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ScienceDirect
Talanta 74 (2008) 1603–1607
Talanta
www.elsevier.com/locate/talanta

Pharmaceutical powders analysis using FT-Raman spectrometry: Simultaneous determination of sulfathiazole and sulfanilamide

Macarena López-Sánchez, María José Ruedas-Rama, Antonio Ruiz-Medina, Antonio Molina-Díaz, María José Ayora-Cañada *

Department of Physical and Analytical Chemistry, Faculty of Experimental Sciences, University of Jaén, 23071 Jaén, Spain

Received 20 June 2007; received in revised form 7 September 2007; accepted 3 October 2007
Available online 16 October 2007

Abstract

A procedure for rapid quantitative analysis of pharmaceutical powders is described. Powdered samples were measured in a rotating cell in order to avoid sub-sampling problems by increasing the irradiated area. Quantitative determination of sulfathiazole and sulfanilamide, using a simple univariate calibration model is proposed. Even though both antibacterials are of the same chemical family (sulfonamides), the richness of structural information contained in the Raman spectra allowed their determination using the area of two selected bands (1255 and 1629 cm^{-1} for sulfathiazole and sulfanilamide, respectively). Relative standard deviation (R.S.D.) values ($n = 10$) of 3.35% and 3.46% for sulfathiazole and sulfanilamide, respectively, demonstrate the good reproducibility of the measurement technique with the rotating cell. The method was successfully applied to the analysis of synthetic mixtures and commercial pharmaceutical powders. The procedure is suitable to be applied to pharmacopoeial uniformity of content testing of batches.

Keywords: Pharmaceuticals; Raman spectrometry; Solids; Powders; Quantitative determination; Sulfonamides; Sulfathiazole; Sulfanilamide

1. Introduction

Raman spectrometry is a rapid, non-destructive, non-invasive and reliable tool that is finding increasing application in the field of pharmaceutical analysis [1,2]. The richness of the vibrational spectroscopic information allows qualitative and quantitative analysis even of polymorphic crystal forms. Quantitative analysis can be performed either by manually selecting some of the bands due to each of the target compounds [3] or by using multivariate data analysis techniques [4,5] (i.e. partial least squares regression (PLS)). Raman spectroscopy is becoming an excellent analytical tool for both process control and finished product control in pharmaceutical production. The technique can be used to study solids, liquids, powders, gels, slurries and aqueous solutions without requiring any special sample preparation. It means that many studies may be performed in situ. Several approaches to direct active ingredient quantification in pharmaceuticals and audits on polymorphs have already been reported but there is still a lack of widespread acceptance of the technique in routine pharmaceutical analysis.

The major problem in the analysis of solid samples by Raman spectrometry appears because tablets or powders are heterogeneous on length scales greater than the size of a typical focused laser spot, which illuminates only a tiny area (50–500 μm) to collect spectral information. Two different approaches have been described to overcome this problem. One of them consists on measuring several spectra for each sample, with the position of the sample being changed randomly for each measurement. The average spectrum is then taken for the analysis [6]. A second useful approach to represent average sample composition is rotation of the sample during Raman collection to cover a wider surface area. It has been demonstrated that this procedure leads to improved calibration performance [7].

When dealing with powdered samples, the use of immersion probes with increased sampling area and continuous rotation of the sample in a vial have been demonstrated to provide good reproducibility [8,9]. Without the use of probes, the most common approach to rotate pharmaceutical powders and to measure them by means of Raman spectrometry involves grinding in a mortar for a few minutes and then preparing a pellet in a sim-

* Corresponding author. Fax: +34 953212940.
E-mail address: mjayora@ujaen.es (M.J. Ayora-Cañada).

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doi:10.1016/j.talanta.2007.10.015

ilar way to that used in IR spectroscopy [10–12]. This pellet can be then easily rotated. Another previously described procedure to increase sampling area consisted in placing the powders in a NMR-tube and rotating it with one motor while moving it up and down with a second motor [13]. In this work, a novel procedure for quantitative analysis of powders avoiding the time-consuming step of preparing pellets will be evaluated. It involves the use of a dedicated cell which facilitates the rotation of the powders achieving a large sampling area by using only one motor. Furthermore, the feasibility of quantifying closely related chemical substances on the basis of their distinct Raman spectral features using simple univariate calibration will be evaluated. Two sulfonamides (sulfathiazole and sulfanilamide), an important class of antibacterial agents used in medicine and veterinary practice, have been chosen as model analytes.

2. Experimental

2.1. Materials

Sulfathiazole and sulfanilamide were obtained from Aldrich (Madrid, Spain). Commercially available powder (Wilfe, containing g: 69.7 g sulfathiazole and 30.3 g sulfanilamide per 100 g *Ltd. Pérez Giménez*) was purchased in a local pharmacy.

2.2. Raman spectrometer and measurement cell

Raman spectra were recorded using a Bruker RFS (FT)-Raman Spectrometer fitted with a liquid nitrogen-cooled Ge detector. The excitation radiation was the 1064 nm line from a Nd–YAG laser (Coherent) with a laser power of 1.3 W using a non-focused laser beam. The Raman scattered radiation was collected at 180° geometry. All spectra were recorded with a resolution of 4 cm^{-1} and were averaged over 64 scans.

The measurements were made in a homemade cell (see Fig. 1). This consisted of a metallic washer over a glass window. The powdered sample was introduced into the washer hole, covered with an adhesive label and attached to a magnet. The cell was fixed to a synchronous motor mounted in the sample compartment by means of the magnet. The sample remained in the space between the magnet and the glass (20 mm inner diameter and 2 mm depth). The motor rotated the sample cell around the axis of the laser beam (5 r.p.m.) to yield an irradiation pattern of a circumference with a radius of 3 mm.

2.3. Procedure

To obtain the calibration curves, standards with suitable weight ratios of sulfathiazole and sulfanilamide were prepared by mixing accurately weighed amounts of both pure solids in a mortar and grinding for a few minutes to homogenise the powders properly. Powder samples of commercial formulations were also grinded in the mortar.

Approximately 300 mg of powder were placed into the homemade cell. Standards and samples were analysed by triplicate and calibration graphs were obtained by plotting selected band areas against the sulfonamides concentration expressed as a

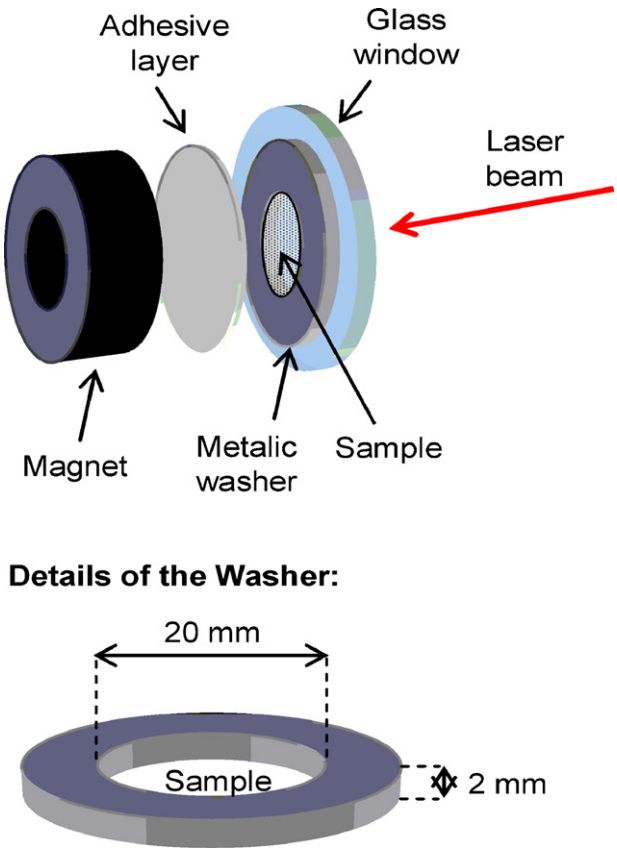

Fig. 1. Scheme of the measurement cell.

weight percent. Band areas were calculated employing one-point baseline correction. The range 1624–1636 cm^{-1} was used for sulfanilamide. A baseline point obtained averaging four points in the range 1650–1660 cm^{-1} was employed. Sulfathiazole was quantified using the band area between 1246 and 1276 cm^{-1} (baseline point average of four points between 1220 and 1230 cm^{-1}).

3. Results and discussion

3.1. Raman spectra of sulfathiazole and sulfanilamide

The FT-Raman spectra of sulfathiazole and sulfanilamide in solid state are presented in Fig. 2. The most intense spectral features, common to both sulfonamides, are located around 1595 and 1135 cm^{-1}. They can be assigned to the stretching of the benzene ring and the symmetric stretching of the SO_2 group, respectively [14]. In addition to these common bands, each sulfonamide showed spectral singularities. Thus, the S–N stretching is observed at 900 cm^{-1} in the spectrum of sulfanilamide [15] and characteristic bands of thiazole ring involving the C–S stretching mode are observed in sulfathiazole spectrum at 633 and 732 cm^{-1} [16]. Two bands, 1629 and 1255 cm^{-1} were selected for quantification of sulfanilamide and sulfathiazole, respectively. These bands are specific for each sulfonamide, without any contribution from the other one. The assignment of the band at 1255 cm^{-1} characteristic of sulfathiazole is dif-