| NO. | Abstract Title | Names of Author (s) | Authors' details | Presentation Type |
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| 1 | EVOLUTION OF PELLET SHAPE DURING INITIAL STAGES OF SPHERONISATION | **Syahmeer M. How** [1,2], Sarah L. Rough[1], Liguang Wang[1,3] & Ian D. Wilson[1] | 1 Department of Chemical Engineering and Biotechnology, University of Cambridge, Philippa Fawcett Drive, Cambridge, CB3 0AS, UK<br><br>2 Department of Process and Food Engineering, Faculty of Engineering, Universiti Putra Malaysia, 43400, Serdang, Malaysia<br><br>3 School of Chemical Engineering, The Universityof Queensland, Brisbane, Queensland 4072, Australia | Poster |
| 2 | ROLLER COMPACTION; DECREASE THE AMOUNT OF FINES IN MILLING STAGE | **Mohamed N. Mohamed**[1], Riyadh B Al-Asady, Manfred Felder[2], James D. Litster & Agba D Salman | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK.<br><br>2 Alexanderwerk AG, Remscheid, North Rhine-Westphalia, Germany | Poster |
| 3 | ADVANCED 3D AND 4D ICROSTRUCTURE STUDY OF SINGLE GRANULE FORMATION USING SYNCHROTRON IN-SITU X-RAY IMAGING | Sima Zeinali Danalou[1], Carter Blocka[1], Jingsi Yang[1], Xiao Fan Ding[2], Ning Zhu[1,2,3], Heather N. Emady[4], Ellen Wasan[5] & **Lifeng Zhang**[1] | 1 Department of Chemical and Biological Engineering, University of Saskatchewan, SK, Canada,<br><br>2 Department of Biomedical Engineering, University of Saskatchewan, SK, Canada,<br><br>3 Canadian Light Source Inc., SK, Canada,<br><br>4 School for Engineering of Matter, Transport and Energy, Arizona State University, AZ, USA.<br><br>5 College of Pharmacy and Nutrition, University of Saskatchewan, SK, Canada | Oral |

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| 4 | DEVELOPING A COMMERCIAL SCALE SEMI-CONTINUOUS FLUID BED WET GRANULATION PROCESS VIA DESIGN OF EXPERIMENTS BASED ON A MULTIVARIATE MODEL AND STATISTICAL ANALYSIS | **Maitraye Sen**, Sydney Butikofer, Chad N. Wolfe, Shashwat Gupta & Adam S. Butterbaugh | Lilly Research Laboratories, Eli Lilly & Company, 1400 West Raymond Street, Indianapolis, Indiana 46221, USA | Oral |
| 5 | STRUCTURATION OF PLANT-BASED MILK POWDER FOR IMPROVED CONSTITUTION | **Kathrin Kramm**[1], Jana Kammerhofer[2], Vincent Meunier[3], Swantje Pietsch-Braune[1] & Stefan Heinrich[1] | 1 Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Denickstraße 15, 21073 Hamburg, Germany<br><br>2 Nestlé Product Technology Center, Nestléstrasse 3, 3510 Konolfingen, Switzerland<br><br>3 Nestlé Research, Vers-Chez-Les-Blanc, 1000 Lausanne 26, Switzerland | Poster |
| 6 | MODEL-DRIVEN AND DATA-DRIVEN SOFT SENSING OF SOLID MOISTURE CONTENT IN FLUIDIZED BED DRYERS | **Robert Kräuter**, Xiye Zhou & Stefan Heinrich | Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Germany | Oral |
| 7 | TWIN PRO® - FUSION OF TWO ROCESSES: HIGH SHEAR GRANULATION AND FLUIDIZED BED DRYING IN ONE PROCESS | **Soeren E. Lehmann**[1] & Lars Steinke[2] | 1 Glatt Pharmaceutical Services GmbH & Co.KG, Werner-Glatt-Straße 1, 79589 Binzen, Germany<br><br>2 Glatt GmbH, Werner-Glatt-Straße 1, 79589 Binzen, Germany | Poster |
| 8 | CORRELATING PARTICLE PROPERTIES WITH PROCESS PARAMETERS IN FLUIDIZED BED SPRAY GRANULATION AND ITS APPLICATION IN DYNAMIC FLOWSHEET SIMULATION | **Xiye Zhou** , Robert Kräuter & Stefan Heinrich | Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Denickestr. 15, 21073 Hamburg, Germany | Poster |
| 9 | DEVELOPMENT OF GRANULAR NEUTRAL AMINO ACIDS WITH CALCIUM HYDROXIDE COMPOSITION | **Min Kyung Kwon**[1], Jun-Woo Kim[1] & DongHyun Lee[2] | 1 CJ BIO Institute, CJ Blossom Park, 42, Gwanggyo-ro, Yeongtong-gu, Suwon, Gyeonggi-do 16495, Republic of Korea | Oral |

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| | | | 2 School of chemical Engineering, Sungkyunkwan University (SKKU), 2066 Seobu-ro, Jangan-gu, Suwon, Gyeonggi-do 16419, Republic of Korea | |
| 10 | DEM MODELLING OF DRY POWDER SPREADING PROCESS FOR LITHIUM-ION BATTERY ELECTRODE MANUFACTURING | **Hamza Mohamed**[1,2], Ruihuan Ge[1,2], Denis Cumming[1,2] & Rachel Smith[1,2] | 1 Department of Chemical and Biological Engineering, The University of Sheffield, Sheffield, S10 2TN, UK<br><br>2 The Faraday Institution, Quad One, Harwell Science and Innovation Campus, Didcot, OX11 0RA, UK | Poster |
| 11 | SCALE AND BOUNDARY EFFECTS ON DRUCKER-PRAGER CAP MODEL PARAMETERS IN DIE COMPACTION | Gweni Alonso Aruffo[1], Driss Oulahna[2], Olivier Lecoq[2] & **Abderrahim Michrafy**[2] | 1 Université de Toulouse, Mines Albi, Centre ICA, Albi, France<br><br>2 Université de Toulouse, Mines Albi, CNRS, Centre RAPSODEE, Albi, France | Oral |
| 12 | TABLET MICROSTRUCTURE INDUCED BY EMBOSSED FEATURES OF COMPACTING PUNCH: CASE STUDY ANALYSIS | **Gweni Alonso Aruffo**[1], Driss Oulahna[2] & Abderrahim Michrafy[2] | 1 Université de Toulouse, Mines Albi, Centre ICA, Albi, France<br><br>2 Université de Toulouse, Mines Albi, CNRS, Centre RAPSODEE, Albi, France | Poster |
| 13 | OPEN-SOURCE FLOWSHEET SIMULATION ENVIRONMENT FOR DYNAMIC SIMULATION OF PARTICULATE PROCESSES | Vasyl Skorych & **Stefan Heinrich** | Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology (TUHH), Denickestrasse 15, 21073 Hamburg, Germany | Poster |
| 14 | THE EFFECT OF PROCESSING CONDITIONS ON DRY SOLIDS RECOVERY AND MOISTURE ABSORPTION CAPACITY OF SPRAY DRIED FISH PROTEIN HYDROLYSATES | **Kudzai Chiodza** & Neill J. Goosen | Department of Chemical Engineering, University of Stellenbosch University, Banghoek Road, Stellenbosch Central, Stellenbosch, 7599, South Africa | Oral |
| 15 | CONTINUOUS IN FEED FRAME LUBRICATION FOR TABLETS DURING DIRECT COMPRESSION | **René Brands**, Christopher Mathias, Jens Bartsch & Markus Thommes | Laboratory of Solids Process Engineering, TU Dortmund University, Emil-Figge-Straße 68, Dortmund, 44227, DE | Oral |

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| 16 | MICROCOAT™ FOR SUSTAINED RELEASE ORALLY DISINTEGRATING GLICLAZIDE TABLETS | **Kavil Patel**[1], Darragh Murnane[2] , Craig Richardson[1] & Fang Liu[1,2] | 1 Fluid Pharma Ltd., Windsor House, Harrogate, UK<br><br>2 University of Hertfordshire, College Lane, Hatfield, UK | Poster |
| 17 | DEM SIMULATION OF LOW SHEAR AGGLOMERATION | **William K. Walls**, James A. Thompson & Stephen G.R. Brown | Faculty of science and engineering, Swansea University, Fabian Way, Swansea SA1 8EN, Wales, United Kingdom | Oral |
| 18 | SUBMICRON AG-COATED CU PARTICLES AS FILLER IN SINTERING PASTE: CONTROL OF AG DEWETTING AND IMPROVEMENT OF SINTERABILITY THROUGH SURFACE MODIFICATION USING CARBOXYLIC ACID | Yeongjung Kim & **Jong-Hyun Lee** | Department of Materials Science and Engineering, Seoul National University of Science and Technology, 232 Gongneung-ro, Nowon-gu, Seoul 01811, Republic of Korea | Poster |
| 19 | DRYING BEHAVIOUR USING THE QBCON® 1 CONTINUOUS DRYER | **Katharina Kiricenko**, Peter Kleinebudde | Heinrich Heine University, Institute of Pharmaceutics and Biopharmaceutics, 40225 Duesseldorf, Germany | Poster |
| 20 | THE EFFECT OF ROLL SPEED ON THE PREDICTION OF RIBBON SOLID FRACTION | **Martin Lück**[1], Matthias De Saeger[2] & Peter Kleinebudde[1] | 1 Institute of Pharmaceutics and Biopharmaceutics, Heinrich Heine University Duesseldorf, Universitaetsstrasse 1, 40225 Duesseldorf, Germany<br><br>2 Department of Pharmaceutics, Laboratory of Pharmaceutical Technology, Ghent University, Ottergemsesteenweg 460, 9000 Ghent, Belgium | Poster |
| 21 | EMPLOYING A NOVEL MULTI-RESONANCE MICROWAVE SENSOR FOR IN-LINE MOISTURE MONITORING OF FLUIDIZED BED AGGLOMERATION | **Gero Stöckl**, Aitor Atxutegi & Stefan Heinrich | Hamburg University of Technology (TUHH), Institute of Solids Process Engineering and Particle Technology, Denickestrasse 15, 21073 Hamburg, Germany | Poster |
| 22 | HOMO AND HETERO AGGLOMERATE FORMATION OF NANOPARTICLES IN A SPOUTED | **Subash R. Kolan**, Rui Wang, Dr.-Ing. Torsten | Thermal Process Engineering Department, Otto von Guericke University Universitätsplatz. 2, 39106 Magdeburg | Oral |

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| | | Hoffmann & Evangelos Tsotsas | | |
| 23 | EMULSION STABILITY OF SPRAY-DRIED INFANT FORMULA | **Mariana Rodríguez Arzuaga** [1,2] Analía G. Abraham[2], Lilia Ahrné[3] & María C. Añón[2] | 1 Latitud, LATU Foundation. Montevideo, Uruguay<br><br>2 Centro de Investigación y Desarrollo en Criotecnología de Alimentos, Buenos Aires, Argentina<br><br>3 University of Copenhagen. Denmark | Oral |
| 24 | FOOD VS PACKAGING: MODELLING MASS TRANSFER FROM POWDER COMPACTS INTO PACKAGING | **Luc Dewulf**[1], Michael K. Hausmann[2], Annabel Bozon[3], Gerhard Niederreiter[2], Stefan Palzer[2], & Agba D. Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, United Kingdom S2 3JD<br><br>2 Nestlé Research, 1010 Lausanne, Switzerland<br><br>3 Nestlé Product Technology Centre, Lange Straße 21, 78221, Singen, Germany | Oral |
| 25 | MIMICKING THE STRUCTURE OF NATURAL COMPOSITES BY MERGING SPRAY DRYING AND WARM COMPACTION PROCESS | **Sophia Rothberg**[1], Swantje Pietsch-Braune[1], Stefan Heinrich[1] | 1 Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Denickestraße 15, 21073 Hamburg, Germany | Poster |
| 26 | COMPARISON OF DEM SOFTWARE FOR THE SIMULATION OF COMPACTION OF BIPLANAR TABLETS | **Amine Ait Ouazzou**[1], Yogesh M. Harshe[2], Vincent Meunier[2] Jan H. Finke[3], Stefan Heinrich[1] | 1 Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Hamburg, Germany<br><br>2 Nestlé Research, Route du Jorat 57, Lausanne 1000, Switzerland<br><br>3 Institute for Particle Technology and Center of Pharmaceutical Engineering - PZV, Technical University of Braunschweig, Germany | Poster |
| 27 | AN INNOVATIVE SETUP TO STUDY THE INFLUENCE OF SHEAR STRESS ON THE BREAKAGE OF AGGLOMERATES | **Hanin Atwi**[1], Guillaume Dumazer[1], Sylvain Martin[1] , Guilhem Kauric[2], | 1 Mines Saint-Etienne, Univ Lyon, CNRS, UMR 5307 LGF, Centre SPIN, F-42023 Saint-Etienne France | Oral |

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| 28 | NOVEL STRATEGIES FOR RECOVERY OF ZINC AS ZINC- SULFIDE BY FLUIDIZATION BED HOMOGENEOUS CRYSTALLIZATION | **Kai-Yang Chang**, Po-Lin Liao, Nicolaus Nezha Nunez Mahasti, Yao-Hui Huang | Department of Chemical Engineering, National Cheng Kung University, Tainan City, Taiwan | Oral |
| 29 | PREDICTION OF DROPLET SIZE DISTRIBUTION<br>FROM TWIN FLUID NOZZLES | **Leander Vinzenz Mehlis**[1,2], Jens Bartsch[1], WernerHoheisel[2], Patrick Kranz[3] & Markus Thommes[1] | 1 Laboratory of Solids Processing, TU Dortmund, Dortmund 44227, Germany<br>2 Formulation Technology, Invite GmbH, Cologne 51061, Germany<br>3 Process Modelling and Design, Bayer AG, Leverkusen 51373, Germany | Poster |
| 30 | ELECTROSTATIC SPRAY DRYING: ADVANTAGES FOR THERMOSENSITIVE ACTIVES | **Elodie Beaupeux** [1], Audrey Maudhuit [1], Akaber Dokmak [1,2] , Preethi Jayaprakash[1,3], Thomas Deleau [2] , Claire Gaiani [3] | 1 Fluid Air Europe, Division of Spraying Systems CO., Treillières France<br>2 Toulouse University, RAPSODEE, Albi France<br>3 Université de Lorraine, LIBio, Nancy, France | Oral |
| 31 | A NON-DIMENSIONALISED QUADRATURE METHOD OF MOMENT MODEL FOR WET GRANULATION | **Timo Plath**[1], Stefan Luding[1]& Thomas Weinhart[1] | Multi-Scale Mechanics, TFE, ET, MESA+, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands | Oral |
| 32 | REGIME ANALYSIS APPROACH FOR HIGH-SHEAR WET GRANULATION SCALE UP | Matthew Reading[1], **Stefan Bellinghausen[1]** & Dana Barrasso[2] | 1 Siemens Process Systems Engineering, London, UK<br>2 Siemens Process Systems Engineering, Parsippany, NJ, U | Poster |
| 33 | COMPACTION PROCESS DESIGN AND TECH TRANSFER AT DIFFERENT STAGES OF DEVELOPMENT | **Stefan Bellinghausen**[1], Jianfeng Li[2] & Dana Barrasso[2] | 1 Siemens Process Systems Engineering, London, UK | Oral |

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| | | | 2 Siemens Process Systems Engineering, Parsippany, NJ, USA | |
| 34 | MICROPELLET COATING FOR TASTE IMPROVEMENT OF PAEDIATRIC FIXED DOSE COMBINATION ANTIMALARIAL THERAPIES | Dina Shokry[1], Alan Reader[1], Sangeetha Marri1, Daniel Baker[1], **Kavil Patel**[2] & Fang Liu[1,2] | 1 University of Hertfordshire, College Lane, Hatfield, UK<br><br>2 Fluid Pharma Ltd., Windsor House, Harrogate, UK | Oral |
| 35 | INFLUENCE OF SPRAY PARAMETERS ON COATING STRUCTURE IN FLUIDIZED BED GRANULATION | **Maike Orth**, Swantje Pietsch-Braune & Stefan Heinrich | Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Denickestrasse 15, 21073 Hamburg, Germany | Poster |
| 36 | POWDER GRANULATION TO REDUCE LUMP FORMATION DURING RECONSTITUTION OF SWELLING FOOD POWDERS: CASE STUDY AND RESEARCH GAPS | **Klara Haas**, P. Bhargav, J. Kammerhofer, M. Kindlein & V. Meunier | Nestlé Research, Lausanne, Switzerland | Oral |
| 37 | INVESTIGATION OF ISLAND GROWTH ON PARTICLES COATED BY MEANS OF AEROSOL | **Serap Akbas**, Torsten Hoffmann, Kaicheng Chen & Evangelos Tsotsas | Thermal Process Engineering, Otto-von-Guericke-University, Universitätsplatz 2, 39106 Magdeburg, Germany | Oral |
| 38 | CONTINUOUS MELT GRANULATION WITH PLANETARY ROLLER GRANULATORS | Tom Lang[1], Thomas Birr[2], Markus Thommes[1] & **Jens Bartsch**[1] | 1 Laboratories of Solids Process Engineering, TU Dortmund University, Emil-Figge-Str.68, 44227 Dortmund, Germany<br><br>2 Entex Rust & Mitschke GmbH, Heinrichstr. 67a, 44805 Bochum, Germany | Oral |
| 39 | EFFECT OF HYDROPHOBIC POWDERS ON THE TENSILE STRENGTH OF THE TABLET | **Zoe Chu**[1 2], Christopher Windows-Yule[1], Ian Gabbott[2], Gavin Reynolds[2], Rachael Shinebaum[2] & Andy Ingram[1] | 1 School of Chemical Engineering, University of Birmingham, Edgbaston, B15 2TT<br><br>2 Oral Product Development, Pharmaceutical Technology & Development, Operations, AstraZeneca, Macclesfield, UK | Oral |

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| 40 | ADVANCED ON-LINE MEASUREMENT TECHNIQUES TO CONTROL MILK POWDER CHARACTERISTICS DURING CONTINUOUS FLUIDIZED BED SPRAY AGGLOMERATION | **Tobias V. Raiber**, Jennifer Frank, Laura Grotenhoff & Reinhard Kohlus | Department of Process Engineering and Food Powders, University of Hohenheim, Garbenstraße 25, 70599 Stuttgart, Germany | Oral |
| 41 | MODELING THE PARTICLE SIZE DISTRIBUTION OF AGROCHEMICAL POWDER BLENDS: A DATA ANALYSIS ON THE OPERATING CONDITIONS OF A PILOT SCALE JET MILL | **Srishti Khurana**[1], Sweta Somasi[2], Samual R. Zukowski[1] & Ryan Berner[1] | 1 Formulation Process Science and Technology, Corteva Agriscience, 9330 Zionsville Rd, Indianapolis, IN, 46268, USA<br><br>2 Small Molecules Discovery and Development, Corteva Agriscience, 9330 Zionsville Rd, Indianapolis, IN, 46268, USA | Poster |
| 42 | DEM ANALYSIS OF MIXING PERFORMANCE OF COHESIVE POWDERS IN A HIGH SHEAR MIXER | Abul Hassan Syed[1,2], Hasan S. Elmsahli[1] & **Csaba Sinka[1]** | 1 School of Engineering, University of Leicester<br><br>2 Department of Chemical and Process Engineering, University of Surrey | Oral |
| 43 | PREDICTING TABLET PROPERTIES USING IN-LINE MEASUREMENTS AND EVOLUTIONARY EQUATION DISCOVERY | **Issa Munu**[1,2], Leonard Nicusan[1], Jason Crooks[2], Kendal Pitt[2], Christopher Windows-Yule[1] & Andrew Ingram[1] | 1 School of Chemical Engineering, University of Birmingham, Edgbaston, B15 2TT, United Kingdom<br><br>2 GSK Global Supply Chain, Priory Street, Ware, SG12 0DJ, United Kingdom | Poster |
| 44 | INVESTIGATING THE HEAT SENSITIVITY OF HYPROLOSES WITH DIFFERENT PARTICLE SIZES DURING TABLETING | **Hanna D. Grumann** & Peter Kleinebudde | Heinrich Heine University Duesseldorf, Institute of Pharmaceutics and Biopharmaceutics, Universitaetsstr. 1, 40225 Duesseldorf, Germany | Poster |
| 45 | A REGIME MAP FOR DRY POWDER COATING | Marv Khala[1], **Colin Hare**[1], Vikram Karde[2] & Jerry Heng[2,3] | 1 School of Engineering, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK<br><br>2 Department of Chemical Engineering, Imperial College London, London SW7 2AZ, UK | Oral |

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| 46 | MIXING AND SEGREGATION RATES AND MECHANISMS IN AN AGITATED VESSEL | Marv Khala[1], **Colin Hare[1]**, Chuan-Yu Wu[2], Navin Venugopal[3] , Martin J. Murtagh[4] & Tim Freeman[5] | 1 School of Engineering, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK<br><br>2 Department of Chemical and Process Engineering, University of Surrey, Guildford, GU2 7XH, UK<br><br>3 Corning Inc., Corning, NY 14870, United States<br><br>4 Materials Science & Engineering, Cornell University, Ithaca, NY 14850, United States<br><br>5 Tewkesbury GL20 8DN, UK | Poster |
| 47 | EVALUATION AND DIFFERENTIATION OF DAMAGING INFLUENCES ON COATED PELLETS IN TABLETING MACHINES | Lara Stein[1,2,3], Luisa Enders[1,2], Gernot Warnke[3] & **Jan H. Finke**[1,2] | 1 Institute for Particle Technology, TU Braunschweig, Volkmaroder Str.5, 38104 Braunschweig, Germany<br><br>2 Center of Pharmaceutical Engineering – PVZ, TU Braunschweig, Franz-Liszt-Str. 35A, 38106 Braunschweig, Germany<br><br>3 JRS PHARMA GmbH & Co. KG, Rosenberg, Germany; Holzmühle 1, 73494 Rosenberg | Oral |
| 48 | PAT MONITORING OF COATING PAN BY NIR: PLS METHOD CALIBRATION APPROACH | **Andrea Gelain**, Giuseppe Buratti & Gabriele Inverni | Freund-Vector European Laboratory, viale Enrico Mattei 2, Villasanta (MB), Italy | Oral |
| 49 | SPRAY DRYING AND TABLETING OF LIVING MICROORGANISMS | **Karl Vorländer**[1,2], Arno Kwade[1,2], Jan H. Finke[1,2] & Ingo Kampen[1,2] | 1 Technische Universität Braunschweig, Institute for Particle Technology (iPAT), Volkmaroder Str. 5, 38104 Braunschweig, Germany | Oral |

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| | | | 2 Technische Universität Braunschweig, Center of Pharmaceutical Engineering (PVZ), Franz-Liszt-Str. 35A, 38106 Braunschweig, Germany | |
| 50 | MANUFACTURE OF MINI-TABLETS AND THEIR CONTINUOUS ROBOTIC COMPOUNDING INTO MULTI-UNIT DOSAGE SYSTEMS | Elizaveta Mutylo[1, 2], Erik Sonntag[1, 2], David Smrčka[2], Jan Vrba[3], Daniel Pecek[2] & **Frantisek Stepanek**[1, 2] | 1 Department of Chemical Engineering, University of Chemistry and Technology Prague, Technicka 3, 166 28 Prague 6, Czech Republic<br><br>2 Zentiva, k.s., U Kabelovny 130, Prague 10, Czech Republic<br><br>3 Department of Computing and Control Engineering, University of Chemistry and Technology Prague, Technicka 3, 166 28 Prague 6, Czech Republic | Poster |
| 51 | ENSURING PRODUCT STABILITY, QUALITY, AND SAFETY WHILE INTRODUCING NOVEL SUSTAINABLE PACKAGING SOLUTIONS | **Linda Brütsch**[1] & Vincent Meunier[2] | 1 Nestle Research, Lausanne, Switzerland Lausanne<br><br>2 Nestle Research, Lausanne, Switzerland Lausanne | Oral |
| 52 | STRUVITE (MGNH4PO4.6H2O) GRANULATION FROM SEAWATER USING FLUIDIZED BED HOMOGENEOUS CRYSTALLIZATION TECHNOLOGY | Thi Hanh Ha[1], Nicolaus N.N. Mahasti[1], **Ming Chun Lu**[2] & Yao Hui Huang[1] | 1 Department of Chemical Engineering, National Cheng Kung University, Tainan City, Taiwan<br><br>2 Department of Environmental Engineering, National Chung Hsing University, Taichung City 40227, Taiwan | Poster |
| 53 | MECHANISTIC REDUCED ORDER MODELS FOR INTEGRATING DRY GRANULATION AND TABLETING PROCESSES | **Sunidhi Bachawala**[1], Rexonni Lagare[2], Yan-Shu Huang[2], Katherine Young[2], Phoebe X. Bailey[2], David J. Sixon[2], Zoltan K. Nagy[2], Gintaras V. Reklaitis[2] & Marcial Gonzalez[1,3] | 1 School of Mechanical Engineering, Purdue University, West Lafayette, IN 47907<br><br>2 Davidson School of Chemical Engineering, Purdue University, West Lafayette, IN 47907<br><br>3 Ray W. Herrick Laboratories, Purdue University, West Lafayette, IN 47907, USA | Oral |

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| 54 | USING POSITRON EMISSION PARTICLE TRACKING (PEPT) TO EVALUATE MIXING IN AN AXIAL INCLINE BLENDER FOR CONTINUOUS DIRECT COMPRESSION (CDC) | **Owen Jones-Salkey**[1,2], Andrei L. Nicusan[1], Dominik Werner[1], Kit Windows-Yule[1], Andrew Ingram[1], Sean Clifford[2] & Gavin K. Reynolds[2] | 1 School of Chemical Engineering, University of Birmingham, Birmingham, B15 2TT, UK<br><br>2 Oral Product Development (R&D), AstraZeneca, Charter Way, Macclesfield, SK10 2NA, U | Poster |
| 55 | HYBRID MODELLING OF PHARMACEUTICAL MIXTURE PROPERTIES: PREDICTIVE SOLUTIONS FOR PARTICLE SIZE, SHAPE, FLOW, AND DENSITY | **Mohammad Salehian**[1,2], Jonathan Moores[2], Isra' Ibrahim[2] & Daniel Markl[1,2] | 1 Digital Medicines Manufacturing (DM2) Research Centre, Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC), Strathclyde Institute of Pharmacy & Biomedical Sciences, University of Strathclyde, Glasgow, UK.<br><br>2 Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC), Strathclyde Institute of Pharmacy & Biomedical Sciences, University of Strathclyde, Glasgow, UK. | Poster |
| 56 | PRE-NUCLEATION IN HIGH-SHEAR WET GRANULATION | **Diana S. Kumar**[1], Sarang Oka[2] & Heather N. Emady[1] | 1 School for Engineering of Matter, Transport, and Energy, Arizona State University, 501 E Tyler Mall, Tempe, AZ 85287, USA<br><br>2 Hovione, Drug Product Continuous Manufacturing, 40 Lake Dr, East Windsor, NJ 08520, USA | Oral |
| 57 | WATER SOLUBLE TABLET FORMULATOIN FOR FAST INTRA TABLET COATING VARIABILITY DETERMINATION | Rok Šibanc[1], Branko Vukosavljević[1], Anja Ehrig[2], Blaž Grilc[3], Ilija G. Ilić[3] & **Rakulan Sivanesapillai**[2] | 1 Bayer AG, Chemical and Pharmaceutical Development, Wuppertal, 42117, Germany<br><br>2 Bayer AG, Engineering and Technology, Leverkusen, 51368, Germany<br><br>3 Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Ljubljana, Ljubljana, 1000, Slovenia | Oral |

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| 58 | THE ROLE OF INTERPARTICLE FORCES IN THE FLOWABILITY FOR GRANULATION PROCESSES | **Jordan E. Monroe** & Heather N. Emady | School for Engineering of Matter, Transport and Energy, Arizona State University, 501 E Tyler Mall, Tempe, AZ 85287, USA | Poster |
| 59 | STRUCTURAL AND FUNCTIONAL ANALYSIS OF A NEW CO-PROCESSED TABLETING EXCIPIENT | René Rösemeier-Scheumann[1,2], **J. H. Finke**[1,2], U. Bobe[3], A. Bozon[3] & A. Kwade[1,2] | 1 Institute for Particle Technology (iPAT), TU Braunschweig, Germany<br><br>2 Center of Pharmaceutical Engineering (PVZ), TU Braunschweig, Germany<br><br>3 Nestlé Product Technology Centre, Singen, Germany | Poster |
| 60 | RECLAMATION OF ALUMINUM AS ALPHA-AL(OH)3 PELLET FROM AQUEOUS SOLUTION VIA FLUIDIZED-BED HOMOGENEOUS CRYSTALLIZATION TECHNOLOGY | **Kai-Yang Chang**, Nicolaus N.N. Mahasti & Yao-Hui Huang | Department of Chemical Engineering, National Cheng Kung University, Tainan City, Taiwan | Poster |
| 61 | DEVELOPMENT OF AN ACOUSTIC EMISSION TECHNIQUE IN COMBINATION WITH MACHINE LEARNING TO CHARACTERIZE THE PARTICLE SIZE DISTRIBUTION IN SOLID-GAS FLUIDIZED BEDS | **Fria Hossein**[1], Matteo Errigo[1], Sibo Cheng[2], Panagiota Angeli[1], Massimiliano Materazzi Matterazzi[1], Paola Lettieri[1]& Rossella Arcucci[2] | 1 Department of Chemical Engineering, University College London, London, UK, WC1E 7JE<br><br>2 Data Science Institute, Department of Computing, Imperial College London, London, UK, SW7 2AZ | Oral |
| 62 | MICRO SCALE INVESTIGATIONS OF AGGLOMERATION AND DEAGGLOMERATION DUE TO SINGLE COLLISIONS BETWEEN WETTED PARTICLES | **Falk Bunke** & Stefan Heinrich | Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology (TUHH), Denickestrasse 15, 21075 Hamburg, Germany | Poster |
| 63 | INVESTIGATION OF FLUIDIZATION- AND MIXING BEHAVIOR OF NANO- AND MICRON PARTICLES IN A VIBRATED FLUIDIZED BED WITH PULSATED GAS FLOW | **Zhi Cheng Hua**, Swantje Pietsch-Braune, Aitor Atxutegi & Stefan Heinrich | Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Germany | Poster |

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| 64 | MULTIVARIATE ANALYSIS AND PROCESS OPTIMIZATION OF MECHANOCHEMICAL SYNTHESIS USING TWIN SCREW EXTRUSION: PRODUCTION 4,4 BI-PYRIDINE BASED MOF | **Ahmed Metawea**[1], Rodrigo Soto[1,2], Majeda Khraisheh[3], Gavin Walker[1] & Ahmad B. Albadarin[4] | 1 Department of Chemical Sciences, Bernal Institute, University of Limerick, Limerick, Ireland.<br><br>2 Department of Chemical Engineering and Analytical Chemistry, University of Barcelona, Marti i Franquès 1-11, 08021 Barcelona, Spain.<br><br>3 Department of Chemical Engineering, College of Engineering, Qatar University, P.O. Box 2713, Doha, Qatar<br><br>4 B&WB Department of Chemical Engineering and Advanced Energy, Maroun Semaan Faculty of Engineering & Architecture, American University of Beirut | Oral |
| 65 | MECHANISMS OF RIBBON SPLIT IN ROLLER COMPACTION | **Christian Eichler**[1], Vasyl Skorych[1,2] & Stefan Heinrich[1] | 1 Hamburg University of Technology, Institute of Solids Process Engineering and Particle Technology, Hamburg, Germany<br><br>2 DyssolTEC GmbH, Hamburg, Germany | Oral |
| 66 | PARTICLE AGGLOMERATION VIA RESONANT ACOUSTIC MIXER FOR DRY POWDER INHALATION | **Qingzhen Zhang** [1], Zheng Wang[1,2] & Philip Hall[1,3] | 1 Department of Chemical and Environmental Engineering, University of Nottingham Ningbo China, Ningbo 315100, People's Republic of China<br><br>2 Key Laboratory for Carbonaceous Wastes Processing and Process Intensification Research of Zhejiang Province, University of Nottingham Ningbo China, Ningbo 315100, People's Republic of China<br><br>3 Nottingham Ningbo China Beacons of Excellence Research and Innovation Institute, Ningbo 315100, PR China | Oral |

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| 67 | VIRTUAL PROTOTYPING OF WET GRANULATION PROCESSES | **Timo Plath**, Stefan Luding & Homas Weinhart | Multi-Scale Mechanics, TFE, ET, MESA+, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands; | Poster |
| 68 | INFLUENCE OF REFILLING ON DOSING ACCURACY OF LOSS-IN-WEIGHT POWDERS FEEDER IN CONTINUOUS MANUFACTURING | **Fabiola N. Santamaría Alvarez**[1], Peter Kleinebudde[2] & Jochen Thies[1] | 1 New Technologies Innovation Center, Glatt GmbH, Werner-Glatt-Str. 1, 79589 Binzen, Germany<br><br>2 Institut for Pharmaceutical Technology & Biopharmacy, Heinrich-Heine-University Düsseldorf Universitätsstr. 1, 40225 Düsseldorf | Oral |
| 69 | TAKING A MECHANISTIC APPROACH TO UNDERSTANDING THE EFFECT OF AGITATION ON UNDESIRED AGGLOMERATION IN AN AGITATED FILTER DRYER | **Suruthi Gnanenthiran**[1], Pari Rao[2], Christopher Hewitt[2], James Litster[1] & Rachel Smith[1] | 1 Particle Technology Group, Department of Chemical and Biological Engineering, University of Sheffield, Mappin St, Sheffield, S1 4NL UK<br><br>2 Chemical Development, Pharmaceutical Technology & Development, Operations, AstraZeneca, Macclesfield, UK | Poster |
| 70 | PROCESS FOR SPRAY FOAMING OF A POLYMER - SURFACTANT SOLUTION BY USE OF A TWO-FLUID NOZZLE TO CREATE A CONTINOUS COATING | **Björn Düsenberg**[1], Heike Kreuder[2], Lothar Seidemann[2], Frank Kleine Jäger[2] & Andreas Bück[1] | 1 Friedrich-Alexander-Universität Erlangen-Nürnberg, Institute of Particle Technology, Cauerstraße 4, D-91058 Erlangen, Germany<br><br>2 BASF SE, Carl-Bosch-Strasse 38, D-67056 Ludwigshafen am Rhein, Germany | Oral |
| 71 | INDUSTRIAL CASE STUDY ON APPLICATION OF ROLLER COMPACTION MODELLING FOR SCALE UP AND TECH TRANSFER | Lorenzo Poloni[1], Martin Lubej[1], **Arnesh Palanisamy**[1] & Bindhu Gururajan[1,2] | 1 Novartis Pharma AG, Novartis Campus, 4056 Basel, CH<br><br>2 School of Engineering, University of Edinburgh, Edinburgh EH8 9YL, UK | Poster |
| 72 | DRUM COATING OF NON-SPHERICAL TABLETS: SIMULATIONS AND EXPERIMENTAL STUDIES OF INTRA- AND INTER-PARTICLE LAYER THICKNESS DISTRIBUTION | Abhinandan K. Singh[1], Vanessa Götz[1], Pradeep Muramulla[2] & Andreas Bück[1] | 1 Institute of Particle Technology (LFG), Friedrich-Alexander University Erlangen-Nuremberg, Cauerstraβe 4, 91058 Erlangen, Germany | Oral |

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| | | | 2 Pharmaceutical Development, Daiichi-Sankyo Europe GmbH, Luitpoldstraβe 1, 85276 Pfaffenhofen an der Ilm, Germany | |
| 73 | TRANSFORMATIONAL CONICAL MILL SCREEN DESIGN: A PARADIGM SHIFT IN SCALABLE ORAL SOLID DOSAGE POWDER SIZE REDUCTION | **Wilf Sanguesa**[1] & Yang Su[2] | 1 Quadro Engineering, Colby Drive, Waterloo, Ontario, Canada, N2V1A1<br><br>2 Microfluidics, Glacier Drive, Westwood, MA, USA, 02090 | Oral |
| 74 | FLUIDISED BED GRANULATION – ADVANCED PROCESS CONTROL FOR CONSISTENT PRODUCT QUALITY | **Samuel Solomon**[1], Chris O'Callaghan[2], Caroline McCormack[2], Marcus O'Mahony[3], Ian Jones[2], Gavin Walker[1,4] & Patrick Cronin[5] | 1 University of Limerick, Dep. Of Chemical Sciences, Limerick, Ireland.<br><br>2 Innopharma Technology, Dublin, Ireland.<br><br>3 Pharmaceutical Manufacturing Technology Centre, Bernal Institute, University of Limerick, Limerick, Ireland.<br><br>4 Solid State Pharmaceutical Centre, Bernal Institute, University of Limerick, Limerick, Ireland<br><br>5 Dairy Processing Technology Centre, Bernal Institute, University of Limerick, Limerick, Ireland. | Poster |
| 75 | DESIGN AND EVALUATION OF STERCULIA TRAGACANTHA AS A RELEASE MODIFIER IN THEOPHYLINE SUSTAINED RELEASE TABLET FORMULATION | **Timma O. Uwah** , Ekaete I. Akpabio, Daniel E. Effiong & Godwin E. Jacob | Department of Pharmaceutics & Pharmaceutical Technology, Faculty of Pharmacy, University of Uyo, Uyo, Akwa Ibom State, Nigeria | Oral |
| 76 | INFLUENCE OF DRYING TECHNIQUE ON STRUCTURAL PARAMETERS AND LIPID OXIDATION STABILITY OF PLANT-BASED MILK POWDERS | **Teresa Kurtz**[1], Klara Haas[2], Olivier Schafter[2], Vincent Meunier[2] & Stefan Heinrich[1] | 1 Solids Process Engineering and Particle Technology, Hamburg University of Technology, Denickestraße 15, 21073 Hamburg, Germany<br><br>2 Nestlé Research, Route du Jorat 57, 1000 Lausanne, Switzerland | Poster |

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| 77 | STATIC AND DYNAMIC VAPOR SORPTION OF HYDROPHOPIC STARCH ESTER POWDERS AND CORRESPONDING TABLETS | **Ioannis Partheniadis**, Georgios Stathakis & Ioannis Nikolakakis | Laboratory of Pharmaceutical Technology, School of Pharmacy, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece 54124 | Poster |
| 78 | GRANULATION OF FLY ASH RESOURCES FOR WASTE UTILIZATION AND MATERIAL RECYCLING – A REVIEW | **Gabriel Borowski** | Faculty of Environmental Engineering, Lublin University of Technology, 40B Nadbystrzycka Str., 20-618 Lublin, Poland | Poster |
| 79 | STEAM GRANULATION VERSUS WET GRANULATION: IMPACT ON GRANULE AND TABLETS PROPERTIES | Erica Franceschinis[1], Elena Fontanel[1], Giulia De Santi[1], Nicola Realdon[1], Greta C. Magnano[2] & Dario Voinovich[2] | 1 PharmaTeG-Pharmaceutical Technology Group- Department of Pharmaceutical and Pharmacological Science, University of Padua, via Marzolo 5, 35131 Padova, Italy<br><br>2 Department of Chemical and Pharmaceutical Sciences, University of Trieste, P.le Europa 1, Trieste, Italy | Poster |
| 80 | EFFECT OF THE DRYING TYPE ON THE PROPERTIES OF GRANULE AND TABLETS PRODUCED BY HIGH SHEAR WET GRANULATION | **Erica Franceschinis**[1], Valentina Bressan[1], Simone Bernardotto[1], Margherita Morpurgo[1], Marco Luperini[2] & Andrea C. Santomaso[3] | 1 Department of Pharmaceutical and Pharmacological Sciences, University of Padova, via Marzolo 5, 35131 Padova, Italy<br><br>2 Luperini Production S.p.A., Via delle Gavine 1709, San Macario in Monte, 55100 Lucca, Italy<br><br>3 APTLab-Advanced Particle Technology Laboratory Department of Industrial Engineering University of Padova, via Marzolo 9, 35131 Padova, Italy | Oral |
| 81 | EFFECT OF FEED RATE AND ROTATION SPEED ON PROPERTIES OF AGGLOMERATES PRODUCED WITH THE FLEXOMIXTM SYSTEM | **Olukayode I. Imole** & Peter G. J. van der Wel | Research and Development, Hosokawa Micron B.V., Gildenstraat 26, 7005 BL, Doetinchem, The Netherlands | Poster |
| 82 | THE EFFECT OF TEMPERATURE ON PHARMACEUTICAL POWDER ADHESION TO COMPACTION TOOLING | **Vishal V. Shinde**, Ahmad D.A. Ramahi & I. Csaba Sinka | University of Leicester, University Road, Leicester LE1 7RH, United Kingdom | Oral |

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| 83 | NUMERICAL ANALYSIS OF INTER TABLET COATING UNIFORMITY OF TABLETS IN A LAB SCALE DRUM COATER | **Pradeep Muramulla**, Srikanth Gopireddy, Thomas Profitlich & Nora Urbanetz | Daiichi Sankyo Europe GmbH, Luitpoldstrasse 1, Pfaffenhofen, Germany | Poster |
| 84 | FORMULATION AND CHARACTERISATION OF HETERO-AGGREGATES FROM CONTINUOUSLY OPERATED OPPOSED-JET FLUIDIZED BEDS | **Ali Massomi**, Jochen Schmidt & Andreas Bück | Friedrich-Alexander-Universität Erlangen-Nürnberg, Lehrstuhl für Feststoff- und Grenzflächenverfahrenstechnik, Cauerstr. 4, 91058 Erlangen, Germany. | Poster |
| 85 | HEAT TRANSFER STUDIES IN A ROTATING DRUM CONTAINING NON-SPHERICAL PARTICLES | Satchit Nagpal[1], Sourabh Jogee[1], **Pradeep Muramulla**[2], Partha S. Goswami[1] & Srikanth Gopireddy[2] | 1 Department of Chemical Engineering, IIT Bombay, Mumbai, India<br><br>2 Daiichi Sankyo Europe GmbH, Luitpoldstrasse 1, Pfaffenhofen, Germany | Oral |
| 86 | THERMAL DESIGN AND SCALE-UP OF FLUID BED GRANULATION | **Ian C. Kemp** | Independent Consultant, 36 Wickenfields, Ware, Hertfordshire SG12 0XH, United Kingdom. | Oral |
| 87 | DEM SIMULATION OF A SINGLE SCREW GRANULATION: THE EFFECT OF LIQUID BINDER ON GRANULE PROPERTIES | Tony B. Arthur & Nejat Rahmanian | Department of Chemical Engineering, Faculty of Engineering & Informatics, University of Bradford, Bradford, BD7 1DP, UK. | Oral |
| 88 | PHARMACEUTICAL TWIN SCREW GRANULATION OF ALPHA-D-LACTOSE MONOHYDRATE WITH POLYETHYLENE GLYCOL 4000; AN INVESTIGATION OF GRANULE AND TABLET ATTRIBUTES | **Nana K. G. Sekyi**[1], Adrian L. Kelly[1], Nejat Rahmanian[1] & Anant Paradkar[2] | 1 Department of Chemical Engineering, Faculty of Engineering & Informatics, University of Bradford, Bradford, BD7 1DP, UK<br><br>2 School of Pharmacy & Medical Sciences, Faculty of Life Sciences, University of Bradford, Bradford, BD7 1DP, UK | Poster |
| 89 | INFLUENCE OF MIXING ELEMENTS ON GRANULE AND TABLET PROPERTIES IN HOT MELT TWIN SCREW GRANULATION | **Nana K. G. Sekyi**, Nejat Rahmanian & Adrian L. Kelly | Department of Chemical Engineering, Faculty of Engineering & Informatics, University of Bradford, Bradford, BD7 1DP, UK | Poster |
| 90 | MIXER TORQUE RHEOMETER - A CORRELATION BETWEEN THE MULTIPLE ADDITION AND VARIABLE MIX TIME METHODS | **Bruna R. Belem**, Gustavo V. Carapeto, Bruna F. do Rosário, | Department of Pharmacy, University of São Paulo, Professor Lineu Prestes Avenue, 580, São Paulo,<br>Brazil. | Oral |

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| | | Michele G. Issa & Humberto G. Ferraz | | |
| 91 | ASSESSMENT AND CHARACTERIZATION OF GRANULES PRODUCED IN A SINGLE SCREW EXTRUDER | Aaran Chauhan[1] & **Nejat Rahmanian**[2] | 1 43 Huggett Close, Leicester, LE4 7PY, United Kingdom<br><br>2 Richmond Road, University of Bradford, Bradford, BD7 1DP, United Kingdom | Poster |
| 92 | QUANTITATIVE ANALYSIS OF THE EFFECTS OF MULTICOMPONENT FORMULATION VARIATIONS ON GRANULE QUALITY ATTRIBUTES | **Ashley Dan**[1] , Haresh Vaswani[1] , Aleksandra Grząbka-Zasadzińska[3] , Jingzhe Li[2] , Koyel Sen[2] , Shubhajit Paul2 , Yin-Chao Tseng[2] & Rohit Ramachandran[1] | 1 Department of Chemical and Biochemical Engineering, Rutgers, The State University of New Jersey, Piscataway, NJ, USA 08854<br><br>2 Boehringer Ingelheim Pharmaceuticals Inc, 900 Ridgebury Rd, Ridgefield, CT 06877<br><br>3 Institute of Chemical Technology and Engineering, Poznan University of Technology, ul. Berdychowo 4, 60-965 Poznań, Poland. | Oral |
| 93 | DEVELOPMENT AND OPTIMIZATION OF DIRECT PELLETIZATION TECHNIQUE BY USING PROCEPT GRANULATOR | **Azza A. Mahmoud**, Géza Regdon jr. & Katalin Kristó | Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged, Eötvös u. 6, H-6720, Hungary | Poster |
| 94 | MIXER TORQUE RHEOMETER - EVALUATION OF THE PHYSICAL QUALITY OF FURAZOLIDONE GRANULES PRODUCED WITH DIFFERENT LIQUID/SOLID RATIOS | **Gustavo V. Carapeto**, Bruna R. Belem, Bruna F. do Rosário, Michele G. Issa & Humberto G. Ferraz | Department of Pharmacy, University of São Paulo, Professor Lineu Prestes Avenue, 580, São Paulo, Brazil | Oral |
| 95 | VALIDATION OF SCALED-UP PARTICLE MODEL IN DEM FOR COHESIVE PARTICLES | **Kimiaki Washino**, Yuze Hu, Ei L. Chan, Takuya Tsuji & Toshitsugu Tanaka | Department of Mechanical Engineering, Osaka University, Japan | Oral |
| 96 | DUST RELEASE AND SIMULTANEOUS SEPARATION BY MEANS OF ELECTROSTATICALLY ASSISTED SPRAY | **Marcus Weidemann** & Eberhard Schmidt | University of Wuppertal, Institute of Particle Technology, Rainer-Gruenter-Strasse Building FF, 42119 Wuppertal, Germany | Poster |

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| | NOZZLE SYSTEMS - EXPERIMENTAL PROCEDURES | | | |
| 97 | IN-LINE PARTICLE SIZE MEASUREMENT IN DRY GRANULATION: DEVELOPMENT AND APPLICATION OF A NOVEL SAMPLING FUNNEL FOR CONTINUOUS SAMPLING | **Marcus Weidemann**[1], Manfred Felder[2] & Eberhard Schmidt[1] | 1 University of Wuppertal, Institute of Particle Technology, Rainer-Gruenter-Strasse Building FF, 42119 Wuppertal, Germany<br>2 Alexanderwerk GmbH, Kippdorfstrasse 6-24, 42857 Remscheid, Germany | Oral |
| 98 | EVALUATION OF EFFECT OF PROCESS AND FORMULATION VARIABLES ON THE SIZE ENLARGEMENT MECHANISMS IN HIGH SHEAR MIXERS – AN EIRICH MIXER STUDY | Charlotte Sloan & **Chirangano Mangwandi** | School of Chemistry & Chemical Engineering, Queen's University Belfast, David Kier Building Stranmillis Road, Belfast, BT9 5AG, UK | Oral |
| 99 | SOLID DISPLACEMENT METHOD TO DETERMINE ENVELOPE DENSITY OF ROLLER COMPACTED RIBBONS AND ITS APPLICATION IN MATHEMATICAL MODELLING IN TECHNOLOGY TRANSFER OF THE DRY GRANULATION PROCESS | **Nikita Marinko**[1], Petr Zámostný[1] & Michaela Gajdošová[2] | 1University of Chemistry and Technology, Prague, Department of Organic Technology, Technická 5, Prague 6, 166 28, Czech Republic<br><br>2 Zentiva k,s,, U Kabelovny 130, Prague 10, 102 37 Czech Republic | Oral |
| 100 | THE EFFECT OF VARYING COMPRESSION FORCE AND SPEED ON PHARMACEUTICAL TABLET CRITICAL QUALITY ATTRIBUTES | **Jeanina-Monica Bungau**, Riyadh B. Al-Asady & Agba D. Salman | Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK | Poster |
| 101 | FORMULATION IN A DROP - TEMPLATED GRNAULATION AND COMPACTION ANALYSIS | Paola Medina Martinez[1], Line Koleilat[1], Joshua Hanson[2], Jonathan Wade[2] & **Paul Mort**[1] | 1 Purdue University, West Lafayette, IN, USA<br><br>2 Eli Lilly & Company, Indianapolis, IN, USA | Oral |
| 102 | INTEGRATED MODEL CONTROL OF FLUIDIZED BED GRANULATION | Line Koleilat[1], Joshua Hanson[2], Jonathan Wade[2], Christian Karl Paasche[3], Carl Wassgren[1] & **Paul Mort**[1] | 1 Purdue University, West Lafayette, IN, USA<br><br>2 Eli Lilly & Company, Indianapolis, IN, USA<br>3 Hüttlin GmbH, Syntegon Company, Schopfheim, Germany | Poster |

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| 103 | INDUSTRIAL CASE STUDY ON SCALE UP AND SYSTEM DYNAMICS CHARACTERIZATION OF PHARMACEUTICAL CONTINUOUS PRODUCTION LINE | **Ahmad Mohamad**, Yves Roggo, Markus Krumme | Novartis Pharma AG, Novartis Campus, 4056 Basel, CH | Oral |
| 104 | COMPARATIVE ANALYSIS OF POROSITY MEASUREMENT TECHNIQUES USING PHARMACEUTICAL MATERIALS | **Arnesh Palanisamy**[1], Lizbeth Martinez[1] & Bindhumadhavan Gururajan[1,2] | 1 Novartis Pharma AG, Novartis Campus, 4056 Basel, CH<br><br>2 Department of Materials and Processes, University of Edinburgh, Old College, South Bridge, Edinburgh EH8 9YL, UK | Poster |
| 105 | RESTRUCTURING OF MILK POWDER: SINGLE DROPLET DRYING IN THE SPRAY DRYER | **Xuqian Li**[1], Riyadh B Al-Asady[1], Constantijn Sanders[2] & Agba.D.Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK<br><br>2 Nestec Ltd., Nestlé Product Technology Centre, Nestlé Strasse 3, CH-3510 Konolfingen, Switzerland | Oral |
| 106 | INFANT MILK RECONSTITUTION: INVESTIGATION OF THE HOMOGENEITY OF PARTICLE SUSPENSION | **Zheng Wang**[1], Riyadh B Al-Asady[1], Constantijn Sanders[2] & Agba D Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK<br><br>2 Nestlé Product Technology Centre, Nestlé Strasse 3, CH-3510 Konolfingen, Switzerland | Poster |
| 107 | INVESTIGATION OF HEAT TRANSFER ON MOIST SPRAY-DRIED PORCELAIN PARTICLES | **Carine. L. Alves**[1], Agenor de Noni Jr.[2], Sergio Y. Gómez González[2], Irina Smirnova[3] & Stefan Heinrich[1] | 1 Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology (TUHH), 21073 Hamburg, Germany<br><br>2 Department of Chemical Engineering (EQA), Federal University of Santa Catarina (UFSC), 88040-900 Florianópolis, SC, Brazil<br><br>3 Institute of Thermal Separation Processes, Hamburg University of Technology (TUHH), 21073 Hamburg, Germany | Oral |

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| 108 | FLOWSHEET SIMULATIONS APPLIED FOR OPTIMIZATION AND SUSTAINABILITY OF PORCELAIN TILE MANUFACTURING | **C. L. Alves**[1], V. Skorych[1], A. de Noni Jr.[2], D. Hotza [2], S.Y. Gómez González[2], & S. Heinrich[1] | 1 Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology (TUHH), 21073 Hamburg, Germany<br><br>2 Department of Chemical Engineering (EQA), Federal University of Santa Catarina (UFSC), 88040-900 Florianópolis, SC, Brazil | Poster |
| 109 | THE INFLUENCE OF CALCIUM IONS ON THE PROCESSABILITY OF CROSCARMELLOSE SODIUM IN EXTRUSION/SPHERONIZATION | **Finn Siebel** & Peter Kleinebudde | Institute of Pharmaceutics and Biopharmaceutics, Heinrich Heine University Düsseldorf, Universitätsstraße 1, Düsseldorf, 40225, Germany | Poster |
| 110 | EVALUATION OF DIFFERENT MANNITOL GRADES IN DRY GRANULATION PROCESS BY ROLLER COMPACTION | M. Cerea, L. Palugan, A. Foppoli, **A. Gelain**, A. Cozzi, G. Macleod, A. Melocchi, A. Gazzaniga | 1 Università degli Studi di Milano, dip. di Scienze del Farmaco, Via G.Colombo 71, Milano, Italy<br><br>2 Freund-Vector corp. Via Enrico Mattei 2, Villasanta (MB), Italy<br><br>3 Disproquima, Via Mauro Venegoni, 73, 20025 Legnano (MI)<br><br>4 SPI Pharma, Rockwood Office Park, 503 Carr Road, Wilmington, Delaware | Poster |
| 111 | A MODELLING FRAMEWORK BASED ON SERIAL ARTIFICIAL NEURAL NETWORKS FOR THE MODELLING OF A CONTINUOUS TABLETTING LINE | **Wafa' H. AlAlaween**[1], Mahdi Mahfouf[2], Chalak Omar[3], Riyadh B Al-Asady[3], Daniele Monaco[3] & Agba D. Salman[3] | 1 Department of Industrial Engineering, The University of Jordan, Jordan<br><br>2 Department of Automatic Control and Systems Engineering, The University of Sheffield, UK<br><br>3 Department of Chemical and Biological Engineering, The University of Sheffield, UK | Oral |
| 112 | DEVELOPING AFFORDABLE GRANULATION METHODS | **Yashodh H Karunanayake**[1], Linda Brütsch[2], | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK | Oral |

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| | | Vincent Meunier[2] & Agba D Salman[1] | 2 Nestle Research Lausanne, 1010 Lausanne, Switzerland | |
| 113 | A SIMPLIFIED JOHANSON MODEL TO PREDICT ROLL FORCERIBBON DENSITY RELATIONSHIP IN PHARMACEUTICAL ROLLER COMPACTION | **Chen Mao**, Chi So, Lap Yin Leung, & Ariel R. Muliadi | Small Molecule Pharmaceutical Sciences, Genentech, Inc., South San Francisco, CA, 94080, USA | Oral |
| 114 | LACTOBACILLUS LOADED POROUS HYDROXYAPATITE (HAP) PELLETS USING DIFFERENT HAP GRADES AND PORE FORMERS | Theodora Papanikolaou[1], Ioannis Partheniadis[1], Dimitrios Fatouros[1], Antonia Sipaki[1], **Ioannis Nikolakakis**[1], Suzan Vergkizi[2] | 1 Laboratory of Pharmaceutical Technology, School of Pharmacy, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece 15124<br><br>2 Laboratory of Microbiology, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece 15124 | Oral |
| 115 | RESTRUCTURATION OF FOOD POWDER USING ROLLER COMPACTOR TO INCREASE THE SHELF LIFE | **Yang S. Mohamad**[1], Riyadh Al-Asady[1], Manfred Felder[2], Vincent Meunier[3], James Litster[1] & Agba D. Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK<br><br>2 Alexanderwerk AG, Remscheid, North Rhine-Westphalia, Germany<br><br>3 Nestle Research, 1010 Lausanne, Switzerland | Poster |
| 116 | MODUL P ROTARY TABLET PRESS: INVESTIGATING THE FORMULATION VARIABLES | **Shengda Hou**, Riyadh B Al-Asady & Agba D Salman | Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK | Poster |
| 117 | TO IMPROVE MILK POWDER QUILITY BY DRY COATING | **Yongang Ma**, Riyadh B Al-Asady & Agba D Salman | Department of Chemical and Biological Engineering, University of Sheffield Sir Robert Hadfield Building, Mappin Street, Sheffield, United Kindgom S2 3JD | Poster |
| 118 | COARSE-GRAINED DISCRETE ELEMENT SIMULATION AND EXPERIMENTAL STUDY OF WET GRANULATION PROCESS | **Roxana Saghafian Larijani**[1], Vanessa Magnanimo[1], | 1 Soil MicroMechanics, Faculty of Engineering Technology, University of Twente, Drienerlolaan 5, Enschede, 7522NB, Netherlands | Poster |

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| 119 | PREPARATION AND EXAMINATION OF THE COMPRESSIBILITY OF TITANATE NANOTUBE-API COMPOSITES | **Tamás Sovány**, Dalma Erdei, Ranim Saker, Yasmin Ranjous, Géza Regdon jr. | Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Eötvös u 6. H-6720 Szeged, Hungary | Poster |
| 120 | A NOVEL MECHANISTIC MODEL TO DESCRIBE THE SWELLING OF DISINTEGRATING GRANULE | **Peyman Mostafaei**, Bilal Ahmed, Francesca Magnasco, Faraj Shmam, Neeru Bala & Rachel Smith | Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield S1 3JD, UK | Poster |
| 121 | EFFECTIVENESS OF PREDICTING SPHERICAL AGGLOMERATE PROPERTIES USING A POPULATION BALANCE MODEL | **Victoria R Kitching**, Bilal Ahmed, Kate Pitt, James D. Litster & Rachel M. Smith | Department of Chemical and Biological Engineering, The University of Sheffield, Mappin Street, Sheffield, S1 3JD | Poster |
| 122 | VOLUME-INTERACTING LEVEL SET DISCRETE ELEMENT METHOD: THE ANGLE OF REPOSE OF ANGULAR AND CONCAVE PARTICLES | **Dingeman L.H. van der Haven**[1], Ioannis S. Fragkopoulos[2] & James A. Elliott[1] | 1 Department of Materials Science & Metallurgy, University of Cambridge, 27 Charles Babbage Road, Cambridge, CB3 0FS, United Kingdom<br><br>2 Future Manufacturing & Digital Innovation, Novo Nordisk A/S, Måløv, Denmark | Oral |
| 123 | FLUID BED PROCESSING OF NANOCRYSTAL FORMULATIONS WITH PERSONALISED DISSOLUTION PROFILES | Ondřej Navrátil[1,2], Elizaveta Mutylo[1,2], **Filip Hládek**[1,2] & František Štěpánek[1] | 1 Department of Chemical Engineering, University of Chemistry and Technology Prague, Technická 5, 166 28 Prague 6, Czech Republic | Oral |

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| 124 | PREDICTION OF GRANULE CRITICAL QUALITY SIZE ATTRIBUTES IN A TWIN SCREW WET GRANULATOR USING POPULATION BALANCE MODELLING | **Neeru Bala**[1], Jeremiah Corrigan[1,2], Bilal Ahmed[1], Jonathan Meyer [2], Marek Schongut[2], Kai Lee[2], Martin Rowland[2], James D. Litster[1], Neil Dawson[2] & Rachel Smith[1] | 1 Particle Technology Group, Department of Chemical and Biological Engineering, University of Sheffield, Newcastle Street, Sheffield, S1 3JD, UK<br><br>2 Pfizer Inc., Sandwich, Kent, UK | Poster |
| 125 | A NOVEL METHOD FOR RAPID SCREENING OF SPRAY-DRIED FORMULATIONS | **Vojtěch Klimša**[1,2], Gabriela Ruphuy Chan[1,2] & František Štěpánek[1] | 1 University of Chemistry and Technology Prague, Technická 3, 166 28 Prague, Czech Republic<br>2 Levare s.r.o., Jičínská 226/17, 130 00 Prague, Czech Republic | Oral |
| 126 | IDENTIFICATION OF LETHAL MECHANISMS AND CONTROL STRATEGIES IN DEVELOPING PROBIOTIC TABLETS | **Bide Wang**[1], Andrew Middleton[2], Rachael Gibson[2], Jayant Khanolkar[2], Oleksiy Klymenko[1] & Charley Wu[1] | 1 School of Chemistry and Chemical Engineering, University of Surrey, Guildford, GU2 7XH, UK<br><br>2 P&G Innovation Centre, 452 Basingstoke Road, Reading, Berkshire, RG2 0QE, UK<br>Email: c.y.wu@surrey.ac.uk | Oral |
| 127 | INVESTIGATING PROCESS VARIABLES THAT AFFECT LOGO-BRIDGING | **Euan F. Murgatroyd** & Ian P. Gabbott | Pharmaceutical Technology and Development, AstraZeneca, Charter Way, Macclesfield, SK10 2NA, UK | Poster |
| 128 | DEM-CFD SIMULATION OF VOLUMETRIC EXPANSION OF GRANULAR MATERIALS | Chuan-Yu Wu & **Jiawei Hu** | School of Chemistry and Chemical Engineering, University of Surrey, Guildford GU2 7XH, UK | Poster |
| 129 | ACTIVE MATERIAL-CARBON BLACK (AM-CB) SPHERICAL CO-AGGLOMERATES FOR IMPROVED HANDLING OF LI-ION BATTERY MATERIAL | **Kunal Pardikar**, Jediah Capindale, Kate Pitt, Denis Cumming, & Rachel Smith | Department of Chemical and Biological Engineering, The University of Sheffield, Sheffield, S10 2TN, UK | Poster |

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| 130 | NUMERICAL INVESTIGATION OF GRANULE FLOW | Ali Z. Al hassn[1], **Kimiaki Washino** [2] , Ei L. Chan[2] & Agba D. Salman[3] | 1 Department of Chemical Engineering, College of Engineering, University of Diyala, Iraq<br><br>2 Department of Mechanical Engineering, Osaka University, Osaka, Japan<br><br>3 Department of Chemical and Biological Engineering, University of Sheffield, Newcastle Street, Sheffield, S1 3JD, UK | Poster |
| 131 | TOWARDS BETTER SUSTAINABILITY:SPRAY-DRYING OF HIGHLY VISCOUS CONCENTRATES | **Riyadh B Al-Asady**[1], Vincent Meunier[2], Gerhard Niederreiter[3] & Agba D. Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Newcastle Street, Sheffield, S1 3JD, UK<br><br>2 Nestlé Research, Vers-Chez-Les-Blanc, 1000 Lausanne 26, Switzerland<br><br>3 Nestlé Research, 1010 Lausanne, Switzerland | Oral |
| 132 | CONTINUOUS MANUFACTURING OF PHARMACEUTICAL TABLETS: EFFECT OF DIFFERENT UNITS AND FORMULATION PARAMETERS | **Riyadh B Al-Asady**[1], Chalak S.Omar[2], Jeanina M. Bungaue [1] & Agba D. Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Newcastle Street, Sheffield, S1 3JD, UK<br><br>2 Multidisciplinary Engineering Education, The Diamond, University of Sheffield, Leavygreave Road, Sheffield, S37RD, UK | Poster |
| 133 | FAST TO CLINIC: MATERIAL SPARING PLATFORM APPROACH TO ROLLER COMPACTION PROCESS DEVELOPMENT | **Ranjit Dhenge** [1], Chandan Bhugra[2], Parind Desai[2], Stephanie Lam[2] & Daniel Goodwin[3] | 1Global Supply Chain, GlaxoSmithKline, Ware, UK<br><br>2 Research and Development, GlaxoSmithKline, Upper Providence, USA<br><br>3 Research and Development, GlaxoSmithKline, Ware, UK<br>E-mail: ranjit.x.dhenge@gsk.com | Poster |

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| 134 | REPLICATING RING-DIE PELLETING PROCESS WITH SINGLE-DIE PELLET PRESS: EVALUATION AND OPTIMIZATION | **Prutha Nagaraja** [1], Dejan Miladinovic [2] Laurent Cavin[3], Thomas G Gfroerer[3], Andreas Thuermer [3], Odd Ivar Lekang [1] & Kristian Berland [1] | 1 Department of Mechanical Engineering and Technology Management, Norwegian University of Life Science, Elizabeth Stephansens v. 15, 1430 Ås, Norway<br><br>2 Department of Animal and Aquacultural Sciences, Norwegian University of Life Science, Elizabeth Stephansens v. 15, 1430 Ås, Norway<br><br>3 Form giving and Customer Specific Blends, Plastic Additive, BASF Schweiz AG, Postfach, 4005 Basel, Switzerland | Poster |
| 135 | SYSTEMATIC STUDY TO IMPROVE THE POWDER FLOWABILITY AND REDUCING THE PERCENTAGE OF FINES IN ROLLER COMPACTOR | **Yang S. Mohamad**[1], Riyadh Al-Asady[1], Mingzhe Yu[1], Manfred Felder[2], Vincent Meunier[3], James Litster[1] & Agba D. Salman[1] | 1Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK<br><br>2 Alexanderwerk GmbH, Remscheid, North Rhine-Westphalia, Germany | Oral |
| 136 | FOOD VS PACKAGING: DYNAMICS OF OIL-MIGRATION FROM PARTICLE SYSTEMS INTO FIBROUS MATERIAL | **Luc Dewulf**[1], Michael K. Hausmann[2], Annabel Bozon[3], Gerhard Niederreiter[2], & Agba D. Salman[1] | 1 Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, United Kingdom S1 3JD<br><br>2 Nestlé Research, 1010 Lausanne, Switzerland<br><br>3 Nestlé Product Technology Centre, Lange Straße 21, 78221, Singen, Germany | Poster |
| 137 | REAL-TIME GRANULE SIZE MEASUREMENT IN A TABLET PRODUCTION LINE: INVESTIGATION OF GRANULE SIZE IN FLUDIZED BED DRYER | **Shengda Hou,** Jeanina M. Bungău, James D. Litster & Agba D. Salman | Department of Chemical and Biological Engineering, University of Sheffield, Mappin Street, Sheffield, S1 3JD, UK | Poster |

# 1.EVOLUTION OF PELLET SHAPE DURING INITIAL STAGES OF SPHERONISATION

Syahmeer M. How [1,2], Sarah L. Rough[1], Liguang Wang[1,3] & Ian D. Wilson[1]

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Extrusion-spheronisation is used to generate pellets with high sphericity in the pharmaceutical sectors. Cylindrical extrudates are generated by forcing a cohesive paste (powdered solids with a small amount of liquid binder) through a screen or extrusion die on to a rotating friction plate which promotes breakage of the cylinders into shorter lengths: simultaneously, collisions between pellets and with the wall promotes rounding and densification. The breakage stage is important in determining the final size distribution of the pellets and the time taken for spheronisation to be completed.

This paper reports a systematic analysis of the breakage stage in extrusion-spheronisation. Microcrystalline cellulose-water extrudates were generated by ram extrusion through a single-holed die and either added to the spheroniser as a set of extrudates of equal length, or by mass. Spheronisation was run for short lengths of time to capture the evolution of pellet length and shape (determined by image analysis of photographs, see below). Breakage kinetics were fitted to a simple first order reaction model (described in detail in [1]) while the evolution of pellet shape is compared with geometrical models. The effect of spheroniser speed and extrudate diameter were investigated. Approaches for modelling the associated population balance model are discussed.

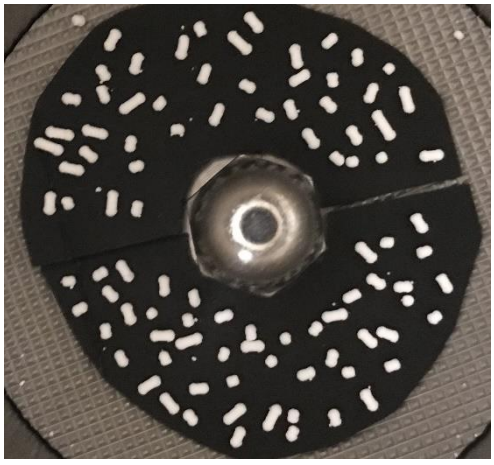
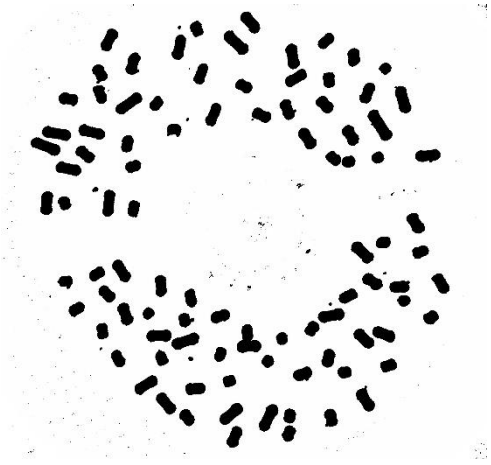
(a)  (b) 

Figure 1. Photograph (a) and binarised image (b) used for shape analysis

[1] L. Wang, C.W. Lim, G.Z.L. Ng, S.L. Rough, D. Ian Wilson, Modeling the breakage stage in spheronization of cylindrical paste extrudates, AIChE Journal. 67 (2021) 1-11.

# 2. ROLLER COMPACTION; DECREASE THE AMOUNT OF FINES IN MILLING STAGE.

Mohamed N. Mohamed[1], Riyadh B Al-Asady, Manfred Felder[2], James D. Litster & Agba D Salman

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Dry granulation by roller compactor is a size enlargement technique, widely used in pharmaceutical industry because it has several advantages such as no need for liquid binder, can be suitable for heat sensitive materials, low cost comparing to wet granulation and it is a continuous process. however, one of its major drawback is forming of fines which can lead to manufacturer problems such as poor flow ability that can lead to tablet weight variation due to inconsistent die filling during tableting and un acceptable content due to segregation of fine from granules [1].

The aim of this study is to investigate into the possibility of decreasing the amount of fine in the outcome granules by concentrating on milling stage as one of the main source of fines during the process. The work will focus on the flack crusher and the miller in order to decrease the amount of fine in the final granules.

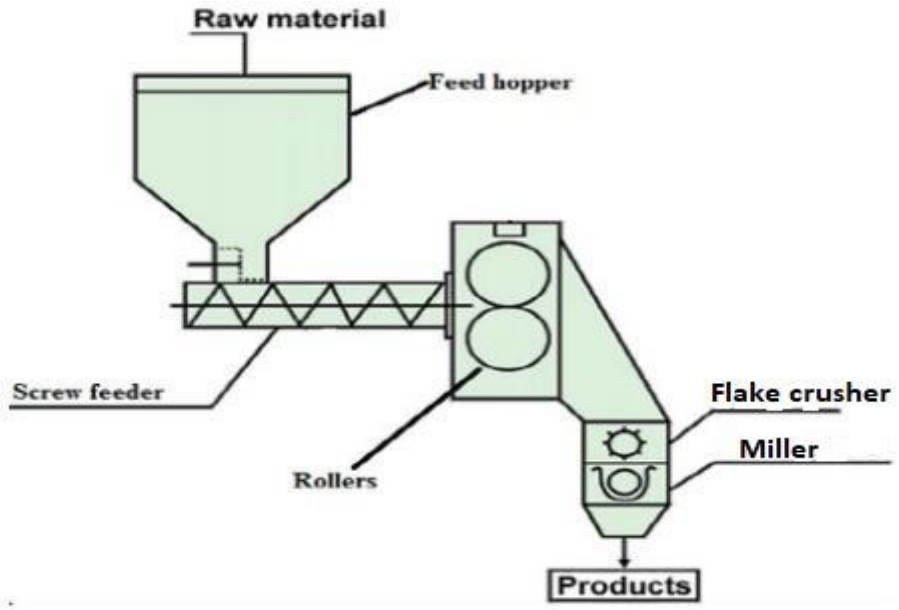


Figure 1. Diagram shows the main parts of roller compactor machine [2]

[1] C.S. Omar, R.M. Dhenge, J.D. Osborne, T.O. Althaus, S. Palzer, M.J. Hounslow, A.D. Salman, Roller compaction: Effect of morphology and amorphous content of lactose powder on product quality, International Journal of Pharmaceutics, 496 (2015) 63-74.

[2] D. Sonam, P. Kulkarni, V. Kashikar, B. Jitendr and T. Manoj. A Review: Roller Compaction for Tablet Dosage Form Development. Journal of pharmacy and pharmaceutical science. 2 (2013) 68-73.

# 3. ADVANCED 3D AND 4D MICROSTRUCTURE STUDY OF SINGLE GRANULE FORMATION USING SYNCHROTRON IN-SITU X-RAY IMAGING

Sima Zeinali Danalou[1], Carter Blocka[1], Jingsi Yang[1], Xiao Fan Ding[2], Ning Zhu[1,2,3], Heather N. Emady[4], Ellen Wasan[5] & Lifeng Zhang[1]

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2 Department of Biomedical Engineering, University of Saskatchewan, SK, Canada,
3 Canadian Light Source Inc., SK, Canada,
4 School for Engineering of Matter, Transport and Energy, Arizona State University, AZ, USA.
5 College of Pharmacy and Nutrition, University of Saskatchewan, SK, Canada
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Wet granulation is the most common granulation method used in the pharmaceutical and chemical industries. Monitoring the microstructure of the granule in the granulation process could play a decisive role in obtaining high-quality granules. Due to the complexity, fast and opaque nature of wet granulation, it cannot be captured by conventional methods such as lab-based X-ray imaging techniques. In this study, synchrotron X-ray imaging was employed for the first time to investigate the internal real-time pore evolution during the granule nucleation process taking place in seconds, based on the single droplet impact method. Binary mixtures consisting of acetaminophen (APAP) as the active pharmaceutical ingredient with lactose monohydrate (LMH) and microcrystalline cellulose (MCC), and deionized water as a liquid binder were used. It was found that granules from coarser and more homogenous powders experienced a higher rate of pore evolution during nucleation with a more uniform pore distribution. Dynamic wetting studies showed that the crater mechanism was found for most binary mixtures with 50 wt. % excipients. The spreading mechanism occurred for MCC with the greatest droplet diameter increase, and the Tunneling happened for 90% of fine LMH with the highest penetration length. The final granules resulting from the spreading and the Tunneling mechanism showed the highest and lowest porosity, respectively. The tensile strength and dissolution test results showed that the granules with lower porosity and finer pores exhibited higher hardness and a slower dissolution rate.

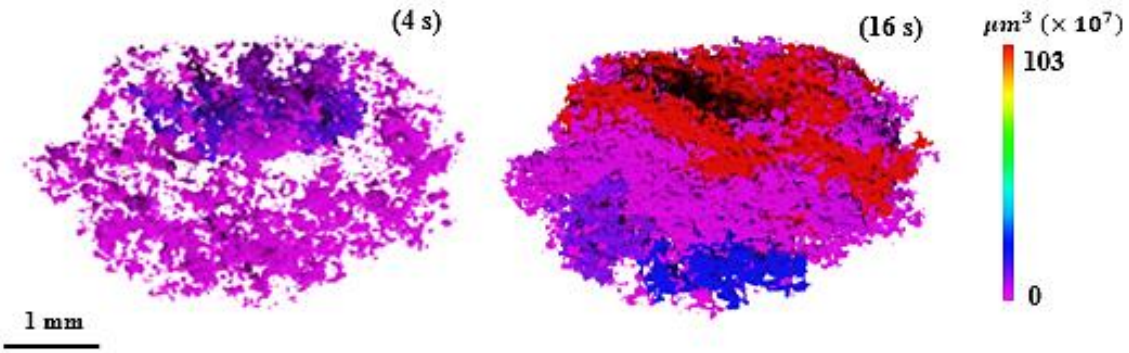


Figure 1. 3D pores volume rendering over time for 50%MCC-50%APAP.

# 4. DEVELOPING A COMMERCIAL SCALE SEMI-CONTINUOUS FLUID BED WET GRANULATION PROCESS VIA DESIGN OF EXPERIMENTS BASED ON A MULTIVARIATE MODEL AND STATISTICAL ANALYSIS

Maitraye Sen, Sydney Butikofer, Chad N. Wolfe, Shashwat Gupta & Adam S. Butterbaugh

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Although fluid bed wet granulation provides several benefits, such as ease of automation and enhanced manufacturing efficiency by reducing process footprint and cost, it is a time consuming and complex unit operation to develop. The granulation rate processes in a fluid bed are influenced by several primary input variables (e.g., raw material properties, fluid dynamics and granulation/drying operating parameters) [1]. Due to this complexity, several aspects of fluid bed wet granulation are often developed either empirically or through trial and error in a univariate manner, as means to simplify development. However, these approaches typically result in less process knowledge, and ultimately, in a commercial process with a higher likelihood of deviations in product quality attributes due to any common-cause variability that is not fully understood.

This work presents a multivariate approach to develop a robust commercial design space of a semi-continuous fluid bed wet granulation by reducing development time and resource usage. The initial work was performed in a bench top fluid bed granulator to map the interactions among the primary input variables and granule quality attributes via a partial least squares (PLS) model. This understanding was then used to streamline the experimental design at the commercial scale. The dimensionality of the process space was reduced by identifying two intermediate variables: moisture accumulation rate (dominant during spraying) and moisture removal rate (dominant during drying). Effects of selected primary input variables were combined into these intermediate variables, which were then connected to the granule quality attributes (e.g., the span of granule size distribution as a function of moisture accumulation rate and processing batch size is shown in the below figure). The process knowledge space was built combining PLS analysis with experiments followed by a statistical analysis to understand the process variability, resulting in the proposal of the final commercial operating design space.

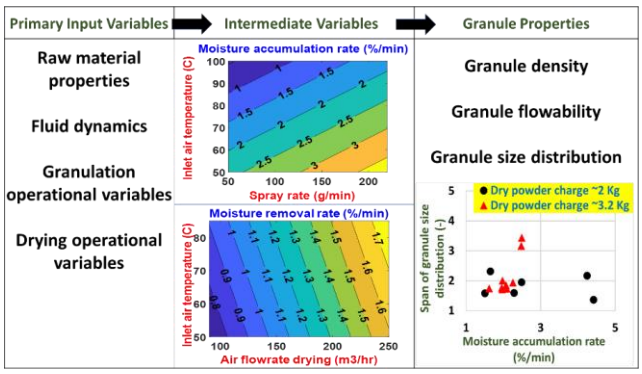


Figure 1. Connecting granulation process inputs with granule properties via intermediate variables

[1] V.N. Emenike, I. Kulla, M. Maus, A. Staab, D. Schröder, A linear scale-up approach to fluid bed granulation, Int. J. Pharm. 598 (2021) 120209

# 5. STRUCTURATION OF PLANT-BASED MILK POWDER FOR IMPROVED RECONSTITUTION

Kathrin Kramm[1], Jana Kammerhofer[2], Vincent Meunier[3],
Swantje Pietsch-Braune[1] & Stefan Heinrich[1]

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Food products in powder form are widely produced due to advantageous properties including better physical and chemical stability, easy weighing, efficient transport and smaller volume for storage [1]. Milk powder in particular has numerous applications in various products, but a growing number of consumers are tending towards plant-based alternatives. The Plant-Based Milk Alternative (PBMA) model powder investigated in this project, consists of maltodextrin, plant protein, vegetable oil and a soluble fiber source, and has tendency to form lumps during reconstitution. This lump formation is most likely correlated with the bulk power structure as well as the viscosifying and swelling properties of the plant ingredients. For more efficient wetting behavior and facilitated water imbibition, the fine food powders are often agglomerated. To design targeted particle structures, PBMA powder is produced by spray-drying of homogenized emulsions followed by fluid-bed agglomeration process.

To understand how to obtain an optimized structure of PBMA powder for subsequent applications, the influence of material properties and process parameters on the formation, structure and qualities of the agglomerated powder has to be investigated. Therefore, the material properties were examined in dependency of the fluidized bed process parameters for different formulations covering various type and quantity of PBMA components. The produced agglomerates were analysed regarding particle size distribution, moisture content, surface roughness and wettability. The results show that the plant proteins and fibers have a predominant influence on the process and product properties.

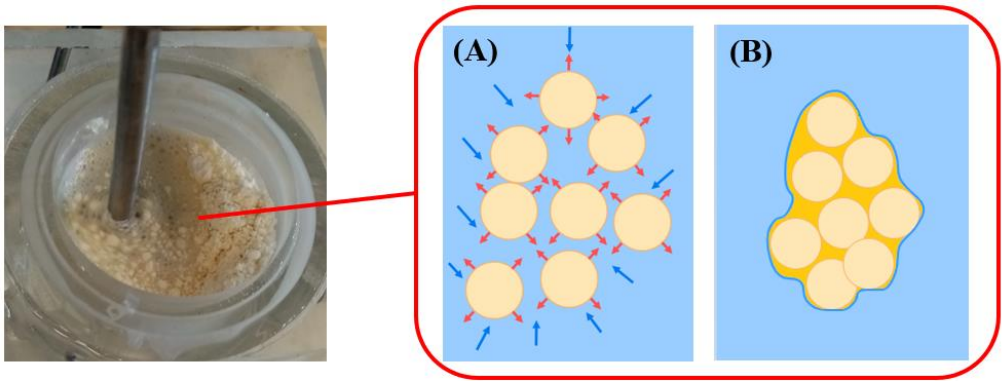


Figure 1. Lump formation during reconstitution, (A) particles start to swell (red arrows) due to water contact (blue arrows); (B) formation of a viscous outer layer leading to the aggregation of swelling particles

[1] B. Cuq, E. Rondet, J. Abecassis, Food powders engineering between know how and science: Constraints, stakes and opportunities, Powder Technology, 208 (2011) 244-251

# 6. MODEL-DRIVEN AND DATA-DRIVEN SOFT SENSING OF SOLID MOISTURE CONTENT IN FLUIDIZED BED DRYERS

Robert Kräuter, Xiye Zhou & Stefan Heinrich

Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Germany
E-mail: robert.kraeuter@tuhh.de

Solid moisture content is an important particle property in many applications of fluidized beds. The importance on the quality of pharmaceutical formulations make an in-line measurement of the moisture content desired. However, this particle property is often measured off-line by loss over drying during or after the process which results in a delayed process control. Beside the usage of more advanced and expensive methods, such as near-infrared spectra-based measurements or the microwave resonance technology (MRT), a promising strategy for in-line monitoring of the moisture content is soft-sensing.

In this work we compare model-driven and data-driven implementation of a soft sensor for the drying of Cellets® in a fluidized bed in terms of accuracy and computing speed. The model driven implementations are based on mechanistic models and the data-driven implementations are based on correlation techniques and machine learning methods such as artificial neural networks. The algorithms are developed with experimental data and MRT measurements in lab scale and we analyze the influence of different process parameters and material properties on the soft sensor's ability to generalize across other production scales. We then use the predicted moisture content together with other in-line measurements as inputs for real-time flowsheet simulations of the drying process. These flowsheet simulations pave the way towards the development of a digital twin for the autonomous control of fluidized bed dryers.

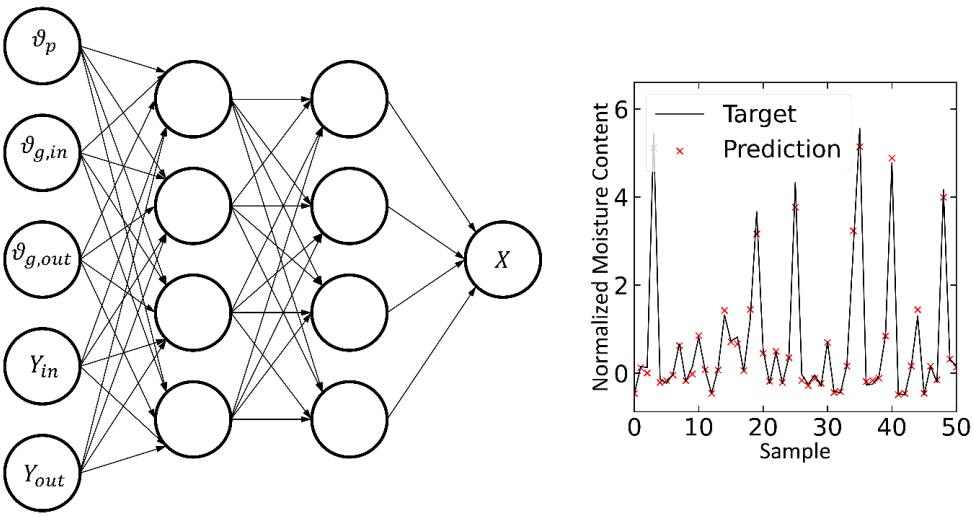


Figure 1. Artificial neural network for the prediction of solid moisture content based on process parameters bed temperature $\vartheta_p$, temperature of fluidization and exhaust gas $\vartheta_{g,in}$ and $\vartheta_{g,out}$ and moisture content of fluidization and exhaust gas $Y_{in}$ and $Y_{out}$. The topology is shown on the left and a prediction on random samples of a batch dying of Cellets®200 is shown on the right.

# 7. TWIN PRO® - FUSION OF TWO PROCESSES: HIGH SHEAR GRANULATION AND FLUIDIZED BED DRYING IN ONE PROCESS

Soeren E. Lehmann[1] & Lars Steinke[2]

1 Glatt Pharmaceutical Services GmbH & Co.KG, Werner-Glatt-Straße 1, 79589 Binzen, Germany
2 Glatt GmbH, Werner-Glatt-Straße 1, 79589 Binzen, Germany
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Granulation is an important process in the manufacture of solid dosage forms in the pharmaceutical industry. Traditionally, the production of the granules is split into different unit operations: High shear granulation, wet milling, conveying of wet granules and fluid bed drying. Especially, the wet milling and conveying of wet granules are often challenging process steps.

For the first time, the revolutionary, patent pending TwinPro® system unites two previously separate processes, high shear granulation and fluid bed drying, in one batch process. The revolutionary fusion of two processes into a single system eliminates the often-critical wet milling and conveying of the wet granules. By adjusting the position of the bottom plate, the TwinPro® enables classical high shear granulation (closed position) and subsequent fluid bed drying in the same unit by lowering the bottom plate, allowing for inflow of drying air into the system.

The unification of high shear granulator and fluid bed drying unit in one plant as well as the removal of wet milling and conveying steps results in a reduced footprint of the entire granulation process line as well as lowered investment costs in systems and building technology. Additionally, overall process time and cleaning demand are reduced, while process efficiency and robustness are increased. Furthermore, highly reproducible product quality is achieved by precise end point detection via torque measurement.

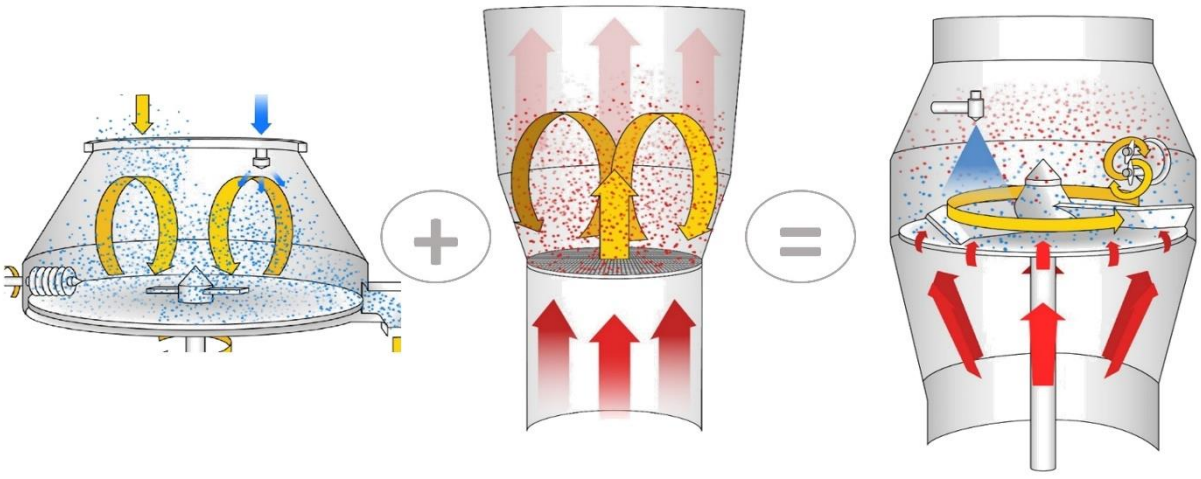

Figure 1. Schematic overview of fusion of traditional high shear granulation and fluidized bed drying into the TwinPro® process.

# 8.CORRELATING PARTICLE PROPERTIES WITH PROCESS PARAMETERS IN FLUIDIZED BED SPRAY GRANULATION AND ITS APPLICATION IN DYNAMIC FLOWSHEET SIMULATION

Xiye Zhou , Robert Kräuter & Stefan Heinrich

Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology, Denickestr. 15, 21073 Hamburg, Germany
E-mail: xiye.zhou@tuhh.de

In fluidized bed spray granulation, the particle moisture content and bed temperature during operation are key parameters, which significantly influence the later product properties such as flowability and hardness. However, the particle moisture content is usually determined by offline measurements based on loss on drying, which is time-consuming and leads to delayed process control. Hence, an inline measurement of the moisture content becomes crucial. Moreover, the influence of process parameters on the particle moisture content and bed temperature should be modeled with the purpose of faster process prediction, which contributes to the development of a digital twin for the autonomous control of fluidized bed processes.

In this work, Cellets® are coated using fluidized bed spray granulation. The particle moisture content is measured inline based on microwave transmission. Important process parameters, such as the flow rate and the temperature of the fluidization air, the water spray rate and the atomization pressure in the nozzle, are varied according to a design of experiments approach. The resulting inline particle moisture content and bed temperature are correlated with the process parameters using the response surface methodology. Additionally, the dynamic behaviour of particle moisture content and bed temperature according to the change of process parameters is investigated. The established models are then implemented in the open-source dynamic flowsheet simulation software Dyssol [1] and serve for a model-driven soft sensing.

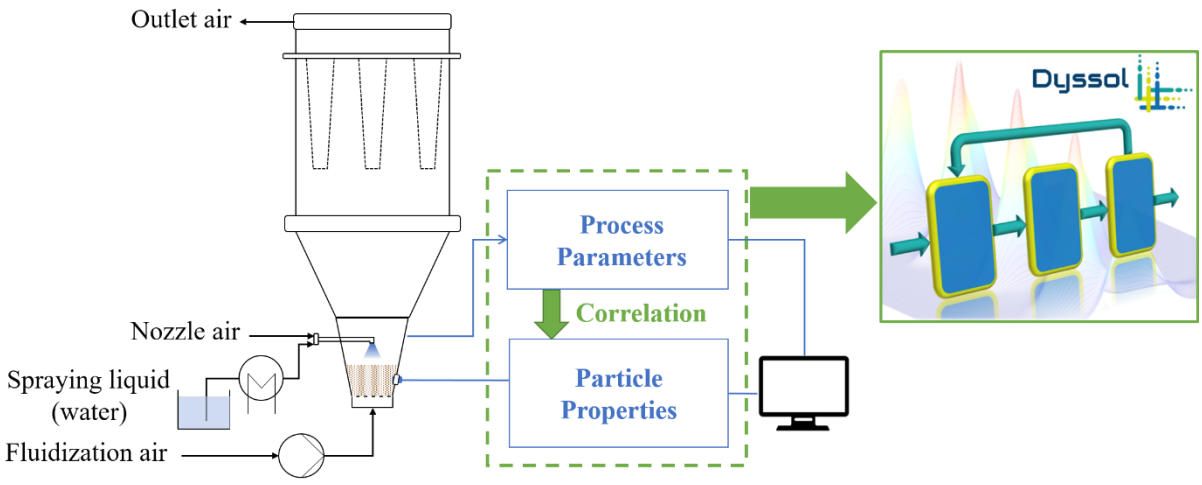


Figure 1. Schematic experimental setup with inline measurement of process parameters and particle properties. The correlation is implemented in the dynamic flowsheet simulation tool Dyssol.

[1] V. Skorych, M. Dosta, S. Heinrich, Dyssol—An open-source flowsheet simulation framework for particulate materials, SoftwareX, 12 (2020) 1-7.

# 9. DEVELOPMENT OF GRANULAR NEUTRAL AMINO ACIDS WITH CALCIUM HYDROXIDE COMPOSITION

Min Kyung Kwon[1], Jun-Woo Kim[1] & DongHyun Lee[2]

1 CJ BIO Institute, CJ Blossom Park, 42, Gwanggyo-ro, Yeongtong-gu, Suwon, Gyeonggi-do 16495, Republic of Korea
2 School of chemical Engineering, Sungkyunkwan University (SKKU), 2066 Seobu-ro, Jangan-gu, Suwon, Gyeonggi-do 16419, Republic of Korea
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In general, amino acid granules for feed are manufactured in such a way that all moisture in the fermentation broth is removed by the evaporation and fluidized bed granulation process. Evaporation is one of the most energy-efficient way to remove water, however fluidized bed granulation process involving drying is relatively inefficient method in removing water. Industrially, the energy efficiency of the evaporation and fluidized bed granulation process can be differed up to 10 times or more. For example, in a 5-stage falling film evaporator, about 4-5 tons of water is removed with 1 ton of steam, whereas in a fluidized bed granulator, about 0.4-0.5 tons of water can be removed with 1 ton of steam. Therefore, it is good way to remove as much water as possible in advance from the evaporation process in order to manufacture granules efficiently in terms of energy saving. Viscosity of process liquid is highly increased with induction of crystals during the evaporation process, and it is closely related to the maximum allowable concentration of the evaporator. Surely, improvement of solubility of the amino acid is good strategy in order to increase the maximum allowable concentration in the evaporation process. Neutral amino acids such as threonine, tryptophan, valine, isoleucine, and leucine have very low solubility in aqueous solution at room temperature of 2-10 g/100 g H2O. In this study, the manufacturing method of the neutral amino acid granule for the feed additive using calcium hydroxide was developed. Solubility of neutral amino acid is increased with increasing the amount of calcium, and it has the high nutritional value as a feed additive. In addition, the energy saving by this process was calculated and commercial examples were introduced. Fig. 1 shows the effect of mole ratio of calcium to amino acid on maximum allowable concentration during the evaporation process of various amino acids.

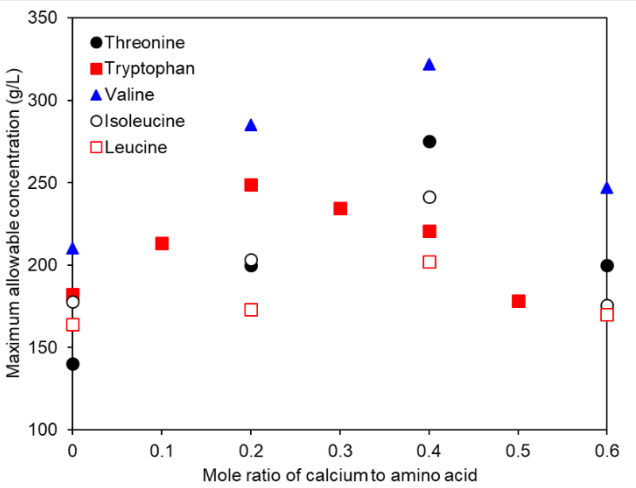


Figure 1. Effect of mole ratio of calcium to amino acid on maximum allowable concentration during the evaporation process of various amino acids

# 10. DEM MODELLING OF DRY POWDER SPREADING PROCESS FOR LITHIUM-ION BATTERY ELECTRODE MANUFACTURING

Hamza Mohamed[1,2], Ruihuan Ge[1,2], Denis Cumming[1,2] & Rachel Smith[1,2]

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Lithium-ion batteries have been widely used in energy storage. Dry production techniques show great potential to replace the conventional slurry casting approach [1] [2]. Dry powder spreading has been widely used in industries such as metal additive manufacturing [3], and can be implemented in battery production. In this work, this method is used with battery material.

By using Discrete Element Method (DEM), powder spreading of battery material onto the current collector was investigated. The effect of different parameters such as blade height, blade speed, surface energy and particle shape was investigated. It was found that increasing the particle-current collector (PC) surface energy has little effect on powder spreading while increasing the particle-particle (PP) surface energy reduces uniformity. It was also found that decreasing the speed of the blade increases the uniformity of the powder layer. The increase in PP surface energy increases the formation of agglomerates and large clusters which shows a non-uniform spreading of the powder. The results presented here offer a basis for the future application of powder spreading in battery production.

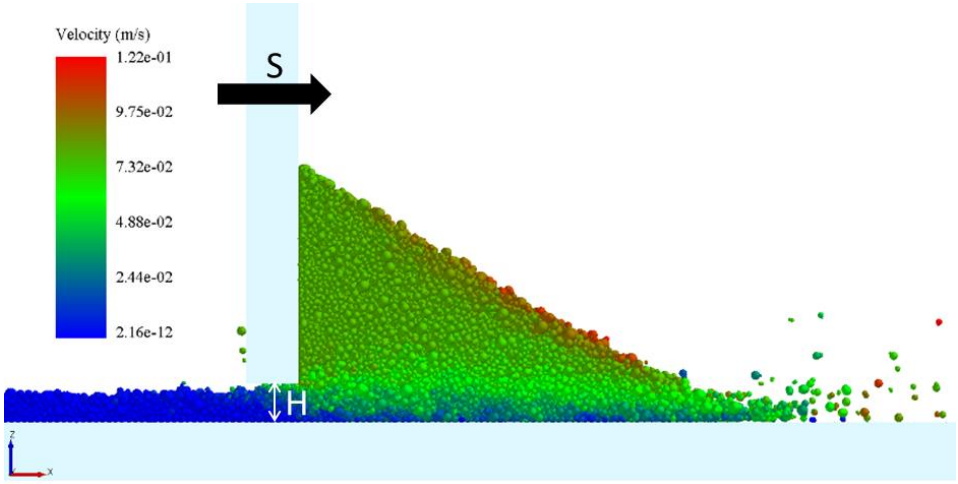


Figure 1. Illustration of powder spreading in EDEM

[1] Ludwig, B., et al., Simulation of Micro/Nanopowder Mixing Characteristics for Dry Spray Additive Manufacturing of Li-Ion Battery Electrodes. Journal of Micro and Nano Manufacturing, 2017. 5(4): p. 1-8.

[2] Schälicke, G., et al., Solvent-Free Manufacturing of Electrodes for Lithium-Ion Batteries via Electrostatic Coating. Energy Technology, 2020. 8(2): p. 1900309.

[3] Frazier, W.E., Metal Additive Manufacturing: A Review. Journal of Materials Engineering and Performance, 2014. 23(6): p. 1917-1928.

# 11. SCALE AND BOUNDARY EFFECTS ON DRUCKER-PRAGER CAP MODEL PARAMETERS IN DIE COMPACTION

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The Drucker-Prager Cap model (DPC) is a widely used for modelling the die compaction behavior of metallic, ceramic and pharmaceutical powders. For a good prediction of the density distribution using Finite Element Method (FEM), accurate input data (elastic and plastic properties) are required [1,2]. Generally, such properties are identified using a commonly standard calibration method [3]. In this method, the necessity of measuring the radial stress, using instrumented die, enables the determination of elastic properties, hydrostatic and deviatoric stress components for the constitutive equations of DPC. By definition, material properties are considered as intrinsic to the material and can then be used to simplify larger-scale finite element simulation of the compaction (other shape and size). However, due to the boundary conditions during experiment, the determined material parameters seem depending on size and shape of the sample.

The aim of this paper is to address the question whether the elastic and plastic properties of DPC model, obtained by the standard calibration method using full instrumented die, can accurately predict compressive behaviors of other compact sizes and shapes using finite element simulations. By Considering Microcrystalline Cellulose powder (MCC 102), we demonstrate that elastic and plastic parameters of DPC determined using small instrumented die of 1 cm3 of volume, failled to predict the compaction cycle of a parallelepiped compact measuring 16x54x13 mm3. To overcome this difficulty, a mixed procedure of calibration combining data from small instrumented die and compaction cycle of larger-size compact is proposed and applied to cylindrical compacts with diameters of 11, 20, 30 mm and a parallelepiped compact (16x54x13 mm3) leading to new material parameters. These latest data were implemented in FEM simulations and showed good predictions of the experimental compaction cycle and the mean relative density of the tablet. This validation motivated the interest of the proposed approach as a compromise between the need for additional radial instrumentation and the generation of compaction cycle at the compact scale.

[1] M.D. Riera, J.M. Prado and P. Doremus, Model input data - elastic properties, Modelling of Powder Die Compaction, Springer-Verlag London Limited, (2008) 65-76.

[2] P. Doremus, Model Input data - Plastic properties, Modelling of Powder Die Compaction, Springer-Verlag London Limited, (2008) 77-93.

[3] P. Doremus, Model Input data –Failure, Modelling of Powder Die Compaction, Springer-Verlag, London, (2008) 95–103.

# 12. TABLET MICROSTRUCTURE INDUCED BY EMBOSSED FEATURES OF COMPACTING PUNCH: CASE STUDY ANALYSIS

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The powder die compaction process is widely used in many industrial sectors and allows to produce tablets of diverse sizes and shapes. However, the presence of engravings on the compacting punch surface induces complex flows leading to heterogeneous density distributions. Previous studies using X-ray tomography [1,2] investigated the impact of prints, present only on a single surface of the tablet, on the density distribution. Furthermore, a recent study [3] analysed the effect of two grooves on the top and bottom surfaces of the tablet on its microstructure. The shape of the latter is presented in Fig. 1. However, the question whether more grooves, their geometrical parameters and their position on the surface, which can have an impact on the density distribution, has not yet been studied.

In this work, a study of the compaction behaviour of microcrystalline cellulose powder under identical punches, with five engravings each one, was conducted. The density distribution was then characterized using X-ray tomography and predicted by modelling using the finite element method. Afterwards, a parametric study relative to the position and the geometrical parameters of the groove was carried out numerically. The impact on the density gradient is discussed.

Results showed that the presence of engravings, on both the upper and lower punches, generated a localized density gradient that can lead to defects in the tablet. The sensitivity analysis with respect to the shape and the position of the groove allowed to better understand the flow of powder in its vicinity. Future prospects towards the optimization of the groove shape are proposed.

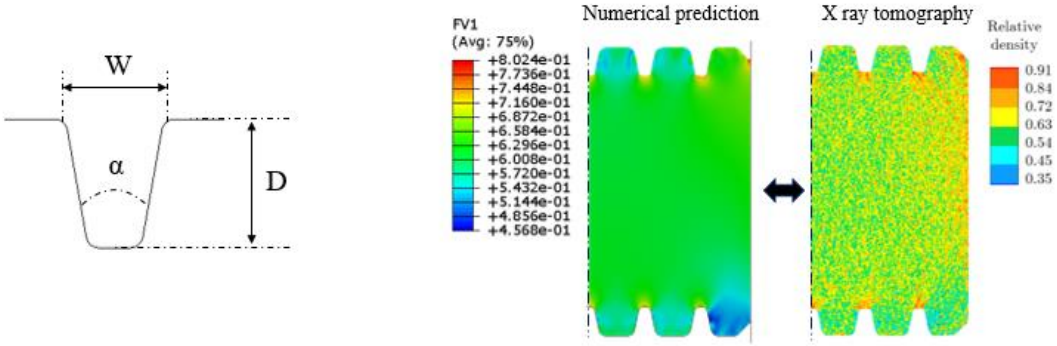


Figure 1. Groove shape (left), relative density distribution of grooved tablet (right)

[1] P.R. Laity, Effects of punches with embossed features on compaction behaviour, Powder Technol. 254 (2014) 373–386.

[2] S. Swaminathan, J. Hilden, B. Ramey, C. Wassgren, Modeling the formation of debossed features on a pharmaceutical tablet, J. Pharm. Innov. 11 (3) (2016) 214–230.

[3] Alonso Aruffo, G., Michrafy, M., Oulahna, D., & Michrafy, A. (2022). Modelling powder compaction with consideration of a deep grooved punch. Powder Technology, 395, 681-694.

# 13. OPEN-SOURCE FLOWSHEET SIMULATION ENVIRONMENT FOR DYNAMIC SIMULATION OF PARTICULATE PROCESSES

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In this contribution, we present a flowsheet simulation system Dyssol [1], which can be used to model a wide variety of interconnected production processes including agglomeration, granulation, compaction, or drying [2,3]. The framework is being developed since 2012 within a consortium of over 15 German universities and industrial partners. Although the main focus of Dyssol is the simulation of dynamic processes in granular materials, it is also able to handle steady-state models and fluid phases. The program is open-source and available under the permissive BSD license that allows distribution, modification, private and commercial use [4]. Due to its flexibility, Dyssol can be easily expanded and supplemented with new models, making it easy to customize for specific purposes. It is available for both Windows and Linux platforms and comes with comprehensive documentation that covers all aspects of usage and model development.

Financial support from the German Research Foundation is gratefully acknowledged.

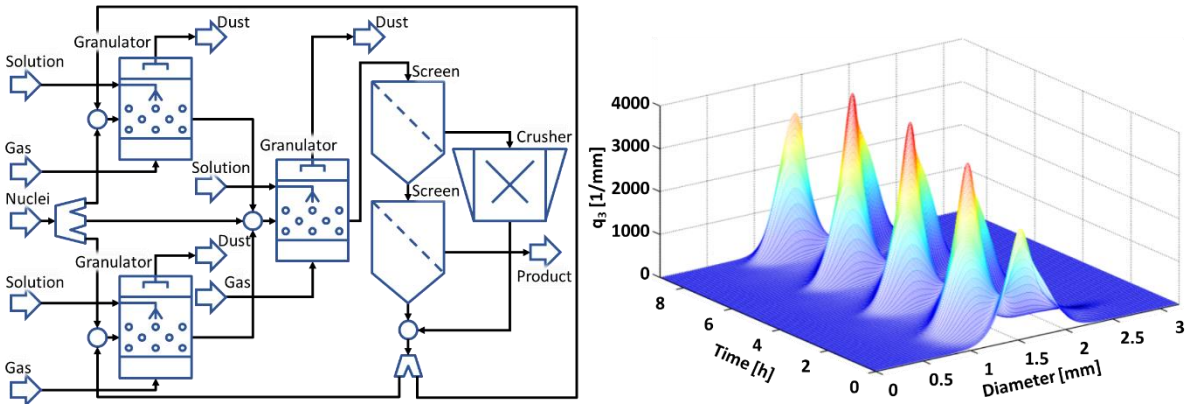


Figure 1. An example flowsheet of a two-stage granulation process with external classification and milling (left) and a time-dependent change in particle size distribution of granules (right).

[1] V. Skorych, M. Dosta, E.-U. Hartge, S. Heinrich, Novel system for dynamic flowsheet simulation of solids processes, Powder Technology, 314 (2017) 665-679.

[2] M. Buchholz, J. Haus, S. Pietsch-Braune, F. Kleine Jäger, S. Heinrich, CFD-aided population balance modeling of a spray drying process, Advanced Powder Technology, 33(7) (2022) 103636.

[3] S.E. Lehmann, M. Buchholz, A. Jongsma, F. Innings, S. Heinrich, Modeling and Flowsheet Simulation of Vibrated Fluidized Bed Dryers, Processes (2021) 9 52.

[4] V. Skorych, M. Dosta, S. Heinrich, Dyssol - An open-source flowsheet simulation framework for particulate materials, SoftwareX, 12 (2020) 100572.

# 14. THE EFFECT OF PROCESSING CONDITIONS ON DRY SOLIDS RECOVERY AND MOISTURE ABSORPTION CAPACITY OF SPRAY DRIED FISH PROTEIN HYDROLYSATES

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Production of dried, powdered fish protein hydrolysates from fish processing by-products is a method to add value to a low-value by-products. Sardines are a rich source of protein, essential oils and minerals, and the processing of sardines into tinned food results in more than 25% of their mass ending up as processing by-products [1]. These by-products, heads, tails, viscera, like their source, are also rich in nutrients that can be harnessed [2]. This study employed enzymatic protein hydrolysis to produce fish protein hydrolysates (FPH) from a mixture of sardine heads and tails, and evaluated how the degree of protein hydrolysis (DH), spray drying temperature and maltodextrin (stabilizer) concentration affected dry powder recovery and powder equilibrium moisture content after spray drying.

Dry powder recovery for low DH ranged from 0.456 to 0.565 g/g dry feed while that of high DH ranged from 0.233 to 0.323 g/g dry feed. A significant amount of dry powder was recovered from the walls of the dryer chamber, accounting for 0.332 - 0.452 g/g dry feed for low DH sample and 0.624 - 0.817 g/g dry feed for high DH. The difference in dry solids recovery could be due to the differences in zeta-potential, where FPH obtained at high DH has a high negative zeta-potential. Furthermore, higher DH resulted in higher hygroscopicity in the FPH powder.

The addition of maltodextrin produced powders with high equilibrium moisture content ($X_e$) at low water activity ($a_w$) of 0.113 and 0.328, regardless of DH or drying temperature. More stabiliser reduced $X_e$ for powders exposed to $a_w$ above 0.529, but there was no clear relationship between maltodextrin concentration and $X_e$. Qualitative analysis also showed that FPH powders lost their flow properties at $a_w$ greater than 0.328. Some powders became sticky solid lumps, some caked, while others collapsed. The practical significance of this result is that FPH powders can be easily handled in any process environment where the $a_w$ is less than 0.328 without any loss of flow properties. This prevents the unnecessary dilution of protein and the negative effects that high maltodextrin levels has on other physicochemical properties such as powder solubility and foaming capacity [3].

[1] X. Wang, “Natural bioactive compounds from fish,” in Natural Bioactive Compounds, Academic Press, 2021, pp. 393–408.

[2] N. Greyling, A. Bordoloi, and N. J. Goosen, “Optimising enzymatic conditions of monkfish (Lophius vomerinus) heads hydrolysis towards potential waste biomass valorisation,” Biomass Convers. Biorefinery, pp. 1–12, Mar. 2020, doi: 10.1007/s13399-020-00650-z.

[3] Y. N. Fawzya, S. M. Nursatya, R. Susilowati, and E. Chasanah, “Characteristics of Fish Protein Hydrolysate from Yellowstripe Scad (Selaroides leptolepis) Produced by a Local Microbial Protease,” in E3S Web of Conferences, 2020, vol. 147, doi: 10.1051/e3sconf/202014703017.

# 15. CONTINUOUS IN FEED FRAME LUBRICATION FOR TABLETS DURING DIRECT COMPRESSION

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Powder compression executed with rotary tablet presses requires traditionally an internal lubrication to reduce friction between dies, punches and powder. Here, after pre-blending the drug and excipients, a subsequent blending step is executed to blend lubricant and pre-blend before the material is fed into the feed frame. This may lead to overlubrication due to shear forces applied by feed frame paddles and negatively effects tablet hardness, disintegration and dissolution time. To overcome these negative effects, a method was tested, where the lubricant is directly dosed into the feed frame of the rotary tablet press.

In this work, internal lubrication and feed frame lubrication were systematically compared with focus on tablet properties. The design space included variation of feed frame speed from 40-120 rpm and lubricant content from 0.5-1.5 wt%. Responses were wetting angle, tensile strength, disintegration time, dissolution time and ejection force. Tablets produced with feed frame lubrication showed less negative influence on tablet properties compared with internal lubrication. Figure one shows exemplary the reduction of disintegration time for variation in feed frame speed and lubricant content.

Due to the additional blending step during internal lubrication, more shear forces are applied to the powder, which leads to particle coating with lubricant and overlubrication. However, the mixing capacity in the feed frame itself is sufficient for the required blending of lubricant, which is consistent with Zimmermann's results [1]. Overall, the feed frame lubrication method reduces the need for an additional blending step and has less negative impact on tablet properties.

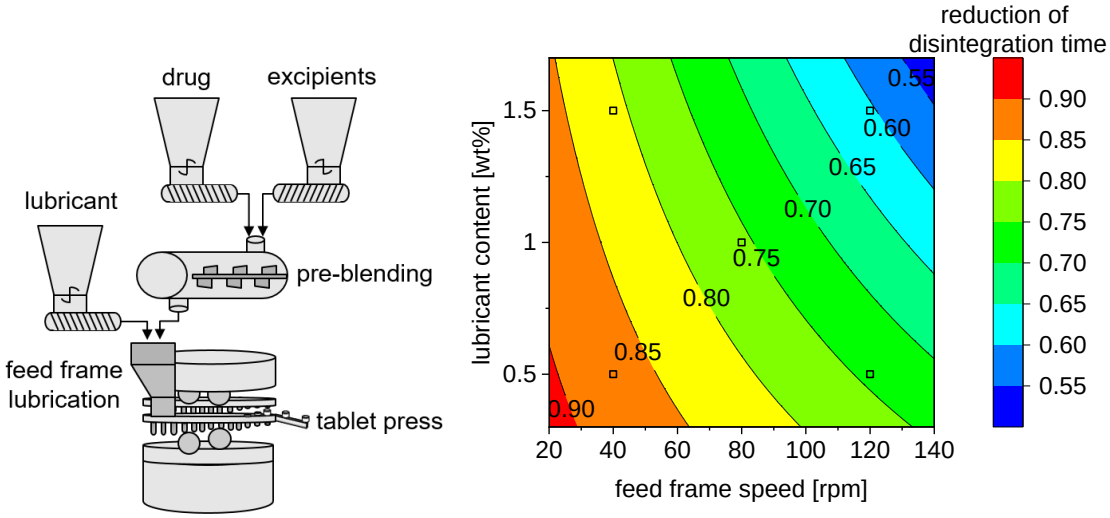


Figure 1. Schematic representation of the feed frame lubrication (left) and contour plot with disintegration time reduction for feed frame speed and lubricant content variations (right).

[1] M. Zimmermann, M. Thommes, Residence time and mixing capacity of a rotary tablet press feed frame, Drug Dev. Ind. Pharm. 47 (2021) 790–798.

# 16. MICROCOAT™ FOR SUSTAINED RELEASE ORALLY DISINTEGRATING GLICLAZIDE TABLETS

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Gliclazide is used in the treatment of type II diabetes mellitus and requires twice daily dosing using immediate release oral tablets with an average diameter of 11 mm. The aim of this research is to prepare appealing orally disintegrating tablets (ODTs) comprising gliclazide layered and sustained release (SR) coated micropellets smaller than 250 µm by applying the novel MicroCoat™ technology.

Gliclazide layered microcrystalline cellulose (MCC) spheres were SR coated with aqueous dispersions of ethyl cellulose and hypromellose (80:20) using a fluid bed coater. During SR coating the MicroCoat™ technology was applied whereby magnesium stearate (MS), sodium stearyl fumarate (SSF) or colloidal silicon dioxide (SD) were periodically added as dry powder glidants into the coating chamber to facilitate micropellet flow and eliminate agglomeration [1]. ODTs were prepared by compressing (6, 8 and 10 kN force) 69.5 % w/w co-processed mannitol, MCC, carmellose and crospovidone, 30 % w/w SR micropellets and 0.5 % w/w MS). ODT hardness, friability and disintegration were measured according to USP standards. An additional disintegration method was applied using texture analysis (TA) [2]. *In vitro* drug release from SR micropellets and ODTs was observed using the USP II (paddle) method.

The application of MicroCoat™ technology led to high coating process yields of 95-99 %. A compression force of 10 kN was found to cause coating rupture so 8 kN was used successfully. Regarding the MicroCoat™ effect on ODT performance, hardness was highest following the addition of SD. ODTs comprising MS disintegrated more slowly compared to when SSF and SD were used but still occurred in <30 s. SR lasting 15 h was observed from ODTs where MS and SSF were added during micropellet coating whereas SD inclusion caused fast release.

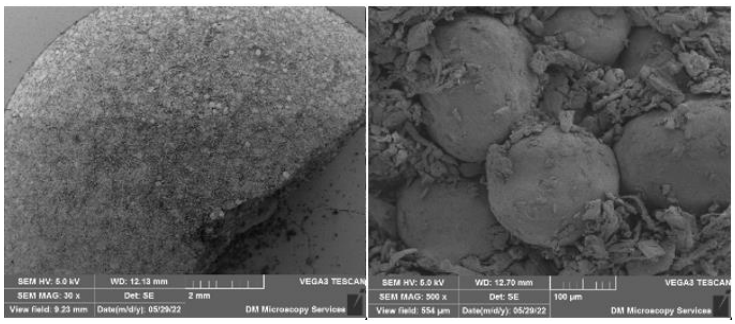


Figure 1. Prepared ODTs with intact singular coated micropellets present in the tablet matrix

[1] Mohylyuk V, Patel K, Scott N, Richardson C, Murnane D, Liu F. Wurster fluidised bed coating of microparticles: towards scalable production of oral sustained-release liquid medicines for patients with swallowing difficulties. AAPS PharmSciTech. 2020 Jan;21:1-0.

[2] Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier JP, Piccerelle PH. Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. International journal of pharmaceutics. 2005 Mar 23;292(1-2):29-41.

# 17. DEM SIMULATION OF LOW SHEAR AGGLOMERATION

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Size control in granulation is of great importance yet is often difficult to achieve. Different methods of modelling the growth behaviour and from this determining the size distribution have been implemented, with population balance models being common. Discrete Element Methods (DEM) Models have been used to obtain collision behaviour statistics, which is then fed into other models, but only rarely has it been used to directly model the agglomeration behaviour itself. Even then, the behaviour is modelled through the adhesion of a subset of particles in the greater bulk.

Here a novel approach is used which instead models the coalescence (where two or more granules combine into a single larger granule) of granules directly, based on the criteria required for merging [1]. The criteria for the merging can be tracked directly within the DEM simulation, which additionally tracks the porosity and the consolidation (the reduction of porosity and subsequent increase in saturation over time) of the granules. The simulation can also be observed in detail, which allows insights into behaviours which are difficult to track with large scale experiments, such as the differences in locations where consolidation occurs compared to coalescence.

By directly modelling the merging behaviour within the DEM simulation, the effect of altering the physical properties of the particles can be observed. Further, by including the intrinsic spatial variation induced by segregation, the DEM model demonstrates a distribution in the output size. These two outcomes allow for understanding what affects the product distribution and in turn may give insights on how to go about narrowing this distribution.

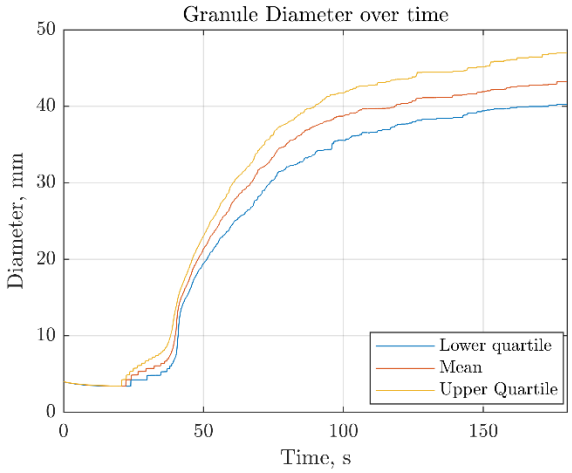


Figure 1. Granule growth behaviour within the DEM simulation, demonstrating induction growth and the distribution of sizes.

[1] W.K. Walls, J.A. Thompson, S.G.R. Brown, Towards a unified theory of wet agglomeration, Powder Technology, 407 (2022) 117519.

# 18. SUBMICRON AG-COATED CU PARTICLES AS FILLER IN SINTERING PASTE: CONTROL OF AG DEWETTING AND IMPROVEMENT OF SINTERABILITY THROUGH SURFACE MODIFICATION USING CARBOXYLIC ACID

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While a sintering paste containing Ag-coated Cu particles is expected to be widely used for formation of electrodes and die attachment owing to price competitiveness, change in contact states between particles and early oxidation of core Cu during the process, derived from dewetting of Ag shells at temperatures near 200 ℃, severely deteriorate the electrical, thermal, and mechanical properties by decrease in sinterability.

In this study, submicron Ag-coated Cu particles were fabricated, which was followed by surface modification using dilute carboxylic acids so as to suppress the Ag dewetting. Carboxylate groups binded on the surface of Ag-coated Cu particles, and then organo-metallic surfaces (COO-Ag) of a rough morphology were formed to reduce surface energy [1], which was verified by X-ray photoelectron spectroscopy and Fourier transform infrared spectroscopy. The paste containing Ag-coated Cu particles was prepared by mixing with a reducing solvent and was printed on a slide glass. Subsequently, a printed film was sintered at 300 ℃ for different times (1−10 min). Electrical resistivities of the films sintered using surface-modified Cu@Ag particles were significantly lower than those by non-treated ones. The organo-metallic surface effectively suppressed the dewetting of Ag shells during heating. Hence, promoted necking between particles resulted in the decrease of electrical resistivity.

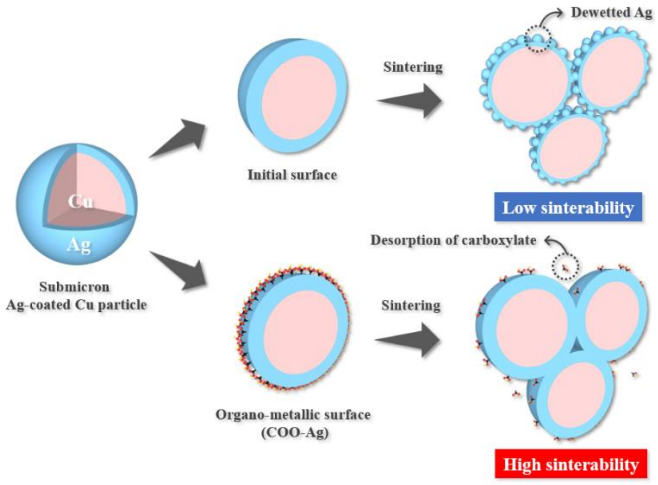


Figure 1. Schematic illustration of different sintering methods using submicron Ag-coated Cu particles

[1] H. Zhan, J. Guo, X. Yang, B. Guo, W. Liu, H. Shen, X. Wang, W. Tang, F. Chen, Silver frameworks based on self-sintering silver micro-flakes and its application in low temperature curing conductive pastes, Journal of Materials Science: Materials in Electronics, 30 (2019) 21343-21354.

# 19. DRYING BEHAVIOUR USING THE QBCON® 1 CONTINUOUS DRYER

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Twin-screw granulation offers in comparison to high-shear granulation or fluidized-bed granulation a continuous wet granulation method. Afterwards a drying step is necessary for further processing of the granules. QbCon from L.B. Bohle offers the possibility to dry the granules immediately after granulation in a truly continuous fluid bed dryer. Wet granules are fluidized through incoming air and transported forward using vibration to the outlet of the dryer and meanwhile exposed to hot and dry air [1].

The drying behaviour of the continuous twin-screw granulator and dryer QbCon® 1 (L.B. Bohle, Germany) using temperature and humidity sensors in the drying chamber was investigated. The temperature and humidity profiles were recorded using 12 wireless RHTemp 1000Ex (MadgeTech Inc., US) 0.5 cm above the distributor plate. Dependend on the layer thickness of the granules in the dryer, either the granules temperature or surrounding air was measured. The dryer was preheated and granulation and drying were performed place for 1 hour. Only the last 10 minutes of recorded temperature and humidity were used for evaluation of the drying process. Profiles were investigated for two different placebo formulation with the same drying parameters. Using the profiles, the different drying stages are displayed not in the time domain as in traditional batchwise fluid-bed dryer but in the space domain as the granules are drying while transportation. The loss-on-drying of the dried granules were 1.76 ± 0.13 % (lactose formulation) and 0.67 ± 0.07 % (mannitol formulation).

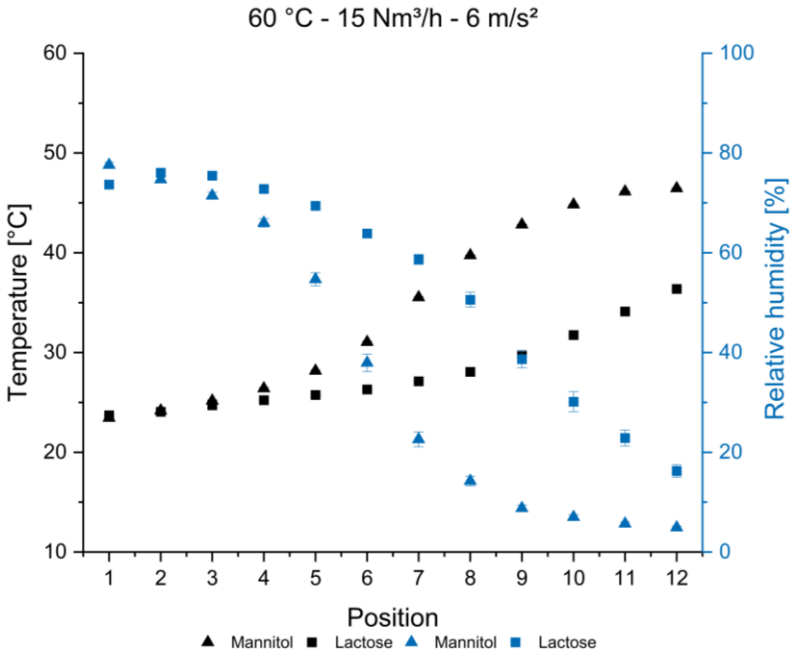


Figure 1. Temperature- and humidity profiles of lactose and mannitol formulation along the drying chamber of QbCon® 1.

[1] R. Meier, D. Emanuele, P. Harbaum, Important elements in continuous granule drying processes, TechnoPharm, 10 (2020) 92-101.

# 20. THE EFFECT OF ROLL SPEED ON THE PREDICTION OF RIBBON SOLID FRACTION

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Influence of the roll speed (RS) during roll compaction (RC) on the ribbon solid fraction prediction is often neglected. Many postulated models to predict the ribbon solid fraction e.g. the Midoux number [1], which can be used for equipment transfer and upscaling, exclude the RS as a process parameter. The authors themselves noted that increased RS could weaken the predictive accuracy (PA) of the model [1]. The RS can be transferred into a dwell time (DT), which was defined the time where the pressure is above 90 % of $P_{max}$. The applied values for RS were chosen to have equidistant DT steps.

The effect of the RS on the ribbon solid fraction prediction was systematically investigated compressing microcrystalline cellulose (MCC) at several maximum roll pressures ($P_{max}$) and DT combinations using the gap controlled roll compactor BRC25 (L.B. Bohle Maschinen + Verfahren GmbH, Enningerloh, Germany). The PA of the ribbon solid fraction using the Midoux number, a simplified Johanson model, was determined. For a more plastically deformable material such as MCC the PA drops from 1.15 to below 0.9 with the highest accuracy between a DT of 100 and 66 ms, which corresponds to RS of 2 and 3 rpm. This led to prediction accuracies over all $P_{max}$ of $1.02 \pm 0.03$ and $0.98 \pm 0.04$, respectively ($\bar{x} \pm s$). Thus, RS seems to be an important factor in the prediction of roll compaction processes and prediction models should include RS as parameter to improve their accuracy.

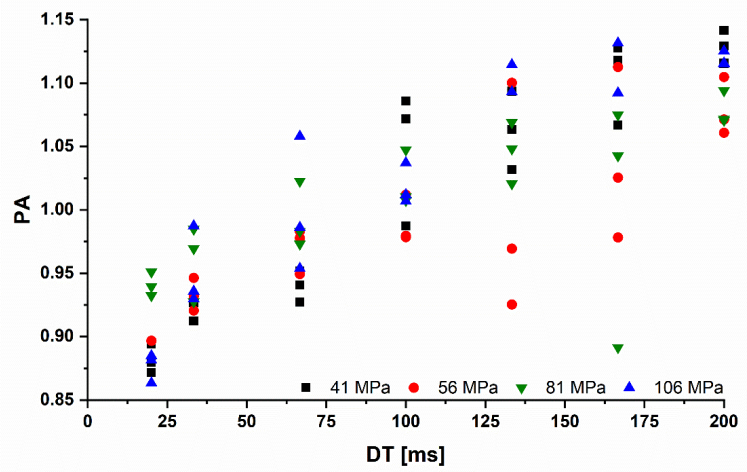


Figure 1. Prediction accuracy of the ribbon solid fraction with changing DT; individual values; $n = 3$.

[1] R. Sousa, P.C. Valente, M. Nakach, L. Bardet, M. Wacquet, N. Midoux, J.R. Authelin. Roller Compaction Scale-Up Made Simple: An Approximate Analytical Solution to Johanson's Rolling Theory, J. Pharm. Sci. 109 (2020) 2536-2543.

# 21. EMPLOYING A NOVEL MULTI-RESONANCE MICROWAVE SENSOR FOR IN-LINE MOISTURE MONITORING OF FLUIDIZED BED AGGLOMERATION

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Previous studies have successfully measured granule moisture content in fluidized beds with microwave sensors [1]. This allows to operate a fluidized bed at optimal conditions even for critical substances, such as amorphous granules. Amorphous substances are relatively common in food industry and their characteristics depend highly on the moisture content. In order to control the product quality of the agglomerates the inlet gas temperature can be changed, which then has to be accounted for. This leads to two major challenges: Precise moisture content measurements of amorphous granules at (i) different temperatures and for (ii) a wide granule moisture content range.

Previous sensor systems operating with a single resonance frequency showed limitations at high granule moisture content and were not able to cover a wide range of granule moisture contents. This paper describes the application of the novel microwave sensor TEWS MW 4200 working at resonance frequencies of 2 and 6 GHz. The moisture sensor is calibrated with batch experiments (Figure) and validated with continuous experiments. Calibration data is gained by taking samples throughout the experiment and offline analysis using the gravimetric method. For agglomeration in the fluidized bed water is sprayed on maltodextrin DE 20 (Figure). Rapid, reliable in-process moisture control at a wide range of moisture contents and different temperatures is achieved. Additionally, it is shown how to gain information of the particle size from the measurement data.

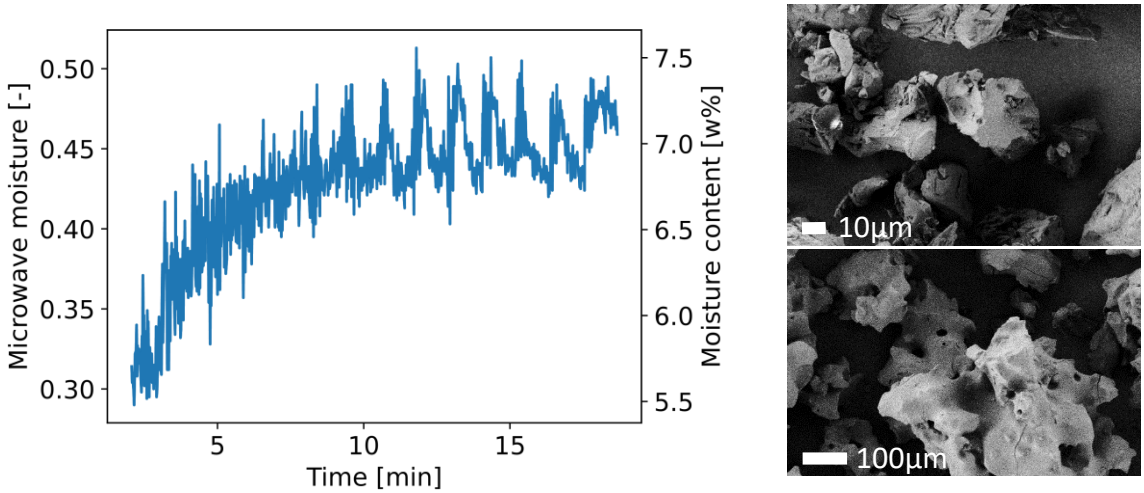


Figure 1. Moisture content over time during batch agglomeration (left), SEM pictures of original maltodextrin particles (right top) and maltodextrin agglomerates (right bottom)

[1] C.B. Buschmüller, W. Wiedey, C. Döscher, J. Dressler, J. Breitkreutz, In-line monitoring of granule moisture in fluidized-bed dryers using microwave resonance technology, European Journal of Pharmaceutics and Biopharmaceutics, 69 (2008) 380-387.

# 22. HOMO AND HETERO AGGLOMERATE FORMATION OF NANOPARTICLES IN A SPOUTED

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Hetero agglomerates of nanoparticles (NPs) can exhibit novel and superior properties compared to their pure components. The new properties can emerge from direct contact of different particles (hetero contact) as a result from transfer of charges, mass, heat, forces, or moments without the need of chemical reaction of components. The cohesion in nano powders (Geldart group C) have long been seen as a problem [1] and it is the cause for fluidizing NPs in form of agglomerates. Fluidization of NPs can be assisted in many ways [2]: by mechanical stirrers, pulsed gas flow, admix of large particles, centrifugation, acoustic waves, microjets, impactor plates, vibration.

The present study investigates the homo and hetero agglomerate formation of NPs in a spouted bed equipment. The spouted bed technique imposes a similar circular motion to the solids with additional feature of high air inlet flow velocity that can be adjusted by rolls and slits of variable width. It makes issues of expansion, Geldart group obsolete, because particles can be intensively mixed and processed quite independently from size, shape, or density [8]. It would be easy to combine the spouted bed air jets with centrally placed inverted nozzle to improve the stability of process. Hetero agglomeration of nanoparticles in fluidized beds can be route to new and superior products. The main objective is to break path for the mixing of very small, fluidized particles to hetero agglomerates with new and superior properties. Bridge the gap between classical NPs and conventional fluidized particles by including submicron particles into the investigation. Additionally, find the level of sub-agglomerate mixing and push the level towards individual NPs by application of non-flame, i.e., not sintered, raw material. Agglomerate morphology is ideally assessed by imaging technique that resolves single primary particles to identify the change of composition in different agglomerates. A method to quantify the mixing at sub agglomerate level using EDX analysis will be developed.

[1] J.P.K. Seville, C.D. Willett, P.C. Knight, Interparticle forces in fluidisation: a review, Powder Technology. 113 (2000) 261–268.

[2] J.R. van Ommen, J.M. Valverde, R. Pfeffer, Fluidization of nanopowders: a review, J Nanopart Res. 14 (2012) 737.

[3] E. Tsotsas, S. Heinrich, M. Jacob, M. Peglow, L. Mörl, Intensification of Fluidized-Bed Processes for Drying and Formulation, in: Modern Drying Technology, John Wiley & Sons, Ltd, (2014) 85–130.

# 23. EMULSION STABILITY OF SPRAY-DRIED INFANT FORMULA

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Emulsion-based powders, such as infant formulas are produced by spray drying, and the stability of the emulsions after reconstitution is of major importance to provide a safe feeding of the baby. However, during the production of infant formula, pre-spray drying processing parameters, such as concentration of the feed and heat treatment temperature, affect the properties of the emulsion powders and consequently may affect the stability of the emulsion after reconstitution. Previous studies showed that a significant reduction in energy consumption could be achieved by producing spray-dried infant formula from feeds with 60% total solids (TS) pasteurized at 75 °C, compared to 50% TS and 100 °C; while obtaining powders with less than 7% whey protein denaturation, no loss of available lysine during processing, and improved wettability and rehydration [1, 2]. However, limited studies are found regarding the stability of reconstituted emulsion powders.

This study aimed to assess the effect of pasteurization temperature and concentration of TS in the feed on the stability of the reconstituted emulsions powders. For this purpose, infant formula wet-mixes with 45 or 55% TS were pasteurized at 75 or 100 ºC for 18 s and the powders obtained were produced at pilot scale using a GEA Mobile Minor I spray dryer. The characteristics of the emulsion feeds and the reconstituted emulsions (12.5% TS) were compared.

The emulsion feeds with 55% TS were flocculated, with large particle size, high apparent viscosity, and pseudoplastic behavior. Light microscopy observations of the reconstituted powders showed that the flocs were disrupted during spray drying in 55% emulsions pretreated at 100°C, while the 55% emulsions treated at 75°C remained flocculated, reducing its stability post-reconstitution. The four reconstituted emulsions were mainly stabilized by caseins, although β-Lactoglobulin was also detected at the oil-water interface in emulsions preheated at 75 °C and aggregated in the continuous phase of emulsions preheated at 100 °C.

In conclusion, pre-processing steps such as heat treatment and concentration of the feed can be optimized to improve the energy consumption and powder properties but their impact on the properties of the reconstituted powders need also to be assessed in the final product application.

[1] M.R. Arzuaga, D.F. da Silva, E. Xanthakis, K. Aalaei, T.P. Czaja, L. Ahrné. Impact of wet-mix total solids content and heat treatment on physicochemical and techno-functional properties of infant milk formula powders, Powder Technology 390, (2021) 473-481

[2] M. R., Arzuaga, K. Aalaei, DF da Silva, S. Barjon, M.C. Añón, A.G. Abraham & L. Ahrné. Infant milk formulae processing: effect of wet-mix total solids and heat treatment temperature on rheological, emulsifying and nutritional properties, Journal of Food Engineering. 290, (2021), 110194

# 24. FOOD VS PACKAGING: MODELLING MASS TRANSFER FROM POWDER COMPACTS INTO PACKAGING

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Mass transport phenomena between food, packaging, and the environment is of increasingly major concern for the consumer food industry. Growing global pressure on food manufacturers to employ less packaging demands understanding and predictability of food microstructure stability and substance migration to ensure environmentally friendly packaging with high shelf-life, while maintaining food safety and organoleptic properties. This work for the first time applies dimensional analysis to characterise and model the phenomena of small molecule transport from a porous powder compact into the contacting packaging material. It is suggested that the extent of mass transfer from the food into its contacting packaging depends on the ratio of viscous forces of the migrating substance to the capillary forces due to the porosity of the compact. Key physical properties of both forces were summarised in the single dimensionless capillary number for both the food compact and packaging. Employment of a single nondimensional quantity allowed a direct comparison between the two governing phenomena in both materials, leading to a food capillary number $Ca_{food}$ and packaging capillary number $Ca_{pack}$. Experimental substance migration tests performed with food analogues and model packaging were compared to literature values of oleogels de-oiling into paper substrates. This technique could be applied to link barrier performance of various food-packaging systems to their physical microstructural and rheological properties, and act as a tool to predict and select best packaging candidates.

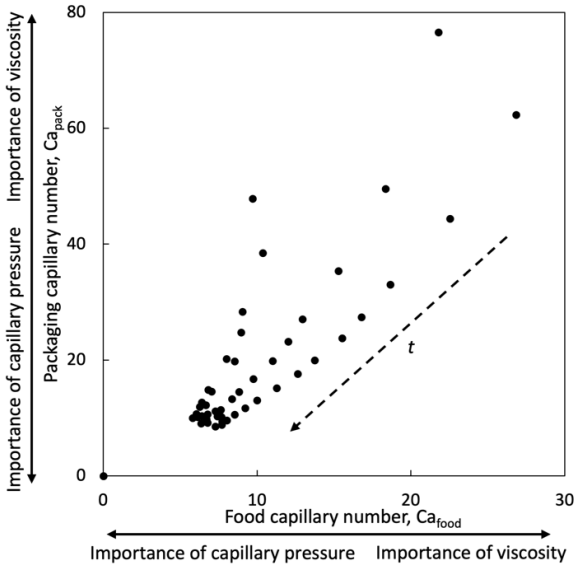


Figure 1. Experimental food capillary number against packaging capillary number, $t$ = time

# 25. MIMICKING THE STRUCTURE OF NATURAL COMPOSITES BY MERGING SPRAY DRYING AND WARM COMPACTION PROCESS

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Bio-composites such as nacre or bone show outstanding mechanical properties which surpass those of their single components. This is due to their complex structure, in which the building blocks of the hard component are embedded in a soft matrix, thus combining strength and toughness. The combination of both properties makes such materials particularly interesting for several structural applications for instance scratch resistance, lightweight and highly-stable coatings and screens. Therefore, there is a great interest to develop scalable processes for the production of artificial composites with strong mechanical properties. In our previous work, a process route combining a spray drying process with a subsequent warm compaction step was identified for the production of those composites. Therefore, submicron particles (alumina or iron oxide) are coated with a soft polymer. Through warm compaction of the coated particles, a polymer matrix is formed where the hard particles are embedded, thus mimicking the structure of bio-composites such as nacre. Several studies with commercial particles and polymers, using this process route, were conducted and the interface between the polymer matrix and the particles was identified as the weakest point in the produced composite. For this reason, the focus of the actual work lies in the optimization of the mechanical properties by improving the interaction of the hard and soft components in the composite. By creating functionalized particles and coating them with a polymer, that is capable of forming covalent bonds to the ligands on the particle's functionalized surface, a stronger interface and with that, stronger composites are generated. The mechanical properties of the produced composite material are measured by nanoindentation while the composite structure is analyzed by SEM and porosity measurements.

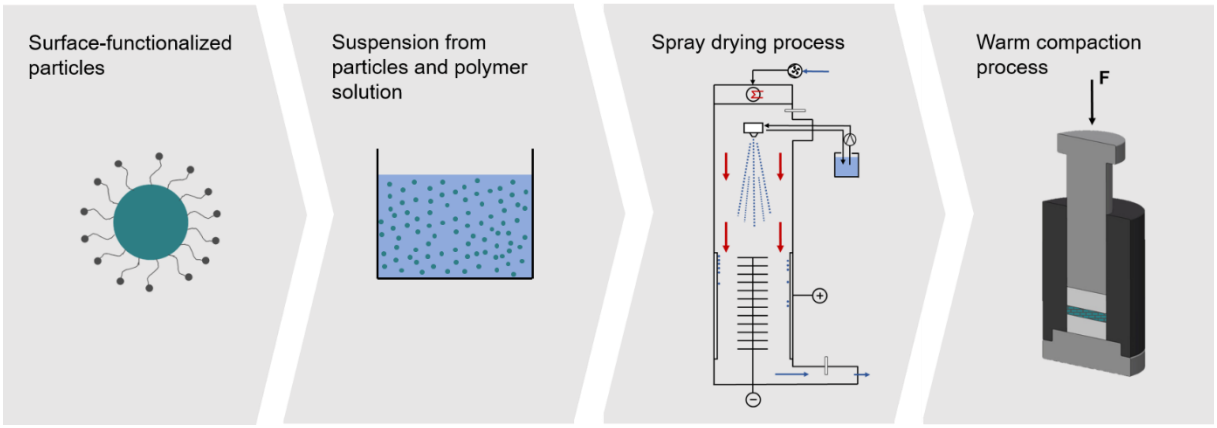


Figure 1. Process route for the production of composite pellets using functionalized particles by spray drying and warm compaction.

We gratefully acknowledge financial support from the German Research Foundation (DFG) via the collaborative research center SFB986 (project number 192346071).

# 26. COMPARISON OF DEM SOFTWARE FOR THE SIMULATION OF COMPACTION OF BIPLANAR TABLETS

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Several industries, including the food, pharmaceutical and chemical sectors, frequently use powders. In the compression process known as tableting, a powder that has been packed into a small volume is subjected to a uniaxial force. The mechanical strength and porosity of tablets are affected by the particle size distribution [1] as well as process variables including compression speed and compaction force [2].

In this study, the Discrete Element Method (DEM) was used to simulate the compaction of dry particles in a tableting process *(Fig.1)*. The purpose of this work is to compare the capability of different cohesion contact models from two DEM software namely EDEM (Altair Engineering, Troy, Michigan, USA) namely the Hertz-mindlin with JKR and the Edinburgh elasto-plastic adhesion model, to simulate the compaction profile during the tableting process and predict the porosity/solid fraction and the elastic recovery of the tablets with increasing compaction force and dwell time.

These simulations were then validated and compared with experimental data conducted on the STYL'One Evo compaction simulator (*Medel'Pharm, Beynost, France*) to identify needs for more precise model calibration or model extension.

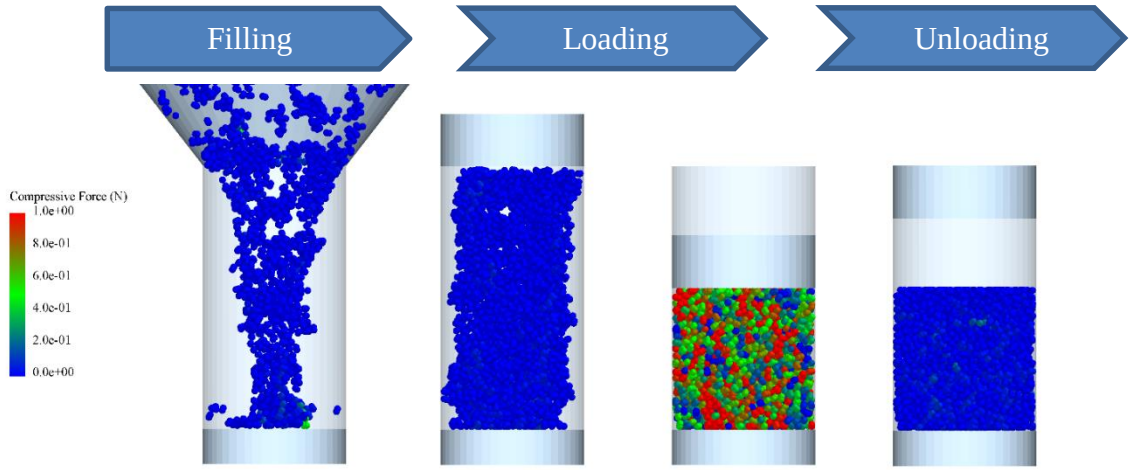


Figure 1. Snapshot of a DEM simulation for particles clipped up to the middle plane in an in-die uniaxial compression test, EDEM (Altair Engineering)

[1] I. Wünsch, J. H. Finke, E. John, M. Juhnke, A. Kwade, International journal of pharmaceutics, 2021, 599

[2] W. R. Mitchell, L. Forny, T. Althaus, D. Dopfer, G. Niederreiter, and S. Palzer, Chemical Engineering Science, 2017, 167, 29–41

# 27. AN INNOVATIVE SETUP TO STUDY THE INFLUENCE OF SHEAR STRESS ON THE BREAKAGE OF AGGLOMERATES

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Many industrial processes use agglomerated powders, composed of various particles, which adhere to one another [1]. During powder mixing operations, agglomerates experience a complex variety of mechanical stimulations. The agglomerates often break and fragments may recombine to form new agglomerates with a different structure. The aim of this work is to study the fragmentation phenomenon of agglomerated powders in order to better understand the causes and factors affecting the fragmentation process [2,3].

An innovative experimental setup has been built, where an inclined blade applies a controlled stress on a thin bed of precipitated silica agglomerates. The shear stress is controlled by the translation speed of the blade and the normal stress by the weight of a mass set on the blade. A parametric study is performed and the local internal stress tensor, inside the powder, is derived from force transducers instrumenting the setup. Granulometric measurements as well as qualitative observation of the granular material after shearing is done to complete this study. In addition, a theoretical study is carried out using a population balance model in order to develop a general predicting tool for the fragmentation behaviour of any sheared powders [4].

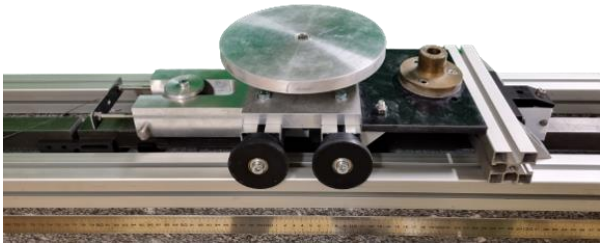

Figure 1. Prototype trolley

[1] Pietsch, Wolfgang B. Agglomeration processes: phenomena, technologies, equipment. John Wiley & Sons, 2008.

[2] Dumas, T., 2012. Renforcement des pneumatiques par la silice. Caracterisation physio-chimique et dispersion des granules de silice (Thesis, Ecole Nationale Supérieure des Mines de Saint-Etienne).

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[4] Kumar, J., Peglow, M., Warnecke, G. and Heinrich, S., 2008. An efficient numerical technique for solving population balance equation involving aggregation, breakage, growth and nucleation. Powder Technology, 182(1), pp.81-104.

# 28. NOVEL STRATEGIES FOR RECOVERY OF ZINC AS ZINC-SULFIDE BY FLUIDIZATION BED HOMOGENEOUS CRYSTALLIZATION

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This study aims for amelioration of drawbacks by implemented in fluidized-bed homogeneous crystallization(FBHC) system and crystallization zinc sulfide on the granule continuously. In this study, the FBHC was used to research impact parameters. The operating parameters for FBHC include the pH and [S]/[Zn] and these are optimized to maximize the crystallization efficiency of nickel. 99.9% of total removal (TR) and 99.5% of crystallization ratio (CR) at [S]/[Zn] = 1.5, pH 8.6 ± 0.3 and an input nickel level of 1960 mg-Zn/L. The crystal phases of FBHC products are respectively characterized as ZnS by XRD analysis. The product morphology explains the reaction path and mechanism for homogeneous crystallization of zinc sulfide. The high crystallization ratio demonstrated that ZnS granule is more competitive than the sludge conducted ZnS in batch reactor in terms of solid water content between granule and sludge.

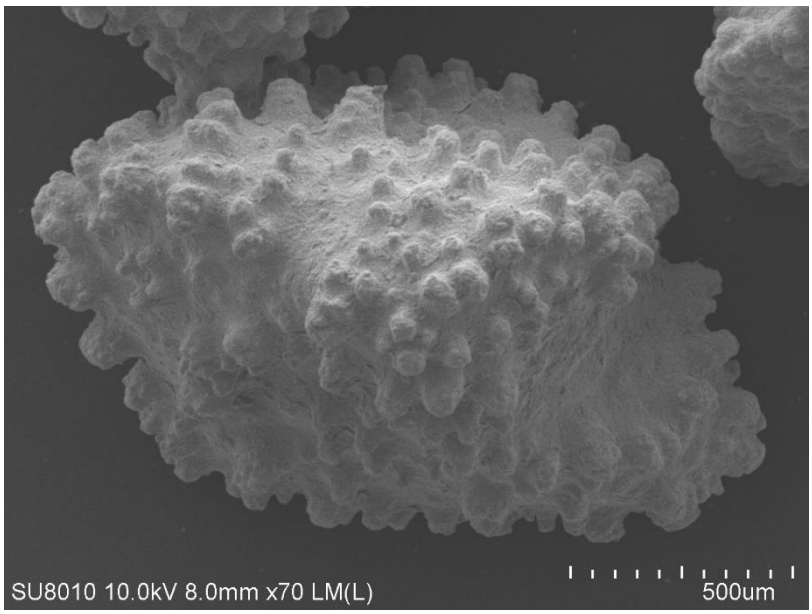


Figure 1. Recovery particle as zinc sulfide using fluidized bed homogeneous crystallization

# 29. PREDICTION OF DROPLET SIZE DISTRIBUTION FROM TWIN FLUID NOZZLES

Leander Vinzenz Mehlis[1,2], Jens Bartsch[1], Werner Hoheisel[2], Patrick Kranz[3] & Markus Thommes[1]

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2 Formulation Technology, Invite GmbH, Cologne 51061, Germany
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The droplet-size distribution of twin-fluid nozzles is a relevant parameter for wet and melt granulation. Conventional models only consider the mean value of the droplet-size distribution. Therefore, a predictive model for droplet-size distribution was developed.

The droplet-size distribution was determined for a twin-fluid nozzle (970 S4, Schlick) experimentally (Spraytec, Malvern) using different spray rates (0.9 to 2.1 kg/h) and atomization pressures (50 to 236 kPa). Experimental data were required to parametrize the new model and subsequently validate the model performance. For the model development, the Aliseda approach [1] predicting the Sauter diameter (eq. 1) and the Maximisation of Entropy Generation [2] predicting the distribution (eq. 2) were considered. Each of those models utilizes two parameters, which need to be estimated from experimental data. These parameters characterize a specific nozzle but are independent from material properties and process conditions.

The new model predicts the droplet-size distribution adequately (Figure 1). Applied to wet or melt granulation processes, it is seen to be a sufficient tool to predict particles-size distribution and porosity of granules.

$$x_{32} = f(Re, Oh, We, D_l, b_g, \alpha_{liq}, \rho_{liq}, \rho_{gas}, \eta_{gas}) \quad \text{(eq. 1)}$$

$$Q_3(x) = d(x_{32}, p, T, \rho_{liq}, \kappa, \sigma) \quad \text{(eq. 2)}$$

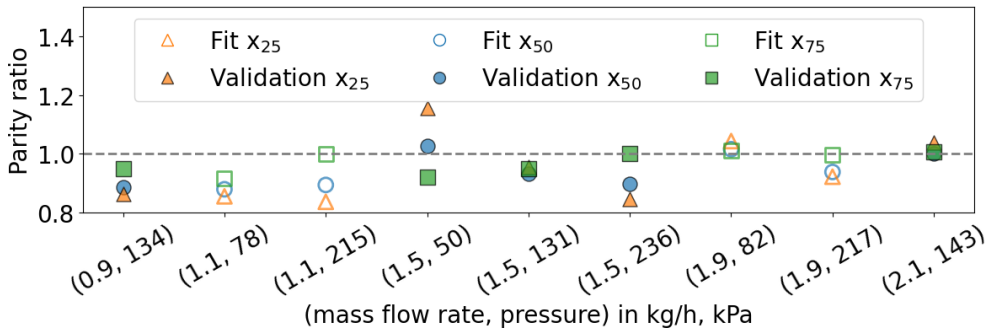


Figure 1. quotient between predicted and observed quantities of size distribution of the process conditions

[1] A. Aliseda, et al., Atomization of viscous and non-newtonian liquids by a coaxial, high-speed gas jet, Experiments and droplet size modeling, Int. J. Multiph Flow, 34 (2008) 161-175

[2] X. Li, M. Li and H. Fu, Modeling the initial droplet size distribution in sprays based on the maximization of entropy generation, At. Sprays, 15 (2005) 295-321

# 30. ELECTROSTATIC SPRAY DRYING: ADVANTAGES FOR THERMOSENSITIVE ACTIVES

Elodie Beaupeux[1], Audrey Maudhuit[1], Akaber Dokmak[1,2], Preethi Jayaprakash[1,3,] Thomas Deleau[2] & Claire Gaiani[3]

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2 Toulouse University, RAPSODEE, Albi France
3 Université de Lorraine, LIBio, Nancy, France
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In many industries, spray drying and freeze drying are mainly used to obtain a powder form in the final product. On one hand, spray-drying is a continuous process, scalable and widely used for different application such as dairy products, active pharmaceutical compounds, oil encapsulation …However, high temperature is needed to reach moisture content expectations and leads to the degradation of heat-sensitive compounds. On the other hand, freeze-drying is a batch process using sublimation to preserve the active during drying. It is mainly used for pharmaceutical products, microorganism, ...The main limits of the process are energy cost and time consumption. An alternative continuous technology, namely electrostatic spray dryer, is emerging for drying sensitive product reducing the production cost to compare to freeze dryer [1], [2]. In this process, in the presence of the electrostatic field, there is a migration of solvent to the surface of the droplet which allows to have a complete drying at low temperatures [3].

In this work, this phenomenon is studied to quantify the benefits to avoid degradation to the active products like probiotics, enzymes, oil encapsulation and to evaluate the life cycle of this new technology.

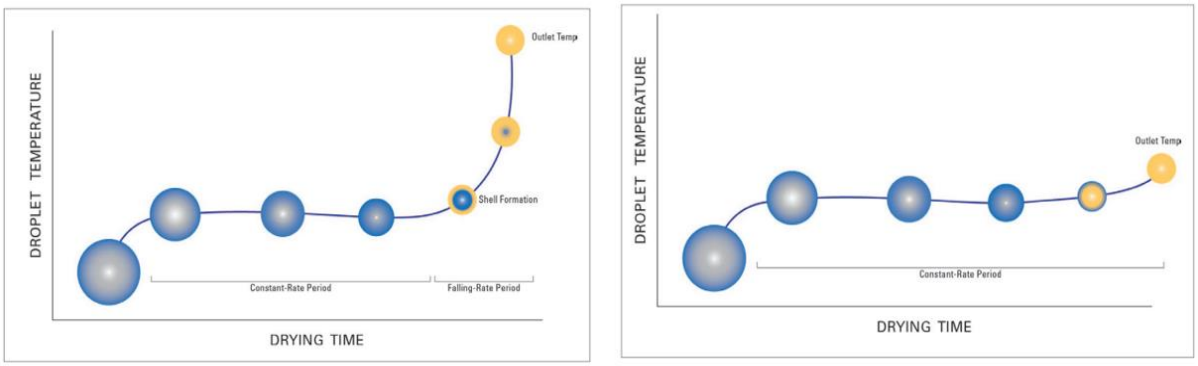


Figure 1. Drying curve of droplet temperature in conventional spray drying and electrostatic spray drying

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[2] T. T. Mutukuri, Y-F. Maa, R. Gikanga, R. Sakhnovsky, Q. T. Zhou, Electrostatic spray drying for monoclonal antibody formulation, International Journal of Pharmaceutics, 607 (2021) 120942

[3] A.K. Masum, J. Saxena, B. Zisu, 13-Elctrostatic spray drying of high oil load emulsions, milk and heat sensitive biomaterials, Food Engineering Innovations Across the Food Supply Chain, Ed Academic Press (2022) 237-246

# 31. A NON-DIMENSIONALISED QUADRATURE METHOD OF MOMENT MODEL FOR WET GRANULATION

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Wet granulation, such as twin-screw wet granulation, is a multiphase process utilized to produce aggregate particles with defined properties from very fine powders. Simulating these processes on the microscale is challenging because of the large number of particles involved, which differ widely in both size and material properties. Macroscale methods, tracking only the particle bulk properties, are efficient but do not resolve disperse particle properties such as the particle size distribution (PSD), which is key information for downstream processing. These deficiencies are addressed by multiscale methods like population balance modeling (PBM), which tracks distributed properties, such as the particle size, by adding them as internal variables to the macroscale (CFD) model. Most of available methods to track disperse properties are either inaccurate (method of moments) or computationally expensive (Monte Carlo, class methods) [1]. Recently a new closure for the method of moments, the quadrature method of moments (QMOM), was introduced which allows accurate moment tracking of a PSD with the efficiency proportional to a CFD simulation [2]. In this study we propose a framework of a maximum entropy reconstruction (MER), which has proven to reliably reconstruct PSDs from its moments, coupled to a QMOM as a fast and reliable evolution and reconstruction algorithm. Coupling of both methods has several advantages for the reconstruction algorithm. Special cases (growth, aggregation or breakage) are utilized to verify the framework (see Figure 1 for an example on constant aggregation of particles) and relevant numerical as well as theoretical issues are discussed. For validation the framework is successfully tested on a twin-screw wet granulation dataset [3].

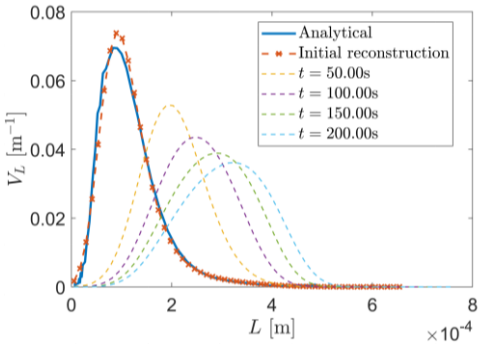


Figure 1. Time evolution of a volumetric particle size distribution subject to spatially homogeneous constant aggregation.

[1] M. Shiea, A. Buffo, M. Vanni, D. Marchisio, Numerical Methods for the Solution of Population Balance Equations Coupled with Computational Fluid Dynamics, Annu. Rev. Chem. Biomol. Eng. 11 (2020) 339–366.

[2]D.L. Marchisio, R.O. Fox, Computational Models for Polydisperse Particulate and Multiphase Systems, Cambridge University Press, 2013.

[3] T. Plath; C. Korte, R. Sivanesapillai, T. Weinhart, Dataset as a basis for process modeling of twin-screw wet granulation: A parametric study of residence time distributions and granulation kinetics, 2021, 4TU.ResearchData. Dataset.

# 32. REGIME ANALYSIS APPROACH FOR HIGH-SHEAR WET GRANULATION SCALE UP

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Wet granulation processes are difficult to scale up because conventional methods require ample experimental data at scale to determine the most favourable operating conditions. Therefore, an approach is required which is based on scientific understanding of the wet granulation process, key operating conditions and performance indicators. A systematic model-driven framework can facilitate this scale-up process by reducing the number of experiments required, particularly at large scale. Such an approach helps to design large-scale experiments and reproduce desired experimental outcome observed at small scale which is needed for a successful process scale up.

This case study demonstrates the workflow of a scale-up campaign for high shear wet granulation processes using a dimensionless regime analysis approach. The workflow includes calibration and validation of a regime analysis model for high shear wet granulation. Calculations were made at small scale for dimensionless numbers such as pore saturation, Stokes deformation number, dimensionless penetration time and spray flux. These parameters are used to construct nucleation and growth regime maps at small scale. Additionally, the calibrated maps are validated using large (or pilot) scale experiments. To scale up the granulation process, the calibrated regime maps were applied to identify the optimal operating range at the large scale. The outcomes show that regime analysis approach is useful for high shear wet granulation scale up.

# 33. COMPACTION PROCESS DESIGN AND TECH TRANSFER AT DIFFERENT STAGES OF DEVELOPMENT

Stefan Bellinghausen[1], Jianfeng Li[2] & Dana Barrasso[2]

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Roller and tablet compaction are key process steps in the production of pharmaceutical tablets. Because experimental data is limited or costly at early stages of development, an efficient process development workflow is key to make efficient use of the data available. A range of modelling solutions are available to understand the process behaviour and predict suitable process conditions for the different stages of development. However, the selection of the most appropriate modelling and experimental methodology for a given problem remains a challenge in pharmaceutical process development. The overall objectives of employing these solutions are to design the production process with minimal experimental effort and to reduce process variability to meet product specifications.

In this work, we will present an efficient design workflow for compaction tech transfer from compaction simulator to production equipment. This design workflow is based on science-based models that are calibrated using targeted experimentation, taking into account the typical data available at different stages of pharmaceutical development. Additionally, more advanced modelling solutions will be described that build process understanding under uncertainty and minimise tablet-to-tablet variability.

# 34. MICROPELLET COATING FOR TASTE IMPROVEMENT OF PAEDIATRIC FIXED DOSE COMBINATION ANTIMALARIAL THERAPIES

Dina Shokry[1], Alan Reader[1], Sangeetha Marri[1], Daniel Baker[1], Kavil Patel[2] & Fang Liu[1,2]

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Malaria is one of the most devastating diseases on the planet with children aged 6 months to 5 years amongst the worst affected. Artesunate (AS)-Amodiaquine (AQ) are included as a fixed dose combination in current WHO guidelines, however, AQ is renowned for its poor palatability, leading to incompliance in paediatric populations. The aim of this work is to develop a fixed dose combination of taste masked AS/AQ micropellets (diameter <250 um) for oral administration in young children.

AS and AQ were separately spray layered onto microcrystalline cellulose (MCC) in a modified bench top fluidized bed coater. The AQ layered micropellets were taste mask coated using 80/20, 77.5/22.5 and 75/25 ratios of organic ethyl cellulose (polymer) and hypromellose (pore former) solutions at 10, 15 and 20 % coating levels (CL). MicroCoat™ technology was applied during coating whereby powdered magnesium stearate was added into the coating chamber via an external feeding port. Micropellet diameter was measured using laser diffraction. Drug release from coated micropellets was measured *in vitro* using USP II apparatus. Taste masking was determined *in vitro* by dispersing micropellets in 10 mL of deionised water and comparing release to a known bitterness threshold. Concentrations of AQ and AS were quantified using UV and HPLC analysis, respectively.

By applying MicroCoat™ technology, yield for all coating trials was >95 %. AS release (>90 % in 5 min) was observed from layered micropellets. At 10 % CL AQ release was too slow from micropellets coated with an 80/20 ethyl cellulose/hypromellose ratio and too fast at a 75/25 ratio. At a 77.5/22.5 ratio and 10 % CL AQ release was acceptable, however, taste masking was incomplete with 0.17±0.01 mg/mL release after 1 min (bitterness threshold identified at 0.069 mg/mL). To improve taste masking the 77.5/22.5 coating level was increased from 10 to 15 %. As the thickness of the coating increased, AQ release remained within the acceptable limits and taste masking was achieved (0.01±0.00 mg/mL). The AS layered micropellets and taste masked AQ micropellets were measured to have an average particle diameter of 179 and 225 µm, respectively.

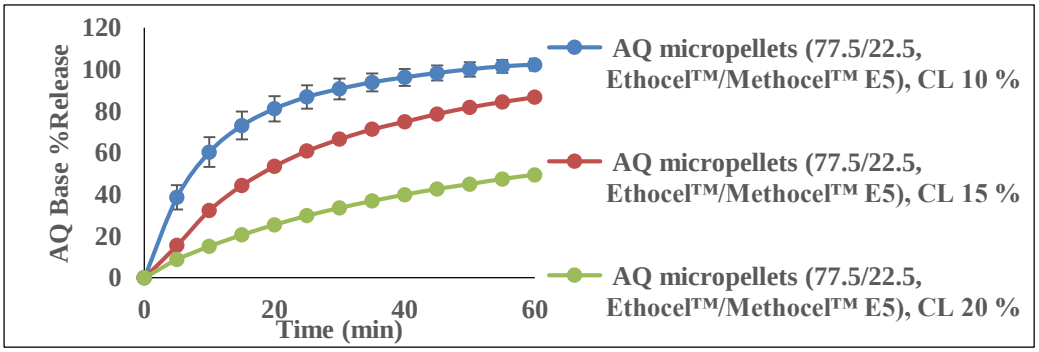


Figure 1. Percentage of AQ released from 77.5/22.5 (Ethocel™/Methocel™ E5) coated micropellets at different coating levels versus time (minutes).

# 35. INFLUENCE OF SPRAY PARAMETERS ON COATING STRUCTURE IN FLUIDIZED BED GRANULATION

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In fluidized bed granulation and coating, the spraying of the liquid is one if not the most critical step in terms of later product properties and application. The injection of the solid-containing solution into the particle bed and atomization into droplets depends on several parameters such as the type and location of the nozzle, the liquid properties, and the spray related process parameters, e.g. the liquid mass flow. By influencing the characteristic of the injected droplets, these parameters also have an effect on the solid-liquid interaction at the particle surface and, thus, the structure of the produced granules.

In this work, the liquid injection in the granulation process and its influence on the granule structure are investigated. First, the spray pattern of the two-fluid nozzle is analyzed by recording the spray cone with a highspeed camera at varied spray parameters and evaluating the recorded images with regard to the cone angle. It was found that the shape of the spray cone is mostly influenced by the air pressure applied at the two-fluid nozzle. Furthermore, granulation experiments were performed in a lab-scale fluidized bed using Cellets®500 as primary particles and sodium benzoate as coating material. Experiments were carried out at varied spray conditions. In order to investigate the influence of the changed parameters, the granules were characterized concerning their surface morphology using confocal laser-scanning microscopy and scanning electron microscopy. A significant effect of the liquid spray rate and spray air pressure on the surface structure could be observed. However, to fully understand the phenomena causing these different coating structures, thermal conditions in the fluidized bed also have to be considered.

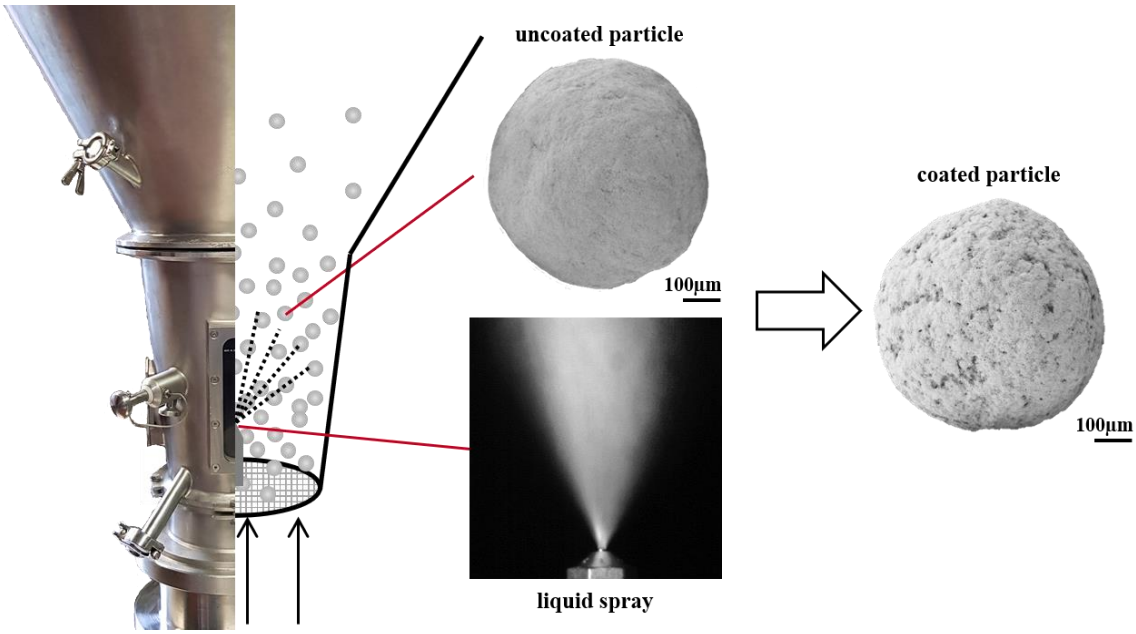


Figure 1. Scheme of a fluidized bed spray granulation with highspeed camera image of the spray cone and SEM images of uncoated and coated particles.

# 36. POWDER GRANULATION TO REDUCE LUMP FORMATION DURING RECONSTITUTION OF SWELLING FOOD POWDERS: CASE STUDY AND RESEARCH GAPS

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During reconstitution of food powders, material swelling can lead to extensive lump formation and thus a significant delay in complete rehydration. Powder granulation has been a frequently applied approach in the food industry to improve reconstitution by reducing the wetting time and reducing the risk for lumps. The positive effect of powder granulation can be partially ascribed to the resulting lower surface to volume ratio of particles and higher inter-particle pore space leading to slower particle swelling upon water contact and reduced pore clogging by swelling respectively. Changes in recipes of food powders which includes the use of an ingredient with higher swelling capacity, can lead to more pronounced lump formation if the particle structure is not adapted accordingly. To avoid a deterioration of reconstitution performance upon recipe adaptation, a prediction of swelling behaviour of material mixes as well as the tendency of lump formation for a given powder structure is required.

In the presented study we showcase how an analysis of the swelling behaviour of food materials in combination with advanced structural analysis of a powder bulk can be used to predict the lump formation tendencies of food powders. For this purpose, powders with different structures were produced by spray drying and a subsequent granulation step (roller compaction, fluidized bed agglomeration) and subjected to XRD-scans to get accurate data of the powder bulk structure. Stepwise digital dilation of the powder bulk 3-D structure was used to imitate the swelling of the powder bulk and thus predict the order in which the powders would clog in contact with water in a Washburn set-up (Figure 1). Water penetration was simulated using the software Geodict. The prediction from the digital swelling simulation were successfully validated in imbibition experiments with powder containing pea protein.

To implement similar prediction tools for industrial application, faster and simpler methods as well as a better understanding of the role of material swelling during the reconstitution are needed and should be investigated in future studies on powder reconstitution.

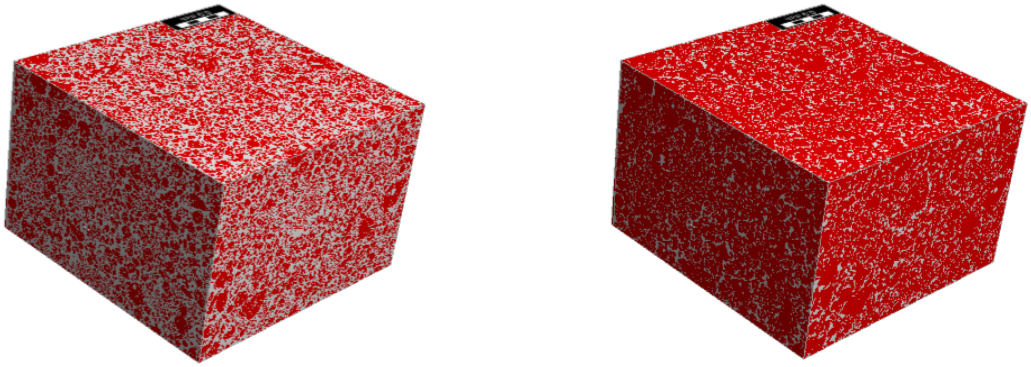

Figure 1. 3D visualization of a food powder before digital swelling (left) and after (right)

# 37. INVESTIGATION OF ISLAND GROWTH ON PARTICLES COATED BY MEANS OF AEROSOL

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The coating processes of particles have importance for many industries such as pharmaceutical, food, and chemical industries. Fluidization is one of the most important processes for particle formation. Fluidized beds (FB) are preferred to mechanically agitated beds because of good mixing, homogeneity, high heat and mass transfer rates. Coating particles in a spray fluidized bed (SFB) is the conventional way of coating particles. The coatings with SFB are usually thicker than 30 µm since the droplet size is large, the mean droplet size is around 40 µm in diameter [1,2].

In this study, an aerosol fluidized bed (AFB) is used to coat particles. A new aerosol generator is used to get coating solution droplets smaller than 1 µm in diameter. Glass particles, which have a mean diameter of 653 µm, were used as a non-porous core material and the coating solution was sodium benzoate (NaB). Scanning electron microscope (SEM) pictures were analyzed by MATLAB image processing program for evaluating the coverage with the curvature effect. Monte - Carlo (MC) simulation was used to simulate the coating of fluidized particles by aerosol droplets. The purpose of this work is the determination of possible island growth on particles, and the investigation of the reasons of it by comparing the experimental and simulation results with innovative changes.

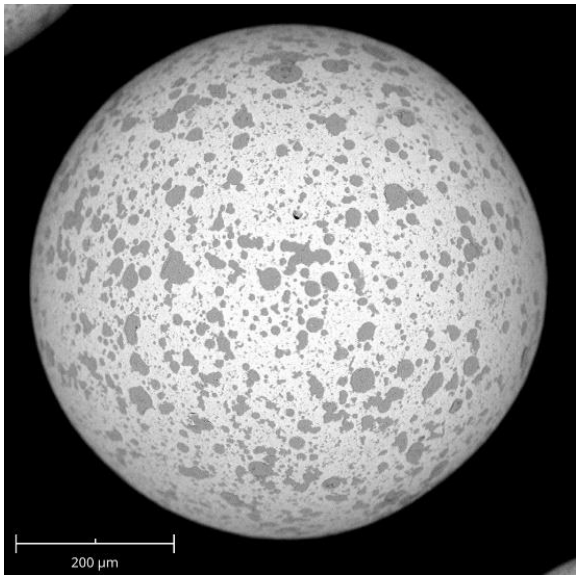


Figure 1. SEM picture of the patchy coated particle

[1] R. Zhang, T. Hoffmann, and E. Tsotsas, Novel Technique for Coating of Fine Particles Using Fluidized Bed and Aerosol Atomizer, Processes, 8 (2020) 1525.

[2] M. Mezhericher, C. Rieck, N. Razorenov, and E. Tsotsas, Ultrathin coating of particles in fluidized bed using submicron droplet aerosol, Particuology, 53 (2020) 23–29.

# 38. CONTINUOUS MELT GRANULATION WITH PLANETARY ROLLER GRANULATORS

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Over the last decades a major challenge in pharmaceutical technology is to establish methods for continuous operation due to a switch of the production focus [1]. For granulation as a key unit operation in powder handling to enlarge the particle size and enhance the flowability [2], the use of planetary roller granulators is a promising alternative for melt processing.

The fundamental of the modular process concept (Figure 1) is the rotation of a central spindle, which drives free-flowing planetary spindles in a surrounding roller cylinder due to the toothing of all these components. Therefore, the orbital motion is commutated, while the rotation is opposed. In addition, the central spindle as well as the roller cylinder are heated independently. This leads to an enhanced ratio of free process volume to generated and heated surface, which is favourable in terms of process control.

In this work, continuous melt granulation with planetary roller granulators has been evaluated experimentally for a constant formulation with a focus on several process related aspects. This includes the identification of an operating window with respect to processing and equipment limitations as well as the impact of process parameters (feed rate, rotation speed, free process volume) and equipment parameters (screw configuration) on the processing conditions. Thereby the particle size distribution of the product is the key indicator for the granulation performance, while the mechanical and thermal energy input represent the heating mechanism and the residence time distributions is a feedback on the transport mechanisms.

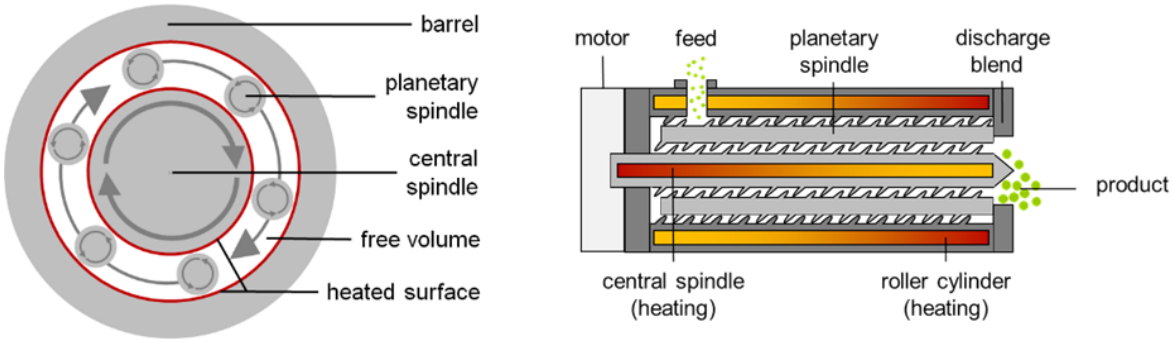


Figure 1. Radial cross section of a planetary roller granulator (left) and axial cross section of the modular machine concept (right)

[1] H. Leuenberger, New trends in the production of pharmaceutical granules: batch versus continuous processing, European Journal of Pharmaceutics and Biopharmaceutics, 52(3) (2001) 289- 296.

[2] P. Serno, P. Kleinebudde, K. Knop, Granulieren: Grundlagen, Verfahren, Formulierungen, Editio-Cantor-Verlag, (2007).

# 39. EFFECT OF HYDROPHOBIC POWDERS ON THE TENSILE STRENGTH OF THE TABLET

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A tablet consists of the drug, the active pharmaceutical ingredients (API), and the other components, excipients. The tensile strength of a tablet is one of the most important outcome parameters of compression as it will need to withstand coating, packing, and shipping stresses but also not affect the dissolution time. Currently, there is a lack of understanding of why excipients improve the bulk powder properties and the bonding mechanisms of the powder during compression. This makes tablet formulation development an inefficient trial-and-error process that is needed for every new API (1). Therefore, there is a need to understand the fundamentals of the bonding mechanisms of the powder during compaction. In literature, surface energy of the powders contribute a significant amount towards the tensile strength (2) as hydrophobic powders, which have a lower surface energy (3), are seen to disrupt the tablet strength significantly (4,5).

Additives with differing levels of hydrophobicity were mixed into microcrystalline cellulose (MCC) at different mass fractions to measure the effect the additives had on MCC tabletability. There was focus on a lower mass fraction (0.02-0.1 V/V) with increasing increments of 0.02 V/V as well as gaining a full picture (0.2-1 V/V) with increments of 0.2 V/V.

The aim was to investigate the impact of the hydrophobicity of additive powders on tabletability of microcrystalline cellulose (MCC). This was done by mixing powders of varying hydrophobicity into MCC at varying mass fraction. There was focus on a lower mass fraction (0.02-0.1 V/V) with increasing increments of 0.02 V/V as well as gaining a full picture (0.2-1 V/V) with increments of 0.2 V/V.

It was found at low mass fractions (0.02-0.4 V/V) of additive added the hydrophobic powders disrupted the tablet strength more compared to hydrophilic powders which could be attributed to the levels of surface energy of the additive. In contrast, at higher mass fractions (0.6-0.8 V/V), it is hypothesised that the deformation mechanisms of the additives which governed the tensile strength of the tablet.

[1] Reynolds GK, Campbell JI, Roberts RJ. A compressibility based model for predicting the tensile strength of directly compressed pharmaceutical powder mixtures. Int J Pharm. 531(1) (2017) 215–24.
[2] Sun CC. 4 Role of Surface Free Energy in Powder Behavior and Tablet Strength. In: Adhesion in Pharmaceutical, Biomedical and Dental Fields. 2017. p. 75–88.
[3] Sunkara D, Capece M. Influence of Material Properties on the Effectiveness of Glidants Used to Improve the Flowability of Cohesive Pharmaceutical Powders. AAPS PharmSciTech.19(4) (2018) 1920–30.
[4] Zuurman K, Maarschalk KVDV, Bolhuis GK. Effect of magnesium stearate on bonding and porosity expansion of tablets produced from materials with different consolidation properties. 179 (1999) 107–15.
[5] Mishra SM, Rohera BD. Mechanics of tablet formation: a comparative evaluation of percolationtheory with classical concepts. Pharm Dev Technol. 24(8) (2019) 954–66..

# 40. ADVANCED ON-LINE MEASUREMENT TECHNIQUES TO CONTROL MILK POWDER CHARACTERISTICS DURING CONTINUOUS FLUIDIZED BED SPRAY AGGLOMERATION

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To ensure constant powder properties of agglomerated skim milk powder, suitable product quality characteristics and monitoring of the spray drying and agglomeration process parameters are necessary. On the one hand, data such as mass flow, temperatures and air moisture are already being recorded continuously. Product quality characteristics such as particle moisture or particle size, on the other hand, are frequently only analyzed off-line in the laboratory. Slowdowns occur as a result of manual sampling, transportation from the plant to the laboratory, preparation and execution by the operator.

Continuous on-line measurement techniques overcome the disadvantages of sampling, especially if multiple process parameters or replication measurements are desired. Furthermore, any undesirable changes in the process can be addressed directly by using this data within the process control strategy. In this work, near-infrared spectroscopy (NIR), capacitive moisture measurement (CM) and in-line particle size measurement using spatial frequency filters (IPP) are employed. The scope of this work was to calibrate these sensors within a two-stage continuous pilot scale spray agglomeration production process for skim milk powder.

A fluidized bed is mounted underneath the spray drying chamber in this configuration. The particles generated in the spray dryer are agglomerated directly in the fluid bed, which is equipped with a variety of sensors (NIR, CM, IPP). Fluidization velocity, temperature, and the amount of moisture injected into the system were varied using a full factorial design as a framework. IPP was used to monitor particle size growth, while CM and NIR were used to determine particle moisture. The acquired NIR spectra are used to develop a mathematical model using multivariate data analysis (PLS regression). Several pre-processing methods were evaluated and tested for their suitability as a basis for model building. The off-line moisture content determined by Karl Fischer titration of the taken samples was used to validate the moisture content predictions (CM and NIR). Beyond product moisture, NIR measurement reveals spectral pattern fluctuations such as the light scattering by the fluidized bulk or baseline shifts, which can be used to correlate other derived quality characteristics such as particle size distribution or atomizing nozzle condition. Predictions for the particle size could be validated using IPP.

Complex processes such as continuous spray agglomeration require advanced measurement technology for dynamic control. The generated model should allow an assessment of the current agglomeration behavior based on the recorded NIR spectra. Hence, process control can be improved, such as determining the optimal injection of binders or responding to raw material fluctuations, consequently increasing operation time and yields. In the context of large-scale industrial food manufacturing, long process times and constant process conditions make it challenging to expand the data set that would be needed for the application. The specific application in the continuous semi-industrial pilot scale process can serve as a bridge to the industrial application, where the goal of on-line measurement has been defined for many years, but has only been applied in a few cases.

# 41. MODELING THE PARTICLE SIZE DISTRIBUTION OF AGROCHEMICAL POWDER BLENDS: A DATA ANALYSIS ON THE OPERATING CONDITIONS OF A PILOT SCALE JET MILL

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Agrochemical formulations like Water Dispersible Granules (WG) and Water Soluble Granules (SG) are prepared from blended powders constituting of solid active ingredients and co-formulants. These powder blends are subjected to particle size reduction in order to meet a certain particle size specification. Particle size reduction of the powder blends is attained by using Jet (or Air) Mill - a technology capable of reducing primary particle size to <10 µm (D50), often, with a single pass.

Particle Size Distribution (PSD) is a critical confounding variable that impacts downstream granulation and performance. Traditionally, identifying the jet milling conditions for a product's PSD has relied on trial-and-error. The efficient alternative to the trial-and-error method is - a precision and data-driven approach of defining a model for the jet mill parameters. Models are particularly necessary for difficult-to-mill powder blends, where optimal processing conditions may not be intuitive.

In this work, complex powder blends, were subjected to a comprehensive range of milling conditions, yielding an expansive dataset. The ultimate target was to optimize the jet mill process and establish better controls using the predictive model. This work explored the relationship between the independent variables: feed pressure (psi), grind pressure (psi), Δ between both pressures and product inlet feedrate (kg/hr), and dependent variable: particle size distribution (D50, D90) of the outlet product. Additionally, interactions amongst the independent variables, were also studied when defining the fit model, to gauge the influence on the resultant particle sizes.

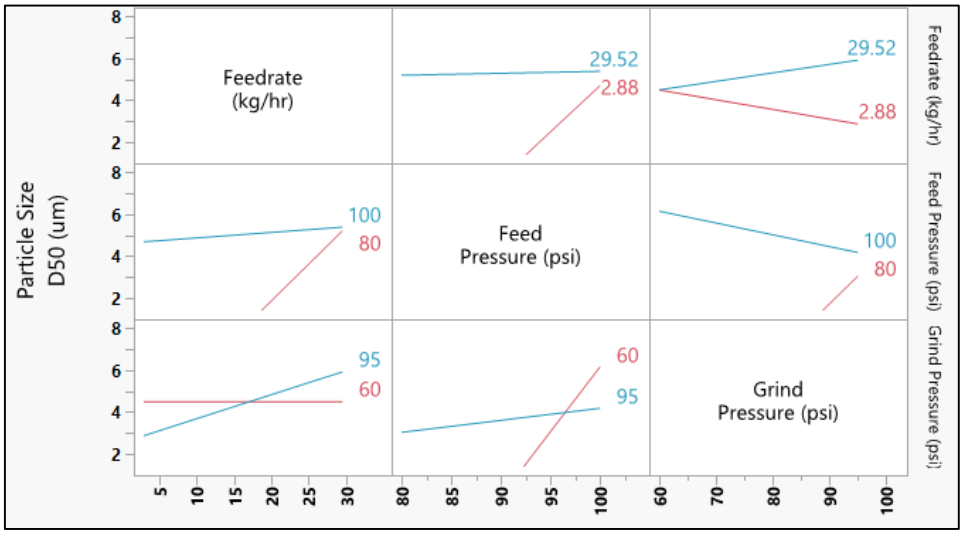


Figure 1. Particle Size D50 vs. Interaction Profiles generated via Fit Model

# 42. DEM ANALYSIS OF MIXING PERFORMANCE OF COHESIVE POWDERS IN A HIGH SHEAR MIXER

Abul Hassan Syed[1,2], Hasan S. Elmsahli[1], I. Csaba Sinka[1]

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The cohesiveness of powders causes formation and breakage of agglomerates, yet cohesiveness is broadly ignored in Discrete Element Modelling (DEM) powder mixing. This paper presents a DEM investigation into the effect of cohesiveness on the mixing performance in a geometrically realistic high-shear mixer. The adhesive contact law of Johnson-Kendall-Roberts (JKR) [1] and the Hertz-Mindlin [2] are employed to compare the behaviour of cohesive and non-cohesive particles. The quality of mixing is quantified using a non-sampling Subdomain Mixing Index (SMI) [3] method. The mixing quality is analysed considering particles with properties within the representative range for pharmaceutical formulations. The flow regimes are also characterized for different fill ratios to determine the optimum loading of the mixer. SMI regime maps are obtained as functions of surface energy (which determines adhesion between particles) and fill ratio (a process parameter) at different times during the mixing process.

The paper has two contributions. First, it shows particle clustering under the effect of adhesive forces in a high shear mixer; these clusters may break down under the effect of the impeller. Optimal mixing requires a certain level of cohesion; however, highly cohesive powders present poor mixing behaviour. Second, an inherent limitation of the SMI methods was identified with regard to the selectio of the subdomains in terms of both size and geometry; therefore, the SMI values should be interpreted relatively for practical purposes.

[1] K. L. Johnson, K. Kendall and A. D. Roberts, “Surface energy and the contact of elastic solids,” Proceedings of the Royal Society of London, vol. 324, pp. 301-313, 1971.

[2] R.D. Mindlin and H. Deresiewicz, “Elastic spheres in contact under varying oblique forces,”

[1] M. Cho, P. Dutta and J. Shim, “A non-sampling mixing index for multicomponent mixtures,” Powder Technology, vol. 319, pp. 434-444, 2017.

# 43. PREDICTING TABLET PROPERTIES USING IN-LINE MEASUREMENTS AND EVOLUTIONARY EQUATION DISCOVERY

Issa Munu[1,2], Leonard Nicusan[1], Jason Crooks[2], Kendal Pitt[2], Christopher Windows-Yule[1] & Andrew Ingram[1]

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High shear wet granulation (HSWG) is an common unit operations in manufacturing of tablets that minimises segregation, facilitates desired content uniformity within granules, improves powder flowability thus preventing tablet weight variability [1], [2]. This shows that HSWG is an important unit operation that can influence granule and tablet CQAs.
This study presents an opportunity of predicting granule and tablet properties through torque measurement of the granulation bowl and the force exerted on a probe within the powder bed.

The results showed that the torque and Lenterra force in-line measurements are providing unique rich information about the granulation process (see Figure  and Figure ). The Lenterra force probe is more sensitive during the water addition phase (see Figure ). The model developed from Design of Experiment (DoE) matrix and evolutionary equation discovery show that the cumulative force during water addition in high shear granulation process has a strong contribution towards tablet tensile strength. The capability to predict tablet tensile strength and rotary press compaction force from upstream data will minimises waste and eliminates operator trial runs to get the best compression machine settings.

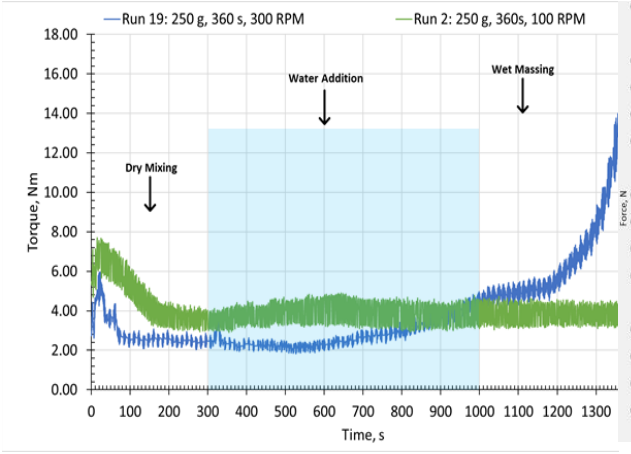


Figure 1. Torque measurement during granulation

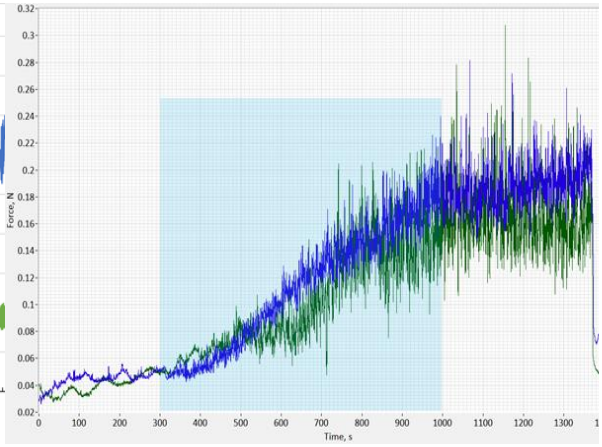


Figure 2. Force measurement during granulation

[1] I. P. Gabbott, F. Al Husban, and G. K. Reynolds, “The combined effect of wet granulation process parameters and dried granule moisture content on tablet quality attributes,” Eur. J. Pharm. Biopharm., vol. 106, pp. 70–78, 2016

[2] J. Dun and C. C. Sun, “Structures and properties of granules prepared by high shear wet granulation,” Handb. Pharm. Wet Granulation Theory Pract. a Qual. by Des. Paradig., pp. 119–147, 2018

# 44. INVESTIGATING THE HEAT SENSITIVITY OF HYPROLOSES WITH DIFFERENT PARTICLE SIZES DURING TABLETING

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Powders and granules are commonly compressed into tablets. During production, heat evolving from friction, elastic and plastic deformation and fragmentation of materials can affect tablet characteristics [1]. In that respect, the evaluation of tensile strength serves the assessment of tablet quality, due to its importance for handling and possible influence on disintegration and drug release [2].

In this study, the heat sensitivity of two commonly used binders with identical chemical composition but varying particle size distribution was investigated. The binders used were either HPC SSL ($x_{50}$ = 61 µm) or the finer quality HPC SSL-SFP ($x_{50}$ = 18 µm) (Nippon Soda, Japan). Binary mixtures composed of lactose and the binder were produced at a ratio of 9:1. The temperature increase during tableting was mimicked using a tablet press equipped with a thermally controlled die set to either 22, 30, 50 or 70 °C (STYL'One Evo, Medelpharm). The die was filled manually after lubrication with magnesium stearate.

The tabletability of both mixtures was evaluated and compared. When tableting is performed under elevated temperatures, the mixture containing HPC SSL-SFP (b) proved to be more sensitive to heat, as the increase in tensile strength is more pronounced than for the mixture with HPC SSL (a).

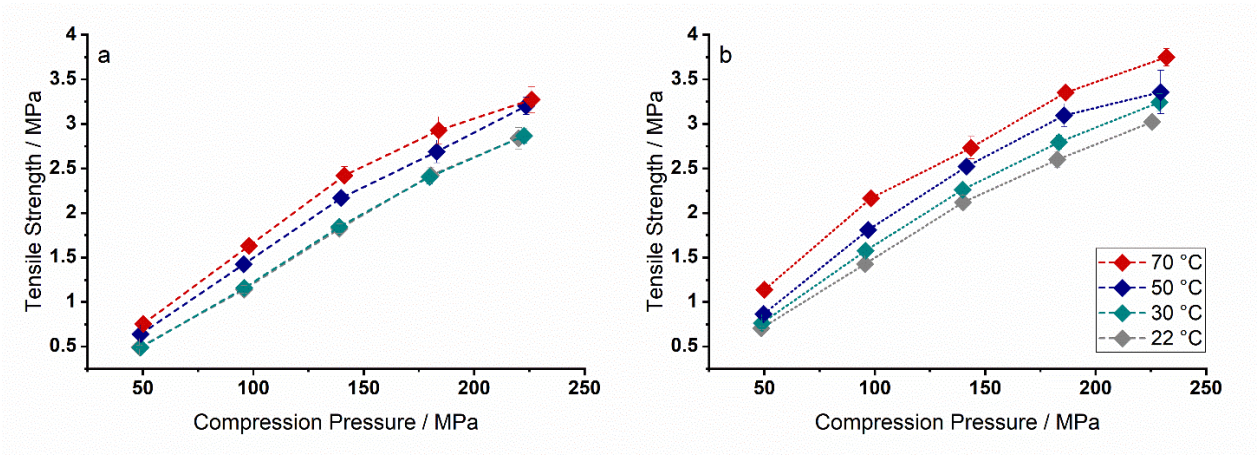


Figure 1. Change in tensile strength for different tableting temperatures. Binary blend containing lactose and (a) HPC SSL (b) HPC SSL-SFP ($\bar{x} \pm sd$, n=10).

[1] E.J. Hanus, L.D. King, Thermodynamic effects in the compression of solids, J Pharm Sci. 57 (1968) 677–684.

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# 45. A REGIME MAP FOR DRY POWDER COATING

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Many products are coated to protect against damage or moisture ingress, to change dissolution rates or to provide functional surface properties. Dry powder coating is often favourable to traditional liquid coating approaches due to the environmental benefit of being solvent-free. However, dry powder coating is often wasteful, with excess coating material added and mixing time applied to ensure sufficient coverage.

In this work we present a regime map for dry powder coating of particles, whereby the surface area coverage of the host material is related to particle properties and process conditions of the coating system. From DEM simulations we demonstrate that the relevant properties of guest and host particles can be accounted for by a single value, namely the granular bond number. Process parameters are shown to be well represented by the Stokes deformation number, a ratio of mixing energy to the cohesive energy of the particles. The developed regime map enables the number of impeller revolutions required to achieve the desired surface coverage to be defined, based on the size, density and surface energy of the guest and host materials.

Furthermore, some powders exhibit significant surface energy heterogeneity. Here we introduce approaches for simulating such heterogenous particles and show the influence this has on the overall surface coverage.

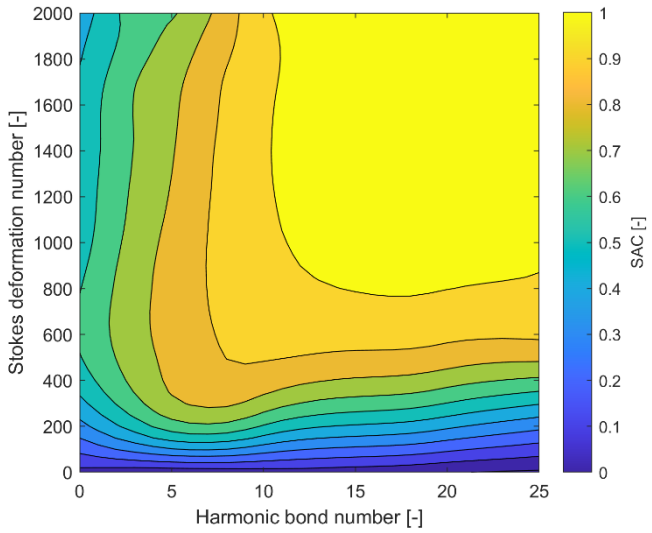


Figure 1. Regime map showing Surface Area Coverage (SAC)

# 46. MIXING AND SEGREGATION RATES AND MECHANISMS IN AN AGITATED VESSEL

Marv Khala[1], Colin Hare[1], Chuan-Yu Wu[2], Navin Venugopal[3] Martin J. Murtagh[4] & Tim Freeman[5]

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Most powder products contain a mixture of materials which vary in terms of particle size, density and cohesion. These differences in particle properties lead to segregation phenomena through a variety of mechanisms. In this work we present an experimental approach to assess mixing rates and segregation tendencies in an agitated vessel using a modified FT4 Powder Rheometer. Mixing rates are determined based on size and density ratios.

We also present DEM simulations of this system, which show the influence of absolute particle size and size and density ratio effects which agree with the experiments. DEM is also used to establish the influence of cohesion on the mixing/segregation rate; with a relationship developed to predict the degree of mixture quality (mixing index) from the energy input and the energy of particle contacts. The energy of particle contacts can be determined from the surface energy of the powders along with either (i) DEM contact information, or (ii) the particle size distribution. The former gives a more robust relationship, but requires simulation of the system, whilst the latter still gives a strong relationship and only requires information which can be experimentally measured, thus lending itself to industrial application.

Furthermore, the DEM simulations establish the influence of impeller speed on mixing rates. For cohesionless systems it is shown that increasing impeller speed reduces mixing rate since fines have less time to backfill transient voids, whilst for cohesive systems mixing improves with impeller speed due to cohesive clusters of fines being more easily dispersed.

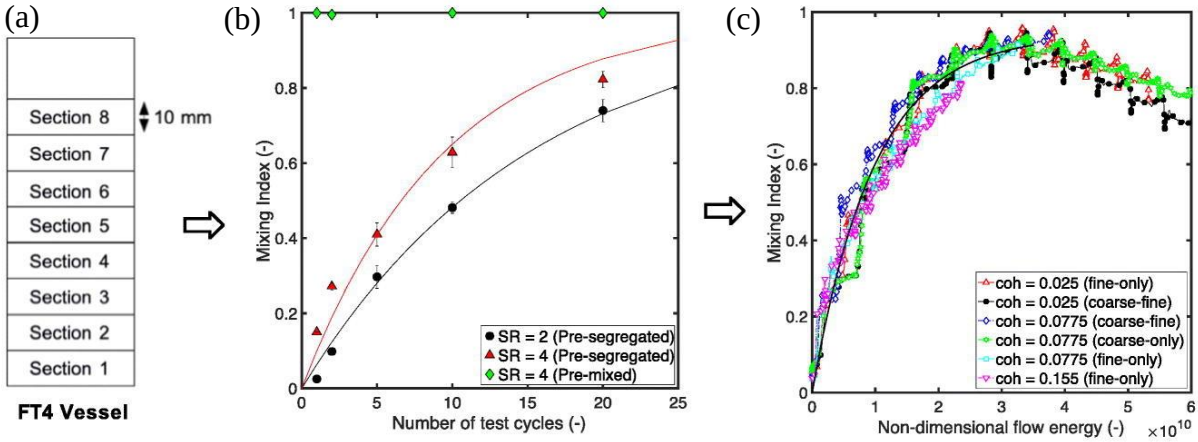


Figure 1. (a) the sectioned FT4 vessel used to assess mixing index (b) influence of particle size ratio on mixing rate (c) the developed relationship to predict mixing rate (black line) mapped against systems of varying cohesion

# 47. EVALUATION AND DIFFERENTIATION OF DAMAGING INFLUENCES ON COATED PELLETS IN TABLETING MACHINES

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Multiple Unit Pellet Systems (MUPS) are frequently applied to deliver drugs in small entities (pellets) with modified drug release. To achieve this, drug-containing pellets are coated with functional polymer layers that delay or sustain the drug release. To protect the API-containing core during the whole process chain of blending the coated pellets with excipients, flowing, feeding, and finally compacting the blend to a tablet, the coating layer around the pellets must stay perfectly intact.

In this study, the influence of different sub-processes in rotary tablet presses, namely feeding and compaction, on pellet coating integrity was systematically elucidated. On the formulation side, different pellet coating approaches, including the application of outer cushioning layers, and different deformation behaviours of the blended powders were studied. The compaction sub-process showed the greatest influence on coating integrity by the main compression stress. Here, an additional (non-enteric) cushioning coating could shield the enteric coating from mechanical stresses and improve the integrity of pellets also at high compaction stresses. Additionally, this can economically reduce the necessary amount of enteric coating applied.

In the feeding process, a forced paddle feeder was investigated as it is commonly applied on industrial rotary presses. Here, shear stresses are applied to the pellets. The shape of the spokes of the paddle wheel as well as small changes in characteristic geometric measures within the feed frame showed a distinct influence on the damage of the pellet coating. Coating damage, measured as premature model drug release, was shown to linearly increase with residence time in the stressing volume of the paddle feeder, but could be reduced by formulation parameters (cushioning coating, lubrication) or technical changes in the feed frame. Further, the additivity of the damaging effects of these subsequent sub-processes, feeding and compaction, is studied.

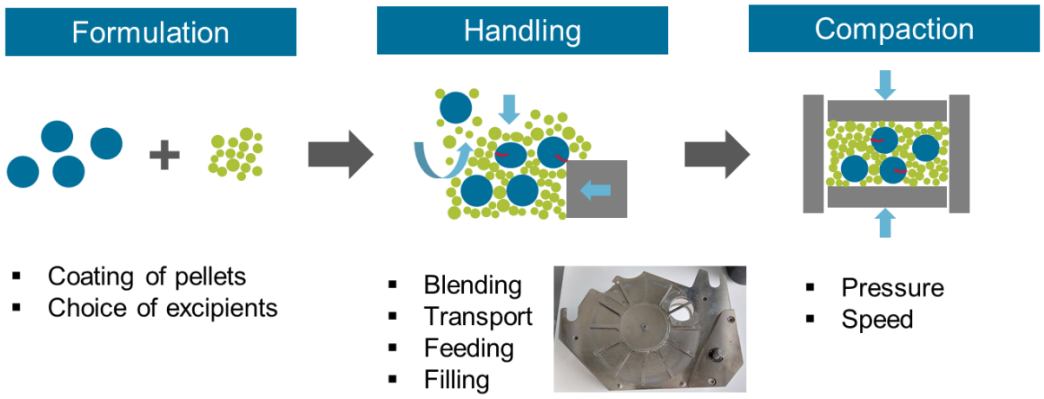


Figure 1. Illustration of influences on pellet coating integrity over a typical tabletting process chain

# 48. PAT MONITORING OF COATING PAN BY NIR: PLS METHOD CALIBRATION APPROACH

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The importance of real-time controlling the production processes in pharmaceutical industry is growing, to ensure a precise reproducibility, especially regarding modified release solid dosage forms, and to spare materials, shorten the process time and, consequently, save money. In this study the coating process in pan was taken in consideration, different coating materials were tested, the process was monitored by NIR to determine the weight gain and the coating thickness of the coated tablets in real time. To establish the correlation between the physical properties of the tablets and the response of the NIR device, the tablets were coated in coating pan (Freund-Vector LDCS Pilot) monitoring the process by a full-spectrum NIR device (Viavi Solutions MicroNIR PAT-U) and measuring the thickness and the weight gain off-line. The measured values were compared with the NIR response using chemometric methods: PCA, PLS, calibration and cross-validation method. To demonstrate the independency from the coating material used to achieve a correct process monitoring different coating polymers were tested. The data were analysed using CAMO Unscrambler X multivariate analysis software.

The process shows a very strong correlation between the absorbances read by the NIR instrument and the determined coating thickness and weight gain. This indicates that the model is reproducible. The reproducibility and the precision of the PAT monitoring can allow process control without the need for constant sampling and at-line analysis. This allows precise in-process control over the product and provides the possibility to spare process time, energy and raw materials. Future development of this study can lead to an integration of the PAT technology with the control software of the coating pan and a real time control of the process in terms of product characteristics instead of the process parameters, with the aim of integration with the automatic control system. This integration can also be developed to design a continuous manufacturing process that must be kept constantly under control to guarantee the reproducibility of the final product.

# 49. SPRAY DRYING AND TABLETING OF LIVING MICROORGANISMS

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The production of tablets containing living microorganisms is of special interest for the administration of probiotic microorganisms. These microorganisms provide health benefits to the patient when administered in viable form and adequate doses. Understanding the influence of different process steps, their specific process parameters and formulation aspects is crucial for improving the quality of probiotic tablets, especially with regard to microbial survival.

Different drying technologies can be used to dry microorganisms preserving their viability, for example freeze-drying or granulation. In this study, spray drying was used to dry the yeast *Saccharomyces cerevisiae* as a model microorganism. The influence of various process parameters such as inlet temperature, outlet temperature, spray rate, spray pressure and nozzle diameter was investigated. The influence of formulation aspects such as cell concentration as well as type and concentration of protective additives was also considered. The microbiological results indicate a critical specific energy input that is crucial for life-sustaining drying.

Selected products from the spray drying process were further processed into tablets using a compaction simulator. Here, process and formulation parameters such as compression stress as well as type and concentration of filler and binder were again varied and their influence on mechanical and microbiological tablet properties was examined. In principle, the higher the compression stress, the lower the survival rate, although the deformation behavior of the filler as well as its proportion also show effects.

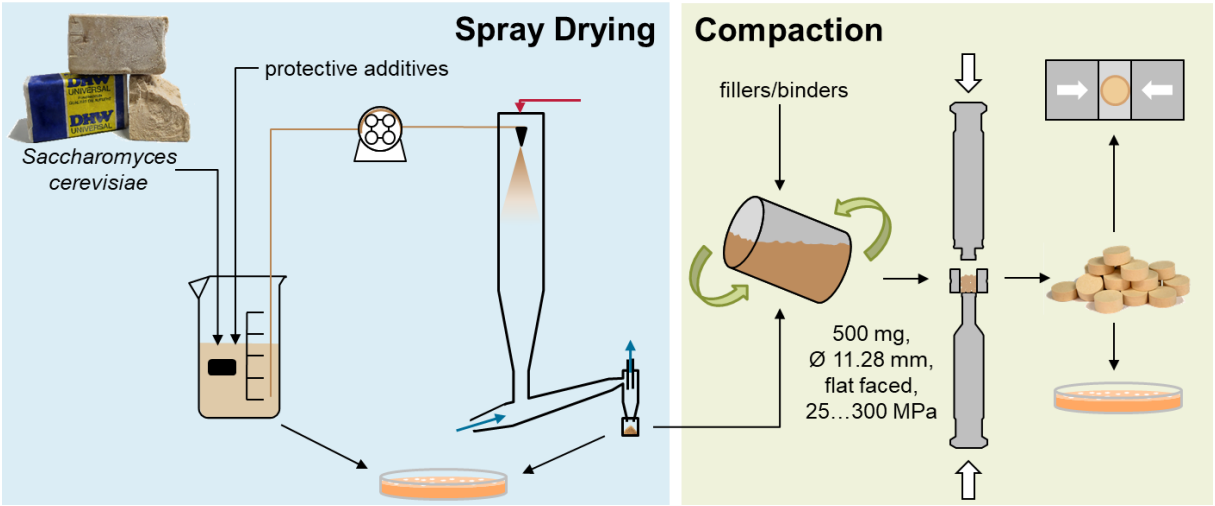


Figure 1. Overview of the process chain

# 50. MANUFACTURE OF MINI-TABLETS AND THEIR CONTINUOUS ROBOTIC COMPOUNDING INTO MULTI-UNIT DOSAGE SYSTEMS

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Recent advances in the fields of pharmacy and technology have led to the demand for therapeutic treatment that takes into account the patient's personal medical history and condition. In response, scientists and engineers are striving to develop drug dosage forms with well-defined therapeutic benefits tailored to the needs of a specific patient. This has led to the rapid spread of personalised medicine, which aims to develop customised drug delivery systems.

The Multi-Unit Dosage System (MUDS), consisting of mini-tablets filled into a hard gelatin capsule, is an effective therapeutic alternative to conventional dosage forms. So-called MUDS is designed so one mini-tablet represents the minimum strength of one API, and by counting and filling the required number of subunits in a capsule, can be achieved the right dose for each patient. The principle of MUDS capsules is thus to develop a single dosage form containing several active ingredients (in different mini-tablets) that the patient must take at a specific time. By the composition of mini-tablets and various process-related parameters (homogenization, granulation, compression) can be obtained the required dissolution behavior and convenient mechanical properties of subunits

The aim of the present study was to prepare mini-tablets with high drug loading content that retain equivalent dissolution profiles to original products and develop a multi-unit dosage system. Two APIs used for combination therapy for the prevention of cardiovascular diseases were used as model drugs. In order to achieve appropriate weight and content uniformity, we had to ensure good flow properties of tableting blends. For this purpose, wet granulation was added as a manufacturing step. By optimizing of the composition of the tableting blend and binder solution, size of granules, and other parameters of wet granulation, we were able to achieve the desired release kinetics of API from produced mini-tablets. By subsequent adjustment of tableting parameters, we managed to ensure appropriate mechanical properties. Mini-tablets with predefined release profiles were filled into a capsule, the overall release profiles were determined by an appropriate dissolution method with HPLC analysis.

Also, in this project, we are introducing an innovative manufacturing technology for the fully automated production of personalised drug dosage forms. This technology is based on a very precise and fast automatic compounding of small mini-tablets into hard gelatine capsules. With the proposed technology, it is possible to manufacture patient-specific batches of MUDS capsules on an industrial scale, which would contain a set of capsules for a period of 30-90 days. In this way, it would be possible to produce dosage forms tailored to individual patients while taking the advantages of industrial continuous production such as speed, quality and traceability.

# 51. ENSURING PRODUCT STABILITY, QUALITY, AND SAFETY WHILE INTRODUCING NOVEL SUSTAINABLE PACKAGING SOLUTIONS

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The rapidly evolving consumer trends and rising awareness about the ecological impact of their products makes it vital for packaging, food and ingredient manufacturers to be capable of quickly adapting processes to meet the consumer demands. The most striking and discussed topic is most likely the concern about the use of non-recyclable packaging materials and their impact on the environment including waste in the oceans and sustainable use of resources. However, manifold attempts to remove or replace undesired ingredients or packaging materials, one often faces hurdles linked to product stability, quality and safety, particularly in products with a large overall surface area such as food powder. To overcome this drawback material-science driven approaches are required tackling all aspects of the value chain – modifying product recipes, processes, storage & distribution and packaging materials.

In the present talk we will address the arising challenges in developing recyclable packaging materials with strong enough barrier properties as well as the impact of lowering the barrier properties (moisture transmission) on the product properties of food powders. Different approaches targeting novel product formats for powders especially by increasing the particle size are highlighted. Such increase in particle size by granulation, compaction, or other aim at increasing the stability towards temperature and humidity. Nevertheless, attention also needs to be drawn on the functional behaviour such as reconstitution of such novel formats to meet consumer demands while going to more sustainable food production.

# 52. STRUVITE ($MgNH_4PO_4.6H_2O$) GRANULATION FROM SEAWATER USING FLUIDIZED BED HOMOGENEOUS CRYSTALLIZATION TECHNOLOGY

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Struvite ($MgNH_4PO_4.6H_2O$) that could be recovered from phosphorus–contained wastewater has a high potential as an alternative source of phosphorus fertilizer. However, the cost and availability of current commercial $Mg^{2+}$ sources hinder the downstream transfer of struvite precipitation. Additionally, mass production of sludge in batch operation is the limitation of conventional precipitation for struvite production. This study aims to circumvent these drawbacks by investigating seawater as a magnesium source for phosphorus recovery as struvite granule by fluidized bed homogeneous crystallization (FBHC) system. The operating parameters, including up-flow velocity (U, m $h^{-1}$) and cross-sectional loading (L, kg $m^{-2}$ $hr^{-1}$) were optimized in the FBHC system. Under optimum conditions at pH 9.5, molar ratio of Mg: P: N=1.0:1.1:1.2, up-flow rate of 30 m $h^{-1}$, and cross-sectional loading of 1.1 kg $m^{-2}$ $hr^{-1}$, the crystallization ratio (CR) and total removal (TR) of phosphorus reached 60% and 85%, respectively. Based on the XRD pattern, it was confirmed the solid products consist of struvite ($MgNH_4PO_4.6H_2O$) with an average size of 3.0mm.

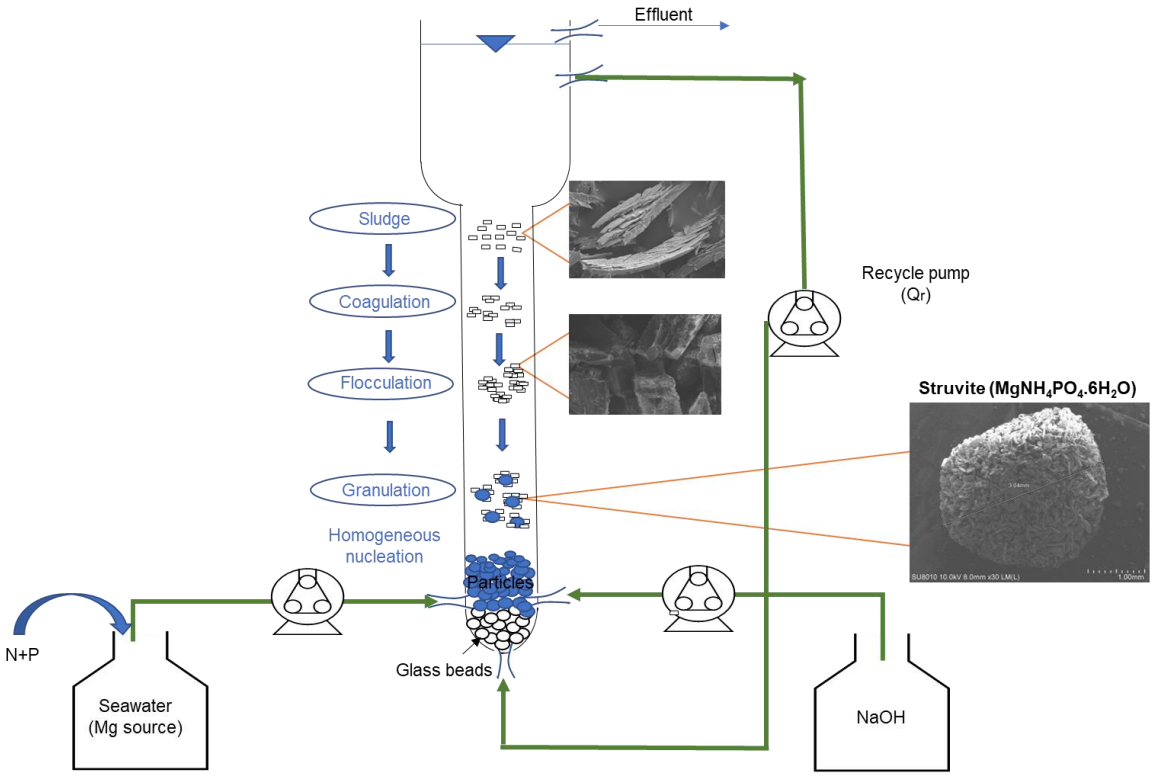


Figure 1. Fluidized bed homogeneous reactor (FBHC) arrangement.

# 53. MECHANISTIC REDUCED ORDER MODELS FOR INTEGRATING DRY GRANULATION AND TABLETING PROCESSES

Sunidhi Bachawala[1], Rexonni Lagare[2], Yan-Shu Huang[2], Katherine Young[2], Phoebe X. Bailey[2], David J. Sixon[2], Zoltan K. Nagy[2], Gintaras V. Reklaitis[2] & Marcial Gonzalez[1,3]

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Dry granulation is often used before tableting to improve the flowability and content uniformity of the blend. However, the process modifies particle porosity and imparts plastic work, which can negatively impact the tabletability of the granules [1]. Understanding this phenomenon is instrumental to improving the control of the continuous operation of a dry granulation line. This goal can be achieved via mechanistic modelling, but existing models for roller compaction [2] and tableting [3] were developed independently, and do not consider the effect of the former over the latter. In this work, we present a mechanistic approach to developing reduced-order models capable of capturing the relationship between dry granulation and tableting critical process parameters (CPPs) and the tablet critical quality attributes (CQAs). Specifically, we develop models to predict tablet tensile strength and tableting compaction force based on roll gap and roll pressure. The models were developed using roll compaction and tableting data of a powder blend composed of 10% APAP with MCC. The granules were made under varying levels of roll pressures and roll gaps, while the tablets were made under varying dosing positions and main compression thicknesses. The models showed that the roll pressure and roll gap used during granulation have high predictability for the tensile strength and compaction force during the tableting of those granules. The models also reveal that the tensile strength is sensitive to roll pressure and roll gap while the compaction force is less sensitive to roll pressure as compared to the roll gap.

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# 54. USING POSITRON EMISSION PARTICLE TRACKING (PEPT) TO EVALUATE MIXING IN AN AXIAL INCLINE BLENDER FOR CONTINUOUS DIRECT COMPRESSION (CDC)

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Pharmaceutical products being manufactured via Continuous Direct Compression (CDC) are on the rise. Through the application of prior studies which demonstrated relationships between processing conditions and effective mixing [1]. Despite our increase in understanding of macro responses, our understanding of the micro-behaviour is lacking. Through the use of Positron Emission Particle Tracking (PEPT) we can uncover some detail about the discrete paths particles take through a blender.

A prototype of the CDB-1 axial powder blender (seen on GEA's Consigma® CDC-50 line) was placed in the ADAC detector to undergo PEPT analysis. The bulk and tracer of choice 1mm MCC, Vivapur 1000 (JRS Pharma, Germany). The experiment was conducted over a range of RPM's (225, 300, 375) and two blade configurations (8 and 16 mixing blades, helically arranged). Through utilising PEPT's unique advantage, the ability to understand systems from a micro-up perspective, the detail of each discrete trajectory can be statistically scrutinised. Accordingly, the following distributions are discussed: trajectory's standard deviation across an axis, path length, velocity & residence time distribution. All of which highlight the material's propensity to behave to processing conditions on a micro scale. In addition, methods have been applied to evaluate the mixing- in an attempt to relate the micro-characteristics to macro-mixing performance.

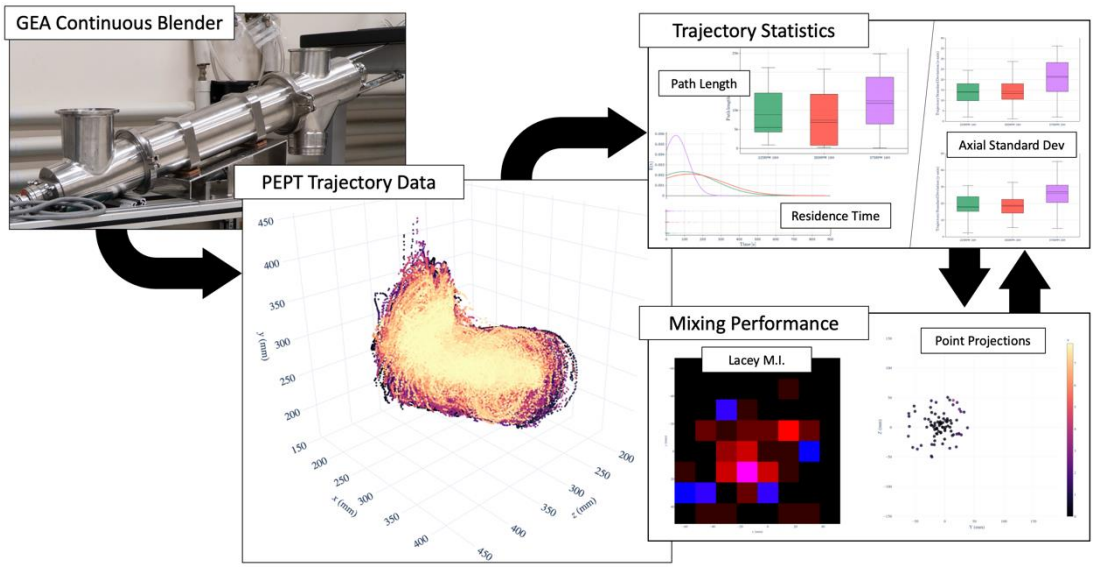


Figure 1. Pipeline showcasing the PEPT experiment and the subsequent analysis.

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# 55. HYBRID MODELLING OF PHARMACEUTICAL MIXTURE PROPERTIES: PREDICTIVE SOLUTIONS FOR PARTICLE SIZE, SHAPE, FLOW, AND DENSITY

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Efficient and cost-effective drug products development requires accurate prediction of pharmaceutical mixture characteristics to support the decision-making in formulation design and process optimization. This paper presents a system of hybrid models that combine both mechanistic and data-driven approaches to predict characteristics of pharmaceutical mixtures. The system model establishes a link between raw material properties and formulation to critical mixture attributes. Mechanistic, probabilistic models were developed to predict the particle size and aspect ratio distributions of pharmaceutical mixtures using those of the raw components. Additionally, the accuracy of two existing mechanistic mixture rules for predicting the mixture's true density and bulk density was assessed. Two data-driven models were developed that utilise principal component analysis to reduce the dimensionality of the predicted particle size and shape distributions, along with the predicted true density and bulk density as input data to predict the flowability (represented by the Flow Function Coefficient, FFC) and tapped density of the mixture (Figure 1).

The proposed particle size and shape mixture models outperformed one existing approach (weighted average of percentiles) whilst providing insights into the full distribution of the mixture. The presented models accurately predicted blend properties of different formulations and components, utilising raw material properties to avoid time-consuming and material-intensive blend preparation and characterisation. The system model proposed in this study holds the potential to accelerate the process of developing new drug products with new Active Pharmaceutical Ingredients (APIs) by predicting key mixture characteristics to help inform the decisions on formulation and process conditions during the process development.

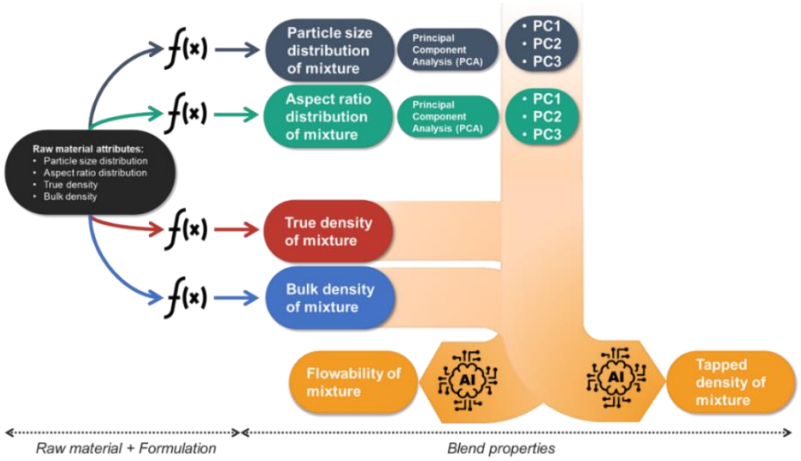


Figure 1 - Flow diagram of the proposed hybrid framework for mixture modelling. $f(x)$ and AI represent mechanistic and data-driven models, respectively.

# 56. PRE-NUCLEATION IN HIGH-SHEAR WET GRANULATION

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Wet granulation can be broken down into three rate processes: Wetting & Nucleation, Consolidation & Growth, and Breakage & Attrition [1]. These stages are often inseparable from each other, which hinders the characterization of the relationship between operating conditions and product properties in wet granulation processes. Single-drop granulation is a form of drop-controlled nucleation intended to isolate the Wetting & Nucleation rate process by allowing a single droplet to form a single granule upon impacting a static powder bed [2-4]. This work explores the high-shear granulation of a pre-nucleated bulk material. Single-dropped granules (pre-nucleated granules) are charged to a mixer granulator under varied conditions to observe how the remaining rate processes and resulting granulated product are affected by various pre-nucleation conditions.

Single-dropped granules are generated under various conditions that are intended to produce nucleated granules of varying size, shape, liquid content, and formation mechanism [5]. These nuclei are charged to the mixer granulator, along with differing amounts of additional liquid binder and additional dry powder, and then granulated for controlled amounts of time. Experiments are performed using Avicel micro-crystalline cellulose (MCC) as the raw powder, paired with DI water as the liquid binder. The raw MCC is sieved into three particle size ranges before use. Each size range was characterized by optical microscopy for the $d_{43}$ projected area diameter: small (51 ± 13 µm), medium (95 ± 18 µm), and large (153 ± 24 µm). The resulting granulated bulk is analysed for the mass-based size distribution by sieving and granule yield [6]. A representative sample of individual granules are also evaluated for their shape (circularity, vertical aspect ratio) by the prism method and image analysis software, ImageJ. This is the first study, to our knowledge, to apply the single-drop granulation technique to a traditional high-shear wet granulation process.

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# 57. WATER SOLUBLE TABLET FORMULATOIN FOR FAST INTRA TABLET COATING VARIABILITY DETERMINATION

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Tablet coating is a common unit operation in production of tablets and is performed for cosmetic purposes and/or taste masking, protection of the active ingredient or controlled release. Important quality attribute of coating is its thickness or amount per surface area. Every tablet in a batch must have sufficient coating amount in order that the function of the coating is achieved. This is typically described as the intra-tablet coating variability. Determination of the coating amount can be time consuming already for one tablet for some measurement methods such as microtomography. Additionally, to get statistically sound values of the coating variability, many tablets must be measured. Ideally that number should be at least 100.

Since none of the conventional analytical methods were fast enough for our purposes, we developed a dedicated placebo tablet formulation. The goal was to have a fully soluble tablet core and coating with an embedded colour tracer. For the analysis the coated tablets were dissolved in water and the solution was measured photometrically without any additional preparation steps such as filtration, centrifugation or dilution. The measured absorbance is then directly proportional to the amount of coating on the tablet.

Besides the good water solubility, the tabletting mixture had to have good flowability to enable direct compression, low hygroscopicity, low absorbance in solution, low ejection stress and high mechanical strength. The final formulation that satisfied all of the criteria consisted of: isomalt and sodium lauryl sulphate for the tablet core and hypromellose, polyethylene oxide and tartrazine for the coating. A series of coating experiments using this formulation was performed on different drum coaters with two different tablet shapes.

# 58. THE ROLE OF INTERPARTICLE FORCES IN THE FLOWABILITY FOR GRANULATION PROCESSES

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In granulation processes, from roller compaction to high shear wet granulation, the physical properties of the dry and wet material can influence the granules and final product quality. On the microscale, interparticle forces, such as adhesion and capillary, influence the flowability of a bulk powder. It is expected that the motion of a particle is restricted as interparticle forces increase [1]. The contact area between two particles, or a particle and a surface, directly correlates to the adhesive force between the materials. The primary parameters that affect the contact area and flow of a bulk powder include particle size, particle size distribution, and particle shape. The capillary forces of liquid bridging between particles also affects the particle flow and depends on the level of moisture present.

This work focuses on investigating the effects of particle size, moisture content, and particle shape on the flowability of micro-crystalline cellulose (MCC), measured by the FT4 Powder Rheometer. The raw MCC was sieved into five size fractions and characterized by a Malvern Morphologi G3 particle analyzer for the $d_{43}$ (51 ± 13 µm, 80 ± 30 µm, 109 ± 25 µm, 141 ± 47 µm, 173 ± 59 µm). The powder bulk's moisture levels, resulting from added deionized water, range from 0 – 50 wt%. Using particle size and shape measurements from the particle analyzer, particle size, shape, and moisture content were correlated with the FT4 flowability results. This is the first study, to our knowledge, to quantify the effects of particle shape, size, and moisture content on the flowability of powders in granulation processes.

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# 59. STRUCTURAL AND FUNCTIONAL ANALYSIS OF A NEW CO-PROCESSED TABLETING EXCIPIENT

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The tableting of powders is a process used to convert powdery bulk materials into a suitable form for industry and customer needs, whereat the compact properties of resulting tablets depend on the complex interplay of material, formulation and process parameters. Due to the high number of different materials and property variations, tableting excipients are used in tablet formulation to improve bulkiness, tablet strength, disintegration and dissolution behaviour. The list of excipients covers for example diluents, binders, lubricants and superdisintegrants.

In this work, the cause of the superiority of a newly developed co-processed binder excipient called Salt-Starch is investigated. The component's benefits on the final formulation properties demonstrated, especially its content-dependent effects. For a fundamental understanding of its binding mechanisms, the structure of Salt-Starch is investigated. It is shown that aside from the particle size distribution, the specific structure of the excipient has super-additive effects regarding the resulting tablet strength (tensile strength) compared to sole components NaCl and starch and their binary mixtures, respectively. One reason for the benefit of Salt-Starch in this comparison is the lower elastic recovery, which is quantified by applying a kinetic dependency indicator.

The results pronounce the benefits of Salt-Starch compacted purely and in formulation compared with simple binary mixtures of NaCl and starch regarding the tableting parameters compressibility, compactability and tabletability. The systematic evaluation of compaction results of the individual components with varied particle sizes and of binary mixtures and Salt-Starch enable the derivation of essential rules of structural influence. SEM and µ-CT measurements support the effect of the specific structure of Salt-Starch on the compaction results and clarify tableting behaviour based on the structure resulting from the production process of Salt-Starch. As a further impression, the independency of Salt-Starch of compaction kinetics is presented and discussed to supplement its superiority.

# 60. RECLAMATION OF ALUMINUM AS ALPHA-AL(OH)$_3$ PELLET FROM AQUEOUS SOLUTION VIA FLUIDIZED-BED HOMOGENEOUS CRYSTALLIZATION TECHNOLOGY

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Aluminum is the most widely used non-iron metal that is considered a highly toxic compound in the water. Adsorption and conventional chemical precipitation are commonly used to remove aluminum from water. However, the sludge produced from the chemical precipitation process created a new problem due to its low separability and high cost of the handling process. In this study, fluidized-bed homogeneous crystallization (FBHC) technology was applied to treat 700 mg-Al/L solutions by synthesizing low moisture and high crystallinity particles and reducing the production of excessive sludge. A sedimentation tank was also installed after the effluent stream of FBHC to minimize the level of small particle in the final water discharge. Sodium hydroxide (NaOH) was added as a precipitant to generate Al(OH)$_3$ pellets. Under the optimum condition of pH 9.7, up-flow velocity of 45 m/h, and reflux ratio of 42, the total removal efficiency achieved up 99 % corresponding to the aluminum residual concentration of 0.2 mg-Al/L. The crystalline ratio also reached over 90% meant the sludge generated was decreased over 90% by converting it to crystalline aluminum hydroxide pellets.

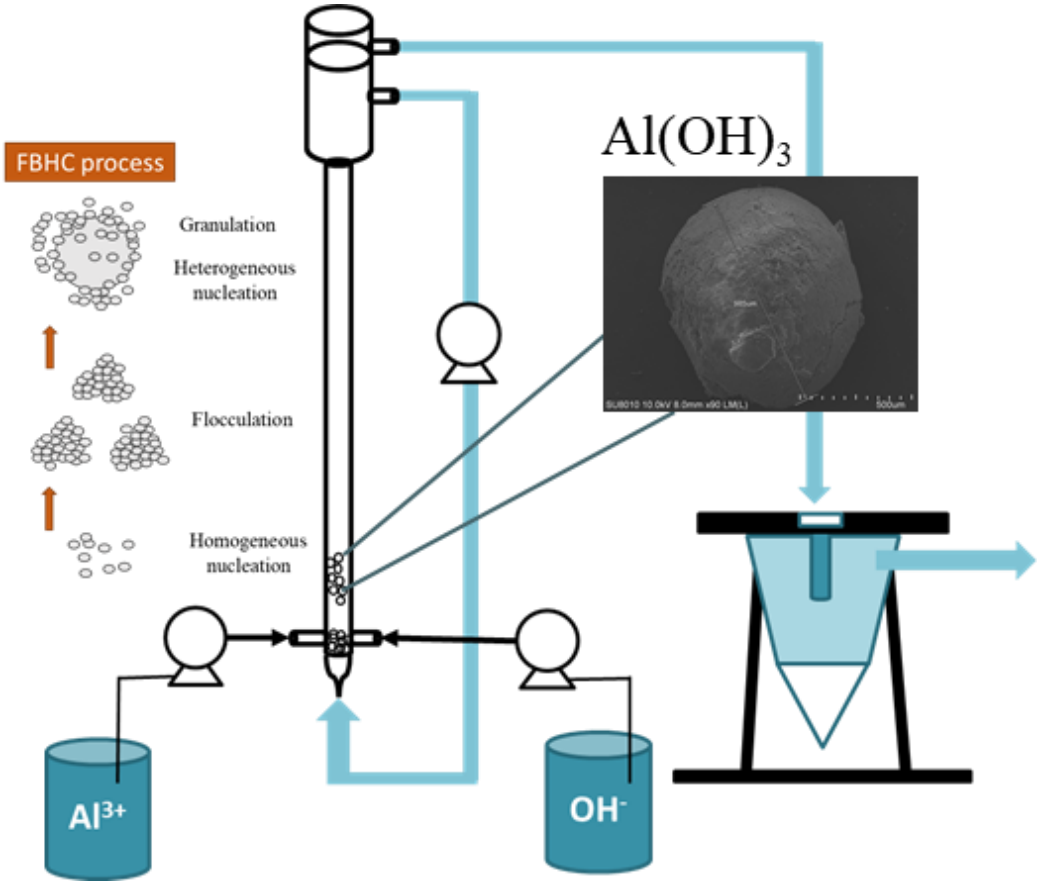


Figure 1. The concept of granulation by fluidized bed homogeneous techmology (FBHC).

# 61. DEVELOPMENT OF AN ACOUSTIC EMISSION TECHNIQUE IN COMBINATION WITH MACHINE LEARNING TO CHARACTERIZE THE PARTICLE SIZE DISTRIBUTION IN SOLID-GAS FLUIDIZED BEDS

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In this work, an acoustic emission (AE) technique in combination with a machine learning (ML) algorithm (Principal Component Analyses) are developed to characterize the particle size distribution in a solid-gas fluidized bed. A theoretical approach to explain the generation of acoustic emission signal in solid-gas flows is explained. An AE signal is generated in gas-solid fluidized beds due to the collisions and friction between fluidized particles as well as between particles and the bed inner walls. The generated AE signal is in the form of an elastic wave with frequencies >100 KHz and it can propagate through the gas-solid mixture. An inversion algorithm to extract information about the particle size starting from the energy of the AE signal is also explained. The development of an AE technique is important because it provides a cheap, sensitive, non-intrusive, radiation-free diagnostic, which is suitable for on-line measurement. Combining AE with machine learning algorithms (ML) is beneficial for applications to industrial settings, reducing the cost of signal post processing, while being able to model both small and large-scale experiments. Experiments were carried out in a pseudo-2D flat fluidized bed with four glass bead samples with different sizes, ranging from 100 µm to 710 µm. AE signals were recorded with sampling frequency 5 MHz. The AE signal post processing and data preparation for ML process are also explained. For the ML process, the AE frequency data sets were divided in training (60%), cross validation (20%) and test sets (20%). Two ensemble ML approaches, namely Random Forest and Gradient Boosting are applied to predict particle sizes based on the AE signal features with an accuracy greater than 99.5% and a R squared score larger than 0.999. Experimental results indicate that the AE technique is a powerful tool for the characterization of solids in solid-gas flows.

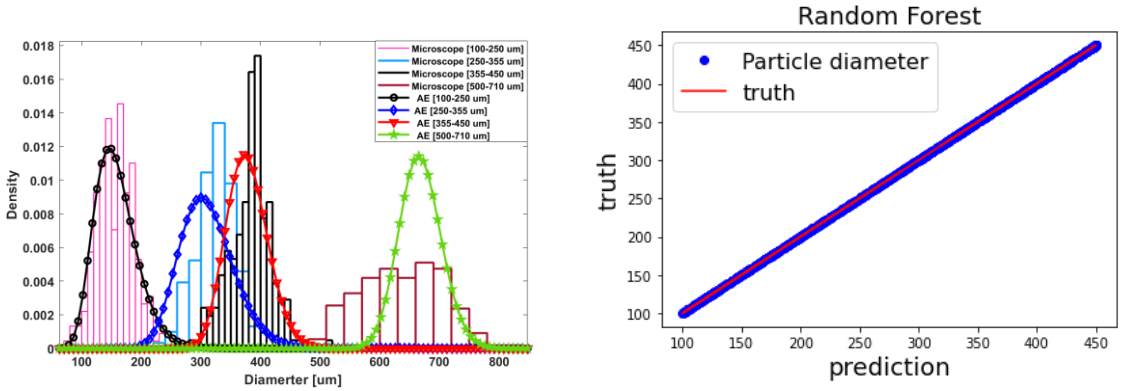


Figure 1. A) Inverted particle size distribution from the measured AE energy, B) Prediction Vs the truth of dataset.

# 62. MICRO SCALE INVESTIGATIONS OF AGGLOMERATION AND DEAGGLOMERATION DUE TO SINGLE COLLISIONS BETWEEN WETTED PARTICLES

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During fluidized bed spray agglomeration wetted particles stick together, resulting in blackberry shaped and porous particles. The extend of agglomeration of the bed material will determine its further transport within the system and the product quality and morphology.

This work aims to provide a fundamental understanding of the micro-mechanisms of agglomeration as well as deagglomeration of particles. To investigate the mechanisms, single particle experiments were performed by means of a newly developed setup to realize binary collisions of two particles under dry and wet conditions. The collisions are recorded by two high-speed cameras, enabling motion analysis in three-dimensional space by methods of digital image analysis. The positions, translational velocity, rotational velocity and orientation of the rotation axis are determined both before and after the collision. In the case of moistened collisions, one particle or both are coated with a homogeneous liquid layer before the collision by using the liquid ring method of Buck et al. [1], which has already been successfully applied in particle-wall collisions. In this case, the thickness of the liquid layer is also determined. The results allow a direct comparison with DEM collision models, both with and without additional liquid phase.

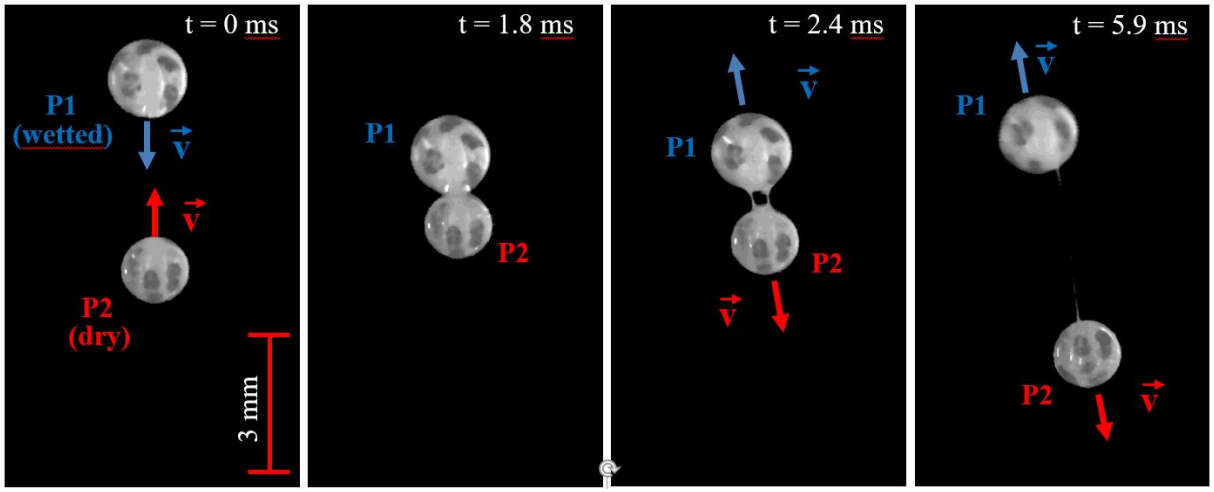


Figure 1. Wetted binary particle collision between two spherical $ZrO_2$ particles with a diameter of 1.5 mm. The upper particle (P1) is wetted with a 116.3 µm thick layer of silicon oil with a kinematic viscosity of $150 \cdot 10^{-6}$ $m^2/s$ at 20°C, while the lower particle (P2) is dry. The white particles are additionally marked with grey markers to track the rotation. They collide with a relative velocity in the normal direction of 1.57 m/s, which results in a complete rebound.

[1] B. Buck, Y. Tang, N. G. Deen, J. A. M. Kuipers, and S. Heinrich, Dynamics of wet particle-wall collisions: influence of wetting condition, Chemical Engineering Research and Design, 135 (2018) 21-29.

# 63. INVESTIGATION OF FLUIDIZATION- AND MIXING BEHAVIOR OF NANO- AND MICRON PARTICLES IN A VIBRATED FLUIDIZED BED WITH PULSATED GAS FLOW

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All-Solid-State-Batteries (ASSBs) are set to provide high energy densities along with a safer energy storage medium than conventional batteries, which could become crucial in the electrification of transport systems. One of the main challenges of ASSBs is the upscaling of the production process [1]. To that end, the use of a vibrating fluidized bed is proposed for the mixing, coating and aggregation of the battery materials. Thus, the fluidization and mixing behaviour of lithium iron phosphate (LFP), carbon black (CB) and sodium chloride (SC) is investigated in a vibrated fluidized bed with pulsated gas flow. SC is used as a model material for solid electrolytes, which often react with moisture. The vibration was realized through the rotation of an eccentric plate (Fig. 1A) whose movement is translated into a linear shaft onto which the fluidized bed is mounted, while the pulsated gas flow was implemented via solenoid valves. First, the mixing and fluidization qualities of the bed material were evaluated. Second, a parametric study including vibration parameters, pulsated gas flow parameters and pre-conditioning of the particles via drying or sieving was explored. The success of the hetero-agglomerate and aggregate production was determined by SEM and TEM images (Fig. 1D) in conjunction with particle size measurements. Additionally, the macroscopic electrical powder conductivity was measured via a four-point probe method using an Ohmmeter and a material testing machine.

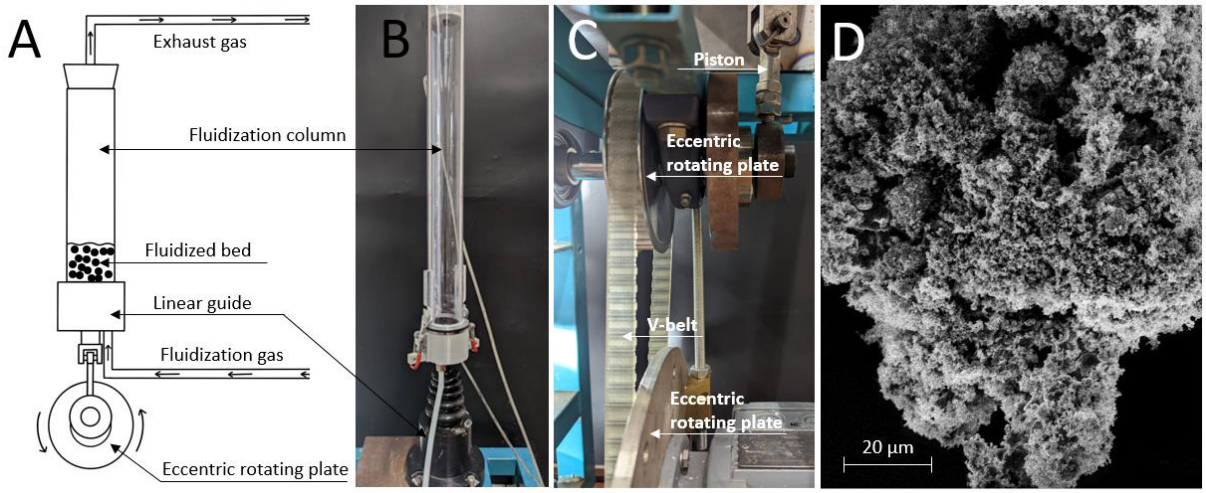


Figure 1. Schematic of a vibrated fluidized bed (A) Upper part of fluidized bed (B) Motorized v-belt system for translation of vibration frequency (C) and an SEM image of LFP coated with CB obtained by fluidization (D).

[1] J. Schnell, T.Günther, T. Knoche, C. Vieider, L. Löhler, A. Just, M. Keller, S. Passerini, G. Reinhart, All solid stat Lithium-Ion and Lithium Metal Batteries - Paving the Way to Large-Scale-Production, J. Power Sources. 382 (2018), 160-175.

# 64. MULTIVARIATE ANALYSIS AND PROCESS OPTIMIZATION OF MECHANOCHEMICAL SYNTHESIS USING TWIN SCREW EXTRUSION: PRODUCTION 4,4 BI-PYRIDINE BASED MOF

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The process optimization of 4,4-bipyridine based metal organic framework (MOF) synthesis by twin screw extrusion (TSE) has been investigated using cobalt nitrate hexahydrate (Co(NO3)2·6H2O) as a metal precursor with molar ratio 1:1, the reported ratio to form a 1-dimensional MOF. Multivariate analysis (MVA) was employed to investigate the effects of twin screw extruder (TSE) operating parameter's including amount of solvent added (L/S ratio), screw speed and feeding rate on the product composition. Partial least square (PLS) analysis has been applied as a robust chemometric approach to obtain a predictive model from the collected Raman data that are able to quantify the composition of the MOF product. Based on the results from the best predictive model obtained, a maximum MOF purity percentage of 86.91 %wt. has been obtained at 0.5 L/S, a feeding rate of 50 g/h and a 100 rpm of screw speed.

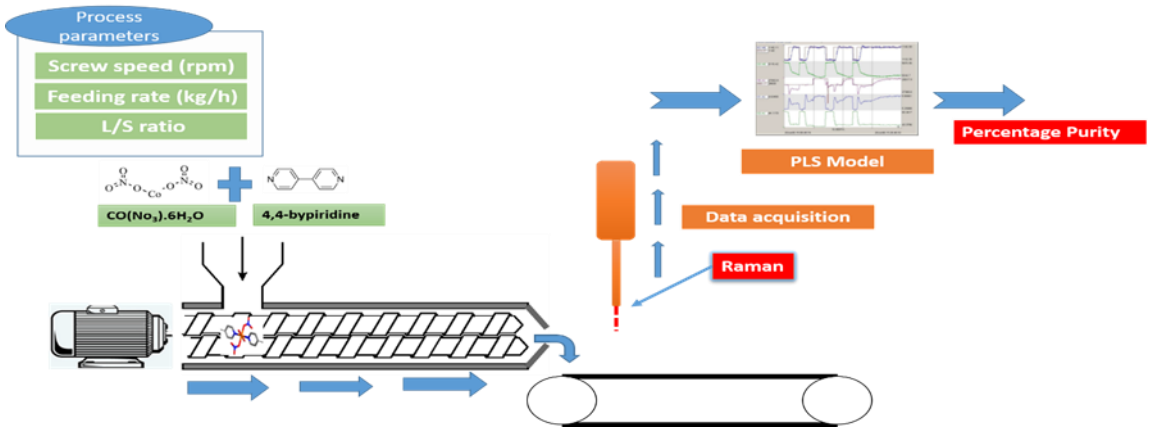


Figure1. Equipment set-up, process parameters and process tools for measuring the purity of the MOF

# 65. MECHANISMS OF RIBBON SPLIT IN ROLLER COMPACTION

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Dry granulation, which includes compaction and grinding, is an economical process to improve the flowability of heat- and moisture-sensitive powders. Roller compaction enables a continuous process of powder compaction between two counter-rotating rollers, resulting in the formation of ribbons. Subsequently, these ribbons are comminuted by rotating or oscillating screen mills into granules of any desired size.

After compaction, the ribbons often split into different parts. Common is the transversal split, where the ribbons split to follow both rollers, as presented in figure. In the literature, this behavior is usually attributed to adhesion to the roller surface. In order to gain a deeper understanding of the ribbon split, DEM (discrete element method) simulations were performed in this study. For this, the open-source MUSEN framework was utilized, which supports GPU-accelerated computations, enabling simulations with a large number of particles. In addition, MUSEN allows the analysis of cohesive and frictional effects within the bulk material. Hence, an elastoplastic Edinburgh contact model [1] was used and calibrated by compaction tests and shear tests to suit experimental data.

Finally, by analyzing the simulations of the roller compaction process, a horizontal stress gradient was found in the region of the smallest gap. This gradient results in shearing and weakening of the ribbon material in the center between the rollers. Besides the transversal split, as in Fig. 1, a longitudinal split may occur in this process, too. Here the ribbon does not follow the rollers but splits instead towards the sealing plates. This behavior has also been related to a stress profile in the smallest gap but acting perpendicular to the plan of the figure below.

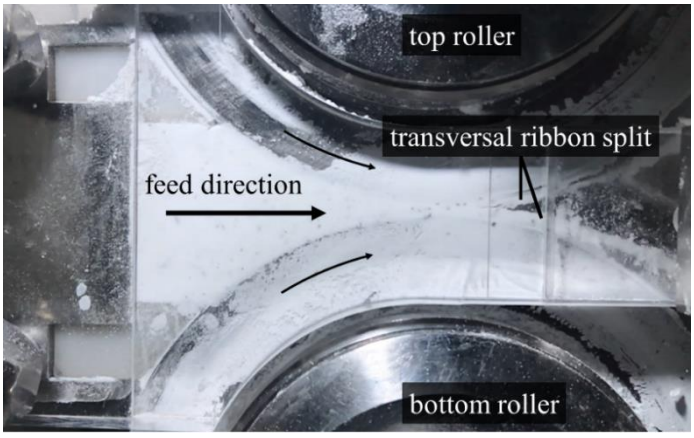


Figure 1. Insides of roller compactor WP120 by Alexanderwerk AG during production with smooth roller surface.

[1] S.C. Thakur, J.P. Morrissey, J. Sun, J.F. Chen, J.Y. Ooi, Micromechanical analysis of cohesive granular materials using the discrete element method with an adhesive elasto-plastic contact model, Granular Matter. 16 (2014) 383–400.

# 66. PARTICLE AGGLOMERATION VIA RESONANT ACOUSTIC MIXER FOR DRY POWDER INHALATION

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2 Key Laboratory for Carbonaceous Wastes Processing and Process Intensification Research of Zhejiang Province, University of Nottingham Ningbo China, Ningbo 315100, People's Republic of China
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Utilizing the cohesiveness of fine particles is a versatile way to prepare agglomerate formulation for efficient pulmonary delivery. Vibration process is often applied to facilitate the formation of particles used in agglomerate formulation to achieve appropriate particle size distribution and mechanical strength, which can significantly influence the metering dose and aerodynamic performance of the final product [1].

In this work, the feasibility of resonance acoustic process for agglomerate formulation preparation was investigated [2]. The effect of vibration intensity and grid pattern was studied. The effect on particle size distribution and aerodynamic performance due to interparticle collision was evaluated by applying different levels of acceleration force and a chessboard-like grid in the mixing process. It was found that the existence of the grid significantly affected the particle size distribution, and subsequently the metering dose in Turbuhaler®. Acceleration significantly affected the tapped density and mechanical strength of agglomerates resulting in different fine particle fraction (FPF). The novel particle agglomeration method can improve the agglomerates production efficiency by utilizing the volume of the mixer to induce more particle collision instead of conventional rotation method with finite vibration areas.

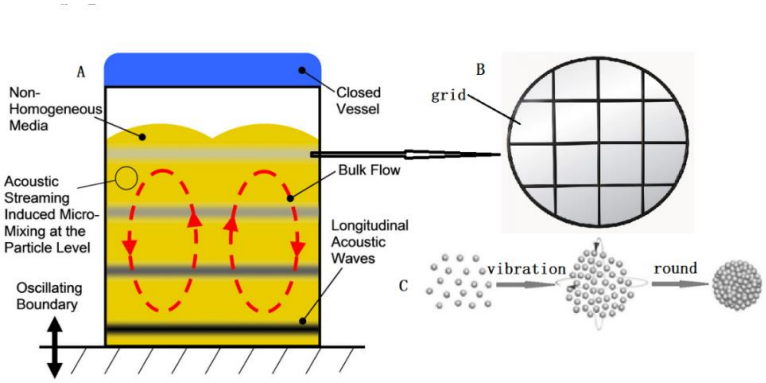


Figure 1. Particle agglomeration with resonant acoustic mixer, A represent the resonant acoustic mixer, B is the grid in the mixer, C shows the brief process of particle agglomeration [2]

[1] Etschmann, Christian, and Regina Scherließ. "Formulation of rifampicin softpellets for high dose delivery to the lungs with a novel high dose dry powder inhaler." International journal of pharmaceutics vol. 617 (2022): 121606

[2] Juan G. Osorio, Fernando J. Muzzio, Evaluation of resonant acoustic mixing performance, Powder Technology, 278(2015), 46-56,

# 67. VIRTUAL PROTOTYPING OF WET GRANULATION PROCESSES

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Wet granulation is a multiphase process utilized to produce aggregate particles with defined properties from very fine powders. Industrial approaches to wet granulation are mainly carried out by batch processes (rotating drum, tumblers) on a basis of quality by testing. Recently, a growing interest to improve the manufacturing sites changed the paradigms to continuous processes (twin-screw, fluidized bed, extrusion) in a quality by design (QbD) approach [1] which can provide variable throughput, consistent quality and reduced operator involvement [2]. However, a QbD approach process is challenging, especially in the pharmaceutical and bio-pharmaceutical sector critical where quality attributes are stringent and numerous [3]. Empirical methods for process optimization are still predominant and yet the field is lacking a comprehensive computer model to predict wet granulation processes. Simulating these processes on the microscale using discrete particle methods (DPM) is challenging because of the large number of particles involved, which differ widely in both size and material properties. Macroscale methods, tracking only the particle bulk properties, are efficient but do not resolve disperse particle properties such as the particle size distribution (PSD), which is key information for downstream processing. Multiscale methods like population balance modeling (PBM) can track distributed properties, such as the particle size, by adding them as internal variables to the macroscale (CFD) model but they do lack information on particle dynamics. A promising solution to address these deficiencies is to develop a comprehensive DPM–PBM–CFD heterogeneous multiscale model [4] which allows exploration of virtual design spaces, see Figure 1. The DPM micro-model will run in a certain parameter space and provide particle dynamics data for the PBM macro-model to derive mechanistic kernels for macroscale simulations. New microscopic simulations are only necessary, when the parameter space has to be expanded. Constitutive modeling, utilizing the insights of this framework, can help to develop an application-specific PBM for design optimizations and enable transitioning from real to virtual prototyping of wet granulation processes.

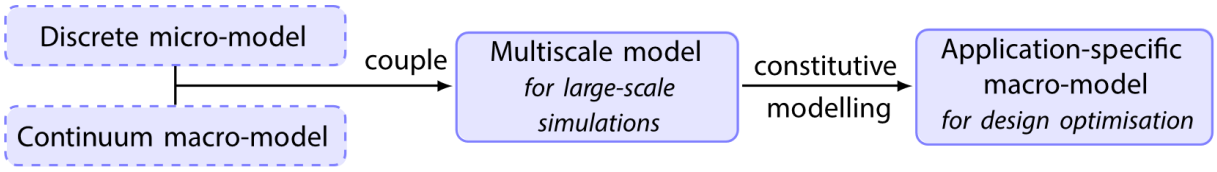


Figure 1. Modeling framework for the virtual prototyping of wet granulation processes

[1] J. Rantanen, J. Khinast, The Future of Pharmaceutical Manufacturing Sciences, J. Pharm. Sci. 104 (2015) 3612–3638.

[2] A. Kumar, K. V. Gernaey, T. De Beer, I. Nopens, Model-based analysis of high shear wet granulation from batch to continuous processes in pharmaceutical production - A critical review, Eur. J. Pharm. Biopharm. 85 (2013) 814–832.

[3] P. Suresh, I. Sreedhar, R. Vaidhiswaran, A. Venugopal, A comprehensive review on process and engineering aspects of pharmaceutical wet granulation, Chem. Eng. J. 328 (2017) 785–815.

[4] Weinan, E.; Engquist, B. The Heterognous Multiscale Methods. Commun. Math. Sci. 2003, 1, 87–132.

# 68. INFLUENCE OF REFILLING ON DOSING ACCURACY OF LOSS-IN-WEIGHT POWDERS FEEDER IN CONTINUOUS MANUFACTURING

MSc. Fabiola N. Santamaría Alvarez[1], Univ.- Prof. Dr. Dr. h.c. Peter Kleinebudde[2] & Dr. Jochen Thies[1]

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Continuous manufacturing is nowadays a novel concept to produce high quality drug products. The manufacture of solid dosage forms starts with the feeding of materials, which is a critical step to ensure the quality of the final product [1]. Therefore, loss in weight (LIW feeder) have been developed by various equipment manufacturers to ensure the accurate dosage that allows obtaining products in compliance with the specifications. As the feed hopper is of limited capacity, it must be refilled on regular basis to maintain continuous manufacturing. During refilling, dosing must be done in volumetric mode which can have an impact on dosing accuracy.

The present work studies the impact of the refill and the different factors such as the feed rate, the refill system and the filling level at which the refill starts on the accuracy of the dose. Four performance indicators were used to evaluate this impact: the refilling time, the time out of the limits, the Maximum or minimum feed rate during the refilling and the total deviation from the set point.

It was found that the refiller type and the filling level at which the refill starts plays an important role and should be selected considering to the material´s characteristics to be fed. As a general rule a faster and shorter refill is always preferable, however, depending on the refiller and the material a positive or negative deviation from the feeding dose can be observed.

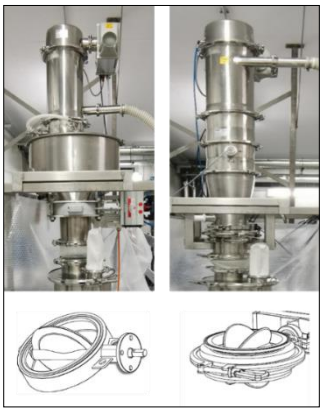

Figure 1. Refillers: TT-refiller (left), G-refiller (right).

[1] Blackshields, C., & Crean, A. (2017). Continuous powder feeding for pharmaceutical solid dosage form manufacture: a short review. Pharmaceutical Development and Technology, 23(6), 554–560.

# 69. TAKING A MECHANISTIC APPROACH TO UNDERSTANDING THE EFFECT OF AGITATION ON UNDESIRED AGGLOMERATION IN AN AGITATED FILTER DRYER

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2 Chemical Development, Pharmaceutical Technology & Development, Operations, AstraZeneca, Macclesfield, UK
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Agitated filter dryers (AFDs) are increasingly used in the pharmaceutical industry due to their combined filtration and drying operations which minimise product loss and exposure to workers, occupy *minimal* floor space and give s*hort* overall cycle times. Using an agitator enhances mass and heat transfer during drying and allows for more homogeneous mixing. However, the use of highly agitated drying conditions can lead to particle agglomeration [1]. This undesired agglomeration can cause issues in the manufacturing process and lead to out of specification products which need further milling, as well as unfavourably long cycle times.

The exact causes and mechanisms underlying agglomeration during drying in AFDs is not yet fully understood. This work aims to bridge these gaps by applying existing knowledge of wet granulation processes by investigating the effect of agitation on agglomeration whilst isolating the drying component. Drying in AFDs involves not only agitation of the wet cake but also heating which can contribute to the formation of solid bridges, leading to agglomerate formation. By isolating the effect of agitation rate in the dryer, the correlation between this and agglomeration can be determined. In this work, the effect of varying agitation periods in a lab-scale agitated vessel are presented and the relationship between agitation time and measured attrition and agglomeration are investigated.

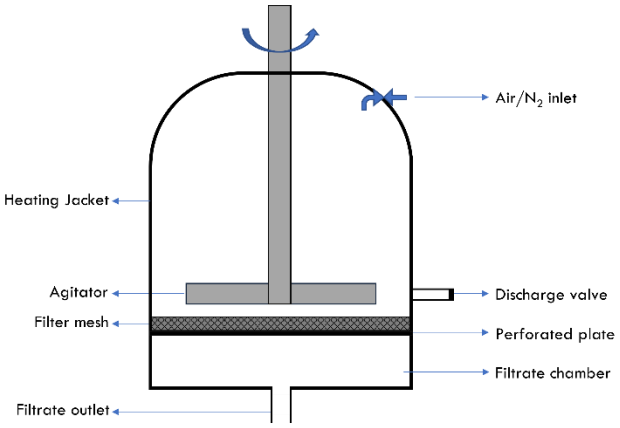


Figure 1. Cross-sectional representation of an AFD.

[1] A. Tamrakar, A. Gunadi, P. M. Piccione, R. Ramachandran, Dynamic agglomeration profiling during the drying phase in an agitated filter dyer: Parametric investigation and regime map studies, Powder Technology, 303 (2016) 109–123.

# 70. PROCESS FOR SPRAY FOAMING OF A POLYMER - SURFACTANT SOLUTION BY USE OF A TWO-FLUID NOZZLE TO CREATE A CONTINOUS COATING

Björn Düsenberg[1], Heike Kreuder[2], Lothar Seidemann[2], Frank Kleine Jäger[2] & Andreas Bück[1]

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Coating processes can be divided into wet coating, e.g. spray coating in a fluidized bed, and dry coating processes, where nanoparticles are deposited on the host particle surface due to a mixing process. The difference is, that spray coating achieves a continuous coating, while in a dry process the coating is formed by discrete particles. The advantage of dry coating, however, is that no downstream drying process is required. Coating by means of foam represents a combination of both methods, in which a likewise continuous coating can be produced, but the amount of liquid to be dried is significantly less than that of spray coating.

In this work, a method to create foams via a two-fluid nozzle is established and it is proven, to coat particles using the produced foam. To achieve this goal, a formulation consisting of water, a polymer and a surfactant is used. Process parameters, such as liquid volume flow and gas volume flow, are varied to evaluate the parameters influence on the foam. Subsequently the foam is used to coat cellulose particles by dye them with methylene-blue within an all-purpose mixer. The foams are analysed in term of stability over the time and bubble diameter. The coating is analysed by image analysis and microscopy.

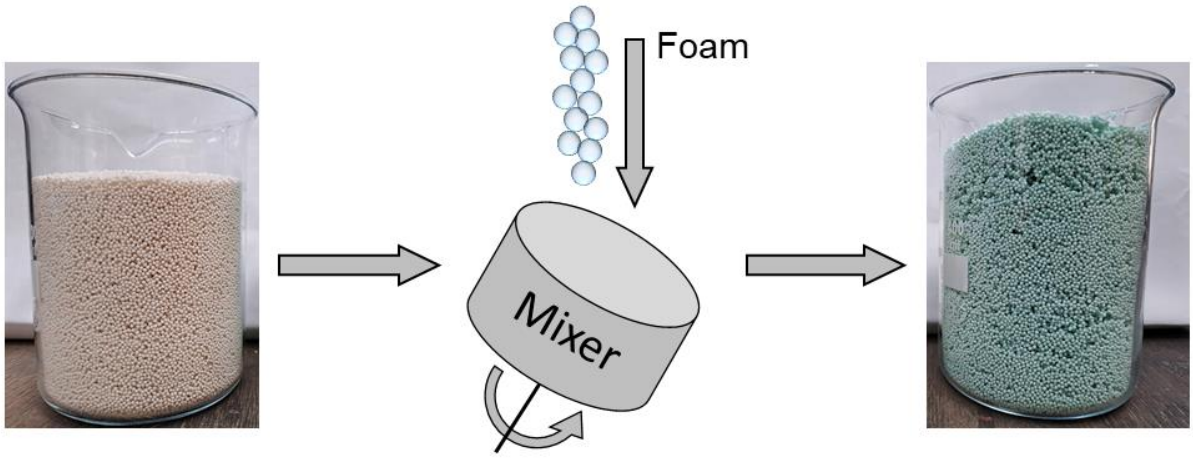


Figure 1. Foam coating of cellulose pellets

# 71. INDUSTRIAL CASE STUDY ON APPLICATION OF ROLLER COMPACTION MODELLING FOR SCALE UP AND TECH TRANSFER.

Lorenzo Poloni[1], Martin Lubej[1], Arnesh Palanisamy[1] & Bindhu Gururajan[1,2]

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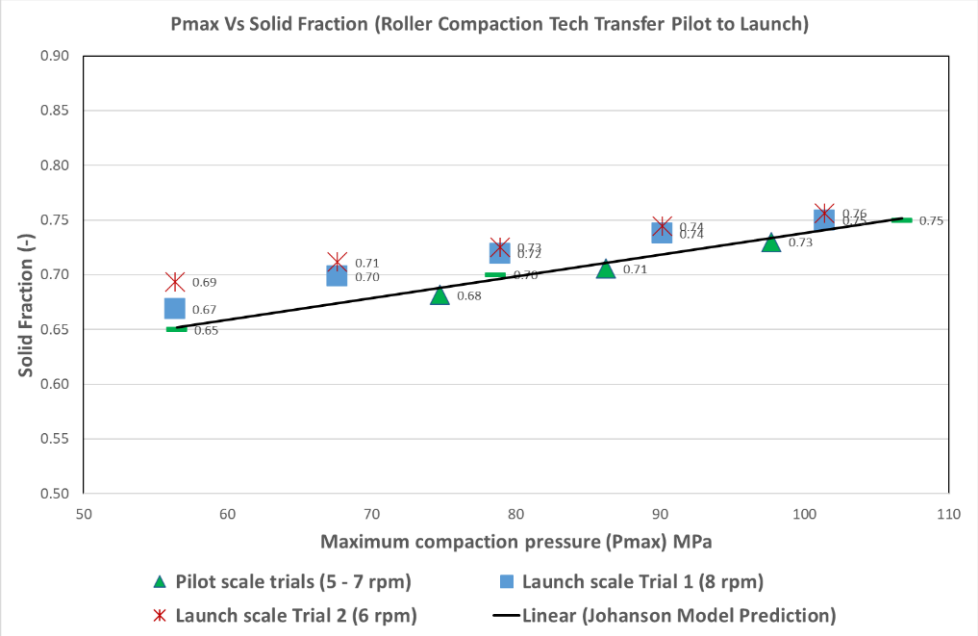
Dry granulation of pharmaceutical powders by the roller compaction process is gaining increasing popularity in the pharmaceutical industry for its simplicity, cost, potential stability benefits and continuous processing options. It offers unique advantages compared with wet granulation for processing physically or chemically moisture-sensitive materials, since the use of a liquid binder is not required. Another advantage is that it does not require a drying stage and therefore it is suitable for compounds that either have a low melting point or degrade rapidly upon heating [1,2]. Due to the limited availability of drug substances for initial granulation studies, it is important to devise methods to overcome this issue and establish robust processes. The industrial application of the Johanson model [1,2,3] for the tech transfer and scale up of experimental drug product formulation A from pilot plant to commercial site is presented in this work. The impact of the calculated pressure between the rolls (Pmax) on the ribbon porosity measured using Geopyc was investigated. The relationship between Pmax and the ribbon porosity in the pilot phase (Bepex with roll width 3 cm) was used to predict the roller compaction force range at the commercial scale (Bepex with roll width 5 cm). The approach permitted the production of tablets at commercial scale with the same quality as the pilot scale and the satisfaction of all the in-process control specifications with no tablet defects.




Scale up and tech transfer of roller compaction process - Pressure (Pmax) vs Solid Fraction.

[1] J R Johanson, 1965, ASME, Journal of Applied Mechanics Series E, 32 (4), 842–848.

[2] Bindhumadhavan, G., Seville, J.P.K., Adams, M., Greenwood, R. and Fitzpatrick, S., Roll compaction of a pharmaceutical excipient - Experimental validation of rolling theory of granular solids, Chemical Engineering Science, Volume 60, Issue 14, July 2005, pp. 3891-3897.

# 72. DRUM COATING OF NON-SPHERICAL TABLETS: SIMULATIONS AND EXPERIMENTAL STUDIES OF INTRA- AND INTER-PARTICLE LAYER THICKNESS DISTRIBUTION

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Coating of tablets is an essential process in the pharmaceutical industry. Tablet coating is often performed in rotary drums using single or multiple spray nozzles. In this process, the solid-containing droplets (coating material) are sprayed onto a bed of moving tablets. The liquid evaporates, generating an increasing coating layer on the tablet surface over time. The thickness of the coating layer of tablets depends on droplet characteristics, the geometry of the tablet, and operation parameters of the drum. The coating layer thickness distribution on individual tablets and across all tablets has a major influence on the subsequent product properties.

In order to predict the coating thickness distribution of non-spherical tablets, numerical simulation of the entire tablet coating process is preferred over the time-consuming experiments. Here, a discrete stochastic Monte Carlo model has been developed incorporating tablet coating sub-mechanisms such as droplet-tablet interaction, droplet deposition or rebound, droplet drying, film formation, and film drying (schematic workflow is shown in Fig. 1). Parameterization of sub-models is performed using recent experimental results [1]. Simulation results of intra- and inter-particle coating layer thickness distribution are compared to own measurements, giving insight on the complex interplay between material properties and process conditions.

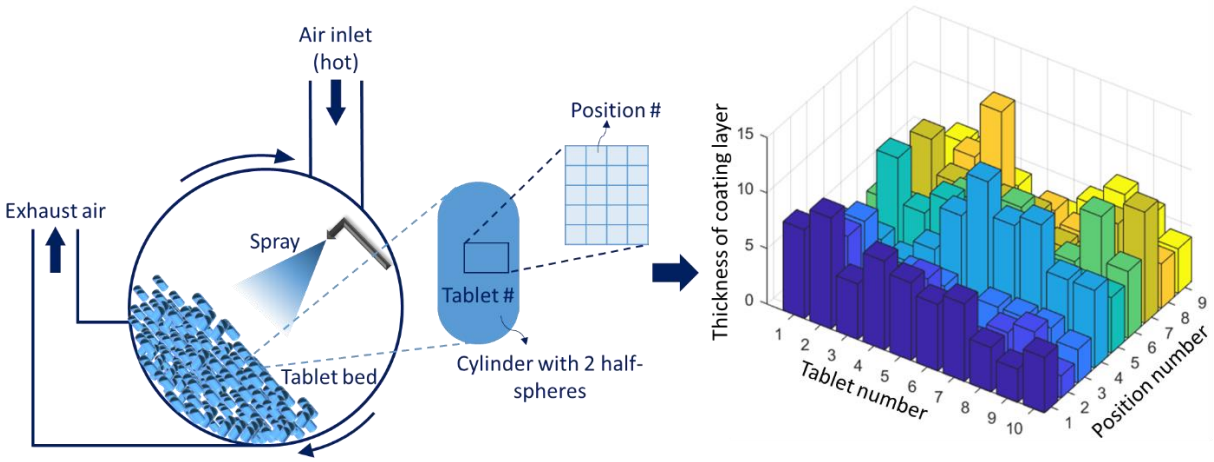


Figure 1. A schematic diagram for analyzing the tablet coating thickness.

[1] L. Pasternak, M. Sommerfeld, P. Muramulla, F. L. Yuan, S. Gopireddy, N. Urbanetz, T. Profitlich, Tablet coating in lab-scale drum coaters: Combining DEM simulations and spray experiments to predict tablet coating, Powder Technology, (2022) [in revision].

# 73. TRANSFORMATIONAL CONICAL MILL SCREEN DESIGN: A PARADIGM SHIFT IN SCALABLE ORAL SOLID DOSAGE POWDER SIZE REDUCTION

Wilf Sanguesa[1] & Yang Su[2]

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Conical milling is a granule size reduction/calibration technique commonly used in the pharmaceutical industry. The primary goal for a mill is to increase surface area and thus improve bulk density, powder flow and tablet compressibility properties of oral solid dosage (OSD) formulations [1].

Some of the disadvantages of a milling process are the potential generation of unwanted heat, wide particle size distribution (PSD) curves and too many fines [2]. The avoidance of heat generation is particularly challenging when the starting material has a low melting or glass transition temperature. Since heat can lead to screen blinding or smearing, particular attention needs to be paid to the profile of the calibrating screens being utilized.

In this Study, the behaviour of dry particles in a conical mill equipped with a new "high efficiency" conical screen-hole design was simulated using computation fluid dynamics (CFD). The mass flow and velocity of the particles was then compared to empirical data derived from experimental DoE results using various products with differing material properties. It was found that the new screen-hole pattern design reduced milling temperatures while increasing capacities when compared to traditional screen designs; without changing or shifting particle size distributions, thus ensuring validated processes and results remain unaffected.

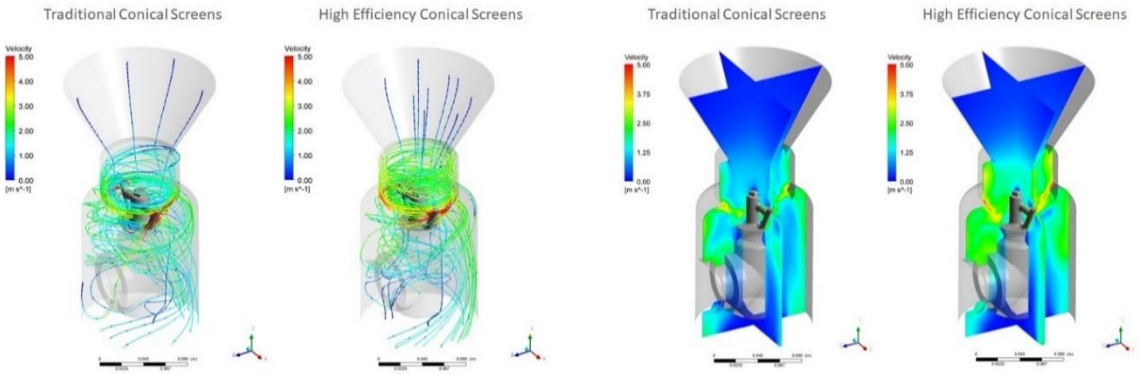


Figure 1. Air Flow (left) and Mass Flow (right) Across Traditional vs. New Hole

[1] R.P. Patel, A.H. Baria, N.A. Patel, An Overview of Size Reduction Technologies in the Field of Pharmaceutical Manufacturing. Dep of Pharmaceutics, College of Pharma. Ed. and Res., India; 2(4) (2008) 216-220

[2] S. Sunil, Jambhekar, Bioavailability and Granule Properties, South University School of Pharmacy, Savannah, GA, USA; Handbook of Pharmaceutical Technology, Chapter 19; Taylor and Francis (2005)

# 74. FLUIDISED BED GRANULATION – ADVANCED PROCESS CONTROL FOR CONSISTENT PRODUCT QUALITY

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2 Innopharma Technology, Dublin, Ireland.
3 Pharmaceutical Manufacturing Technology Centre, Bernal Institute, University of Limerick, Limerick, Ireland.
4 Solid State Pharmaceutical Centre, Bernal Institute, University of Limerick, Limerick, Ireland
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Active pharmaceutical ingredients (APIs) exhibit poor flow characteristics thereby hindering the efficient manufacture of oral solid dosage forms (OSDs). As a result, intermediate processing steps such as wet granulation via fluidised bed granulation (FBG) have become standard practice in the manufacturing cascade for OSDs. Given the complexity of the FBG process, the industry approach has been largely recipe driven, resulting in a black box type of approach during operation of FBG.

In the current research, we present an advanced process control strategy by feeding data from associated PAT tools and sensors into semi-mechanistic models in real time, which serve as basis for the process control & automation module of the SmartX platform – a process control and data analytics software. In doing so, the moisture content is predicted in real time whilst the fluidisation airflow is controlled for consistent powder bed fluidisation during live FBG runs. As a result, common issues, which have otherwise led to product failure are mitigated.

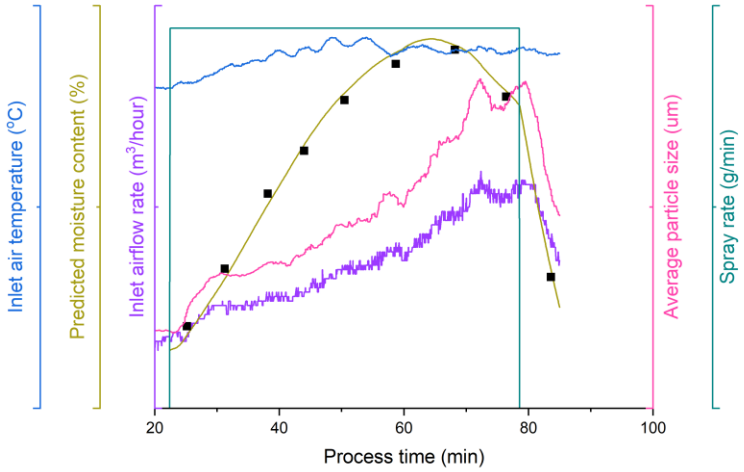


Figure 1. Real time prediction of powder bed moisture content and dynamic control of fluidisation air flow rate during fluidised bed granulation. Black points represent the measured moisture content

# 75. DESIGN AND EVALUATION OF STERCULIA TRAGACANTHA AS A RELEASE MODIFIER IN THEOPHYLINE SUSTAINED RELEASE TABLET FORMULATION

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The investigation of indigenous plants as possible sources of pharmaceutical excipients has seen quite a surge in recent times with hydrophilic polymers being preferred for their cost friendliness, good drug release profile and biocompatibility. This research was aimed at the design and formulation of sustained release tablets using a locally sourced gum from a plant against commercially available polymers usually employed as drug release modifier in drug production.

The gum powder of the leaves of *Sterculia tragacantha* (STG) was extracted, characterized and compared against tragacanth gum (TG) and hydroxypropyl methylcellulose (HPMC) in a sustained release theophylline tablet formulation via wet granulation. Tablets were evaluated for hardness, friability, thickness, content uniformity. Swelling behaviour in three media – distilled water, phosphate buffer (pH 7.4) and 0.1N HCl, drug-polymer compatibility using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared (FTIR) spectroscopy and *in vitro* drug release profile in simulated intestinal fluid (SIF) and simulated gastric fluid (SGF) for 12 hours were studied.

The extracted gum powder showed 82.25% carbohydrate composition, 2.52% moisture content, viscosity 8.0275mPaS (25 $^{o}$C), pH 7.61, water holding capacity 11.5 g/g of water, Hausner's Ratio (HR) 1.589 and Carr's Index (CI) 37.080. The STG tablet granules showed excellent flow comparable to HPMC and TG with granule density 1.35, porosity 71.51%, HR
1.11 and CI 10.26. Drug-polymer compatibility was also confirmed. At 20% tablet composition, physical evaluation of formulated tablets showed characteristics mainly within acceptable limits, tensile strength 1.142 ± 0.069 and porosity 10.770. Swelling studies in distilled water and acidic medium presented a behaviour similar to TG showing minimal erosion up to the 8$^{th}$ hour. In the phosphate medium, STG compared favourably with HPMC but erosion was observed after the fifth hour. In SGF, percentage release of theophylline was 61.1, 55, 66% and 70.8, 67.7, 72.5% in SIF at the 12$^{th}$ hour for HPMC, TG and STG respectively against an almost 100% release from a commercial brand of sustained release theophylline tablet. Release kinetics in SIF followed a Korsemeyer Peppas model indicating drug release was by diffusion and erosion and in SGF a zero-order model indicating release by diffusion. The results showed satisfactory potential of *S. tragacantha* leaf gum as a substitute release retarding agent in matrix tablet formulations.

# 76. INFLUENCE OF DRYING TECHNIQUE ON STRUCTURAL PARAMETERS AND LIPID OXIDATION STABILITY OF PLANT-BASED MILK POWDERS

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Dried emulsions such as milk powders have been widely used for decades across multiple categories and applications, from infant formula to milk chocolate. In recent years, environmental, health and animal welfare concerns have strongly increased the demand for plant-based milk alternatives, and with it the interest in plant-based milk powders [1]. In milk powder substitutes, milk fat, protein and carbohydrates are replaced by plant-based counterparts to form a milk-like emulsion with consecutive drying, aiming to achieve similar nutritional and organoleptic properties compared to dairy milk [2]. In order to achieve the long shelf-life required for milk powder substitutes, present lipids and proteins need to be protected in the powder matrix against oxidation by environmental oxygen.

Particle structure is considered a crucial impact factor for shelf stability of dried emulsions. Changes in surface to volume ratio, size and porosity of dried emulsion particles influence the access of oxygen towards encapsulated oil droplets as well as the amount of non-encapsulated, unprotected fat (free fat). Furthermore, vacuole size inside spray dried particles determines the amount of entrapped air available for lipid oxidation [3]. Drying methods such as spray- or freeze drying and structuration techniques like spray granulation are established methods to alter particle structure.

The present work investigates and compares the influence of different particle structures created by different drying and structuration techniques such as spray and freeze drying on lipid oxidation of dried emulsions stabilized by plant protein. Results show differences for particle morphology, encapsulation efficiency (ratio of encapsulated to non-encapsulated fat) and oxidation stability for powders produced with various drying and structuration techniques. The obtained data reinforces the significance of particle structure for the production of shelf stable powders.

[1] S.K. Vanga, V. Raghavan, How well do plant based alternatives fare nutritionally compared to cow's milk? J. Food Sci. Technol. 55 (2018) 10–20.

[2] C.Vega, Y.H. Roos, Invited Review: Spray-Dried Dairy and Dairy-Like Emulsions—Compositional Considerations, J. Dairy Sci. 89 (2006) 383–401.

[3] K. Haas, J. Obernberger, E. Zehetner, A. Kiesslich, M. Volkert, H. Jaeger, Impact of powder particle structure on the oxidation stability and color of encapsulated crystalline and emulsified carotenoids in carrot concentrate powders, Journal of Food Engineering 263 (2019) 398–408.

# 77. STATIC AND DYNAMIC VAPOR SORPTION OF HYDROPHOPIC STARCH ESTER POWDERS AND CORRESPONDING TABLETS

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Hydrophobic starch esters have demonstrated high potential as matrix formers in controlled-release drug delivery systems [1]. The mechanical properties and tableting performance of native starch (SN), starch acetate (SA) and starch propionate (SP) have been reported in a previous work [2].

In the present work tablets of the SN, SA and SP starch grades were prepared using 6 mm diameter round flat-face punches by direct compression at low (120 MPa) or high (174 MPa) compression pressure. Changes of tablet weight and of the corresponding uncompacted powders, as well as changes of the axial tablet expansion were followed with relative humidity (RH) under static and dynamic mode of vapor sorption. Static sorption measurements were made by placing the tablets or powders in desiccators over saturated salt solutions, whereas dynamic vapor sorption was performed using an in-house developed device previously described [3]. Vapor sorption effects on tablet tensile strength were studied at different RH levels between 0% and 85%. Furthermore, molecular changes in the starch structure due to moisture sorption were followed by recording Raman spectra.

It was found that SP and SA tablets and uncompacted powders exhibited lower weight increase (Δw) compared to SN. Tablets of SA grade exhibited the lowest increase. For SA and SP tablets, vapor sorption showed differences with the compression pressure. SA and SP tablets prepared at 174 MPa showed greater Δw compared to those compressed at 120 MPa. On the other hand, vapor sorption by the SN tablets was unaffected by the compression pressure. Finally, there was no indications of any effect of vapor sorption on tablet strength and the chemical structure of the studied starch grades.

[1] N. Sakhnini, N. Al-Zoubi, G.H. Al-Obaidi & A. Ardakani, Sustained release matrix tablets prepared from cospray dried mixtures with starch hydrophobic esters. Die Pharmazie 70 (2015) 177-182.

[2] N. Al-Zoubi, A. Ardakani, F. Odeh, N. Sakhnini, I. Partheniadis & I. Nikolakakis, Mechanical properties of starch esters at particle and compact level - Comparisons and exploration of the applicability of Hiestand's equation to predict tablet strength European Journal of Pharmaceutical Sciences 147 (2020) 105292.

[3] I. Partheniadis, D. Kopanelou, M. Gamlen & I. Nikolakakis, Monitoring the weight and dimensional expansion of pyridostigmine bromide tablets under dynamic vapor sorption and impact of deliquescence on tablet strength and drug release. International Journal of Pharmaceutics 609 (2021) 121150.

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# 78. GRANULATION OF FLY ASH RESOURCES FOR WASTE UTILIZATION AND MATERIAL RECYCLING – A REVIEW

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In this review, the granulation process was described for the utilization of industrial waste called fly ash. Granulated fly ash of coal incineration was used i.e., for the production of cement and cement mortar. The addition of granules had an effect on drawing out of setting time, as well the hardening of mortar. The compressive strength and flexural strength of the mortar with the addition of phosphogypsum were comparable to the mortars made from standard cement mixtures. The waste phosphogypsum contained in the granules can replace the natural gypsum commonly used in the cement industry.

Other results showed, the granules from the coal fly ash had a satisfy mechanical properties, when made under the specific technological conditions, such as: grain fraction, material humidity, type and binder share, disc pelletizer tilting angle, and curing time. Depending on the ash type from incineration, it should be mixed with binders and water-spray should be added during the mixing. The disc granulator parameters, such as the rotational speed and the inclination angle of disc, were also important. The final mechanical strength of the granules was attained by curing from several hours to several dozen days.

Concluding, the granulation process of waste remains as a model for meeting the goals of circular economy – it completely meets the requirements for sustainable development of the environment. The fly ash granules were fully utilized thanks to the harmful substances reduction, and the material recycling as well.

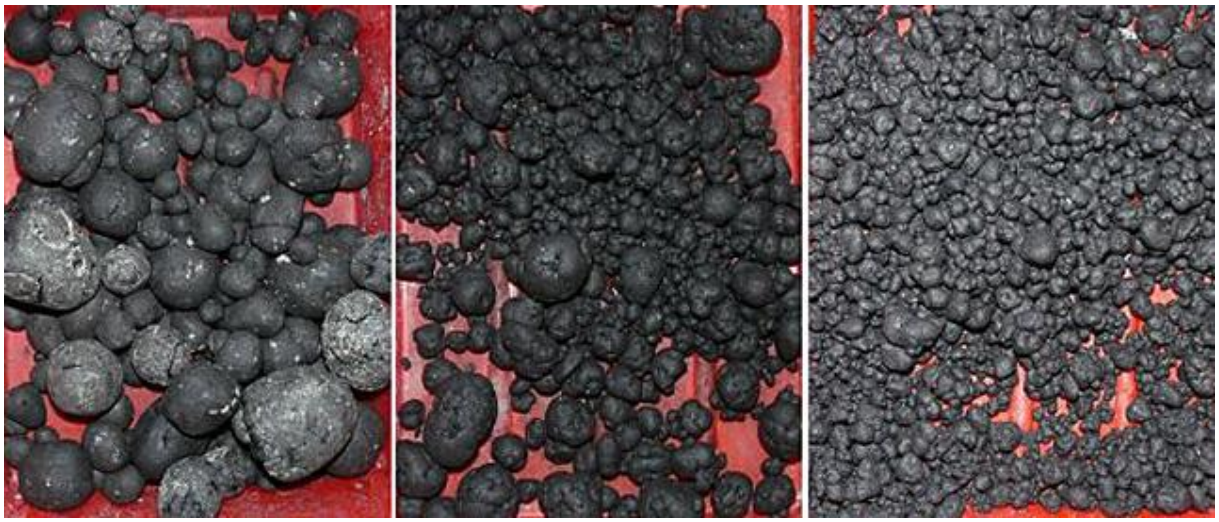

Figure 1. Granules size and shape depending of technological parameters and type of binder

# 79. STEAM GRANULATION VERSUS WET GRANULATION: IMPACT ON GRANULE AND TABLETS PROPERTIES

Erica Franceschinis[1], Elena Fontanel[1], Giulia De Santi[1], Nicola Realdon[1], Greta C. Magnano[2] & Dario Voinovich[2]

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2 Department of Chemical and Pharmaceutical Sciences, University of Trieste, P.le Europa 1, Trieste, Italy
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Steam granulation (SG) involves the use of steam as the granulating medium instead of traditional liquid water [1]. Steam provides a higher diffusion rate into the powder bed and a more favourable thermal balance during the drying step. Due to the ability of the steam to diffuse, a reduction of up to 50% of the amount of water necessary for granulation is possible. Furthermore, the literature reports that the granules produced by SG have a larger surface area than those obtained with wet granulation (WG) [2]. However, no articles have been published on the effect of steam on the compressibility characteristics of the granules.

The purpose of this study was to compare the technological properties of granules and their relative tablets obtained with SG and WG. To evaluate the effect of the solubility and thickening power of the diluents on process performance, different formulations were used containing 20% (w/w) caffeine as a model drug, 50% (w/w) microcrystalline cellulose as granulating aid and 30% (w/w) diluent (maltodextrin, sorbitol, lactose or corn starch) were used. The preliminary rheological characterizations performed on the four formulations highlighted that SG requires a lower amount of liquid binder than conventional WG; moreover, SG generally allows better control of granule growth because it occurs more slowly than WG. Granulation experiments were performed using a standardized experimental procedure, and the granules, after drying in a ventilated oven, were characterized by sieve analysis to evaluate the particle size distribution and by measuring the tensile strength and uniformity of the content. A compression study was also performed to identify the compression mechanism. The granules obtained with SG are generally smaller, with a narrow particle size distribution and lower crushing strength. The granules were then compressed in a single punch tablet machine using different compression forces, and the tablets that had a tensile strength of 1-2 MPa were characterized by mass and content uniformity tests, disintegration and dissolution tests. The results demonstrate that the granules manufactured through SG have better compression properties and the tablets present shorter disintegration time and a faster caffeine release than those achieved through WG.

[1] S. Shanmugam, Granulation techniques and technologies : recent progress. BioImpacts (2015) 5 (1) 55-63.

[2] M. Vialpaldo, B. Albertini, N. Passerini, D. Bergers, P. Rombaut, J.A. Martens, G. Van Den Mooter, Agglomeration of mesoporous silica by melt and steam granulation. Part I: A comparison between disordered and ordered mesoporous silica. Journal of Pharmaceutical Sciences, 102 (2013) 3966-3977.

# 80. EFFECT OF THE DRYING TYPE ON THE PROPERTIES OF GRANULE AND TABLETS PRODUCED BY HIGH SHEAR WET GRANULATION

Erica Franceschinis[1], Valentina Bressan[1], Simone Bernardotto[1], Margherita Morpurgo[1], Marco Luperini[2] & Andrea C. Santomaso[3]

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Although the wet granulation process can be performed with different equipment, the use of high-shear mixers (HSMs) may offer many advantages. Among these, the most relevant is the possibility of performing all the granulation steps (mixing, wetting, and massing phases) on the same equipment, leading to a reduction in dustiness, risk of cross-contamination, and toxic exposure. However, in general, the drying phase is performed in other equipment to reduce the process time (fluid bed) or the cost (ventilated oven). However, drying can be performed in HSM if the instrument is equipped with a heating jacket and a vacuum pump.

The purpose of this research is to evaluate the effect of the type of drying technique on the properties of granules and tablets. In particular, the two techniques evaluated were drying in a ventilated oven (D-O) or inside the HSG using the heating jacket and vacuum pump (D-J/V). The three formulations selected for this study contain: 40% (w/w) microcrystalline cellulose as granulation aid, 34% (w/w) lactose as diluent, 3% (w/w) polyvinylpyrrolidone K30 as binder, 3% (w/w) sodium starch glycolate as disintegrant and 20% (w/w) of three model molecules as actives (caffeine, paracetamol or citric acid). The actives are characterized by different water solubility and particle size. The study started with a rheological characterization performed using a mixer torque rheometer to identify the amount of water necessary for granulation and to predict the growth mechanism. Granules were produced following a standard procedure and dried in a ventilated oven set at 60°C or inside the HSM using the jacket temperature set at 60°C and a vacuum pressure of 200 mbar. The process was carried out until a LOD of 3% was reached.

As expected, the data highlighted that D-J/V allows for a reduction in drying time ranging from 30 to 45%. The granules were then characterized by sieve analysis (PSD), content uniformity, flowability, tensile strength, and compression studies. The results showed that the granules obtained by D-J/V are generally smaller, with a higher yield and a lower crushing strength. As regards the granule structure, the data and SEM imagines show that the effect of the drying type depends on the solubility of the active; in fact, if the active is very soluble in water, faster migration and crystallization of the active can occur on the granule surface. Granules with a particle size <500 μm were then compressed using different compression forces and tablets with a tensile strength of approximately 1 MPa were then characterized by mass and content uniformity tests, disintegration and dissolution tests. Results showed that compressibility, tabletability, and compactability of the granules were improved using D-J/V when the active was sparingly soluble in water, but the disintegration and dissolution performances were not modified. On the contrary, when a highly soluble active is present, D-O allows for an increase of compression properties owing to the crystals present on the surface, but it produces a drastic worsening of disintegration and dissolution performances.

# 81. EFFECT OF FEED RATE AND ROTATION SPEED ON PROPERTIES OF AGGLOMERATES PRODUCED WITH THE FLEXOMIX™ SYSTEM

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In powder processing, it is a rather common process to spray or introduce a liquid medium on to a powder. Such process is done with the goal to change or enhance the properties or functionality of the base powder. For example, for tuning the bulk density, increasing particle size, reducing dust or fines in the product, for improving material handing and process safety, among other reasons. While this process is common, achieving the desired properties is a non-trivial endeavour given the number of factors or process parameters that play a role during the process. As is often the case, another complexity is introduced when the goal is to translate trials performed on a small, pilot scale to larger production scale.

In the current work, trials were performed on two sizes of a commercially available continuous vertical agglomerator - the Flexomix™ [1]. The goal was to study the effect of increasing feed capacity and rotation speed on the consistency of the properties of the agglomerates produced before and after drying in a batch fluidized bed. Using flour as the test sample and water as the agglomerating medium, it is shown that it is possible to achieve stable agglomerate properties, namely bulk density, moisture content and particle size distribution, within a wide operating range when the process parameters are properly tuned. Particularly, changes in agglomerate characteristics due to increasing the number of nozzles to accommodate increasing liquid capacity is reported. Finally, it is shown that comparable results can be obtained across the two equipment sizes - an indicator of process robustness for scalability.

Figure 1. The Flexomix™ continuous agglomerator

[1] O.I. Imole, M. Ypma, P. van der Wel, Tuning agglomeration across different scales: a study of the Flexomix™ agglomeration system, The Micromeritics. 64 (2021) 35-41.

# 82. THE EFFECT OF TEMPERATURE ON PHARMACEUTICAL POWDER ADHESION TO COMPACTION TOOLING

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Undesired adhesion of powder to metal surfaces (sticking) is a significant problem in powder pressing sectors including pharmaceuticals, food, detergents, catalysts etc. Sticking is difficult to predict in early stage product formulation and process development and usually manifests only at full production scale. For example, in pharmaceuticals it is believed that 25% of solid dosage forms are affected by sticking [1]. Many factors affect the propensity of a powder to stick. One of the most important factors is the temperature evolution of the powder during the compaction process.

In this work, the effect of temperature on sticking was investigated. A heated punch/die system was used to replicate the temperature experienced by the powder in full-scale production. The sticking of ibuprofen, aspirin, paracetamol and microcrystalline cellulose (MCC) was investigated at room temperature and at 50 ˚C. For ibuprofen, the sticking tendency increases with temperature while for aspirin it decreases. Temperature has no significant effect on paracetamol. Certain excipients such as microcrystalline cellulose do present sticking under any of the conditions studied. The results are discussed the context of sticking hypotheses presented in the literature.

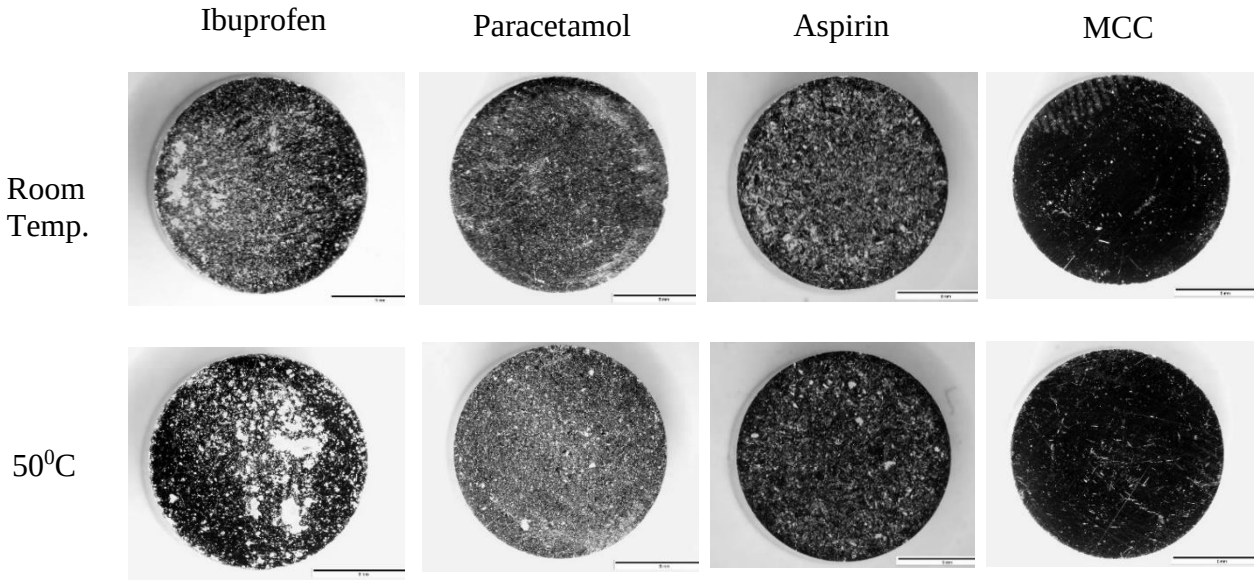


Figure 1. Microscopic images of powder sticking to punch surface at room and elevated temperature.

[1] S. Chattoraj, P. Daugherity, T. McDermott, A. Olsofsky, W.J. Roth, M. Tobyn, Sticking and Picking in Pharmaceutical Tablet Compression: An IQ Consortium Review, Journal of Pharmaceutical Sciences. 107 (2018) 2267–2282.

# 83. NUMERICAL ANALYSIS OF INTER TABLET COATING UNIFORMITY OF TABLETS IN A LAB SCALE DRUM COATER

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The most common form of drug products are tablets which are often coated to mask the taste and controlled release of active pharmaceutical ingredients (API). The coating process of tablets is commonly done in a rotating drum, where tablets are moved continuously due to drum motion during which coating solution is sprayed and hot air is blown simultaneously so that the solvent evaporates, and the solute deposits on the tablet surface forming a film. Achieving a homogeneously coated tablet is a very important and challenging task to maintain quality standards [1].

In this work, to predict the homogeneity of tablet coating, inter-tablet coating variability is calculated for tablets of different shapes by combining Discrete Element Method (DEM) simulations with experimental spray data [2]. Experiments were performed to measure the DEM parameters like the coefficient of restitution, and coefficient of friction to accurately model the DEM simulations. The DEM simulations were validated against the experiments by comparing the tablets surface velocity and residence time in spray zone. The coefficient of variation (COV) in residence time was calculated for different tablet shapes (SRC and oblong), pan loads, and drum speeds. For the rate of decay of COV as a function of time, an empirical fitting using power law correlation was performed. It was found that, the oblong tablets show a higher COV than the SRC tablets at 15 and 20 rpm drum speeds for the same pan load. At 30 rpm drum speed, the COV values for all tablet shapes for the same pan load were very similar close.

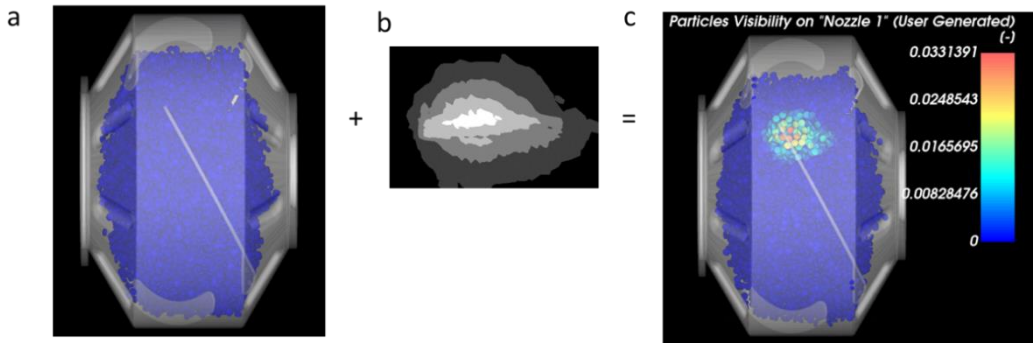


Figure 1. (a) Tablets in a drum coater, (b) spray distribution contour, and (c) snapshot of coated tablets with spray.

[1] W.R Ketterhagen, Modeling the motion and orientation of various pharmaceutical tablet shapes in a film coating pan using DEM, International Journal of Pharmaceutics, 409(1-2) (2011) 137-149.

[2] L. Pasternak and M. Sommerfeld, Spray characterisation for modelling the tablet coating process. In International Conference on Liquid Atomization and Spray Systems (ICLASS). 1(1) (2021).

# 84. FORMULATION AND CHARACTERISATION OF HETERO-AGGREGATES FROM CONTINUOUSLY OPERATED OPPOSED-JET FLUIDIZED BEDS

Ali Massomi, Jochen Schmidt & Andreas Bück

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Aggregation of two or more types of particles is one of most important processes to get access to hetero-aggregates, which are often outperforming homo-aggregates in different applications like catalysis [1] or anti-cancer therapy [2]. In order to create hetero-aggregates, it is essential to develop and use an appropriate setup that is able to break down the starting material to its primary particles.

In our work, we are following a simple approach to process $TiO_2$ and $ZrO_2$ in a fluidized bed, which is generated with air pressure from opposed jet nozzles (Figure 1). The air pressure causes the initial homo-aggregates to deaggregate into their primary particles. Due to attractive interaction forces (Van-der-Waals, electrostatic, etc.) the fluidized primary particles reaggregate and form hetero-aggregates, which will be characterised regarding their structural, optical, electronic and chemical properties. Characterisation methods are chosen in order to compare the properties between the single aggregate and the bulk product. Methods like SEM and EDX are used to investigate the structures of single aggregates as well as the spatially resolved element composition within. Next to that, methods like XRD provide information about the averaged composition of the bulk phase. Furthermore, the setup parameters will be varied in order to investigate their impact on the properties of the hetero-aggregates.

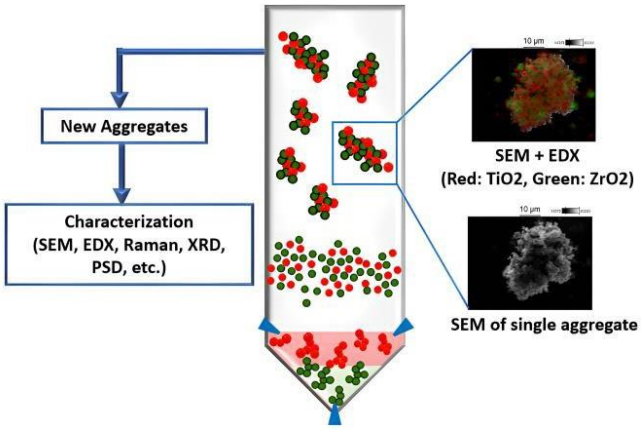


Figure 1. Experimental setup of the opposed-jet fluidized bed.

[1] Q. Zhang, C. X. Caiyun, H. Yin, S. Zhou, Enhanced Catalytic Hydrogenation Performance of Rh-Co2O3 Heteroaggregate Nanostructures by in Situ Transformation of Rh@Co Core– Shell Nanoparticles, ACS Omega, 4 (2019) 20829-20837.

[2] N. Kutsevol, Y. Kuziv, T. Bezugla, V. Chumachenko, V. Chekhun, Multicomponent Nanocomposites for Complex Anticancer Therapy: Effect of Aggregation Processes on Their Efficacy, International Journal of Polymer Science, (2020) 9627954.

# 85. HEAT TRANSFER STUDIES IN A ROTATING DRUM CONTAINING NON-SPHERICAL PARTICLES

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In chemical and process industries, rotating drums are commonly used as mixers, dryers, granulators, and reactors for processing particulate materials [1]. Most of the earlier studies are limited to the spherical particles and have focused on understanding granular flow in drums operating under a rolling regime. However, there are numerous industrial operations in which non-spherical particles are heated by hot air flowing through the porous wall of a rotating drum operating in the cascading regime.

In the present work, we attempt to understand the heat transfer mechanism between hot air (using CFD) and non-spherical particles (using DEM) in a rotating drum using open-source CFDEM software. Non-spherical particles, considered for the simulations mimic pharmaceutical tablets having standard round convex (SRC) and oblong shapes. The multi-sphere approach is used to model the tablet shapes. Collisions between the tablets are captured through the interaction between candidate spheres of non-spherical particles. The focus here is to study the heat transfer between hot air and particles and the heat conduction between the particles. The effects of drum speed and air inlet temperature on the bed temperature distribution are investigated. It is observed that the average temperature of the tablet bed correlates positively with the air inlet temperature, but the drum speed has no significant effect.

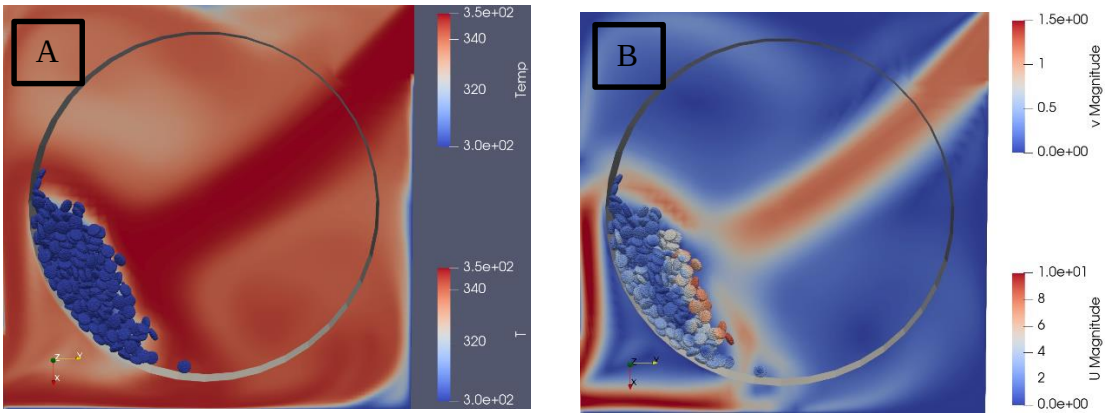


Figure 1. (A) Temperature profile of Tablets (T) and air (Temp). (B): Velocity plot of tablets (v) and air (U)

[1] Santomaso, A.C., Ding, Y.L., Lickiss, J.R. and York, D.W., 2003. Investigation of the granular behaviour in a rotating drum operated over a wide range of rotational speed. Chemical Engineering Research and Design, 81(8), pp.936-945.

# 86. THERMAL DESIGN AND SCALE-UP OF FLUID BED GRANULATION

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Fluid bed granulation combines two unit operations in a single item of equipment; granulation and drying. Much research has been reported on the differences this can cause in terms of the granulation mechanisms, for example a greater degree of layering growth compared to agglomeration of separate particles [1]. However, much less has been published on the effects on thermal design, operation and control.

Both theoretical modelling and practical experience show that successful operation of a fluid bed granulation process requires much tighter control of operational variables compared to separate granulation and drying processes. For pharmaceutical processes, the feasible design space is much smaller for fluid bed granulation rather than fluid bed drying, even in the same dryer, and as a result, inlet air temperature, air flowrate, spray rate and sometimes inlet air humidity become critical process parameters in regulatory terms, which does not apply to fluid bed drying [2]. This is because the applied spray rate must be kept in close balance with the evaporation rate of liquid from the bed. Too high a spray rate leads to overwetting and "wet quenching", uncontrolled agglomeration and defluidisation of the bed; whereas too low a spray rate gives poor surface wetting and weak fragile granules.

The Design Space for fluid bed granulation is most effectively expressed in terms of total heat input rate (combining effects of air temperature, flowrate and humidity) and spray rate [2,3]. The region for successful reliable operation plots as a trapezium or parallelogram. Effective scale-up can be achieved by expressing in terms of specific heat input and specific spray rate per kg of solid. The theoretical basis is a heat balance over the bed. Even so, considerable care is required in the calculations. For example, if the air and liquid flows are cut off during filter bag shaking, both the relative durations of the cutoff periods and the pattern of the transient flows to regain setpoint values have significant effects on the feasible operating region.

[1] L. Mörl, S. Heinrich, M. Peglow, Fluidized bed spray granulation. Chapter 3, 23-188, in “Granulation”, Handbook of Powder Technology Vol. 11, ed. Salman, Hounslow and Seville. Elsevier, Amsterdam, (2007).

[2] I.C. Kemp, A. van Millingen, H. Khaled, Development and verification of a novel design space and improved scale-up procedure for fluid bed granulation using a mechanistic model. Powder Technology, 361 (2020), 1021-1037.

[3] I.C. Kemp, A. van Millingen, H. Khaled, L. Iler, M. Mavani and L. Li, Simultaneous wetting and drying; fluid bed granulation and tablet film coating. Drying Technology, 39:2 (2021), 187-202 (special issue; papers from IDS2018).

# 87. DEM SIMULATION OF A SINGLE SCREW GRANULATION: THE EFFECT OF LIQUID BINDER ON GRANULE PROPERTIES

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The single-screw Variable Density Extruder (manufactured by Caleva, UK) is a continuous mode powder processing equipment which has the capability of performing granulation, spheronization, and extrusion. The Variable Density Extruder (VDE) is a new equipment developed and designed for the purpose of evaluating the properties of formulation at varying densities. Product formulation has been a challenge in the development of granules, pellets, and tablets in the major powder processing industries. This challenge is not only limited to pharmaceutical industries but also agricultural, food and detergent processing industries. The EDEM software has been used to model the particle collision pattern to understand the agglomeration behaviour under different formulations in VDE.

This paper assesses the applicability of VDE for granulation purposes using calcium carbonate (CaCO3) powder with mean particle size 65 µm as the primary feed powder and aqueous polyethylene glycol (PEG) 4000 as the liquid binder medium. For this work, eight different experimental runs at four different binder concentrations (i.e., 0.1, 0.2, 0.25 and 0.3 w/w) and under liquid-to-solid ratios (L/S) of 0.1 and 0.15 have been investigated. From the experiments conducted, it was concluded that increasing the binder concentration produced a more consistent product with less fines while low-level concentrations of binder produced inconsistent products with more fines. It was also observed that formulations at low L/S ratios produced fragile products with more fines, and a large range of particle size distribution (PSD). The EDEM simulations indicate an increasing contact force with increasing liquid-to-solid ratios. The bondstatus and number of particles from simulation result brings an understanding to the production of fines as experienced in experimental work. Also, granule strength is a factor of a contact force, thus increasing contact force in simulation is directly proportional to the granule strength.

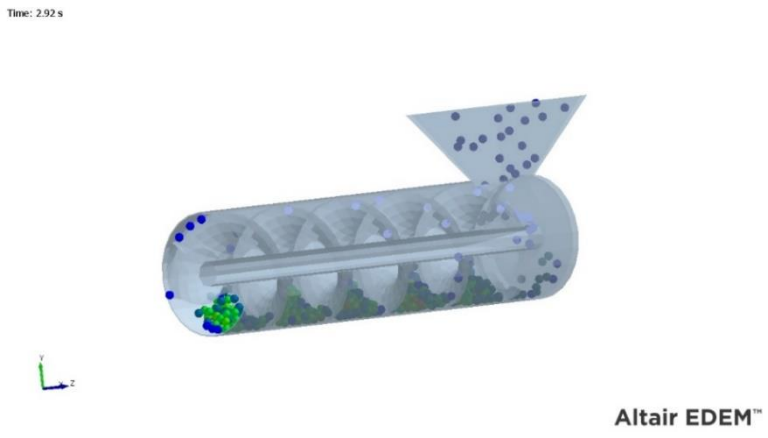


Figure 1. Particle Flow in Variable Density Extruder (VDE)

[1] S. Sarkar, B. Chaudhuri, DEM modelling of high shear wet granulation of a simple system, Asian Journal of Pharmaceutical Sciences, 13 (2018) 220-228.

# 88. PHARMACEUTICAL TWIN SCREW GRANULATION OF ALPHA-D-LACTOSE MONOHYDRATE WITH POLYETHYLENE GLYCOL 4000; AN INVESTIGATION OF GRANULE AND TABLET ATTRIBUTES

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A detailed study of hot melt granulation has been carried out to investigate the effect of materials and process conditions on granule and tablet properties. A pharma 16 twin screw extruder manufactured by Thermo Fisher Scientific has been used to granulate a model pharmaceutical formulation consisting of an active pharmaceutical ingredient (API), excipient and binder. Ibuprofen was used as the API with alpha-d-lactose monohydrate as the excipient and polyethylene glycol (PEG 4000) used as a binder, initially in solid form. These were granulated under a predetermined temperature with the resulting granular material collected for analysis. Two forms of PEG 4000 are considered in this study, an amorphous PEG and a more crystalline PEG form. To establish the influence of these two forms of PEG as well as the other operating and formulation conditions, properties such as granule size distribution and strength, tabletability and tablet attributes of hardness, friability and dissolution were analysed. Tablet friability and hardness improved with the amorphous PEG form, while use of the crystalline PEG resulted in faster dissolution time with corresponding higher drug release. This study reveals the influence of initial material properties/characteristics on the final granulated products (see Figure 1), emphasizing the challenging and complex nature of the granulation process. The study also offers an insight into how optimised granulation can be achieved by understanding of the relationship between the formulation, process and granule properties.

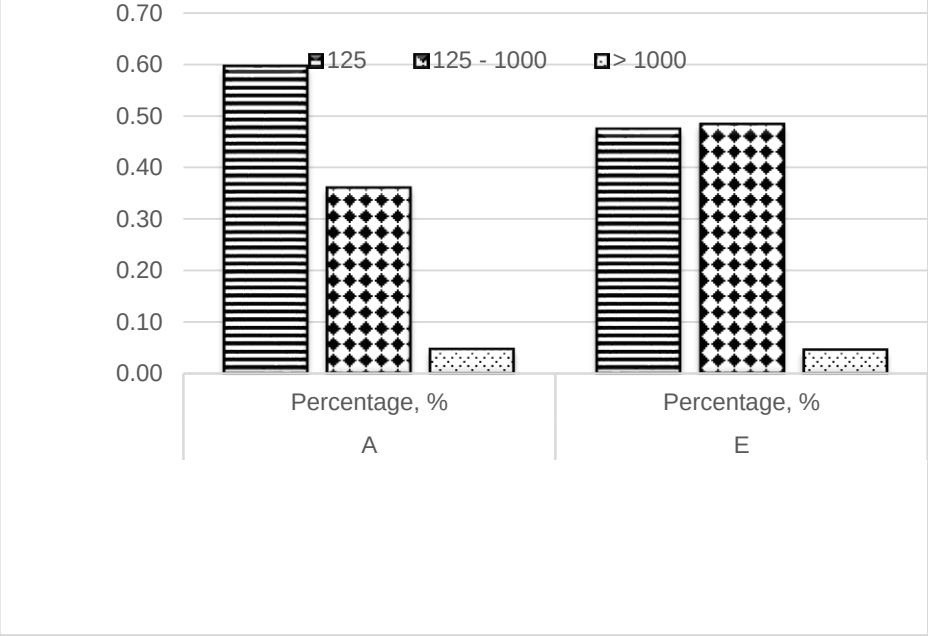


Figure 1. GSD comparison using crystalline PEG (A) versus amorphous PEG (E)

# 89. INFLUENCE OF MIXING ELEMENTS ON GRANULE AND TABLET PROPERTIES IN HOT MELT TWIN SCREW GRANULATION

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Twin screw granulation (TSG) has in recent times become a popular manufacturing technique in the pharmaceutical industry, adapted from widespread use in the plastics industry. Continuous manufacturing such as TSG can provide benefits such as lower residence time, improved process efficiency and higher product quality when compared to batch granulation processes. This study uses calcium carbonate (CaCO3) with a polyethylene glycol (PEG) 4000 binder to investigate the contribution of two types of mixing elements: chaotic and kneading on the performance of the granulation process. Granule properties are assessed in relation to process operating conditions and the most significant contributing factor(s) are identified. Properties such as granule shape, structure and strength are characterised in addition to associated tablet properties of friability, disintegration time and hardness. Results suggest that the type of mixing element has a clear effect on granule properties. Depending on the end use and product characteristics, a choice between the two mixing elements can be made more readily and wisely. Higher tablet strength is observed to result from the use of chaotic elements over kneading elements, with associated longer disintegration times. For tablets of shorter disintegration times, especially for the purposes of fast release dosage forms, kneading elements would be preferred. An understanding of the influence of designs of mixing elements on final products thus enables better engineering considerations for sustained manufacturing.

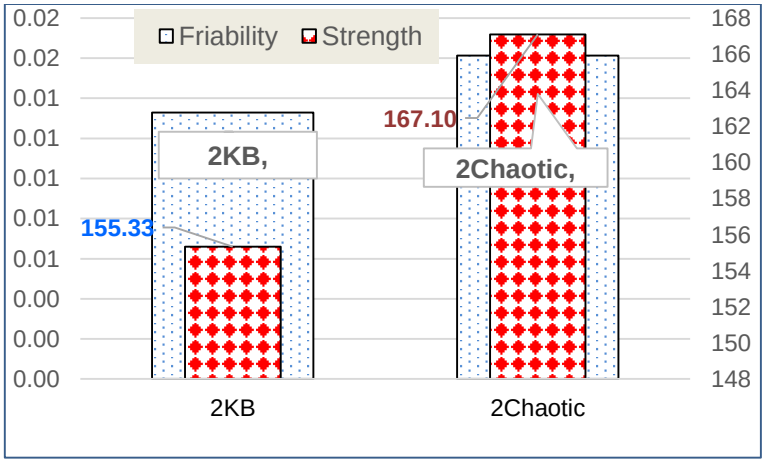


Figure 1. Comparison of mixing elements for tablet friability and strength

# 90. MIXER TORQUE RHEOMETER - A CORRELATION BETWEEN THE MULTIPLE ADDITION AND VARIABLE MIX TIME METHODS

Bruna R. Belem, Gustavo V. Carapeto, Bruna F. do Rosário, Michele G. Issa & Humberto G. Ferraz

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Techniques based on rheology were developed to improve granulation processes, relating the particle's agglutination degree with the measured torque [1]. The mixer torque rheometer (MTR 3 - Caleva, UK) relies on the multiple addition method as a quick way to estimate the binder ratio (mL/g) needed to produce granules with desirable characteristics. However, this method provides a limited description of the formulation mixing kinetics. For that, the MTR also relies the variable mix time method, which furnishes a torque response to mixing time [2]. In this work, a granule formulation (60% ibuprofen, 1% PVP K30, 39% microcrystalline cellulose 101) was evaluated by both methods. Three different binder ratios were selected by means of the first torque derivative and tested in two mixing speed. A complete factorial experimental design $2^1.3^1$ was elaborated (triplicate), resulting in 18 tests.

There was an influence of both factors, so that higher rotation provides higher torque and an increase in water amount results in lower torque or the need for longer mixing time. The literature describes that the binder ratio necessary to achieve the highest torque value (multiple addition test) can be considered a good approximation of the ideal granulation endpoint. In this case, it is understood that 0.833 mL/g ($Torque_{max}$. = 0.565 N.m) would be recommended to obtain ibuprofen granules. However, Fig.1 illustrates that a smaller amount of liquid is capable of providing a torque value above 0.500 N.m, depending on the sample mixing time. It is concluded that a combinatorial study between the multiple addition and variable mix time methods is ideal for a better understanding of the formulation and, consequently, definition of the granulation endpoint and process characteristics. Therefore, it is an important tool for the development of formulations by QbD approach.

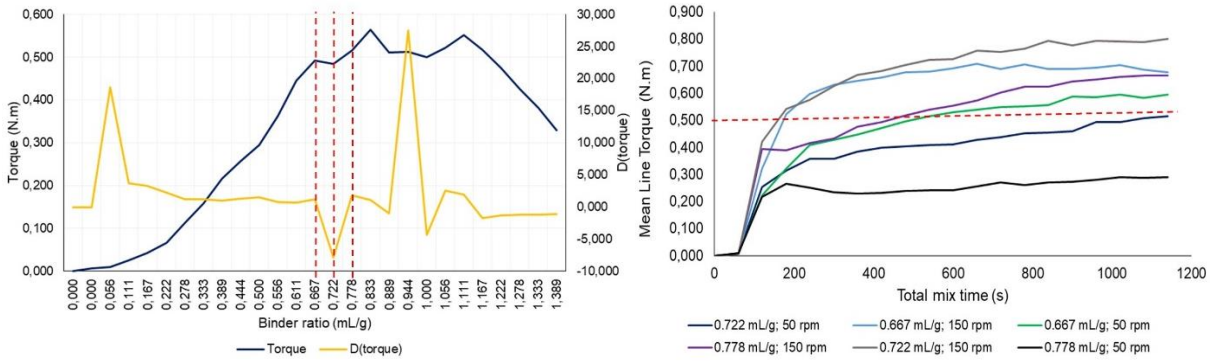


Figure 1. Multiple Addition and Variable Mix Time results obtained in MTR assays.

[1] B.R. Belem, H.G, Ferraz, Rheological profile in mixer torque rheometer of samples containing furazolidone and different binders, Chemical Engineering Research and Design, 160 (2020) 533 - 539.

[2] Caleva Process Solutions Ltd, Installation and Operation Manual, Version A-01 (2013).

# 91. ASSESSMENT AND CHARACTERIZATION OF GRANULES PRODUCED IN A SINGLE SCREW EXTRUDER

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2 Richmond Road, University of Bradford, Bradford, BD7 1DP, United Kingdom
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Granulation is a size enlargement technique, used in many industries and commonly in the food and pharmaceutical industries, to enhance the flowability of materials that would otherwise flow poorly. This provides the option for tableting in the latter case, allowing active pharmaceutical ingredients (APIs) to be delivered in the correct dosage when administered. Both high and low-shear processes are employed for granulation, using either batch or continuous processes. This study uses the latter to combine Durcal 65 as the main component, and aqueous polyethylene glycol (PEG) 4000 as the binder, to increase the average particle size of the main component in a single screw extruder. Using such an extruder has not been covered extensively in the literature, so an insight into the fidelity of this process is gained in this work. The operating parameters changed in this work include the screw speed of the single screw extruder and the coarse/fine ratio of the powder feed. The narrowed particle size distribution was determined, in addition to the enhanced flowability properties and suitability for tableting.

# 92. QUANTITATIVE ANALYSIS OF THE EFFECTS OF MULTI-COMPONENT FORMULATION VARIATIONS ON GRANULE PROPERTIES

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Wet granulation is a complex process that often incorporates two or more components in its formulation to produce robust granules. Due to the individual properties of each component, altering the blend formulation can introduce large variability in granule properties and its microstructure via the different rate mechanisms. The ability to characterize blend formulation based on each component's fundamental material attributes and predict its effect on the granulation process will significantly improve process understanding and expedite product development.

This work analyzes the effects of blend properties on the quality of the granules formed, which includes the dynamic particle size and granule microstructure. We formulated a multi-component blend that is industrially relevant, with the goal of determining the contribution of each component to the blend properties and its effect on granule properties. Additionally, this study also aims to propose the appropriate operating range for each formulation, to produce granules of desired quality attribute. A d-optimal DOE and mechanistic formulation-dependent population balance was used to improve process understanding and quantify the effects of each variable. The usage of soft sensors and in-line measurements for real-time monitoring was also explored as a quantitative method of determining rate mechanisms and identifying granulation endpoints. As seen in Figure 1, the torque profile indicates the different stages that occur during the granulation process, and the responses of granule attribute, such as median diameter (d50) and microstructure.

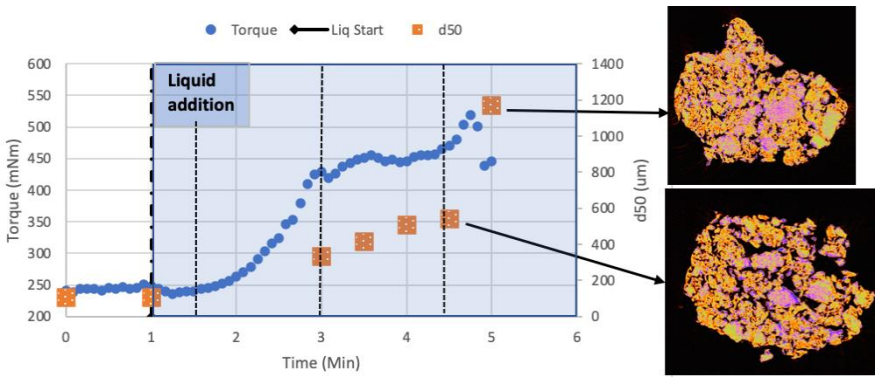


Figure 1. Dynamic median diameter overlayed with torque profile and microstructure images

# 93. DEVELOPMENT AND OPTIMIZATION OF DIRECT PELLETIZATION TECHNIQUE BY USING PROCEPT GRANULATOR

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Pelletization process is used to enhance the physical properties of powder (shape, size distribution, flowability and solubility). Although it can be carried out by different techniques, the use of direct pelletization method by a high shear granulator reduce the process cost and the time. The quality of resulted pellets are highly affected by material attributes and process parameters [1].

This study aimed at preparation of low dose drugs pellets with an acceptable content uniformity by using ProCepT granulator. Central composite design was carried out on five process parameters which are: impeller speed, chopper speed, amount of granulating liquid, amount of binder and liquid addition rate for formulations containing microcrystalline cellulose, mannitol and water as granulating liquid. Size distribution, sphericity, hardness, and friability tests were selected as optimized responses to determine a good design space for direct pelletization by ProCepT granulator.

The process resulted in pellets with good yield within the specified size range, an acceptable aspect ratio, content uniformity, hardness, friability, and good flow properties. The optimum combination range of process parameters were achieved in design space.

[1] J.L.P. Soh, S. Sarkar, P.W.S. Heng, C.V. Liew, Pelletization Techniques, Encyclopedia of Pharmaceutical Science and Technology, Fourth Edition (2013) 2515-2524.

# 94. MIXER TORQUE RHEOMETER - EVALUATION OF THE PHYSICAL QUALITY OF FURAZOLIDONE GRANULES PRODUCED WITH DIFFERENT LIQUID/SOLID RATIOS

Gustavo V. Carapeto, Bruna R. Belem, Bruna F. do Rosário, Michele G. Issa & Humberto G. Ferraz

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Wet granulation is a process widely used by the pharmaceutical industry to improve physical characteristics of raw materials. Despite being well established, one of the main challenges of the process is to determine the best granulation point for the formulation. In this scenario, Mixer Torque Rheometer (MTR) studies help in precising the wet mass endpoint, however there is no consensus regarding the stage of optimal granulation [1].

In this study, a formulation (79% furazolidone, 1% sodium alginate, 20% microcrystalline cellulose 101 and water as binder) was evaluated by multiple addition method (triplicate). Different binder ratios were selected (0.360 mL/g, 0.380 mL/g, 0.400 mL/g and 0.440 mL/g) for granule production and characterization by particle size distribution, friability and density.

The granules produced with binder ratio at $Torque_{max}$ (capillary stage) showed higher density, thus indicating that the particles are at their most agglutinated state. However, the granules obtained with 0.440 mL/g showed less friability and greater particle sizes, exhibiting higher mechanical resistance when produced at droplet stage. Therefore, the granulations were feasible in all selected ratios. Since it is also known that each formulation has particularities, it should also be evaluated which stage provides the Quality Target Product Profile (QTPP) considering it may be a Critical Material Attribute (CMA) of the specific product.

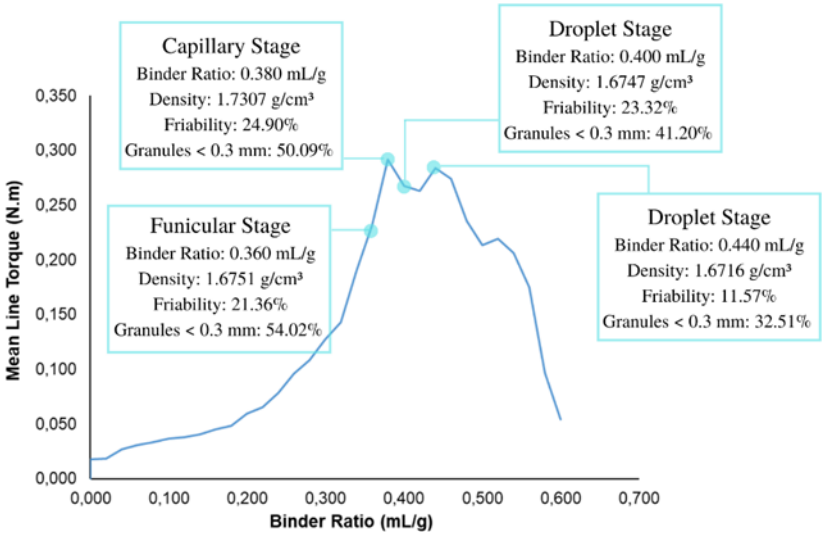


Figure 1. Rheological profile and granule characterization results for different binder ratios.

[1] B.R. Belem, H.G, Ferraz, Rheological profile in mixer torque rheometer of samples containing furazolidone and different binders, Chemical Engineering Research and Design, 160 (2020) 533 - 539.

# 95. VALIDATION OF SCALED-UP PARTICLE MODEL IN DEM FOR COHESIVE PARTICLES

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In a granulation process, small particles are adhered together by various types of cohesion forces, e.g., liquid bridge forces for wet granulation and surface adhesion forces for dry granulation, to form large particle assemblies called granules. Therefore, it is of paramount importance to understand the influence of cohesion forces to fine powder flows. However, it is difficult to observe particle-level interactions by experiment, and our knowledge today is still far from complete. Numerical simulation can be a powerful alternative tool to understand the underlying physics of cohesive powder flows. Discrete Element Method (DEM) has become a popular choice of simulating particulate flows where the movement of particles is tracked in a Lagrangian manner. One of the main advantages of DEM over the Eulerian model is that the individual particle properties and the subsequent inter-particle interactions can be directly considered. On the other hand, one of the major challenges of DEM is the high computational cost with large number of particles. This makes it difficult or practically impossible to perform simulation of fine powders in a large-scale system.

The scaled-up particle model, which is sometimes referred to as coarse grain or discrete parcel model, has been increasingly popular to overcome the aforementioned problem: large particles are used in simulation to represent the original small particles. Recently, the authors proposed a novel scaled-up particle model based on the continuum approximation of powder flow [1-3]. The scaling criteria for inter-particle and body forces are derived separately, and in principle they can be universally applied regardless of the forms of the cohesion force and particle shape models. In the present study, the scaled-up particle model proposed is used to simulate various applications to investigate the validity of the model. It is found that the model can reasonably predict the original particle motion with different cohesion forces in terms of the bulk motion, velocity distribution and torque applied to the impeller of a granulation mixer.

[1] E.L. Chan, K. Washino, Coarse grain model for DEM simulation of dense and dynamic particle flow with liquid bridge forces, Chemical Engineering Research and Design, 132 (2018) 1060-1069.

[2] K. Washino, E.L. Chan, T. Kaji, Y. Matsuno, T. Tanaka, On large scale CFD-DEM simulation for gas-liquid-solid three-phase flows, Particuology, 59 (2021) 2-15.

[3] Y. Hu, E.L. Chan, T. Tsuji, T. Tanaka, K. Washino, Geometric similarity on interparticle force evaluation for scaled-up DEM particles, Powder Technology, 404 (2022) 117483.

# 96. DUST RELEASE AND SIMULTANEOUS SEPARATION BY MEANS OF ELECTROSTATICALLY ASSISTED SPRAY NOZZLE SYSTEMS - EXPERIMENTAL PROCEDURES

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The use of various raw materials in the form of bulk materials takes place in the building materials industry, agriculture and the food industry, among others. Bulk material handling, transport and storage result in the particle emissions, referred to as dusting.

The aim of the project is to demonstrate the effectiveness of the dust reduction measure "use of spray nozzles" in combination with the effect of electrostatic charging. The special feature here is that the investigations are oriented to the type of stress and the material and thus take into account the character of the dust emissions in a macroscopic scale. Different test set-ups are used to realistically illustrate the bulk handling operations during which dust is released. The effectiveness of the reduction measure is investigated using different operating parameters for dust emission as well as separation. The subsequent electrostatic charging of the spray mist allows the use of water and compressed air to be reduced. An evaluation method for spray nozzle systems is being developed, which considers the economics of the used resources and the material-related efficiency of the dust reduction, with a focus on the fine particle fractions PM2.5 and PM1.

An existing wind tunnel was extended to measure the dust release from a bulk material pile, from falling bulk material dropped of a conveyor belt, from falling material hitting the bulk pile as well as a combination of those cases. The spray nozzles are placed downstream followed by an optical particle counter (OPC) and a cascade impactor (CI). The combination of OPC for online particle-droplet measurement and CI for fractionized sampling of dust particles give a comprehensive insight into particle release and particle separation. This publication will show the experimental setup and methods as well as first results for calcium carbonate (Ulmer Weiß XMF).

# 97. IN-LINE PARTICLE SIZE MEASUREMENT IN DRY GRANULATION: DEVELOPMENT AND APPLICATION OF A NOVEL SAMPLING FUNNEL FOR CONTINUOUS SAMPLING

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In the dry granulation by roller compaction process two counter rotating rollers are used to compress a powder into a dense, compact ribbon. In a second, subsequent step, the ribbon is milled down using a sieve mill. This process is continuous by nature and produces granules with a defined particle size distribution (PSD), raising the need for in-line PSD monitoring to ensure continuous quality control.

This work aims to provide a method for representative in-line sampling and PSD measurement in dry granulation. A 4 by 10 testing tube grid was placed directly at the sieve of the milling unit of an Alexanderwerk WP 120 Pharma roller compactor. The PSD of each individual sample was measured by sieve analysis. The measured sieve fractions were plotted in map diagrams according to their position under the mill, see Figure . It was found, that the PSD varies greatly depending on the position along sieve length (row 1 to 10) but is constant along the width of the sieve mill (column A to D). A novel sampling funnel was developed which integrates the sample along the sieve length.

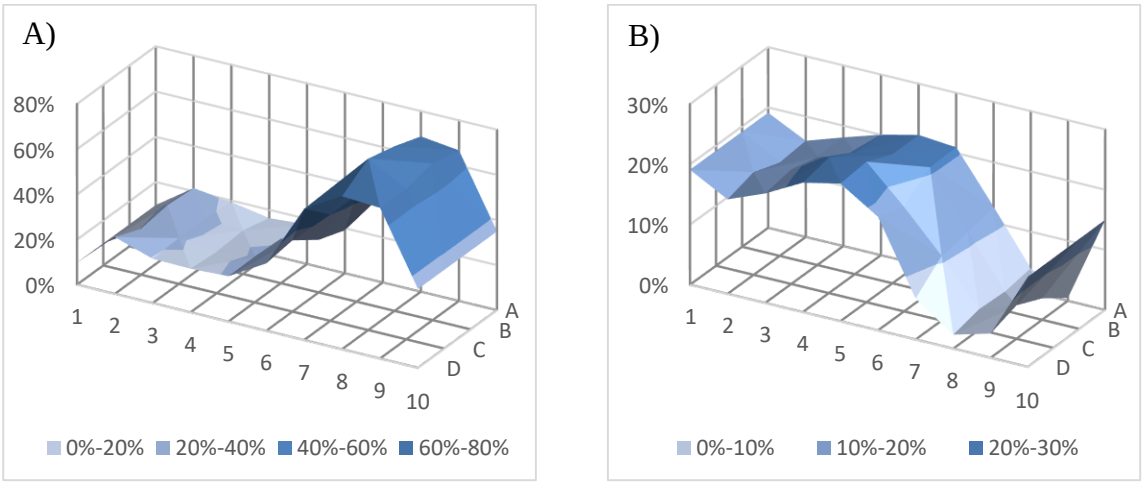


Figure 1. Dependency of different sieve fractions in a PSD on the position under the sieve mill in a roller compactor. A) sieve fraction <0.20 mm, B) sieve fraction 0.40 to 0.63 mm.

The novel sampling funnel was used to take a representative sample for in-line PSD measurement with an in-line particle probe using spatial filter velocimetry. It was possible to measure the PSD in-line and to track changes of the PSD with changing specific compaction force of the roller compactor. The representative in-line measurement was validated using at-line sieve analysis of the complete granule stream.

# 98. EVALUATION OF EFFECT OF PROCESS AND FORMULATION VARIABLES ON THE SIZE ENLARGEMENT MECHANISMS IN HIGH SHEAR MIXERS – AN EIRICH MIXER STUDY

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High shear mixing of powder in the presence of liquid addition can result in growth of the primary powder particles into larger entities called granules. The particle growth can occur either through a layering mechanism or coalescence or a combination of both mechanisms. The dominating mechanism of particle growth is dependent on both process and formulation variables. The influence of process variables such as vessel inclination, direction of rotation of vessel, impeller speed, duration of mixing and rotation seed of vessel pan, on the particle growth mechanism is quantified using image analysis of samples of granules produced under different conditions. The study was also extended to include the effects formulation variables such as particle density of main powder, quantity of binder added, particle size of coating material. Results show that the coating mechanism dominated when the mixing time was short, with a high inclination angle of the mixer vessel and the vessel rotating in a direction opposite to that of the agitator.

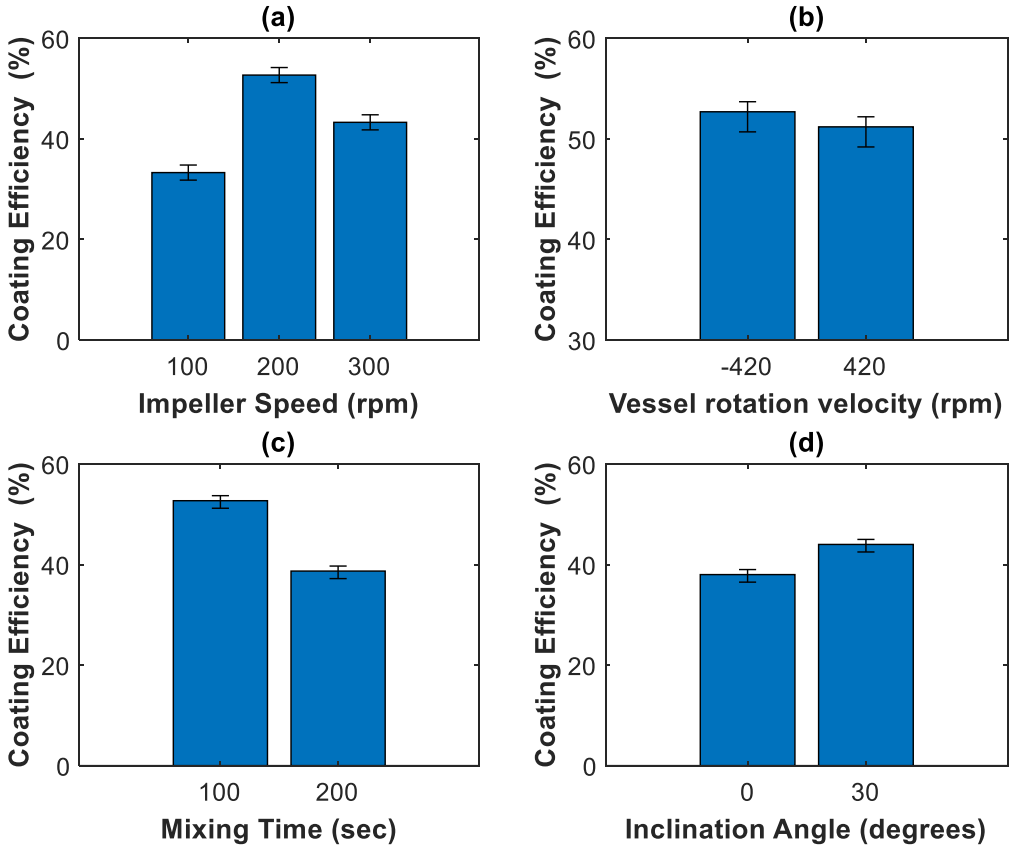


Figure 1. Influence of process variable on coating efficiency.

# 99. SOLID DISPLACEMENT METHOD TO DETERMINE ENVELOPE DENSITY OF ROLLER COMPACTED RIBBONS AND ITS APPLICATION IN MATHEMATICAL MODELLING IN TECHNOLOGY TRANSFER OF THE DRY GRANULATION PROCESS

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Producing the same quality of intermediate products on various roller compaction machinery in dry granulation scale-up operations is essential for robust production of pharmaceutical formulations. The widely accepted criteria for transferability of dry granulation processes lies in the intermediate's physical property which is ribbon envelope density. Through a pilot study on a small-scale roller compactor, it is possible to prepare various batches of granulate under different process parameters to select the most preferrable batch for further development. The ribbon densities of intermediate compacts for each batch differ due to process parameters set during compaction. The method presented in this work allows to determine envelope density of roller compacted ribbons by an accurate measurement of their envelope volume by utilizing solid volume displacement of glass microspheres. The data acquired by the application of this method are demonstrated for utilization in mathematical modelling to predict scale-up process parameters of a pharmaceutical mixture based on samples from pilot studies. It is shown that the method for envelope density measurement is as accurate as mercury porosimetry as it accommodates the pore size neatly (Fig. 1) and its deployment into practice is environmentally safe, fast and inexpensive.

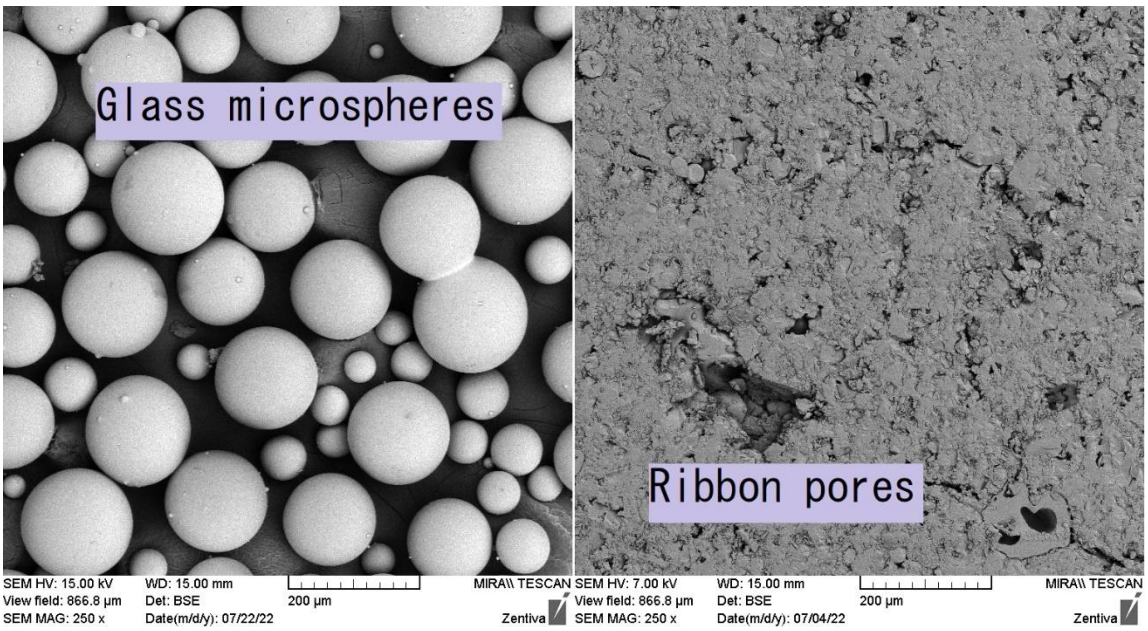


Figure 1. Comparison of glass microsphere size to ribbon pores

# 100. THE EFFECT OF VARYING COMPRESSION FORCE AND SPEED ON PHARMACEUTICAL TABLET CRITICAL QUALITY ATTRIBUTES

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Continuous manufacturing within the pharmaceutical industry is now gaining momentum, and comprehensive understanding of each unit operation is necessary in order to aid in advancing the movement towards complete shifting from batch processes. Solid dosage forms are currently categorised as the most frequently used medicines, highlighting the crucial importance of precise development with regard to product safety, stability and efficacy, as well as efficient manufacturing at industrial scales [1].

Considering that granules compression represents one of the most important manufacturing processes, establishing product's mechanical integrity and bioavailability until administration, this paper focuses on the effect of different applied compression forces and speeds on tablet's critical quality attributes (CQA) such as tensile strength, dissolution and porosity, while aiming the production of solid forms with commercially acceptable properties [2]. The Consigma-25 continuous manufacturing line was employed for powder processing through wet granulation, whereas the integrated GEA Modul-P high-speed rotary tablet press was used for compression force variation. Furthermore, an Instron 3367 single-punch Universal Mechanical Tester aided in effective determination of the impact of different punch speeds on tablets' CQAs. Throughout the experimental work an extensive number of samples have been subjected to comprehensive testing in order to ensure enhanced accuracy of the manufacturing technique. Nevertheless, micro-computed tomography and further critical analysis with respect to scientific and engineering considerations allowed for complete validation of the results achieved experimentally.

[1] D. Markl, J.A. Zeitler, A Review of Disintegration Mechanisms and Measurement Techniques, Pharmaceutical Research. 34 (2017) 890.

[2] I.C. Sinka, F. Motazedian, A.C.F. Cocks, K.G. Pitt, The effect of processing parameters on pharmaceutical tablet properties, Powder Technology. 189 (2009) 276–284.

# 101. FORMULATION IN A DROP - TEMPLATED GRNAULATION AND COMPACTION ANALYSIS

Paola Medina Martinez[1], Line Koleilat[1], Joshua Hanson[2], Jonathan Wade[2] & Paul Mort[1]

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Binder-powder interactions were investigated using single droplet-penetration on static powder beds. Experimental effects included binder type, binder concentration, powder blend ratio (active, excipient), and pre-wetting of the powder. These screening effects are relevant to formulations requiring binder granulation, especially challenging formulations having high levels of micronized active ingredients. Interactions were characterized using two approaches: 1) dynamic droplet imaging, measuring contact angle, drop height, contact area, and penetration time; and 2) mass balance of drop-templated granules which were recovered from the bed and subsequently dried. The structure of the templated granules was analyzed via uniaxial die compaction, focusing on the intermediate range of the compaction curve (granule deformation and closure of interstitial porosity in the compact). The results provide guidance in granule formulation including the dynamics of granule formation and resultant compaction behavior. The approach is especially useful for early-stage development when only small quantities of raw materials are available.

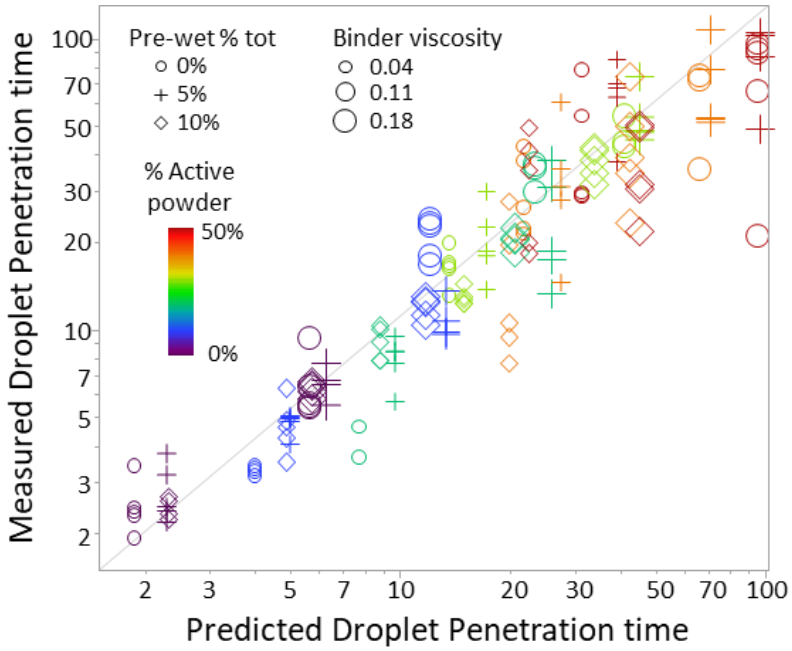


Figure 1. Multi-variate analysis of binder-powder interaction.

# 102. INTEGRATED MODEL CONTROL OF FLUIDIZED BED GRANULATION

Line Koleilat[1], Joshua Hanson[2], Jonathan Wade[2], Christian Karl Paasche[3], Carl Wassgren[1] & Paul Mort[1]

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Fluidized bed granulation processes are used to achieve particle size enlargement, typically with the objective of relative narrow granule size distribution with moderate porosity suitable for a range of commercial product applications. The granule size is controlled according to a balance of growth and breakage transformations in a fluidized flow field where powders are combined with binder, typically an air-atomized aqueous binder solution. Flow control is modeled using fluidization process stability criteria. Mass balance is governed by the addition of binder with concurrent drying. The drying rate is governed by the balance of airflow and product enthalpy. This paper integrates fluidization criteria with mass and energy balances to create a process control model. The model is implemented to optimize process stability and product quality.

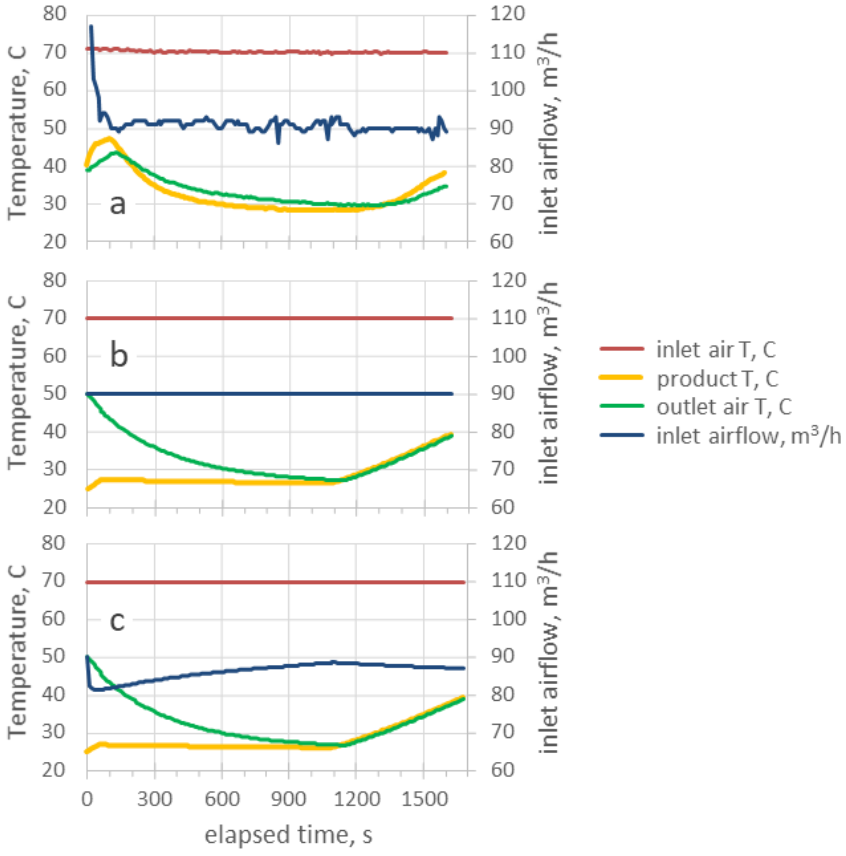


Figure 1. Fluidized bed granulation: a) Process data, Syntegon SolidLab2; b) Feed-forward mass and energy balance at fixed airflow; c) Feed-forward mass and energy balance with integrated fluidization model.

# 103. INDUSTRIAL CASE STUDY ON SCALE UP AND SYSTEM DYNAMICS CHARACTERIZATION OF PHARMACEUTICAL CONTINUOUS PRODUCTION LINE.

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In the pharmaceutical industry, continuous manufacturing (CM) of drug products is becoming more and more prevalent. In comparison to classic granulation techniques, continuous twin-screw wet granulation has several advantages, including flexible batch size in continuous manufacturing that can be adjusted to meet changing market demand. Another benefit is that during development and scale-up studies, continuous manufacturing consumes less time and material than traditional wet granulation procedures.

In this work, a GMP continuous wet granulation line that produces solid oral dosage forms was examined in order to determine the critical scaling up parameters and the system dynamics of the line as a whole. Dosing/feeding, blending, twin-screw wet granulation, fluid-bed drying, sieving, and tableting were the steps that made up the continuous process. To describe the process flow and evaluate the process dynamics, several step experiments in API concentration were carried out. Process Analytical Technologies (PAT) used three Near Infrared (NIR) probes to measure the API content after the blender, after the dryer, and in the feed frame of the tablet press to monitor the API content in real time. The approach allowed for the production of supplies for clinical phase III study, at high throughput and lengthy run times.

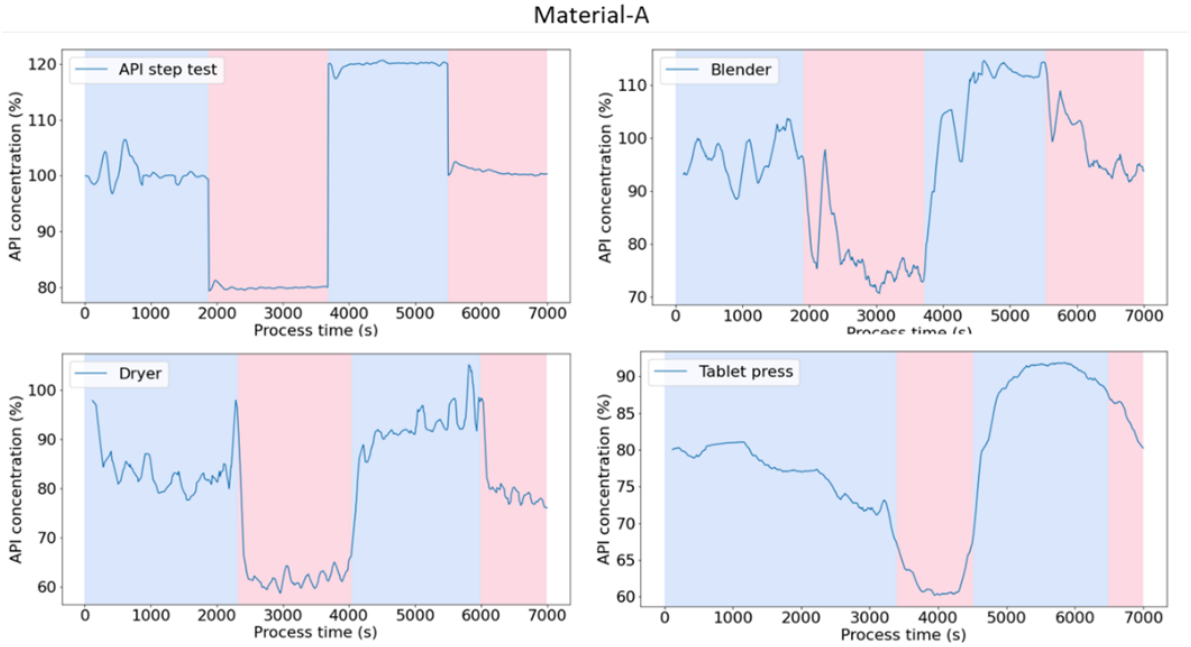


Figure 1. Graphical overview of the detection method for Material-A trials. Legend: background color changes symbolized the change point detection time.

[1] Morgane Jelsch, Yves Roggo, Ahmad Mohamad, Peter Kleinebudde, Markus Krumme, Automatic system dynamics characterization of a pharmaceutical continuous production line, European Journal of Pharmaceutics and Biopharmaceutics, 180 (2022) 137 - 148.

# 104. COMPARATIVE ANALYSIS OF POROSITY MEASUREMENT TECHNIQUES USING PHARMACEUTICAL MATERIALS

Arnesh Palanisamy[1], Lizbeth Martinez[1] & Bindhumadhavan Gururajan[1,2]

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Dry granulation by roller compaction is one of the techniques used to improve the flow properties of pharmaceutical materials where direct compaction of tablets is not possible. It is often preferred over wet granulation due to faster processing times and lower energy consumption. Ribbons are produced during the process and ribbon porosity is considered a critical intermediate material attribute. Ribbon porosity measurements are often used to validate roller compactor modelling and simulations. Various ribbon porosity measurement techniques exist, each with it is own advantages and challenges. The most commonly used techniques in the pharmaceutical industry for ribbon porosity measurements are envelope volume using the Geopyc technique, mercury porosimetry and X-ray Microtomography. However, there are ongoing research activities to find innovative techniques which are simple, faster, non-destructible, precise and accurate. Laser triangulation is one such emerging technique [1]. In this study, the Laser triangulation technique is used for the evaluation of the ribbon porosity and results are compared with the commonly used technique for validation of the results and its suitability as an at-site measurement technique. In this investigation, ribbons were produced using commercially available roller compactors namely Gerteis Mini-pactor and Bepex Pharmapactor. In the initial experiments, ribblets were manufactured using the STYL'One compaction simulator using Microcrystalline Cellulose (MCC) as the model excipient. Ribbons were manufactured using a roller compactor using MCC for further evaluation of the techniques. Experimental compound A was used in the active formulation and further studies were carried out in pilot and launch scales to generate ribbons for further comparison of the technique and validate the suitability of each measuring technique to quantify the porosity data. This paper discusses in detail the importance of the roller compaction process and ribbon porosity as critical intermediate material attributes, different porosity measurement techniques, results obtained and comparative analysis of the data generated.

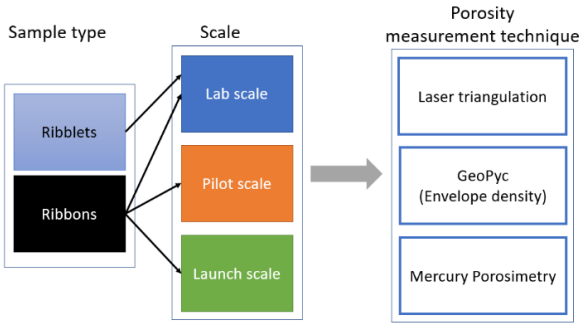


Figure 1. Illustration showcasing sample type and origin used to compare the measurement techniques.

[1] Lillotte, T.D., Bebernik, P., Keck, J., Bommer, M., Schröder, D. and Wagner, K.G., 2021. Laser triangulation as a fast and reliable method for determining ribbon solid fraction; focus on accuracy, precision, and measurement time. International Journal of Pharmaceutics, 610, p.121241.

# 105. RESTRUCTURING OF MILK POWDER: SINGLE DROPLET DRYING IN THE SPRAY DRYER

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The production process of milk powder has attracted much attention these days. Among which spray drying is currently the main industrial method of milk production because of its high drying speed and high process control accuracy. Spray drying is a process where the slurry converted into powder form by spraying the slurry through atomizer and then drying it using high temperature gas. The development of spray drying technology also gives the opportunity to produce food additives with better performance and longer shelf life [1]. Controlling the spray dryer parameters is a key to control the product quality. Researchers used different method including pilot equipment, simulation, modelling to scale-up the process to reduce the cost by reducing the number of trail and error. Meanwhile, by changing parameter or restructure powder so as to reduce package cost also lead energy saving and friendly environment

In this study, dying of droplet attached to a syringe and levitated in the air were both used to compare the accuracy of the model in the spray dryer. Experiments showed that the droplets in the Levitator are more spherical, but the final dry particles shape is like ‘donuts’ due to the compression of the upper and lower sides by the ultrasonic waves. In the syringe drying, the droplets are only suspended on the filament by friction. Due to gravity, the shape of the droplets and dried particles is close to that of water droplets. The final particle morphologies of both cases are significantly different from those in the spray dryer. Thus, a new air suspension device will be developed to study the drying process of single droplets. This device is expected to suspend a single droplet and keep it stable in a part of a tube with hot air to simulate a droplet drying process in spray dryer. Besides, by comparing with other single droplet drying methods, a drying model will be established and validated in a spray dryer for the purpose of controlling product characteristics. The milk powder will be restructured and in the same time remain the other properties such as reconstitution ability.

[1] C.R. Martin, P.R. Ling, and G.L. Blackburn. Review of Infant Feeding: Key Features of Breast Milk and Infant Formula, Nutrients, 8(5) (2016), 279.

# 106. INFANT MILK RECONSTITUTION: INVESTIGATION OF THE HOMOGENEITY OF PARTICLE SUSPENSION

Zheng Wang[1], Riyadh B Al-Asady[1,] Constantijn Sanders[2] & Agba D Salman[1]

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The homogeneity of the reconstituted infant milk formula has attracted more attention in the last decade due to the addition of the water-insoluble nutrients, such as vitamin A, D, E, K and minerals. The water-insoluble particles with different size ranges in the suspension may trigger several issues. The big particles would settle down in a short time driven by gravity, while the fine particles might stick on the wall of the container. On the other side, particles with hydrophobic surface could float on the liquid surface due to capillary force [1]. All these unfavourable phenomena could decrease the bioavailability of the nutrients, which are intentionally added by the manufacturer and reduce the homogeneity of the milk suspension, shown in Fig. 1.

This work investigates the homogeneity of the liquid using the inline and offline methods. The samples at different spots of the suspensions were taken and observed under a microscopy for a long time span. Beyond that, the particle motion was recorded and as the results, a stable suspended particle size was successfully obtained.

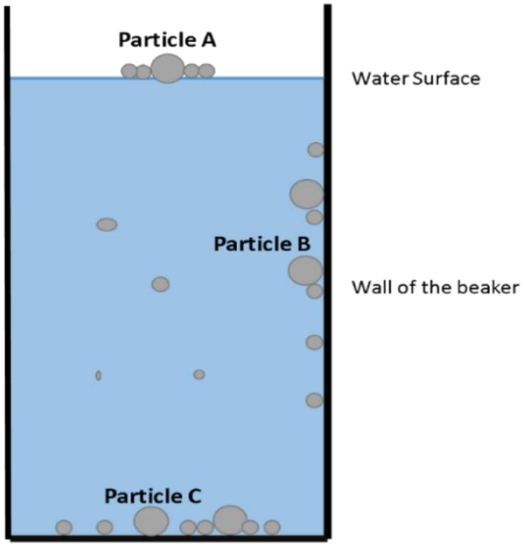


Figure 1. The problem faced when suspending solid particles into liquid. Particle A is floating on the liquid surface. Particle B is sticking on the wall of the beaker. While particle C settles down to the bottom.

[1] A. Bozon, L. Fries, J. Kammerhofer, L. Forny, G. Niederreiter, S. Palzer, and A.D. Salman. Effect of heterogeneous hydrophobic coating on floating of insoluble particles. Powder Technology, 395(2022), 592–603.

# 107. INVESTIGATION OF HEAT TRANSFER ON MOIST SPRAY-DRIED PORCELAIN PARTICLES

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1 Institute of Solids Process Engineering and Particle Technology, Hamburg University of Technology (TUHH), 21073 Hamburg, Germany
2 Department of Chemical Engineering (EQA), Federal University of Santa Catarina (UFSC), 88040-900 Florianópolis, SC, Brazil
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Porcelain tiles are produced by a sequence of steps, including powder processing by wet milling and spray drying, shaping through pressing, and thermal treatments, such as drying and sintering processes. After spray drying, the particles are stored for moisture homogenization and to cool to room temperature. The application of the particles with higher temperatures leads to several operational problems such as increased friction that hinders fluidity into the pressing die which compromises the filling of the die and, consequently, the density of the pressed tile. Moreover, the increased temperature of the particles can lead to cracks before firing and geometrical defects in the final production.

Even though it has been determined by parametric studies the negative influence of the hot temperatures of the spray-dried particles on the process sequence, heat transfer via conduction on wet spray-dried particles bed is not yet fully understood and analytical solutions to heat conduction problems in granular media are scarce.

In this contribution, an experimental setup was developed to investigate heat transfer via conduction on the particle bed (Fig.1). The heating base of aluminium was isolated with polyurethane foam and the particles were placed on a cylinder of the same material. Thermocouples type K were placed on 3 different height positions in the middle of the cross-section area to investigate how the temperature evolved during time on these different heights. The spray-dried porcelain particles were prepared for different moisture contents to analyse the influence of moisture on the system. The built setup allowed the determination of the thermal conductivity of the moist spray-dried porcelain granules, which are for DEM simulations.

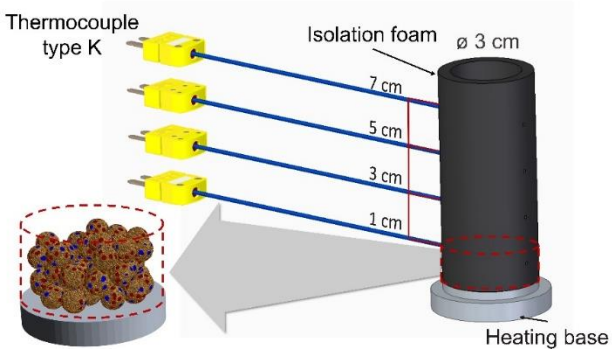


Figure 1. Experimental set up for heat transfer via conduction on moist particle bed

Acknowledge: German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) in the framework of Research Training Group GRK2462: Processes in natural and technical Particle Fluid Systems (PintPFS)

# 108. FLOWSHEET SIMULATIONS APPLIED FOR OPTIMIZATION AND SUSTAINABILITY OF PORCELAIN TILE MANUFACTURING

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Increased degrees of automation may be very helpful in managing the manufacturing process to not only boost productivity and reduce $CO_2$ emissions but also to assure high-quality metrics and reduce production costs. In this regard, flowsheet simulations can be effectively applied for process control. The simulations allow to design and optimize processes, evaluate operation parameters, and forecast of more sustainable productions of complex plants such as

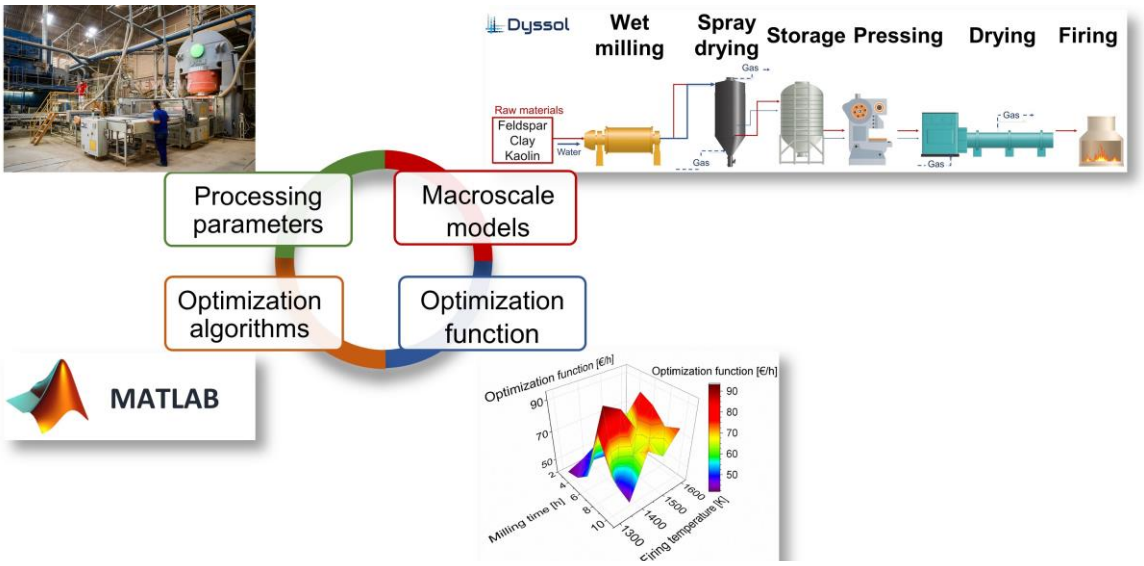


Figure 1. Optimization methodology

manufacturing porcelain tiles.

A flowsheet simulation of the entire porcelain stoneware manufacturing process chain (s. Figure 1) was developed in the open-source framework Dyssol framework [1,2]. A sensitivity analysis of the process parameters was made possible by evaluating the entire process sequence. The coupling between Dyssol and MATLAB allowed for the determination of improved process parameters that reduced energy consumption and $CO_2$ emissions while maintaining product quality. This allowed for the optimization of the process sequence. In the porcelain tile manufacturing sector, the proposed method has demonstrated significant potential to promote digitalization and establish digital twins for further online process control.

[1] V. Skorych et al. (2020). Dyssol – an open source flowsheet simulation framework for particulate materials. Software X12.

[2] C.L. Alves et al. (2021). Integrated process simulation of porcelain stoneware manufacturing using flowsheet simulation. CIRP Journal of Manufacturing Science and Technology, V. 33, p. 473-487.

# 109. THE INFLUENCE OF CALCIUM IONS ON THE PROCESSABILITY OF CROSCARMELLOSE SODIUM IN EXTRUSION/SPHERONIZATION

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In pelletization only a few excipients are suitable for the wet-extrusion/spheronization process [1]. In preliminary tests croscarmellose sodium (CCS) showed promising results to act as a pelletization aid.

In this study we aimed to examine whether calcium ions influence the properties of powder mixtures containing croscarmellose sodium and consequently their ability to form pellets. Therefore, the interaction of water with a mixture of croscarmellose sodium and calcium hydrogen phosphate anhydrous (DCPA) as well as a second mixture which additionally contained calcium chloride dihydrate ($CaCl_2$) was investigated using mixer torque rheometry. The mixtures were extruded and spheronized with different liquid to solid ratios (L/S). After drying, the products were characterized using image analysis. The influence of calcium ions on the swelling of CCS was investigated using laser diffraction by dispersing croscarmellose sodium in demineralised water or in a solution of approximately 20 % $CaCl_2$.

Products of spherical shape could be obtained in both cases. A lower L/S was needed when $CaCl_2$ was included which is also implied by the left shift in the mixer torque rheometry data. On the other hand, $CaCl_2$ led to extrudates of lower mechanical strength so that a slower speed of the spheronizer had to be used to reduce abrasion or even form products. The swelling of croscarmellose was reduced from 59 % to 34 % which was shown by the laser diffraction data.

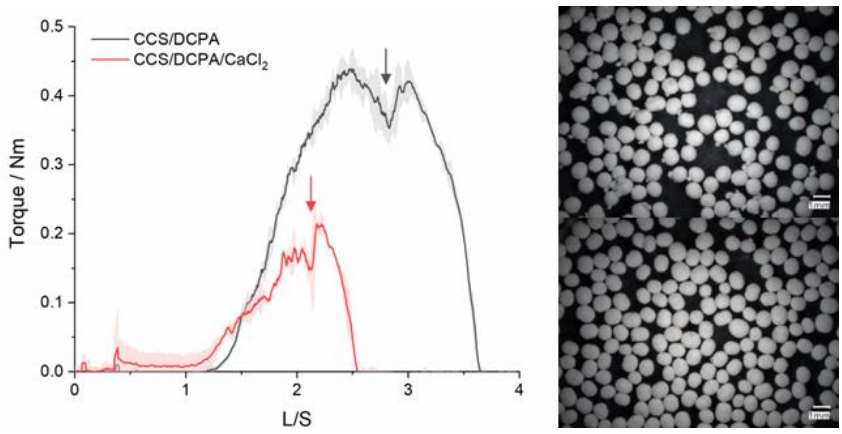


Figure 1. Mixer torque rheometry measurements of the two different mixtures (left) and the resulting pellets (top: CCS/DCPA (50:50), bottom: CCS/DCPA/$CaCl_2$ (50:43:7)) at the optimal L/S (right)

[1] A. Dukic-Ott, M. Thommes, J.P. Remon, P. Kleinebudde, C. Vervaet, Production of pellets via extrusion-spheronisation without the incorporation of microcrystalline cellulose: a critical review, Eur J Pharm Biopharm, 71 (2009) 38-46.

# 110. EVALUATION OF DIFFERENT MANNITOL GRADES IN DRY GRANULATION PROCESS BY ROLLER COMPACTION

Matteo Cerea[1], Luca Palugan[1], Anastasia Foppoli[1], Andrea Gelain[2], Alberto Cozzi[3], Graeme Macleod[4], Alice Melocchi[1] & Andrea Gazzaniga[1]

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Dry granulation technology is increasingly used in the pharmaceutical industry for improving bulk density and flowability of powder mixtures or for preventing segregation issues of highly potent drugs prior to tableting. Compared to wet granulation, dry granulation avoids the use of any liquid binder so is ideal for use with moisture and heat sensitive drugs with added benefits also in terms of costs and lower equipment footprint. In addition, roller compactor for dry granulation can be inserted in a continuous manufacturing system.

The purpose of this work was to evaluate different commercial grades of mannitol to be used in dry granulation by roller compaction (RC), with particular interest in comparing the compactability of dry granules obtained at different RC forces to that of the relevant starting raw materials as such.

Various grades of mannitol were processed in a roller compactor (TFC220, Freund Vector, IA, USA) equipped with screw feeder rotating at 20 rpm, knurled rolls 200mm diameter and 31 mm width operating at 2 rpm under 3 different compression forces (15, 30 and 45 kN). Ribbons were milled using an oscillating mill (Oscillowit, Frewitt, CH) with screen size 1.0 mm, square cross-section wire, operating at 50 rpm. Samples were analyzed for specific surface area (SSA) by the BET method (SA 3100, Beckman-Coulter, I), particle size distribution (PSD) by digital image analysis (Qicpic, Sympatec, D), flow properties according to Ph Eur monograph based on bulk and tapped densities (Stav 2003, J. Engelsmann, D) and morphology by scanning electron microscopy (SEM, Leo1430, Carl Zeiss, CH). 400 mg tablets were obtained using an instrumented rotary tablet press (AM8S, Officine Meccaniche Ronchi, I) equipped with flat punches, 11.28 mm diameter, operating at different compression force (FA=1-50 kN), rotating at 20 rpm. Prior to tableting 0.5% lubricant was blended for 2 min (Turbula mixer, WAB, CH). The mechanical strength of the tablets was characterized as tensile strength (TS according to Fell and Newton. A diametric strength tester (TBH30, Erweka, D) was used to measure the diametrical crushing load of tablets (n=3). Height and diameter were measured by digital micrometer (Digital IDC, Mitutoyo, J). Compactability (CP) of raw materials and granules was calculated by the slope of the regression line from the TS vs pressure profiles (95% i.c., multiplied by factor 105). Calculation of standard deviation of CP and statistics were performed according to Sonnergaard.

Various mannitol grades tested confirmed the ability to be used as filler in dry granulation process by roller compaction. Mannitol granules obtained showed remarkable technological properties in terms of flowability and bulk density while maintaining satisfactory aptitude for enabling tableting process.

# 111. A MODELLING FRAMEWORK BASED ON SERIAL ARTIFICIAL NEURAL NETWORKS FOR THE MODELLING OF A CONTINUOUS TABLETTING LINE

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The shift to continuous manufacturing has brought, on the one hand, with it several advantages particularly in the pharmaceutical industry in terms of capital footprint and time-to-market. On the other hand, it has added more challenges associated with modelling and optimizing the several unit operations included. Therefore, a modelling framework based on serial interconnected artificial neural networks is proposed in this paper to model the various processes of the Consigma25 Continuous Tabletting Line (CTL) at the Diamond Pilot Plant (DiPP). Such interconnected networks are designed to anticipate the properties of granules and tablets by mapping them to the various operational parameters of the CTL, where the outputs of each network in addition to the rest of the parameters are considered as inputs to the other networks. Validated on an experimental data set, the proposed framework has the ability to anticipate the properties of the granules and tablets produced using a specific blend of excipients. In addition, it can be used to control the CTL by controlling its processes.

# 112. DEVELOPING AFFORDABLE GRANULATION METHODS

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The energy consumption of different manufacturing pathways is an aspect of food production that has been gathering more and more attention of late. This is driven by increased demand on manufacturers to produce cheaper products to accommodate financially pressured consumers, especially in developing markets. In developed markets meanwhile, manufacturers face a pressure both from the public and government bodies to adhere to their social responsibility of being sustainable and to reduce their carbon footprint. The most straightforward manner in which manufacturers can display their commitment to reducing food prices and sustainability is by choosing the optimum process route based on energy efficiency.

The consideration and improvement of energy efficiency is something that has gathered a lot of interest, with recent literature heavily focusing on identifying energy saving opportunities in spray drying [1]. Granulation meanwhile is an even more widespread powder process carried out in the powder processing industry with a variety of different pathways existing to produce very different granular products. Existing literature focusing on and comparing between these processes based on energy economy to identify the optimum method is severely lacking. Rather, literature that references the energy consumption of a granulation process usually only does so through the torque parameter (which does not account for the total energy consumption of the process) with the aim of characterising the mix [2] or identifying the end point of various granulation stages [3].

This study will look at the energy consumption of a wide range of different granulation pathways as a whole, from wet granulation techniques (High Shear Granulator, Twin Screw Granulator and Fluidised Bed Granulation) to dry granulation (Roller Compactor) to evaluate the economy of each based on total energy consumption to produce a gram of desired granules. Maltodextrin has been chosen as the model amorphous material due to its commonplace use in the food industry. The impact of key process parameters on the process economy will be evaluated as well. Key granule product attributes such as friability, dissolution time and flowability have been evaluated as well to add a quality dimension when considering between the technologies.

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# 113. A SIMPLIFIED JOHANSON MODEL TO PREDICT ROLL FORCE-RIBBON DENSITY RELATIONSHIP IN PHARMACEUTICAL ROLLER COMPACTION

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Roller compaction is one of the most prevalent means of granulation in drug product development. In practice, it is vital to predict the roll force (RF)-ribbon density ($\rho$) relationship to aid the material-sparing process development and scale up. Although the well-known Johanson model quantitatively describes such relationship, it has not been extensively employed due to the requirement of the effective angle of internal friction ($\delta$) and wall friction angle ($\phi$) of powders at high stress regimes.

In this study, we demonstrated that a simplified Johanson model, devoid of $\delta$ and $\phi$, can be developed for the roller compaction of pharmaceutical powders. Specifically, we provided a theoretical basis showing that the RF-maximum pressure ($P_{max}$) and RF-$\rho$ relationship becomes independent of $\delta$ and $\phi$, beyond a critical nip angle ($\alpha_c$). We also showed that for most pharmaceutical roller compaction, $\alpha_c$ is lower than 17°. Because the nip angle increases with increasing $\phi$, one can maximize $\phi$ in actual roller compaction by using rolls with non-smooth surface, thereby leading to a roller compaction operation with the nip angle greater than 17°. Under this condition, the original Johanson model is drastically simplified to a single equation requiring only one material property (i.e. compressibility, $K$).

By performing manufacturing-scale roller compaction encompassing pharmaceutical powders with diverse $K$ (microcrystalline cellulose and dicalcium phosphate), we demonstrated that the simplified Johanson model is capable of accurately predicting RF-$\rho$ relationship. A predictive tool in the form of graphical user interface (GUI) was created based on the simplified model, and is being extensively used for in-house roller compaction formulation and scale-up development.

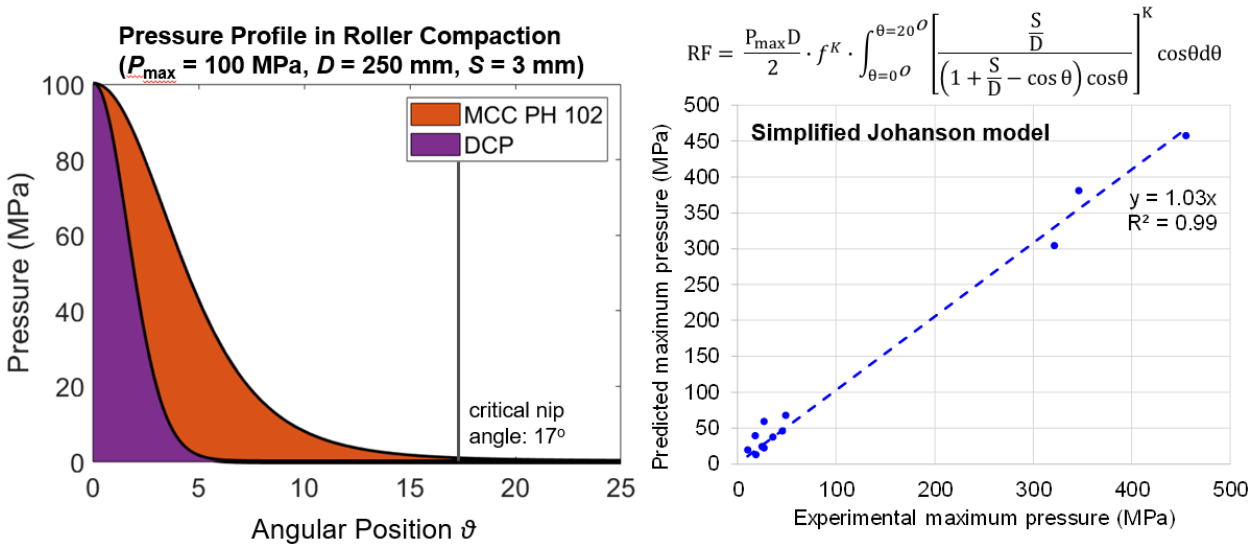


Figure 1. Pressure profile of microcrystalline cellulose and dicalcium phosphate in roller compaction (left), and the experimental $P_{max}$ vs predicted $P_{max}$ using the simplified Johanson model (right).

# 114. LACTOBACILLUS LOADED POROUS HYDROXYAPATITE (HAP) PELLETS USING DIFFERENT HAP GRADES AND PORE FORMERS

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Hydroxyapatite is the main component of bones, and it is used as porous scaffolds for bone substitution. In the last years there is upcoming interest for using HAP as carrier for drug delivery, due to its adsorptive ability and high specific surface area, enabling incorporation of therapeutic agents [1-3]. In this work porous hydroxyapatite (HAP) pellets were prepared by combining extrusion/spheronization with sintering. HAP grades with different specific surface areas (*S*w) were used as pellet's substrates and two microcrystalline cellulose size fractions, a micronized ($MCC_M$) and a large ($MCC_L$) free-flowing size fraction were used as pore formers. After heating to sublime MCC and sintering the remaining HAP at 1150 $^oC$, pellets of high porosity up to 65.3% were obtained. These were characterized by SEM, image analysis, mercury porosimetry, nitrogen sorption and mechanical testing. They were subsequently loaded with Lactobacillus (La-5) by two methods, simple immersion in La-5 suspension or injection of the La-5 suspension into pellets resting in vials under vacuum. The latter method gave significantly higher loading, especially for the $MCC_L$ pellets and there was statistical interaction of the effects of pore former particle size and loading method.

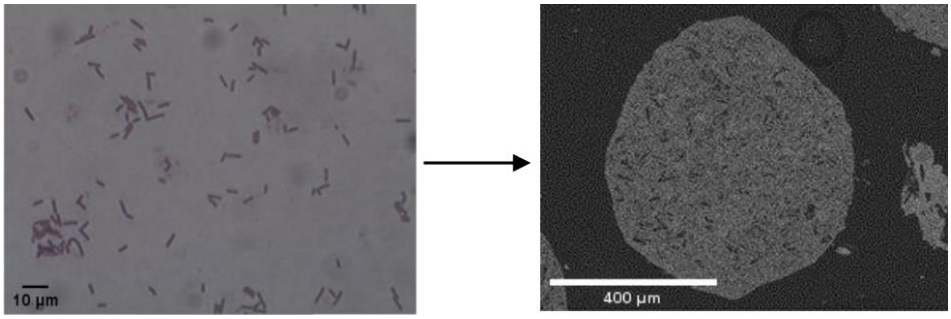


Figure 1. Microscope images of La-5 bacillus (lseft) and porous HAP pellet (right)

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# 115. RESTRUCTURATION OF FOOD POWDER USING ROLLER COMPACTOR TO INCREASE THE SHELF LIFE

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Food powders have been used for many purposes as they offer technological solutions to problems faced during food production, handling and storage due to their low bulk weight, diverse application, high production rate, and most importantly stability [1]. Despite the stability, the physical and chemical characteristics of food powder can still deteriorate when exposed to critical factors which affecting the powder's shelf life. One of the critical factors that influences the shelf life of food powder especially amorphous powder is the exposure to the relative humidity throughout processing, transportation, and storage [2]. The shelf life of food powder can be prolonged by using packaging to protect the powder from relative humidity and preserve the product characteristics. One of the most used packaging types is made from plastic. Plastic is commonly used material in packaging industry due to its low cost, light weight, flexibility, and high barrier moisture properties when exposed to relative humidity. Plastic is also sometimes combined with other types of materials such as aluminium to improve the barrier property. However, plastic is not sustainable, and the usage of plastic has caused a serious impact to the environment which is why the current industries are starting to look for a more sustainable approach through application of paper-based packaging. Unfortunately, such packaging exhibit much lower moisture barrier properties than plastic-based packaging. Therefore, there is a demand in searching for more sustainable method to further increase the shelf life stability of food powder so that the percentage of plastic in the packaging can be reduced.

A method suggested in this study is to restructure the food powder by roller compactor to increase the shelf life by making the powder less sensitive to the relative humidity. Restructuration of food powder will be a more sustainable approach as it enables the usage of lower percentage of plastic in the packaging. Roller compaction is a dry granulation process that is widely used in the pharmaceutical and food industries. In the roller compaction, fine powders are fed into rollers under high pressure to produce a ribbon-like shape compact before being milled into granules. Food powder that undergoes roller compaction process especially the one with amorphous property will experience work hardening phenomena and decrease in porosity. These two factors will help to make the powder less sensitive to the relative humidity which resulted in an increase of shelf life.

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# 116. MODUL P ROTARY TABLET PRESS: INVESTIGATING THE FORMULATION VARIABLES

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Continuous manufacturing technology in pharmaceutical industry in the past few years shows a great potential to replace the traditional batch operation mode in the near future which could improve the pharmaceutical products manufacturing [1]. Tablet is one of the widely used solid dosage forms and considered as an important route for drug administration, thus, scientific research focused more on controlling the tablet quality during the manufacturing process [2]. ConsiGma™ 25 used in this project is a continuous and fully automatic manufacturing system developed for tablet manufacturing from powder to the final product as it is connected with other operation unit including a twin screw granulator, fluidized bed, blenders, conical mill and a tablet press. GEA Modul P rotary tablet press is integrated as the last part of the manufacturing line and aims to provide more efficient way to produce tablets with high rotary speed.

The usage of lubricant is regarded as an important factor for producing tablet as the tablet quality could be affected by the amount of the lubricant. This work investigated the effect of adding different amount of lubricant before tablet machine in ConsiGma™ 25 line. Tablet properties including weight, diameter, thickness and hardness were measured by a multifunctional tablet tester. The tablet strength was also determined and examined. Meanwhile, the tableting process will also be simulated in gPROMS software where different lubricant concentration and percentage use of microcrystalline cellulose and lactose were investigated. The simulation data will be compared with the experimental results.

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# 117. TO IMPROVE MILK POWDER QUILITY BY DRY COATING

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Milk powder is highly susceptible to environmental factors during preservation. These changes may seriously affect the chemical and physical properties (such as particle size, density, flowability, solubility, water activity, etc.) of the milk powder, thereby reducing the sensory quality and shelf life of the product. Coating technology is widely used in the pharmaceutical industry to change the surface composition and properties of materials. The dry coating technology has been expanding into the food industry in recent years although few studies involves in this area [1].

In this study, milk powder was dry coated with whey protein and casein protein layer by using high shear mixer, and the properties (such as particle size, surface morphology, infrared imaging spectroscopy, flowability, water vapor sorption, reconstruction, etc.) of the two products with the original milk powder were compared.

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# 118. COARSE-GRAINED DISCRETE ELEMENT SIMULATION AND EXPERIMENTAL STUDY OF WET GRANULATION PROCESS

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Wet granulation is widely used in various industries, including pharmaceutical, chemical, and food industries. Improvement of powder flowability and enhancement of material strength are some of the advantages of this process. Therefore, it is of great interest for the industry to predict the optimal process parameters. Discrete Element Method is a powerful tool that can let us efficiently simulate the physical behaviour of the system and minimise costly experiments by direct equipment design/selection. In the case of wet particulate systems in a pendular state, the effect of the presence of liquid bridges between particles can be considered by incorporating capillary and viscous force of the liquid bridge force into DEM.

One challenge with DEM simulations on an industrial scale is computational expense as there are millions of particles in the system requiring simulation. In this study, a coarse-grained particle (CG) upscaling approach has been used for the simulation of a drum granulator. In CG-DEM, a group of original particles are represented as a larger particle, and scaling rules will be applied to ensure the conservation of mass, momentum, and energy. This can lead to a significant reduction in the computational cost of industrial scale DEM simulations [1]. To our knowledge, a limited number of studies have been done on CG-DEM simulation of systems containing liquid bridges [2,3]. Hence, it is important to understand how to apply a coarse-graining approach for wet particle systems and compare different scaling rules.

The proposed CG-DEM model will be validated using the experimental data obtained from the wet granulation process of catalyst support material on an industrial lab-pilot scale.

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# 119. PREPARATION AND EXAMINATION OF THE COMPRESSIBILITY OF TITANATE NANOTUBE-API COMPOSITES

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Titanate nanotubes are used in many places, e.g. in the field of environmental protection, food industry or medicine. Due to their biocompatibility, excellent mechanical strength, and chemical resistance, these nanosystems are extremely suitable for drug delivery applications and processing into various solid dosage forms [1].

In present study, the compressibility and tablettability of the composites of unfunctionalized and functionalized titanate nanotubes and active pharmaceutical ingredients were evaluated. The compaction and deformation results obtained with a Korsch EK0 eccentric tablet press using different compression forces, were evaluated using the Kawakita-Lüdde and Walker equations. According to the Kawakita-Lüdde method, the titanate nanotubes show an exceptionally good arrangement after filling, due to the aggregation tendency resulting from the relatively high surface energy. In the case of composites this value was usually much lower, which indicates that the composite formation decreases the surface energy and the resulted aggregation. This also resulted the decrease of the 1/b coefficients which displays the energy demand to reduce the initial volume to its half during the rearrangement phase. In contrast, the Walker equations indicated excellent compressibility of the native nanotubes in the deformation phase which may be due to the flexibility of the spiral structure. During the formation of the composites, nanocrystals of the active substance are formed on the surface and inside of the nanotube, which reduces flexibility and corrupts deformation properties. Nevertheless, the strength of drug carrier interactions and the properties of nanocrystals have a high influence on this property, which is well visible from the results of TNT-hydrochlorothiazide composites made with dimethyl sulfoxide, where the active substance is in amorphous form and shows similarly good results as native TNTs.

In summary, the composite formation may slightly deteriorate the mechanical properties of titanate nanotubes, but with a properly optimized formula, they may still be suitable for tableting without excipients.

Funding: Project no. TKP2021-EGA-32 has been implemented with the support provided by the Ministry of Innovation and Technology of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme.

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# 120. A NOVEL MECHANISTIC MODEL TO DESCRIBE THE SWELLING OF DISINTEGRATING GRANULES

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One of the most common requirements for granular products are desired dispersion and dissolution characteristics. In some cases, rapid disintegration is required while in others, controlled dissolution is preferred. Disintegration agents are typically added to rapid dispersing formulations to promote the break-up of the granular product into the active ingredients through absorption of penetrating liquid inside the product. Which in turn increases the rate of dissolution.

A new mathematical model to describe the swelling mechanism of a single disintegrating granule is presented in this work. The mechanistic model considers important rate processes from liquid uptake to liquid absorption by the disintegrant particles and finally, swelling of the granule. Through these mechanisms, the model can predict the evolving granule size along with the porosity, saturation and size of the primary particles.

Specific estimates of model parameters were initially obtained through single granule experiments with formulations consisting of sodium starch glycolate as the superdisintegrant, microcrystalline cellulose as the filler and polyethylene glycol/water as the binder. To track the individual size of a granule, a bespoke flow cell was developed. The flow cell was coupled with an optical microscope to capture the behaviour of a swelling granule quantified through an in-house image-based algorithm.

To explore the model performance on a swelling granule, four key parameters were chosen for investigating their influence on the disintegration process: initial granule size, initial porosity, superdisintegrant diffusivity and its maximum absorption ratio. The simulations revealed that when increasing the initial granule size, a decrease in the relative swelling rate was observed. This was due to lengthening the time required for the liquid saturation level to reach the threshold value which initiates the absorption phenomena. Increasing the initial porosity displayed interesting behaviour; as more pores are available for greater liquid uptake, disintegrant particles simultaneously reach their maximum absorption ratio leading to faster swelling kinetics. As expected, increasing liquid diffusivity and maximum absorption ratio results in increasing the swelling rate due to an increase in the liquid absorption rate.

In conclusion, the model presented in this work is capable of predicting the essential swelling behaviour of a disintegrating granule using a mechanistic approach. This is a key step in the development of new models capable of predicting the disintegration of populations of other products, such as tablets and granules.

# 121. EFFECTIVENESS OF PREDICTING SPHERICAL AGGLOMERATE PROPERTIES USING A POPULATION BALANCE MODEL

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Population balance models (PBM) are useful tools for the prediction of product properties such as size distributions for many particulate processes e.g., crystallisation, agglomeration and granulation. PBMs are frequently used in the pharmaceutical industry as they allow for process design, sensitivity analysis and predictive capabilities which reduce the cost of process development.

Spherical agglomeration is a particle size enlargement technique that has promising applications for the pharmaceutical industry. The spherical agglomeration process produces agglomerates with enhanced sphericity and density, by using an immiscible bridging liquid to agglomerate particles in suspension. It is particularly useful to engineer particle properties for challenging morphologies such as needle-shaped crystals. Due to the improved properties, the agglomerates are frequently able to undergo direct compression, reducing the number of unit operations needed for manufacture of active pharmaceutical ingredients (API).

Spherical agglomeration is a relatively new particle size enlargement technique, and industrial uptake is hindered by lack of understanding of the process. Recent progress in mechanistic understanding has been made [1], and a PBM for spherical agglomeration has been developed in gPROMS Formulated Products (Siemens PSE, UK). This PBM uses information and mechanistic understanding of high shear wet granulation (HSWG) to predict spherical agglomerate properties which include size and size distribution as well as the average liquid volume fraction of the agglomerates.

In this work, robust experimental validation of this recently developed spherical agglomeration PBM is presented. The effect of primary particles size and mixing intensity in the vessel is investigated. Mixing intensity is varied by changing both impeller speed and geometry, providing varied fluid velocity profiles, particle meeting probability and hydrodynamics. Impeller speed is considered in the model equations however impeller geometry is not; to improve the model the system hydrodynamics should be incorporated.

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# 122. VOLUME-INTERACTING LEVEL SET DISCRETE ELEMENT METHOD: THE ANGLE OF REPOSE OF ANGULAR AND CONCAVE PARTICLES

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Despite the many advances in the numerical modelling of powders using the discrete element method (DEM), the description of realistic particle shapes remains challenging. Current methods that describe particle shapes are either prohibitively expensive or limited to rounded or convex shapes. To address these limitations, we have developed a new method called volume-interacting level set DEM (VLS-DEM) which has no restrictions on particle shape; concave particles of arbitrary complexity can be modelled, even interlocking ones [1].

In this work, VLS-DEM was used to study the effect of varying angularity and concavity on the angle of repose of various particle shapes. To study angularity, the Platonic solids were used. New concave shapes were then created by hyperbolising these five solids. When the original vertices are positioned on the unit sphere, each solid can be hyperbolised by remapping all surface points $\boldsymbol{r}$ according to $\boldsymbol{r} \rightarrow \boldsymbol{r}(\boldsymbol{r} \cdot \boldsymbol{r})^{\boldsymbol{\alpha}}$ with $\alpha$ being the hyperbolicity constant. Changing the constants allows the generation of increasingly concave shapes, creating more spiky or angular shapes for increasingly positive constants and more bubbly or less angular shapes for increasingly negative constants. At $\alpha = -0.5$, all shapes become a unit sphere, thereby also providing a natural reference point for a systematic comparison between all shapes.

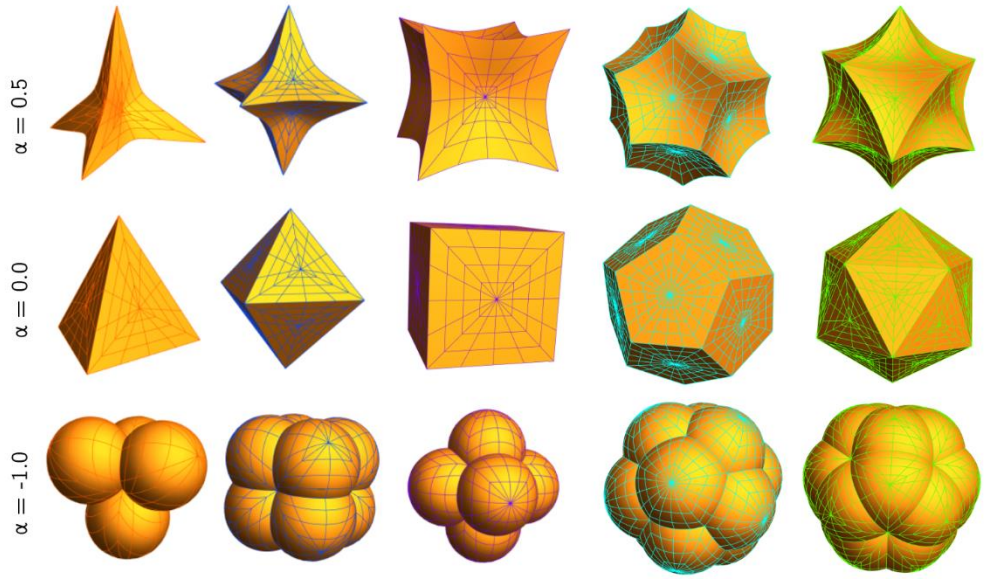


Figure 1. The five Platonic solids and some of their hyperbolised variants.

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# 123. FLUID BED PROCESSING OF NANOCRYSTAL FORMULATIONS WITH PERSONALISED DISSOLUTION PROFILES

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The pursuit of developing personalized drug formulation entails many challenges. The idea is to overcome prevailing problems in drug administration one of which is poor medication adherence due to polypharmacy [1]. Especially in the treatment of cardiovascular diseases, multiple drugs are co-prescribed, many of which a poorly soluble (BCS or BDDCS classes II and IV) [2]. Both the personalization and the efficacy of the administered drug can be improved by using a complex multi-component dosage form.

Transforming poorly soluble active pharmaceutical ingredients (API) into nanosuspensions is a way of improving their solubility and possibly their bioavailability. The preparation of API nanosuspension can be done by wet milling for a wide range of APIs [3]. Further processing of the nanosuspension into a viable drug formulation is the second step in the process.

In this work, we present a possible solution by using a fluid-bed device as a granulator or Wurster coater. Fluid-bed apparatus utilizing the active pharmaceutical ingredient in a form of nanosuspension is a very powerful combination for the development of advanced drug formulations. In the fluid-bed apparatus, the API suspension is used with additional excipients either in the wet granulation process as a binder or with Wurster insert as a functional coating. Availability of choice for the coating additives or powders for granulation presents great variability in the material and release characteristics of the final product.

The granulate preparation is targeted for the preparation of minitablets and is optimized for good flowability. By changing the binder additives or the powdered excipient we alter the dissolution kinetics. The coated pellets are modified by using different coating polymers or additional layers, such as pH-sensitive polymers, further adjusting the release characteristics. These small units used in multi-component capsules present a perfectly adjustable drug formulation tailored to the needs of an individual patient.

[1] M.T. Brown, J.K. Bussell, Medication adherence: WHO cares?, Mayo Clinic proceedings, 86 (2011) 304-314.

[2] L.Z. Benet, F. Broccatelli, T.I. Oprea, BDDCS Applied to Over 900 Drugs, The AAPS Journal, 13 (2011) 519-547.

[3] F. Hládek, S. Chvíla, O. Navrátil, M. Balouch, F. Štěpánek, Systematic Investigation of Wet-Milling Kinetics and Colloidal Stability of Pharmaceutical Nanocrystals, Crystal Growth & Design, 22 (2022) 6928-6940.

# 124. PREDICTION OF GRANULE CRITICAL QUALITY SIZE ATTRIBUTES IN A TWIN SCREW WET GRANULATOR USING POPULATION BALANCE MODELLING

Neeru Bala[1], Jeremiah Corrigan[1,2], Bilal Ahmed[1], Jonathan Meyer[2], Marek Schongut[2], Kai Lee[2], Martin Rowland[2], James D. Litster[1], Neil Dawson[2] & Rachel Smith[1]

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With increasing interest in continuous manufacturing within the pharmaceutical industry, twin screw wet granulation has emerged as a key process within continuous manufacture of solid oral dosage forms. Computational simulation of twin screw wet granulators can lead to reduced costs by minimising experimental burden, allowing the design space for process optimisation to be explored more efficiently. Mechanistic-based population balance models (PBM) can predict key phenomena, such as under-wetting, by accurately predicting the full particle size distribution. This is compared with statistical models used in previous research, such as T-shaped partial least squares, which are limited to predicting granule scalar quantities (D10, D50 and D90) and to the conditions and formulations in the data set.

In this work, a recent breakage kernel, specifically developed for a twin screw wet granulator [1], was implemented in PBM, in addition to other previously developed kernels for the remaining key processes: nucleation, layering and consolidation. Breakage is one of the most dominant processes in the twin screw granulator [2], and by using a kernel developed specifically for this process it is expected model performance will be improved. A global systems analysis was employed in combination with process knowledge to reduce the number of parameters requiring estimation in the PBM, with the aim to understand the required quantity of experimental data, and to ultimately minimise future experimentation for model calibration and subsequently reduce costs. A parameter estimation approach was developed using mechanistic process knowledge of critical process parameters (such as liquid to solid ratio and powder feed number) to reduce experimental design. The proposed method was evaluated on experimental data for both a hydrophobic and non-hydrophobic formulation [3] and compared with alternative experimental designs. Results demonstrate that the PBM captures multi-modal distributions that can highlight certain phenomena. Additionally, the proposed approach to minimising experimental design successfully estimated parameters with fewer experiments than a standard factorial design.

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# 125. A NOVEL METHOD FOR RAPID SCREENING OF SPRAY-DRIED FORMULATIONS

Vojtěch Klimša[1,2], Lucie Mašková[1], Gabriela Ruphuy Chan[1,2], František Štěpánek[1]

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The last decade saw a rise of high throughput screening and combinatorial chemistry – two powerful techniques, which significantly accelerated the rate of discovery of the new active pharmaceutical ingredients (APIs). However, due to the nature of these processes, a majority of these newly discovered molecules are practically insoluble in water. Reportedly, around 40% of the marketed drugs nowadays and nearly 90% of the drugs in the development pipelines are drugs with poor aqueous solubility [1]. Since drug intake into human body is controlled by the ability of the drug to dissolve in water, this poses a challenge for formulation scientists. One of the solutions to this problem is drug amorphization, which can be achieved in different ways, however a literature review [2] reveals spray drying as the most popular technique nowadays. But since spray drying is a batch unit operation, the process has to be stopped and the device has to be cleaned, before product with a different composition can be produced, which significantly increases the time needed for development of a new product.

In this work we introduce a new, highly efficient approach to combinatorial production of spray-dried samples, which is often needed for the design of new drug forms. Our device consists of a series of pumps connected with a mixer, which is able to produce variable inlet and an autosampler capable of collecting multiple particle fractions. This study proposes an efficient and systematic approach consisting of four phases: pre-formulation, polymer screening, composition screening, and process optimization. The approach is tested using a ternary system of two drugs (Ezetimibe and Simvastatin) and one polymer.

All in all, we would like to demonstrate back-to-back development of a pharmaceutical formulation in rapid and efficient manner, but in general the proposed approach has the potential to accelerate the development process for a number of different spray-dried products.

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[2] K. Edueng, D. Mahlin, C.A.S. Bergström, The Need for Restructuring the Disordered Science of Amorphous Drug Formulations. Pharmaceutical Research; 34 (2017) 1754-1772.

# 126. IDENTIFICATION OF LETHAL MECHANISMS AND CONTROL STRATEGIES IN DEVELOPING PROBIOTIC TABLETS

Bide Wang[1], Andrew Middleton[2], Rachael Gibson[2], Jayant Khanolkar[2], Oleksiy Klymenko[1] & Charley Wu[1]

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Tablet is one of the main forms for probiotic delivery and probiotic viability is one of critical product properties for these tablets [1]. However, manufacturing of probiotic tablets is a complex multi-stage process, involving many potential lethal mechanisms. In particular, shearing, compression and local heating were identified as three lethal mechanisms, leading to the reduction of probiotic viability during tableting. Shearing and compression could cause severe mechanical damage to cell walls and membranes while local heating could lead to oxidation and denaturation of cell protein. The most effective control strategies to alleviate the impact of these three lethal mechanisms during formulation development and the manufacturing process include formulation design and process optimisation, such as choice of excipient, probiotics/excipients ratio, and compaction profiles. This work aims to give an overview of these lethal mechanisms and corresponding control strategies, which could serve as a guideline for developing and manufacturing probiotic tablets.

[1] S. Klayraung, H. Viernstein, S. Okonogi, Development of tablets containing probiotics: Effects of formulation and processing parameters on bacterial viability, International Journal of Pharmaceutics, 370.1-2(2009) 54-60.

# 127. INVESTIGATING PROCESS VARIABLES THAT AFFECT LOGO-BRIDGING

Euan F. Murgatroyd & Ian P. Gabbott

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Pharmaceutical tablet film coating is a common process for oral solid dosage forms. A frequently used method is pan coating. In this method, a circular perforated pan, holding the tablets to be coated, rotates and a centrally positioned spray gun sprays the suspension onto the tablet bed.

Pan coating has many process variables and due to the complexity of the process, several defects can occur(1). Several of these defects have been investigated and have a known cause, allowing adjustments to be made that can resolve the defect. One defect that does not have a well-established cause in the literature is logo-bridging. Logo-bridging is one of most severe as it can cause the loss of definition and subsequently identification of the logo, which can be a regulatory requirement.

The results of the study demonstrated that logo/intagliation bridging defects were associated with higher atomising air pressures, higher coating suspension spray rates, lower pattern air pressures and lower drying air flow temperatures. The shape and pattern of the spray at different conditions was also examined and a correlation between the spray pattern and the incidence of logo/intagliation bridging was recorded.

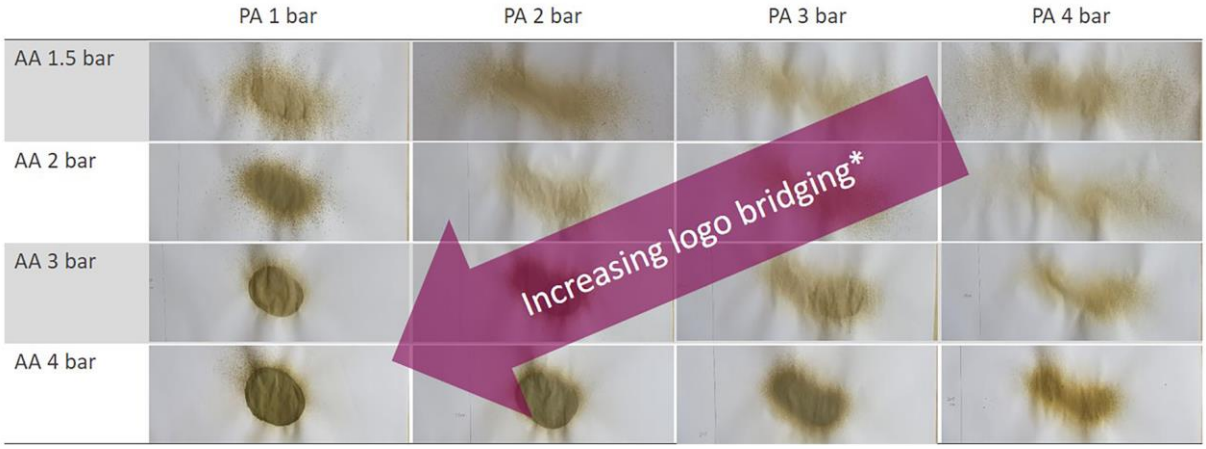


Figure 1. Images of Spray Characterisation with associated Atomization & Pattern air pressures

[1] D. Niblett, S. Porter, G. Reynolds, T. Morgan, J. Greenamoyer, R. Hach, I. Gabbott, Development and evaluation of a dimensionless mechanistic pan coating model for the prediction of coated tablet appearance, Int. J. Pharm. 528 (1–2) (2017) 180–201, https://doi.org/10.1016/j.ijpharm.2017.05.060.

# 128. DEM-CFD SIMULATION OF VOLUMETRIC EXPANSION OF GRANULAR MATERIALS

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Swelling or volumetric expansion is a prevalent phenomenon in many processes of granular materials. For example, swelling of excipients particles affects the performance of the disintegration of tablets in the patient's body and the efficiency of the oral delivery of drugs [1].

In this work, a microscopic diffusion swelling model that considers the change in microstructure of swelling particles is implemented into the discrete element method coupled with computational fluid dynamics (DEM-CFD). The expansion of particle bed consists of super absorbent polymers (SAP) particles, i.e. the swellable particles, and polyformaldehyde (POM) particles, i.e. the non-swellable particles, in a rectangle container is then analysed experimentally and numerically. It is shown that a tapered pattern of SAP particles and an arch pattern of POM particles are formed during the swelling process. The mixing degree of the binary particle system is quantified using the Lacey index, and it is found that the mixing index increases with time until the POM particle layer is encompassed by SAP particles. A close examination of the normal stress distribution reveals that POM particles located in the central area are pushed out by the swollen SAP particles that migrate upwards through a weak passage, i.e. 'low-stress channel'. Moreover, the inter-particle friction and the particle-wall friction play different roles in the upwards migration of the particles.

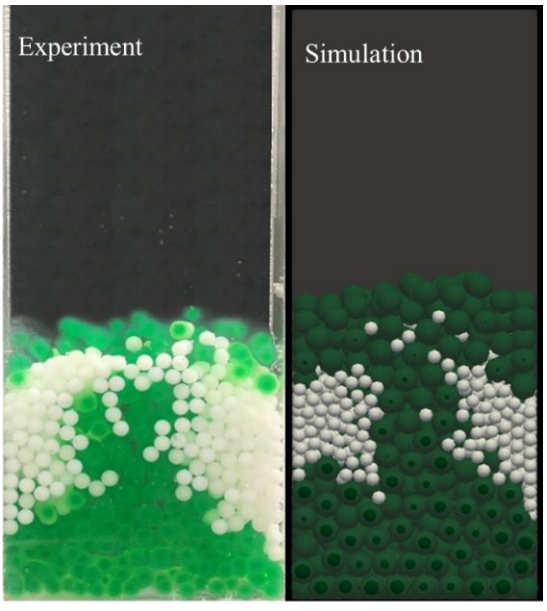


Figure 1. Swelling behaviour of particles in a cubic container

[1] D. Markl, J.A. Zeitler, A Review of Disintegration Mechanisms and Measurement Techniques, Pharm. Res. 34 (2017) 890–917.

# 129. ACTIVE MATERIAL-CARBON BLACK (AM-CB) SPHERICAL CO-AGGLOMERATES FOR IMPROVED HANDLING OF LI-ION BATTERY MATERIALS

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Particle engineering techniques offer an attractive opportunity to improve the handling of Li-ion battery materials and performance of electrodes. Battery nano-materials like carbon black, $LiFePO_4$ are difficult to handle and process due to dust hazard, poor flowability. Furthermore, traditional slurry-casted electrodes suffer from multiple particle-scale issues including slow solid-state diffusion of Li-ions, micro-cracking, inadequate active surface area, poor electronic conductivity network. Some of these handling and performance related issues can be mitigated by generating well-structured particle agglomerates.

In this work, we apply a novel particle engineering technique to generate structured agglomerates. The technique of spherical agglomeration is imported from the pharmaceutical industry and applied to the battery materials. Through use of an immiscible solvent known as the bridging liquid, primary particles are agglomerated in a suspension. This novel methodology is implemented to generate multicomponent co-agglomerates of active material, conductive additives, and polymer binder. The schematics below elaborates on the mechanism behind this co-agglomeration procedure. Obtained agglomerates are characterised in detail to demonstrate tunability of agglomerate properties through mechanistic understanding of the process-structure relationship. Advantages of such structured agglomerates in electrode manufacturing process are also discussed.

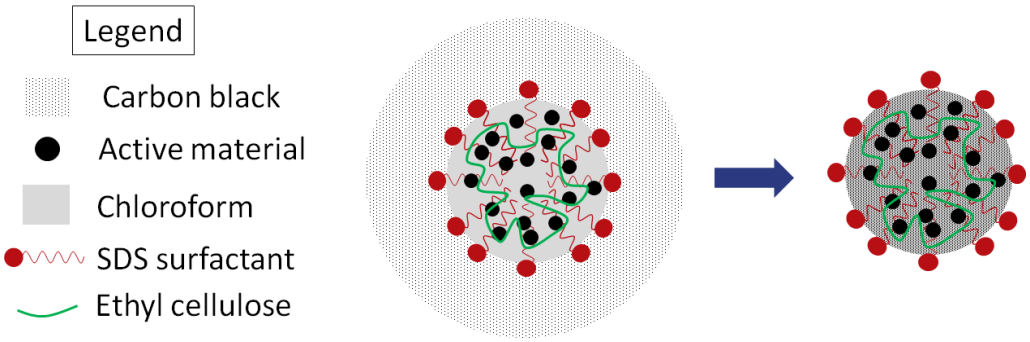


Figure 1. Mechanism of AM-CB co-agglomeration

# 130. NUMERICAL INVESTIGATION OF GRANULE FLOW CHARACTERISTICS IN AN INTENSIVE MIXER USING DEM

Ali Z. Al hassn[1], Kimiaki Washino [2] & Ei L. Chan[2], Agba D. Salman[3]

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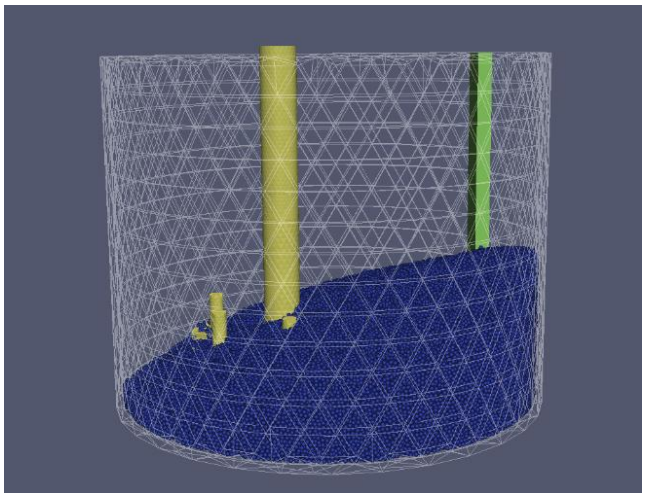
The dynamics of the moving granules in the granulator have a significant effect on the granule attributes. Therefore, studying the particle motion during the mixing process in the high shear mixer is a required step for comprehending the granulation process. In this work, Discrete Element Method (DEM) is used to study the particle motion in an intensive mixer "Eirich EL1" with a specific process called Multi-stage granulation (MSG) which is depicted in the authors' previous work (Al hassn et al., 2018). In MSG, the granulation process is divided into three stages: low impeller speed, high impeller speed, and then low impeller speed again.

The results showed that, the velocity distribution inside the mixer was not analogous in all zones of the mixer. The velocity of particles was the highest at the zone after the contact of impeller with the particle bed. The highest velocity gradient was noticed to be there, as well. In addition, the Lacey's mixing index (LMI) and velocity probability distribution function (PDF) was also used to study the flow characteristics in the MSG process. The LMI was better in the second stage, i.e. at the high impeller speed, compared to the first/third stage. This gives indication that the bed has better homogeneity at the second stage. The area under the curve of the PDF showed that the number of particles influenced by the impeller in the first/third stage was slightly higher compared with the second stage.

[1] Al hassn, A.Z., Jeßberger, S., Hounslow, M.J., Salman, A.D., 2018. Multi-stage granulation: An approach to enhance final granule attributes. Chem. Eng. Res. Des. 134, 26–35.



Flow of particles in Eirich EL1 mixer

# 131. TOWARDS BETTER SUSTAINABILITY: SPRAY-DRYING OF HIGHLY VISCOUS CONCENTRATES

Riyadh B Al-Asady[1], Vincent Meunier[2], Gerhard Niederreiter[2] & Agba D Salman[1]

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## ABSTRACT

There is continuous increasing pressure and demand on food industry to improve the sustainability of different manufacturing processes.

During atomization process, two types of forces are important, stabilizing (viscosity and surface tension of the liquid) and disruptive forces which depends on the nozzle type. For the atomization to happen, the disruptive forces should exceed the stabilizing forces.

Increasing the total solid content (TS) of the spray dryer feed to improve the sustainability leads to increase the stabilizing forces, viscosity and surface tension, which consequently makes the atomization less efficient especially in obtaining the desired droplet size. High viscosity leads to larger droplets size which could be more challenging to dry and may induce more sticking.

In this study, the impact of introducing gas bubbles inside the viscous liquid before spraying is investigated.

Three scales were used to investigate the process efficiency of spray drying of the viscous food materials. These are single droplet scale, atomization and spray dryer.

The results showed an improvement in the efficiency of the spray drying of viscous food solution in term of drying kinetics, particle size, and consumption of energy.

# 132. CONTINUOUS MANUFACTURING OF PHARMACEUTICAL TABLETS: EFFECT OF DIFFERENT UNITS AND FORMULATION PARAMETERS

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Continuous manufacturing of tablets is increasingly attracting more pharmaceutical companies. Continuous tablet manufacturing line, ConsiGma-25, includes different units such as granulators, dryer, mill, mixers at different stages and tableting machine. The effect of different parameters of some units were investigated against the final quality of the tablet in different previous studies.

In this work, the effect of interaction of different ConsiGma-25 units on the granules and tablets properties were investigated. The granules properties were size distribution, porosity and moisture content whereas the investigated properties of the final tables were tablet strength, weight, dimensions, dissolution time. Another investigated factor is the formulation parameters of the primary powders. This is carried out by changing the formulation of the two primary powders, lactose and microcrystalline cellulose.

The results showed a difference in the scale of effect of different units in the manufacturing line on the properties of granules and tablets.

# 133. FAST TO CLINIC: MATERIAL SPARING PLATFORM APPROACH TO ROLLER COMPACTION PROCESS DEVELOPMENT

Ranjit Dhenge [1], Chandan Bhugra[2], Parind Desai[2], Stephanie Lam[2] & Daniel Goodwin[3]

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2 Research and Development, GlaxoSmithKline, Upper Providence, USA
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Continuous processing utilizing dry granulation is an attractive option not only due to ease of scale-up, given an existing equipment train, but also is material sparing. Resource, i.e. API and time savings are mainly attributable to material sparing approach to process development.

Scientific approach utilizing material properties that allow projection of process parameter ranges via API sparing testing of ribbon Solid Fraction versus Tensile Strength have been well documented. Utilisation of ribbon solid fraction data to process parameter allow acceleration to First Time in Human Studies but also do so with minimal utilization of API in early development. Application of scientific principles to scale up between Pilot Scale and Commercial Scale roller compactors make acceleration to commercialization feasible.

Further, use of platform formulation approaches also allows generation of data on multiple formulations/ projects thereby enabling generation of large amount of prior knowledge which can be leveraged.

# 134. REPLICATING RING-DIE PELLETING PROCESS WITH SINGLE-DIE PELLET PRESS: EVALUATION AND OPTIMIZATION

Prutha Nagaraja [1], Dejan Miladinovic [2] Laurent Cavin[3], Thomas G Gfroerer [3], Andreas Thuermer [3], Odd Ivar Lekang [1] & Kristian Berland [1]

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2 Department of Animal and Aquacultural Sciences, Norwegian University of Life Science, Elizabeth Stephansens v. 15, 1430 Ås, Norway
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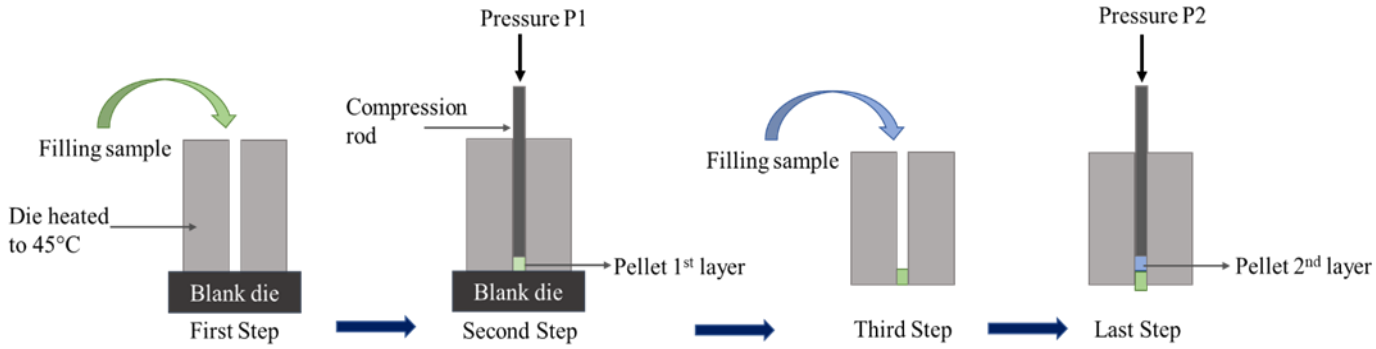
Plastic additives are essential components incorporated during plastic production to enhance the performance of plastic material and modify the properties of the polymer to achieve a specific purpose. Traditionally, plastic additives have been dosed in powder form, but this form comes with several challenges related to dosing, homogeneity of the mixture, dust explosion, and transportation. Therefore, as a solution, plastic additives in pellet form has emerged as an alternative that is easy to handle [1]. To investigate the pelleting process, a single-die pellet press was used as it allows low-cost and lab-scale testing in comparison to the most commonly used ring-die pellet press [2]. After evaluating various methods, we concluded that the pellet-making technique depicted in the figure below is the most suitable for replicating the ring die process. We evaluated the effectiveness of the pelleting process by examining the physical properties of the resulting pellets, including dimensions, tensile strength, surface roughness, and density. Our study indicated that we could produce pellets with comparable tensile strength to those produced by a ring-die pellet press. Furthermore, we estimated the optimal pressure required for producing high-quality pellets. We have used a Scanning Electron Microscope to analyze the surface morphology of the pellets and examine the bonding of particles, and the sintering effect involved in the formation of pellets. Based on our results, we can conclude that the single-die pellet press is a valuable tool for gaining a better understanding of plastic additive pellet processing on a small scale.




A schematic illustration of the pelleting process using a single-die pellet press.

[1] J. Semen, Albemarle Corp, Granular polymer additives and their preparation, US patent 6,821,456, 23 November 2004.

[2] S. J. Rueda, B. Rego de Vasconcelos, X. Duret, J.-M. Lavoie, Lignin Pellets for Advanced Thermochemical Process—From a Single Pellet System to a Laboratory-Scale Pellet Mill, Energies, 15(2022), 3007.

# 135. SYSTEMATIC STUDY TO IMPROVE THE POWDER FLOWABILITY AND REDUCING THE PERCENTAGE OF FINES IN ROLLER COMPACTOR

Yang S. Mohamad[1], Riyadh Al-Asady[1], Mingzhe Yu[1], Manfred Felder[2], Vincent Meunier[3], James Litster[1] & Agba D. Salman[1]

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Roller compaction is a continuous dry granulation process that is widely used in food and pharmaceutical industries as it has high efficiency, low cost and can be easily scaled up. There are three important steps involved in roller compaction; feeding, compaction and crushing stages. During the feeding stage, the rearrangement of powder particles will occur under low pressure before moving into compaction stage where the powder is compressed under two counter- rotating rollers and referred as ribbons. The ribbons will then enter a crushing stage where the ribbons will be milled into granules. The flowability of powder across the rollers in the compaction area is important as it has significant effect on the product quality [1]. The non-uniform powder flowability across the rollers will affect the uniformity of quality distributed at different locations across the ribbon which eventually resulted in non-uniform qualities in granules [2]. Therefore, it is essential to improve the powder flowability across the roller in the compaction area. Another drawback of continuous dry granulation process is the amount of uncompacted fines due to a lack of compaction stress on both sides of the roller edges during the compaction process [3].

This research focuses on a systematic study of a customized guider design to improve powder flowability across rollers and reduce the percentage of fines in the compaction zone. The studies were validated by examining powders with varying flowabilities. The results show a significant trend with improved uniformity of powder flowability across the rollers and reduced production of fines. This offers potential for long-term sustainability and resource conservation in industrial applications by reducing material recycling and energy consumption during continuous processes.

[1] M. Yu, C. Omar, A. Schmidt, J. D. Litster, A. D. Salman. Roller compaction: Infrared thermography as a PAT for monitoring powder flow from feeding to compaction zone. International Journal of Pharmaceutics, (2020) 578.

[2] M. Yu, C. Omar, A. Schmidt, J. D. Litster, A. D. Salman. Improving feeding powder distribution to the compaction zone in the roller compaction. European Journal Pharmaceutical Biopharmaceutical, (2018), 128, 57-68.

[3] M. K. Hwang, S. Y. Kim, T.T. Nguyen, C.H. Cho, & E.S. Park. Use of roller compaction and fines recycling process in the preparation of erlotinib hydrochloride tablets. European Journal of Pharmaceutical Sciences, (2019).

# 136. FOOD VS PACKAGING: DYNAMICS OF OIL-MIGRATION FROM PARTICLE SYSTEMS INTO FIBROUS MATERIAL

Luc Dewulf[1], Michael K. Hausmann[2], Annabel Bozon[3],
Gerhard Niederreiter[2], & Agba D. Salman[1]

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Paper packaging for compacted or tabletted foods is seen as a key sustainable packaging of the future [1]. Yet its fibrous structure is susceptible to absorb oils and other small molecules from the contacting food. Underlying phenomena associated with oil stains from compacted food on fibre-based packaging, such as of viscous liquid flow, capillarity, and gravity from compacted particle systems into fibre networks are not fully understood yet. This work employed for the first time Raman laser spectroscopy coupled with automated image quantification for comparison of oil flow dynamics between a food compact and paper. The extent of oil released from the compact and imbibed into paper showed similar exponential decay with time for both porous systems. Also, for the first time, oil migration dynamics inside the compact was visualised, showing that oil movement within the tabletted food proceeds at different rates depending on the location within the compact, with 4-times variations between tablet top and bottom. This discovery opens the way to further understanding liquid transfer between porous media and harness microstructure engineering to increase food and packaging performance.

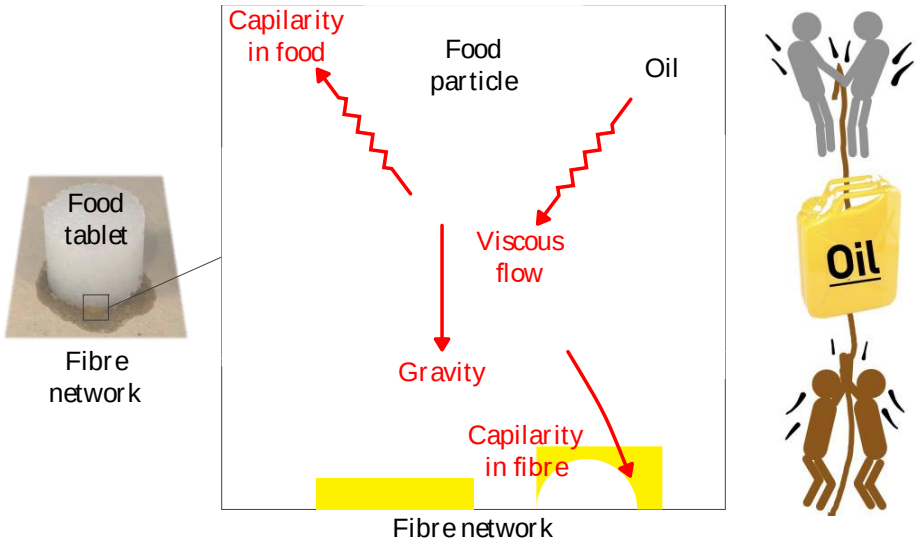


Figure 1. Schematic of different drive and resistance processes occurring during oil-release from particle food systems to fibre-based packaging, in analogy to a tug competition for oil.

[1] B.L. Tardy, J.J. Richardson, L.G. Greca, J. Guo, J. Bras, O.J. Rojas, Advancing bio-based materials for sustainable solutions to food packaging, Nature Sustainability, 6 (2023) 360-367.

# 137. REAL-TIME GRANULE SIZE MEASUREMENT IN A TABLET PRODUCTION LINE: INVESTIGATION OF GRANULE SIZE IN FLUDIZED BED DRYER

Shengda Hou, Jeanina M. Bungău, James D. Litster & Agba D. Salman

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As granulation represents the core process during solid dosage form manufacturing, granules size variability can significantly impact the quality of the tablets produced, which is reflected in both physical aspect and internal structure, as well as content uniformity and disintegration properties [1].

In this work, granule size distribution in the fluidised bed dryer as part of a continuous powder-to-tablet line was measured using a spatial filter velocimetry probe. Figure 1 shows the granule size distribution throughout drying. In the filling stage, an increased percentage of fines are detected. As filling ends and only drying proceeds, the percentage of fines detected by the probe drops and larger granules can be observed. While due to the numerous parameters involved within a continuous manufacturing set-up, understanding the granule size performance during drying can be challenging and further investigation is needed.

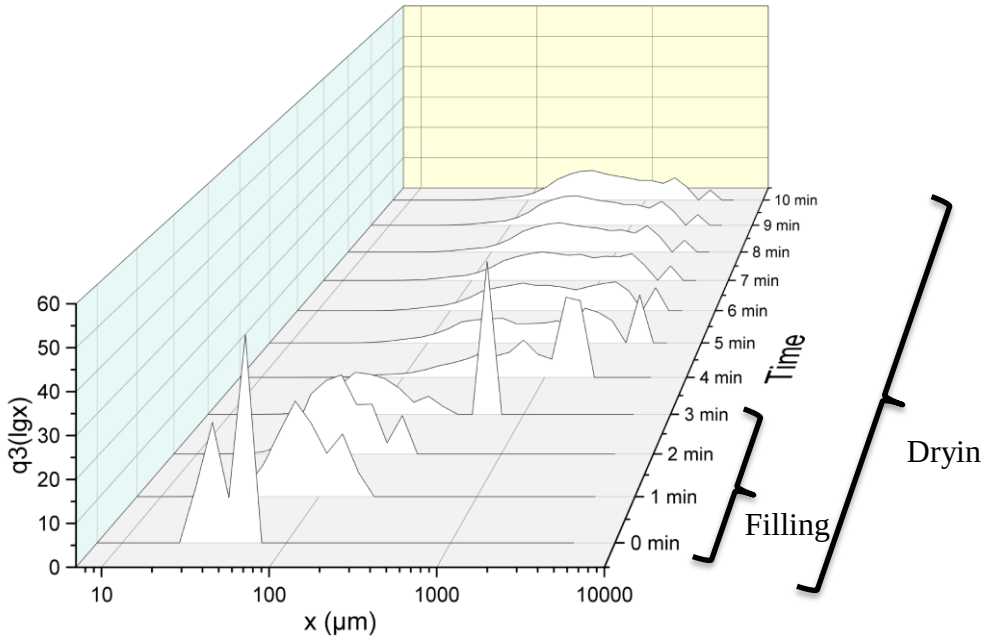


Figure 1. Volume density distribution q3 (lgx) with time,filling stage lasts for 3 minutes and total drying time is 10 minutes. 0 minute is defined as the time granules are detected by the probe.

[1] V. Pauli, Y. Roggo, P. Kleinebudde, M. Krumme, Real-time monitoring of particle size distribution in a continuous granulation and drying process by near infrared spectroscopy, European Journal of Pharmaceutics and Biopharmaceutics. 141 (2019) 90–99.