Quantitative analysis of Piroxicam polymorphs pharmaceutical mixtures by hyperspectral imaging and chemometrics

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Introduction

In the pharmaceutical industry the polymorphic form of drug is very relevant as it affects the solubility, potentiality and the bioavailability of the drug. Much effort is demanded from regulatory authorities and patent attortneys to determine whether polymorphs exist .

The chemical information necessary for the study of pharmaceutical tablets, including polymorphism, is not restricted to the quantification of compounds present in the samples. Important parameters are possible to be obtained through mapping distribution of the constituents. Thus, the imaging spectroscopy using near infrared region may obtain data directly from the tablets surface bringing advantages like: fast and non-destructive sample analysis and it does not produce waste neither require preparation of the sample.

In this work, attempts have been made to apply chemometric methods to imaging analysis of pharmaceutical formulations for quantification and distribution of polymorphic forms in the Piroxicam drug.

Objectives

In this work, attempts have been made to apply chemometric methods to image analysis of pharmaceutical formulations for quantification and distribution of polymorphic forms in the Piroxicam drug.

Methodology

In this work, it was used Piroxicam from EMS Sigma Pharma (Brazil), which was found to correspond to form 1 by comparison with PXRD spectra [3] and [4]. Form 2 was prepared from form 1. The form 2 (needles) was obtained by the crystallization from saturated Piroxicam solution in absolute ethanol (aliphatic alcohol) at room temperature. For the proposed study 55 pharmaceutical formulations containing the two polymorphic forms in the excipients (Lactose, NaHCO3, talc, starch, magnesium stearate) were made. The concentrations of form 1 were made in the range from 1% (w/w) to 90% (w/w) for pharmaceutical formulations while for form 2 the concentrations were from 1% (w/w) to 85% (w/w).

The acquisition of images was performed using the Spotight 400N FT-NIR Imaging by PerkinElmer. For each tablet, a three way array data (100x100 pixels and 239 λ) has been obtained and unfolded for pre-processing by the detrend, orthogonal signal correction and first derivative combination. Thereafter, PCA has been used to obtain distribution of pixels information. The compound distribution maps have been acquired through a PLS model.

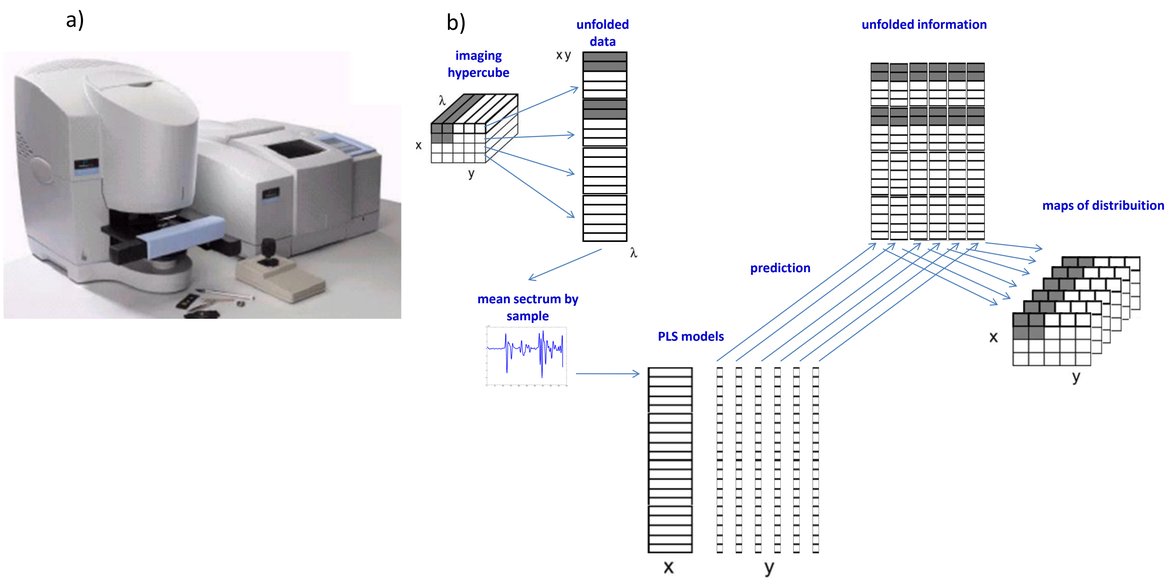

Figure 1: a) – Spotight 400N FT-NIR Imaging; b) PLS model developed

Results

The distribution maps (Fig. 2) have been obtained by PLS for all compounds.

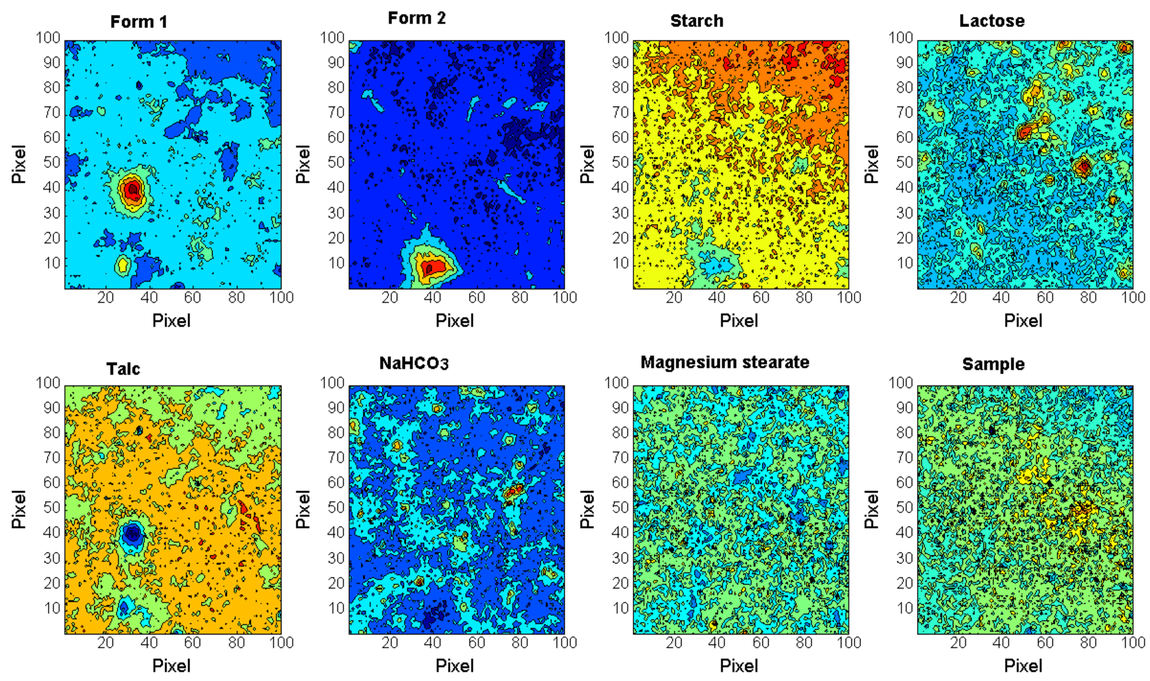

Figure 2 – PLS distribution maps

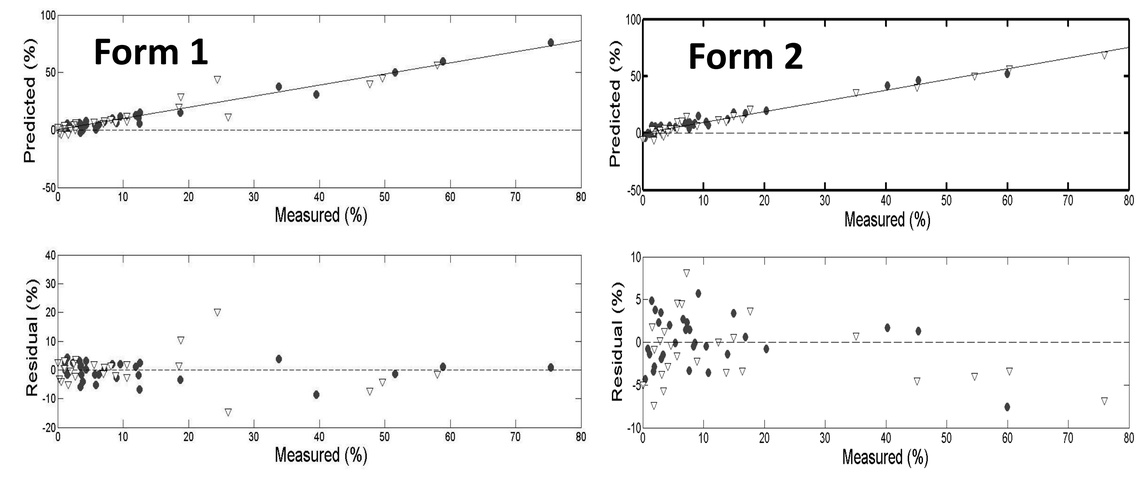

Figure 3 – Plot of predicted versus reference values for Piroxicam by PLS. Calibration (●) and validation (Δ) samples.

Tabel 1 : Results of PLS analysis

	RMSEC (%(w/w))	RMSEP (%(w/w))	$R_{calibration}$	$R_{validation}$
Form 1	3.25	3.72	0.99	0.99
Form 2	2.92	3.66	0.98	0.98

Conclusions

A method to perform partial least squares regression (PLS1) prediction on hyperspectral data was presented. It was possible to reach information with excellent chemical precision per pixel of image. Through this study it was obtained the location and content of the two polymorphic forms in Piroxicam drug satisfactorily.It is believed that using this methodology it is possible to study particle size, interferences detection, quality process, as well as global information of the samples.

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