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Research Article

A CRITICAL INFLUENCE OF SHAPES AND SIZES ON FLOW PROPERTIES OF DIFFERENT GRADES OF MICROCRYSTALLINE CELLULOSE

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ABSTRACT
Microcrystalline cellulose (MCC) has high demand and importance in pharmaceutical industry as fillers and binders. The physical properties like shape and size are one of the major contributor for the flow characteristics of bulk ingredients. The present study was designed to compare and quantify the influence of the size and shape on flow properties of 19 different grades of commercially available microcrystalline cellulose. The parameters evaluated include bulk density, tap density, compressibility index, Hausner's ratio, moisture content, average particle size, shape, angle of repose and sieve analysis as per USP specifications. The result obtained from these parameters showed different particle sizes ranging from 50-200μm and different shapes of particles like oval, spherical and one or both end curved rod shaped particles. The mixed variety size and shaped particles improved flow behavior, while small particle size and similar shaped particles of MCC showed poor flow ability.

Key word: Physical stability, Physical characterization, Physico-chemical properties, Particle size, Excipients.

INTRODUCTION

Cellulose is one of the most abundant and biodegradable polymers that has a promising future in the production of various materials used for variety of applications. Cellulose is a linear polysaccharide consisting of several D-glucose units linked together by ß, 1-4 glycosidic bond. It is tasteless, odorless, white crystalline material, there are about 2000 to 4000 glucose units all linked by ß ,1,4 glycoside bond hence the chain length is not constant. Microcrystalline cellulose can be biodegradable to its constituent glucose units via acid hydrolysis at high temperature and through enzymatic processes. Microcrystalline cellulose today, has brought revolutionaries in tableting technology because of its unique compressibility and carrier capacity. It exhibitsexcellent property as excipient for solid dosage form as it is compacted well under minimum compressional pressure. It is safe and physiologically inert. Commercially available MCC is derived from both Gymnosperm and other soft wood and from hard wood dicotyledon. Microcrystalline cellulose has many uses in both food, cosmetics and pharmaceutical industries as an anticaking agent, emulsifier, stabilizer, dispersing agent, thickeners and gelling agent and one of the most used filler-binder in direct tablet compression is due to its excellent binding properties, where it is use as a dry binder. The objective of this study is to investigate the effect of shape and size on flow properties ofdifferent grades and brands of MCC in view of its angle of repose, Carr's and Hausner's index. [1, 2, 3,4,5]

MCC (Fig. 1) is a partially depolymerized cellulose and is composed of crystalline and amorphous domains. The relatively large surface to volume ratio of micro fibrils, due to their small size, and the presence of abundant hydroxyl groups makes MMC hygroscopic. An important property of MCC as an excipient is its moisture content, which should not exceed 7.0 % (m/m) according to the European Pharmacopoeia. Hygroscopicity is one of the main limitations to using MCC in pharmaceutical formulations, since it may induce instability in moisture-sensitive drugs. MCC has been referred to as a »molecular sponge«, because most of the water held by MCC is present as free water that may be readily lost by evaporation. It should be noted that moisture content itself says little about an excipients propensity to promote hydrolysis. It has been shown that while cellulose powders with a lower degree of crystallinity contain more water than their counterparts with a higher degree. The former exhibit lower rates of degradation of acetylsalicylic acid than the latter. The study of the influence of water-binding energy of cellulose on the stability of acetylsalicylic acid revealed that each water molecule formed on average more hydrogen bonds in low-crystallinity cellulose (LCC) than in ordinary MCC and in high-crystallinity cellulose (HCC). Therefore, the stability of acetylsalicylic acid was greater in a binary mixture with LCC, since despite a larger amount of total water content, fewer water molecules were available to induce hydrolysis.[6,7,8,9,10,11,12,13,14, 15]

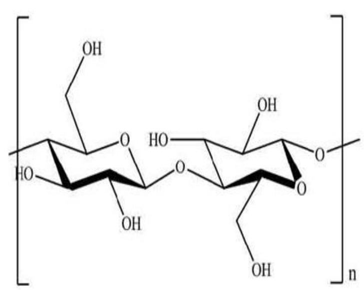


Fig. 1: Structural formula of cellulose

It is well know that particle size and size distribution is one of the many factors that greatly impacts on the flowability of powder during handling, processing and tableting. Flowability is a vital parameter for efficient and effective transport, storage and handling of MCC. It is the ability of the powder to flow in desired manner in a given processing or handling piece of equipment. Flowability remains a crucial factor that affects the design and processing of MCC der in handling equipment such as hoppers, filling and packaging operations, conveying,]. There are many techniques to assess the flowability of powders which includes; measuring the time required to discharge a given amount of powder from a flowmeter, Carr's compressibility index, Hausner ratio, angle of repose and flow function, The higher the flow function of the powder, the better the flowability. As poor powder flow can lead to sticking or caking during storage, prone to cohesion, rat holing, arching, poor content uniformity and poor solubility. The flowability of powder is a multifunctional parameter which depends on particle size and size distribution, shape, particle interactions and moisture content.[14, 15, 16, 17]

Table 1: Materials used

Sr. No.	Raw material	Manufacturer	Supplier	Specification
1	Primecel PH 101	Chemifield Cellulose Pvt. Ltd	Chemifield Cellulose Pvt. Ltd	USP, IH
2	Primecel PH 102	Chemifield Cellulose Pvt. Ltd	Chemifield Cellulose Pvt. Ltd	USP, IH
3	Chemicel PH 101	Chemifield Cellulose Pvt. Ltd	Chemifield Cellulose Pvt. Ltd	USP, IH
4	Chemicel PH 102	Chemifield Cellulose Pvt. Ltd	Chemifield Cellulose Pvt. Ltd	USP, IH
5	Primecel SF 50	Chemifield Cellulose Pvt. Ltd	Chemifield Cellulose Pvt. Ltd	USP, IH
6	Primecel SF 90	Chemifield Cellulose Pvt. Ltd	Chemifield Cellulose Pvt. Ltd	USP, IH
7	Avicel PH 101	FMC Biopolymer Pvt. Ltd.	Signet Chemical corporation Pvt. Ltd.	USP, IH
8	Avicel PH 102	FMC Biopolymer Pvt. Ltd.	Signet Chemical corporation Pvt. Ltd.	USP, IH
9	Ceolus PH 101	Asahi Kasei Chemicals Pvt. Ltd.	ArihantInnochem Pvt. Ltd.	USP, IH
10	Ceolus PH 102	Asahi Kasei Chemicals Pvt. Ltd.	ArihantInnochem Pvt. Ltd.	USP, IH
11	Ceolus US702	Asahi Kasei Chemicals Pvt. Ltd.	ArihantInnochem Pvt. Ltd.	USP, IH
12	Ceolus US 711	Asahi Kasei Chemicals Pvt. Ltd.	ArihantInnochem Pvt. Ltd.	USP, IH
13	Flocel PH 101	GMW JRS Pharma Pvt. Ltd.	JRS Pharma Pvt. Ltd.	USP, IH
14	Acecel pH 101	Accent Microcell Pvt. Ltd.	Accent Microcell Pvt. Ltd.	USP, IH
15	Acecel pH 102	Accent Microcell Pvt. Ltd.	Accent Microcell Pvt. Ltd.	USP, IH
16	Comprecel PH 101	Mingtai Chemical Pvt. Ltd.	Anshul life sciences Pvt. Ltd.	USP, IH
17	Comprecel PH 102	Mingtai Chemical Co. Ltd.	Anshul life sciences Pvt. Ltd.	USP, IH
18	Pharmacel PH 101	DFE Pharma Pvt. Ltd.	Kawarlal& co. Pvt. Ltd.	USP, IH
19	Pharmacel PH 102	DFE Pharma Pvt. Ltd.	Kawarlal& co. Pvt. Ltd.	USP, IH

Table 2: Equipment& Instrument used

Sr. No.	Parameters	Equipment & Instrument name
1	Particle size, Particle shape	Digital Motic Microscope B1 Series
2	Particle size	Sieve shaker
3	Moisture content	Moisture Analyzer (CB-50)
4	Bulk density,Tapped density	Tap density tester USP
5	Flow property	As per USP

Methods

Determination of Bulk density[18]

Procedure

- A 100 ml cylinder was taken which is readable up to 1 ml.
- The powder sample (M) weighed and filled up to more than 60% volume of the cylinder.
- The untapped volume of powder (V_0) in the cylinder was noted.
- Bulk density was calculated.
- The formula of Bulk Density is M/V_0
- The unit of bulk density is g/ml.

Determination of Tap Density[18]

Procedure

- Tap density measured after determination of untapped volume or bulk volume V_0.
- The tap volume of 10, 500, 1250 taps V_{10}, V_{500}, V_{1250}respectively measured to the nearest graduated unit.
- The height of the taps are 3± 2 mm as per USP.
- If the difference between V_{500}, and V_{1250} is more than 2ml then tap should increase more than1250. If not then V_{1250} is the V_fi.e. final tapped volume.
- Tap density was calculated by this formula- M/V_f, where Vf is the final tapped volume and M is powder sample weight.

Determination of CI[18], [19]

Procedure

CI Index was calculated by following formula with the specification as mention in the Table No. 3:-

$$\text{Compressibility Index} = 100(V_0 - V_F)/V_0$$ [19]

Determination of Hausner Ratio[18], [19].

Procedure

Further Hausner Ratio was calculated by following formula with the specification as mention in the Table No. 3 [18], [19].

$$\text{Hausner Ratio} = V_0/V_F$$ [18, 19]

Table 3: Specification of Flowability[19]

Compressibility Index (%)	Flow Character	Hausner Ratio
≤10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>38	Very, very poor	>1.60

Table 4: Flow Properties

Sr. No.	Item Name	Untapped Density (10gm)	Tapped density	Hausner'sRatio	CI index
1	Chemicel PH101	0.303	0.4	1.32	24.25
2	Primecel PH 101	0.303	0.4545	1.5	33.34
3	Avicel PH 101	0.333	0.417	1.252	20.144
4	Ceolus PH 101	0.3125	0.3448	1.1	9.375
5	Accel PH 101	0.33	0.4	1.21	16.66
6	Comprecel PH 101	0.27	0.35	1.28	22.22
7	Flocel PH 101	0.35	0.43	1.21	17.85
8	Pharmacel PH 101	0.37	0.312	1.18	15.62
9	Chemicel PH102	0.333	0.4348	1.306	23.41

10	Primecel PH 102	0.333	0.3846	1.154	13.34
11	Avicel PH 102	0.3125	0.3846	1.231	23.072
12	Ceolus PH 102	0.31	0.37	1.18	15.62
13	Accel PH 102	0.31	0.35	1.14	12.5
14	Comprecel PH 102	0.32	0.38	1.19	16.12
15	Pharmacel PH 101	0.312	0.344	1.1	9.375
16	Chemicel SF50	0.271	0.357	1.317	24.089
17	Ceolus UF 711	0.25	0.3	1.22	18.42
18	Chemicel SF90	0.303	0.37	1.233	18.11
19	Ceolus UF702	0.27	0.32	1.16	13.88

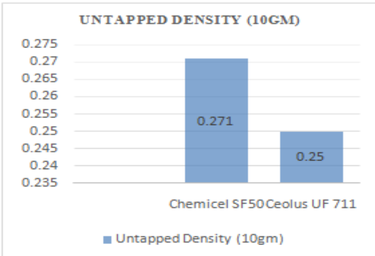


Fig.1: Comparison of CHEMICEL SF50 and CEOLUS 711 Grade

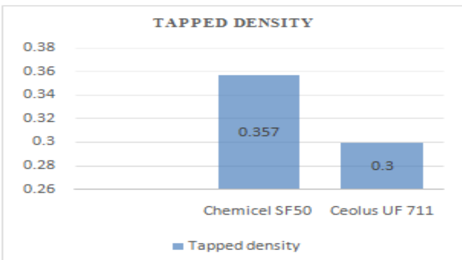


Fig.2: Comparison of CHEMICEL SF50 and CEOLUS 711 Grade

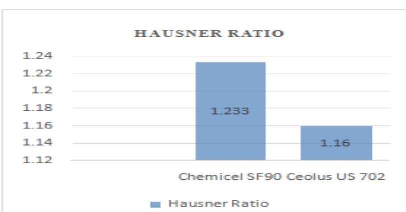


Fig.3: Comparison of CHEMICEL SF90 and CEOLUS 702 Grade

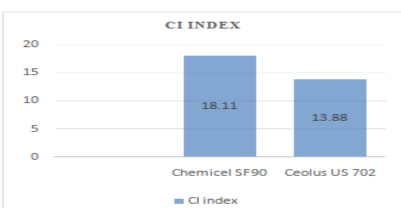


Fig.4: Comparison of CHEMICEL SF90 and CEOLUS 702 Grade

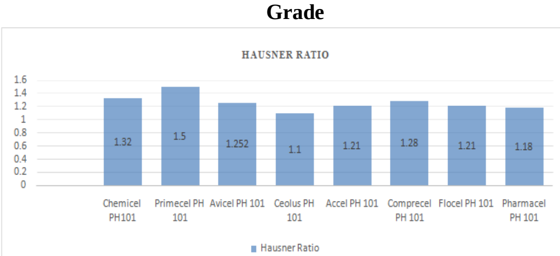


Fig.5: Comparison of all 101 Grade

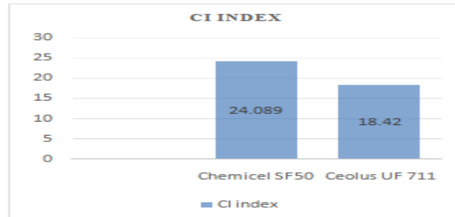


Fig.*6:*Comparison of all 101 Grade

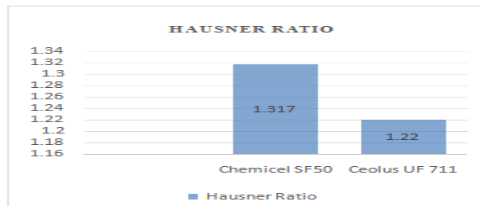


Fig.*7:* Comparison of CHEMICEL SF 50 and CHEMICEL UF 711

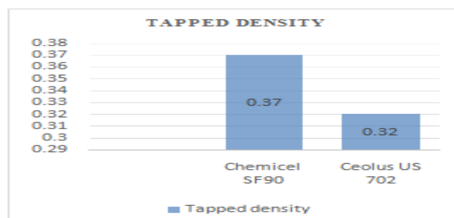


Fig.8: Comparison of CHEMICEL SF 90 and CHEMICEL UF 702

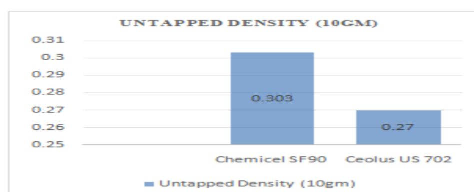


Fig.9; Comparison of CHEMICEL SF 90 and CHEMICEL UF 702 Grade

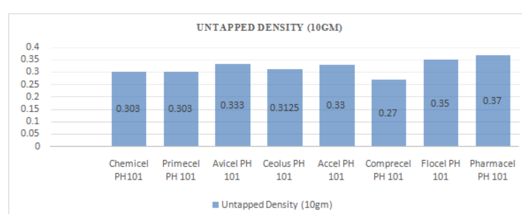


Fig.10: Comparison of all 101 Grade

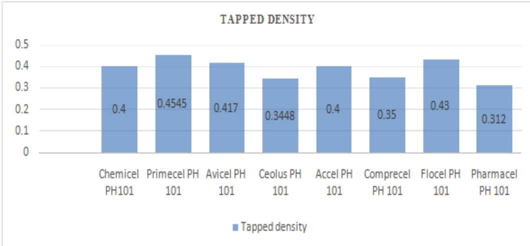


Fig. 11: Comparison of all 101 Grade

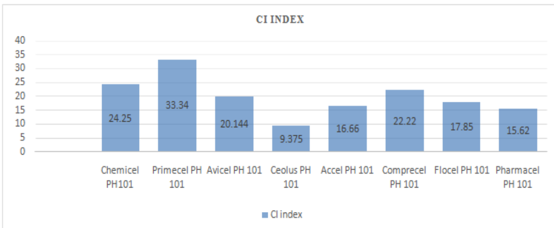


Fig.12: Comparison of all 101 Grade

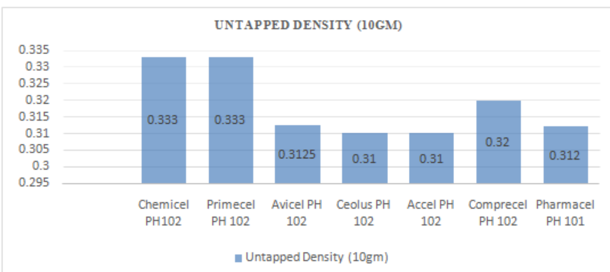


Fig. 13: Comparison of all 102 Grade

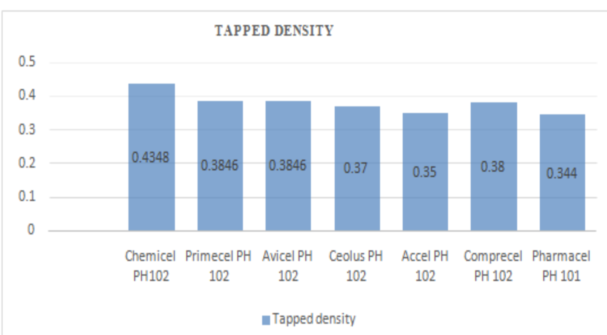


Fig.14: Comparison of all 102 Grade

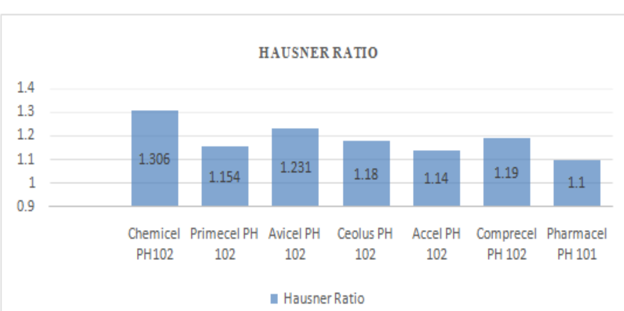


Fig.15: Comparison of all 102 Grade

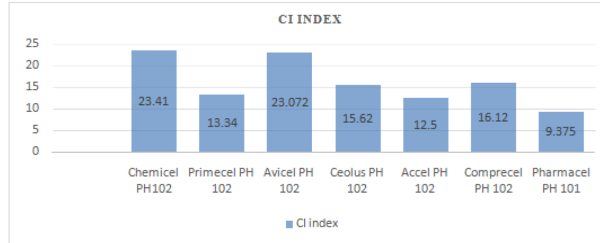


Fig.16: Comparison of all 102 Grade

a) Determination of particle size (Digital Motic Microscope B1 Series) [20]

PROCEDURE

Installing Software

Operation:

The power cabel was connected to a power out let and to the microscope. The microscope head was connected to your computer's USB2.0 port with USB port. The microscope was switched on and adjusted the illumination intensity to a comfort level. The sample was mounted and images were taken with help of installed Motic software.

The sieves were stacked on top of one another in ascending degrees of coarseness, and then placed the test powder on the top sieve.

In this process following sieves were used for determining particle size as mentioned in Table no. 4 [21].

Table 5: Standard sieve of different size

S.no.	Sieve used	Particle Size
1	Sieve no. #20	850 µm
2	Sieve no. #40	425µm
3	Sieve no. #60	250µm
4	Sieve no. #80	180µm
5	Sieve no. #100	150µm

Table 6: Particle Size Range

SR NO	Item Name	Particle size in µm
1	Chemicel PH101	13.33-93.31
2	Primecel PH 101	13.33-93.31
3	Avicel PH 101	26.66-79.98
4	Ceolus PH 101	13.33-106.64
5	Accel PH 101	13.33-133.33
6	Comprecel PH 101	13.33-66.65
7	Flocel PH 101	13.33-119.97
8	Pharmacel PH 101	26.66-119.97
9	Chemicel PH102	13.33-106.64
10	Primecel PH 102	13.33-133.33
11	Avicel PH 102	39.99-106.64
12	Ceolus PH 102	53.22-159.93
13	Accel PH 102	26.66-133.33
14	Comprecel PH 102	53.22-146.30
15	Pharmacel PH 101	26.66-119.97
16	Chemicel SF50	26.66-93.31
17	Ceolus UF 711	13.33-119.97
18	Chemicel SF90	53.22-186.22
19	Ceolus US 702	53.22-226.61

Table 7: Sieve Analysis

Sr. No.	Item Name	Sieve analysis		
		60#	80#	100#
1	Chemicel PH101	0%	1.64%	9.18%
2	Primecel PH 101	0%	1%	4.21%
3	Avicel PH 101	0%	0.09%	1.67%
4	Ceolus PH 101	0%	0%	1.85%
5	Accel PH 101	0.00%	0.00%	2.45%

6	Comprecel PH 101	0.40%	2.08%	4.00%
7	Flocel PH 101	0.00%	1.01%	4.80%
8	Pharmacel PH 101	0.00%	0.00%	0.92%
9	Chemicel PH102	0%	1.71%	12.06%
10	Primecel PH 102	0.84%	10.92%	17.12%
11	Avicel PH 102	0.38%	9.24%	18.44%
12	Ceolus PH 102	0.22%	10.09%	22.00%
13	Accel PH 102	0.00%	3.20%	12.00%
14	Comprecel PH 102	2.00%	7.20%	13.60%
15	Pharmacel PH 102	0.00%	3.52%	14.68%
16	Chemicel SF50	0%	0.20%	0.32%
17	Ceolus UF 711	0.00%	0.00%	2.20%
18	Chemicel SF90	1.68%	12.76%	8.08%
19	Ceolus UF 702	0.69%	17.60%	26.80%

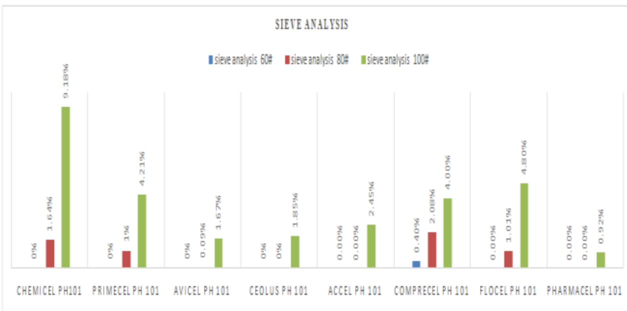


Fig.17: Comparison for all 101 Grade

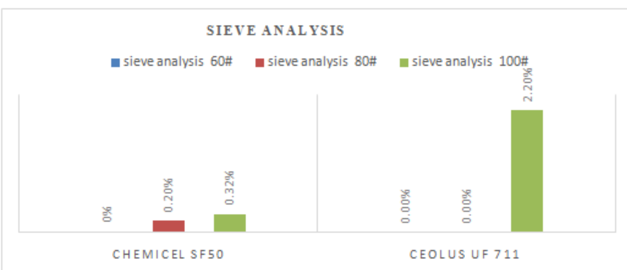


Fig.18: Comparison for all SF and CEOLUS UF Grade

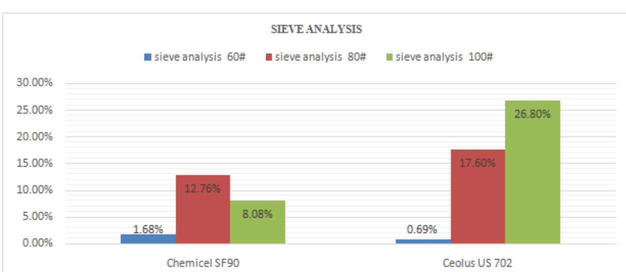


Fig.19: Comparison for all CHEMICEL SF and CEOLUS US Grade

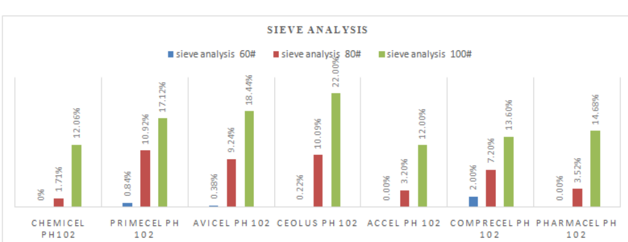
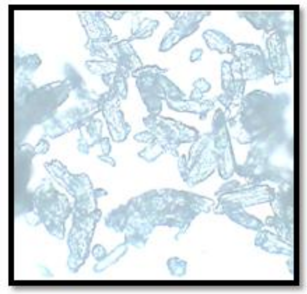
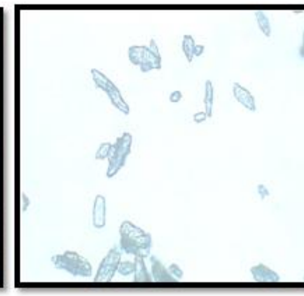


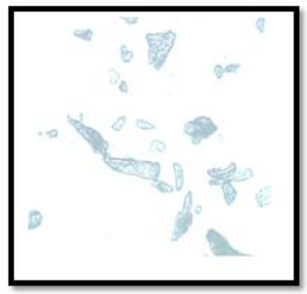
Fig. 20: Comparison for all 102 Grade



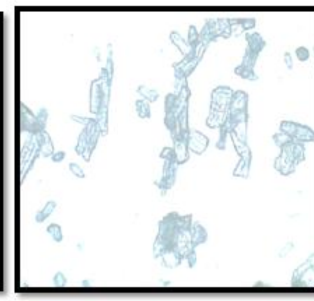
1. Chemicel PH 101



2. Chemicel PH 102



3. Primecel SF50



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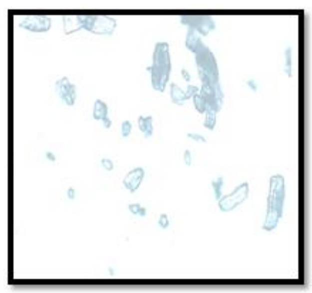

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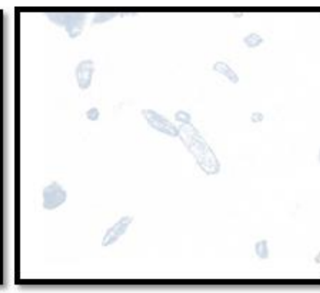

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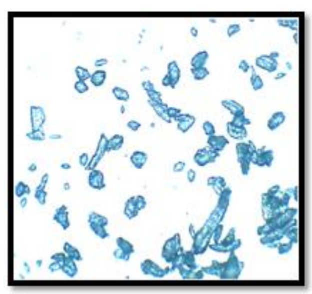
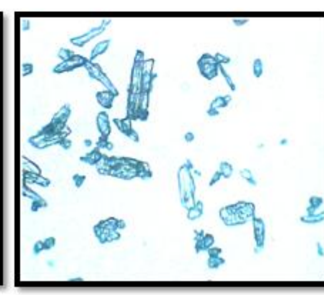


7. Avicel PH 101



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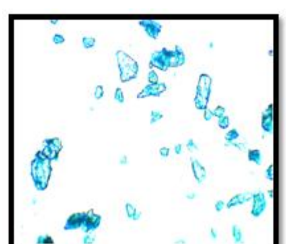
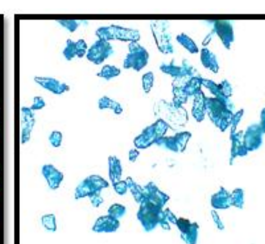
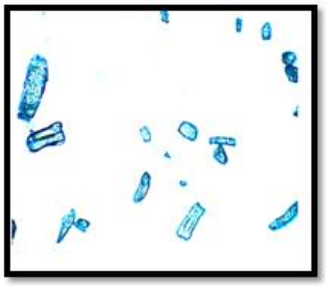


9. Ceolus PH 101

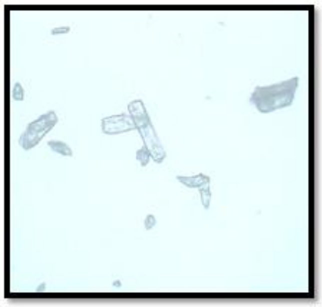


10. Ceolus PH 102

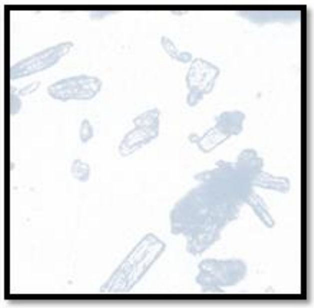


11.Ceolus US 702

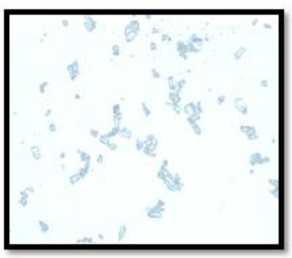
12.Ceolus UF 711



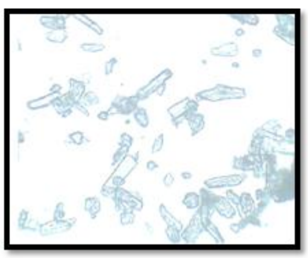
13. Pharmacel PH 101



14.Pharmacel PH 102

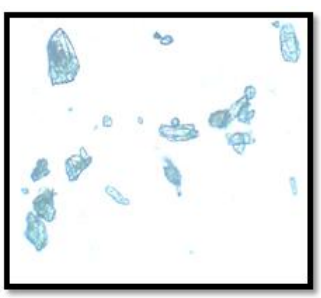


15. Comprecel PH 101

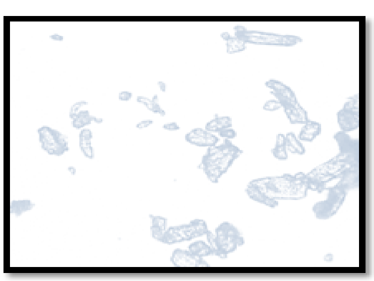


16. Comprecel PH 102

17. Acecel PH 101



18 Acecel PH 102



19. Flocel PH 101

Determination of Angle of repose [19]

Procedure

A funnel was fixed at 2 to 4 cm height (in this study 2.5 cm) from a fixed base. Powder was poured from the top of the funnel very slowly and carefully. The pile of powder can be distorted by the impact of powder from above. By carefully building the powder cone, the distortion caused by impact can be minimized. When the pile touchedthe bottom of the cone then pouring of powder was stopped, and a circle was drawn around the powder. The angle of repose was determined by measuring the height of the cone of powder and calculating the angle of repose, α, from the following equation: tan (α) = height/radius.

Determination of Moisture content: Moisture Analyzer (CB-50)

Procedure

The power supply was connected to the mains outlet and the mains power was switched on. The instrument was switched on using on/ off switch provided at the back side of the instrument. Instrument went through self-test and subsequently displayed the weight as well the calibration of instrument was checked before it was put into use. The tare key was used to make pan weight zero. The sample was placed on the pan and was analyzed by the analyzer. After specified time the display showed the reading which was noted.

Table 8: Moisture Content

Sr. No.	Item Name	LOD**
1	Chemicel PH101	4.84
2	Primecel PH 101	4.62
3	Avicel PH 101	5.64
4	Ceolus PH 101	5.35
5	Accel PH 101	5.2
6	Comprecel PH 101	4.5
7	Flocel PH 101	4.9
8	Pharmacel PH 101	6.15
9	Chemicel PH102	5.15
10	Primecel PH 102	5.33
11	Avicel PH 102	5.24
12	Ceolus PH 102	4.2
13	Accel PH 102	5.1
14	Comprecel PH 102	4.1
15	Pharmacel PH 102	7.27
16	Chemicel SF50	4.21
17	Ceolus UF 711	4.3
18	Chemicel SF90	5.77
19	Ceolus US 702	4.2

**

All grades of MCC showed moisture content within limit.
If moisture increases in any grades then flow property decreases.

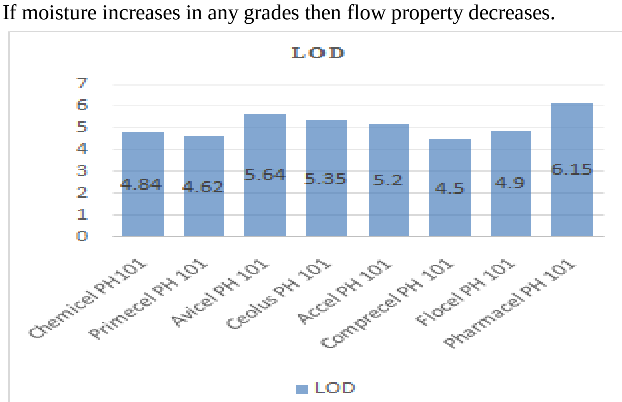


Fig. 21: Comparison of all 101 Grade

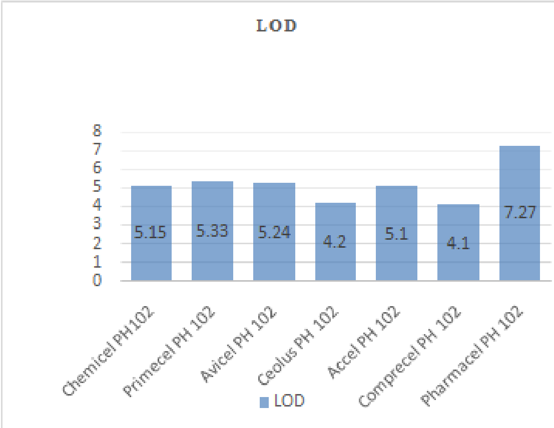


Fig. 22: Comparison of all 102 Grade

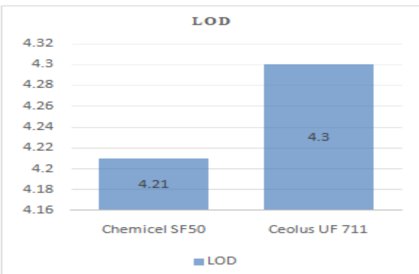


Fig. 23: Comparison of CHEMICEL SF50 and CEOLUS 711 Grade

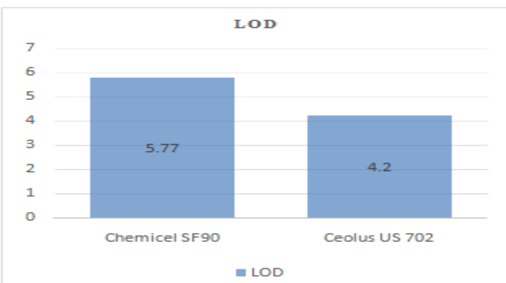


Fig.24 : Comparison of CHEMICEL SF90 and CEOLUS 702 Grade

Result and Discussion

S.no.	Parameter	Result
1	Particle Size	Ø All PH 101 and PH 102 showed the particle size range in specified limit as mentioned in Handbook of excipients [21]. Ø Chemicel SF 50 andCeolus UF 711 also showed the particle size range in specified limit. Ø But Chemicel SF 90 andCeolus UF 70 showed higher particle size.
2	Sieve Analysis	Ø All PH 102 showed more retention compare to PH 101 grades. Ø While UF 702 showed higher retention because of higher particle size.
3	Moisture Analyzer	Ø All grades of MCC revealed the moisture content within limit. If moisture increases in any grades then flow property decreases.
4	Flow Properties	Ø The flow property result of all the MCC PH 101, Chemicel SF50 andCeolus UF 711 showed fair flow limit. Ø While MCC PH 102, Chemicel SF90 andCeolus UF 702 showed good flow limit.
5	Particle Shape	Ø From the study of all brands of MCC it can concluded that the MCC PH 101, Chemicel SF50 andCeolus UF 711 showed small spherical as well as small rod shaped particles. Ø While MCC PH 102, Chemicel SF90 andCeolus UF 702 showed triangular, big rod shaped with one side curved, small and big spherical particles.

CONCLUSION

From the discussed parameters it can be concluded that all PH 101, SF 50 and UF 711grades has exhibit particle sizes ranging from 50-150µm with similar shapei.e. Oval or spherical and rod particles of MCC with poor flowability. While all PH 102, SF 90 and UF 702 711grades has exhibit particle sizes ranging from 50-150µm with different of shapes of particles like oval, spherical and one or both end curved rod shaped particles. The mixed variety size and shaped particles improves flow behavior. The results demonstrate that particle size and particle shape significantly affect the flow characteristics of a powder blend.However, the influence of particle shape and particle sizeof MCC and the dissolution of the compressedMCC tablets require further investigation.

The results, thus obtained, proclaim that all brands and grades of microcrystalline cellulose have closeresemblance in physicochemical properties as well as complying with the official requirements specified in the United States Pharmacopoeia – 37[18-20]and Handbook for Pharmaceutical excipients for microcrystalline cellulose[21].

ACKNOWLEDGEMENT

We are immensely grateful to Chemifield Cellulose Pvt. Ltd.

Table 9: Abbreviation

S.no.	Abbreviated Form	Full Form
1	BD	Bulk Density
2	CI INDEX	Compressibility Index
3	I.e.	That is
4	IH	In-house specification
5	LOD	Loss on Drying
6	MCC	Microcrystalline Cellulose
7	USPNF	United states Pharmacopoeia National Formulary
8	USP	United states Pharmacopoeia

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