**IFPRI (Belgium 2022) Meeting Feedback from Dr. Poom**

1. One of the things that people are asking about is the detail in your experiment. I believe most of what you had shown in your talk and poster are the summary of your finding such as flow aid improve the dissolution performance, or it increases your FFC classification by two ranks. What the members are also interested in is the detail on how you run the experiment as well. What was the experimental design, what was measured, etc. If you can be more specific on the detail of the study that would be very helpful.

* We are developing a set of slides that include relevant details of the experiments so those can be shared with all IFPRI members. Briefly, some of the details are as follows:
  + PSD analysis: For primary particle size of powders, we employ a venturi-based, pressure driven, dry dispersion method using RODOS from Sympatec, along with their laser diffraction system called HELOS). The pressure titration allows us to vary the pressure in a wide range, e.g., 0.1 – 2.0 bar, which could help determine the true PSD without the influence of natural agglomeration or potential attrition due to the pressure-dispersion. Most of the measurements reported are done using 1.0 bar pressure. This yields true PSD including D10, D50, D90 along with D(3,2), which is employed to quantify dry coating nano silica amount.
  + Agglomerate size analysis: Another Sympatec device called QicPic which is a laser imaging system is used. This is done in conjunction with the Gradis system, which dispenses the powder into the size measurement unit without appreciably disturbing the natural agglomerate state of the powders. Thus, gentler dispersion along with image analysis, and statistically relevant agglomerate size distribution is obtained which often indicates how cohesive particles are.
  + True Density measurement: These were done using Helium Pycnometer; for which further details will be provided.
  + Powder bulk properties: Measured using FT4 flow-tester, yielding Flowability via shear-testing (flow function coefficient – FFC) at pre-consolidation stress of 3.00 kPa, and conditional Bulk Density, which is highly reproducible.
  + Estimation of the amount of flow aid for different Surface Area Coverage by Dry coating nano silica based on Mechanistic Model (Chen’s Model mentioned below) which involves the true PSD calculated above (D3,2).

The Surface Area Coverage is calculated from:

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where *d* is guest particle size and *D* is the host particle size.

The Weight Percentage of the guest particles is estimated using below mentioned equation, essentially quantifying the dry coating with mechanistic principles:



involving true density of guest and host as well.

* Based on such estimates of guest silica coverage on host particle different SACs based dry coating is performed on powders using LabRAM (high intensity vibrational mixture).
  + Parameters of operation for dry coating using LabRAM being, 60Hz with acceleration of 75G for a time period of 5 minutes.
  + Correlating uncoated and dry coated properties using scaling parameter (Bond Number) which provides mechanistic correlation of cohesion and bulk properties.

* + Improvements for different silica types and SAC coatings are typically compared with the cases when industry suggsted 1wt% silica coating is done.

1. Related to the previous point. The coverage of the guest particle depended on the mixing/blending step. There are questions of
   * What type of blender was used?
     + Dry coating results reported were done using a lab-scale high intensity vibrational mixer, called, LabRAM. Typical processing parameters used are, Vibrational frequency set at 60 Hz, amplitude set so that equivalent acceleration is 75G (in terms of the gravity of earth), and process time was 5 min.
   * How much blending was done on each sample?
     + The sample amounts typically range from 10-80 grams, most commonly, 50gms. Process parameters are specified above. These are typical and, in some cases, they need to be changed for more challenging, finer powders.
   * How do you ensure that at specific blending you are getting the target %SAC?
     + This is an excellent question. In past, the actual SAC was verified via image analysis. Currently, most example materials have a morphology that does not facilitate image analysis. Therefore, the bulk property improvement after the dry coating is carried out to obtain implicit verification of how well the coating would have taken place. This is augmented by taking typical SEM images of dry coated samples and qualitatively assessing silica coating/dispersion on the host materials.
   * How are you keeping this consistent between experiment with different host particle?
     + So far, we have found that most of the host powders could be well coated with silica using the above mentioned LabRAM parameters along with the previous models to estimate theoretical SAC and hence actual silica amounts. Since theoretical SAC is a function of the host material PSD, we usually get consistency between various hosts. In some cases, we may need to estimate the effective external surface area of the host powder sample more accurately using BET or other means. In cases when the bulk property enhancements are not adequate as compared to typical materials with similar D50 or D3,2 sizes, we need to double-check our silica amounts and/or LabRAM operating parameters. We would be happy to discuss such cases of IFPRI member interest in case their in-house experiments do not yield satisfactory results.
2. The degree of mixing as it related to flow aids effectiveness is of interest to the members can you clarify how the mixing is done. I think you mentioned LabRam in your proposal, but it was not clear from the poster on the blending step.
   * In general, any high-intensity mixer will do the job provided (a) the mixing intensity is high enough for effective simultaneous deagglomeration of guest aggregates and re-distribution of silica particles, and (b) the processing time is sufficient for eventual uniform coating of silica because that depends on the total number of collisions a single host particle undergoes with other host particles and vessel walls (please refer to Zheng et al, *Powder Technology*, 366 (2020) 150–163, for a stick-bounce model providing further details on both these factors). As far as our current work and the results presented in the poster, we used LabRAM, which is meant as a material sparing, batch-mode, lab-scale, benchmarking device. The LabRAM parameters have already been mentioned above.

* It would be helpful if you can explicitly define the mechanism of action of the flow aid. Does it reduce interlocking, does it lower the surface energy, etc. Having that insight clearly define will be very helpful to the member in understanding your work?
  + This topic has been addressed in multiple previous papers and was also covered in the IPFRI presentation. However, it is understandable that the limited time did not allow me to fully explain. I am happy to offer a workshop/tutorial to all IFPRI members down the road and will also include a concise section on this topic in our Annual Report.
  + Briefly stated, the main mechanism is the creation of nano-scale surface roughness when the dry coating process is successful in uniformly dispersing the particles of flow aid such as silica on the host surface. That leads to altered surface morphology, bringing a dramatic change in the inter-particle van der Waals attraction force. That force is governed by: (i) radius of curvature at the contact that becomes the same as silica radius, smaller the radius the better lower the adhesion force, but as long as that contact radius is not too small, e.g., less than ~ 5 nm; (ii) surface energy at contact (which also becomes about the same as that of the silica, thus nullifying potentially higher surface energy of the substrate/host material; and, (iii) hardness at contact, which is also that of silica, harder contact is usually lower attraction forces. To gain the relative impacts, altered contact radius could have over one order of magnitude impact, whereas altered surface energy could only have 10-30 % reduction. That means the main mechanism of improved flowability is the reduced vdW force because of nano-scale surface roughness.
  + Interlocking is a different phenomena and while the reduced inter-particle adhesion due to dry coating will have some impact, the cohesion is a secondary effect and interlocking is a primary effect. That means, flow aids have a limited capability for improving flow if the particles get interlocked due to their high aspect ratios as compared to the vessel/opening/feeder dimensions.
* I realized that your proposal is pharma focus (using silica with host particle being APAP, lactose, etc.) Your work generated a good amount of interest from non-pharma companies. There is a strong appetite to see this work expand to area outside of pharma (into food and detergent). I believed you talked to a few people on this during your poster session. Again, this is different from your original proposal. How receptive are you in expanding the scope of the project? Of course, we would need member from non-pharma company to act as project liaison as well (I believe right now it just Vertex and Roche).  Some comments include
  + First, I would like to have non-pharma representatives in the project liaison group. I will reach out to some of those people but if you and Jim could help, that would be greatly appreciated. I am open to expanding the material scope of the project after I receive (a) more detailed input from those members, and (b) specific examples of the materials and phenomena of their interest. Having said that, the extent of including added examples, test procedures, and models would depend on the state-of-the-art literature related to those mechanisms; for example, the impact of moisture versus electrostatic versus plain vdW forces. By bringing more representatives into the mix, we can better assess the timeline of addressing those items; some of those could be within the first three years of the funded project, some could be by establishing collaborative projects, and some by including such topics in the renewal proposal.
  + Other mechanisms of flow aids: anti-clumping, anti-consolidation, moisture absorption, etc.
    - Flow aids could certainly have an effect on these tendencies of powders, but in those cases, inter-particle forces other than vdW play a more important role. As mentioned above, after gaining a better understanding of the member interest and their materials, I would be able to provide a more educated response.
  + Looking into impact of size and shape of the flow aids
    - Our models are capable of addressing the size of the flow aid for vdW interactions. In terms of shape, I have yet to see anything specific in the literature, largely because of the lack of specificity regarding what type of materials the IFPRI members have in mind. If one is concerned with soapy, waxy, or flaky flow aids, I am interested in developing a better understanding of those in the next 2-3 years. Within the current project period, we are certain of making some progress towards developing a phenomenological understanding of those materials impact on flowability. A potential barrier there is the ability to discern the surface morphology with required accuracy at the scale of interest. I believe there are academics within the currently funded IFPRI projects who could help us through collaborative projects. I would welcome an opportunity to discuss that further.

1. Since you are doing more or less what you outline in your proposal it really up to you whether you want to expand the scope. There are projects that take these types of suggestion into a very good and interesting direction and there are also that ended up losing focus of the original goal. Please let us know your thought on this.

* Some members are picking up that you want some help/input on understanding the effect of electrostatics. Please let us know if you do. There are different routes that we can approach this, it would be good to discuss.

Let us discuss this during our next quarterly meeting and as pertinent, even before that. In line with my response above, these topics need to be examined further; if not now, at a later stage. Regarding electrostatics: (1) There is rich literature coming from the toner industry where numerous papers have shown that unless the powder surface is altered to greatly reduce its vdW forces (like what dry coating could do), the vdW adhesion force is over an order of magnitude higher than electric field forces to enable movement of toner particles. (2) Unlike vdW forces which are mostly prevent during contact, electrostatic forces are “relatively” longer range although the magnitude of forces is inversely proportional to the separation distance squared.

I believe we can clear the smoke if I can better understand what IFPRI members are really talking about and learn more about their specific samples, the powder size ranges, and other material properties.

1. Jim Michaels mentioned that why only silica?

We can coat with any flow additive, although the present results are predominantly based on two types of silica. In past, we have used materials such as alumina, titania, iron oxide, silicon carbide, indium tin oxide (ITO), carbon black, etc. In addition, soapy or waxy materials could also be considered such as magnesium stearate, carnauba wax, leucine, and others. For reduction of cohesion arising from vdW attraction, discrete nanos-zed materials are the best, including fins of the same material as host provided they are about 20 nm in diameter.