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Near-infrared spectroscopic analysis of paracetamol in tablets

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The earliest use of near-infrared spectroscopy (NIR) for the assay of a drug in tablets was in 1968 (Sherken, 1968). This involved the crushing of tablets and it was not until 1987 that the analysis of intact dosage forms as reported (Lodder et al, 1987). There have been a few reported methods of analysing intact tablets by reflectance NIR, but the recent appearance of transmission instruments allowed the application of this form of NIR analysis to the assay of a model drug (paracetamol) in intact tablets.

Samples from production batches (25 batches, 99-102% stated potency) and specially prepared out-of-specification batches (10 batches. 90-110% stated potency) were obtained. They were assayed by the normal BP method using ultraviolet (UV) spectrophotometry (BP 1993). NIR transmission spectra were measured using a NIRTAB system (Buhler AG, Uzwill, Switzerland) between 6000 and 11520 cm^{-1}. Spectral data were processed using NIRCAL (Buhler AG, Uzwill, Switzerland) and also exported into Excel.

Four lots of 20 tablets were scanned 1, 5, 10 and 20 times and the results compared for signal to noise ratio and time taken for analysis. The optimum was 20 tablets scanned 5 times each (taking 20 minutes using a programmable autosampler) and an average spectrum was calculated for each batch of tablets. The batches were divided into a calibration set (20 batches, lying between 90-110% stated potency) and a validation set (15 batches, lying between 95-105% stated potency). Partial Least Squares (PLS) regression models were used to set up regressions between the reference tablet paracetamol concentrations (UV) and the NIR predicted values. Various pre-treatments were tried : transmission, absorbance, first and second derivatives, Savitzky-Golay smoothing and multiple scatter correction as well as examining data from selected parts of the spectral range and correcting the spectra by the weight of 20 tablets. The regression with the smallest Relative Standard Error of Prediction (0.73%) was obtained using data from the whole of the spectral range using the first derivative of the absorbance to correct shifts of the spectra due to physical effects. Using this model, the bias and accuracy of the NIR assay were calculated for the assay of paracetamol in the tablets from the residuals data:

$$\frac{\Sigma(\text{NIR value} - \text{UV value}) \times 100}{\Sigma \text{UV value}}$$

Table 1. Bias and accuracy of NIR assay of paracetamol in tablets (%)

	Bias	Accuracy
Mean	-0.08	0.59
S.D	0.75	0.44
n	15	15

Bias takes into account the algebraic sign of the residuals; accuracy ignores the sign.

Thus, NIR can be used as an accurate, direct, non-destructive method for the assay of paracetamol in tablets.

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