DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 21(18), 2109-2120 (1995)

PELLETIZATION IN ROTARY SHAKER: EFFECT OF EQUIPMENT VARIABLES ON PELLETIZATION OF FERROUS FUMARATE

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ABSTRACT

A novel method and equipment viz. rotary shaker pelletizer has been developed for making spheres of pharmaceuticals. Essentially based on laboratory rotary shaker, the equipment variables that influence pelletization were determined using ferrous fumarate as the model drug and the results were used to optimize equipment design. Variables studied were orbital diameter of the rotary shaker, and diameter and texture of bottom surface of the bowl. The results indicate that the equipment is versatile in producing large quantities of ferrous fumarate pellets in short processing times and that a critical orbital diameter of the shaker and bowl size and roughness of the bottom surface of bowl, preferably with a raised conical bottom, is essential for best output.

INTRODUCTION

The various equipments in common use for manufacture of pellet products are coating pans, fluid-bed machines, centrifugal equipments, extruders/spheronizers(1) and high-shear mixers(2). Little attention has been paid to the possibility of using rotary shaker as a pelletizer for pharmaceuticals. The equipment can be suitably modified to pelletize formulations in a manner similar to that possible with spheronizers. The efficiency of latter lies in short processing times, high yield and ease of method reproducibility. The forces responsible for sphere formation from wet, plastic, cylindrical extrudates in a spheronizer are particle-friction plate collisions, interparticulate collisions and particle-wall collisions, and the spiral rope-like motion of the particles(3). Spiral particle motion and high degree of particle-bowl bottom friction and interparticulate collisions occur in a bowl (fed with plastic extrudates) attached to the platform of a rotary shaker. Such a motion and particle friction may result in plastic deformation of extrudate/granule surface to form spheres. Thus, rotary shaker also possesses potential for pelletizing pharmaceuticals.

The aim of the present study was to investigate the effects of equipment variables on movement and friction of wet extrudates in the bowl attached to the platform of rotary shaker and their subsequent deformation into spheres. The four major equipment variables studied were bowl diameter, bottom surface of the bowl, texture of the bottom surface of the bowl and the orbital diameter of the shaker.

EXPERIMENTAL

Materials

Ferrous fumarate (Zim Laboratories Ltd., Nagpur, India) was used as the active ingredient. Sugar (as a 33.3% aqueous solution) was used as the binder and granulating agent.

Equipment

The laboratory rotary platform shaker (model IEC-50, IEC equipments, Bombay, India) was used as the prototype for equipment design and development. It was modified by replacing the motor with the one of greater power (1 hp) and 1000 rpm and a separate speed reduction gear box of ratio 5:1 (fig. 1). The rotary shaker platform rotates in a horizontal plane and circumscribes a circle. The original orbital diameter of this circle was 3 cm. It was increased on two different occasions to 6 cm and 14 cm by replacing with proportionately larger ex-center rotating shafts (fig. 2). The three different pelletizing cylindrical bowls, having diameter to height ratio 3:1, used on different occasions were 20 cm, 30 cm and 60 cm. Unevenness or roughness on the bottom surface of the bowl, to accentuate friction of particles, was introduced by welding a S.S. wire mesh 40. Further modifications of the bowl design were made by attaching an inverted conical plate (whose vertex was at a distance one-half the bowl height) at the periphery of circular bottom surface of the bowl. Unevenness on this plate was introduced in a manner similar to that for flat bottomed bowl.

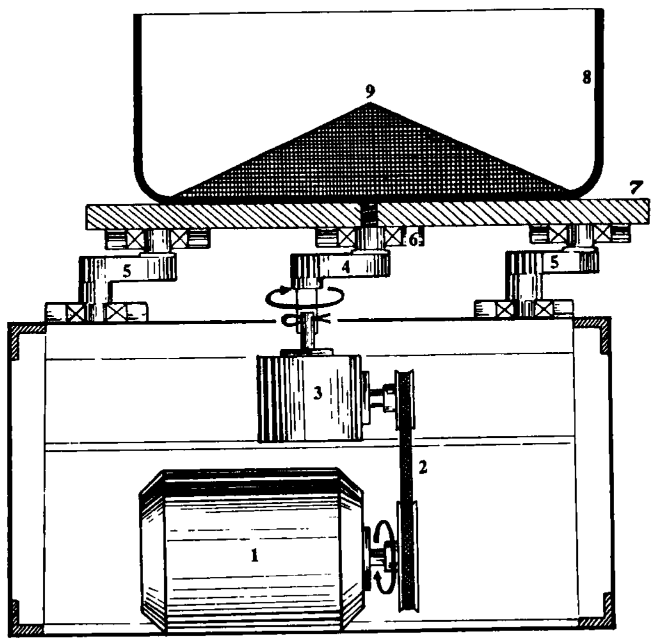

FIGURE 1

Schematic diagram of rotary shaker pelletizer. 1 = drive motor; 2 = belt; 3 = speed reduction gear box; 4 = ex-center rotating shaft; 5 = supportive ex-center rotating shaft(s); 6 = bearing housing; 7 = platform; 8 = cylindrical bowl; 9 = checkered conical plate.

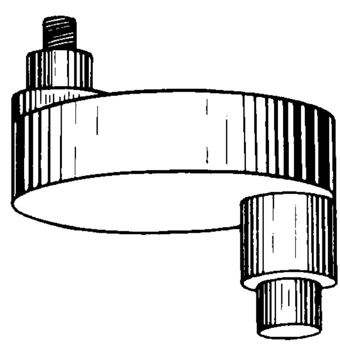

FIGURE 2

Ex-center rotating shaft that gives an orbital motion to the bowl supported on platform.

Formulation

Several concentrations and volume of sugar syrup were screened to find a combination that would yield optimum spheres of ferrous fumarate. The formulation ultimately chosen contained the following:

Ferrous fumarate (200 mesh)	1000 g
Sugar syrup (33.3% w/v)	350 ml

Processing

The materials mentioned in the formula were blended together for 5 minutes and immediately passed through wire mesh 16 by pressing with the hands to form extrudates. The wet extrudates were then charged into the bowl clamped to the platform of the rotary shaker. The feed size was varied depending upon the bowl diameter as shown in table 1. The table also shows the various equipment variables chosen to process the wet extrudates of ferrous fumarate. The shaker was rotated at 200 rpm at all sets of conditions. The processing or dwell time was varied depending upon the formation of pellets but was not more than 5 minutes. After completion of process, the pellets were tray dried at 60°C for 3 hours.

Testing

Sieve Analysis: Percent agglomeration, particle size distribution and mean pellet diameter were estimated by sieve analysis of the samples. Percent agglomeration or amount of lumps was determined from weight fraction larger than 2 mm or 10-mesh. Size distribution of pellets of size smaller than 2 mm was evaluated by shaking 10-, 12-, 16-, 20-, 40-, 60- and 80-mesh (ASTM screens) arranged on an automatic sieve shaker at a frequency of 60 Hz for 5 minutes with a load of 100 g of particles on the topmost sieve. The mean pellet diameter was calculated by the method of Meshali et al(4).

Friability: The friability of pellets was assessed by tumbling 100 g of 16/20 mesh particles in a friability tester for 10 minutes. The material was then sifted to remove fines and weighed. The friability index is the loss in weight expressed as a percentage.

Repose Angle: The angle of repose was determined by the fixed-height method(5). The height of funnel was maintained at 4 cm and the average internal diameter of the funnel stem was 8 mm.

Bulk Density: A 100 g sample of pellets was poured gently through a glass funnel into a 250 ml graduated cylinder, the surface was carefully smoothed and the volume was measured. Bulk density was then calculated and expressed in g/ml.

TABLE 1

Equipment Variables and Feed Size for Processing of Ferrous Fumarate Extrudates in Rotary Shaker Pelletizer

Process-ing Desig-nation	Bowl Diameter (cm)	Bottom Surface of the Bowl	Texture of Bottom Surface of the Bowl	Orbital Diameter of the Rotary Shaker (cm)	Feed Size (g)
A	20	Flat	Smooth	3	200
B	20	Flat	Roughened	3	200
C	20	Raised-Conical	Smooth	3	200
D	20	Raised-Conical	Roughened	3	200
E	30	Raised-Conical	Roughened	3	500
F	30	Flat	Smooth	6	500
G	30	Flat	Roughened	6	500
H	30	Raised-Conical	Smooth	6	500
I	30	Raised-Conical	Roughened	6	500
J	60	Raised-Conical	Roughened	6	2000
K	60	Flat	Smooth	14	2000
L	60	Flat	Roughened	14	2000
M	60	Raised-Conical	Smooth	14	2000
N	60	Raised-Conical	Roughened	14	2000

RESULTS AND DISCUSSION

The results obtained with different equipment variables are shown in table 2. Pellets were successfully prepared on several occasions by utilizing a specific set of equipment variables. Formation of satisfactory pellets was greatly dependent upon motion of the wet extrudates. Processing conditions B, D, G, I, L and N, which could affect spiral movement of particles, resulted in spherical pellets (see fig. 3). Such a spiral motion facilitated excellent interparticulate friction and friction between particles and the bowl base which can be attributed to four equipment variables - bowl diameter, bottom surface of the bowl, texture of the bottom surface of the bowl, and orbital diameter of the shaker.

Bowl Dimensions

The diameter of the bowl in relation to the orbital diameter of the shaker seems to be critical. At a given orbital diameter of the rotary shaker, use of larger bowl may result in an inefficient and insufficient motion of the particles and thus

TABLE 2

Observation of Pelletized Particles

Processing Designation	Processing Time (minutes)	Percent Agglomeration	Pellet Description
A	5	-	None
B	3-4	8.0	Spheres
C	5	-	None
D	1-2	4.6	Spheres
E	5	37.0	Mostly rod shaped
F	5	-	None
G	5	12.3	Spheres
H	5	-	None
I	1-2	3.7	Spheres
J	5	18.6	Mostly rod shaped
K	5	-	None
L	1-2	11.6	Spheres
M	5	21.1	Mostly rod shaped
N	1-2	1.8	Spheres

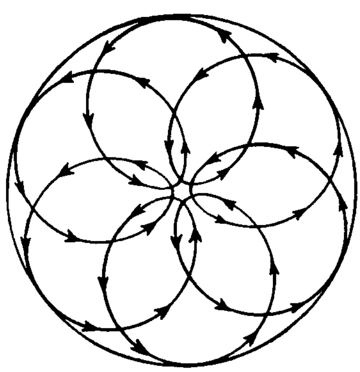

FIGURE 3

Spiral motion of the particles in the bowl of rotary shaker pelletizer

failure to produce pellets. Introduction of an inverted conical plate with an uneven surface tends to improve movement of the mass but may not influence satisfactory pelletization as observed in processing conditions E and J. On the other hand, at large orbital diameters, pelletization is effective even if the bottom surface of bowl is flat and rough.

Bottom Surface of the Bowl

Two variations of the bottom surface were tried in all bowl designs - flat and raised-conical. At a given bowl and orbital diameter and surface roughness, thespiral motion was more perfect and effective when the bottom surface of the bowl was conical. The latter also allowed greater surface for particle movement and friction resulting in better pellets than when the base of the bowl was flat (see fig. 4b and 4c). In each rotary cycle, the mass is directed to the central part of the bowl and then to the periphery, which results in a more convenient movement of the mass.

Texture of the Bowl Base

Observations stated in table 2 demonstrate that surface roughness of the bowl base is essential for improved friction with particles in motion and thus rapid and effective pellet formation as evident from the results of processing conditions B, D, G, I, L and N. Such an unevenness was found to be more efficacious when the bottom of the bowl was raised-conical enabling pellet formation in shorter processing time. Smooth surface of the bowl causes slip-and-slide of particles and poor movement of the mass with the outcome that spheres fail to form even on prolonged processing. Inability in producing pellets even when the bowl has a raised-conical and roughened surface as in processing conditions E and J is attributable to poor movement of the mass because of the larger bowl diameter in relation to orbital diameter of the rotary shaker.

Orbital Diameter of the Rotary Shaker

Direct correlation exists between the bowl and the orbital diameter. It is imperative to increase the orbital diameter of the rotary shaker in order to effect pelletization in a larger diameter bowl. Alternatively, large quantum of material can be processed in small bowls when the orbital diameter of the rotary shaker is also small, by increasing the number of bowls.

Various physical measurements were used to evaluate and characterize the products of experimental conditions which yielded spheres viz. B, D, G, I, L and N (see table 3).

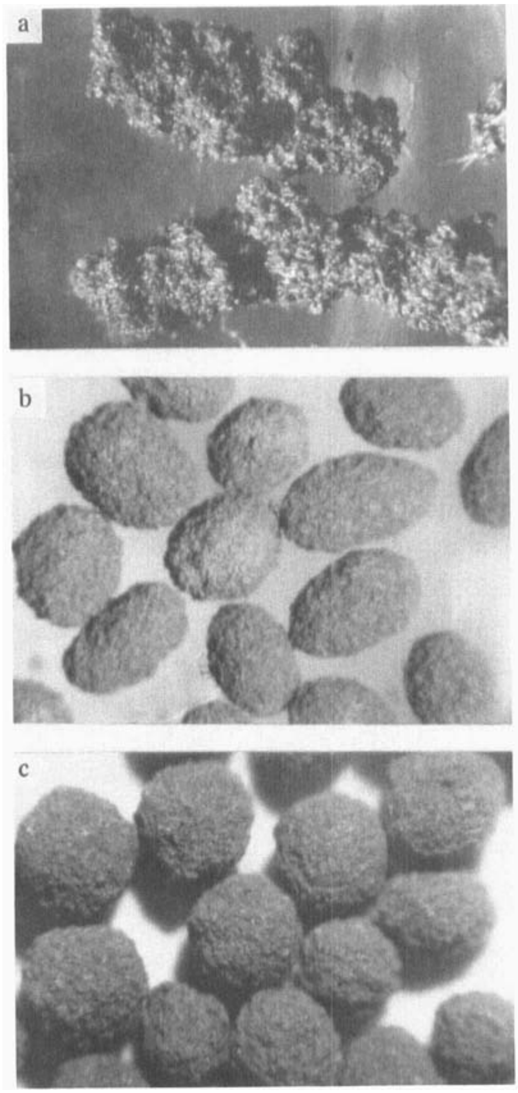

FIGURE 4

Stereomicrographs of extrudates (fig. a), and pellets produced with processing conditions G (fig. b) and I (fig. c) . Magnification 12x.

TABLE 3

Physical Characteristics of Ferrous Fumarate Pellets

Processing Desig-nation	Percent Agglo-meration	Size Distribution of Pellets (< 2 mm)		Mean Pellet Diameter (microns)	Percent Friability	Angle of Repose (degrees)	Bulk Density (g/ml)
		mesh (passed/ retained)	percent weight fraction				
B	8.0	10/12	6.5	953	6.2	26.8	0.826
		12/16	35.7				
		16/20	41.3				
		20/40	12.6				
		40/60	2.7				
		60/80	1.2				
D	4.6	10/12	2.3	1065	2.9	24.2	0.840
		12/16	39.8				
		16/20	50.1				
		20/40	7.1				
		40/60	0.4				
		60/80	0.3				
G	12.3	10/12	12.8	918	7.4	27.1	0.833
		12/16	27.6				
		16/20	39.3				
		20/40	15.1				
		40/60	3.9				
		60/80	1.3				
I	3.7	10/12	4.7	956	5.7	24.7	0.840
		12/16	33.9				
		16/20	45.6				
		20/40	13.2				
		40/60	1.9				
		60/80	0.7				
L	11.6	10/12	8.3	914	6.8	27.6	0.826
		12/16	33.7				
		16/20	43.6				
		20/40	7.3				
		40/60	4.9				
		60/80	2.2				
N	1.8	10/12	3.2	1088	1.8	24.1	0.847
		12/16	42.7				
		16/20	48.8				
		20/40	4.3				
		40/60	0.7				
		60/80	0.3				

Percent Agglomeration

It was found that the amount of lumps formed were greater when flat base bowls were used. The lumps consist of loose agglomerates of irregular shape. A decrease in the quantum of lumps formed when raised-conical and roughened plate was used is because of greater and controlled degree of spiral agitation that cause the loose aggregates to break down easily.

Particle Size Distribution and Mean Pellet Diameter

As evident from table 3 and figure 5, processing conditions in which the bowl with the raised-conical plate were used resulted in pellets with relatively narrow size distribution. More than 85% pellets were of 10/20 mesh and thus, expectedly, the mean pellet diameters were greater under such experimental conditions.

Friability

High correlations were also found between friability and bottom surface of the bowl, and between pellet size and friability. The pellets prepared using flat base bowls were more friable. The two contributing factors to higher friability of such pellets were greater proportion of small size pellets, and the relatively ovoid shape of the final product (fig. 4b) which led to an increase in the surface area of the pellets and thus higher degree of attrition during friability testing.

Repose Angle

A lower angle of repose indicates a greater tendency of particles to flow. Data from this study demonstrated that flow properties of more spherical pellets (conditions D, I and N) were superior to those of the relatively ovoid materials (conditions B, G and L).

Bulk Density

Pellets which were more spherical (conditions D, I and N) had a higher bulk density. Bulk density is partially indicative of packing of the material and denotes that spheres provide the most compact packing.

CONCLUSIONS

The rotary shaker examined was found to be highly suitable for pelletization of ferrous fumarate. By proper choice of equipment variables it is possible to produce dense, spherical pellets with a very narrow size distribution and high content of active drug, in high yields and short processing time. Equipment design that results in greater and controlled degree of spiral agitation of wet extrudates and thus efficient interparticulate friction and friction between particles and the bowl base, is desirable for sphere formation. While a critical orbital

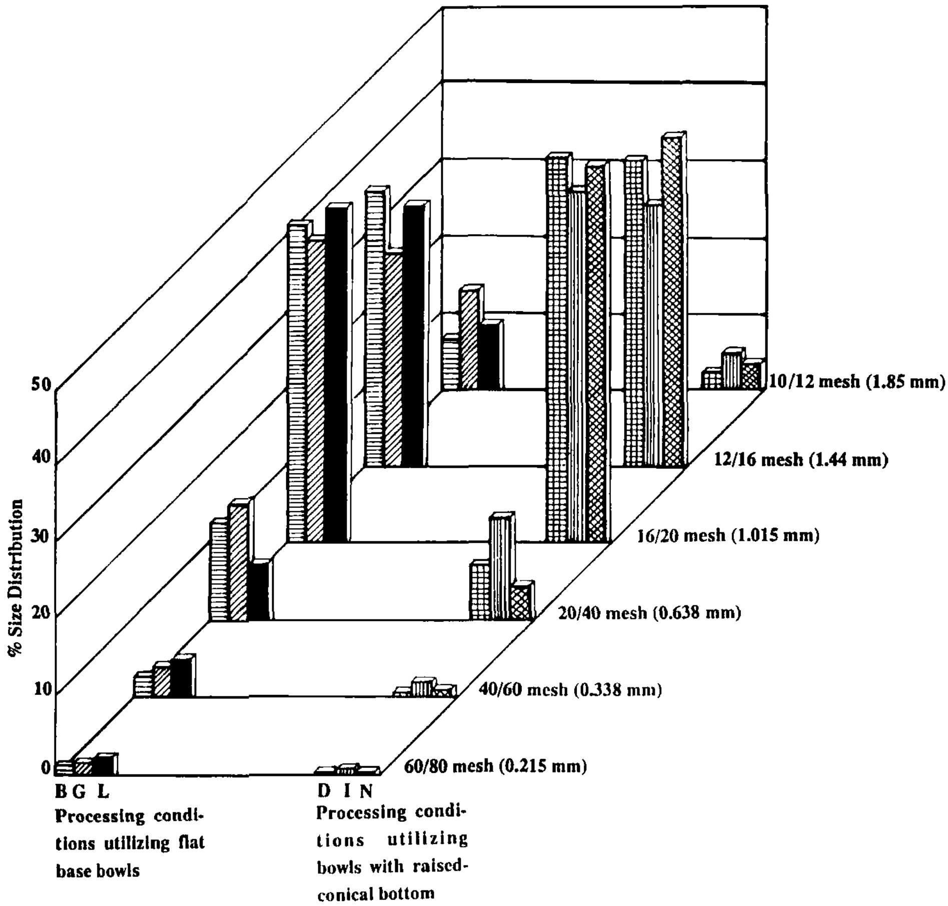

FIGURE 5

Size distribution of pellets produced with processing conditions B, G and L (flat base bowls) and D, I and N (bowls with raised-conical bottom). Particle diameter in mm indicated in parentheses are arithmetic mean of two successive sieve openings.

diameter of the rotary shaker for a given bowl dimension is essential to induce such a spiral motion and interparticulate collisions, the raised-conical plate with a roughened surface is equally necessary to accentuate it as well as facilitate attrition between the wet extrudates and the bottom surface of the bowl. It is highly probable that if the raised-conical plate is indented with grooves in a cross-hatch pattern in a fashion similar to the friction plate of the spheronizer(3), and if the feed materials are cylindrical (and plastic) extrudates such as those prepared by extruders, the rotary shaker pelletizer may prove to be as efficient as spheronizer in pelletizing a wide variety of pharmaceuticals.

ACKNOWLEDGEMENTS

Mr. A.S. Daud, Executive Director, Zim Laboratories Ltd., Kalmeshwar, Nagpur, India, is acknowledged for extending financial support to the project.

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