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A COMPARISON STUDY OF GRANULE AND DRY POWDER PROPERTIES OF CO-PROCESSED LACTOSE MONOHYDRATE AND CELLULOSE EXCIPIENTS USING THERMAL AND RHEOLOGICAL TECHNIQUES WITH WATER AS THE BINDER

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Keywords:

Lactose Monohydrate, Microcrystalline Cellulose, Powdered Cellulose, Wet Granulation, Thermal Effusivity, Powder Rheology

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ABSTRACT: Poor flow and cohesion are the most common problems encountered during manufacturing of a tablet. Tablets are produced by compression of formulation ingredients including the drug and excipients that improve processing properties of the product. Excipients may include fillers, diluents, binders, lubricants etc. which are added to impart good flow. Cellulose and Lactose have been widely used in Pharmaceutical Industry as a binder and filler due to their property of excellent flowability and stability. The aim of the experiment is to prepare granules of two co-processed excipients of lactose monohydrate and cellulose using water as a binder and compare their flow properties. Although these excipients can be directly compressed, we use wet granulation technique since it allows the material to be compressed with better flow properties. In Wet granulation technique, the particle size, shape and size distribution are optimized with the use of binder that bonds the powder particles together forming spherical granules. In Cuisinart mixer, 700g of powder was mixed with continuous addition of water for 30 seconds with the mixing time of 3 minutes for three different concentrations of water. The wet mass was passed through U.S. Standard sieve # 14 and the granules formed were dried at 60°C in an oven. These dried granules were then characterized for their flow properties and compared to the dry powder used for direct compression. Tests performed confirmed that wet granulation technique not only improved the flow of granules but also gave better compression and permeability characteristics than dry powder alone.

INTRODUCTION: Tablets are solid dosage forms that typically contain drug substances or API in combination with one or more non-medicinal substances called excipients [1]. Excipients are inert substances that are added to facilitate powder characteristics including flowability [2].

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For a formulation scientist not only the API, but an excipient used in the formulation of solid dosage forms is of equal importance as they may be used for several purposes like binders, diluents, fillers, disintegrants, taste masking agents, coloring agents etc. [3] Pharmaceutical Industries that manufacture solid dosage forms have to deal with the powder flow properties [4]. Characterization of the powdered excipients usually involves analysis of their physical properties such as particle size, particle shape, texture, surface area, density, porosity, shear strength etc. that directly affect the powder flowability [5]. This helps understand the cohesivity

as well as the shear properties like tensile strength, elasticity, compactibility etc. [6]. Powder flow behavior is determined by its chemical and physical properties as well as the processing parameters such as hopper angle, type of blender, vacuum transfer systems, die filling during compression/ encapsulation etc. and storage [7, 8]. Hence, a range of flow properties and equipment parameters must be studied to avoid common handling problems like content uniformity and segregation in pharmaceutical industry [9, 10]. Measuring these flow properties prior to production will allow powder to flow in a reliable manner through the desired equipment [11, 12]. Failure to achieve reliable flow will have a negative impact on the production and market value of the product [13]. There are various traditional methods to measure flowability like Angle of Repose, Bulk/Tap density, Carr's Index and Hausner's Ratio [14]. Newest technology includes Freeman Technology (FT4) Rheometer which helps us to measure multidimensional flow pattern of a given powder [15]. Our research on these two excipients and their characteristics is intended to achieve product with a good flow property and to compare granules prepared by wet granulation and with direct compression technique.

Two co-processed excipients were used for our research. One with alpha-lactose monohydrate and powdered cellulose in 75:25 ratio and the second excipient containing 75:25 alpha-lactose mono hydrate and microcrystalline cellulose (MCC) [16]. Lactose is widely used as a filler/binder and Cellulose as a binder in a pharmaceutical industry for the manufacture of oral tablets [17]. Microcrystalline cellulose has also been known to exhibit some lubricant and disintegrant properties that lead to optimum granule formation as well as provide an advantage during tableting process [18, 19]. Numerous studies on these excipients have proved that moisture content among them influences the physico-chemical properties of the excipient affecting its compactibility, hardness, dissolution and disintegration, as well as its chemical stability [20, 21]. Our aim is to study the effect of water on flow properties of the two selected excipients and compare them with dry powder (No binder).

Wet granulation technique was used to prepare granules with different concentrations of water as the binder. Often known as size enlargement technique, it is one of the oldest method for production of solid dosage forms like tablets and capsules [22]. It is most popular, as granules prepared by this technique meet optimum physical requirements necessary for compressing good quality tablets [23]. There are many ways to perform wet granulation and selection of proper equipment will optimize the process [24]. Wet granules for our experiments were prepared using Cuisinart mixer and Effusivity testing was carried out simultaneously to optimize the amount of binder used [25]. Based on this data, three batches of granules for Excipient A and Excipient B were selected. These were subjected to a range of flow properties using FT4 Powder Rheometer including flow energy, compressibility, permeability, shear stress, wall friction and aeration [26]. Properties of the dried granules were also determined using Texture Analyser, Sieve Analysis and Hardness tester for compressed tablets.

Granule and dry powder properties of both the excipients were studied to differentiate between wet granulation method and direct compression.

MATERIALS AND METHODS:

Materials: Cellactose 80® (Lactose monohydrate and Powdered cellulose) and MicroceLac 100® (Lactose monohydrate and Microcrystalline cellulose):- Donated by Meggle Excipients and Technology, Germany.

Distilled Water: Barnstead Nanopure, Thermo scientific system, Waltham, MA, USA.

Methods

Preparation of granules using wet granulation method: For our study purpose Cellactose 80® and MicroceLac 100® were named Excipient A and B respectively. Lab scale granules were prepared in a mortar and pestle. 10 grams of each excipient was added to the mortar and water was added gradually as the binder. Increasing concentration of water was added to each batch of powder (10g). Thermal effusivity (C-Therm Technologies, Canada) was tested with water ranging from 5% w/w- 55% w/w of water. Depending on the end-point based on effusivity results, three percentages of water were finalized for large scale wet granulation.

Large scale batch of wet granules were prepared using Cuisinart mixer (East Windsor, NJ) with 700 grams of powder. Wet granulation was carried out for 30% w/w, 35% w/w, 40% w/w of water for Excipient A and for 25%w/w, 30%w/w and 35%w/w of water for Excipient B. Addition time was 30 seconds and mixing time of water was 3 minutes for each of the three batches of two excipients at 40rpm. A sample of wet mass was analyzed for thermal effusivity immediately after mixing. The wet powder blend was then screened through US standard sieve # 14. A portion of these wet granules was analyzed for wet tests in FT4 Rheometer. The rest of the granules were dried in an oven at 60°C, testing for its loss on drying (Ohaus, MB 200, NJ) at every 10 minutes until a constant value is obtained. The dried granules were further analyzed using FT4 Powder Rheometer (Freeman Technology, UK), Sieve Analyzer (Octagon 200, Endecotts, UK.), Texture Analyser (Texture Technologies Corp., NY), Angle of Repose and Hardness Tester (Manchester, NH).

Thermal Effusivity Test [23]**:** Each batch of wet granules is subjected to thermal effusivity test after the mixing process. Approximately 1 gram of wet sample was tested by TC probe that detects the rise in temperature at the interface between sample and the plate. Sensor supplies heat (≈ 2°C) to the sample and measures the heat reflected from it.

$$\textbf{Effusivity} = \sqrt{K\,\rho Cp} \qquad (1)$$

K = Thermal Conductivity (W/m•K)
ρ = Density (kg/m3)
Cp = Heat Capacity (l/kg•K)

FT4 Rheometer Test: [15]

Basic Flowability Energy (BFE): BFE involves downward anti-clockwise motion of blade for inducing high stress flow in the powder. It is the work done during the movement of the blade through the powder bed as it moves from top to the bottom of the vessel. Blade moves at a -5° helix and 100 mm/s tips speed. Work done is calculated by the axial and rotational forces exerted on the powder bed.

Formula:

$$dE = \{T/(R\tan\alpha) + F\}dH \qquad (2)$$

dE = Total energy consumed (mJ)
T = Torque (Nm)
R = Radius of the blade
α = Helical path angle as the blade moves
dH = Distance travelled by the blade during the test
F = Axial force on the blade (Newton)

Specific Energy (SE): Specific Energy is calculated from the energy of upward traverse of conditioning cycles 6 and 7 which is divided by the sample mass. Blade moves at a +5° helix and 100 mm/s tips speed and the powder flows under low stress as the blade lifts the particles gently.

Compressibility: Compressibility program uses a vented piston to compress the sample under increasing normal stress. After conditioning and splitting the blade is exchanged with a vented piston before compression occurs. For each normal stress the distance travelled by the piston is measured. Hold period is usually about 60 seconds. Compression force ranges from 0.5 kPa- 15 kPa.

Compressibility = Percent Change in volume after compression (3)

Permeability: Permeability is similar to compression with the addition of air source in the test. Air is passed simultaneously through the vessel at a constant flow rate as the vented piston compresses the powder under increasing normal stress. The pressure drop across the bed is measured for every applied normal stress. This test subjects the powder to a stress ranging from 1 kPa to 15 kPa at a constant velocity of air 2 mm/s during compression.

Permeability can be calculated from the below equation:

$$Q = \frac{KA}{\mu}\frac{Pa - Pb}{L} \qquad (4)$$

Q = Air Volume/ unit time (cm^3/s)
K = Permeability (cm^2)
A = Cross-sectional area of powder bed (cm^2)
Pa-Pb = Pressure drop across powder bed (Pa)
μ = Viscosity of air (Pa.s)
L = Length of the powder bed (cm)

Aeration: Aeration program is a combination of conditioning and test cycles that assess the change in the flow properties as air is passed through the powder bed. Air supply is off during the first test followed by introduction of air and increasing air velocity for each subsequent test. This test uses a

maximum air velocity of 10mm/s with the blade speed of 100 mm/s throughout the test.

$$\textbf{Aeration Ratio (A.R)} = \frac{Energy\ (Air\ Velocity\ 0)}{Energy\ (Air\ Velocity\ n)} \quad (5)$$

Shear Cell: Shear cell test involves a shear head to induce both vertical and rotational stresses in the powder bed. Conditioning is the first step after which the blade is replaced with a vented piston to allow entrained air to escape from the bed surface. Splitting is done next followed by shearing with the help of shear head. Shear stress measured is then recorded.

Wall Friction: Wall friction test is similar to the shear test but it involves use of wall friction head instead of shear head that induces both vertical and rotational stresses. Velocity with which the head rotates is pre-fixed prior to the test.

Wall Friction Angle:

$$\phi = \tan\text{-}1(\tau_w/\sigma_w) \quad (6)$$

τ_w = Shear stress a
σ_w = Normal stress

Granule Tensile Strength: Strength of granules was measured using TA-XT Plus Texture Analyser where TA 54 probe measures the force required to break a granule. Probe is 4mm in diameter and was fixed at a height of 3mm above the base where the sample is placed. The probe slowly moves downwards and crushes the granule kept in the center of the plate. The point where the granule breaks is known as fracture point.

Fracture point = Average force of 10 tests (7)

Tablet Hardness: Hardness was analyzed using Schleuniger tester. This tester consists of an electric motor that drives an anvil to compress the tablet at a fixed rate. The tablet is pushed against the stationary anvil until it crushes or breaks. The force required to break the tablet is measured. Tablets were formed using Carver single punch tablet press weighing 500 mg for each batch and compressing at three different pressures to compare hardness.

Sieve Analysis: Sieve analysis is carried out to analyze the distribution of granules prepared using different concentration of water. 100 grams of granules were weighed and sieved on Octagon 200 sieve shaker for 10 minutes through a series of US standard sieves numbers 14, 16, 20, 25, 30, 60 and a collecting pan at the bottom to collect fines. Granules retained on each sieve were weighed and percent of the total amount of granules added was calculated.

RESULTS AND DISCUSSION:

Effusivity: Thermal Effusivity results for each batch of granules were obtained using C-Therm sensor. **Fig. 1** shows a sharp rise in effusivity at 40% w/w of binder for Excipient A and 35% w/w of binder for Excipient B confirming the endpoint of granulation.

An increase in Thermal Effusivity is observed with increasing water content due to greater thermal conductivity and heat capacity of the wet sample mass at each point. Formation of sticky mass occurs after endpoint and slurry is observed at 50% w/w of water with effusivity value of around 1500 $ws^{1/2}m^{-2}k^{-1}$ for both the excipients, indicating over-granulation. Effusivity of water alone is 1600 $ws^{1/2}m^{-2}k^{-1}$ confirming the same.

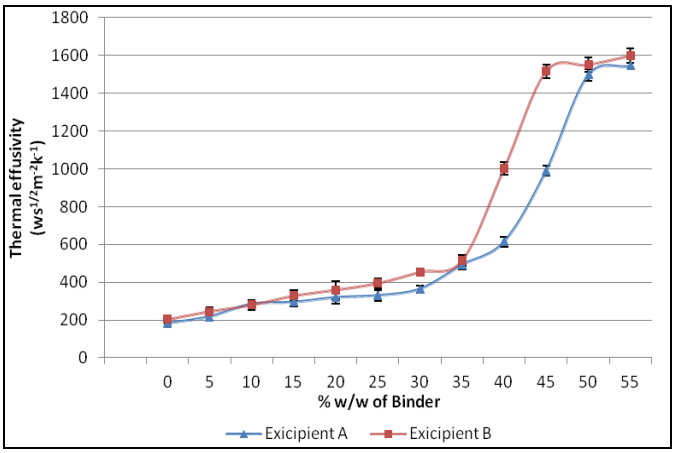

FIG. 1: THERMAL EFFUSIVITY AS A FUNCTION OF BINDER

Basic Flowability Energy: Fig. 2 indicates higher flow energy with increasing water content. This can be attributed to increase in the inter-particulate forces with the increase in binder. At higher concentrations of the liquid, particles are closely bound due to bridge formation between the liquid and particles, resulting in an efficiently packed state. At this point inter-particle spaces disappear as liquid is filled within them resulting in capillary pressure that resists the movement of the blade during the test. This results in higher BFE results.

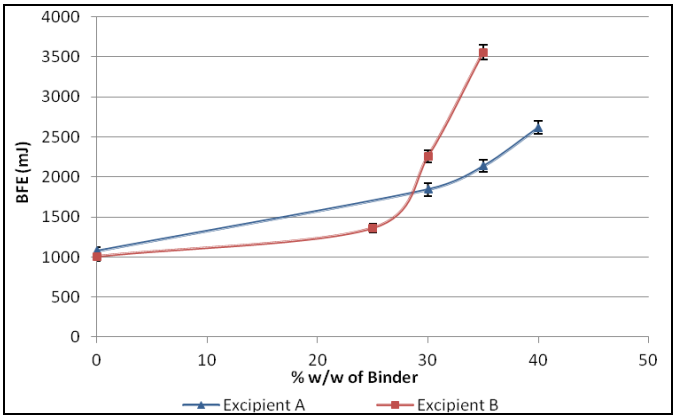

FIG. 2: BASIC FLOWABILITY ENERGY (BFE) OF DRY POWDER AND GRANULES

Specific Energy: As the amount of liquid increases surface tension between the particles increases giving rise to a closely packed cohesive powder bed. The movement of the blade in the upward direction is resisted by this cohesive bed increasing the SE value. Granules formed at the endpoint are bigger in size and have more air pockets in the granule bed compared to the fine dry powder as a result of which the blade moves more swiftly through the granule bed than in dry powder alone. This results in low SE values as seen in **Fig. 3** indicating that the granules have low cohesion and excellent flow properties as compared to dry powder *i.e*. 0% w/w of binder.

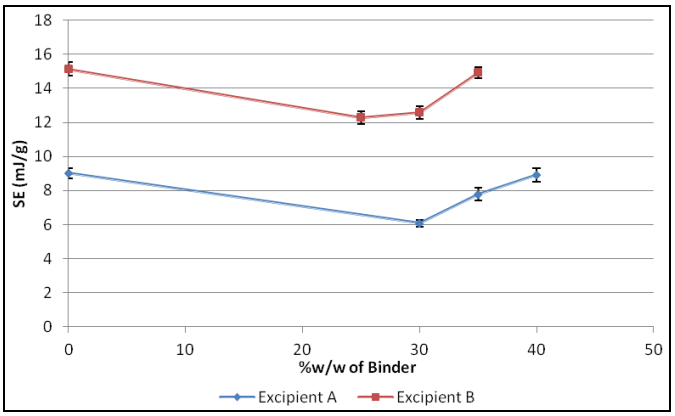

FIG. 3: SPECIFIC ENERGY (SE) OF DRY POWDER AND GRANULES

Compressibility: Dry powder gives lower compressibility value than the dried granules. Addition of granulating liquid leads to formation of liquid bridges between particles which are transformed into permanent bonds on drying, forming granules of high strength. These are larger in size than fine dried powder as two or more particles adhere together to form a granule. Packed spherical granules have more air pockets than the fine dried powder increasing the force required for compressing them. **Fig. 4** confirms that granules formed at the end point provide better compressibility during tablet punching rather than the Excipient A and Excipient B dry powder with no binder.

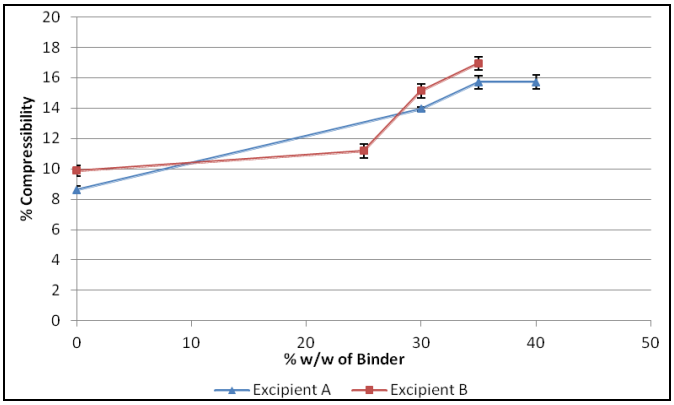

FIG. 4: COMPRESSIBILITY OF DRY POWDER AND GRANULES

Permeability: Cohesive powders will have less permeability to air resulting in high pressure drop values. It results due to small number of channels between particles through which air can pass easily. Decrease in the pressure drop from dry powder to batch of 40% w/w of binder for Excipient A granules and to 35% w/w of binder for Excipient B granules shown in **Fig. 5** suggests that optimum sized granules with low cohesion are formed allowing air to easily pass through the granule bed providing an advantage in processes like feeding through hopper, pneumatic transfer, die filling etc. Dry powder (0% w/w of binder) in both the cases shows higher pressure drop as air has difficulty to pass through the homogenously packed fine powder bed exerting more pressure.

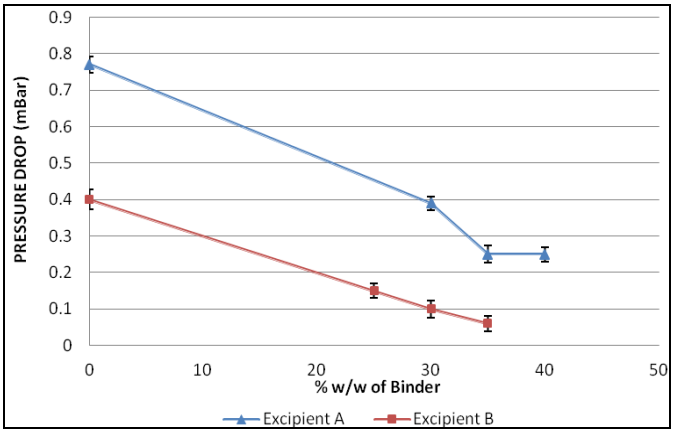

FIG. 5: PRESSURE DROP OF DRY POWDER AND GRANULES

Aeration:
A.R ≈1 Powder is less sensitive to external aeration
2 ≤ A.R ≥ 20 Average sensitivity to aeration
A.R > 20 Highly sensitive to aeration

As seen from **Fig. 6**, increase in the amount of water causes a drop in the A.R ratio and increases aeration energy (AE) respectively. This suggests that as we increase water content granules formed are less sensitive to aeration due to increase in size as compared to the dry powder which has moderate sensitivity to aeration providing advantage during pneumatic transfer and die filling process.

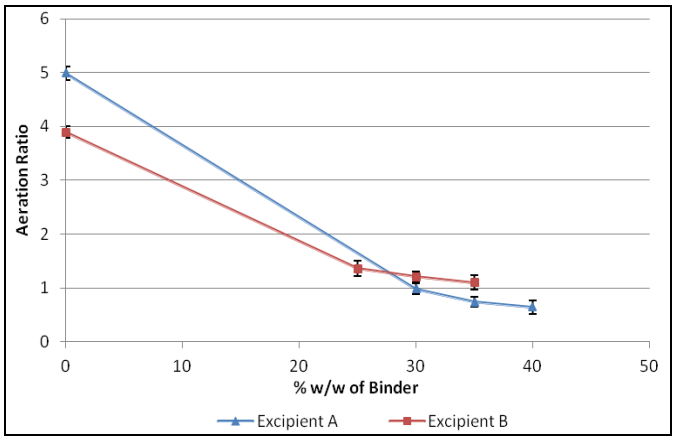

FIG. 6: AERATION RATIO OF DRY POWDER AND GRANULES

Shear Test: The powder initially resists the movement of blade due to which shear stress increases until this resistance is overcome and the powder bed shears. This point is called as the yield point where flow occurs. The greater the shear stress, more difficult it is to induce flow in the powder bed. As seen from **Fig. 7** shear stress goes on decreasing from dry powder to the endpoint in both the excipients.

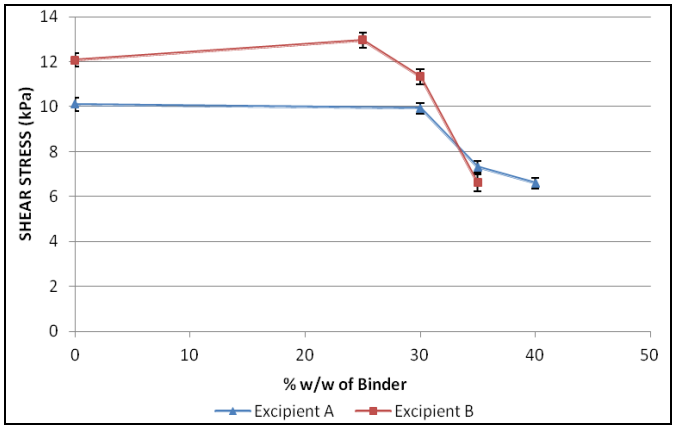

FIG. 7: SHEAR STRESS OF DRY POWDER AND GRANULES

As fine dry powders are packed homogenously with very few channels for air, the flow becomes difficult due to the force exerted by the powder bed. At the endpoint (40% w/w batch of Excipient A and 35% w/w batch of Excipient B) however, formation of optimum granules leads to low resistance offered by the granule bed and air can easily flow around the granules leading to a better flow.

Wall Friction: The larger the Wall Friction angle, the greater is friction exerted by the granules. With the increase in the amount of water the wall friction angle goes on decreasing as shown in **Fig. 8**, suggesting that the granules formed at endpoint are of optimum size as compared to the dry powder.

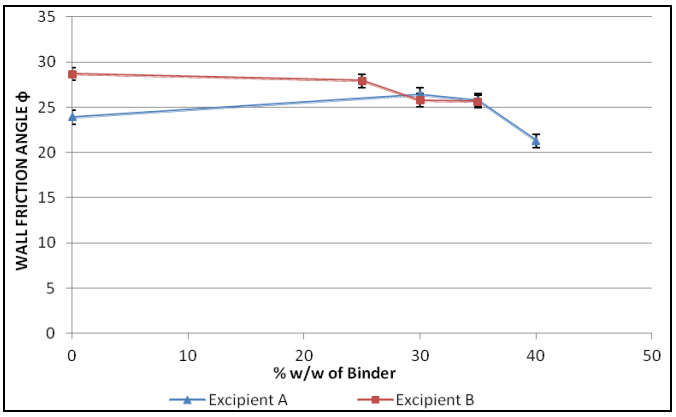

FIG. 8: WALL FRICTION ANGLE OF DRY POWDER AND GRANULES

Texture Analysis: Fig. 9 suggests that Excipient A granules with 40% w/w of binder and Excipient B granules with 35% w/w of binder are stronger and tougher than the rest of the batches of granules.

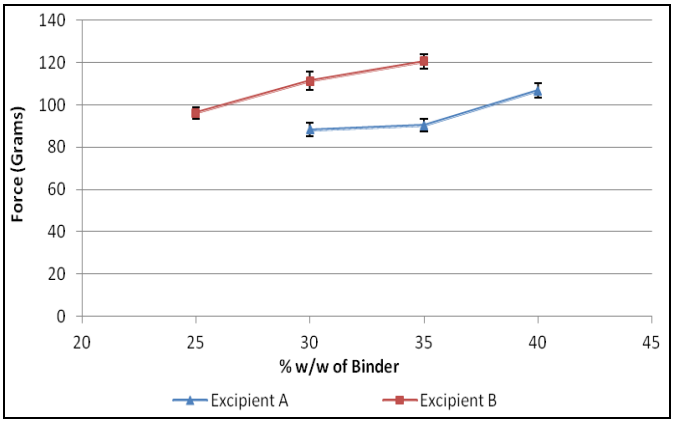

FIG. 9: TEXTURE ANALYSIS OF DRIED GRANULES

The inter-particle forces increase as the spaces between them are filled with liquid binder. Surface tension holds the granules together which form

strong permanent bonds on drying. Hence granules formed at endpoint are stronger providing an advantage during processes like pneumatic transfer which bring about attrition or breaking of granules.

Tablet Hardness: Fig. 10 and **11** suggests that as the concentration of the binder increases, the hardness also increases. The granule hardness given by batch of 40% w/w and 35% w/w of binder for Excipient A and Excipient B respectively, is better at all the three pressures as compared to the other batches of water, indicating optimum granule strength at the endpoint.

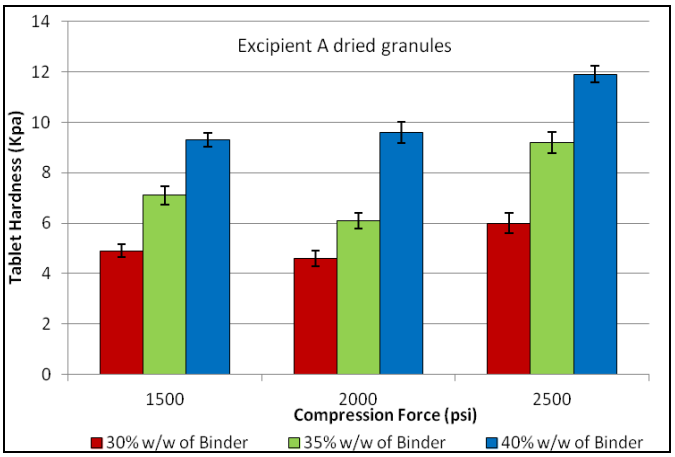

FIG. 10: TABLET HARDNESS FOR EXCIPIENT A DRIED GRANULES

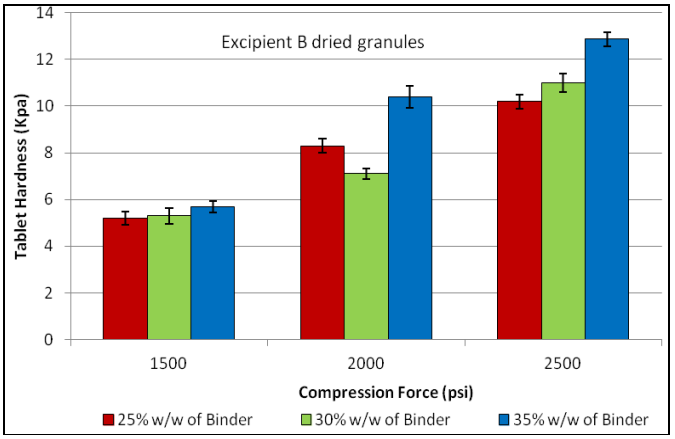

FIG. 11: TABLET HARDNESS FOR EXCIPIENT B DRIED GRANULES

Sieve analysis: Sieve analysis was carried out to check the uniformity of particle size and its distribution. Data from **Fig. 12** and **13** indicates that maximum granules are retained on US standard sieve #16 for 40% batch of binder and 35% w/w of binder for Excipient A and Excipient B respectively indicating better size distribution than the rest. A slight increase in the amount of fines was observed at the endpoint which provides optimum packing of granule bed.

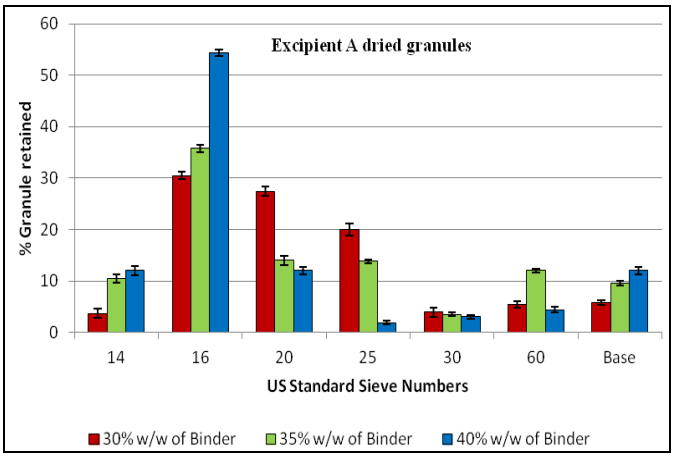

FIG. 12: GRANULES RETAINED FOR EXCIPIENT A

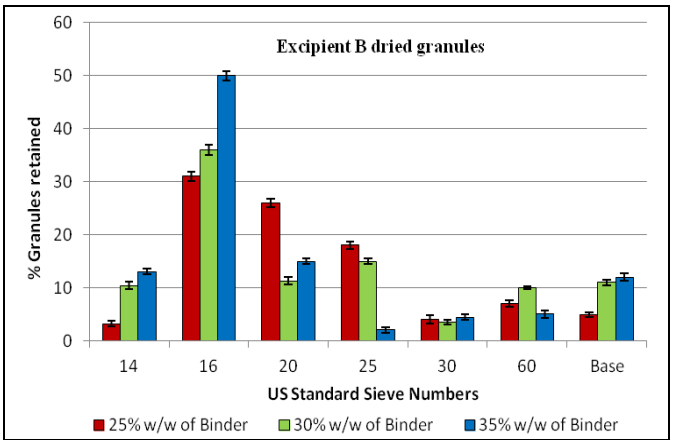

FIG. 13: GRANULES RETAINED FOR EXCIPIENT B

CONCLUSION: Comparison between granules and dry powder of both the excipients confirms the advantage of wet granulation technique over direct compression as it improves flow, permeability and compression properties of the excipients. Characterization of granules using Thermal effusivity probe and FT4 Rheometer indicates that granules formed at the endpoint are stronger and efficiently packed with fines giving optimum size distribution and tablet hardness. This study helps identify optimum binder concentration needed to generate granules with good flow properties. Further studies along with a model drug are needed to understand the impact on powder rheology and tableting properties.

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CONFLICT OF INTEREST: The author declares no conflict of interest.

REFERENCES:

1. Mahato RI and Narang AS: Pharmaceutical dosage forms and drug delivery. CRC Press, Second Edition 2011.
2. Yihong Q, Yisheng C, Geoff GZZ, Lawrence Y and Rao VM: Developing Solid Oral Dosage Forms: Pharmaceutical Theory and Practice. Academic Press, Edition 2, 2016: 151-175.
3. Bhor NJ, Bhusare SE and Kare PT: Multifunctional Excipients: The Smart Excipients. International Journal of Pure & Applied Bioscience 2014; 2(5): 144-148.
4. Rowe RC, Sheskey PJ, Cook WG and Quinn ME: Handbook of Pharmaceutical Excipients. Pharmaceutical Development and Technology. Edition 7, Vol. XVIII, 2013: 544.
5. Sutton S: Optimizing the tableting process with a quality-by-design approach. Pharmaceutical Technology 2012; 36(5): 50-52.
6. Thoorens G, Krier F, Leclercq B, Carlin B and Evrard B: Microcrystalline cellulose, a direct compression binder in a quality by design environment- A review. International Journal of Pharmaceutics 2014; 1-2:64-72.
7. Jager PD, Bramante T, Luner PE: Assessment of Pharmaceutical Powder Flowability using Shear Cell-Based Methods and Application of Jenike's Methodology. Journal of Pharmaceutical Sciences 2015; 104(11):3804-3813.
8. Huang W, Shi Y, Wang C, Yu K, Sun F and Li Y: Using spray-dried lactose monohydrate in wet granulation method for a low-dose oral formulation of a paliperidone derivative. Powder Technology 2013; 246: 379-394.
9. Leturia M, Benali M, Lagarde S, Ronga I and Saleh K: Characterization of flow properties of cohesive powders: a comparative study of traditional and new testing methods. Powder Technology 2014; 253: 406-423.
10. Barnum RA and Khambekar J: Going with the flow: Using powder flow behavior as part of the design process for implementing new formulations and handling equipment. Pharmaceutical Processing 2010; 25(3): 22-24.
11. Schulze D: Shear testing of powders for process optimization. Annual Transactions of the Nordic Rheology Society 2013; 21: 99-106.
12. Prescott JK and Barnum RA: Improving powder flow during pharmaceutical operations. Rx Times Pharmacy, Jenike and Johanson Inc., 2010.
13. Fayed ME, Otten L: Handbook of powder science & technology. Springer Science & Business Media, Second Edition 2013.
14. Zettler A, Hilden J, Koenig M, Breslin C, Aburub A, Allgeier M, Patel P and Mitra B: Evaluation of Small-Scale Powder Flow Characterization Tests in the Prediction of Large-Scale Process Failures. Journal of Pharmaceutical Innovation 2016; 11(3):189-199.
15. Freeman R: Measuring the flow properties of consolidated, conditioned and aerated powders- A comparative study using a powder rheometer and a rotational shear cell. Powder Technology 2007; 174(1): 25-33.
16. Mirani GA, Patankar PS, Borole SV, Pawar SA and Kadam JV: Direct compression high functionality excipient using coprocessing technique: A brief review. Current Drug Delivery 2011; 8(4): 426-435.
17. Wang S, Li J, Lin X, Feng Y, Kou X, Babu S, Panicucci R: Novel coprocessed excipients composed of lactose, HPMC, and PVPP for tableting and its application. International journal of pharmaceutics 2015; 486(1):370-379.
18. Dugar RP, Dave RH: To study the effects of solvent and relative humidity on rheological and thermal properties of microcrystalline cellulose granules using hydroxypropyl methylcellulose as binder. International Journal of Pharmaceutical Sciences and Research 2014; 5(9)**:**3616-3626.
19. Chaudhari SP, Dave RH: To prepare and characterize microcrystalline cellulose granules using water and isopropyl alcohol as granulating agents and determine its end-point by thermal and rheological tools. Drug Development and Industrial Pharmacy 2014; 40(5): 744-752.
20. Viljoen JM, Steenekamp JH, Marais AF, Kotzé AF: Effect of moisture content, temperature and exposure time on the physical stability of chitosan powder and tablets. Drug development and Industrial Pharmacy 2014; 40(6):730-42.
21. Crouter A and Briens L: The effect of moisture on the flowability of pharmaceutical excipients. AAPS PharmSci Tech 2014; 15(1):65-74.
22. Shanmugam S: Granulation Techniques and Technologies: Recent Progresses. BioImpacts 2015; 5(1): 55–63.
23. Saikh MA: A technical note on granulation technology: a way to optimise granules. International Journal of Pharmaceutical Sciences and Research 2013; 4(1):55.
24. Kayrak-Talay D, Dale S, Wassgren C, Litster J: Quality by design for wet granulation in pharmaceutical processing: assessing models for a priori design and scaling. Powder technology 2013; 240:7-18.
25. Dave RH, Wu SH and Contractor LD: To determine the end point of wet granulation by measuring powder energies and thermal properties. Drug Development and Industrial Pharmacy 2012; 38(4): 439-446.
26. Freeman T: Quantifying experience in powder processing. Pharmceutical Technolgy Europe 2009; 21(3): 16-21.

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