Journal of Pharmaceutical Analysis 2012;2(2):90–97

Contents lists available at ScienceDirect

Journal of Pharmaceutical Analysis

www.elsevier.com/locate/jpa
www.sciencedirect.com

ORIGINAL ARTICLE

Determination of drug, excipients and coating distribution in pharmaceutical tablets using NIR-CI

Anna Palou[a], Jordi Cruz[b], Marcelo Blanco[a], Jaume Tomàs[c], Joaquín de los Ríos[c], Manel Alcalà[a,*]

[a]*Unitat de Química Analítica, Departament de Química, Facultat de Ciències, Universitat Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain*
[b]*Escola Universitària Salessiana de Sarrià, Passeig Sant Joan Bosco, 74, 08017 Barcelona, Spain*
[c]*Esteve Farma, c/Sant Martí s/n, 08197 Martorelles, Barcelona, Spain*

Received 7 October 2011; accepted 15 November 2011
Available online 22 November 2011

KEYWORDS

Near infrared Chemical Imaging (NIR-CI);
Hyperspectral imaging;
Component distribution;
Tablet coating distribution;
Partial Least Squares (PLS) regression

Abstract The growing interest of the pharmaceutical industry in Near Infrared-Chemical Imaging (NIR-CI) is a result of its high usefulness for quality control analyses of drugs throughout their production process (particularly of its non-destructive nature and expeditious data acquisition). In this work, the concentration and distribution of the major and minor components of pharmaceutical tablets are determined and the spatial distribution from the internal and external sides has been obtained. In addition, the same NIR-CI allowed the coating thickness and its surface distribution to be quantified. Images were processed to extract the target data and calibration models constructed using the Partial Least Squares (PLS) algorithms. The concentrations of Active Pharmaceutical Ingredient (API) and excipients obtained for uncoated cores were essentially identical to the nominal values of the pharmaceutical formulation. But the predictive ability of the calibration models applied to the coated tablets decreased as the coating thickness increased.

1. Introduction

Near Infrared-Chemical Imaging (NIR-CI) is a technique based on conventional NIR spectroscopy with the added advantage that it affords recording of a large amount of both spectral and spatial information in a single image. While the conventional NIR technique only provides the average spectrum for the surface of each sample, NIR-CI gives one spectrum per pixel in each acquired image and hence much more information about the whole sample surface [1]. The easiness to obtain this information through with NIR-CI has aroused interest in NIR-CI in many fields of study. This is

*Corresponding author. Tel./fax: +34 935814899.
E-mail address: manel.alcala@uab.cat (M. Alcalà)

Peer review under responsibility of Xi'an Jiaotong University.
doi:10.1016/j.jpha.2011.11.003

Production and hosting by Elsevier

particularly applicable in the analysis of pharmaceutical products, which is made easy by NIR-CI by virtue of its ability to acquire a vast amount of information in an expeditious manner, all without altering the sample. The increasing interest aroused by NIR-CI in the pharmaceutical field is evident from the variety of studies based on this technique reported in recent years. Such studies include the homogeneity of powder samples [2], particle size determinations [3], product composition [4], the determination of the concentrations and distribution of components in solid tablets [5] and content uniformity [6], among others. Also, the many uses of NIR-CI in the pharmaceutical industry have been the subject of two interesting reviews [1,7].

Film coatings on commercial tablets have been the subject of some study [8,9], but not so much as pharmaceutical components despite their significance. The coating film applied to a drug tablet is primarily intended to improve its esthetics and function. Thus, the coating allows the unpleasant taste of some APIs to be masked and facilitates swallowing of tablets, in addition to preserving their integrity and giving them a uniform appearance. Some coatings, however, are intended to facilitate the controlled or enteric release of the dosage form of a drug [10]. In any case, the exact function of a coating depends largely on its thickness and distribution on the tablet surface. In fact, too thin or too thick a coating can alter the effectiveness of a tablet by making the core more vulnerable to external factors or diminishing the API release rate. Simply measuring the average thickness of the lacquer film on a tablet is inadequate to ensure that the tablet will meet the specifications; rather, this requires obtaining more information about the way the coating is distributed throughout the tablet surface. The capabilities of the NIR-CI technique in this respect make it a suitable choice for quality control in tablet production processes.

However, the vast amount of information contained in a hyperspectral image requires the use of an effective procedure to extract it. In fact, hyperspectral data form a three-way cube that must be unfolded and processed with appropriate two-way multivariate algorithms in order to extract the target information.

In those cases where some components of a pharmaceutical are unknown or a spectrum unavailable, algorithms requiring no calibration set are especially useful; such algorithms include Multivariate Curve Resolution-Alternating Least Squares (MCR-ALS) [11] and its augmented form [12]. However, the process involved in extracting information from chemical images can be slow and cumbersome. One alternative choice in wide use for the quantitative analysis of CI data is Partial Least Squares (PLS) [13]. The Isys software included with the NIR-CI instrument allows the easy application of PLS for a rapid and accurate determination of components distribution in a sample. This algorithm requires a series of data distributed over a wide enough range of specific values of the target property to allow the construction of a suitable calibration model for the samples to be analyzed. Each pixel of the image is assigned to a response matrix based on the similarity of its spectra with those for the pure components [14].

In this work we intend to evaluate the distribution of the components in a tablet and quantify the thickness and surface distribution of the film coating during the development of a new pharmaceutical formulation. Individual calibration models for the components were used to obtain their distribution map and a calibration model derived from the NIR-CI hyperspectral image was used to establish the distribution map for the coating film.

2. Materials and methods

2.1. Samples

We studied three different types of samples, namely: (a) cores (uncoated tablets), (b) tablets with a coating of variable thickness and (c) tablets with the standard coating. The coated tablets (b) included samples with film thicknesses between $0x$ and $3x$, where x is considered the standard coating thickness of tablets (c).

We consider the coating process is constant and reproducible along time. The standard time encompasses a coating thickness namely x. The double or triple of this standard time are named $2x$ and $3x$. The reference coating thickness has been calculated measuring the approximate tablet surface (1.92 cm^2), the tablet weight difference before and after coating (from 290 mg to 317 mg) and the real density of the coating polymer (1.19 g/cm^3). This measurement was 39.4 μm of coating thickness for a x standard coating time, 21.9 μm for $0.5x$, 78.8 μm for $2x$ and 118.2 μm for $3x$. The estimated measurement for a standard x coating time (39.4 μm) was quite similar to the coating thickness obtained by scanning electron microscopy (SEM, 40 μm). However, we could not compare the calculated thickness and the SEM results for all the coating levels. In this work, all the coating thickness results are referred to the x standard coating time instead of the microns measurements, in order to simplify and better understand the conclusions.

The uncoated cores had the same API and excipient composition, namely: 35% API and 65% excipients. The excipient mixture contained 40% of excipient #1, 20% of excipient #2, 2% of excipient #3, 1.5% of excipient #4 and 1.5% of excipient #5. The API and the two major excipients in combination accounted for 95% of the tablet content. The presence of the lacquer in the coated tablets reduced the proportions of API and excipients to an extent dependent on the coating thickness. Table 1 shows the resulting changes in the major components.

The samples in groups a and b were used to determine the concentrations of the tablet components (API and excipients).

Table 1 Composition (% w/w) of API and the two major excipients at different coating levels.

Coating level	Sample composition (% w/w)		
	API	E #1	E #2
$0x$	35.0	40.0	20.0
$0.5x$	34.4	39.3	19.7
$1x$	33.9	38.8	19.4
$2x$	33.0	37.7	18.7
$3x$	32.0	36.6	18.3

$0x$ means uncoated core and $1x$ means nominal standard coating.