Characterisation of pharmaceutical polyols by yield pressure determination.

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Introduction

The aim of the project was to compare the compression properties of a group of excipients called polyols by Heckel testing, as these materials can be used to provide strength to tablet formulations. All of the samples have different chemical structures which may affect, for example, how a tablet formulation performs.
Four different materials were selected, all with approximately the same particle size [200 µm] and from the same supplier [Roquette, France], to be compressed by a hydraulic Compaction simulator in order to characterise the properties of the materials by the compression properties seen.

Materials and methods

Xylitol [Xylisorb 200SD], Sorbitol [Neosorb 200SD], Mannitol [Pearlitol 200SD] and Maltitiol [Sweetpearl 200SD,] were selected and supplied by Roquette, France. Testing was performed using a Phoenix hydraulic Compaction Simulator (Dudley, UK). Heckel testing was performed at two speeds [0.1 mm/s and 300 mm/s] using a 'V shaped' profile (Fig.1). The Heckel equation was used to generate yield pressure values [Eqn.1].
The true density was determined using a Helium Pycnometer (Micromeritics, UK). This value was then multiplied with the volume of the tablet (235.65 mm^3) to give the fill weight required.
The known weight of material is then compacted to theoretical zero porosity using 10 mm diameter die with flat faced punches. The punches and die are lubricated before compression using magnesium stearate suspended in acetone. The data were analysed by the Compaction Analysis software programme to generate values for yield pressure (Py) using the Heckel equation (Eqn.1). A range of 30-150 MPa was selected for the polyols to include the most linear portion of the Heckel plot.

$$\ln \frac{1}{1-D} = kP + A \qquad \text{[Eqn.1]}$$

Where D = the relative density of the compact
P = Pressure applied
K = Gradient of the line in the linear region[1]

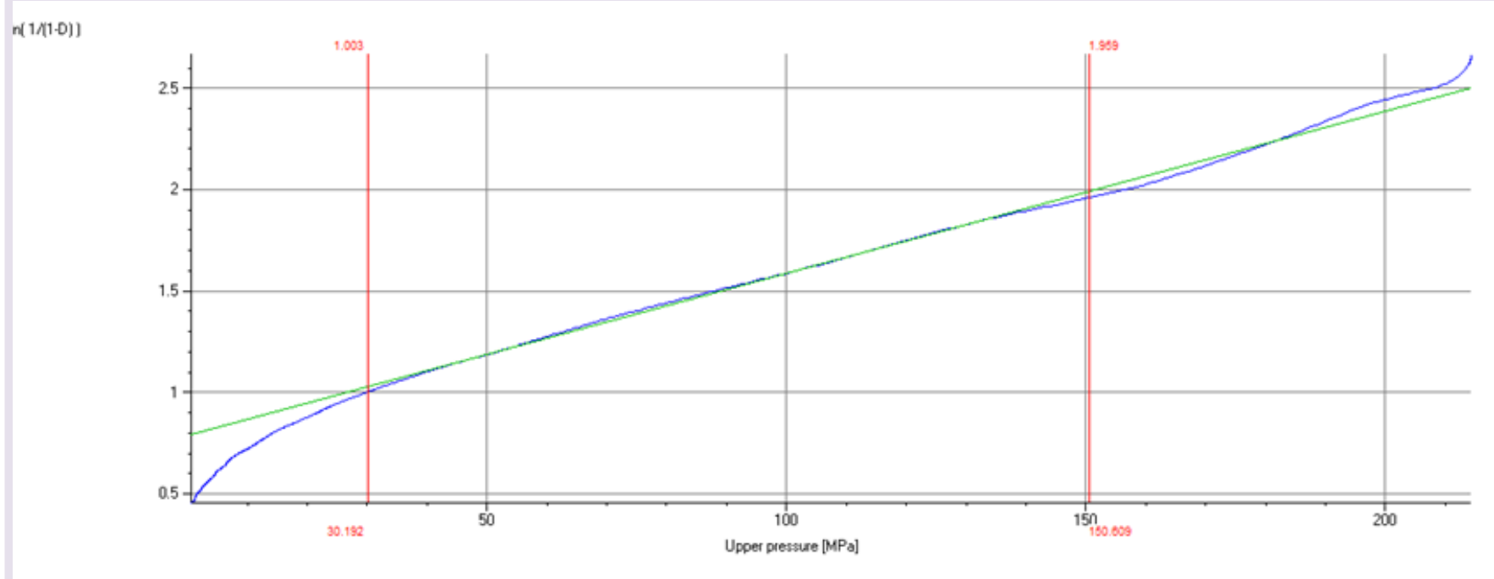

Fig. 2: Example Heckel analysis.

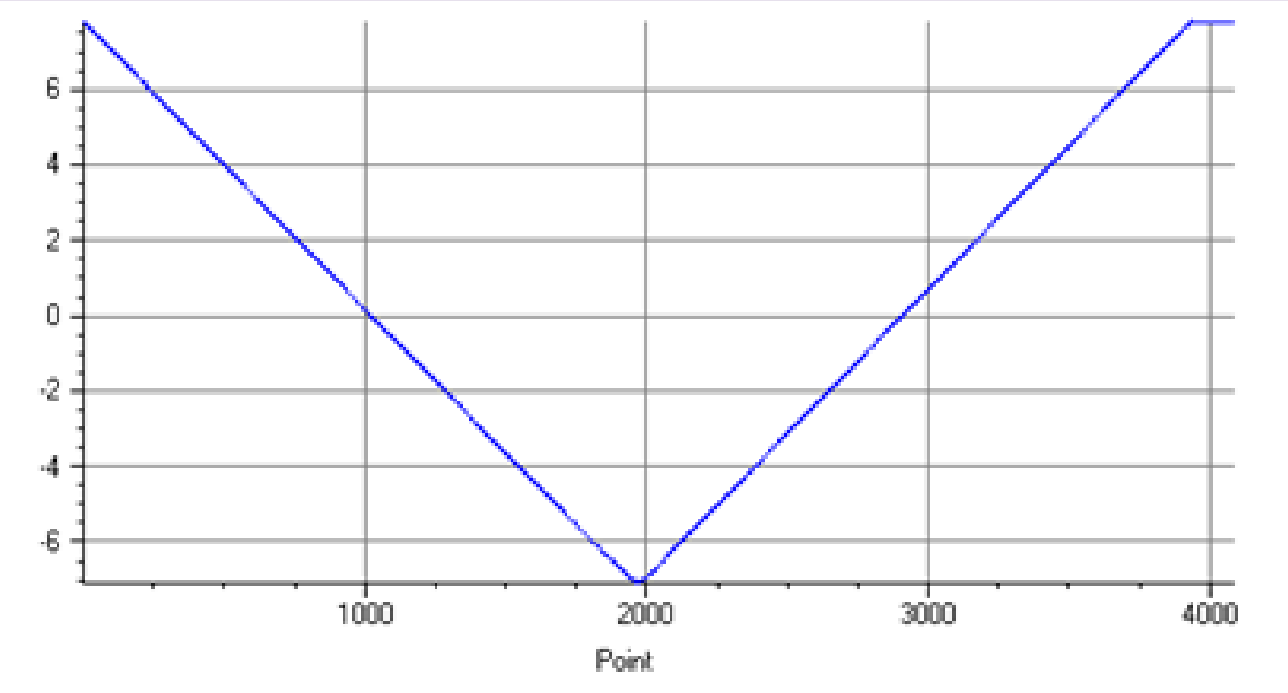

Fig. 1: Example of profile used for Heckel testing

$$\%SRS = \frac{Py\ Fast - Py\ Slow}{Py\ Slow} \times 100 \qquad [2]$$

[Eqn.2]

A material may behave differently depending upon punch speed as the deformation characteristics may change with the rate of applied force. It is for this reason that the Strain Rate Sensitivity is calculated [Eqn.2].
This calculation is based upon a percentage increase between the slow and fast speed yield pressures, combining the yield pressure and Strain Rate Sensitivity data together allows characterisation of the material. This can range from a hard , brittle material to a very soft viscoelastic materials with ductile materials falling in between.

Results

Three of the materials were characterised as moderately hard/brittle due to the low values of Strain Rate Sensitivity and slow speed yield pressures being over 100 MPa at slow speeds. Sorbitol falls into the moderately hard brittle/ ductile category as the Strain Rate Sensitivity is higher than the other materials and the slow speed yield pressure is lower for sorbitol than the other materials (Fig.3).
The Strain Rate Sensitivity (SRS) measures changes in compression behaviour at productions speeds. For the samples classified as moderately hard/brittle, xylitol is least likely to be affected by press speeds with a SRS of 2.3% and maltitol is most likely to be affected with a SRS of 11.6%. Sorbitol will be significantly affected by press speeds due to the high SRS of 41.8%.

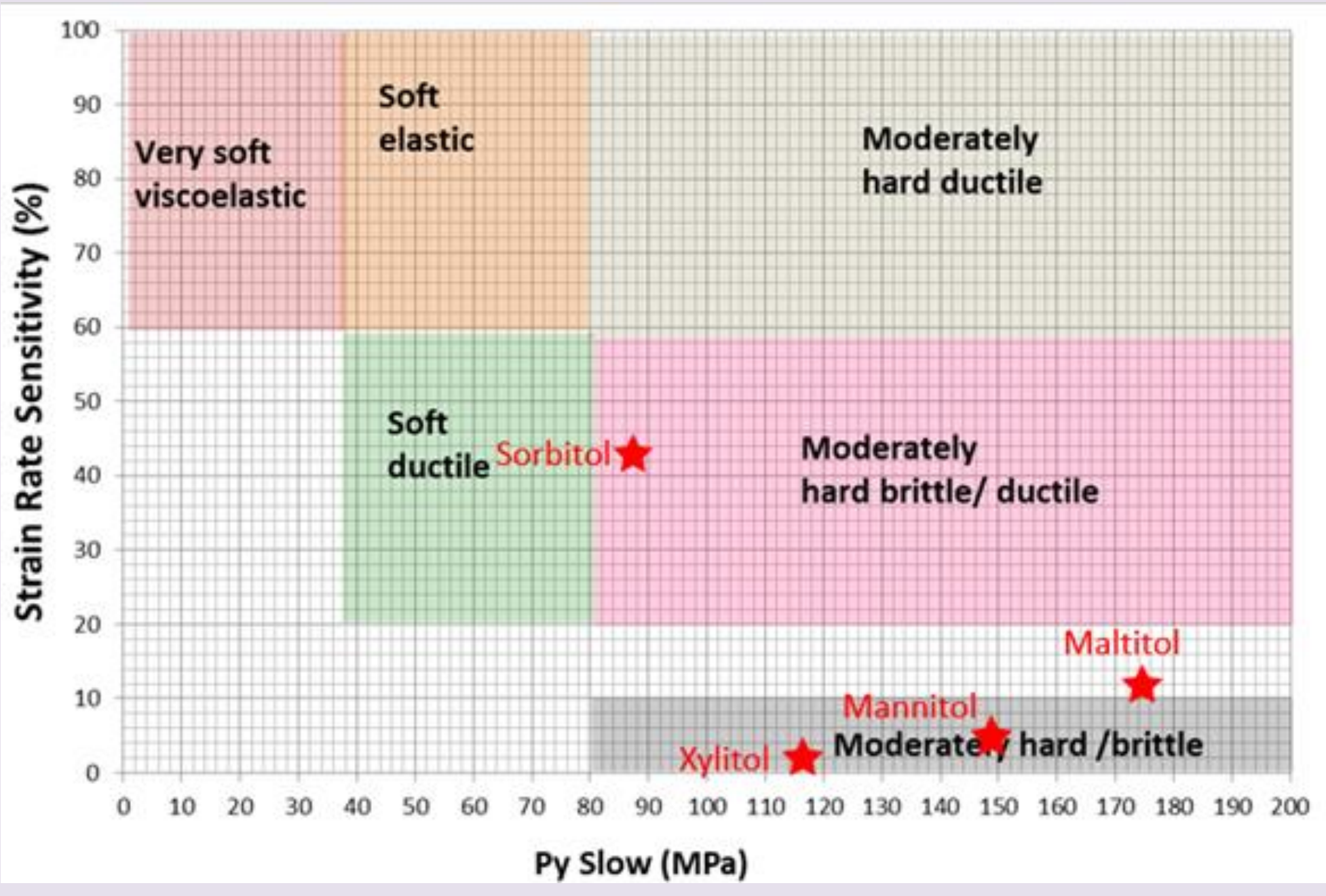

Fig. 3: SRS chart for all materials tested.

Materials with a yield pressure above the ideal range for tablets [80-120 MPa] will be useful in balancing yield pressures of plastic APIs [Mannitol and Maltitol]. Xylitol and Sorbitol fall within this ideal range. Higher forces are needed to deform brittle materials and they are likely to deform by fracture. The polyols show further differences in crushing strength and ejection forces.

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Ejection force and compact strength

Ejection Force: Sorbitol shows the lowest ejection forces at both fast and slow speeds across all of the samples, while xylitol shows the highest ejection forces at fast speed and maltitol shows the highest ejection forces at slow speeds. High ejection forces may promote die wall friction and possible sticking which could results in physical defects within production, however no physical defects were seen in any of the compacts made.
The general trend seen across the samples is that as the speed of compression increases so does the ejection force (Fig.4).

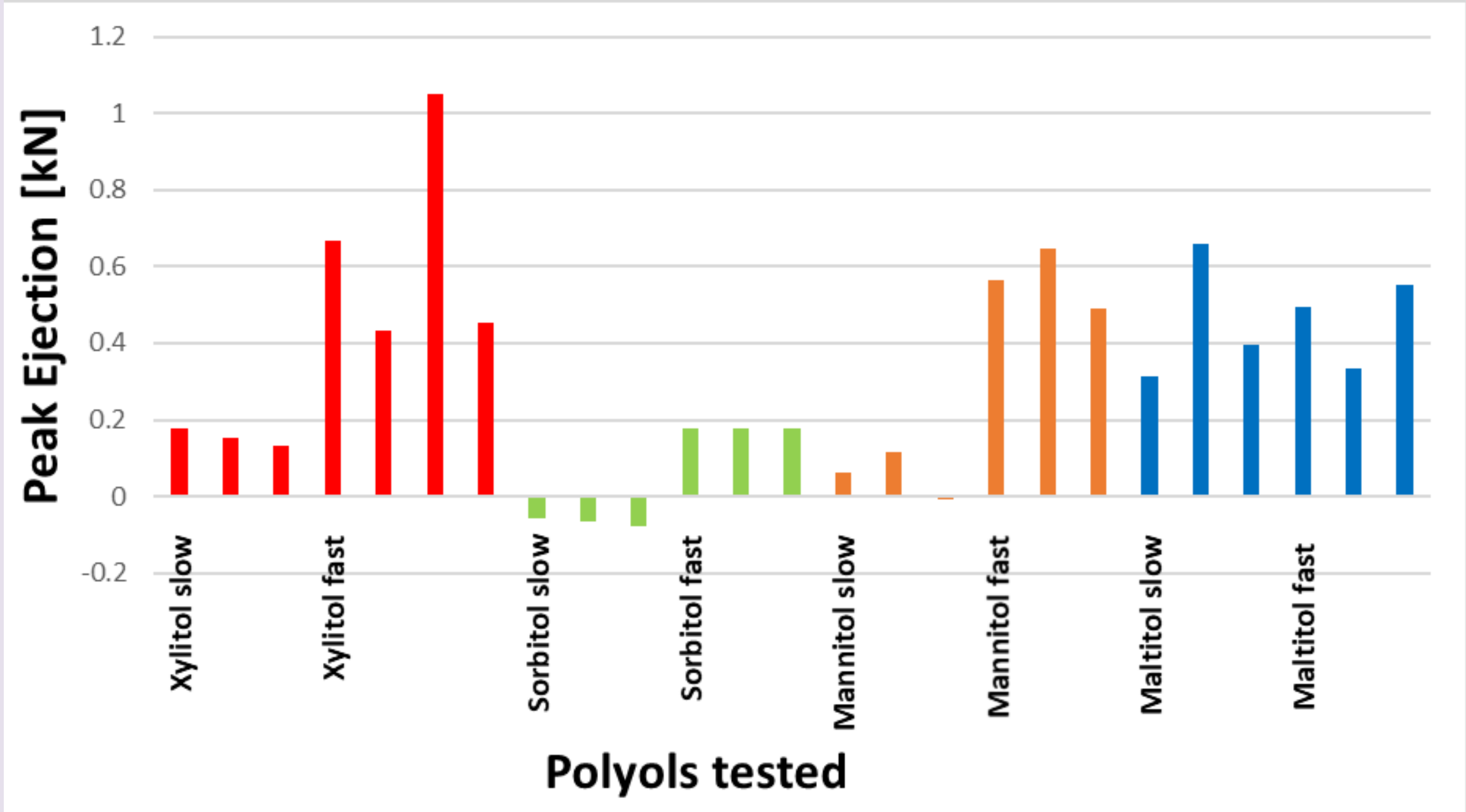

Fig. 4: Graph showing ejection forces for the polyols at slow and fast speed

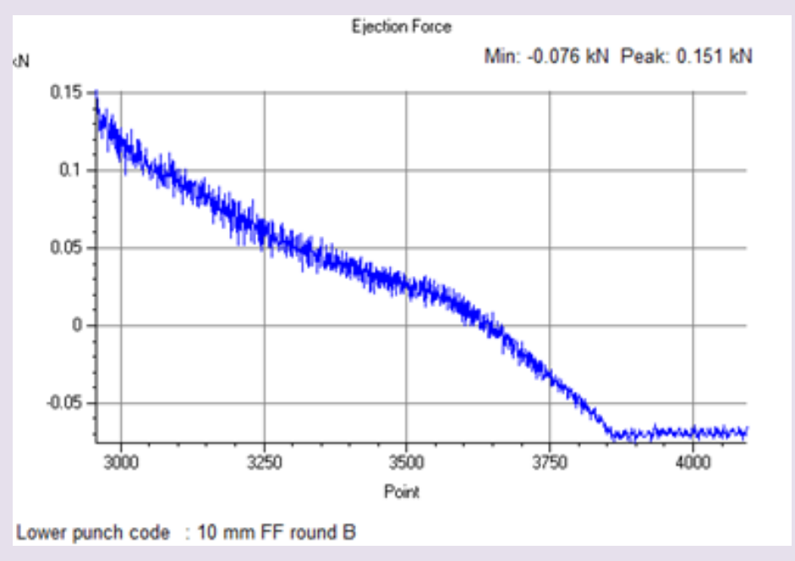

Fig. 5a: Example slow speed ejection force data.

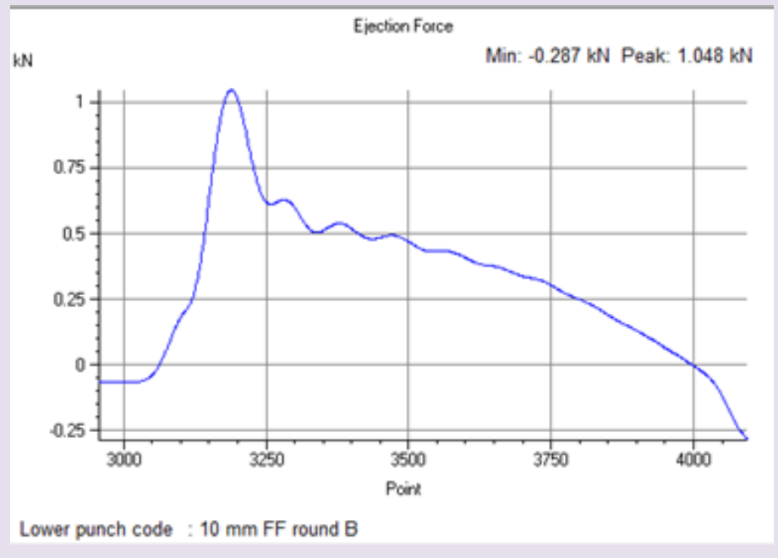

Fig. 5b: Example fast speed ejection force data.

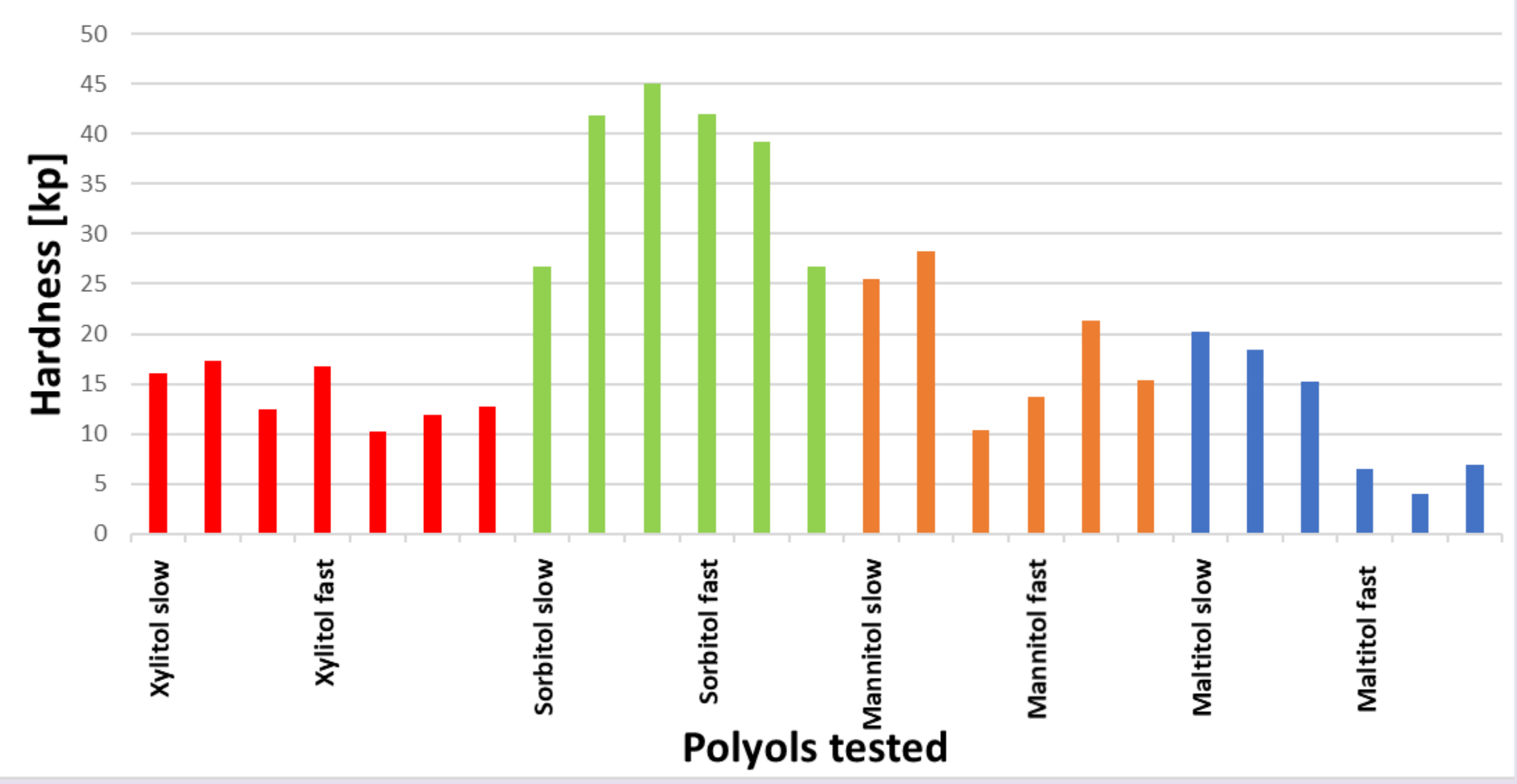

Fig. 6: Graph showing hardness/crushing strength for the polyols at slow and fast speed

In order to gain an understanding of how the dwell time affects the bonding within materials the compact strength needs to be looked at. These excipients generally have a high compact strength due to their use within formulations.

Crushing strength: Generally the crushing strength decreases as speed increases with the exception of sorbitol which has a similar crushing strength across both speeds. Xylitol only shows a slight drop in crushing strength as speed increases. Maltitol has the most obvious change in crushing strength across the two speeds. There are generally high crushing strengths across the polyols tested when compared to APIs or other excipients, this again is due to the role these materials play within a formulation. Sorbitol shows the highest crushing strength across the materials at both speeds. Xylitol and maltitol show similar crushing strengths at slow speed.

Conclusions

General trends could be seen across the materials and these were: as punch speed increases so does the ejection force and crushing strength decreases as punch speed increases.
Sorbitol has the highest crushing strength out of all of the samples and the lowest ejection forces at both speeds. This may be useful to consider with an API that has a poor tensile strength.
Mannitol also has a good crushing strength however, at fast speeds the ejection forces increase so a lubricant may be needed also if this were to be used within a formulation.
Maltitol has a very poor crushing strength at fast speeds compared to all the other samples so this may not be as useful within a formulation.
Xylitol may also not be as useful at providing strength to a formulation as there are two other polyols that are better at providing strength and xylitol exhibits a high ejection force when fast speeds are simulated like that experienced within production.
Sorbitol and mannitol appear to be the best performing polyols in terms of crushing strengths and ejection forces based on Heckel testing with mannitol more useful with plastic APIs.

References

1. R.W. Heckel. Trans. Metall. Soc. AIME 221 (1961)1001-1008
2. R.J. Roberts and R.C. Roe, Chem. Eng. Sci. 42(1987) p903