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NIR based approach to evaluate anhydrate-hydrate transformations

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Outline

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- **Solid forms of Naproxen sodium (NS)**
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  - Scores and loadings plot from NIR spectra
- **Summary**

Need for Process Analytical Technology tools

"QUALITY PHARMACEUTICAL PRODUCT"

Understanding of the solid form during various phases of development : Crucial factor

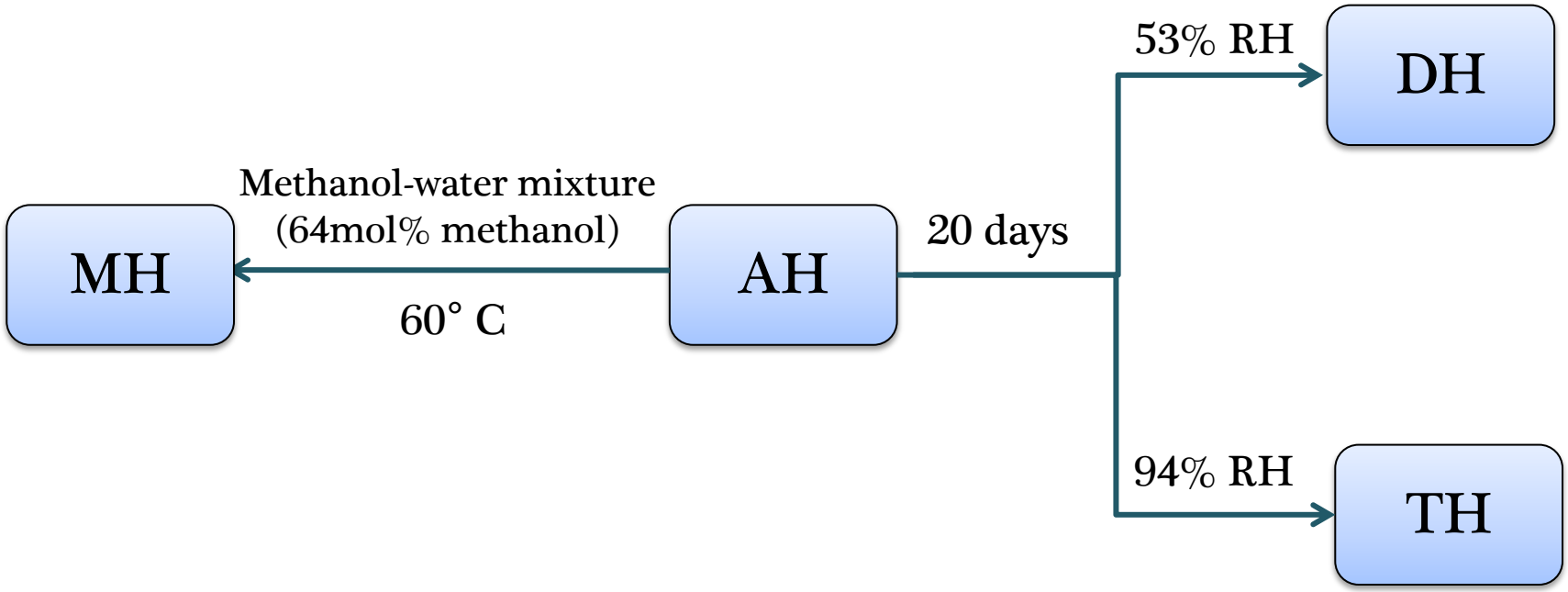
Important to identify suitable technique during early development that can monitor such changes and can be developed as a PAT tool for future manufacturing of pharmaceutical products

NIR Specroscopy as a PAT tool

- Fast, noninvasive and real time data acquisition possibilities makes NIR as one of the ideal PAT tools
- Multivariate data analysis from NIR spectral data can provide simple and quick approach for extracting information from NIR spectral data

Katherine A. Bakeev, Pharmaceutical Technology Europe, *Sep.* **2003**

Solid forms of Naproxen Sodium



AH: Anhydrate, MH: Monohydrate, DH: Dihydrate, TH: Tetrahydrate

Objective of the present work

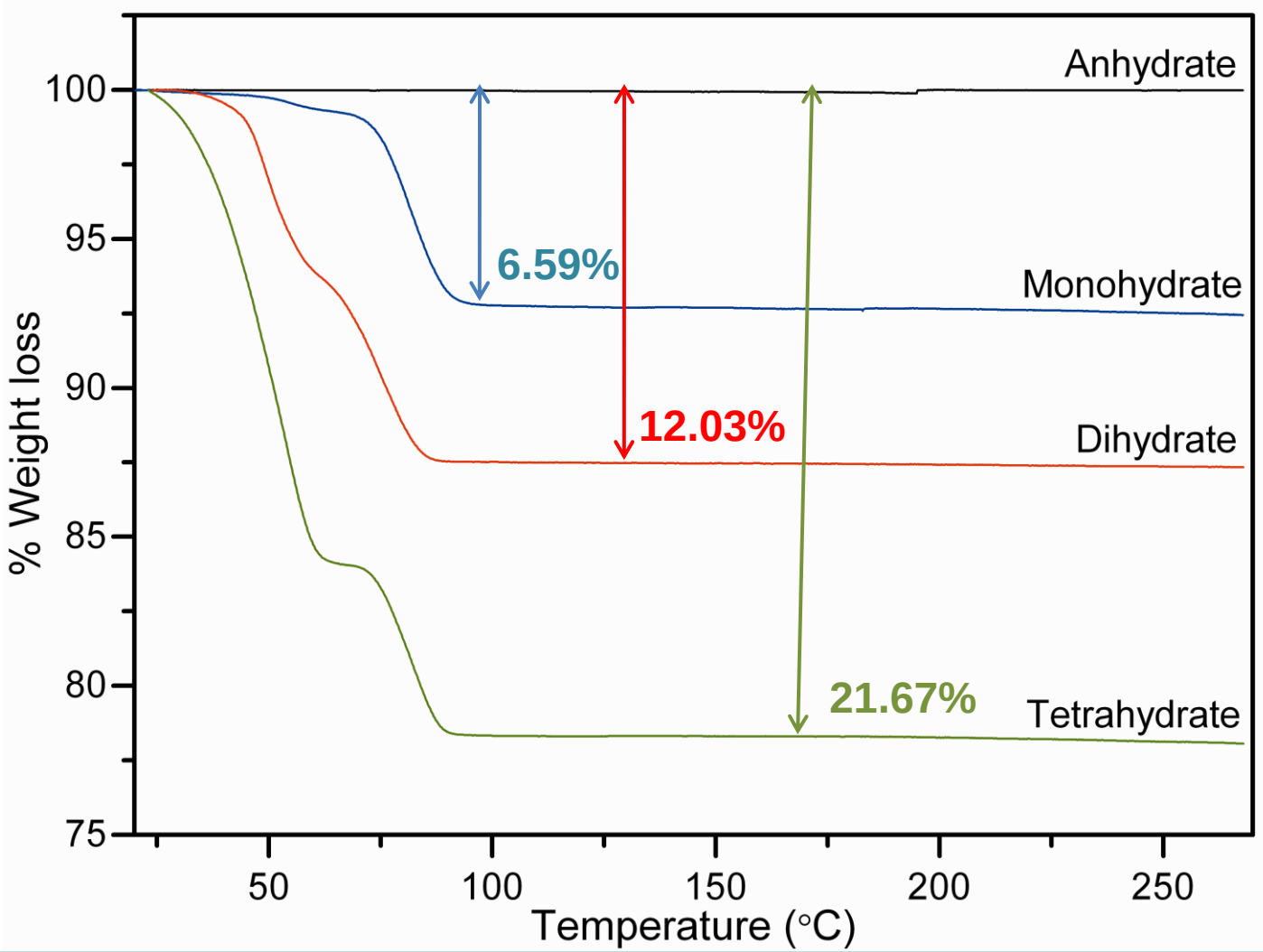
Alteration in physicochemical properties of NS, attributed to the anhydrate to hydrate transformation during processing, has been reported[1,2]

However, till date no PAT tool has been evaluated for monitoring of phase transformation of NS during pharmaceutical processing..!!

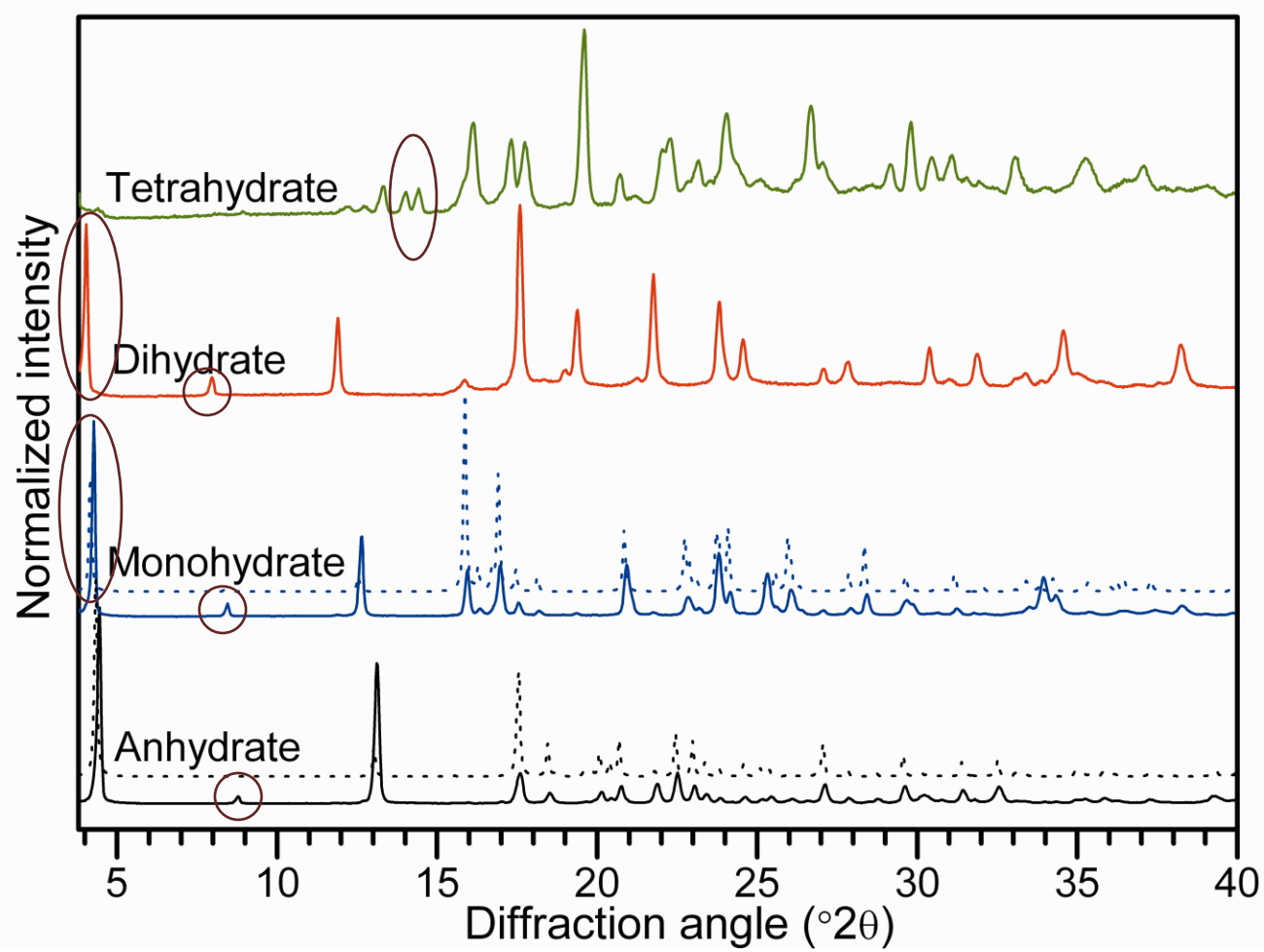
Therefore, the present study focuses on evaluating feasibility of NIR spectroscopy as a real-time monitoring tool

[1]Bansal, P. *et. al. Drug Dev. Ind. Pharm.* **1994**, 20, 2151-2156; [2]Martino, P.D.*et.al*, *J. Pharm. Sci.* **2008**, 97, 5263-5273.

Thermal Gravimetric Analysis

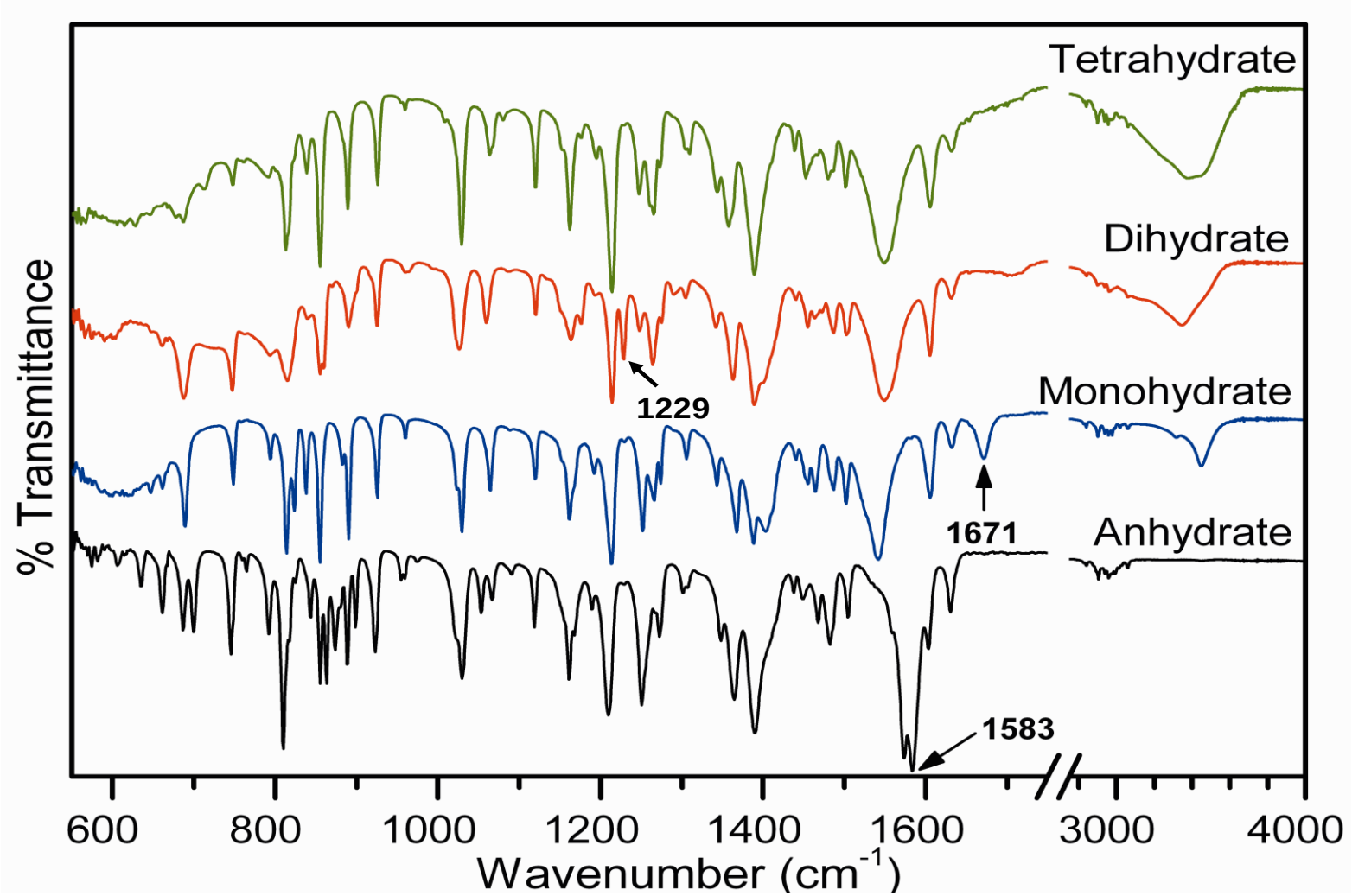


PXRD patterns

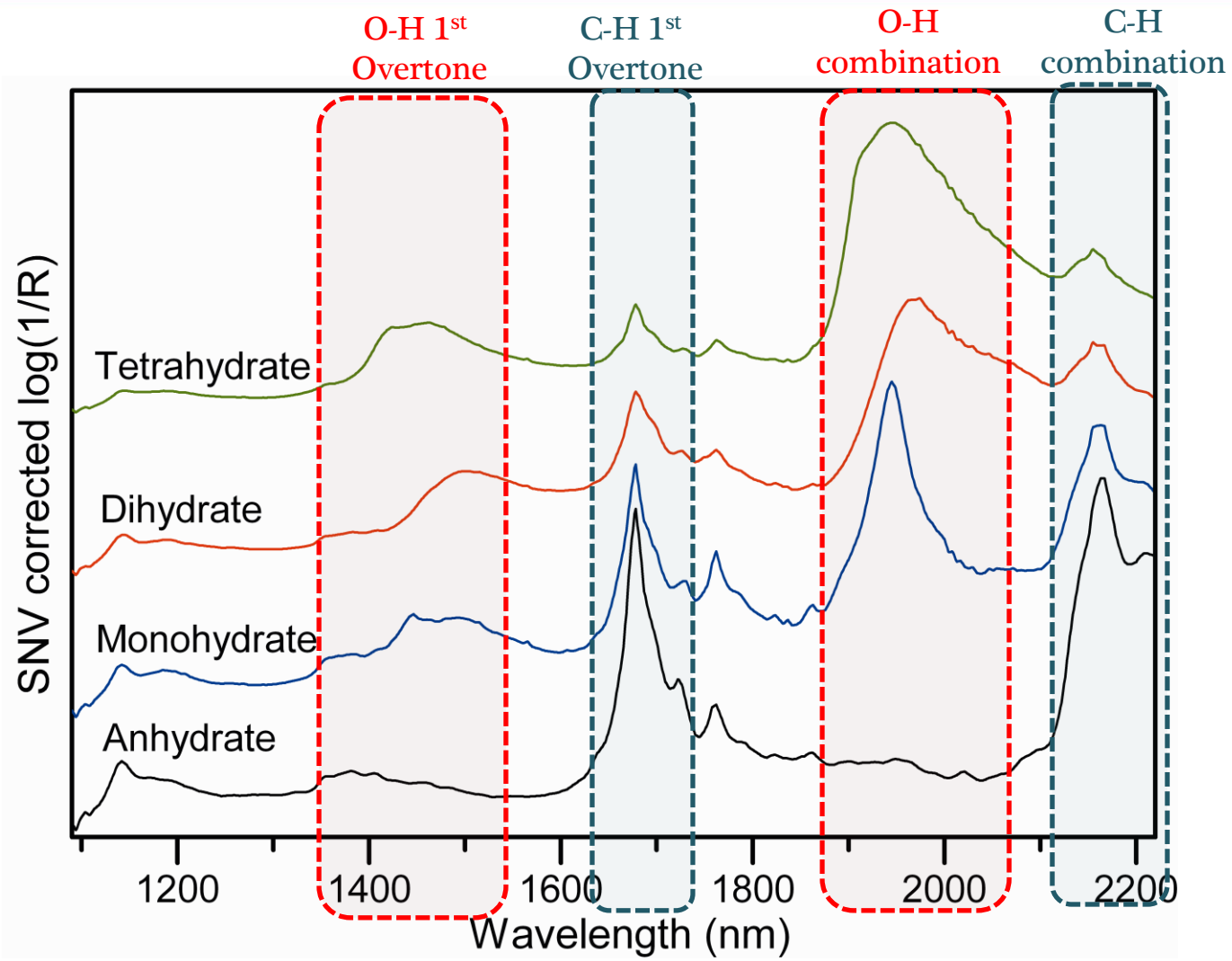


Note:The dotted diffractograms are the calculated patterns for AH and MH forms from their crystal structures

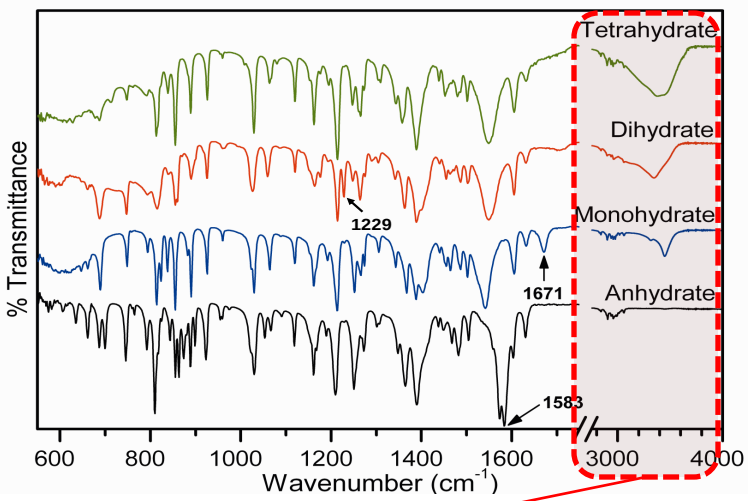
FTIR spectra

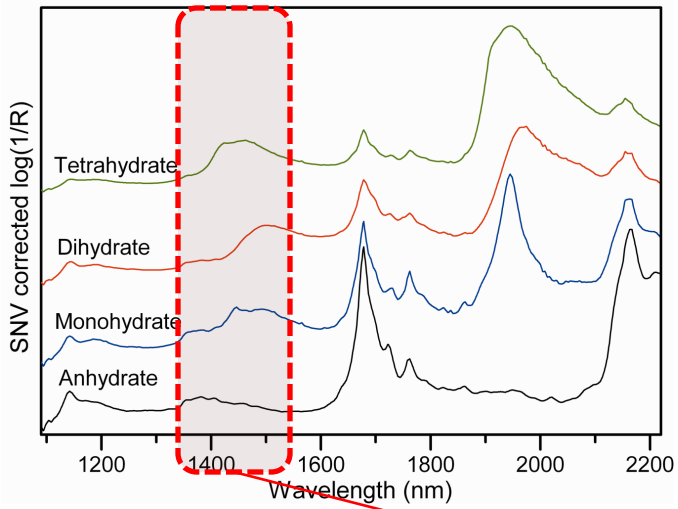


NIR Spectra (SNV corrected)



Chemical information from FTIR and NIR spectra

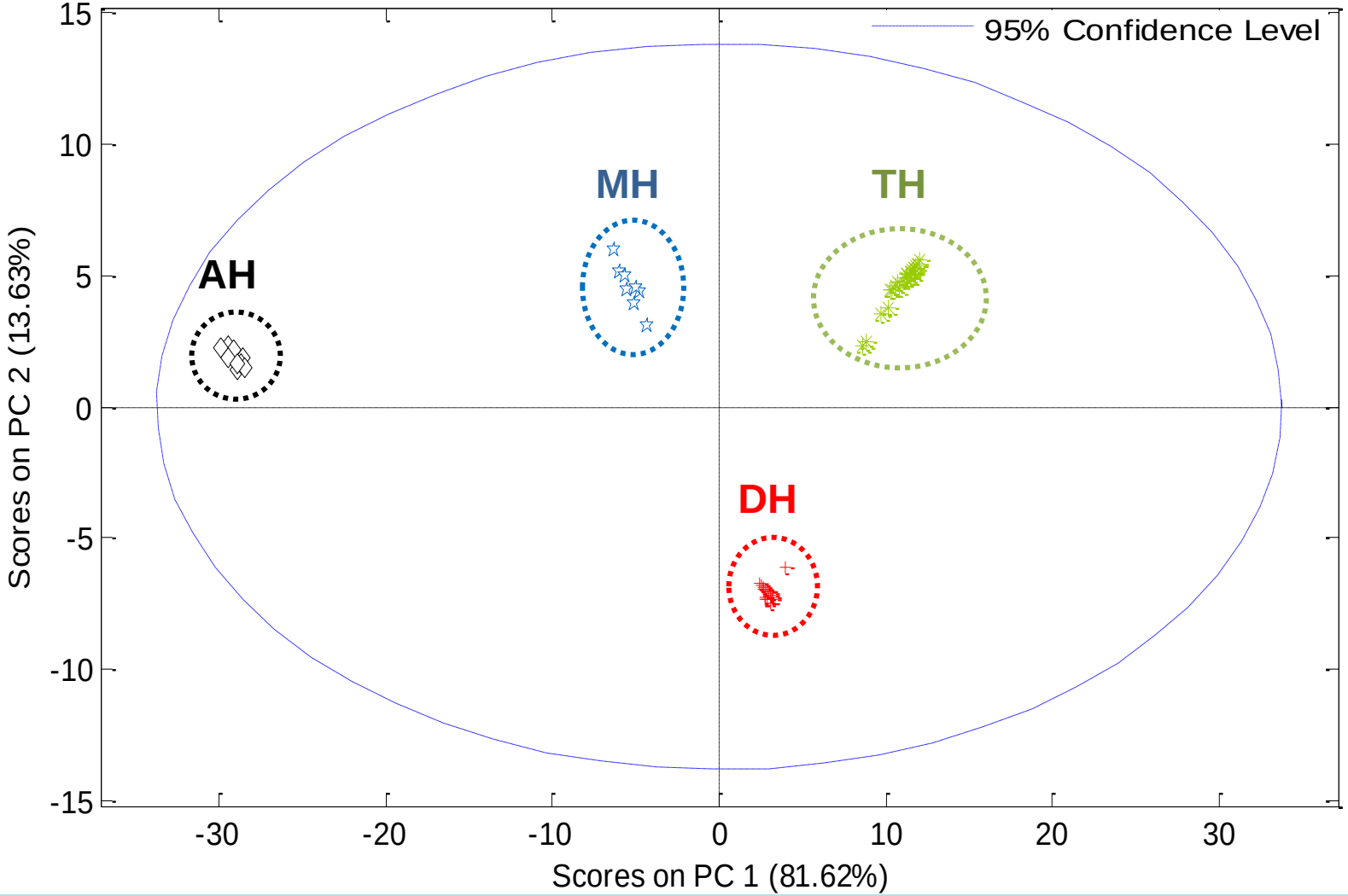




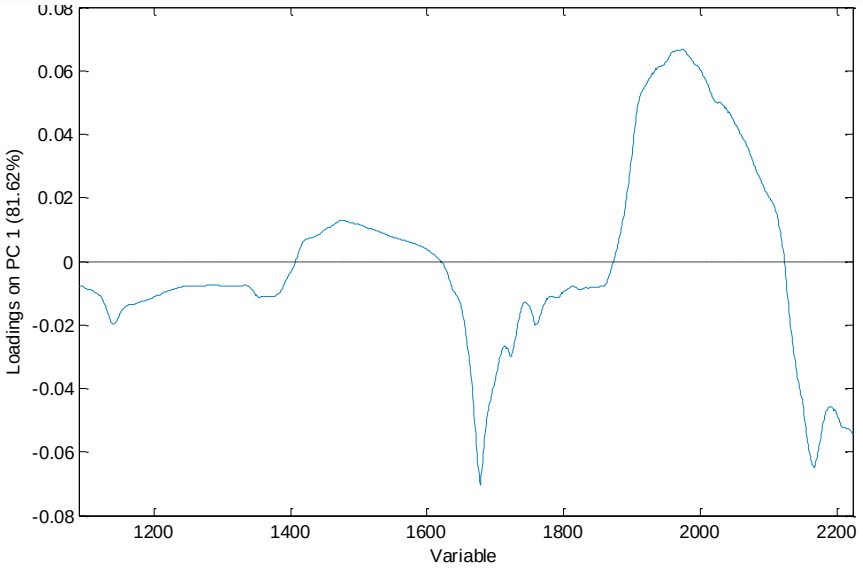
Solid form	O-H stretching (FTIR)	1st O-H Overtone (theoretical*)	1st O-H Overtone (experimental#)
MH	3450 cm^{-1}	6900 cm^{-1} (1449 nm)	1446 nm
DH	3350 cm^{-1}	6700 cm^{-1} (1492 nm)	1496 nm
TH	3450-3380 cm^{-1}	6900-6760 cm^{-1} (1449-1479 nm)	1447-1465 nm

*calculated by multiplying the wave-number values for fundamental vibrations in FTIR spectra by 2; #observed by NIR spectroscopy

PCA Scores plot from NIR spectral data

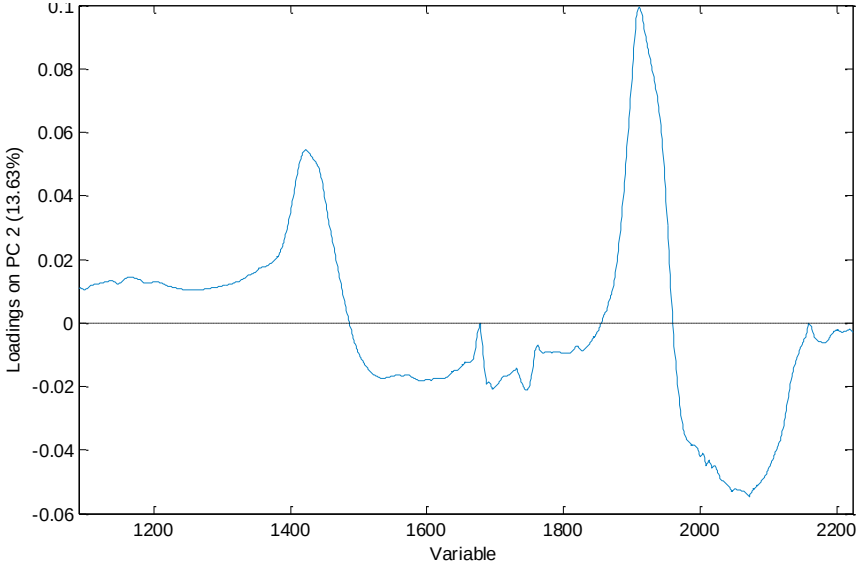


PCA Loadings plot from NIR spectral data



Loadings on PC1

Loadings on PC2



Conclusion

- NIR spectroscopy coupled with multivariate data analysis can efficiently distinguish the NS solid forms
- NIR spectroscopy can be considered as a potential technique to monitor phase transformations
- Further studies will focus on development of NIR based quantitative model that can be applied for real time monitoring of hydrate formation and dehydration behaviour of the NS solid forms during processing and storage


Thank You.