POSTER 69

Understanding the Effect of Spherical Agglomeration on Tablet Manufacturability and Performance

Jack Creswick, Vishal Raval, Alastair Florence, Daniel Markl

Strathclyde Institute of Pharmacy and Biomedical Sciences &
Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC), University of Strathclyde, Glasgow

Introduction

Oral solid dosage (OSD) forms are the most common formulations for marketed pharmaceuticals, while tablets are the most common form of OSD produced. The properties of the materials directly influence the tabletting process; both the former and latter will determine the mechanical and performance properties of the final product. Spherical agglomeration (SA) is the process of organising particles into spherical clusters, and has been shown to improve material properties and overcome flowability issues. A compaction simulator was used to compact tablets containing either spherically agglomerated active pharmaceutical ingredient (API), or the primary crystal form of API. These tablets were assessed for their mechanical strength and porosity. Tablets were also assessed via terahertz time-domain spectroscopy (THz-TDS), followed by dissolution studies, to evaluate their performance.

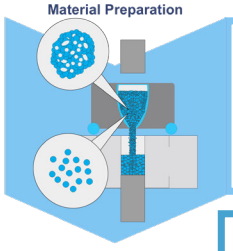
Objectives

- To produce tablets from primary crystal (PC), batch-made spherical agglomerate (AGB), and continuous-made spherical agglomerate (AGC) benzoic acid (BA).
- To study differences between PC, AGC and AGB tablets using compressibility, compactability and tabletability analyses.
- To assess PC, AGB and AGC tablet performance through dissolution studies and understand the impact of agglomerated materials on dissolution outcomes.
- To explore the effect of SA on porosity and content uniformity via terahertz time-domain spectroscopy analysis.

Materials & Experimental Plan

35% w/w continuous made spherically agglomerated (AGC), batch made spherically agglomerated (AGB), and non agglomerated (PC) benzoic acid (BA) make up the API used. 1% Magnesium stearate (MgSt) acts as lubricant, while 64% microcrystalline cellulose (MCC) was chosen as it deforms mostly plastically. Tablets of equal weight (200 mg) are compacted on a compaction simulator (HB50, Huxley-Bertram) at a range of thicknesses and pressures (2.11-2.85 mm and 50-400 MPa, respectively). Breaking force measurements were taken and *in-situ* compaction data were used to asses mechanical properties. Tablets were scanned with THz-TDS (TeraPulse Lx, TeraView) before dissolution studies were used to evaluate performance.

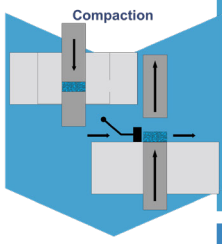
Material Preparation

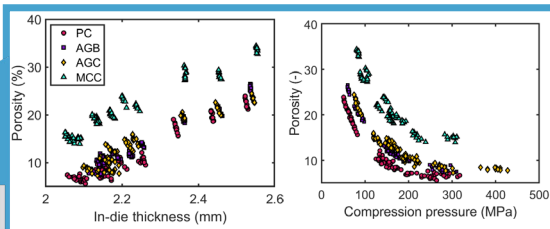


MCC	PC	AGB	AGC
MCC/MgSt % (w/w): 99/01	MCC/API/MgSt % (w/w): 64/35/01	MCC/API/MgSt % (w/w): 64/35/01	MCC/API/MgSt % (w/w): 64/35/01
MCC VMD*(μm): 146	API VMD*(μm): 68	API VMD*(μm): 341	API VMD*(μm): 355
Sphericity (avg, std): 0.623, 0.110	Sphericity (avg, std): 0.703, 0.097	Sphericity (avg, std): 0.661, 0.089	Sphericity (avg, std): 0.703, 0.074
True Density: 1.55	True Density: 1.28	True Density: 1.27	True Density: 1.28

*Volume Mean Diameter, PAQXOS 4.1 EPQC,sphere(EQPC), ISO

Compaction

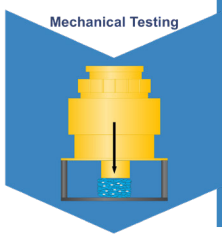




- Custom, simplified single-sided rotary press compaction profile was applied.
- Punch position control → 10 batches clearly separated in terms of the in-die thickness.

Figure 1. (a) Control of punch gap caused (b) wider distribution of resultant pressures.

Mechanical Testing



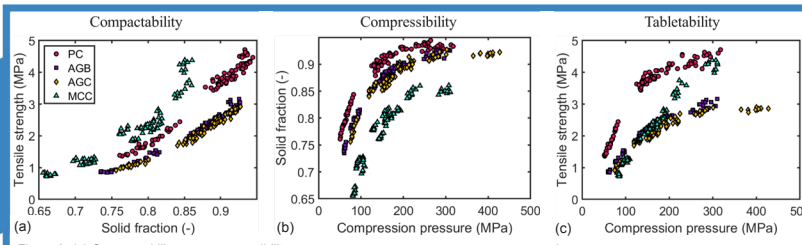


Figure 2. (a) Compactability, (b) Compressibility, and (c) tabletability plots for each batch of tablets.

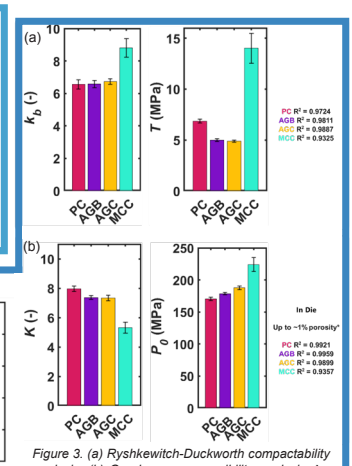
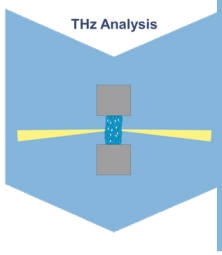
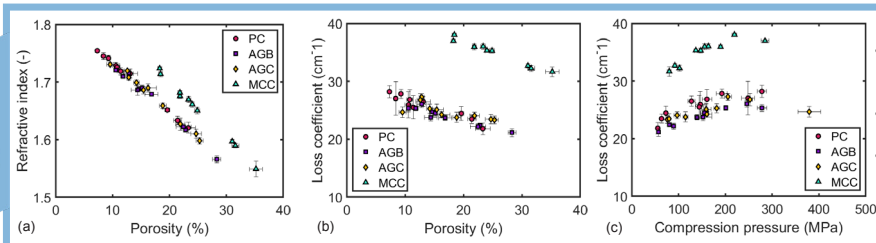


Figure 3. (a) Ryshkewitch-Duckworth compactability analysis. (b) Gurnham compressibility analysis. k_b: bonding capacity; T = tensile strength at 0% porosity; K: resistance to compression; P_0: pressure to reach 0% porosity.

THz Analysis

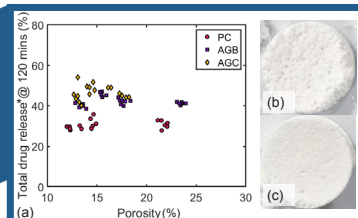




- Clear trend for all batches in Fig. 4 (a), indicative of content uniformity
- Variation in PC > AGB/AGC indicative of inhomogeneity
- Similar trends indicate that AGB/AGC SA particles collapse to size of PC at all compression loads tested.

Figure 4. (a) Refractive index of all tablets tested, Loss coefficient as a function of (b) porosity and (c) compaction pressure.

Dissolution



- Dissolution rate: AGC > AGB > PC
- Observed additional action on tablet surface due to SA
- SA dissolve, increasing exposed surface area leading to improved dissolution
- *Note: No disintegrant was used in formulation*

*Figure 5. (a) Dissolution performance of each blend * of label claim (70 mg), (b) Image of AGC tablet surface, (c) Image of PC tablet surface.*

Conclusions & Next Steps

- SA BA is suitable for direct compression.
- MCC tablets possess the highest porosity and tensile strength at each given pressure.
- PC tablets show highest compressibility at each given pressure.
- THz-TDS findings indicate uniform content and homogenous blending for MCC/AGB/AGC, but not PC
- Dissolution performance is increased with use of SA API
- *In-situ* THz-TDS study