EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 11
Issue: 1
109-115
Year: 2024

CHARACTERIZATION AND PERFORMANCE EVALUATION OF HICEL HFS IN DIRECT COMPRESSION TABLET FORMULATION

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Article Received on 03/11/2023 **Article Revised on 24/11/2023** **Article Accepted on 14/12/2023**

ABSTRACT
Direct Compression is the shortest method to manufacture tablets and co-processed excipient is the best choice for direct compression tablet formulation due to its outstanding physical properties. HiCel™ HFS is manufactured using the co-processed method and contains Mannitol, colloidal silicon dioxide, and a binder. A preferred binder is Microcrystalline cellulose. The composition has improved compressibility, particle size, lubrication sensitivity, and ejection force during tableting and gives higher tablet hardness at low compression force compared to individual excipient dry mix or either alone in the preparation of solid dosage form Tablet formulation. Tablets comprising the co-processed composition, an active, and optionally or more other excipient. This co-processed excipient composition was also suitable for Pharmaceutical, herbal, and nutraceutical tablets, it helps to protect API from moisture, and it will help to improve the flow of herbal extract flow and reduce die-frication during tableting. In this study, we will discuss the superiority of HiCel™ HFS like characterization, evaluation, and tableting.

KEYWORDS: Moisture Sensitive, Compressibility, Direct Compression, Scanning Electron Microscope (SEM), FTIR.

INTRODUCTION
Manufacturing a tablet requires a Pharmaceutical Active Ingredient and a variety of excipients. Excipients are used to provide bulk and essential properties of the dosage form.[1] Solid dosage forms are easy to manufacture and handle. Tablet is the easiest way to administer pharmaceutical activity. When manufacturing a tablet requires a binder to bind the API, a glidant to increase the flow of the blend, a disintegrant to break down the tablet into pieces after administration and enhance the dissolution rate of the tablet, and used lubricant to increase flow and reduce die friction during tableting, and sometimes used taste masking agent to mask taste when API having a bitter taste.[2] Microcrystalline cellulose (MCC), Mannitol, and colloidal silicon dioxide (CSD) are individually used in pharmaceutical industries to manufacture tablet formulations. MCC generally known as dry binder, provides sufficient flow with superior binding properties. Whereas Mannitol is used as a sweetening agent, or as a binder, filler it helps to tablet disintegrate fast. Colloidal silicon dioxide is used as a glidant or flow enhancer in formulation industries.[3]

Generally, three methods are commonly used to manufacture tablet formulation direct compression, wet granulation, and Dry granulation. Direct compression is the shortest and cheapest method to making tablets than wet granulation and dry granulation.[4] But the selection of excipients for the direct compression method is very difficult. In the direct compression method, each excipient should be free-flowable. Direct compression method excipient should have superior physical properties like free-flowing flow, superior binding and enhanced disintegration and dissolution profile. A very important excipient should be Carrie's equal quantity of the API throughout the batch. This means mentioned weight and drug content are uniform in all tablets. In Direct compression method mix binder, glidant and disintegrant together after that added API and mixed again. At the last step mixed lubricating agents and compressed tablet. The direct compression method is less expensive because less equipment is required, less power consumption, less labour consumption.[5] Co-processed excipients are well-suited excipient for DC formulation because co-processed excipient has outstanding flowability. it improves API flowability when it is used in formulation. Co-processing technology makes the individual excipient superior in physical properties.

Improves flow, bulk density, particle size, surface area and morphology but not changes in chemical structure of the product. Whereas wet granulation is old method to make tablet in pharmaceutical Industries.[6] It contains multiple steps, mixing the API with the excipient. Add binder solution to bind API thereafter the dump mass is screened and dry the graduation with the help of a try drier and other suitable driers. Screen the granules and add lubricant to lubricate the material after that compress the tablets. Yield is also loss during multiple stages. However, the Wet granulation method is not suitable for all API because some APIs are heat sensitive, and some APIs are not compatible with solvents and dyes. Dry granulation used where flow is poor and bulk density is less. The method includes mixing the ingredients, roller compacting or slugging the mix, dry screening or milling the coarse dry granulate, lubricating, and finally compressing the lubricated granules. In this article, we will evaluate co-processed excipient HiCel HFS physical parameters and their application in oral solid dosage forms.[7]

Aceclofenac tablets are manufactured using HiCel HFS, whereas Aceclofenac has poor solubility in the water. HiCel HFS helps to increase the solubility of API and the improved dissolution rate of Aceclofenac tablets. We studied characteristics of HiCel HFS through FTIR and SEM and physical properties like bulk density, PSD, compressibility index and angle of repose.[8]

MATERIAL AND METHODS

Material

HiCel™ binder manufactured at Sigachi Industries Ltd. in Dahej, Gujarat, Filler Purchased from Labort Fine Chem Pvt. Ltd Gujarat, Glidant Purchased from Nilkon Corporation, Wacker Germany. Aceclofenac Purchased from Saral Chemtech LLP, Muzaffarnagar, U.P, and other chemicals AR grade are used in this study.

METHOD

Characterization Study

Fourier - Transform Infrared Spectroscopy (FTIR)

Fourier - Transform Infrared Spectroscopy (FTIR) spectroscopy was conducted using an IR Spirit-S (Shimadzu, Tokyo, Japan) and the spectrum was recorded in the wavelength region from 4000 to 400 cm^{-1}. The procedure consisted of dispersing a sample in KBr and compressing it into disc by applying a pressure of 10 tons for 2 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained.[9]

Scanning Electron Microscope (SEM)

Take an approximate 1 to 2 milligram sample and mounted on double-sided taped on aluminum stabs. Placed stabs into sample compartment into microscope. Micrographs were taken at appropriate magnification and particle surface visualization detailed analyzed by Scanning Electron Microscope at SICART University, Anand, Gujarat (India).[10]

Physical Parameters Evaluation

Untapped Bulk Density

Untapped bulk density analyzed by Scott volumeter. Weight empty cup, place it under the chute and 10 g of each sample poured into funnel through volumeter, at a suitable rate to prevent clogging, until the cup overflows. Level the excess powder and taken weight of the filled cup. Calculate untapped bulk density by using below mentioned formula.[11]

$$\text{Untapped bulk density (g/ml)} = \frac{\text{Sample Mass (gm)}}{\text{Volume of Cup (ml)}} \quad \text{(i)}$$

Tapped Bulk Density

Tapped bulk density is determined by placing a graduated cylinder containing a known mass of final blend powder on a mechanical tapper apparatus (Model No. ETD 1020) which is operated at require number of tapped until powder bed reached a minimum volume. Calculate tapped bulk density by using below mentioned formula.[12]

$$\text{Tapped bulk density (g/ml)} = \frac{\text{Sample Mass (gm)}}{\text{Sample Volume (ml)}} \quad \text{(ii)}$$

Hausner's Ratio

It is indirect index for ease of measuring powder flow. Lower Hausner's ratio (<1.25) indicates good flow property. Calculate Hausner's ratio by using below mentioned formula.[12]

$$\text{Hausner's Ratio} = \frac{\text{Tapped density}}{\text{Untapped density}} \quad \text{(iii)}$$

Compressibility Index

Compressibility is also known as carr's index. Based on the apparent bulk density and the tapped density. Percentage compressibility is calculated by the below formula.[12]

$$\text{Compressibility (\%)} = \frac{\text{Tapped density} - \text{Untapped density}}{\text{Tapped dneisity}} \times 100 \quad \text{(iv)}$$

Angle of Repose

Angle of Repose obtained between the free-standing surface of the powder heap and the horizontal plane. It was determined by using the fixed funnel method. 20 gm of final powder blend was poured into the funnel keeping the orifice of the funnel blocked by thumb. When the powder was cleared from the funnel and made a peak, the peak height was measured through a scale.[13]

Table 1: Powder characteristics indicative of the Powder Quality.[13]

Types of flow	Angle of Repose (°)	Compressibility index (%)	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very Poor	56-56	32-37	1.46-1.59
Very Very Poor	>66	>38	>1.60

Particle Size Distribution Analysis

Particle size distribution was analyzed by using dry dispersion method Aero S accessory (Malvern Mastersizer 3000 Instrument v3.81)**.**

Aceclofenac 100 mg Tablet Manufacturing Process

Aceclofenac with HiCel™ HFS

Weigh accurately the required quantity of Aceclofenac, HiLose and HiCel™ HFS using an analytical weighing balance (Mettler Toledo, ME303/A04) and transfer into a powder blender (Reva Pharma Machinery, TRMIX-20), mixed this material for 8-10 minutes at 25 RPM. At last, add Lubricant and mix for 3-5 minutes at 25 RPM, material is ready for tablet punching.

Aceclofenac with Physical Mixing

Weigh accurately the required quantity of Microcrystalline Cellulose (HiCel 90M), HiLose (Croscarmellose sodium) and Colloidal silicon dioxide using an analytical weighing balance (Mettler Toledo, ME303/A04) and transfer into a powder blender (Reva Pharma Machinery, TRMIX-20), blend all ingredient for 5 minutes at 25 RPM after that add Aceclofenac into powder blender and blend again for 8 to 10 minutes at 25 RPM. At last, add lubricant Magnesium stearate into the powder blender and blend the material again for 3-5 minutes, material ready for tablet punching.[14]

Table 2: Aceclofenac 100 mg Tablet Composition.

Ingredients	F1 (With HiCel™ HFS)	F2 (With Physical Mixing)
Aceclofenac	100.0	100.0
HiCel™ HFS	147.0	--
Physical Mixing (Mannitol, MCC and Colloidal Silicon Dioxide)	--	147.0
HiLose (Croscarmellose Sodium)	0.50	0.50
Magnesium Stearate	2.5	2.5
Total Tablet Weight	**250.0 mg**	**250.0 mg**

Pre-compression Parameters

Pre-compression parameters i.e. bulk density, Compressibility, Particle size and angle of repose of Aceclofenac evaluate using above mention method.

Tablet Compression of 100 mg Aceclofenac

Aceclofenac 100 mg tablets were manufactured by using 12 station Eliza Press tablet punching machine using "D" tooling dies and punches with 8.0 mm diameter. Both samples of Aceclofenac tablet manufactured at the same pre-compression and main compression force.[15]

Post-Compression Evaluation of Aceclofenac 100 mg Tablet

Physical Appearance

The general appearance of both formulated tablets was studied visually in shape, colour and texture of formulated tablet.

Weight Variation

Weight variation test was performed by individually weighing of 10 tablets by using an analytical weighing balance (Mettler Toledo, ME303/A04), calculating the average weight of every formulation.[16]

Thickness

All formulated tablet thickness was measured by using Vernier Calliper, a sample size of 10 tablets. The tablet was put in between two jaws vertically and the thickness measured.

Hardness

Randomly 10 tablets were taken from each sample. Tablet hardness measured by using a digital hardness tester machine (TH1050M). A single tablet was placed between two anvils, force was applied to the anvils and the tensile strength that was just required to break the tablet was recorded. Finally, the reading was noted in [N].[17]

Friability

30 tablets were taken and weighed by using an analytical weighing balance (Mettler Toledo, ME303/A04). which was considered as the initial weight. All the tablets were placed in the drum of the friability tester (FT1020) and allowed to rotate at 100 revolutions for 4 minutes. After 100 revolutions, 30 tablets were removed and re-weighed, which was considered as the final weight. The percentage friability was calculated by below mention

formula. As per USP, the tablets should not lose more than 1% of their total weight.

$$\text{Friability (\%)} = \frac{\text{Initial weight (gm)} - \text{Final weight (gm)}}{\text{Initial Weight (gm)}} \times 100 \quad \text{(v)}$$

In Vitro Disintegration Time

The disintegration time of Aceclofenac tablets was analyzed by using a tablet disintegration tester (Lab India, DT1000) at 37±2°C in 900 ml De-mineralized water. Six tablets were taken and one tablet was introduced in each tube, disk was placed and the basket was positioned in a liter beaker containing 37±2°C temperature of water. Note down tablet disintegration time.[18]

In Vitro Dissolution Profile

Aceclofenac tablet drug released profile was analyzed by using a dissolution test apparatus (Labindia, DS8000) and followed by IP method, apparatus no 1 (paddle), speed 50 rpm for 45 minutes in 900 ml of phosphate buffer pH 7.5 at 37±0.5°C medium temperature. Randomly select 6 tablets and one tablet introduced in each beaker of dissolution. 5 ml samples were withdrawn from each beaker at different time intervals 5, 15, 30, 40 and 45 minutes.Samples filter through Whatman filter paper (No. 42). Take 1 ml filtrate sample from the beaker and transfer it into 10 ml of volumetric flask and dilute up to 10 ml by using a dissolution medium. Repeat the same procedure for all remaining 5 tablets containing samples. Take standard and samples absorbance by using UV Visible Spectrophotometer UV-1900 (Shimadzu) at λ=273 nm wavelength. Calculate aceclofenac drug released profile with the help of below mentioned formula.[19]

Amount of Drug Released (mg) = Concentration of released drug × Dilution factor × Volume of dissolution medium / 1000

Drug Released (%) = Amount of drug released (mg) / label claim (mg) x 100 (Vi)

RESULTS AND DISCUSSION

Characterization

Fourier - Transform Infrared Spectroscopy (FTIR)

In Co-Processing processes, Mannitol and colloidal Silicon Dioxide Particles are coated on Microcrystalline Cellulose because when comparing with individual excipient scan peeks are shifted of HiCel HFS, shown in Fig 1.

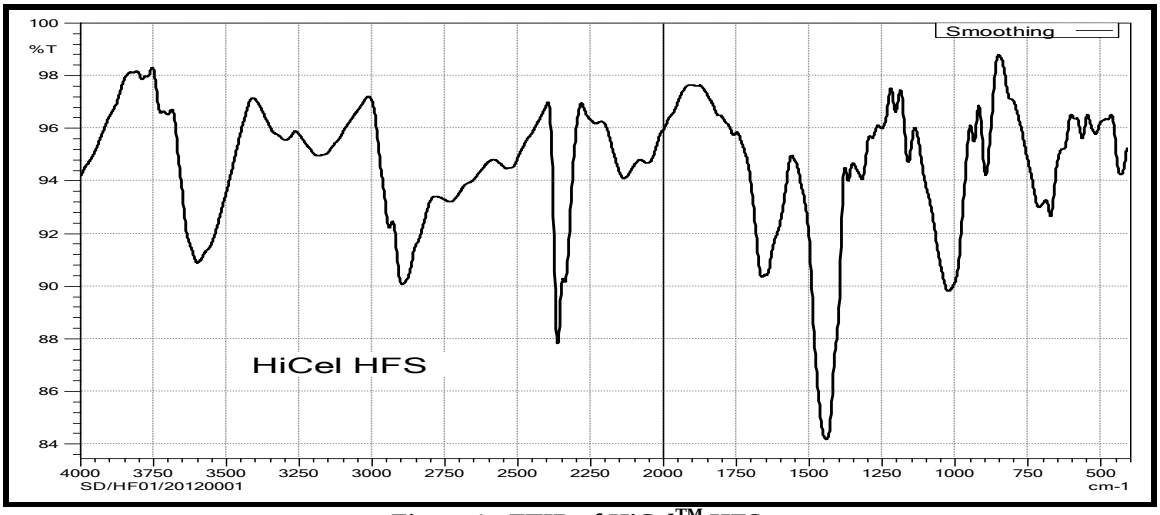

Figure 1: FTIR of HiCel™ HFS.

Scanning Electron Microscope (SEM) Images

Binder, filler and glidant are all present in HiCel™ HFS single particles. According to all HiCel™ HFS SEM picture and as indicated in figure 2, all materials have been covered with one another. HiCel™ HFS increased surface area and particle size, which made it easier to combine API components uniformly. Improved compressibility, specific surface area, flowability and tablet weight uniformity.

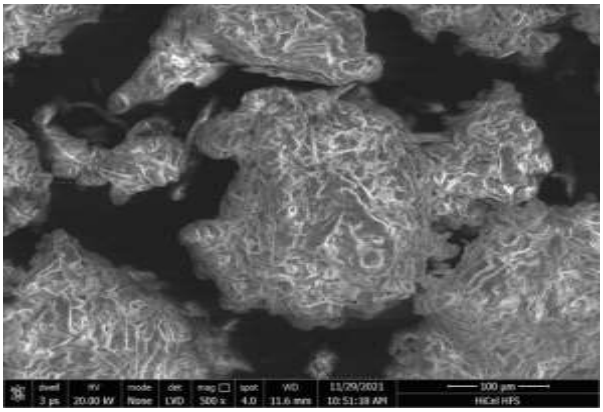

Figure 2: Scanning Electron Microscope (SEM) images of HiCel™ HFS at 100 µm magnifications.

Physical Evaluation of HiCel™ HFS

Physical parameters of powder are very important for the direct compression tablet manufacturing method, physical parameters help during tablet manufacturing, control tablet rejection, and help to run the tablet punching machine smoothly at high RPM. HiCel™ HFS untapped density 0.36 g/ml and tapped density 0.45 g/ml. Higher bulk density improved the flowability of the powder whereas Hausner's ratio and compressibility index are considered indirect measurements of powder flowability, Hausner's ratio is indicative of friction between inter-particles, while the Compressibility index shows the aptitude of a material to diminish in volume. As the values of these increase, the flow of the powder decreases. HiCel™ HFS 1.26 Hausner's ratio and 20.70 Compressibility index. The flow properties of powders are essential in determining the suitability of a material as a direct compression excipient. Increasing value is an indication of decreasing flowability. It has excellent flowability, which is represented by the angle of repose and it has 32° angle of repose. Particle size plays a very important role in direct compression formulation, it helps to carry a uniform quantity of API into each tablet. HiCel™ HFS average particle size mean (D50) 135 µm. All physical parameters are mentioned in table no.3.

Table: 3 Physical Evaluation of HiCel™ HFS.

Parameters	HiCel™ HFS Results
Untapped Bulk Density (g/ml)	0.36
Tapped Bulk Density (g/ml)	0.45
Hausner's Ratio	1.26
Compressibility Index (%)	20.70
Angle of Repose (°)	32
Average Particle Size (µm) D50	135.0

Pre-Compression Parameters Evaluation of Aceclofenac Final Blend

Aceclofenac blend containing HiCel HFS having good angle of repose, low carr's index value comparative to physical mix comparative results are mentioned in below table,

Table 4: Pre - Compression Parameters of Aceclofenac Tablet.

Formulation Code	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner's Ratio	Carr's Index (%)	Angle of Repose (°)
F1	0.454	0.625	1.377	27.36	35
F2	0.436	0.606	1.389	28.05	41

Evaluation of Aceclofenac Tablet

Physical Appearance

All tablets are white in color Round, Concave with both sides embossed on the tablet surface and 8.00 mm in diameter. Aceclofenac tablets containing HiCel™ HFS are free from all tablet defects. However, Aceclofenac tablets containing physical mixing have capping defects on the tablet surface.

Weight Variation

We have found weight uniformity in HiCel™ HFS containing Aceclofenac tablets as compared to physical mixing containing Aceclofenac tablets. Due to coarser particle size, the excellent flowability of HiCel™ HFS maintained equal filling of die-cavity resulting found minimum tablet weight variation. The average tablet weight is mentioned in table 5.

Thickness

HiCel™ HFS and physical mixing containing Aceclofenac tablet thickness 5.75 mm. We have made Aceclofenac Tablet with HiCel™ HFS and physical mixing at same thickness.

Hardness

Aceclofenac tablet made with HiCel™ HFS having found more tablet hardness as compared to Aceclofenac tablet made with physical mixing. Average tablet hardness of both samples mentioned in Tablet 5.

Friability

Aceclofenac tablet containing HiCel™ HFS found less friability test, however, physical mixing containing Aceclofenac tablet found more friability. The friability of both sample tablets is mentioned in Table 5.

In Vitro Disintegration Time

Aceclofenac tablet containing HiCel™ HFS found less disintegration time as compared to physical mixing containing Aceclofenac tablet. Average disintegration time of both samples mentioned in Table 5.

In Vitro Dissolution Profile

Aceclofenac drug released fast from HiCel™ HFS containing Aceclofenac tablet as compared to physical mixing containing Aceclofenac tablet. Average Aceclofenac tablet drug release profile of both tablet samples shown in Fig:3.

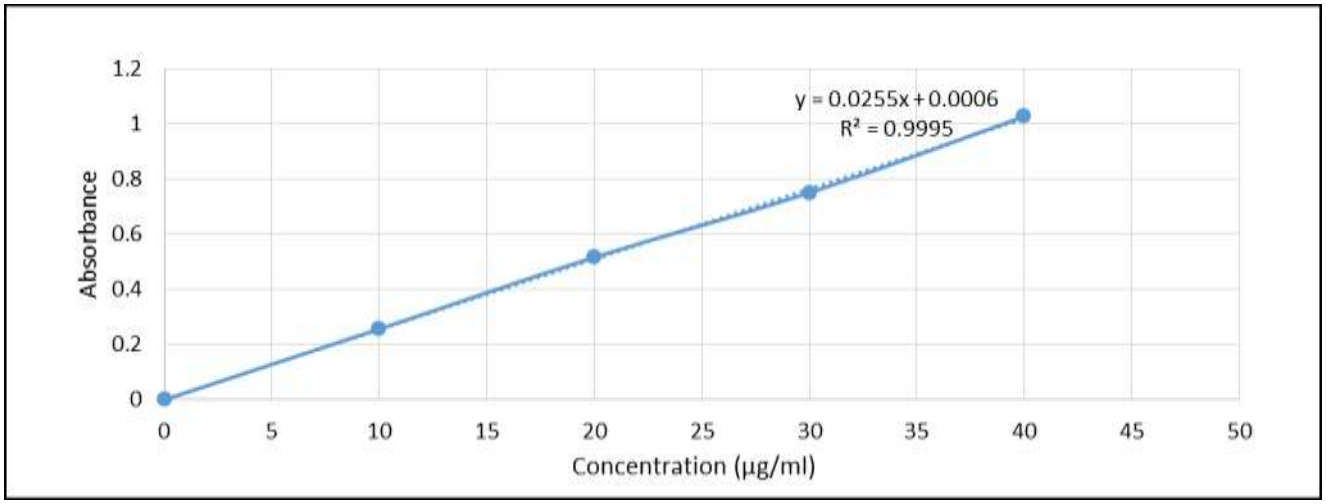

Figure 3: Standard Calibration Curve of Aceclofenac.

Table 5: Post Compression Parameters of Aceclofenac Tablet

Parameters	Results	
	F1 (with HiCel™ HFS)	F2 (with Physical Mixing)
Tablet Description	Round, Concave, White Color Tablet with both side embossing.	
Avg.Tablet Weight (mg)	250.1	249.9
Avg.Tablet Hardness (N)	98.6	83.3
Tablet Thickness (mm)	5.75	5.75
Tablet Diameter (mm)	8.00	8.00
Friability (%)	0.047	0.284
Avg. Disintegration Time (sec)	21.67	28.54
% Drug Released After 45 min	101.65	90.12

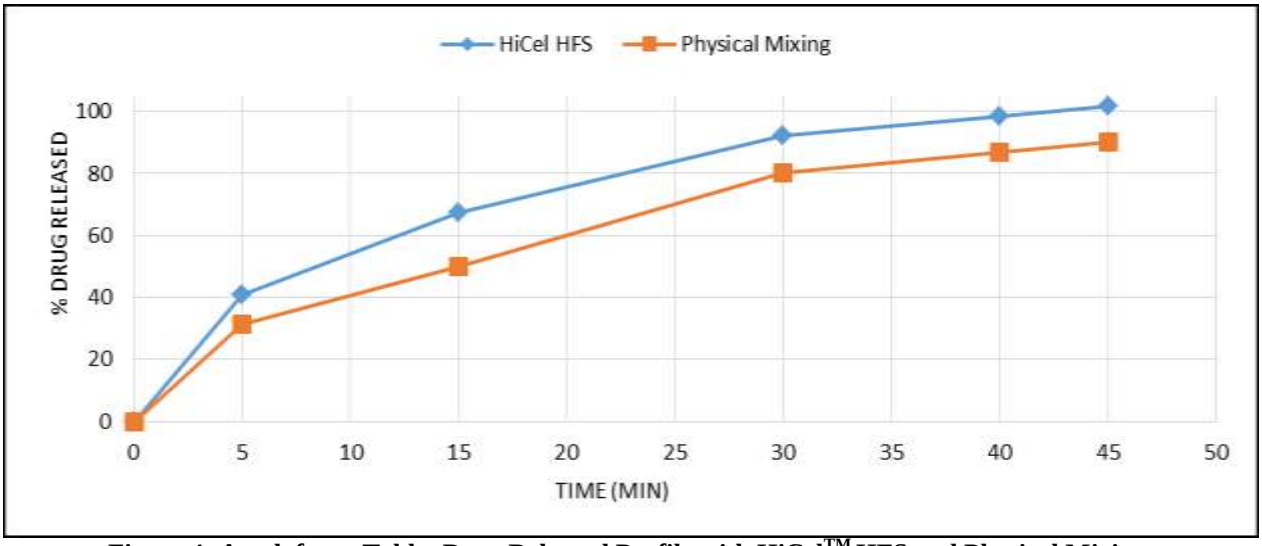

Figure 4: Aceclofenac Tablet Drug Released Profile with HiCel™ HFS and Physical Mixing.

CONCLUSION

In this study, We have found High Functional Excipients having outstanding physical properties i.e. bigger and homogeneous, higher bulk density, lower compressibility and angle of repose, which improved Aceclofenac blend flowability and helped to minimize tablet weight variation during tablet compression and improve tablet appearance by reducing die-friction and tablet defects. HiCel™ HFS provides higher tablet hardness, less disintegration time, friability, and improved drug released profile in comparison to the physical blend. In the physical blend, all materials are not blended well due to different particle sizes and bulk densities of different excipients. Due to heterogeneous blending caused more weight variation and drug content variation. Observed few tablet defects such as capping, less tablet hardness, with more friability, more disintegration time. In dissolution Aceclofenac released is slow in comparative to HiCel™ HFS.

ACKNOWLEDGMENT

The authors are thankful to the Sophisticated Instrumentation Centre for Applied Research and Testing (SICART), Anand, Gujarat, India for providing SEM testing facility.

Conflict of Interest

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

REFERENCES

1. Liew KB, Anand G and Uttam KM. (2019). A review on co-processed excipients: Current and future trend of excipient technology. International Journal of Pharmacy and Pharmaceutical Sciences, 11(1): 1-9.
2. Ayyappan J, Umapathi P and Darlin Q. (2010). Development and evaluation of a directly compressible coprocessed multifunction sustained released agent for tablets. International Journal of Pharmacy and Pharmaceutical Sciences, 2(4): 1-10.
3. Ujjwal D, Rohini C, Priti M and Ruchira C. (2012). A review: co-processed excipients. International Journal of Pharmaceutical Sciences Review and Research, 12(1): 93-105.
4. Aljaberi A, Ardakani A, Khdair A, Abdel-Rahim AS, Meqdadi, Ayyash M, Alobaidi GM and Al-Zoubi N. (2013). Tableting functionality evaluation of Prosolv Easytab in comparison to physical mixtures of its individual components. Journal of drug delivery of science technology, 23(2): 499-504.
5. Bhowmik D., Chiranjib B., Krishnakanth, Pankaj, Chandira R.M. (2009). Fast dissolving tablet: An overview. Journal of Chemical and Pharmaceutical Research, 1(1): 163-177.
6. Srinivas M., Parambil A., Krishnan M., AchuthaN.U. (2008). Enhancement of dissolution rate and bio availability of aceclofenac. International Journal of Pharmaceutics, 350: 279–290.
7. Wagh M.P., Yewale C.P., Zate S.U., Kothawade P.I. and Mahale G.H. (2010). Formulation and evaluation of fast dispersible tablets of aceclofenac using different superdisintegrants.
8. Seema Atram. (2014). Recent development of herbal formulation: A novel drug delivery system. International Ayurvedic Medical Journal, 2(6): 953-958.
9. Mutalik S., Naha A, Usha, A. N., Ranjith A. K., Musmade P., Manoj K., Anju, P. and Prasanna S., Preparation, in vitro, pre clinical and clinical evaluations of once daily sustained release tablets of aceclofenac, Arch Pharm Res, 2007; 30(2): 222-234.
10. Donovan N, Leonard Gary W and Chandler SS. (2012). Characterization of Materials, second edition. Wiley online library.
11. Monika T, Amit RS and Ajay KS. (2017). Process and development of co-processed excipient Silicified Microcrystalline Cellulose and manufacture paracetamol tablet by direct compression. International Journal of Pharmaceutical Sciences review and research, 32(2): 191-196.
12. United States Pharmacopoeia. (2018). General Chapter: Bulk density, 40-NF 35.
13. United States Pharmacopoeia. (2018). General Chapter: Powder flowability, 40(1): NF 35.
14. Tomar M; Shah Jilika; Sinha A.R; Singh A.K. "Silicified Microcrystalline cellulose.
15. Armin H. Gerhardt. "Moisture Effects on Solid Dosage Forms—Formulation, Processing, and Stability" Journal of GXP Compliance, 2009; 13: 58-66.
16. Aulton ME. (2002). Pharmaceutics the science of dosage design Churchill Livingstone. Second edition, 134.
17. Rojas J, Lopez A, Guisao S and Carlos O.(2011). Evaluation of several Microcrystalline cellulose obtained from agricultural by-products. Journal of advanced pharmaceutical technology & research, 2(4): 144-150.
18. United States Pharmacopoeia. (2018). General chapter: Dissolution and disintegration, 40-NF, 35: 2270-2274.
19. Indian Pharmacopoeia (2018). Aceclofenac Tablet monograph, 1145.