NEAR INFRARED SPECTROSCOPY – MULTIVARIATE ANALYSIS: A PROOF-OF-CONCEPT STUDY FOR NON-DESTRUCTIVE QUALITY CONTROL OF PHARMACEUTICAL PREPARATIONS

Marion Barrieu[1], Joëlle Claves[2], Mouloud Yessad[2], Yassine Bouattour[2], Mireille Jouannet[2], Philip Chennell[1]

[1] Université Clermont Auvergne, CHU Clermont Ferrand, Clermont Auvergne INP, CNRS, ICCF, F-63000 Clermont-Ferrand, France ; [2] CHU Clermont-Ferrand, Pôle Pharmacie, F-63003 Clermont-Ferrand, France

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INTRODUCTION

Quality control (QC) of pharmaceutical preparations (PP) is an essential part of the pharmaceutical drug compounding activity. However, qualitative and quantitative analytical assays nearly always require either a sample of the preparation (liquid forms) and can be destructive (solid forms). Near infrared spectroscopy - multivariate analysis (NIR-MVA) is a novel technology that could possibly be used for QC of PP in their primary container (syringes or bags) or dosage forms (capsules). **However, NIR-MVA is as of yet mostly untested in a hospital setting.**

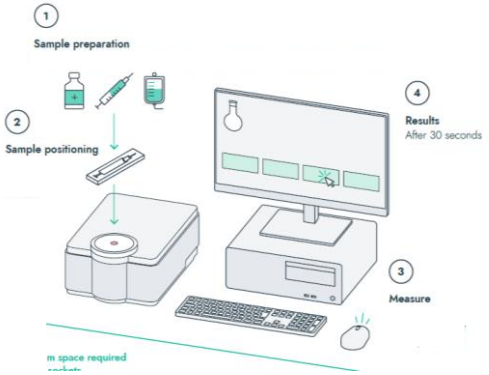
OBJECTIVE

The objective of this proof-of-concept study was to investigate the analytical capabilities of NIR-MVA for the QC of several PP.

MATERIALS AND METHODS

1. Materials

- Fourier-Transformation-NIR - spectrometer (TANGO-R®, Bruker)
- OPUSLAB software (Ayna Analytics) for signal interpretation and MVA.



2. Methods

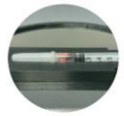
A. Quantification capabilities

- Spironolactone capsules
- Amikacin ophthalmic solution in amber glass vials
- Bevacizumab solutions (in polypropylene syringes or IV-bags)

➡ Results compared with local measurement methods

B. Discriminative capabilities (identification confirmation)

- Tested using multiple anticancer IV preparations (blinded analysis): 5 fluorouracil, gemcitabine, paclitaxel, carboplatine, oxaliplatine, nivolumab and bevacizumab.
- The preparations were conditioned in 100 or 250 mL multilayer polyolefin Freeflex IV-bags (Fresenius Kabi), depending on the available preparations.
- Data base: the spectra for each compound was acquired at least once (drug dependant).



NB: Each preparation was analysed either directly in its primary packaging (IV-bags, syringes, glass vials) or individual dosage form, without extraction (capsules).

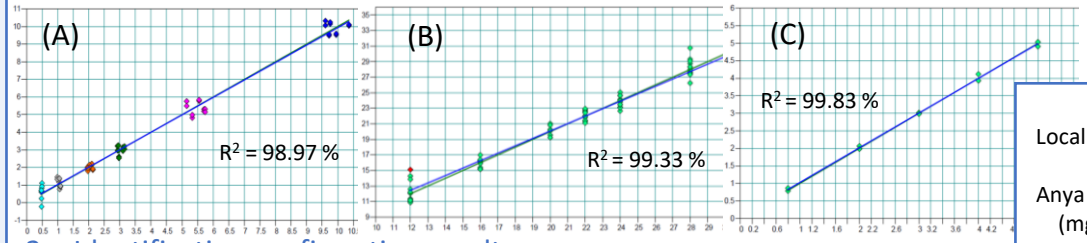
CONCLUSION

NIR-MVA seems to be a very promising analysis tool for QC in PP. The ability to correctly quantify a compound directly in its primary packaging container or dosage form could offer new possibilities to the hospital pharmacist looking to perform fast and safe QC on PP, as it nullifies the need to withdraw a sample.

RESULTS AND DISCUSSION

1. Quantification results

Obtained correlation curves ((A) spironolactone capsules, (B) amikacin solutions and (C) Bevacizumab solutions (IV-bags). The system was able to quantify (within the quantification range) the content of 5 additional and independent 3 mg spironolactone capsules (average trueness bias of -0.32%).



X axis : Local measurement
Y axis : Anya measurement (mg or mg/mL)

2. Identification confirmation results

Despite the very small number of reference spectra included into the database, the system correctly identified the nivolumab, carboplatin and gemcitabine preparations

Compound and theoretical concentration	Identified compound	Interpretation
Nivolumab 240 mg/124 mL in NaCl 0.9%	Nivolumab	Correct (multiple model spectra in the data base)
5FU 340 mg/106.80 mL in NaCl 0.9%	Gemcitabine	Incorrect (but only 1 model spectra of 5FU in the data base)
Paclitaxel 102 mg/267 mL in NaCl 0.9%	Not identified, unknown	Incorrect (but only 1 model spectra of paclitaxel in the data base and of different concentration)
Bevacizumab 275 mg/111 mL in NaCl0.9%	Nivolumab	Suspected lab manipulation error
Oxaliplatine 155 mg/281 mL in glucose 5%	Not identified but on hit list	Incorrect (but only 1 model spectra of oxaliplatin in the data base and of different concentration?
Gemcitabine 1640 mg/293 mL in NaCl0.9%	Gemcitabine	Correct (multiple model spectra in the data base)
Carboplatine 500 mg/300 mL in glucose 5%	Carboplatin	Correct (despite low number of spectra in the data base