



JOURNÉES DE RECHERCHE EN SCIENCES DE LA SANTÉ
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Identification of pharmaceutical products using Handheld NIR and Raman spectrophotometers.

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Plan de la présentation

1. Introduction
2. Methodology
 - PCA et data preprocessing
 - Modelization
3. Results
4. Conclusion et prospect

1. Introduction

1.1. vibrational spectroscopy

Table 1. Comparaison of NIR and Raman spectroscopy

Critères	PIR	Raman
Nature of signal	Absorption	Diffusion (inelastic)
Selectivity	Low	High
Sensitivity	Medium	Low
Interference	Water and physical properties	Fluorescence and degradation of the sample
Applications	Identification, quantification, falsification detection, water dosing	Identification, quantification, falsification detection, study of polymorphic forms

1.2. objective

- Evaluate the performance of different spectrophotometers in the identification of pharmaceutical products directly in their primary packaging (eg blister)

Statistical comparison using the chemometric method of supervised classification: DD-SIMCA (Data-driven soft independent modeling of class analogy)

1.3. Context

Instruments: Market representatives: technology and performance

<u>Vibrational spectroscopy</u>	<u>Manufacturer</u>	<u>Model</u>	<u>Spectral range (cm⁻¹)</u>	<u>Data points</u>	<u>Pixel resolution (cm⁻¹)^a</u>	<u>Spectral resolution (cm⁻¹)^b</u>	<u>Weight (kg)</u>	<u>Price (k€)</u>
dispersive NIR	Tellspec Inc.	Enterprise scanner	11111 - 5882	256	20,4	N/A	0,14	~ 1,4
Raman (785 nm)	Ocean Optics Inc.	IDRaman version 1	400 - 2300	1901	1	28,9	0,35	~ 17

^acomputed as the analysed spectral range divided by the number of data points

^bcomputed following the ASTM E2529-06 guidance

Drug Samples

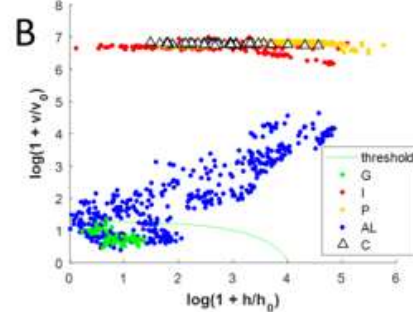
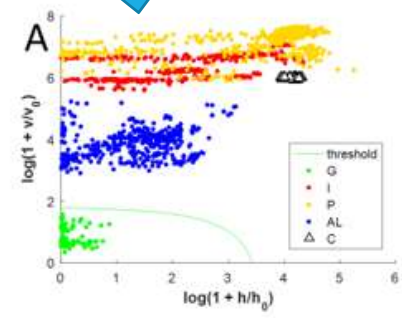
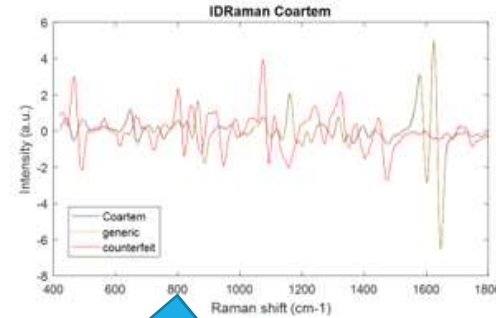
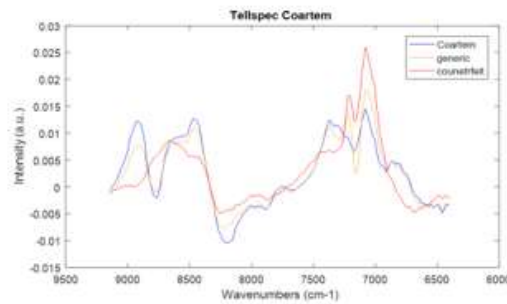
- **Paracetamol and various combinations:** highly dosed, high Raman scattering, and wide variety of possible combinations
- **Ibuprofen:** wide variety of colors and pharmaceutical forms (auto-fluorescence of a colored coating, soft capsules ...).
- **Artemether-lumefantrine:** falsifications.

2. Methodology

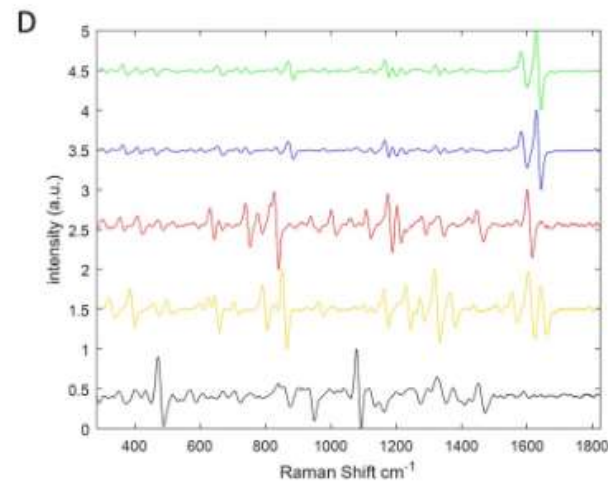
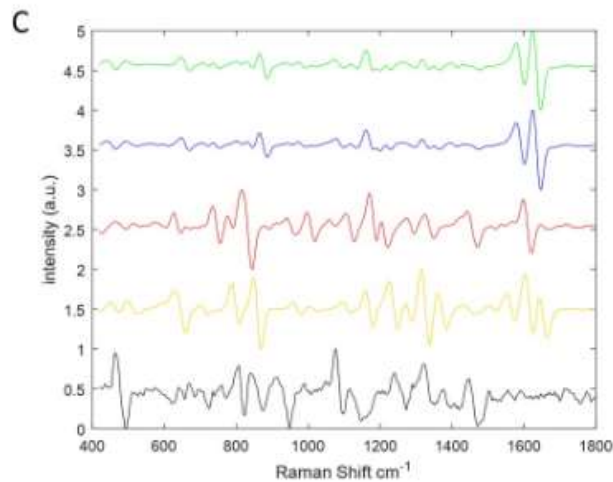
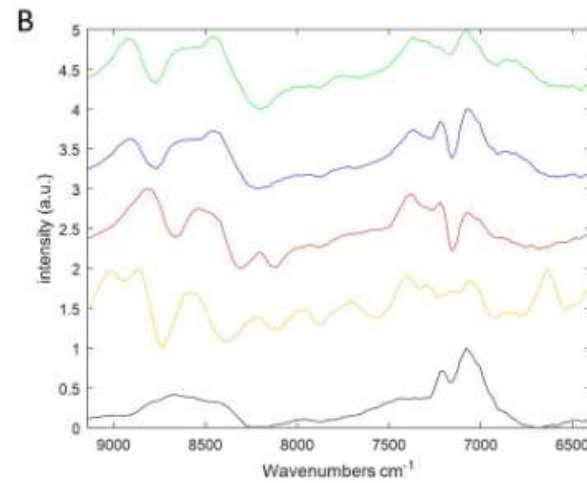
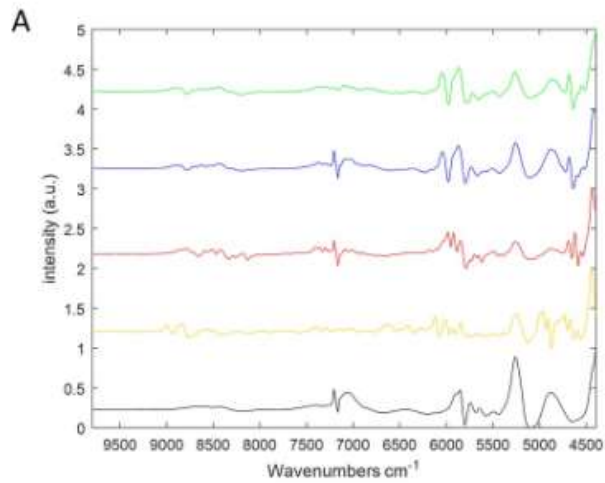


NIR and Raman handheld devices

Modelling



Comparing



Preprocessing methods

- The first derivative:
- Normalization: SNV

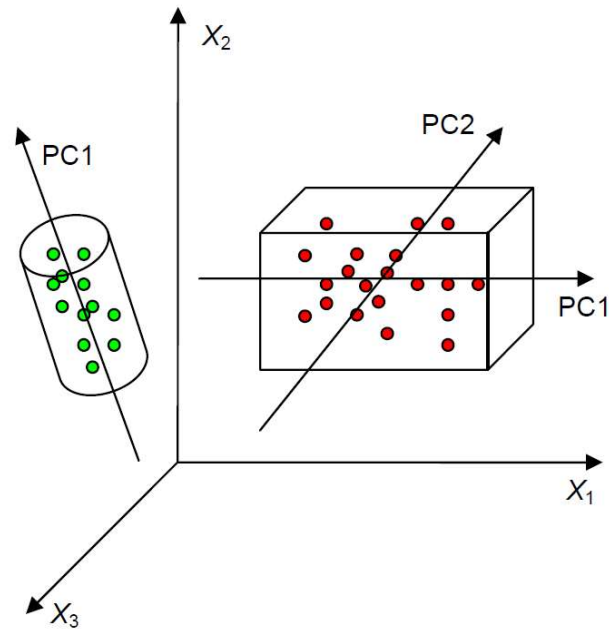
legends :

- Green spectra = median G-AL
- Blue spectra = median AL
- Red spectra = median I
- Yellow spectra = median P
- Black spectra = median C

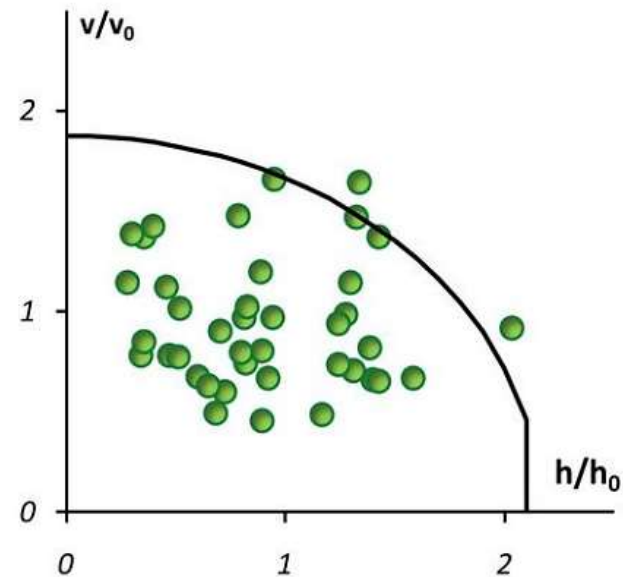
3. Results

Méthode 1. One class classification Model (DD-SIMCA)

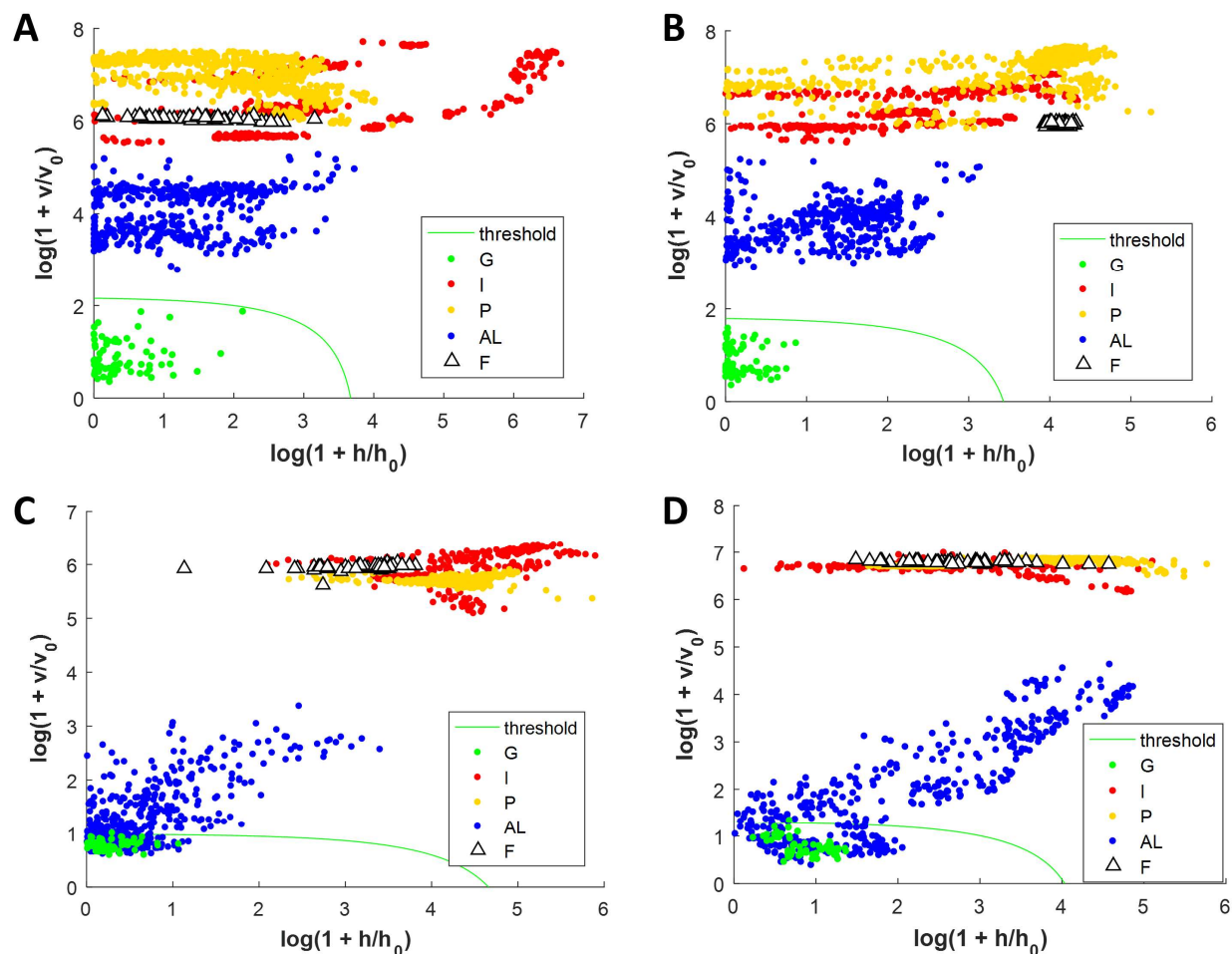
Figures 1. PCA, scores plots



Acceptance area



Figures 2. G-C DD-SIMCA acceptance plots



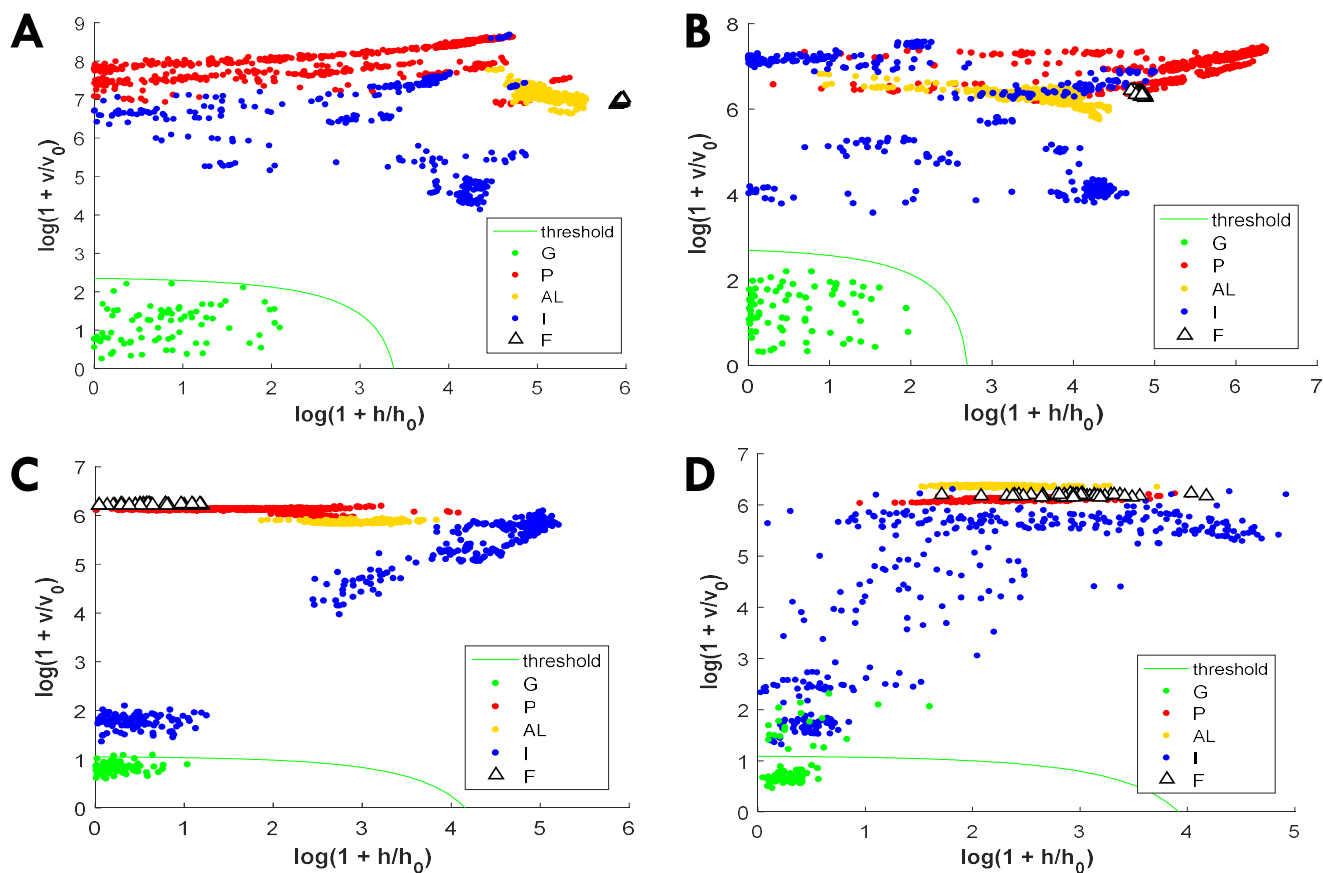
Model settings

- **Figure 2A:** NIR-A: autoscaling, 1PC, $\alpha=0.00001$
- **Figure 2B:** NIR-B: autoscaling, 1PC, $\alpha=0.0001$
- **Figure 2C:** Raman-A: autoscaling, 2PC, $\alpha=0.001$
- **Figure 2D:** Raman-B: autoscaling, 3PC, $\alpha=0.0001$

legends :

- "G" Coartem = reference artemether-lumefantrine samples;
- "I" ibuprofen samples;
- "P" paracetamol and paracetamol combination samples;
- "AL" artemether-lumefantrine generic samples
- "F" falsified coartem samples

Figures 3. G-I DD-SIMCA acceptance plots



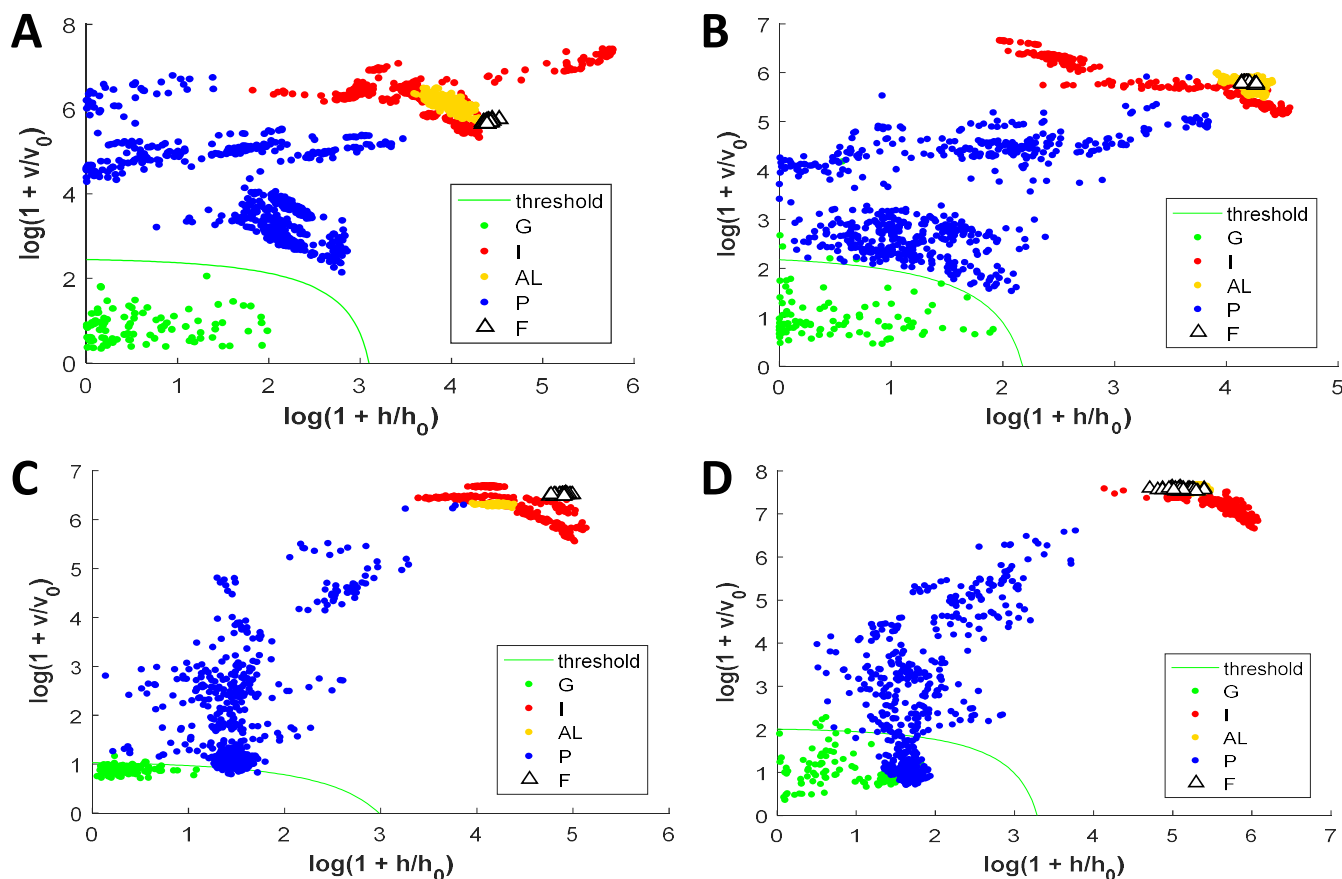
Model settings

- **Figure 2A:** NIR-A: autoscaling, 1PC, $\alpha=0.00001$
- **Figure 2B:** NIR-B: autoscaling, 1PC, $\alpha=0.001$
- **Figure 2C:** Raman-A: autoscaling, 2PC, $\alpha=0.000001$
- **Figure 2D:** Raman-B: autoscaling, 3PC, $\alpha=0.0001$

Legends:

- “G ” Ibuprofen EG = reference;
- “P” paracetamol and paracetamol combination samples;
- “AL” artemether-lumefantrine generic samples
- “I” ibuprofen samples;
- “F” falsified coartem samples

Figures 4. G-P DD-SIMCA acceptance plots



Model settings

- **Figure 2A:** NIR-A: autoscaling, 1PC, $\alpha=0.0001$
- **Figure 2B:** NIR-B: autoscaling, 1PC, $\alpha=0.02$
- **Figure 2C:** Raman-A: autoscaling, 6PC, $\alpha=0.0001$
- **Figure 2D:** Raman-B: autoscaling, 5PC, $\alpha=0.0001$

Legends:

- “G” Dafalgan = reference Paracetamol samples;
- “I” ibuprofen samples;
- “AL” artemether-lumefantrine generic samples
- “P” paracetamol and paracetamol combination samples;
- “F” falsified coartem samples

Table 2 : Figures of merit of NIR and Raman systems for DD-SIMCA model

Metrics	IBUPROFEN				PARACETAMOL				COARTEM			
	NIR-A	NIR-B	Raman-A	Raman-B	NIR-A	NIR-B	Raman-A	Raman-B	NIR-A	NIR-B	Raman-A	Raman-B
spectral range (cm ⁻¹)	6500-5000	9143-6399	284-1825	420-1800	9797-4397	9143-6399	284-1825	420-1800	9797-4397	9143-6399	284-1825	420-1800
preprocessing	SG(1,2,15) UA	SG(1,2,5) UA	SG(1,2,35) SNV	SG(1,2,25) SNV	SG(1,2,15) UA	SG(1,2,5) UA	SG(1,2,35) SNV	SG(1,2,25) SNV	SG(1,2,15) UA	SG(1,2,5) UA	SG(1,2,15) SNV	SG(1,2,25) SNV
Matthews correlation coefficient	1.000	1.000	0,977	0,842	1.000	0,971	0,891	0,337	1.000	1.000	0,421	0,472

SG: Savitzky-Golay (derivative, polynomial order, window size)

UA: unit area normalization

SNV: standard normal variate

$$MCC = \frac{TP \times TN - FP \times FN}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}}$$

4. Conclusion et perspectives

No ideal spectrophotometer.



The choice = final objectives of the analysis.

NIR system

For the identification of the specific product

Low cost equipment

Raman System

less effective in terms of brand recognition and discrimination

More interesting in chemical interpretation

In conclusion, portable vibrational spectroscopy devices are promising tools for identifying substandard and falsified drugs.



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