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Classification of microcrystalline cellulose grades using near-infrared spectroscopy

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Microcrystalline cellulose is an important, widely used pharmaceutical excipient which is commercially available in different grades. These possess different physicochemical properties which give the material a range of pharmaceutical applications, from adsorbent and suspending agent to tablet and capsule disintegrant and diluent.

Importantly, the grade of this material is classified by nominal median particle size (Wade et al 1994) and this is usually determined by forward angle laser light scattering (FALLS). However, this analysis suffers from the disadvantages that it is sample-destructive and time consuming. For these reasons, manufacturers and users of this material have sought alternative methods of measuring particle size which, once calibrated by a suitable reference method, do not suffer from these problems. For example, one suitable technique is near-infrared spectroscopy.

Recently, O' Neil et al (1997) have shown that near-infrared (NIR) spectra of pharmaceutical raw materials contain useful particle size information that could be used to measure median particle size, d_{50}.

Using this spectroscopic technique, a method has been developed which can accurately and non-destructively determine the median particle size of this material by applying two wavelength multiple linear regression to spectral and FALLS data.

Batches of different grades of commercial material (Avicels PH101, PH102 and PH200, total = 36 batches) were used along with machine sieved material (sieve diameters: 150 μm, 90 μm, 63 μm, 45 μm, 38 μm and 32 μm) to provide a suitable particle size range and data set (n = 77). Randomised sieved and bulk samples were assigned to a calibration (60%) and validation set (40%) three times. A six scan average spectrum of each sample was recorded using a fibre-optic probe FT-NIR spectrometer (Buhler AG, Uzwil, Switzerland).

Multivariate regression of log d_{50} on reflectance at two wavelengths was found to give the best fit to the experimental data. Plots of NIR predicted log d_{50} vs. FALLS log d_{50} for the calibration and validation sets are shown in Fig. 1. The standard error of calibration and prediction were typically 0.1 (logarithmic scale).

These results clearly demonstrate the ability of NIR spectroscopy to classify microcrystalline cellulose by median particle size.

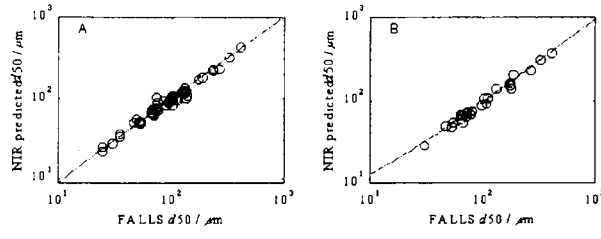

Fig. 1. NIR predicted median particle size, d_{50} vs. FALLS d_{50} for one data set. (A) Calibration set and (B) Validation set.

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O' Neil, A. J., Jee, R. D., Watt, R. A., Moffat, A. C. (1997) Journal of Pharmacy and Pharmacology 49 Supplement 4: 19

Wade, A., Weller, P. J., eds. (1994) Handbook of Pharmaceutical Excipients. 2nd edn., American Pharmaceutical Association, Washington, The Pharmaceutical Press, London, pp 84-87