Adhesion of powders to metal surfaces during compaction

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Background and objectives

Adhesion of powders to metal surfaces during compaction (referred to as "sticking") is a significant problem in powder pressing sectors including pharmaceuticals, food, detergents, catalysts etc. Sticking is difficult to predict in early stage of product formulation and process development and usually manifests during full production scale where high productivity machines such as rotary tablet presses are used. The remedy consists of stopping production, remove, clean, reassemble tooling and continue processing until the material builds up on the tooling surfaces again. In pharmaceuticals it is believed that 25% of solid dosage forms are affected by sticking.

Objectives:
1. Establish a test method to quantify material adhesion on compaction tooling over an industrially relevant range of process and environmental conditions.
2. Identify the key factors affecting the amount and/or rate of powder adhesion on compaction tooling including: powder properties (e.g. mechanical, thermal), powder tool interactions (friction, adhesion), tooling materials and finish, compaction parameters (stress, rate) and environmental conditions (temperature, relative humidity).
3. Establish a predictive criteria for the propensity of adhesion given a set of molecular/crystal properties and process/environmental conditions.

Sticking hypotheses:
1. Temperature. Sticking can be understood as a coupled thermo-mechanical problem with two sources of heat: 1) Powder compaction involves dissipative processes that generate heat and 2) At the tool interface heat is also generated due to friction. As sticking (gradual deposition of the material to surfaces) progresses the properties of the materials and surfaces evolve, e.g. phase transformations due to stress, strain rate, temperature.
2. Humidity. Moisture uptake by hygroscopic materials leads to water acting as a binder at the interfaces, leading to sticking.
3. Particle breakage. Brittle materials or granules break during compaction, creating new surfaces. These new unlubricated surfaces give cohesion/strength to compact but also lead to sticking.

## Experimental characterisation of sticking
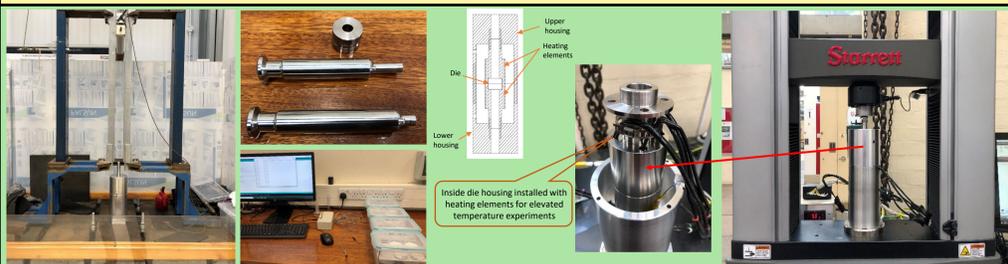
Sticking observations
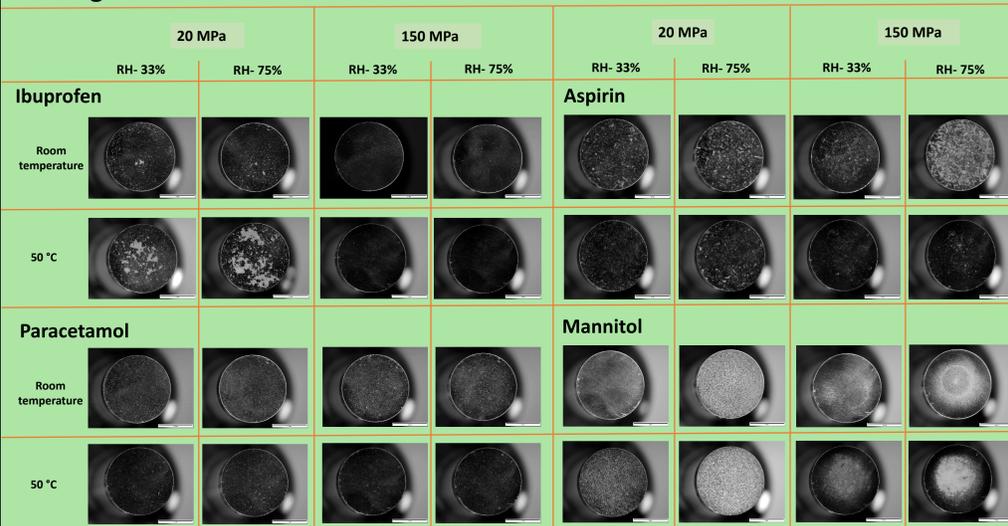
- Ibuprofen exhibited less sticking than expected (from the literature) during low speed compaction at the humidity and temperature levels tested. However, at high compaction speed, sticking was severe. Note: we use brand new "B" tooling manufactured by I Holland (representative tool material and surface finish).
- Aspirin exhibited more sticking than the other APIs at both humidity levels. However, at 75% RH sticking was severe .Interestingly, sticking was reduced at elevated temperature.
- Paracetamol showed more hazing at room temperature. However, at elevated temperature hazing was reduced significantly at both humidity levels.
- Mannitol showed more sticking at RH 75% compared to RH 33%. Also, at 75% RH and elevated temperature, sticking was increased further.
- Sorbitol showed no sticking at room temperature. However, at 50 °C a small amount of sticking was observed, which was reduced at RH 75%.
- Maize starch and Microcrystalline cellulose did not exhibit any sticking behaviour
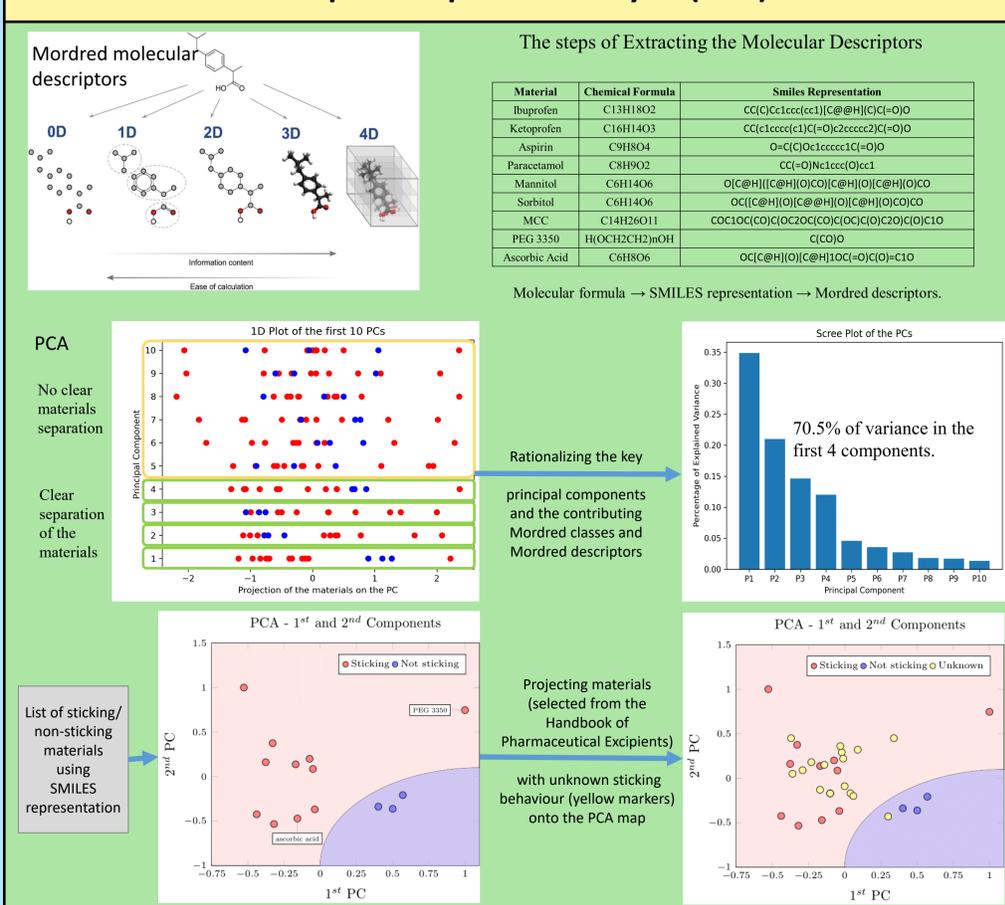
High speed compaction
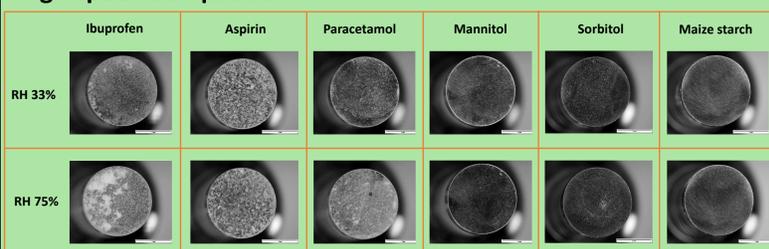
- Ibuprofen, Aspirin and Paracetamol: severe sticking
- Mannitol, Sorbitol and Maize starch: compaction rate did not present significant effect

Materials and testing parameters

Material	Formula	Type	Sticking/ Not Sticking	Parameters				
				Pressure (MPa)	% RH	Temperature	Strain rate	20 successive tabletting
				20, 50, 75, 100, 150, 200, 250	33% and 75%	Room and 50 °C	Impact test	
Ibuprofen	$CH_{13}H_{18}O_2$	API	Sticking	✓	✓	✓	✓	✓
Acetylsalicylic Acid (Aspirin)	$C_9H_8O_4$	API	Sticking	✓	✓	✓	✓	✓
Paracetamol	$C_8H_9NO_2$	API	Not Sticking	✓	✓	✓	✓	✓
Mannitol	$C_6H_{14}O_6$	Excipient	Sticking	✓	✓	✓	✓	✓
NEOSORB (Sorbitol)	$C_6H_{14}O_6$	Excipient	Sticking	✓	✓	✓	✓	✓
Maize Starch B	$(C_6H_{10}O_5)_n +(H_2O)$	Excipient	Not Sticking	✓	✓	✓	✓	-
Microcrystalline Cellulose (MCC)	$(C_6H_{10}O_5)_n$	Excipient	Not Sticking	✓	✓	✓	✓	-

Principal Component Analysis (PCA)

Mordred molecular descriptors

The steps of Extracting the Molecular Descriptors

Material	Chemical Formula	Smiles Representation
Ibuprofen	C13H18O2	CC(C)Cc1ccc(cc1)[C@@H](C)C(=O)O
Ketoprofen	C16H14O3	CC(c1cccc(c1)C(=O)c2ccccc2)C(=O)O
Aspirin	C9H8O4	O=C(C)Oc1ccccc1C(=O)O
Paracetamol	C8H9O2	CC(=O)Nc1ccc(O)cc1
Mannitol	C6H14O6	O[C@H]([C@H](O)CO)[C@H](O)[C@H](O)CO
Sorbitol	C6H14O6	OC[C@H](O)[C@@H](O)[C@H](O)CO)CO
MCC	C14H26O11	COC1OC(CO)C(OC2OC(CO)C(OC)C(O)C2O)C(O)C1O
PEG 3350	H(OCH2CH2nOH	C(CO)O
Ascorbic Acid	C6H8O6	OC[C@H](O)[C@H]1OC(=O)C(O)=C1O

Molecular formula → SMILES representation → Mordred descriptors.

PCA

No clear materials separation

Clear separation of the materials

Rationalizing the key principal components and the contributing Mordred classes and Mordred descriptors

70.5% of variance in the first 4 components.

List of sticking/ non-sticking materials using SMILES representation

Projecting materials (selected from the Handbook of Pharmaceutical Excipients) with unknown sticking behaviour (yellow markers) onto the PCA map

Summary and deliverables

Database of sticking behaviour:
- Comprehensive characterisation of 7 materials
- Hypotheses/mechanisms: compaction pressure, rate, temperature, humidity
- Mordred descriptors
- PCA to predict sticking of a new molecule

Work remaining:
- Identify key Mordred categories (20+ => 5): polarity, acid/base, autocorrelation
- Identify key Mordred descriptors (1800 => 100): molecular weight, no. of H donors/acceptor, no of cyclic structures
- Refine sticking prediction maps
- Consider particle and bulk properties (e.g. physical, mechanical and thermal properties)

Deliverable: Python package:
- Input: SMILES representation (new molecule)
- Output: yes/no sticking prediction and representation on map
- Graphical user interface

Sticking 2 (renewal proposal): Sticking science

Incorporating crystal and particle descriptors

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