The Use of Compaction Simulation as a Tool to Aid Successful Tablet Formulation

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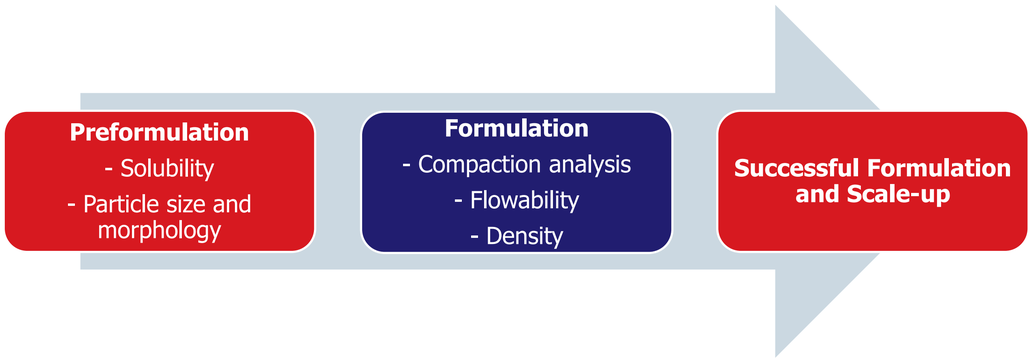
Introduction

Early consideration of API properties allows intelligent formulation design and manufacturing process selection to be achieved despite limited API availability[1,2].



Compaction simulation has been demonstrated to be predictive of production scale[3], and can help to de-risk the costly and time-consuming process of scaling up from R&D to production scale.

Materials and Methods

Compaction analysis of 3 model small molecule APIs (paracetamol (APAP), metoclopramide hydrochloride (MTH), diclofenac sodium (DCFS)) and a 25% APAP formulation (directly compressed (DC) and dry granulated (DG)), was carried out using a Gamlen D500 powder compaction analyser, tablet tensile analyser (TTA) and Gamlen Dashboard Software. Figure 1.

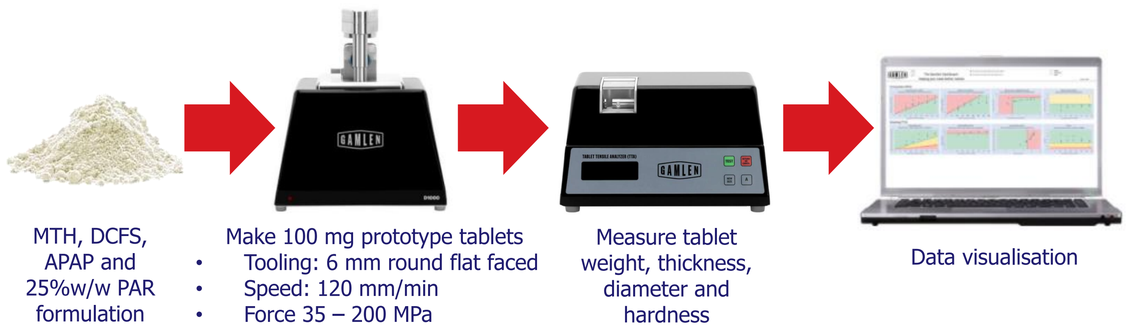


Figure 1: Compaction analysis method

Results and Discussion

API Compaction Analysis

Tabletability and compressibility profiles for APAP, MTH and DCFS are shown in Figure 2. Significant differences in compaction properties can occur between APIs. As expected, APAP demonstrated the worst tabletting and compressibility properties[4], followed by MTH and DCFS, respectively. This information, along with other API properties (flowability, solubility, melting point etc) and dosage form properties (tablet size and strength) can guide formulation decisions and strategies.

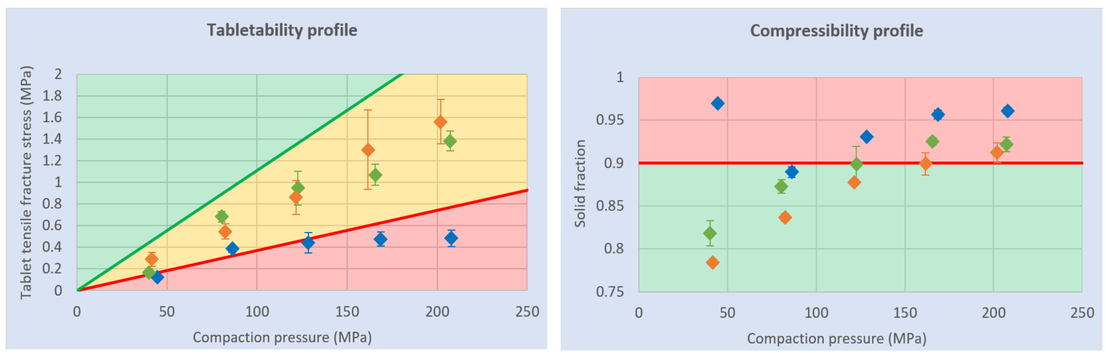


Figure 2: APAP (Blue), MTH (Green), DFCS (Orange)

Formulation Compaction Analysis

Excipients are added to aid manufacturing processes or improve API properties (Table 1) such as compaction, flowability or dissolution. Compaction analysis, in combination with flowability data and API particle size/morphology data, can aid selection of an appropriate manufacturing process. DG can improve the flowability of a formulation, however, it risks reducing compressibility and tablet tensile strength as a result of double compression[5]. The flowability of 25% w/w DC formulation has been improved by granulating, without compromising the compressibility or tablet tensile strength of the formulation (Figure 3). Prototype tablets prepared during compaction simulation can be used to measure other attributes such as disintegration time, friability and dissolution. Formulation compaction simulation has also be shown to assist wet granulation of a poorly compressible material such as APAP and reduce the risk of tablet defects[6].

Table 1: APAP properties

APAP Properties	
Molecular weight (g/mol)	151.16
Melting point (°C)	169
Particle size (µm)	D_{10}: 22.21 D_{50}: 85.22 D_{90}: 204.5
Flowability	Carrs Index (%): 47 Hausner Ratio: 1.9

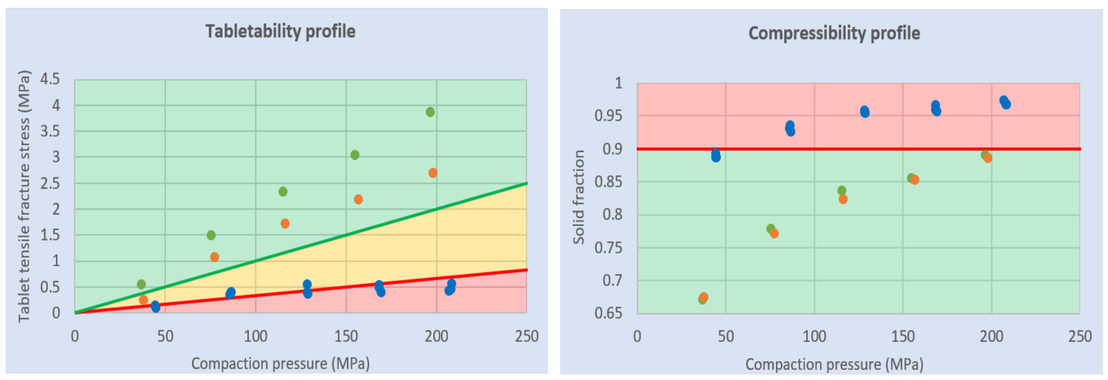


Figure 3: APAP (blue), APAP DC blend (Green), APAP Granules (Orange).

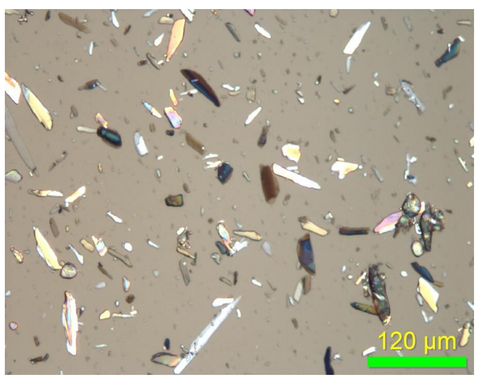


Figure 4: Microscopic APAP image

Conclusion

Compaction analysis of APIs and formulations alongside information about API properties was shown to be a useful tool and allows informed decisions to be made about formulation design and manufacturing process despite minimal API resources expected in early development.

References

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