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HIGH-FUNCTIONAL SELF-LUBRICATING EXCIPIENT PERFORMANCE COMPARISON WITH PHYSICAL BLEND

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ABSTRACT

A microcrystalline cellulose-based excipient having improved lubrication sensitivity and flowability, whether utilized in oral solid dosage forms, in direct compression, wet and dry granulation tablet manufacturing, or hard capsule filling and dry syrup formulation. Self-lubricating excipient BARETab Lub is an agglomerate of microcrystalline cellulose particles and from 0.1 to 0.8 % lubricant Magnesium stearate, by weight of the Microcrystalline cellulose, wherein the microcrystalline cellulose and magnesium stearate particles are in intimate association with on each other. The lubricant magnesium stearate is used in pharma and Nutra as a novel lubricant to make solid oral dosage forms. Self-lubricating excipients don't affect tablet properties like hardness, disintegration time, and dissolution of the tablet, BARETab Lub improves Particle BET surface area, and Physical properties. In this study, we will blend the self-lubricating excipient physical properties, BET surface area, FTIR, SEM, and the impact of blending time on the Self-lubricating excipient and physical mix of MCC and Magnesium stearate.

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INTRODUCTION

A list of excipients is used to manufacture dosage forms. It is a pharmaceutical drug product in the form in which they are marketed for use. Dosage forms are a specific mixture of active and inactive ingredients. It is divided into three types solid, liquid, and semi-solid. Solid dosage forms like Capsules and Tablets are the most popular, easy to handle, and have better patient compliance (Bowden, 2001). In manufacturing Tablets, there are three methods that basically are used. Wet granulation is the old, lengthy, and costly method as compared to the other two methods. The wet granulation method is suitable for all the APIs, but various steps are involved. The dry granulation method is used very rarely, this method contains mechanical compression (slugs) or compaction (roller compaction) to facilitate the agglomeration of dry powder particles. Whereas the direct compression method is the fastest method to manufacture tablets. Nowadays, many formulations are manufactured using this method. Lubricants are added in the last step of blending in all three processes (Wang, 2010). The selection of lubricants is crucial for tableting, although they might alter the tablet's properties in an undesired way. A lubricant is thought to be required to enable the compressed form or tablet to be released from the device (Goldberg, 2012).

Even so, it is also contended that the lubricant may coincide with the necessary binding between the various carrier components and, in the case of hydrophobic lubricants like magnesium stearate, adversely affect tablet disintegration properties (Bolhuis, 1996). Lubricants have a tendency to coat excipient components, making it difficult for them to adhere to one another. Water plays a vital role in disintegration, so a hydrophobic lubricant coat resists it. As a result, the use of lubricant prior to the actual compression step helps to minimize contact time between the lubricant and other tablet components (Wang, 2010). However, there is a perpetual need to optimize the process for producing ready-to-use co-processed Self-lubricating excipient combinations in the art. Although the principal goal of lubricants and glidants is to enhance tableting and flowability into the tablet press, some lubricants can also promote flow. Lubricants are regularly used in several formulations to ease in the tableting step. A tablet must be ejected from the tablet press die after compression. Lubricants contribute to reducing friction between the tablet and the die metal surface, minimizing the ejection force, and ensuring that the tablet is discharged cleanly and without breaking or fracture (Miller, 1988). In this study, we will discuss high functional excipient BARETab Lub physical properties, BET surface area, and morphological characteristics by SEM, Fourier-transform infrared spectroscopy, and Compression difference between a physical blend and co-processed excipients. We will evaluate the impact of blending

time on BARETab Lub and the Physical mix of MCC and Magnesium stearate and also discuss the weight variation difference between BARETab Lub and the Physical mix.

MATERIALS AND METHODS

Material: BARETab® Lub, binder at Sigachi Industries Ltd. in Dahej, Gujarat. Glidant purchased from Nikon Corporation, Wacker Germany, lubricant purchased from Sunshine Private Limited, India other chemicals of AR grade are used in this study.

Method

BET Surface Area Analysis: Take 0.1380 g sample in the sample cell and charge nitrogen gas at a low-pressure dose of 10.00 cm^3/g STP and -195.73 ^0C temperature (Busignies Virginie, 2011). The Surface area of both samples was analyzed by using a Micromeritics surface analyser at Shah-Schulman Centre for Surface Science & Nanotechnology Dharmsinh Desai University, Nadiad, Gujarat.

Fourier-transform infrared spectroscopy: 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 the 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 (Mutalik, 2007).

Scanning Electron Microscope: Take an approximate 1 to 2-milligram sample and mount it on double-sided taped-on aluminum stabs. Placed stabs into sample compartment into a microscope. Micrographs were taken at appropriate magnification and particle surface visualization was detailed and analyzed by scanning electron microscope at SICART University, Anand, Gujarat (India) (Donovan, 2012).

Physical Evaluation of BARETab® Lub

Untapped density: Untapped bulk density analyzed by Scott volumeter. Weight the empty cup, place it under the chute and 10g of each sample is poured into a funnel through a volumeter, at a rate suitable to prevent clogging, until the cup overflows. Level the excess powder and weigh the filled cup (Monika, 2017).

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

Tapped density: Tapped 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 reaches a minimum volume (United States Pharmacopoeia, 2018).

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

Hausner's ratio: It is the indirect index for ease of measuring powder flow. Lower Hausner's ratio (<1.25) indicates good flow property (United States Pharmacopoeia, 2018).

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

Compressibility: Compressibility is known as Carr's index. Based on the apparent bulk density and the tapped density. Percentage compressibility is calculated by the below formula (United States Pharmacopoeia, 2018).

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

Angle of repose: Angle of repose obtained between the freestanding surface of powder heap and the horizontal plane. It was determined by using the fixed funnel method. 20 gm of final blend powder 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 (United States Pharmacopoeia, 2018).

Particle size distribution analysis: Particle size was analyzed using laser diffraction (Malvern instrument, Mastersizer 3000).

Blending of BARETab Lub and individual excipient Magnesium stearate and Microcrystalline Cellulose: Take the required material into a powder blender (Reva Pharma machinery, TRMIX-20), and blend both samples at 25 RPM for 5, 10, 15, and 20 minutes (Tomar, 2016).

Manufacturing Method of Placebo Tablet: Weight accurately required quantity of Microcrystalline cellulose, Magnesium stearate, BARETab Lub, Disintegrant, and Glidant and transfer into powder blender (Reva Pharma machinery, TRMIX-20), blend the material for 8 minutes at 25 RPM. The material is now ready for tablet punching (Tomar, 2016).

Tablet compression: All sample tablets were manufactured by using Pare-Elizabath (EP-200) using D tooling manufactured at the same compression force (Armin, 2008).

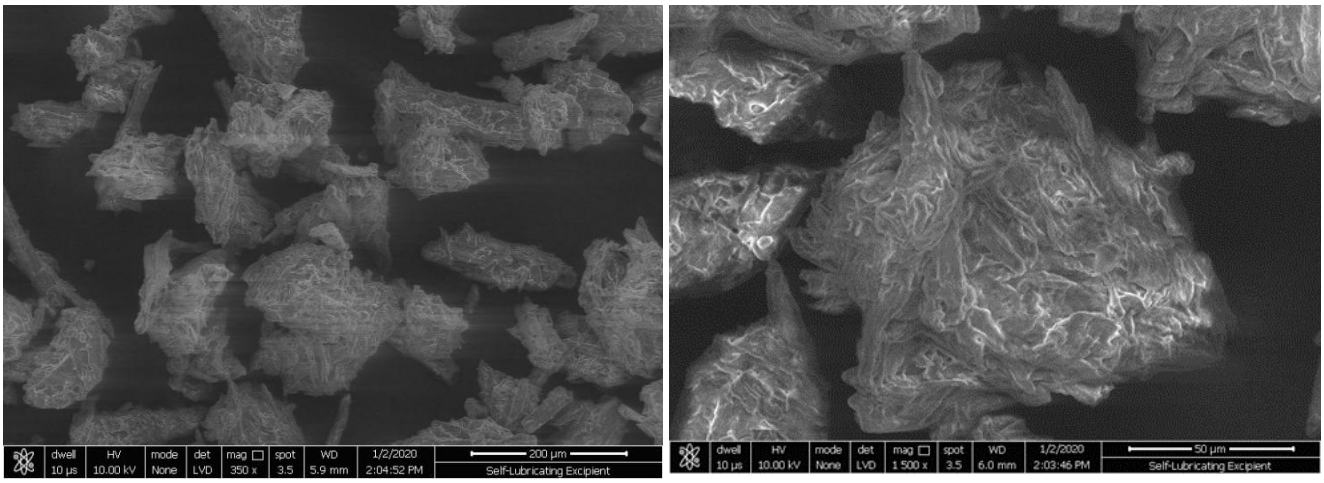
Placebo Tablet Evaluation: Take randomly 10 tablets and visualizing general appearance of all formulated tablets were studied visually in shape, color, texture amend defects. Weight variation test was performed by weighing 10 tablets individually using a four-digit digital weighing balance (Mettler Toledo, MS304S/A01), calculating the average weight of every formulation (Aulton, 2002) and tablet thickness was evaluated using Vernier calipers, The Tablet sample was put in between two jaws vertically and the thickness measured. Tablet hardness was tested by an Electronic digital hardness test machine (TH1050 M). A single tablet was placed between two anvils, force was applied to the anvils, and the tensile strength that was required to break the tablet was recorded. Finally, the reading was noted in Newton [16]. For friability 10 tablets were taken and weighed by using an electronic digital balance which was considered as the initial weight. All the tablets were placed in the drum of the friability tester (FT1020) and allowed to rotate 100 times at 25 rpm. After 100 revolutions, 10 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.

In vitro disintegration time: The disintegration time of paracetamol tablets was analyzed by using a tablet disintegration tester (Labindia, DT 1000) at 37±2°C in 800 ml Demineralized water. Six tablets were taken, and one tablet was introduced in each tube, disk was placed and basket was positioned in one litre beaker containing 37±2°C temperature of water. Note down tablet breaking time. Noted the time when the tablet broke down into smaller particles (United States Pharmacopoeia, 2018).

RESULTS AND DISCUSSION

BET Surface area: The BET-specific surface areas of BARETab® Lub was 4.52m^2/g. larger surface area results in higher interarticular bonds which impact on tablet hardness. When particle surface is larger than chances of the presence of interparticle bonds is more, and the force of these bonds helps to achieve higher tablet hardness.

Scanning electron microscope Images: BARETab® Lub single particle contains microcrystalline cellulose and magnesium stearate and Magnesium stearate homogeneously coating on Microcrystalline cellulose.



(A) BARETab Lub SEM image on 350 magnifications (B) BARETab Lub SEM image on 1500 magnification
Fig. 1. SEM image of BARETab Lub self-lubricating Excipient at different magnification

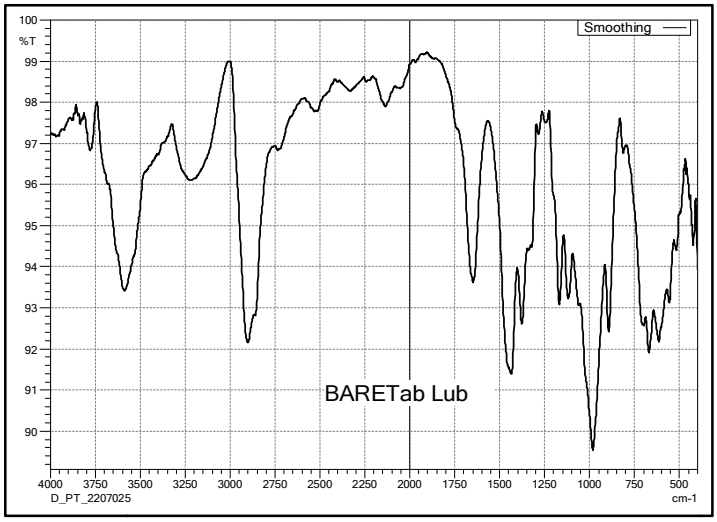


Fig. 2. FTIR Spectra of BARETab Lub

Table 1. Physical parameter evaluation of BARETab Lub and Physical mix of MCC and Magnesium stearate

Comparative physical parameter evaluation of BARETab Lub and Physical mix of MCC and 0.5% Magnesium stearate		
Parameter	BARETab Lub (Self Lubricating Excipient)	Physical Mix of MCC and Magnesium Stearate
Untapped density (g/ml)	0.30	0.30
Tapped density (g/ml)	0.45	0.41
Hausner Ratio	1.50	1.35
Compressibility (%)	33.33	25.93
Angle of Repose (°)	41	38
Average Particle size (µm)	98	120

Table 2. Impact of blending time on BARETab Lub and Physical mix of MCC and Magnesium stearate (0.5%)

comparative Physical parameter evaluation of BARETab Lub and Physical mix of MCC and 0.5% Magnesium										
Parameter	Physical Mixing of Microcrystalline cellulose and Magnesium stearate					BARETab Lub (Self-Lubricating Excipient)				
Blending Time (Mints)	Initial MCC	5 mins	10 mins	15 mints	20 mints	Initial	5 mins	10 mins	15 mints	20 mints
Untapped density (g/ml)	0.30	0.33	0.35	0.37	0.38	0.30	0.30	0.30	0.30	0.30
Tapped density (g/ml)	0.45	0.49	0.504	0.524	0.524	0.405	0.405	0.405	0.405	0.405
H.Ratio	1.50	1.48	1.44	1.38	1.38	1.35	1.35	1.35	1.35	1.35
Compressibility Index (%)	33.33	32.65	30.56	29.39	27.48	25.93	25.93	25.93	25.93	25.93
Angle of Repose (°)	41	41	40	40	41	38	38	38	38	38

Fourier - Transform Infrared Spectroscopy (FTIR): FTIR spectra, we can see clearly that microcrystalline cellulose peaks are shifted due to co-processing of MCC and Magnesium stearate spectra shown in Fig. 2.

Physical parameters evaluation: The physical Parameters of the self-lubricating Excipient and Physical mix of Microcrystalline cellulose and Magnesium stearate are mentioned in Table No. 1.

BARETab Lub and the Physical Mix of MCC and Magnesium stearate untapped density are the same. Flow properties denoted by H. ratio, compressibility, and angle of repose, BARETab Lub having good flowability. When blending time has increased bulk density and flowability increased of physical mix of MCC and magnesium stearate whereas , no impact shown on BARETab Lub material after 20 mints Physical parameters shown in Table 2.

Table 3. Comparative Evaluation of BARETab Lub and Physical Mix of MCC and Magnesium Stearate (0.5%) Tablet

comparative Placebo tablet parameter evaluation of BARETab Lub and Physical mix of MCC and 0.5% Magnesium										
Parameter	Physical Mixing of Microcrystalline cellulose and Magnesium stearate					BARETab Lub (Self-Lubricating Excipient)				
Blending time	Initial MCC	5 mins	10 mins	15 mints	20 mints	Initial	5 mins	10 mins	15 mints	20 mints
Tablet weight (mg)	500.0	500.0	500 .0	500.0	500.0	500.0	500.0	500.0	500.0	500.0
Hardness (N)	10.00	7.81	5.57	3.71	1.89	10.89	10.83	10.84	10.89	10.87
Thickness (mm)	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Friability (%)	00	0.061	0.145	0.321	0.976	00	00	00	00	00
Disintegration Time (Sec)	10.00	12.00	15.00	17.00	25.00	12.00	12.00	12.00	12.00	12.00

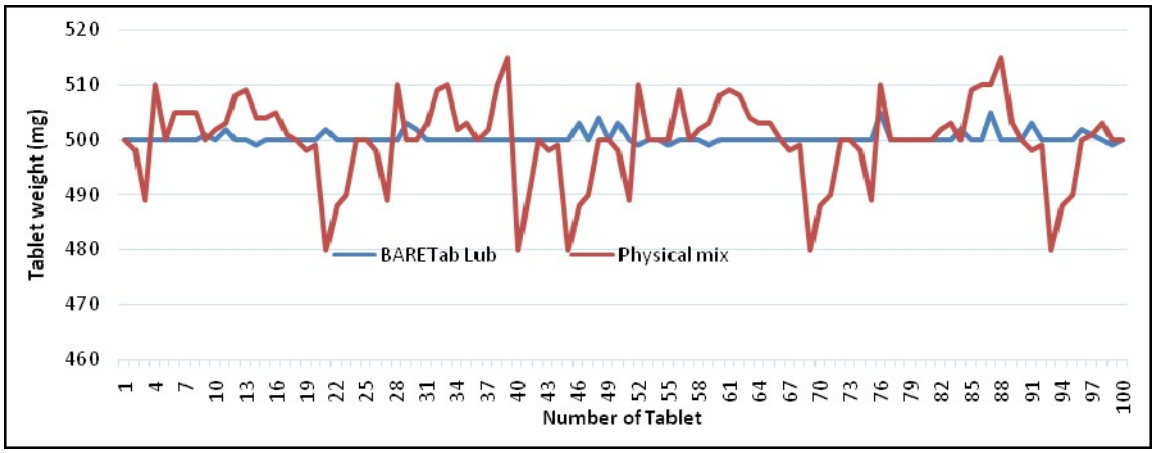


Fig. 3. Weight uniformity (weight variation) comparison of BARETab Lub and Physical mix of MCC and Magnesium stearate

Placebo Tablet evaluation of BARETab Lub and Physical mix of MCC and magnesium stearate: All sample tablets are compressed with the same force and thickness and diameter are also the same. All tablets are white in color, elongated in shape. BARETab Lub has more hardness, less friability, and less disintegration time than a physical mix of MCC and magnesium stearate as shown in Table No. 3. When the blending time increased of both samples, tablet hardness decreased and friability and disintegration time has increased which are shown in Table no.3.

Weight uniformity data of BARETab Lub and Physical mix of MCC and magnesium stearate (0.5%) Placebo Tablet data: Standard weight of placebo tablet was 500 mg , we can see in the Fig. 3 BARETab Lub tablet weight is more unform comparative to physical Mix of MCC and magnesium stearate.

CONCLUSION

In this study, we have observed magnesium stearate shows a negative impact on bulk density and tablet profile especially on tablet hardness, friability, and disintegration time, when blending time is increased. It drops tablet hardness and increases table disintegration time, when disintegration has increased then dissolution will also increase. A physical blend of MCC and magnesium stearate also impacted on weight variation. As per this study co-processed excipient having better physical and tableting result and there are no impact of blending time shown on it.

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