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Characterization and evaluation of isomalt performance in direct compression

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Abstract

Isomalt is a sugar substitute with a wide range of potential pharmaceutical applications as a result of its physicochemical properties. Four grades of this material were evaluated for their physical characteristics. Only Palatinit® C and F exhibited potential characteristics for direct compression. As expected, the products required lubrification for tabletting. A level of 1% lubricant gave the best performance for Palatinit® C, the most compressible grade as shown by compaction profiles generated using a single-punch machine. However, its flow behaviour had to be improved by including 0.5% Aerosil® 200 as shown by tablet weight uniformity data. Further evaluation by Heckel analysis showed that isomalt exhibited plastic behaviour and underwent elastic recovery primary in the die. Its dilution potential was examined using powdered paracetamol. Acceptable tablets were produced up to 30% drug dilution, but the tensile strength values were reduced, disintegration time and friability increased as expected. Drug dissolution profiles showed a decreasing dissolution rate with the increase of compression force and drug concentration, but considerable improvement was noted when a disintegrant was included. The physical characteristics of the tablets were relatively stable after half a year storage at different humidities as a result of the low hygroscopicity of isomalt.

Keywords: Isomalt (Palatinit®); Physical characteristics; Direct compression; Compaction profiles

1. Introduction

Nowadays, there is an increasing interest in sugar substitutes (mono- and disaccharide alcohols, also called polyols) in pharmaceutical formulations. The reason for this interest is the recognition of their natural tasting sweetness, reduced calorie content and non-cariogenic characteristics. In addition, the majority of these polyols can be consumed by diabetics without any significant increase in body glucose, insuline or lactic acid concentration unlike the conventional saccharides such as sucrose, glucose and lactose. Furthermore, the polyols have shown very good industrial and technical properties in pharmaceutical manufacturing, above all in the area of direct tabletting. Among all polyols, isomalt is the only sugar alcohol derived from sucrose. By enzymatic

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transglucosidation (Protaminobacter rubrum), the nonreducing sucrose is converted into a reducing disaccharide α-D-glucopyranosyl-1,6-D-fructose whose generic name is isomaltulose. This new sugar is considerably more resistant to acids and microbial influences because of its more stable 1–6 bond between glucose and fructose (isomer of the 1–2 weaker sucrose one). In the second processing step, isomalt, an equimolecular mixture of the isomers α-D-glucopyranosyl-1,1-D-mannitol (GPM) and α-D-glucopyranosyl-1,6-D-sorbitol (GPS), is obtained by hydrogenation of isomaltulose in a neutral aqueous solution using Raney nickel as a catalyst (Strater, 1989). During crystallization, GPM crystallizes with two molecules of water, therefore isomalt contains approximately 5% of water.

In addition to the technical advantages of the other polyols, isomalt has the advantage to be more comparable to sucrose, much less hygroscopic and with better organoleptic qualities (Strater, 1989). Because of the above cited characteristics, isomalt seems a promising excipient for tablet manufacturing by direct compression.

An excipient intended for direct compression tabletting should be free-flowing, chemically, physically and physiologically inert, relatively inexpensive and show excellent compressibility in order to produce tablets with a high tensile strength, a low friability, a low weight variation, a short disintegration time and a high drug dissolution rate (Bolhuis and Lerk, 1973; Armstrong, 1997).

The purpose of this investigation was the evaluation of isomalt as a directly compressible vehicle.

Table 1
Different types of isomalt

Product	Batch number	Supplier
Palatinit® F (0.2–0.6 mm)	L615 IDD	Palatinit-Süßungsmittel GmbH, Mannheim-Germany
Palatinit® C (<0.4 mm)	L643 IMB	Palatinit-Süßungsmittel GmbH, Mannheim-Germany
Palatinit® P.F (<100 μm)	L704 OMB	Palatinit-Süßungsmittel GmbH, Mannheim-Germany
Ground isomalt (<0.3 mm)	–	Eridania Béghin-Say Group, Vilvoorde, Belgium

2. Materials and methods

2.1. Materials

The different types of isomalt used are listed in Table 1. Magnesium stearate (< 90 μm) (Pharmachemic, Wevelgem, Belgium) was used as the lubricant and Aerosil® 200 (< 90 μm) (Ludeco S.A, Brussels, Belgium) as a glidant. Paracetamol dense powder (Mallinckrodt Chemical Ltd, Raleigh, USA), was used as a model drug for the testing of the dilution potential of the isomalt in direct compression. In some cases, Explotab® (Pennwest, Patterson, New York) was used as a disintegrant. Neosorb® P100 T-sorbitol, Pearlitol SD 200-mannitol and Xylisorb® 300-xylitol (Roquette Frères, Lestrem, France) were used in a comparative study.

2.2. Methods

2.2.1. Powder primary characterization

The isomalt granules (0.5–3.5 mm) (Eridania Béghin-Say Group, Vilvoorde, Belgium) were milled using a mill operating at 12 000 rpm with a feed rate of 20 g/s (model USCH, H. Bavermeister Maschinenfabrik GmbH, Hamburg, Germany) and a sieve of 300 μm.

The particle size distribution of each isomalt powder was determined using laser diffraction (Mastersizer, Malvern, Worc's, UK).

The true density was measured using a helium pycnometer (Accupyc 1330 Micromeritics®, Norcross, USA). The bulk and tapped densities were measured by pouring a 50 g sample into a 100 ml graduated cylinder. Next, the cylinder was submitted to tapping (J. Engelsmann, Ludwigshafen, Germany) until a constant volume was obtained. The packing characteristics were evaluated by the Hausner factor.

The flow properties were evaluated by determining the angle of repose and the flow rate. The flow rate was determined according to Amidon (1995) using a standard funnel as described in the Ph. Eur. III. For poor flowing samples, an electric shaker Type 370 (Retsch, Wiesbaden, Germany) was used. The angle of repose was measured by pouring the powder through a funnel on a circular disk and measuring the maximum height of the cone obtained.

The total powder surface area was measured with the aid of the BET method (Gemini 2360 Analyser, Micromeritics, Norcross, USA) with nitrogen as adsorbate gas.

The powder porosity was determined by a mercury intrusion porosimeter (Auto Pore III 9410, Micromeritics, Zaventem, Belgium) in a pressure range between 0.003 and 413 MPa.

X-ray diffraction analysis was performed using a X-ray diffractometer (D 500, Cu-Kα, Siemens, Germany), $\lambda = 1.5406$ Å.

The hygroscopicity was determined by submitting the samples of isomalt types P.F, C and F to different relative humidities (RH) at ambient temperature (20 ± 2°C) until a constant water content was obtained. The water content was measured using a Karl Fischer Titrator, DL 35 (Mettler-Toledo, Beersel, Belgium).

2.2.2. Compression and tablet characterization

The isomalt grades with potential characteristics for tabletting (Palatinit® C and F) were selected for evaluation of lubricant requirements and compression properties. The samples were blended with magnesium stearate (< 90 μm) at 0.25, 0.5, 0.75 and 1% lubricant level for 5 min. All mixing operations were carried out using a Turbula mixer type T2A (W.A. Bachofen, Basel, Switzerland). Each blend was visually evaluated for lubrification problems during compression.

The compaction behaviour of isomalt combined with the optimal lubricant level (1% w/w), was evaluated by means of the Heckel tablet in-die method at different compression times (Rue and Rees, 1978; Roberts and Rowe, 1985; Paronen, 1987), using a compaction simulator (PuuMan Oy, Kuopio, Finland) fitted with 12 mm circular flat punches. The Heckel plot representing the powder densification in the die versus the applied pressure was used to interpret the powder deformation behaviour.

The formulations were compressed on a single-punch tabletting machine (Korsch Type Eko, Frankfurt, Germany), fitted with 13 mm circular flat punches equipped with a piezoelectric cell for compression force measurements. The tablet average weight, the standard deviation (SD) and relative standard deviation (RSD) were obtained from 20 individually weighed tablets according to Eur. Ph. III. Because of the poor flow properties observed for the Palatinit® C formulation, 0.5% Aerosil® 200 (< 90 μm) was added to improve the blend flowability. For each formulation, a compaction profile was generated using the average tablet tensile strength versus the compaction force over a force range of 5–25 kN. The tablet tensile strength was calculated from the diametral crushing force (mean of ten tablets) measured using a strength tester, Type PTB 311 (Pharma Test, Hainburg, Germany). Tablet friability was calculated as the percentage weight loss of 20 tablets after 100 rotations in a friabilator machine, Type PTF (Pharma Test, Hainburg, Germany). The results are presented as a mean value ($n = 3$). Tablet disintegration time (mean of six tablets) was measured according to Eur. Ph. III (Pharma Test disintegrator, Type PTZ, Hainburg, Germany) in 0.1 N HCl at 37 ± 0.5°C with disks.

The formulation with 30% paracetamol was selected to evaluate the precompression effect on the tensile strength. Tablets of 250 mg were prepared by single compression (10 and 20 kN) and by combination of precompression/main compression (10/20 and 20/10 kN) with an interval of 530 ms and a compression speed of 45.7 mm/s, using the compaction simulator fitted with 9 mm circular flat punches.

The dissolution profile for paracetamol was tested in triplicate according to USP XXIII (paddle apparatus) with a paddle speed of 50 rpm in 900 ml phosphate buffer pH 5.8 at 37 ± 0.5°C, using a VK 7000 automatic dissolution tester (VanKel, Edison, New Jersey, USA). Samples were withdrawn at regular intervals through a filter with replaced pure medium. The drug content of each sample was determined by measuring

Table 2
Physical properties of different types of isomalt[a]

Parameters	Palatinit P.F	Ground <300 μm	Palatinit C	Palatinit F
Mean diameter Dm (μm)	35.57	67.17	151.94	403.70
Surface area S.A (m^2/g)	1.8309	1.3145	0.8195	0.5753
Porosity (%)	75.3	73.4	65.9	51.5
Bulk density ρ_b (g/cm^3)	0.48 ± 0.01	0.52 ± 0.01	0.64 ± 0.00	0.79 ± 0.00
Tapped density ρ_t (g/cm^3)	0.76 ± 0.01	0.80 ± 0.00	0.88 ± 0.00	0.85 ± 0.00
Compressibility index Ci (%)	36.5 ± 0.6	35.3 ± 0.2	27.2 ± 0.1	7.1 ± 0.4
Hausner factor, Hf	1.58 ± 0.01	1.54 ± 0.02	1.38 ± 0.01	1.08 ± 0.00
Flow rate, Vf (g/s)	6.9 ± 0.5[b]	7.5 ± 1.6[b]	8.3 ± 0.8[b]	14.7 ± 0.4
Angle of repose, α (°)	53.0 ± 0.1	52.1 ± 0.1	46.2 ± 0.1	38.0 ± 0.2

[a] True density: 1.5211 ± 0.0002 (g/cm^3).
[b] Use of electric shaker.

the absorbance spectrophotometrically at 243 nm (UV-VIS Spectrometer Lambda 12, Perkin-Elmer, Ueberlingen, Germany).

The physical stability of 600 mg tablets containing 30% drug was evaluated after storage at ambient temperature (20 ± 2°C), 45 and 85% RH, for 6 months.

3. Results and discussion

3.1. Primary physical properties

The primary physical properties of the different types of isomalt are summarized in Table 2. All isomalt types examined showed major differences in mean particle size, particle size distribution (Fig. 1) and particle shape (results not shown), bulk and tapped densities, surface area and porosity indicating different flow and compression properties as demonstrated by the compressibility index, Hausner factor, flow rate and angle of repose. All these differences greatly affected the tabletting behaviour. Only Palatinit® C and F showed acceptable physical characteristics regarding to flowability and direct compressibility. Palatinit® C seemed to be more directly compressible than Palatinit® F as shown by the compressibility index. However, Palatinit® F showed the narrowest particle size distribution with a very low amount of fine particles and a free flowability required for low tablet weight variation, especially in direct compression.

X-ray diffraction patterns (Fig. 2) confirmed the crystalline nature of the different types of isomalt and did not show any polymorphic behaviour. Fig. 3 shows the water sorption isotherms for the different particle sizes of isomalt. Only above 85% RH (20°C), an important increase of the water content reaching values around 20% (w/w) was seen. This is unusual for polyols because of their hydrophilic nature (Hancock and Shamblin, 1998) and is an important consideration when an extremely moisture-sensitive active ingredient has to be incorporated into a direct compression formulation and has to be seen as a main advantage for stability especially at high relative humidity (Sangekar et al., 1972).

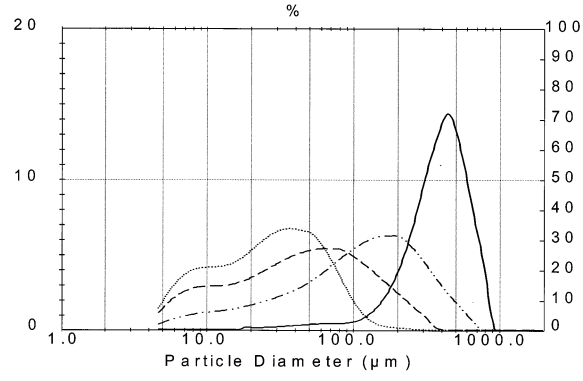

Fig. 1. Particle size distribution as determined by laser diffraction analysis for different types of isomalt. Keys: type F (—); C (– · · –); ground <300 μm (– –); and P.F (· · ·).

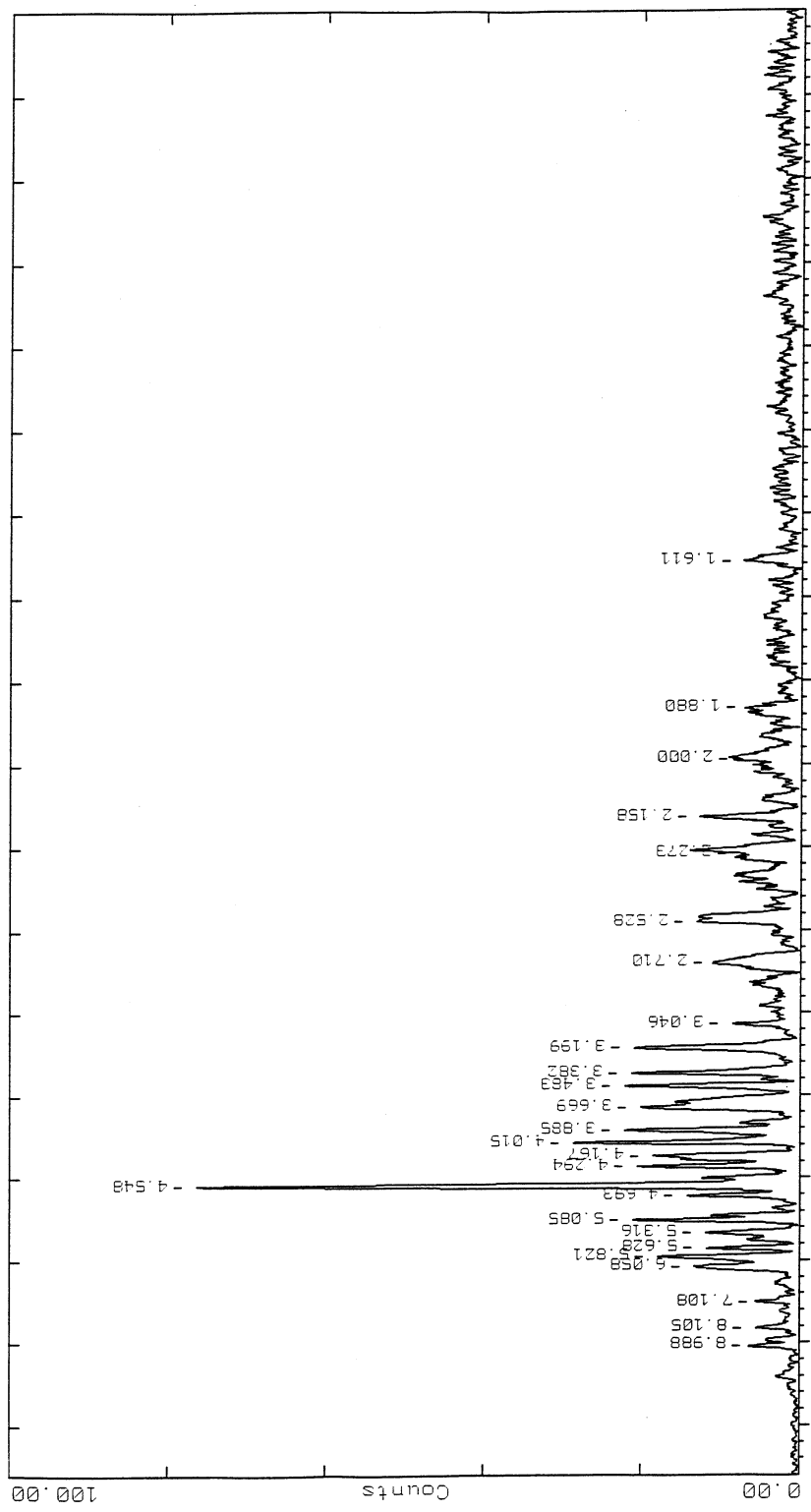

Fig. 2. X-ray diffraction pattern of isomalt type F.

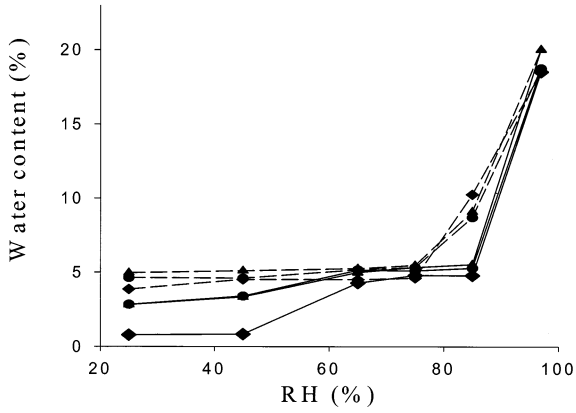

Fig. 3. Water sorption isotherms: absorption (—) and desorption (– – –) for Palatinit® P F (▲); C (●); and F (◆) at 20°C and different relative humidities (RH).

3.2. Compaction properties and tablet characteristics

3.2.1. The lubricant requirements and flow properties

The compaction profiles for lubricated Palatinit® C and F at different concentrations of magnesium stearate are shown in Fig. 4. Isomalt compression without lubricant was impossible. During compression lubrification problems such as die wall sticking, capping and lamination were observed at different compression forces for the formulations containing less than 1% magnesium stearate. This lubricant concentration was the optimal lubrification level for Palatinit® C, while for Palatinit® F it was 0.25%. For Palatinit® F, the tablet tensile strength decreased more rapidly when the lubricant level was increased than in the case of Palatinit® C tablets so that the measurements were impossible above the optimal lubricant level. These differences in lubrification sensitivity for these two grades are evident because the surface area of the type F is much smaller than for the type C (Bolhuis and Hölzer, 1995). The tensile strength reduction phenomenon is caused by the formation of a lubricant film and is typical for mainly plastic deforming materials. The dissolution rate can also be markedly affected in the presence of a hydrophobic film. For Palatinit® C, tablet tensile strength increased more proportionally to the applied compression force than Palatinit® F tablets. As for Palatinit® C, the same optimal lubricant level was reported by Basedow et al. (1986) for sorbitol and by Arm-

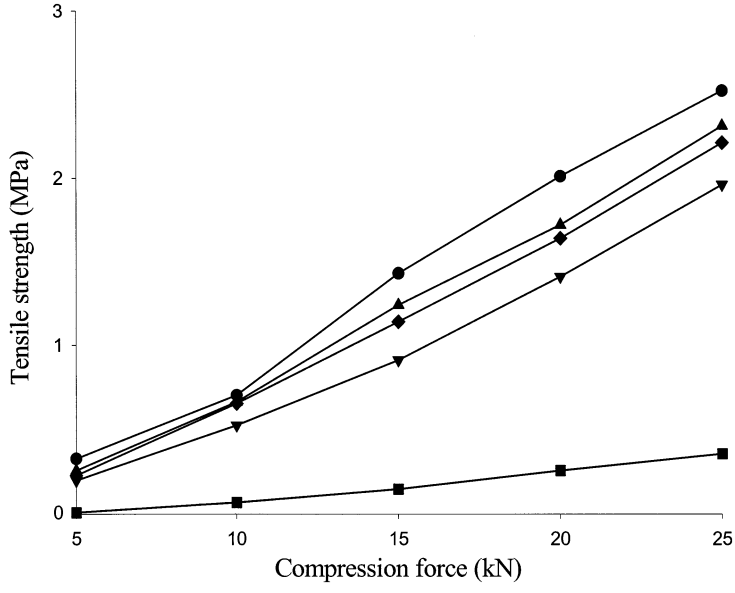

Fig. 4. Palatinit® F and type C profiles at different concentrations of magnesium stearate. Keys: 0.25% (F: ■; C: ●); 0.5% (▲); 0.75% (◆); 1% (▼) for only type C.

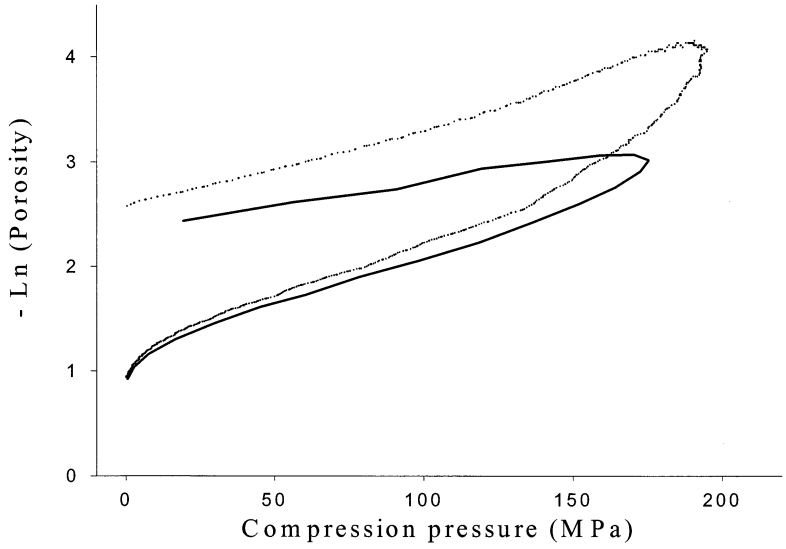

Fig. 5. Densification vs applied pressure plots of Palatinit® C combined with 1% magnesium stearate, at different compression times. 0.05 s (—); and 1.5 s (· · ·).

strong (1998) for lactitol. According to these authors, no significant effect of the lubricant level on the tablet tensile strength was noted for both materials.

With the optimal lubrification level the tablet tensile strength for Palatinit® C was around 0.80 and 1.90 MPa at compression forces of 15 and 25 kN, respectively. For Palatinit® F, only a tablet tensile strength of 0.35 MPa was obtained at a compression force of 25 kN. The flow behaviour on the tablet press was excellent for Palatinit® F as shown by the tablet weight uniformity data with a RSD value of 0.3%, while for Palatinit® C formulations the RSD value was 0.8%. With addition of 0.5% Aerosil® 200 to the Palatinit® C formulations the RSD value decreased to 0.4%, the lubrification properties were still acceptable and the tablet tensile strength increased. At the optimal lubrification level, an increase of 36.5% (1.20 ± 0.06 MPa) and 20.9% (2.33 ± 0.18 MPa) was observed at compression forces of 15 and 25 kN, respectively.

For mixtures of Palatinit® C and F (4:1 and 6:1), 0.2% Aerosil® 200 was found to be sufficient to improve the tablet weight uniformity. The optimal lubrification level (0.75%) was lower than for pure Palatinit® C and the tablet tensile strength increased with increasing Palatinit® C concentration in the mixture.

3.2.2. The deformation behaviour

Heckel plots obtained for Palatinit® C at different compression times showed an increased densification with increased contact time (Fig. 5) and this effect tended to decrease the value of yield pressure, Kd (reciprocal of the slope determined from the upward linear part of the Heckel plot). This phenomenon justifies the deformation behaviour of isomalt similarly to sorbitol (Schmidt, 1983; Reyss-Brion et al., 1986), mannitol (Roberts and Rowe, 1985) and in contrast to other polyols such as xylitol (Garr and Rubinstein, 1990; Morris et al., 1996) and lactitol (Armstrong, 1998) which are mainly brittle materials. The decrease in the yield pressure with increasing contact time could be as a result of a time dependent deformation and bond formation of the material and/or a decrease in brittle behaviour. The Kd values were 107.2 and 94.4 MPa at compression times of 0.05 and 1.5 s, respectively with corresponding punch velocities of 102.0 and 3.4 mm/s. The strain rate sensitivity (SRS) calculated from both Kd values $[(Kd2 - Kd1) \times 100/Kd2]$ was not very high (11.9%). This suggests that a certain degree of

fragmentation occurred especially at low compression force. The degree of immediate elasticity was quantified by the reciprocals of the slopes obtained from the downward linear section of the Heckel plot (decompression phase). The values obtained, 117.5 MPa for a compression time of 1.5 s and 207.0 MPa for 0.05 s showed that isomalt undergoes a fast elastic recovery primarily in the die.

3.2.3. The dilution potential

The dilution capacity of isomalt was examined for formulations based on Palatinit® C with the lubricant and the glidant added in optimal concentrations. When combined with paracetamol, the tablet tensile strength was reduced with increasing drug concentration in the blend (Fig. 6). Palatinit® C was successfully diluted with 30% drug, but a force of 20 kN was required for a tablet tensile strength of ± 0.95 MPa. Further dilution caused a continual decrease of tablet tensile strength and at a dilution of 50% drug, the tensile strength was reduced to 0.56 MPa at a force of 20 kN. The tablet tensile strength did not significantly change when a disintegrant was added to the formulation containing 30% drug concentration.

A comparison was made between the compressibility of isomalt and other polyol blends containing 30% paracetamol with magnesium stearate and Aerosil® 200 in the same optimal concentrations for all mixtures (Fig. 7). The compression properties of the mixtures decreased in the order sorbitol, mannitol, isomalt and xylitol. An acceptable tablet tensile strength (>0.80 MPa) was found at a force of 10 kN for sorbitol, 15 kN for mannitol and 20 kN for isomalt. Very weak tablets were obtained for xylitol at all compression forces. Several authors already indicated the excellent compression characteristics of sorbitol (Shangraw et al., 1981; Schmidt, 1983; Du Ross, 1984; Guyot-Hermann and Leblanc, 1985; Basedow et al., 1986). The blends based on mannitol and xylitol showed serious lubrification problems as already mentioned in literature (Debord et al., 1987; Morris et al., 1996) even at a lubricant level of 2% magnesium stearate.

Precompression at 10 and 20 kN for the 30% paracetamol formulation, did not have any influence on the tablet strength.

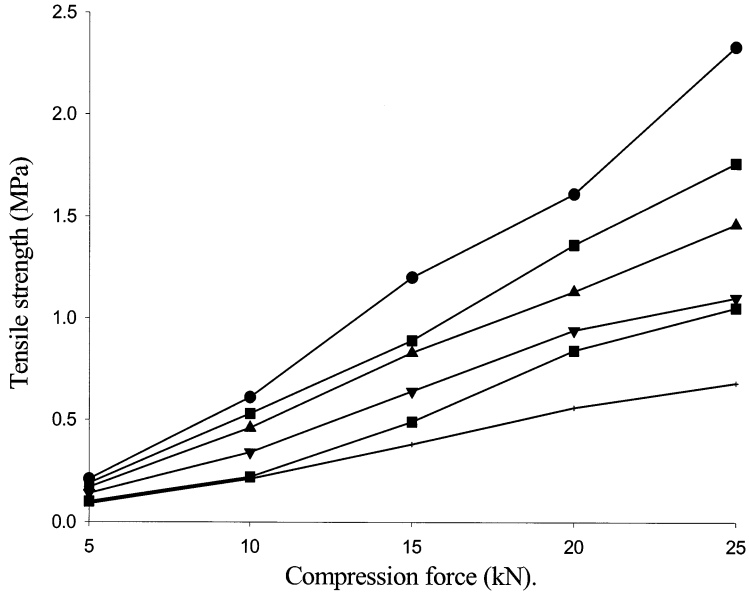

Fig. 6. Compressibility of Palatinit® C mixtures with different concentrations of paracetamol, 0.5% Aerosil® 200 and 1% magnesium stearate. Keys: 0% (●); 10% (■); 20% (▲); 30% without (▼); and with 5% Explotab® (◆); and 50% (+) paracetamol.

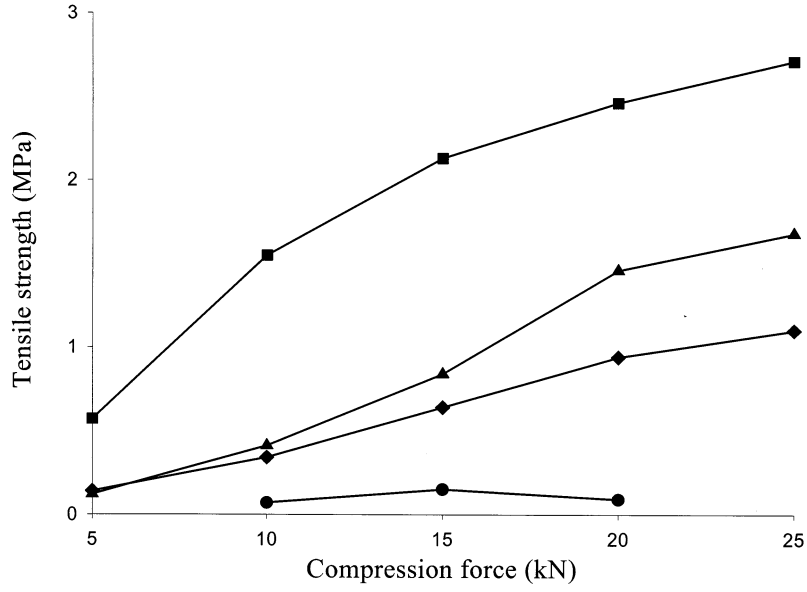

Fig. 7. Isomalt compressibility compared to the other polyols blends containing 30% paracetamol, 0.5% Aerosil® 200 and 1% magnesium stearate. Keys: sorbitol (■); mannitol (▲); isomalt (◆); and xylitol (●).

Table 3
Tablet friability and disintegration time

Compression force (kN)	Drug concentration (% w/w)							
	0	10	10[a]	20	30	30[a]	30/sorbit.	50
1. Friability (%)								
15	2 ± 0	2 ± 1	7 ± 1	3 ± 0	4 ± 0	13 ± 1	0.6 ± 0.1	6 ± 0
20	1 ± 0	2 ± 0	2 ± 0	2 ± 0	3 ± 0	3 ± 0	0.4 ± 0.1	4 ± 0
25	1 ± 0	1 ± 0	1 ± 0	2 ± 0	2 ± 0	3 ± 0	0.3 ± 0.1	4 ± 0
2. Disintegration (s)								
15	282 ± 13	293 ± 16	269 ± 8	334 ± 20	435 ± 12	274 ± 8	461 ± 28	613 ± 14
20	316 ± 14	326 ± 8	297 ± 8	462 ± 24	518 ± 27	315 ± 8	497 ± 37	795 ± 8
25	341 ± 15	343 ± 14	305 ± 7	478 ± 22	564 ± 11	335 ± 6	579 ± 40	907 ± 32

[a] Addition of 5% Explotab®.

The friability and disintegration time increased with an increasing drug concentration (Table 3). In addition, an increasing compression force resulted in a friability decrease, while the disintegration time increased. The disintegration was fast (≤ 300 s) (Cirunay and Plaizier-Vercammen, 1997a) up to 10% drug concentration at a compression force below 25 kN. The friability was around 1%, above a compression force of 20 kN for placebo tablets and 25 kN for a 10% drug formulation. Higher drug concentrations increased the disintegration time and the drug dissolution rate decreased. Similar observations were reported for lactitol by Armstrong (1998) and for xylitol by Cirunay and Plaizier-Vercammen (1997a,b). Tablets based on sorbitol also showed a slow disintegration time but a very low friability (Table 3) which is in correlation with the literature data (Shangraw et al., 1981; Guyot-Hermann and Leblanc, 1985; Basedow et al., 1986). The

addition of 5% Explotab® to the Palatinit® C formulations containing 10 and 30% drug decreased the disintegration time only for the formulation containing 30% drug.

3.2.4. The drug dissolution and tablet physical stability

The drug release profiles of the tablets prepared with the formulations containing 10 and 30% drug are shown in Fig. 8. The dissolution rate decreased with an increasing drug concentration and compaction force. For the formulation with 30% drug, the drug release was below the U.S.P XXIII recommended limits for paracetamol tablets ($\geq 80\%$ in 30 min). Only 68.6 (± 4.7) and 61.2 (± 2.3)% dissolved in 30 min for tablets prepared at 20 and 25 kN, respectively. For a 10% drug concentration, the amount of drug dissolved was 92.0 (± 0.9)% and 83.0 (± 3.8)% in 20 min at a compression force of 20 and 25 kN, respectively. Dörr and Willibald-Ettle (1996) reported that the drug dissolution rate was significantly lower for model melts (lozenges) and tablets made of isomalt than for conventional saccharide formulations. Likewise, the slow drug release was also mentioned for hard confections based on isomalt formulations by Coia and Lynch (1990). The addition of a disintegrant resulted in a considerable increase of the dissolution rate particularly for the formulation with 30% drug.

The paracetamol tablets based on isomalt, conserved during 6 months at 45 and 85% RH, kept their physical aspect. After storage at 45% RH, an increase of the tablet tensile strength and a decrease of the friability were observed at all compression forces (Table 4) as a result of some crystallization which must have occured during storage. Similar phenomena were reported in several studies for sorbitol, mannitol (Sangekar et al., 1972; Guyot-Hermann and Leblanc, 1985), xylitol (Cirunay and Plaizier-Vercammen, 1997a) and for paracetamol tablets (Khattab et al., 1993). At 85% RH, a small decrease of the tablet tensile strength was observed, but the corresponding fri-

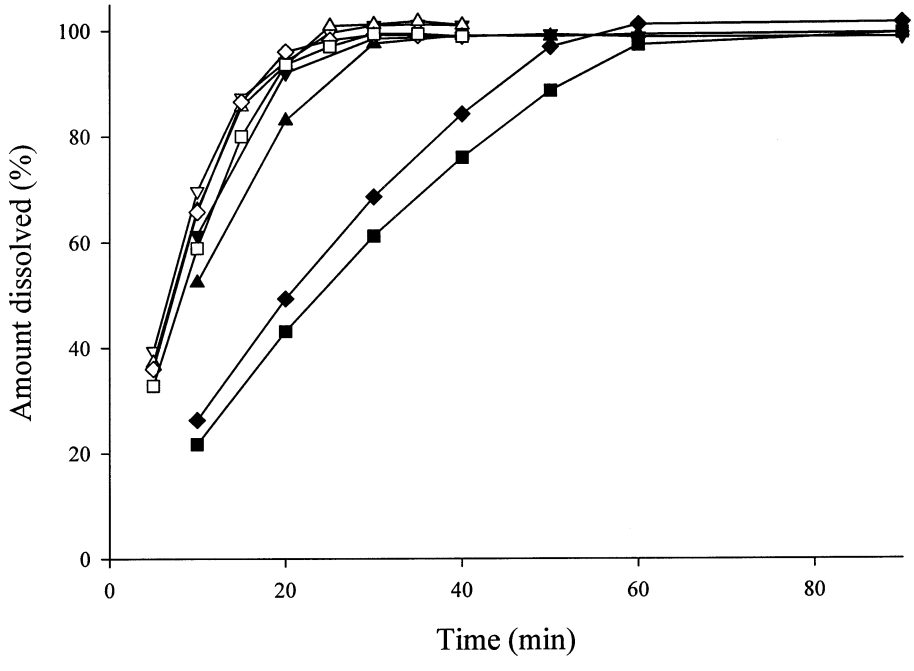

Fig. 8. Paracetamol release from tablets based on the formulations with 10%, 30% drug, 1% magnesium stearate and 0.5% Aerosil® 200, with and without 5% disintegrant (Explotab®) at a compression force of 20 and 25 kN. Without disintegrant: 10%/20 kN (▼); 10%/25 kN (▲); 30%/20 kN (◆); 30%/25 kN (■); with disintegrant: 10%/20 kN (▽); 10%/25 kN (△); 30%/20 kN (◇); 30%/25 kN (□).

Table 4
Hardness, friability and disintegration time of Isomalt tablets containing 30% paracetamol prepared by direct compression at 20 and 25 kN, before and after storage at different humidity levels (45 and 85% RH) at 20 ± 2°C

Force (kN)	Tensile strength (MPa)	Friability (%)	Disintegration (s)
1. Initial values			
20	0.94 ± 0.13	2.6 ± 0.1	518 ± 27
25	1.10 ± 0.05	2.2 ± 0.1	564 ± 11
2. Values after $\frac{1}{2}$ year storage at 45% RH			
20	1.14 ± 0.07	2.1 ± 0.1	500 ± 11
25	1.34 ± 0.16	1.9 ± 0.1	550 ± 31
3. Values after $\frac{1}{2}$ year storage at 85% RH			
20	0.75 ± 0.06	1.8 ± 0.2	523 ± 14
25	0.97 ± 0.08	1.6 ± 0.1	533 ± 14

ability decreased even more than for 45% RH level. This could be the consequence of some moisture pickup by isomalt which reduced the tablet strength but increased their plasticity. No significant differences in tablet breaking were noted (all tablets broke more or less diametral) and no considerable changes in tablet disintegration were observed. Compared to the commonly used directly compressible sugar alcohols, tablets made with isomalt seem to be more stable than with sorbitol (Sangekar et al., 1972; Shangraw et al., 1981; Guyot-Hermann and Leblanc, 1985; Basedow et al., 1986), xylitol (Laakso et al., 1982; Cirunay and Plaizier-Vercammen, 1997a) and have a comparable stability as those made with mannitol (Debord et al., 1987).

4. Conclusions

Among all isomalt types studied, only palatinit C exhibited acceptable properties as a direct compression tablet excipient. Levels of 1% magnesium stearate and 0.5% Aerosil 200 were found to give the best performance, respectively in terms of lubrication requirements and flow behaviour. An acceptable tablet tensile strength (>0.80 MPa) was obtained up to 30% drug dilution at a compression force of 20 kN, but an acceptable tablet friability was reached only at a 10% drug concentration. Compared to sorbitol, isomalt was less directly compressible, but its low hygroscopicity can be of some interest in pharmaceutical manufacturing. A relatively slow drug dissolution profile was observed, but can be considerably improved by the addition of a disintegrant. The tablet physical characteristics did not significantly change after 6 months of storage up to 85% RH.

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