

# Development of a Model for Roller Compaction Formulations Based on Tableability Performance - Part IV: Ibuprofen Blends

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## ABSTRACT

**Purpose:** To evaluate the effect of increasing ibuprofen content on the tableability performance of roller compacted Avicel PH200™ and Prosolv HD90™ blends as a part of a larger study towards development of a model for roller compaction formulations.

**Methods:** Ibuprofen was blended with either Avicel PH200™ or Prosolv HD90™ in different proportions and the blends were roller compacted and milled. Pre-roller compacted blends and post-roller compacted and milled granules were compressed on a single station carver press. Tablets were made at compression forces ranging from 0.2 to 2.6 metric tons. Physical properties such as blend bulk and tap densities, tablet thickness and breaking force were measured. Carr's indices and tensile strengths were calculated. The effect of increasing the ibuprofen content on the compressibility, compactibility and tableability of the formulations was investigated.

**Results:** In the case of Avicel PH200™ ibuprofen blends, Carr's indices increased on addition of ibuprofen in the pre-roller compacted blends, indicating a reduction in flowability. This effect was not observed in the post-roller compacted granules. For Prosolv HD90™ ibuprofen blends, no major change in flowability was observed before or after roller compaction. Compressibility of the formulations decreased with an increase in ibuprofen content across all blends prior to and after roller compaction. Compactibilities did not show a major change on addition of ibuprofen in the pre-roller compacted blend, but increased slightly with ibuprofen content in the post-roller compacted granules. Tableability reduced with increasing ibuprofen content for all blends. In the post-roller compacted material, the increase in tableability on addition of ibuprofen was less prominent as compared to pre-roller compacted blends.

**Conclusions:** The tableability performance decreased with an increase in ibuprofen content of the blend. In the pre-roller compacted blends, compressibility is the dominant factor that determines tableability. In the post-roller compacted material, the strong influence of compressibility is mitigated by the reverse trend observed in compactibility.

## OBJECTIVES

To build a model for roller compaction formulations based on tableability performance. The overall aim of the project is to investigate the suitability of the roller compaction process for different excipients and API blends. Part IV of this project involves the use of ibuprofen/excipient blends for evaluation of tableability performance for pre-roller compaction blends and post-roller compaction granulation.

## BACKGROUND

For the purposes of Part IV of this project, various formulations of ibuprofen with Avicel PH200™ or Prosolv HD90™ was studied. The same response variables were studied as in Part I of the project, such as Tableability, Compressibility, and Compactibility.

Tableability of a blend is a measure of the blend's ability to make a strong and compact tablet on application of mechanical pressure. The final tableability of a blend depends on the compressibility and the compactibility of the blend. Compressibility is the ability to undergo reduction in volume as a result of applied pressure. It is represented by a plot of Solid Fraction vs Compression Force. Compactibility is the ability of material to produce tablets of sufficient strength under densification and is represented by a plot of Tablet Tensile Strength vs Solid Fraction. Finally, Tableability can be described as the capacity of a powder to be transformed into a tablet of appreciable strength under effect of compaction pressure, and is represented by a plot of Tablet Tensile Strength vs Compression Force.

## METHODOLOGY

Ibuprofen was blended in different proportions with Avicel PH200™ and with Prosolv HD90™. These blends were roller compacted using a Chilsonator IR220 (The Fitzpatrick Co. Elmhurst, IL), and milled using a Fitzmill model M5A (The Fitzpatrick Co. Elmhurst, IL). The bulk and tap densities of the resulting final blends and roller compacted granulations were measured. The Carr's index was calculated to provide an indication of the flow. The composition of the blends is listed in Table 1.

The final blends (pre-roller compaction) and the roller compacted milled granulations were then compressed on the Carver press at 7 different compression forces ranging from 0.2 to 2.6 metric tons. Tablet thickness and breaking force were measured, and tensile strengths of the tablets were calculated for both the pre-roller compaction and post-roller compaction samples. Effect of roller compaction and Ibuprofen drug loading was evaluated in Avicel PH200™ and Prosolv HD90™ blends using plots of Compressibility, Compactibility and Tableability.

## RESULTS AND DISCUSSION

Carr's indices of the blends (pre-roller compacted) and the milled granulations are listed in Tables 1 and 2. In the case of the Avicel PH200™ blends, the flowability of milled granulations was marginally better than pre-roller compacted blends. A similar trend is not obvious for the Prosolv HD90™ blends. Also in the case of both pre-roller compacted blends, the flow appears to be better at lower drug loading compared to higher drug loading and this is more apparent in the case of the Avicel PH200™ blends.

Table 1—Carr's Indices of Final Blends (Pre-Roller Compaction)

Ibuprofen (%)	Avicel PH200™ (%)	Carr's Index
10	90	24
40	60	30
75	25	40
Ibuprofen (%)	Prosoolv HD90™ (%)	Carr's Index
10	90	28
40	60	30
75	25	36

Table 2—Carr's Indices of Milled blends (Post-Roller Compaction)

Ibuprofen (%)	Avicel PH200™ (%)	Carr's Index
10	90	27
40	60	27
75	25	25
Ibuprofen (%)	Prosoolv HD90™ (%)	Carr's Index
10	90	30
40	60	34
75	25	29

The compressibility of the all blends shows that at low compression forces the compressibility is similar across the drug loadings (Figures 1 – 4). As the compression force is increased, the trend emerges that the higher the drug loading the lower the compressibility. This feature can also be observed for the post roller compacted granulations. Compressibility does not appear to decrease upon roller compaction.

Figure 1—Compressibility Profile of Ibuprofen/Avicel PH200™ Pre-Roller Compacted blends

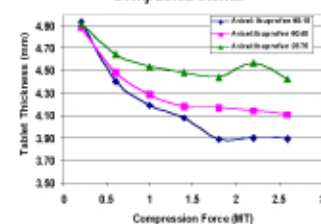


Figure 2—Compressibility Profile of Ibuprofen/Prosoolv HD90™ Pre-Roller Compacted blends

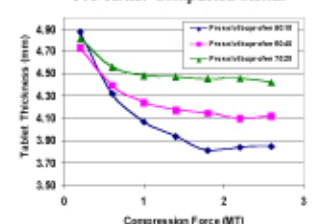


Figure 3—Compressibility Profile of Ibuprofen/Avicel PH200™ Post-Roller Compacted blends

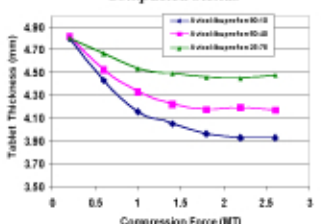
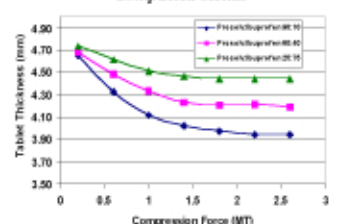


Figure 4—Compressibility Profile of Ibuprofen/Prosoolv HD90™ Post-Roller Compacted blends



It appears that drug loading does not have an effect on compactibility of the pre-roller compacted blends. At the post-roller compaction stage, the compactibility of the blends slightly increased with increasing drug loading for the Avicel PH200™ and Prosolv HD90™ blends (Figures 5 – 8).

Figure 5—Compactibility Profile of Ibuprofen/Avicel PH200™ Pre-Roller Compacted blends

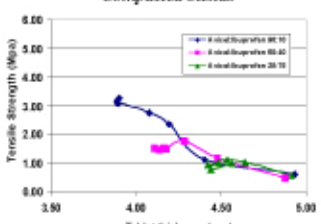


Figure 6—Compactibility Profile of Ibuprofen/Prosoolv HD90™ Pre-Roller Compacted blends

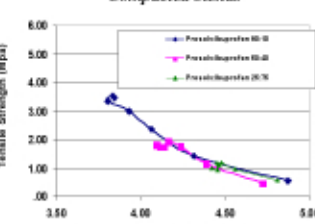


Figure 7—Compactibility Profile of Ibuprofen/Avicel PH200™ Post-Roller Compacted blends

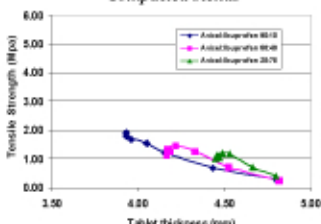
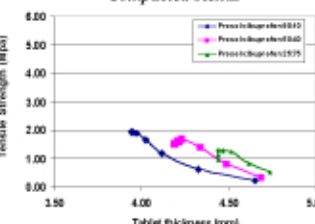


Figure 8—Compactibility Profile of Ibuprofen/Prosoolv HD90™ Post-Roller Compacted blends



The tableability of the blends decreases with increasing drug loading for all blends (Figures 9 – 12). Tableability was found to decrease upon roller compaction. Within the post-roller compacted blends there is a slight trend indicating a decrease in tableability with an increase in drug loading, although this is not as prominent as in the case of the pre-roller compacted blends.

Figure 9—Tableability Profile of Aspirin/Avicel PH200™ Pre-Roller Compacted blends

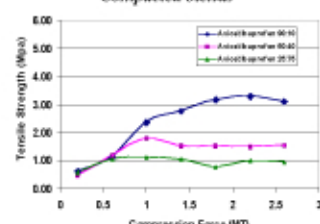


Figure 10—Tableability Profile of Aspirin/Prosoolv HD90™ Pre-Roller Compacted blends

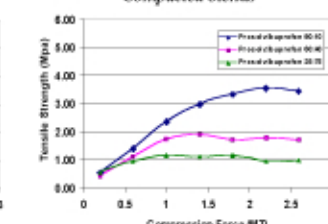


Figure 11—Tableability Profile of Ibuprofen/Avicel PH200™ Post-Roller Compacted blends

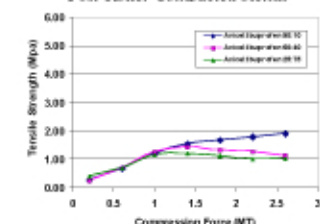
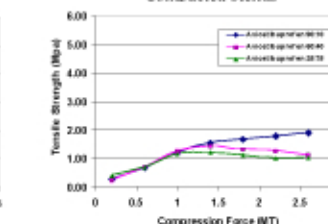


Figure 12—Tableability Profile of Ibuprofen/Prosoolv HD90™ Post-Roller Compacted blends



## CONCLUSIONS

The blends showed a gradual reduction in compressibility with an increase in Ibuprofen drug loading. The tableability is a function of the compressibility and compactibility  $\{T = f(\text{compressibility}, \text{compactibility})\}$ . It appears, from the results that the compressibility is the dominant factor in determining tableability in the case of the Ibuprofen pre- and post-roller compacted blends. Compactibility appears to not be a factor in the case of pre-roller compacted blends, although it gains more dominance after roller compaction.

## ACKNOWLEDGEMENTS

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