WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 10, 841-852. Research Article ISSN 2277– 7105

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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Article Received on
07 July 2017,

Revised on 28 July 2017,
Accepted on 17 Aug 2017

DOI: 10.20959/wjpr201710-9377

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ABSTRACT

Direct compression is an admired method for manufacturing the solid dosages form tablets. Now a days many excipients are used to manufacture the tablets. Physical parameters (bulk density, Particle size, moisture content, Carr's index and angle of repose) and degree of polymerization are very important to manufacture tablets by direct compression. Out of this bulk density plays a vital role in direct compression method. It affects 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. It is 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 second correlation between tensile strength and friability of their tablets. In this study, we will make tablets using different bulk density samples of HiCel™MCC 90M and HiCel™SMCC 90M grade and without adding pharmaceutical active ingredient, after that evaluate quality parameter of tablet.

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

INTRODUCTION

There are a list of pharmaceutical excipients available in the pharmaceuticals market. Microcrystalline cellulose (MCC) is one of them. Microcrystalline cellulose is native form of cellulose.[1] It is isolate from wood pulp by hydrolysis reaction. Hydrolysis reaction is done in the presence of mineral acids and water at required temperature and pressure.[2] In wood pulp, cellulose chains are packed in layers held together by a cross-linkage polymer and strong hydrogen bond.[3] Cellulose consists of liner chain of ß-14-D anhydroglucopyranosyl units.[4] In hydrolysis reaction, high degree of polymers convert into low degree of polymers.[5] HiCel^{TM}MCC is perfect excipient for direct compressible formulations. It is one of the most frequently used, to formulate solid dosage forms. It is non-reactive, free-flowing and versatile pharmaceutical excipient.[6] It has strong binding property to bind the pharmaceutical active ingredient, most extensively used filler and has inherent disintegrant properties.[7] However, its flow is cohesive in nature that's why sometimes it may cause flow problems with some API, Sigachi Industries recommends co-processed excipient HiCel^{TM}SMCC (Silicified Microcrystalline Cellulose) to eliminate this problem and for improved tablet manufacturing process and final product tablet.[8,9] HiCel^{TM}SMCC 90M has very good compaction and compressibility.

Co-processed excipients are manufactured by using co-process technology. Co-processing is also the most extensively explored method to prepare directly compressible adjuvant.[10] 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, just change the physical properties of final product.[9] At the present, lots of co-processed excipients are used in pharmaceutical industries i.e. HiCel^{TM}MCG and HiCel^{TM}SMCC. HiCel^{TM}Silicified Microcrystalline Cellulose (HiCel^{TM}SMCC) is high functionality multifunctional co-processed excipient.[9,10] It is a synergistic intimate physical mixture of two compounds, microcrystalline cellulose and silicon dioxide.[11] It is unique and novel tableting co-processed excipient which can enhance binding capacity and gives desire tensile strength in tablet formulation. It requires no complex processing, making it ultimate for direct compression process.[12]

Different physical parameters (moisture content, particle size, bulk density) of both product HiCel^{TM}MCC and HiCel^{TM}SMCC are directly affecting the tablet compaction and other tableting parameters too.[13] Tablets require certain amount of strength to withstand

mechanical shocks of handling during packing and shipping, thus tablets should possess optimum strength.[14] 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.

MATERIALS AND METHODS

Materials

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 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.

Methods

Manufacturing Process of HiCel™MCC

Dissolving grade wood pulp was cut into small pieces, charged in 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.[15] Then prepare slurry 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.

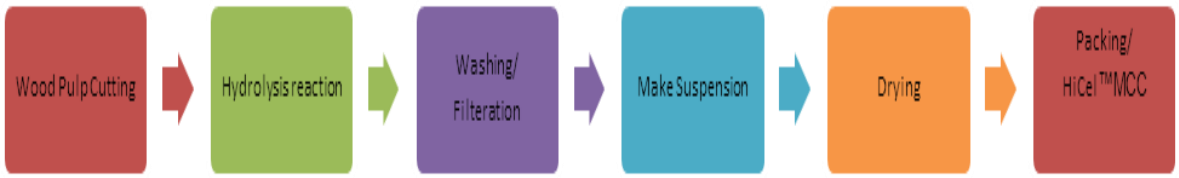

Fig1: Manufacturing process of HiCel™MCC.

Manufacturing Process of HiCel™SMCC

Take colloidal silicon dioxide 2% and wet microcrystalline cellulose 98% on dried bases. Make slurry of both combination and dry with spray dryer.[9]

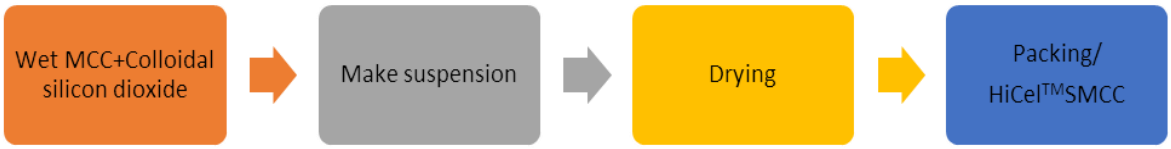

Fig2. Manufacturing process of HiCel™SMCC.

SEM Analysis of HiCel™MCC and HiCel™SMCC

Morphology of HiCel™MCC was carried out at CSMCRI Bhavnagar, Gujarat and HiCel™SMCC study was carried out at AMITY University Noida using with scanning electron microscope.[15]

Untapped Bulk Density[2]

Weigh accurately 20g sample by using electronic digital balance (Mettler Toledo, 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 equation1.

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

Tapped Density[2]

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

Flow of powder was measured by "Hausner Ratio". H.Ratio is calculated by using equation[2] 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[10] 4.

$$Carr's\ Index = \frac{Tapped\ density - Untapped\ Bulk\ density}{Tapped\ bulk\ density} \times 100 \quad (4)$$

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^{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.[10] Take tare weight again and calculate moisture content by using the equation 5.

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

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 pressures.

Evaluation of HiCel^{TM}MCC and HiCel^{TM}SMCC Tablets

Weight Variation of Tablet[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.

$$Average\ weight\ (mg) = \frac{Total\ tablet\ weight}{No.of\ tablet} \quad (6)$$

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

Tensile Strength of Tablet[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 just required to break the tablet was recorded. Finally the reading was noted in kp[kgf] unit.

Friability of Tablet

10 tablets were taken and weighed by using 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 lose more than 1% of their total weight.[16]

$$\% \, Friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100 \quad (7)$$

Disintegration of Tablet

This test was carried out at 37±2°C in 800 ml Demineralized water. Six tablets was taken and one tablet was introduced in each tubes, disk was placed and basket was positioned in one litre beaker containing 37±2°C temperature of water. Note down tablet breaking time. Noted the time when the tablet broke down into smaller particles.[16]

RESULT AND DISCUSSION

Powder Profile Evaluation of HiCel™MCC and HiCel™SMCC

SEM Analysis of HiCel™MCC and HiCel™SMCC

We found all particles of both products HiCel™MCC and HiCel™SMCC are free flowing and images are shown in Fig3 and Fig4 respectively.

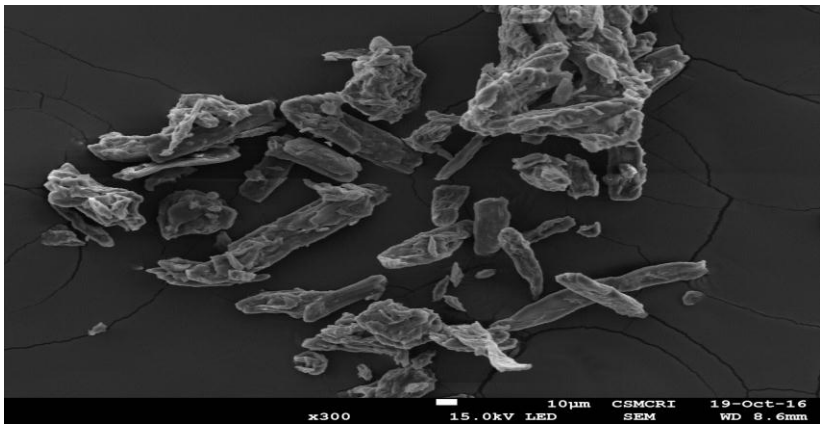

Fig3. SEM image of HiCel™MCC (Microcrystalline Cellulose).

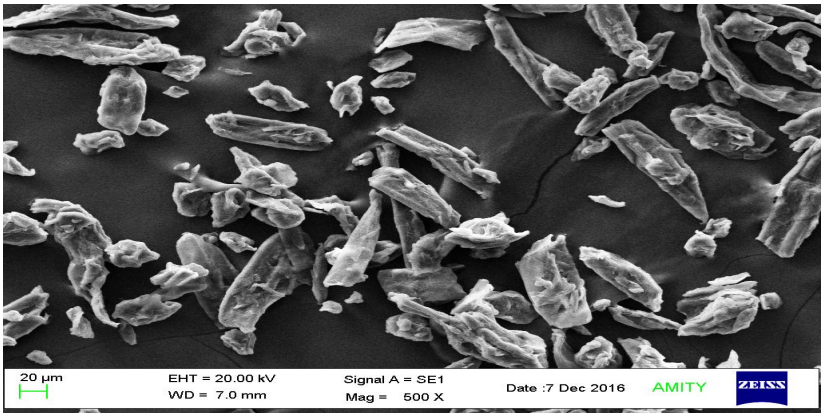

Fig4. SEM image of HiCel™SMCC (Silicified Microcrystalline Cellulose).

Physical parameter of HiCel™MCC and HiCel™SMCC

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

Table 1: Physical properties of HiCel™MCC and HiCel™SMCC.

Bulk Density (g/cc)	HiCel™MCC 90M			HiCel™SMCC 90M		
	Moisture content (%)	H.Ratio	Carr's Index (%)	Moisture content (%)	H.Ratio	Carr's Index (%)
0.28	4.52	1.41	28.21	4.62	1.30	22.22
0.30	4.56	1.42	30.23	4.64	1.31	23.08
0.32	4.53	1.43	30.43	4.61	1.32	23.81
0.34	4.55	1.44	32.00	4.63	1.33	24.44
0.36	4.54	1.45	30.77	4.62	1.34	25.00
0.38	4.54	1.46	30.91	4.62	1.36	26.92
0.40	4.56	1.48	32.20	4.64	1.38	27.27

General Appearance

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

Weight Variation

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

Table 2: Weight uniformity of HiCel™ MCC90M tablets at different bulk density.

Tablet No.	Weight Uniformity of HiCel™MCC 90M						
	0.28	0.30	0.32	0.34	0.36	0.38	0.40
1.	500	501	503	500	502	500	501
2.	500	501	502	500	500	503	503
3.	503	502	502	502	500	501	500
4.	502	503	503	501	503	502	503
5.	500	502	503	502	501	500	501
6.	502	502	500	502	503	500	502
7.	503	500	501	503	502	503	500
8.	503	502	500	500	500	503	502
9.	500	501	503	502	502	503	503
10.	500	503	501	500	500	500	503
Average	**501.5**	**501.7**	**501.8**	**501.2**	**501.3**	**501.5**	**501.8**

Table 3: Weight uniformity of HiCel™SMCC90M tablets at different bulk density.

Tablet No.	Weight Uniformity of HiCel™SMCC 90M						
	0.28	**0.30**	**0.32**	**0.34**	**0.36**	**0.38**	**0.40**
1.	502	501	500	501	500	501	500
2.	500	503	503	503	502	500	503
3.	503	500	501	500	500	503	500
4.	503	503	502	500	503	502	502
5.	502	502	500	502	500	503	500
6.	500	501	503	500	500	500	501
7.	500	503	503	503	503	502	501
8.	501	500	501	502	502	500	501
9.	503	503	503	502	503	502	500
10.	503	501	500	500	502	500	502
Average	**501.7**	**501.7**	**501.6**	**501.3**	**501.5**	**501.3**	**501.0**

Tensile Strength

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

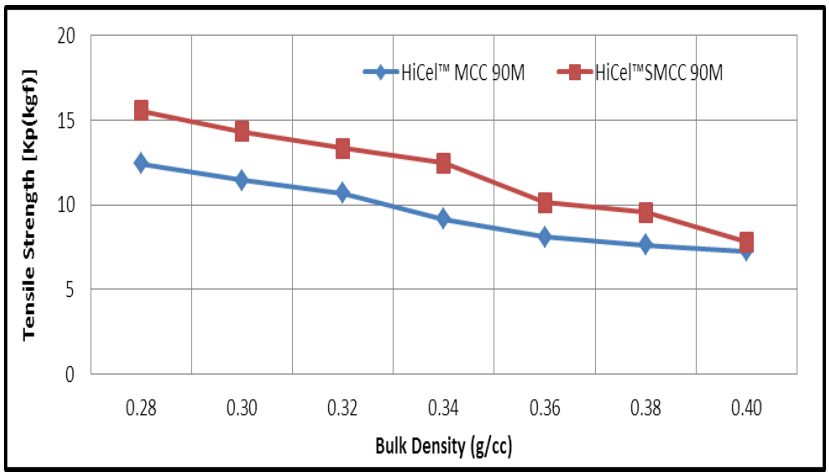

Fig 5. Average tensile strength of HiCel™MCC 90M and HiCel™SMCC 90M tablets at different bulk density.

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 mentioned in Fig6.

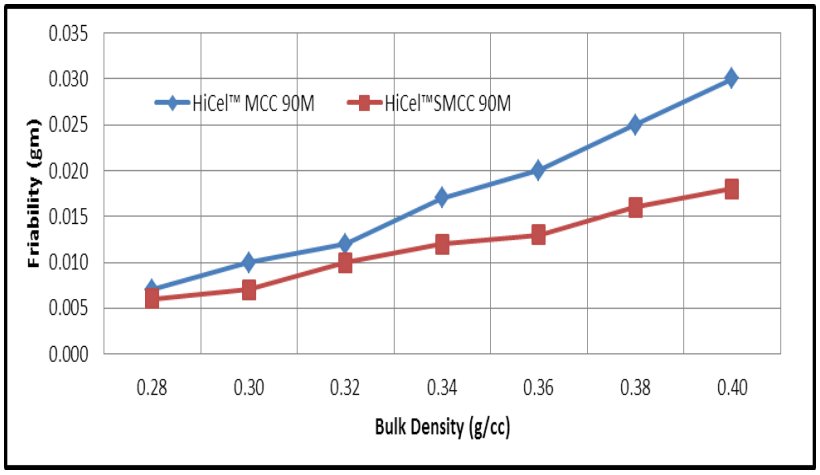

Fig6. Friability of HiCel™MCC90M and HiCel™SMCC 90M tablets at different bulk density.

Disintegration Time

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

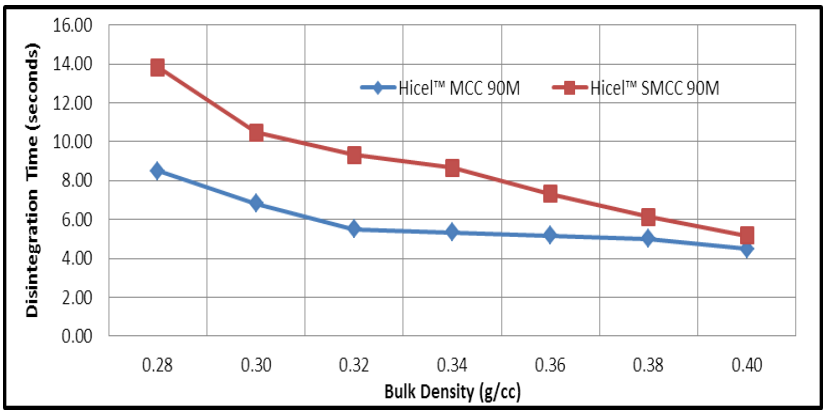

Fig7. Average disintegration time of HiCel™MCC 90M and HiCel™SMCC90M tablets at different bulk density

Table4. Average tensile strength, percentage friability and disintegration time of HiCel™MCC and HiCel™SMCC tablets at different bulk density

Bulk Density (g/cc)	HiCel™MCC 90M			HiCel™SMCC 90M		
	Avg. Tensile strength [Kp(kgf)]	Friability (%)	Avg. Disintegration Time (seconds)	Avg. Tensile strength [Kp(kgf)]	Friability (%)	Avg. Disintegration Time (seconds)
0.28	12.45	0.14	8.50	15.56	0.11	13.83
0.30	11.46	0.20	6.83	14.33	0.14	10.47
0.32	10.68	0.23	5.50	13.35	0.20	9.33
0.34	09.17	0.34	5.33	12.46	0.23	8.66
0.36	08.10	0.39	5.17	10.13	0.25	7.33
0.38	07.64	0.50	5.00	09.55	0.31	6.14
0.40	06.24	0.59	4.50	07.80	0.36	5.17

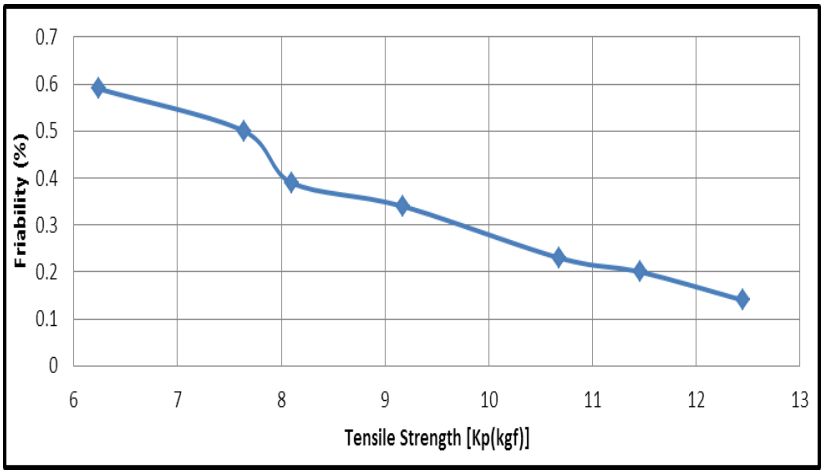

Fig 8. Tensile strength v/s friability of HiCel™MCC 90M.

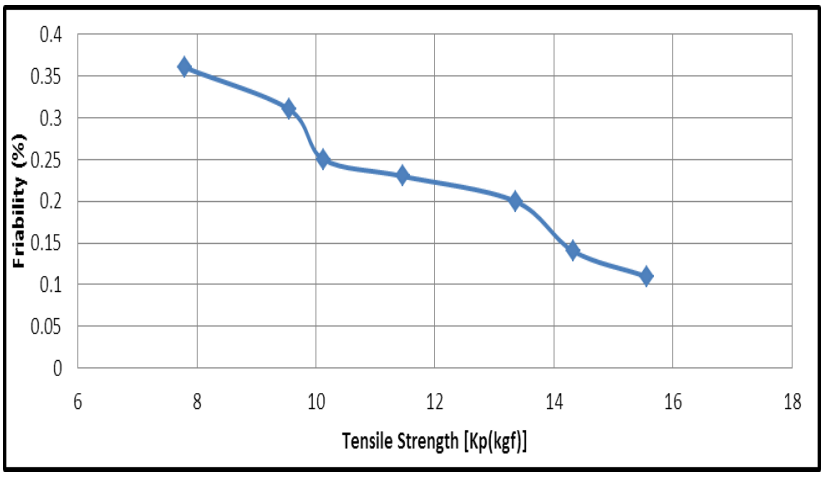

Fig 9. Tensile strength v/s friability of HiCel™SMCC 90M.

ABBREVIATIONS

API: Active pharmaceutical ingredient, β: beta, ˚C Degree Celsius, g: Gram, g/cc: Gram per cubic centimeter, H.Ratio: Hausner Ratio, mg: Milligram, ml: Milliliter, MCC: Microcrystalline cellulose, µS/cm: Micro Siemens per centimeter, %: Percentage, SEM: Scanning electron microscopy, SMCC: Silicified microcrystalline cellulose, USP: United states pharmacopoeia, V/V: Volume by volume.

CONCLUSION

In this study, we have elucidated that the bulk density affects tablet properties of HiCel™MCC 90M and HiCel™SMCC 90M. First correlation we have 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.

ACKNOWLEDGEMENT

The authors are thankful to Production department for provide us required samples of both grade and especially thanks to Mr. Gaurav Tripathi and C.Maity for support and co-operation.

CONFLICTS OF INTERESTS

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

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