Comparison of two methods for instant moisture content measurement of tablets, by NIR-SRS and by 3D-MRT

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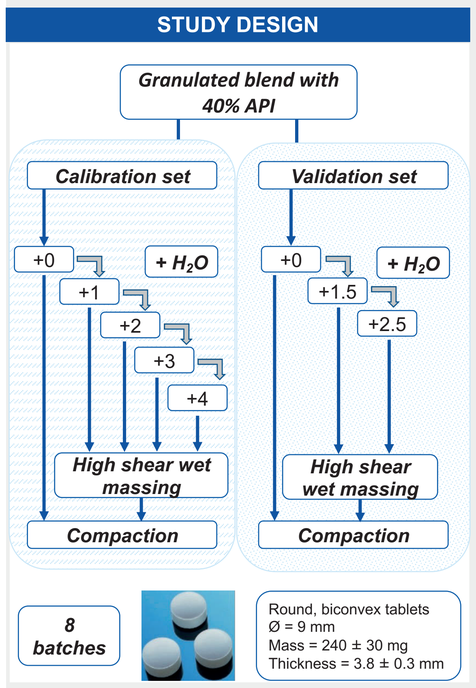
INTRODUCTION

Moisture content (MC) is a key quality attribute in pharmaceutical tablets, affecting stability, shelf life, and disintegration. Near infrared (NIR) spectroscopy is commonly used as a fast, non-destructive method for moisture analysis. Microwave Resonance Technology (MRT) is gaining attention for its ability to measure moisture in solid, inhomogeneous products due to its greater penetration depth. The CU–120 inspection system (Pharma Technology – Belgium) combines near infrared spatially resolved spectroscopy (NIR-SRS) and 3D-MRT technologies, enabling real-time, non-destructive moisture monitoring and direct comparison of both methods.

METHODOLOGY

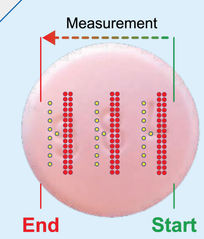
STUDY DESIGN



- Calibration: 25 tablets (5/batch)
- Validation: 15 tablets (5/batch)
- Test: 160 tablets (20/batch)
- Reference: 40 tablets

RM: Coulometric Karl Fischer (KF)

Fig. 1 Wavelength and frequency ranges



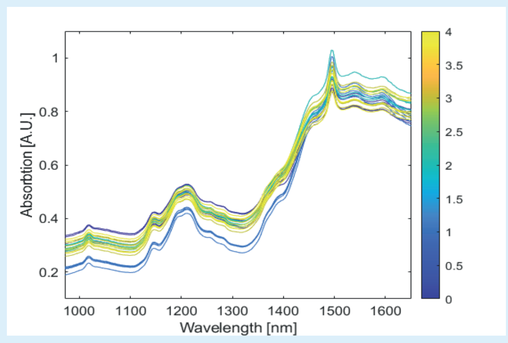
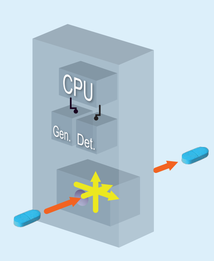


Fig. 2 Raw NIR spectra colored by the added water amount

- Multipoint probe – 9 active fibers – larger surface covered than with single point NIR
- Measurement depth ~ 1 mm
- Measurement range: 900-1650 nm
- Speed 1.056 mm/ms
- Integration time 0.89 ms
- Modeling using chemometric multivariate analysis techniques



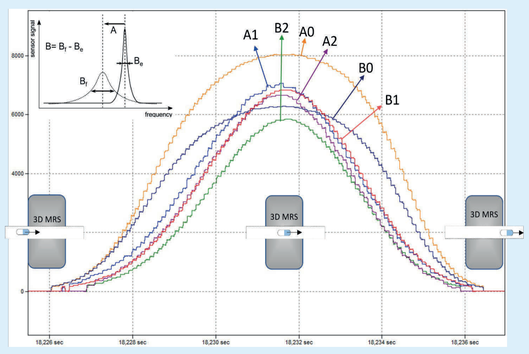


Fig. 3 Frequency shift (GHz) and half-width broadening vs. time

- Three resonance modes 2 – 2.3 – 2.6 GHz
- Continuous measurement of the resonance frequencies (A_0, A_1, A_2) and the half-width of the resonance peaks increase (B_0, B_1, B_2)
- Maximum values are kept only
- Modeling via multiple linear regression

Shift of the resonance frequency A:
$A = f_e - f_f$ f_e: res. freq. – empty resonator [Hz]; f_f: res. freq. – filled resonator [Hz]

Increase of the half-width B:
$B = B_f - B_e$ B_e:half-width of the res. peak – empty resonator; B_f:half-width of the res. peak – filled resonator

RESULTS

- Calibration models were developed by correlating either the NIR spectra or the MRT data with water content, based on a calibration set consisting of 25 tablets with five different water concentrations was used to evaluate model performance.

NIR – SRS

- The NIR-SRS data were modeled using partial least squares (PLS) regression after preprocessing with Standard Normal Variate (SNV), Gap Segment First Derivative (gap: 5, segment: 5), and Generalized Least Squares (GLS) weighting (α = 0.09). As cross-validation 'venetian blinds' were applied.

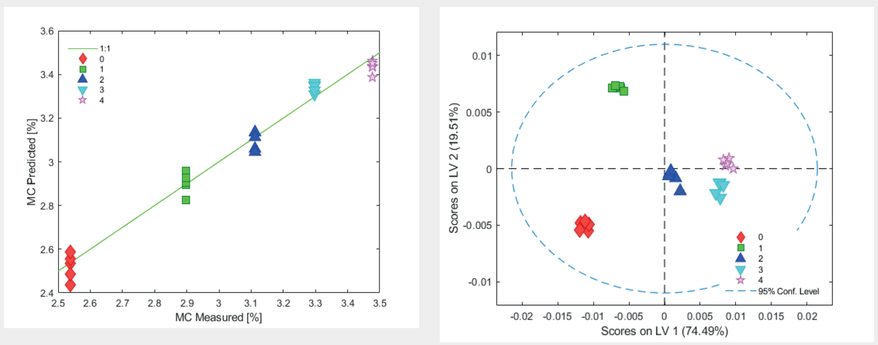


Fig. 4 Prediction plot (left) and the scores plot (right) for the calibration samples

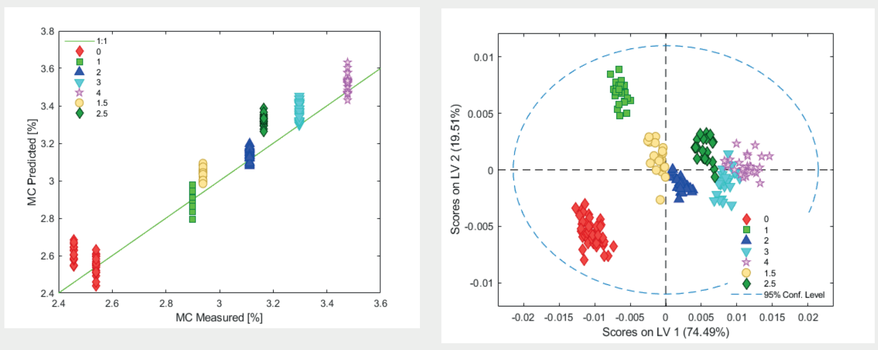


Fig. 5 Prediction plot (left) and the scores plot (right) for the test samples

3D – MRT

- Multiple linear regression (MLR) was applied to the derived data.

$$RH = k_0 \frac{B_0}{A_0} + k_1 \frac{B_1}{A_1} + k_2 \frac{B_2}{A_2} + k_3$$

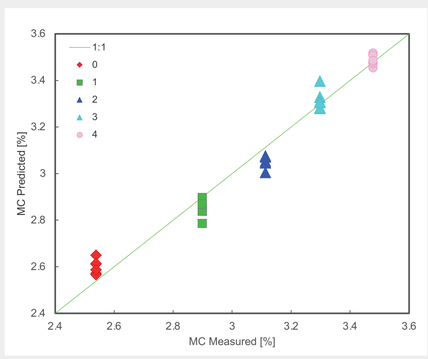


Fig. 6 Prediction plot for the calibration samples

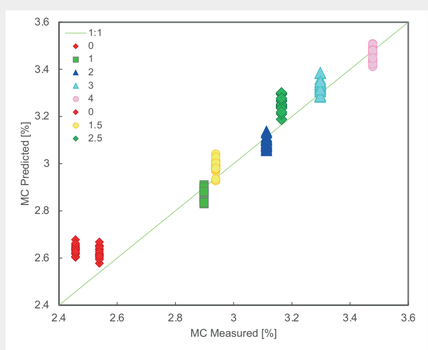


Fig. 7 Prediction plot for the test samples

MODEL PERFORMANCE

- Water content of each tablet used for calibration and validation was determined by Karl Fischer (KF) titration.
- The measured moisture contents were between 2.5% and 3.5%.
- For the calibration and prediction of moisture content, an average value was used (based on five measurements at each water addition level).

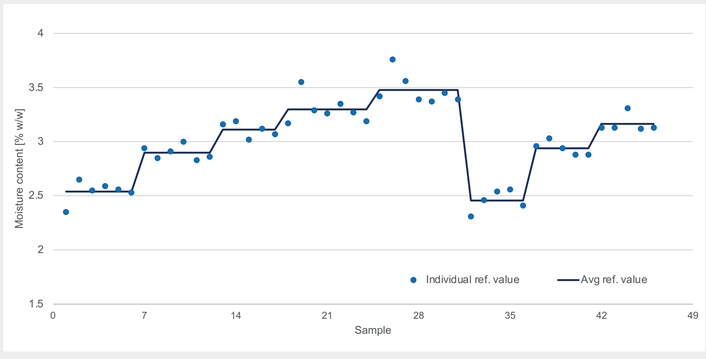


Fig. 8 Reference moisture content of the calibration and validation samples, where blue dots are individual values and the solid line is the averaged value

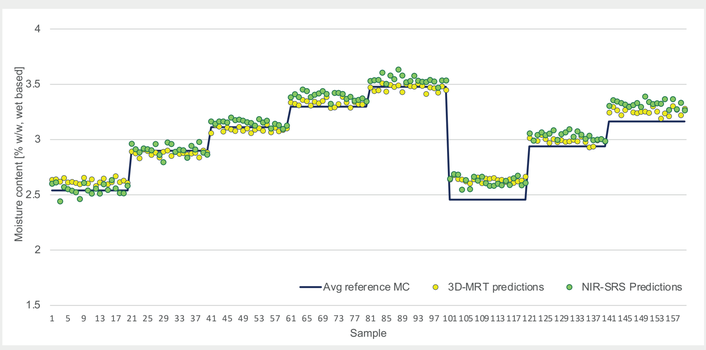


Fig. 9 Reference moisture content (line) plotted with predicted values of the test batch through 3D-MRT (yellow dots) and NIR-SRS (green dots)

	3D-MRT	NIR-SRS
R^2	0.973	0.995
RMSEC / RMSECV	0.0577 / 0.0659	0.02328 / 0.0477
RMSEP (final)	0.0850	0.1041

Table 1 Performance indices of the predictive models of both techniques

- Both NIR-SRS and 3D-MRT enabled precise modeling of water content in low-moisture tablets (2.5–3.5% w/w, KF reference), achieving calibration errors of 0.023% w/w (NIR-SRS) and 0.058% w/w (3D-MRT), with $R^2 > 0.97$. Prediction errors were 0.104% w/w (NIR-SRS) and 0.085% w/w (3D-MRT), confirming ~0.1% w/w accuracy.
- Our findings show that both NIR (inline NIR-SRS, 1 scan) and MRT (inline 3D-MRT at 2.0, 2.3, and 2.6 GHz) exhibit calibration errors on the order of 0.1% w/w, comparable to benchtop methods reported by Corredor et al. (2011) [1] (FT-NIR, 64 scans; 1D-MRT at 2.5 GHz).

CONCLUSIONS

- The CU–120 system is a unique combination of NIR-SRS and 3D-MRT technologies that enables fast, accurate, and reliable moisture content determination through high-speed data acquisition — even within low water concentration ranges..
- Both integrated technologies deliver a similar level of precision (with average errors around 0.1% w/w for both NIR-SRS and 3D-MRT), comparable to leading benchtop methods, but with the added advantage of enabling inline, real-time measurement.
- Despite the product's low water content range (2.5–3.5% w/w), remarkable precision is achieved with both methods.

REFERENCES

1. Corredor, C. C., Bu, D., & Both, D. (2011). Comparison of near infrared and microwave resonance sensors for at-line moisture determination in powders and tablets. *Analytica Chimica Acta*, 696(1-2), 84-93.

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