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COMPACTION BEHAVIOUR OF MUSOL, A NEW DIRECT COMPRESSION VEHICLE

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ABSTRACT

The compaction characteristics of Musol, a new autocompressible vehicle derived through chemical modification of mucuna gum was investigated. Avicel PH 101, Zeparox and Encompress were used as reference tablet vehicles. Values of the mean yield stress derived from the analysis of Heckel plots indicate that Musol consolidates principally by plastic deformation. The effect of lubrication and recompression on friability, tensile strength and re-working potential of the tablets prepared with the vehicles were determined. While Avicel PH 101 yielded the strongest tablets, Musol showed the highest re-working potential for lubricated and un-lubricated slugs. On the basis of friability, tensile strength and re-working potential, Musol performed better than the grades of Zeparpx or Encompress used in the study.

INTRODUCTION

The mode of densification or consolidation of powdered substances offer useful information in the development of compressed tablets(1). Consolidation to a given voidage gives an indication of the strength of the material if the porosity approaches zero (2). By varying the porosity of the compact and hence its relative density through the application of different compaction loads, Heckel plots (3) are obtained. From these, the value of the mean yield stress of the powdered material is obtained. Studies of the mean yield stress show that low values may indicate intense plastic flow of a material whereas high values often indicate densification principally by fragmentation (4). A number of investigators (5-8) have used this approach in the study of the compaction characteristics of some pharmaceutical powders. The compaction behaviour of Musol has been investigated in the present study in order to determine its potentials as a direct compression vehicle. Although available autocompressible agents such as microcrystalline cellulose form extremely strong tablets, certain inherent disadvantages, such as high moisture sorption properties (9-11), low bulk density (12,13) and poor flow (13) necessitate continuous search for new excipients that can supplement or substitute existing raw materials.

MATERIALS

Avicel PH 101[1], Encompress E2995[2], Zeparox EP Lactose[3] and magnesium stearate[4] were used as supplied by the manufacturers. Musol was processed and crystallised in our laboratory.

METHODS

Bulk and Particle densities.

The mean particle size of Musol used was 150 μm. All the powdered vehicles were passed through 250 μm aperture sieve and dried for an hour in a hot air oven[5] set at 60°C. The powders were allowed to attain equilibrium at 30°C before any determination. The fluff bulk density D_o, and the consolidated bulk density at equilibrium D_e, of each vehicle were determined using a dry 250 ml measuring cylinder while the powder was poured. The apparent particle density of each vehicle was determined using an air pycnometer.[6]

Compression of tablets

A 600 mg sample of each vehicle was placed in a 1.31 cm diameter die of a hydraulic press[7] fitted with flat-faced punches. Batches of blank tablets were prepared using compaction loads of 10, 20, 40 and 60 KN. In order to compress Encompress or Zeparox powders with which sticking occured during preliminary experiments, the punch and die surfaces were lubricated with a thin film of magnesium stearate before each compression.

For the purpose of determining the effect of magnesium stearate lubricant on the strength of directly compressed vehicles, tablets in which 2 % magnesium stearate was incorporated were also prepared. The compression load was also varied between 10 and 60 KN. Each batch of tablets was stored at 25°C for 24 h in well closed containers prior to their use in subsequent investigations.

Tablet dimensions.

Twenty tablets were selected randomly from each batch. The thickness and diameter of each tablet was measured with a micrometer[8].

Diametral crushing strength and Tensile strength.

Each of the selected tablets was placed between the platens of a precision physical testing machine[9]. The compressor speed was set at 10^{-1} cm per minute. The sensitivity of the instrument was ensured by selecting loads nearest the expected crushing strength for tablets in each batch. On the activation of the motor, the diametral crushing strength was automatically displayed by the recorder. The mean diametral crushing strength was determined for the various batches of the tablets. The tensile strength S, of each tablet was calculated from the relationship (5,7),

$$S = {}^{2P}/_{\pi dh} \quad \ldots \quad (1)$$

where P is the breaking load, d the diameter and h the thickness of the tablet.

Friability

Twenty tablets were selected randomly from each batch and accurately weighed. The dusted tablets were placed in a friabilator[10] and subjected to shock for 4 min. at a motor speed of 25 rpm. At the end of the period the tablets were de-dusted and weighed. The friability was calculated as the percent loss in weight.

Re-working potential

Tablets from a given batch were selected and milled to the original particle size of the starting direct compression

vehicle. Several 600 mg samples of each powdered tablets were respectively re-compressed at 10, 20, 40 and 60 KN. The tablet dimensions, friability, diametral crushing strength and tensile strength were determined as described earlier.

RESULTS AND DISCUSSION

The Heckel equation which usually relates the relative density D_r, of a compressed powdered solid to the applied load, P, is given as (3)

$$\ln \frac{1}{(1-D_r)} = KP + A \quad \cdot \quad \cdot \quad (2)$$

The constant K, is the reciprocal of the mean yield stress P_y, while A is a constant usually considered as the sum of the densification by particle rearrangement. A low value of P_y often indicates intense plastic flow of a material while very high values or a curvilinear portion in the zone of low compaction loads may indicate densification principally by fragmentation or brittle fracture (4, 7, 14). The term D_r, is the ratio of the apparent density of the compact to the particle density. Though the Heckel relationship may elicit some criticisms (15), it still continues to provide an adequate method of quantifying differences between the compaction behaviour of starting materials used in tabletting (5-8).

The Heckel plots for the un-lubricated and re-worked tablets are shown in Figures 1 and 2. The effect of lubrication on the densification of Musol and Avicel PH 101 is presented in Figure 3. At both low and high compaction loads good tablets were not obtained with the grade of Zeparox used in the study.

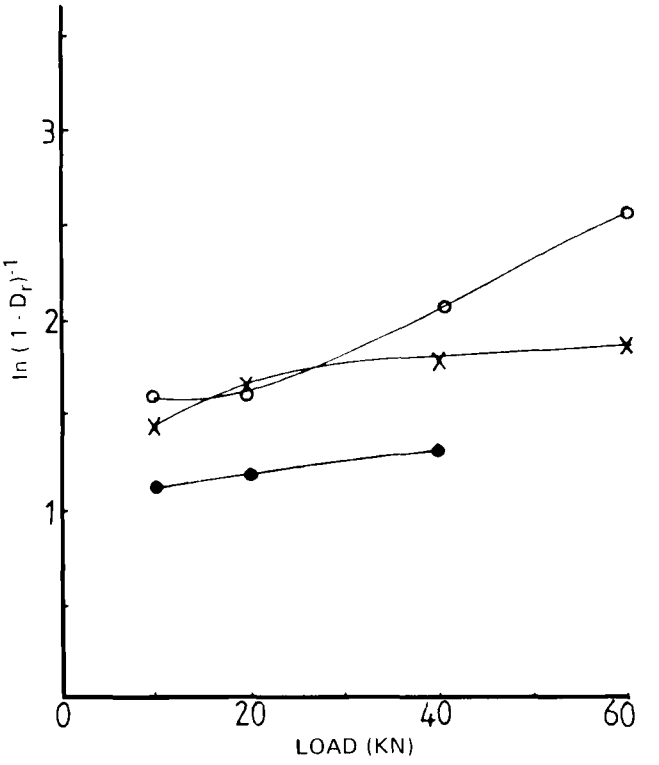

FIGURE 1.
Heckel plots for unlubricated blank tablets of some direct compression diluents. X, Avicel PH 101; O, Musol; ● Encompress.

It is shown in Table 1 that a high value of mean yield stress was obtained with un-lubricated Encompress. This agrees with the consolidation by fragmentation or brittle failure under pressure reported for this substance (16,17). In contrast to Encompress, relatively low values of mean yield stresses were obtained with un-lubricated Musol and Avicel PH 101 respectively. The low value of the mean yield stress obtained with Avicel PH 101 at low compaction loads agrees with plastic flow reported for this

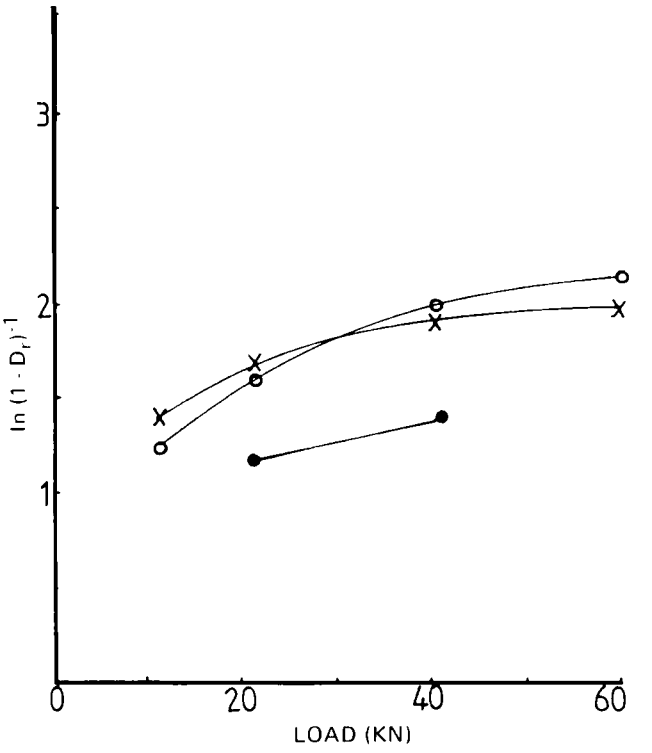

FIGURE 2.
Heckel plots for unlubricated slugs of some direct compression diluent X, Avicel PH 101; O, Musol; ● Encompress.

substance (18-20). On the basis of the relatively low values of mean yield stresses obtained for re-worked and lubricated Musol, it can be reasonably assumed that its mode of densification is principally by plastic deformation. Re-working of the tablets generated smaller particles and this may have led to closer packing of the particles and the low mean yield stresses observed for all the three vehicles. Lubrication with 2% magnesium stearate significantly increased the P_y values of Avicel PH 101 and Musol

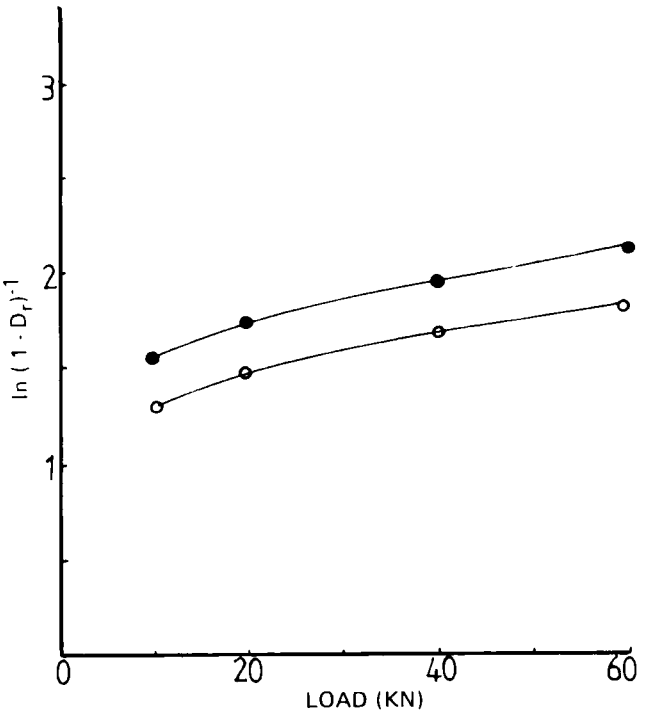

FIGURE 3

Heckel plots for lubricated slugs. ●, Avicel PH 101; ○, Musol.

TABLE 1

Mean Yield Stress KN, of Named Vehicles

Vehicle	Un-lubricated Tablets	Reworked Tablets	Lubricated Tablets
Avicel PH 101	40.00	32.08	47.6
Musol	38.50	31.40	47.0
Encompress	138.90	87.72	-

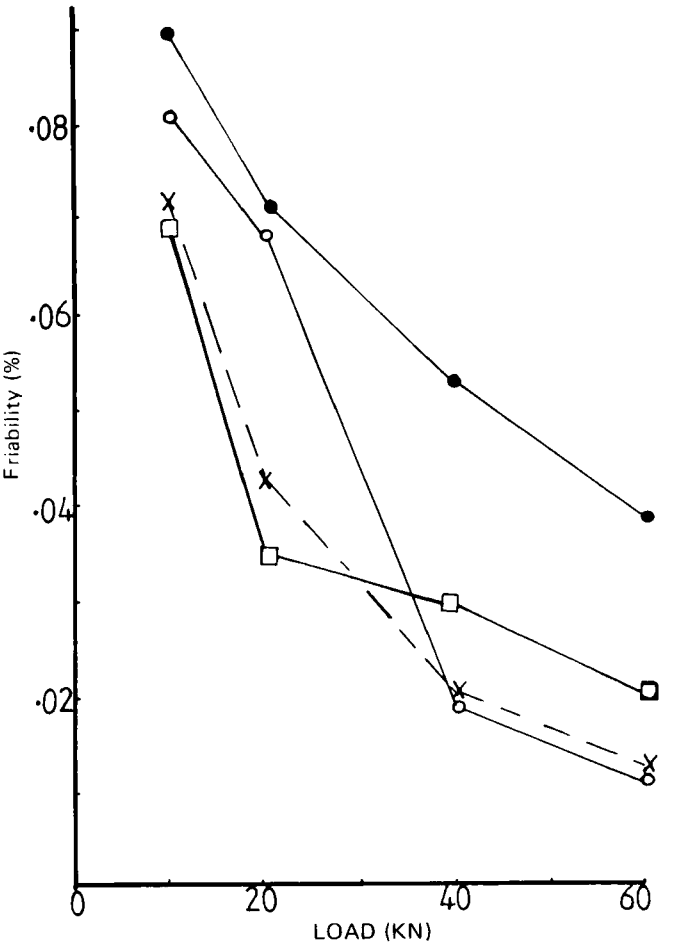

FIGURE 4.

Effect of increasing compaction load on the friability of slugs. X, Unlubricated Avicel PH 101
O, Reworked Avicel PH 101; □, Unlubricated Musol;
●, Reworked Musol.

respectively. The tablets produced with Encompress were too soft for further consideration. The effect produced by the lubricant is probably due to induction of elastic stress in the compacts and this is known to oppose increased plastic flow of materials during compression (21).

Friability and Reworking Potential

The effect of re-compression and increasing compaction load on the friability of un-lubricated tablets prepared with Musol and Avicel PH 101 respectively are shown in Figure 4. Tablets produced with either Encompress or Zeparox were soft and therefore did not merit further consideration. The tablets of Avicel PH 101 and Musol were not friable. Though re-working increased the friability in each case, the maximum friability at the lowest compaction load of 10 KN were 0.09 and 0.08 % for Musol and Avicel PH 101 respectively. These are by far less than the 1-2 % friability values reported as satisfactory for some directly compressed tablets (16).

Figure 5 shows that lubrication of the vehicles with 2 % w/w magnesium stearate increased the friability of the tablets. This is not surprising since the lubricant generally softens tablets thereby reducing their strength and resistance to shock. The highest friability of 0.7 % obtained for lubricated Musol at a compaction load of 10 KN is considered satisfactory. Figures 6 and 7 show that lubrication and re-working reduced the tensile strength of all the tablets tested. The highest values of tensile strength were obtained for Avicel PH 101 at all compaction loads. However, the reduction in tensile strength of its tablets by lubrication was more marked than the reduction obtained for tablets prepared with Musol. Figure 6 shows that Encompress tablets had the least tensile strength of all the three vehicles. Above 40 KN, the Encompress tablets capped. This is probably due

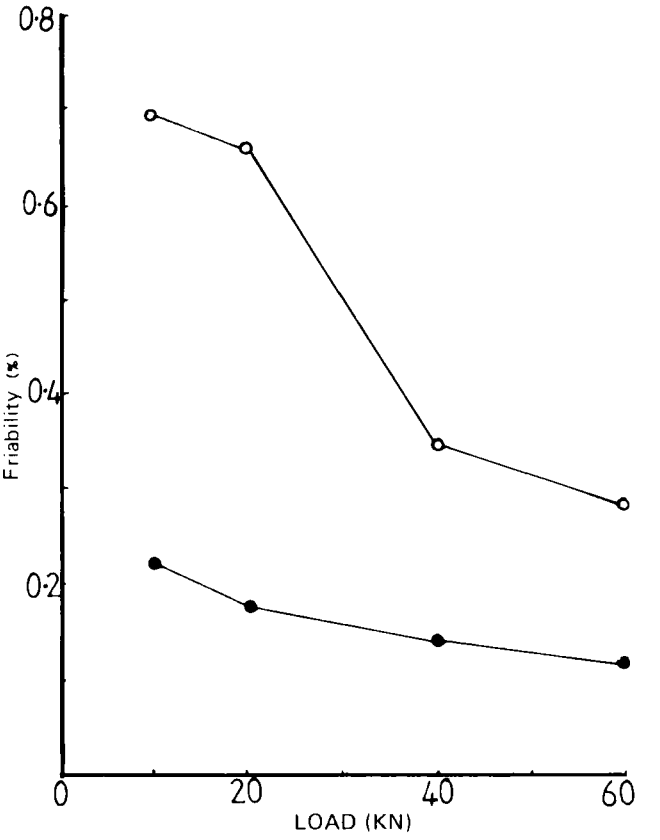

FIGURE 5.

Effect of increasing compaction load on the friability of lubricated slugs. ●, Avicel PH 101; O, Musol

to resistance of the particles to deformation. Encompress consolidates by brittle fracture during compression and above an optimum load, the particles no longer withstand higher compressive forces. This may have caused the capping of the tablets prepared with this vehicle.

Table 2 shows the re-working potentials for the lubricated and un-lubricated tablets prepared with either Musol, Avicel

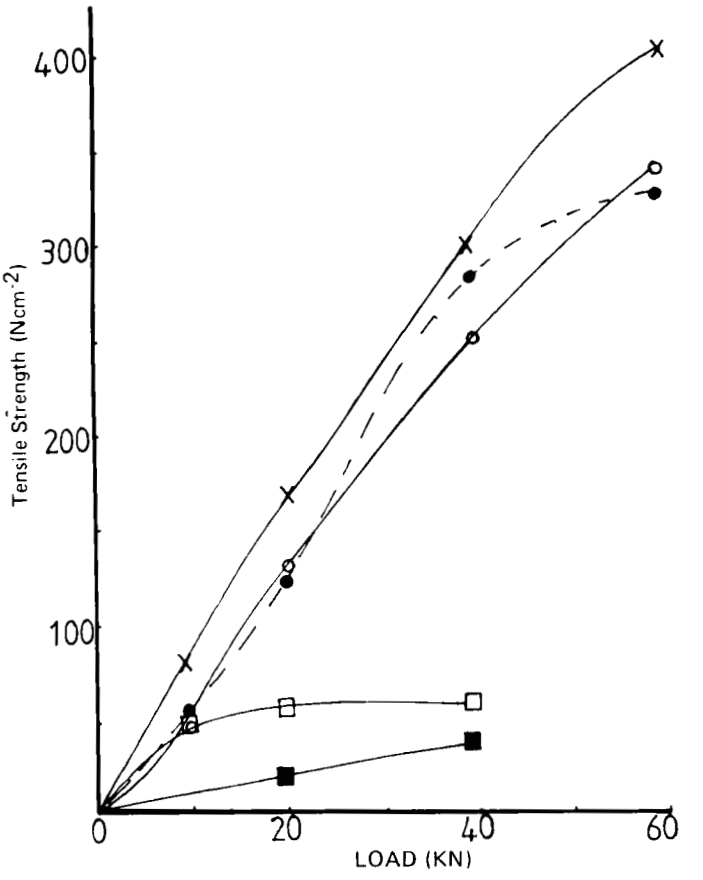

FIGURE 6.

Effect of lubrication and recompression on the tensile strength of slugs.

X, Unlubricated Musol; O, Reworked Musol; ●, Musol + 2% Magnesium stearate; □, Unlubricated Emcompress; ■, Reworked Encompress.

PH 101, or Encompress. The values were derived from Figures 6 and 7 according to the method reported by Malkowska and Khan (22). The re-working potentials for Avicel PH 101 and Musol are quite high, indicating that these vehicles do not lose much of their compressibility characteristics after compression. It can be

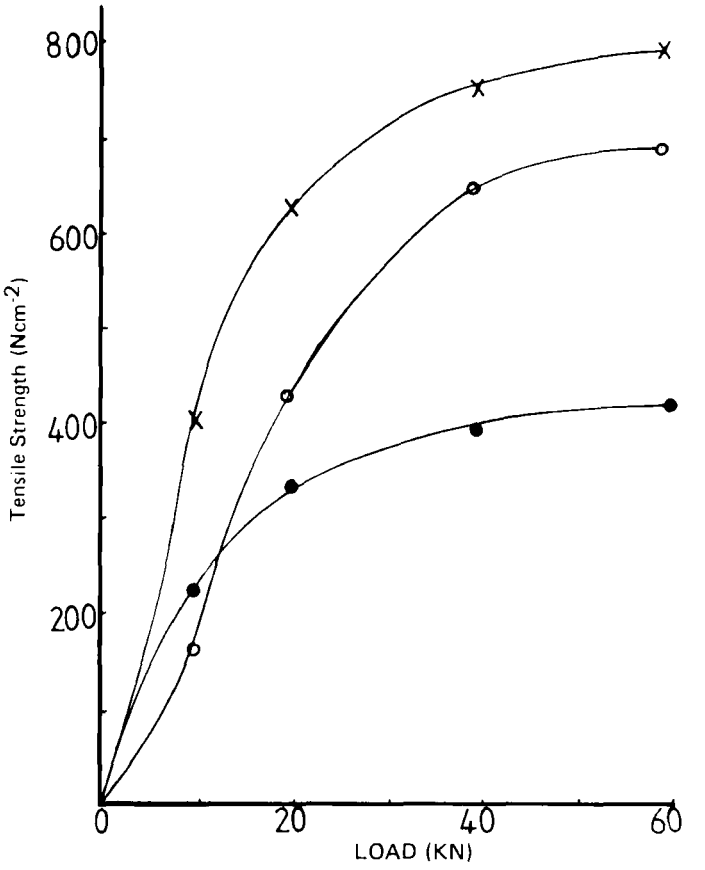

FIGURE 7.

Effect of lubrication and recompression on the tensile strength of slugs.

X, Unlubricated Avicel PH 101; O, Reworked Avicel PH 101; ● Avicel PH 101 + 2% Magnesium stearate.

TABLE 2

Re-working Potentials of Named Vehicles

Vehicle	Reworking Potential (%)	
	Lubricated Tablets	Un-lubricated tablets
Avicel PH 101	54.05	79.73
Musol	81.48	85.15
Encompress	-	45.00

seen that Musol withstands re-working more than Avicel PH 101 even though tablets of the latter had more tensile strength at all compaction loads investigated. The very low re-working potential obtained for un-lubricated Encompress is characteristic of materials which consolidate by fragmentation under pressure (13). It is a disadvantage if defective tablets can not be re-worked if the need arises.

CONCLUSION

The fluff bulk density and consolidated bulk density at equilibrium obtained for Musol were 0.70 and 0.82 respectively. These gave percent compressibility (4-7) and Hausner ratio (4,5) of 16.7 and 1.2 respectively indicating very good flow and compressibility characteristics for Musol. Low values of mean yield stress were obtained from the analysis of the Heckel plots This is indicative that the mode of densification of Musol is mainly by plastic deformation. The tensile strength of the tablets compressed at compaction loads of 10 to 60 KN shows that Musol is autocompressible. Its tablets were not as friable as those of Encompress and Zeparox. Although the tensile strengths of tablets prepared with Avicel PH 101 were much higher than the tensile strength of tablets produced with Musol, the latter showed the highest re-working potential of all the vehicles tested including Avicel PH 101. Musol may therefore be used to impart strength to poorly compressible powdered drugs.

FOOTNOTES

1. FMC Corp, Philadelphia

2. Cambrian Chemicals, Croydon, U.K.

3. Dairy Crest, Surrey, U.K.

4. BDH

5. Manesty Ltd, England

6. Beckman Model 930

7. Pye Unicam

8. EHB Germany

9. RDP Howden Ltd, Warks, England

10. Erweka Apparatebeau.

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