Advantages of near infrared transmission measurement for the analysis of intact pharmaceutical tablets

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Introduction

In the course of increasing quality consciousness, near infrared (NIR) spectroscopy is of growing importance. In raw material control at the warehouse NIR spectroscopy has become a standard method. This is true especially in the pharmaceutical industry, which is dependent on a fast and reliable identification of their raw materials because of severe regimentation through GMP. Now there are initial efforts underway to extend NIR spectroscopy to the control of final products in order to replace conventional analysis methods, which lead, especially for tablets, to a high expense for sample preparation.

In the literature one finds some reports which demonstrate the potential of NIR spectroscopy, both for the qualitative analysis as well as for the quantitative determination of the active ingredient's content.[1–4] Since tablets generally have a compact structure, these reports exclusively deal with measurements of the diffuse reflectance. The danger with the application of this measuring method is that mainly data of the regions slightly underneath the surface of the tablet are recorded. Thus, inhomogenities of the sample are not considered and the measurement may lead to a wrong result. This becomes clear if sugar covered dragees or tablets with a layer construction are examined.

In order to solve this problem, as well as for investigating tablets of any kind, Buhler Ltd ANATEC measured the tablets by means of NIR transmission spectroscopy. Despite a strong reduction of the light intensity at the passage through a compact sample of a few millimetres, the method shows a very good sensitivity to quantitative investigation of the active ingredient's content. This is demonstrated in a preceding publication[5] in which the results of measurements performed on a synthetic set of tablets containing salicylic acid acetate as an active component are reported. In the present paper the utility of the method for dragees is demonstrated.

Details of the apparatus

The system consists of two basic elements: the NIR spectrometer, which is used with an external light source, and the autosampling system. The experimental set-up can be seen in Figure 1. The NIR spectrometer is a polarisation interferometer based on the principle of a moving quartz

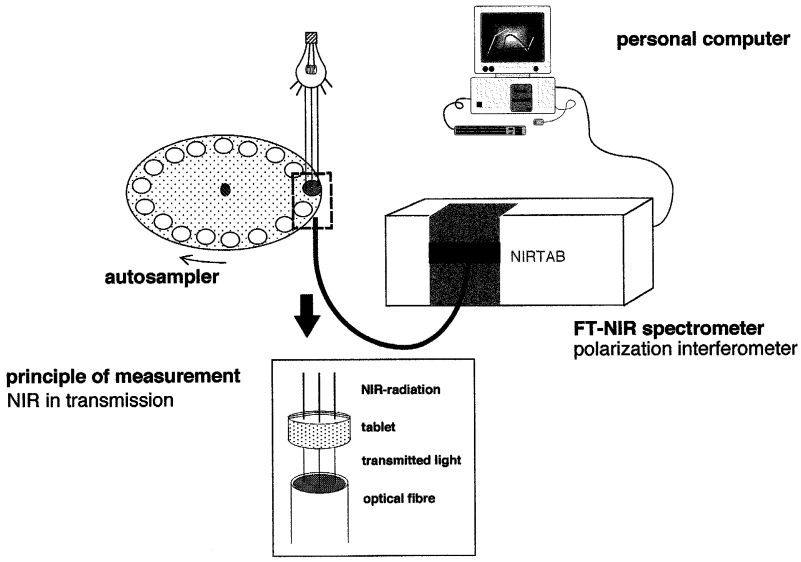

Figure 1. Set-up for the examination of intact tablets by NIR transmission spectroscopy.

wedge. The second part of the apparatus is formed by an autosampling system containing a high power tungsten halogen lamp and a programmable rotational sampling unit. The tablets are positioned on a plate with 45 peripheral holes exactly adapted to the size and the shape of the tablet under examination. When brought into the optical path the tablets are homogeneously illuminated in order to cover the complete top area of the sample only. Different spectral regions are removed by optical filters in order to avoid both electronic excitation and heating effects inside the tablets. Light diffusely transmitted through the tablet is collected by a bundle of optical fibres and conducted to the interferometer. Spectral data can be taken between 6500 and 12,000 cm^{-1}. The NIR measurements are done against a Spectralon disk (Labsphere Inc., North Sutton, USA) as a transmission reference standard having a thickness comparable to that of the tablet.

The precision of the system was demonstrated by the subsequent measurement of one single tablet being positioned in different holes of the sample plate. The repeatability was proven by the repeated measurement of one tablet whilst moving the autosampler between the reference position and the position of the sample. In the same run, the long-term stability was shown as the experiment lasted for five days during eight hours a day.

Advantages of the transmission principle

Simple compressi without any polymer or sugar coating, in principle, can be examined by either using diffuse reflectance or transmission NIR spectroscopy. But when dealing with polymer coated tablets or even sugar coated dragees the method of diffuse reflectance might not reach the exactness required for quantitative analysis of the active ingredient's content.

We carried out comparative experiments on sugar coated tablets both in diffuse reflectance and in transmission NIR spectroscopy. As diffuse reflectance measurements mainly provide information on the regions slightly underneath the surface of the tablet, we do observe the spectral bands characteristic of the sugar cover. That is mainly the absorption band at 6944 cm^{-1} (OH first overtone), see Figure 2(a), curve I. Removing the sugar cover from the dragee leads to a complete

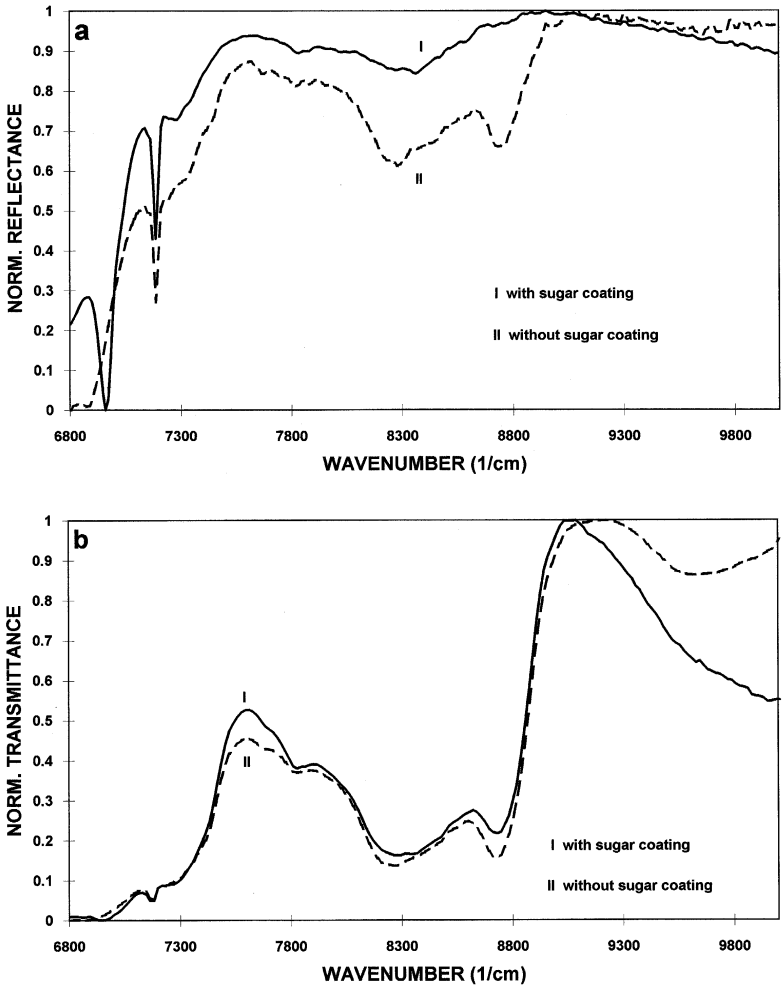

Figure 2. Comparison of NIR spectra for dragees with and without sugar coating: (a) reflectance data and (b) transmittance data.

disappearance of the band at 6944 cm^{-1} and a reduction at 7168 cm^{-1}. This band may be attributed to an intermediate polymer layer. At the same time, we can observe more prominent bands characteristic for the active and inactive content of the tablet, especially at 8749 cm^{-1} where we can find the absorption of the aromatic CH stretch second overtone [Figure 2(a), curve II]. For comparison we measured the same samples in the transmission mode. As is seen in Figure 2(b), curve I, the sugar cover has much less influence on the spectra. At the same time, the absorption bands, being characteristic for the active and inactive components (i.e. around 8300 and 8800 cm^{-1}) can clearly be observed for the sugar coated dragee as well as for its nucleus.

Further experiments are performed on the influence of the build-up of multi-layered dragees. Figures 3(a) and 3(b) show spectra for diffuse reflectance and diffuse transmittance, respectively. Curve I characterises the nucleus with the first active ingredient. Curve II shows the spectrum of

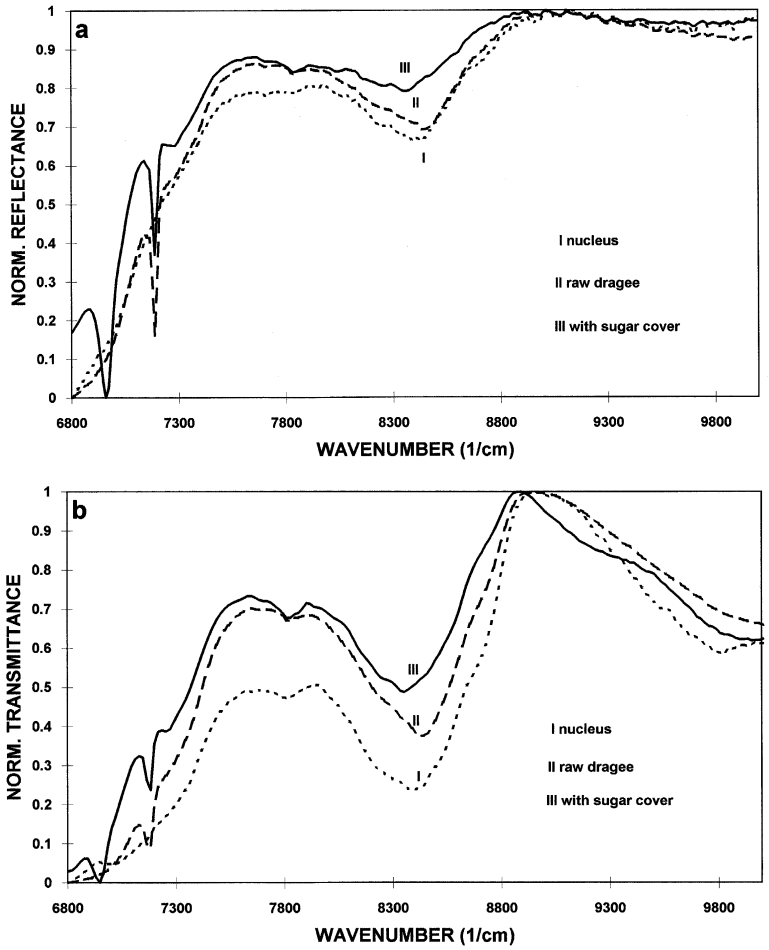

Figure 3. Comparison of NIR spectra for multi-layered dragees: (a) reflectance data and (b) transmittance data.

the raw dragee containing additionally a second active ingredient and a polymer layer. Curve III is the spectrum for the dragee completed with a sugar coating. In all three cases we get much more spectral information with the measurement of transmission spectra.

Transmission NIR spectroscopy can be regarded as an useful tool for the examination of dragees and tablets having a multi-layered structure. On such premises a calibration for the amount of chemically well-defined active ingredients in dragees seems to be promising, especially when expecting an accuracy comparable to that of conventional analytical methods such as HPLC or UV spectroscopy.

Acknowledgement

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