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Compactibility characterization of granular pectin for tableting operation using a compaction simulator[1]

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Abstract

Pectin has great potential as a tableting excipient and drug carrier to the colon. It is a non-toxic, soluble polysaccharide which passes through the stomach and small intestine with limited digestion, but is totally metabolized by the colonic microflora. In the past, drug–pectin matrices coated with pH-dependent polymers have been investigated for possible drug delivery to the colon. Although many scientists have used pectin, its feasibility in terms of tablet manufacturability with a high-speed machine has never been evaluated. In this report compactibility of different pectin types (low and high methoxylated) for large-scale tableting operation have been evaluated. The compactibility behavior of granular pectins were studied by a compaction simulator. It was found that pectin on its own does not produce tablets of acceptable quality even at a punch velocity as low as 20 rpm (e.g. low tensile strengths, capping and lamination irrespective of applied compression force). Heckel plots were constructed and changes in porosity at different compaction pressures and punch velocities were determined. Yield pressures for the pectin at a maximum punch velocity of 50 and 250 mm/s were 200 and 213 MPa, respectively. Such close values indicate that this material primarily consolidates by fragmentation with little plastic deformation. This was further evidenced from a low strain rate sensitivity value (SRS = 6.1%) for high methoxylated pectin. The high apparent porosity of 13.8% at 160 MPa shows significant resistance to densification, and compacts underwent substantial elastic recovery (18–25%) during decompression and ejection. These findings suggest that pectin is hard, rigid and poorly compactible. To improve tabletability of pectin, a 50/50 binary mixture with microcrystalline cellulose was evaluated and excellent compacts were produced at all compaction rates and pressures. It is concluded that frequent structural failures observed in both pectin types are due to lack of plastic deformation, poor compactibility and high elastic recovery. © 1998 Elsevier Science B.V.

Keywords: Pectin; Compactibility; Compaction simulator; Drug delivery; Consolidation mechanism; Tableting; Punch velocity; Strain rate sensitivity; Plastic deformation

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[1] This work is dedicated to Professor Dr W.A. Ritschel, one of the pioneers in the area of Industrial Pharmacy, Biopharmaceutics and Pharmacokinetics, on the occasion of his retirement.

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1. Introduction

It is known that, apart from various pH-sensitive synthetic polymers and prodrugs which have been used (Hardy et al., 1987) for colonic delivery of drugs, the major substrates for bacterial growth in the human large intestine are polysaccharides (i.e. pectin, starches), proteins that escape digestion, azo aromatic molecules, exfoliated cells, mucins and other carbohydrate moieties. These macromolecules are broken down to smaller subunits by a variety of hydrolytic enzymes. Thus, drug targeting to the colon is investigated as a potential route (Friend, 1991) for drug delivery by employing pectin as a drug carrier.

Pectin is non-toxic and almost totally metabolized by colonic bacteria, is present in fruits and vegetables, and consists of D-galacturonic acid and its methyl ester linked via (1–4) glycosidic linkages. It is commercially available and is marketed as low-methoxylated (degree of methoxylation 30–37%) and high-methoxylated (degree of methoxylation 65–72%) pectin. Various published work suggests that pectin as an excipient and a drug carrier to the colon may be of value (Hardy et al., 1985; Rubinstein et al., 1990; Ashford et al., 1993; Cook et al., 1993; Kim and Fassihi, 1996). Investigations to assess behavior of pectin tablets and matrix-type tablets under conditions mimicking mouth-to-colon transit (Coupe et al., 1991; Ashford et al., 1994) suggest that both high and low methoxylated pectin formulations can optimally protect a drug with a high susceptibility to enzymatic attack during its transit to the colon (Hardy et al., 1985). It is also shown that drug-containing pectin matrices rapidly break down (degrade) in the presence of pectinolytic enzyme (Kim and Fassihi, 1996) in the dissolution media. Furthermore, as an excipient, viscosity modifier and gelling agent, pectin has been used in the development of controlled release drug delivery design when blended and tabletted together with other polymers in a binary or ternary polymeric matrix system (Kim and Fassihi, 1997a,b,c).

In general, an ideal excipient for tableting should be free flowing, inert, non-toxic, inexpensive, chemically compatible with drugs, compressible, and have good bonding/consolidation properties. These characteristics are rarely embodied in a single excipient, and in practice a combination of both brittle and plastic materials at predetermined ratios offers advantages over a single material (Fassihi et al., 1994, 1995). Furthermore, it is presently not possible to predict the type and amounts of desired excipients from the knowledge of the compaction properties of the active or individual excipient(s) during the formulation development. Nevertheless, useful conclusions based on the compaction behavior can be drawn when relevant parameters, such as porosity changes with increasing pressure, Heckel plots, strain–rate sensitivity values, force–displacement curves and percent elastic-recovery of tablets are taken into consideration (Humbert-Droz et al., 1983; Ragnarsson and Sjogren, 1985; Roberts and Rowe, 1985, 1986; Yang et al., 1996).

The objectives of the present study were: (i) to characterize the physicochemical and physicomechanical properties of pectin granules/powder; (ii) to investigate compressibility/compactibility of pectin by itself and in combination with plastically deforming microcrystalline cellulose using a compaction simulator under tableting conditions used in production as opposed to compression on a Carver press; and (iii) to investigate the influence of punch velocity on compaction behavior and determine the strain rate sensitivity of pectin.

2. Experimental

2.1. Materials

Pectin Type 170 (designated as low methoxyl pectin with a degree of methoxylation (DM) of 30–37%) and Pectin Type 621 (designated as high methoxyl pectin with a DM of 65–72%), obtained from Pectagel Co. (Great Neck, NY, USA) were used for compaction studies. Microcrystalline cellulose NF (Avicel PH-101, FMC Co., Philadelphia, PA, USA) and magnesium stearate (Amend Drug & Chemical Co., Irvington, NJ, USA) were used as received.

2.2. Methods

2.2.1. Bulk powder characterization

Pectin samples with different degrees of methoxylation were characterized by a Micromeritics Gemini surface area tester (Model 2360, Micrometrics, Norcross, GA, USA) and a Micromeritics mercury porosimeter (Model 9320). The true density of each pectin powder was determined using a Micromeritics Helium AccuPyc 1330 autopycnometer. The moisture content of pectins was determined using Karl Fisher titration (Mettler DL 18 titrator). Standard US sieves and a laboratory sieve vibrator (Derrick MFG. Co., Buffalo, NY, USA) were used for determining particle size distribution of pectin samples. The powder properties of bulk pectin samples including numerically evaluated flowability and floodability indices are listed in Table 1.

2.2.2. Compaction simulator data acquisition and treatment

Compaction Profiling was carried out on a Mand Compaction Simulator (Abacus Industries Ltd., formerly Mand Testing Machines Ltd, Stourbridge, UK), equipped with a Nicolet Model 440 Oscilloscope, and a personal computer. The compaction cycle used to drive the simulator was that of a Manesty Betapress, i.e. double-ended compression (both punches moving) operated over a range of velocities. Typically, tablet production at 20 rpm is equivalent to a maximum punch tip velocity of about 50 mm/s with a dwell time comparable to that of rotary presses, such as a Stokes B2, and a speed of 100 rpm (i.e. punch velocity of 250 mm/s) is equivalent to a dwell time on a typical production press if the punch head flatness is considered. The required time–displacement profiles for the upper and lower punches were calculated according to the Rippie and Danielson equation (Rippie and Danielson, 1981):

$$Z = [(r_1 + r_2)^2 - (r_3 \sin \omega t - x_2)^2]^{1/2} \quad (1)$$

where Z is the vertical displacement of the punch (upper or lower) at time t; r_1, r_2, r_3, and x_2 are mechanical constants of the tablet press, while ω is the turret angular velocity. This equation, and hence the waveforms, do not take into consideration the punch head flatness. These waveforms were used to characterize and interpret behavior of pectin types as well as their 50/50 (w/w) pectin/microcrystalline cellulose blends. The latter blends were prepared in V-mixer for 10 min with pectin and microcrystalline cellulose and lubricated with 1.0% (w/w) magnesium stearate for another 5 min. Pure pectin samples failed to form intact tablets due to poor compactibility. Hence, waveforms with increased dwell times (flatness considered) were also used for compaction profiling of pure pectin type.

Compacts were prepared using a constant volume of pectin powder in the die equivalent to 0.225 cm^3 (compact weight = true density × 225 mg). A 1-cm die and flat-faced round tooling were used. Seven compacts of different pectin samples and their blends were compressed to obtain a residual porosity in the range of 2–20% at each compaction speed. Thickness, weight and hardness (Tablet Hardness Analyzer VK 2000, Vankel Corp.) of tablets were measured immediately after ejection unless otherwise indicated. The data (loads on and displacements of upper and lower punches as a function of time) from three representative compaction cycles at each test conditions were subsequently down-loaded from the Nicolet Oscilloscope to the PC and converted into Microsoft Excel (version 5.0) for further manipulation. Tensile strengths of tablets were calculated according to the method of Fell and Newton (1970, 1971).

2.2.3. Analysis of compaction data

Many techniques and compaction equations have been used to characterize the consolidation behavior of pharmaceutical solids (Bateman et al., 1989; Celik and Marshall, 1989; Marshall and York, 1993). However, due to the complexity of the compressional process, many of the expressions have been shown to have limitations. A simple and most widely used approach is analysis of Heckel plots which can be constructed according to Heckel equation (Heckel, 1961a,b):

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

where D is the ratio of the density of the powder mass at pressure P to the true density of the powder mixture (i.e. relative density). The reduction in porosity or the resistance to volume reduction is reflected by the slope (K) of the profile and A is a constant. The yield pressure, P_y, is usually calculated as the reciprocal of the linear portion slope 'K' of the Heckel plot.

Although the Heckel equation has limitations, it has been successfully and widely used by many authors to differentiate between compression by brittle fracture and plastic deformation (Hersey and Rees, 1970; Yang et al., 1996).

3. Results and discussion

3.1. Powder characteristics

Powder flowability and compactibility are the most important parameters that the formulation scientist takes into consideration when developing a solid dosage form. In the commercial production of solid dosage forms using high-speed machines, uniform and continuous powder flow is essential in order to minimize production losses due to wide variations in tablet weight (Fassihi and Kanfer, 1986). Some of the variables that can influence powder flow include powder cohesiveness, particle size and size distribution. According to Carr (1965), powder flowability could be best assessed by four parameters: angle of repose, angle of spatula, compressibility and cohesiveness. Table 1 outlines all powder characteristics as determined. Although the above-mentioned four parameters tend to be within acceptable range, the uniformity of powder flow and the degree of flowability were poor for both high- and low-methoxylated pectin (see Table 1). Other properties were very similar for both pectins.

3.2. Force–time profiles for normal and prolonged dwell times

A typical upper punch force profile during a compression cycle at a compaction speed of 20 rpm for both pectins under normal and prolonged dwell times are shown in Fig. 1. As can be seen, the force–time peak under normal dwell time conditions is not symmetrical for both pectin types (i.e., slightly skewed). For example, the calculated area under the curve for the compression and decompression phases for high- and low-methoxylated pectins (Fig. 1a and c) are $AUC_{comp} = 312.5$ and 298.1 kN·s and $AUC_{decomp} = 192.8$ and 201.1 kN·s, respectively. The accuracy of AUC values and interpretation of complex events that occur during decompression phase are highly questionable, however, the determination of degree and intensity of symmetry between the phases of compression and decompression may be of value. It is reported that for a fully elastic body (steel ball) the force–time profile is symmetrical (Dwivedi et al., 1991). Synonymous behavior has been observed for plastically deforming (i.e. Avicel PH 101, PH 102, and

Table 1
Powder and micromeritic properties of bulk Pectin samples

Pectin	High-methoxylated	Low-methoxylated
Degree of methoxylation (%)	67–72	30–37
Angle of repose (°)	38.8	36.9
Angle of fall (°)	30.6	25.1
Angle of difference (°)	8.2	11.8
Aerated bulk density (g/mm^3)	0.64	0.66
Packed density (g/mm^3)	0.85	0.85
True density (g/mm^3)	1.595	1.592
Compressibility (%)[a]	24.4	22.8
Cohesiveness (%)	46.3	43.6
Angle of spatula (°)	56.1	57.9
Dispersibility (%)	6.5	10.3
Degree of floodability	Tends to flush	Fairly high
Floodability index	55	66
Flowability index	57	57
Degree of flowability	Not good	Not good
Mean particle size (μm)	175	180
Porosity (%)	50.2	47.7
Surface area (m^2/g)	0.400	0.345

Note: no single type of measurement adequately assesses the powder properties. In order to use these values as a rough guide the technique developed by Carr (1965) should be consulted.

[a] Values in the range of 21–25 are considered as passable.

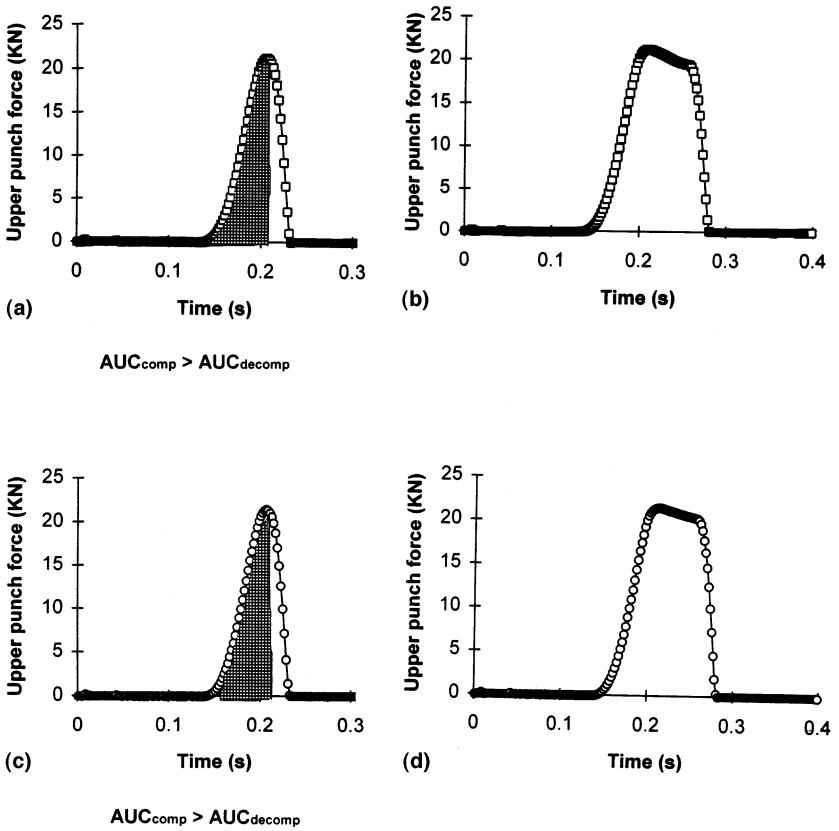

Fig. 1. Representation of upper punch force versus time for high-methoxylated (□) and low-methoxylated (○) pectin samples at 20 rpm, generated under normal (a,c) and prolonged (b,d) dwell times.

Klucel) and brittle (i.e. Emcompress and lactose) materials in relation to 'peak offset time' or 'punch stress maxima' (Dwivedi et al., 1991; Morhead and Rippie, 1990). These reports indicate that the duration of 'peak offset time' or 'punch stress maxima' is longer for materials that consolidate by plastic flow, while short values are characteristic of brittle fracture behavior. The latter materials do not show intense symmetrical pressure–time profiles at the point where the derivative of pressure with respect to time is zero, while under similar conditions viscoelastic substances show apparent asymmetrical pressure–time profiles (Dwivedi et al., 1991, 1992). Thus, Fig. 1a and c may indicate that pectin is rigid and brittle. When a prolonged dwell time is used (Fig. 1b and d) significant reduction in peak upper punch force is apparent (declining slopes during dwell time). This phenomena is likely to be associated with internal stress relaxation (i.e. changes in the magnitude of the stress distribution within the compact), and reduction in porosity.

3.3. Compactibility characteristics

The compaction cycle includes powder compression, reduction in volume of the material leading to lower residual porosities, consolidation and bonding with the formation of a coherent tablet, decompression and ejection of the tablet from the die. It is believed that consolidation of powdered material in a die takes place by one of the two known mechanisms, fragmentation and plastic deformation, or both. In general, the dynamics of the process of compact formation and compactibility depend on both the physicochemi-

cal properties of the material and the tableting conditions. Consolidation is also affected by particle characteristics (i.e. amorphous or crystalline), size and size distribution, ability to bond following deformation, moisture content and elastic recovery during decompression, resulting in bond breakage. Typically most amorphous materials tend to exhibit varying degrees of viscoelasticity, while elasticity and brittleness is often associated with crystalline substances. However, pharmaceutical solids rarely exist as 100% crystalline or 100% amorphous phases (Hancock and Zografi, 1997). The profiles of residual porosity examinations at different thicknesses are shown in Fig. 2. The initial reduction in porosity is very high as compression force increases. However, at higher applied forces the resistance against further densification is dramatically increased and, consequently, further volume reduction as reflected by the percent reduction in porosity requires significantly higher applied pressures. For example, in order to achieve porosity of 12% a pressure of 200 MPa is required, while for further reduction in porosity to approximately 8% a pressure of 400 MPa is necessary. Obviously pectin's resistance to compression (see Fig. 2) is extremely high, indicating that this might result in the structural failures during the postcompression cycle (decompression and ejection) as observed (i.e. tablets produced under these conditions laminated upon ejection). Since most pharmaceutical solids are viscoelastic in nature and undergo consolidation by a combination of mechanisms (i.e. brittle fracture and plastic deformation), it is essential to ensure that the newly formed compacts will remain bonded during the postcompression phase. In the tableting operation, the expression 'compression force' describes the force–time profile of a compression event, and compression and decompression strokes of the upper punch usually follow a sine wave function. As discussed earlier, the contact time of about 100 ms corresponds to that of a Betapress or equivalent tableting machine, operating at a compaction speed of approximately 20 rpm. In the case of high-methoxylated pectin at or below of 20 rpm, no compact failure occurred during decompression and tablet ejection, possibly due to the slow rate of compaction, more uniform distribution of forces, internal viscoelastic relaxation in the die and, consequently, fewer bonds being broken. On the contrary, low-methoxylated pectin failed to produce tablets of appreciable strength even at this lowest rate of compaction (i.e. 20 rpm). In addition, lamination and capping were evident and became more pronounced for all pectin types as the compaction speed was increased (i.e. >20 rpm). These findings indicate that all pectin types are hard, rigid and poorly compactible and undergo extensive elastic recovery during decompression and ejection, as will be discussed in a later section. Hence, to produce coherent tablets of acceptable quality, pectins need to be blended with a plastically deforming, highly compactible excipient in order to improve their tabletability.

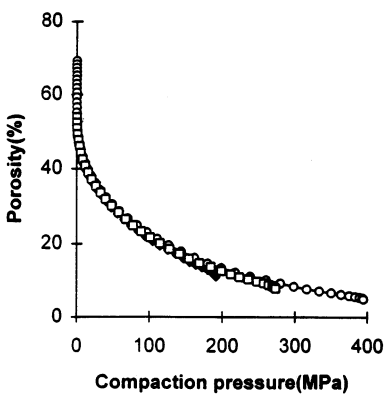

Fig. 2. Residual porosity of high-methoxylated pectin sample versus mean compaction pressure for different thicknesses: 2.6 (○), 2.8 (□) and 3.0 (◆). Tablets were produced at 20 rpm ($n=3$).

3.4. Force–displacement (F–D) analysis

It is apparent that materials which form strong interparticulate bonds show greater resistance to the compression process. However, the ability to flow under conditions of compaction and relief of internal stresses will eventually contribute to the physical strength of the tablet. Thus, measurement of the total energy transferred by the punches and absorbed by the material may reflect the nature of particle behavior, elasticity, viscoelastic flow, brittle fracture and breaking of

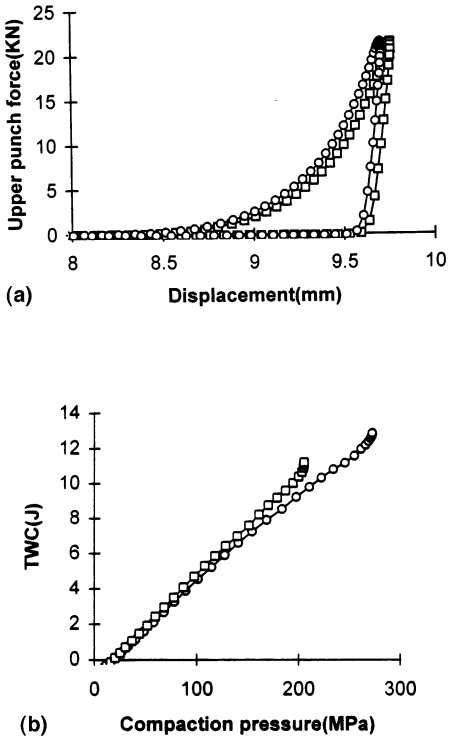

Fig. 3. A typical F–D profiles (a) and total work as a function of increasing compaction pressure (b) for high-methoxylated (□) and low-methoxylated (○) pectin samples at 20 rpm and a thickness of 3.0 mm.

bonds in the material. This can be calculated directly using the integral equation:

$$\mathrm{TWC} = \int_{D_o}^{D_{\max}} F \cdot \mathrm{d}D \tag{3}$$

where TWC is the total work of compaction involved and the entire force (F)–displacement (D) plot and area under the curve can be determined. Although this approach oversimplifies the true picture of the stress/strain relationship during consolidation, its utility for overall comparison of total energy consumption under a standardized rate of compression conditions will be valuable. Fig. 3a shows a typical F–D profile obtained under standardized conditions (i.e. constant force–time compression cycle) by plotting the upper punch force versus its displacement for two pectin types. The area under the F–D curves has been used by many researchers to estimate the total energy consumption during tableting (DeBlaey and Polderman, 1971; Ragnarsson and Sjogren, 1985). Total work of compaction (TWC) versus applied pressure is also given in Fig. 3b. It appears, that during compression, high-methoxylated pectin consumes significantly more energy (based on Student's t-test, $p < 0.05$) at equivalent compaction pressure when compared with low-methoxylated pectin. It is suggested that powders with different physicochemical and packing arrangements will absorb varying amounts of energy and that the work of compaction is utilized both for volume reduction and bonding (Krycer et al., 1982; Fell and Newton, 1971). Thus knowledge of total energy consumption by itself may not necessarily be a sensitive criterion of tablet strength and consolidation behavior. The data in Fig. 3 seems to indicate that in the comparative analysis of pectins more coherent and stronger tablets were produced from high-methoxylated pectin where higher total work was involved. In addition, in this study powder characteristics including particle size and moisture content of both pectins were similar. Furthermore, since the compaction rates and other experimental conditions were identical during this study, it may be assumed that a higher degree of methoxylation results in more coherent and, hence, stronger compacts.

3.5. Heckel analysis and influence of punch velocity on compression behavior of pectin

Fig. 4 presents typical Heckel plots for both low- and high-methoxylated pectins obtained at compaction speed of 20 rpm and a tablet thickness of 3.0 mm. Both profiles follow the same trend with little difference in their densification/consolidation behaviour. Fig. 5a is representative of Heckel profiles for high-methoxylated pectin at compaction speeds of 20 and 100 rpm, keeping the in-die thickness at 3.0 mm. The variation of Heckel plot gradients are significantly different ($p < 0.05$) from each other. This clearly signifies that pectin has some degree of viscoelastic properties. The calculated mean yield values 'P_y' (using the linear portion of the profile from 25 to 125 MPa, $r^2 = 0.9999$ based on linear regression anal-

ysis) at 20 and 100 rpm are 200 and 213 MPa, respectively. These values are relatively large and indicative of great resistance to compression and volume reduction. In general, a low value of P_y (steep slope) reflects low resistance to pressure, good densification and easy compression. A low P_y value, however, may not necessarily reflect that compact has acceptable tensile strength. In the case of pectin the P_y values at both punch velocities are relatively large. This indicates that pectin resists consolidation. The nature of the consolidation mechanism can be best described by the apparent strain rate sensitivity (SRS) value (Roberts and Rowe, 1985). This is calculated by using the equation (Roberts and Rowe, 1985):

$$\text{Apparent SRS} = \frac{P_{y2} - P_{y1}}{P_{y2}} \times 100\% \quad (4)$$

where P_{y1} and P_{y2} are the calculated yield pressures at low and high punch velocities, respectively. The calculated strain rate sensitivity (SRS) for pectin derived from profiles presented in Fig. 5a was 6.1%. A low SRS value suggests that the material consolidation is largely by brittle fracture. The corresponding porosity profiles are given in Fig. 5b. In the original work (Roberts and Rowe, 1985), determinations of SRS values were based on constant punch velocities of 0.033 and 400 mm/s using saw-tooth waveforms, and SRS values for a variety of materials were in the range of 1.8 to 54.1. High values of SRS indicate that material is strain rate sensitive, a property seen with plastically deforming materials, while low SRS values are associated with brittle fracture substances. In contrast to pectin, plastically deforming materials such as PEO (Yang et al., 1996) (MW, 7×10^6, SRS = 18.5%) and Avicel PH 101 value (Roberts and Rowe, 1985) (SRS = 38.9%), exhibit high SRS values.

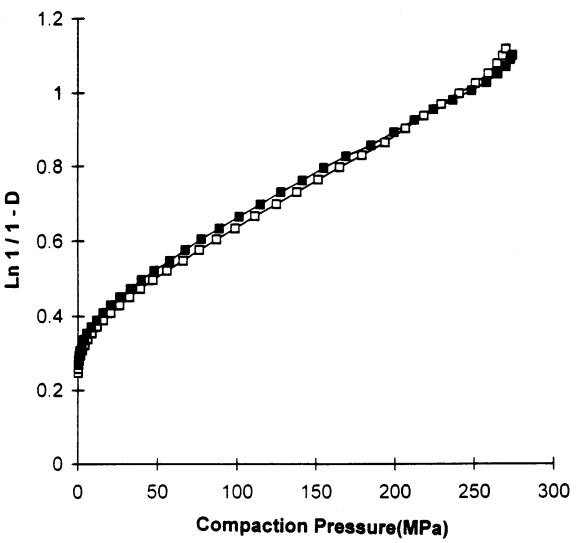

Fig. 4. Heckel plots for high-methoxylated (□) and low-methoxylated (■) pectin samples at 20 rpm and a thickness of 3.0 mm.

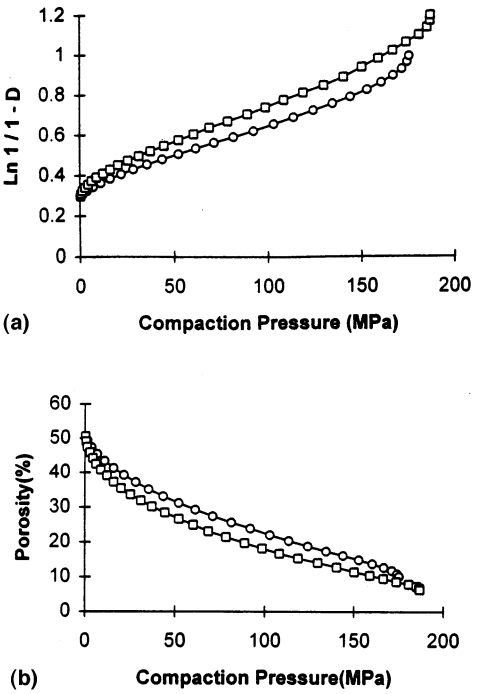

Fig. 5. Heckel plots (a) and porosity changes (b) for high-methoxylated pectin produced at 20 (□) and 100 rpm (○) to a constant thickness of 3.0 mm.

3.6. Apparent axial recovery

In general, excipients and pharmaceutical solids are considered as viscoelastic systems and show significant reversible (representing elastic behavior) or irreversible changes (plastic deformation) when compressed. In this study the percentage of

apparent axial recovery of each ejected compact was calculated according to the following expression (Armstrong and Haines-Nutt, 1972):

$$\text{Apparent axial recovery} = \frac{H - H_{\text{in-die}}}{H_{\text{in-die}}} \times 100\% \quad (5)$$

where $H_{\text{in-die}}$ and H are the minimum thicknesses of the tablet in the die and after ejection.

Calculated apparent elastic recovery profile for high-methoxylated pectin at a compaction speed of 20 rpm is presented in Fig. 6. The nature of plastic flow can be interpreted in terms of viscoelasticity. Hence, the changing thickness of the compact due to elastic recovery during unloading can be used to obtain plastoelasticity. As shown in Fig. 6, pectin compacts underwent a substantial elastic recovery in the range of 18–25% during decompression and ejection. Thus, it is clear that all pectin types are rigid and require very high applied loads for compression. They undergo very little plastic deformation during compression. As discussed earlier they form compacts, largely by brittle fracture mechanism, and undergo substantial elastic recovery during the decompression and ejection phase of the compression cycle, resulting in frequent structural failures, especially at high rates of compaction.

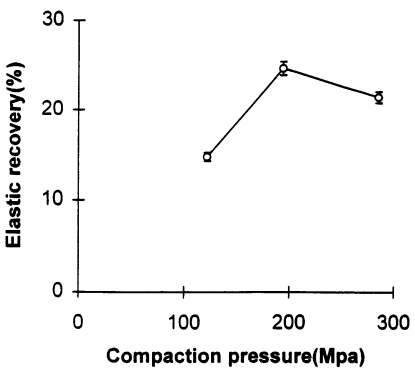

Fig. 6. Relationship between apparent elastic recovery and compaction pressure for high-methoxylated pectin compacts produced at 20 rpm ($n = 3$).

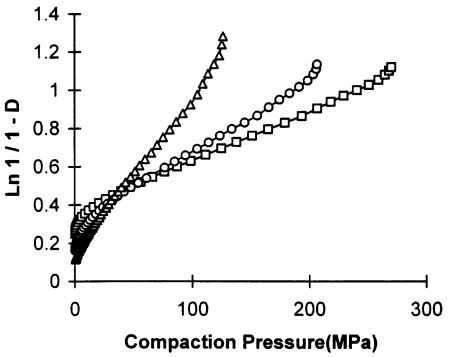

Fig. 7. Heckel plots for high-methoxylated pectin (□), Avicel PH 101 (△) and 50/50 pectin/Avicel blend (○) at a thickness of 3.0 mm and compaction speed of 20 rpm.

3.7. Compactibility profiles of pectin–microcrystalline cellulose blends

Based on the earlier results (see compactibility characteristics and axial recovery sections) and in order to circumvent problems of capping, lamination, and structural failures, pectin types were blended with the plastically deforming, highly compactible microcrystalline cellulose at a level of 50/50. The Heckel plots for the high-methoxylated pectin, microcrystalline cellulose and their 50/50 blend are presented in Fig. 7. Microcrystalline cellulose exhibits a low yield pressure. As expected, the sensitivity of each material in terms of compressibility and consolidation is in the order of Avicel > Avicel/pectin blend > pectin (see Fig. 7). The relationship between porosity reduction and tensile strengths with increasing compaction pressure for the Avicel/pectin blend and high-methoxylated pectin is shown in Fig. 8a and b, respectively. Hard compacts were obtained at all compaction rates and the blends showed high strain rate sensitivity and, hence, the mechanism of consolidation of the 50/50 blend was predominantly plastic deformation. These studies suggest that blending of pectin and plastically deforming materials is the most economical way for pectin tablet production. Further refinements and optimization of the powder mixtures (blends ratio) is obviously necessary and will be determined in future studies.

4. Conclusions

From the evidence provided in this study it may be concluded that pectin, which on its own is a hard, rigid material, does not produce intact compacts when the compaction speed is greater than 20 rpm. The cause of this may be related to a low plastic flow as reflected by small changes in porosity at higher applied pressures, low strain rate sensitivity values, and large axial recovery after ejection. When compressed at very high compaction pressures some increase in tensile strength at a compaction speed of 20 rpm could be achieved in the case of high-methoxylated pectin. To improve tabletability of pectin, binary mixtures of pectin types and microcrystalline cellulose at 50:50 ratio were prepared and these blends, as might have been expected, provided excellent compacts at all punch velocities and compaction pressures. Though pectin by itself exhibited a low strain rate sensitivity (e.g. a brittle material), the 50/50 blends consolidated largely by plastic deformation. The frequent structural failures (lamination and capping) observed in all pectin types could be attributed to lack of plastic deformation, poor compactibility and high elastic recovery. High methoxylation resulted in more coherent, still weak compacts. Examination of compaction profiles presented here may be useful to research scientists who are involved in use of pectin as a drug carrier and can be used as formulation 'finger-prints' and may aid in troubleshooting.

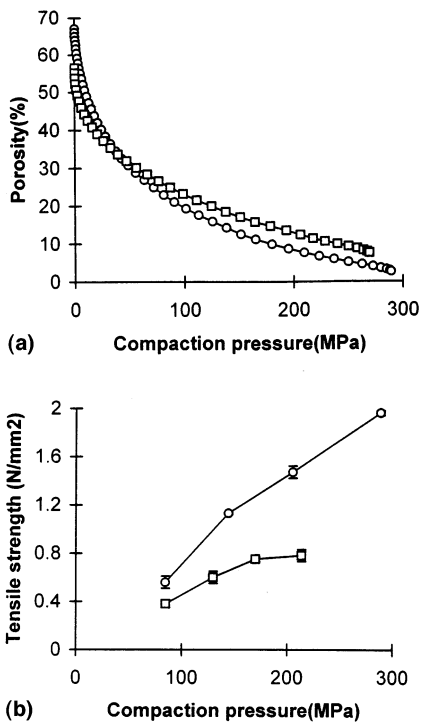

Fig. 8. Relationship between residual porosity (a) and tensile strength (b) for high-methoxylated pectin (□) and pectin/Avicel blend (○) as a function of increasing compaction pressure at 20 rpm.

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