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Article · January 2024

DOI: 10.20959/wjpr20245-31066

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WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 13, Issue 5, 1093-1105. Research Article ISSN 2277–7105

THE ROLE OF BARETAB NUTRA DS IN DIRECT TABLET COMPRESSION METHOD

Rauf Pathan[1]*, Monika Tomar[1] and Amit Raj Sinha[2]

[1]Sigachi Industries Limited, Dahej SEZ, Bharuch, Gujarat, India.

[2]Sigachi Industries Limited, 2nd Floor, Kalayan's Tulsiram Chambers, Madinaguda, Hyderabad, Telangana (India).

Article Received on
17 Jan. 2024,

Revised on 07 Feb. 2024,
Accepted on 27 Feb. 2024

DOI: 10.20959/wjpr20245-31066

***Corresponding Author**
Rauf Pathan
Sigachi Industries Limited,
Dahej SEZ, Bharuch,
Gujarat, India.

ABSTRACT

BARETab Nutra DS is a novel Co-Processed excipients which is a combination of three Pharmacopeial excipients made by Co-Processing Technology. BARETab Nutra DS contains Dibasic Calcium Phosphate Anhydrous [DCPA] (Filler), Microcrystalline Cellulose (Binder) and Crosscarmellose Sodium (Disintegrant). BARETab Nutra DS offers excellent compressibility, good flowability with higher tablet hardness with less percentage friability and less disintegration time as compared to physical mixing and individual excipients. This is the main requirement for Direct Compression (DC) tablet formulation mainly in Nutraceutical tablet formulation. However, most individual excipients have insufficient physical characteristics, particularly in flowability and compressibility. Co-processed excipients are beginning to be used in the manufacturing of tablets and capsules to fulfill these requirements. All co-processed excipients have excellent flowability and higher compressibility and they have now carved out a niche for themselves in the Pharmaceutical and Nutraceutical sectors. In this study, We will make a Placebo Tablet of BARETab Nutra DS, Physical Blend, and Individual Excipient (MCC) by using direct compression method at the same thickness and same tablet weight and evaluate in-vitro parameters such as Weight Uniformity, Tablet Hardness, Friability and Disintegration time. BARETab Nutra DS is a high-functionality excipients to provides excellent tablet hardness, less friability and less disintegration time with superior flowability.

KEYWORDS: Co-Processed Excipient, Higher Compressibility, Direct Compression (DC), Nutraceutical, Flowability, Compression Force, FTIR.

1. INTRODUCTION

Co-processed excipients have been used in the formulation industries for quite some time. It is most commonly used to make directly compressible tablet formulations.[1] A co-processed excipients is a unique combination of two or more two excipients created through co-processing technology.[2] Excipients used in co-processing have superior physical properties such as higher bulk density, greater surface area, excellent compressibility, and homogeneous particle size distribution that provide good quality tablets with reduced tablet ejection force, reduced percentage friability, higher tablet hardness, less disintegration time, and uniform API distribution in each tablet.[3] When API is combined with a binder, filler, and disintegrant, however. When a physical mixing blend is created for tabletting, the quality of the tablets may differ from batch to batch.[4]

BARETab Nutra DS is a novel high-functionality co-processed excipient, which is the combination of Dibasic Calcium Phosphate Anhydrous [DCPA], Microcrystalline Cellulose (MCC) and Crosscarmellose Sodium (CCS). BARETab Nutra DS is specially designed for herbal extract as well as vitamin tablet formulation which is very hygroscopic in nature, has poor flowability, and lower compressibility. BARETab Nutra DS is a good choice for nutraceutical and pharmaceutical tablets by direct compressible formulation which has lower compressibility and poor flow properties. BARETab Nutra DS provides synergistic properties and excellent benefits as compared to individual excipients and physical mixing used in directly compressible tablet formulations. BARETab Nutra DS improved lubrication selectivity, increased blending properties, improved binding properties, higher tablet hardness with less disintegration time, and also less percentage friability with improved drug release profile of dosage form.

BARETab Nutra DS is specially designed for nutraceutical formulations. It is very helpful to deliver good-quality tablets and it controls rejections during tabletting in production.[5] Direct compression method for tablet compression is a popular choice because it provides the shortest, most effective, and least complex way to produce tablets. The manufacturer can blend an API with the excipient and the lubricant, followed by compression, which makes the product easy to process. No additional processing steps are required. Moisture or heat-sensitive ingredients, which would be contraindicated in wet granulation, can also be used in

this type of process. However, it does require a very critical selection of excipients in comparison to granulation processes because the raw materials must demonstrate good flowability and compressibility for successful operation.[6]

In this article, We will discuss about high functionality excipient BARETab Nutra DS physical properties and morphological properties by SEM, Fourier-transform infrared spectroscopy (FTIR) and tablet compression difference between physical mixing, individual excipient and Co-processed excipient of placebo tablet. We will evaluate impact of BARETab Nutra DS (Co-Processed Excipient), Physical mixing and Individual excipient (MCC) during tablet compression and also discuss about impact on tablet weight variation, tablet hardness and disintegration time difference between BARETab Nutra DS, Physical mixing and Individual excipient.

2. MATERIAL AND METHODS

Material

HiCel^{TM} binder and BARETab Nutra DS manufactured at Sigachi Industries Ltd. in Dahej, Gujarat, Filler Purchased from SBF Pharma, Ahmedabad, Gujarat, Disintegrant Purchased from Ascot Pharma, Ahmedabad, Gujarat and others chemicals are AR grade used in this study.

Method

Characterization of BARETab Nutra DS

Fourier - Transform Infrared Spectroscopy (FTIR)

Fourier - Transform Infrared Spectroscopy (FTIR) spectroscopy was conducted by 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.[7]

Scanning Electron Microscope (SEM)

Take an approximate 1 to 2 milligram sample and mount on double-sided taped on aluminum stabs. Placed stabs into sample compartment into microscope. Micrographs were taken at appropriate magnification and particles surface visualization detailed analyzed by Scanning Electron Microscope (SEM) at SICART University, Anand, Gujarat (India).[8]

Physical Parameters Evaluation of BARETab Nutra DS

Untapped bulk density

Untapped bulk density analyzed by Scott volumeter. Weight empty cup place it under the chute and 10 g of sample poured into funnel through volumeter at a suitable flow 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.[9]

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

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 fixed number of tapped (500) until powder bed reached a minimum volume. Calculate tapped bulk density by using below mentioned formula.[10]

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

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.[10]

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

Compressibility Index (Carr's Index)

Compressibility is also known as carr's index. Based on the apparent bulk density and the tapped density. Percentage compressibility is calculated by below formula.[10]

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

Angle of repose

Angle of Repose obtained between free standing surface of powder heap and the horizontal plane. It was determined by using the fixed funnel method. Take about 30 gm of sample was poured into funnel keeping the orifice of the funnel blocked by thumb. When powder was cleared from funnel then the peak height was measured.[11]

Particle Size Distribution (PSD) Analysis

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

Manufacturing method of placebo tablet

Weight accurately required quantity of individual excipient and transfer into powder blender (Reva Pharma Machinery, TRMIX-20), blend the material for 10 minutes at 25 RPM. This material is now ready for tablet compression.[12]

Tablet compression

All Placebo tablets were manufactured by using Eliza Press (EP-200) tablet punching machine with the help of "D" tooling. All Placebo tablets manufactured at the same thickness.

Evaluation parameters of placebo tablet

Physical appearance

The general appearance of all Placebo tablets was studied by visually in shape, colour and texture of Placebo tablets.

Weight variation

Tablet Weight variation test was performed by individually weighing of 10 tablets by using analytical weighing balance (Mettler Toledo, ME303/A04), Calculating the average weight of every Placebo tablet samples.[13]

Thickness

All placebo tablets thickness was measured by using digital tablet thickness tester, sample size is 10 tablets. Tablet was placed in between two jaws vertically and tablet thickness measured.

Hardness

Randomly 10 tablets were taken from each Placebo tablet samples and tablet hardness measured by using digital tablet hardness tester machine (TH1050M). Each individual 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 Newton [N].[14]

Friability

15 tablets were taken and weigh by using analytical weighing balance (Mettler Toledo, ME303/A04). Which was considered as a initial weight. All tablets were placed into the drum of friability tester (FT1020) and allow to rotate at 100 RPM for 4 minutes. After completion of 100 RPM, Tablets were removed from friability drum and weigh again, Which was considered as a final weight. The percentage friability was calculated by below mentioned formula. As per United States Pharmacopeia (USP) Percentage friability should not be more than 1%.

$$\text{Percentage Friability} = \frac{\text{Initial weight (gm)} - \text{Final weight (gm)}}{\text{Inital weight (gm)}} \times 100 \text{ (v)}$$

In vitro disintegration time

Disintegration time of all placebo tablets were analyzed by using tablet disintegration tester (Lab India, DT1000) at 37±2°C temperature in 900 ml De-mineralized water. Six tablets were taken and one tablet was introduced in each tube of basket, After that disk was placed on the tablet to avoid floating of tablet during disintegration test and basket was positioned in one liter beaker containing 37±2°C temperature of water. Note down the tablet disintegration time.[14]

3. RESULTS AND DISCUSSION

Characterization of BARETab Nutra DS

Fourier - Transform Infrared Spectroscopy (FTIR)

BARETab Nutra DS FTIR image shown in Fig 1.

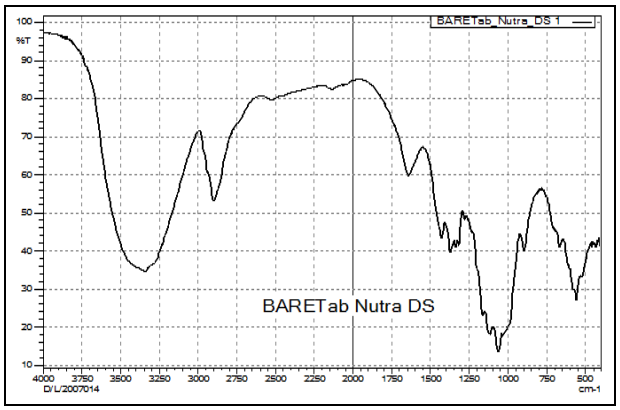

Figure 1: FTIR image of BARETab Nutra DS.

Scanning Electron Microscope (SEM) Images

Binder (MCC), Filler (DCPA) and Disintegrant (CCS) all are present in BARETab Nutra DS single particles. According to BARETab Nutra DS SEM images and as indicated in figure 2, all materials have been covered with one another. BARETab Nutra DS increased surface area and particle size, which made it easier to combine with API uniformly. BARETab Nutra DS particles are more or less spherical in shape. Which helps to improved compressibility, specific surface area, flowability and tablet weight uniformity as well as tablet hardness and disintegration time.

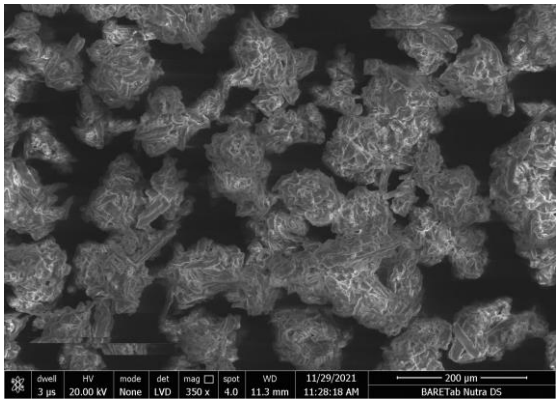

Figure 2: Scanning Electron Microscope (SEM) image of BARETab Nutra DS at 350 X magnifications.

Physical Parameters Evaluation of BARETab Nutra DS, Physical Blend and Individual Excipient

Physical parameters of powder highly impact on tablet compressibility. Powder flow is influenced by bulk density, particle shape and particle size. Lower bulk density facilitates compressibility however low bulk density hindered flowability. It helps to reduce tablet rejection and ran tablet punching machine smoothly at high RPM. BARETab Nutra DS untapped bulk density is 0.41 g/ml and tapped density 0.53 g/ml higher bulk density improved flowability of powder. Hausner's ratio and compressibility index are considered as indirect measurements of powder flowability. The Hausner's ratio is indicative of friction between inter-particles, while the compressibility index shows the aptitude of material to diminish in volume. As the values of these increase the flow properties of the powder decrease due to increase value of angle of repose. BARETab Nutra DS 1.29 Hausner's ratio and 22.64 compressibility index. The flow properties of powder is essential for determining the suitability of a material used as a direct compression excipient. Increasing value is an indication of decreasing flowability. BARETab Nutra DS excellent flowability, which is

represented by angle of repose and it has 34° angle of repose. Particle size of powder play a very important role in direct compression tablet formulation, It helps to carry uniform quantity of API into the each tablets. BARETab Nutra DS average particle size is (D50) 108 µm. Whereas we have found physical parameters of physical blend and other individual excipient having poor flowability due to higher angle of repose and less average particle size as compare to BARETab Nutra DS. which is highly impact during tablet manufacturing by using direct compression (DC) method. All physical parameters results of BARETab Nutra DS, Physical Blend and other Individual Excipient are mentioned in table no.1&2.

Table 1: Physical Parameters Evaluation of BARETab Nutra DS and Physical Mixing.

Physical parameters	Results	
	P-1	P-2
Untapped Bulk Density (g/ml)	0.410	0.420
Tapped Bulk Density (g/ml)	0.530	0.580
Hausner's Ratio	1.29	1.38
Compressibility Index (%)	22.64	27.59
Angle of Repose (°)	34	45
Average Particle Size (µm) D50	108.0	92.0

[**P-1:** BARETab Nutra DS, **P-2:** Physical Mixing (MCC, CCS and DCPA)]

Table 2: Physical Parameters Evaluation of Individual Excipient and Physical mixing.

Physical Parameters	Results		
	P-3	P-4	P-5
Untapped Bulk Density (g/ml)	0.320	0.340	0.440
Tapped Bulk Density (g/ml)	0.490	0.480	0.600
Hausner's Ratio	1.53	1.41	1.36
Compressibility Index (%)	34.69	29.17	26.67
Angle of Repose (°)	38	37	39
Average Particle Size (µm) D50	102.0	91.0	84.0

[P-3: Microcrystalline Cellulose, **P-4:** MCC + DCPA Co-Processed, **P-5:** Physical Mixing (MCC and DCPA)]

Evaluation parameters of placebo tablet

Physical appearance

All Placebo tablets are white in color with 14.00 mm diameter and elongated, concave shape. All Placebo tablets containing BARETab Nutra DS are free from all types of tablet defects such as Capping, Sticking, Lamination etc. However, Placebo tablets containing physical mixing having found Capping tablet defect during tablet compression.

Weight variation

We have found good tablet weight uniformity with BARETab Nutra DS containing Placebo tablets as compared to physical mixing and individual excipient containing Placebo tablets. Due to coarser particles size, excellent flowability of BARETab Nutra DS maintain equal filling of die-cavity resulting found minimum tablet weight variation as compared to physical mixing and individual excipient containing Placebo tablets. Average tablet weight of all placebo tablets is mentioned in table 4.

Thickness

All Placebo tablets containing BARETab Nutra DS, individual excipient and physical mixing tablet thickness 6.00 mm. We have made all placebo tablets containing BARETab Nutra DS, individual excipient and physical mixing at same thickness. Average tablet thickness all placebo tablets mentioned in table 4.

Hardness

Placebo tablets made with BARETab Nutra DS found good tablet hardness as compared to placebo tablets made with physical mixing and individual excipient. Average tablet hardness of all placebo tablets mentioned in Table 4.

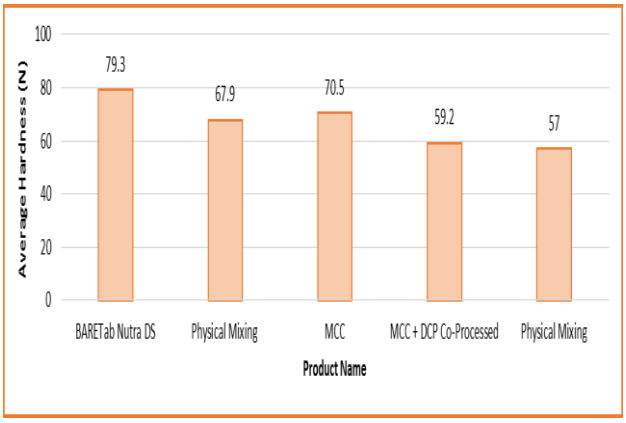

Figure 3: Hardness Comparison of Placebo Tablet made with BARETab Nutra DS, Physical Mixing and Individual Excipient.

Friability

Placebo tablets containing BARETab Nutra DS found less percentage of friability, however physical mixing and individual excipient containing placebo tablet having found more percentage of friability as compared to placebo tablets containing BARETab Nutra DS. Percentage of friability of all placebo tablets mentioned in Table 4.

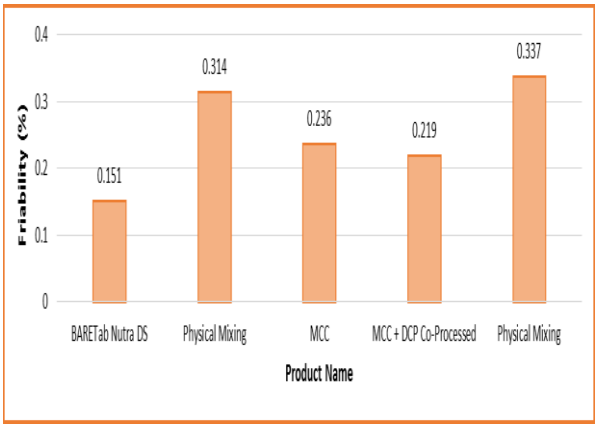

Figure 4: Friability (%) Comparison of Placebo Tablet made with BARETab Nutra DS, Physical Mixing and Individual Excipient.

In vitro disintegration time

Placebo tablets containing BARETab Nutra DS found less disintegration time as compared to physical mixing and individual excipient containing placebo tablets. Average disintegration time of all placebo tablets mentioned in Table 4.

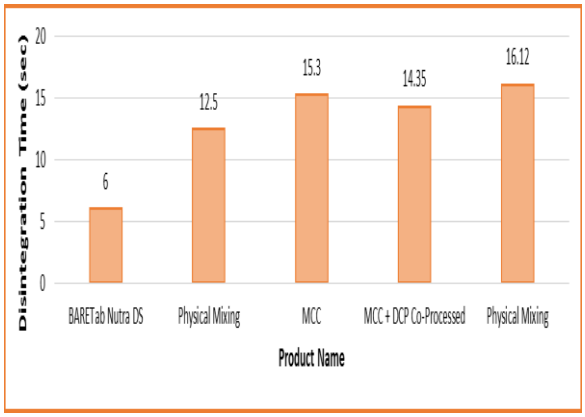

Figure 5: Disintegration Time Comparison of Placebo Tablet made with BARETab Nutra DS, Physical Mixing and Individual Excipient.

Table 3: Pre - Compression Parameters of Placebo Tablet of BARETab Nutra DS, Physical Mixing and Individual Excipient.

Product Name	Pre-Compression Force (kN)	Main Compression Force (kN)	Ejection Force (kN)
BARETab Nutra DS	0.9	2.7	112.6
Physical Mixing (MCC, CCS and DCPA)	0.7	3.0	175.2
Microcrystalline Cellulose	1.1	3.6	158.7
MCC + DCPA Co-Processed	0.8	2.9	142.5
Physical Mixing (MCC and DCPA)	0.6	2.6	245.8

Table 4: Post Compression Parameters Placebo Tablet of BARETab Nutra DS, Physical Mixing and Individual Excipient.

Parameters	Results				
	P-1	**P-2**	**P-3**	**P-4**	**P-5**
Tablet Description	Elongated, Concave, White in Color Tablet				
Avg. Tablet Weight (mg)	500.4	512.2	503.6	502.1	504.5
Avg. Tablet Hardness (N)	79.30	67.90	70.50	59.20	57.00
Tablet Thickness (mm)	6.00	6.00	6.00	6.00	6.00
Tablet Diameter (mm)	14.00	14.00	14.00	14.00	14.00
Friability (%)	0.151	0.314	0.236	0.219	0.337
Avg. Disintegration Time (sec)	6.00 sec	12.5 sec	15.30 sec	14.35 sec	16.12 sec

[**P-1:** BARETab Nutra DS, **P-2:** Physical Mixing (MCC, CCS and DCPA), **P-3:** Microcrystalline Cellulose, **P-4:** MCC + DCPA Co-Processed, **P-5:** Physical Mixing (MCC and DCPA)]

4. CONCLUSION

In this study, we have concluded that BARETab Nutra DS has outstanding physical properties. It has particles more homogeneous, and have higher bulk density and higher compressibility, which improves flowability and final product parameters, like helping to minimize tablet weight variation during tablet compression. BARETab Nutra DS gives less ejection force as compared physical blend and the machine runs smoothly at high RPM and ejects tablets without any tablet physical defect as well as improving the tablet appearance. When it compares with individual excipient Microcrystalline Cellulose, Co-processed excipient combination of Microcrystalline cellulose, Dibasic calcium phosphate Anhydrous (DCPA) and Crosscarmellose Sodium (CCS). Physical mix of Microcrystalline Cellulose and Dibasic calcium phosphate Anhydrous (DCPA) and Crosscarmellose Sodium (CCS). BARETab Nutra DS having higher flow and good tablet profile parameters like hardness, friability and disintegration time.

ACKNOWLEDGMENT

The authors are thankful to Quality and the pilot plant team for helping us.

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. A review on co-processed excipients: Current and future trend of excipient technology. International Journal of Pharmacy and Pharmaceutical Sciences, 2019; 11(1): 1-9.
2. Ayyappan J, Umapathi P and Darlin Q. Development and evaluation of a directly compressible co-processed multifunctional sustained released agent for tablets. International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(4): 1-10.
3. Ujjwal D, Rohini C, Priti M and Ruchira C. A review: co-processed excipients. International Journal of Pharmaceutical Sciences Review and Research, 2012; 12(1): 93-105.
4. Aljaberi A, Ardakani A, Khdair A, Abdel-Rahim AS, Meqdadi, Ayyash M, Alobaidi GM and Al-Zoubi N. Tabletting functionality evaluation of Prosolv Easytab in comparison to physical mixtures of its individual components. Journal of drug delivery of science technology, 2013; 23(2): 499-504.
5. BARETab™. The beginning of end of single excipient usage. Express pharma journal, 2019; 16(1): 129.
6. Upendra N, Ashok KP, Charu B and Neha G. Formulation and evaluation of nutraceutical tablets using herbal drugs by direct compression method. Journal of drug delivery & therapeutics, 2014; 4(2): 47-51.
7. 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.
8. Donovan N, Leonard Gary W and Chandler SS. Characterization of Materials, second edition, 2012 Wiley online library.
9. Monika T, Amit RS and Ajay KS. 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, 2017; 32(2): 191-196.
10. United States Pharmacopoeia. General chapter: Bulk density, 2018; 40-NF: 35.
11. United States Pharmacopoeia. General chapter: Powder flowability, 2018; 40(1)-NF: 35.
12. Tomar M; Shah Jilika; Sinha A.R; Singh A.K. “Silicified Microcrystalline Cellulose”,
13. Rojas J, Lopez A, Guisao S and Carlos O. Evaluation of several Microcrystalline cellulose obtained from agricultural by-products. Journal of advanced pharmaceutical technology & research, 2011; 2(4): 144-150.

14. United states pharmacopoeia. General chapter: Dissolution and disintegration, 2018; 40-NF 35: 2270-2274.