

Investigation on a cost effective, non-sticking direct compression method for Ibuprofen

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Introduction

Development of Ibuprofen (IBU) tablets suffers from several drawbacks, e.g. cost pressure, sticking tendency, bad compression properties and the high dosages needed. To overcome those drawbacks a methodical approach to evaluate the impact of drug quality, tablet composition, processing parameters and punch quality on the compressibility of Ibuprofen formulations was initiated. Experiments were performed on laboratory scale and verified on pilot scale.

Materials and Methods

Different types of IBU were purchased from Sanaq Pharmatrans (D), Hubei Biocause, Shandong (both CN), Shasun or Dr. Reddy's Albemarle (both IND). One Shasun type was a granulate with 90% IBU content, the Sanaq type was a granulate with 100% IBU content. Different punch types were purchased from Notter, Schwarz (both D) and Senss (CH). All excipients were standard pharmaceutical grade purchased by Temmler Werke Muenchen. Reference tablets consisted of Microcrystalline Cellulose (MCC), Corn Starch, Carboxymethylcellulose Sodium XL, Colloidal Silicon Dioxide (CSD; 200m²/g), Stearic Acid, Magnesium Stearate and 400mg granulated Ibuprofen. Equipment and methods employed are summarized in Table 1.

Purpose	Equipment
Light Microscopy	VHX-600 (Keyence, D)
SEM / EDX	JSM-6500F (Jeol, Jp; detectors by Oxford Instruments, UK)
Surface tension	Testing inks (Arcotest; Plasmatrete, both D)
Sieve analysis	Vibration sieve analyser (Retsch AS-200, D; 10g, 1.5mm amplitude, 3min)
Compression	FS 8 rotary press (Ronci, I); XL 400 rotary press (Korsch, D)
Coating	BTC 400 (Bohle, D)
Dissolution (DISS)	Basket in phosphate buffer pH 7.2 at 150rpm; N=3
Hardness and mass of tablets	WHT (PharmaTest, D); Multicheck (Erweka, D); N=10

Table 1: Equipment and methods employed.

Results and Discussion

IBU qualities differed greatly in particle shape and size distribution, as well as in compressibility and sticking tendency during tableting (Table 2). Usage of coarsely graded types could reduce sticking but led to lowered breaking strength. Finely graded types did not allow to produce adequate tablets by direct compression. Sticking tendency decreased markedly with increasing compaction force and increasing content of CSD. CSD coated the IBU particles as evaluated by SEM/EDX (Figure 1) [1]. Coarsely graded IBU is more easily coated than finely graded types due to lower specific surface area.

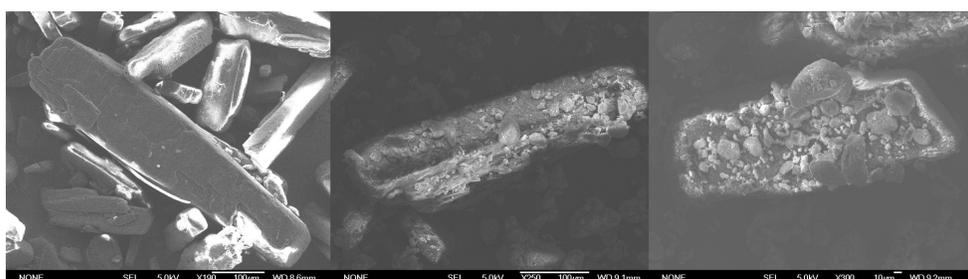


Figure 1: SEM images of IBU blended with (from left to right) increasing amounts of CSD form 0% up to 4.33w%.

Type	Fine	Coarse	Granulated
Particles <180/ <355µm [w%]	88/100	1 /31	51/74
Hardness [N] (Srel %)	84.0 (8.7)	77.7 (5.7)	131.3 (8.4)
DISS [w% after 10/ 20/ 30min]	no data	86/ 99/ 100	90/ 99/ 100
Capping tendency	High	None	Very low
Sticking tendency	High	Low	Medium

Table 2: Exemplary data of three different Ibuprofen qualities.

The CSD effect could also be seen on a 360kg scale using common punches and coarsely graded Ibuprofen. The resulting breaking strengths were sufficient for tablet coating without tablet breakage. No other excipients or production parameters evaluated showed markedly positive impact on sticking tendency (Figure 2).

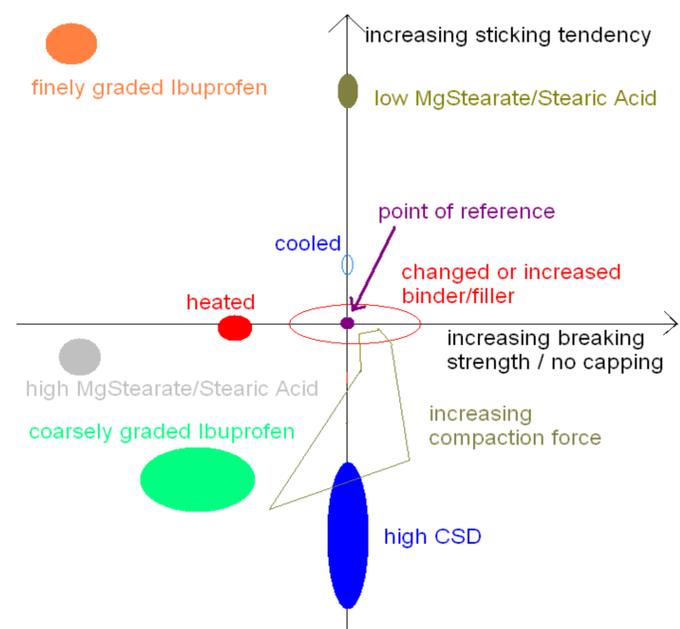


Figure 2: Schematic plot of the obtained results.

The tested punches showed differences in surface structure (Figure 3), surface tension, durability and sticking tendency. Impact of surface structure on sticking tendency of IBU formulations as reported in [2] could not be evaluated. Also ejection force measurements showed no significant correlation with sticking tendency.

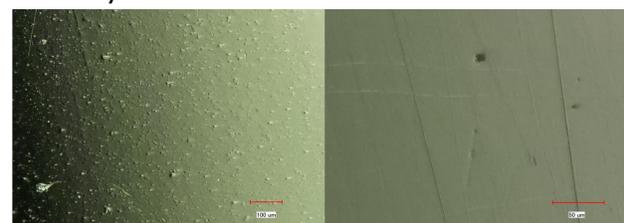


Figure 3: Exemplary pictures of two punch types with different surface structure.

Conclusion

Several qualities of IBU with different particle size distributions are available. Sticking tendency of IBU formulations is greatly influenced by compaction force, Colloidal Silicon Dioxide content and the API's particle size. Other formulation parameters showed only little impact. A method of direct Ibuprofen compression with reduced sticking tendency was successfully established on pilot scale. Punch characterisation revealed differences in surface structure, surface tension, durability and sticking tendency.

References

- [1] K. Meyer, I. Zimmermann; Powder Technol; 139 (2004), 40-54
- [2] M. Roberts et al.; J Pharm Pharmacol; 55 (2003), 1223-1228