

# Influence of Formulation and Excipient Variables on the Pellet Properties Prepared by Extrusion Spheronization

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**Abstract:** Four commercial grades of microcrystalline cellulose, Avicel PH 101, Avicel PH 102, Avicel PH 112 and Avicel PH 302 were compared for extrusion spheronization. Model mixes containing Avicel PH 101 with different proportions of fillers like lactose and dicalcium phosphate dihydrate (DCPD) were also compared to observe the influence of these fillers on the pellet properties. The amount of water used for granulation of Avicel/ Avicel mixes was kept constant so as to evaluate and quantitate the influence of these excipients/fillers on the pellet properties. The various pellet properties evaluated included, drug release, size and size distribution, shape, density, friability and flow.

Mean pellet diameter did not vary among the Avicel grades. Pellets prepared with different proportions of Avicel PH 101 and lactose were more or less similar in mean diameter. The same phenomena were observed in case of DCPD as well. Plain lactose pellets were the largest in size. Therefore, it can be inferred that the presence of Avicel suppressed the change in pellet size.

Circularity was found to be significantly linear function of log of bulk density of Avicel powders. As revealed by the SEM photographs, pellets of Avicel PH 101 were fairly round where as those containing Avicel PH 302 were dumbbell shaped. Formulations containing DCPD showed the highest circularity.

Drug release rate varied in all the formulations. Among the Avicel grades, Avicel PH 302 showed the highest drug release rate where as Avicel PH 101 showed the least. Drug release also varied as a function of the type of filler and their proportion in the pellets. For both the fillers, the drug release increased with an increase in their proportion. Less water was required for formulations containing higher amounts of lactose and DCPD. Plain DCPD failed to spheronize, although pellets of plain lactose could be formed at the investigated level of water.

**Keywords:** Avicel, extrusion, spheronization, pellets, lactose, dicalcium phosphate dihydrate.

## INTRODUCTION

Pellets are increasingly being used as multiple unit dosage forms. Pellets possess many pharmacological advantages as they disperse freely in the gastrointestinal tract, maximize drug absorption, reduce peak plasma fluctuations and minimize potential side effects without appreciably lowering the bioavailability [1]. They avoid high local concentrations of bioactive agents, which may inherently be irritative or anesthetic to stomach [2]. Additionally they reduce intra and inter subject variability of plasma profiles by reducing variations in gastric emptying rates and overall transit times.

Extrusion-spheronization is the most commonly used method for pellet production [3]. Use of suitable excipients and fillers can be made to produce pellets of desirable quality [4]. Different excipients from a variety of sources have been evaluated for the formation of spherical pellets [5,6]. Spherical pellets possess many advantages, including a low surface area to volume ratio, good flow properties and uniformity in packing [7]. This ideal shape of pellets makes

them excellent substrates for coating as desired for aesthetic purposes or controlled release of active ingredients [1]. Microcrystalline cellulose (MCC) is the most commonly used excipient in extrusion / spheronization. It leads to the formation of round spheres with desirable characteristics. During spheronization, the moisture entrapped in the MCC microfibrils adds plasticity to the extrudates and helps to round the short extrudates into spherical pellets [8]. MCC may also act as a crystallite gel [9] or as a sponge [10] to aid the production of pellets by extrusion-spheronization. However, MCC obtained from different sources varies widely in properties. There have been many reports on the inherent variability in physical properties that exist between MCCs of different batches/ manufacturers.

Lactose and dicalcium phosphate dihydrate (DCPD) are very widely used tableting excipients, but little information is available about the impact in pellet properties by the use of these two fillers in combination with MCC. In the current study, the influence of Avicel grades, obtained from a single manufacturer, on the critical pellet properties has been investigated. Also the possibility of improving the pellet properties by the incorporation of the two fillers, lactose and dicalcium phosphate dihydrate (DCPD) and the spheronization behavior of such mixtures have been studied.

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## MATERIALS AND METHODS

### Materials

Piroxicam was a generous gift from Lark Laboratories, New Delhi, India. The Avicel grades used for the purpose, Avicel PH 101 (Mean particle size 50  $\mu\text{m}$ , Bulk density 0.298g/ml), Avicel PH 102 (mean particle size 100 $\mu\text{m}$ , Bulk density 0.353 g/ml), Avicel PH 112 (mean Particle size 100 $\mu\text{m}$ , Bulk Density 0.342g/ml) and Avicel PH 302 (mean particle size 100 $\mu\text{m}$ , Bulk density, 0.423g/ml) were obtained from FMC Corporation, Philadelphia, USA. Lactose monohydrate was purchased from Loba Chemie, Mumbai, India. Dicalcium phosphate dihydrate was obtained from E. Merck Ltd. Mumbai, India. All other chemicals and reagents used were of Analytical grade.

### Methods

#### Preparation of Pellets

The drug content of all pellets was kept constant to 5%. Pellets were prepared according to the formula given in Table 1. Distilled water was used as the moistening liquid. The amount of water used for moistening of different Avicel grades (E1-E4) was kept constant. For all the rest batches the amount of water required for moistening was as per quantities mentioned in Table 1. Fifty grams of the powder mass was moistened and extruded through an extruder (Caleva extruder 25) and subsequently spheronized on a spheronizer (Caleva spheronizer 120) at a fixed rpm for 2 mins. The spheronization time was kept low so as to clearly differentiate the effect of the excipient and/or fillers on the

pellet properties (particularly on pellet shape). The wet pellets thus obtained were dried in a tray dryer (Narang, New Delhi) at 50° C for 24 h.

#### Size Analysis

The size analysis of the pellets was done by carrying out the sieve analysis of the prepared batches. A sieve shaker (Nippon, India) vibrating at 1 mm amplitude for 20 minutes was used for separating the pellets into various size fractions. The mass median diameter and span were employed to characterize the pellet size and size distribution. The mass median diameter of the pellets was taken to be the pellet diameter at the 50% mark on the respective cumulative percent oversize plot. The span of the pellet size distribution was calculated as the ratio of the difference between the pellets diameter at the 90% and at the 10% to the pellets diameter at the 50% [11].

The modal class fraction referred to the size fraction obtained from sieving with the highest weight of pellets.

#### Shape Analysis

At least 50 pellets from each batch were randomly selected from the modal class fraction obtained from size analysis by sieving for shape analysis. The pellets were mounted on a light microscope fitted to a Camera Lucida and the images of the pellets were drawn manually on a graph paper. The area of the images (A) and the maximum and minimum radii were calculated from which the various shape factors were calculated as reported by Koo and Heng, 2001 [3], as per the following formulae:

**Table 1. Details of the Various Batches Prepared for Extrusion-Spheronization**

EXCIPIENT VARIABLES		
FORMULATION CODE	EXCIPIENTS	% OF WATER USED FOR GRANULATION (DRY BASIS)
E1	Avicel PH101	80%
E2	Avicel PH102	80%
E3	Avicel PH112	80%
E4	Avicel PH302	80%
FORMULATION VARIABLES		
FORMULATION CODE	EXCIPIENTS	
FL1	Avicel PH 101(75%)+ Lactose (25%)	64%
FL2	Avicel PH 101(50%)+ Lactose (50%)	48%
FL3	Avicel PH 101(25%)+ Lactose (75%)	32%
FL4	Lactose (100%)	16%
FD1	Avicel PH101 (75%)+ DCPD (25%)	64%
FD2	Avicel PH101 (50%)+ DCPD (50%)	48%
FD3	Avicel PH101 (25%)+ DCPD (75%)	32%

$$\text{Roundness} = \frac{\text{area}}{x (\text{max. rad})^2}$$

$$\text{Elongation} = \frac{\text{Max. radius}}{\text{Min. radius}}$$

$$\text{Rectang} = \frac{\text{area}}{4x \text{max.rad} x \text{min.rad}}$$

The Electron micrographs of the pellets were taken with the help of a scanning electron microscope (JSM 6100 JEOL JAPAN). The pellets were mounted onto stubs using double-sided adhesive tapes. The pellets were then coated with gold palladium alloy (150-200A<sup>0</sup>) using fine ion coat sputter (JEOL, fine ion sputter JFC-1100), before being examined under the scanning electron microscope.

#### Bulk, Tapped and Granule Densities

Pellets were poured gently through a glass funnel into a graduated cylinder cut exactly to 10 ml mark. Excess pellets were removed using a spatula and the weight of the cylinder with pellets was determined. Weight of the pellets required for filling the cylinder volume was calculated. The cylinder was then tapped from a height of 2 cms until the time when there was no more decrease in the volume. Bulk density ( $\rho_b$ ) was calculated as the quotient of the weight of the pellets and the volume of the cylinder used. Tapped density ( $\rho_t$ ) was calculated as the quotient of the weight of the pellets and its final volume after tapping. Hausner ratio ( $H_R$ ) and Carr index ( $I_c$ ) were calculated according to the two equations given below:

$$H_R = \rho_t / \rho_b$$

$$I_c = (1 - \rho_t / \rho_b) / \rho_t$$

For the determination of granule density, exactly 1 g of the pellets were poured into 5 ml of petroleum ether taken in a 5 ml volumetric flask. The volume of the ether displaced was measured. The quotient of the weight of pellets and the volume of petroleum ether displaced was taken as the granule density ( $\rho_g$ ). All the determinations were done in triplicate and the average  $\pm$  S.D was calculated.

#### Flow Properties

The flow properties were characterized in terms of angle of repose and flow rate. For the determination of angle of repose, the pellets were poured gently through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2 cm above a hard surface. The pellets were poured till the time when the upper tip of the

pile surface touched the lower tip of the funnel. The  $\tan^{-1}$  of the (height of the pile / radius of its base) gave the angle of repose.

The flow rate was calculated as the time taken for 10 g of pellets to flow through a funnel of 5 mm internal diameter. All the determinations were repeated in triplicate and the average  $\pm$  S.D was calculated.

#### Friability

5 g accurately weighed pellets were taken from the modal class fraction of the pellets and placed in a friabilator (Macro, New Delhi) and tumbled for 200 revolutions at 25 rpm. Twelve steel balls (diameter 6.3mm, weighing 1.028 g each) were used as attrition agents. After friability testing, the pellets were sieved through a sieve of 355 $\mu$ m aperture. The weight loss (%F) after friability testing was calculated as:

$$\%F = \frac{W_i - W_r}{W_i} \times 100$$

Where  $W_i$  was the initial weight of the pellets before friability testing, and  $w_r$  was the weight of pellets retained above the sieve after friability testing.

#### Dissolution Studies

400 mg of the pellets (equivalent to 20 mg drug) of 18/25-mesh fraction were used for the drug release studies. A constant sieve fraction of the pellets were used for each batch so as to minimize the effect of change in total surface area upon dissolution rate. USP dissolution apparatus Type I was used for the studies at 50 rpm. Simulated gastric fluid (without pepsin) was used as the dissolution media, samples were withdrawn after predetermined time intervals and were analyzed by UV spectrophotometry at a  $\lambda_{\text{max}}$  of 333.0 nm. The dissolution studies were conducted in triplicate and the average drug release  $\pm$  S.D. calculated.

## RESULTS AND DISCUSSION

#### Size and Size distribution

The results of the size analysis data are shown in Table 2. The mean pellet diameter did not differ much among the different Avicel grades keeping the processing conditions constant. The inclusion of higher concentrations of lactose or DCPD however changed the pellet size. Pure DCPD failed to spheronize. Pure lactose pellets (FL4) showed the largest mean pellet diameter. When lactose constituted 75% of the

Table 2. Size Analysis of Different Formulations

	E1	E2	E3	E4	FL1	FL2	FL3	FL4	FD1	FD2	FD3
Arithmetic Mean diameter(mm)	0.662	0.659	0.686	0.664	0.638	0.654	0.703	0.894	0.684	0.665	0.547
Geometric Mean diameter(mm)	0.601	0.587	0.616	0.600	0.574	0.589	0.639	0.805	0.616	0.599	0.492
Span	0.619	0.509	0.594	0.646	0.470	0.463	0.456	0.403	0.683	0.729	0.743

total excipients (FL3), the mean pellet size was larger than Avicel PH 101 pellets (E1). Like wise, the mixture containing 75% DCPD (FD3) had different pellet diameter than pellets prepared with Avicel PH 101 (E1). At lower concentration (up to 50%), both lactose and DCPD did not have much effect on the mean pellet diameter as compared to Avicel PH 101 pellets (E1). This may be attributed to the fact that Avicel acts as a molecular sponge [10] and suppresses the change in pellet size induced by the presence of lactose or DCPD. According to the sponge model, the extrusions and subsequently the spheronization properties of MCC depend on the microfibrils of the MCC and the void spaces in between them. Apart from the water present inside the pores of the fibers, water present in this void space provides adequate rheological properties to the wet mass, which further helps in extrusion-spheronization. When small molecules like lactose or DCPD are added to this mass in small concentrations (i.e. up to 50%), they could well reside in these void spaces and the fibers will be able to retain their own properties with a little effect of the presence of the fillers. This is also supported by the decrease in the water requirement with increase in the concentration of the fillers.

The span values among the four Avicel grades differed from one another. However, no correlation could be found among them.

### Shape Analysis and SEM

Circularity is an important pellet characterization parameter as the shape of the pellets can affect other properties such as flowability and coating performance. It can be seen from Table 3 that, the circularity parameter differed among the different Avicel grades. This finding is in agreement with the report published by Koo and Heng, 2001 [3]. For the same processing conditions, Avicel PH 101 (E1) gave fairly round pellets (Fig. 2,a), where as dumbbell shaped pellets were obtained with Avicel PH 302 (E4) (Fig. 2,d). This difference in roundness can be attributed to the density differences of the pure Avicel powders. With an increase in Avicel density, the roundness decreased and a good correlation ( $r^2 = 0.98$ ) could be obtained when the circularity values were plotted against the log Bulk density of Avicel powders (Fig. 1). High-density MCC grades have low void volumes and are poorly compressible. Thus, when subjected to attrition and rounding forces during extrusion

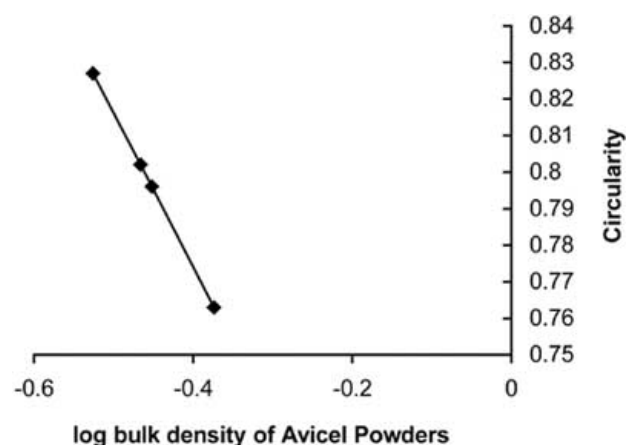


Fig. (1). Circularity vs. log Bulk density of Avicel powders.

spheronization process, these Avicel grades are inherently more resistant to deformation and spheronization. The Avicel grades with lower densities allowed pellets to deform more quickly and easily into more spherical pellets.

The incorporation of Lactose or DCPD, also affected the circularity parameters. Lactose decreased the circularity where as DCPD increased the circularity. Pellets containing 75% DCPD (FD3) were highly spherical and had smooth surfaces.

SEM photographs of some selected batches are shown in Fig. 2. The change in the shape of the pellets resulting from a change in the formulation parameters can be clearly seen here. The pellet shape changed from fairly spherical (Fig. 2,a) to fairly dumbbell shape (Fig. 2,d) as the densities of the Avicels used in the study increased. The pellet shapes of E2 and E3 (Fig. 2,b, and c) are intermediate between those of E1 (Fig. 2,a) and E4 (Fig. 2,d). Further it is clearly visible that when DCPD is added to the formulation (FD3), the sphericity and smoothness of the pellets increased (Fig. 2,e), where as by incorporation of lactose (FL4), the opposite results were obtained (Fig. 2,f).

### Density of Pellets

Table 4 shows the various densities of the formulations. All the three, bulk, tapped and granule densities differed

Table 3. Shape analysis of Different Pellet Formulations

	E1	E2	E3	E4	FL1	FL2	FL3	FL4	FD1	FD2	FD3
Circularity	0.832	0.790	0.800	0.767	0.821	0.818	0.804	0.794	0.891	0.923	0.936
±	±	±	±	±	±	±	±	±	±	±	±
S.D	0.067	0.045	0.052	0.064	0.053	0.040	0.072	0.078	0.041	0.035	0.063
Elongation	1.250	1.391	1.341	1.406	1.259	1.293	1.316	1.346	1.161	1.110	1.056
±	±	±	±	±	±	±	±	±	±	±	±
S.D	0.091	0.097	0.089	0.098	0.098	0.083	0.096	0.089	0.094	0.068	0.089
Rectang	0.830	0.836	0.831	0.837	0.833	0.836	0.841	0.849	0.799	0.789	0.791
±	±	±	±	±	±	±	±	±	±	±	±
S.D	0.057	0.068	0.065	0.063	0.071	0.059	0.072	0.059	0.063	0.058	0.064

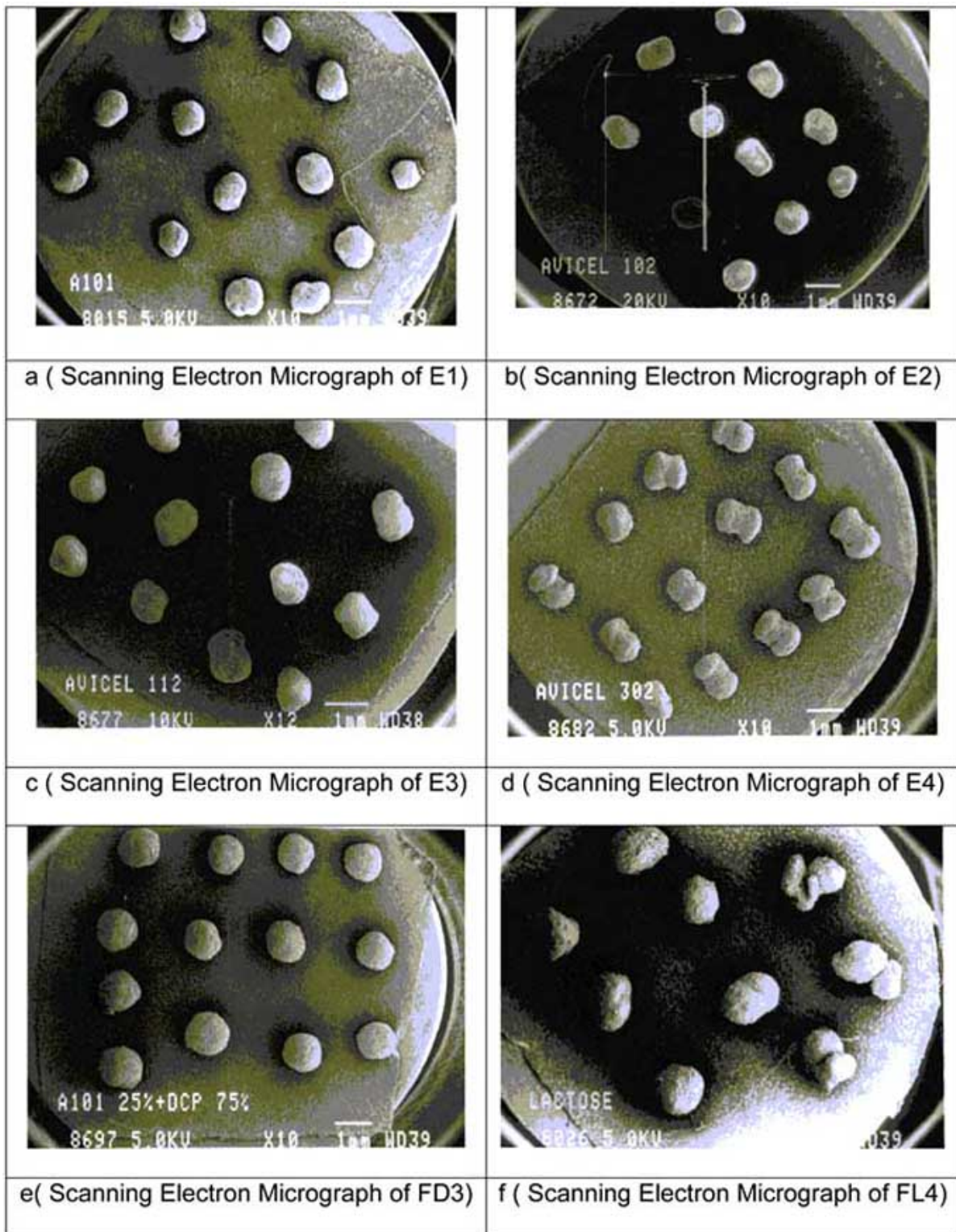


Fig. (2). Scanning Electron Photographs of different batches.

with the different Avicel grades. It depended on the density of pure Avicel grades. High Hausner ratio of pellets containing Avicel PH 101 may be attributed to a higher span value of the size distribution. Pellets containing lactose with Avicel PH 101 showed higher bulk densities, which may be

due to the particle size and higher density of lactose. Similar results have been reported by Heng and Koo, 2001 [12].

Pellets containing DCPD showed high bulk and tapped densities, which may be due to their highest circularity. The

**Table 4. Densities of Different Pellets**

	E1	E2	E3	E4	FL1	FL2	FL3	FL4	FD1	FD2	FD3
Bulk density	0.767	0.774	0.793	0.880	0.770	0.778	0.794	0.707	0.839	0.873	0.895
Mean $\pm$ SD	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
(gm/ml)	0.013	0.007	0.013	0.007	0.004	0.017	0.014	0.008	0.018	0.017	0.026
Tapped density	0.881	0.812	0.832	0.949	0.791	0.813	0.827	0.762	0.919	0.961	1.073
Mean $\pm$ SD	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
(gm/ml)	0.015	0.013	0.007	0.008	0.005	0.018	0.014	0.009	0.019	0.015	0.023
Granule density	1.177	1.277	1.304	1.462	1.221	1.279	1.312	1.393	1.356	1.391	1.432
Mean $\pm$ SD	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
(gm/ml)	0.019	0.062	0.059	0.071	0.049	0.053	0.016	0.066	0.058	0.063	0.075
Hausner ratio	1.145	1.049	1.049	1.078	1.027	1.045	1.042	1.079	1.095	1.101	1.199
Carr Index	0.127	0.047	0.047	0.073	0.027	0.043	0.040	0.073	0.087	0.092	0.166

high Hausner ratio may be a result of their higher size distribution. Pure lactose pellets (FL4) had the minimum bulk density, which may be due to the larger pellet size and greater surface irregularities. High density of mixed pellets can also be attributed to the setting of lactose or DCPD within the void spaces of MCC micro fibrils, thereby making the pellets denser.

#### Flow Properties

Table 5 shows the angle of repose and flow rates of the different formulations. It was observed that among the Avicel grades (E1-E4), pellets containing Avicel PH 302 (E4) had the minimum angle of repose. Pellets containing DCPD (FD1-FD3) had both good circularity as well as high density and as a result they showed very low angle of repose as well as a very high flow rate (Table 5). Pellets containing lactose had the least satisfactory flow properties which may be attributed to their surface and shape irregularities.

#### Friability

The percent friabilities of all the formulations containing pure Avicels (E1-E4) were below 1%. With increase in the concentration of lactose or DCPD, percent friability increased, but still the presence of even 25% Avicel PH 101 reduced the % friability of the pellets from 8.98% (FL4) to

2.48% (FL3). Similar findings have been reported by Sousa *et al.*, 2002 [13] who found that the higher the proportion of MCC in the pellets, the greater was the mechanical strength of the pellets. Further, friability of pellets containing DCPD was almost same to those containing lactose. Friability of pellets containing Avicel PH 302 (E4) was more than the pellets prepared with other Avicel grades, which may be due to the inability of Avicel PH 302 to form hard compacts at the fixed attrition forces inside the spheronizer, due to the high density of the said Avicel grade (PH 302).

#### Dissolution Studies

*Effect of different Avicel grades:* The dissolution profiles of the pellets prepared with different Avicel grades are shown in Fig. 3a and 3c. The dissolution profiles of the drug differed significantly within the Avicel grades (ANOVA,  $P < 0.05$ ) but in all cases the dissolution could be described by the Higuchi equation [14]. The percent release vs.  $\sqrt{\text{time}}$  in all the formulations was found to be linear ( $r^2 = 0.98$  to 0.999). Thus it is concluded that Avicels acted as an inert matrix from which the drug release occurred via diffusion.

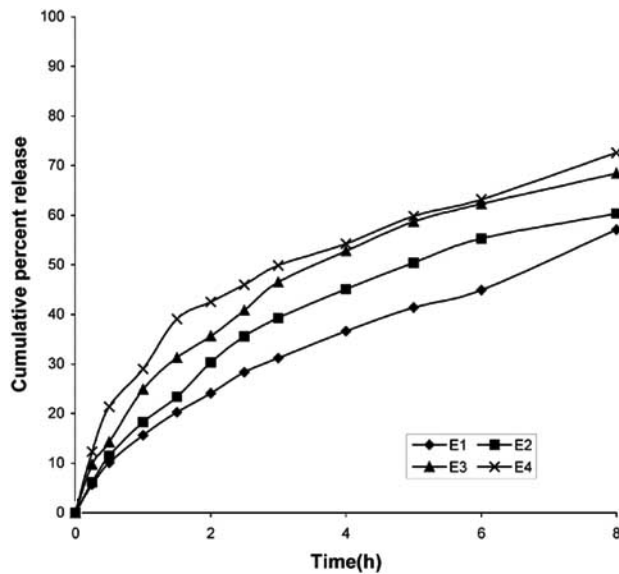
The difference in the release rate from different Avicel grades can be attributed to many factors. According to Alvarez *et al.*, 2002 [15], MCC with larger particle size has higher porosity. The average particle size of Avicel PH 101

**Table 5. Flow Properties of Different Pellet Formulations**

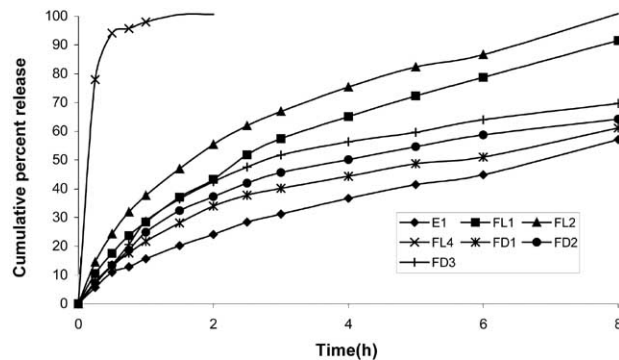
	E1	E2	E3	E4	FL1	FL2	FL3	FL4	FD1	FD2	FD3
Angle of repose (degrees)	29.858	32.977	32.321	27.622	30.739	32.545	32.919	36.743	27.136	25.015	25.901
Mean $\pm$ SD	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
	0.926	0.956	1.261	0.525	0.473	0.892	0.793	2.190	0.921	0.340	0.456
Flow rate (g/s)	1.537	1.382	1.495	1.385	1.491	1.320	1.316	1.256	1.913	1.908	1.839
Mean $\pm$ SD	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
	0.021	0.039	0.026	0.037	0.041	0.046	0.043	0.061	0.053	0.038	0.075

**Table 6. Friability Values of Different Pellet Formulations**

	E1	E2	E3	E4	FL1	FL2	FL3	FL4	FD1	FD2	FD3
% F	0.56	0.58	0.72	0.93	0.80	1.88	2.48	8.98	0.96	1.08	5.00



**Fig. (3a).** Cumulative percent release vs. Time of formulations E1-E4.

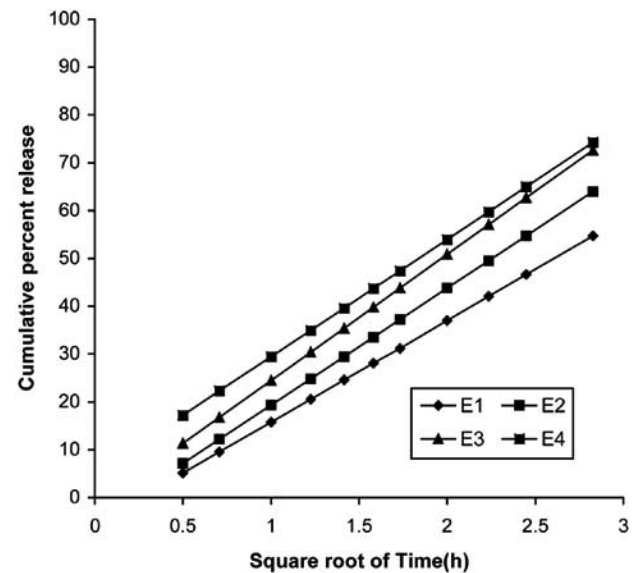


**Fig. (3b).** Cumulative percent release vs. time of formulations E1, FL1, FL2, FL4, FD1-FD3.

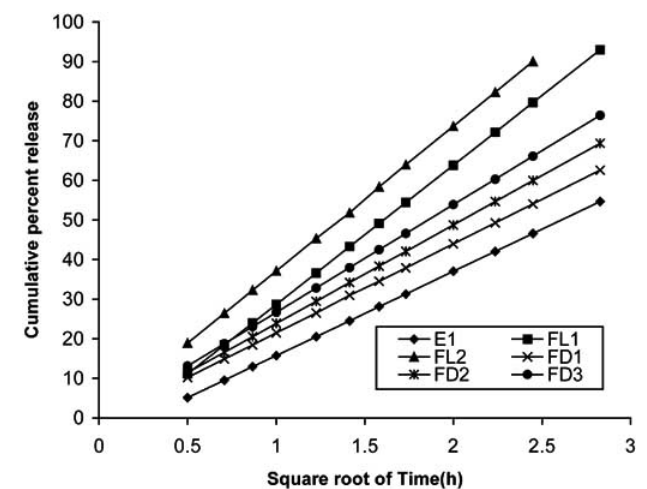
being the smallest among the four different grades used should have the minimum porosity and thus maximum retardation of the release should be caused. Avicel PH 102 and PH 112 have similar mean particle size, but Avicel PH 112 has lesser moisture content than Avicel PH 102 [16]. The lower moisture content of the PH 112 grade, made it more hygroscopic and it absorbed more water when put into the aqueous dissolution media, thus forming channels which facilitated drug diffusion from the inert matrix structure of the Avicels. The highest drug release from Avicel PH 302 can be attributed to the fact that, being the Avicel of the highest density, it could not be spheronized well at the investigated spheronization time, and formed only dumbbell shaped pellets. This may be due to poor compaction of the Avicels, which prevented the formation of well-formed

matrix structure and this facilitated drug diffusion and the highest release was obtained.

*Effect of addition of lactose/ DCPD on drug release from Avicel PH 101:* The effects of addition of fillers like lactose or DCPD on Avicel PH 101 pellet properties are shown in Fig. 3b & 3d. An increase in lactose concentration in the matrix increased the drug release. These results are in agreement with the results obtained by Blanque *et al.*, 1995



**Fig. (3c).** Cumulative percent released vs. Square root of time of formulations E1-E4.



**Fig. (3d).** Cumulative percent release vs. Square root of time of formulations E1, FL1, FL2, FD1-FD3.

[17], who found that the high solubility of lactose provides the possibility of highly porous spheres during the dissolution process, which allows a faster drug release. Pure lactose pellets did not show Higuchian release, rather the pellets were disintegrated immediately when put into the dissolution media giving a burst effect. Thus, pure lactose pellets showed enhanced drug release. DCPD also showed an increase in drug release ( $P < 0.05$ ) but this increase was far less as compared to that by lactose.

## CONCLUSION

The prepared pellets varied in pellet properties such as drug dissolution profile, size, size distribution, shape, flow properties, densities and friability. All pellets showed different drug release behaviors. Drug release occurred by diffusion of the pellet matrix except in pure lactose pellets, which disintegrated in the dissolution media giving burst release. Mean pellet diameter did not differ much ( $P < 0.05$ ) among different Avicel grades. Pure lactose pellets showed the largest mean diameter. Pellets containing dicalcium phosphate dihydrate (75%) and Avicel PH101 (25%) showed the smallest mean diameter. All other pellet formulations had almost similar size. Presence of Avicel suppressed the change in mean particle size. However different Avicel grades differed in their circularity parameters. A linear relationship was found between the pellet circularity and log bulk density of pure Avicel powder. With increase in density of Avicel, roundness decreased. MCC was found to be a very suitable excipient for the process of extrusion spheronization. Among the different grades of Avicels used, Avicel PH 101 was found to be the most satisfactory in terms of the pellet properties.

Plain DCPD could not be spheronized even at a water content where plain lactose could be spheronized satisfactorily. Pellets containing DCPD were found to be the most circular. Plain lactose pellets had the minimum bulk density. Pellets containing DCPD had high bulk and tapped densities and a high Hausner ratio. Densities of pellets of different Avicel grades were a function of their powder

densities and circularity. Pellets containing DCPD showed the best flow properties owing to their greater circularity and a high density. Among the Avicel grades pellets of Avicel PH 302, showed the best flow properties. Flow properties of pellets containing lactose were the least satisfactory. Friability increased with increase in the concentration of lactose or DCPD. Plain lactose pellets showed the highest and unacceptable friability parameter. Pellets of all the Avicel grades showed little friability. When used as an adjuvant to Avicels, DCPD was far more satisfactory than lactose in improving the pellet properties.

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