Do you know what’s going in? Analysing tablets by NIR spectroscopy

Drug analysis needs to be cost effective without compromising on accuracy. This is an important principle for both routine quality control and the identification of potentially harmful counterfeit medicines. Near-infrared spectroscopy, or NIRS for short, is a useful part of the pharmaceutical analysis toolbox – and a winning choice thanks to the minimal time and labour resources it consumes, as well as the fully automated online analyses it offers. Not only that, but it also takes simultaneous analysis of multiple substances in its stride. This article illustrates what it can do.
QUALITY by Design (QbD) and process analytical technology (PAT) are two concepts that have become watchwords for the US Food and Drug Administration (FDA). These approaches aim to increase efficiency in the development and production of drugs. In QbD’s case, trial-and-error processes are replaced with a design which, from the outset, is optimally tuned to the ways in which the drug will be used further down the line. In other words, it is adapted to suit the patient population, the manner in which it will be administered, and so on.

The hope is that this will result in a production that delivers the desired results from the very start. Without PAT, however, the QbD approach could not survive. Process analysis is used to monitor production in real time. Thus, it allows alterations to be made during the process itself in order to achieve the intended quality. Not only that, but it also helps to improve understanding of the product and process.

**Original or counterfeit?**

Besides routine analyses of active ingredient content, NIR spectroscopy can also be used as a fast and cost-effective way of testing whether drugs are genuine. While counterfeit medicines may not present much of a problem to first-world countries, both agencies and patients in the developing world are continually faced with the dangers associated with these non-genuine products.

A 2013 publication discussed the use of NIRS to classify tablets containing the three active ingredients metamizole, caffeine, and orphenadrine. The method is non-destructive and fast – enabling the use of a large sample quantity.

**More than one route to the destination**

The authors of this study developed the method on the basis of four preparations from different manufacturers. They defined one of these as the reference and then developed models for differentiating it from the other three products. To do this, they used a range of algorithms: SIMCA (soft independent modelling of class analogies); GA-LDA (genetic algorithm-linear discriminant analysis); and SPA-LDA (successive projection algorithm-linear discriminant analysis).

**The models: ranging from simple to elaborate**

The models that arose from these algorithms came in varying degrees of complexity. Modelling with the SIMCA algorithm used the entire measured wavelength range of the spectra. Meanwhile, GA-LDA and SPA-LDA used only 12 and two selected wavelengths, respectively. All three models proved capable of classifying the preparations with 100% accuracy. The latter two algorithms offer the advantage of fast, inexpensive modelling and are able to deliver reliable predictions if appropriate validation is performed. Figure 1 shows the results of SPA-LDA modelling.

**Growing significance**

The profile of near-infrared spectroscopy is rising more and more in the pharmaceutical industry – this is in large part thanks to the FDA’s PAT initiative. Already an established tool for process and quality control, in the future it is hoped that NIRS will help to boost efficiency in the development and production of drugs even further. Using NIRS and an appropriate model, pharmaceutical products can be identified, and their various ingredients determined – whether these be APIs or excipients. Not only does this allow for rapid, straightforward quality control at the manufacturing plant, but it also makes it possible to verify whether preparations are genuine – in customs or pharmacy contexts for instance.

**References**