J. Pharm. Pharmacol. 1998, 50 (Supplement): 46

The case for the use of near-infrared spectroscopy as a primary method of analysis

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Although a relatively new analytical technique, near-infrared spectroscopy (NIR) has been validated extensively against primary (the usual well used and understood) technologies in the scientific literature. However, it is still often quoted as a secondary technique, i.e. one where a set of calibration samples must first be analysed by a reference (standard) method so that the analyte concentrations are known and then these samples used as a teaching set for the NIR calibration (Osborne et al, 1986; Workman, 1992). This paper makes the case for the use of NIR as a primary method of analysis.

For quantification purposes, there is no reason why the spectral values measured by NIR (e.g. reflectance or absorbance) cannot be directly related to the mass, volume or concentration of a drug in a sample. The calibration would be set up by measuring the NIR values of prepared samples of either known composition or of known amounts of a drug, i.e. standards. Typically analysed matrices are:

- Mixture of two liquids, e.g. water in chloroform
- Solution of a solid in a liquid, e.g. meprobamate in chloroform, meglumine and meglumine diatrizoate in parenteral products
- Mixture of two solids, e.g. propranolol and magnesium carbonate
- Liquid in a solid, e.g. water in lactose where the water can be determined by loss-on drying

Where the matrix is complex, e.g. intact tablets, setting up calibration samples may be very complicated and NIR may best be used in these situations as a secondary quantification method if direct, fast analyses are required. However, as with chromatographic techniques, the tablets could be ground to a powder, extracted with a solvent to separate the drug from the matrix and then analysed by NIR. An example is the assay of meprobamate in tablets. Alternatively, the tablets could be ground to a powder and then analysed by a method of standard additions, e.g. aspirin in solid dosage forms.

Drugs may be identified directly by measuring their NIR spectra and comparing them with a library of spectra previously generated from pure drugs just as is currently done in mid-infrared spectroscopy. Whilst NIR spectra do not have the fundamental absorption bands of the mid-infrared region (because it has overtone and combination bands), chemical assignments can be made to many bands in the NIR information rich spectrum (e.g. some X-H and O-H stretching overtone bands). NIR has the great advantage that active drugs may be directly identified in intact tablets (Khan et al, 1997).

NIR can also be used for measuring the particle size of powders from a calibration curve generated using sieved fractions. This is because the diffuse reflectance of a powder increases as the mean particle size decreases.

NIR can be used empirically and pragmatically in many process control applications without the need to involve another (primary) method. Examples include blending solids, drying to constant weight and synthesising materials for optimal yield.

In conclusion, the above examples show that NIR can be used as a primary method of analysis.

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