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Relationship between vibration produced during powder handling and segregation of pharmaceutical powder mixes

John N. Staniforth

Pharmaceutics Group, School of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY (U.K.)

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Summary

The vibration signatures of different pharmaceutical processing equipment were monitored in order to determine vibration intensities likely to influence powder segregation. It was found that an orbital screw-blender was virtually vibration-free, but that several of the tabletting machines had critical areas which vibrated at frequencies and accelerations within the range previously tested in a model vibration system. Both the powder feed hopper and the force feeder were found to be points at which pharmaceutical powder mixes were particularly susceptible to segregation. The model systems showed that drug and excipient powder mixes had segregation tendencies which were increased by combinations of low-vibration frequency and high acceleration such as those found in the rear feed-frame of a Manesty double-rotary tabletting compressor and also on the top main pressure roller bearing of the Manesty Layerpress multi-layer tabletting compressor. Despite the segregation produced when some powder mixes are vibrated, vibratory force-feeders are still frequently used to promote powder discharge from tote bins, bulk containers and hoppers. The results obtained in this study demonstrate that vibration conditions produced by many types of pharmaceutical processing machinery could lead to powder segregation.

Introduction

Vibration is a major cause of segregation during processing of many powders ranging from coal to pharmaceuticals. The Pharmaceutical Codex (1979) recognized that "there is a possibility of segregation of the constituents if powders for mixtures are stored for long periods or subjected to mechanical vibration".

Coarse particle constituents of a vibrating powder move up or down the bed according to the packing arrangement of the particles (Brown, 1939). In a moving bed, Hirst (1937) showed that elimination of interparticle contact forces allowed large particles to sink. However, Williams (1963) found that under most conditions, particles much larger than the rest of the powder rose to the surface. This phenomenon was further studied by Khan and Smalley (1973) who found that reducing the vibration frequency at any acceleration reduced the time taken for a large sphere to rise to the surface of a packed bed of sand. Similarly, the segregation time could be reduced by increasing the acceleration at any vibration frequency. The size of the large particles also affected the rise time. The higher the ratio of large particle diameter to particle size of sand the larger the segregation effect.

In powders containing smaller particles and where particle size distributions are narrower, different behaviour occurs. Lawrence and Beddow (1968/69) showed that vertical vibration of lead mixtures in a die produced downward movement of fines. This probably occurs by the mechanism of percolation and is affected by the stability of the powder bed. At low amplitudes and frequency, Lawrence and Beddow found that dilation of the powder bed was minimal and segregation did not occur.

Harwood (1977) studied the effect of vertical vibration on free-flowing and cohesive powders. He found that whilst segregation could be readily produced in free-flowing systems, truly cohesive powders exhibited very little tendency to segregate. Upward movement of fine iridium-192-labelled sand was produced in a vibrated powder bed of flint particles. Harwood explained this action in terms of vibratory mixing. Use of banding sand with a particle size distribution closer to that of the tracer sand caused segregation in both directions although upward movement was more marked; the time required for segregation was also somewhat increased.

The effect of vibration-induced segregation produced during processing has been less widely studied. Turczyn (1979) discussed the implications of different types of vibration profiles on the contents of containers during transportation. The effect of shock waves on the packing of granular materials has been studied by Nunziato and Walsh (1978). They showed that the way in which different materials respond to shock depends on the initial porosity of the solid; this was found to alter the wave behaviour as it passes through the granules and thus affects the stress on the material.

In the present study, a system was developed to analyze the frequency and acceleration of vibrations produced by pharmaceutical process machinery during various stages of mixing and tabletting, so that a comparison could be made with vibration conditions producing segregation in the model systems studied previously.

Materials and methods

In order to monitor vibration signals of process equipment an accelerometer (type DJB 101, Bruel and Kjoer, Naerum, Denmark) was used to detect acceleration

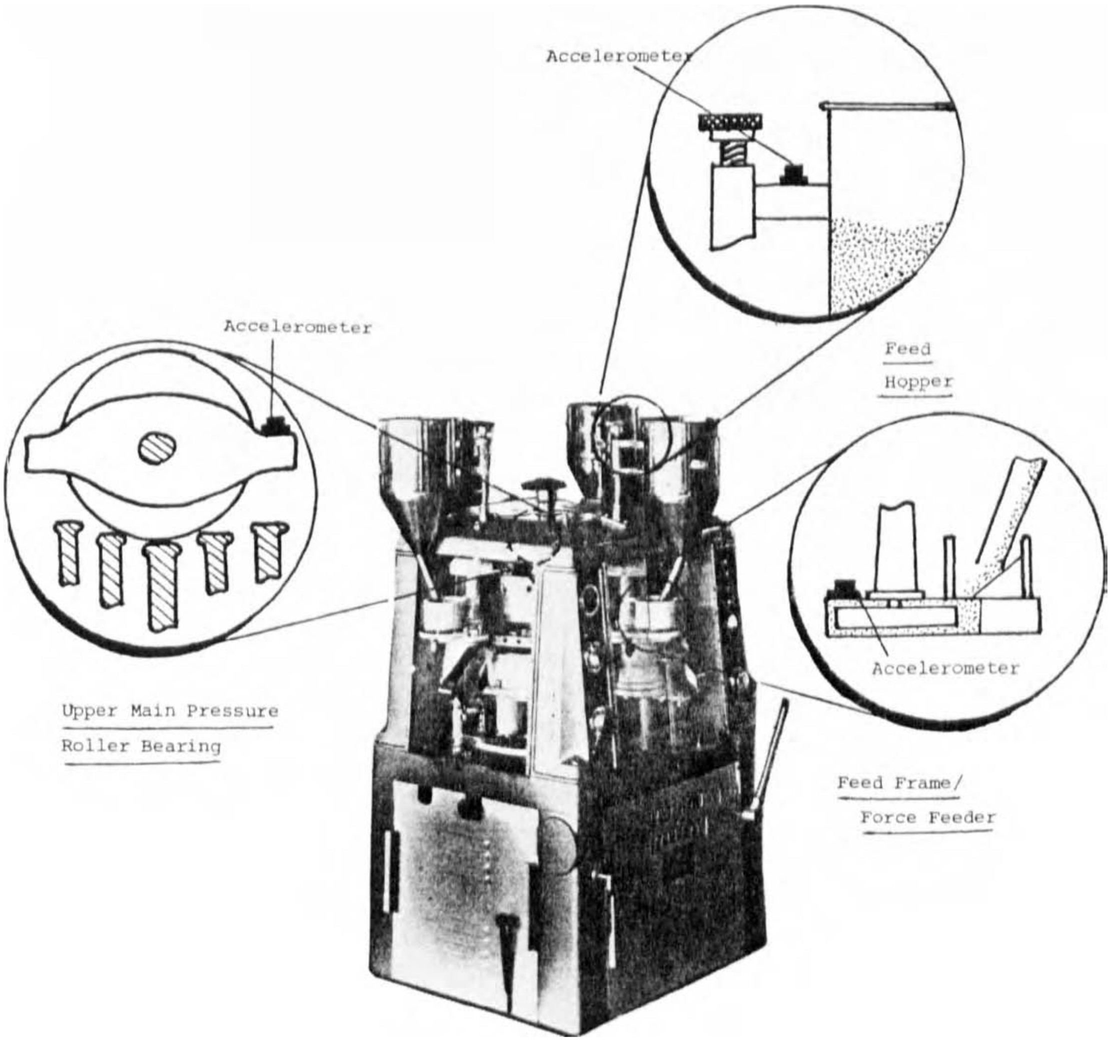

Fig. 1. Diagram showing location of accelerometers on rotary tabletting machines.

magnitudes at specific frequencies. The output from the accelerometer was connected to a tunable band-pass filter (type 1621, Bruel and Kjoer) which filtered out frequency signals in the range 0.2–20,000 Hz and passed on a specific pre-selected frequency to a precision sound level meter (type 2203, Bruel and Kjoer) which measured the corresponding vibration acceleration.

An accelerometer with a permanent magnet attached at its base was used to monitor the vibration frequencies and accelerations by placing the accelerometer on different horizontal flat metal surfaces of the process equipment. Positions for location of the accelerometer were chosen to reveal the vibration intensity to which the powder was subjected at critical positions in each process. For this reason the locations of accelerometers on tabletting compressors included the powder feed hopper, feed-frame or force-feeder and the main pressure roller bearings as shown in Fig. 1.

Several different types of rotary tabletting machines were monitored: Manesty type RD; Manesty type BB3B; Manesty Layerpress (Manesty Machines, Speke, U.K.). In addition, the compressors were equipped with different quantities of punches and die sets and were rotated at different turret speeds.

Results and discussion

Accelerometers connected to the hopper and feed frame of a Manesty RD rotary tabletting machine produced different vibration signatures (Fig. 2). The hopper was found to vibrate at two principle frequencies around 200 Hz and 2500 Hz with corresponding peak accelerations of 0.75 *g* and 2.5 *g*. There were also two broad-band vibrations around 50 Hz at 0.23 *g* and 800 Hz at 0.68 *g*. The tabletting machine feed-frame vibrated less intensely at one main frequency around 3 kHz with an acceleration of approximately 0.8 *g*.

A similar difference in vibration measurements was found at separate points in a dual compression tabletting machine with smaller diameter compression tooling, the Manesty BB3B. Fig. 3 shows the vibrations measured in the front feed-frame and front hopper at different turret speeds with 9 sets of punches and dies which was equivalent to one-third full tooling complement. The vibrations which occurred in the front hopper of the dual compression rotary machine were found at two main frequencies: 150 Hz with 0.16 *g* acceleration and at 300 Hz with 0.12 *g* acceleration.

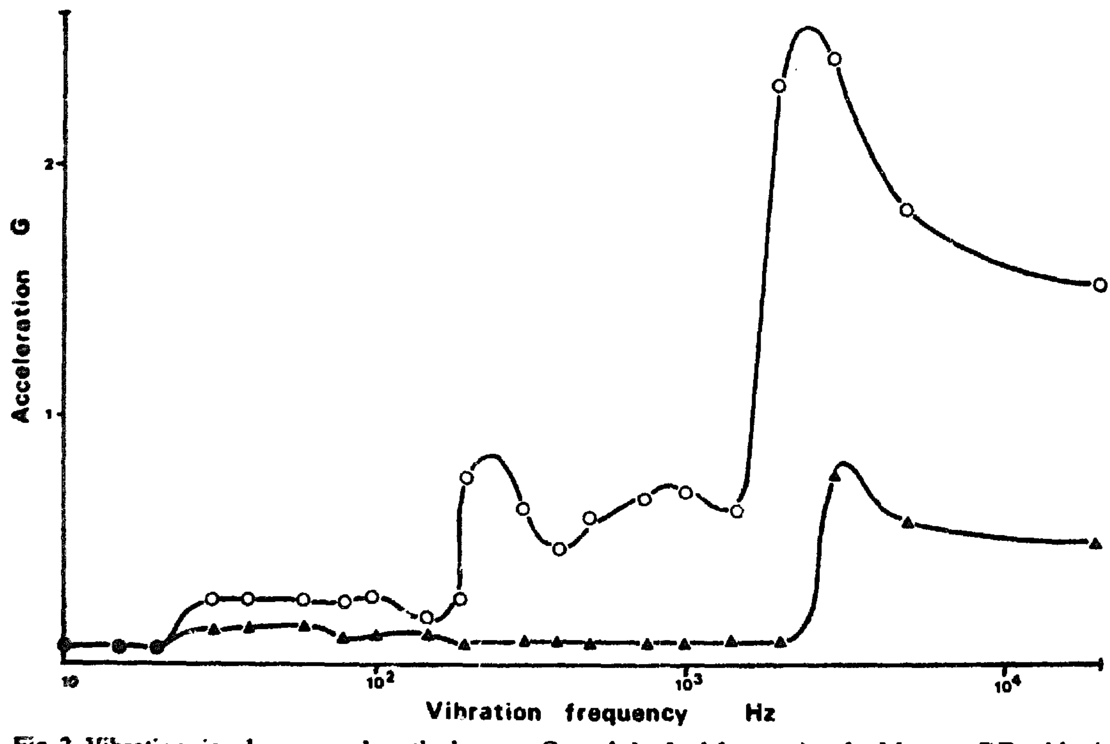

Fig. 2. Vibration signals measured on the hopper, O, and the feed frame, ▲, of a Manesty RD tabletting machine.

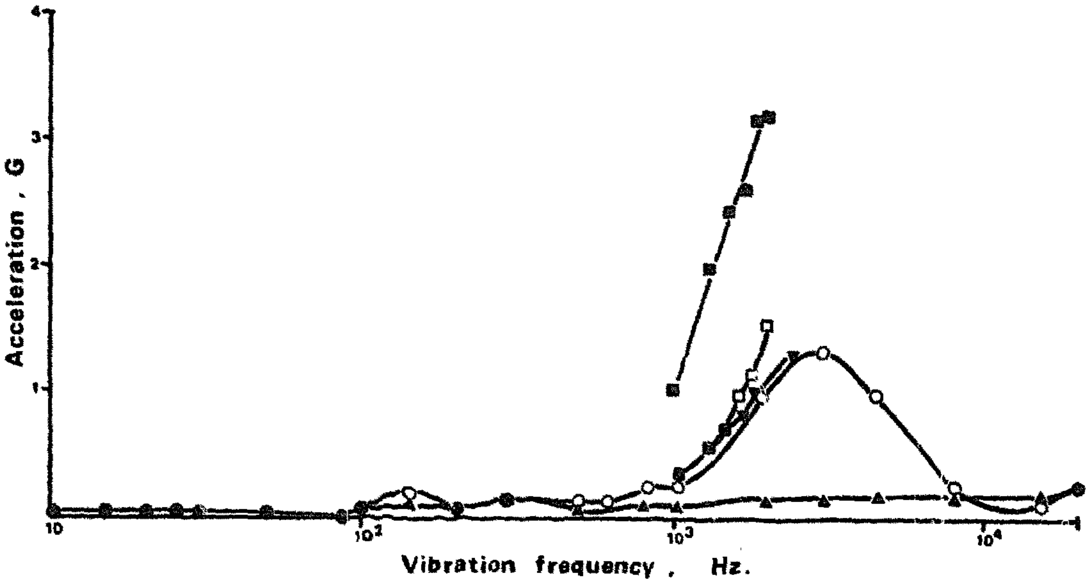

Fig. 3. Vibration signals measured on the front hopper at 18 rpm, ▲, and on the front feed-frame at 18 rpm, ○; 22 rpm, ▼; 26 rpm, □; and 28 rpm, ■ of a Manesty BB3B rotary tabletting machine with 9 sets of punches and dies.

The front feed-frame vibrated more intensely with a peak acceleration at 3 kHz. At a turret speed of 18 rev · min^{-1} this peak acceleration was 1.25 *g*. A similar high value occurred at 22 rev · min^{-1}, although there was a slight reduction in vibration frequency. A further increase in turret speed to 26 rev · min^{-1} produced a vibration acceleration of 1.6 *g* at 2 kHz and at 28 rev · min^{-1} the acceleration increased to 3.2

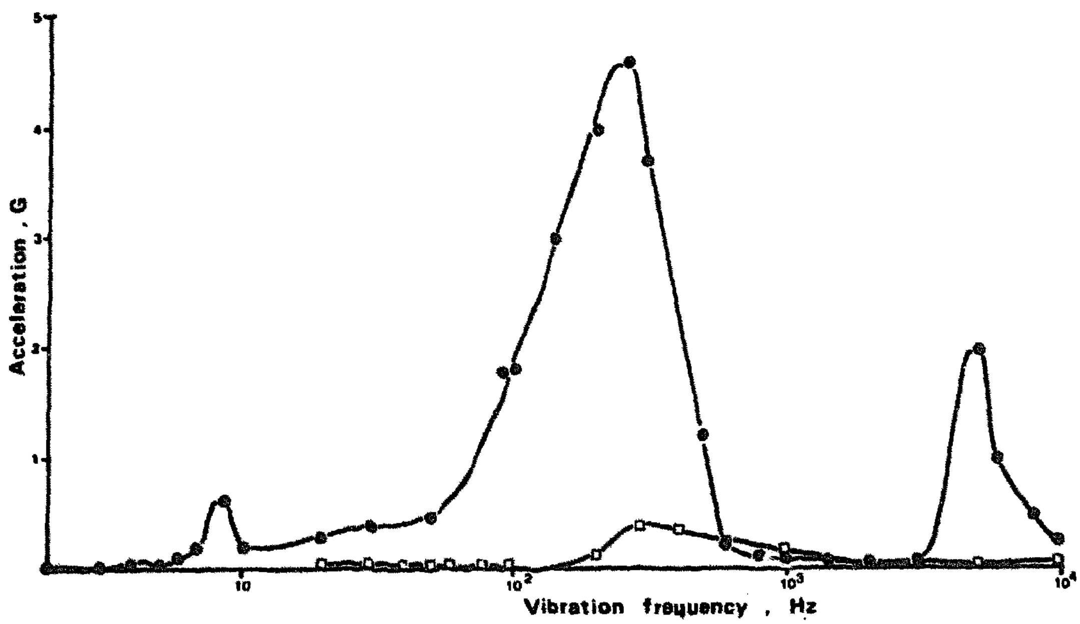

Fig. 4. Vibration signals measured on the rear hopper, □; and the rear feed-frame, ●, of a Manesty BB3B rotary tabletting machine with a complete set (27) of punches and dies.

g at the same frequency. These changes in vibration frequency and acceleration were caused by changes in the damped and un-damped oscillations of the tabletting machine at different speeds, usually referred to as machinery rumble. Another change in the vibration signature of the tabletting compressor was produced by forming tablets using a full complement of punches and dies (27 sets). The vibrations were measured on the rear hopper and feed frame of the dual compression rotary (Fig. 4). The hopper vibrated at one main frequency centered at 350 Hz with a maximum acceleration of 0.4 *g*. The rear feed-frame vibrated strongly at 3 main frequencies: 9 Hz; 200 Hz and 5000 Hz with corresponding accelerations of 0.6 *g*, 4.5 *g* and 2 *g*.

A third tabletting machine capable of making layered tablets, was also tested (Manesty Layerpress). The tabletting machine had two precompression stages and a single main compression stage. Vibration measurements were carried out on the upper main pressure roller bearing (close to the gear box of the force feeding unit) and also on the third hopper feeding the last layer, before final compression (Fig. 5). The hopper was found to vibrate at two principle frequencies centered around 100 Hz with an acceleration of 0.25 *g* and around 700 Hz with an acceleration of 0.8 *g*. The pressure roller bearing vibrated at 3 main frequencies, 150 Hz, 500 Hz and 2 kHz with vibration accelerations of 0.78 *g*, 3 *g* and 2.1 *g*, respectively.

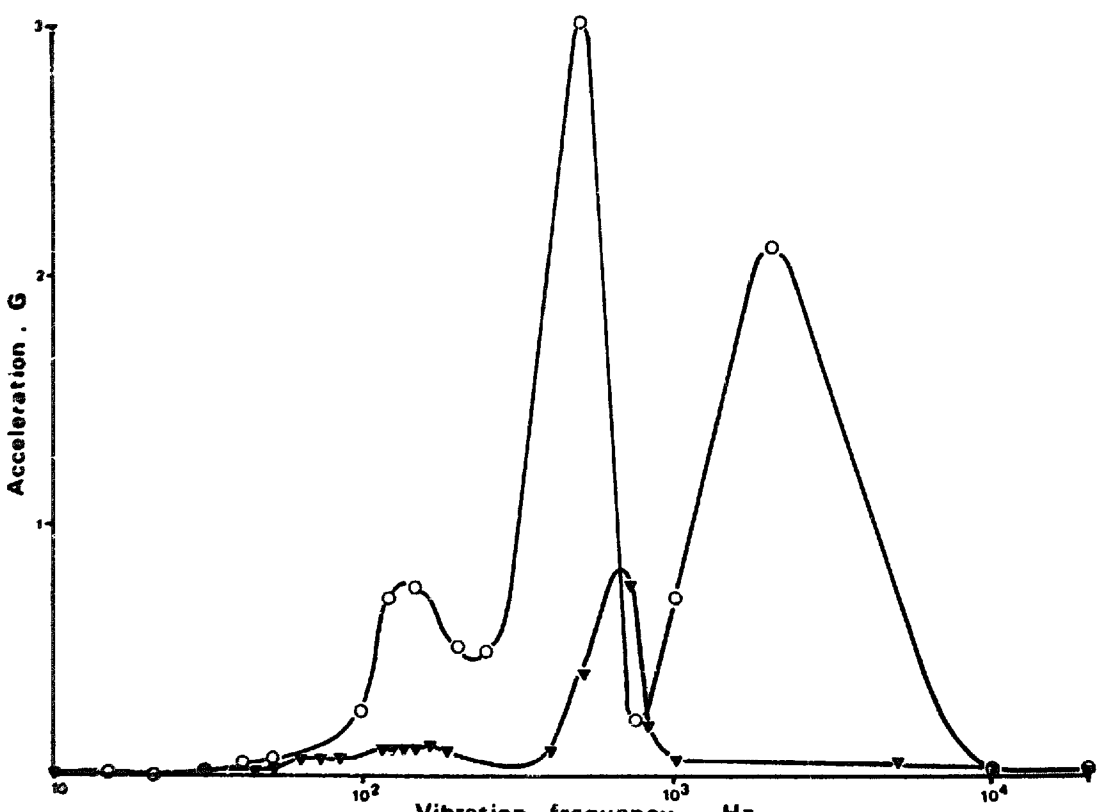

Fig. 5. Vibration signals measured on the third hopper, ▼, and the upper main pressure roller bearing, ○, of a Manesty Layerpress rotary tabletting machine.

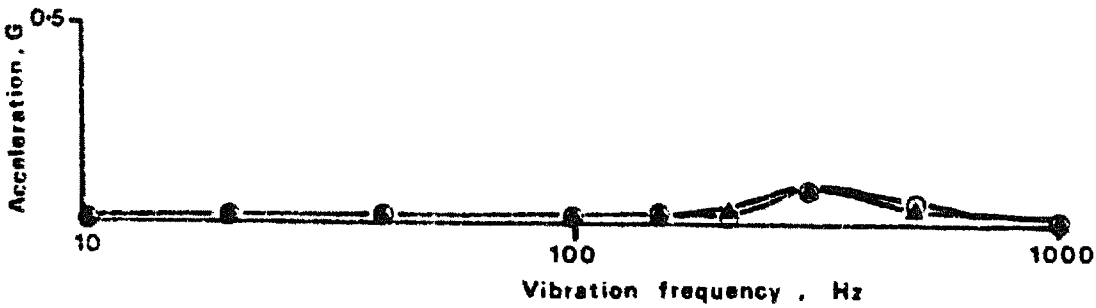

Fig. 6. Vibration signals measured on a Nauta mixer half-filled, ▲, and completely filled, O, with dry powder.

In addition to the different tabletting machines, an orbiting screw powder mixer (Nautamix, Haarlem, Holland) was also tested. Vibrations were measured on the bottom main load-bearing frame. Fig. 6 shows the vibrations produced with the mixer half-full and fully charged with powder. It was found that the charge-size made virtually no difference to the vibration signature—which was in any case small, consisting of a single broad frequency centered on 300 Hz with a peak acceleration of approximately 0.1 *g*.

The vibration signature of the different pharmaceutical processing equipment can be compared with the effects of similar combinations of frequencies and accelerations on powder segregation in a vibration model reported elsewhere by Staniforth and Rees (1982). Powder mixes containing a fine-particle model drug, potassium chloride, were formed with 3 different coarse-particle direct compression tabletting excipients: Dipac (Amstar, New York, U.S.A.); Emdex (Edward Mendell, New York, U.S.A.) and crystallite lactose (Staniforth, 1980). It was found that the 3 powder mixes behaved differently for reasons explained elsewhere (Staniforth and Rees, 1982), but in general conditions of low frequencies and high accelerations produced maximum powder segregation. (Table 1).

Table 2 shows vibration conditions which gave rise to the maximum powder segregation for each system. It should be stressed that all of the powders were mixed by very high content uniformity with homogeneities given by coefficients of variation well below 2% prior to vibration.

TABLE 1

EFFECT OF VIBRATION FOR 15 MIN AT A FREQUENCY OF 50 Hz AND ACCELERATIONS OF 2 *g* ON THE SEGREGATION OF POWDER MIXES (COEFFICIENT OF VARIATION = cv%)

Excipient	cv% of different concentrations of potassium chloride following vibration				
	0.5%	1%	2%	5%	10%
Dipac	21.4	47.5	59.5	256.6	500.1
Emdex	1.3	14.3	25.7	76.2	123.4
Crystallite lactose	2.2	18.7	31.1	93.0	15.7

TABLE 2

MAXIMUM SEGREGATION TENDENCIES OF DIFFERENT POWDER MIXES AND CORRESPONDING VIBRATION CONDITIONS (COEFFICIENT OF VARIATION = cv)

	Vibration frequency (Hz)	Vibration acceleration (g)	cv (%)	Error limits
Dipac and 0.5% potassium chloride	50	2.25	61.48	± 28.3%
Crystallite lactose (710–1000 μm size fraction)	50	2.25	19.57	± 5.5%
and 0.5% potassium chloride	30	2.25	21.15	± 13.5%
Dipac and 10% potassium chloride	50	2.25	500.1	±175.6%
Emdex and 10% potassium chloride	50	2.25	118.9	± 4.5%
Crystallite lactose (250–500 μm size fraction)	50	2.25	93.2	± 0.2%

Table 2 shows that massive segregation of drug particles from excipient particles occurred at frequencies and accelerations comparable with some of those encountered in conventional production equipment used to produce pharmaceutical tablets. Since vibrations within the segregation producing range—frequencies below approximately 100 Hz and accelerations above approximately 2 *g*—were found at critical points such as the powder hopper and the force feed unit where powder mixes are charged into the tabletting dies, it can be seen that conditions exist for producing segregation.

In order to minimize the scale or intensity of segregation of a given powder mix during processing, the vibration signature of all equipment should be monitored at critical points. If vibration conditions with low frequencies and high accelerations are found to exist it would be desirable to modify the equipment so as to minimize or eliminate the vibrations.

Conclusions

It was found that pharmaceutical processing equipment produced different vibrations at different areas. Although the orbiting screw blender was virtually vibration free, several of the tabletting machines had points on the powder hopper or on the feed-frame/force feeder which vibrated at frequencies within the range previously tested in a model vibration system by Staniforth and Rees (1982).

In the vibration model it was found that accelerations above approximately 2 *g* were capable of producing powder segregation. Similarly, segregation was most pronounced in vibration conditions of low frequency and generally less than 100 Hz. Powder segregation was found to be most intense in conditions with combinations of low frequencies and high accelerations, such as those found during normal pharmaceutical tabletting operations using a Manesty Layerpress or RBB3B rotary tabletting machine.

The results suggest that vibration conditions produced by normal processing equipment could lead to powder segregation and content uniformity problems in the final product. In conditions where content uniformity falls below desired or given limits these results suggest that minimizing or eliminating low frequency/high acceleration vibrations could reduce powder segregation and improve homogeneity.

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