

Investigation of porosity of tablets using photoacoustic spectroscopy



Lauri Kurki
Optical Instruments, VTT, Finland
Helsinki Drug Research 2008
10 June 2008




VTT TECHNICAL RESEARCH CENTRE OF FINLAND

Contents

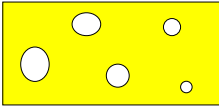
- Porosity of pharmaceutical tablets
- Photoacoustic spectroscopy
- Results of the laboratory study
- Conclusions

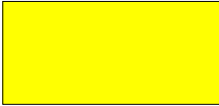



2

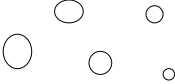
VTT TECHNICAL RESEARCH CENTRE OF FINLAND

Porosity (of cheese)




$$\epsilon = \frac{V_{\text{holes}}}{V_{\text{piece}}}$$


V_{piece}



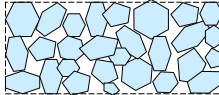
V_{holes}

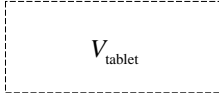


3

VTT TECHNICAL RESEARCH CENTRE OF FINLAND

Porosity of compressed powder




$$\epsilon = \frac{V_{\text{pores}}}{V_{\text{tablet}}} = 1 - \frac{\rho_{\text{tablet}}}{\rho_{\text{crystal}}}$$


V_{tablet}


$$\rho_{\text{tablet}} = \frac{m_{\text{tablet}}}{V_{\text{tablet}}}$$

Calculated by weighing and measuring the outer dimensions



$$\rho_{\text{crystal}} = \frac{m_{\text{crystal}}}{V_{\text{crystal}}}$$

Measured using Helium pycnometry

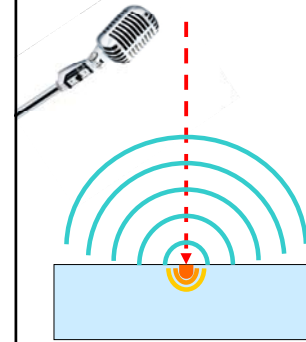


4

About the study

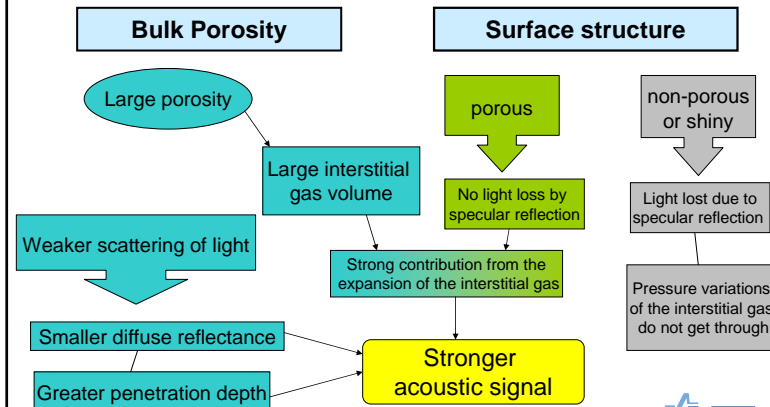
- Tablet porosity strongly affects pharmaceutical and biopharmaceutical properties of the tablet.
- The present aim was to develop a novel non-destructive porosity measurement technique for tablets using photoacoustic spectroscopy (PAS).

Photoacoustic phenomenon in a solid porous sample

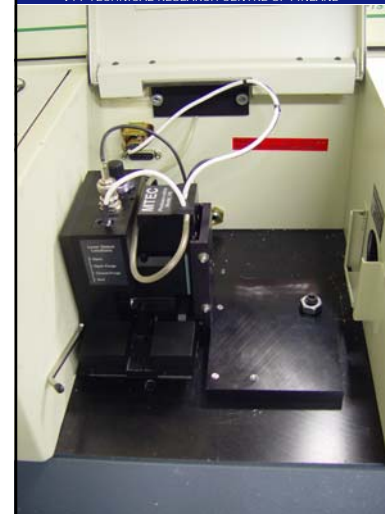


- Amplitude-modulated or chopped light is sent continuously to the sample
- Part of the light is continuously reflected
- The rest is continuously absorbed
- Absorption produces periodic heating of the solid sample and the gas within it
 - Heat conducted to the surface causes the nearby gas to expand periodically
 - Pressure signal from the interstitial gas also proceeds to the surface
- These effects produce the total photoacoustic signal (sound)

What affects the Photoacoustic Spectroscopic (PAS) response?



PAS Equipment



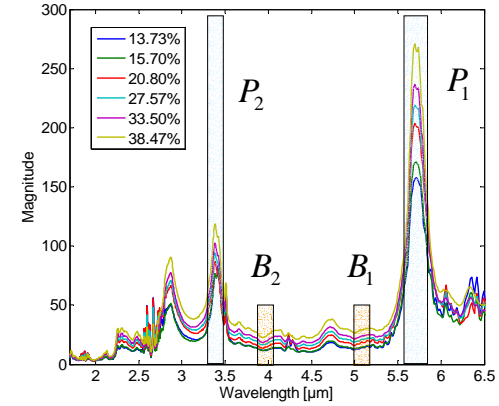
- Bio-rad FTS6000 Fourier-transform spectrophotometer
- MTEC Model 300 Photoacoustic cell
- Helium used as the purge gas
- We used step-scan mode with 100 Hz modulation frequency
 - Sound frequency: 100 Hz

Sample tablets

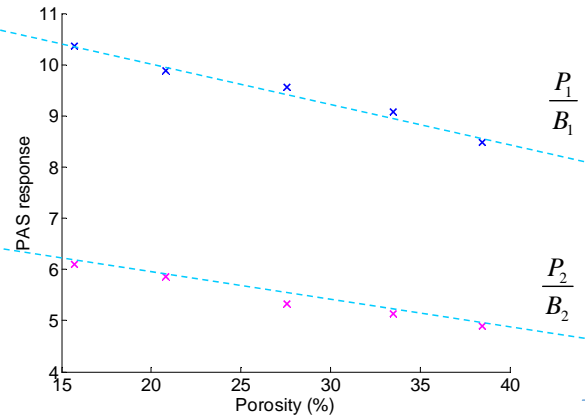
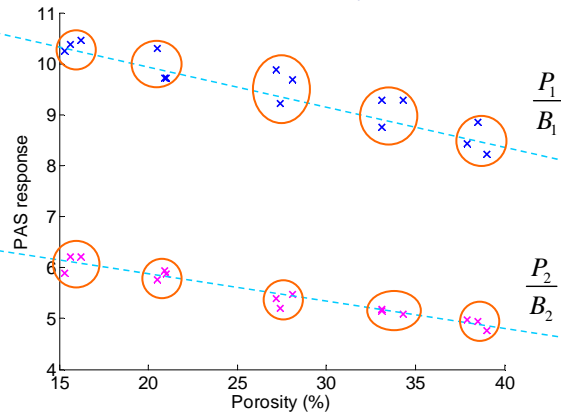


- Material: Starch Acetate
- Form: cylindrical
- Diameter: 10 mm
- 3 series made of different particle size distributions

Photoacoustic magnitude spectra in the infrared range



Is there a linear porosity response?



Technical note:
Calibration model for porosity estimation from PAS spectra

Measured bands: P_1, B_1, P_2, B_2

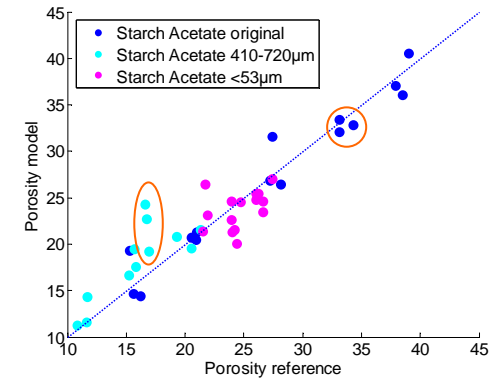
Calibration model: $\varepsilon_{PAS} = a_0 + a_1 \frac{P_1}{B_1} + a_2 \frac{P_2}{B_2}$

Fitting parameters: a_0, a_1, a_2

13



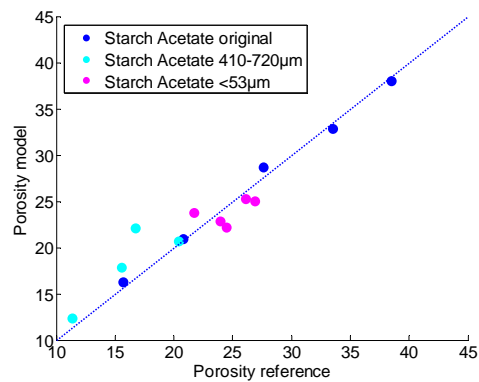
All samples



14



Mean porosities



15



Notes & Questions for further study

- Materials other than Starch Acetate require different calibrations.
- What is the sampling depth at the chosen wavelength and modulation frequency ranges?
- Problems are posed by inhomogeneity of porosity especially at the tablet surface.
- Is it possible to get the same performance using mere infrared diffuse reflectance spectroscopy?

16



Final remarks

- We developed a prediction model for measuring the porosity of Starch Acetate tablets using PAS
- Prediction was rather independent of the particle size and had mean relative error of 10%
- Photoacoustic spectroscopy is thus a potential method for nondestructive tablet porosity measurement.

17



Thank you for your attention.

Workgroup:

- Lauri Kurki, Janne Paaso
Optical Instruments, VTT Technical Research Centre of Finland
- Marko Kuosmanen, Mikko Hakulinen, Jarkko Ketolainen, Kristiina Järvinen
Department of Pharmaceutics, University of Kuopio

References:

- *Generalized theory of the photoacoustic effect*, F. Alan McDonald and Grover C. Wetsel, Jr., J.Appl.Phys. 49(4), pp. 2313-2321, (1978)
- *Photoacoustic spectroscopy of thick powdered or porous samples at low frequency*, J.-P. Monchalain, L. Bertrand, and G. Rousset, J.Appl.Phys. 56(1), pp.190-210, (1984)



UNIVERSITY OF KUOPIO

18

