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EFFECT OF MOISTURE CONTENT OF EXICIPIENT (MICROCRYSTALLINE CELLULOSE) ON DIRECT COMPRESSIBLE SOLID DOSAGE FORMS

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Keywords:

Quality parameters, Microcrystalline cellulose, Moisture content, Tablet hardness, Weight variation, Percentage Friability

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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 a very 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.

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].

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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 excipients and 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 final product 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 on 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 hydroxyproply methyl cellulose (HPMC) [7, 8, 9].

HiCel™ Microcrystalline cellulose is a common excipient used for tabletting 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 % which is good for direct compression formulation, while USP monograph specification limit is not more than 7%. A number of studies have confirmed that higher and extra low moisture content of Microcrystalline Cellulose influence the hardness of direct compressible tablets. We are using Hicel™ 90M and AceCel™ 102G Microcrystalline Cellulose for this study.

MATERIAL AND METHOD:

Material: HiCel™ 90M (Spray Dried Microcrystalline Cellulose) and AceCel™ 102G (Air Stream dried Microcrystalline 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. Proton mini press (model 10 STN "D") "D" type tooling machine was used for makeing the tablets. Digital tablet hardness taster (Labindia model no.TH1050M) was used for test tablet hardness. Friability test done at Baroda analytical services in Vadodara, Gujarat.

Method:

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 ™ 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, Calculate moisture content by using the following formula.

Moisture content =

$$\frac{\text{After drying weight of shallow bottle} - \text{empty weight of shallow bottle}}{\text{Sample weight in gram}} \text{ X } 100 \quad \text{..... (1)}$$

Tablet Compaction: [5, 6, 15] 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.

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 2) The pharmacopeial limit of weight variation is mentioned in (**Table 1**) .

$$\text{Average weight of tablet} = \frac{\text{Total weight of tablets}}{\text{Total no.of tablets}} \quad \text{..... (2)}$$

TABLE 1: WEIGHT VARIATION TEST LIMITS FOR TABLETS (USP)

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 %

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.

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 3). According to USP the tablets should not lose more than 1% of their total weight.

$$\% \text{ Friability} = \frac{\text{Tablet weight befor friability} - \text{Tablet weight After friability}}{\text{Tablet weight beforefriability}} \times 100 \quad \text{..... (3)}$$

RESULT AND DISCUSSION:

Moisture Content: Moisture content of both grades (HiCel™ 90M and AceCel™ 102G) of Microcrystalline Cellulose were investigated and summarized in the **Table 2**.

TABLE 2: 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

Compaction and General Appearances of tablet: Tablets of both grades (HiCel™ 90M and AceCel™ 102G) are ~500mg weight; all tablets are made at 3.25 tone release pressure, and other related data of tablets mention in **Tablet 3**.

TABLE 3: GENERAL APPEARANCES OF TABLET

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

Weight variation of Tablet: All the tablets of both grades are passed in uniformity weight test, i.e. weight variation was found within the pharmacopeial limit shown in **Table 4** and **5**, and **Fig.1** and **2**.

TABLE 4: WEIGHT VARIATION OF HICEL™ 90M 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 5: WEIGHT VARIATION OF ACECEL™ 102 G 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

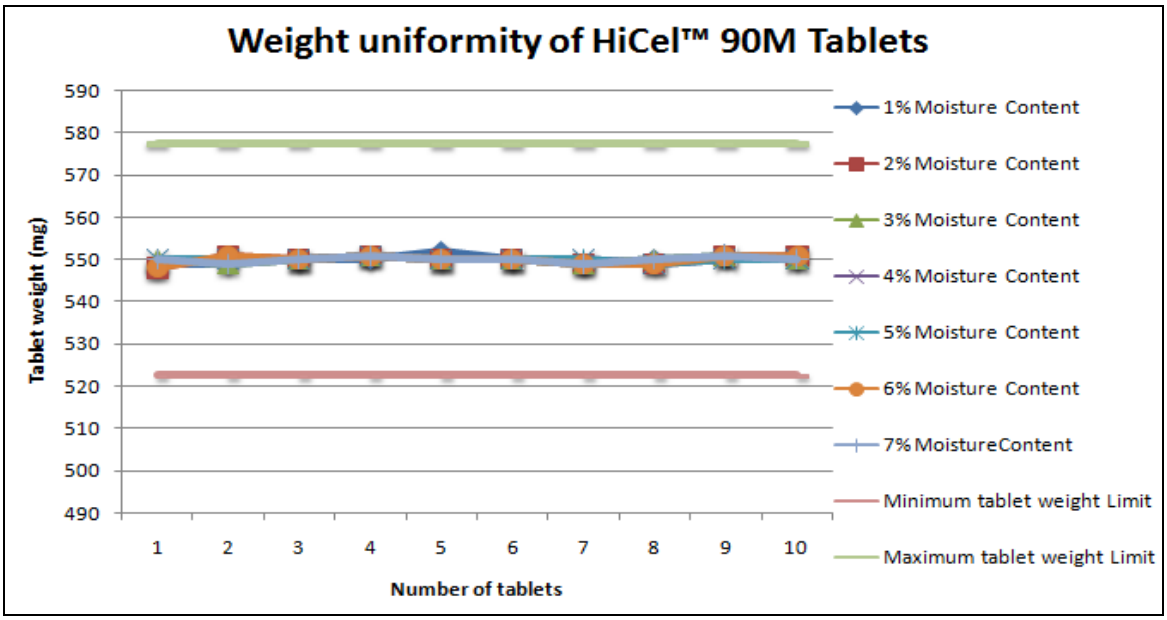

FIG.1: WEIGHT VARIATION OF HICEL™ 90 M TABLETS AT DIFFERENT MOISTURE CONTENT WITH MINIMUM AND MAXIMUM PHARMACOPEIAL LIMIT

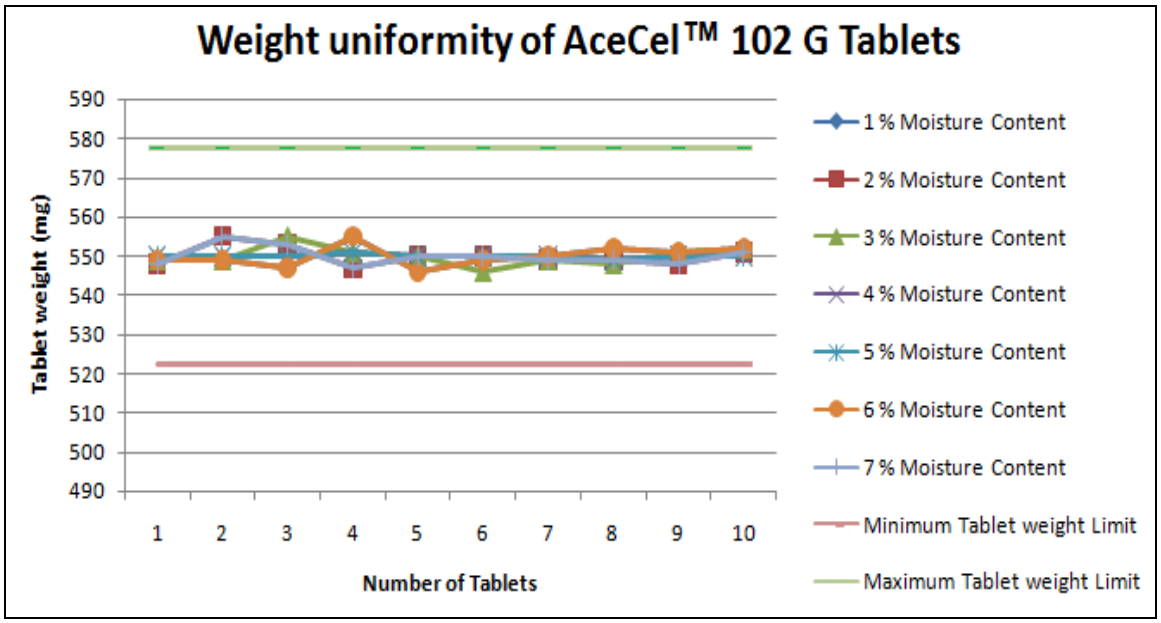

FIG.2: WEIGHT VARIATION OF ACECEL™ 102 G TABLETS AT DIFFERENT MOISTURE CONTENT WITH MINIMUM AND MAXIMUM PHARMACOPEIAL LIMIT

Hardness variation of Tablet: Tablet hardness of both grades are decreasing with increasing the moisture content of both grades of microcrystalline cellulose related details are mentioned in **Table 6** and **Fig.3**.

Note [18]: It is to be noted that atmospheric condition of room i.e. temperature and humididty may affect the tablet hardness. In case may be excerissed to maintain relative humidity (RH) range of 53% and temperature 23±1 ^{o}C.

TABLE 6: DIFFERENT MOISTURE CONTENT AND AVERAGE HARDNESS OF HICEL™ 90M AND ACECEL™ 102G TABLETS

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

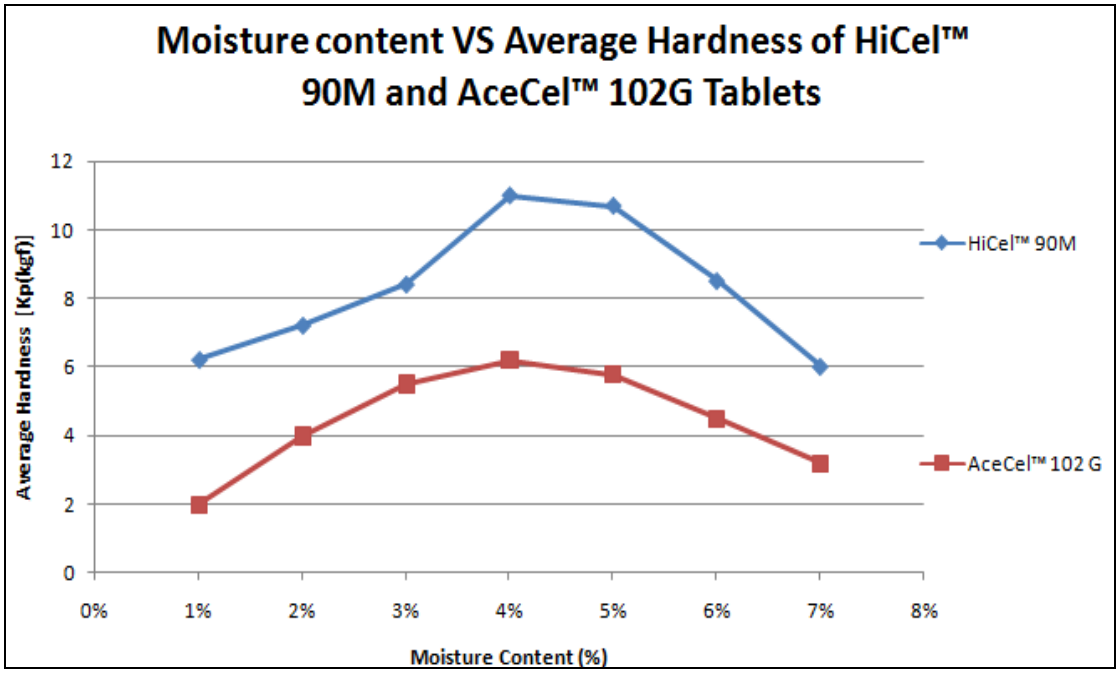

FIG.3: AVERAGE HARDNESS OF HICEL™ 90M AND ACECEL™ 102 G TABLETS AT DIFFERENT MOISTURE CONTENT

Friability of Tablet: 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 7** and **Fig. 4.**

TABLE 7: AVERAGE PERCENTAGE FRIABILITY OF OF HICEL™ 90M AND ACECEL™ 102G 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

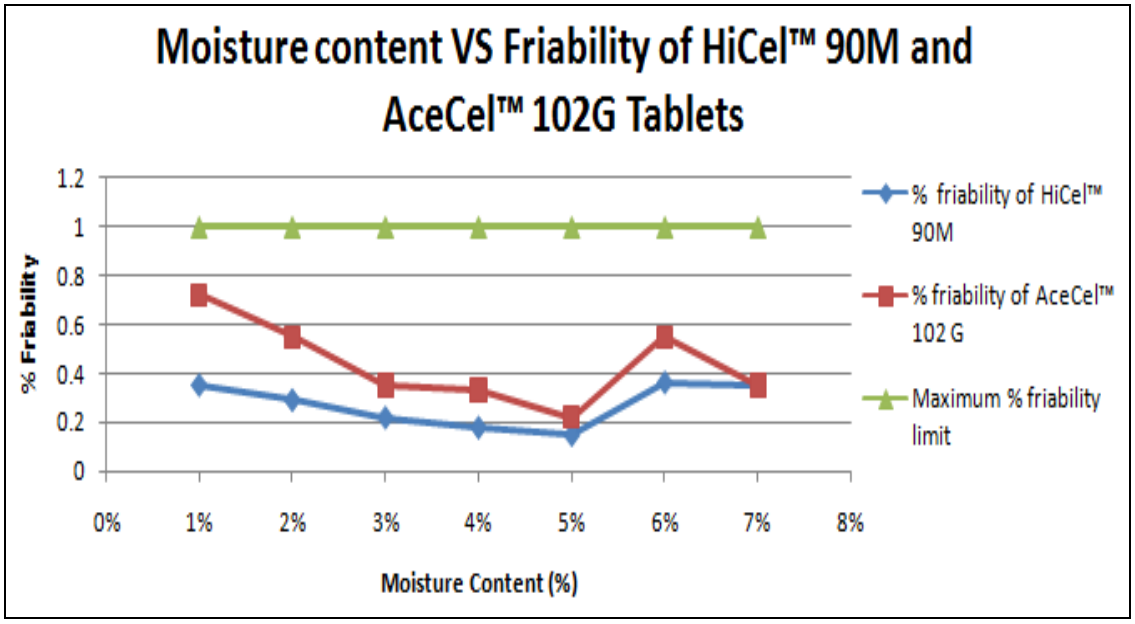

FIG. 4: AVERAGE % OF FRIABILITY OF HICEL™ AND ACECEL™ 102 G TABLETS AT DIFFERENT MOISTURE CONTENT WITH MAXIMUM ACCEPTABLE PHARMACOPEIAL LIMIT

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.

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