Heinrich Heine Universität Düsseldorf

Heinrich-Heine-Universität Düsseldorf 40204 Düsseldorf
Dekanat der Mathematisch-Naturwissenschaftlichen Fakultät

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Mathematisch-Naturwissenschaftliche Fakultät

Dekanat

Promotionsangelegenheiten
Universitätsstraße 1
40225 Düsseldorf
Telefon: +49 (0)211 81 15092
E-Mail: promotionmnf@hhu.de

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Promotionsverfahren von **Frau M.Sc. Katharina Kiricenko**
Auslage der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

Continuous twin-screw granulation with vibrated fluidised-bed drying

von den Berichterstattenden Prof. Dr. Dr. h.c. P. Kleinebudde und Prof. Dr. J. Breitkreutz beantragt. Sie kann zusammen mit den Gutachten in der Zeit

vom 04.12.2024 bis 15.12.2024

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen (§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

18.12.2024 um 15:00 Uhr

im **Hörsaal 6D** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Juniorprof. Dr. M. Hacker, Prof. Dr. Dr. h.c. H. Stark und Prof. Dr. N. Teusch.

Die Öffentlichkeit ist bei der Befragung zugelassen.

Mit freundlichen Grüßen
im Auftrag

Amina Diekmann

Name, Vorname: Kiricenko, Katharina

Zusammenfassung

Dissertation: Continuous twin-screw granulation with vibrated fluidised-bed drying

Common continuous manufacturing setups use twin-screw wet granulation (TSG) and segmented fluidised-bed dryers (FBDs), but challenges like limited drying capacity and variability in air temperature can lead to inconsistent moisture content and granule breakage. An alternative drying technique using vibrated fluidised-bed dryer (VFBD) after wet granulation, as implemented in the QbCon®-System, improves heat and mass transfer and allows easier adjustment of residence time.

This thesis explored the application of TSG and VFBD in the QbCon® 1 through three studies, along with a fourth on screw configuration impact. First, the drying behaviour of granules was studied using two different formulations: one with mannitol and another with alpha-lactose and microcrystalline cellulose (MCC). Due to MCCs water absorption capacity, lactose-MCC granules showed higher loss-on-drying (LOD) under constant drying conditions thus requiring increased drying capacity. Changes in temperature along the drying chamber showed that lactose-MCC granules did not reach the second drying stage and the critical moisture content, as indicated by the absence of a temperature increase in the granules which corresponded to high LOD values. LOD is reduced with higher drying temperatures or air flow and decreased vibration acceleration. Decrease in vibration acceleration and air flow led to longer residence time. The drying parameters including the vibration showed no effect on granule size.

Stepwise deviation of mass and energy balances provided insights into heat loss and mass flow in the empty state and during drying of granules by using logged sensor data. This approach presents an alternative to NIR spectroscopy and microwave resonance technology for real-time LOD monitoring as a potential PAT tool. Building on these results, the combination of mass balance together with NIR spectroscopy was demonstrated as an orthogonal PAT system. Both methods, mass balances and NIR spectroscopy, independently predicted the LOD thus providing accurate LOD values. If a sensor problem occurs with the NIR spectroscopy, the mass balance can still provide LOD values. Furthermore, in the case of deviations between the two PAT methods, the cause can be investigated, such as a sensor issue with the NIR spectroscopy. However, moisture and temperature sensors used in the mass balance can also be faulty. The correlation between both measurements was observed up to a LOD of 16 % using different drying conditions and formulations. Additionally, a statistical model was developed to predict the LOD based on the set process parameter such as the L/S ratio and powder feed rate in granulation and drying temperature, air flow and vibration acceleration in drying. The model was developed and verified with additional experiments beside the design of experiment. A benefit of the developed model is its ability to predict one of the five process parameters to target a defined LOD value.

The investigation of screw configurations for hydrophilic and hydrophobic formulations showed minimal impact from variations in the kneading zone (number of kneading elements, thickness or offset angle). The L/S ratio was the most influential factor affecting granule friability and size. Using more kneading elements, larger offset angle or thickness led to longer residence time. Including tooth-mixing elements at the end of a screw configuration led to a high fraction of oversized granules. For hydrophobic ibuprofen formulations, at least one kneading zone was necessary to produce granules with sufficient strength with fewer fines thus improving tablet strength. This study assumed that the influence of screw configuration may depend on the formulation and requires further investigation. Overall, the findings indicate that TSG followed by a VFBD is a promising approach for continuous manufacturing.