Sample presentation in near infrared spectroscopy—limited only by man's imagination

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Introduction

The ability of near infrared (NIR) spectroscopy to be applied to any material is limited only by man's ability to concoct a way of presenting the sample. In this paper, four presentation devices will be described that are testimony to the versatility of NIR spectroscopy. Pfizer market a veterinary product which is essentially a plastic floor tile embedded with drug. Fibre optic transmission measurements to predict drug release rate will be described. The efficient scanning of solvents and hazardous liquids in a sealed container is a requirement at all Pfizer manufacturing sites. A transflectance system that uses disposable, low-volume HPLC vials will be described. Penetration of NIR radiation into pharmaceutical blend is low. This presents a problem when all of the sample (100–500 mg) must contribute to the spectrum for regulatory acceptance. A moving blend cell designed to overcome this problem will be described. Automation of NIR scanning is essential if the maximum benefit is to be gained from the technique's versatility of sample presentation. A system of robotics to bring the sample to the instrument will be described.

Experimental

Equipment

All spectra were acquired using a NIRSystems (Silver Spring, MD, USA) 6500 instrument equipped with transmission fibre optics for "bolus sheets", and a direct contact module for solvents and solids.

A sample transport module was used for the blend cell work. Automation was achieved using a Zymark (Warrington, Cheshire, UK) Zymate II robot arm.

Software

Spectral collection and quantitative calibrations were achieved using the NSAS software supplied with the instrument. Principal component analysis (PCA) was performed in the Pirouette software (Infometrix, Seattle, WA, USA).

Predicting dissolution rates of paratect bolus

A paratect bolus is a rolled plastic sheet which consists of 50% active material mixed with ethyl vinyl acetate. The rolled sheet is placed into the rumen of cattle, where the slow release of drug protects the animal from worm infections for three months.

The conventional method for quality testing the bolus is to punch it with 55 holes and measure its active release rate in an agitated water bath over a three week period. These HPLC results are

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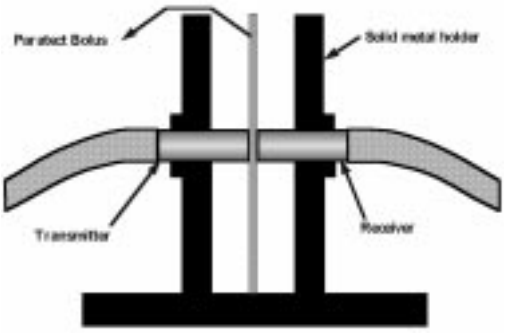

Figure 1. Paratect flex bolus scanned using a transmission pair.

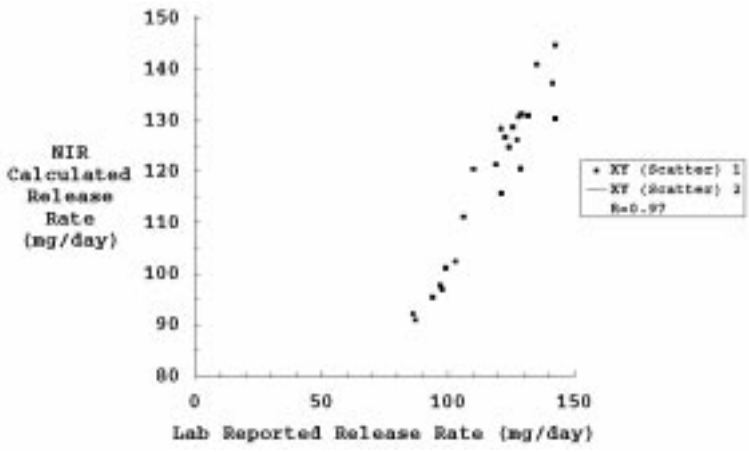

Figure 2. Paratext flex bolus release rate.

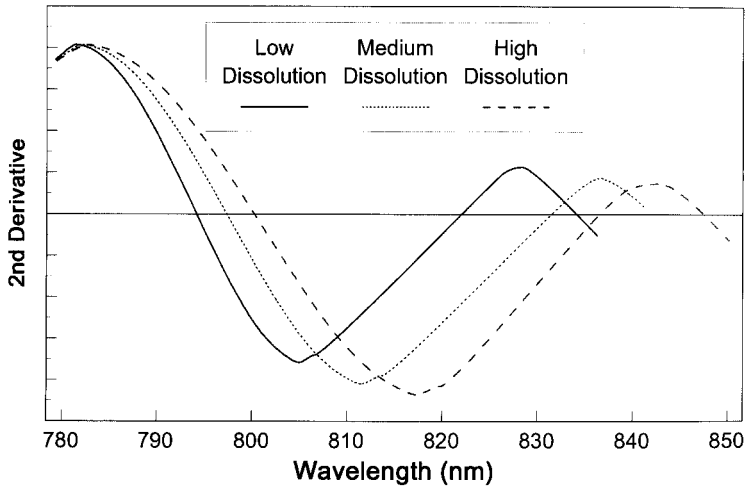

Figure 3. Effect of dissolution rate on paratect spectra.

Sample	301-18915		401-18805		401-18808		401-18811		401-18814		401-18817	
	HPLC (av)	NIR	HPLC (av)	NIR	HPLC (av)	NIR	HPLC (av)	NIR	HPLC (av)	NIR	HPLC (av)	NIR
D1L							122.30	109.48				
D1M	110.00	99.77	135.20	131.84							94.25	90.99
D1R												
F1L			132.90	140.70	129.50	129.43					97.10	94.62
F1M			138.00	130.39			107.70	107.84			89.35	88.97
F1R									103.15	108.26		
F2L									104.85	97.69		
F2M			138.30	131.03								
F2R	128.15	132.72	143.70	137.06	125.15	131.83	115.30	111.51	104.25	101.64	89.95	92.37
F3L					124.25	127.31	115.95	113.05	95.05	99.75		
F3M												
F3R									94.65	103.11		
F4L							106.50	104.38				
F4M					115.45	109.82	103.10	109.72				
F4R												
Average	119.08	116.25	137.62	134.20	123.59	124.60	111.81	109.33	100.39	102.09	92.66	91.74
Difference	2.83		3.42		-1.01		2.48		-1.70		0.92	

Figure 4. Results for validation samples.

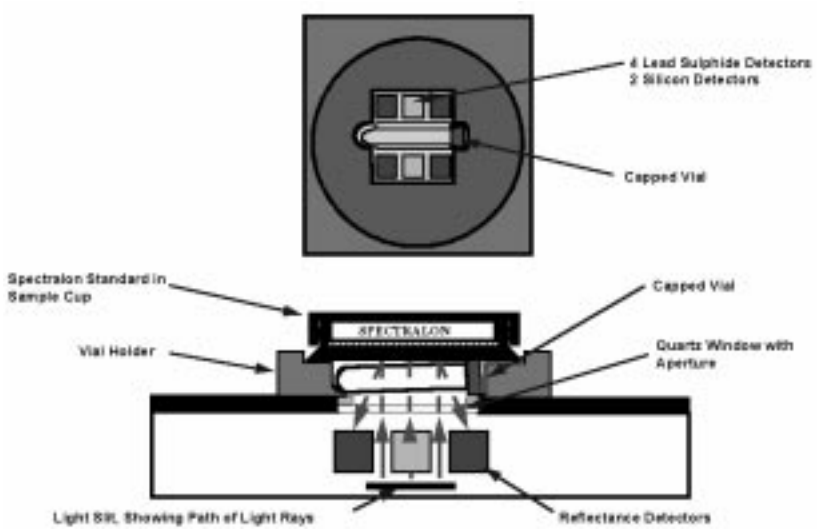

Figure 5. Horizontal setup for scanning liquids.

then used to determine an increased or decreased number of holes to punch in the bolus to adjust the release rate to within specification. The ability of NIR to predict the water bath release rate has significant plant throughput and reduced inventory cost advantages. Figure 1 shows the fibre optic transmission system for scanning the bolus sheets, Figure 2 shows the calibration that can be obtained using partial least squares (PLS) across a selected wavelength region 744–850 nm. Figure 3 illustrates the peak shifts that facilitates calibration. Figure 4 tabulates results for a validation set of boluses which required a range of hole numbers to achieve specification

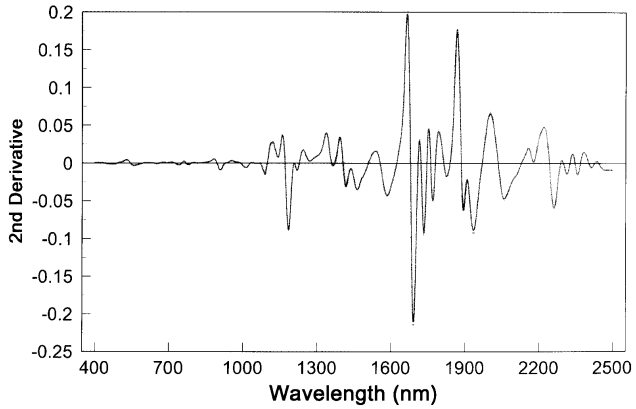

Figure 6. Same ethanol sample scanned in six separate vials.

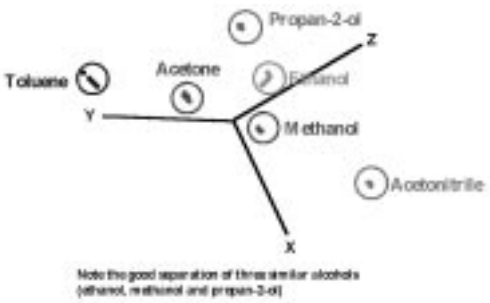

Figure 7. PCA scores plots for six solvents.

dissolution rate. The NIR calibration successfully predicts the conventional release rate and number of holes that are required.

Scanning solvents and hazardous liquids in disposable HPLC vials

In many European countries there is a requirement to identify positively each container of raw material including drums of solvent and some hazardous liquids. Scanning such liquids in low volume disposable HPLC vials provides many benefits in terms of efficiency and safety.

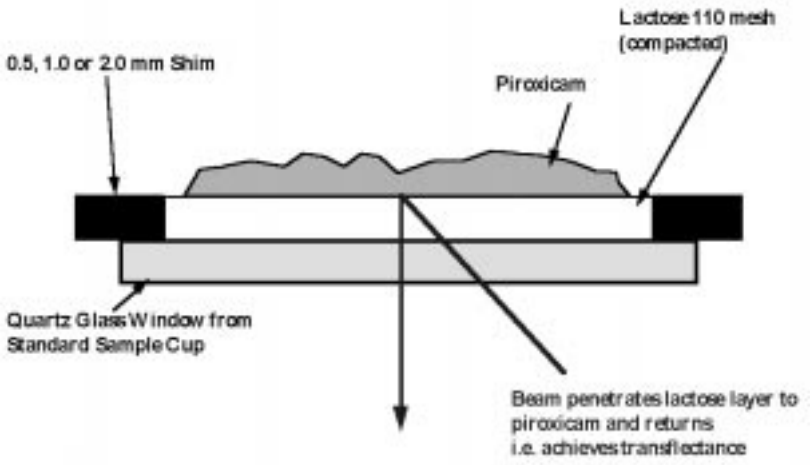

Figure 8. Determination of depth of penetration of NIR radiation.

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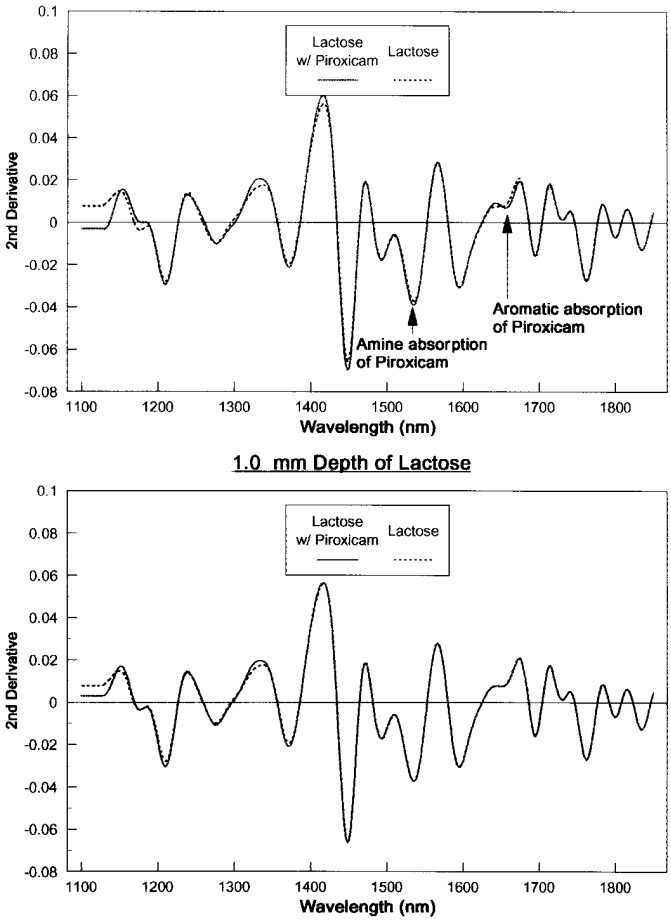

Figure 9. NIR penetration of lactose.

The optical configuration shown in Figure 5 has successfully provided a means of obtaining high quality reproducible transflectance spectra of these materials. Figure 6 shows the spectra of ethanol scanned in six different vials. Figure 7 shows the spectra of several solvents represented as a PCA scores plot, and illustrates the excellent reproducibility. The close clustering of the scores for individual solvents illustrates the excellent identification and qualification ability of the system, particularly the separation of similar alcohols.

Analysis of pharmaceutical blends

The weight of sample contributing to the spectrum of a pharmaceutical blend must be tightly controlled. Regulatory guidelines enforce a maximum limit of the tablet or capsule weight, typically 100–500 mg. Production managers will require analysis of no less than this dose weight to avoid over stringent assessment of their products. Depth of penetration measurements for blends were performed using the scheme shown in Figure 8, in which defined layers of carrier material,

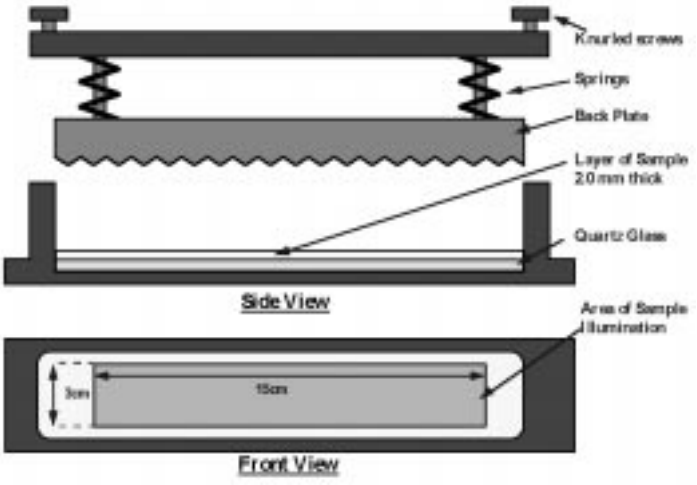

Figure 10. Design of blend cell.

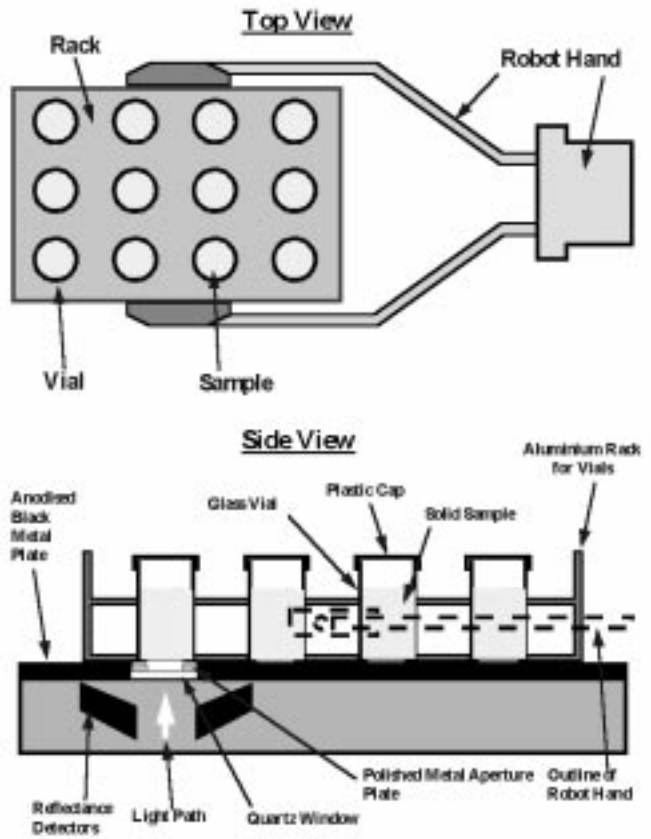

Figure 11. Rack of vials for scanning solids.

which constitutes the major part of the blend matrix, were coated with active material. The ability to see specific absorptions of the active material through the carrier provides effective depth of penetration data.

Figure 9 shows typical results of these experiments where penetration was measured at 0.5 mm in the critical aromatic/amine absorptions region. These measurements have revealed that between 30–50 mg of blend contribute to the spectra of a sample scanned in a standard sample cup. To overcome this limitation a cell for providing a large surface area of small samples of blend (1–2 g) has been designed and built (Figure 10).

The cell essentially allows movement of a thin layer of sample through the scanning beam during spectral acquisition.

Automation of NIR scanning

The requirement to perform "every container" identity of raw materials has prompted a need to fully automate the testing. Sucrose for example may arrive at the UK plant contained in 800 separate bags. The use of disposable vials as sample holder combined with robotics, (Figure 11) has enabled unattended rapid throughput of large numbers of samples.

Conclusions

The ability of NIR to scan neat unprepared samples makes it the most versatile analytical technique available to the chemical industry today. Simple optical systems can be adapted to take a wide range of sample types from liquids to slurries, to dry powders. The variety of samples and presentation techniques that can be used in NIR spectroscopy is indeed limited only by man's imagination.

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