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Non-destructive assessment of mechanical properties of microcrystalline cellulose compacts

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ABSTRACT

In the present study the mechanical properties of microcrystalline cellulose compacts compressed were studied. The resistance to crushing was tested using diametral compression testing and apparent Young's modulus was determined using consecutive uniaxial compression of the full cross-sectional area of single tablets. As non-elastic deformation during the first compression cycle and reverse plasticity were discovered, the loading phase of the second compression cycle was used to determine Young's modulus. The relative standard deviation of 10 consecutive measurements was 3.6%. The results indicate a direct correlation between crushing strength and Young's modulus, which found further support when comparing surface roughness data and radial recovery of the tablets to Young's modulus. The extrapolated elastic modulus at zero-porosity was found to be 1.80 ± 0.08 GPa, which is slightly lower than previously reported values, confirming the complexity of measuring the elastic properties of microcrystalline cellulose compacts. The method can be used for non-destructive assessment of mechanical properties of powder compacts for example during storage studies.

1. Introduction

According to the European pharmacopoeia, sufficient mechanical strength of tablets should be ensured e.g., by testing the resistance to crushing (European Pharmacopoeia, 2014, 8th ed.). As explained in a thorough review by Podczeck (2012), when diametral compression is applied on a tablet during crushing strength measurements, the tablet is subjected to three kinds of stress: shear, compressive and tensile stress. Ideally, when the tensile forces increase, the tablet undergoes elastic deformation until failure along the diameter of the tablet. It has been shown, however, that the deformation before failure is not fully elastic (Edge et al., 2000). The simplicity of crushing strength and tensile strength measurements have been criticized by e.g., Podczeck (2012), showing there is a need for more extensive knowledge on testing mechanical properties of tablets.

The elasticity of materials in general has traditionally been described using Young's modulus. Young's modulus has also been used to measure the elasticity of pharmaceutical compacts as reviewed by Jain (1999) and Podczeck (2012). Microcrystalline cellulose is a widely used plastically compressing tablet diluent and has been extensively studied (Thoorens et al., 2014), and there are several reports available describing Young's modulus of microcrystalline cellulose (Table 1). In addition to the most commonly used 3- and 4-point-bending methods there are several other methods that have been employed in assessing the elasticity of pharmaceutically relevant materials, such as uniaxial compression, indentation testing, acoustic and photoacoustic methods and AFM. Compact solid fraction and tensile strength have been found to increase with increasing compression forces, and tensile strength at zero-porosity has been suggested as a measure of the strength of materials (Adolfsson and Nyström 1996). Young's modulus at zero-porosity also has been reported as a measure of the hardness of the tablet (Roberts and Rowe 1991). Wu et al. (2005) were able to predict the tensile strength at zero porosity of binary tablets, demonstrating that this could be used as a tool in pharmaceutical formulation.

The mechanical properties of tablets change during storage due to physicochemical changes in the materials or structure arising from exposure to various storage conditions (e.g., Suihko et al., 2001; Edge et al., 2000; Kiekens et al., 2000). Tablets undergoing solid-state changes during storage show differences in e.g., strength, dimensions, porosity or moisture absorption over time (Suihko et al., 2001; Picker, 2001). Given the known inaccuracies in crushing strength testing, there is a clear need for an accurate and

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Table 1
Examples of Young's moduli at zero porosity (E_0) of microcrystalline cellulose.

Technique	Reference	MCC	Details	RH (%)	n	Method	E_0
4-point	Bassam et al. (1988)	Avicel PH102	100 × 10 mm beams	45 ± 5	10	Spriggs	8.17
		Avicel PH101					9.01
		Avicel PH105					10.21
		Emcocel 90M					9.35
		Emcocel					9.00
		Unimac MG200					7.98
		Unimac MG100					8.83
		Avicel PH101		75			5.54
4-point	Bassam et al. (1990)	Avicel PH102	100 × 10 × h mm beams	40 ± 5		Spinner	8.67
		Avicel PH101					9.19
		Avicel PH105					9.43
		Emcocel 90M					8.87
		Emcocel					7.13
		Unimac MG200					7.34
		Unimac MG100					8.03
4-point	Mashadi and Newton (1987)	Avicel PH101	100 × 10 × h mm beams	N/A	7	Spriggs	10.3
4-point	Raatikainen et al. (1997)	Avicel PH101	60 × 6 × 2 mm beams	45	8	Spriggs	4.88–9.58
3-point	Gupta et al. (2005)	Avicel PH200	40 × 15 mm × h	15–75		Spriggs	2–6
3-point	Hancock et al. (2000)	Avicel PH101	8 × 4.5 × h mm, un-notched beams	0	15	Spriggs	9.2
				22	15		9.0
				53	15		6.5
				75	15		5.1
			8 × 4.5 × h mm, notched beams	0	15		5.7
				22	15		5.1
				53	15		4.2
				75	15		3.2
3-point	Raatikainen et al. (1997)	Avicel PH101	60 × 6 × 2 mm beams	45	8	Spriggs	5.70–7.93
Cantilever	Raatikainen et al. (1997)	Avicel PH101	60 × 6 × 2 mm beams	45	8	Spriggs	7.21–7.27
Photoacoustic	Ketolainen et al. (1995)	Avicel PH102	Tablet, width 13 mm, 1–8 Hz	N/A	8	Spriggs	7.09
Uniaxial, small area	Holman and Leuenberger (1988)	Avicel PH102	Tablet, Brinell's testing machine	40 ± 10	8	Spriggs	1.924
Uniaxial	Kachrimanis and Malamataris (2004)	Avicel 101	Single tablets (d = 13 mm)	N/A	5	Phani–Niyogi	4.4–5.5
			(d = 10 mm)				6.3–8.4
			(d = 5 mm)				2.9–3.1
			(d = 13 mm)			Spriggs	5.3–6.9
			(d = 10 mm)				7.8–12.9
			(d = 5 mm)				3.0–3.3
			Superimposed tablets (d = 13 mm)		5	Phani–Niyogi	2.6–3.5
			(d = 10 mm)				2.8–4.1
			(d = 5 mm)				2.5–2.9
			(d = 13 mm)			Spriggs	2.9–4.3
			(d = 10 mm)				2.9–6.5
			(d = 5 mm)				3.1–3.4

reproducible method for testing mechanical properties of tablets. Non-destructive testing of mechanical properties as a function of time could reveal changes in internal structure possibly affecting product performance (Williams et al., 2004; Picker, 2001; Kiekens et al., 2000). Consequently, the aim of the present study was to investigate the relation between crushing strength and Young's modulus of microcrystalline cellulose compacts in order to clarify whether Young's modulus could be used as a non-destructive method to estimate mechanical strength of tablets.

2. Materials and methods

2.1. Materials

In the present study the mechanical properties of microcrystalline cellulose (MCC; Emcocel LP200, JP JRS Pharma GmbH & Co. KG, Germany) compacts were studied. The particle size of MCC was $d_{10} = 74 \pm 4$ μm, $d_{50} = 211 \pm 9$ μm and $d_{90} = 376 \pm 11$ μm (mean ± SD; $n = 3$) as measured with a SympaTec HELOS/KF laser diffractometer (SympaTec GmbH, Germany). The true density of microcrystalline cellulose was 1.59 g/cm^3 as measured with a Multivolume helium pycnometer 1305 130/50000/10 (Micrometrics, USA) from a 3.22 g sample. The measurements were repeated until no considerable change in density could be detected, upon which three consecutive measurements were made and the results were averaged.

2.2. Tablet compaction

The powder was stored in controlled conditions of 50% RH and 25 °C for a minimum of 14 days prior to compaction. The moisture content of the acclimatized powder was measured by heating in an oven at a temperature of 170 °C, and the loss on drying was measured by weighing the samples ($n = 4$) with 30 min intervals