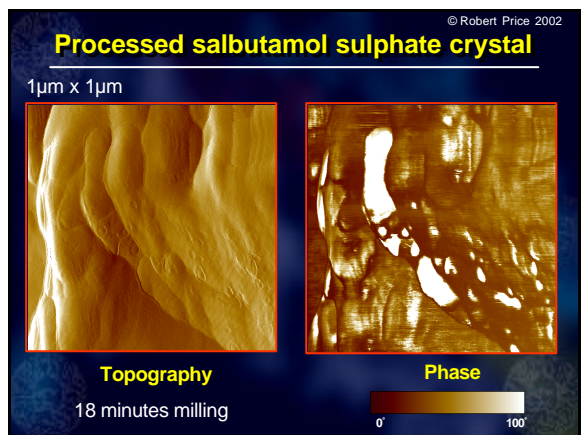
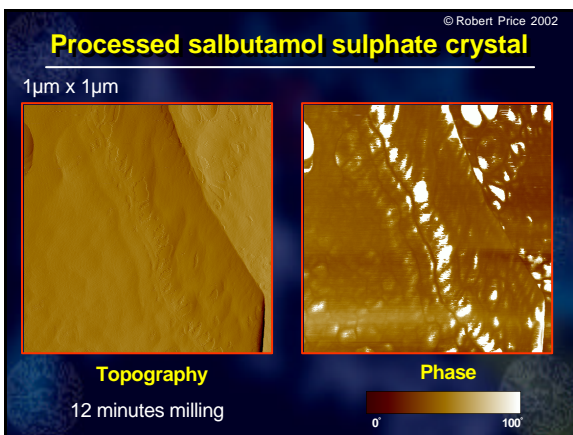
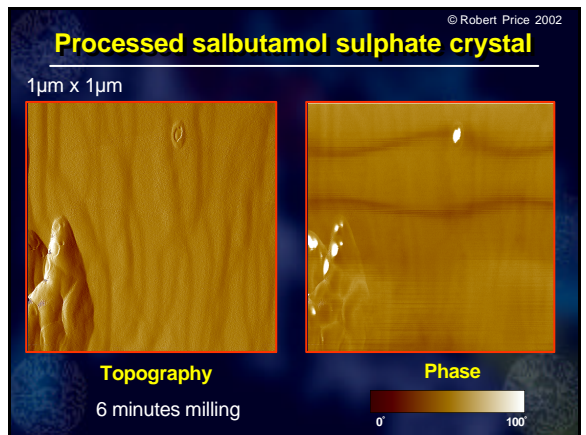
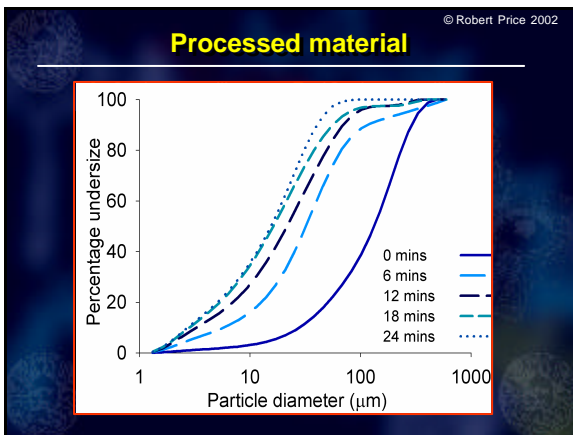
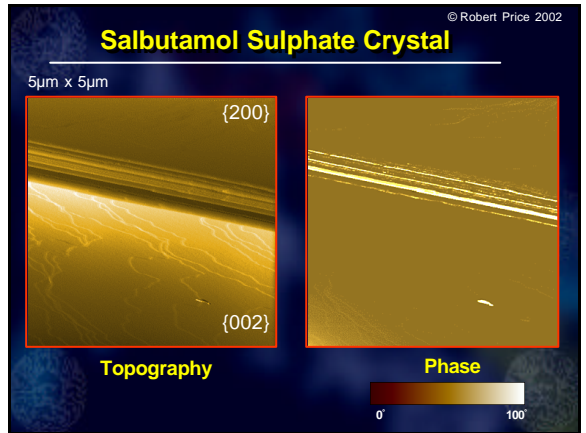
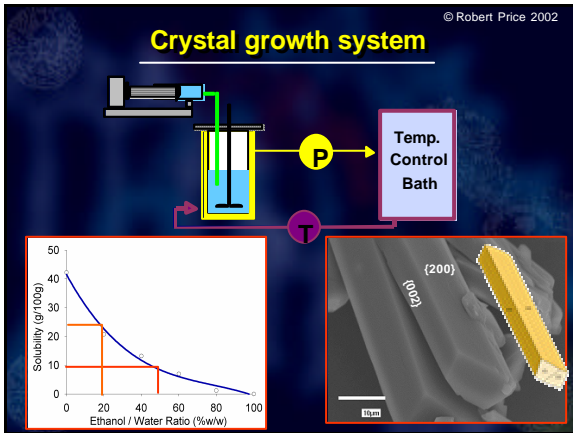


## Cross section of a Starch particle

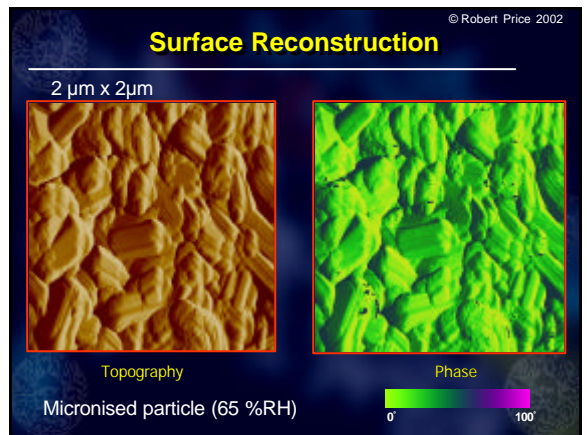
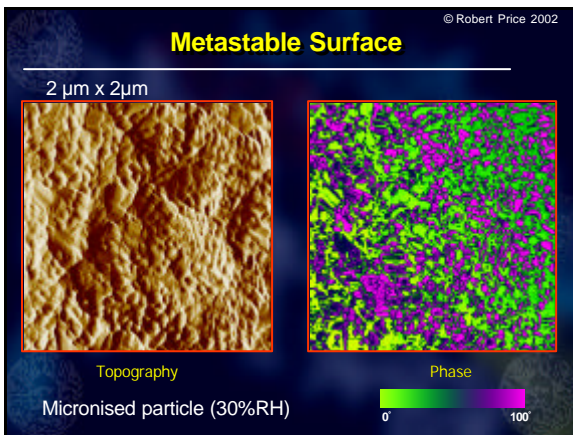
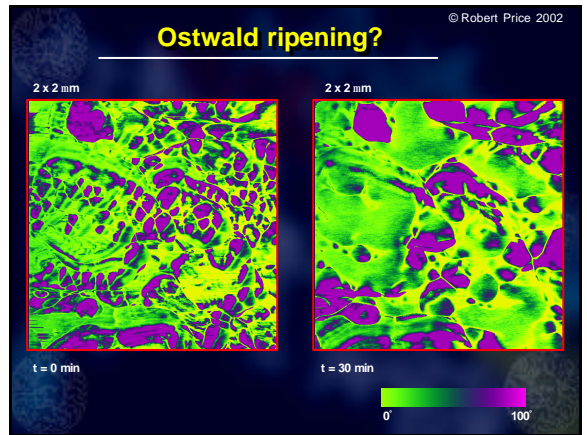
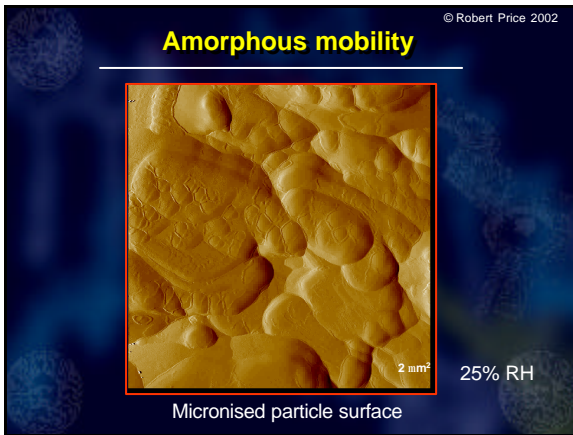
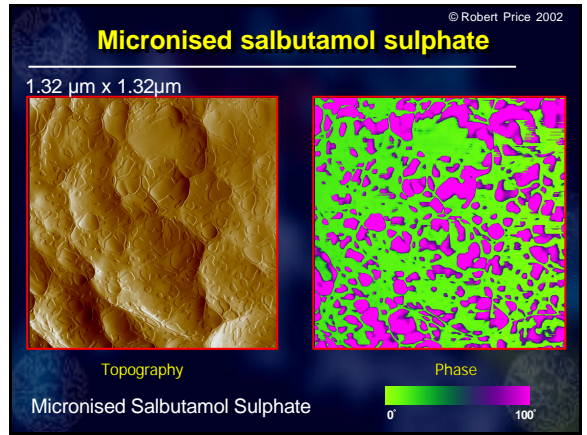
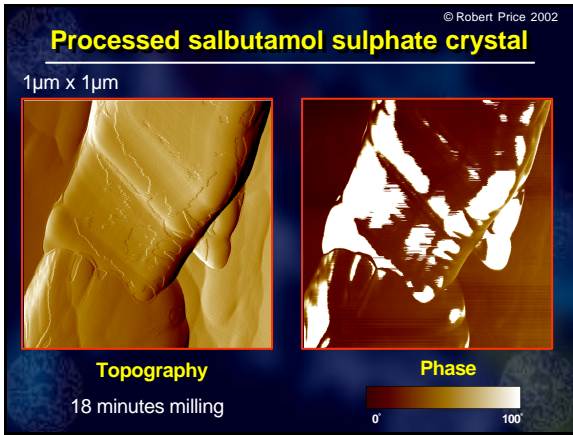


Amplitude

Phase





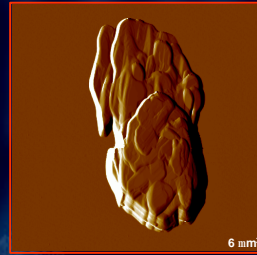
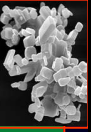


## Conclusion

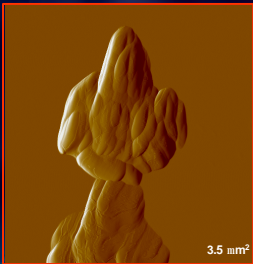
- Amorphous regions will adversely affect the stability and characteristics of a DPI formulation.
- For certain processed materials, the surface will reconstruct to a thermodynamically stable crystalline state.
- Development of new methodologies are required in the conditioning and processing of inhalation material

**SEDS: A potential long term solution ?**

## SEDS produced Salbutamol Sulphate



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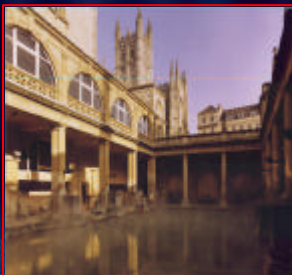


## General Conclusions

The AFM can be used, in real time, to characterise:

- Thermodynamically metastable amorphous domains, at a nanometre level.
- Physical transformations on particle surfaces.
- Long term stability of the powdered systems.

## Acknowledgements



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