Comparison of traditional ring shear cell measurement to novel SSSpinTester for more predictive powder flow analysis

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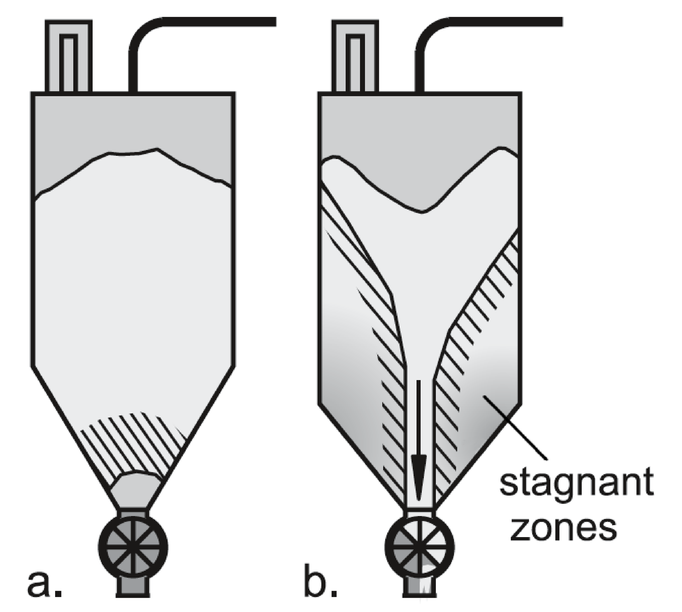
1 – The Importance of Flowability

Consistent and reliable powder flow is of crucial importance to produce high-quality drug products. Flow problems can lead to costly process interruptions:

- Formation of arches and rat holes
- Subsequent flooding
- Content inhomogeneity and dosing inaccuracy due to segregation

Flowability is influenced by:

- Particle size and shape
- Surface properties
- Moisture content and environmental conditions



Flow obstructions: a. **arching**, b. **rat hole**[1]

Improvement of the flowability can be achieved through changes in the *formulation* and / or in the *process equipment*.
Thus, early assessment is needed when only limited sample is available.

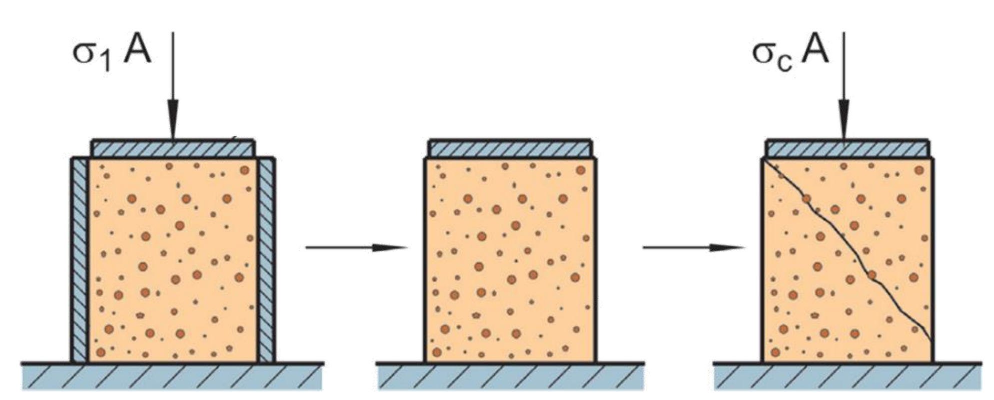
Quantification of flowability happens in the form of the flow function coefficient FFC. The general measuring principle consists of two steps:

1. Formation of a stable powder cake by consolidating with a defined major principal stress.
2. Applying an increasing pressure and measuring the required force to break the cake.

The FFC can then be calculated: FFC = major principal stress σ_1 / unconfined yield strength σ_C and sorted into different categories.

Flow categories

FFC < 1	not flowing
1 < FFC < 2	very cohesive
2 < FFC < 4	cohesive
4 < FFC < 10	easy-flowing
10 < FFC	free-flowing



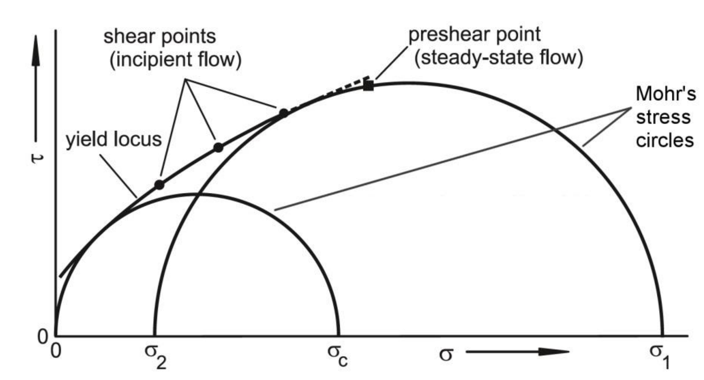
Uniaxial compression test: illustration of determination of FFC-value[1]

2 – Ring Shear Cell Measurement

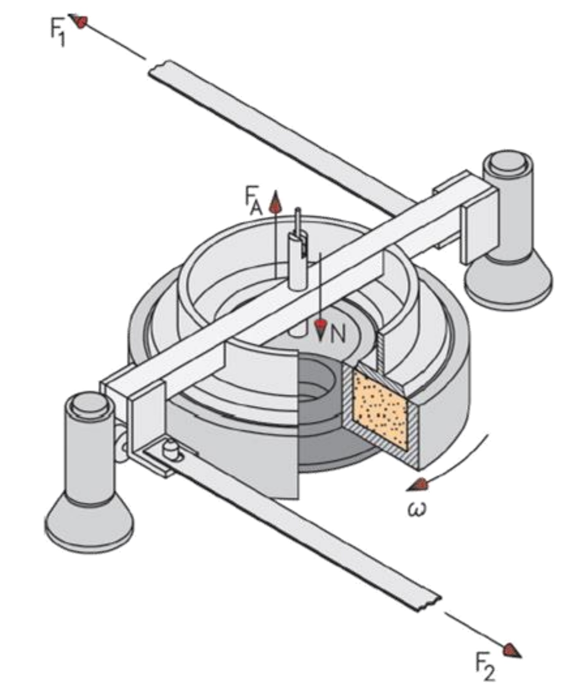
The current industry standard is measuring with a ring shear cell. A powder cake is consolidated with a defined pressure and sheared laterally until constant shear stress reached. The normal pressure is reduced and the procedure is repeated. The normal load and the corresponding constant shear stress are plotted to generate the yield locus.

Limitations:

- **High pressure** (> 1000 Pa) is not representative for conditions later on faced in the production process
- **Sample amount** (> 30 ml)
- Time consuming (> 15 min)



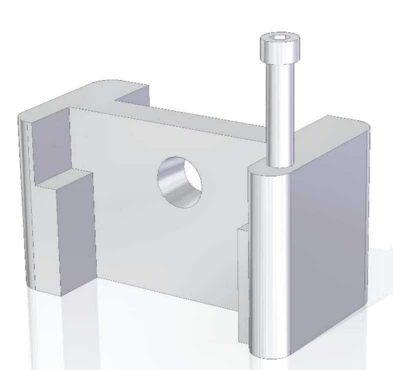
Yield locus diagram with two Mohr's stress circles[1]



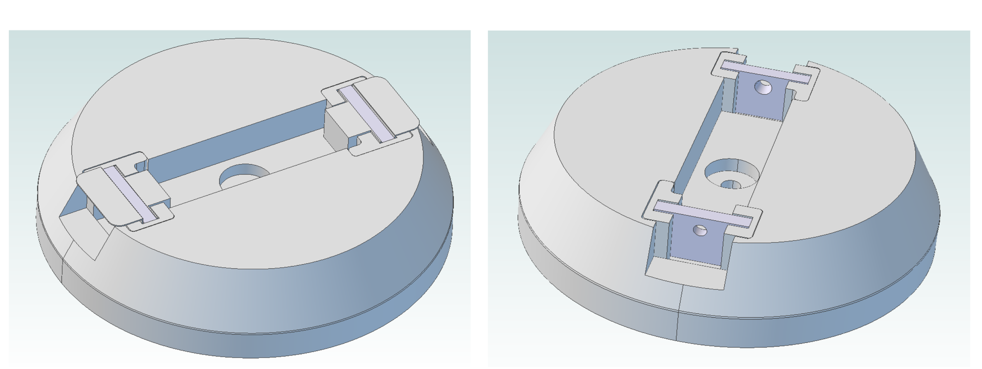
Experiemental setup of ring shear cell[1]

3 – Novel SSSpinTester Technology

To overcome the current challenges, the SSSpinTester makes use of **centrifugal forces** to consolidate the powder specimen. The filled cell is placed in a rotor and spun at the necessary rotational speed to consolidate with the intended major principal stress. For the second run, the two gates are removed. The cell is spun until the cake breaks, the powder flows out and a laser detects the free path. From the rotational speed at failure and the weight of the sample, the unconfined yield strength can be calculated.
The cell volume is only **0.38 cm³** and the powder consumption thereby significantly less than for the ring shear cell. Furthermore, the SSSpinTester is able to measure at much lower pressures when compared to the ring shear cell. Reasonable values at pressures **as low as 50 Pa** can be obtained.

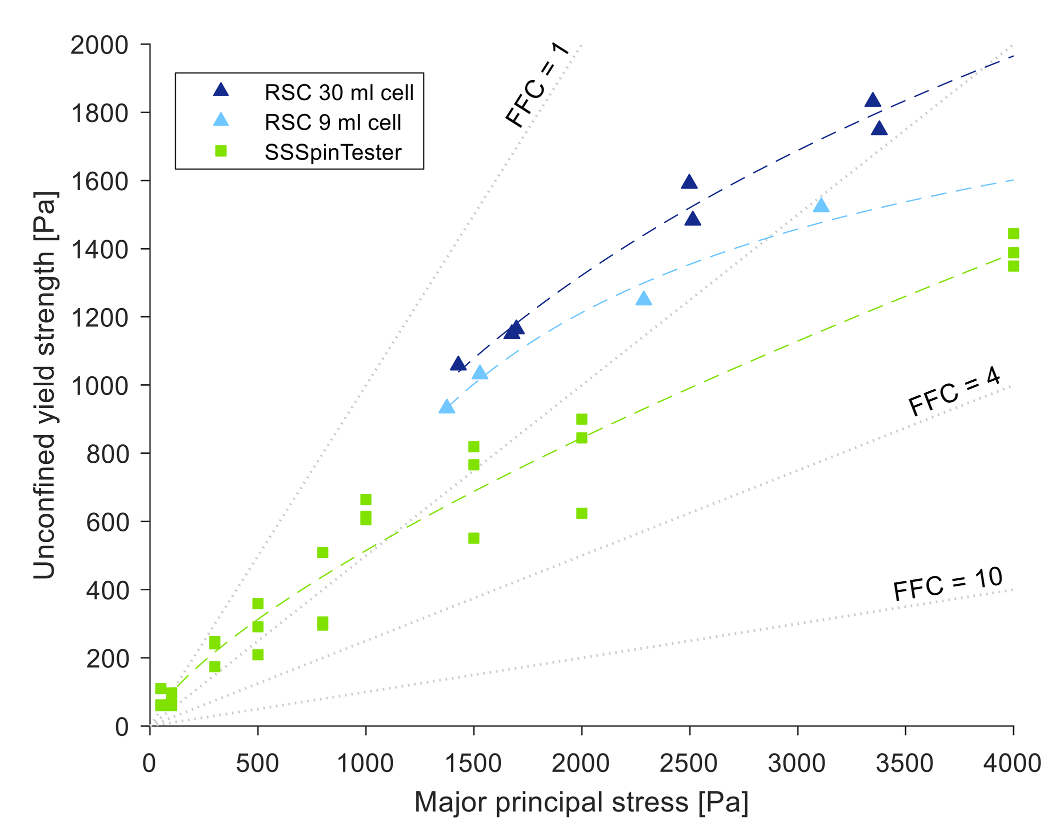


SSSpinTester cell

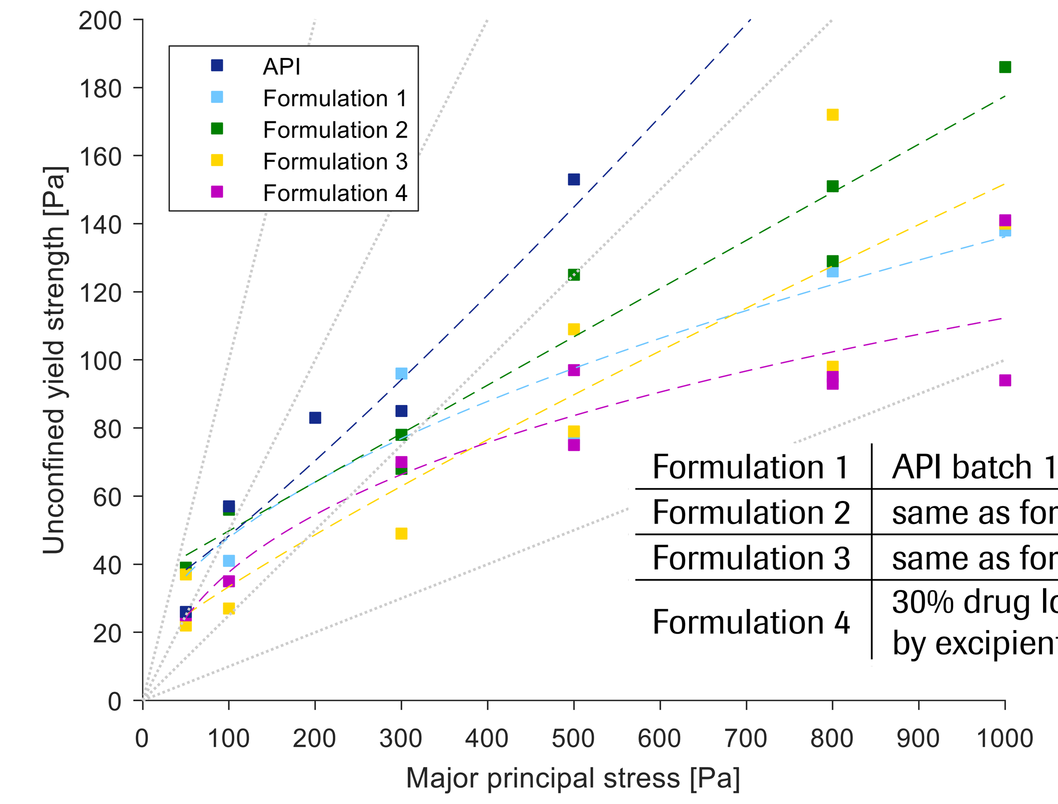


Cell placed in the rotor, for the first run with the gates (left), for the second without for the laser to pass through (right)

4 – Results

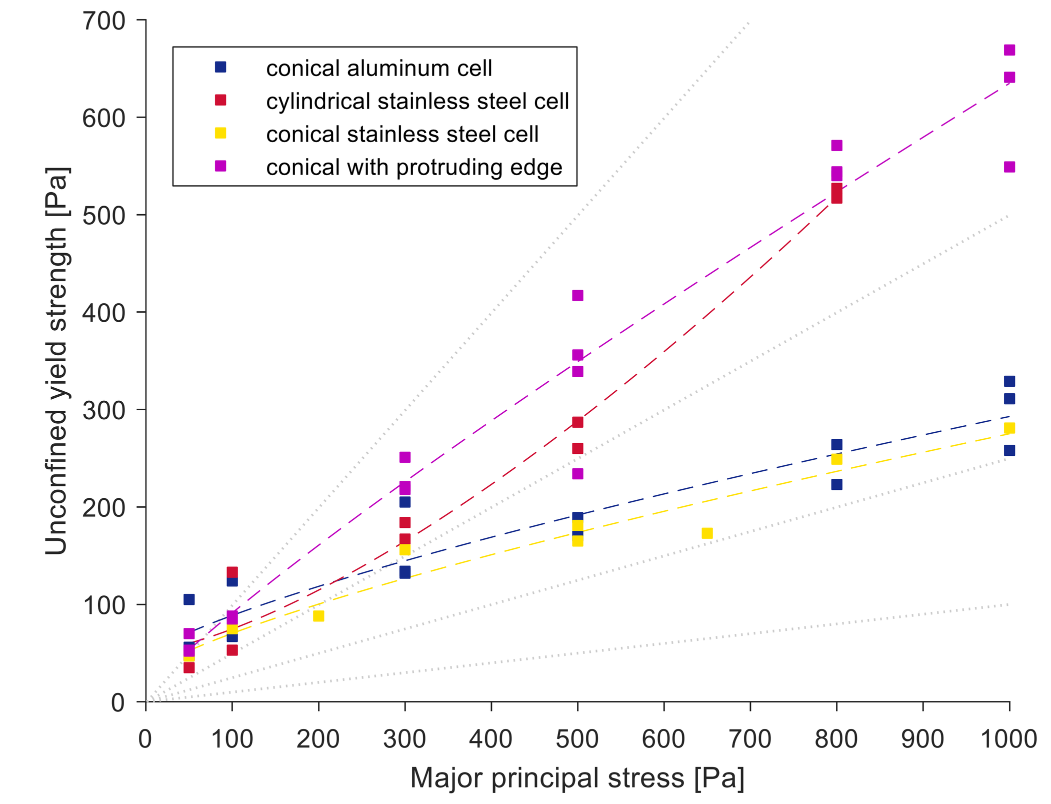


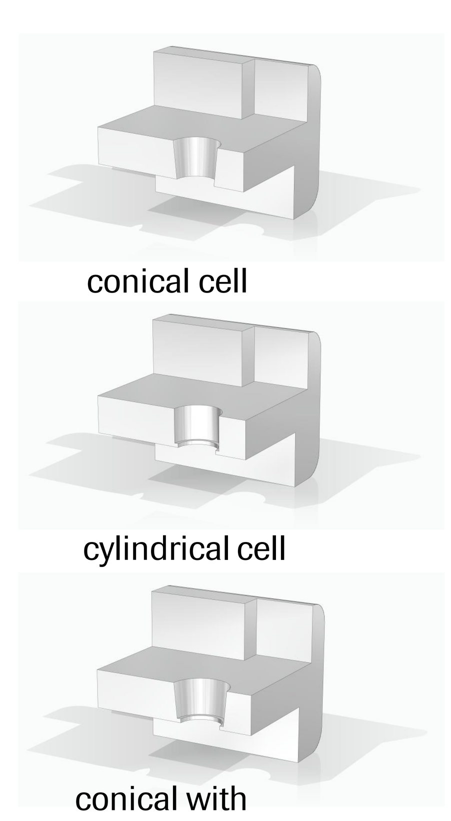
Flow function of corn starch as obtained with two different cell sizes of the ring shear cell (triangles) and the SSSpinTester (squares).



Comparison of flow behaviour of a pure API and various corresponding formulations.

Formulation 1	API batch 1, 40% drug load
Formulation 2	same as formulation 1, + 1% Aerosil®
Formulation 3	same as formulation 1, + 2% Aerosil®
Formulation 4	30% drug load, proportionally replaced by excipients, + 1.5% Aerosil®





Influence of the cell geometry and material on the results as obtained with lactose.

5 – Preliminary Evaluation and Outlook

The SSSpinTester…

- is able to generate values in the process-relevant low-pressure-range of 50-500 Pa
- requires minimal amount of sample, only 0.38 cm³ of powder per run
- is mainly suited for fine, cohesive powders

The challenges faced with the SSSpinTester so far were:

- flowability data highly depend on the method with which they were determined
- high influence of the sample preparation
- difficult to reach sufficient weight for reproducible consolidation

The reproducibility could be improved through design of a new cell geometry.

For future use in routine measurement:

- a robust, operator-independent routine method needs to be defined
- the full flow function needs to be reported
- subclasses of powders with a certain cut-off in particle size need to be identified, for which the SSSpinTester gives meaningful results

Further optimization of the cell geometry may facilitate the measuring process.

6 – References

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7 – Acknowledgement

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