Physico-mechanical Characterization of POLYOX™ for Tablet Manufacture

INTRODUCTION

Polyethylene oxide (PEO) polymers available commercially under the trade name of POLYOX™, water soluble resins (WSR), are novel materials with unique properties. They have found a number of uses in pharmaceutical applications. PEO can be used in extended release (ER) matrices[1, 2], osmotic pumps, in mucosal bio-adhesives, in melt extrusion and in gastro-retentive dosage forms.

POLYOX™ polymers are free flowing white crystalline powders with an average particle size of around 150 μm. They are nonionic, highly swelling, thermoplastic and soluble in water and selected organic solvents.

The purpose of this work was to characterize the physical and mechanical properties of POLYOX™ in relation to the tablet manufacturing processes, for extended release (ER) matrix applications.

MATERIALS AND METHODS

Materials

Table 1 shows the grades of POLYOX™ materials used in this study.

Table 1. POLYOX™ materials tested in the study

POLYOX materials used in the study	Approximate molecular weight	Viscosity range at 25ºC (cP)		
		5% solution	2% solution	1% solution
WSR-1105	900,000	8,800 – 17,600		
WSR N-60K	2,000,000		2,000 – 4,000	
WSR-301	4,000,000			1,650 – 5,500
WSR-303	7,000,000			7,500 – 10,000

Moisture Content

Moisture content of the POLYOX™ samples was determined by using a loss on drying (LOD) method in an oven (Heraeus, UK) at 105ºC. The test was conducted on 1 g samples. The samples were re-weighed after drying in the oven for 60 minutes.

Particle Appearance

Appearance of powder particles was assessed with the aid of a stereomicroscope (S8 APO, Leica Microsystems Ltd, UK). Photomicrographs of the samples were taken using a digital camera (DFC420, Leica Microsystems Ltd, UK) at x40 magnification.

Powder Flow

Flow properties of POLYOX™ powders were determined by calculating the Carr's index [3, 4], as shown below, Equation 1. A tap density tester (Sotax, UK) was used to measure the bulk volume (V_0) and the final tapped volume (V_f) of a 100 g sample for all tested materials. The Carr's index, or the % compressibility of a powder due to tapping, can give some indication of material flow properties.

Equation 1: $$\text{Compressibility Index} = \frac{(V_0 - V_f)}{V_0} \times 100$$

In addition, powder flow was assessed during rotary tablet manufacture (see below) by measuring weight variation of the produced compacts.

Compact Manufacturing and Testing

POLYOX™ compacts with a target weight of 350 mg were manufactured using an instrumented 10 station rotary tablet press (Riva, Piccola, Argentina), fitted with 10 mm flat faced tooling and operated at various speeds (20, 30 or 40 rpm) and compression forces (4-24 kN). Upper compression force and ejection force values were recorded.

Tablet weight, diameter, thickness and breaking force values were determined using an automatic tablet tester (Pharmatron AT4, Dr Schleuniger-Pharmatron, Germany) and friability using a friability tester (Copley, UK).

RESULTS AND DISCUSSION

POLYOX™ powders have a low moisture content of less than 0.5% (Figure 1).

Figure 1. POLYOX™ loss on drying (n = 4)

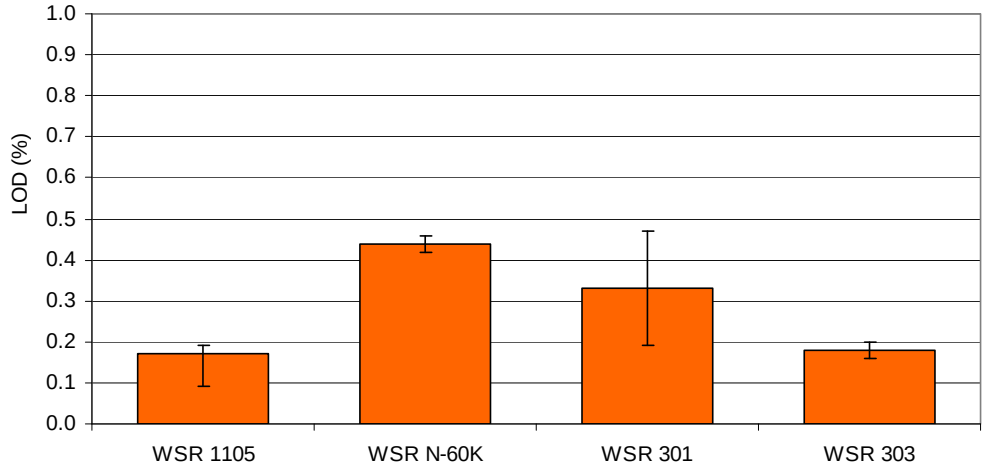


Figure 2 shows a microphotograph of POLYOX™ 1105 powder particles that appear to be spherical and have a wide range of size distribution.

Carr's compressibility index for the tested POLYOX™ powders was 17-21%, indicating good to fair powder flow (Figure 3). This is further supported by the consistent weight uniformity of compacts produced with a weight variation of equal or less than 1.2% at all tablet press speeds used in this study.

Figure 2. Microphotograph of POLYOX™ 1105 powder (x40 magnification)

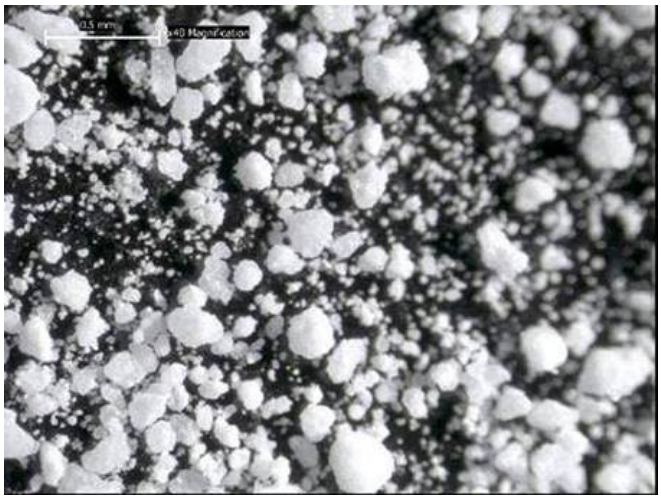
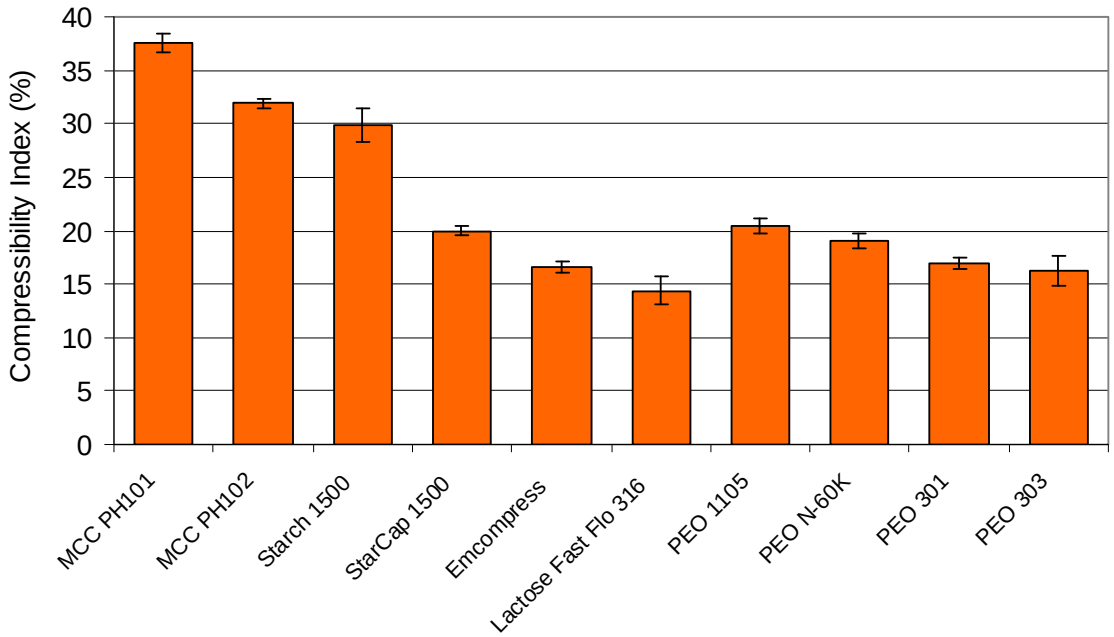


Figure 3. Carr's compressibility index values for POLYOX™ powders and other commonly used tableting excipients



During compression of POLYOX™ powders very low ejection forces were obtained for all tested PEO materials. Figure 4 shows the data for POLYOX™ 1105 compacts only. Similar results were produced for other PEO grades, i.e. N-60K, 301 and 303. This may suggest that POLYOX™ powders are self-lubricating materials and will probably require a reduced amount (i.e. 0.25-0.5% w/w) of lubricants added to the formulations.[5]

Slightly higher ejection force values were produced at a very low compression force of 4 kN. This can be explained by the fact that thickness of the compacts produced at 4 kN was significantly higher compared to the compacts manufactured at 8-24 kN (Figure 5). Due to this, higher side wall friction during tablet ejection resulted in higher ejection force values.

Figure 4. Ejection force values for POLYOX™ 1105 compacts

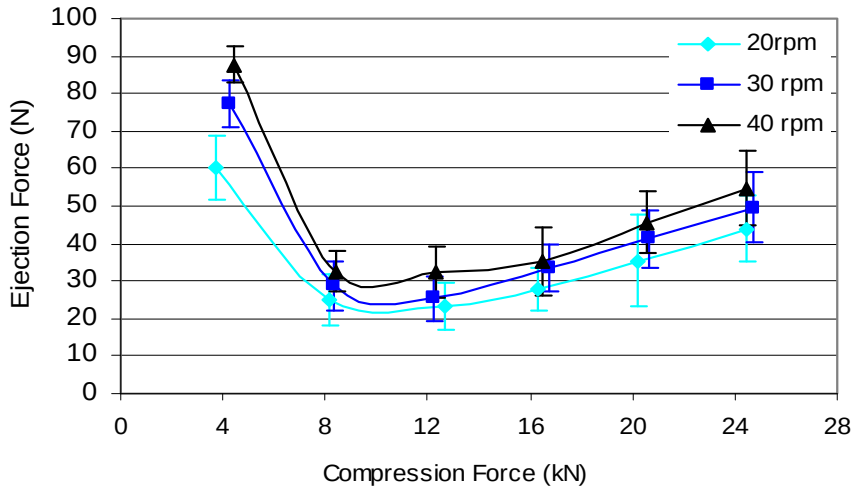


Figure 5. Thickness of POLYOX™ 1105 compacts (n = 20)

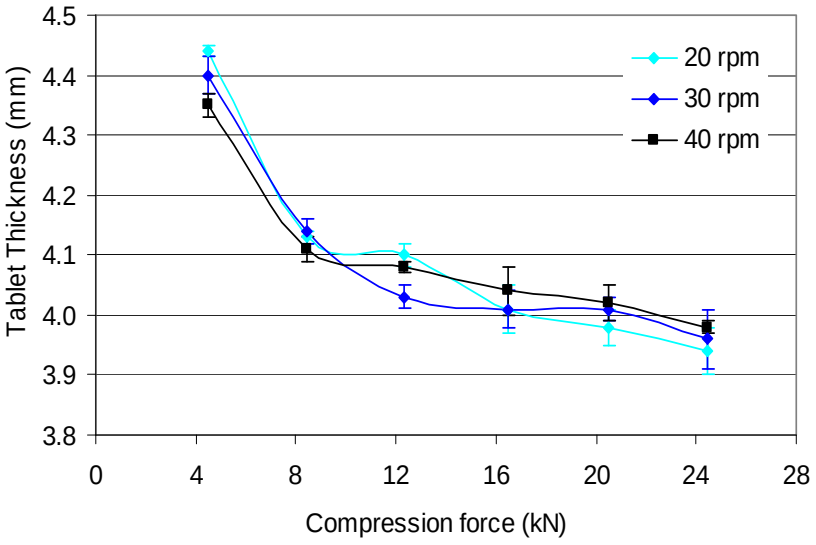


Figure 6 shows that tablets with high breaking force values (up to 22-24 kp) were produced for all tested POLYOX™ samples. It was also noticed that during the test, tablets deformed without fragmentation (Figure 7) indicating that the material deforms plastically.

It was also found that with an increase in tablet press speed compact mechanical strength was not reduced significantly (Figure 8), probably due to a relatively low elastic recovery. Similar results were produced for N-60K, 301 and 303.

Compact friability values for POLYOX™ 1105 (Figure 9) and other tested grades were less than 0.2% and largely independent of compression force and tableting speed used.

Figure 6. Breaking force values for POLYOX™ compacts (n = 20)

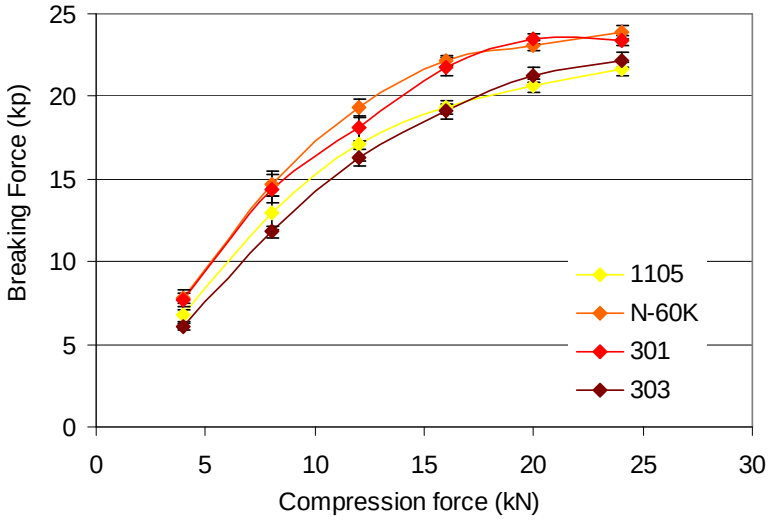


Figure 7. Pictures of compacts after breaking force testing (a) POLYOX™ 1105 (b) POLYOX™ 301 (c) POLYOX™ 303

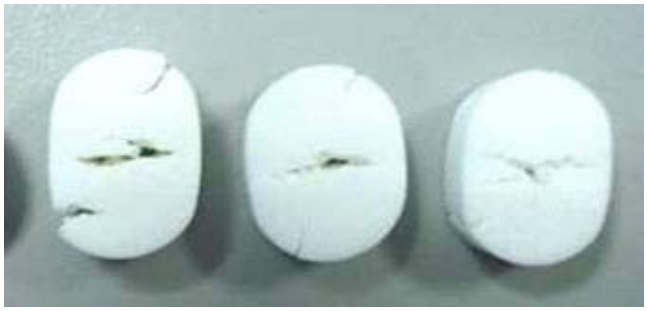


Figure 8. Effect of tablet press speed on PEO 1105 compact breaking force

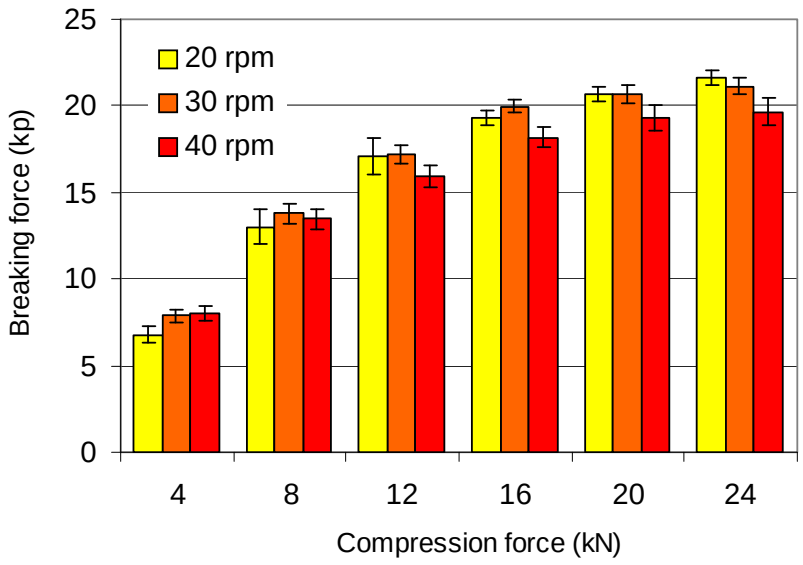
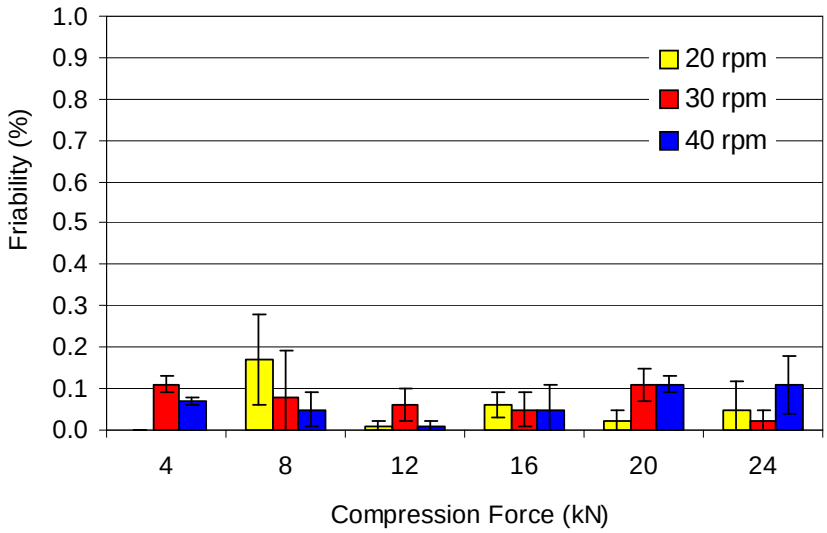


Figure 9. Friability of PEO 1105 compacts



CONCLUSIONS

- POLYOX™ powders are comprised of spherical particles with a low moisture content of less than 0.5%.
- Carr's compressibility index for the tested POLYOX™ powders was 17-21%, indicating good to fair powder flow. This resulted in consistent compact weight uniformity with weight variation of 1.2% or less at all tablet press speeds used.

- Very low ejection forces (less than 100 N) were obtained when producing POLYOX™ compacts. A typical PEO ER matrix formulation will probably require approximately 0.5% w/w of magnesium stearate.[5]
- Tablets with high breaking force values (up to 22-24 kp) were produced for all tested POLYOX™ samples independent of tablet press speed, due to highly plastic nature of POLYOX™ and a relatively low elastic recovery.
- Friability values for POLYOX™ compacts were less than 0.2% and largely independent of compression force and tableting speed.

The flowability, compactibility and lubricity provide POLYOX™ with desirable properties to be utilized in direct compression applications, specifically for its use in hydrophilic ER matrix tablets.

REFERENCES

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