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Evaluation of substrate–binder interaction in a model granule system

F. Kiekens [a], R. Zelko [b], I. Antal [b], J.P. Remon [a,*]

[a] *Laboratory of Pharmaceutical Technology, University of Gent, Harelbekestraat 72, B-9000 Gent, Belgium*
[b] *Pharmaceutical Institute, Semmelweis University of Medicine, Hogyes E. u. 7., H-1092 Budapest, Hungary*

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Abstract

The real binder function in granules made of PVP and glass ballotini as model substrates, and its effect on the mechanical properties of rectangular beam specimens consisting of these granules was investigated by use of the four-point beam-bending technique. The mechanical properties of the rectangular beam specimens were correlated with the granulation liquid characteristics (contact angle, surface tension and binder concentration). The mechanical strength and Young's modulus of the specimens both reached a maximum value when the binder concentration in the granulation liquid was increased to 20% (w/v) for all granulation liquid volumes used. Above a 20% PVP concentration, the increasing granulation liquid contact angle hindered the binder spreading, creating weak regions in the compact and decreasing its mechanical strength. This was confirmed by scanning electron microscopy pictures showing a non-homogeneous distribution of the PVP in the granulated mass. No differences were observed in the stress/strain behaviour of the beams made with PVP of different molecular weight. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Substrate–binder interaction; Four-point beam bending; PVP

1. Introduction

Several studies have investigated the substrate–binder interaction in granule systems to determine the real function of the binder and its effect on granule properties (Mullier et al., 1987; Adams et al., 1989; Mullier et al., 1991; Hancock et al., 1993). In these studies, different techniques were developed for this purpose, all having their own advantages and disadvantages. In contrast to the standard diametrical breaking test of tablets, additional information on the mechanical properties of excipients was obtained with the four-point beam-bending technique which was used by Church and Kennerley (1983), Mashadi and New-

* Corresponding author. Tel.: +32 9 2648056; fax.: +32 9 2228236; e-mail: JeanPaul.Remon@rug.ac.be

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ton (1987), Bassam et al. (1990) and York et al. (1990). The influence of the granulation liquid characteristics and of the molecular weight of PVP on the mechanical behaviour of rectangular beam specimens made of glass ballotini as a model substrate, using the four-point beam-bending technique were the two main objectives in this study. The importance of sample preparation, experimental test and storage conditions when applying the four-point beam-bending method, was also shown.

2. Materials and methods

Glass sphere granules were produced using glass spheres (500 g Microperl-AQ, Sovitec-Glaverbel, Fleurus, Belgium) and polyvinylpyrrolidone Kollidon 25 and 90 (BASF, Ludwigshaven, Germany), in a planetary mixer (Hobart, Troy, OH) and a high shear mixer (Grall 10, Colette Machines, Wommelgem, Belgium). The mixing time and speed were kept constant at 5 min and 150 rpm, respectively, when using the planetary mixer. The rotor and the chopper speed were fixed at 600 and 1500 rpm, respectively, for the experiments with the high shear mixer. Eighteen different batches were produced using, for each of them, a specific PVP concentration and granulating solution volume (Table 1). The 10% 80 ml, 15% 70 ml and 20% 65 ml combinations were used in order to produce granules in the capillary state. These volumes were determined with the mixer torque rheometer as described by Hancock et al. (1994).

Table 1
PVP binder concentration (%, w/v) and granulating solution volumes (ml) used for the production of 18 different Microperl granule batches

	PVP conc.				
	5%	10%	15%	20%	25%
Volumes (ml)	10	10	10	10	10
	30	30	30	30	30
	50	50	50	50	50
	—	80	70	65	—

Rectangular beam specimens ($100 \times 10 \times 6$ mm) were produced by compressing the wet glass sphere granules in specially designed PTFE dies, using a force of 100 N. The punch and the bottom part of the die were removed and the die, filled with the compacted granules, was placed in an oven at a temperature of 50°C for 48 h. After this period, the dies were opened and the beams were stored at room temperature and 45% R.H. prior to the testing. Some beams, prepared with 500 g Microperl and 30 ml 15% Kollidon 25, were also stored at 45 and 65% R.H. in order to investigate the influence of moisture uptake during storage on the maximal tensile stress. The 100 N compressional force did assure samples of equal porosity after drying, since the mean beam porosity value ($\pm$ S.D., $n = 6$) measured by use of mercury porosimetry (Autopore III, Micromeritics, Atlanta) was $51 \pm 2\%$.

In order to examine the mechanical behaviour of the PVP binder inside the beams, they were tested for their strength and elasticity using the four-point beam-bending technique.

The beams were carefully placed on a specially designed stainless steel/aluminum breaking rig which was fixed and tested in a Lloyds Testing Machine (Lloyds L1000R, Fareham, UK) (Fig. 1). The dimensions of the support span and the load span were 80.0 and 40.0 mm, respectively, and the crosshead-speed was 0.5 mm/min. Because no indentation occurred at the contact points, the deflection of the beam was visualized by the displacement of a 500-N DLC-loadcell. The load was measured by a strain gauge inside the loadcell. The load-deflection diagram was recorded and saved as a table-format file, smoothed, transformed to a stress–strain diagram and evaluated. The maximal tensile stress (σ) and strain (ϵ) were calculated and evaluated according to the following formulas:

$$\sigma = \frac{3}{2} \cdot \frac{F \cdot (o - i)}{w \cdot h^2} \tag{1}$$

$$\epsilon = \frac{D \cdot h}{2\left(\frac{i^2}{8} + \frac{(o-i)i}{4} + \frac{(o-i)^2}{12}\right)} \tag{2}$$

while

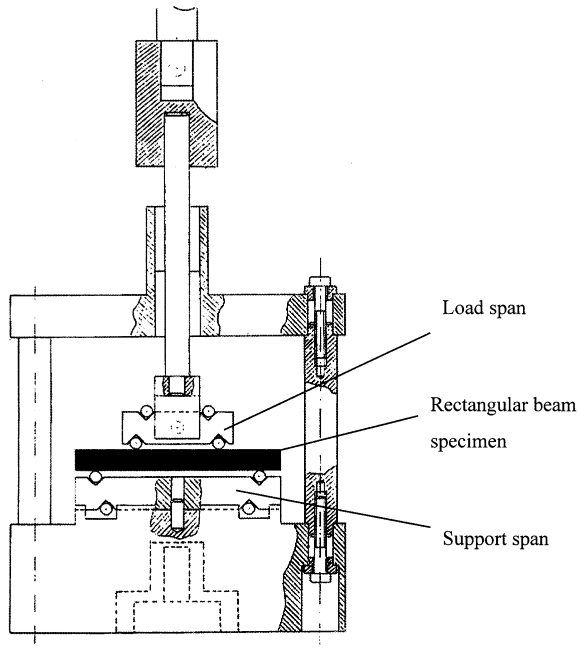

Fig. 1. Cross-section of the four-point beam-bending construction.

$$D = \frac{D'}{2} \cdot \frac{2o^3 + i^3 + 6oi^2}{o^3 i^3 + 3oi^2} \quad (3)$$

where F = force (N); o = support span (mm); i = load span (mm); w = specimen width (mm); h = specimen height (mm); D = central beam deflection (mm); D' = loadcel displacement (mm).

Eq. (1) and Eq. (2) were taken from Timoshenko (1968), while Eq. (3) was derived from the general beam-bending theory. Calculation of the Young's modulus (MPa) was performed by the slope determination of the stress–strain curve at 50% of the maximal tensile stress. This ensured that the curve was in the linear elastic region.

A two-factor, three-level face-centered central composite design (Franz et al., 1988) was applied to construct a second-order polynomial model describing the effect of formulation factors (amount of granulation liquid, binder concentration) on the mean maximum tensile stress values of the rectangular beam specimens. The two factors as well as their levels are shown in Table 2. The levels for each parameters are represented by a (−) sign for the lower level, a (+) sign for the higher level and by (0) for the base level. Table-Curve 3D (Jandel Scientific) software was applied for the multiple regression analysis. The expected form of the polynomial equation is as follows:

$$y = b_0 + b_1x_1 + b_2x_2 + b_{11}x_1^2 + b_{22}x_2^2 + b_{12}x_1x_2 \quad (4)$$

where y is the response, x are the factors, and b are the coefficients characterizing the main (b_1,b_2), the quadratic (b_{11},b_{22}), and the interaction (b_{12}) effects.

Scanning electron microscopy pictures (Zeiss, DSM 9200, 3.00 kV, 5 mm) were taken from the 500–760-μm granule size range. The samples were taken from the wet mass of 500 g Microperl AQ granulated with 30 ml liquid using the five different PVP concentrations and forced through a 1-mm sieve. After the breaking tests the fracture plane of the beam was also examined by SEM.

The dynamic surface tension of the Kollidon 25 solutions at five different concentrations was determined by the Du Nouy ring method using a computer-controlled and programmable tensiometer (KSV Sigma 70, Helsinki, Finland) after equilibration at 20°C for 1 h.

After equilibration at 20°C, the dynamic contact angle of the aqueous solutions for the different PVP concentrations was determined using the Wilhelmy plate method and the KSV Sigma 70.

Diffuse reflectance spectrometry was applied to investigate if the binder was uniformly spread in the wet granulated mass or had agglomerated at certain locations within the mass. A 500–760-μm granule sample was placed into a 5-mm layered cell with 4 × 5-cm sides and placed into the sample container of the UV/VIS/NIR spectrophotometer (Hitachi U-3501, Japan) equipped with an integrating sphere (diameter = 60 mm) and PbS detector. The reflectance (R%) was measured between 200 and 2500 nm:

Table 2
Experimental design with factors and their levels

Levels	x_1, amount of granulation liquid (ml)	x_2, binder concentration (%, w/v)
Lower (−)	10	5
Base (0)	30	15
Higher (+)	50	25

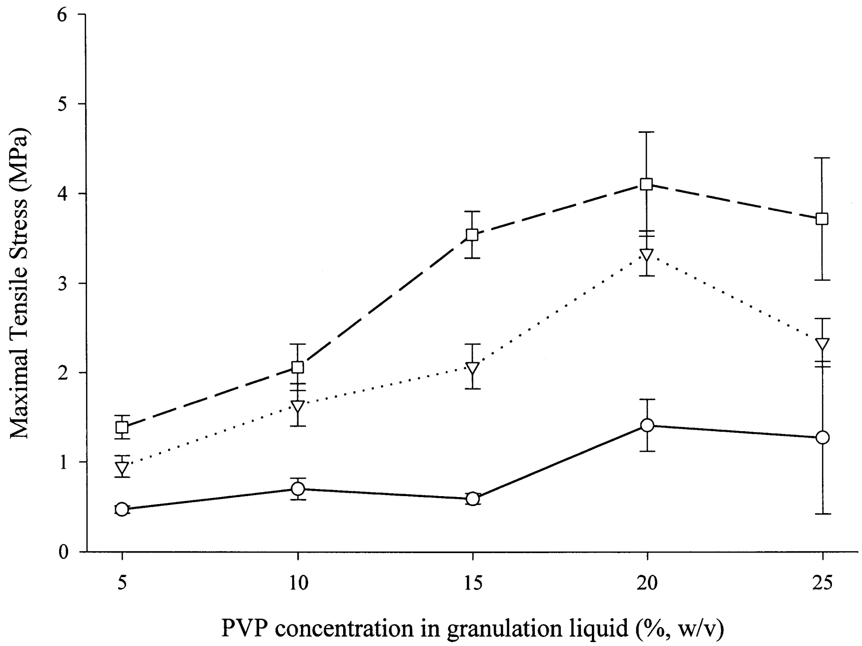

Fig. 2. The maximal tensile stress values shown per volume of granulation liquid added: (○) 10 ml; (▽) 30 ml; (□) 50 ml.

$$R\% = I_R/I_0 \times 100. \quad (5)$$

where I_R is the intensity of the diffusely reflected light collected by the integrating sphere and I_0 is the intensity of the incident light.

3. Results and discussion

The maximal tensile stress values resulting from the four-point breaking test were related to the volume of the granulation liquid and the PVP concentration. The data are shown in Fig. 2. When the binder concentration increased from 5 to 20% (w/v), the strength of the beams also increased for all the granulation liquid volumes used. The strongest beams were produced with a 20% binder concentration. The relative strength enhancement for a PVP concentration increase from 5 to 20% was around 33% and similar for the three granulation volumes used (10, 30 and 50 ml).

The same profiles were observed for the corresponding Young's moduli, reflecting the elasticity of the beam (Fig. 3). It is clear that the beams not only became stronger, but also more elastic when both the granulation liquid volume and the binder concentration were increased. The similar profile obtained for the three different granulation liquid volumes, indicated that the mechanical properties of the dried compacts were influenced by the dry binder concentration. Hancock et al. (1993) reported an increasing Young's modulus with increasing PVP binder volume fraction. The binder concentration in the granulation liquid was not specified but varied in order to produce dry agglomerate specimens with a 1.99 and 3.90% volume fraction of dry binder. Adams et al. (1989) reported that their compacted beam specimens containing sand and PVP became stiffer and stronger as the concentration and molecular weight of the binder increased.

Diffuse reflectance measurements allowed the evaluation of a homogeneous distribution of PVP in the granulated mass. A non-linear reciprocal relationship was found between the amount of Kollidon 25 added and the reflectance measured. The reflectance ($R\%$) decreased with increasing binder concentration indicating an increased binder presence in the granules (Table 3).

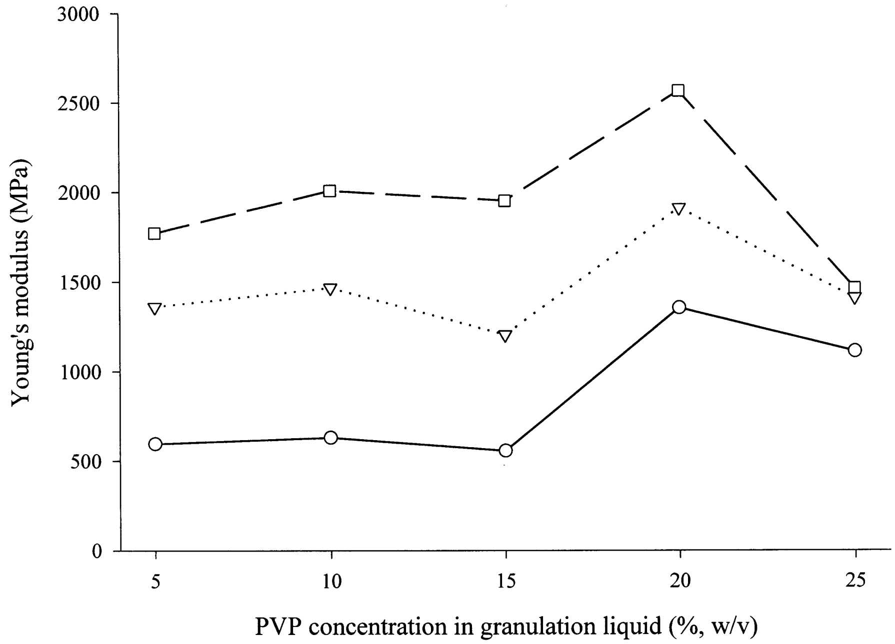

Fig. 3. The Young's modulus values shown in function of the granulation liquid volume added: (○) 10 ml; (▽) 30 ml; (□) 50 ml.

SEM pictures revealed that with the lowest amount of PVP added, the binder-film formed at the Microperl surface was often too brittle and too fragile to remain intact. Probably due to internal tensions in combination with the drying process, the PVP film showed numerous cracks and flaws (Fig. 4a). When higher amounts of PVP were added, a more uniform binder layer was formed around and between the Microperl spheres (Fig. 4b). Hancock et al. (1994) described the characteristics of granules prepared using glass ballotini and probably 70 ml of a 5% PVP (Kollidon 90) solution, reflecting exactly our findings on the granules prepared with 30 ml 25% Kollidon 25. It has to be mentioned that a 5% Kollidon 90 solution has a higher viscosity (± 40 mPa s^{-1}) than a 5% Kollidon 25 solution (± 2 mPa s^{-1}). From the comparison of the characteristics of the granules prepared with different amounts of granulation liquid, it was obvious that not only the amount of liquid but also the binder concentration determined the granule properties. The fracture plane of the beams prepared with four different volumes (10, 30, 50 and 65 ml) of a 20% PVP solution, was examined. In all cases, the beam fracture seemed to be primarily caused by adhesive failure since 'cup' formation was frequently observed (Fig. 5) and torn or fractured binder film indicating cohesive failure, was not detected. Cutt et al. (1986), who used lead glass ballotini, Kollidon 25 and dry PVP addition, reported, on the contrary, that in the broken granules cohesive failure was dominantly present. This observation was explained by the strong adherence of PVP to the ballotini and failure inside the binder film. As those granules were prepared by dry binder addition, a comparison with our results should be done with caution.

A decrease in the dynamic surface tension with increasing binder concentration was observed up to a concentration of 10% PVP. Above this concentration no surface tension changes were seen. A possible explanation for this phenomenon could be found in the ratio of polymer/water molecules at the liquid surface. Once all water molecules at the liquid surface are replaced by PVP molecules, the surface tension levels out to approximately constant values. This phenomenon was also reported by Parker et al. (1990). With increasing binder concentration, the dynamic con-

Table 3
The mean (± S.D.) surface tension and contact angle values of the granulation liquids and reflectance values of granules for the different PVP concentrations ($n = 5$)

Concentration of Kollidon 25 solution (%, w/v)	Surface tension (mN/m, S.D.; temperature, 20°C)	Contact angle (°; temperature, 20°C)	Reflectance values (%, $\lambda = 1900$ nm; granule-size, 0.5–0.76 mm)
Water	72.80 ± 0.14	67.3 ± 0.70	—
5	58.84 ± 0.19	69.8 ± 0.85	65.15 ± 0.55
10	51.60 ± 0.44	75.1 ± 1.26	62.83 ± 0.47
15	45.82 ± 0.31	80.2 ± 1.54	58.53 ± 0.63
20	47.51 ± 0.32	86.0 ± 1.67	57.67 ± 0.51
25	44.17 ± 0.19	92.2 ± 1.82	54.40 ± 0.38

tact angles of the granulation liquid measured against a Wilhelmy plate also increased (Table 3). This indicated that the system became less hydrophilic at higher PVP concentrations, hindering a homogeneous spreading of the granulation solution on the hydrophilic Microperl surfaces. This could result in a non-homogeneous binder distribution and in a different fracture behaviour of the beams. But the strength-increasing effect of a higher PVP concentration in the granulation liquid (5–20%) seemed more predominant than a non-homogeneous binder spreading. Also, the granulation liquid viscosity could have had an influence on the mixing efficacy during granulation. As for the production of the different batches the operational mixing conditions, such as speed and time, were kept constant this could have resulted in an inefficient mixing. A comparative study was performed using three different mixing procedures: a planetary mixer (Hobart) used at a low and a high mixing speed and a high shear mixer. All batches were produced using 50 ml of a 25% (w/v) PVP solution. No significance difference was observed between the mechanical properties of the beams (Kruskal–Wallis test; $p = 0.14$). After the mixing process, two major binder liquid characteristics, the surface tension and the contact angle, determine the binder draining and droplet coalescence on the Microperl surface. During drying, the PVP forms bridges between the substrate spheres and the strength of these bonds determines the final granule (beam) strength. As the contact angle of the granulation liquid increased with increasing PVP concentration, making the solution less hydrophilic, the draining process was more explicit causing 'storage areas' with clustered PVP. Subsequently weak areas were created where the spheres had only a thin PVP film around them, and where no solid bridges were present. In the case of the 25% PVP solution this negative 'contact angle effect' dominated the positive strengthening effect of the concentration increase of the binder. Because the beam strength is dependent on the weakest area in the beam, the 25% PVP beam strength determination resulted in lower stress and Young's modulus values. This was supported by the statistical analysis using factorial design.

The following polynomial equation ($r^2 = 0.9518$, root mean square = 1.4752), obtained after a significance test at 95% confidence level, represents the effect of formulation factors (x_1,x_2) on the mean maximum tensile stress values of the rectangular beam specimens (y). To avoid the artifact caused by the different magnitude of the factors, coded levels were applied.

$$y = 2.04 + 1.05x_1 + 0.75x_2 + 0.045x_1^2 - 0.38x_2^2 + 0.38x_1x_2 \quad (6)$$

The positive sign of the coefficients indicate an increasing effect, while the negative signs indicate a decreasing effect on the corresponding response. Both the coefficients of the independent variables are positive ($b_1 = 1.05$; $b_2 = 0.75$), which indicates their increasing effect on the corresponding response. Due to the negative quadratic effect ($b_{22} = -0.38$) of the binder concentration, caused by the 'negative contact angle effect', its main effect is less dominant at higher binder concentrations. Table 4 summarizes the measured and the predicted mean maximum tensile stress values of the rectangular beam specimens. The second-order polynomial model described the effect of the selected independent variables with good correlation.

Critical stress intensity factors and strain energy release rates were not determined because it required a modification of the four-point beam-bending technique by inserting a small notch across the center of the surface of the testbeam. Although this technique has been used by several authors (Mashadi and Newton, 1987; Mullier et al., 1987; Adams et al., 1989), it was impossible to

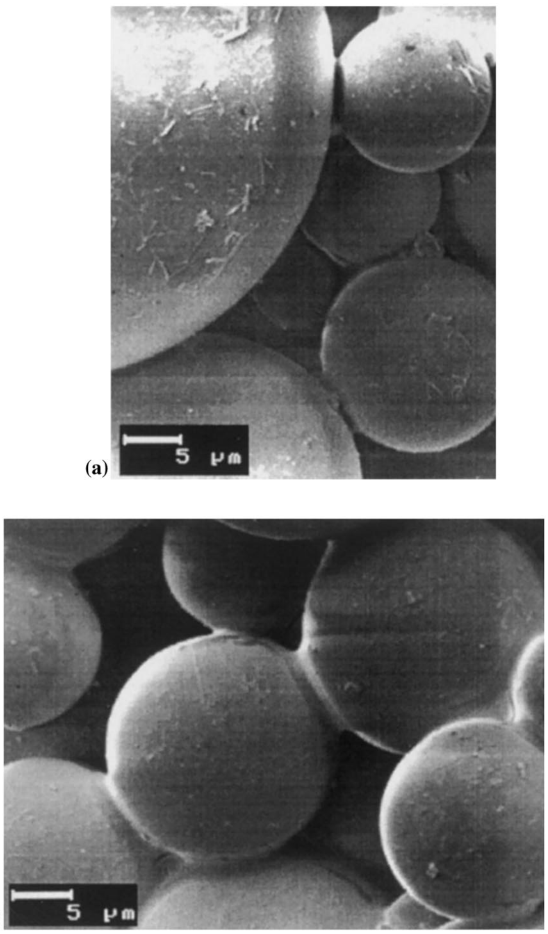

Fig. 4. (a) SEM pictures of Microperl granules, granulated with 30 ml 5% (w/v) Kollidon 25 showing cracks and flows in the PVP films. (b) Microperl granules, granulated with 30 ml 25% Kollidon 25, showing uniform binder films.

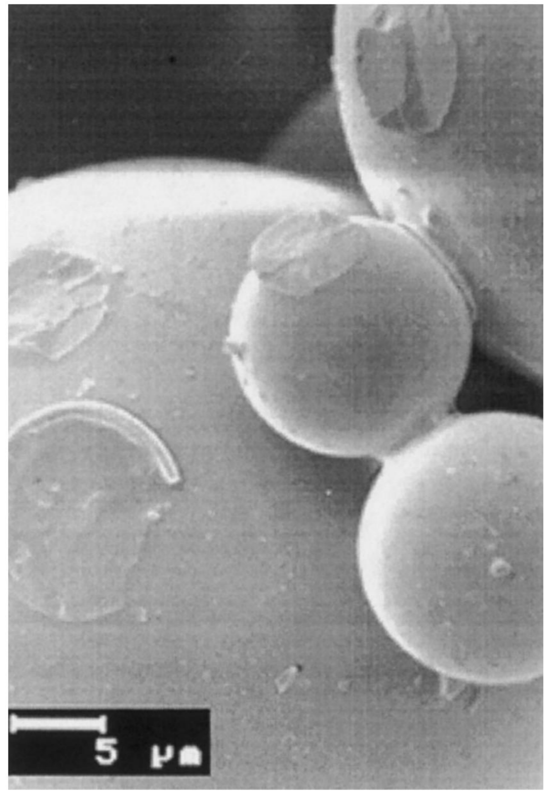

Fig. 5. The fracture plane of a beam prepared with 50 ml 20% PVP solution.

obtain a sharp and well-defined notch in the surface of our glass beams.

The relative humidity during the storage decreased the strength of the rectangular beam compacts, confirming the importance of environmental storage and test conditioning. The maximum tensile stress values for beams produced with 30 ml of 15% PVP solution and stored at 35, 45 and 65% R.H. were 1.77 ± 0.32, 1.44 ± 0.20 and 1.40 ± 0.06 MPa, respectively.

Both with the Kollidon 25 and the Kollidon 90 a linear relationship was observed between the maximal tensile stress and the total amount of binder added. No significant difference was observed between the stress–strain curves of the two polymer grades. Although Adams et al. (1989) reported that the effect of an increasing PVP molecular weight was consistent with the rapid increase in toughness with molecular weights above a value of about 10^5, it can be said that in

Table 4
Randomized matrix of the two-factor, three-level face-centered central composite factorial design (average of 20 beams)

Trial	Controlled factors		Response parameter, y	
	x_1 (ml)	x_2 (%, w/v)	Measured (MPa)	Predicted (MPa)
1	+	0	3.54	3.13
2	−	−	0.47	0.28
3	0	−	0.95	0.91
4	−	+	1.27	1.02
5	0	0	2.07	2.04
6	+	−	1.39	1.62
7	0	+	2.33	2.41
8	+	+	3.71	3.88
9	−	0	0.59	1.03

our study the molecular weight of the PVP binder had no effect on the strength of the beams.

It can be concluded that the mechanical properties of the PVP/glass spheres granule system were determined by the balance between the weakening effect of the inhomogeneous binder distribution, caused by the less hydrophilic character of the more concentrated granulation liquid and the strengthening effect of the increased binder concentration. This was supported by SEM pictures and by a second-order polynomial model.

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