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# Direct compression characteristics of xylitol

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## Summary

A study of the compaction characteristics of xylitol, a naturally occurring non-cariogenic sugar alcohol, employed as a sweetener in tableting has been made, using a wide range of compression speeds (24–850 mm/s). Heckel analysis, radial tensile strength, elastic recovery, net compaction energy and the compaction force/tensile strength relationship have been used as the basis of the investigation. The mean yield pressure, radial tensile strength and elastic recovery of xylitol tablets appear to be independent of compression speed, indicating a dominant fragmentation mechanism of consolidation. A good correlation was observed between the net compaction energy of xylitol and compression speed and an equation has been proposed to describe the relationship. Xylitol was observed to exhibit significant sensitivity to compaction force at compression speeds up to 500 mm/s and a maximum compaction force of 22.43 kN has been recommended in an effort to optimise tablet tensile strength.

## Introduction

Xylitol is a sweet, odourless, white crystalline pentavalent sugar alcohol, similar to mannitol and sorbitol. Sweeteners employed in pharmaceutical tablets fufill the purpose of providing bulk and also mask the possible unpleasant taste of active ingredients.

The connection between sucrose and tooth decay is indisputable, depending primarily on the frequency of sucrose intake. Xylitol has gained interest as a tablet excipient, because it is the only naturally occurring sweetener which is non-cariogenic, this effect being ascribed to the possible inability of caries-causing microorganisms living in saliva and the buccal cavity to use xylitol for their nutrition. The initial metabolism of xylitol is independent of insulin, and does not cause rapid variation in blood glucose levels and can therefore be used in small doses in diabetics (Ylikahri, 1979).

Kristoffersson and Halme (1978) previously investigated xylitol as an excipient for oral lozenges and found that, due to the hygroscopicity of xylitol and the strong polarity of water, the granulation required the addition of 5% spiritus gelatinae.

In 1982, Laakso et al. reported the suitability of xylitol as a tablet excipient in direct compression and granulation using spiritus gelatinae as the granulation solution and concluded that xylitol in combination with Avicel was more suitable for use as an excipient in direct compression than in wet granulation methods.

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The aim of the present study was to assess the fundamental direct compression characteristics of xylitol using a wide range of compression speeds (24–850 mm/s). Heckel analysis, radial tensile strength, elastic recovery, net compaction energy and the compaction force/tensile strength relationship were used as the basis of the evaluation.

## Materials and Methods

### *Materials*

Xylitol (milled with mean particle size 0.17 ± 0.03 mm) was obtained from Forum Chemicals (Surrey, U.K.) whilst magnesium stearate was from BDH Chemicals (Poole, U.K.).

### *Methods*

*Compression*

The compressions were carried out using The Liverpool School of Pharmacy High Speed Compaction Simulator (Bateman, 1988a), fitted with 12.5-mm flat-faced punches. A sawtooth time displacement profile was used to control both upper and lower punches. 500 mg constant weight of xylitol was compressed to a maximum force of 22.0 kN, and five tablets were produced at seven compression speeds from 24 to 850 mm/s, The die wall was cleaned with acetone and prelubricated with 4% w/v of magnesium stearate in carbon tetrachloride before each compression.

During compression, upper punch load and punch separation were monitored to an accuracy of ±0.05 kN and ±12 μm respectively. The compression data were manipulated in an identical manner to that previously described by Bateman (1988a,b).

*Radial tensile strength*

Tensile strength was determined from the force required to fracture tablets by diametral compression on a motorised tablet hardness tester (Model 2E, Schleuniger, Switzerland) and the corresponding tensile strength calculated according to the equation of Fell and Newton (1971).

*Compaction force / tensile strength relationship*

The compaction force is likely to affect other characteristics of the tablets. The sensitivity of xylitol to changes in compression force was determined at three compression speeds (24, 300 and 500 mm/s), by subjecting 500 mg of the material to an applied compaction force in the range 5–32 kN and the corresponding tensile strengths of the compressed tablets were determined 24 h after ejection.

*Elastic recovery*

The elastic recovery of xylitol tablets was calculated using the equation reported by Armstrong and Haines-Nutt (1972) and Malamataris et al. (1984):

$$ER = \left[(H_0 - H_p)/H_p\right] \times 100\%$$

where $H_p$ and $H_0$ are the heights of the tablet under pressure and 24 h after ejection, respectively. Whilst it could be argued that the expression for elastic recovery does not allow for the possibility of recovery in a radial direction, nevertheless it seems reasonable to expect ER as defined above to provide some comparative measure of the changes in the decompression phase of xylitol as the compression speed is increased.

*Net compaction energy*

The net compaction energy of xylitol tablets at varying speeds of compression was determined using energy analysis. A computer program was

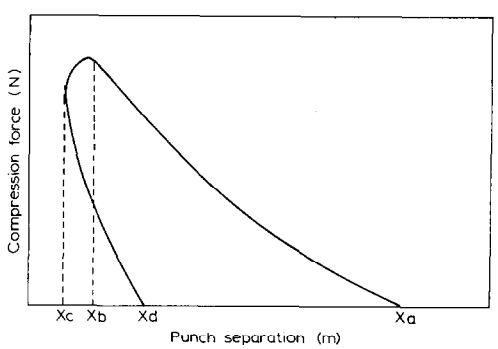


Fig. 1. Schematic diagram of force-displacement plot used in the energy analysis.

employed to calculate compression and decompression energies from the transient recorder data.

Fig. 1 illustrates schematically the force-displacement plot, where Xa is the punch separation at the first measurable force, Xb denotes the first occurrence of peak force, Xc represents the minimum punch separation and Xd is the decompression force (less than or equal to zero). The area under the curve XaXb (AUC XaXb) gives the compression energy, whilst that under curve XcXd (AUC XcXd) corresponds to the decompression energy (Bateman, 1988b).

The net compaction energy ($E_c$) was determined as

$$E_c = (\text{AUC XaXb}) - (\text{AUC XcXd}).$$

## Results and Discussion

The compressibility of pharmaceutical powders can be estimated from the mean yield pressures evaluated from the Heckel analyses. The mean yield pressure of xylitol appears to be independent of compression speed over the range 24–850 mm/s (Fig. 2), which encompasses the range of speeds encountered during research using physical testing machines (0.05–5.0 cm/min) and single-punch machines (50–150 mm/s), and the range well above that of compression speeds during production, using rotary machines (100–400 mm/s). This observation can be ascribed to the fact that xylitol consolidates primarily by fragmentation, the mean yield pressure only varying between 66.65 and 70.85 MPa. Fragmentation is rapidly achieved and changes in compression speed would be expected to have little or no effect.

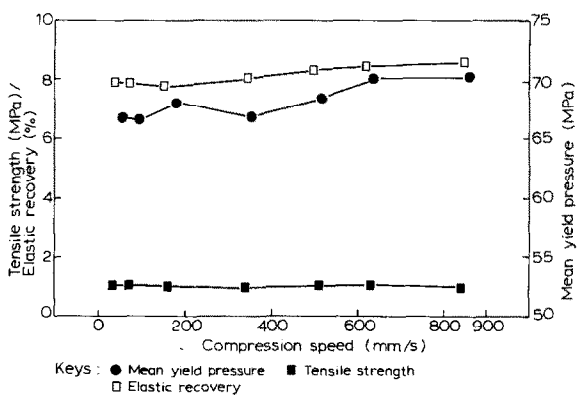


Fig. 2. Effect of compression speed on the mean yield pressure, tensile strength and elastic recovery of xylitol tablets. (●) Mean yield pressure, (■) tensile strength, (□) elastic recovery.

There was no significant change in radial tensile strength and elastic recovery with increasing speed of compression, which appears to correlate with the hypothesis that consolidation occurs by fragmentation (Fig. 2).

The net compaction energy was found to increase with compression speed, and there was a good correlation between the natural logarithm of net energy and compression speed (correlation coefficient of 0.96). It can be described by the equation:

$$\ln E_c = A + B[\text{Cs}]$$

where $E_c$ is the net compaction energy of xylitol, Cs is the compression speed, $A$ is the intercept (1.74) and $B$ is the slope of the line ($7.12 \times 10^{-4}$). With increasing speed of compression, more compaction energy appeared to be required for elastic deformation, fragmentation of particles and formation of bonds. There is a possibility that part of the net energy might be utilised in particle rearrangement, die-wall friction and increased interparticulate friction that may occur at high compression speeds. The equation described above holds for xylitol and would be interesting to determine its applicability to other pharmaceutical powders that deform primarily by a fragmentation mechanism.

The relationship between compaction force and tensile strength of xylitol tablets at different speeds of compression is illustrated in Fig. 3. The compaction force is the mean of the upper and lower punch forces. It is particularly important to avoid error often associated with substantial die wall friction (Ragnarsson and Sjogren, 1983). The compaction force is an important parameter which may significantly affect other tablet characteristics and it is essential that it is accurately known. The sensitivity of some direct compression excipients, such as microcrystalline cellulose, to compaction

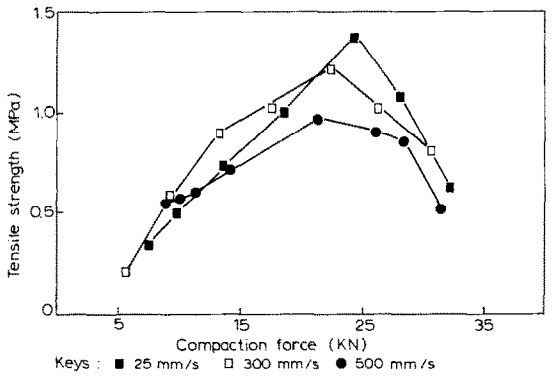


Fig. 3. Effect of compression speed on the relationship between compaction force and tensile strength of xylitol tablets. (■) 25 mm/s, (□) 300 mm/s, (●) 500 mm/s.

force puts greater demands on the need to control this parameter (Marshall, 1989).

Xylitol exhibited significant sensitivity to changes in compaction force at varying speeds of compression (Fig. 3). As the force is increased, the tensile strength increases almost linearly up to 23.90 kN at a speed of 25 mm/s, 22.15 kN at 300 mm/s and 21.25 kN at 500 mm/s (mean value 22.43 kN). Further increases in compaction force resulted in a decrease in tablet tensile strength. This can be ascribed to the possibility that the work associated with compaction above 22.43 kN is being recovered during elastic relaxation which results in a weakening of the tablet structure.

It follows from this observation that, in order to optimise tensile strength for xylitol, it is necessary to keep the compaction force below 22.43 kN at compression speeds up to 500 mm/s.

## Conclusion

A study of the direct compression characteristics of xylitol using a wide range of compression speeds has been performed. Heckel analysis, tensile strength, elastic recovery, net compaction energy and the compaction force/tensile strength relationship were used as the basis of the evaluation.

The mean yield pressure, radial tensile strength and elastic recovery of xylitol tablets appear to be independent of compression speed in the range 24–850 mm/s, indicating that the dominant mechanism of consolidation is fragmentation, which is known to be independent of compression speed.

A good correlation occurred between the net compaction energy of xylitol and compression speed and an equation has been proposed to describe the relationship. Xylitol exhibited significant sensitivity to compaction force at varying speeds of compression; the tensile strength increasing almost linearly with compaction force up to an average value of 22.43 kN. Further increases in compaction force resulted in a progressive decrease in tensile strength, implying that the additional force is being recovered during elastic relaxation. It appears from this observation that the compaction force of xylitol at compression speeds up to 500 mm/s should be maintained at a value lower than 22.43 kN so as to maximise tablet tensile strength.

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