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Evaluation of Physical Properties of Selected Excipients for Direct Compressible Tablet

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Abstract

Excipients play important roles in the manufacturing of direct compressible tablet. The physical properties of excipients like flow properties, bulk density, tapped density, compressibility and diameter of particles are the most important studies which should be taken under consideration. Excipients like lactose, ludipress, avicel, povidone, sodium starch glycolate, sodium lauryl sulfate, sodium carboxy methyl cellulose, polyethylene glycol 4000 (PEG 4000) and maize starch are used and found that PEG 4000, avicel PH-101, ludipress and sodium lauryl sulfate showed an angle of repose below 40^0 which indicates good flow properties and others are not. The highest compressibility value is obtained from lactose and compressibility value was lowest for PEG 4000. It was found from the average diameter of excipients that sodium starch glycolate is very fine graded powder because all particles pass through a sieve (100 mesh) and the highest value is obtained from PEG 4000.

Key words: Flow property, Compressibility, Direct Compression.

Introduction

Tablet is the most widely used and stable preparation as well as cost effective among the solid dosage forms (Alderborn, 2007; King, 1980). Tablet is manufactured by preparing granules first. Wet granulation and dry compaction are used for preparing granules (Alderborn and Wikberg, 1996; Kleinebudde, 2004). Direct compression is another suitable and efficient method of tablet manufacturing for water degradable active pharmaceutical ingredients (API). Flow property, bulk density, tapped density, particle size, size distribution of particle and compressibility play an important role in manufacturing tablet. Poor flow property of powder from hopper to die cavity is one of the common problems of pharmaceutical industry. Problem in flow property mainly gives rise to wet variation and tablet problems may be happened during manufacturing (Wu, *et al*., 2007). To know about flow property, it is important to determine the angle of repose as well as tapped and untapped density of different excipients (Govedarica *et al*., 2011). Usually bulk density is of great importance when one considers the size of a high-dose tablet product or the homogeneity of a low-dose formulation in which there are big differences in drug and excipients densities. Compressibility of the excipients is directly related to the powder flow property and bulk density (Carr, 1965). Some drugs have very poor compressibility e.g. vitamin E and these drugs are very difficult to formulate into tablet. Direct compression method of tablet preparation can only be used with high compressible graded excipients (Liberman, 1981). Particle size and size distribution governs the flow property and compressibility of the excipients (Maja *et al*., 2012). Generally particle size has a proportional relationship with the flow property of the excipients. Excipients with higher particle size exhibits good flow property and vice versa. The main purpose of this research work is to find out the appropriate excipient(s) by comparing their physical properties from a selected list of

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excipients so that suitable excipient(s) can be short listed in order to know which excipient(s) can be used for direct compressible tablet to get the best and effective result.

Materials and Methods

Materials: Lactose, ludipress, avicel PH-101, avicel PH-102, povidone K-30, sodium starch glycolate, sodium lauryl sulfate, sodium carboxy methyl cellulose, polyethylene glycol and maize starch were used in preparing tablets and they were purchased from local market. All other chemicals used were of analytical grade.

Measurement of angle of repose: The angle of repose of the powdered excipients was measured by using a funnel and a petridish. At first, the funnel was fixed with a funnel holder above 6 inch height from the petridish. Then the powder was allowed to fall freely through the funnel until a cone is formed on the petridish. When the cone is formed then powder passing was stopped, because further powder passing may cause fall of powder from the petridish. Then the height and the diameter of the cone were determined by a scale. By using the following formula angle of repose of all the excipients were determined,

$\tan\theta = 2h/D$, where **"D"** is the diameter of the cone and **"h"** is the height of the cone.

*Measurement of bulk density (Untapped density)***:** For determining the bulk density of the excipients a certain amount of powder was weighed. Then the powder was poured into a graduated cylinder and from the cylinder volume was measured. During pouring the powder into the cylinder, the cylinder was kept at 45^0 angle to avoid the initial taping of the powder. If the powder is poured into the cylinder keeping it at 90^0 angle then the powder will be tapped and the actual bulk density will not be obtained. Then by using the following formula we determined the bulk density of the excipients,

Bulk density = Mass/Volume

Measurement of tapped density: In order to determine the tapped density of the powdered excipients a certain amount of powder was weighed by taking it in a measuring cylinder. Then the measuring cylinder was placed on a mechanical tapper apparatus, which was operated for 100 times tapping. After tapping the powder bed volume reached a minimum. Using the weight of the powdered excipients in the cylinder and this minimum volume, tapped density was computed.

Measurement of percent compressibility: Percent compressibility of the powdered excipients was determined directly from the following formula,

$$Compressibility\ Index = 100 \times \left(\frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} \right)$$

Determination of particle size and size distribution: The particle size distribution of each excipient was characterized by sieve analysis. A weighed quantity of the excipients was passed through a set of nested sieves consisting of United States standard sieves of 40, 60, 80, 100 and 120 corresponding to opening sizes of 425, 250, 175, 150, and 125 μm. The bottom of the nested assembly was fitted with a collection pan and shaken. The weight of powder on each sieve was calculated and from there particle size distribution was obtained.

Particle diameter was determined by a series of calculation. At first, the arithmetic mean opening of the sieves was determined. Then the percentage of retained powder on each sieve was calculated. After that the multiplied value of arithmetic mean opening and % retained was divided by total percent retained i.e.100. This value represents the diameter of the excipient. In this way the diameter of the other excipients was calculated.

$$\text{Particle diameter} = \frac{\text{Arithmetic Mean Opening of the sieves x \% of the retained powder on each sieve}}{\text{Total \% retained}}$$

Results and Discussion

Physical parameters of excipients play an important role in manufacturing tablets. Without maintaining the physical properties like angle of repose, tapped and bulk density, hausner ratio and particle

diameter, it is difficult to manufacture a quality tablet. If physical properties are not maintained then it will not be possible to get the tablet with desired quality as the compression will not be done properly and various problems like picking, chipping etc will be occurred. These will cause the loss of products and patient compliance will be hampered. If the physical properties of excipients are not selected carefully than the flow rate of powders will not be satisfactory. Different manufacturing problems of tablets may occur because of this unsatisfactory flow rate. For better direct compressible tablet formulation these criteria of excipients should be maintained.

Incase of flow property it was observed from the table1 and figure 1 that lactose, maize starch, sodium starch glycolate and avicel PH 102 reflects unsatisfactory flow property having the angle of repose 50.18º, 50.05º, 49.25º and 43.35º respectively. On the other hand, ludipress, sodium lauryl sulfate, avicel PH 101, PEG 4000, povidone K 30 showed good flow property having the angle of repose 37.67º, 36.87º, 34.77º, 30.24º and 38.90º respectively. Value for angle of repose $\leq 30^0$ usually indicates a free- flowing material and angles $\geq 40^0$ suggest a poorly flowing material (Carr., 1965). No free flowing material was found. From table 1 and figure 2, untapped density was found higher incase of ludipress and PEG 4000 which were 0.637g/ml and 0.540g/ml respectively. Tapped density was found higher incase of lactose and ludipress having the value 0.714g/ml and 0.703g/ml respectively. From table 1 and figure 2, it was also seen that, avicel PH 102, avicel PH 101, sodium starch glycolate, sodium lauryl sulfate and maize starch showed comparatively low untapped and tapped density. Hausner ratio was minimum for PEG 4000 and maximum for lactose having the value of 1.05 and 1.83 respectively (Table 1). A hausner ratio greater than 1.25 is considered to be an indicator of passable flow property but not excellent one (Carr., 1965). Lactose and Maize starch reflected higher compressibility than others. Povidone K 30 and avicel PH 101 exhibited almost similar compressibility. But PEG 4000 and sodium carboxymethyl cellulose showed very low compressibility compared to others. In case of particle size and size distribution povidone K30, ludipress, lactose, avicel PH 102 and maize starch showed high percentages particles in 0.18-0.25 mm size range. Avicel PH 101, sodium carboxymethyl cellulose, sodium lauryl sulfate and polyethylene glycol showed high percentages particles in 0.25-0.42 mm size range. No particles of sodium starch glycolate retained in 0.25-0.42 mm, 0.18-0.25 mm and 0.12-0.15 mm range. That means the particles are very fine graded. High percentages particles of sodium starch glycolate retained in 120 mesh sieve. But it requires more than 120 mesh sieves to get an idea about its particle size and size distribution.

PEG 4000 showed the highest diameter which was 0.32 mm, among the others (Table 1). Avicel PH 102, maize starch, lactose, ludipress, povidone K 30, sodium lauryl sulfate showed comparatively lower particle

Table 1. Comparison of physical properties of selected excipients.

Excipients	Angle of repose (Degree)	Untapped density (g/ml)	Tapped density (g/ml)	Hausner ratio[a]	Compressibility index	Particle diameter (mm)
Polyethylene glycol 4000	30.24	0.540	0.571	1.05	5.42	0.32
Avicel PH-101	34.77	0.289	0.338	1.16	14.49	0.26
Sodium lauryl sulfate	36.87	0.285	0.338	1.18	15.70	0.24
Ludipress	37.67	0.637	0.703	1.10	17.95	0.23
Povidone K-30	38.90	0.370	0.434	1.17	14.62	0.23
Sodium carboxymethylcellulose	40.90	0.454	0.489	1.07	7.05	0.27
Avicel PH-102	43.35	0.282	0.350	1.24	19.17	0.20
Sodium starch glycolate	49.25	0.305	0.382	1.25	20.34	
Maize starch	50.05	0.305	0.441	1.44	31.99	0.21
Lactose	50.18	0.389	0.713	1.83	45.45	0.21

a = Tapped Density/Untapped Density

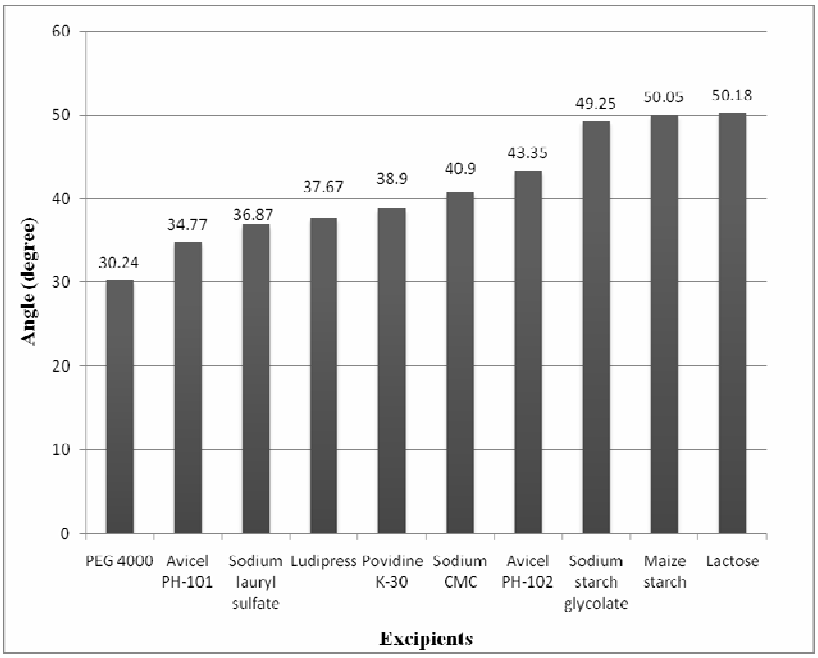

Figure 1. Angle of Repose of selected Excipients.

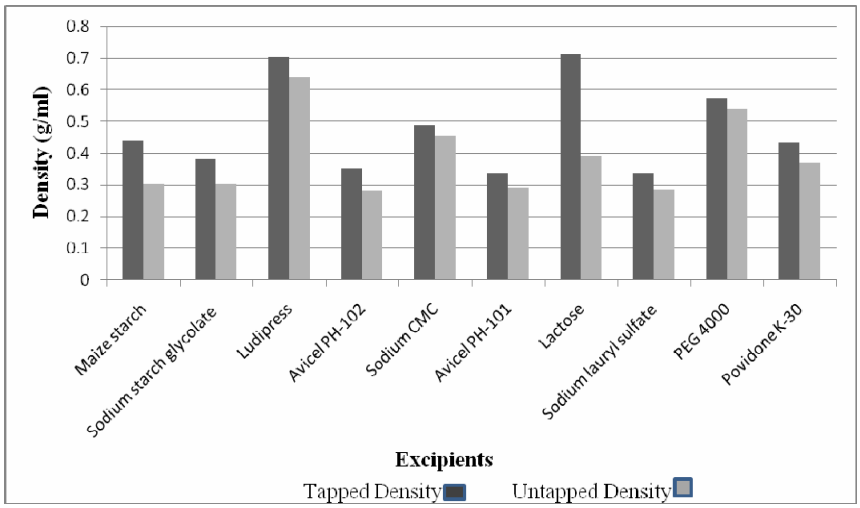

Figure 2. Untapped and tapped density of selected excipients.

diameter which was 0.20mm, 0.21mm, 0.21mm, 0.23 mm, 0.23 mm, 0.24 mm respectively. It is observed that most of the excipients with higher particle size showed good flow property.

Conclusion

From the current study it was found that, PEG 4000 met most of the physical properties like angle of repose, tapped and untapped density, hausner ratio, compressibility index and compressibility when it was compared to the reference standard rather than other selected excipients. Future studies can be done by taking other excipients with similar process which will definitely give an idea of better excipients for better direct compression of tablet.

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