BØHLE

First Continuous Granulator with Integrated Truly Continuous Dryer

QbCon® 1

QbCon® 1 – Revolutionary System for Your R&D

Challenges

- Lack of solutions for continuous drying and continuous wet granulation in the pharmaceutical industry.
- No continuous fluid-bed dryer on the market that is suitable for long process times and meets all quality requirements.

Solution

THE L.B. Bohle QbCon® 1 is the ideal device for the introduction of continuous wet granulation

- QbCon® 1 achieves truly continuous drying and granulation for the first time with very narrow and reproducible residence time distributions in the dryer. It also maintains a stable quality of the granules with regard of moisture and particle size.
- QbCon® 1 is a system with fully-integrated software and unit operations consisting of different components by L.B. Bohle (liquid feeding, wet granulation, drying, automatization) and Gericke AG (powder feeding).
- By use of PAT it is possible to monitor the production process inline. This leads to constant production of high-quality products, high patient safety, lower costs, better process understanding and optimized process control.
- The entire process is controlled and monitored via a touch panel.
- The design of QbCon® 1 is very space-saving, and the nominal throughput of the system is 0.5–2.5 kg/h, but can significantly deviate upwards.

Study on the proof of quality attributes in relation to

- A short residence time of the granules in the dryer with simultaneous narrow residence time distribution.
- Traceability of the continuous process
- Reproducible drying of all granules – especially of different sizes – over the entire process.
- A small process chamber to keep the volume in the drying process as low as possible
- A long service life of the product filter without having to interrupt the drying process or even replace the filter

Materials

A **powder mixture** (proportions: 80/17/3) consisting of α-lactose monohydrate (Granulac 200), microcrystalline cellulose (Avicel PH 101) and povidone (Kollidon 30) **was used for granulation**. Purified water was used as **granulation liquid**.
The blue, water-soluble dye FD&C Blue No.1 was used to **assess the residence time distribution of the granules in the dryer**.

Production of the granules

The powder mixture was filled into the gravimetric powder feeder and dosed in the first zone of the QbCon® 1 twin-screw granulator (TSG). The granulation liquid was fed into the second zone of the granulator.

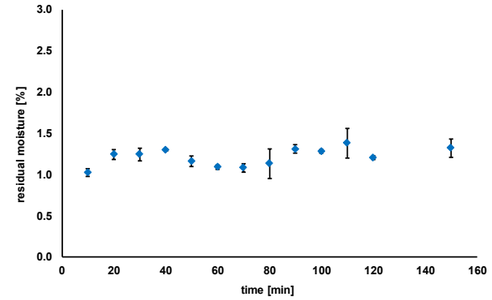
Wet granules leave the twin-screw granulator and land on the distributor plate of the continuous dryer via a direct connection, where they are immediately subjected to hot air and conveyed in the direction of the outlet by vibration.

The conveying of the granules and the air flow are independently adjustable so that the drying effect of the granules can be controlled via the air flow, the supply air temperature and the conveying speed.

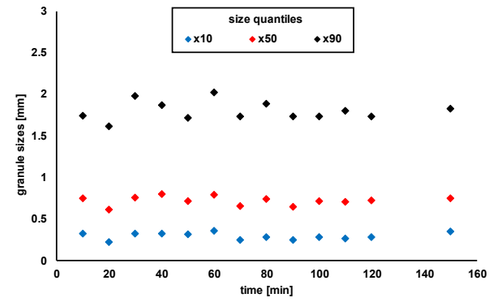
The product filter surface for the air is permanently kept free by means of a cleaning process that is based on a new principle. Thus, for the first time, a continuous granulation without interrupting the process is possible. The dry granules leave the QbCon® 1 via a pneumatically operated valve and can be further analyzed and processed.
A prepared mechanical interface for a NIR probe or any other similar probe also allows in-line quality determination and thus control of the process based on quality (e.g. moisture, active ingredient content or product temperature) of the granules.

Results

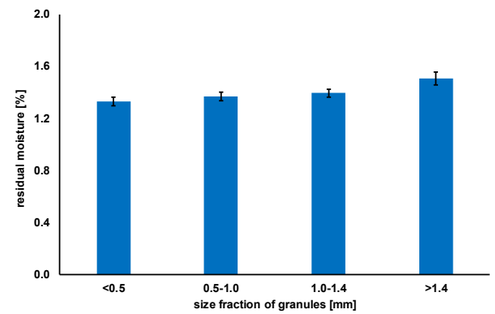
- The continuous granulation and drying tests could be carried out without interrupting or disturbing the process.
- All critical process parameters (feeding, granulation and drying) were consistent over the entire test period.
- Particularly noticeable was that the product filter was covered with only a small portion of the fines content of the granules, therefore the cleaning interval of the product filter has been reduced to 20 minutes. The filter could be cleaned completely without any product residues after cleaning.
- The residual moisture of the granules averaged 1.21 ± 0.11%. The drying was so effective and efficient



Residual moisture content of the produced granules after continuous drying over a process time of 2.5 hours; n=3, mean ± standard deviation.



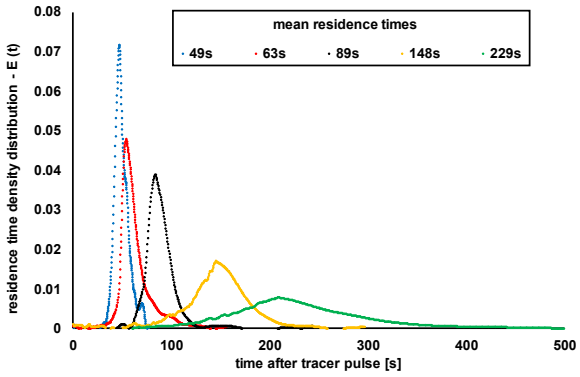
Size quantiles of the granule size distribution after continuous drying over a process time of 2.5 hours.



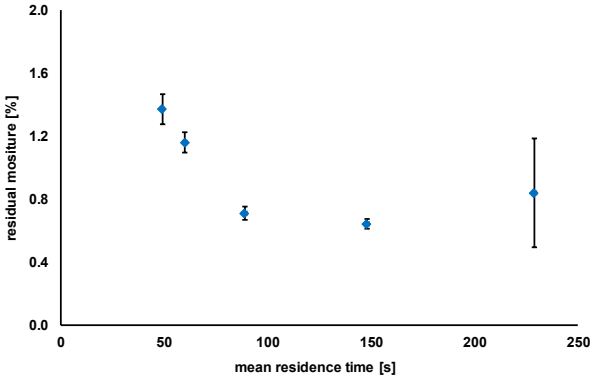
Residual moisture content of the different size fractions of the dried granules; n=3, mean ± standard deviation.

that the value was sometimes even lower than the initial moisture content of the raw material (1.28%).

- The granule size distributions show that the continuous granulation and drying process leads to constant granule sizes.
- The small width of the measured distributions is ideal for a continuous dryer. The aim must be to move all granules through the dryer at the same speed to achieve a similar drying performance.
- By increasing and decreasing the conveying speed of the granules through adjustment of the vibratory system, the limits of formulation and throughput were tested. The mean residence times show a high symmetry.



Measured residence time distributions of the granules in the continuous dryer at different conveying speeds. The legend of the graphic shows the calculated mean residence times associated with the curve progressions.



Residual moisture content of the produced granules as a function of the mean residence times; n=3, mean ± standard deviation.

Conclusion

- The present tests have shown the great potential of this novel drying process which uses a fluid bed.
- Thanks to a very short residence time and a narrow residence time distribution, constant, continuous drying of the granules was achieved even among the different size classes, and the particle size distributions were also constant over the process time.
- The innovative cleaning method for the product filter allows for infinite operation of the dryer, without the necessity to stop the machine and to exchange or clean them offline.

QbCon® achieves unique results in continuous wet granulation and demonstrates the superiority over known processes.

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