Emerging Scientist 2019

Qi (Tony) Zhou

- PhD from Monash University
- Postdoctoral training at University of Sydney
- Dept. of Industrial and Physical Pharmacy, Purdue University
- Over 80 research papers and >$8M funding
- Recipient of several fellowships and research awards

PURDUE UNIVERSITY

Formulation, Characterization and Drug Delivery of Dry Powder Inhalers

Qi (Tony) Zhou

Assistant Professor

PURDUE UNIVERSITY | College of Pharmacy

BACHELOR OF ENGINEERING IN PHARMACEUTICAL SCIENCES FROM SHENYANG PHARMACEUTICAL UNIVERSITY (1997 - 2001)

FORMULATION SCIENTIST IN SHENZHEN NEPTUNE PHARMACEUTICALS (2001 - 2003)

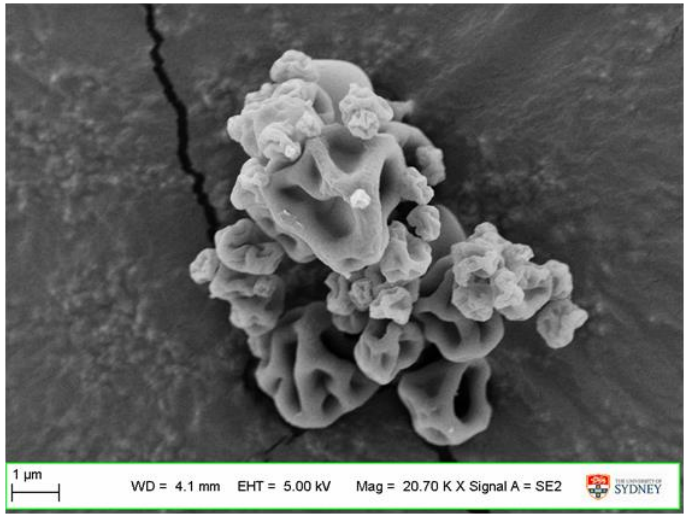
- **Freeze-dried Polydatin powder for injection (US patent application 10/492405)**
- **Freeze-dried Zoledronic Acid powder for Injection**
- **Freeze-dried Calcium Folinate powder for Injection**
- **King Drink (oyster) tablets**

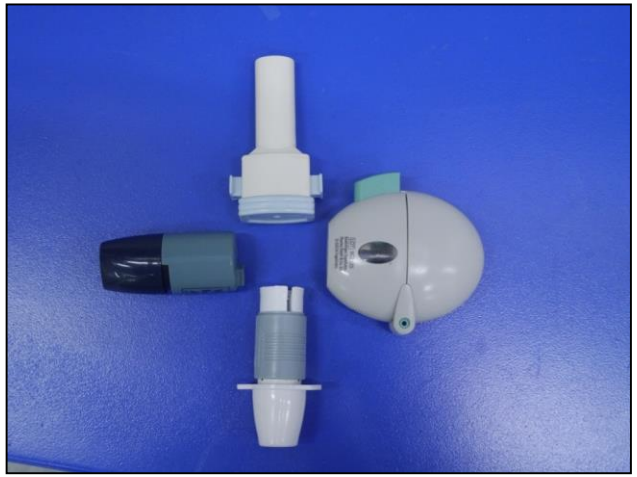
MASTER OF SCIENCES IN PHARMACEUTICS (2004 – 2006) NATIONAL UNIVERSITY OF SINGAPORE

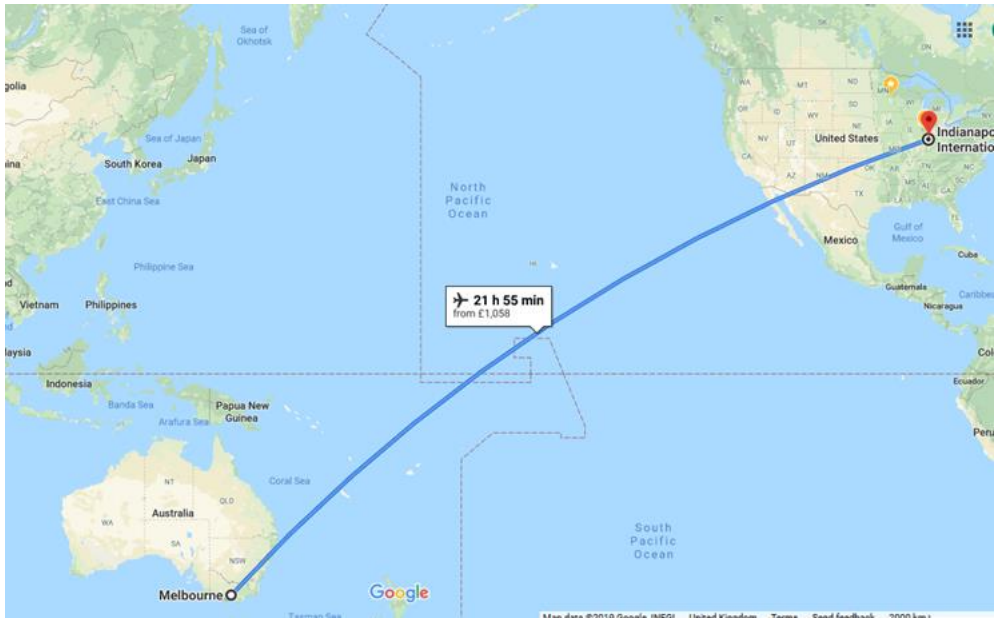
PURDUE UNIVERSITY

PHD IN PHARMACEUTICS (2007 - 2011) MONASH UNIVERSITY OF AUSTRALIA

POSTDOCTORAL FELLOW
THE UNIVERSITY OF SYDNEY (2012 – 2015)



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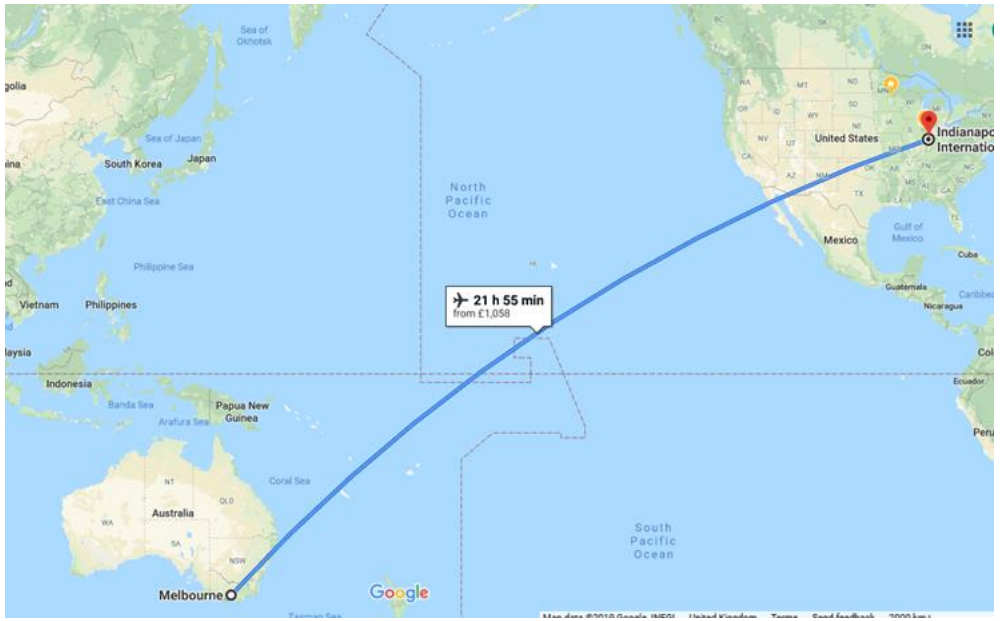
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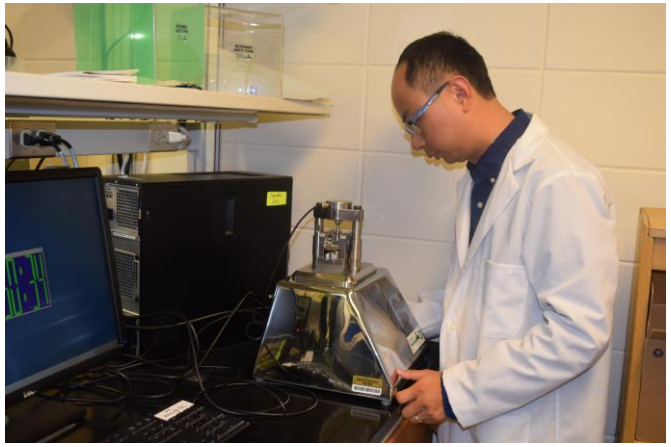
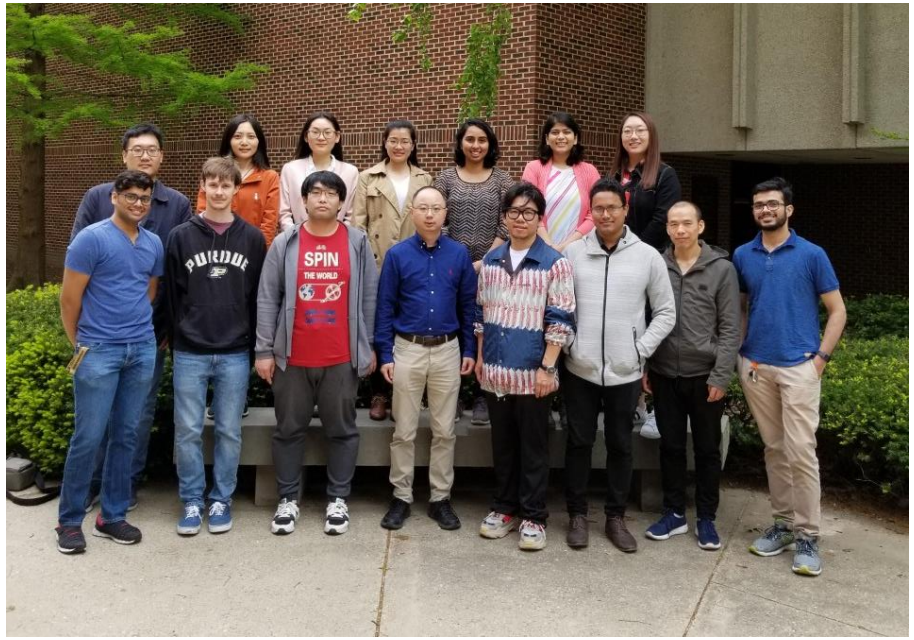
Purdue University (Oct 2015 – present)

Assistant Professor
Department of Industrial and Physical Pharmacy





Outline

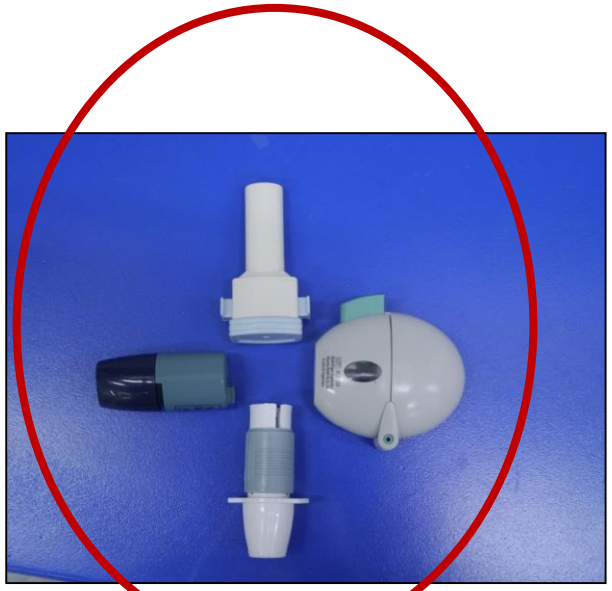
Part 1. Particle engineering and characterization for inhalation formulations

Part 2. Pulmonary drug delivery systems

Part 3. Particle engineering for biological solids

INHALER DEVICES

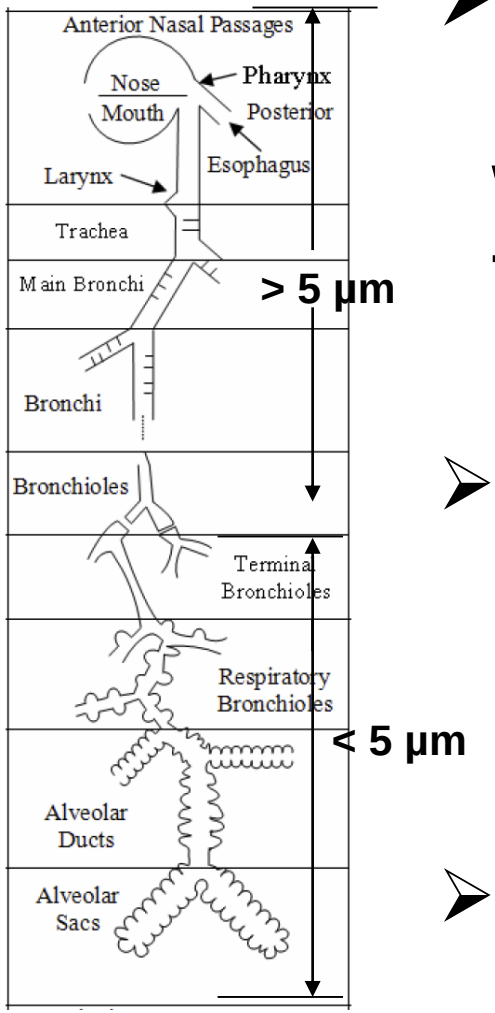
Nebulizer



Dry powder inhaler

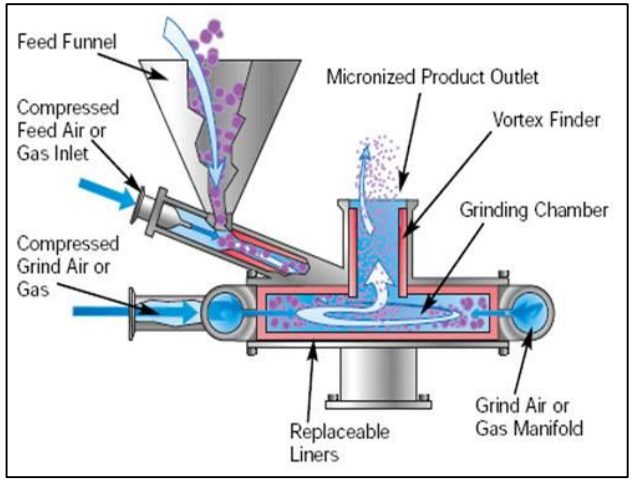
Metered dose inhaler

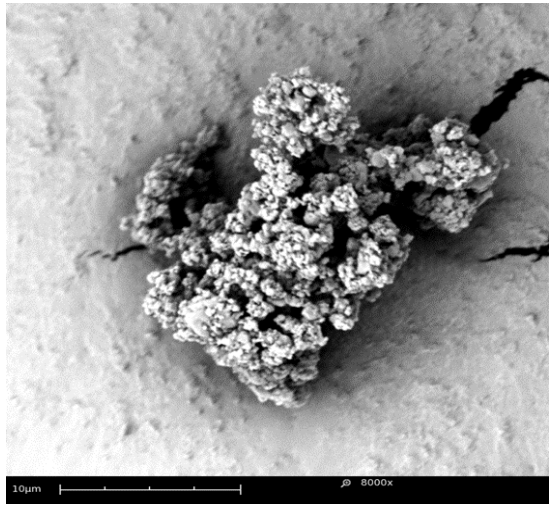
- http://www.manufacturingchemist.com/technical/article_page/Improving_inhalers/57725
- Nazrul Islam, Ellen GladkiDry innovationInternational Journal of Pharmaceutics, Volume 360, Issues 1–2, 6 August 2008, Pages 1–11



- **In pulmonary drug delivery system, particles with aerodynamic diameter > 5 µm will normally deposit in upper airways due to inertial impaction**
- **Particles with aerodynamic diameter 1-5 µm will mostly deposit in lower airways**
- **Particles with aerodynamic sizes < 1 µm may be exhaled**

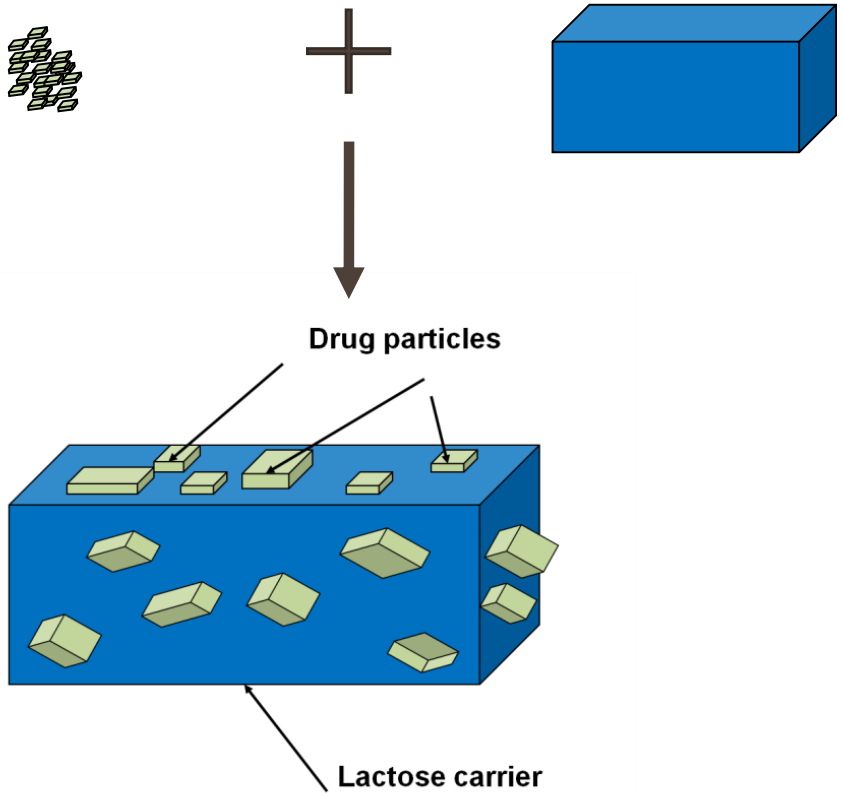
Jet-milling produces cohesive drug particles with poor aerosol performance





DRY POWDER INHALER FORMULATION

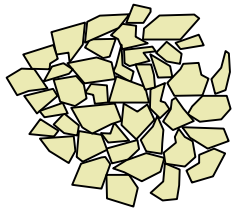
Fine drug powder



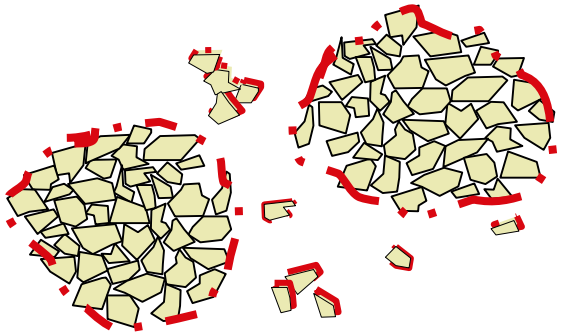
Coarse carrier

Dry coating cohesive particles with anti-sticking materials to improve their powder flow

Agglomerates of fine particles



Traditional blending



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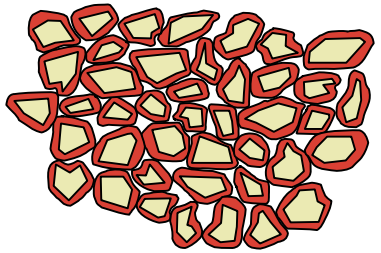
Coating materials (e.g. lubricant)

Mechanical dry coating



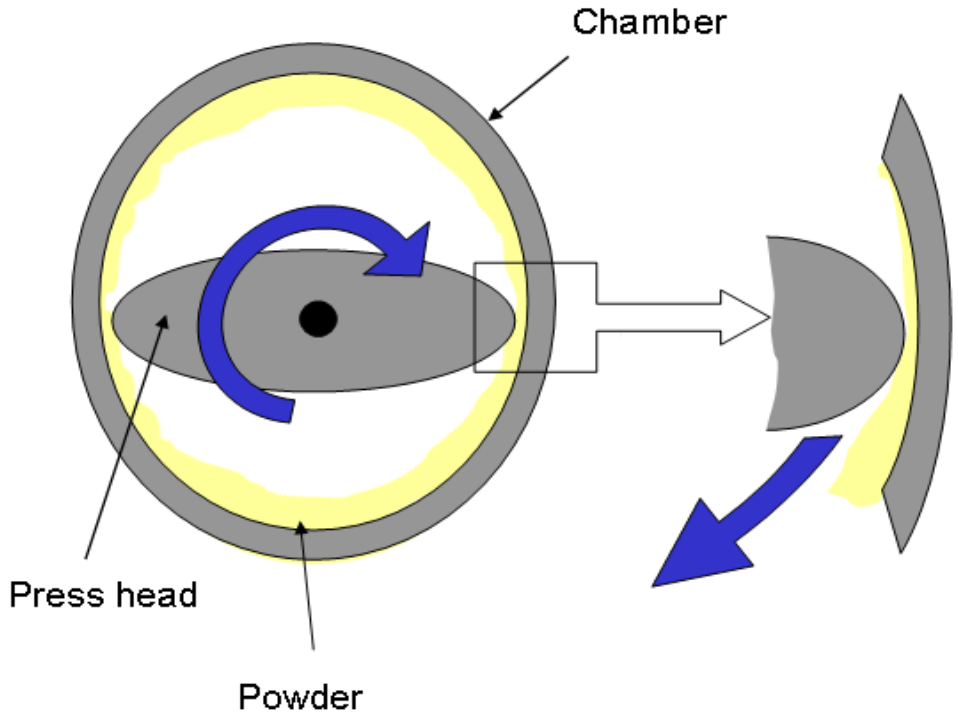
- Mixing: Cannot break agglomerates - coat agglomerates not particles
- Mechanofusion: Break agglomerates and coat individual particles

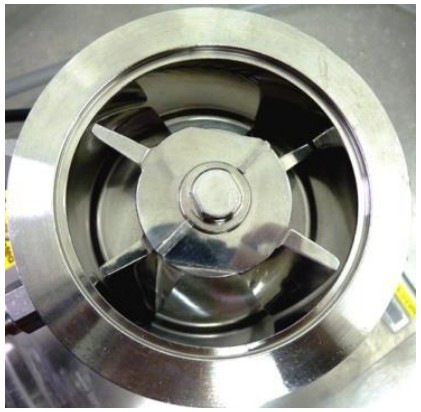
Dry coating approach

- **Simpler – less steps and process parameters than spray drying or solvent coating**
- **Safer – No organic solvents**
- **Greener**
- **Cheaper– Less energy consumption (save energy and reduce carbon emission)**

http://www.greatest-money-saving-tips.com/energy-saving-tips.html

MECHANOFUSION DRY COATING

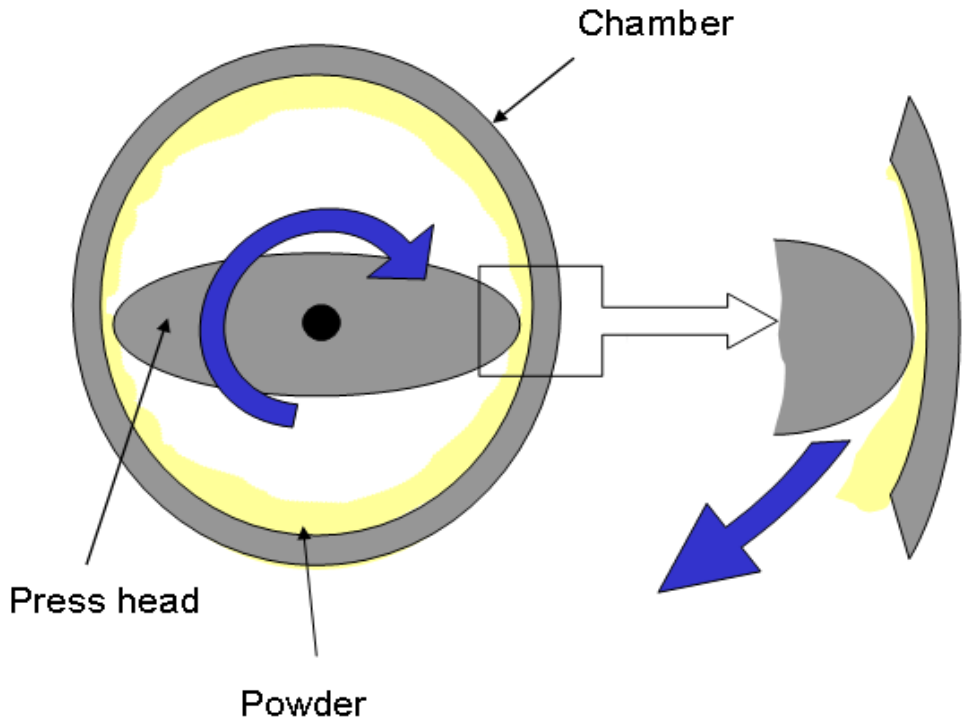


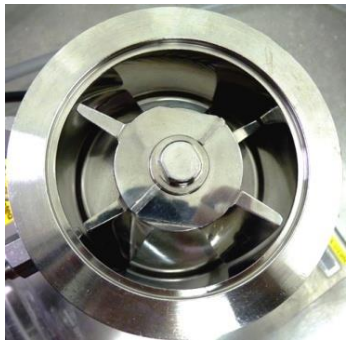


- **Simple process**
- **Complex mechanisms:**
  - **particle/particle**
  - **particle/press head**
  - **particle/chamber wall**

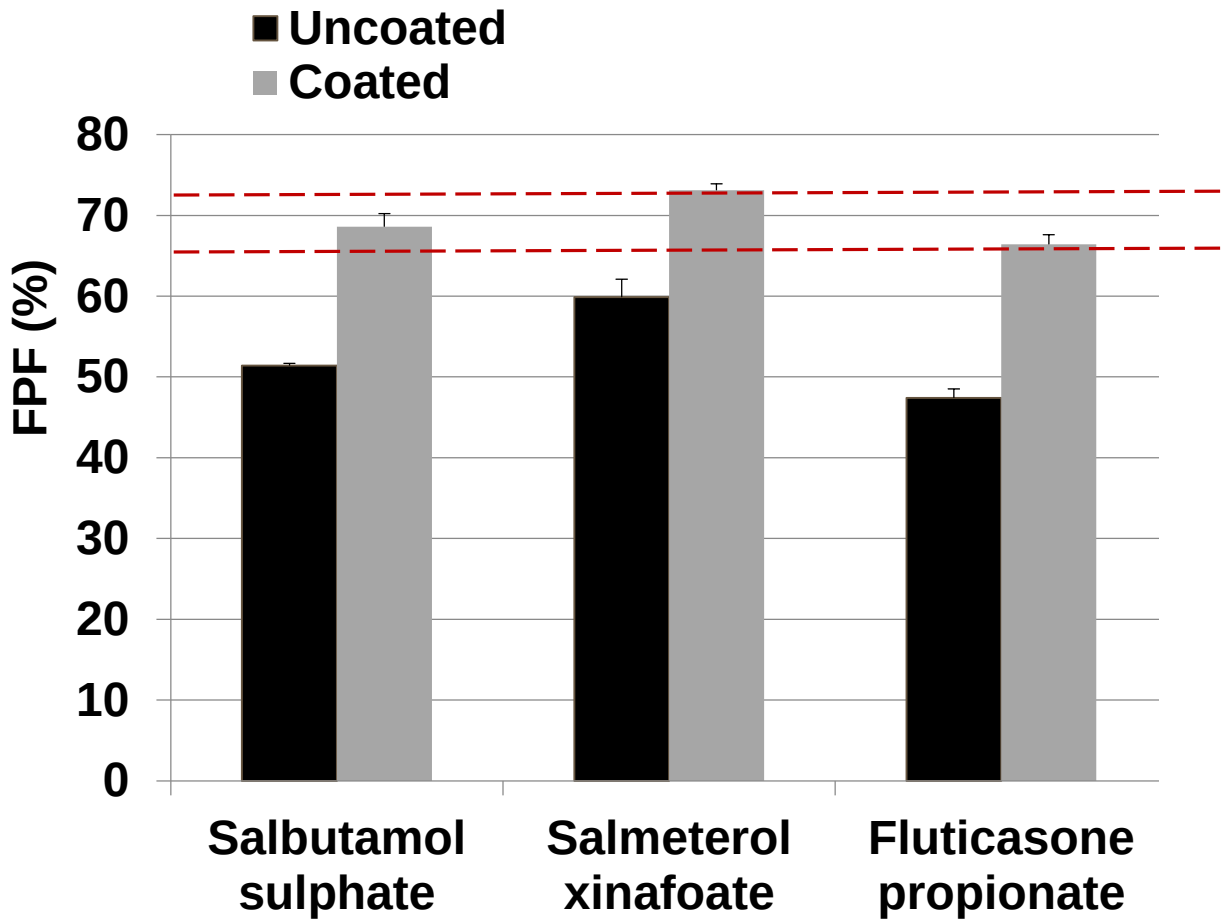
Courtesy: Dr. David Morton and HOSOKAWA micron Ltd.

MECHANOFUSION DRY COATING





Courtesy: Dr. David Morton and HOSOKAWA micron Ltd.

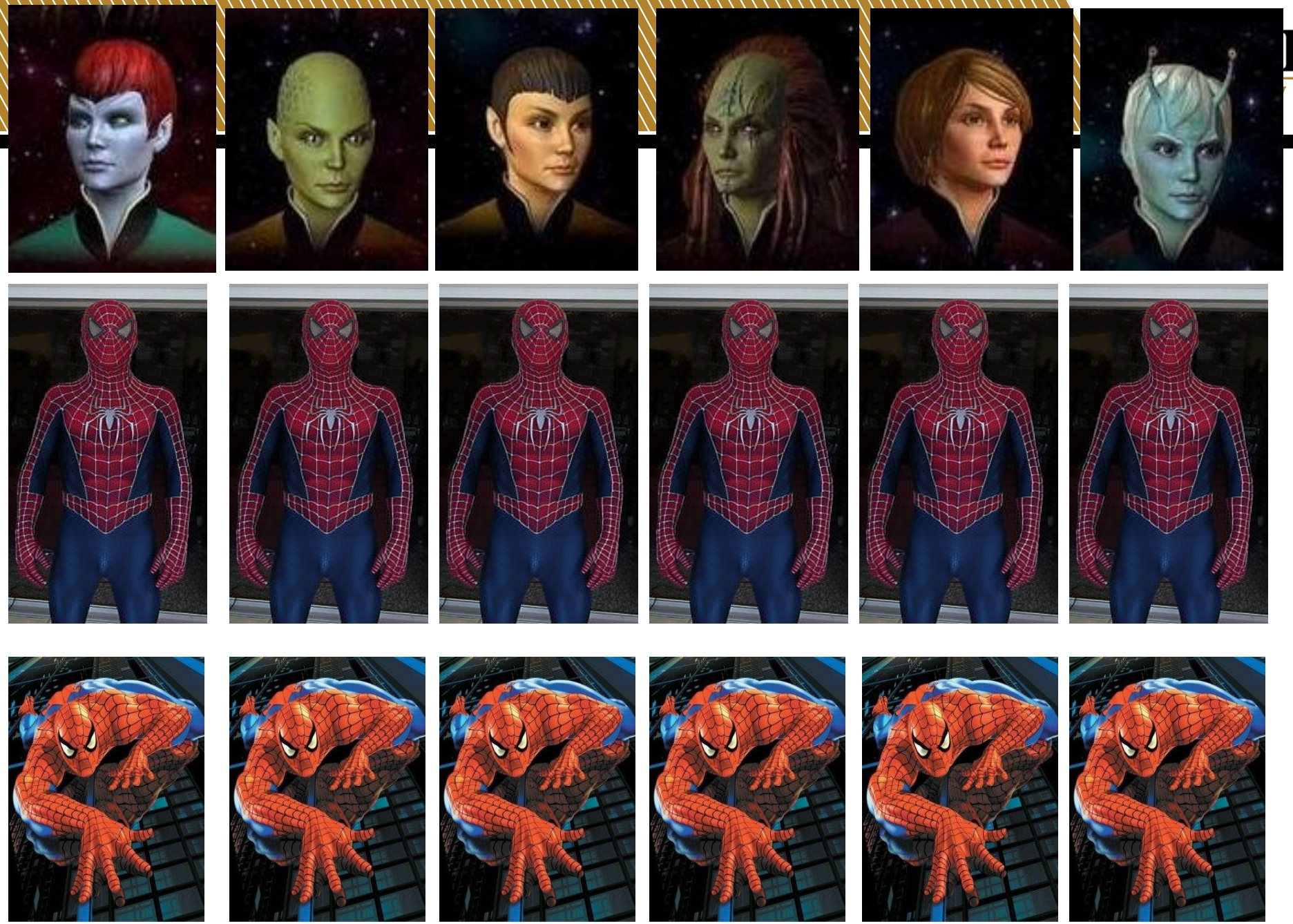


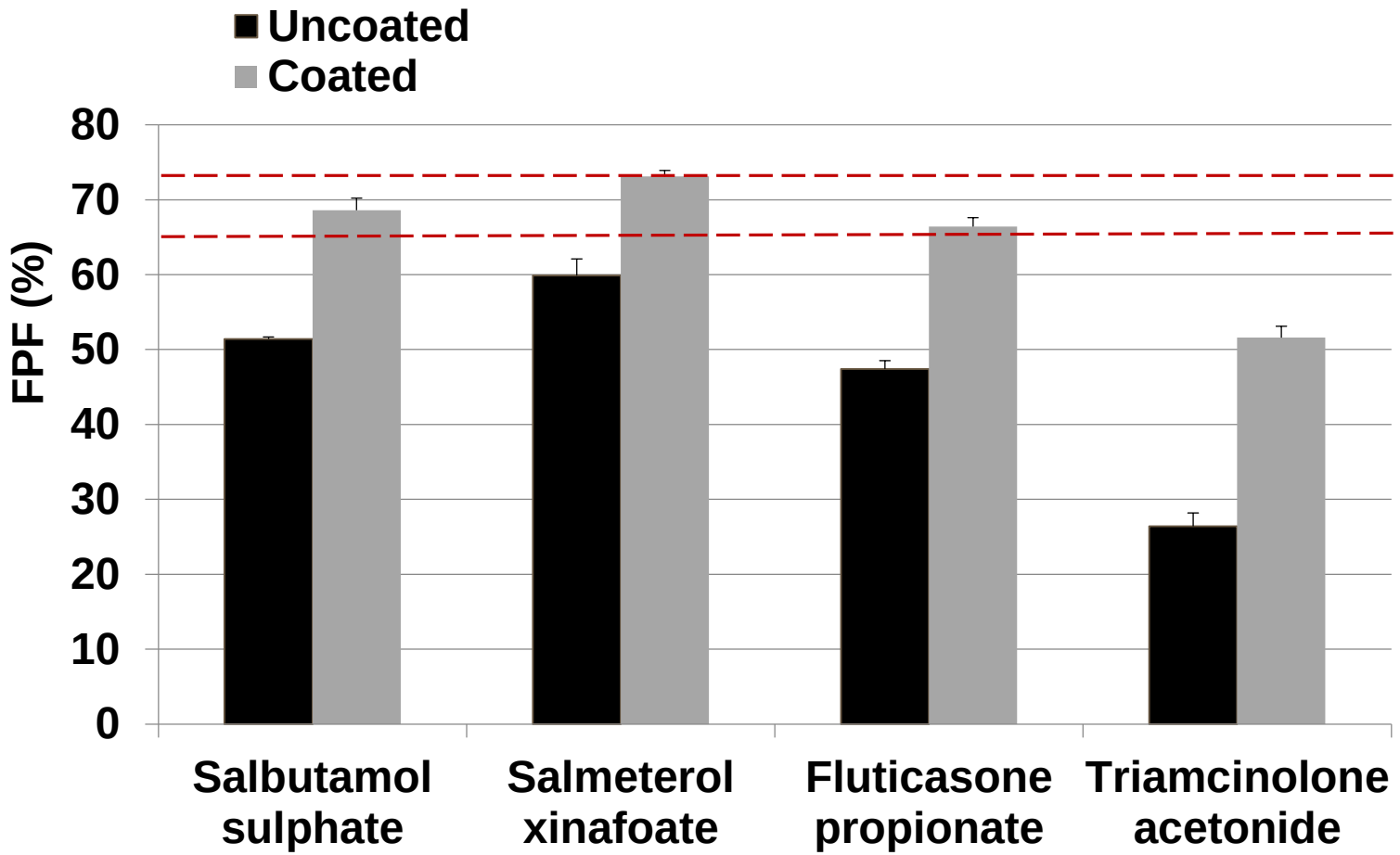
2010. International Journal of Pharmaceutics, 394 (1-2), pp. 50-59.

- Can we make all drugs behave in the same way by homogenize their surface chemistry via dry coating?

- To solve the problems due to different surface properties of the particles (quality by design)

RDUE
ERSITY





2010. International Journal of Pharmaceutics, 394 (1-2), pp. 50-59.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Magnesium stearate has been used in DPI products

SkyePharma

Foradil® Certihaler™ Novartis / Schering-Plough

- Foradil® Certihaler™ now approved in 24 markets (Europe, Mid-East, S America…)
- launched in Germany Sep ′05 and Switzerland Oct ′05 but batches withdrawn by Novartis from both markets Jan ′06
  - a few patients mishandled the device and received an incorrect dose
  - SkyePharma working with Novartis to investigate cause and correct
- FDA “approvable” letter Apr ′06 – device modifications will be required for final approval

21 Jun 06 83

Lack of fundamental understanding on surface coating quality and its effects on aerosol performance

Objective

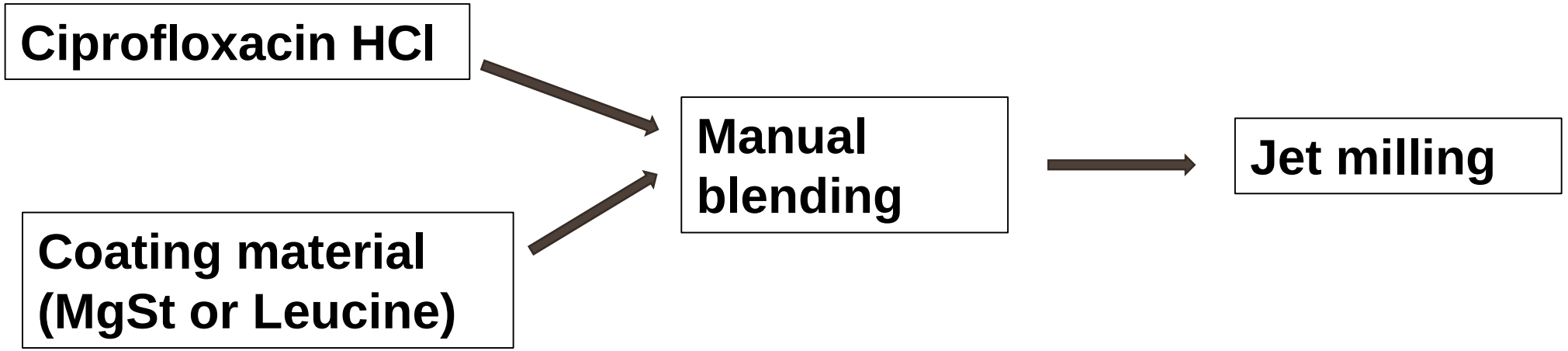
Understand the correlations between surface coating of lubricants and the aerosol performance of carrier-free dry powder inhaler formulations using a ultra-surface-sensitive imaging platform

Specific Aims

(1) Develop a cutting-edge imaging platform to evaluate coating quality of the DPI formulations processed with pharmaceutical lubricants;

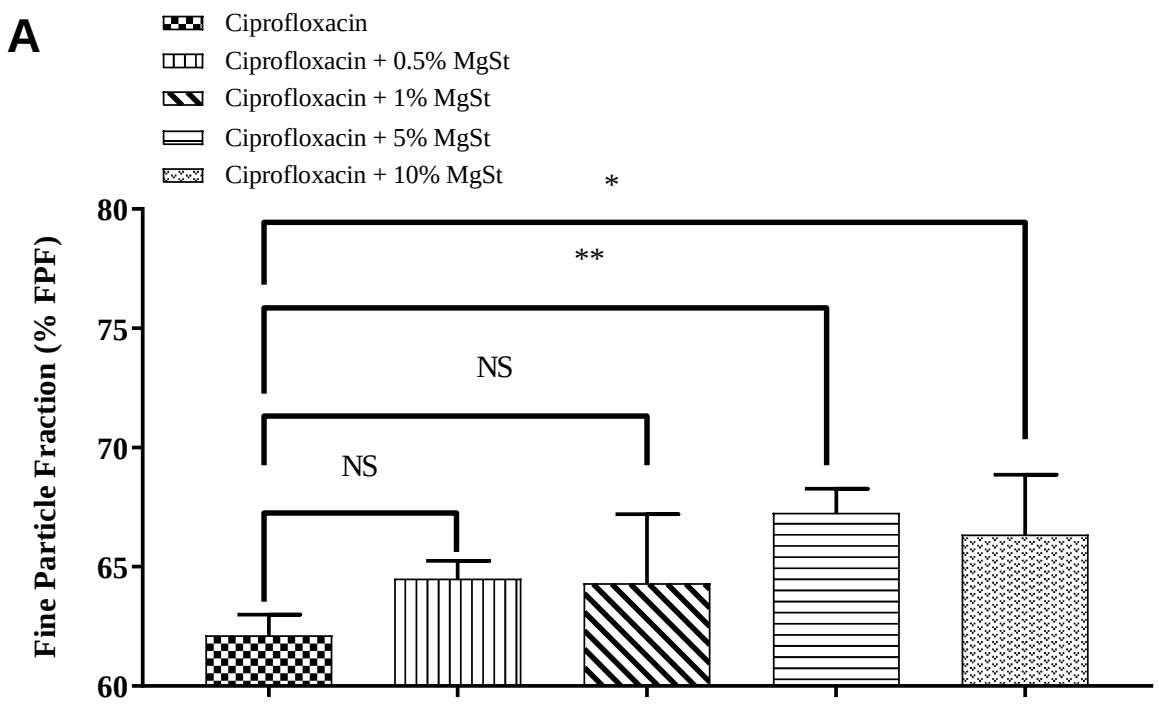
(2) Establish the correlations between surface coating quality and aerosol performance.

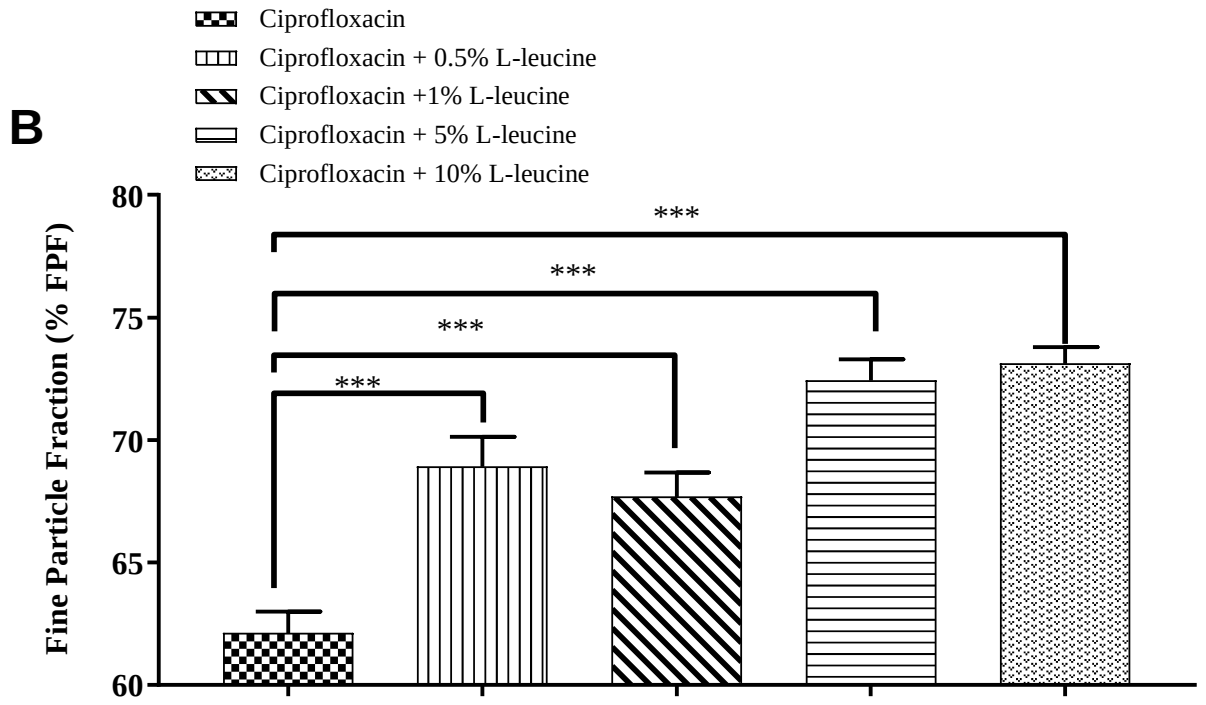
MANUFACTURING PROCESS FOR COATED INHALABLE DRUG PARTICLES



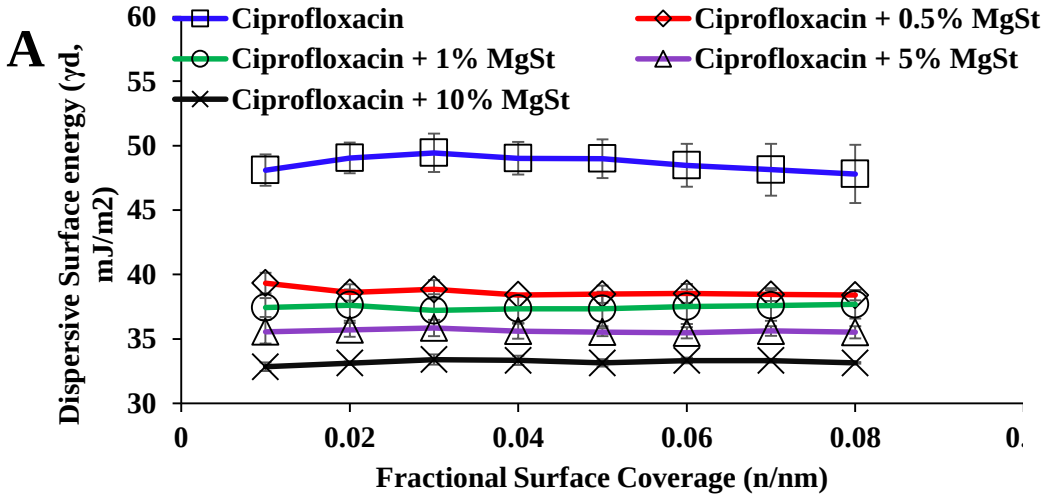
		D_{10} (µm)	D_{50} (µm)	D_{90} (µm)	Span
Ciprofloxacin	Mean	1.0	2.0	4.9	2.0
	SD	0.0	0.0	0.7	0.3
Ciprofloxacin +0.5% MgSt	Mean	0.9	1.9	4.4	1.9
	SD	0.0	0.0	0.1	0.1
Ciprofloxacin +1% MgSt	Mean	0.9	1.9	4.7	2.0
	SD	0.0	0.0	0.3	0.1
Ciprofloxacin +5% MgSt	Mean	0.9	1.8	3.7	1.6
	SD	0.0	0.0	0.1	0.0
Ciprofloxacin +10% MgSt	Mean	0.9	1.9	4.3	1.8
	SD	0.0	0.0	0.0	0.0
Ciprofloxacin +0.5% L-leucine	Mean	1.0	2.0	4.0	1.6
	SD	0.0	0.0	0.0	0.0
Ciprofloxacin +1% L-leucine	Mean	1.0	1.9	3.7	1.4
	SD	0.0	0.0	0.1	0.0
Ciprofloxacin +5% L-leucine	Mean	0.9	1.9	3.8	1.5
	SD	0.0	0.0	0.01	0.0
Ciprofloxacin +10% L-leucine	Mean	0.9	1.8	3.5	1.4
	SD	0.0	0.0	0.1	0.0

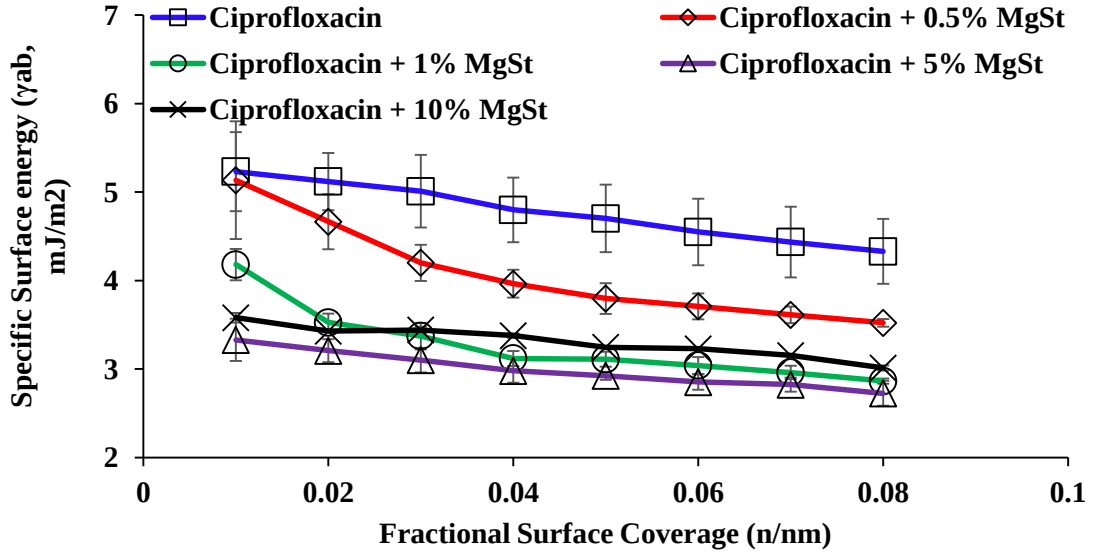
Table 1: Particle sizes of the selected jet-milled ciprofloxacin samples (n=3).

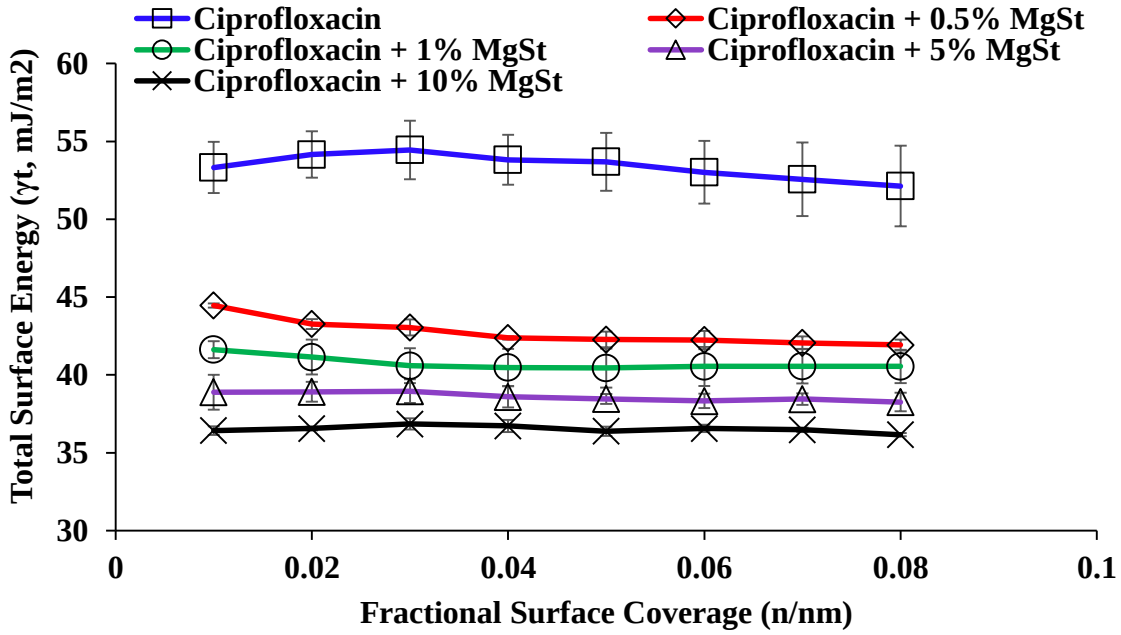

A
Ciprofloxacin
Ciprofloxacin + 0.5% MgSt
Ciprofloxacin + 1% MgSt
Ciprofloxacin + 5% MgSt
Ciprofloxacin + 10% MgSt
*
**
NS
NS
Fine Particle Fraction (% FPF)
80
75
70
65
60


B
Ciprofloxacin
Ciprofloxacin + 0.5% L-leucine
Ciprofloxacin +1% L-leucine
Ciprofloxacin + 5% L-leucine
Ciprofloxacin + 10% L-leucine
***
***
***
***
Fine Particle Fraction (% FPF)
80
75
70
65
60

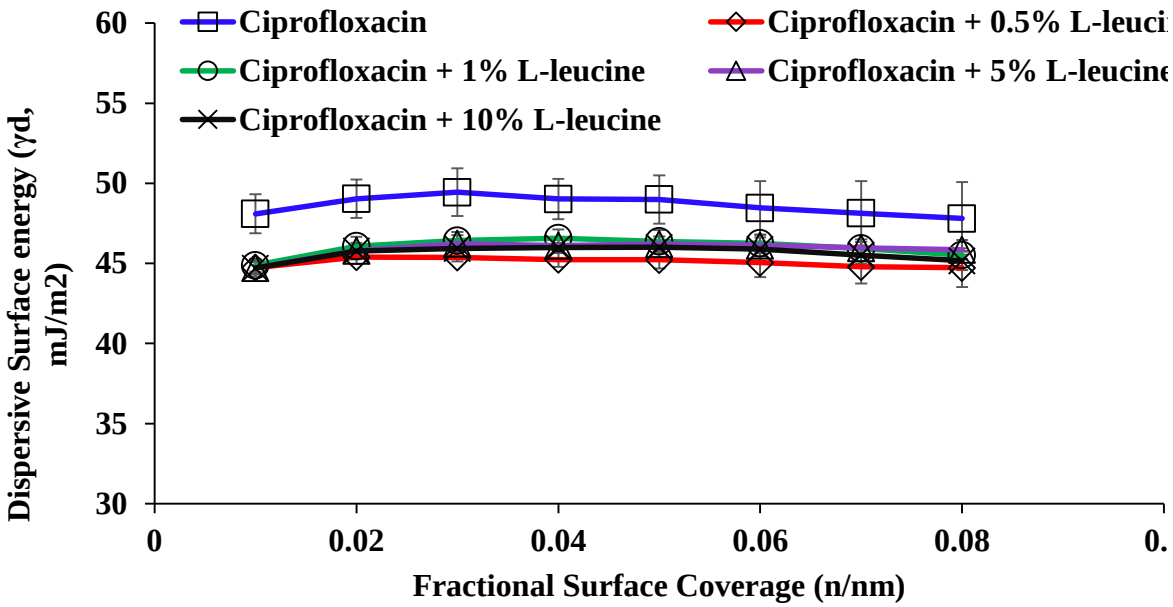
A

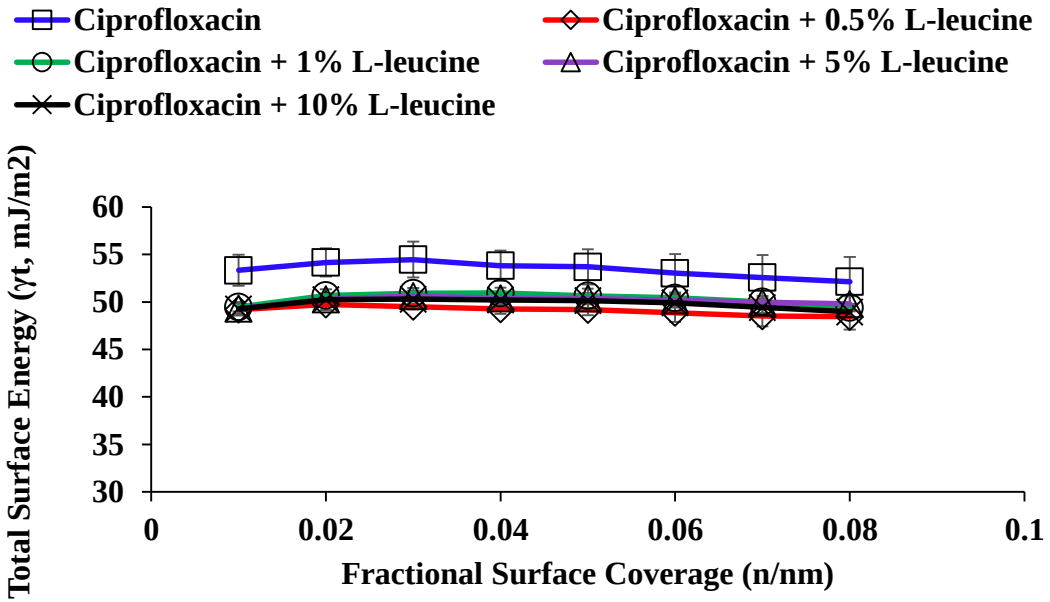

Ciprofloxacin
Ciprofloxacin + 0.5% MgSt
Ciprofloxacin + 1% MgSt
Ciprofloxacin + 5% MgSt
Ciprofloxacin + 10% MgSt
Dispersive Surface energy (γd, mJ/m2)
60
55
50
45
40
35
30
0
0.02
0.04
0.06
0.08
Fractional Surface Coverage (n/nm)

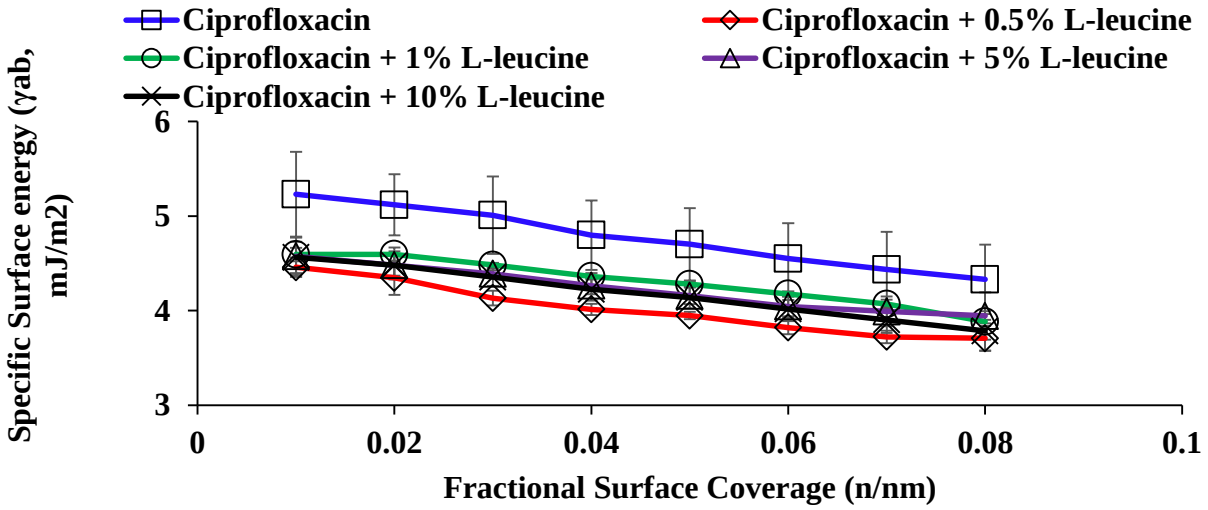

Ciprofloxacin
Ciprofloxacin + 0.5% MgSt
Ciprofloxacin + 1% MgSt
Ciprofloxacin + 5% MgSt
Ciprofloxacin + 10% MgSt
Specific Surface energy (γab, mJ/m2)
7
6
5
4
3
2
0
0.02
0.04
0.06
0.08
0.1
Fractional Surface Coverage (n/nm)

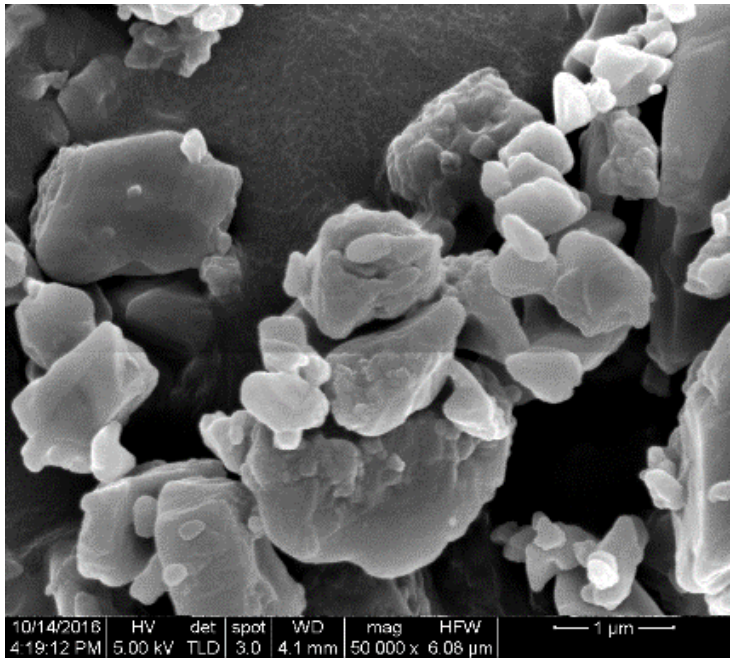

Ciprofloxacin
Ciprofloxacin + 0.5% MgSt
Ciprofloxacin + 1% MgSt
Ciprofloxacin + 5% MgSt
Ciprofloxacin + 10% MgSt
Total Surface Energy (γt, mJ/m2)
60
55
50
45
40
35
30
0
0.02
0.04
0.06
0.08
0.1
Fractional Surface Coverage (n/nm)

B

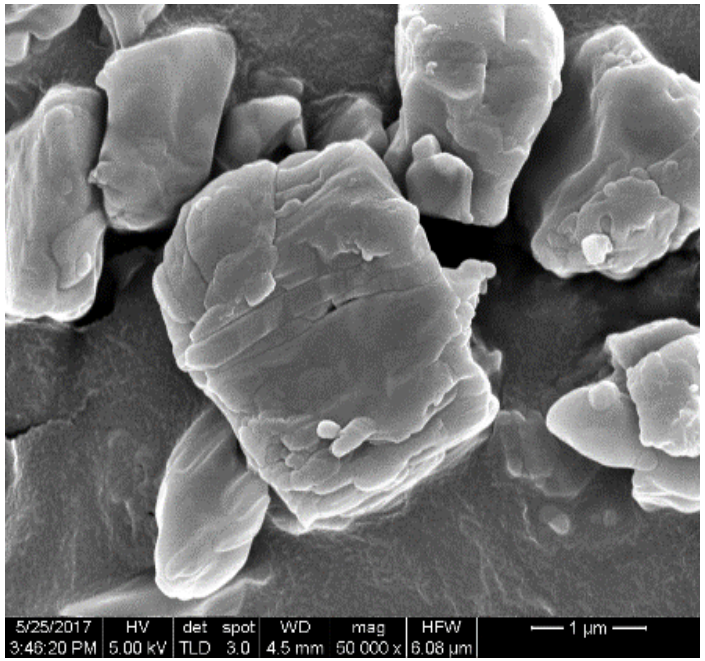

Ciprofloxacin
Ciprofloxacin + 0.5% L-leuci
Ciprofloxacin + 1% L-leucine
Ciprofloxacin + 5% L-leucine
Ciprofloxacin + 10% L-leucine
Dispersive Surface energy (γd, mJ/m2)
60
55
50
45
40
35
30
0
0.02
0.04
0.06
0.08
0.
Fractional Surface Coverage (n/nm)


Ciprofloxacin
Ciprofloxacin + 0.5% L-leucine
Ciprofloxacin + 1% L-leucine
Ciprofloxacin + 5% L-leucine
Ciprofloxacin + 10% L-leucine
Total Surface Energy (γt, mJ/m2)
60
55
50
45
40
35
30
0
0.02
0.04
0.06
0.08
0.1
Fractional Surface Coverage (n/nm)

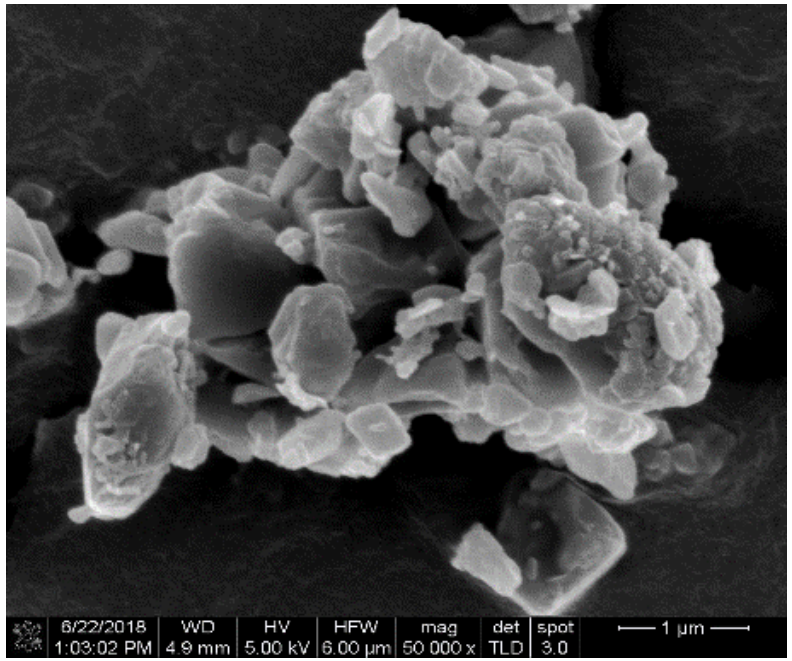

Ciprofloxacin
Ciprofloxacin + 0.5% L-leucine
Ciprofloxacin + 1% L-leucine
Ciprofloxacin + 5% L-leucine
Ciprofloxacin + 10% L-leucine
Specific Surface energy (γab, mJ/m2)
6
5
4
3
0
0.02
0.04
0.06
0.08
0.1
Fractional Surface Coverage (n/nm)



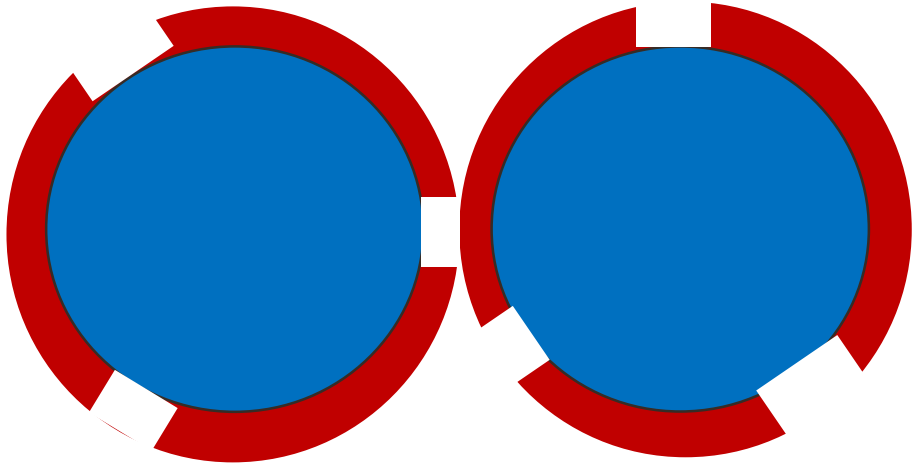
Jet milled drug alone



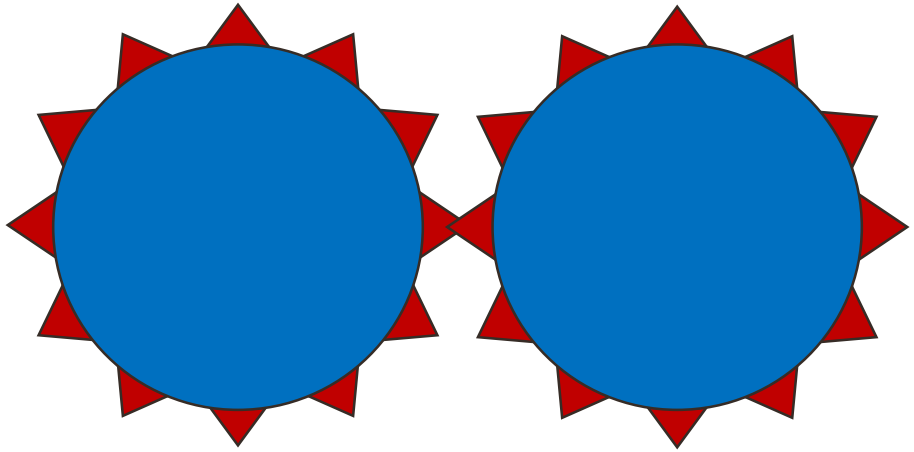
Jet milled drug + 5% w/w MgSt



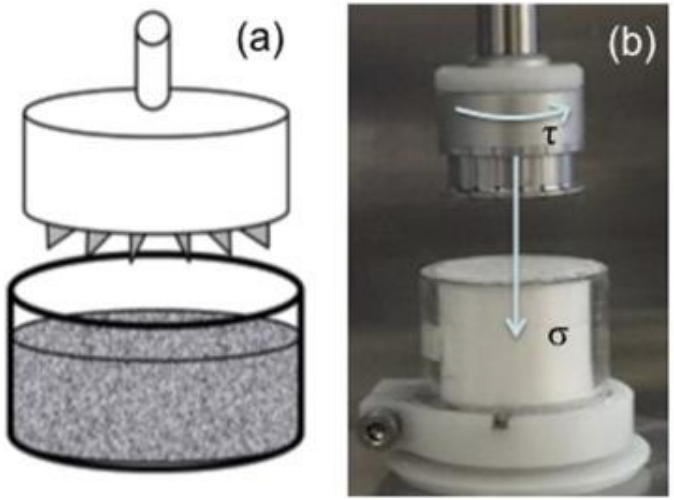
Jet milled drug + 5% w/w Leucine

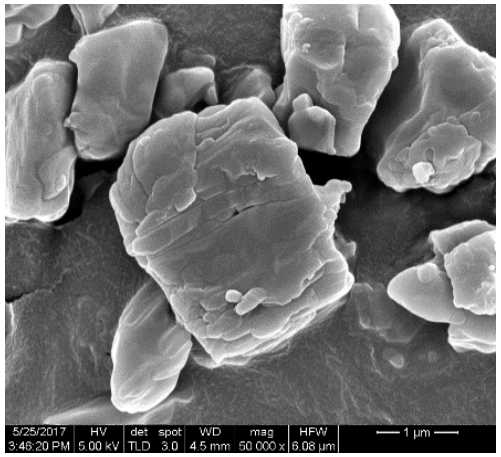


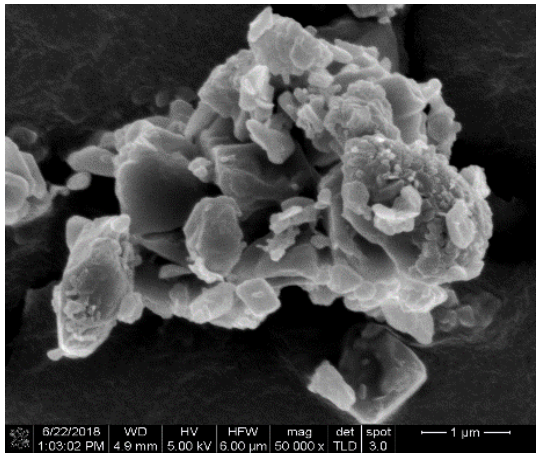
Magnesium stearate forms a non-cohesive film



Leucine creates asperities between particles

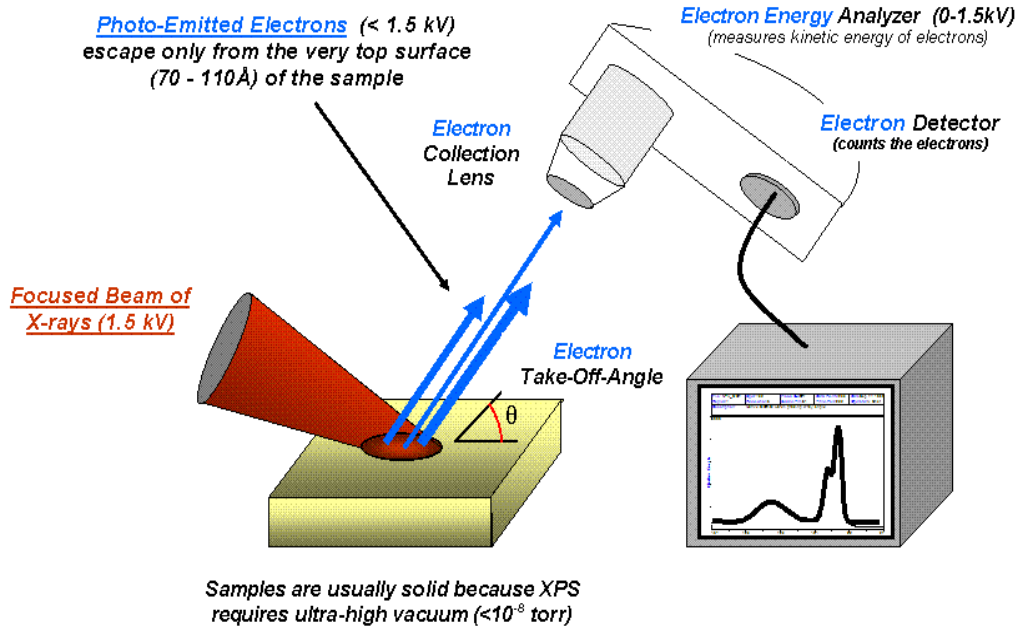


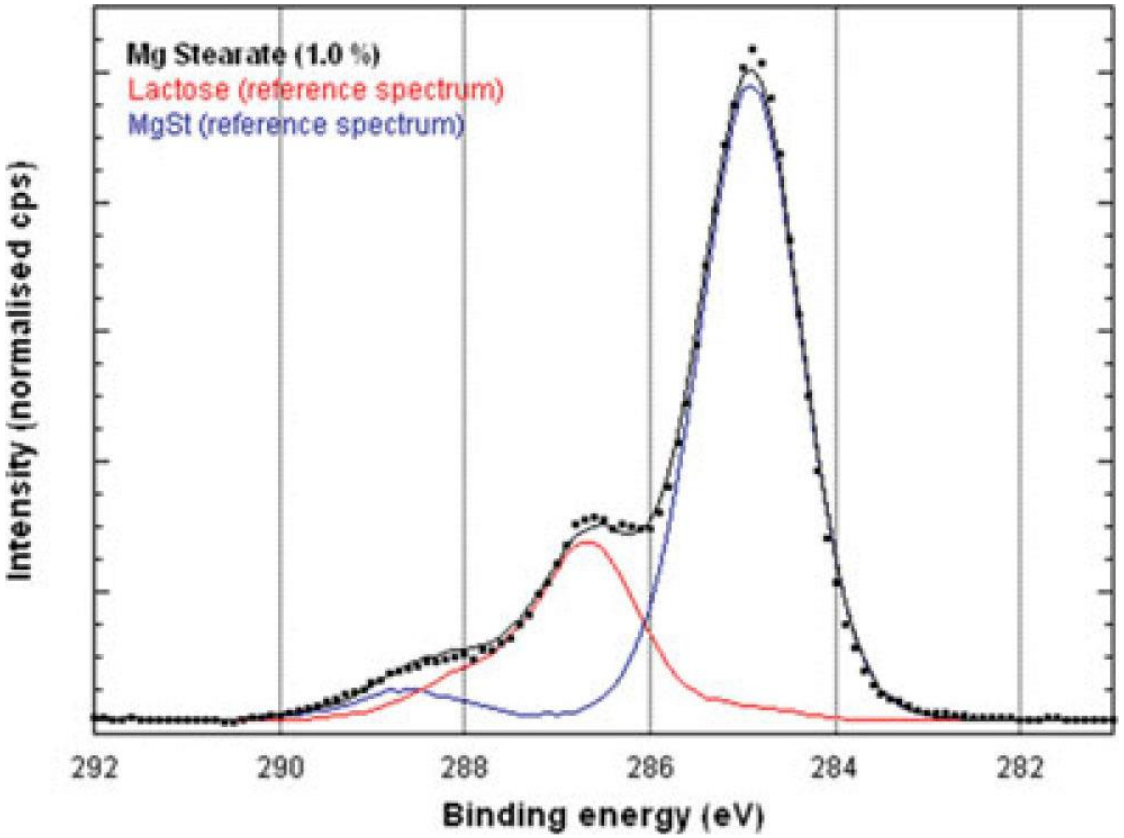




	Cohesion (kPa)
Jet-milled ciprofloxacin	3.7 ± 0.2
Co-jet-milled ciprofloxacin + 5% MgSt	2.1 ± 0.3**
Co-jet-milled ciprofloxacin + 5% L-leucine	3.8 ± 0.3

X-RAY PHOTOELECTRON SPECTROSCOPY (XPS)

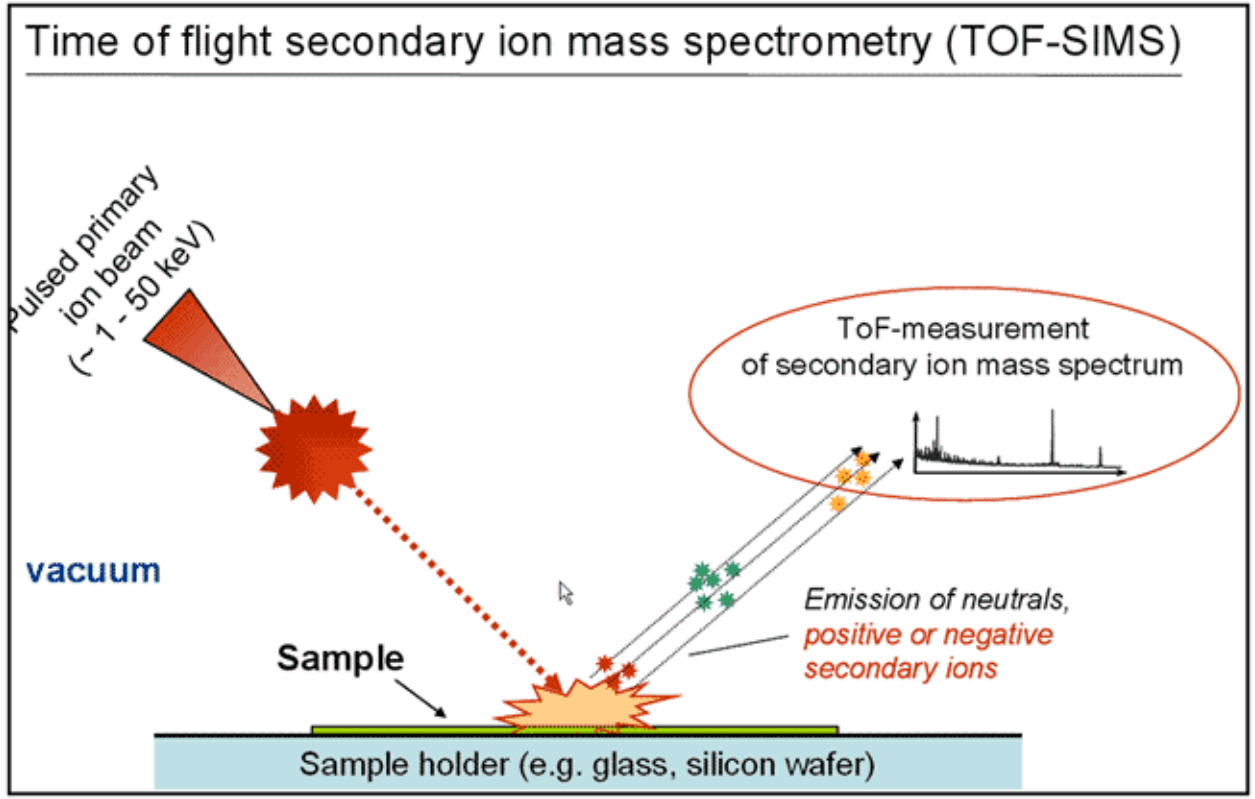




- **Quantitative measurement of surface composition**
- **Measure upmost surface up to 10 nm**
- **Unable to provide imaging or mapping in micron level**

Modified from: http://upload.wikimedia.org/wikipedia/commons/f/f2/System2.gif

TIME OF FLIGHT SECONDARY ION MASS SPECTROSCOPY (NANO TOF-SIMS)



- **Semi-Quantitative**
- **Measure upmost surface up to 1 molecular levels (very sensitive)**
- **Mapping or distribution at resolution up to 200 nm**

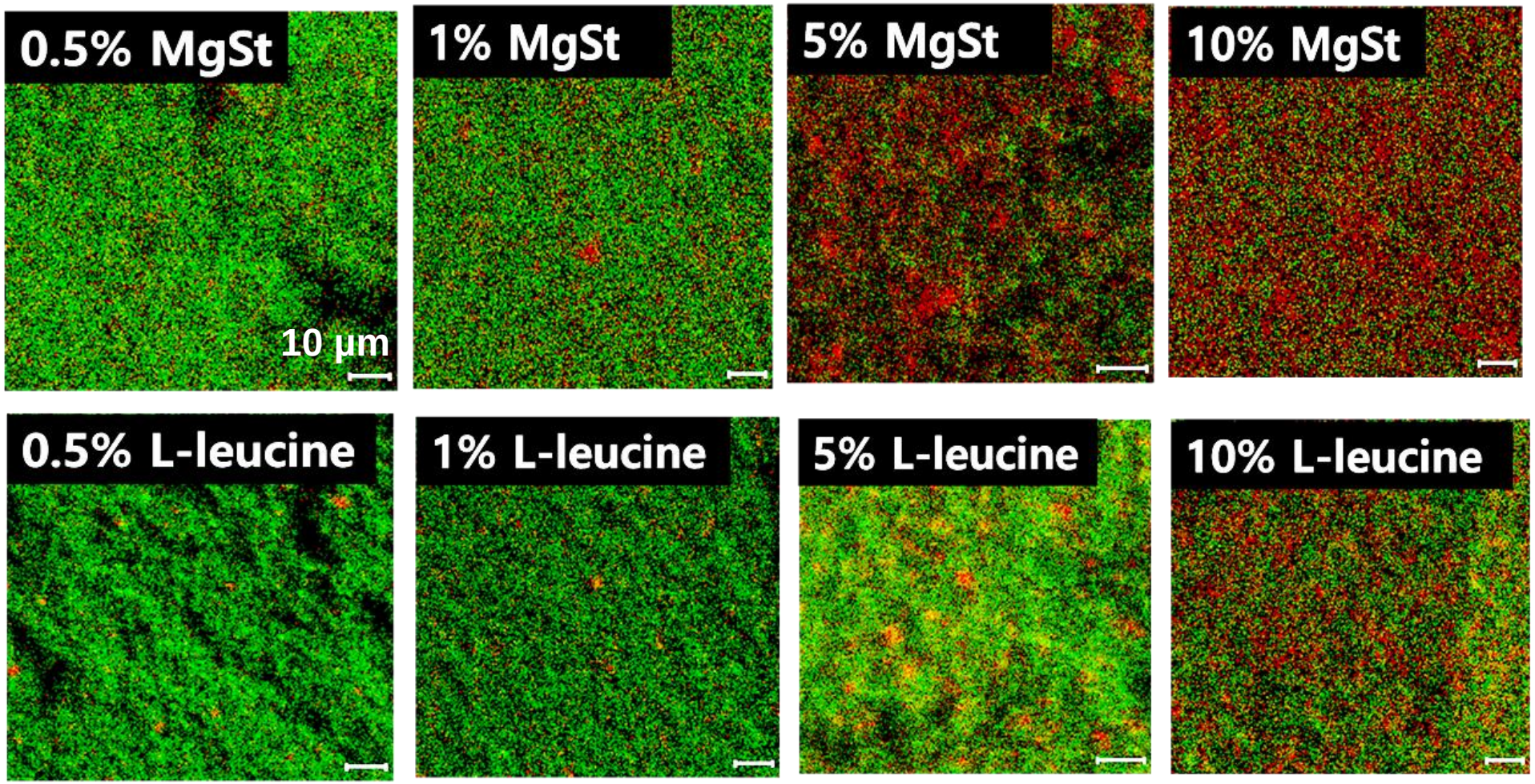
http://www.geomuseum.uni-goettingen.de/people/vthiel/tof_sims.shtml

XPS data

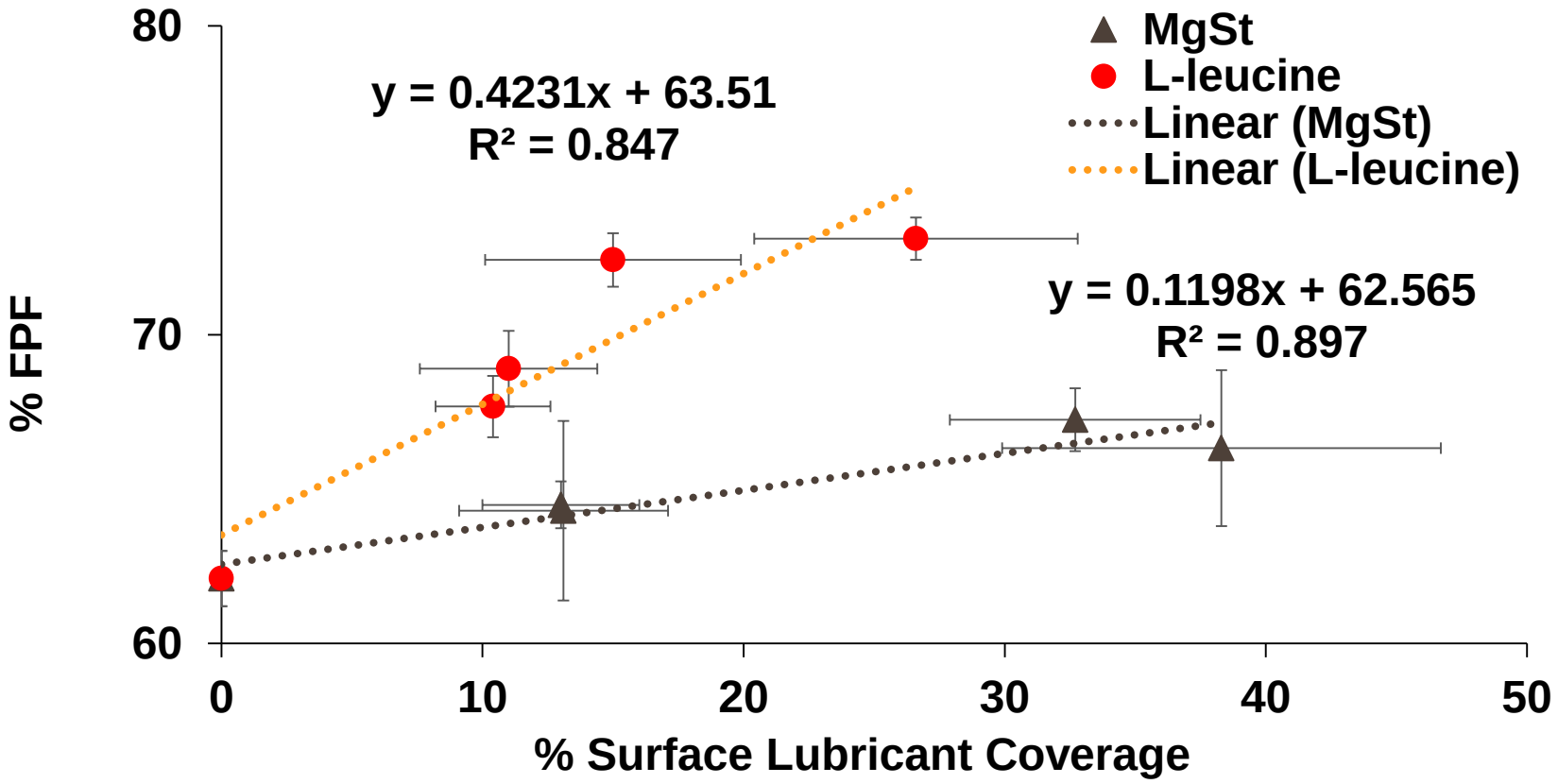
Formulations (w/w %)	% Theoretical Surface Composition		% Measured Surface Composition	
	Ciprofloxacin	Lubricant	Ciprofloxacin	Lubricant
Ciprofloxacin + 0.5% MgSt	99.7	0.3	87.0±3.0	13.0±3.0
Ciprofloxacin + 1% MgSt	99.3	0.7	86.9±4.0	13.1±4.0
Ciprofloxacin + 5% MgSt	96.5	3.5	67.3±4.8	32.7±4.8
Ciprofloxacin + 10% MgSt	92.9	7.1	61.7±8.4	38.3±8.4
Ciprofloxacin + 0.5% L-leucine	99.5	0.5	89.0±3.4	11.0±3.4
Ciprofloxacin + 1% L-leucine	99.0	1.0	89.6±2.2	10.4±2.2
Ciprofloxacin + 5% L-leucine	94.8	5.2	85.0±4.9	15.0±4.9
Ciprofloxacin + 10% L-leucine	89.7	10.3	73.4±6.2	26.6±6.2

PURDUE UNIVERSITY

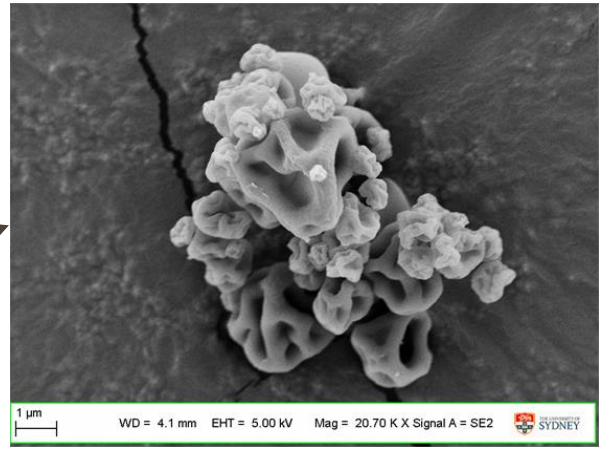
ToF-SIMS images (red signal: coating material; green signal: drug)



Correlations between aerosol performance and surface coverage of coating material based on XPS data

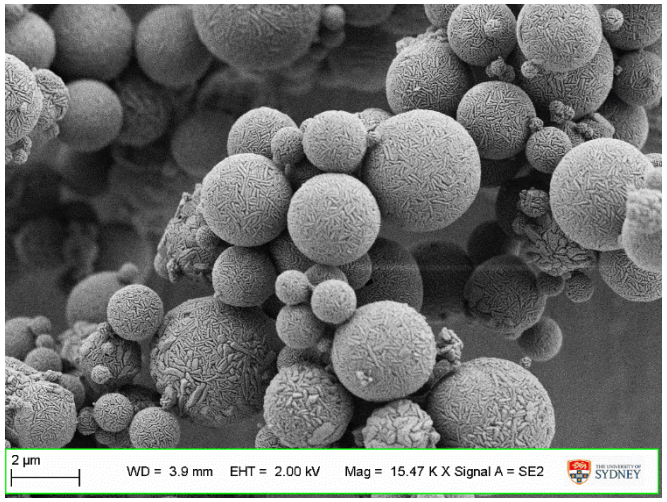


Spray drying for particle engineering



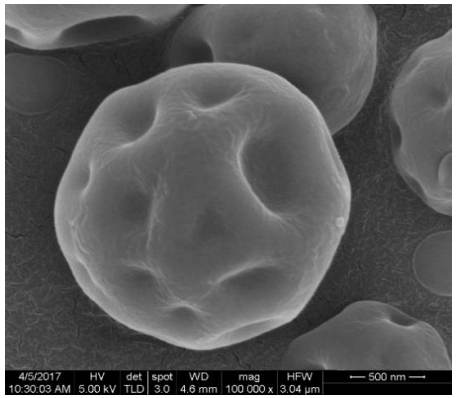
- TOBI Podhaler – tobramycin dry powder inhaler

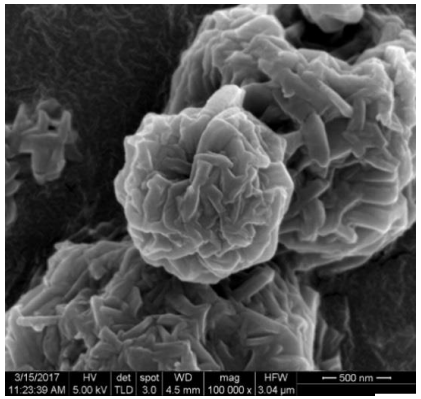
www.tobipodhaler.com



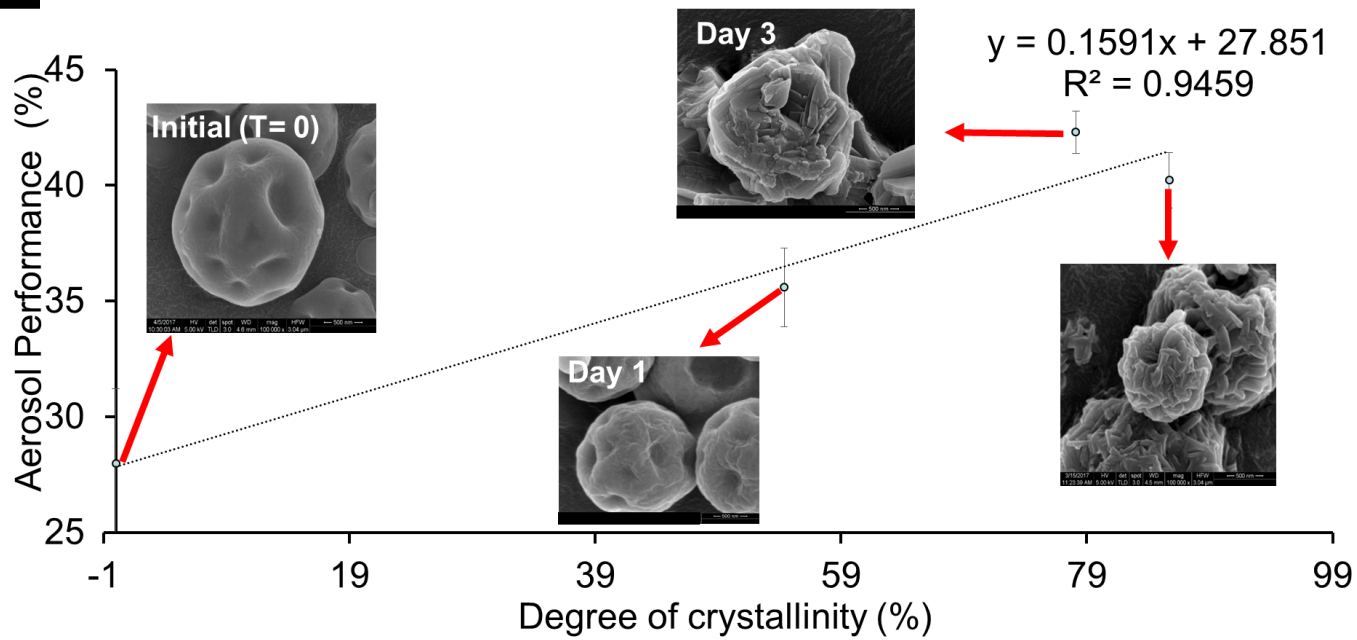
www.aridol.info

Challenges in Spray drying - Amorphous



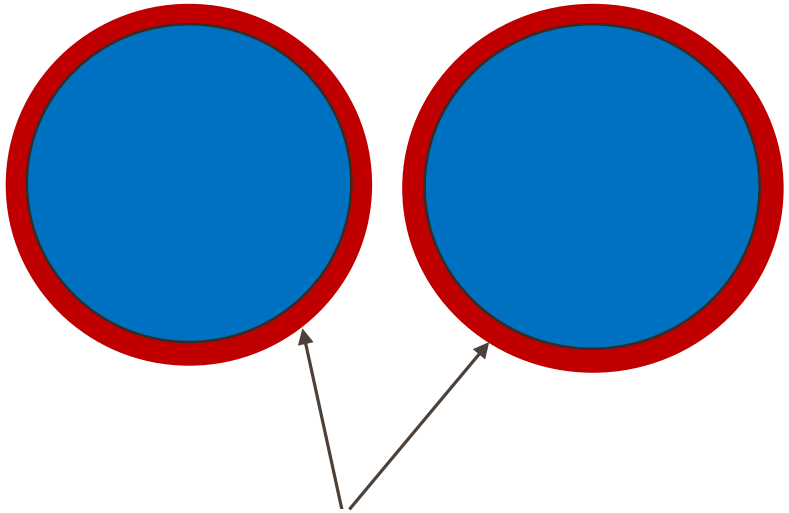


- **Ciprofloxacin HCl hydrate**

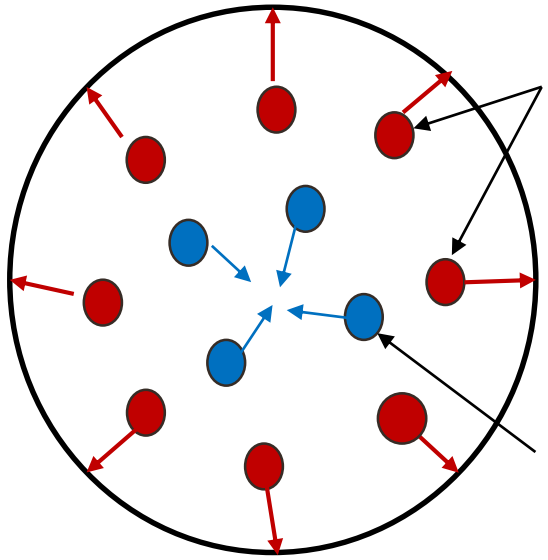


2018. Pharmaceutical Research 35 (1), 7

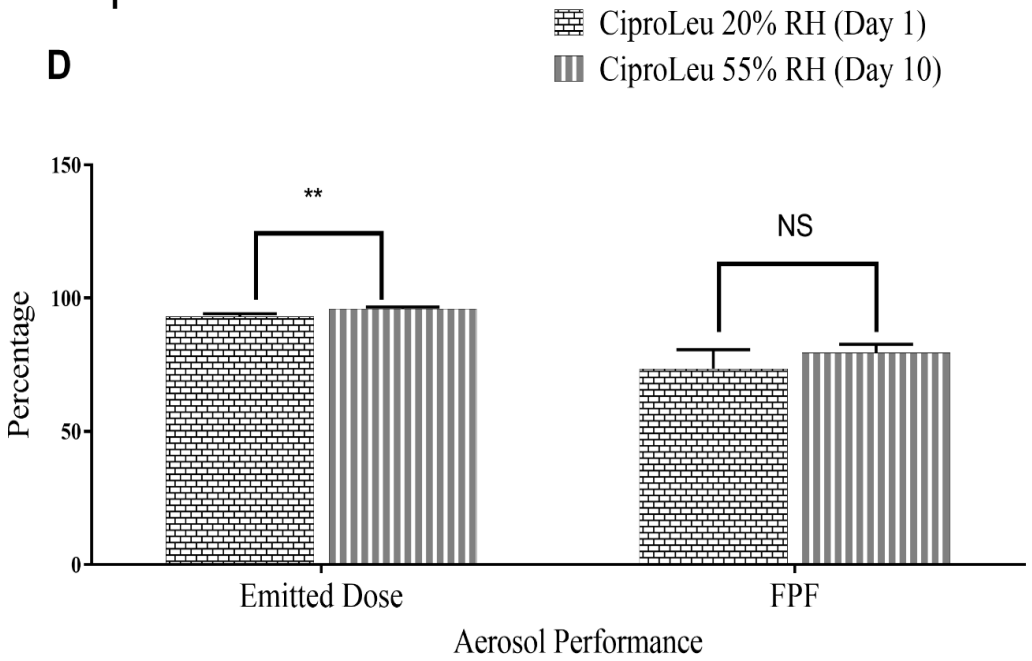
SURFACE PROTECTIVE COATING BY SPRAY DRYING



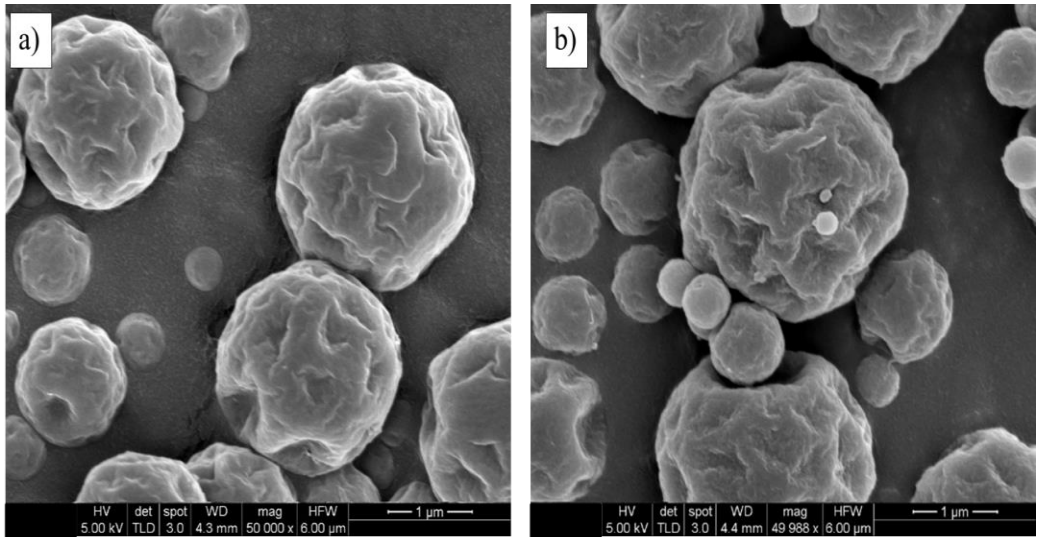
Protective coating layer



Cipro:leu=1:1 w/w

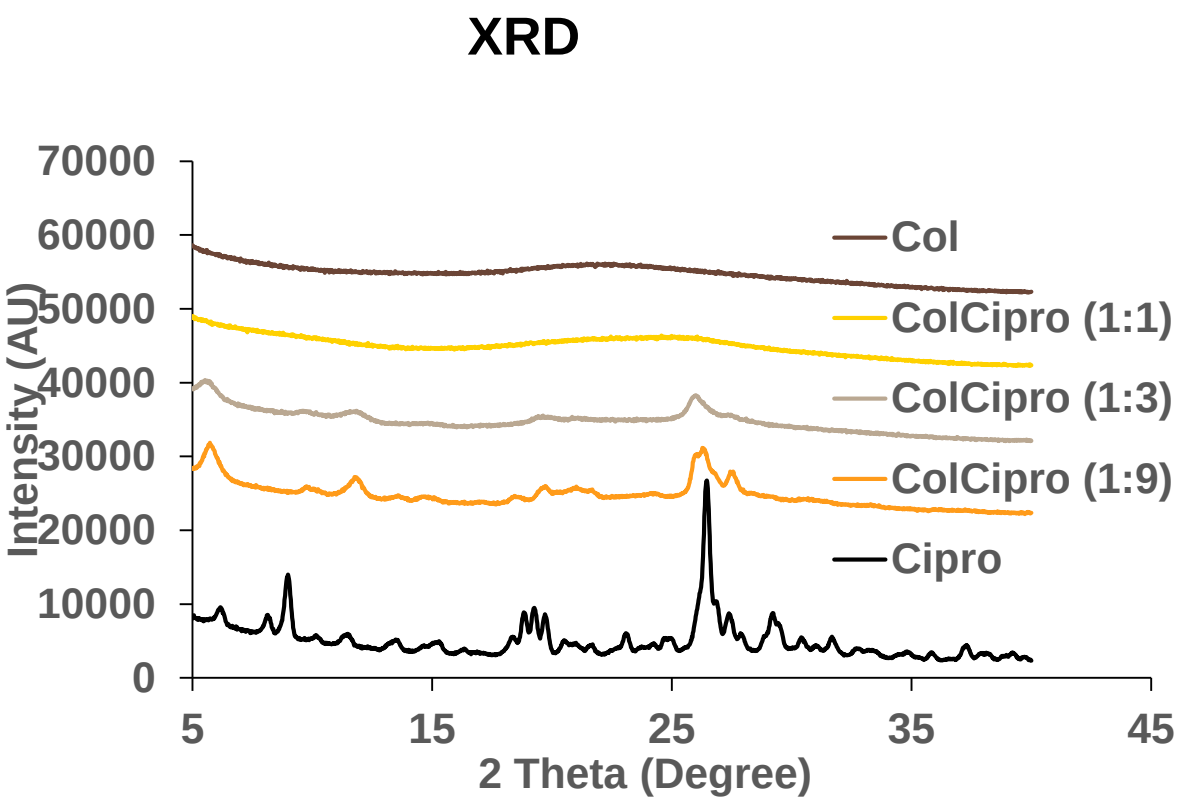


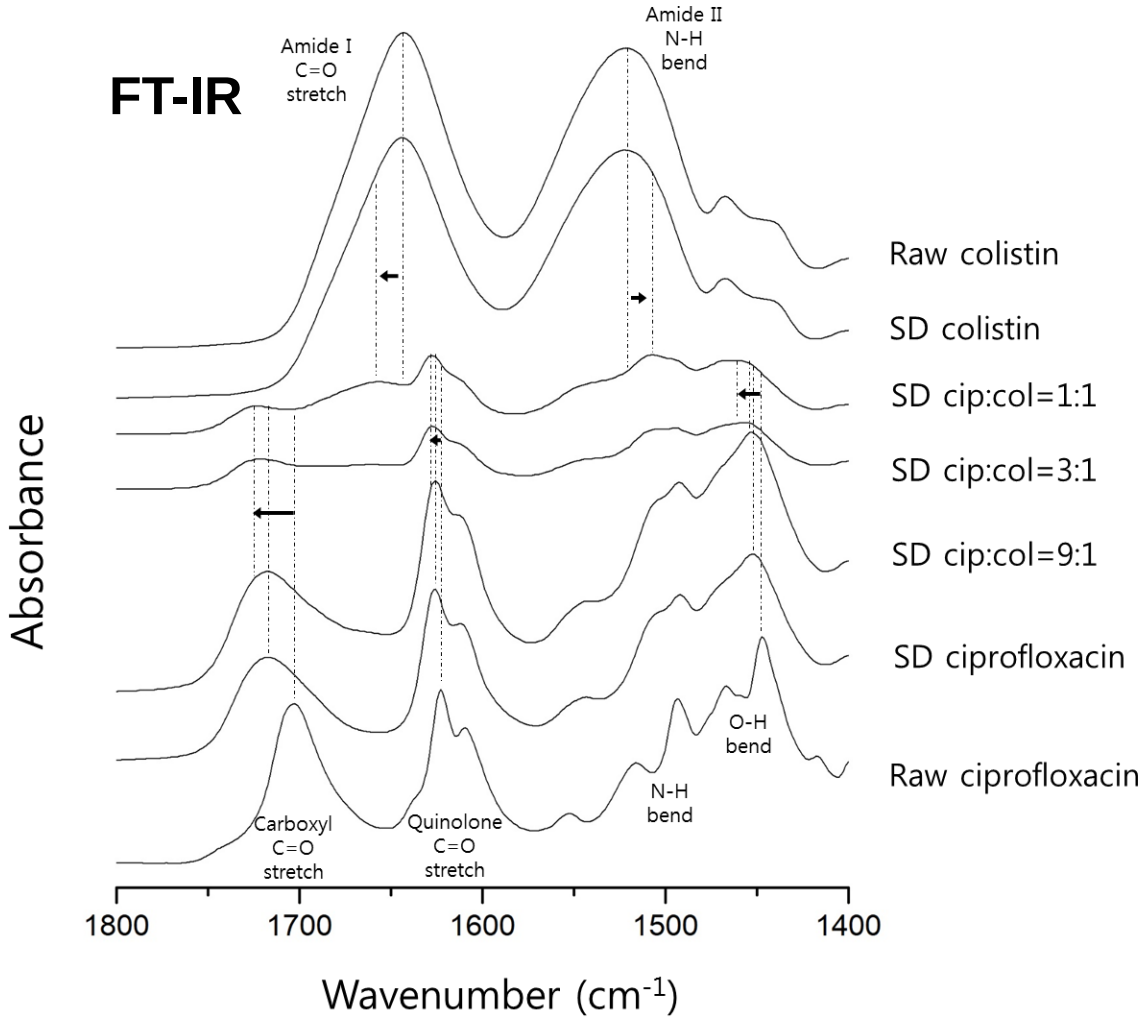
Cipro:leu=9:1 w/w



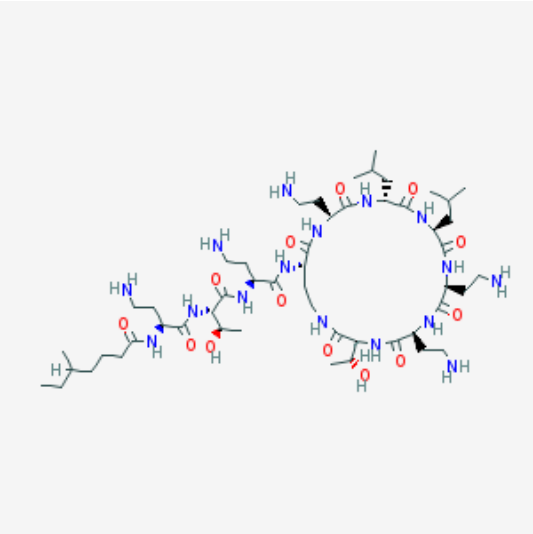
Formulations	% Surface Composition (Theoretical)		% Surface Composition (Measured)	
	L-leucine	Ciprofloxacin	L-leucine	Ciprofloxacin
CiproLeu_1:1	50	50	70	30

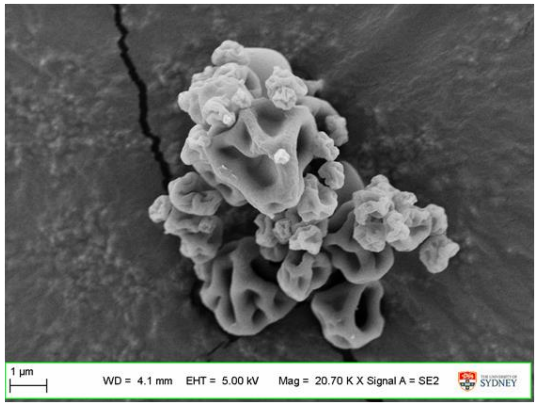
Co-spray drying ciprofloxacin with colistin improved stability up to 60 days

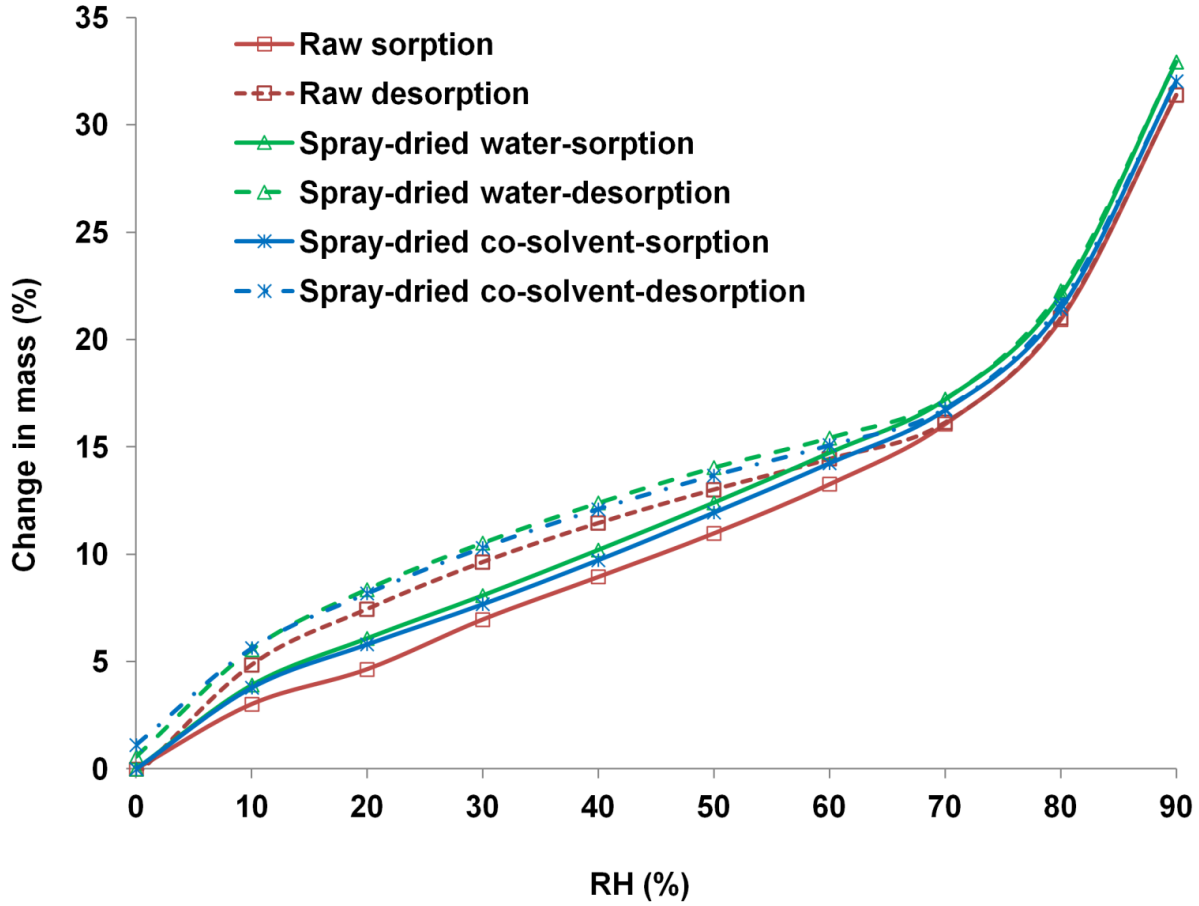




➢ COLISTIN – A POLYPEPTIDE ANTIBIOTIC THE LAST-RESORT AGAINST MULTI-DRUG RESISTANT (MDR) GRAM-NEGATIVE INFECTION

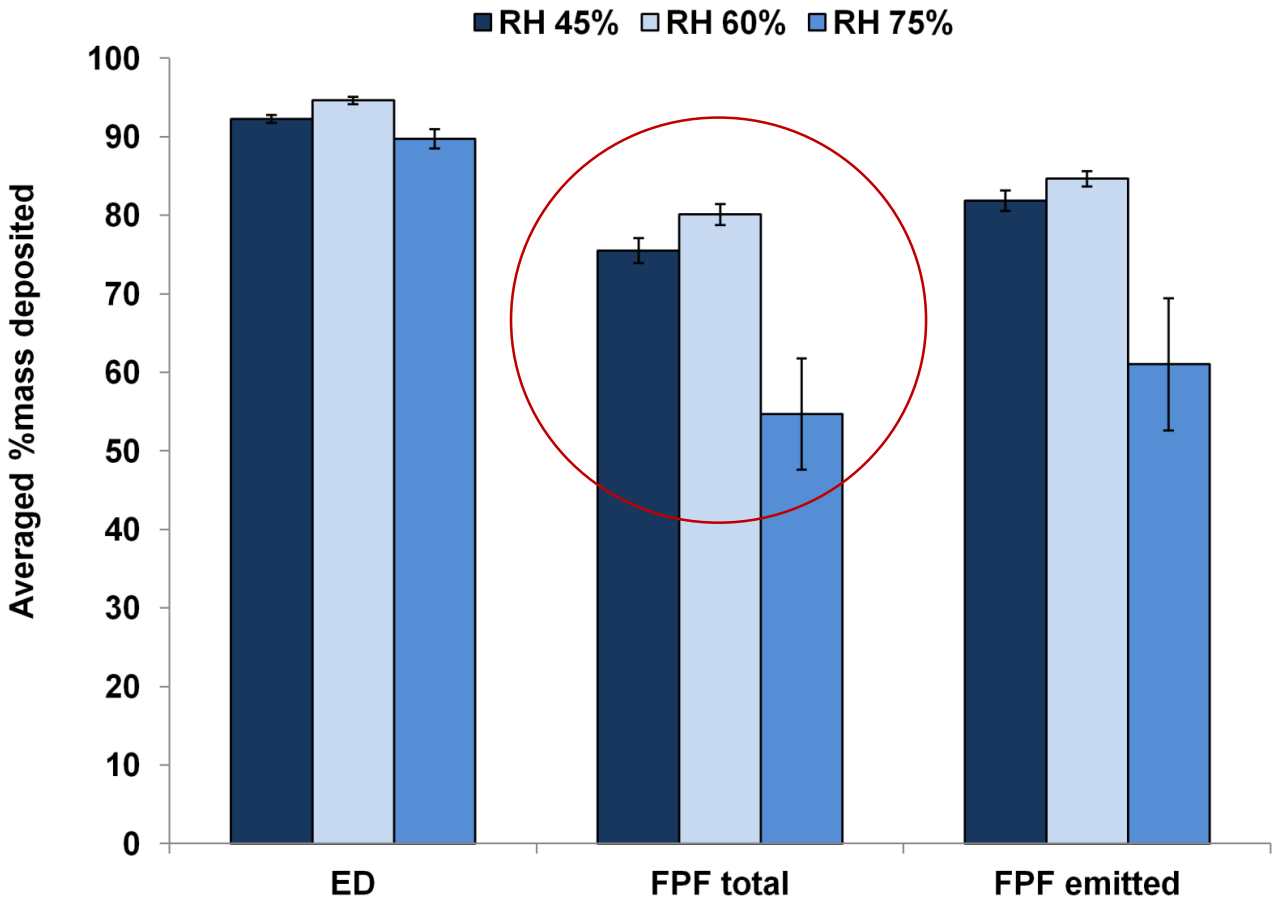


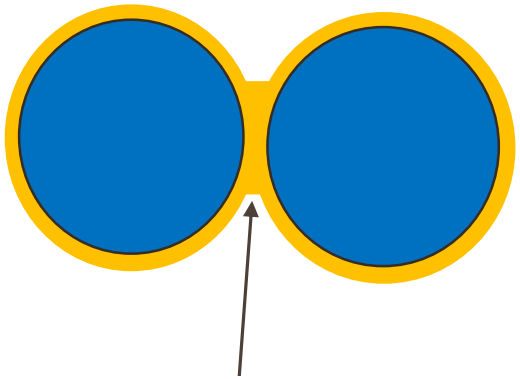




2013. Journal of pharmaceutical sciences 102 (10), 3736-3747

➢ MOISTURE SORPTION CAUSED REDUCTION IN AEROSOL PERFORMANCE

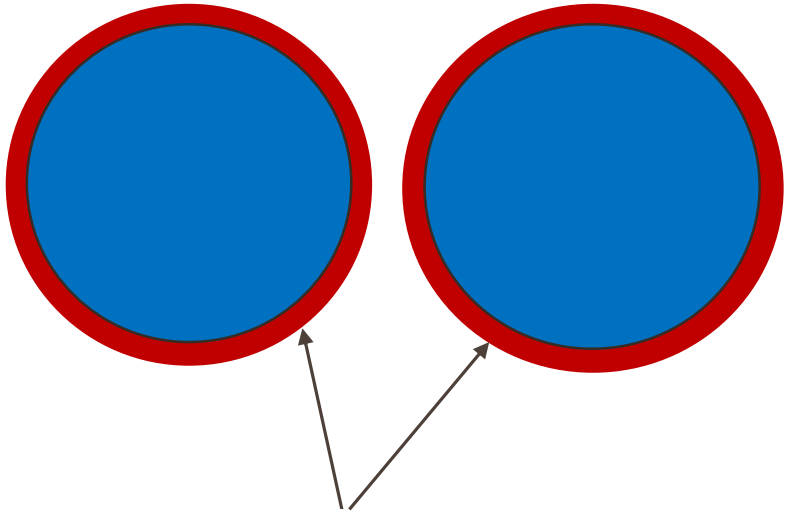




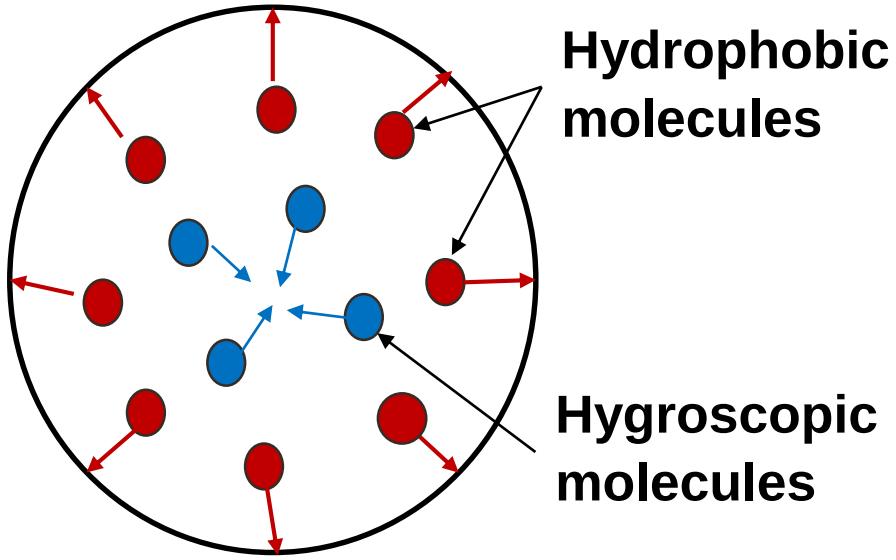
Moisture condensation

2013. Journal of pharmaceutical sciences 102 (10), 3736-3747

SURFACE PROTECTIVE COATING BY SPRAY DRYING

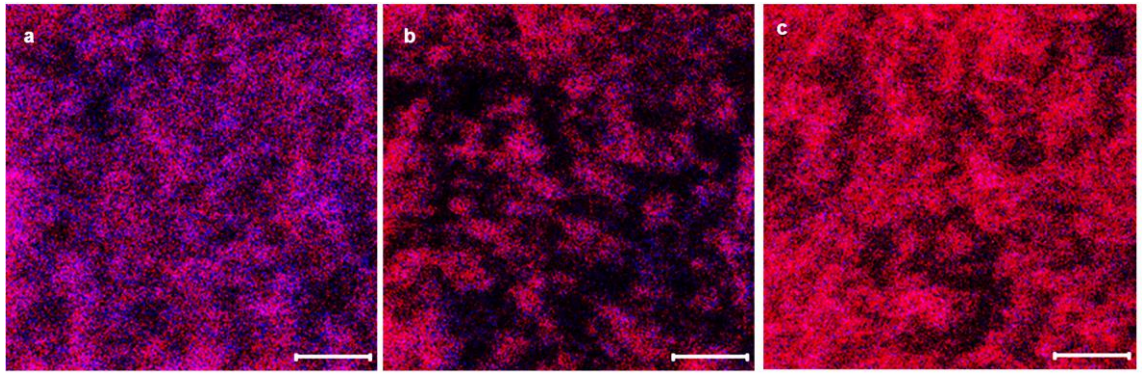


Protective coating layer



SURFACE PROTECTIVE COATING BY SPRAY DRYING

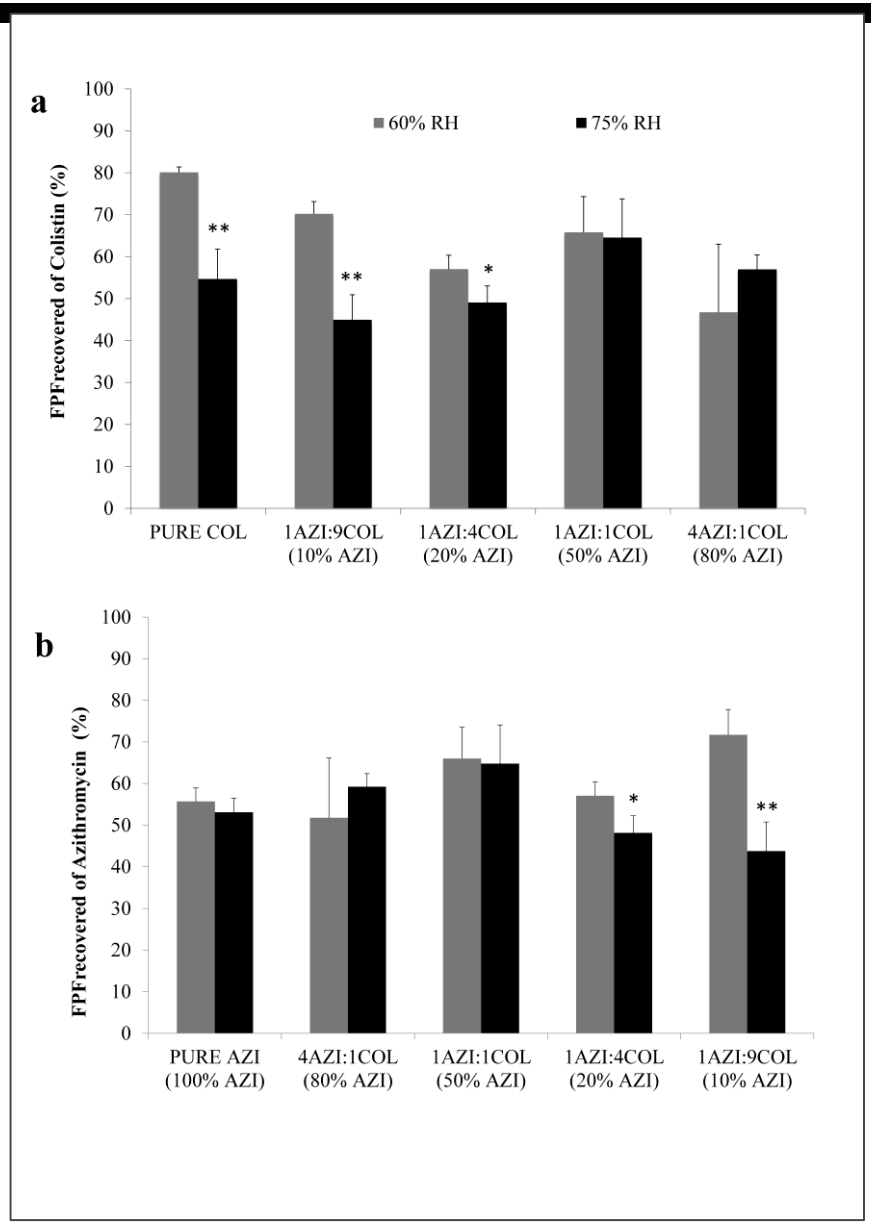
COLISTIN COATED WITH A SYNERGISTIC ANTIBIOTIC, AZITHROMYCINE



Distribution of colistin (blue) and azithromycin (red) on a) Col:Azi 4:1; b) Col:Azi 1:1; c) Col:Azi 1:4 (scale bar = 10 µm).

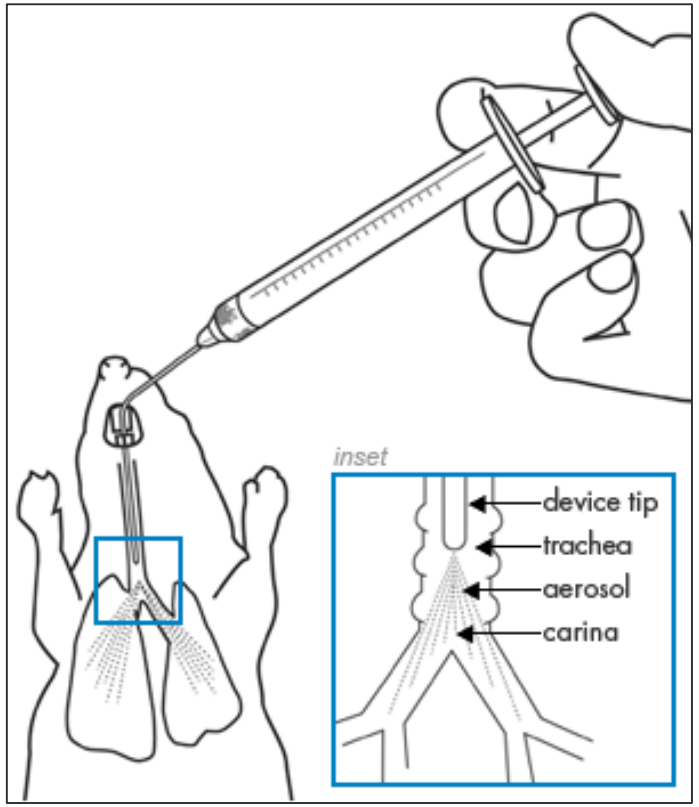
	1Col:4AZI	1Col:1AZI	Pure Col
Col	1.0 %	3.5 %	100.0 %
AZI	99.0 %	96.5 %	0.0 %

2014. The AAPS journal 16 (1), 37-47

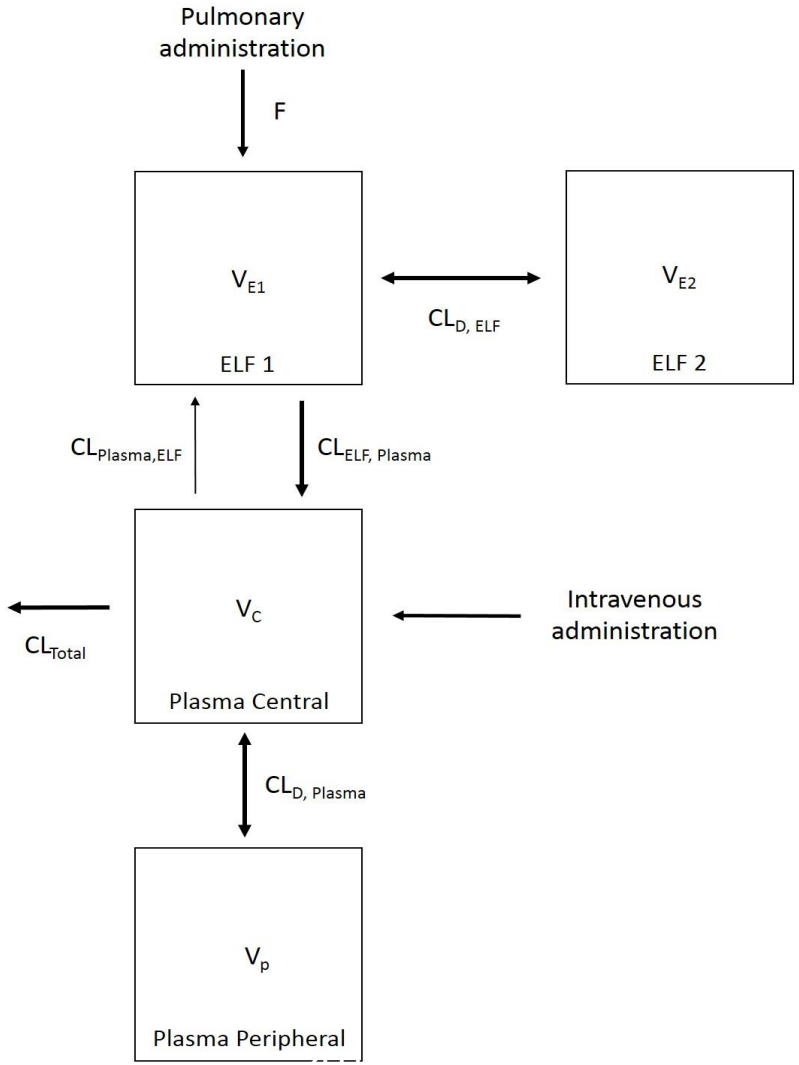


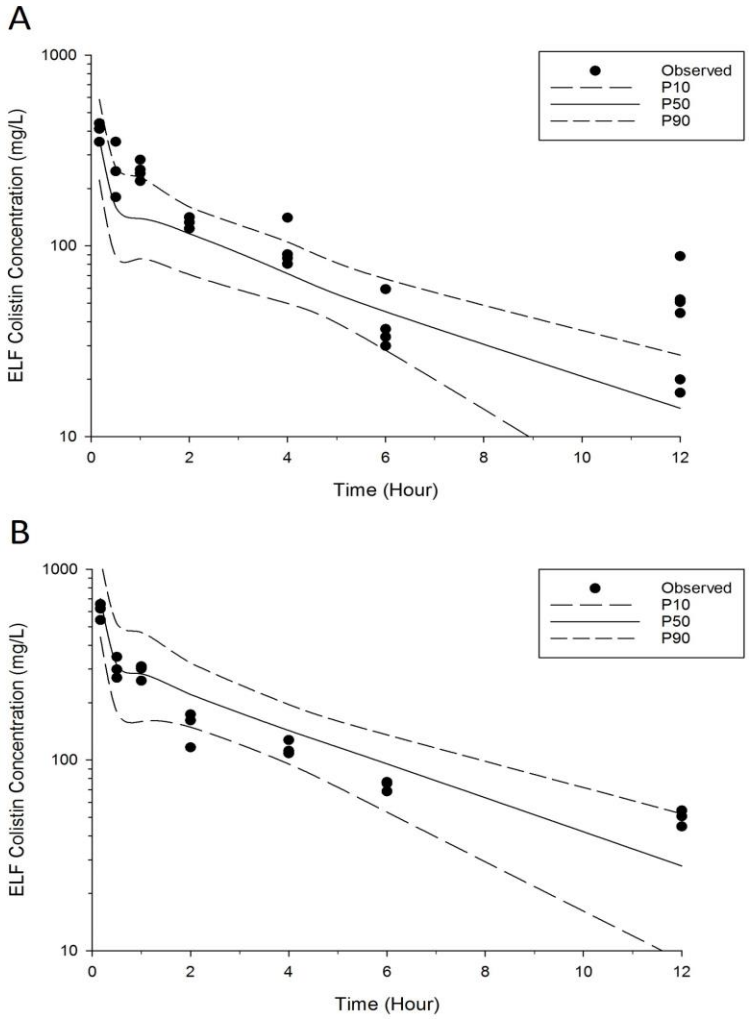
PK AND PK/PD MODELS FOR PULMONARY DRUG DELIVERY SYSTEMS

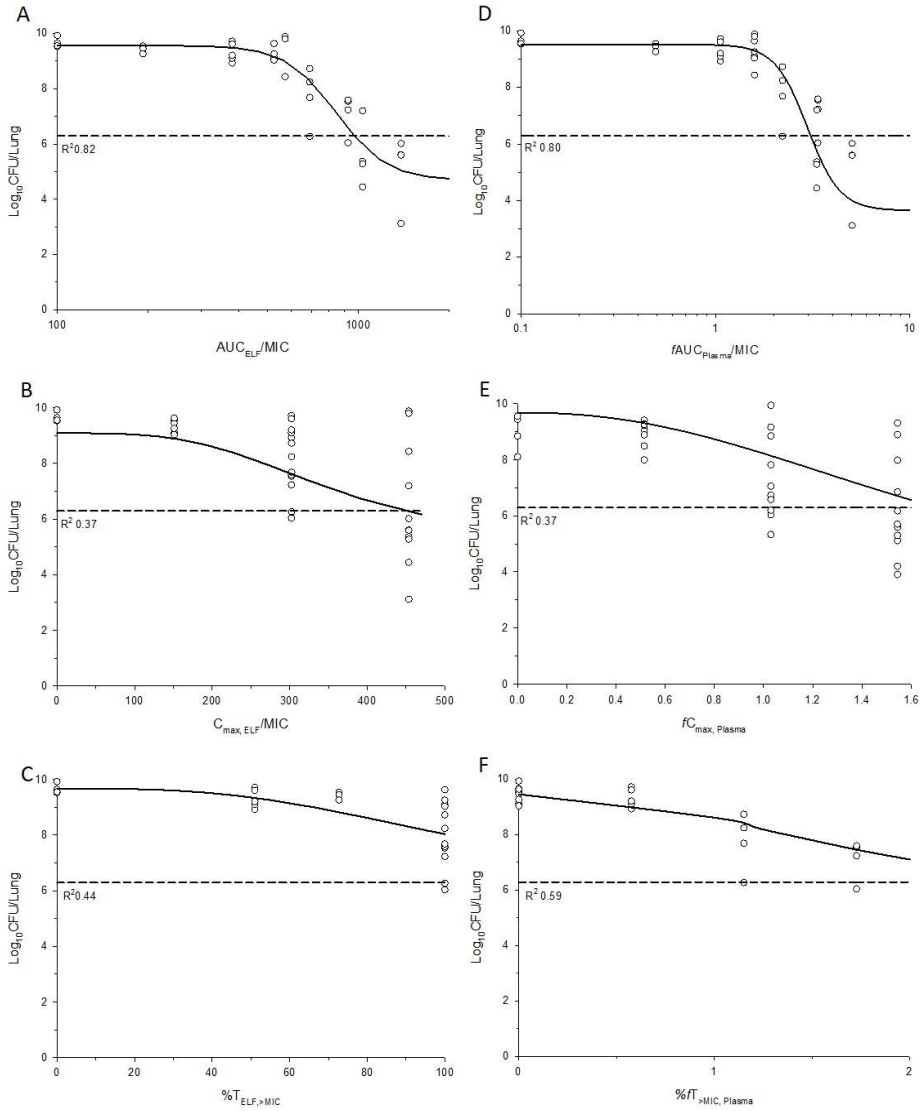
In-vivo animal models for inhaled medicines



Population PK model for inhaled colistin powder formulation







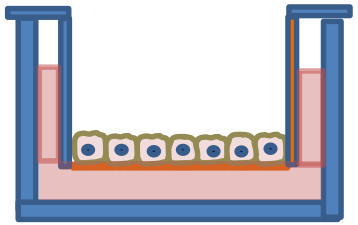
PK/PD in mouse lung infection model

AUC_{ELF}/MIC are the most predictive PK/PD index for pulmonary delivery of colistin

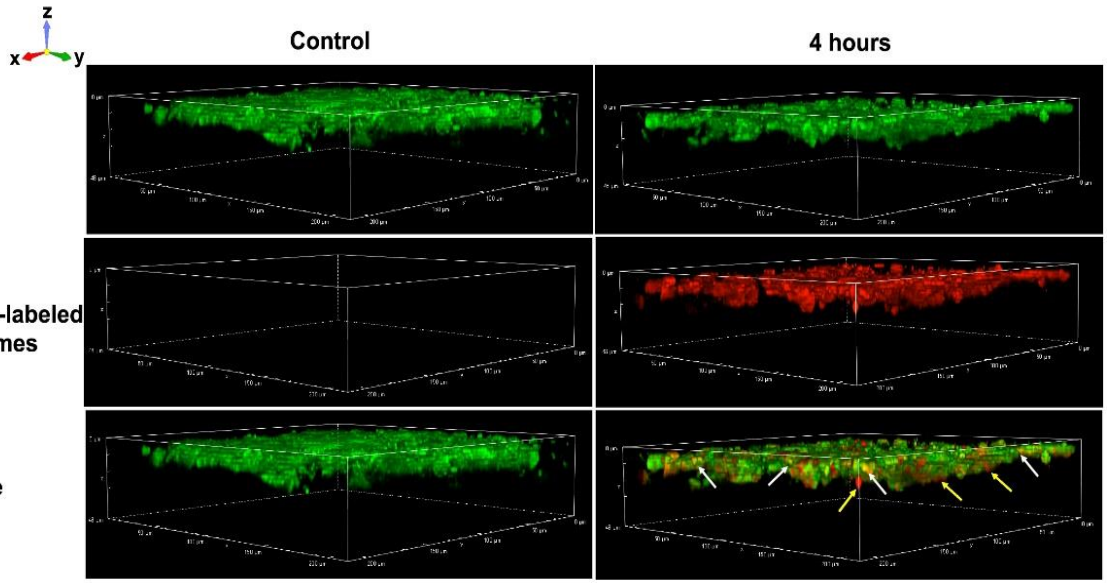
2017. Antimicrobial Agents and Chemotherapy 61 (3), e02025-16

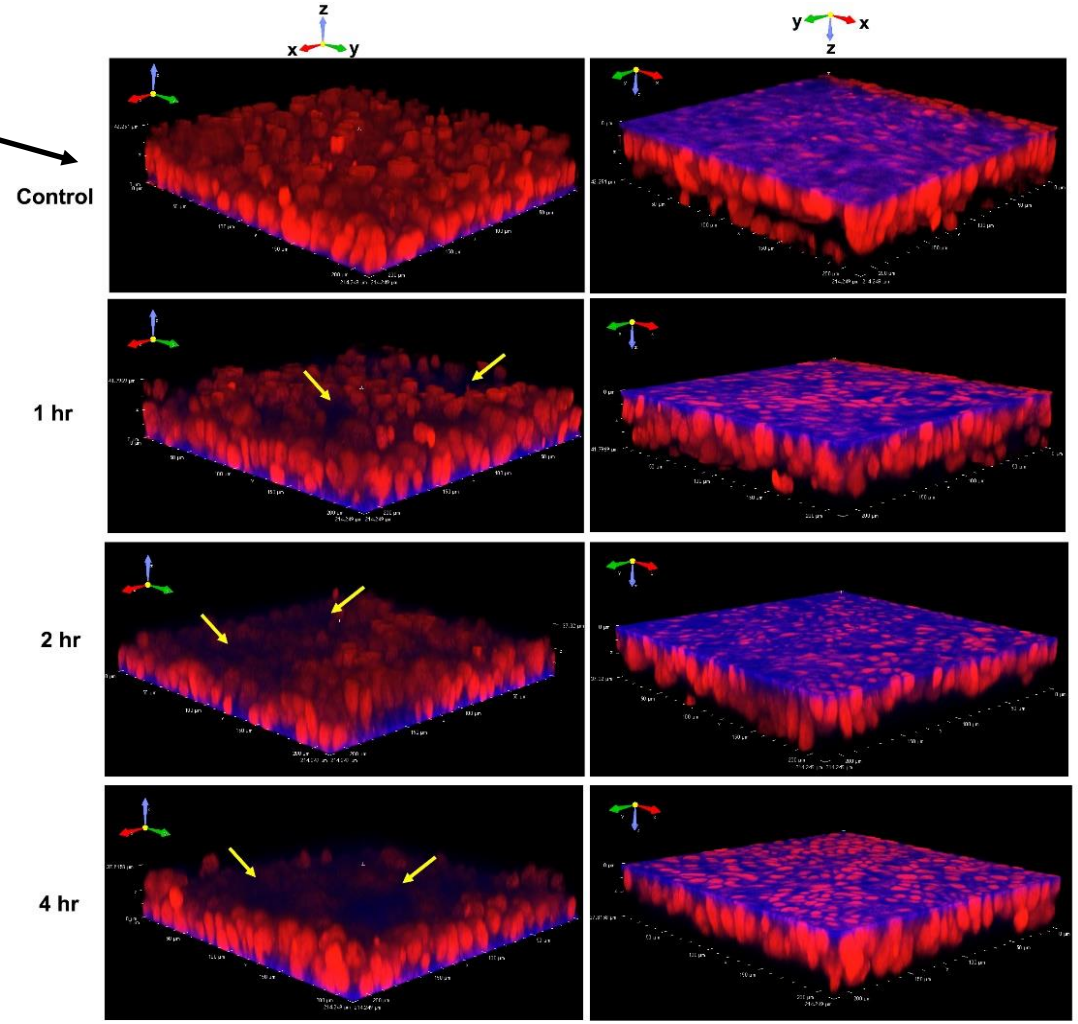
In-vitro human lung epithelial cell model (Calu-3)

Air-interfaced culture (AIC)



Red: cell nucleus
Blue: ciprofloxacin

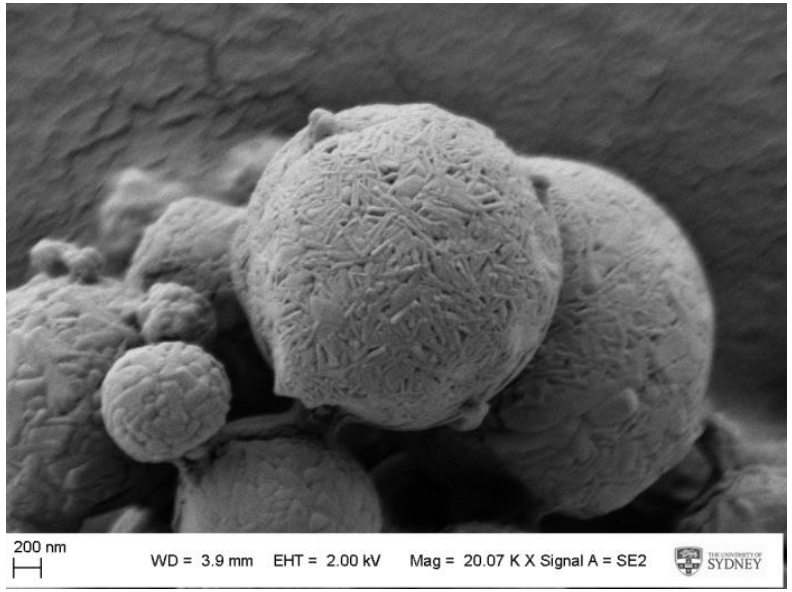




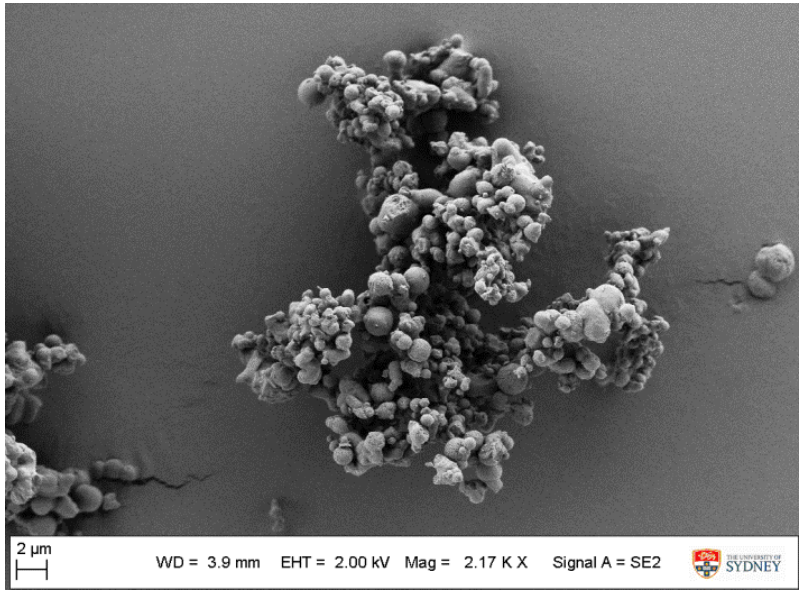
2019 International journal of pharmaceutics 569, 118616

PLATFORMS FOR SPRAY DRIED BIOLOGICS

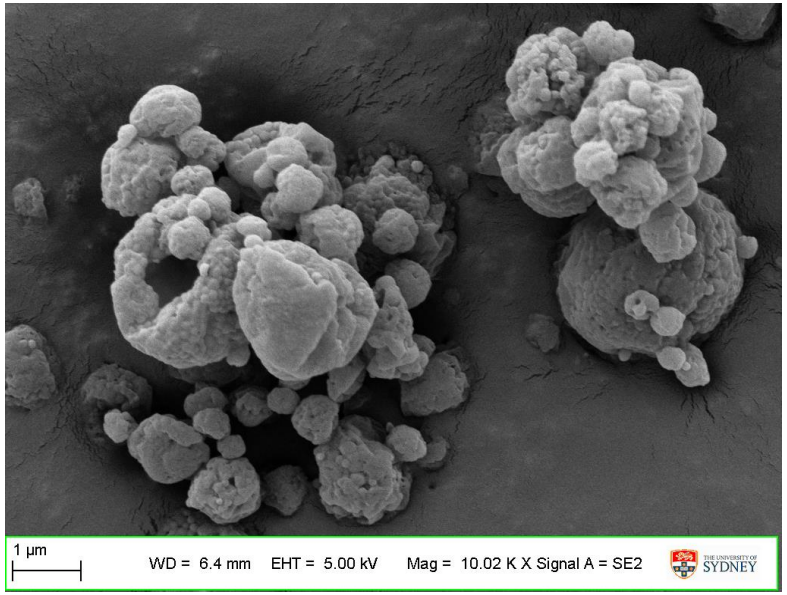
siRNA



Polypeptide



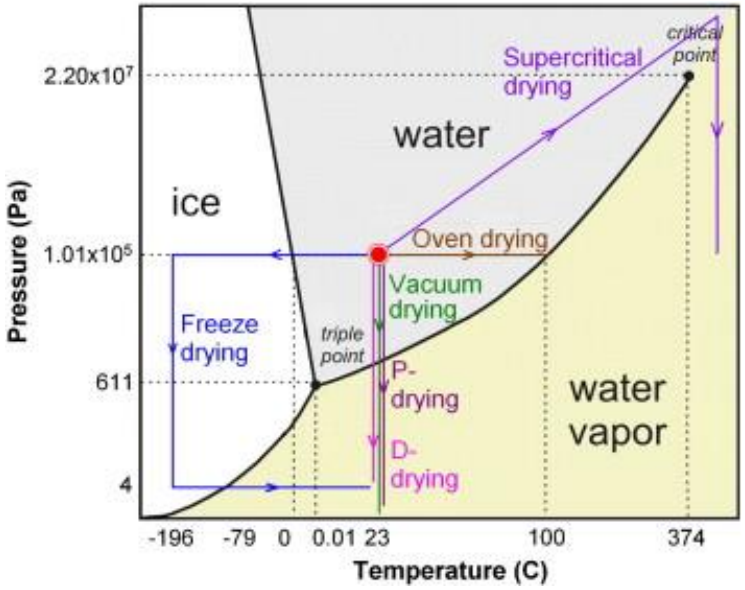
Nanoparticles



2015 . Molecular pharmaceutics 12 (3), 910-921

2016. Journal of pharmaceutical sciences 105 (2), 650-656

Traditional manufacturing of biological solids - Freeze drying (lyophilization)



FIRST FDA-APPROVED STERILE SPRAY DRIED PROTEIN PRODUCTS

Share

Raplixa case study: Enabling an innovative drug presentation through aseptic spray drying

FDA approved the Raplixa, the first spray-dried fibrin sealant, in May 2015 to help control bleeding in adults during surgery.

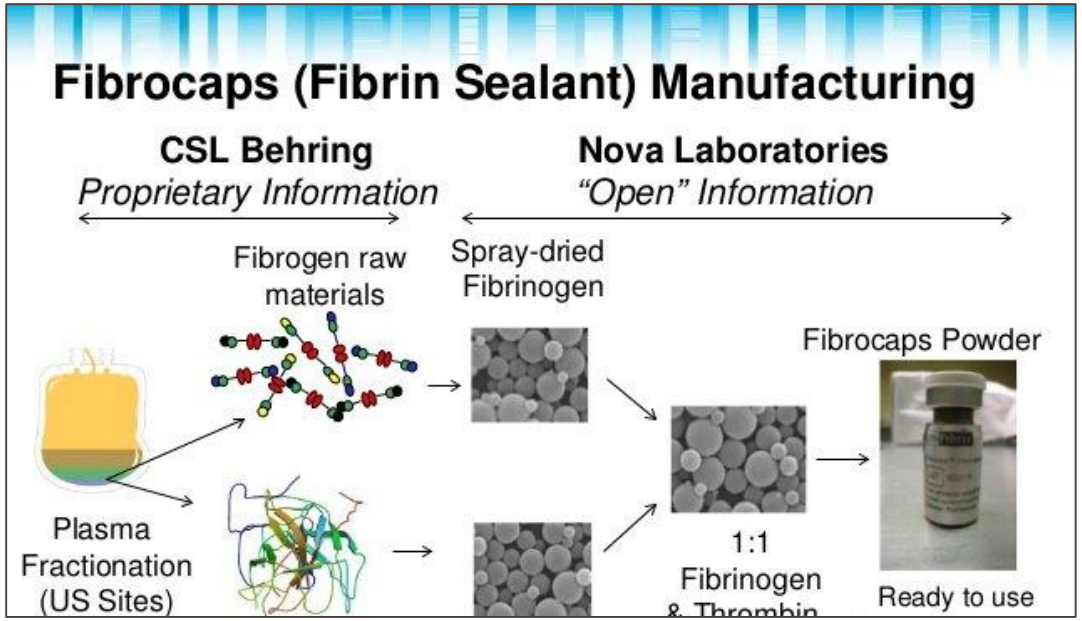
Jul 02, 2016 By Sam de Costa
Pharmaceutical Technology
Volume 40, Issue 7, pg 26

In May 2015, FDA approved Raplixa, the first spray-dried fibrin sealant. Raplixa is used to help control bleeding in adults during surgery. The approval was based on a Phase III, multicenter clinical trial involving 721 patients who underwent different surgical procedures across four countries. Clinical supplies of Raplixa were manufactured by Nova Laboratories at its sterile manufacturing facilities. The product comprised of spray-dried thrombin and spray-dried fibrinogen, which are blended and filled aseptically.

Raplixa needs no thawing, reconstitution, or mixing, and can be applied directly from the vial or with a device. The Raplixa spray device, also approved by FDA, is a low-pressure spray applicator that can be used to apply the fibrin sealant to the bleeding site where the product then dissolves in the blood and starts a reaction between the two proteins, leading to clotting of the blood to help stop bleeding. The approval of Raplixa provides surgeons with an extra option to control bleeding during surgery when needed.

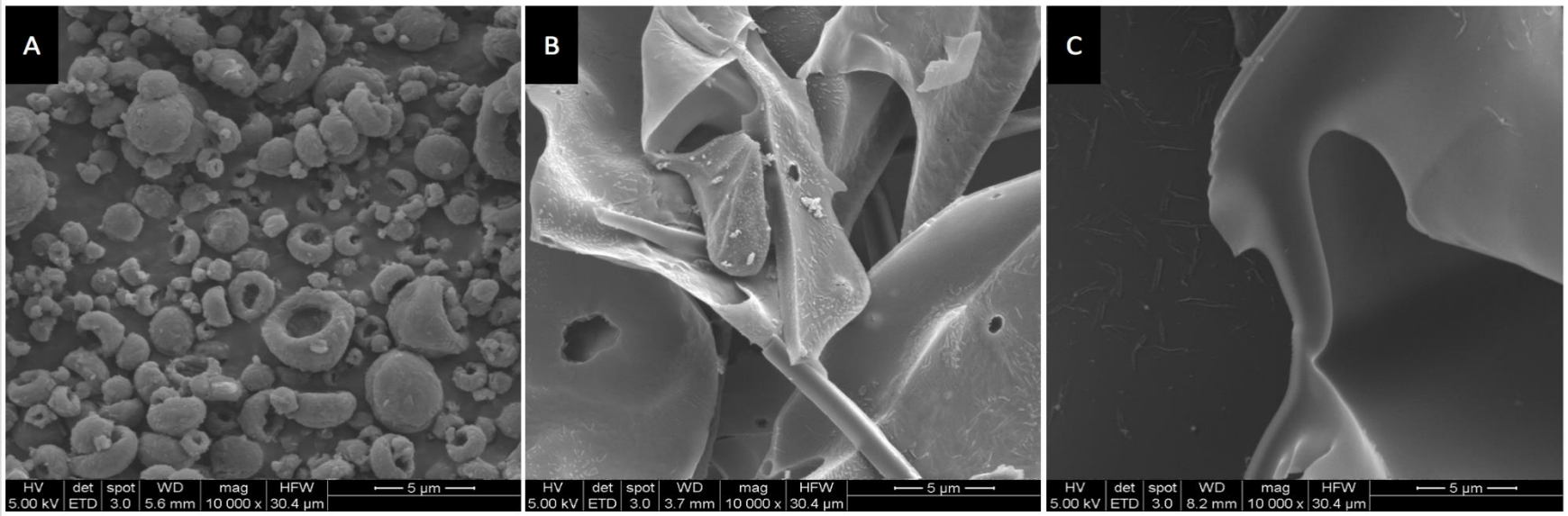
The spray-drying process used to manufacture Raplixa produces dried powders that can be combined into a single vial, eliminating the need to mix the fibrinogen and thrombin before use, and allowing the product to be stored at room temperature. Commercial supplies of Raplixa are now being manufactured by Nova Laboratories.

Article Details
Pharmaceutical Technology
Vol. 40, No. 7
Pages: 26



Karen Midthun, M.D., director of the FDA's Center for Biologics Evaluation and Research "The spray-drying process used to manufacture Raplixa produces dried powders that can be combined into a single vial. This eliminates the need to combine the fibrinogen and thrombin before use and allows the product to be stored at room temperature."

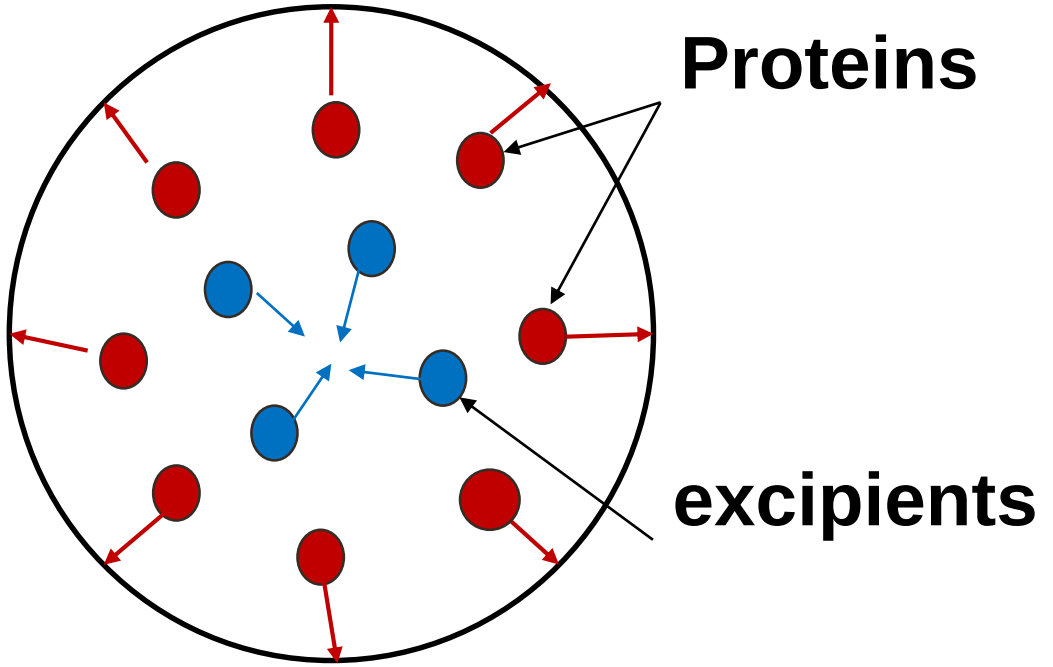
Comparison between lyophilized and spray dried IgG1 mAb using solid state hydrogen-deuterium exchange (ssHDX) analysis

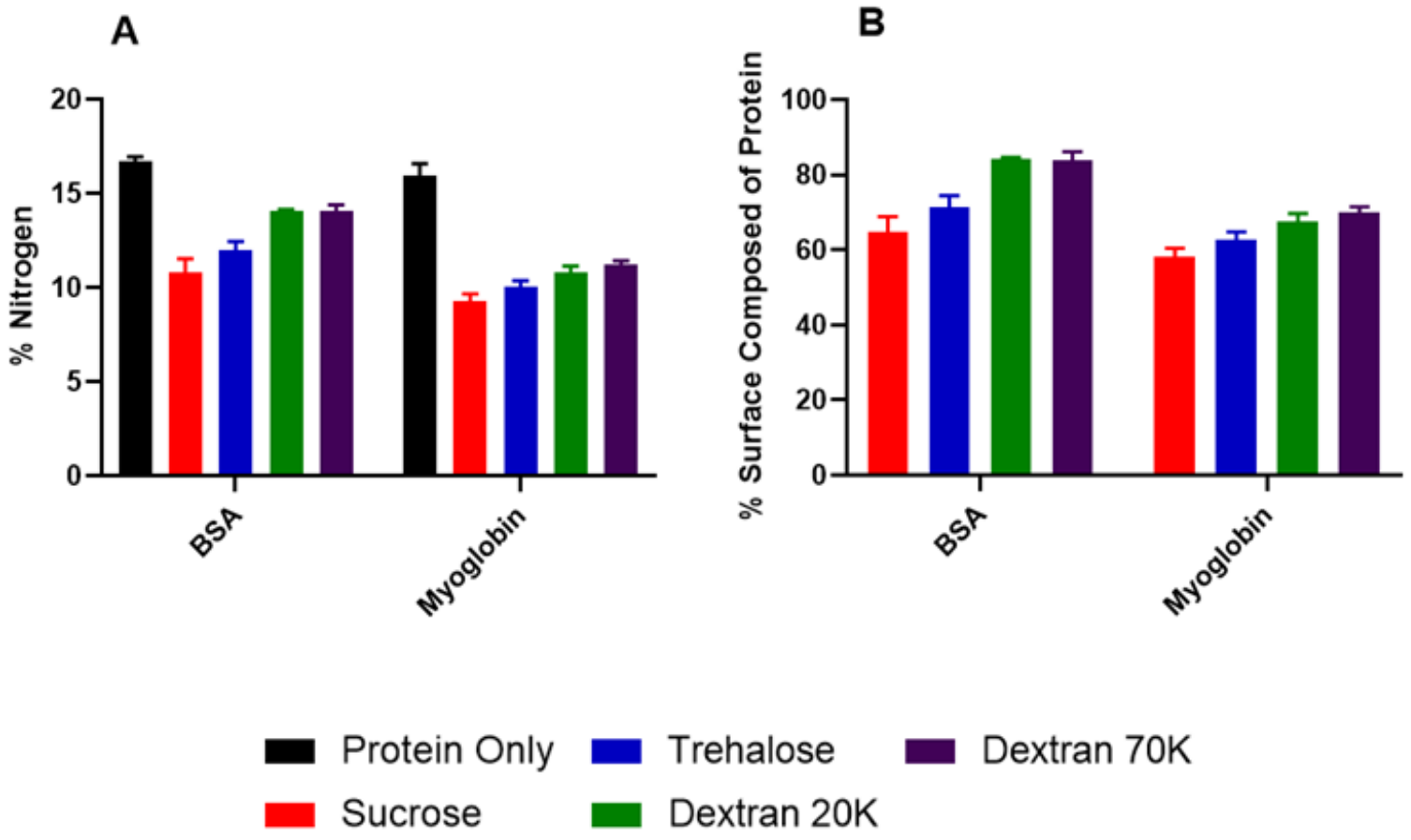


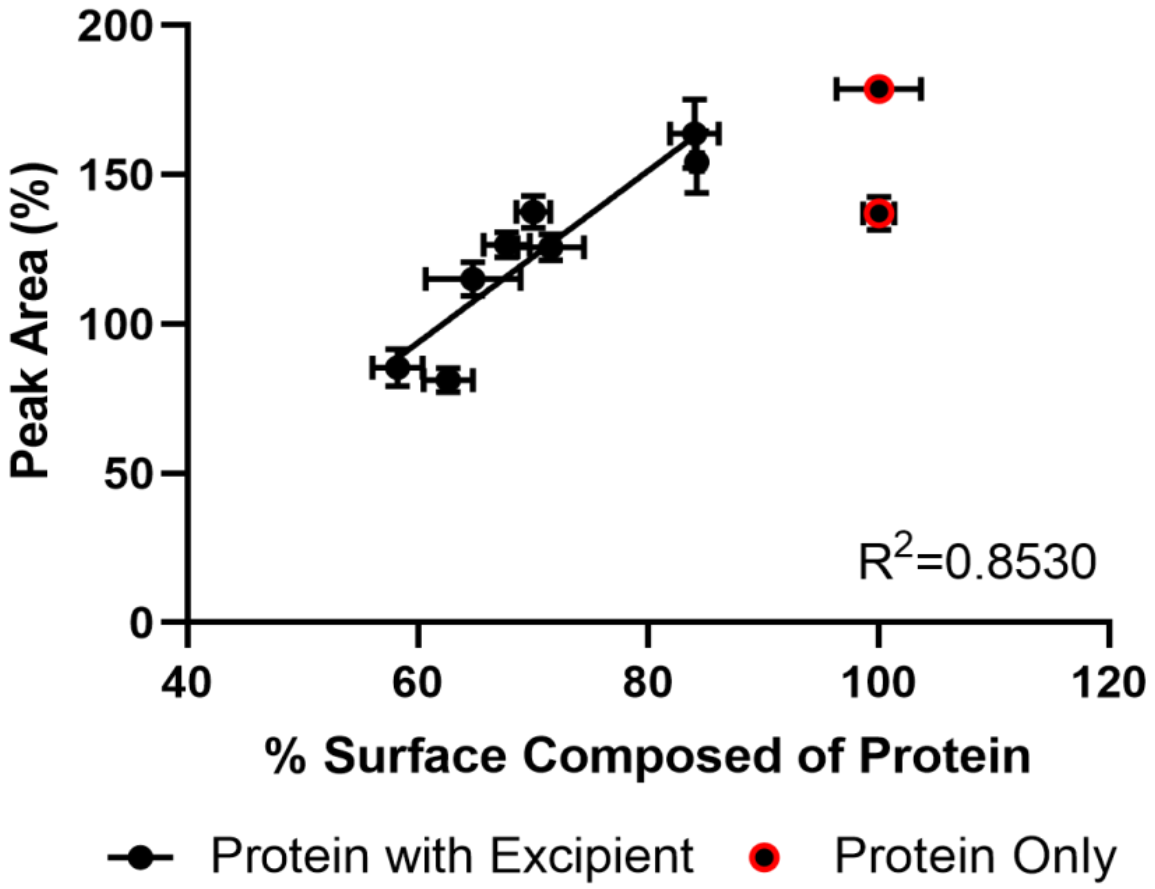
Scanning electron micrographs of mannitol formulations. (A) Spray dried. (B) Lyophilized with uncontrolled ice nucleation (C) Lyophilized with controlled ice nucleation.

2018 Pharm Res (2018) 35: 12.

Surface enrichment of proteins may compromised excipient protection and lead to aggregation

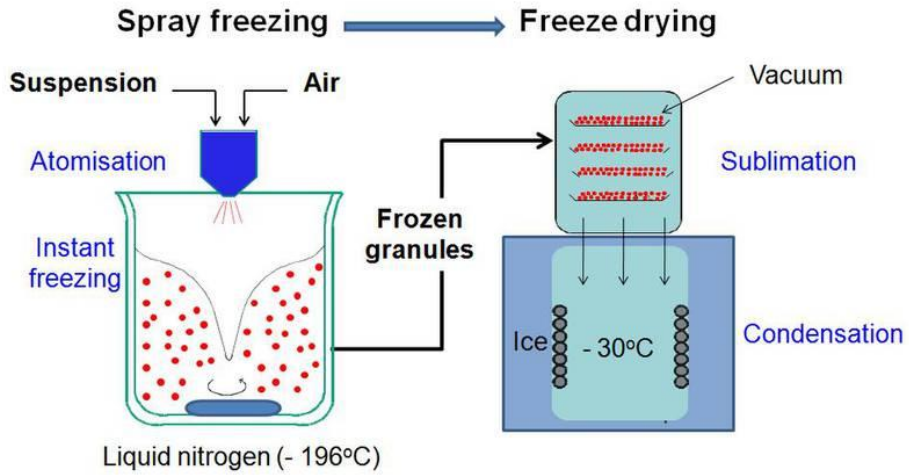


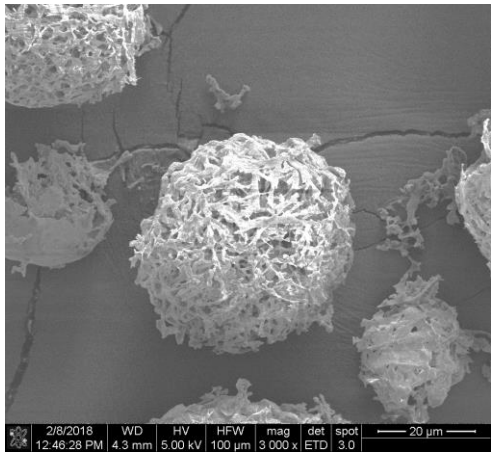

A
% Nitrogen
20
15
10
5
0
BSA
Myoglobin
B
% Surface Composed of Protein
100
80
60
40
20
0
BSA
Myoglobin
Protein Only
Trehalose
Dextran 70K
Sucrose
Dextran 20K

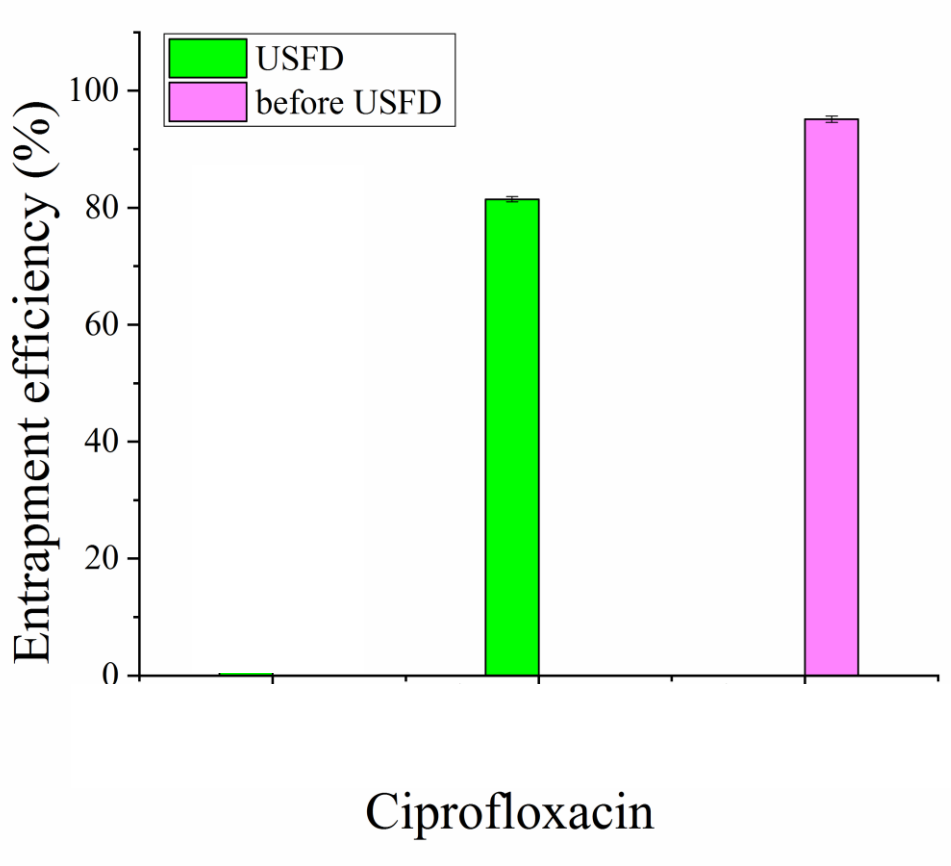


2019 International journal of pharmaceutics 569, 118616

Spray freeze drying for heat sensitive biologics

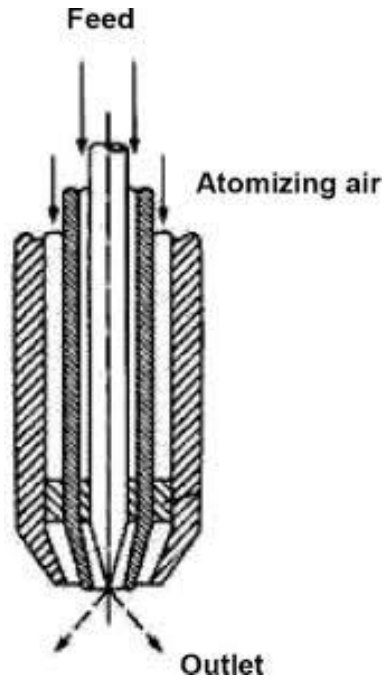




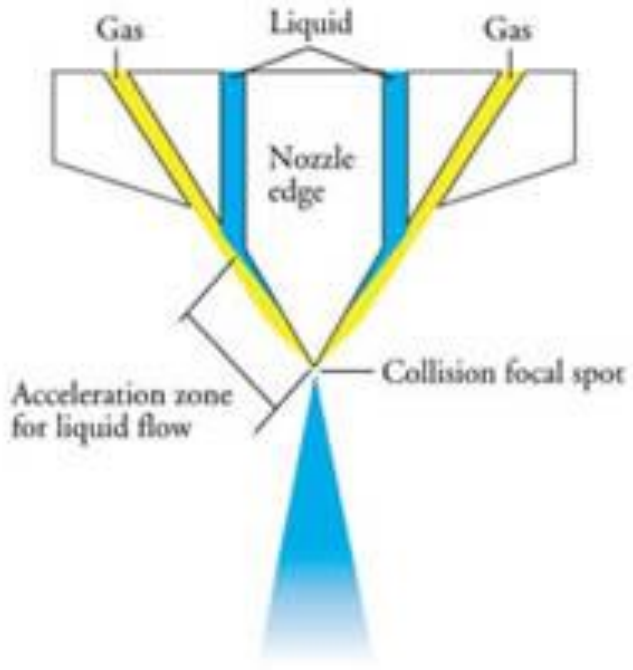


2019 International journal of pharmaceutics 118915

Two-fluid atomizing nozzle



Three-fluid atomizing nozzle



Collaborators:

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Alan Forrest, Gauri Rao (University of North Carolina)

Hak-Kim Chan, Fanfan Zhou (University of Sydney)

Jian Li, David Morton (Monash University)

John Denman, Alex Cavallaro (University of South Australia)

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Guihong Chai
Heejun Park
Nivedita Shetty
Shaoning Wang
Junhong Lin
Jianting Chen
Jian Guan
Nathan Wilson

Current Team members:

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ACKNOWLEDGMENTS

Total funding support: $8.5M

80 journal articles (55 published at Purdue in the past 4 years) and 6 patent applications

AAPS: Outstanding Graduate Student Research Award in Pharmaceutical Technologies, Postdoctoral Fellow Award

IPEC: Excipient Graduate Student Award, Emerging Researcher Award

Australian Government: Australian Endeavor Fellowship, Australian Early Career Fellowship

ISAM New investigator Award

NIPTE Rising Star Scholar Award

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WELCOME TO VISIT PURDUE!

"That's one small step for a man, one giant leap for mankind."

goBOLD

PURDUE UNIVERSITY

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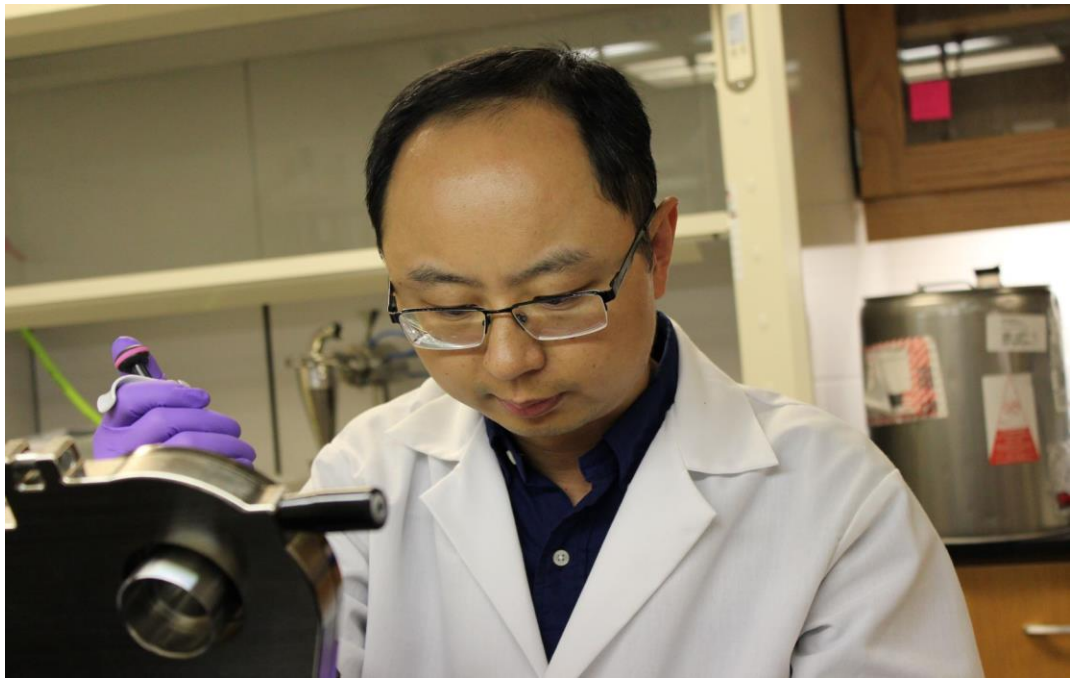
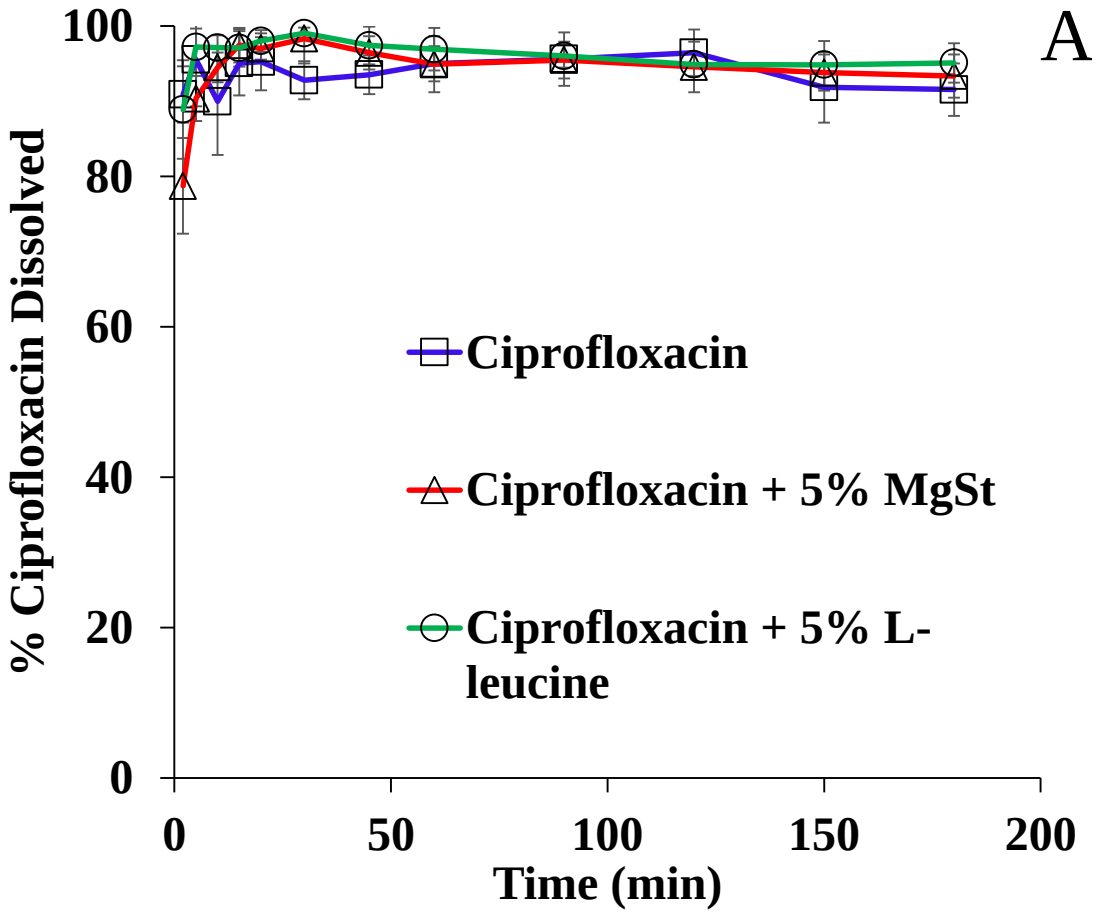
GO BALD

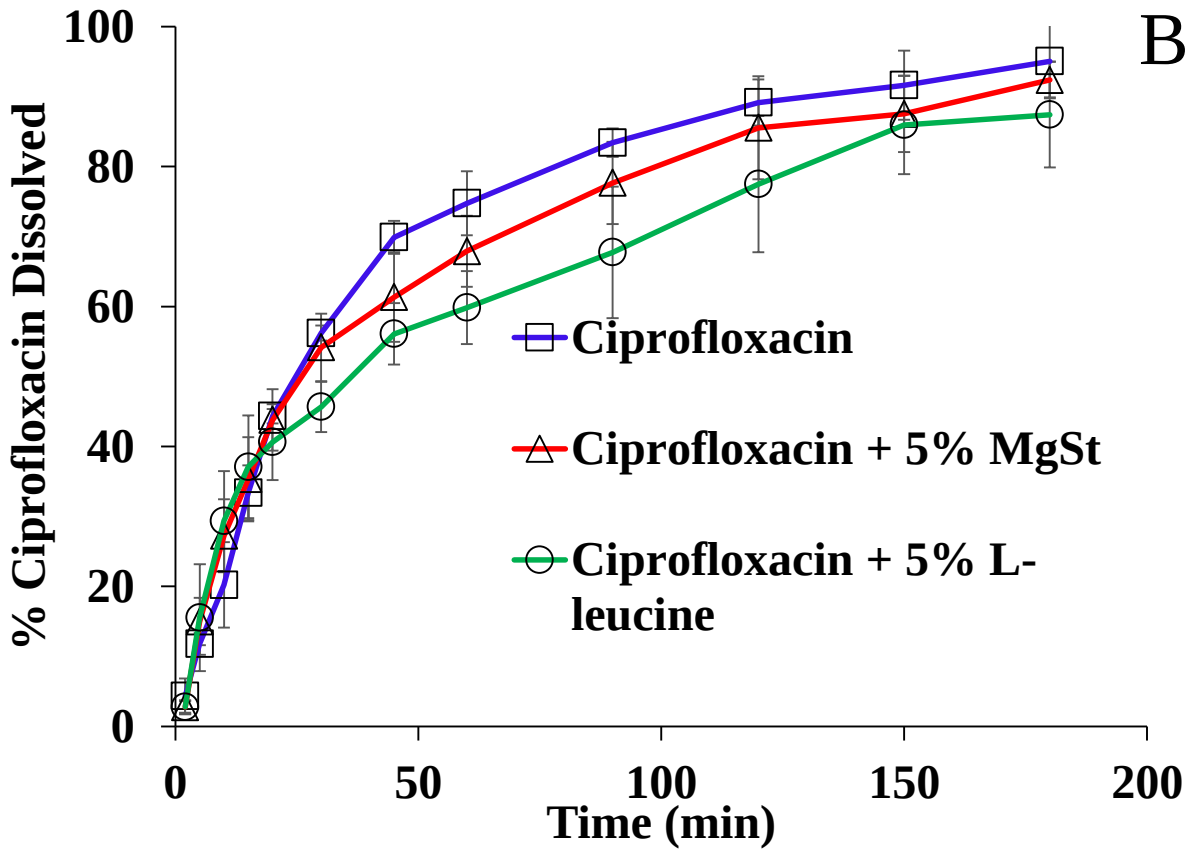


Thank you for your attention!

Any questions?



Stirring in a beaker



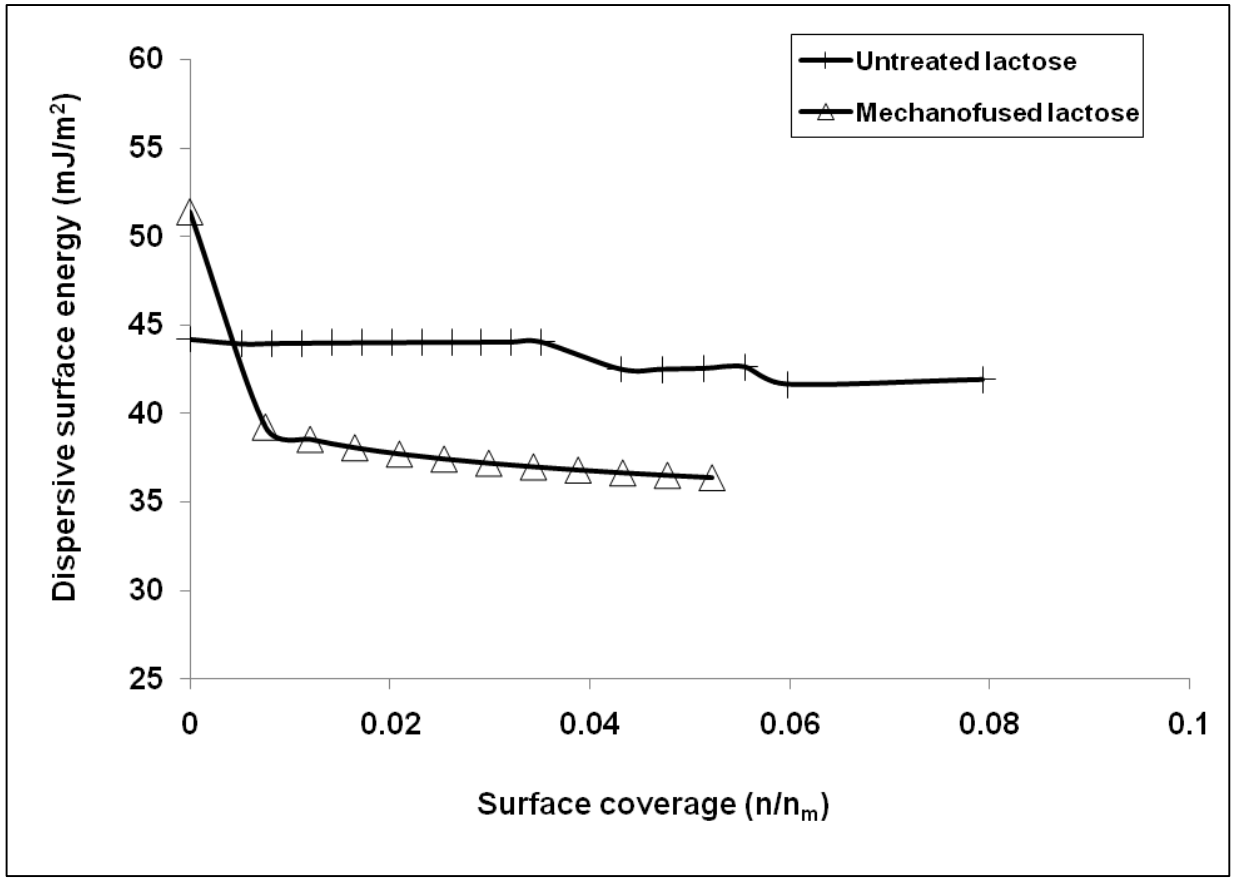
Franz diffusion cell

SURFACE ENERGY – MEASURED BY INFINITE DILUTION OF INVERSE GAS CHROMATOGRAPHY

- Higher of the surface energy, the more sticky of the powder
- Literatures and our data showed surface energy of dry coated powders increased, which was contradictory to the improved powder flow
- A more reliable surface energy measurement is needed

Sample	Dispersive Energy (mJ/m^2)	Polar Energy (mJ/m^2)	Total Energy (mJ/m^2)	Work of Cohesion (mJ/m^2)
Untreated lactose	45.4 ± 1.2	164.0 ± 6.4	209.3 ± 7.3	418.7 ± 15.1
MgSt	36.2 ± 0.2	74.1 ± 1.5	110.4 ± 1.7	220.8 ± 3.4
Mechanofused lactose	51.4 ± 1.1	135.1 ± 4.0	186.5 ± 5.0	373.0 ± 10.2

SURFACE ENERGY – NEW FINITE DILUTION MEASUREMENTS ARE MORE REPRESENTATIVE OF THE PARTICLE SURFACES

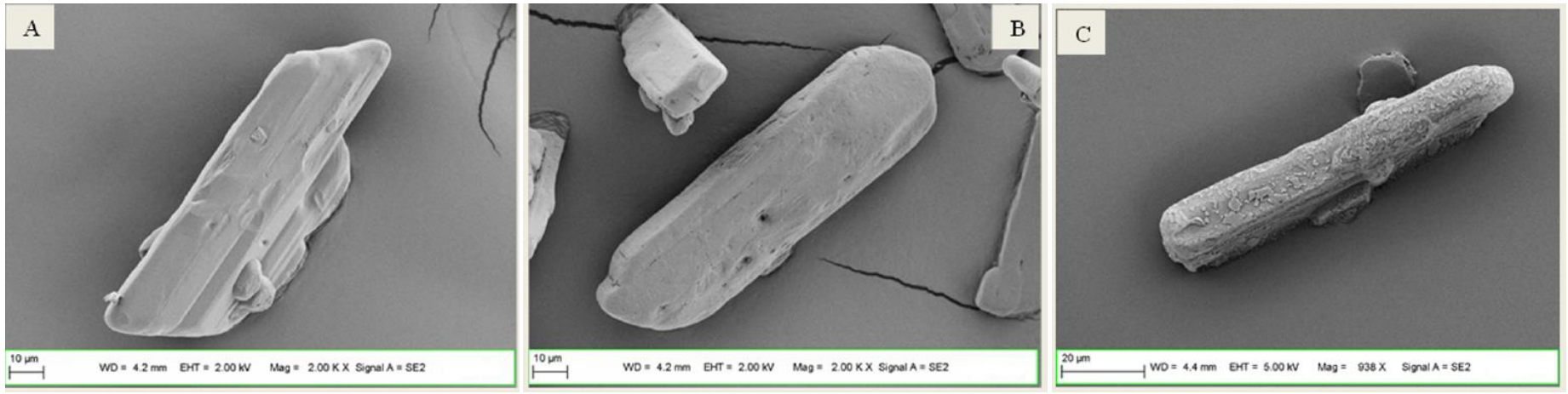


Zhou et al., 2011. Journal of Pharmaceutical Sciences, 100 (8), pp. 3421-3430.

Das et al., 2011. European Journal of Pharmaceutical Sciences, 43 (4), pp. 325-333.

MECHANISMS FOR FLOW IMPROVEMENT ARE DIFFERENT BETWEEN MGST (FILM FORMING) AND LEUCINE (CREATING ROUGH SURFACE)

Raw ibuprofen | **Coated with MgSt** | **Coated with Leucine**



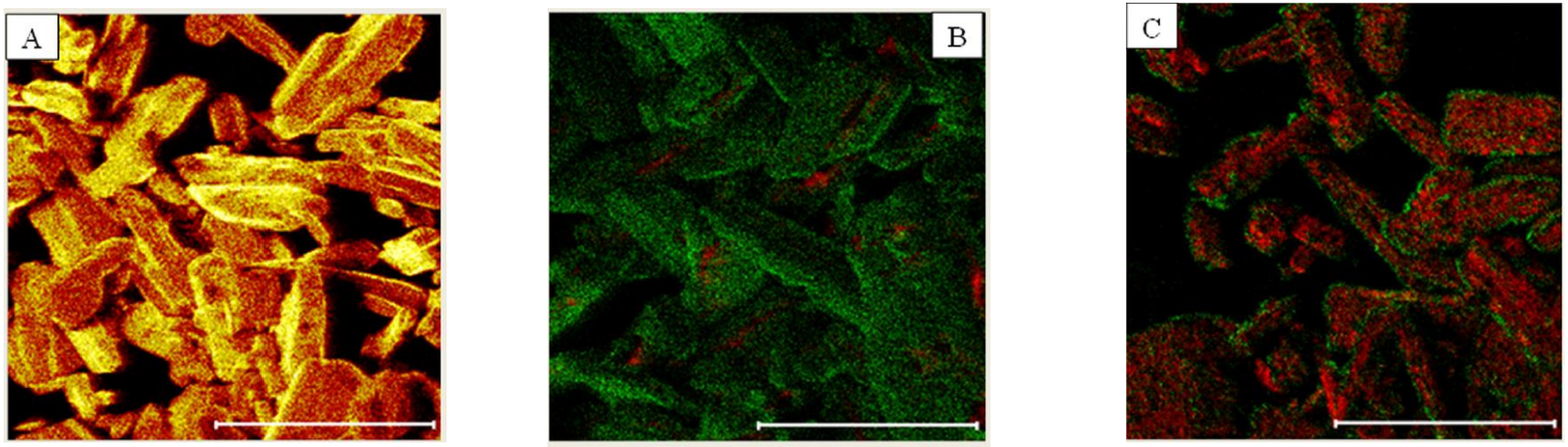
Qu, Zhou et al., European Journal of Pharmaceutical Sciences 78 (2015) 264–272

TOF-SIMS DATA PROVED FLOW IMPROVEMENT ARE DIFFERENT BETWEEN MGST (FILM FORMING) AND LEUCINE (CREATING ROUGH SURFACE)

Raw ibuprofen

Coated with MgSt

Coated with Leucine



Red signal – ibuprofen **Green signal – coating material**

Such imaging platform can be used to understand other surface-related functions, such as lubrication and aerosolization

Qu, Zhou et al., European Journal of Pharmaceutical Sciences 78 (2015) 264–272

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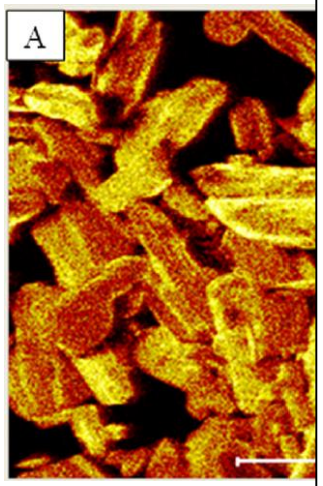
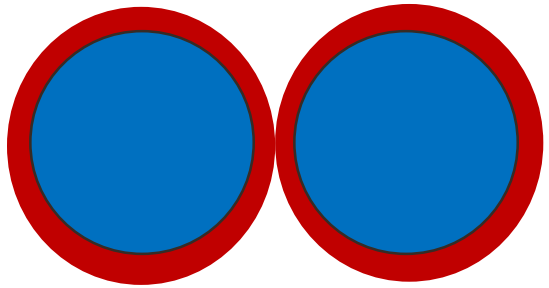
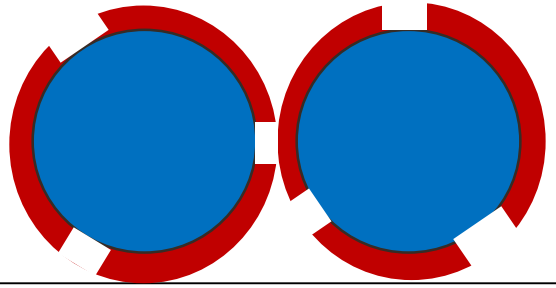
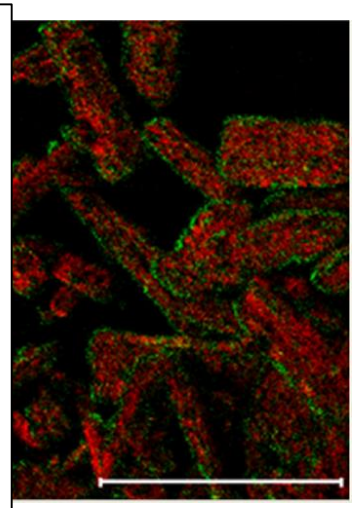




Magnesium stearate forms a non-cohesive film



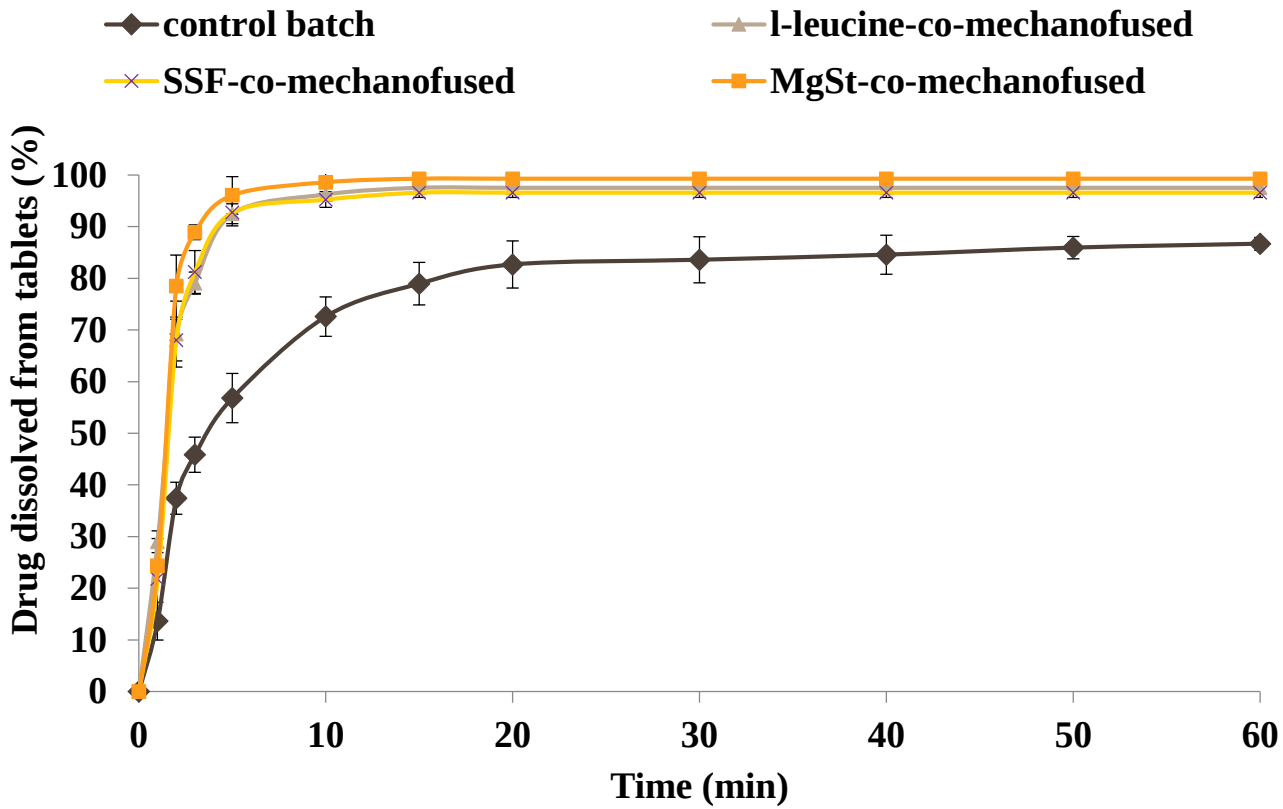
Leucine creates asperities between particles



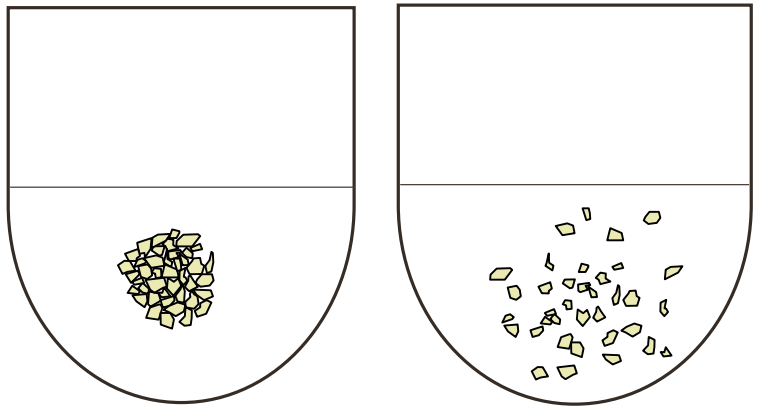
Re material

Such imaging platform can be used to understand other surface-related functions, such as lubrication and spray drying phase separation

DISSOLUTION OF TABLETS



Qu et al., Journal of Pharmaceutical Sciences 106 (2017) 159-167



$$C = C_d * \exp(-k_d * x)$$

$$C = C_d * \exp(-k_d * x) + C_a * \exp(-k_a * x)$$

$$C = C_d * \exp(-k_d * x) + C_{a1} * \exp(-k_{a1} * x) + C_{a2} * \exp(-k_{a2} * x)$$

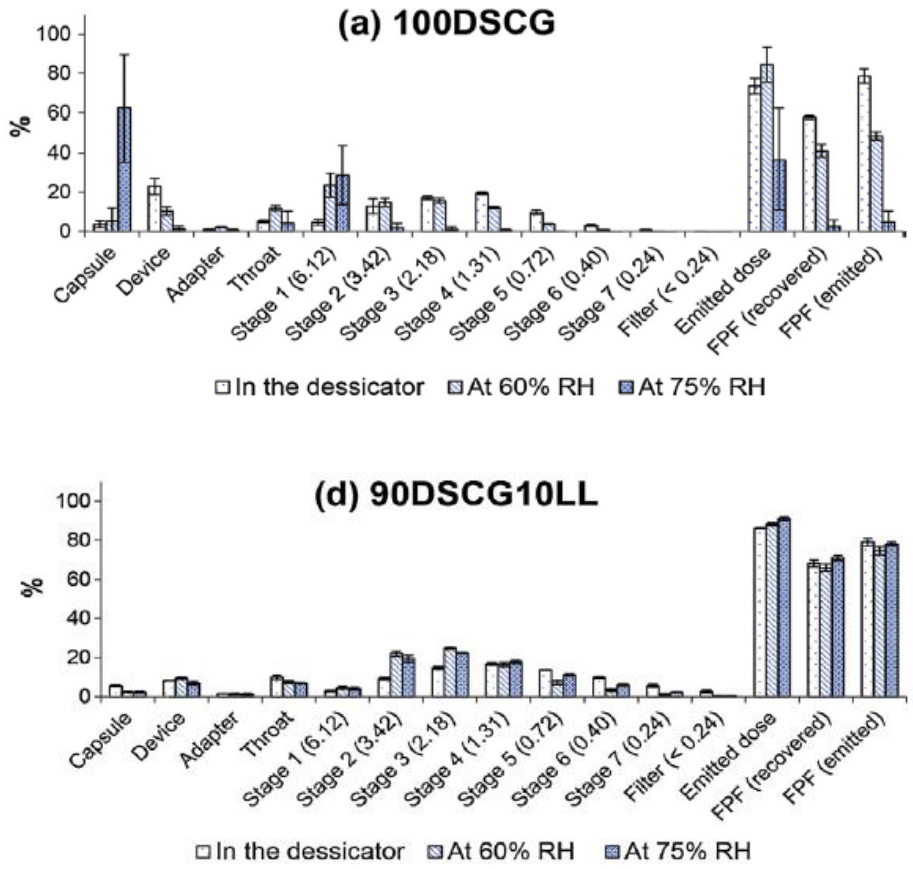
where C is the concentration of undissolved drug (%) at time t; C_d and C_a are the initial concentrations (%) of dispersed particles and agglomerates, respectively; k_d and k_a (min_1) represent the dissolution rate constants for dispersed and agglomerated particles, respectively.

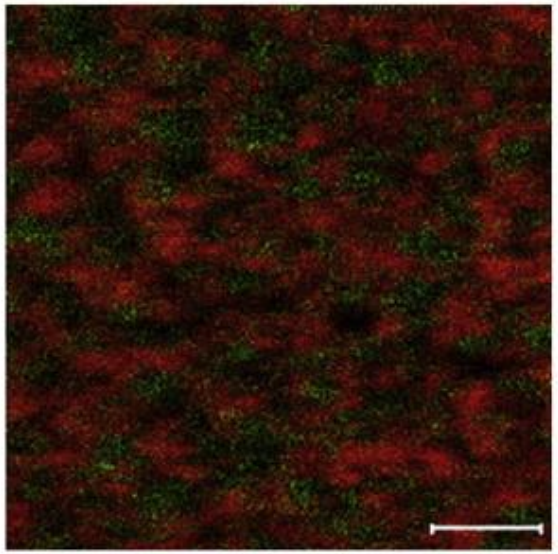
	Raw	MgSt-mechanofused	L-leucine-mechanofused
C_d (%)	60.0 ± 25.8	107.3 ± 0.3	106.8 ± 0.5
C_a (%)	43.0 ± 23.1	–	–
k_d (min^{-1})	0.34 ± 0.06	0.66 ± 0.01	0.61 ± 0.03
k_a (min^{-1})	0.02 ± 0.01	–	–

Qu et al., Journal of Pharmaceutical Sciences 106 (2017) 159-167

SURFACE PROTECTIVE COATING BY SPRAY DRYING

DISODIUM CROMOGLYCATE (DSCG) COATED WITH AN EXCIPIENT, L-LEUCINE





(d) 90DSCG10LL

European Journal of Pharmaceutics and Biopharmaceutics 102 (2016): 132-141.

$$Pe_i = \frac{k}{8D_i}$$

Pe: Peclet number

k: Droplet evaporation rate

D_i: Diffusion motion

Pe<1, particles are likely solid

Pe >1, particles are low density