SYLOID® XDP Silica
Pharmaceutical Excipient

Application Note

Moisture Activated Dry Granulation (*MADG*) with Syloid® XDP Silica

Introduction

Moisture activated dry granulation (MADG) has been presented to pharmaceutical formulators as an innovative way to modify wet granulation. It provides a way to address common problems such as endpoint detection, drying and milling [1]. This technique offers an efficient, cost-effective granulating process utilizing a limited amount of water and does not require a drying step [2]. Because this process depends on the addition of a moisture absorber to facilitate even moisture distribution and drying of the granulated powder, careful selection of excipients is critical for the effective utilization of this technique [3]. Syloid® XDP mesoporous silica excipient is an effective moisture absorber for this technique. The high surface area and pore volume coupled with an active silica surface makes Syloid® XDP silica a highly efficient adsorbent for moisture, effectively "locking" it away in its pores to create a stable, dry powder. In addition, the large particle size of Syloid® XDP silica helps promote a blend with improved flow characteristics for easier processing.

MADG Formulation

A MADG formulation was developed by using Paracetamol as the API of interest with the final dose content of 200mg per tablet. Initially API, fillers and dry binder were added into a rapid mixer-granulator followed by the addition of 5% water spray onto the dry mixture, allowing the process to form granules by activation of dry binder upon contact with the water spray. After 3-5 minutes of granulation, Syloid® XDP silica is added to distribute the moisture evenly and dry the granulated powder. Once the granulated powder is dry then the remaining excipients, such as disintegrant, glidant and lubricant are added. The final lubricated blend was subjected for compression study to evaluate the in-process quality control parameters. For the comparison purpose the same composition was used for direct compression without any addition of water.

Formula

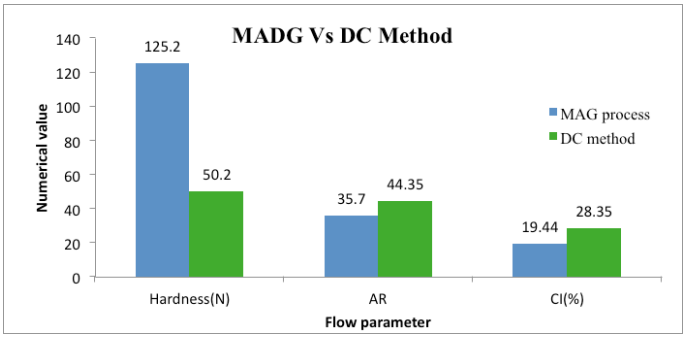
Ingredients	Description	Composition % W/W
Paracetamol	API	40
Di-CalciumPhosphate (anhydrous)	Filler	12.5
Poly Vinyl Pyrrolidone K-30	Dry Binder	5
Micro crystalline cellulose 102	Filler	33.5
Syloid® XDP3050 silica	Adsorbent	2.5
Ac-Di-Sol	Disintegrant	5
Syloid® 244FP silica	Glidant	1
Magnesium Stearate	Lubricant	0.5

Flow Parameters

Flow Parameters	MADG	Direct Compression
Angle of Repose°	35.7	44.35
Bulk Density (g/mL)	0.417	0.448
Tapped Density (g/mL)	0.517	0.625
Compressibility Index (%)	19.44	28.35
Hausners Ratio	1.241	1.396

Tabletting Parameters

Tabletting Parameters	MADG	Direct Compression
Average Weight (mg)	501.3	501.7
Hardness (N)	125.2	50.2
Thickness (mm)	4.68	5.13
Disintegration (min)	0.50	0.50
Friability (%)	0.27	0.35



Conclusion

- MADG process is advantageous over conventional wet granulation in terms of reduced process time.
- Syloid® XDP silica acts as an effective adsorbent which eliminates the drying step.
- Syloid® XDP silica helps to distribute drug uniformly in the formulation and generates uniform sized granules.
- Tablet blend can be generated in single piece equipment (rapid mixter granulator).
- Flow characteristics of the powder blend is improved vs direct blending.
- Tablet hardness is improved vs direct compression.
- Useful for moisture sensitive drugs where wet granulation is not possible.

References

1 Ullah et al., Pharmaceutical Technology, Vol.II, 48-54, 1987
2 Ullah et al., Pharmaceutical Technology, PharmTec, March 7, 2011
3 Ullah et al., Pharmaceutical Technology, November 2009

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