EFFECT OF BULK DENSITY ON TENSILE STRENGTH OF TABLETS PREPARED BY USING HICEL™MCC (MICROCRYSTALLINE CELLULOSE) AND HICEL™SMCC (SILICIFIED MICROCRYSTALLINE CELLULOSE)

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ABSTRACT

Direct compression is a Preferred method for manufacturing solid dosages forms. Functionality Related Characteristics (FRCs), (bulk density, particles size, moisture content, Carr’s index and angle of repose) of Excipients have become increasingly critical in the manufacture of tablets by Direct Compression. Out of this, bulk density plays a vital role in direct compaction method. It affects the tensile strength of tablets. Tensile strength of tablet also depends on wood pulp sources, it varies from pulp-to-pulp. In this research work, we have used HiCel™MCC 90M (Microcrystalline Cellulose) and HiCel™SMCC 90M (Silicified Microcrystalline Cellulose) grade containing dissolving wood pulp. HiCel™SMCC is a co-processed excipient having superior flowability and 25-30% better compaction than HiCel™MCC. It gives very good tablet profile in terms of tensile strength, friability, disintegration time and dissolution time. The main objective of this study is to find the correlation between bulk density of HiCel™MCC and HiCel™SMCC and tensile strength and secondly the correlation between tensile strength and friability of the tablets.

In this study, tablets were made using different bulk density samples of HiCel™MCC 90M and HiCel™SMCC 90M grade without adding pharmaceutical active ingredient, followed by evaluation of tablet properties.

Keywords: Excipients, HiCel™MCC 90M(Microcrystalline Cellulose), HiCel™SMCC 90M(Silicified Microcrystalline Cellulose), Bulk density, Tensile strength and Friability.
INTRODUCTION

Microcrystalline cellulose is the most widely used excipient in the manufacture of Solid oral dosage forms. It is an isolate from wood pulp. Hydrolysis reaction is carried out in the presence of mineral acids and water at required temperature and pressure. In wood pulp, cellulose chains are packed in layers held together by a cross-linkage polymer and strong hydrogen bond. Cellulose consists of linear chain of β-14-D anhydroglucopyranosyl units. In the hydrolysis reaction, high degree polymers convert into low degree polymers. HiCelTMMCC is a perfect excipient for direct compression formulations. It is non-reactive, free-flowing and versatile pharmaceutical excipient. It has strong binding property to bind the pharmaceutical active ingredient, widely used as a filler and has inherent super disintegrant properties. However, its flow is cohesive in nature and this may sometimes cause flow problems with some APIs. Sigachi Industries (EXCIPACT CERTIFIED) recommends co-processed excipient, HiCelTMSMCC (Silicified Microcrystalline Cellulose) to eliminate this problem and for improved tablet manufacturing process and final product tablet. HiCelTMSMCC 90M has very good compaction and compressibility.

Co-processed excipients are manufactured by using co-process technology. Many Methods of Co processing exist, of which Spray Drying is quite Popular. Co-processing is also the most extensively explored method to prepare directly compressible adjuvant. In co-process technology, two established pharmaceutical excipients in certain quantity are mixed and spray dried. The co-processed excipients have no change in their chemical structure, but result in change of the physical characteristics of final product. At present, many co-processed excipients are used in the pharmaceutical industry i.e. HiCelTMMCG and HiCelTSMCC. HiCelTMSilicified Microcrystalline Cellulose (HiCelTSMCC) is high functionality multifunctional co-processed excipient. It is a synergistic intimate physical mixture of two compounds, microcrystalline cellulose and silicon dioxide. It is an unique and novel tableting co-processed excipient which can enhance binding capacity and give desire tensile strength to the tablet formulation. It requires no complex processing, making it the most preferred Co processed excipient for direct compression process.

Functionality Related Characteristics (moisture content, particle size, bulk density) of both product HiCelTMMCC and HiCelTSMCC have a direct impact on the tablet compaction and other tableting parameters. Tablets require certain amount of strength to withstand mechanical shocks of handling during packing and shipping. Thus tablets should possess optimum strength. In this study, we are examining the correlation between bulk density and
tensile strength of tablets and correlation between tensile strength and friability using HiCel™MCC 90M and HiCel™SMCC 90M.

EXPERIMENTAL SECTION

HiCel™Microcrystalline Cellulose 90M and HiCel™Silicified Microcrystalline Cellulose 90M powders of different bulk densities were manufactured at Sigachi Industries Pvt. Ltd. Dahej, Gujarat. Digital weighing balance (Mettler Toledo, Model No. ML802/A01) was used for weighing the samples. Hot air oven (Model no. PNX-14) was used for testing the moisture content of sample. Proton mini press (10 Station) “D” type tooling machine was used for manufacturing the tablets. Digital tablet hardness tester (LABINDIA Model No. TH1050M) was used for testing the tablet tensile strength. Friability tester (LABINDIA Model No. FT1020) was used for analyzing the percentage friability. Disintegration tester (LABINDIA Model No. DT1000) was used for analyzing tablet disintegration time.

Manufacturing Process of HiCel™MCC

Dissolving grade wood pulp was cut into small pieces, charged in a glass line reactor with mineral acid and water, hydrolyzed V/V acid concentration at specific temperature, pressure, and time. After hydrolysis, wood pulp breaks down into slurry. Thereafter, it is washed and filtered with ammonia with the help of filter press for getting the conductivity below 75 µS/cm, pH is neutral. Then a slurry is prepared by addition of water in wet cake of MCC and dried with the help of spray dryer and process flow chart mentioned in fig.1.

Fig1. Manufacturing process of HiCel™MCC

Manufacturing Process of HiCel™SMCC
Colloidal silicon dioxide 2% and wet microcrystalline cellulose 98% was taken on dried basis. This was followed by Slurry preparation and final drying with a Spray Drier.

![Manufacturing process of HiCel™SMCC](image)

**SEM Analysis of HiCel™MCC and HiCel™SMCC**

Morphology study of HiCel™MCC was carried out at CSMCRI Bhavnagar, Gujarat and HiCel™SMCC Particle Morphology study was carried out at AMITY University Noida using a scanning electron microscope.

**Untapped Bulk Density**

Weigh accurately 20g sample by using electronic digital balance (MettlerToledo, Model No-ML802/A01) and poured slowly from side wall into 100 ml capacity “Class A” graduated measuring glass cylinder. Level the surface of sample in cylinder by slow movement and observed the occupied volume. Calculate the untapped bulk density by using equation 1.

\[
Bulk \ Density = \frac{Weight \ of \ powder \ (gm)}{Occupied \ volume \ (ml)} \quad (1)
\]

**Tapped Density**

Tapped density was analyzed by using tapped density machine. (Electro lab instrument, Model No. ETD1020) Measuring cylinder was placed in tapped density machine and insert required taps. After that measure the volume of measuring cylinder and calculate the tapped density by using equation 2.

\[
Tapped \ Density = \frac{Weight \ of \ powder \ (gm)}{Occupied \ volume \ (ml)} \quad (2)
\]

**Hausner’s Ratio**

The flow of powder was measured by “Hausner Ratio”. H.Ratio is calculated by using equation 3.

\[
Hausner’s \ Ratio = \frac{Tapped \ density}{Untapped \ bulk \ density} \quad (3)
\]
Carr’s Index

It measures the tendency of powder to be compressed and the flow ability of powder. Carr’s index is calculated by using equation 4.

\[
\text{Carr’s Index} = \frac{Tapped \ density - Untapped \ Bulk \ density}{Tapped \ bulk \ density} \times 100 \ (4)
\]

Moisture content

Heat the shallow bottle in a hot air oven (Model no. PNX-14) at 105°C for 30 minutes. Cooled it in desiccator for 15 minutes. Weigh the shallow bottle by using electronic digital balance (Mettler Toledo, Model No-ML802/A01) and take about 1 g of HiCel\textsuperscript{TM}MCC in shallow bottle, set oven at 105°C and kept for 3 hours. Take out the shallow bottle after 3 hours and allow to cool in desiccator for 15 minutes\textsuperscript{10}. Take tare weigh again and calculate moisture content by using the equation 5.

\[
\text{Moisture Content} (\%) = \frac{ \text{Final weight} - (\text{Weight of bottle} + \text{sample}) }{\text{Weight of sample (gm)}} \times 100 \ (5)
\]

Tablet Compression

500 mg tablets were manufactured by using 10 station Proton Mini Press (Model no. MINI PRESS 10 “D”) using D tooling dies and punches. Tablet punching machine was operated between 10 to 60 KN pressure.

Evaluation of HiCel\textsuperscript{TM}MCC and HiCel\textsuperscript{TM}SMCC Tablets

Weight Variation of Tablet\textsuperscript{16}

Randomly 10 tablets were taken from each batch. Each tablet was weighed individually by using electronic digital balance (Mettler Toledo, Model No. ML802/A01). The average weight of all tablets was calculated by using equation 6.

\[
\text{Average weight (mg)} = \frac{\text{Total tablet weight}}{\text{No.of tablet}} \ (6)
\]

As per pharmacopoeia limits ±5 % variation is allowed for 500 mg tablets.

Tensile Strength of Tablet\textsuperscript{16}
Randomly 10 tablets were taken from each batch. Electronic digital hardness test machine (Labindia tablet hardness tester, Model No.-TH1050 M) was used to analyze tensile strength of tablets. Single tablet was placed between two anvils, force was applied to the anvils, and the tensile strength that is required to just break the tablet was recorded. Finally the reading was noted in kp[kgf] unit.

**Friability of Tablet**

10 tablets were taken and weighed using an electronic digital balance which was considered as the initial weight. All the tablets were placed in the drum of friability tester (LABINDIA, Model No. FT1020) and allowed to rotate 100 times at 25 rpm. After 100 revolutions, 10 tablets were removed and re-weighed which was considered as the final weight. The percentage friability was calculated by equation 7. As per USP, the tablets should not loss more than 1% of their total weight\(^\text{16}\).

\[
\% \text{ Friability} = \left( \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \right) \times 100 \quad (7)
\]

**Disintegration of Tablet**

This test was carried out at 37±2°C in 800 ml Demineralized water. Six tablets were taken and one tablet was introduced in each of the tubes, disk was placed and basket was positioned in one litre beaker containing 37±2°C temperature of water. Tablet breaking time was recorded i.e. when the tablet broke down into smaller particles\(^\text{16}\).

**RESULT AND DISCUSSION**

**Powder Profile Evaluation of HiCel\textsuperscript{Tm}MCC and HiCel\textsuperscript{Tm}SMCC**

**SEM Analysis of HiCel\textsuperscript{Tm}MCC and HiCel\textsuperscript{Tm}SMCC**

We found particles of both products HiCel\textsuperscript{Tm}MCC and HiCel\textsuperscript{Tm}SMCC are free flowing and images are shown in Fig3 and Fig4 respectively.
Physical parameters of HiCel\textsuperscript{TM}MCC and HiCel\textsuperscript{TM}SMCC

Physical parameters of both samples (HiCel\textsuperscript{TM}MCC 90M and HiCel\textsuperscript{TM}SMCC 90M) are mentioned in Table1.

<table>
<thead>
<tr>
<th>Physical parameters of HiCel\textsuperscript{TM}MCC and HiCel\textsuperscript{TM}SMCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table1. Physical properties of HiCel\textsuperscript{TM}MCC and HiCel\textsuperscript{TM}SMCC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HiCel\textsuperscript{TM}MCC 90M</th>
<th>HiCel\textsuperscript{TM}SMCC 90M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture content (%)</td>
<td>Moisture content (%)</td>
</tr>
<tr>
<td>H.Ratio</td>
<td>H.Ratio</td>
</tr>
<tr>
<td>Carr’s Index</td>
<td>Carr’s Index</td>
</tr>
</tbody>
</table>
### General Appearance

All tablets of HiCel™MCC 90M and HiCel™SMCC 90M are white colored elongated in shape. All tablets of both grades are free from all physical defects.

### Weight Variation

Weight variation results of HiCel™MCC and HiCel™SMCC tablets were within pharmacopoeia limits ±5% of 500 mg. Individual weight and average weight of both grade tablets mentioned in the Table2 and 3.

**Table2. Weight uniformity of HiCel™MCC 90M tablets at different bulk density**

<table>
<thead>
<tr>
<th>Tablet No.</th>
<th>Weight Uniformity of HiCel™MCC 90M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.28</td>
</tr>
<tr>
<td>1.</td>
<td>500</td>
</tr>
<tr>
<td>2.</td>
<td>500</td>
</tr>
<tr>
<td>3.</td>
<td>503</td>
</tr>
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<td>4.</td>
<td>502</td>
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<tr>
<td>5.</td>
<td>500</td>
</tr>
<tr>
<td>6.</td>
<td>502</td>
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<tr>
<td>7.</td>
<td>503</td>
</tr>
<tr>
<td>8.</td>
<td>503</td>
</tr>
<tr>
<td>9.</td>
<td>500</td>
</tr>
<tr>
<td>10.</td>
<td>500</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>501.5</strong></td>
</tr>
</tbody>
</table>
Table 3. Weight uniformity of HiCel™SMCC 90M tablets at different bulk density

<table>
<thead>
<tr>
<th>Tablet No.</th>
<th>Weight Uniformity of HiCel™SMCC 90M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.28</td>
</tr>
<tr>
<td>1.</td>
<td>502</td>
</tr>
<tr>
<td>2.</td>
<td>500</td>
</tr>
<tr>
<td>3.</td>
<td>503</td>
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<tr>
<td>4.</td>
<td>503</td>
</tr>
<tr>
<td>5.</td>
<td>502</td>
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<tr>
<td>6.</td>
<td>500</td>
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<tr>
<td>7.</td>
<td>500</td>
</tr>
<tr>
<td>8.</td>
<td>501</td>
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<tr>
<td>9.</td>
<td>503</td>
</tr>
<tr>
<td>10.</td>
<td>503</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>501.7</strong></td>
</tr>
</tbody>
</table>

Tensile Strength

Average tablet tensile strength of both samples mentioned in Table 4 and Fig 5.

Fig 5. Average tensile strength of HiCel™MCC 90M and HiCel™SMCC 90M tablets at different bulk density

Friability of tablet
According to USP, the tablets should not lose more than 1% of their total weight. All tablets have passed friability test under pharmacopoeia limit. Percentage friability of both grades mentioned in Table 4. Loss of weight is mentioned in Fig6.

![Fig6](image-url)  
**Fig6. Friability of HiCel™MCC90M and HiCel™SMCC 90M tablets at different bulk density**

**Disintegration Time**

Average Disintegration times of both grade tablets are mentioned in Table No-4 and Fig7.

![Fig7](image-url)  
**Fig7. Average disintegration time of HiCel™MCC 90M and HiCel™SMCC90M tablets at different bulk density**

**Table4. Average tensile strength, percentage friability and disintegration time of HiCel™MCC and HiCel™SMCC tablets at different bulk density**
<table>
<thead>
<tr>
<th>Bulk Density (g/cc)</th>
<th>HiCel™MCC 90M</th>
<th>HiCel™SMCC 90M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg. Tensile Strength [Kp(kgf)]</td>
<td>Friability (%)</td>
</tr>
<tr>
<td>0.28</td>
<td>12.45</td>
<td>0.14</td>
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<tr>
<td>0.30</td>
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<tr>
<td>0.32</td>
<td>10.68</td>
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<tr>
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<td>09.17</td>
<td>0.34</td>
</tr>
<tr>
<td>0.36</td>
<td>08.10</td>
<td>0.39</td>
</tr>
<tr>
<td>0.38</td>
<td>07.64</td>
<td>0.50</td>
</tr>
<tr>
<td>0.40</td>
<td>06.24</td>
<td>0.59</td>
</tr>
</tbody>
</table>

**Fig 8.** Tensile strength v/s friability of HiCel™MCC 90M

**Fig 9.** Tensile strength v/s friability of HiCel™SMCC 90M
ABBREVIATIONS


CONCLUSION

In this study, we have elucidated that the bulk density has a significant impact on tablet properties of tablets manufactured using HiCel™MCC 90M and HiCel™SMCC 90M. Firstly, correlation was found between bulk density and tensile strength. Both parameters are inversely proportional to each other, as there is an increase in bulk density of powder, the tensile strength of the tablet decreases.

Second correlation has been found between tensile strength and friability. Both parameters are inversely proportional to each other, as there is decrease in tensile strength of tablet, the percentage friability of tablet increases that have shown in fig 8 and fig 9. Thus, with an increase in bulk density of powder the percentage friability also increases. It may however be noted that the co-relation between the two is not linear, but non-linear.

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CONFLICTS OF INTERESTS

The authors state and confirm no conflict of interests. No direct funding was received for this study.

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