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RESEARCH ARTICLE

A COMPARATIVE STUDY OF MOISTURE SORPTION ON HICEL™SMCC, HICEL™MCC AND PHYSICAL BLEND OF HICEL™MCC AND COLLOIDAL SILICON DIOXIDE, FORMULATION AND EVALUATION OF DISPERSIBLE TABLET OF ACETYL SALICYLIC ACID

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ABSTRACT

Moisture content is a critical parameter for manufacturing oral solid dosage forms. It should be maintained as per requirement moisture content beyond the limits of less than 4% or higher than 5.5% affect tablet properties i.e. hardness, friability and disintegration time. In this article, we will done comparative study of moisture sorption on HiCel™ MCC 90M (Microcrystalline cellulose), HiCel™SMCC 90M (Silicified Microcrystalline cellulose) and physical blend of HiCel™MCC 90M(Microcrystalline cellulose) and colloidal silicon dioxide and also discuss manufacturing process of HiCel™MCC 90M, HiCel™SMCC 90M and Physical blend with HiCel™MCC and Colloidal silicon dioxide. We will make dispersible Acetyl salicylic acid tablet using them and evaluate the comparative study. HiCel™SMCC 90M would show improved tablet properties in terms of better compaction, hardness, friability and disintegration than HiCel™MCC 90M and physical blend of HiCel™MCC and Colloidal silicon dioxide.

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INTRODUCTION

Powder properties and behavior are critical to efficient manufacturing of pharmaceutical tablets. The presence of moisture content in excipients (MCC and SMCC) play an important role in the manufacturing process of tablets. Moisture content of excipients should be maintained in a specified limit, if it is more or less from specify limit, it affects the tablet profile (Crouter, 2004). The ability of a powder to take up water vapor from the atmosphere is called "hygroscopicity" (Armin, 2009). It is classified based on the rate and amount of water uptake from the atmosphere with changes in the air humidity. A non-hygroscopic powder shows almost no changes in moisture content with exposure to air below 90% relative humidity while very hygroscopic power moisture content would increase rapidly in air with low relative humidity (Nokhodchi Ali, 2005). MCC and SMCC can absorb water from atmosphere which are in different physical states: (a) Condensed water on the surface of particles, (b) Absorbed by monolayer, (c) Absorbed by multilayers on the surface of particles, (d) absorbed water within the particle physically and (e) Chemisorbed water(Crouter Allison, 2014).

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The state and distribution of water depends on the amount of water taken up through exposure to humid air and temperature. Generally pharmaceutical industries maintain possible range in relative humidity from 25 to 75% at a temperature of 25-30°C (Ahmad Iqbal, 1994). Many literatures report moisture content of 5–6% for microcrystalline cellulose (MCC) during routine handling under ambient conditions (25-30°C temperature and 40–50% relative humidity. As per reported data the moisture content of a powder can vary during pharmaceutical handling and manufacturing and that these variations could have an impact upon the process and final tablet quality (Crouter Allison, 2014 and Islam, 2008). HiCel™MCC is widely used in the pharmaceutical industry. The effect of moisture content on the behavior of MCC has been investigated in a number of studies. Many literatures found that if moisture content is between 4 to 5.5 %, it is acting as a plasticizer due to presence of water (Tomar, 2017). The most suitable and acceptable moisture content in the range of 4 to 5.5% with a selective humidity of 20-50%, below 4%, there are almost no changes while above 4% the behavior of the MCC powder changes significantly, higher than 5.5% moisture content adversely effects the MCC powder profile and also the tableting profile (Tomar, 2017; Shlieout, 2002). Flow is critical issue during tablet manufacturing. HiCel™MCC flow is good and uniform flow into the tablet dies ensures tablet weight uniformity and production of tablets with consistent and reproducible

properties (Peter Peciar, 2016) HiCel^{TM}MCC flows from the hopper into the tablet dies when gravitational forces become higher than particle–particle interaction forces. Friction and cohesion are the major particle–particle interaction forces. Friction acts at contact points between particles to oppose the relative motion of the particles. Particle shape and surface morphology affect contact and therefore can increase friction if contact area is increased (Tomar, 2017; Saigal, 2009). Water on the particle surface can act as a lubricant decreasing friction. Cohesion refers to the attraction between particles and includes Vander-Waals forces, capillary force, electrical force, and electrostatic force (Islam, 2008.) Water primarily affects cohesion by increasing capillary forces through strengthening liquid bridges between particles (Fechner, 2013). In this study, we elucidate effect of moisture sorption on HiCel^{TM}MCC90M, HiCel^{TM}SMCC90M and physical blend of HiCel^{TM}MCC90M and colloidal silicon dioxide at different temperature, relative humidity and ambient conditions and compare the result of all the three. Manufacturing Aspirin tablet using HiCel^{TM}MCC90M, HiCel^{TM}SMCC90M and Physical blend of HiCel^{TM}MCC90M and Colloidal silicon dioxide by direct compression and evaluate comparative tablet profile.

MATERIALS AND METHODS

HiCel^{TM}MCC90, HiCel^{TM}SMCC90M manufactured at "Sigachi Industries Pvt. Ltd" and colloidal silicon dioxide purchased from "Wacker", were used to investigate this study**.** Acetyl Salicylic acid purchased from "The Andhra sugars limited" Povidone K-30 taken form "Anshul Life science and Purified Talc were used for manufacturing dispersible Acetyl salicylic acid tablet. Two stability Chambers (Thermolab, Model no-TS0000325 S) were used for state of water in powder. Digital weight balance (Model no-ML802/A01, MS 303 S/A01, MS204S /A01) used for weighing 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 making the tablets. Digital tablet hardness taster (Labindia model no.TH1050M) was used for test tablet hardness. Friability tester (Labindia, model no- FT 1020) used for analysis tablet friability test.

METHODS

Preparation of HiCel^{TM} MCC

Dissolving grade 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 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. Slurry is made from the above and spray dried (Tomar, 2015).

Preparation of HiCel^{TM} SMCC

Take Colloidal silicon dioxide 2% and HiCel^{TM}MCC 98%, make slurry of the both combination and dry with the help of spray dryer (Tomar, 2017).

Preparation of physical blend with HiCel^{TM} MCC and Colloidal silicon dioxide: Take Colloidal silicon dioxide 2% and HiCel^{TM}MCC 98%, both samples are blended with the help of blender, in a 3 stages blending process (Tobyn, 1998).

Evaluation of Moisture Sorption

State of water in HiCel^{TM}MCC and HiCel^{TM} SMCC (Nokhodchi, 2005)

In this study we used three different samples HiCel^{TM}MCC 90M, HiCel^{TM}SMCC 90M and physical blend with HiCel^{TM}MCC90M and colloidal silicon dioxide and carried out moisture sorption at different temperature and relative humidity (1) 65% RH, 30°C, (2) 75% RH, 40°C using stability chambers (Thermolab, Model no-TS0000325 S) and (3) ambient condition (Temperature 25°C ±3°C and relative humidity 42%±10%) for 30 hrs. Samples were exposed in a polyliner bag. Took samples at different-different time intervals from each sample (intervals mentioned in the table).

Moisture Content

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 MCC sample 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 (United state pharmacopoeia 39 NF 34)

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

…… (2)

Preparation of dispersible tablets of Aspirin

Dispersible tablets containing 300mg Acetyl salicylic acid were prepared by direct compression method and by using various excipients which is shown table no.5. Each formulation having different excipients used in same quantity. Required material was measure accurately and mixed uniformly. The prepared blend powder was evaluated for various parameters like untapped density, tapped density, angle of repose and hausner ratio. After evaluation of blend powder, the tablets were compressed with 10-station proton mini press tableting machine (Model no. MINI PRESS 10 "D") using D tolling dies and punches. The operating pressure ranges of machine is 10 to 60 KN (Zachariah Markose, 2016).

Evaluation of powder blend

Angle of repose

Pour 30g of sample through pour on powder flow tester (#10 mesh size), 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 check natural tangents chart for angle of repose and reported (Tobyn, 1998).

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

Where
h = height of S.S cylinder
d = diameter of S.S cylinder

Bulk density (Tomar, 2016)

Untapped density

Untapped density is analyzed through graduated measuring cylinder class A. Take 20 gm of sample using weight balance (Toledo, Model No.-ML 802 /A01) and poured into a graduated A grade 100 ml capacity cylinder slowly from the sidewall. Level the surface of sample in cylinder by slow movement, note down the occupied volume, and calculate the untapped density of sample by using following formula.

$$\text{Untapped density} = \frac{Weight\ of\ powder\ in\ gram}{Occupied\ volume\ in\ mL} \quad \ldots\ldots\ldots\ldots\ (3)$$

Tapped density

Tapped density was anlaysed by using (Electro lab instrument, Model No. ETD1020), measuring cylinder placed in tapped density machine and fixed 500 tapped. After 500 tapes measured the volume of measuring cylinder and calculate the tapped density by using following formula.

$$\text{Tapped density} = \frac{Weight\ of\ powder\ in\ gram}{Occupied\ volume\ in\ mL} \quad \ldots\ldots\ldots\ldots\ (4)$$

Hausner's ratio

Hausner ratio is another method to check flow of powder. The flow of powder was measured by "Hausner ratio". Tapped density is divided by untapped density. Formula is mention below.

$$\text{H.Ratio} = \frac{Tapped\ density}{Untapped\ density} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ (5)$$

Evaluation dispersible tablet of acetyl salicylic acid

Weight Variation test

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 (Jayaprakash, 2012).

$$Average\ weight\ of\ tablet = \frac{Total\ weight\ of\ tablets}{Total\ no.of\ tablets} \quad \ldots\ldots\ (6)$$

Tablet Hardness

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 (Jayaprakash, 2012).

Tablet Thickness

10 tablets were taken from each batch. Each tablet place between two arms of the Varnier calipers, note down the reading from the scale (Horhata, 2012).

Tablet Friability

At first 10 tablets were taken. The tablets were carefully dusted prior to testing, then the 10 tablets were weighed electronic digital balance (Mettler Toledo, Model no. MS303/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, then tablets were removed and re-weighted. This was the final reading. The percentage was calculated by following formula. According to United state pharmacopoeia (USP) the tablets should not lose more than 1% of their total weight (Lachman, 1987).

$$\%\ Friability = \frac{Tablet\ weight\ befor\ friability - Tablet\ weight\ After\ friability}{Tablet\ weight\ beforefriability} \times 100 \quad \ldots\ldots\ldots\ (7)$$

Table 1. Physical analysis of HiCel^{TM}MCC 90M, HiCel^{TM}SMCC 90Mand physical blend of HiCel^{TM}MCC90M and Colloidal silicon dioxide

Name of parameter	HiCel^{TM} MCC	HiCel^{TM}SMCC	Physical blend of HiCel^{TM}MCC90M and Colloidal silicon dioxide
Untapped density (g/cc)	0.32	0.32	0.32
Tapped density (g/cc)	0.46	0.44	0.50
Hausner ratio	1.44	1.38	1.56
Angle of repose	38	36	37°30'

In-vitro disintegration time

This test was carried out at 37±2°C in 900 ml of dematerialized water. Six tablets were taken and one tablets was introduce in each tube disk was placed and basket was positioned in 1 liter beaker containing 37±2°C temperature of water. Note down tablet disintegration time.

RESULTS

HiCel^{TM} SMCC, HiCel^{TM}MCC and Physical blend of HiCel^{TM}MCC90M and Colloidal silicon dioxide

HiCel^{TM}MCC 90M, HiCel^{TM} SMCC 90M and physical blend were free flowing, granular powder. Physical parameters are shown in Table no.1.

Note- Colloidal silicon dioxide has dusting nature; it is very difficult to handle duration of physical blend.

Moisture content

We have checked the moisture content of the three samples (HiCel^{TM}MCC 90M, HiCel^{TM} SMCC 90M and Physical blend of HiCel^{TM}MCC90M and Colloidal silicon dioxide at

different-different time intervals. The results of all samples are mentioned in Table no.2, 3 and 4 respectively.

Manufacturing formula of dispersible tablet of acetyl salicylic acid

Weight required quantity of all samples and blend properly. All required material mentioned in Table no.5.

Physical parameters evaluation of acetyl salicylic acid powder blend: After blending analysis below mention parameter of all batches and proceed for making tablets.

Evaluation of Dispersible Acetyl Salicylic Acid

Weight variation: All batches tablets are under pharmacopoeia acceptable limits (±5 %.individual tablet weight shows in the Fig no.1.

Table no.2.Moisture content analyses of HiCel^{TM}MCC 90M at different temperature and relative humidity

Moisture content study of HiCel^{TM} MCC 90M			
Temperature and relative humidity Time Intervals (Hrs)	30±2 °C /65±5 % RH	40±2 °C /75±5 % RH	Ambient condition (Temperature 25°C ±3°C and relative humidity 42%±10%)
Initial	4.60	4.60	4.60
02	5.05	4.98	4.94
04	5.30	5.27	5.28
08	5.46	5.39	5.43
16	6.29	6.23	6.25
20	6.85	6.70	6.66
24	7.13	7.11	7.09

Table 3. Moisture content analyses of HiCel^{TM}SMCC 90M at different temperature and relative humidity

Moisture content study of HiCel^{TM} SMCC 90M			
Temperature and relative humidity Time Intervals (Hrs)	30±2 °C /65±5 % RH	40±2 °C /75±5 % RH	Ambient condition (Temperature 25°C ±3°C and relative humidity 42%±10%)
Initial	4.58	4.58	4.58
02	4.75	4.73	4.69
04	4.97	4.95	4.86
08	4.98	4.97	4.92
16	5.67	5.59	5.63
20	5.98	5.97	5.95
24	6.07	6.03	6.00

Table 4. Moisture content analyses of physical blend with HiCel^{TM}MCC and Colloidal silicon dioxide at different temperature and relative humidity

Moisture content of physical blend with HiCel^{TM}MCC and Colloidal silicon dioxide			
Temperature and relative humidity Time Intervals (Hrs)	30±2 °C /65±5 % RH	40±2 °C /75±5 % RH	Ambient condition (Temperature 25°C ±3°C and relative humidity 42%±10%)
Initial	4.65	4.65	4.65
02	4.90	4.89	4.69
04	5.00	4.97	4.86
08	5.02	4.99	4.92
16	5.67	5.59	5.58
20	6.07	5.97	5.90
24	6.35	6.27	6.15

Table 5. Tablet manufacturing formula of dispersible tablet of acetyl salicylic acid

Description	Quantity (mg)		
	HiCel^{TM} MCC	HiCel^{TM}SMCC	Physical blend
Batch no.	A1	A2	A3
Actyl salicylic acid	300 mg	300 mg	300 mg
HiCel^{TM} MCC 90M	240 mg	--	--
HiCel^{TM} SMCC 90M	--	240mg	--
Physical blend (HiCel^{TM}MCC 90M+ Colloidal silicon dioxide)	--	--	240
Povidone	58 mg	58 mg	58 mg
Purified talc	2mg	2mg	2mg
Total mass of tablet	600 mg	600 mg	600 mg

Table no.7. Pre compression parameter data for Acetyl salicylic acid powder blend

Name of parameter	A1	A2	A3
Untapped density (g/cc	0.534	0.519	0.541
Tapped density (g/cc	0.70	0.615	0.635
Hausner ratio	1.31	1.18	1.17
Angle of repose	33°40’	31°	32°10’

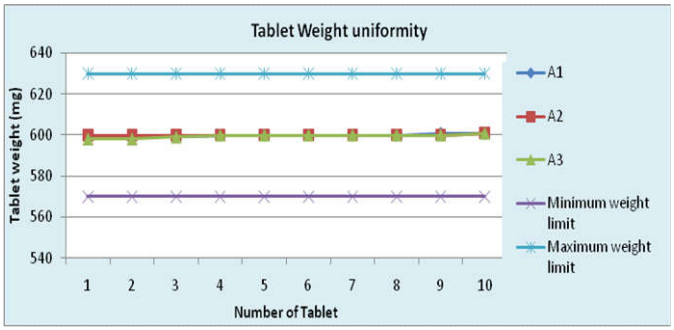

Fig. 1. Weight uniformity of Acetyl salicylic acid tablet (A1- tablet manufacturing with HiCel™MCC, A2- HiCel™SMCC and A3- Physical blend)

Hardness

Tablet hardness of all batches mention in Fig. no. 2.

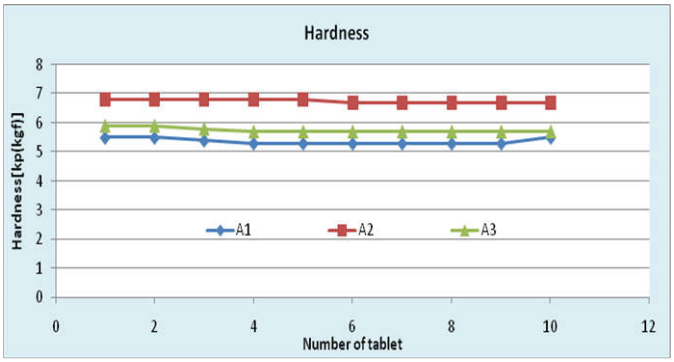

Fig. 2. Hardness of individual Acetyl salicylic acid tablet (A1- tablet manufacturing with HiCel™MCC, A2- HiCel™SMCC and A3- Physical blend)

Thickness

Average tablet thickness of all batches has 6mm and is shown in Table no.8.

Friability

Percentage loss of tablets of all batches mentioned in Fig no.3.

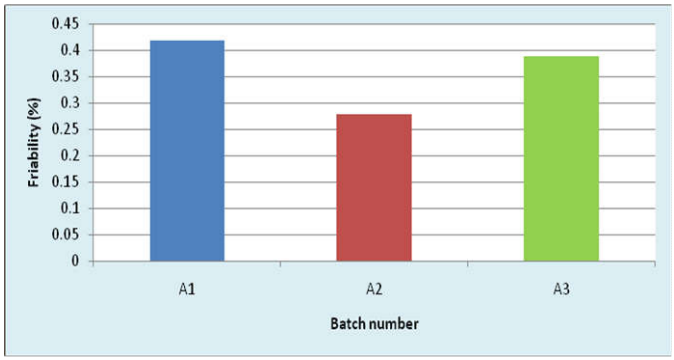

Fig. 3. Friability of Acetyl salicylic acid tablet (A1- tablet manufacturing with HiCel™MCC, A2- HiCel™SMCC and A3- Physical blend)

Disintegration

Tablets disintegration of all batches mentioned in Fig no.4.

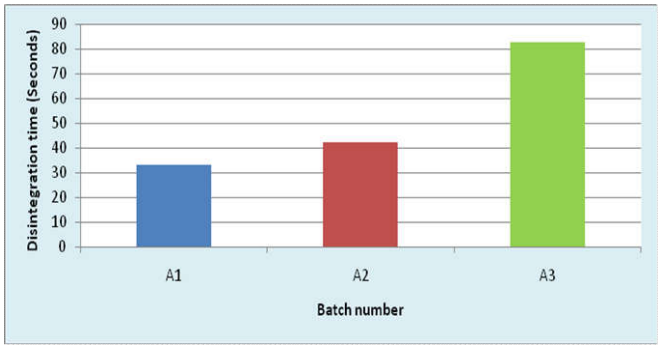

Fig. 4. Average disintegration time of Acetyl salicylic acid tablet (A1- tablet manufacturing with HiCel™MCC, A2- HiCel™SMCC and A3- Physical blend)

DISCUSSION

HiCel™MCC and HiCel™SMCC both are manufactured by spray dryer, physical blend of HiCel™MCC and colloidal silicon dioxide is dry blending. HiCel™MCC (Microcrystalline cellulose) 90M is more hygroscopic than HiCel™SMCC and colloidal silicon dioxide. All three samples at ambient condition absorbed lowest moisture. 40±2°C and 75±5% RH and 30±2°C and 65±5% RH absorbed about to same moisture content, related data mentioned in fig.no.6,7 and 8.We manufactured dispersible Acetyl salicylic acid tablet using HiCel™MCC, HiCel™ SMCC and physical blend, SMCC has superior powder profile with respect to angle of repose and hausner ratio before and after blend than MCC and physical blend. All batches tablets were manufactured at same compaction force. No weight variation observed. Batch no. A1, A2 and A3 tableting profile (weight, hardness, friability and disintegration time) summarize in Table no. 8.

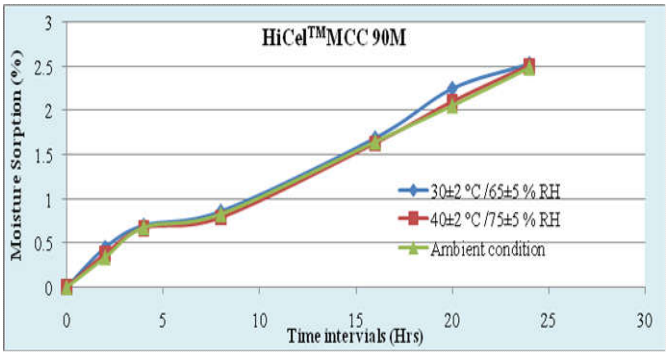

Fig. 5. Moisture sorption in percentage of HiCel™MCC (Microcrystalline Cellulose)

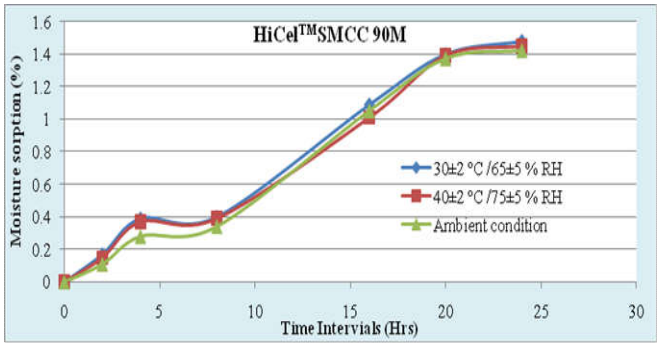

Fig . 6. Moisture sorption in percentage of HiCel™SMCC (Silicified Microcrystalline Cellulose)

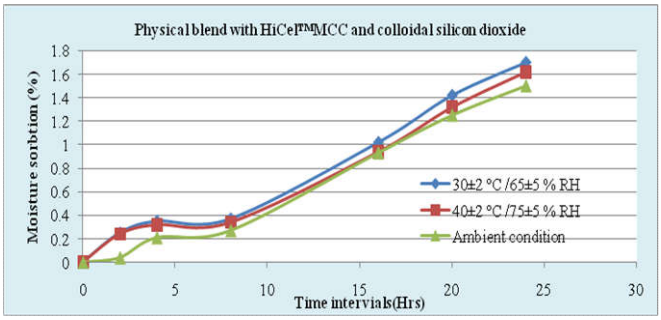

Fig. 7. Moisture sorption in percentage of Physical blend with HiCel™MCC and colloidal silicon dioxide

Table 8. Tablet profile of dispersible tablet of acetyl salicylic acid

Name of parameter	A1	A2	A3
Average Weight (mg)	600	600	600
Average Hardness [kp(kgf)]	5.37	6.75	5.75
Thickness (mm)	6.00	6.00	6.00
Friability (%)	0.42	0.28	0.39
Disintegration Time (Seconds)	33	42.5	83

Conclusion

HiCel^{TM} SMCC 90M has superior flow property than physical blend of HiCel^{TM}MCC and Colloidal silicon dioxide and HiCel^{TM}MCC 90M. The moisture sorption of HiCel^{TM}MCC, HiCel^{TM}SMCC and Colloidal silicon dioxide varies with temperature and relative humidity. HiCel^{TM}SMCC 90M absorbed less moisture than HiCel^{TM}SMCC 90M.Tablet profile of dispersible acetyl salicylic acid Batch A2 has excellent tablet profile Hardness 6.75[kp(kgf)], friability is 0.28% and Disintegration time 42.5 seconds i.e. proved that HiCel^{TM} SMCC has improved tablet profile.

Abbreviation

MCC: Microcrystalline Cellulose, SMCC: Silicified Microcrystalline Cellulose, RH: Relative humidity, Temp: Temperature, STN: Station, FT: Friability, g: gram, mg: milligram, L: liter, S.S: Stain less steel, °C: centigrade, °: degree, %: percentage, H: Height, L: length, d: diameter, USP: United state pharmacopoeia, ml: milliliter, g/cc: gram per cubic centimeter square, Hrs: Hours, mm: millimeter.

Conflicts of interests

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

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