HiCelTM Microcrystalline Cellulose is a stable hygroscopic material, which is widely used in Direct Compression Tabletting. The Plasticity of MCC is one of the main reasons for it's exceptional binding properties. The hygroscopicity of MCC is attributable to the abundant hyrodxyl groups on cellulose chains. The sorption of moisture results in water molecules being tightly bound to the amorphous region of MCC, which are more hydrophilic than the crystalline region of MCC.This moisture reaches an equilibrium in the range of 4 to 5% and this is the range, when the tablet hardness of the tablets are the best.

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Effect of Moisture Content of Exicipient (Microcrystalline Cellulose) on Direct Compressible Solid Dosage Forms

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INDEX OF ABBREVIATIONS

SNO	Abbreviation	Full forms
1.	API'S	Active pharmaceutical ingredients
2.	BD	Bulk density
3.	℃	Degree centigrade
4.	DC	Direct compression
5.	gm	Gram
6.	HR	Hausner Ratio
7.	HPMC	Hydroxy propyl methyl cellulose
8.	MCC	Microcrystalline cellulose
9.	mg	Milligram
10.	PEG	Polyethyleneglycol
11.	%	Percentage
12.	RH	Relative humidity
13.	S.S	Stainless steel
14.	TBD	Tapped density
15.	USP	United state pharmacopoeia

INDEX OF CONTENTS

INDEX OF TABLES

INDEX OF FIGURES

ABSTRACT

Quality of pharmaceutical product is very important because pharmaceuticals drugs should be safe and therapeutically active formulation performance should be consistent and predictable. Final product quality depends on all ingredients which is used for making the final product tablet. Final product tablet is made by the addition of bulk drug and excipients. The continuous evolution of the bulk drugs and excipients can only ensure the quality of final product. Moisture content of API'S and excipients plays avery important role to manufacture the final product. It is may affect the physical and chemical properties of final product. Moisture content affects the physical, chemical and microbiological properties of pharmaceutical finished dosage forms. In direct compression process,high and extra low moisture content could be it affects the hardness of tablet. For satisfactory hardness of tablet, room temperature and humidity must be maintained in a specific limit. Tablet hardness is also most import parameter for any solid dosage form.

Chapter 1

INTRODUCTION

INTRODUCTION

Quality is the collection of feature and characteristics of a product that contribute to its ability to meet requirements and also creating standards for producing acceptable products. Quality can be defined as the measurement of excellence and significant variations or free from defect deficiencies. Quality is measured by the degree of conformance to predetermined specification and standards. To the ethical pharmaceutical manufacturer, it implies a detail system of inspection and control covering the production, evaluation, distribution of every drug bearing the company's label[1,2]. It is the purpose of these operations to produce medication of superior efficacy, safety and elegance and to provide assurance to physician, pharmacist and the consumer that the given product performs uniformly and in a manner satisfactory for the purpose for which it is recommended. Quality of a pharmaceutical product i.e. solid dosage form (tablet) can be guaranteed by evaluating different physical, chemical and microbiological test of from raw materials to finished product[1,3]. All parameters of excipients and API's should lie under limit such as bulk density, particle size and moisture content etc. If moisture content of excipientsand API'S are above limit, it may effect the physical, chemical and microbiological quality of final product[4].

Moisture content plays an important role in final product. Moisture in finalproduct comes from many sources. Moisture may come from the bulk drug or inactive excipients in the formulation. In pure chemicals, moisture may be present as water of crystallization and/or as adsorbed water.When moisture is above limit, however it may be affecting stability of product and could increase chances of microbial contamination[5]. Moisture content affects manufacturing of the solid formulation. Higher moisture content in the powder is not good. It can result in poor powder flow, which could further result in irregular tablet parameter performance[4,5,6]. It may also result in sticking problems on the surface of the tablet. When moisture is present

under limits it helps the API and excipients in binding[6]. In direct compression formulation,different type of excipients are used i.e. starch, microcrystalline cellulose (MCC), Polyethyleneglycol(PEG) and Hydroxy propyl methyl cellulose (HPMC)[7,8,9]. HiCel^{TM}Microcrystalline cellulose is a common excipient used for tableting in pharmaceutical industries for wet granulation and direct compression formulations[5,10]. It consists of purified partially de-polymerised cellulose prepared by hydrolyzing dissolving grade wood pulp with mineral acid[11,12].It exists as partial crystalline regions and serves a number of functions in solid dosage formulations[13,14]. The moisture content of microcrystalline cellulose is about 4% to 5.5%which is good for direct compression formulation, while USP monograph specification limit is not more than 7%.

In this study,the higher and extralow moisture content of Microcrystalline Cellulose may be influencingthe flow of powder and tablet hardness of direct compressible tablets. It may be effecting product stability and microbial growth. We are using two grades HiCel^{TM} 90M and AceCel^{TM}102GofMicrocrystalline Cellulose for this study.Secondly we investigated the temperature and relative humidity effect on HiCel^{TM} 90M grade MCC at three different condition in packed and unpacked condition (in polylinner bag and paper bag).

Chapter 2

MATERIAL USED IN THIS STUDY

MATERIAL USED IN THIS STUDY

MATERIAL

HiCel^{TM} 90M(Spray Dried Microcrystalline Cellulose) and AceCel^{TM} 102G(Air Stream driedMicrocrystalline Cellulose) were used for manufacturing the tablet direct compression technique.Digital weight balance(Mettler Toledo,Model no. ML802/A01) used for weighting the sample. Hot air oven (Model no. PNX-14)used for testing moisture content. Untapped bulk density analysed with Class A grade graduated measuring cylinder capacity 100 ml and dia 30mm, tapped density checked by tapped density tester(ElectrolabModel No. ETD1020)Proton mini press (model 10 STN "D")"D" type tooling machine was used for making the tablets. Digital tablet hardness taster(Labindia model no.TH1050M) was used for test tablet hardness. Friability test done at Baroda analyticalservicesin Vadodara, Gujarat. For effect of humidity and temperature on MCC used two different stability chamber (one was 30±2 ℃/65±5%RH, second was 40±2 ℃/75±5%RH) both stability chamber make by Thermolab (model no-TS0000325 S).

Chapter 3

EXPERIMENTAL SECTION

EXPERIMENTAL SECTION

Manufacture process of HiCel^{TM}90M Microcrystalline Cellulose (MCC)

Fibrous wood pulp cut into the pieces, charged in reactor with mineral acid and water, and hydrolyzed V/V at specific temperature, pressure, acid concentration and time. Mineral acid, temperature, pressure and time used as a catalyst for fast the reaction. 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 75µs/cm, pH is neutral.Makes slurry using wet MCC cake and Water (suspension), and drying with spray drying and pack. Related details are mentioned in the figure no-1.

Manufacture process of AceCel^{TM} 102G Microcrystalline Cellulose

Chemically AceCel^{TM} 102G and Hicel are same, only drying process is different. AceCel^{TM} 102G is Flash/bulk dried and HiCel is spray dried. Related details mentioned in fig. 1.

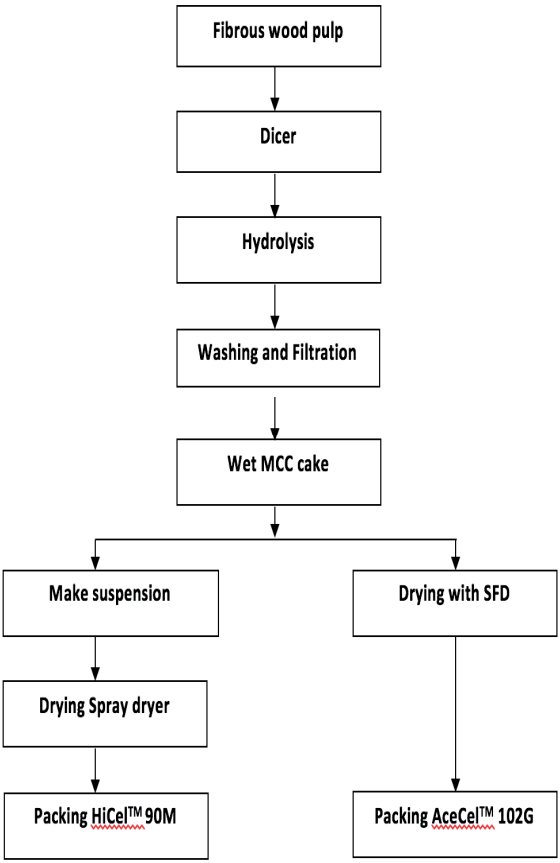

Fig.1 Manufacture process of HiCel™ and AceCel™ microcrystalline cellulose

Moisture content[5, 6, 10]

Heat the shallow bottle in a hot air oven (Model no. PNX-14) at 105°C for 30 minutes after that cool it in desiccator at room temperature.Tare weight the Shallow bottle and take about 1 gm of HiCel™ 90M MCC in shallow bottle, set oven at 105°C and kept for 3 hours. After 3 hours take out the shallow bottle,allow to cool in desiccator at room temperature.

When the shallow bottle is cool take weight again, calculatemoisture content by using the following formula.

$$\text{Moisture content} = \frac{Afterdryingweightofshallowbottle - emptyweightofshallowbottle}{Sampleweightingram} \text{ X } 100 \qquad (1)$$

Moisture content of both grades (HiCel™ 90M and AceCel™ 102G) of Microcrystalline Cellulose were investigated and summarized in the table no-2.

Angle of repose[4]

Pour 30gm of dry MCC through pour on powder flow tester funnel), powder comes on the S.S cylinder surface until a pile build on the top of S.S cylinder. Measure the total height (S.S cylinder & pile) by scales. Using following formula find the calculated value. This value checks natural tangents chart for angle of repose.

$$\text{Angle of Repose} = \frac{2h}{d} \qquad (2)$$

Where

h = height of S.S cylinder

d = diameter of S.S cylinder

Fig.2 Angle of repose analysis

Angle of repose of both grades of microcrystalline cellulose (HiCel^{TM} 90M and AceCel^{TM} 102G were shown in table no.2.

Table.1 Moisture content and Angle of Repose of HiCel™90M and AceCel™ 102G Microcrystalline cellulose

Sr.No	HiCel™ 90M		AceCel™ 102G	
	Moisture Content (%)	Angle of Repose(°)	Moisture Content (%)	Angle of Repose(°)
1	7%	43	7%	36
2	6%	42	6%	34
3	5%	40	5%	33
4	4%	39	4%	33
5	3%	38	3%	32
6	2%	38	2%	32
7	1%	37	1%	31

Bulk density [17][18]

Untapped Density

Untapped density was analyzed through graduated measuring cylinder. Take 20 gm of dry MCC powder pours into a graduated A grade 100 ml capacity cylinder slowly from the sidewall. Level the surface of sample in cylinder by slow movement and note down the occupied volume and calculate the untapped density of MCC by using following formula.Untapped of HiCel^{TM} 90M and AceCel^{TM} 102G shown in table no-3.

$$\text{Untapped density (BD)} = \frac{Weightofpowderingram}{Occupiedvolumeinml} \quad (3)$$

Tapped Density(TBD)[5]

Tapped density(TBD) was anlaysed by using (Electro lab instrument, Model No. ETD1020), measuring cylinder placed in tapped density machine and fixed 500 tapped. After 500 tapped measured the volume of measuring cylinder and calculate the tapped density of HiCel^{TM} using following formula.Tapped density of HiCel^{TM} 90M and AceCel^{TM} 102G shown in table no-3.

$$\text{Tapped density (TD)} = \frac{Weightofpowderingram}{Occupiedvolumeinml} \quad (4)$$

Fig.3 Tapped density tester

Hausner's Ratio [17][18]

Hausner ratio is another method to check flow of powder.The flow of powder was measured by "Hausner ratio". Tapped density(TBD) is divided by untapped density(BD).Formula is mention below. Result mention is mention in table no-3.

Hausner's Ratio (H.Ratio) = $\frac{TBD}{BD}$ (5)

Carr's index[6]

Carr's index is known as Compressibility index, it indicates compressibility of powder.Carr's index of both grades HiCe^{TM} 90M and AceCel^{TM} 102G shown in the table no-3.

$$\text{Carr's index} = 100 \times \frac{Tapped\ density - Untapped\ density}{Tapped\ density} \quad (6)$$

Average Particle size analysis[6]

Average particle size was analyzed by Sieve shaker make (Retch-Japanese instrument). Take cleaned mesh sieve with bottom pan and top cover. Check sieve shaker and set mesh sieve with sample being analyzed on sieve jet. Arrange the sieve mesh sequence top 60, 200 mesh and bottom. Set the amplitude at 1.5 to 2.5 mm, timer at 5 minutes and interval time at 15 sec. Weight 10 gm of MCC powder with the help of weight balance (Mettler Toledo,Model no. ML802/A01) and put into top of sieve. After 5minutes take out the sieves and weight the retention separately. Brush the mesh slowly from bottom and collect the all particles retained in between the mesh and consider as retention. Calculate the retention in percentage for each mesh sieve as per the following formula-

$$\text{Retention \%} = \frac{S(R)}{S(W)} \text{ X } 100 \quad (7)$$

Whereas; S(R) = Sample retention weight (gram), S(W)= Sample taken weight (gram)

Average particle size of both sample shows in table 2.

Table.2 Physical parameter of HiCel™90M and AceCel™102G Microcrystalline cellulose

Sr.No	Parameter	HiCel™ 90M	AceCel™ 102G
1.	Untapped Density	0.30	0.30
2.	Tapped Density	0.43	0.40
3.	Hausner ratio	1.43	1.33
4.	Carr's index	30.23	25.00
5.	Retention on 75µm	52.05	64.25

Tablet manufacturing process

Manufacturing process that may be impact the product moisture content of susceptible product should be carefully monitored. Seasonal humidity and temperature variation may be effect the product quality during manufacturing, packing and storage; air-condensing units need to have sufficient capacity to control processing within the specifications.

A manufacturing area may easily run below facility limits during low humidity seasons but may struggle to be compliant during rainy season. Complies personnel must e watchful of changes to equipment associated with environmental controls.

Tablet Compaction[5,6,15]

Moisture is an important factor in compaction of blended powders or dried granulation to manufacture tablets. Tablet hardness is generally low at low moisture content. As the moisture, content level increase, the tablet hardness also increases to a maximum level; but higher moisture content lead to decrease tablet hardness.Compacts of ~500 mg tablet were made on 10 station proton mini press (Model no. MINI PRESS 10 "D") using D tolling dies and punches. Machine operating pressure ranges 10 to 60 KN.

Fig.4 Direct compression tablet machine

General Appearances of tablet

Tablets of both grades of microcrystalline cellulose (HiCel™ 90M and AceCel™ 102G)are ~500mg weight and shown in fig.2 and 3; all tablets are made at 3.25 Ton release pressure, and other related data of tablets are mentioned in tablet no-3.

Table.3 General Appearances of both grades of microcrystalline cellulose tablets

Sr.No.	Description	Result
1	Shape	Round
2	Color	White
3	Odor	Odorless
4	Taste	Tasteless

Fig.5 HiCel^{TM} 90M microcrystalline cellulose tablets

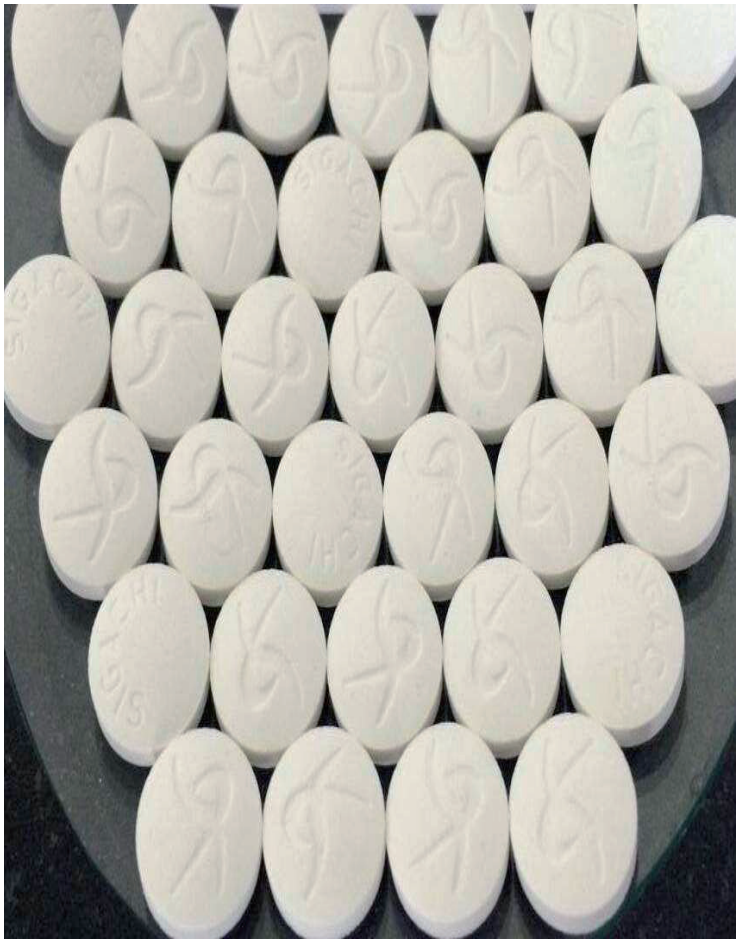

Fig.6 AceCel^{TM} 102G microcrystalline cellulose tablets

Weight variation of Tablets[14,15]

Random 10 tablets were taken from each batch and each tablet was weighted individually using electronic digital balance (Mettler Toledo, Model No.-MS204S /A01) The average weight of all tablets was calculated following formula (equation 8)The pharmacopoeial limit of weight variation is mentioned in (Table no.4) .

$$Averageweightoftablet = \frac{Totalweightoftablets}{Totalno.oftablets} \quad (8)$$

Table .4 Weight variation test limits for tablets as per USP Pharmacopoeia

Sr.No.	Average weight of tablets	Maximum percentage difference allowed
1.	130 mg or less	±10 %
2.	More than 130 mg	±7.5 %
3.	324 mg and above	±5 %

All the tablets of both grades are passing in uniformity weight test, i.e. weight variation was found within the pharmacopoeial limit shown in table 5 or 6, and Fig 7 or 8.

Table 5. Weight variation of HiCel™ 90M microcrystalline cellulose tablets at different moisture content

Tablet No.	HiCel™ 90M Moisture Content (%)						
	1%	2%	3%	4%	5%	6%	7%
1	549	548	550	550	550	548	550
2	549	551	549	550	550	551	549
3	550	550	550	550	550	550	550
4	550	551	551	551	551	551	551
5	552	550	550	550	550	550	550
6	550	550	550	550	550	550	550
7	549	549	549	550	550	549	549
8	550	549	550	549	549	549	550
9	551	551	551	550	550	551	551
10	550	551	550	550	550	551	550
Average	550	550	550	550	550	550	550

Table.6 Weight variation of AceCel^{TM} 102 G microcrystalline cellulose tablets at different moisture content

Tablet No.	AceCel™ 102 G Moisture Content (%)						
	1%	**2%**	**3%**	**4%**	**5%**	**6%**	**7%**
1	549	548	549	550	550	549	548
2	549	555	549	550	550	549	555
3	547	553	555	550	550	547	553
4	555	547	551	551	551	555	547
5	546	550	550	550	550	546	550
6	549	550	546	550	550	549	550
7	550	549	549	550	550	550	549
8	552	549	548	549	549	552	549
9	551	548	551	550	550	551	548
10	552	551	552	550	550	552	551
Average	**550**	**550**	**550**	**550**	**550**	**550**	**550**

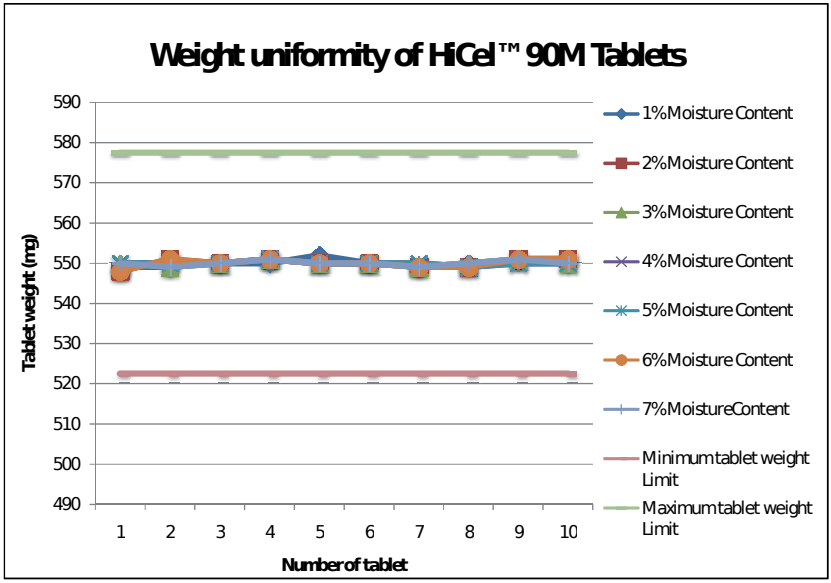

Fig.7 Weight variation of HiCel™ 90 M microcrystalline cellulose tablets at different moisture content with minimum and maximum pharmacopoeial limit

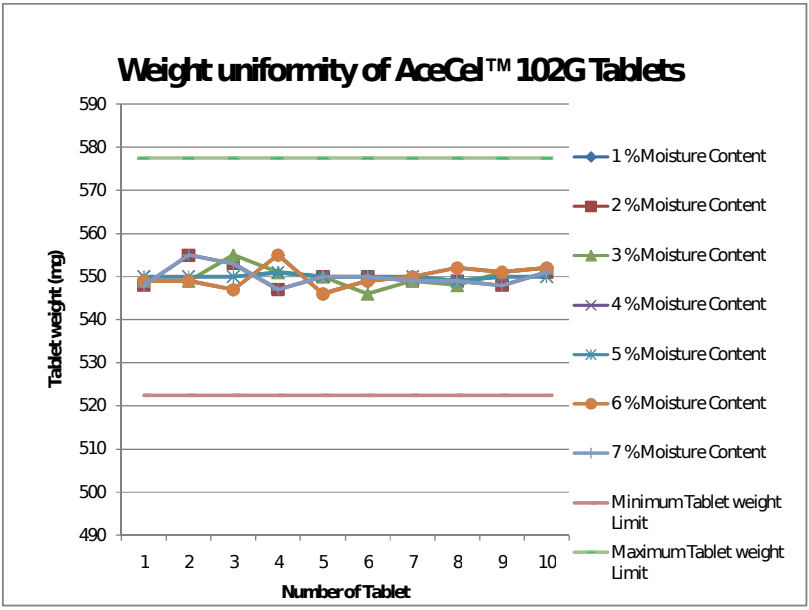

Fig.8 Weight variation of AceCel™ 102 G microcrystalline cellulose tablets at different moisture content with minimum and maximum pharmacopoeial limit

Hardness of Tablet[15,16]

Random 10 tablets were taken from each batch. Electronic digital hardness test machine (Labindia tablet hardness tester, Model No.-TH1050 M) was used for hardness test. Individually, a tablet was placed between two anvils, force was applied to the anvils, and the crushing strength that just caused the tablet to break was recorded. Finally the reading was taken in kp[kgf] on display of hardness machine.

Tablet hardnessof both grades are decreasing with increasing the moisture content of both grades of microcrystalline cellulose related details are mentioned in table 7 and Fig 9 or 10, average hardness of both grades mention in fig 11.

Note[18]- It is to be noted that atmospheric condition of room i.e. temperature and humidity may effect the tablet hardness. In case may be exercised to maintain relative humidity (RH) range of 53% and temperature 23±1°C.

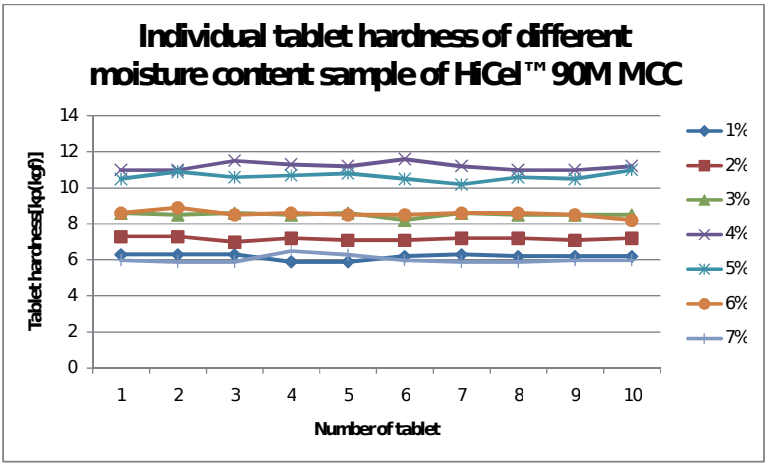

Fig.9 Individual tablet hardness of different moisture content sample of HiCel™90M microcrystalline cellulose

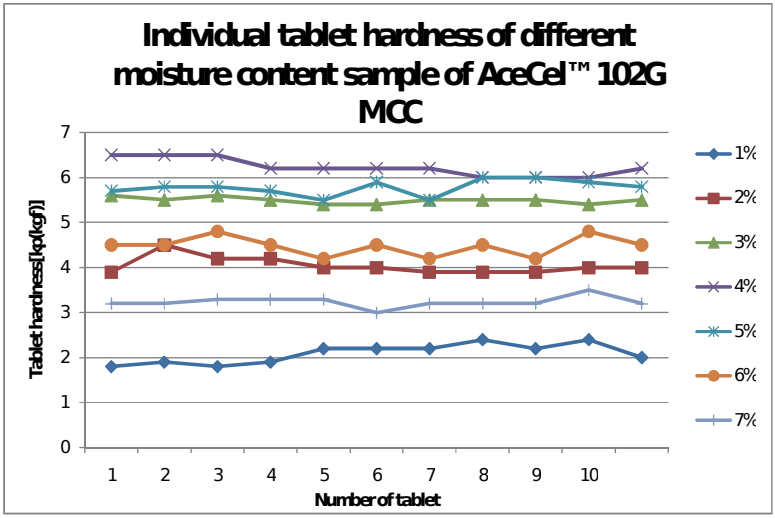

Fig.10Individual tablet hardness of different moisture content sample of AceCel™102G microcrystalline cellulose

Table.7 Different moisture content and average hardness of HiCel™ 90M and AceCel™ 102G microcrystalline cellulose Tablets

Sr.No.	Moisture Content (%)	Average Tablet Hardness [Kp(kgf)]		Average Tablet Thickness (mm)	
		HiCel™ 90M	AceCel™ 102 G	HiCel™ 90M	AceCel™ 102 G
1	1 %	6.2	2.0	5.00	5.01
2	2 %	7.2	4.0	5.01	5.01
3	3 %	8.4	5.5	5.00	5.00
4	4 %	11.0	6.2	5.01	5.01
5	5 %	10.7	5.8	4.99	5.02
6	6 %	8.5	4.5	5.00	5.00
7	7 %	6.0	3.2	5.00	4.99

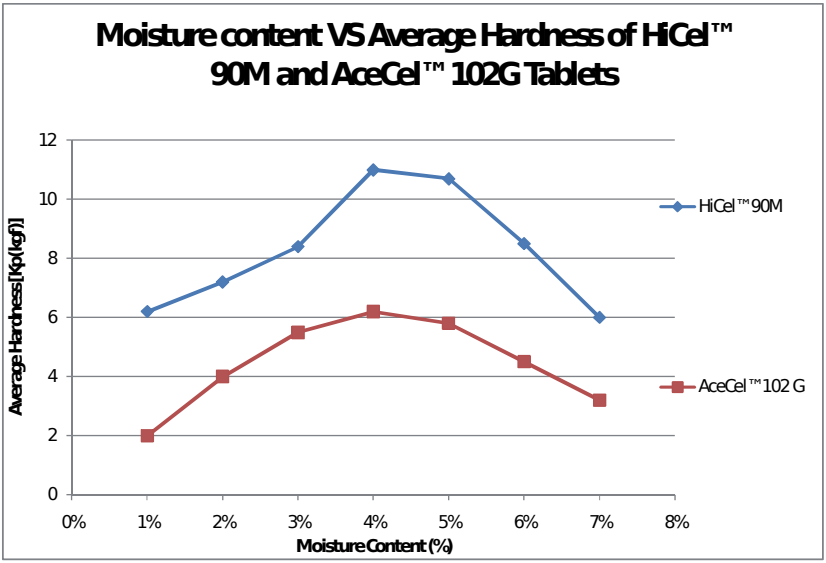

Fig .11 Average hardness of HiCel™ 90M and AceCel™ 102 G microcrystalline cellulose tablets at different moisture content

Thickness of Tablet

Random 10 tablets were taken from each sample. Vernier caliper (M&W Precision tools serial no-11071909) was used for thickness test. Individually, a tablet was placed between two external jaws and take reading in millimeter (mm).

Thickness of tablets mentioned in table 7 and average thickness is shown in fig.12 of both samples HiCel^{TM} 90M and AceCel^{TM} 102G MCC.

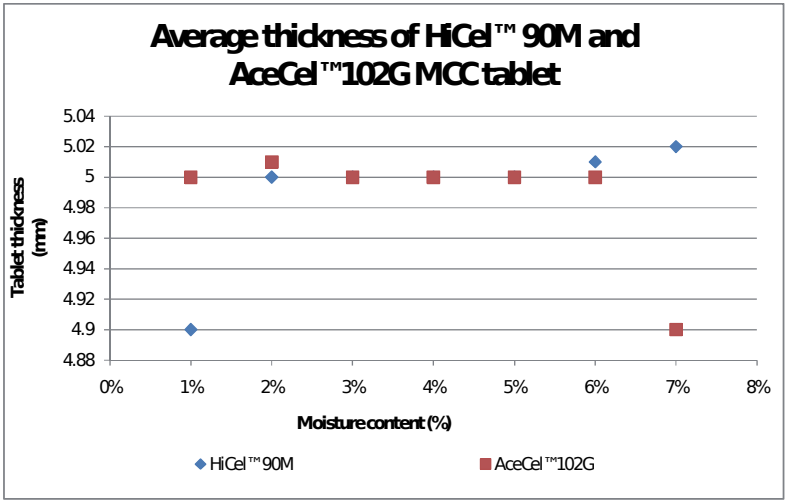

Fig.12 Average thickness of different moisture content sample of HiCel™ 90M and AceCel™102G microcrystalline cellulose

Friability of Tablet[17]

At first 10 tablets were taken. The tablets were carefully dusted prior to testing, then the 10 tablets were weighted electronic digital balance (Mettler Toledo,Model no. ML802/A01). Which was considered as the initial reading. After weight the tablets, all the tablets were placed in the drum of friability tester and rotate 100 times at 25 rpm. After 100 revolutions the 10 tablets were removed and re-weighted. This was the final reading. The percentage was calculated by following formula (equation 9). According to USP the tablets should not lose more than 1% of their total weight.

$$\%\,Friability = \frac{Tabletweightbeforfriability - TabletweightAfterfriability}{Tabletweightbeforefriability} \times 100 \qquad (9)$$

Friability of both grades tablets of microcrystalline cellulose decreases with decreased tablet hardness and increased moisture content of HiCel™ 90M and AceCel™ 102G. Investigated data are reported in table 8 and Fig 13.

Table8. Average Percentage Friability of HiCel™ 90M and AceCel™ 102G microcrystalline cellulose Tablets at different moisture content

Moisture Content (%)	HiCel™ 90M			AceCel™ 102G		
	Initial Weight (mg)	After Friability Weight (mg)	% of Friability (%)	Initial Weight (mg)	After Friability Weight (mg)	% of Friability (%)
1%	550	548.0	0.35	550	546.0	0.72
2%	550	548.4	0.29	550	547.0	0.55
3%	550	548.8	0.22	550	548.0	0.35
4%	550	549.0	0.18	550	548.2	0.33
5%	550	549.2	0.15	550	548.8	0.22
6%	550	548.1	0.36	550	547.0	0.55
7%	550	548.0	0.35	550	548.0	0.35

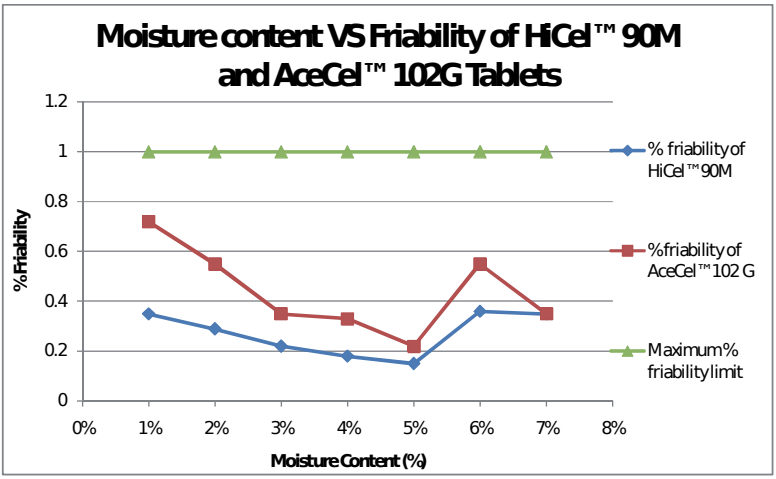

Fig.13Average % of friability of HiCel™ and AceCel™ 102 G microcrystalline cellulose tablets at different moisture content with maximum acceptable pharmacopoeial limit

EFFECT OF TEMPERATURE AND RELATIVE HUMIDITY ON HICEL^{TM}90MMCC

Microcrystalline cellulose (MCC) is one of the most commonly used tableting excipients and many of its properties depend on its moisture content However, moisture sorption by MCC has also been reported to cause stability problems for moisture sensitive drugs. The aim of this study was to investigate the influence of temperature and relative humidity on microcrystalline cellulose. However, the moisture of an unpacked material increases very quickly until the saturation point has been reached as evidenced by the isotherm.

The relationship between moisture content and relative humidity of microcrystalline cellulose was displayed graphically by a curve, the so-called moisture sorption isotherm. For each relativehumidity value, a sorption isothermindicates the corresponding moisture content value at a given, constant temperature.

Generally MCC is manufactured with 4-5% moisture content and for moisture sensitive drugs, low moisture grade are also available (1.5% moisture), however, these appear hygroscopic, and the moisture content of the samples is plotted as absorption of their facility at three different relative humidity.

Table 9.Moisture content of unpacked MCC sample at different humidity and temperature

Conditions: 30°C ± 2°C/65% RH ± 5% RH, open in polylined paper bag.					
Time	Initial	4 hrs	8 hrs	16 hrs	24 hrs
Moisture content %	4.60	5.30	5.46	6.29	7.13
Conditions: 40°C ± 2°C/75% RH ± 5% RH, open in polylined paper bag.					
Time	Initial	4 hrs	8 hrs	16 hrs	24 hrs
Moisture content %	4.60	5.27	5.39	6.23	7.11
Conditions: At room temperature, open in polylined paper bag.					
Time	Initial	4 hrs	8 hrs	16 hrs	24 hrs
Moisture content %	4.60	5.28	5.43	6.25	7.09

Table10.Moisture content of packed MCC sample at different humidity and temperature

Conditions: 30°C ± 2°C/65% RH ± 5% RH, in polylined paper bag				
Time	Initial	4 hrs	12 hrs	24 hrs
Moisture content %	4.60	4.62	4.62	4.63
Conditions: 40°C ± 2°C/75% RH ± 5% RH, in polylined paper bag				
Time	Initial	4 hrs	12 hrs	24 hrs
Moisture content %	4.60	4.62	4.63	4.63
Conditions: At room temperature, in polylined paper bag.				
Time	Initial	4 hrs	12 hrs	24 hrs
Moisture content %	4.60	4.61	4.61	4.62

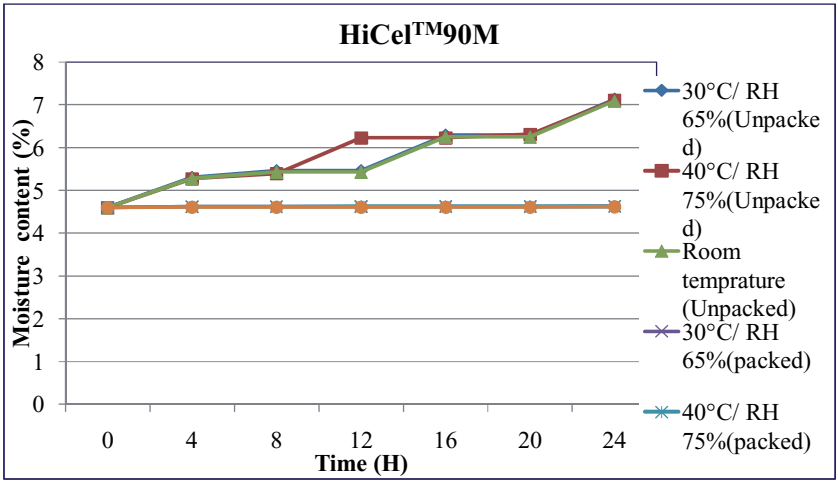

Fig.14 Moisture absorption behavior for theHiCel™90MMCC on different relative humidity and temperature

HiCel™ 90M MOISTURE STABILITY DURING BLENDING & TABLETING IN UNCONTROLLED AREA

HiCel™90M grade MCC is moisture stable even when being blended and tableting in an uncontrolled area. The variation of Moisture content as a %, wrt time is brought out below

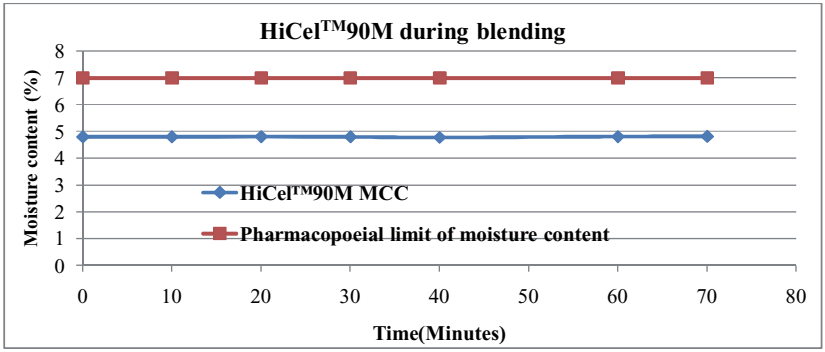

Fig.15:HiCel™90M during blending in ambient area

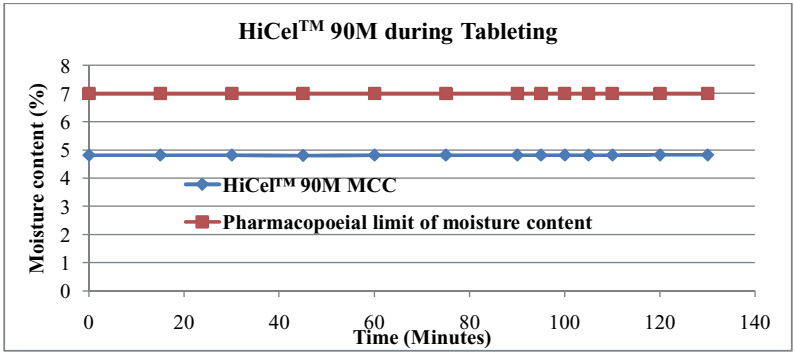

Fig.16 HiCel™ 90M during tableting in ambient area

Chapter 4

CONCLUSION

CONCLUSION

The variation of moisture content of microcrystalline cellulose is the quality parameter of product. It affects the quality of final product. In this study a correlation between moisture content and tablet hardness could be found. The hardness of tablet was lower at higher moisture content of both grades (HiCel™ 90M and AceCel™ 102G) of microcrystalline cellulose powder. No significant difference in resultant hardness was found between moisture content 4% and 5%. When Moisture content of HiCel™ 90M and AceCel™ 102G are 4% to 5%, hardness of tablet is high with low percentage of friability. This study found that high and extra low moisture content affects the tablet hardness and percentage of friability. HiCel™ 90M grade MCC absorbed 7.13% moisture on 30±2℃ and 65±2%RH in 24 hrs. When it's packed in polyliner bag and paper bag, no effect of humidity and temperature on HiCel™ 90M MCC. When HiCel™ 90M MCC is used in uncontrolled area, for the duration of blending and tableting the moisture level over the duration was found to be stable.

Chapter 5

REFERENCES

REFERENCES

1. Silverstein : Excipient quality and selection: Pharmaceutical technology Europe 2016; 28 (2):16-20.
2. Parsant, Nadavadekar, Sheeja Koliyote: Co-processed excipient for orally disintegrating dosase form. International Journal of Pharma Research and review 2014; 3(4):95-100.
3. H.Gerhardt Armin: Moisture effects on solid dosage forms –formulation, processing and stability. Journal of GXP Compliance 2009;(1):58-66.
4. Monika Tomar, Ajay Kumar Singh and Amit Raj Sinha: Physicochemical parameter of microcrystalline cellulose and the most acceptability in pharmaceutical Industries. Journal of Innovations in Pharaceuticals and biological Sciences 2015;2(4):570-578.
5. Monika Tomar, Ajay Kumar Singh and Amit Raj Sinha: Powder and tablet profile of microcrystalline cellulose (MCC) of different with degree of polymerization. International Journal of recent scientific research 2016; 7(6):12044-12047.
6. C.Ahlneck and G.Zografi:The molecular basis of moisture effects on the physical and chemical stability of drugs in the solid state. International Journal of Pharmacy 2004; 62:87-95.
7. Christensen H.,Johansen H.E. andSchaefer: Moisture activated dry granulation in a high shear mixture.Drug Devlopment and Industrial Pharmacy 2008; 14:2195-2213.
8. Gregory Thoorens, Fabrice Krier, Bruno Leclercq, Brain Calin and Brigitte Evard: Microcrystalline Cellulose, a direct compression binder in a quality by design environment-A review. International Journal of Pharmaceutics 2014; 473(1-2):64-72.
9. Anna Penkina, Osmo Antikainen, maija Hakola Sirpa Vuorinen, Timorepo, Jouko Yliruusi Peep Veski, Karin Kogermannn and Jyrki Heinamaki: Direct

compression of cellulose and lignin isolated by a new catalytic treatment. Journal of AAPS PharmaSciTech 2013; 14(3):1129-1136.

10. Alfonso R Gennaro:Remington-The Science and Practices of Pharmacy.Lippinocott Williams & Wilkins, twenty edition 2001.
11. Liliana A., Mlinea,M.Rajendra, M.Kallam, James A.,Farina and Deorkar Nandu: Evaluation and characteristics of a new direct compression performance excipient 2011; 3:1-8.
12. Shlieout G., Arnold K. and Muller G.:Powder and Mechnical properties of microcrystalline cellulose with different degree of polymerization2002; 3:1-10.
13. United State Pharmacopeia 38: NF332015;6596-6597.
14. Martin Alfred: Physical Pharmacy.B.I.Waverey,sixth edition 2011.
15. Lachman:The Theory and Practice of Industrial Pharmacy.Varghese Publishing House, Third edition1987.
16. Soppela Ira,Airaksinen Sari, Motti Murtoma,Tenho Mikko, HataraJuha,Raikkanen Heikki,Y.Jouko,S.Niklas:Investigation of powder flow behavious of binary mixture of microcrystalline cellulose & paracetamol. International Journal of recent science of research 2015;2(5):1123-1125.
17. United State Pharmacopeia 39: NF34.
18. Horhata ST, Burgio J, Lonski L and Rhodesb CT: Effect of storage at specified temperature and humidity on properties of the direct compressible tablet formulation. Journal of pharmaceutical Science 2012;5(12):1746-1749.