W5334

Powder Density Measurement for Respirable Powders Using Uniaxial Compression Under Temperature and Humidity Control

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Particle Engineering

Abstract

Purpose

Pharmacopeial powder density tests use large powder samples and compact the powder by tapping, a method that is poorly suited for powders with small particle size, where interparticle forces are more important than inertial forces. A newly developed technique is presented to measure the Compressed Bulk Density (CBD) of respirable powders by uniaxial compression. This technique uses a sample volume < 0.15 cm³ and has moisture and temperature control, because moisture has been shown to play an important role in consolidation and densification behavior of pharmaceutical powders (1,2).

Methods

An automatic actuator is exerting an increasing pressure on a known mass of powder confined within a small cavity. The pressure is measured using a load cell and NI Lab view software is used to control the setup. The correlation between strain and stress is plotted and processed into a graph that shows density as a function of pressure on the powder bed. For this study, several samples, including Trehalose (Feret diameter: ~500 µm) and L-Leucine (aerodynamic diameter: 2 µm) were analyzed.

Results

Graph 1 shows a strong effect of relative humidity on measured CBD. The low-pressure region shows large experimental scatter that was consistently observed for more than 40 respirable powders tested so far and is attributed to sampling history. Due to this inconsistency of the poured density, parameters like Hausner ratio or Carr Index are not useful measures for respirable powders. In contrast, the Trehalose powder was already compacted to a large extent when poured into the cavity and was not influenced strongly by changes in RH. The corresponding Carr indices for this particle are confirming the high flowability of powders with such large particle size.

Conclusion

Conventional methods that were used for measuring the density of powders with large particle size are not well suited for respirable powders, in which interparticle forces dominate the compaction behavior and the relative humidity during the compaction test impact the results. For these powders a density test based on uniaxial compression under environmental control is advantageous.

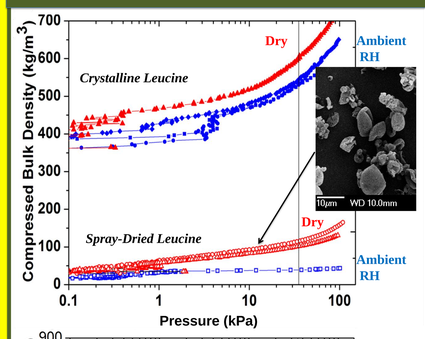
Purpose

Compressed bulk density (CBD) describes the bulk density of a powder under different levels of applied load and is an established method for the analysis of density and compressibility of pharmaceutical powders (3). A new instrument has been developed to determine the Compressed Bulk Density of powder and to evaluate the various types of compression profiles of pharmaceutical powders at a very small scale.

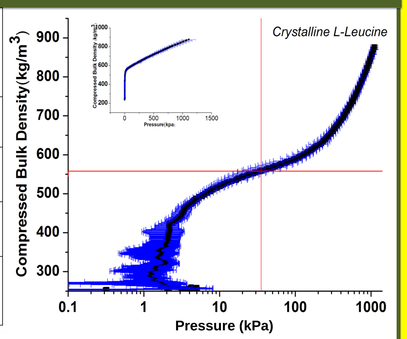
Methods

A pressure of 35 kPa was selected as equivalent measure for tap density based on a previously published correlation (4,5).
For the humidity test, samples were stored at <5 %RH and 20 ± 2 °C in a desiccator cabinet prior to initiating the experiment. During testing, samples were exposed to laboratory conditions, (30 ± 3 %RH).

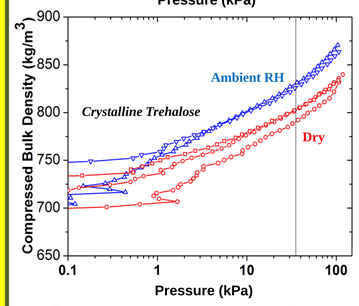
Results



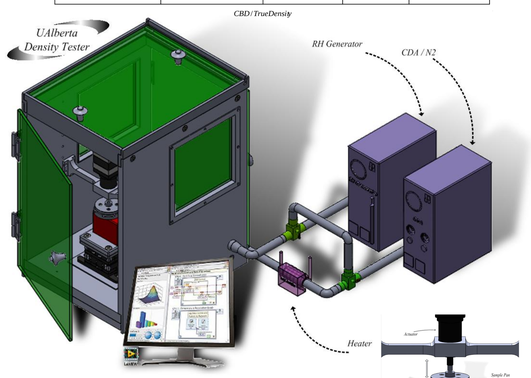
Instrument Comparison	Micromeritics Geopyc 1360	Freeman FT4	USP Tapped Density	UAlberta Density Tester
Sample Volume	> 0.35 cm³	10 cm³	>25 cm³	< 0.15 cm³
Operating Temperature	15 – 35 °C	Ambient	N/A	-24 – 60 °C
Operating RH	20 – 80 %	Ambient	N/A	0 – 90 %
Measurement Time	420 – 780 s	300 – 600 s	> 300 s	30 – 70 s

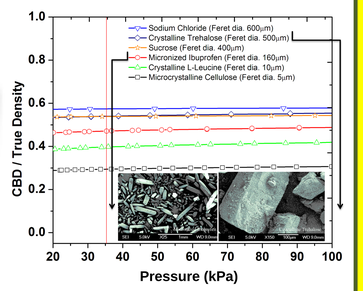


Compressed Bulk Density Profile



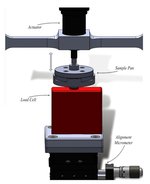
Relative humidity has a strong effect on compressibility of spray dried leucine.

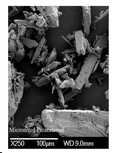


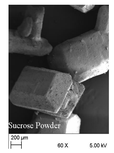


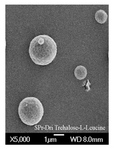
Packing factor is a function of particle size at 35 kPa

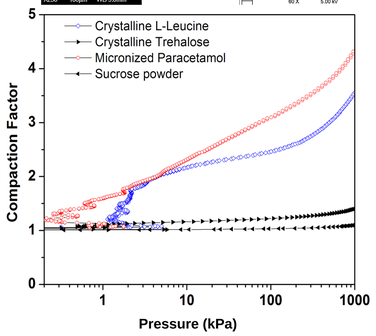
Sample Pan



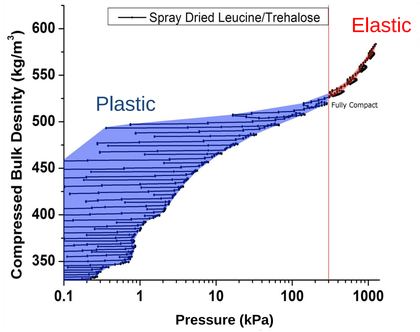


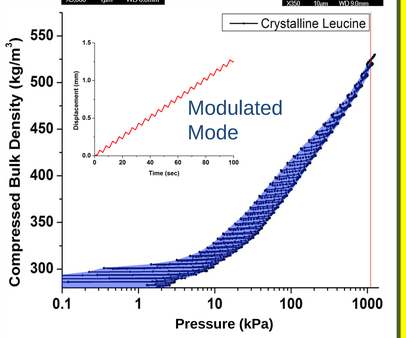






Graph representing the compressibility of four different samples





Modulated compression mode differentiates between plastic and elastic powder response

Conclusion

Classical powder density tests that were developed for powders with large particle size are not well suited for respirable powders. Interparticle forces are large compared to inertial forces for small particles sizes and these powders do not fully compact under external load comparable to tap density tests.

Single value density measurements are not sufficient to describe the packing behavior of powders with small particle size. The entire compression curve should be considered.

Relative humidity during the compaction test impacts the results and should be controlled.

The sampling history affects the initial state of compaction of respirable powders which reduces the usefulness of classical parameters of powder behavior such as Hausner ratio or Carr index. The complete compression graph should be used to determine equivalent information.

The new instrument has the capability to differentiate between elastic and plastic behavior of the powders using a novel modulated compression mode.

The presented technique is a fast and efficient method to analyze the compression behaviour of various types of powder with different physical properties , including pharmaceutical, respirable powders. Sample mass requirements are < 40 mg

References

1. Mir, V. G., Heinamaki J., Antikainen O., Colarte A.I.. Airaksinen S., Karjalainen M., Revoredo O. B., Nieto O. M., Yliruusi J. (2011), Effect of Moisture on Tablet Compression", Carbohydrate Polymers, 86(2), 477-483.
2. Garr J.S. M., Rubinsten M.H. (1992), "The Influence of Moisture Content on the Consolidation and Compaction Properties of Paracetamol", International Journal of Pharmaceutics, 81(2-3), 187-192.
3. Svarovsky, L. (1987), "Powder Testinjg Guide: Methods of Measuring the Physical Properties of Bulk Powders", Elsevier Applied Science, New York, USA
4. Feng A.I., Boraey M.A., Gwin M.A., Finlay P. R., Kuehl P. J., Vehring R. (2011), "Mechanistic Models Facilitate Efficient Development of Leucine Containing Microparticles for Pulmonary Drug", Interrnational Journal of Pharmaceutics, 409(1-2), 156-163.
5. Thalberg K., Lindholm D. and Axelsson A. (2004), "Compression of Different Flowability Tests for Powders for Inhalation", Powder Technology, 143(3), 206-213.

Acknowledgement

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