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A rapid quantitative assay of intact paracetamol tablets by reflectance near-infrared spectroscopy

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There are many analytical applications of near-infrared (NIR) spectroscopy in the pharmaceutical industry both as a qualitative and quantitative method (Burns & Ciurczak 1992). It is a rapid technique involving the absorption of electromagnetic radiation in the range 800 - 2500 nm due to overtones and combinations primarily from hydrogen vibrations in C-H, N-H, O-H and S-H chemical bonds. When preparing a calibration data set for a quantitative NIR method using intact tablets, the variability of active drug in production samples is usually too narrow and the range needs to be expanded using under and overdosed samples.

Reference UV analysis was performed in duplicate using the BP 1993 UV spectroscopic assay for paracetamol tablets and each NIR spectrum was an average of 32 scans over the range 1100 to 2500 nm using a FOSS NIRSystems 6500 near-infrared spectrophotometer equipped with a reflectance detector and sample transport module. Approximately 100 tablets were transferred to a coarse sample holder and scanned, the sample holder being refilled between duplicate scans. The instrument was governed by NSAS version 3.30 software and the data processed using Vision chemometric software. The paracetamol tablets analysed were 25 production batches of Sterwin tablets, 84% *w w* and 10 development batches containing 76 to 92% *w w* paracetamol.

Prior to performing the NIR calibration the tablet ingredients were scanned to identify unique spectral features of paracetamol. Characteristic features were at ~ 1525 and 1625 to 1675 nm, however at 1525 nm there was less interference from excipients. The spectra of three development batches containing 76, 84 and 93% *w w* paracetamol were then compared, the absorbance at ~ 1525 nm correlating with an increase in paracetamol concentration. The NIR spectra were transferred into Vision together with the corresponding mean UV assay values for each spectrum and 20 batches assigned to a calibration set and mathematically treated with standard normal variate and second derivative transformations. Forward search multiple linear regression was applied which gave a correlation of 0.927 at 1530 nm and a correlation of 0.986 when a second wavelength of 1426 nm, selected by Vision, was added. The calibration equation was validated by predicting the concentration of the remaining 15 batches which were assigned to a validation set and the results plotted (Fig 1). The intercept (0.35) and the slope (1.00) were not significantly different from zero and one respectively ($p = 0.05$).

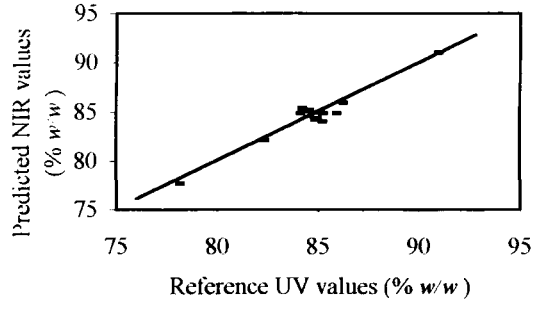

Figure 1. Validation plot of NIR vs. UV data

Statistical analysis of the data indicated that at the 95% probability level the NIR method was comparable to the UV reference method for the assay of paracetamol in Sterwin tablets. No sample preparation was required and the NIR method had the advantage of being rapid and non-destructive.

Burns, D., Ciurczak, E. (1992) Handbook of Near-Infrared Analysis, 1st edn. Marcel Dekker, New York.