IFPRI Gift Project # 130A, #132B

Selection of Flow Aids: Model-based Prediction of Flow Properties Enhancements

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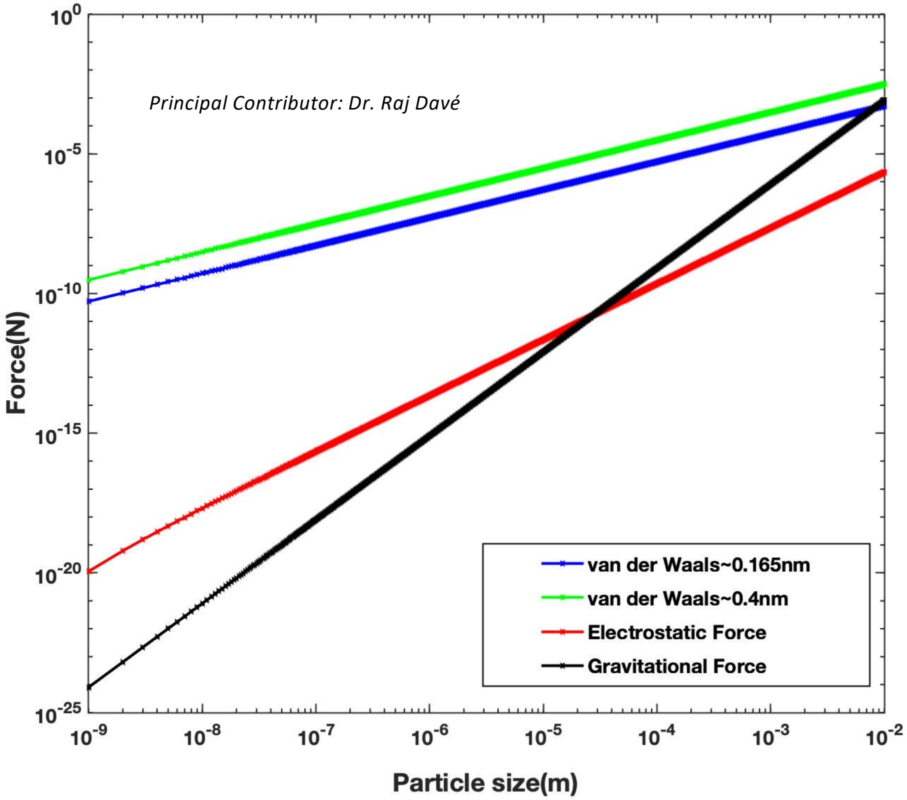
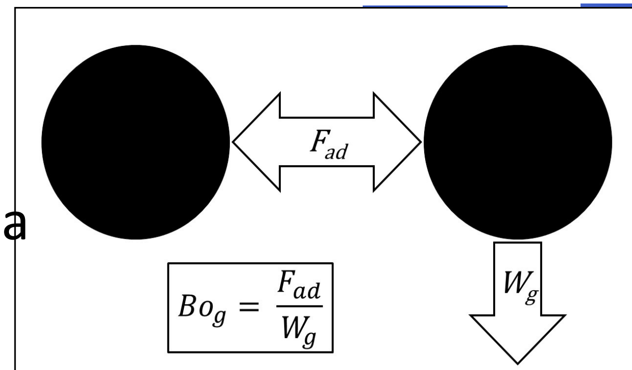
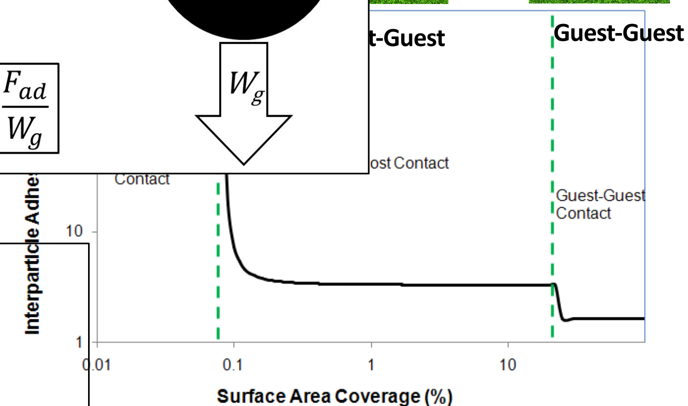
Overview

- Project Objective
  - Mechanistic prediction of flow and its enhancements from particle scale measures
  - Models and decision tools for flow aid selection with minimal experimentation
- Approach
  - Use van der Waals (vdW) contact models to account for cohesion reduction of micro-sized powders coated with nano additives
    - Account for guest-host suitability, amount of guest, non-ideal shapes, surface roughness of host, along with validation through multi-faceted characterization and test materials
- Recent Results
  - Detailed testing of dozen plus materials at varied silica amounts (SAC -25, 50, 100 %)
  - Model improvements for macro-rough particles and the need for higher silica amounts
  - Linking particle to bulk scale – estimation of natural asperities is critical
  - Examination of unexpected advantages in blends
    - Positive synergistic effect on blend (low and medium amounts of a dry coated fine constituent) flowability, content uniformity, and predictability
      - Powder agglomeration of both the dry coated constituent and its blend is a key material sparing indicator

Mechanistic Approach



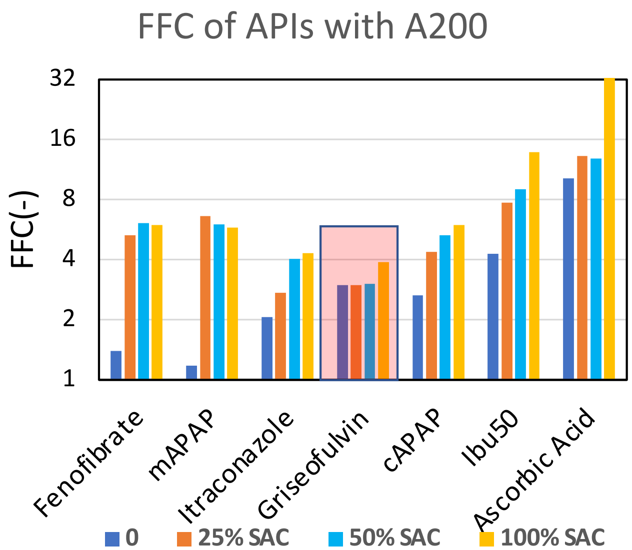


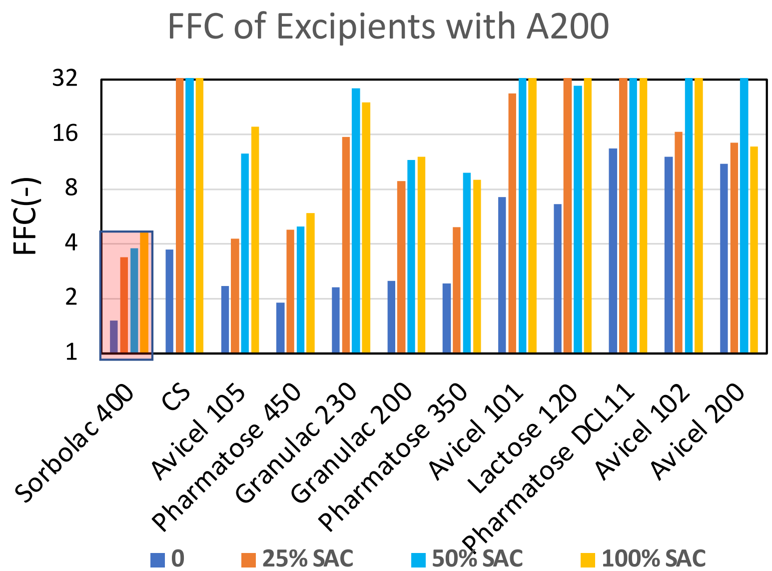


Estimate Van der Waals forces through available contact models

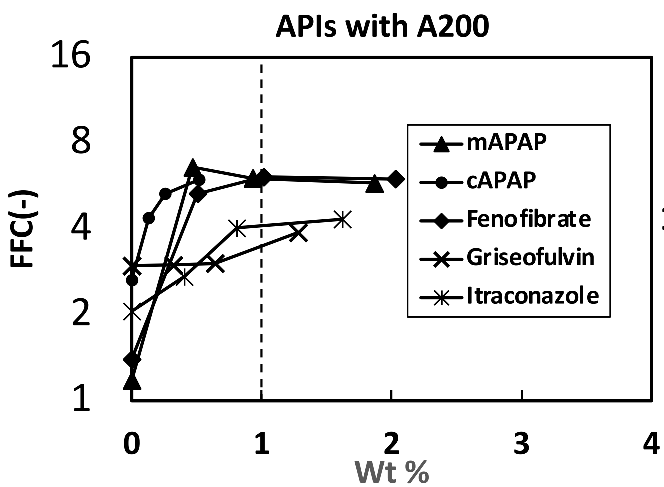
$$\mathrm{Wt}\ \% = \frac{(Nd^3\rho_d)}{(D^3\rho_D) + (Nd^3\rho_d)} \times 100\%$$

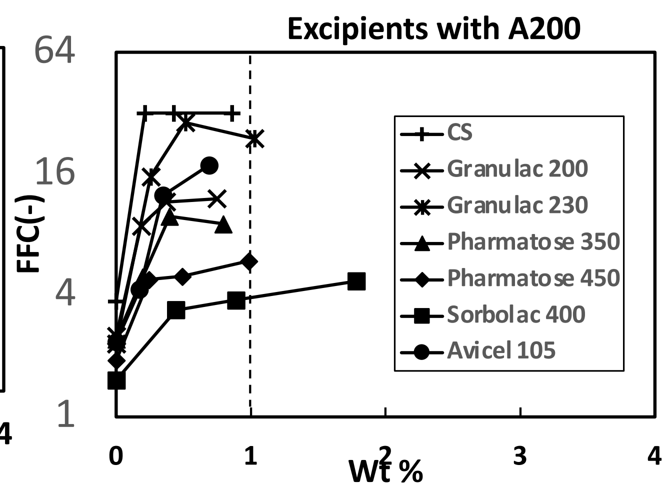
The effect of the amount of silica





Macro rough powders behave differently!

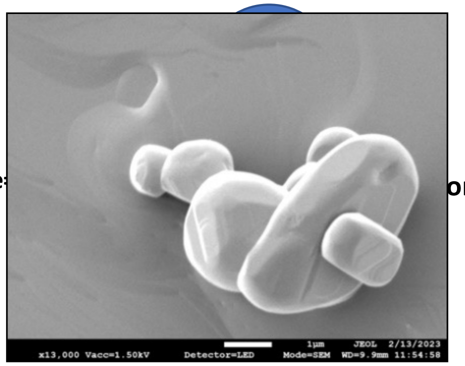




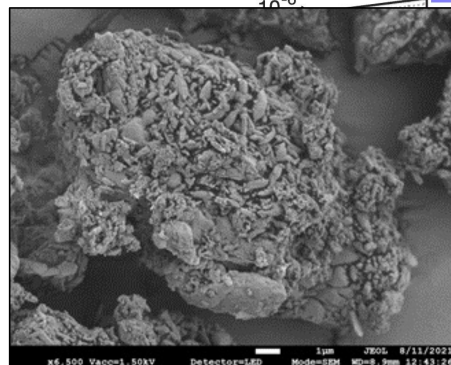
- All particles show improvement in Flow after dry coating
- Theoretical estimates validated experimentally
- Surface area coverage based Wt% estimation better than standard 1wt%

Different Morphologies

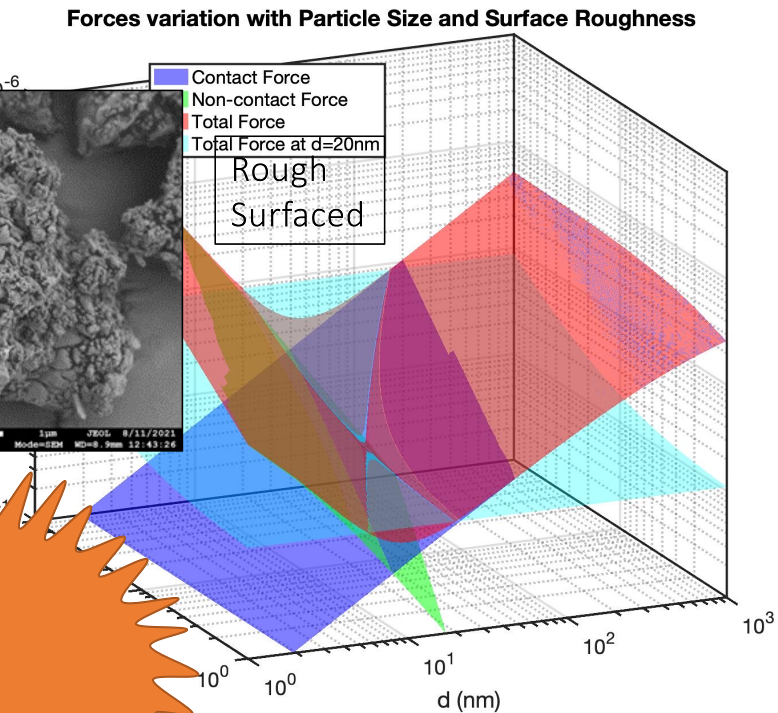
Smooth Surfaced

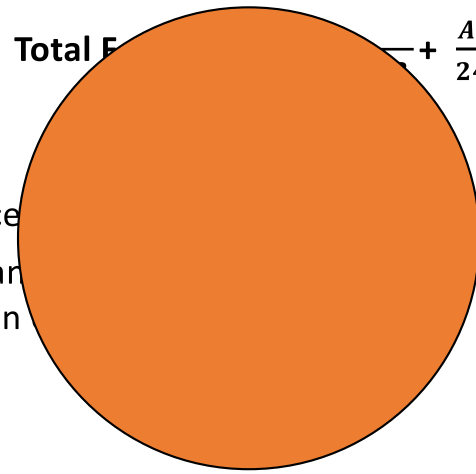
Non-Contact Force  **orce =** $\frac{Ad_{asp}}{24Z_0^2}$

VS



Rough Surfaced

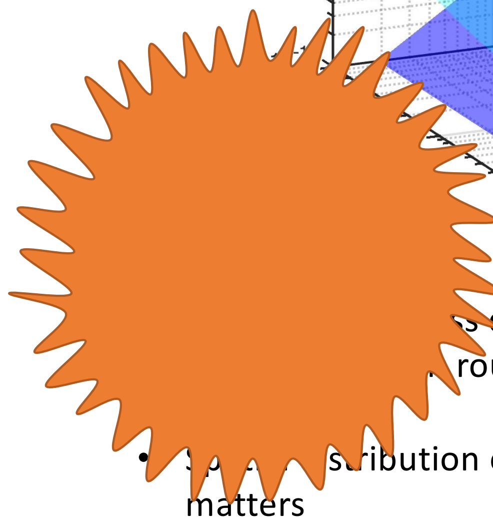


Total F  **+** $\frac{Ad_{asp}}{24Z_0^2}$

Total force

Contact ar

dimension



s dominates in interaction

roughness scale.

- S stribution of roughness also matters

Rough particles have less cohesion before dry coating and the enhancement may be lesser unless more sili silica is used

Particle roughness and specific surface area (SSA)

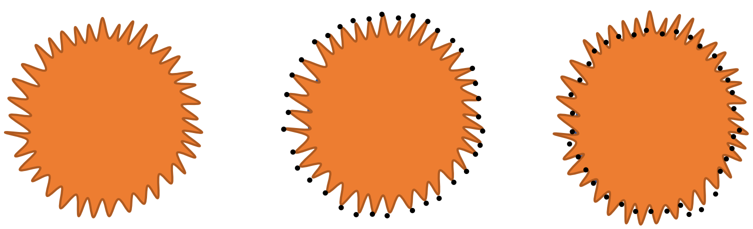
- Roughness may be estimated from an SEM image or through SSA values

Material	D(3,2)um	d50	SSA(m2/gm)	FFC	Dry coated(FFC)
mAPAP	**4.82**	**16**	**0.77**	**1.18**	**5.12**
GF	6.37	19	5.03	2.87	4.46
Sorbolac 400	4.29	16.19	2.62	1.82	4.43

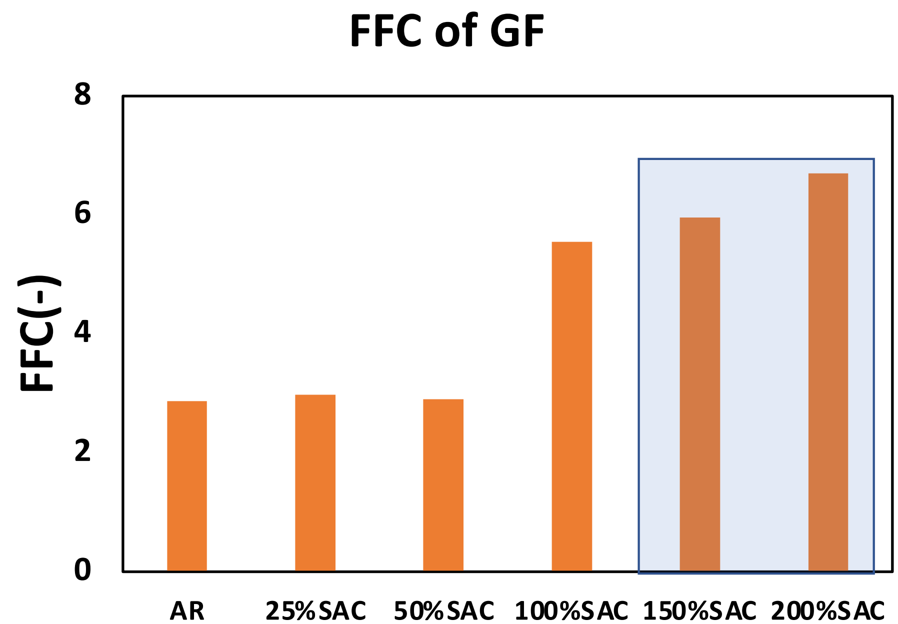
Rough Particles show less improvements too after dry coating

Does more silica beyond theoretical estimates improve Bulk Property?

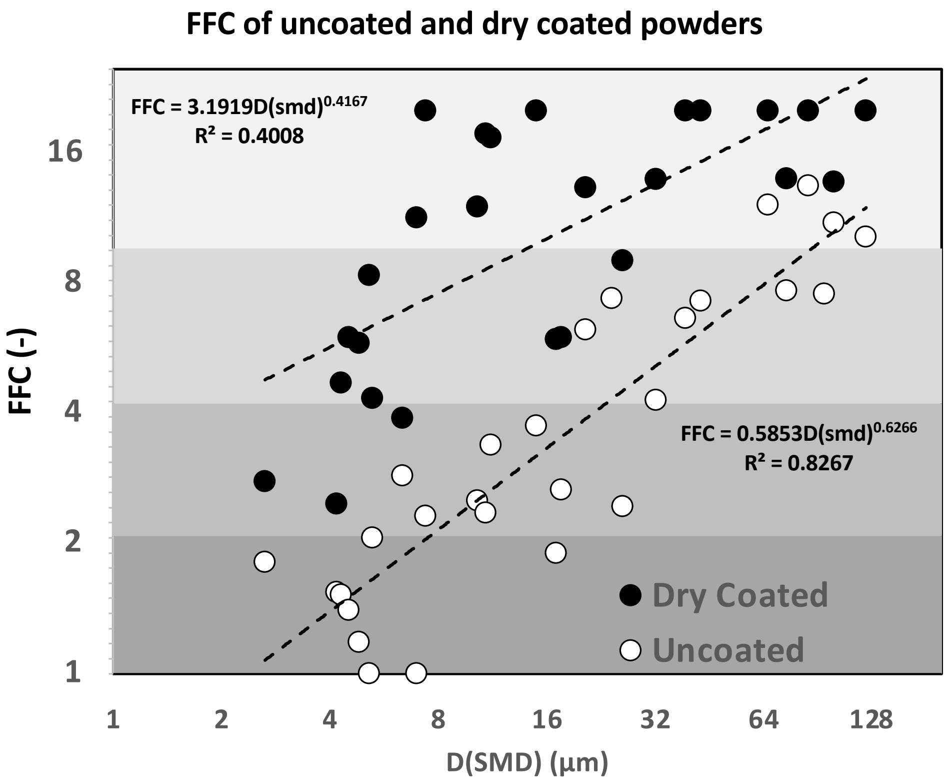
Bulk property improves beyond theoretical estimates of 100% SAC only for macro rough powders



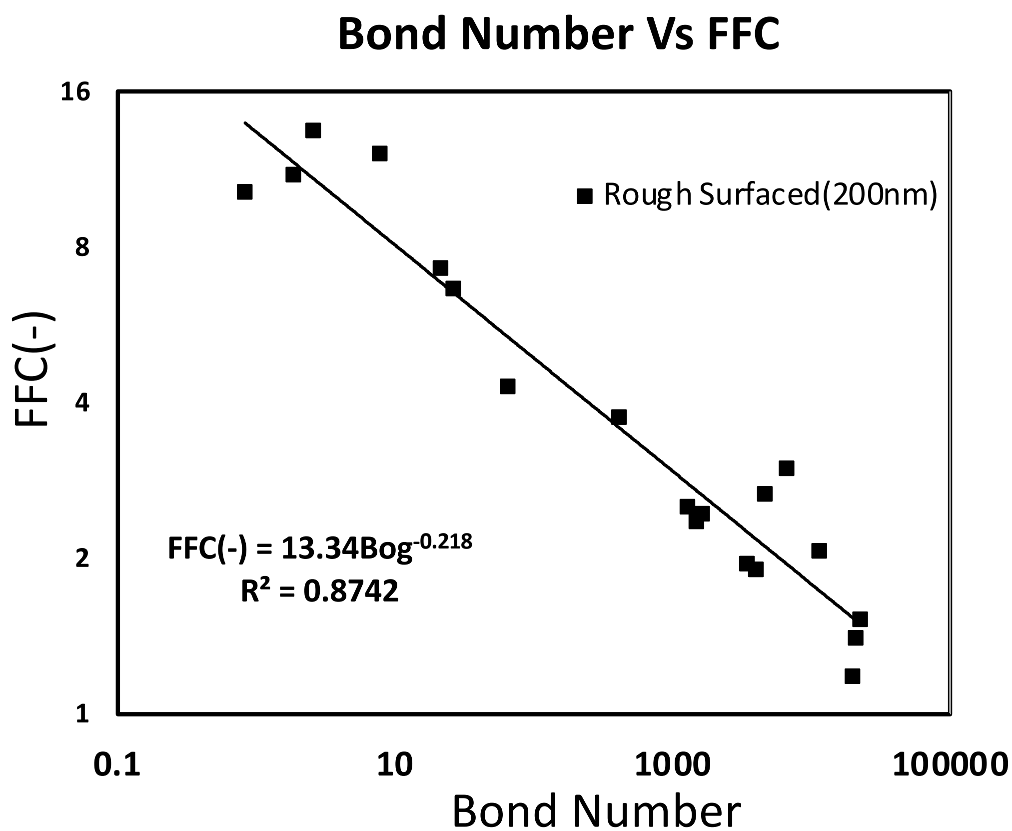
- Silica likes to stay in troughs because of stable equilibrium
- Therefore, more than theoretical estimates may be required
- The effectiveness of dry coating is challenged



Linking particle-scale to bulk-scale: Bond number to capture key parameters

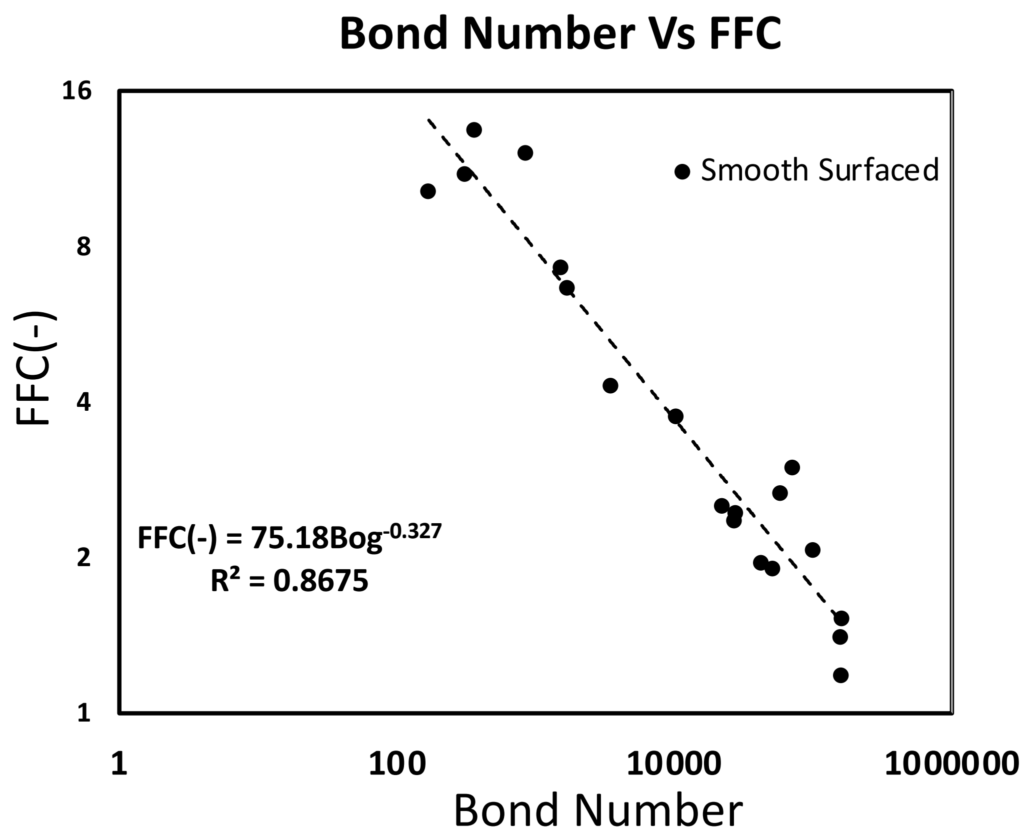


The particle size alone cannot capture bulk property such as FFC

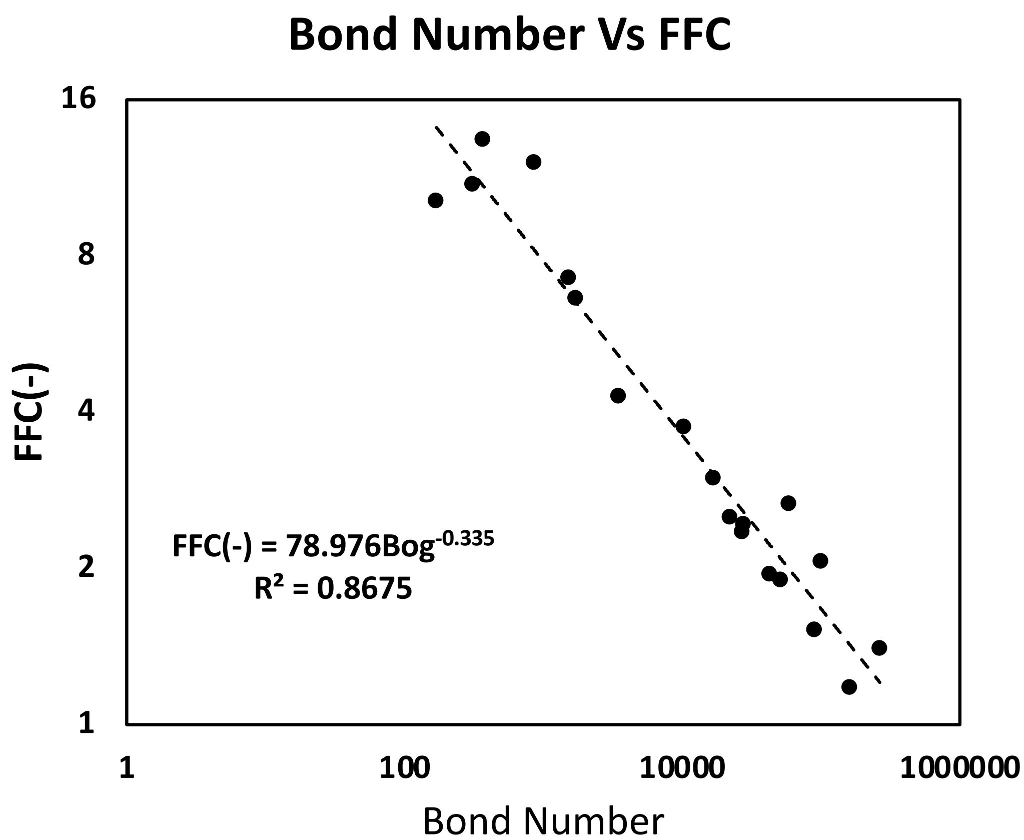


The 200nm roughness assumption may work for uncoated powders

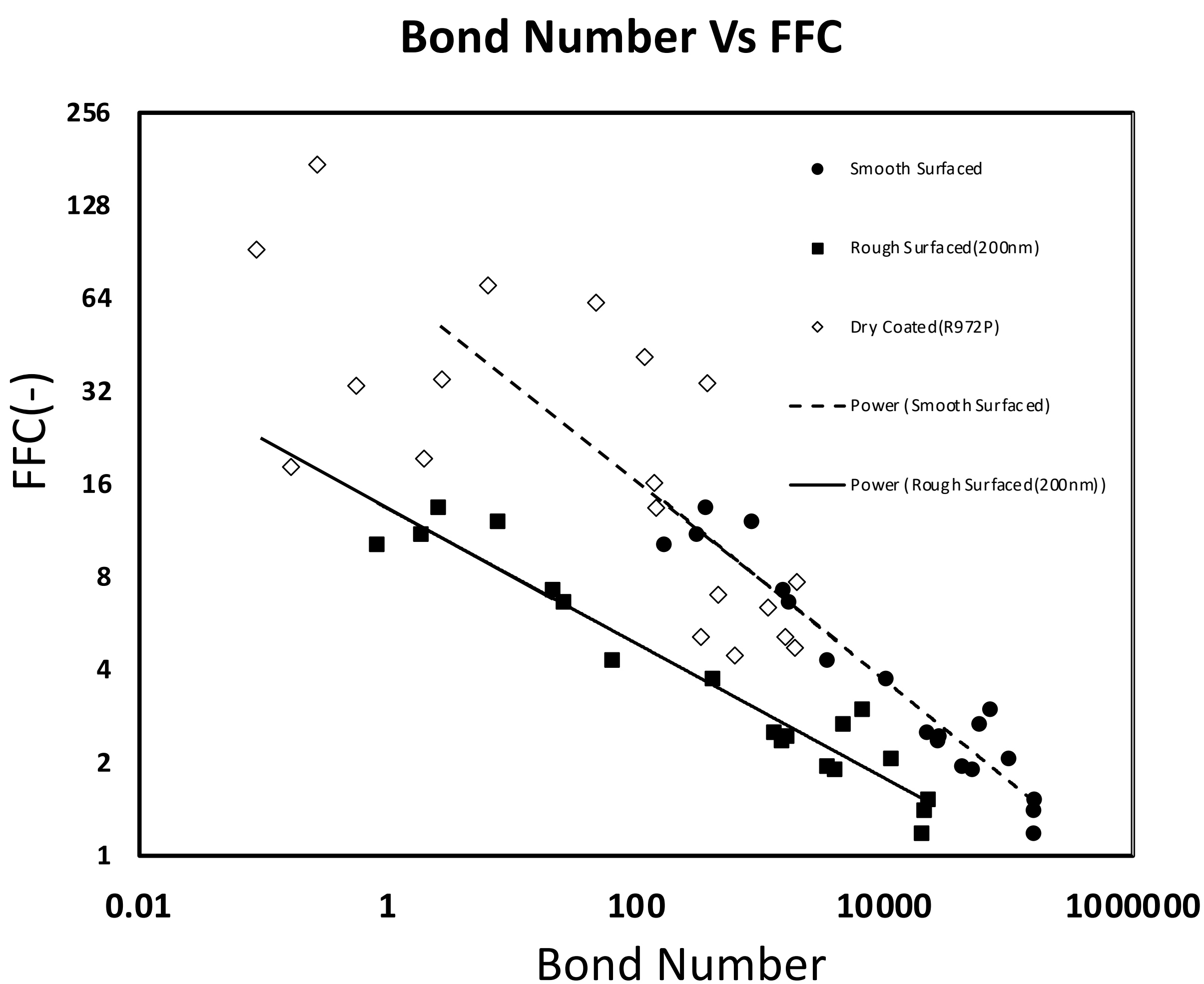
Smooth surfaces assumption may also work well



- Using estimated roughness values of GF (0.5um), Sorb400 (0.8um) and Fenofibrate (~2-5 nm)
- Scatter reduced significantly
- Surface asperity size estimation may be necessary for each powder

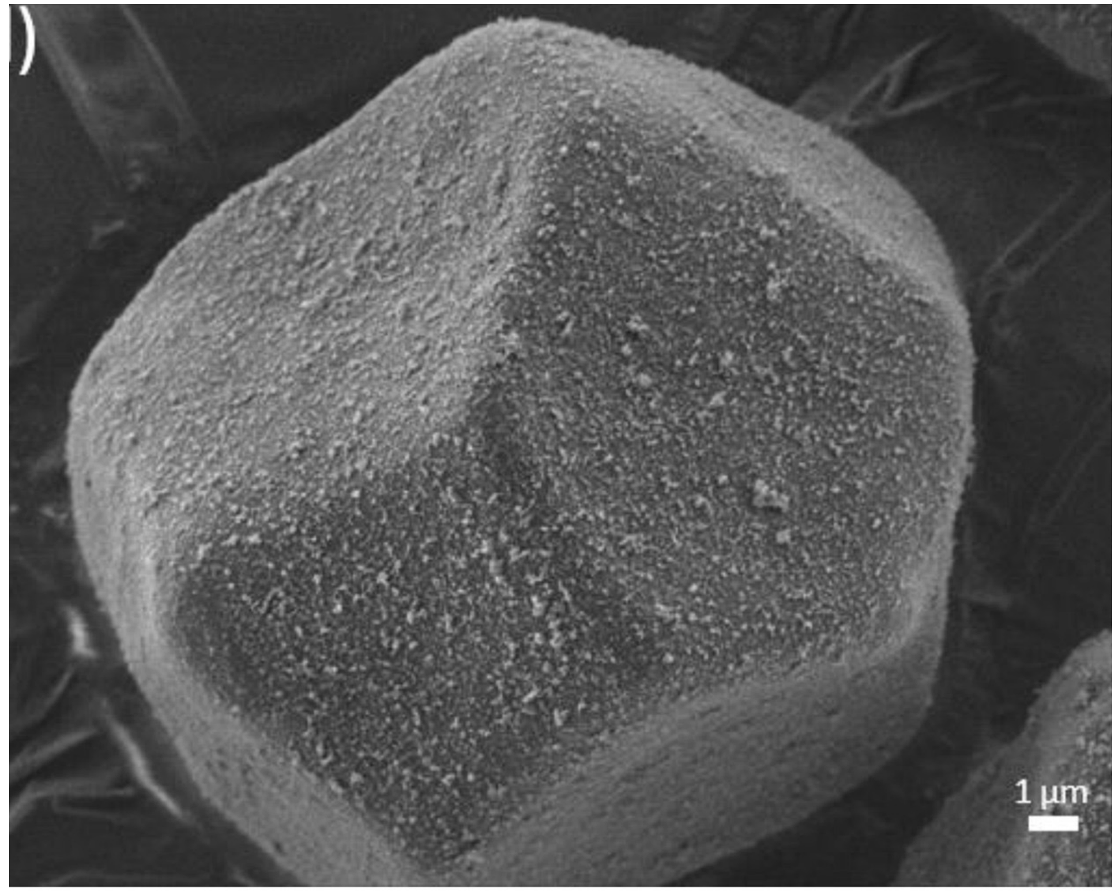


- Since dry-coated particle Bond numbers are less dependent on initial roughness, they are better matched with smooth surface assumptions.
- Most of the powders may not be “naturally rough”



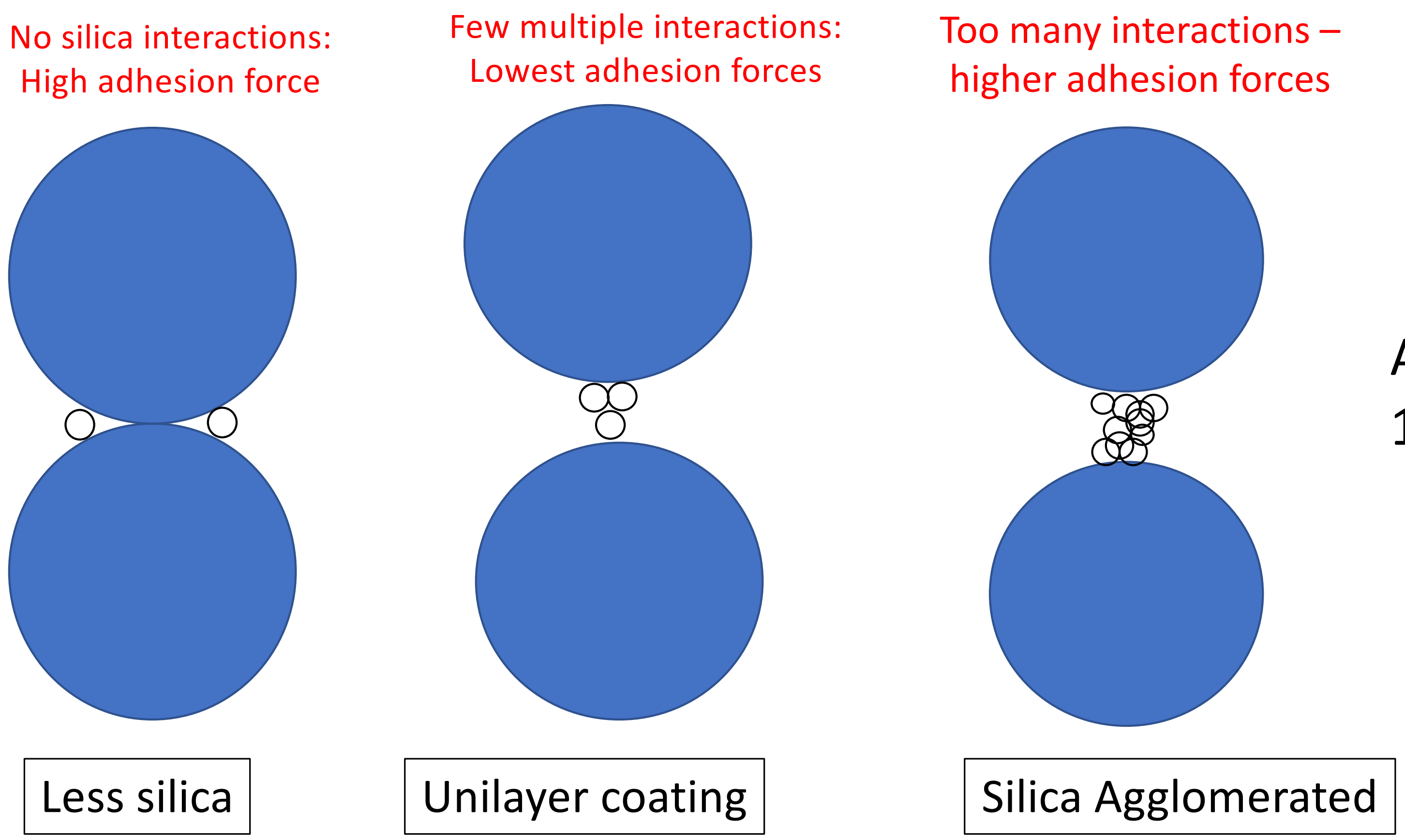
Silica or flow aid may aggregate on host surface

- Generally good coating but small aggregates form on the surface of coated particles
- Potential synergy for blend property enhancements as some of the silica particles from aggregates could transfer to uncoated constituents



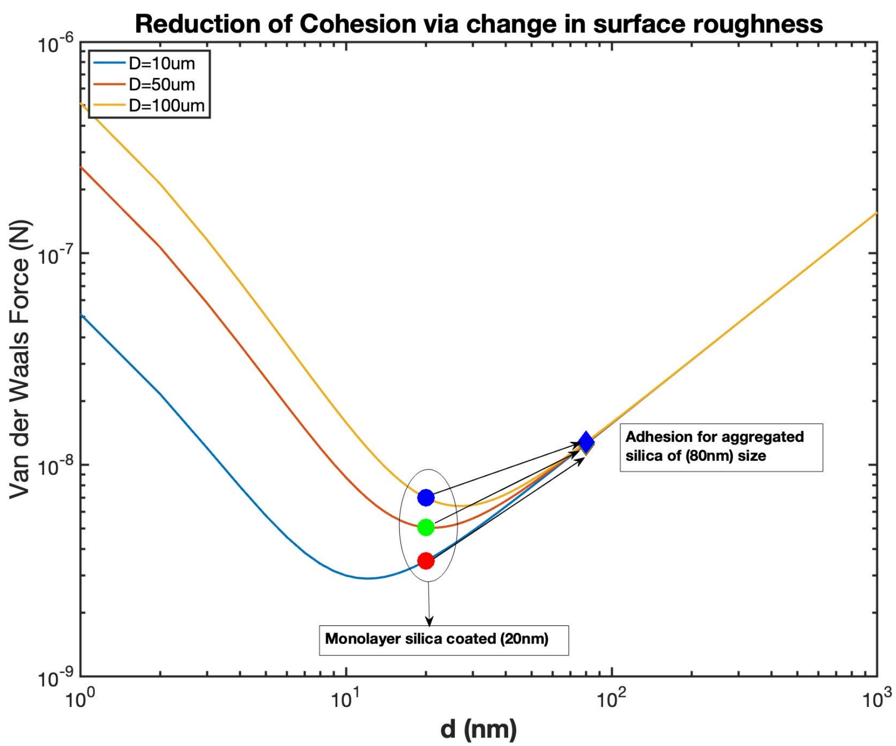
SEM images of cornstarch (10um) coated with Aerosil R972

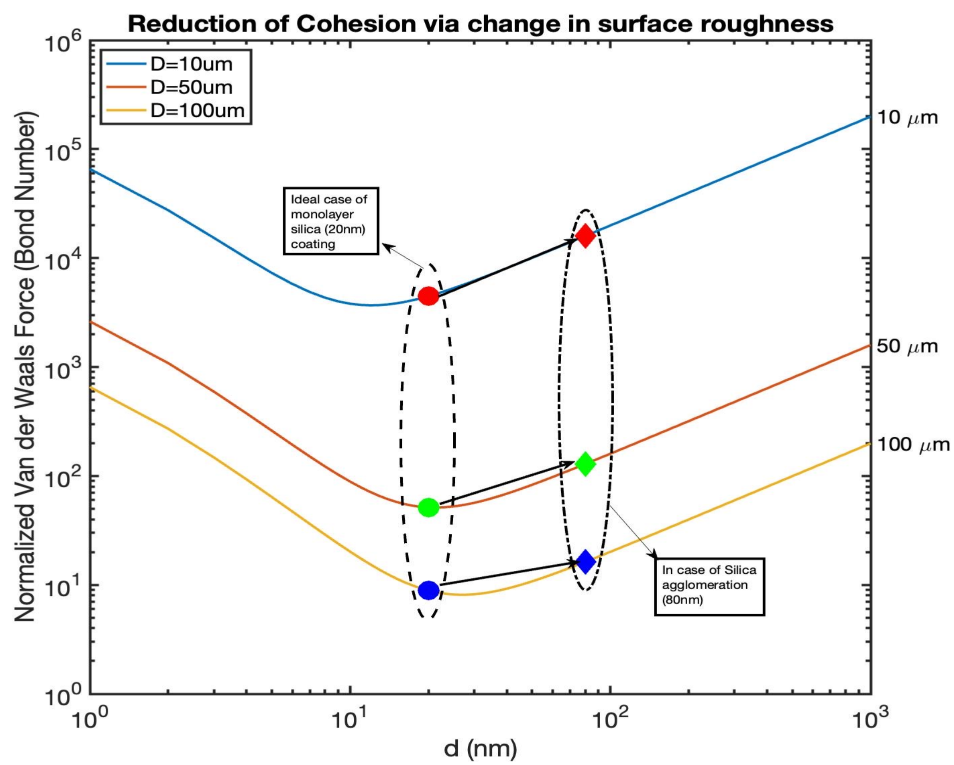
Analyzing silica amount effect and its agglomeration



Aggregate Porosity =
$1- \alpha(Dagg/Dp)^{\beta}$

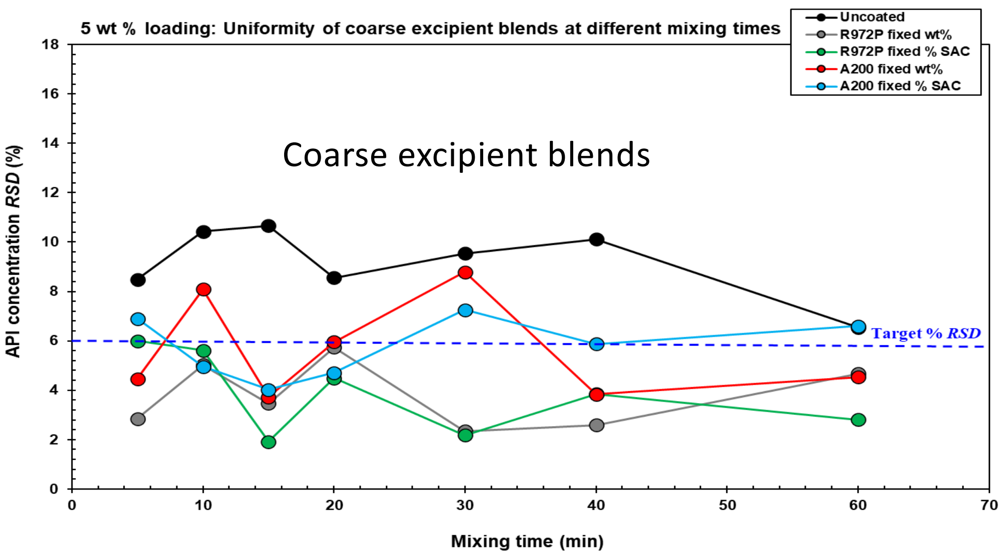
Silica agglomeration increases adhesion force

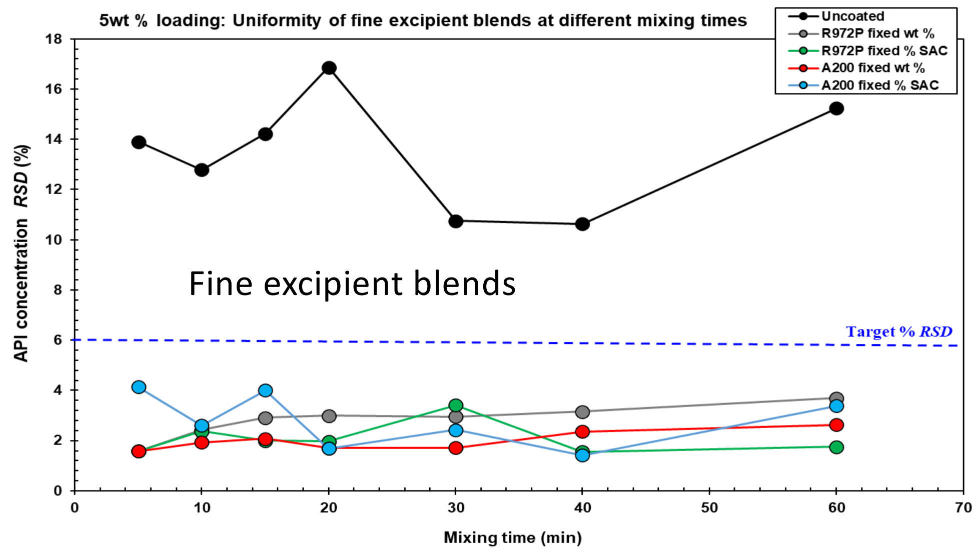




Blends containing a dry-coated constituent (5 wt%): Enhanced fine powder blend uniformity attributed to synergy of silica transfer

- Model API: Milled ibuprofen (d_{50} ~**15 µm**)
- Two excipient types: Fine (AvPH105 & Pharm450 d_{50} ~**20 µm**) or Coarse (AvPH102 & PharmDCL11 d_{50} > **100 µm**)

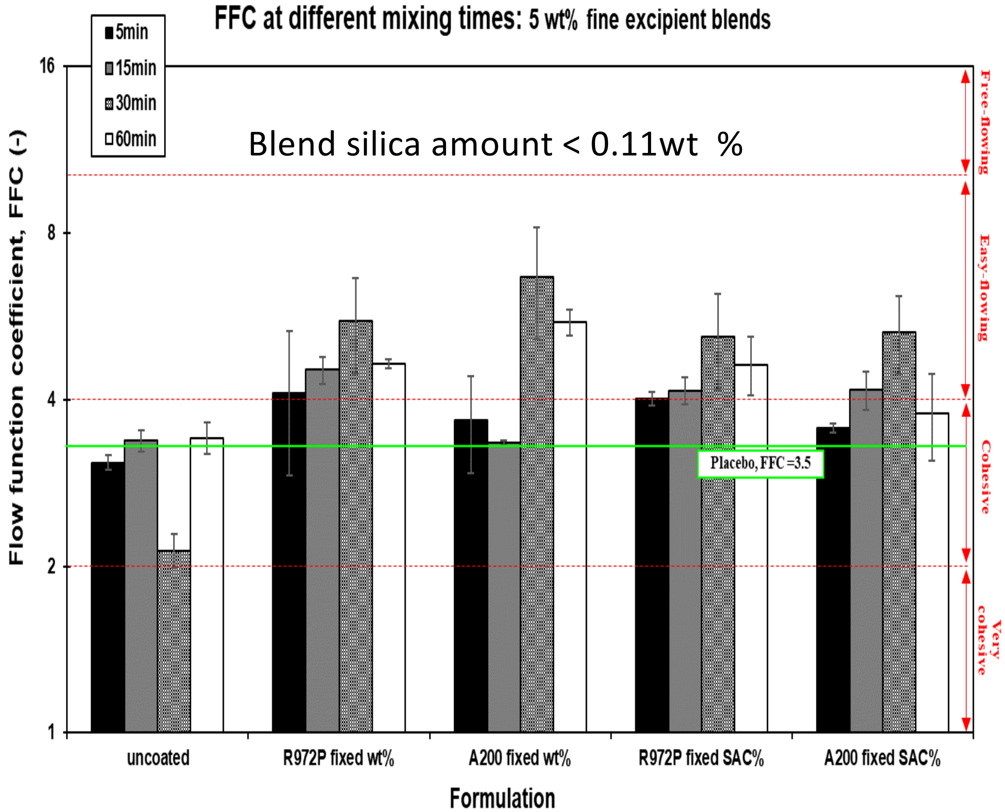


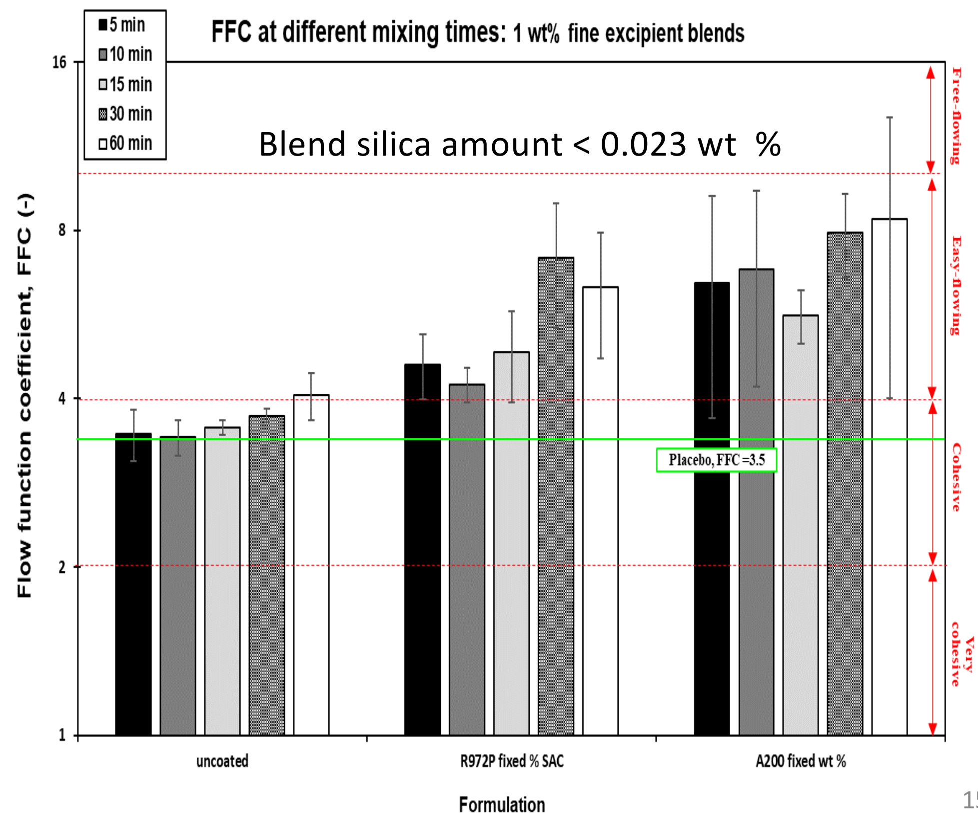


Fine excipients showed better uniformity than coarse excipients
Fine excipient blends with dry coated API was robust against the mixing time and silica type/amount

Flowability of blends with very low amount of a dry-coated constituent (5 & 1 wt %): Examining the dynamics of mixing and silica transfer

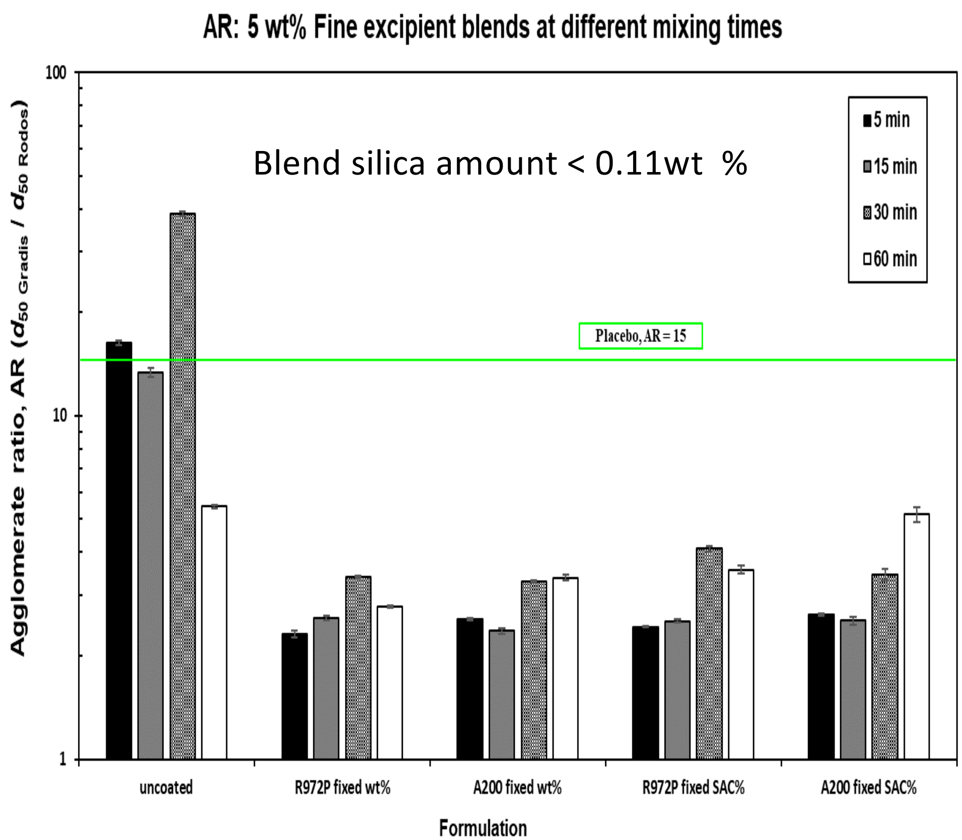
- Flowability of blends should be governed by excipients (95 – 99 wt%)
- *Miraculously* dry coated API fine excipient blends showed notable increase in FFC

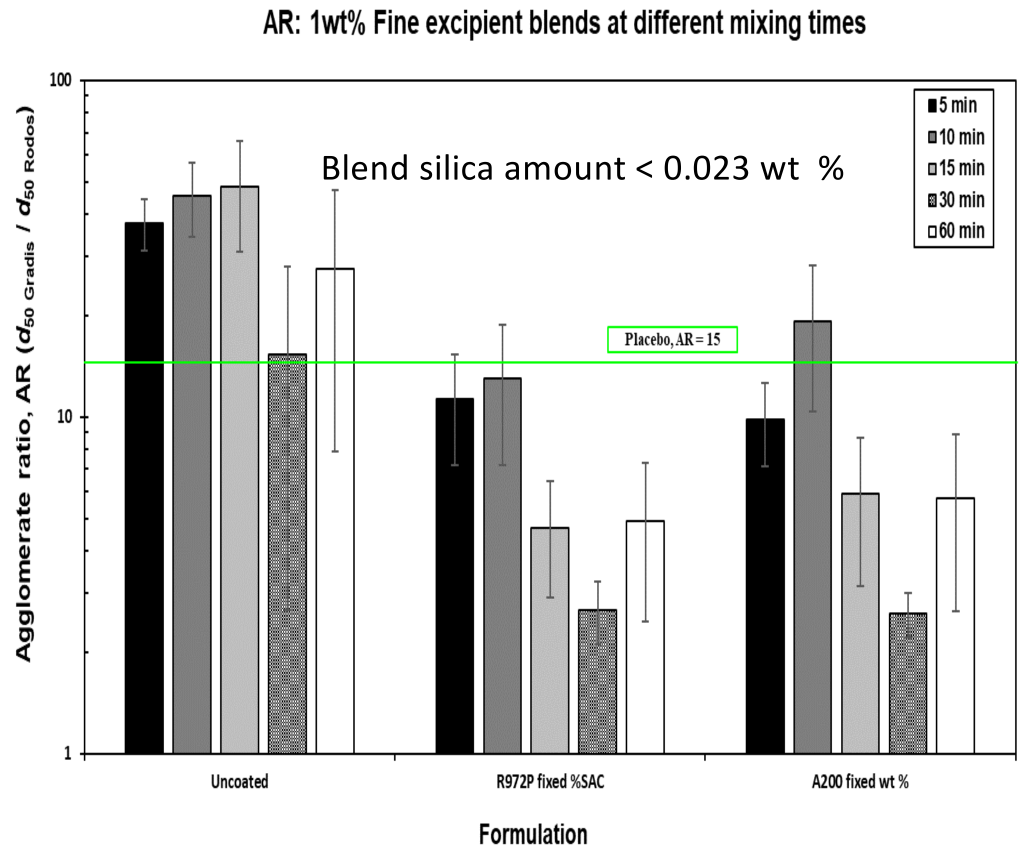




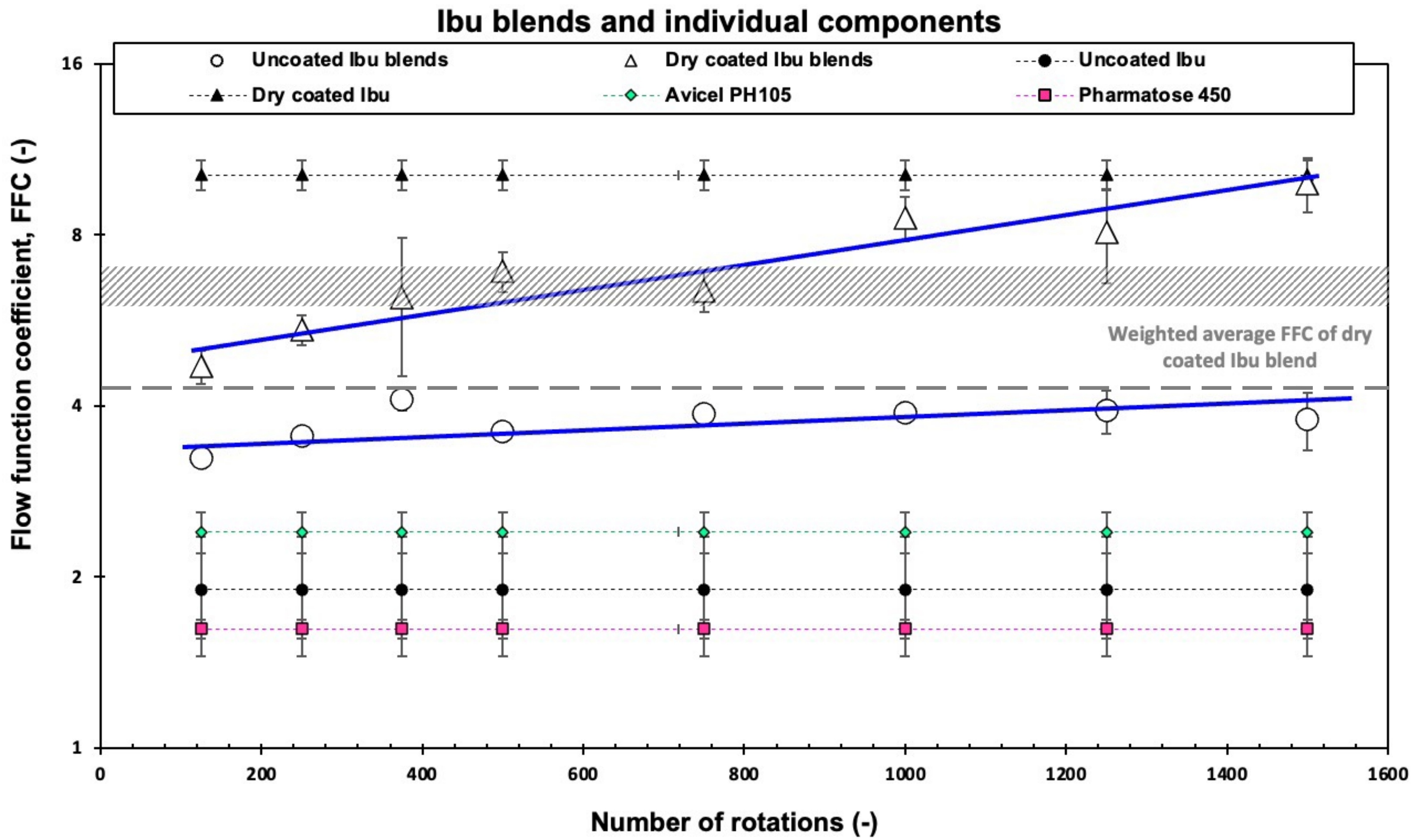
Agglomeration of blends containing very low amount of a dry-coated constituent (1 wt %): Examining the dynamics of mixing and silica transfer

- Blends agglomeration should be governed by excipients (95 – 99 wt%) – [Coarse excipients AR is < 2, yet failed blend content uniformity]
- Dry coated API fine excipient blends showed significant reduction in AR, even for 1 wt % API





Flowability of blends with medium amount of a dry-coated constituent (30 wt %): Examining the dynamics of mixing and silica transfer – fine excipients



Summary and ongoing work

- Key outcomes
  - Particle-contact models along with SAC based normalization is a good way to select the amount and type of silica
    - Validated through dozen plus materials
  - Enhanced contact model explains the behavior of macro-rough particles – they may require higher silica amounts
  - Normalized adhesion force via Bond number helps linking particle to bulk scale
    - For uncoated particles, estimation of natural asperities is necessary
  - Flow aids applied via dry surface coating enhances not only coated powder bulk properties but also their blends even those including low (1-5 wt%) amounts of one dry coated fine constituent
    - Powder agglomeration of both the dry coated constituent and its blend is a leading indicator of blend flowability and blend content uniformity
- Deliverables on track – collaborations sought for the future work
  - Effect of silica aggregation, incorporate other flow measures, coating process intensity – DEM may be needed