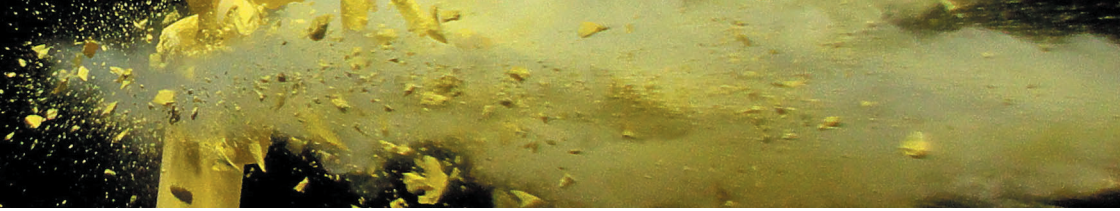
Powder Flow 2011:

Controlling, Regulating and Modifying Powder Flow

Tuesday 6th December 2011, RIBA, London, UK



Powder Flow 2011:

Controlling, Regulating and Modifying Powder Flow

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The Formulation Science and Technology Group is a subject group of the Royal Society of Chemistry, London (U.K.)

It is the leading scientific organisation dedicated to product formulation.

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- Cosmetics
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The FSTG organises many events during the year for the benefit of its members; *conferences, training days, and networking events.*

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Formulation Science & Technology Group

Foreword - Welcome to Powder Flow 2011!

It is a pleasure to welcome you to the RIBA for this very special event on powder flow science and technology.

This years theme "Controlling, Regulating and Modifying Powder Flow" builds on Powder Flow 2009, and explores new aspects of powder rheology. We have been able to secure the participation of the leaders in the field, and hope you will discover and learn new way to measure powder flow and interpret its meaning to further this field of science. There are a number of difficulties with powder flow measurements; first the measurements themselves, as they must be relevant to the powders and processes we study; second the meaning of those measurements, as they need to be related to principals of physics and inform us about our samples; finally, how to use this information to control and modify those processes. A day will not be enough to answer these questions, but we will certainly plant the seeds of future developments and collaborations.

Powder rheology is of importance to a number of disciplines and industries. I am very pleased to see many of them present at the event: specialists from the pharmaceutical industry, formulation scientists, chemical engineers, food science technologists, physics and chemistry academics. This diversity makes the strength of the meetings organised by The Formulation Science and Technology Group (FTSG) of the Royal Society of Chemistry.

Powder Flow 2011 is growing in strength. One of the reasons for holding the meeting at the RIBA this year is indeed because the RSC was too small in 2009 to accommodate us. This year event is also more diverse as we are able to hold a poster session in addition to the exhibition as well as a structured networking session. I hope you will enjoy the B2B networking at the beginning of the day, which will help us to get to know each other and ensure we do meet new people and make full use of the rest of the day. The FSTG has started to hold these speed networking sessions which have proven to be very popular.

Thank you to all the authors who sent in abstracts and are contributing to the poster session. I am also very grateful to all the sponsors and exhibitors who are joining us. I am sure you can imagine that without their support, we could not hold such meetings. Please visit their stands and check out their websites: they are your partners in powder rheology.

Allow me to thank as well the committee of Powder Flow 2011 who have helped me make this event happen: Prof Mojtaba Gadhiri, Prof Mike Bradley, Mr Tim Freeman, Prof Antonio Castellanos, Dr Jag Shur and Prof Rob Price.

Powder Flow 2011 might be a one day event, but it is also a discussion group on Linked In: join the group today and continue your discussions online. Please note that the slides of the speakers will also be available on the Powder Flow 2011 website, and on the FSTG website, alongside the Powder Flow 2009 slides; these can be found at: **www.formulation.org.uk**, and at **www.powderflow2011.com**

I look forward to greeting you during the day, and wish you a very successful Powder Flow 2011, and a very good Christmas.

Philippe Rogueda

On behalf of the committee of Powder Flow 2011

Powder Flow 2011:

Controlling, Regulating and Modifying Powder Flow

Programme

09:00 Register

09:00 Welcome by Philippe Rogueda, B2B networking session

Session One: Interparticulate forces

Chair – Mike Bradley, Greenwich University

10:30 Cohesive interparticle forces and bulk flow properties in fluidisation and powder flow: is a coordinated view possible and convenient?
Prof. Massimo Poletto (Milan)

11:15 Micro- and Macromechanics of Particle Contacts, Flow and Compression of Ultrafine Cohesive Powders
Prof. Juergen Tomas (Magdeburg)

12:00 Lunch, Poster session and exhibition
Poster Session and Prize sponsored by Freeman Technology

Session Two: Flow Properties

Chair – Mojtaba Ghadiri, University of Leeds

13:15 Micro- and Macromechanics of Particle Contacts, Flow and Compression of Ultrafine Cohesive Powders
Dr. Ali Hassanpour (Leeds)

14:00 Dense flows of cohesive materials
Prof. Alain de Ryck (Albi)

14:30 Coffee Poster session and exhibition

Session Three: Case Studies

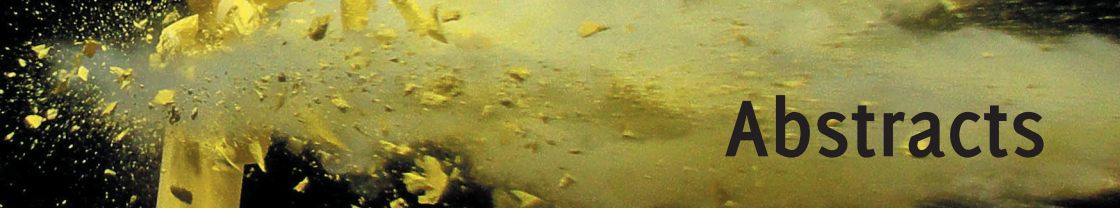
Chair – Jag Shur, University of Bath

15:00 Modelling of adhesive frictional material for powder handling applications
Prof. Jin Ooi (Edinburgh)

15:45 Taming the material; Techniques for modifying the flow properties of powders
Prof. Mike Bradley (Greenwich)

16:30 Determination of the macroscopic cohesion of fine powders by the rain-off experiment
Prof. Brunello Formisani (Calabria)

17:00 Concluding remarks, Ends



Abstracts

Session One Abstracts: Interparticulate forces

Cohesive interparticle forces and bulk flow properties in fluidisation and powder flow: is a coordinated view possible and convenient?

Massimo Polletto – University of Salerno

Binary cohesive interparticle forces are often used to describe the aggregative behaviour of particles in gas fluidization applications of fine powders and, sometime, to explain other phenomena in fluidization such as the delayed bubbling in aeratable powders. These forces can be theoretically estimated but hardly measured. The direct measurement of bulk flow properties is a common procedure to predict the powder flow in silos and piles. Rumpf and Molerus suggest some approaches to relate interparticle cohesive forces with bulk properties. In theory, therefore, it would be possible to use the measurement of bulk flow properties to estimate interparticle forces in order to predict the aggregative behaviour of particles in fluidized systems.

In this presentation some recent experimental results will be reported trying to demonstrate the direct relationship between bulk flow properties and the aggregative behaviour of cohesive powders in vibrated fluidization and aerated discharge of solids. Other experiments will be also reported to validate the possibility of using the Rumpf approach to relate cohesive interparticle forces to the measurement of bulk flow properties.

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Session One Abstracts: Interparticulate forces

Micro and Macromechanics of Particle Contacts, Flow and Compression of Ultrafine Cohesive Powders

Prof. Juergen Tomas - Otto-von-Guericke Universität, Magdeburg

The rapid production of ultrafine, and therefore cohesive to very cohesive powders ($d<10$ µm, e.g. very adhering pigment particles) in biotechnology, pharmaceuticals, auxiliary materials in catalysis or chromatography, generates a number of serious technical problems and issues due to inadequate apparatus and reliability of processing plants. These problems include particle adhesion or sticking during processing (generation or conversion) as well as issues with powder handling and transportation, and particle agglomeration, formulation or coating at the point of use. The understanding of particle adhesion fundamentals is therefore essential to improve product quality and process performance in powder technology.

These fundamentals of cohesive powder compression, consolidation and flow behaviour can be explained using a reasonable combination of particle and continuum mechanics.

Comprehensive models are shown that describe the elastic-plastic force-displacement, viscous damping and frictional moment-angle behaviour of adhesive particle contacts. Using the stiff particles with soft contacts model, a sphere-sphere interaction of van der Waals forces without any contact deformation describes the stiff attractive term. The soft micro-contact response generates a flattened contact, i.e. plate-plate interaction, and increasing adhesion.

These increasing adhesion forces between particles directly depend on this frozen irreversible deformation. Thus, the adhesion force is found to be load dependent. It essentially contributes to the tangential forces in an elastic-plastic frictional contact with partially sticking or microslip within the contact plane. The load dependent rolling resistance and torque of mobilized frictional contact rotation (spin) are also shown.

With this as the physical basis, incipient powder consolidation, yield and cohesive steady-state flow, consolidation and compression functions, compression and pre-shear works are explained. These constitutive models are used to design process apparatuses and to ensure reliable powder flow. Finally, conclusions are drawn concerning particle stressing, powder handling behaviour and product quality assessment in processing industries.

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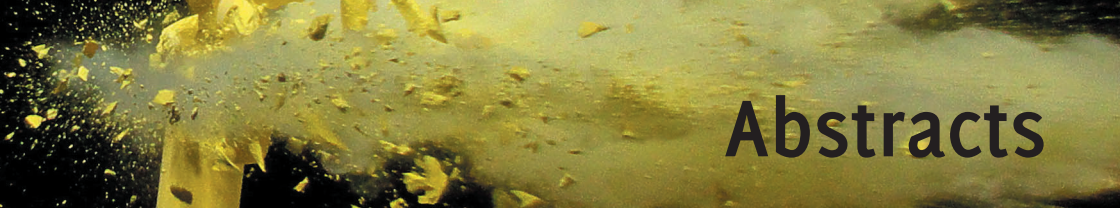

Abstracts

Session Two Abstracts: Flow Properties

Characterisation of Flowability of Cohesive Powders by Indentation

Dr. Ali Hassanpour - University of Leeds

The characterisation of bulk behaviour of cohesive powders is very important in processing of particulate solids, e.g. for reliable powder flow out of storage vessels. Therefore the bulk mechanical properties of cohesive powders have been analysed extensively at large operational scales and applied stresses, typical of those prevailing in storage vessels. However for filling and dosing of small quantities of powders in capsules and for dispersion in dry powder inhalers, the interest is on the behaviour of loosely-compacted powders in small quantities and under very low applied loads. Furthermore at the early stages of drug development, the quantity of the powder available is often very small and the traditional bulk testing methods are neither possible nor applicable. Therefore the ability to successfully predict the flowability of fine cohesive powders from a small quantity or even from the properties of individual particles and their interactions under various physical conditions and in various processes is of great importance. This forms the scope of an on-going research programme at the Institute of Particle Science and Engineering, University of Leeds.

In this presentation the current progress on evaluating the indentation method on a powder bed for assessing bulk powder flow properties is reported. The proposed test method can be carried out on very small quantities, typically a few mm3 and at low consolidation pressures (less than 1 kPa). During indentation, the deformation area around the indentation zone is constrained by the rest of powder bed. The constraining of the deformation in the indentation process in powder beds is far more complicated as compared to continuum solids due to the discrete nature and degree of freedom of particle movement for which no published work has been reported in the literature. In order to gain an understanding of the process of deformation around the indentation zone the Discrete Element Method (DEM) is used to simulate the indentation process. Single particle properties are characterised using the common existing techniques and used as input parameters in DEM simulation with a view to predict cohesive powder behaviour. In this work, particle adhesion is characterised using the newly developed “drop test” technique at the Institute of Particle Science and Engineering (IPSE), University of Leeds.

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Session Two Abstracts: Flow Properties

Dense flows of cohesive materials

Prof. Alain de Ryck - Ecole des Mines d'Albi Carmaux

Flows of granular media still attract attention due to the difficulty to accurately model them. The continuum closure equation allowing predicting such flows are still to be assessed, including in the simplest situations: parallel or steady state dense flows. It has been developed in the recent year a non-Newtonian rheology, so-called μ(I)-rheology, where some viscosity is introduced by a dependency of the friction coefficient on the strain rate: μ depends on the Inertial number, which compares the collisional stress with the mean pressure.

In simple configurations (parallel and steady-states flows), we explore the consequences of this dependency for surface slows on slopes and annular flows. In both cases, the boundary between the dead zones and sheared zones are semi-analytically obtained.

These solutions allow us to predict the slope stability for cohesive materials, the thickness of the sheared zones and their localisation. This last point is of importance in the case of modified Couette shear cells if they are used in the purpose to build a granular rheometre.

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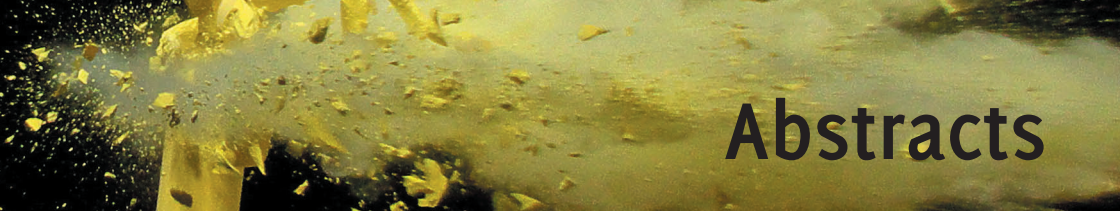

Abstracts

Session Three Abstracts: Case Studies

Modelling of adhesive frictional material for powder handling applications

Prof. Jin Ooi – The University of Edinburgh

Particulates and powders constitute over 75% of material feedstock in industry. Many of these solids exhibit complex cohesive behaviour, leading to handling problems including arching and rat-holing in silo discharge. It is generally recognised that the cohesive strength of a bulk solid is dependent on the prior consolidation stress exerted on the solid. Such cohesive behaviour must be investigated if a numerical model depicting these powder flow problems is to be successful. This presentation describes the development of a DEM model coupled with a calibration methodology to produce quantitative predictions of powder flow problems.

A new contact model was devised to account for the stress history dependent frictional-adhesive behaviour. The model used a bi-linear hysteretic spring to model elastic-plastic permanent contact deformation and a single adhesive force parameter which was defined as a function of the maximum contact overlap for each contact. The model was used to predict the uni-axial unconfined loading to failure of a bulk solid that has been subjected to increasing consolidation stress levels.

The results show that the adhesive frictional model can capture the failure mode (hardening followed by softening at larger strains) and also the stress dependent cohesive strength that is often observed in industrial solids.

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Session Three Abstracts: Case Studies

Taming the material; Techniques for modifying the flow properties of powders

Professor Mike Bradley – The University of Greenwich

Powder flow properties can now be measured in ways that give a good indication of the likely behaviour of the powder in a given process, or conversely allow us to design a process so that it will work reliably with a given powder. The next logical step in powders research, is to understand ways to modify the flow properties of the powder so it will behave more favourably in the process we want to use.

Industrial practice in powder flowability modification is well established, usually to reduce a powder's resistance to flow, through altering the moisture content, the size distribution, applying surface coatings and/or adding so-called "flow aids" or "glidants" to the powder. There are also some relatively new options on the scene, including for example "mechano-fusion". However, many of these are used on a "trial-and-error" basis, chosen according to company tradition and with relatively little understanding of how to optimise their use or which might be a better option for a given application. "Improved flowability" can also have unwanted side-effects, for example increasing segregation tendencies and dustiness of a blend, so occasionally it is necessary to make powders less free flowing.

This paper will give a quick review of what "powder flowability" is and how it can be measured, then will concentrate on an overview of the different methods of powder flowability modification, how they work, their success in different applications, various side-effects and how to measure and control them. It will conclude with a review of some latest research going on in the area.

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Session Three: Case Studies

Determination of the Macroscopic Cohesion of Fine Powders by the Rain-off Experiment

Prof. Brunello Formisani – Università della Calabria

The interparticle attraction forces acting between particles or a particle and a device wall play an important role in many powder handling processes such as fluidisation, dry dispersion, transportation etc. In macroscopic modelling of these operations, a popular method of accounting for the effect of internal forces within a bulk powder is to measure the cohesion of the particulate material from its yield locus, to be determined by a shear tester. Although widely used in the design of storage bins and hoppers, it is unclear whether results obtained by this technique can fit operations where particles are subjected to the dragging action of a fluid, a condition that cannot be analysed in a shear tester.

An alternative approach, suitable for determining bulk solid cohesion in the presence of gas flow, is the so-called "rain-off" experiment, in which a bed of solids is supported against gravity by a rising air flow. Subsequently, the gas flow rate is slowly reduced, thus the supporting drag force is gradually decreased until particles rain down in thin layers or in lumps. At this stage the cohesion of the solid phase can be measured by determining the balance of forces acting at the moment the powder bed fails.

This paper aims to compare the results obtained by the "rain-off" procedure with data provided by a standard shear tester. Several samples of fine powders of interest for the chemical and pharmaceutical industries are discussed. Results are investigated to evaluate the possible influence of gas flow at various degrees of bulk consolidation.

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Poster Abstracts

Flow properties of spray dried granules in dependence of production conditions

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Granules are important in the processing of ceramic components as base material for dry compaction shaping operations. Thereby, flowability of these granules is one important property within processing e.g. handling during storage and transport as well as the homogeneity of the die filling in compaction process. In the latter case the flow properties can have strong influence on the quality of the compacts and finally the sintered products.

One of the most common granulation processes is spray-drying, including the upstream processing steps preparation of raw materials and suspension. Thereby, the process parameters have an important influence on primary granule properties and those on flow behaviour of the bulk. Therefore in-depth knowledge about the correlation of material - formulation - technology and resulting flow behaviour is necessary for ceramic industry to improve quality level and production time of the compacts as well as the fabrication of more complex shaped parts.

The effects of spray drying parameters on the flow properties of granules are studied by the use of Design of Experiments. Nineteen experiments with varying formulation (solid content, composition of organic components) and technological parameters (nozzle pressure, drying gas temperature and mass flow of the suspension) had been carried out in according to the DoE-design. The flow properties of the resulting granules were measured with the Hallflow Meter, a simple and common method in industry.

Besides a direct correlation between varied parameters and the flow properties also interactions higher order could be analysed. In addition, flow properties were linked to primary properties of the granules e.g. granule size, shape and density.

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Poster Abstract

Powder flow properties of bulk lyophilised formulations

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Bulk freeze dried Active Pharmaceutical Ingredients (API's) have seen nascent aseptic automated lyophilisers for fill to finish operations developed. Implications of flow behaviour across the production line during processing or conveying of powders to dosing systems needs addressing. Tablets of freeze dried powder have been proposed, requiring uniform hopper feeding and reproducible filling of dies. This study has investigated powder flow properties of lyophilised mannitol and sucrose solutions as potential carrier agents for bulk freeze dried proteins. Five batches of lyophilised mannitol and sucrose powder were produced from solutions (1, 3, 5, 10 and 15% w/v) using a lyophilisation cycle consisting of -30_ primary drying (32 hr), -20_ secondary drying (4 hr) under a constant vacuum of 20 Pascal. Powder flow and other properties were assessed using angle of repose, compressibility index, Hausners ratio, Karl Fischer, helium pycnometry, X-ray micro computer tomography, light microscopy and thermal analysis. Flow of the produced powder was very poor, a significant positive correlation was noted with increasing solute concentration in the lyophilised solution. Significant* differences in both compressibility index and Hausners ratio were noted, however significant* angle of repose measurements conflicted with the flow when assessed through other methods. Lyophilisation was concluded to confer poor flow properties to mannitol and sucrose powders; however increases of the solute concentration of the initial feed solution did improve flow of the final product.

* p< 0.0001 One Way Anova.

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Poster Abstract

Bulk Powder Hygroscopicity and Caking

G. Calvert[1,2], N. Curcic[2], C. Redhead[2], D. York[2], H. Ahmadian[2] and M. Ghadiri[1]

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[2]Procter and Gamble, NIC, Newcastle upon Tyne

The undesirable transformation of powders, such as caking of a free flowing powder into a coherent mass or deliquescence of a highly hygroscopic material, is a common problem that stretches across many industries. There are a number of mechanisms that may lead to powder transformation and a basic understanding of the microscopic mechanisms involved in the process is needed for a comprehensive holistic approach in addressing the problem of caking.

It is a commercial advantage to research, develop and utilise products that improve both performance and environmental impact. Unfortunately, new performance enhancing ingredients may be sensitive to environmental and operating conditions and their propensity to transform in the supply chain and manufacturing is currently unpredictable. Consequently, high performance materials are either not used or steps are taken to mitigate possible problems.

Recently a collaborative programme between Procter and Gamble, the University of Leeds and Escubed Ltd, as part of a Knowledge Transfer Partnership (KTP), has begun. The main focus of the project is to develop analytical and modelling capability for the characterisation of powder behaviour when subjected to different processing and environmental conditions. A greater knowledge of powder hygroscopic and caking behaviour will lead to a predictive capability that will enable development of optimally performing products and reduce costs.

In this poster the proposed strategy for investigating hygroscopicity and caking is presented.

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Poster Abstract

The use of powder rheology to understand de-aggregation of inhalation powders

E Cordts & H Steckel

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In most of the dry powder inhaler (DPI) formulations on the market the active pharmaceutical ingredient (API) is not administered on its own due to a variety of problems arising upon handling, dosing and inhalation. The necessity to formulate micronized drug particles with a size < 5 µm in order to obtain satisfying API lung deposition led to the fact that nowadays binary or ternary interactive powder mixtures are most commonly used for dry powder inhalers [1]. The addition of excipient fines as a ternary component has been found to increase the drug's inhalable fraction compared to a binary mixture significantly [2]. The exact mechanisms between powder particles responsible for this behaviour still lack mechanistic understanding.

This study has used powder rheology analysis to characterize differences in bulk properties of binary (consisting of lactose carrier and lactose fines) and ternary (including budesonide fines) powder blends.

With the diverse techniques provided by the Freeman FT4 powder rheometer, it was expected to gain a better understanding of interactions within the powder blends. It was of particular interest to investigate how the measured forces are affected by the induction of air through the powder and how this data can be correlated to other dispersion measurements. Starting off with the drug free binary powder blends, its fine particle fraction (fraction , 5.20 µm) was determined via laser diffraction. The powder sample was dispersed through a model device, which was meant to simulate laminar air flow as far as possible.

It was found that increasing amounts of fine lactose within the sample led to a linear increase in cohesion forces under compression. However, this increase in cohesion forces did not correlate with the fine particle fraction measured via laser diffraction. The following aeration test results supported the theory of the formation of non-dispersible agglomerates above a certain amount of added fines.

Consequently, the tests were repeated with ternary mixtures containing additional micronized budesonide. Again, the fine particle fraction (FPF) was determined, this time for the active drug using a Next Generation Pharmaceutical Impactor (NGI). At first, the drug FPF showed a significant increase with increasing amounts of lactose fines (up to 7,5 % added lactose fines). Yet, higher amounts of lactose fines led to a clear drop in fine particle fraction again.

When trying to correlate these findings with powder rheology measurements, neither permeability nor aeration testing has been found to match the trend seen with NGI measurements. However, the powder rheology results correlated to the overall amount of fines within the mixture, but were not able to discriminate between overall and pure drug FPF.

[1] N. Islam, E. Gladki. Dry powder inhalers (DPIs)-A review of device reliability and innovation. Int J Pharm 360, pp. 1-11 (2008)

[2] M.D. Jones, R. Price, J.C. Hooton, M.L. Dawson, and A.R. Ferrie. Using AFM To Investigate How Fines Improve DPI Performance. Proceedings of DDL 16, The Aerosol Society, Edinburgh, UK, pp. 11-14 (2005)

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Poster Abstract

The impact of loaded drug dose and the surface roughness of the coarse lactose carrier to the fluidisation characteristics of dry powder inhaler formulations

Hanne Kinnunen[1], Jag Shur[1], Gerald Hebbink[2] and Robert Price[1]

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In dry powder inhaler (DPI) formulations, the micronised drug that is a Geldart C group powder is blended with coarse lactose carrier (Geldart A). This is done not only to facilitate the handling and dosing of the cohesive drug during manufacturing, but also, ultimately, to enable the fluidisation and thus the pulmonary delivery of the drug. The aim of the current study was twofold. Firstly, the study aimed to investigate the impact of increasing drug concentration on the fluidisation properties of dry powder inhaler (DPI) formulations prepared with carriers with different surface characteristics. Second objective was to gain understanding of how different Geldart group C materials affect the fluidisation characteristics of the formulations.

The lactose carriers used in the study, LH100 and SV010, were obtained from DFE Pharma (Borculo, Netherlands). The drug used was fluticasone propionate (FP) and the placebo formulations were prepared with micronised lactose LH300 (Also from DFE Pharma). To study the fluidisation properties of the formulations, a method for measuring the pressure drop across the powder bed using the Freeman Technology FT4 powder rheometer (Freeman Technology, Tewkesbury, UK) was developed.

The results indicated that the fluidisation properties of the formulations prepared with the carrier demonstrating a higher degree of surface roughness were less susceptible to change in fluidisation properties when the concentration of the drug was increased. This was attributed to the surface asperities and the intrinsic fines of the rougher coarse carrier masking the impact of the added fine particles. It was also found that the fluidisation properties of the carrier with rougher surface and more intrinsic fines were not sensitive to the type of fines (drug vs. lactose). These results can be used in the pursuit of understanding the mechanisms governing DPI performance.

Acknowledgements: DFE Pharma for funding HK.

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Poster Abstract

The effect of temperature on flow properties of powders

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Changes of cohesive flow properties of powders at high temperature are observed in many industrial process units, such as fluidized bed reactors, granulators and dryers. Many authors investigated the behaviour of powders at high temperature through fluidization experiments (Formisani et al., 1998; Lettieri et al., 2000), measurements of the interparticle forces (Pagliai et al., 2007) and direct measurements at the bulk level (Kanaoka et al., 2001; Kamiya et al., 2002). However, the understanding of the effect of temperature on interparticle interactions and flow properties of bulk solid is not still clear. Furthermore, conventional testers and procedures are not suitable for measuring the powder flow properties at high temperature.

In this work, an annular Schulze shear cell, modified in order to measure yield loci at high temperature, was used up to 500°C to directly evaluate the effect of the temperature on the flow properties of samples of fluid cracking catalyst powder, fly ashes, corundum, porous alumina and glass beads. A limited effect of temperature was observed for the cases in which only van der Waals' forces were present.

In order to give an interpretation of the experimental evidences and to correlate the macroscopic flow properties of powders with interparticle interactions, a theoretical framework was developed according to the the particle-particle approach of Rumpf (1974) and Molerus (1985). In particular, the tensile strength of the powder was related to the van der Waals' forces acting between particles coupling the Rumpf equation with the alternative assumption of elastic or plastic deformation at the contact point of particles. The results of the analysis suggests that the increase of the cohesive behaviour with increasing consolidation or the slight increase of the cohesive behaviour with the temperature are mostly related to the plastic deformation of contact points and, therefore, to the strength of the material.

References

Formisani B., Girimonte R., Mancuso L., 1998, Analysis of the fluidization process of particle beds at high temperature, Chemical Engineering Science 53, 951-961

Lettieri P, Yates J.G., Newton D., 2000, The influence of interparticle forces on the fluidization behaviour of some industrial materials at high temperature, Powder Technology 110, 117-127

Kamiya H., Kimura A., Yokoyama T., Naito M., Jimbo G., 2002, "evelopment of a split-type tensile strength and analysis of mechanism of increase of adhesion behaviour of inorganic fine powder bed at high-temperature conditions, Powder Technology 127, 239-245

Kanaoka C., Hata M., Makino H., 2001, Measurement of adhesive force of coal flyash particles at high temperatures and different gas composition, Powder Technology 118, 107-112

Molerus O., 1985, Theory of yield of cohesive powders, Powder Technology 12, 259-275

Pagliai P., Simons S.J.R., Rhodes D., 2007, A novel experimental study of temperature enhanced cohesive interparticle forces, Powder Technology 174, 71-74

Rumpf H., 1974, Die Wissenschaft des Agglomerierens, Chemie Ingenieur Technik 46, 1-11

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Poster Abstract

Early Stage Drug Development Flow Properties and Their Relevance to Full Scale Dosator Operations

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Dosator filling machines have been on the market over forty years or so, and their mechanisms have been evolved over the time; in parallel with this development formulation scientists have progressively increased the potency of blends. Despite the work that has progressed in both of these important fields, there has been a limited improvement in the understanding of how the formulations interact with production line equipment. Typical problems include variation in potency and bulk density - both being issues that can be difficult to predict and / or effectively set-up equipment to counter measure (especially where mainly the manufacturing process is undertaken on a batch basis).

Many manufacturing problems can be traced back to a lack of adequate understanding of consideration of the bulk properties of the powders at the formulation stage. Common issues encountered during full scale production include extended commissioning; high levels of out of specification materials (specifically dose weight variation). Variation of the dose weight in dosator filling applications, like dry inhaled powders, could seriously affect the patient health.

The project aims to provide a predictive tool to industry, the use of which can improve manufacturing efficiency, minimise costs and minimise risk when launching new products. The approach adopted lies in focussing on established powder characterisation techniques and an improved understanding of dosator machine factors affecting output performance and uniform fill dose weight. Although this project has focussed on dosators, the general concept is applicable to other volumetric powder filling systems.

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Poster Abstract

A Dry Powder Jet Printer for Pharmaceutical Powders Dispensing

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In many laboratory situations powders must be weighed out or dispensed for routine analyses such as those often found in industrial settings, where a chemist is required to prepare dozens of samples daily either from a single stock powder or from various powder samples. In a pharmaceutical research and development setup, the process of synthesizing new chemical entities and identifying them as potential drug candidates leads to a limited availability of a few grams of synthesized powders. This warrants the need to develop techniques to dispense precisely microgram or even nanogram quantities of these powders for its application in high-throughput screening enabling faster drug development. Dry powder micro-dispensing can be used in many fields, such as production line filling, solid freeform fabrication, drug delivery and pharmaceutical screening. Micro-dispensing of powders also provide a large landscape in terms of formulation designs for high throughput experimentation in the pharmaceutical industry. Micro to milligrams of powders are metered and dispensed for application in combinatorial chemistry of drug development. Conventional dispensing methods involving use of skilled operators have limitations such as high capital cost, time consumption, operational complexity, constant use of weighing balances and lower fill yield due to fine powders loss at the filter. The process is more challenging when dispensing cohesive and adhesive micron-sized inhalation powders. The mass content uniformity of each dose in such formulations is especially crucial as it assures consistent therapeutic benefits in the patient.

The aim of the present work was to demonstrate the feasibility of a novel dry powder micro-dosing system, developed based on a dry powder jet printer technology, for dispensing pharmaceutical powders (30µg - 5000mg doses) at high precision and speed. The computer-controlled micro-dosing system employs acoustic vibration to initiate and control the powder dispensing from small nozzles. The powder flow arrest was brought about by the formation of domes in the capillary. It has been well established that the dispensing mechanism of powder is strongly related to the powder properties (i.e. particle size, cohesion force), diameter of the capillary tube and intensity of the ultrasonic vibration.

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Poster Abstract

Characterisation of Adhesion by Drop Test Method

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Assessing the flowability of bulk powders is of great importance for various particulate processes, such as filling, transportation and storage of cohesive powders. Bulk powder behaviour is affected by the single particle properties; therefore, characterising single particle properties and in particular, measuring the adhesive force between particles is essential. There are various methods for the measurement of adhesive forces, e.g. Atomic Force Microscopy (AFM), but most of them are very costly and time consuming. For engineering applications there is a need to develop a quick test method for the characterisation of inter-particle adhesion. The drop test method has been designed and developed for this purpose. In this test particles that are adhered to a surface are jolted, and based on the conditions for their detachment, the adhesion force is determined. Here the particles are adhered to the surface of a stub which is then impacted against a stopper ring by dropping the stub from a controlled height. If the detachment force exceeds the adhesive force of a given particle it is detached from the stub, otherwise it is retained. The ratio of the detachment force to adhesion force increases with particle size. Therefore, there is a critical particle size above which particles are detached and below which they remain on the stub. The adhesive force between the particles and the surface is estimated using the JKR theory. The detachment force is estimated by Newton's second law of motion, using the particle mass, and estimated particle acceleration. In this work interface energy of silanised glass beads, avicel, lactose and starch, has been quantified from which the interface energy is obtained. The particle and surface morphology was investigated and showed that the force required to detach spherical particles is higher as compared to the irregular particles due to contact area. For that reason, the interface energy of spherical particles is greater than irregular particles. Due to a smaller contact area for irregular particles, the surface asperity variability has a large impact on the interface energy of the irregular particles, resulting in a reduced reliability of the critical diameter measurement of these particles. The trends of the results obtained with the drop test are similar to those shown in studies by other researchers using established methods like AFM and the centrifuge method.

Key words: Interface Energy, Particle Adhesion, Pull off force

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Poster Abstract

Characterisation of Cohesive Powder Flowability Using Ball Indentation

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The study of bulk behaviour of cohesive powders is very important in the processing of particulate solids such as flow out of storage vessels, filling and dosing of small quantities of powder in capsules and dispersion in dry powder inhalers. Although the mechanical properties of bulk cohesive powders have been analysed extensively at large scales and applied stresses, these analyses are often invalid to deduce the behaviour of loosely compacted powders in small quantities and under very low applied loads. Therefore it is of interest to develop a methodology suitable for assessing the flow behaviour of powders at small scales and low level of compaction (Hassanpour and Ghadiri 2007). In an exploratory programme, the use of indentation on powder beds was investigated for assessing the flowability of powders for a number of powders. The proposed test method can be carried out on very small quantities. The flow function of powder is the ratio of unconfined yield stress and major principle stress. The unconfined yield stress (Y) is inferred from the measurement of hardness (H) by a linear relationship of the form, Y=H/C, where C is the constraint factor, due to the constraint of powder around the indentation zone. The constraining of the deformation in the indentation process in powder beds is far more complicated as compared to continuum solids due to the discrete nature and degree of freedom of movement of the particles for which limited published work has been reported in the literature (Wang et al., 2008). Therefore this work constitutes an attempt to gain an understanding of the process of plastic deformation, (experiments and simulation) during indentation by analysing the shear stress around the indentation zone in a powder bed with a view to predict cohesive powder flowability, an issue of great technological importance. For that purpose, the ball indentation measurement presented for model materials (silanised glass beads, durcal, Avicel, lactohale and limestone) correlates well with DEM simulations (spherical particles) and with shear cell measurements.

Key words: Flowability, Cohesive powders, Ball Indentation, DEM

References

Hassanpour, A., and Ghadiri, M., (2007) Characterisation of flowability of loosely compacted cohesive powders by indentation. Particle & Particle Systems Characterization, Volume 24, Issue 2, pp. 117-123

Wang, C., Hassanpour, A., and Ghadiri,M., (2008). Characterisation of flowability of cohesive powders by testing small quantities of weak compacts. Particology Volume 6, Issue 4, pp. 282-285.

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Poster Abstract

Use of surface energy heterogeneity to relate the effect of surface modification to powder flow properties

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In this study, detailed surface energetics of a model pharmaceutical excipient: D-mannitol was determined using iGC-Surface Energy Analyzer (Surface Measurement Systems Ltd.), and related to Powder Flow measurements with the Freeman FT4.

D_mannitol (M4125 .98%; Sigma Aldrich) was silanised by functionalising hydroxyl surface groups with methylene groups. Surface energy measurements determined the dispersive (.SD) and specific (.SAB) surface energy distributions. Powder flow tests were conducted using FT4 Powder Rheometer (Freeman Technology).

Surface energy results show that untreated D-mannitol is energetically more active and heterogeneous (fig 1). The .SD of untreated D-mannitol varied from 37.51 to 52.63mJ/m2. Silanised D-mannitol is fairly homogenous with mean .SD of 34.10mJ/m2 (±4%).

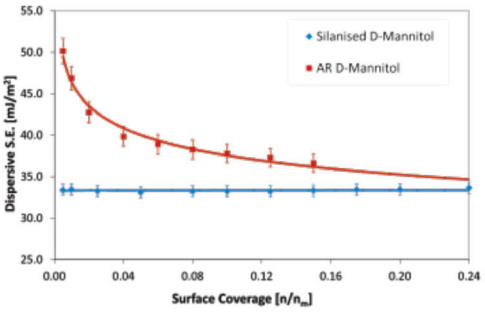

Fig. 1 Dispersive surface energy profiles (as a function of surface coverage).

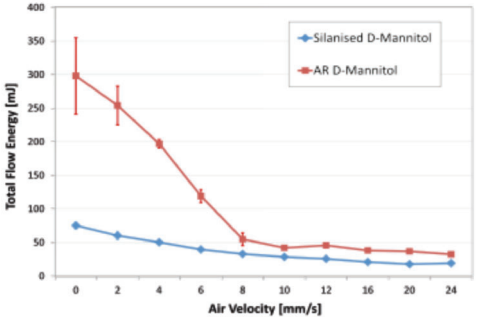

Fig. 2 Flowability energy as a function of aeration.

Powder flow aeration tests show that untreated D-mannitol exhibited unstable flow behaviour (Fig. 2). Flowability energy of untreated D-mannitol decreased from 333.0 to 50.0mJ, before full aeration at at 32.4mJ. Silanised D-mannitol has much lower flowability implying a less cohesive powder.

In summary, silanisation process has clearly improved the flow properties of D-mannitol in a low-stress environment. Powder behaviours of D-mannitol are in excellent agreement with the detailed surface energy distributions determined from iGC-SEA.

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Poster Abstract

Reducing Magnesium Stearate use during Roller Compaction

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The deleterious effects of magnesium stearate (MgSt) on the properties of roller compacted ribbons and hence tablets are well documented [1]. The extent of these effects can be limited through the implementation of a two-step mixing operation [2], in which a formulation is blended to homogeneity prior to the addition of MgSt. It is necessary to characterise the role MgSt during roller compaction and to determine the need for its inclusion.

The formulation consisted of microcrystalline cellulose (Avicel PH102), lactose anhydrous, croscarmellose sodium (Ac-Di-Sol) and MgSt (Mallinckrodt Inc, USA). Roller compactor was an Alexanderwerk WP120. Powder blends were mixed with a low shear tumble blender. Tablets were compacted with a Stylcam 100R rotary tablet press simulator.

The presence of MgSt had a marked influence on the roller compaction process; mass throughput was greatly increased with increasing in roll gap; the latter had a negligible impact on the in-gap ribbon porosity. Evidence of further mixing within the feeding system was observed (see figure 1) which could have the undesirable effect of increasing the formulation lubricity. The beneficial effects of MgSt were apparent at lower levels than 0.5 % w/w.

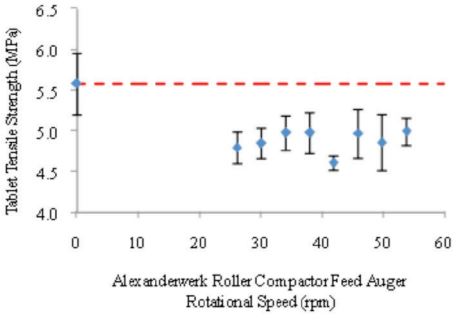

Fig. 1. Comparison of tablet tensile strength of tablets compressed from 'virgin' powder blend (7 minutes at 15 rpm) and powder recovered from roller compactor feeding system.

The beneficial effects of MgSt on the roller compaction behaviour of a placebo formulation can be achieved at a much lower level than is commonly used, if it is homogeneously distributed within a formulation. Blending to homogeneity eliminates the need for a two step blending process, i.e. MgSt can be added during the first blending stage. This affords both a reduction in processing time and potentially a more practical approach to continuous manufacturing.

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[1] X. He, P.J. Secreast, G.E. Amidon, "Mechanistic study of the effect of roller compaction and lubricant on tablet mechanical strength". J. Pharm. Sci 96(5) (2007) 1342-1355.

[2] G. Ragnarsson, A.W. Holzer, J. Sjogren "The influence of mixing time and colloidal silica on the lubricating properties of magnesium stearate". Int. J. Pharm (1979) 3 127-131.

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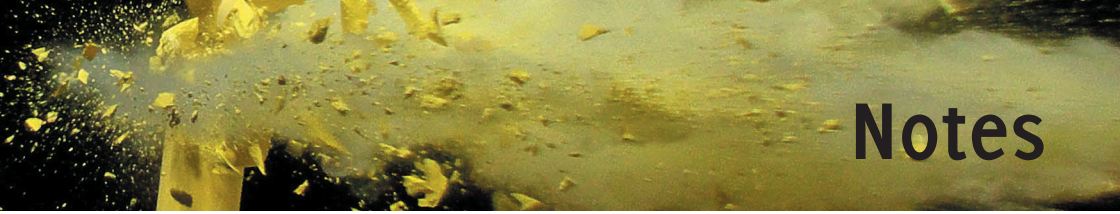

Notes

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