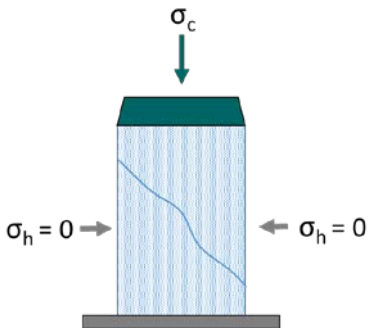
Uniaxial Unconfined Yield Strength (uUYS) can be used to assess and rank powder flowability for a wide range of powder handling processes in various industries, including Chemical, Food, Construction and Pharmaceutical. This application note presents a study using the Uniaxial Powder Tester (UPT) to characterise a range of pharmaceutical blends and the corresponding granulates to illustrate how uUYS values can clearly differentiate between the formulations and quantify the impact of the granulation process conditions.

UNIAXIAL POWDER TESTER (UPT)

Uniaxial testing first involves the construction of a powder column at a given Major Principal Stress (MPS or σ_1), the confining sleeve is then removed, before the freestanding column of material is fractured. The force required to break the column informs on the uUYS (σ_C) of the powder. The UPT also allows bulk powder properties such as density and compressibility to be determined.

Consolidation studies can also be conducted in a range of environments using an off-instrument Consolidation Station. Samples can be consolidated for extended periods of time, at a specific humidity and/or temperature.



EXPERIMENTAL SET-UP

Mixtures containing different ratios of lactose and microcrystalline cellulose (MCC) were dry mixed for 3 minutes in a turbula mixture (total powder volume 750 ml). The resulting dry mixtures were then subjected to a wet granulation process, where the necessary volume of water was added over a 90 s period. The granulation process was continued for a further 180 s. The resulting wet mass was then screened through an 850 µm sieve, dried at 60 °C for 7 hours and then re-screened through a 2 mm sieve.

Dry Mix		*% Water*
% Lactose	*% MCC*	
15	*85*	*0, 40*
30	*70*	*0, 40*
50	*50*	*0, 10, 20, 30, 40*
70	*30*	*0, 40*
85	*15*	*0, 40*

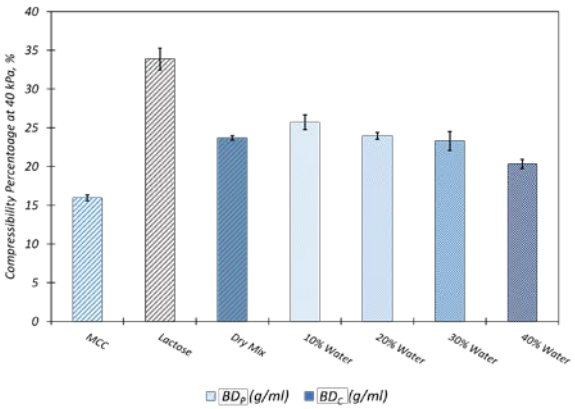
During uniaxial testing, the powder was pre-consolidated at 8 kPa for 5 s. An MPS of 40 kPa was then applied for 30 s, using a unique double-ended compaction method, and the uUYS was measured, alongside the Poured Bulk Density (BD_P), Consolidated Bulk Density (BD_C) and Compressibility.

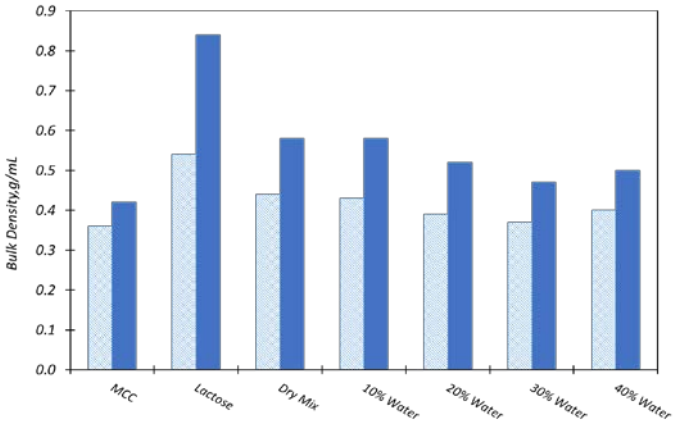
The first phase of the experiment evaluated a 50:50 mixture of lactose and MCC with varying levels of water content used during granulation. The second phase studied varying ratios of lactose:MCC with fixed 40% water content.

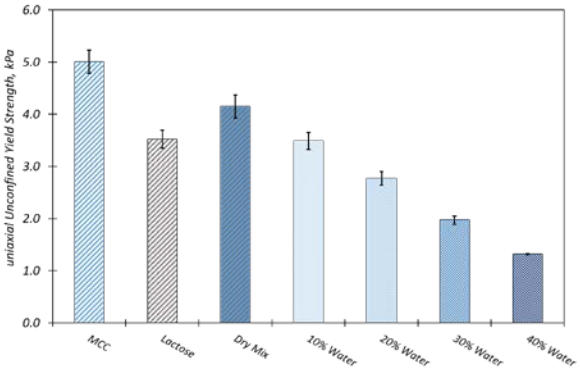
RESULTS – WATER CONTENT

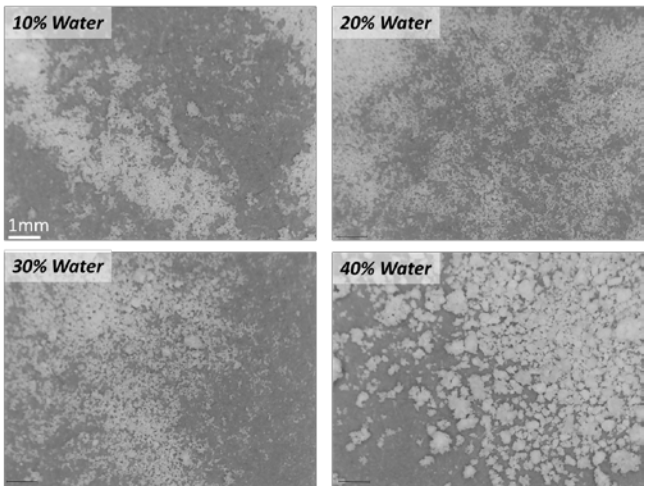
The following observations relating the flow properties of the dry mix and granules were made:

- The Dry Mix of 50:50 lactose:MCC exhibited intermediate behaviour compared to the raw components of lactose and MCC.
- The addition of water, even at 10% content, resulted in a decrease in uUYS, suggesting improved flow for the granules compared to the Dry Mix. This is likely due to a reduction in fines and/or changes in surface properties.
- A clear correlation exists between flow properties and water content with uUYS continuing to decrease with increasing water content, indicating further improvements in the flow properties of the granules.
- As shown in the optical microscopy images, a visual assessment of the wet mass suggested that granule formation started at 30% water content and became dominant at 40%.
- Compressibility exhibits a similar but less pronounced trend, indicating improved packing efficiency as water content increases.
- A similar trend is generally observed with the density measurements, with the exception of 40% water content where BD_P and BD_C values exhibit slight increases, possibly as a result of granule densification.

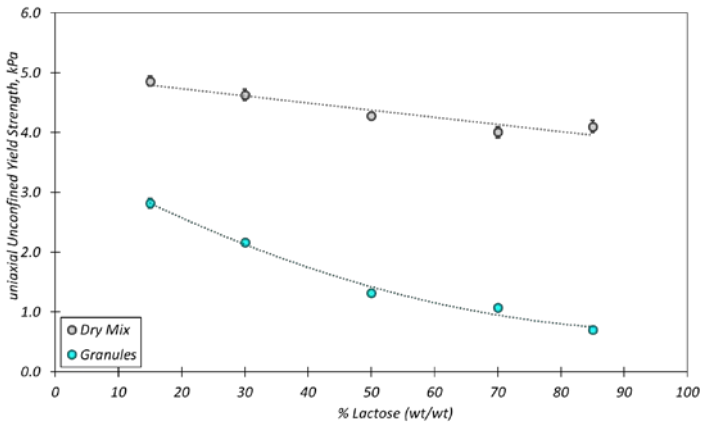


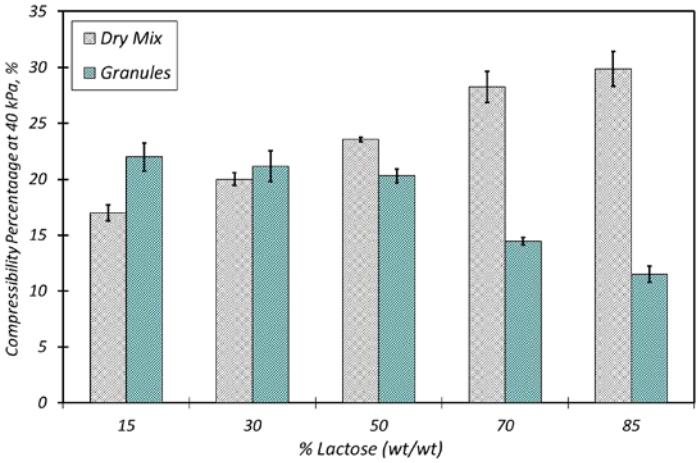


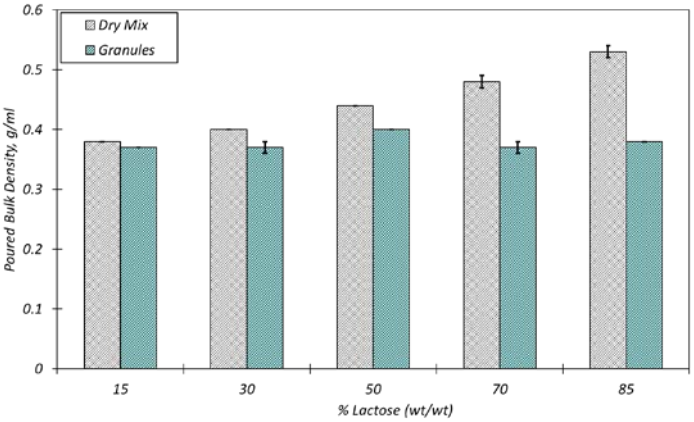


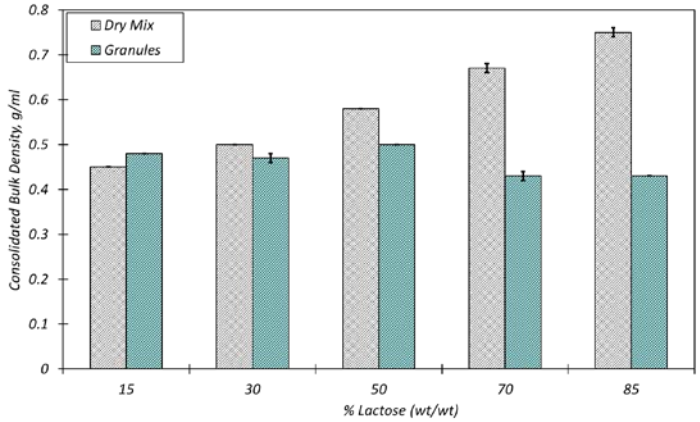


RESULT – EXCIPIENT RATIO









Clear correlations were observed between the flow properties of the dry mix and corresponding granules with increasing lactose content:

- The uUYS for the granules is lower than that of their dry mix counterpart. This demonstrates the effectiveness of the granulation process, and the ability of the UPT to quantify the impact of the process.

- There is a decrease in uUYS with increasing lactose content for the both the dry mixes and granules, suggesting that a higher lactose content results in a less cohesive formulation. Interestingly, the change in uUYS with respect to lactose content is not linear for the granules. Therefore, the properties of the granules cannot simply be predicted from knowledge of the raw components alone.

- For the dry mixes, compressibility increases with increasing lactose content. Higher compressibility is typically associated with greater cohesion. An inverse trend is observed for the granules. Measuring compressibility alone does therefore not accurately or sufficiently inform on the flow properties.

- BD_C and BD_P for the granules remain relatively consistent. Density is therefore not a reliable differentiator and provides limited information on behaviour of the samples.

CONCLUSIONS

The data presented demonstrate the high sensitivity and repeatability of the UPT, enabling the influence of formulation and process changes to be quantified. The granules exhibited a consistent improvement in flow compared to the dry mix. Clear trends were observed between water content, excipient formulation and the flow properties of the resulting granulate. Increasing water or lactose content both reduced uUYS and Compressibility of the resulting granules.

The benefits of uniaxial powder testing can now be employed in industrial applications. A robust, reliable and simple uniaxial tester capable of constructing consistent, free-standing powder columns from a wide range of commonly used powders, means that even inexperienced users can achieve precise and repeatable results. Those looking for a fast and reliable method of troubleshooting process issues, or rapid screening of raw materials, intermediates and finished products, now have an additional and more cost-effective option.

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