

Comparison of Granules Obtained from Roller Compaction of BCS Class IV Drug with a Soluble and Insoluble Carrier



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Introduction

Roller compaction (RC) is a dry granulation process used to mass fine powders into larger, denser granules, without the use of liquids.

The process typically places powder in a hopper, and this powder is fed between two rollers, which have pressure applied to them, in order to press the powder into a ribbon. Subsequently, the ribbon is milled into particles having a larger particle size distribution (PSD) than the starting raw material powders. The reasons for using RC to augment PSD are varied, but include improvement of bulk powder flow for tableting operations, uniform dispersion of an active pharmaceutical ingredient (API) throughout a granulation, and improving the solubility of a poorly water soluble API by associating it closely with a water soluble carrier material. Mannogem® 2080 is a granulated mannitol (Fig 1) with a surface area of 3800 cm²/g and a mesopore diameter of around 10.7 µm. Mannogem 2080 is a direct compression material that is rapidly water soluble. Microcrystalline cellulose (MCC) is a fibrous material which is an insoluble carrier (Fig 2).

Figure 1: SEM Mannogem EZ (1000x)

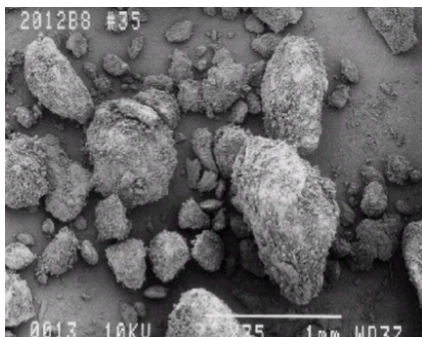
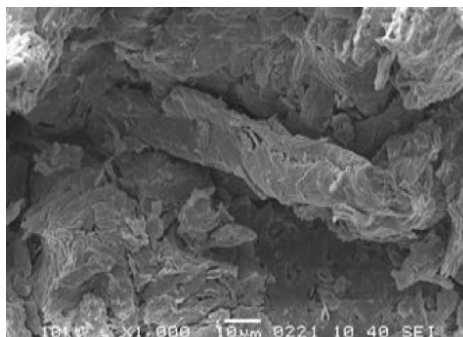


Figure 2: SEM of MCC (1000X)



Method

150 g blends, containing 10% micronized furosemide [D(4.3)=5.926 µm] and either Mannogem 2080 or MCC, were mixed in a 5-quart V-blender at 25 rpm for 15 minutes, followed by lubrication blending for 5 minutes at 25 rpm. Subsequently, the blends were roller compacted using a Clit Mini Roll Compactor (Model: CPMMRC), employing both two tons and five tons of roll pressure at 5 rpm roller speed. The resulting ribbons were milled using a Karnavati oscillating mill (Model: HD- 410 AC) outfitted with a 1 mm screen. 800 mg aliquots (equivalent to 80 mg of micronized Furosemide) of each of the respective granulations were analyzed for blend uniformity and drug release.

Objective

To compare blend uniformity and drug release of a BCS class-IV poorly water soluble drug, furosemide, from granulations manufactured by RC, employing either a soluble carrier (Mannogem 2080, granulated mannitol) or an insoluble carrier (MCC).

Materials

Mannogem 2080 and Lubripharm® are products of SPI Pharma and MCC was obtained from a US source.

Results

Blend uniformity and dissolution (media- 900 ml of pH 5.8 phosphate buffer, Apparatus 2- 50 rpm, samples at 5, 10, 20 & 30 minutes) results were as follows:

Table 1: Granulation Blend Uniformity

Sample	Mannogem 2080-2 Ton	Mannogem 2080-5 Ton	MCC-2 Ton	MCC-5 Ton
1	98.1	98.2	102.7	98.0
2	97.8	100.1	101.9	97.3
3	96.9	97.4	103.3	96.6
4	97.5	95.1	102.6	97.8
5	97.7	98.5	101.6	96.1
6	98.1	96.4	102.5	97.2
7	97.7	97.8	103.0	97.7
8	97.6	96.9	98.3	97.2
9	96.4	97.3	103.5	97.4
10	97.5	97.0	102.5	96.6
Mean	97.5	97.5	102.2	97.2
Min	96.4	95.1	98.3	96.1
Max	98.1	100.1	103.5	98.0
% RSD	0.53	1.36	1.37	0.61

Fig 3: Comparison of furosemide release from granules obtained using 2 ton roll pressure

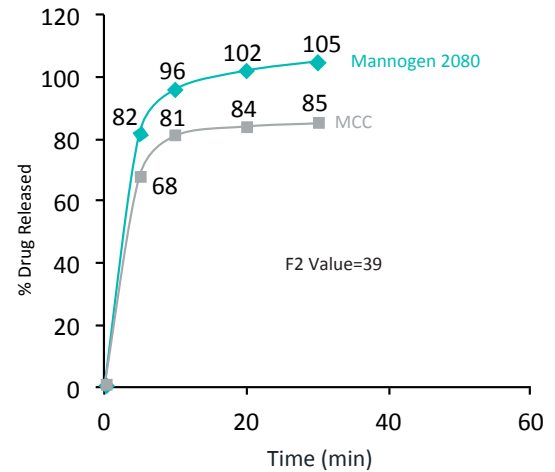
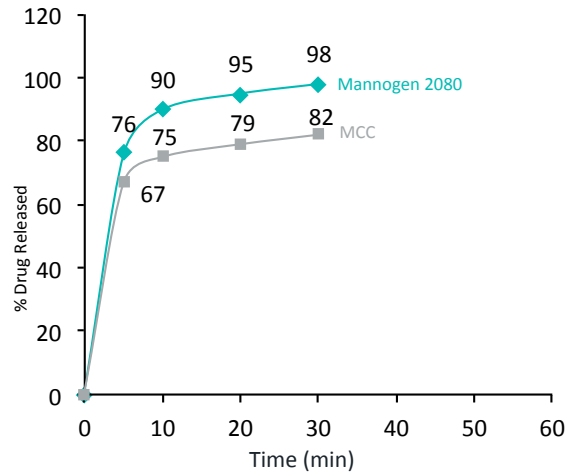


Fig 4: Comparison of furosemide release from granules obtained using 5 ton roll



Conclusion

Both granulations manufactured with Mannogem 2080 and MCC exhibit consistent blend uniformity. The release of furosemide from the Mannogem 2080 granulation was significantly faster than the release of furosemide from the MCC granulation as determined by f2 analysis ($f_2 < 50$). Additionally, at the 30 minute time point, the release from the Mannogem 2080 granulation was complete, whereas release from the MCC granulation for the 2ton compaction and the 5ton compaction were 85% and 82%, respectively. These results demonstrate the advantage of using Mannogem 2080, a water soluble carrier, in the roller compaction of a poorly water soluble API.

References

- 1) United States Pharmacopeia 34. <905> Uniformity of dosage units Pharmacopeial Forum, 35 (3) (2011), p. 724

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