Monitoring dehydration on pharmaceutical tablets using temperature-series near-infrared hyperspectral imaging and chemometrics

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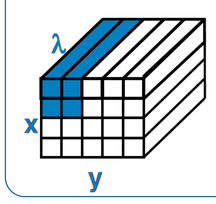
The formation of hydrates is a concern in the pharmaceutical development for the industry, once the hydrate forms have distinct physicochemical and pharmacological properties comparing with their respective anhydrate counterparts. In this sense, the understanding of the dehydration process of pharmaceuticals is relevant for assuring the final quality of the end products[1]. In this study, the dehydration of the mohonydrate (MH) forms of piroxicam (anti-inflammatory drug) and lactose (excipient) were investigated in tablets formulations using temperature-series NIR-hyperspectral imaging and chemometrics.

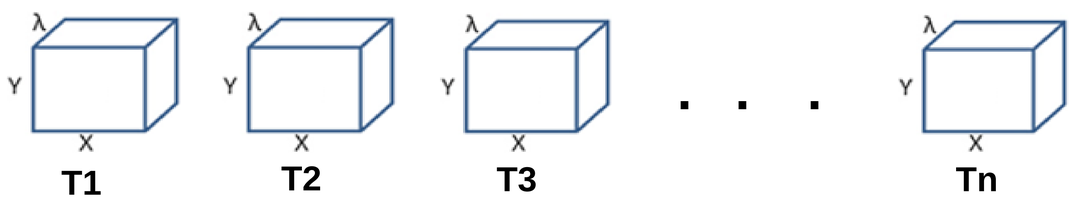
Hyperspectral Imaging



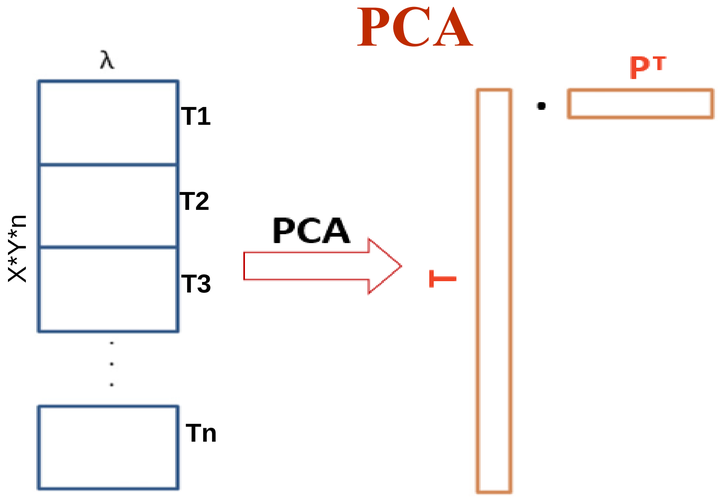
x and y = pixels coordinates in the sample surface

λ = spectrum variables

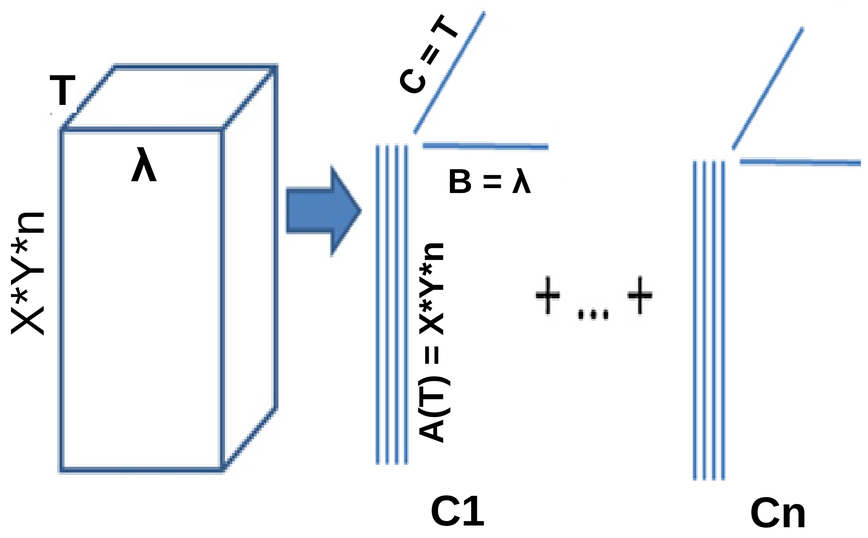
Temperature-series hyperspectral images and chemometrics



PCA

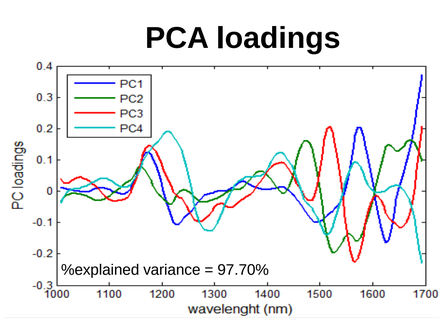


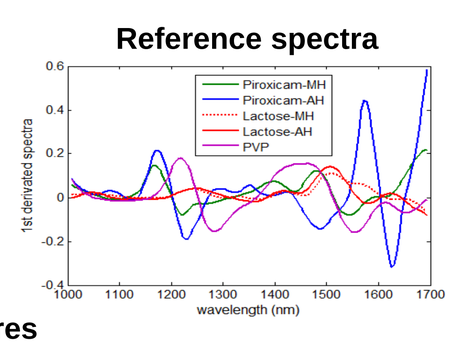
PARAFAC2

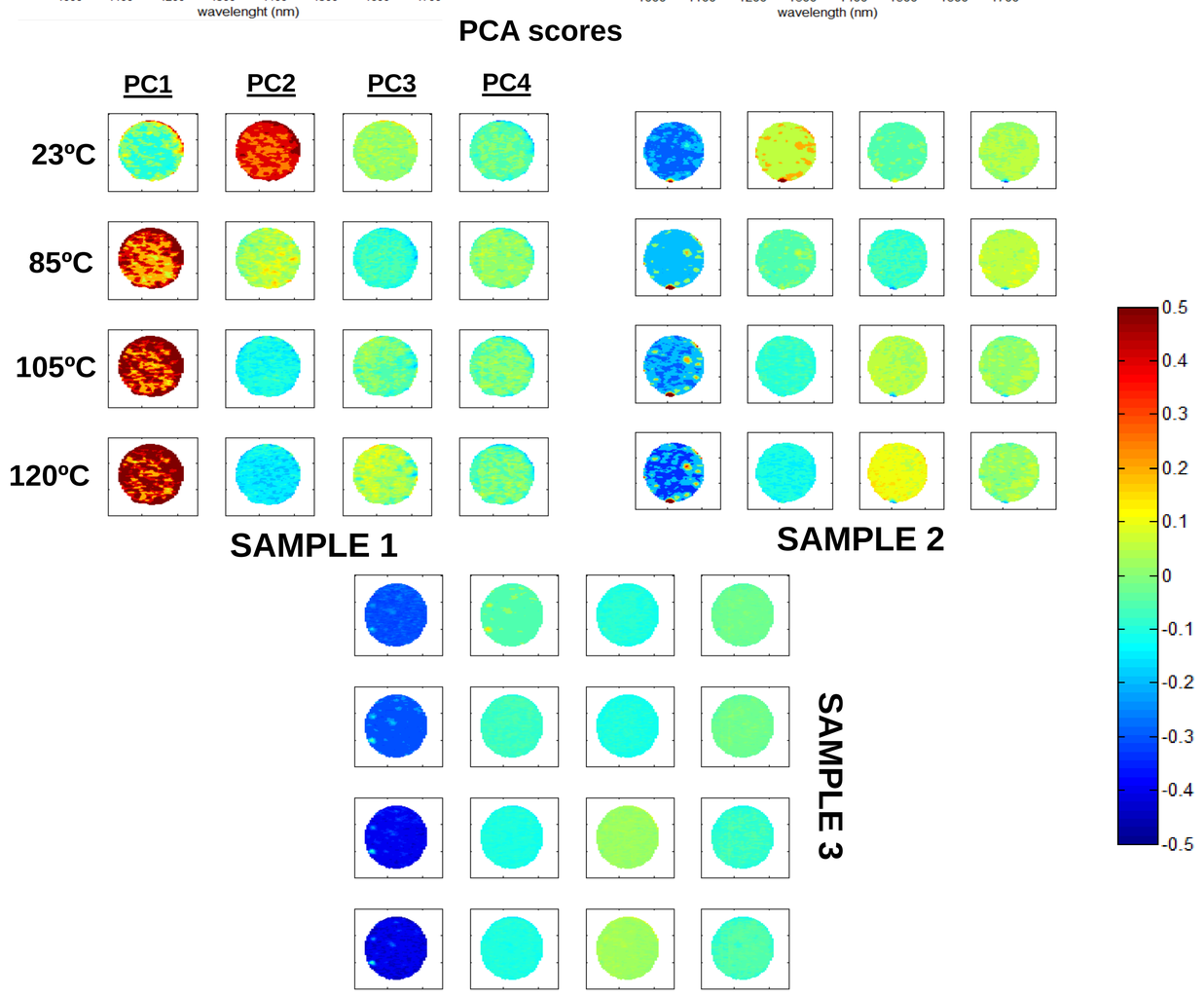


• RESULTS AND DISCUSSIONS

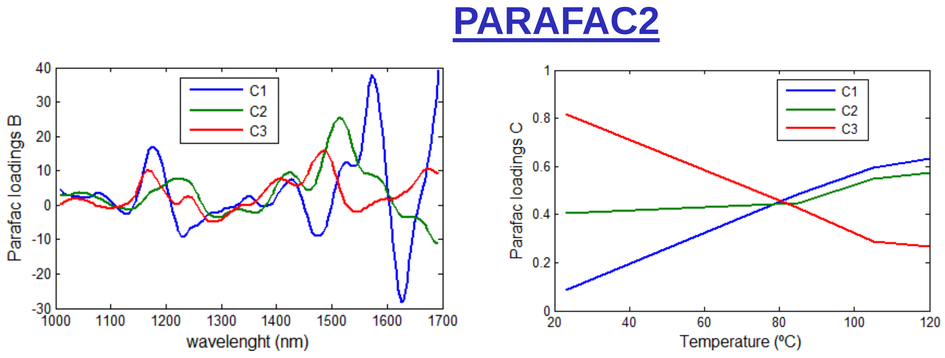
PCA







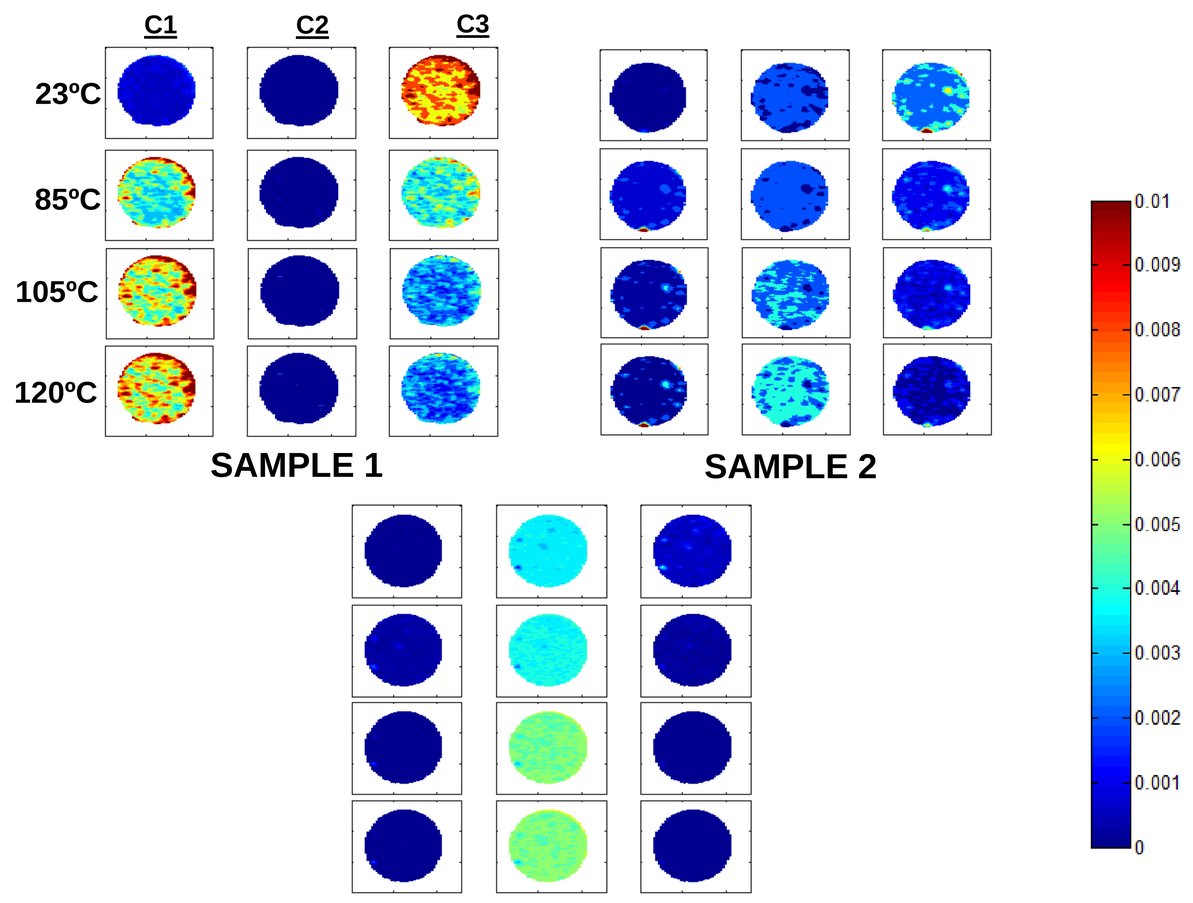
PARAFAC2



Core Consistency Diagnostic (CORCONDIA)

99.27

Parafac loadings – Mode A (Pixels)



- **Experimental**

Tablets composition:

Sample	Lactose-MH (mg)	Piroxicam-MH (mg)	PVP (mg)
1	45	210	45
2	105	105	90
3	210	45	45

Tablets compacted till 5.5 ton

Monitoring the dehydration of the tablets:

NIR-hyperspectral images of each tablets obtained after oven-heating in 4 different temperatures:

23ºC **85ºC** **105ºC** **120ºC**

Hyperspectral images acquisition:

The NIR-hyperspectral images were obtained with a spectrometer (Headwall photonics model 1002A-00371) working in the wavelength range of 1000–1700 nm with a spectral resolution of 7 nm and a line mapping configuration with a line of 320 pixels. The camera is a prototype kindly provided by FOSS (FOOS A/S, Denmark). Spectra were recorded in the reflectance mode, with pixels size (XxY) of 300x50 µm.

PCA: Loadings of PC1 and PC2 could be related to piroxicam-MH, piroxicam-AH, respectively, in which the last one being formed through the dehydration of the monohydrate form. PC3 describes mostly the formation of lactose-AH, more evidenced in sample 3. PC4 can be related to PVP (see ref. spectra).

PARAFAC2: A simpler model was obtained with only compounds that were affected by the tablet heating, *i.e.;* piroxicam-MH, piroxicam-AH and lactose-AH (see ref. spectra). The images are unambiguous for all the samples (differently from PCA), and the temperature mode reveals information about the dehydration kinect of the compounds.

[1] J.A. Zeitler,et al. *Drug hydrate and dehydration processes studies by terahertz pulsed spectroscopy.* Int. J. Pharm. 334 (2007) 78-84.

Acknowledgments: CAPES, CNPq