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Quantitative analysis of solid samples using modified specular reflectance accessory

Tomasz Czaja, Sylwester Mazurek, Roman Szostak*

Department of Chemistry, University of Wrocław, 14 F. Joliot-Curie, 50-383 Wrocław, Poland

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ABSTRACT

Diffuse reflectance Fourier transform infrared spectroscopy (DRIFTS) is a fast, reliable and cost effective analytical method, requiring minimal or no sample preparation. It is commonly used in the course of qualitative and quantitative analysis of pharmaceutical ingredients and food. We demonstrate that simpler and cheaper specular reflectance (SR) accessory working in a DRIFTS like mode (SR-DL) can be an alternative for DIRFTS attachment. An application of a modified SR accessory for quantitative analysis of solids samples is presented. As a case study the concentration of cinnarizine in commercial tablets has been determined from DRIFTS and SR-DL infrared (IR) and near-infrared (NIR) spectra recorded using DTGS (deuterated triglicine sulphate) detector in the IR and NIR regions and InGaAs (indium-gallium arsenide) detector in the NIR range. Based on these spectra Partial Least Squares (PLS) models were constructed and relative standard errors of prediction (RSEP) were calculated for the calibration, validation and analysed data sets. They amounted to 2.4–2.5%, 2.1–2.7% and 2.0–2.6% for the DRIFTS attachment while 2.1–2.2%, 2.0–2.3% and 1.9–2.6%, respectively, for the modified SR accessory. Obtained error values indicate that modified SR accessory can be effectively used for quantification of solid pharmaceutical samples in the mid- and near-infrared regions.

1. Introduction

Diffuse reflectance FTIR spectroscopy (DRIFTS) is one of the most important solid-state sampling techniques which has found an extensive use in pharmaceutical and food industry [1–6]. DRIFTS has a number of benefits over other analytical methods. It is fast, reliable, non-destructive, cost effective method, requiring minimal or no sample preparation. An important advantage is that different components present in the analysed sample can be determined simultaneously from a single spectrum. Depending on the spectral range and optical properties of samples they can be investigated 'as-received' or after dilution with a non-absorbing material, such as KBr or KCl [5].

An alternative to DIRFTS attachment can potentially be simpler and cheaper specular reflection (SR) accessory which is usually applied for registering spectra of films on metallic substrates and of polymers [7,8]. This device is not commonly used in quantitative analysis of solid samples. In this work, an application of SR accessory working in a DRIFTS like mode [9], for quantitative analysis of solids samples is described. A case studies were performed using cinnarizine tablets.

Cinnarizine, 1-benzhydryl-4-[(E)-3-phenylprop-2-enyl] piperizine is a nootropic and antihistamine drug. It is mainly used for the control of vomiting due to motion sickness but also to promote cerebral blood flow and cerebral arteriosclerosis treatment [10]. European Pharmacopeia describes a non-aqueous titration for cinnarizine assay [11]. Several other procedures of cinnarizine quantification including high performance liquid chromatography [12], electrochemical [13,14], spectrometric [13,15] and fluorometric [16] methods were also reported.

Infrared radiation directed onto the surface of a thick solid sample can be absorbed or reflected. The specular component of the reflected radiation obeys Fresnel's reflection law. Specular reflection dominates in the case of smooth surfaces. Instead for rough surfaces mainly diffuse reflection takes place. An incident ray is reflected in all directions, at angles different from the angle of incidence.

To relate concentration C of an analyte quantified in diffuse reflection experiment to the measured intensity of reflected radiation one can use Kubelka Munk equation:

$$f(R) = \frac{(1-R)^2}{2R} = kC, \quad (1)$$

where the absolute remittance $R=J/I_0$ is the ratio of the intensity of reflected radiation J and the intensity of the incident beam I_0, while the coefficient k depends on the absorption and scattering properties of the studied substance [17].

In Fig. 1 optical ray diagrams for a representative DRIFTS attachment and for the modified SR accessory are shown. In the former one,

* Corresponding author.
E-mail address: roman.szostak@chem.uni.wroc.pl (R. Szostak).

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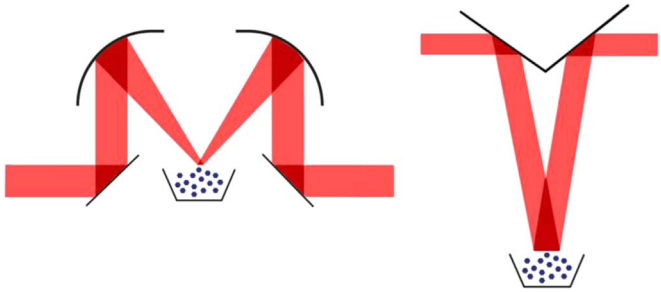

Fig. 1. Optical ray diagrams for DRIFTS (left) and modified SR (right) accessories.

infrared radiation from the source reflected by a plane mirror is focused by a spherical mirror at the sample. The radiation diffusely reflected by the sample is collected by another spherical mirror and directed by the second plane mirror to the detector. The area probed by the ray depends on the particular construction of DRIFTS accessory and on its alignment [3]. The set-up of SR accessory is much simpler. It consists just of two plane mirrors joined at an angle α, in our device α=120°. In that case the only possibility of alignment is connected with the vertical movement of the sample what enables modification of the probed area. Despite their simplicity SR accessories usually transmit smaller portion of the spectrometer source energy to the detector than typical DRIFTS ones.

In the present work, the application of a modified SR accessory for quantitative analysis of solids samples is presented. Based on the DRIFTS and SR-DL infrared and NIR spectra, commercial cinnarizine tablets containing 12.1% of the active pharmaceutical ingredient (API) were quantified. Simultaneous quantification of cinnarizine was performed using FT-Raman spectroscopy.

2. Experimental

2.1. IR and NIR spectra

IR and NIR spectra were recorded using a Nicolet Magna 860 FTIR spectrometer equipped with a DTGS detector. A KBr beamsplitter was applied during mid-infrared measurements while a CaF_2 beamsplitter was used in the NIR region (Thermo Nicolet, Madison, USA). NIR spectra were recorded also using a Nicolet Nexus FTIR (Thermo Nicolet, Madison, USA) spectrometer equipped with a InGaAs detector and a CaF_2 beamsplitter. The interferograms were averaged over 128 scans, Happ-Genzel apodized and Fourier transformed, with a zero filling factor of 2, giving IR and NIR spectra with the resolution 4 cm^{-1} in the 400–4000 cm^{-1} and in the 4000–9500 cm^{-1} ranges, respectively. It took approximately 2 min to obtain a spectrum. Diffuse reflectance spectra were obtain using a Seagull (Harrick, New York, USA) optical assembly set to the DRIFTS mode while rotated by 180° degrees (upside-down) Spec Series (Pike technologies, Madison, USA) specular reflectance unit was applied to collect DRIFTS like spectra with a sample placed in a steel cups of 20 mm diameter and 1–2 mm depth.

2.2. Raman spectra

Raman spectra were recorded using a Thermo Nicolet Magna 860 FTIR spectrometer interfaced with an FT-Raman accessory. A CaF_2 beam splitter and indium-gallium arsenide (InGaAs) detector were used. Samples in the form of pellets were placed in a rotating sample holder. They were illuminated by Nd:YVO_4 laser line at 1064 nm with a power of 300 mW at the sample, and the backscatter radiation was collected. The interferograms were averaged over 256 scans, Happ-Genzel apodized and Fourier transformed using a zero filling factor of 2 to give spectra give spectra in the 100–3700 cm^{-1} range at a resolution 8 cm^{-1}. The samples were rotated at a constant speed of about 200 rpm.

2.3. Reference analysis

Reference quantification of cinnarizine was performed according to the method described by Abdine et al. [15]. Ultraviolet-visible (UV–vis) spectra of cinnarizine chloroform solutions were collected in 1 cm quartz cell in a 200–600 nm range with a resolution of 1 nm using a Carry Varian 100 (Agilent, Santa Clara, USA) spectrometer.

2.4. Materials and sample preparation

Using cinnarizine of pharmacopoeial purity (Hasco Lek, Wrocław, Poland) 45 calibration samples were prepared. The excipients, namely lactose, sodium starch glycolate, silicon dioxide and magnesium stearate were of analytical purity. The mass fraction varied in the 0.07–0.19 range for cinnarizine, 0.67–0.80 for lactose, 0.01–0.11 for silicon dioxide, 0.01–0.13 for sodium starch glycolate and 0.005–0.033 for magnesium stearate (Table S1 in the Supplementary Material). The samples were prepared by mixing constituents in a mortar for a few minutes, to homogenise them properly. Approximately 8 mg of each mixture was diluted with 400 mg of dried KBr to collect DRIFTS and SR-DL spectra in the MIR region. 220 mg of sample was utilised during NIR measurements and 200 mg was used to prepare a pellet for Raman measurements. Analysed, commercial tablets were processed in a similarly way.

2.5. Software and data analysis

To construct PLS models Nicolet TQ Analyst ver. 7 (Thermo Nicolet, Madison, USA) was used. Principal component analysis (PCA) was performed using MathWorks Matlab combined with PLS Toolbox (Eigenvector, Natwick, USA). To characterize the predictive abilities of the developed models, the relative standard errors of prediction (RSEP) were calculated according to the equation:

$$RSEP(\%) = \sqrt{\frac{\sum_{i=1}^{n}(C_i - C_i^A)^2}{\sum_{i=1}^{n} C_i^{A^2}}}\,100\%, \quad (2)$$

where C^A is the actual component content, C is the concentration found from the analysis and n is the number of samples. The RSEP errors were calculated for calibration, validation and analysed samples. Cross-validation, using leave one-out technique, was used to estimate the performance of constructed models. The root mean squared error of cross-validation (RMSECV) was calculated to select an optimal number of factors for PLS models.

3. Result and discussion

In Fig. 2 mid IR (MIR) spectra, obtained using modified SR accessory, of pure cinnarizine, excipients, commercial tablet and calibration sample are presented. Other analogous sets of DRIFTS, SR-DL and Raman spectra are provided in Supplementary Material (Figs. S1–S6). It can be noticed that spectra recorded using SR accessory and DTGS detector are nosier than the corresponding DRIFTS spectra both in MIR and NIR regions. Application of more sensitive detector (InGaAs) results in an improvement of the quality of SR-DL spectra. Typical values of a signal to noise ratio (SNR) are collected in Table 1.

Thirty one samples were used for training purposes, nine samples constituted the validation set and five samples were treated as outliers (Table S2 in Supplementary Material). The conformity of the composition of the calibration/validation samples and of the analysed tablets was controlled using PCA for each of the applied spectral technique. In Fig. 3 scores plots obtained on the basis of SR-DL and DRIFTS NIR spectra registered with the InGaAs detector are presented. In both