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Research paper

Direct compression properties of chitin and chitosan

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Abstract

Deformation and compaction properties of native amino poly-saccharides chitin and chitosan were studied and compared with those obtained with established pharmaceutical direct compression excipients. An instrumented single-punch tablet machine was used for tablet compaction. The following compression parameters were evaluated: a ratio of crushing strength and compression pressure, plasticity and elasticity factor (PF and EF), tensile strength and *R*-value. Chitin and chitosan was found to have a marked tendency to plastic deformation, and both showed a good compression behaviour compared with other direct compression excipients including microcrystalline cellulose. It is concluded that chitin and chitosan are potential co-excipients for direct compression applications.

Keywords: Chitin; Chitosan; Direct compression; Plastic deformation; Elasticity; Tablets

1. Introduction

Chitin is a polysaccharide composed of β [1–4] linked *N*-acetyl-D-glucosamine unit. It is the most abundant natural amino polymer on earth and the supporting material of crustacean and insects. Chitosan is a partially deacetylated form of chitin, and it has recently received much attention as a new excipient and/or functional material of high potential in pharmaceutical and food industry [1]. Both chitin and chitosan have excellent material (excipient) properties such as biocompatibility, biodegradability, non-toxicity as well as chemical and physical stability. Nowadays, several countries in e.g. Asia, the Caribbean and Scandinavia, produce chitin and chitosan of crustacean origin on a commercial scale.

In the pharmaceutical field, several reports describe the successful use of chitin and chitosan in tablets as disintegrants [2–4] and as direct compression diluents [5–10]. Sawayanagi et al. (1982) reported the fluidity and compressibility of blended powders of lactose, potato starch and mannitol with chitin and chitosan [5,6]. More recently, both Mexican shrimp and Cuban lobster chitins were found excellent direct compression agents, with sound cohesion and disintegration properties [8,10].

To date, very little is known about the consolidation mechanisms (i.e. densification and deformation) and compaction properties of chitin and chitosan as direct compression materials. The fundamental knowledge about the compression and compaction behaviour of pharmaceutical powders is essential for the improvement and control of the quality of the final tablets and for the development of the compaction process. A number of early methods (i.e. research tools) have been introduced and developed for this purpose [11–13] but sometimes their use in characterizing pharmaceutical materials can be questioned. Recently, Antikainen and Yliruusi (2003) developed a new method for the evaluation of the compression behaviour of materials using the information derived from force–displacement curves [14].

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The aim of the present study was to investigate the consolidation (i.e. densification and deformation mechanisms) and compaction properties of native chitin and chitosan of lobster origin, potential novel excipients for direct compression. A new method using the information obtained from the force–displacement curve [14], was applied for the evaluation of the plasticity and elasticity of materials.

2. Materials and methods

The materials studied were native chitin extracted from lobster shell (Cuban Industry, Cuba), chitosan derived from the lobster chitin, microcrystalline cellulose, MCC (Avicel® PH 102, FMC International, Cork, Ireland), dibasic calcium phosphate, DBCP (Emcompress®, E. Mendell, NY, USA) and pregelatinised starch, PGS (Starch Rx® 1500, Colorcon, Indianapolis, USA). The excipients were stored under controlled conditions for at least 48 h (at 21 C and 50% RH) before testing. Magnesium stearate (Ph.Eur.) was used as a lubricant in direct compression.

For compression studies, excipients were weighed out individually and poured into a pre-lubricated die (acetone solution of magnesium stearate 5% w/w). Tablets were manually compressed with an instrumented single-punch tableting machine (Korsch EK-O, Berlin, Germany) using 9-mm punches. The press was operated at a fixed speed of 36 rpm. The tablet height under load was held constant at 3.0 mm. Therefore, the upper punch was adjusted to the lowest position and the lower punch was adjusted using a calibration plate (3.00 mm thick).

The weight and height of each tablet were measured with an analytical balance (Sartorius CP 2245, Raute, Goettingen, Germany) and a digital micrometer (Sony DZ 521, Tokyo, Japan), respectively. The crushing strength of tablets was determined immediately after compression with a tablet hardness tester (Schleuniger 2E, Dr. Schleuniger Pharmatron AG, Solothurn, Switzerland).

The plasticity of the materials under compression was measured by the ratio of two areas (work) obtained from the force–distance curve near the maximum force (Eq. (1)) [14]. The plasticity factor (PF) determines the extent of plastic flow at a certain compression force level and gives a comparable numerical value.

$$\mathrm{PF} = \left(\frac{W1}{W1 + W2}\right) \cdot 100\% \quad (1)$$

W1 and W2 can be calculated from the force–displacement curve according to Antikainen and Yliruusi (2003) [14]. The elasticity factor (EF) was calculated with Eq. (2):

$$\mathrm{EF} = \left(\frac{S_{\max} - S_{\mathrm{od}}}{S_{\max} - S_{\mathrm{o}}}\right) \cdot 100\% \quad (2)$$

where $S_{\max}$ is the maximum upper punch displacement, S_{o} is the displacement of the upper punch when force is first noticed and S_{od} is the displacement of the upper punch in the decompression phase [14].

The pressure dependence of factor PF and EF was investigated between 50 and 250 MPa, which is a common range in tablet compression. The changes of PF as a function of compression pressure were modeled with Eq. (3):

$$\mathrm{PF}(P) = Pl \cdot \mathrm{e}^{v_{\mathrm{p}}P} \quad (3)$$

where Pl is the theoretical maximum of plasticity at zero compression pressure and v_{p} is the rate of plasticity change as a function of compression pressure [14].

For scanning electron microscopy, the chitin tablets were carefully divided using a scalpel and the tablet halves were fixed on double-sided carbon tape and coated with 20 nm platinum with a sputter coater (Agar sputter coater B7340, Agar Scientific Ltd., UK**).** The micrographs were taken with a Zeiss DSM-962 (Carl Zeiss, Oberkochen, Germany) scanning electron microscope.

3. Results and discussion

3.1. Densification and deformation under compression

A recent method introduced by Antikainen and Yliruusi (2003) [14] was used for the evaluation of plasticity and elasticity of the direct compression materials. As seen in Table 1 and Fig. 1, the plasticity factor (PF) decreased exponentially for all materials when the compression pres-

Table 1
Values for plasticity (PF) and elasticity factors (EF) of chitin, chitosan and direct compression reference excipients under different compression pressures (CP)

Material	CP (MPa)	PF (%)	EF (%)	Material	CP (MPa)	PF (%)	EF (%)
MCC	52.8	3.24	1.58	Chitin	52.3	2.30	4.65
	56.0	2.78	1.56		64.6	2.28	4.43
	70.0	3.10	1.64		83.4	1.83	4.61
	98.7	2.21	1.71		97.8	1.58	4.05
	148.9	1.61	1.67		139.4	1.36	4.10
	173.9	1.22	1.69		139.5	1.40	3.76
	186.8	1.09	1.71		176.9	1.23	3.52
	207.0	0.69	1.73		189.4	0.89	3.50
DBCP	50.4	1.06	1.61		228.2	0.75	3.43
	60.4	0.83	1.89	Chitosan	60.5	1.96	4.75
	74.3	0.86	2.36		75.7	1.85	4.19
	85.6	1.09	1.89		94.3	1.69	3.70
	102.9	1.02	2.02		110.3	1.47	3.70
	117.5	0.78	2.26		124.6	1.68	3.61
	120.1	0.69	2.07		139.6	1.09	3.62
	137.0	0.71	2.16		172.2	0.88	3.48
	154.4	0.54	2.23		203.4	0.70	3.41
	176.5	0.54	2.48				
PGS	49.7	1.94	7.45				
	59.8	2.01	6.94				
	70.3	2.36	6.27				
	82.3	2.23	5.53				
	99.0	2.26	5.42				
	117.1	1.82	5.09				
	139.7	1.42	5.20				
	169.4	0.85	4.87				
	217.9	0.17	5.91				

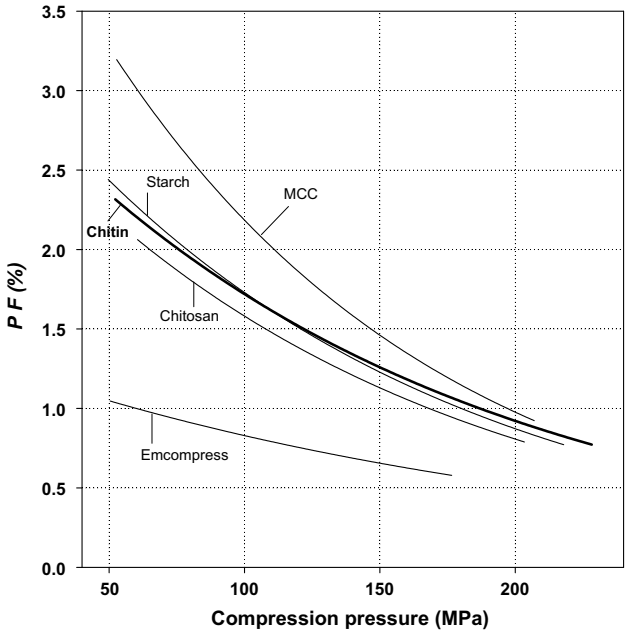

Fig. 1. Effect of compression pressure on the plasticity factor (PF) of chitin, chitosan and direct compression reference excipients ($n = 10$).

sure increased. This change is basically due to the fact that when the compression pressure increases, particles that first deform by plastic flow start to crack and also because the porosity of the tablet decreases. DBCP (dibasic calcium phosphate) was found a less plastic material with the smallest plasticity factor (PF) values at the compression pressure levels studied (i.e. DBCP deforms mainly by fragmentation). With the same range of compression pressures applied, the other materials studied exhibited clearly higher PF values (Fig. 1). Interestingly, chitin and chitosan presented a similar compression behaviour with theoretical maximum plasticity values (Pl) of 3.2 and 3.1, respectively (Table 2 and Fig. 1). It was also demonstrated that MCC maintained its excellent plastic property also with higher compression pressures. The rate of plasticity decrease as a function of compression pressure (v_p) was found similar for all direct compression materials studied, with the exception of that for DBCP which was slightly lower (0.005) (Table 2).

The dependence of elasticity of the materials (i.e. elasticity factor, EF) on the compression pressure is shown in Fig. 2. Chitin and chitosan were clearly more elastic materials than MCC and DBCP, but less elastic than PGS. The EF values for chitin and chitosan ranged from 3% to 4% and, interestingly, the EF values for chitosan increased with low compression pressure levels. In contrast, with MCC and DBCP, the compression pressure applied did not significantly affect the elasticity of the materials. As shown in Figs. 1 and 2, the PF and EF values for PGS were extremely high, providing evidence of a complex nature of PGS as a direct compression excipient. The present results are in accordance with those obtained by Antikainen and Yliruusi (2003) [14].

The SEM images in Fig. 3 showed how chitin particles deformed and oriented in a tablet under a compression. The shapes of deformed chitin particles could be clearly distinguished in a cross-sectional image of the tablet (Fig. 3A), thus supporting the results based on PF and PL values (i.e. chitin deforms under compression mainly by plastic deformation and/or elastic recovery).

Table 2
Coefficients and degree of explanation R^2 for the plasticity factor PF (P)

Material	Pl	$v_p \times 10^{-3}$ (MPa^{-1})	R^2
Chitin	3.2	6.2	0.963
Chitosan	3.1	6.7	0.896
MCC	4.9	8.1	0.957
DBCP	1.3	4.7	0.635
PGS	3.4	6.8	0.717

Pl is the theoretical maximum of plasticity at zero compression pressure and v_p is the rate of plasticity change as a function of compression pressure.

3.2. Compaction properties

The relationship between compression pressure and tablet crushing strength is a simple and widely used method of evaluating the compactibility of pharmaceutical powders. As seen in Fig. 4, a considerable difference in compaction behaviour of the excipients was evident. Chitin and chitosan exhibited an almost identical compression pressure – crushing strength profiles being clearly more compressible than e.g. DBCP and PGS. MCC presented clearly the highest tablet crushing strength values (highest slope of the curve). With DBCP, the tablets exhibited capping with compression pressures higher than 100 MPa. Table 3 pre-

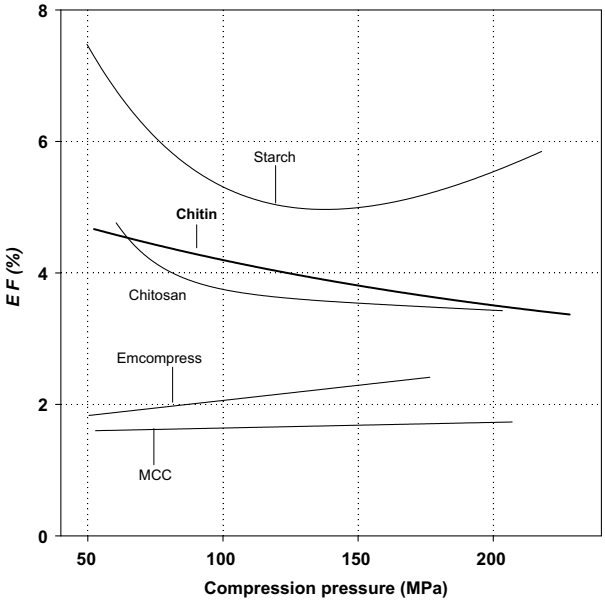

Fig. 2. Effect of compression pressure on the elasticity factor (EF) of chitin, chitosan and direct compression reference excipients ($n = 10$).

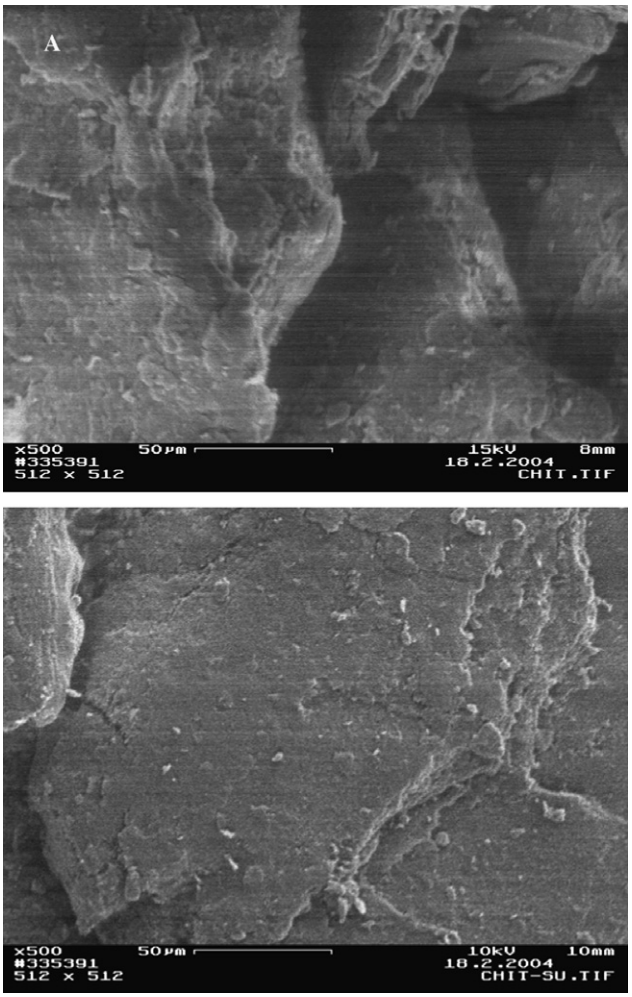

Fig. 3. A scanning electron micrograph on the (A) cross-sectional surface and (B) upper surface of chitin tablet.

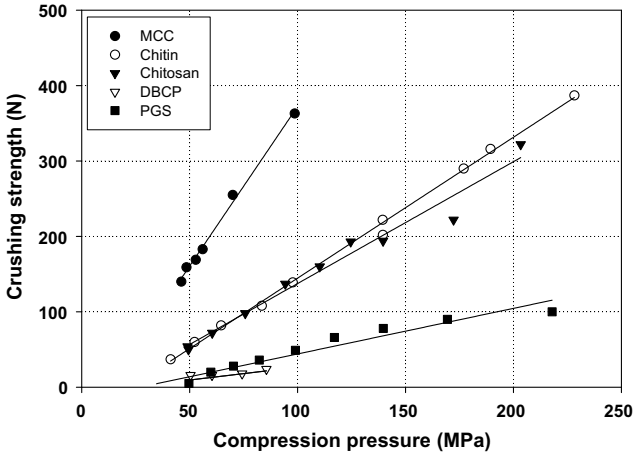

Fig. 4. Effect of compression pressure on the crushing strength of chitin, chitosan and direct-compressed reference tablets ($n = 10$).

sents the experimental equations of the dependence of crushing strength on the upper compression pressure.

To evaluate the compression and friction properties of the excipients (at a compression pressure of 94 MPa), the following parameters were calculated: tensile strength, net work, compactibility (ratio between tensile strength and net work) and R-value (Table 4). Tensile strength and compactibility values for MCC were higher than other excipients, while chitin and chitosan presented similar results of these parameters and DBCP the lowest values. The excipients exhibited the same order with the present parameters as was found with the compression profiles. Lubrication of the die using acetone solution of magnesium stearate was necessary in order to keep the same experimental conditions. Under these conditions, MCC, chitin and chitosan presented the highest R-values. The magnitude of this effect conformed to the following descending rank order: MCC, chitosan, chitin, PGS and DBCP. In summary, the consolidation and compression behaviour of chitin and chitosan was similar, being less plastic and more elastic than MCC and more plastic and elastic than DBCP.

Table 3
Curve fitting and coefficients of determination (R^2) for the dependence of crushing strength (N) on the compression pressure (MPa) ($n = 4$–10)

Material	Curve fitting	R^2
Chitin	$y = 1.869 \times -42.308$	0.997
Chitosan	$y = 1.616 \times -24.226$	0.973
MCC	$y = 4.232 \times -51.065$	0.995
DBCP	$y = 0.341 \times -7.579$	0.721
PGS	$y = 0.604 \times -16.378$	0.944

Table 4
Compression and compaction properties of chitin, chitosan and direct compression reference excipients ($n = 10$)

Materials	Tensile strength (MPa)	R-value	W_{net} (J)	Compactibility (MPa/J)
Chitin	64.91	0.919	4.31	15.06
Chitosan	60.19	0.921	3.74	16.10
MCC	146.87	0.920	5.45	26.93
DBCP	8.96	0.679	2.62	3.41
PGS	18.16	0.726	3.18	5.72

4. Conclusions

Chitin and chitosan of lobster origin exhibit a plastic deformation behaviour under compression and similar elastic recovery with the established direct compression diluents. It is concluded that chitin and chitosan are potential co-excipients for direct compression applications.

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