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Use of a novel multi-frequency microwave sensor for Inline moisture monitoring in fluidized bed granulation

Johanna Peters[1], Kathrin Bartscher[2], Claas Döscher[3], Wolfgang Taute[4], Michael Höft[4], Reinhard Knöchel[4], Jörg Breitkreutz[1]

[1] Institute of Pharmaceutics and Biopharmaceutics, Heinrich-Heine-University, Düsseldorf, Germany, ✉ johanna.peters@hhu.de,
[2] NextPharma, Waltrop, Germany, [3] Döscher Microwave Systems, Hamburg, Germany,
[4] Institute of Electrical and Information Engineering, Microwave Group, Christian-Albrechts-University, Kiel, Germany

Purpose

In this study a novel multi-frequency microwave resonance sensor was developed to investigate and overcome difficulties in inline moisture monitoring in fluidized-bed granulation. It is well known that microwave sensors operating with a single resonance frequency show limitations above certain moisture contents. Higher scattering of measured signals and deviations from reference methods considerably impede the determination of granule moistures higher than approx. 8 % [1, 2]. Recent studies described the benefit of using an additional frequency. In a range where the microwave signal of a lower resonance frequency stays constant, the signal of a higher resonance frequency still showed a linear increase [3]. Therefore, the new multi-frequency sensor was developed and investigated.

Materials and Methods

Maize starch (CPharm Gel, Cargill Deutschland, Krefeld, Germany) and microcrystalline cellulose (MCC, Avicel PH 101, FMC BioPolymer, Philadelphia, USA) were used as model excipients. Granulation was performed using a GPCG1 fluidized-bed granulator (Glatt, Binzen, Germany) using PVP K 30 (Kollidon 30, BASF, Ludwigshafen, Germany) as binder. Microwave setup for moisture determination consisted of a custom-made ring resonator operating at four resonance frequencies (2.8, 6.4, 7.2 and 8.1 GHz) controlled by specifically programmed FPGA (Microwave Group, Christian-Albrechts-University, Kiel, Germany). Matlab software (Mathworks, Natick, USA) was used to record and process measurement data. Reference measurements were performed offline by loss on drying with infra-red light (LOD/IR) using MA45 (Sartorius, Göttingen, Germany).

Results and Discussion

Results from measurements performed by Kollar et al. [3] were confirmed and the investigations extended using the new sensor system. Moisture of conditioned maize starch and MCC was examined offline using four resonance frequencies in the range of 2.8-8.1 GHz.

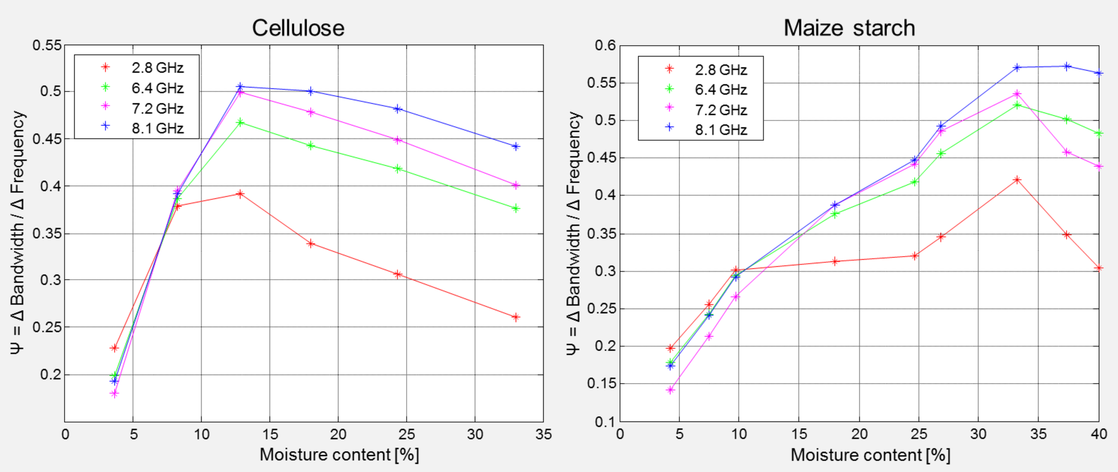

Fig. 1: Microwave signals offline measurements

As expected, the signal of the lowest resonance frequency (2.8 GHz) does not behave linearly above a certain moisture content for both materials. The additional resonance frequencies (6.4-8.1 GHz) showed same effects at different, higher moisture contents. (Fig. 1)

Hence, the results of offline measurements provided an explanation for non-suitability of a single resonance frequency for moisture analysis over a broader moisture range and indicated to follow the approach of combining these different resonance frequencies for inline measurements during fluidized bed granulation.

Fig. 2: MRT sensor (sensor head ø 5.5 cm)

Inline measurements have been performed monitoring the granulation process of a 60:40 mixture of MCC and maize starch.

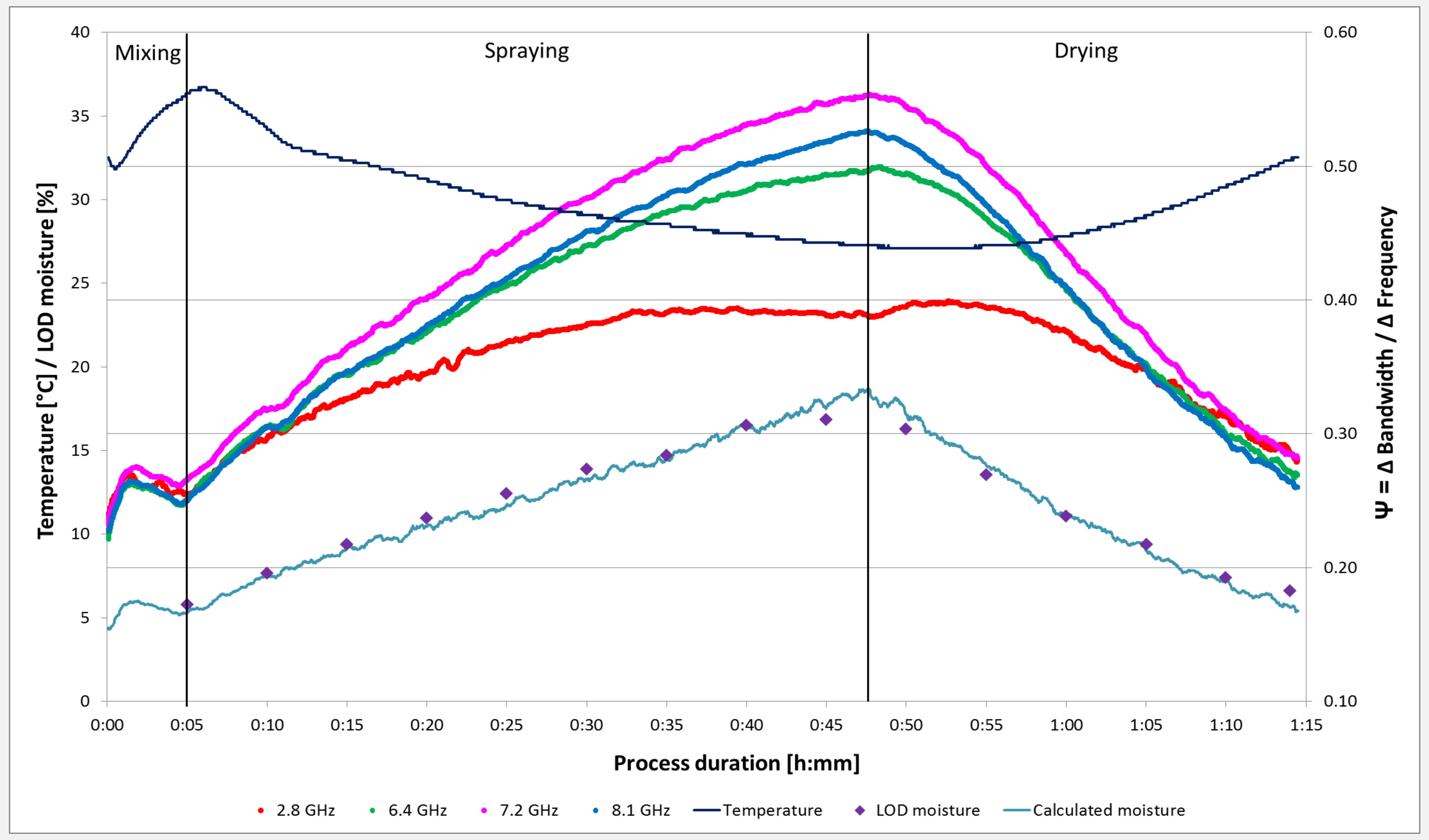

Fig. 3: Inline moisture track of a MCC / maize starch granulation process

LOD values of granule samples collected during granulation and inline microwave moisture values (Ψ) were used to develop a Multiple Linear Regression (MLR) model ($r^2 = 0.9963$).
The model was verified in independent granulation runs and displayed a good level of agreement between the calculated moisture and moisture content obtained offline by LOD/IR during all process stages (Fig. 3). By collection of data sets for each resonance frequency, inline moisture evaluation in fluidized-bed granulation was improved.

Conclusion

Feasibility of a new microwave resonance sensor using four different resonance frequencies to follow the moisture content during granulation processes was demonstrated. By calibration versus experimental LOD moisture values it enables to provide real-time inline data during granulation processes and discontinue offline measurements. For use as a process analytical technology (PAT) tool in development and scale-up of granulation processes a model comprising various drug-excipient mixtures as well as facilitation of further data processing need to be established. Benefit for other applications needs to be further investigated.

References

[1] Buschmüller, C., Diss., HHU Düsseldorf (2009)
[2] Corredor, C.; Bu, D.; Both, D., Analytica Chimica Acta 696, 84-93 (2011)
[3] Kollar, B.; Wiedey, W.; Bartscher, K.; Döscher, C.; Breitkreutz, J., TechnoPharm 3, 317-321 (2013)

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