

Physico-chemical characterization of zein as a film coating polymer A direct comparison with ethyl cellulose

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Abstract

Zein, an alcohol-soluble protein contained in the endosperm tissue of *Zea mais*, occurs as a by-product of corn processing. Although zein has been empirically employed as an edible coating for foods and pharmaceuticals for decades, it has not attracted considerable attention as a possible alternative for film-forming agents in drug formulations such as derivatives of cellulose or polyacrylates. In this report, the thermal, thermomechanical, water sorption and gas barrier properties of zein and plasticized mixtures of zein are discussed. With the objective of classifying these properties within the field of polymers used as pharmaceutical film formers, zein was compared with various types of ethyl cellulose that had a degree of substitution (DS) in the range 1.7–2.6. In order to quantify the plasticizing efficiency of low molecular weight compounds when added to zein, the compatibility of the mixtures was investigated by means of dynamic-mechanical thermal analysis (DMTA). The esters of tartaric acid were found to have superior properties with respect to miscibility, depression of the glass transition temperature and reduced water sorption of the respective mixtures. With regard to solvent-free extrusion, pressure-volume-temperature measurements were performed on mixtures of zein and diethyl tartrate and evaluated according to the Simha-Somcynsky equation of state for multicomponent systems. Generally, the results give reason to believe that zein might serve as an inexpensive and most effective substitute for the fast-disintegrating synthetic and semi-synthetic film coatings currently used for the formulation of substrates that allow extrusion coating.

Keywords: Zein; Ethyl cellulose; Film coating; Properties

1. Introduction

Film-forming polymers are widely used in galenic formulation to ensure physical and chemi-

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cal stability of the active ingredients. They may be subdivided into three categories including: (1) the synthetic compounds, such as polyacrylates, -methacrylates, -aminoalkyl methacrylates and -methacrylesters; (2) the semi-synthetic compounds, such as methyl-, ethyl-, hydroxypropyl-, hydroxypropylmethyl cellulose and several esters, especially cellulose acetate phthalate; and (3) the natural compounds, such as proteins like gelatin, albumin, casein and zein or polysaccharides like starch, alginates, pectin, carrageenan and dextrans. Due to the high amount of hydrophobic amino acids (Landry and Guyon, 1984) zein shows a low water uptake compared with other proteins like casein or gelatin (Bull, 1944; Gennadios and Weller, 1994) and chemically non-modified polysaccharides. Therefore it provides a noticeably narrow variability of the mechanical and gas barrier properties in the range of moderate relative humidity. Since these properties break down at high water activity ($a_w > 0.8$), zein exhibits the necessary compromise for a swellable and fast-disintegrating coating that also ensures sufficient protection.

A knowledge of the thermal, thermomechanical, sorption and diffusion properties of film formers is of fundamental interest, since these properties determine the behaviour of the materials during processing, shelf life and drug release. Extensive experimental work regarding thermomechanical characterization and plasticization of cellulose derivatives has been reported (Entwistle and Rowe, 1979; Porter and Ridgway, 1983; Rowe et al., 1984; Sakellariou et al., 1985, 1986). Studies on the water vapour- and oxygen-permeability of cellulose derivatives and polymethacrylate systems have been performed by Lehmann (1988), List and Kassis (1982a,b) and Gurny et al. (1977).

However, investigations concerning the corresponding properties of zein are comparatively rare. Mechanical and barrier properties of cast zein films from ethanol-glycerol solutions were described and compared with those of wheat protein films by Gennadios et al. (1993a,b) and Ayt et al. (1991). Magoshi et al. (1992) performed X-ray diffraction, calorimetric and thermogravimetric studies on cast films of zein in

order to characterize the transition from random-coil conformation to β -form crystallites and to investigate the thermal degradation of zein.

A large amount of basic work in the characterization of zein has been done by Esen (1980, 1987) and Landry and Guyon (1984) in which zein was separated into fractions of different molecular weight by electrophoresis, chromatography and extraction methods. Other authors have investigated the heterogeneity of zein with respect to disulfide linkages (Turner et al., 1965; Rewa and Brückner, 1979). Larkins et al. (1984) proposed hypothetical structures of the two main proteins of native zein ($M = 19$ and 22 kDa), which contain a similar icosapeptide that is tandemly repeated nine times in the central part of the protein.

Particularly useful information for the processing of zein from solution is contained in an extensive work by Evans and Manley (1941, 1944) and Manley and Evans (1943) who discuss the solubility of zein in primary, binary and ternary solvents. With regard to thermoplastic processing, the contributions of Menjivar and Rha (1981), who investigated the extrudate expansion of concentrated zein solutions in ethanol and of Bruechert et al. (1988), who analyzed volatile compounds generated by extrusion of systems containing zein, have to be mentioned. In addition to coating applications (Autant et al., 1984; Ardaillon and Bourrain, 1987; Haralampu et al., 1991), some efforts have been made to produce thermoplastic materials based on zein (Swallen, 1941; Pinner, 1950; Cole and Daumesnil, 1988).

The reasons that may have prevented zein achieving a wider acceptance are due to the modest efforts made in characterizing its specific properties, resulting in a basic uncertainty about the potential fields of application. Therefore, zein has been rather empirically employed to date. Furthermore, the pharmaceutical industry has predominantly concentrated on water-based formulations due to the strict requirements concerning organic solvent residues in the products, improvements in processing safety, and reduction of solvent emissions.

Although Zein is definitely not water soluble at neutral pH, it is highly swellable compared with

typical structure proteins such as silk and keratins and a solubility of almost 20% in alkaline solutions has been reported (Swallen, 1941). Since zein and mixtures with suitable plasticizers still exhibit a more or less pronounced hydrophilic character, it is difficult to obtain stable aqueous dispersions or emulsions. Hence, investigations regarding the thermoplastic properties seem to be rather promising for the processing and future use of zein.

The goal of the present contribution is to systematically characterize the relevant properties of zein and appropriate mixtures with compounds of low molecular weight with respect to their applicability as film-coating materials. These investigations include the evaluation of pressure–volume–temperature data and the performance of water vapour and oxygen sorption and diffusion measurements. The properties of the zein-based materials are directly compared with those of ethyl cellulose in the degree of substitution (DS) range 1.7–2.6 (Beck and Tomka, 1996).

2. Experimental

2.1. Materials

Zein F 4000 (regular grade) was purchased from Benzian AG (Luzern, Switzerland). The ethyl celluloses (EC) investigated had a DS of 2.60 (Hercules T 200), 2.48 (Hercules N 50), 2.40 (Hercules K 5000), 2.12, 1.90 and 1.69 determined by a modification of the Zeisel method described by Jullander and Lagerström (1963). The latter three products were received from Aqualon East BV (Rijswijk, The Netherlands). The plasticizers were used without further treatment. The following designation for the manufacturers was used: (1) Th. Goldschmidt AG, Essen, Germany; (2) Morflex, Greensboro, NC, USA; (3) Degussa AG, Frankfurt, Germany; (4) Fluka Chemie AG, Buchs, Switzerland; (5) Aldrich Chemie, Buchs, Switzerland.

The plasticizers were selected without considering regulations for food and pharmaceutical additives and it is realised that some of them would not normally be used in film coating because of

their toxicity. Nevertheless, they provide data regarding the plasticizing efficiency of given chemical structural units. The denotations are as follows:

BL:	lacticacid butylester (4)
CLAM:	6-caprolactam (4)
CLON:	6-caprolactone (4)
CV:	carvone (4)
DBT:	tartaricacid dibutylester (4)
DDD:	1,2-dihydroxydodecane (3)
DEG:	diethylene glycol (4)
DET:	tartaricacid diethylester (4)
ELV:	levulinicacid ethylester (4)
GLY:	glycerol (4)
GMS:	glycerol monostearate (1)
LAES:	levulinic acid (5)
LS:	lauric acid (4)
PEG 300:	polyethylene glycol ($M \sim 300$ g/mol) (4)
PS:	palmitic acid (4)
SB:	D-sorbitol (4)
SS:	sebacic acid (4)
TA:	glycerol triacetate (4)
TB:	glycerol tributyrate (4)
TBC:	citricacid tributylester (2)
TEC:	citricacid triethylester (2)
TEG:	triethylene glycol (5)

2.2. Methods

2.2.1. Sample preparation

The samples used for the dynamic–mechanical thermal (DMT) and the pressure–volume–temperature (PVT) analyses were prepared by first thermoplasticizing the premixed polymer–plasticizer systems at 50–180°C for 5–10 min in a Brabender kneader (Brabender OHG, Type W 30). The selection of the mixing temperature depends strongly on the desired viscosity of the melt. In order to protect the pure polymers from thermal degradation, small portions of water were added to lower their glass transition temperature (T_g). The materials were then compression moulded (Given P.H.I. PW-2200) to regularly shaped bodies (dimensions: 40 × 12 × 1 mm) at

185°C, cooled at a rate of 10°C/min, dried to constant weight and annealed in desiccators for 4 weeks at room temperature over P₂O₅.

Films for permeation studies were prepared by dissolving the polymer and the plasticizer in a suitable solvent and casting the solutions on glass (ec) or polystyrene (zein). For this purpose, the solvents selected were dichloromethane/ethanol (4:1) v/v for ethyl cellulose (DS = 1.7) and ethyleneglycol monomethylether for zein. The solvents were allowed to evaporate at room temperature. Upon removal from the plate, the films were placed in a vacuum oven at slightly elevated temperatures to remove residual solvent and subsequently dried over P₂O₅ at 25°C. The average thickness (*d*) of the films was determined from the weight and density of samples that had a defined cross-section.

2.2.2. Density measurement

The density of the materials was determined by weighing the dry samples in air and in paraffin oil at 25°C. The density of the oil was measured with the aid of a standardized glass body of known volume (accessory equipment FNR 33360 for the Mettler analytical balance AE 260).

2.2.3. Dynamic-mechanical thermal analysis (DMTA)

The mechanical measurements were carried out using an Mk II DMT-Analyser (Polymer Laboratories) over a temperature range of 20–200°C (max.) at a heating rate of 2°C/min. The upper temperature was limited due to the rapidly decreasing mechanical stability of the plasticized samples above their glass transition temperature. All experiments were performed under a dry nitrogen atmosphere. In the dual cantilever bending mode, an oscillation frequency of 1 Hz (strain: 32–64 μm) was applied to the center of the sample (5 mm free length of the sample between driving shaft and frame). *T_g* was determined from the maximum of the loss tangent (tan δ).

2.2.4. Pressure-volume-temperature (PVT) analysis

The measurements were performed using a PVT apparatus constructed by Gnomix Research. The

change in the specific volume was recorded over a temperature range 25–200°C and a pressure range 10–100 MPa in the ITS (isothermal standard) mode. Starting at 25°C and 10 MPa, the sample was exposed to a stepwise increase of hydrostatic pressure under isothermal conditions. To account for time-dependent dilatational relaxations, the sample was held for 60 s under constant conditions before recording the specific volume. After reaching 200 MPa, the pressure was reduced to 10 MPa and the sample heated to the next nominal temperature at a heating rate of approximately 1°C/min.

2.2.5. Heat flow calorimetry

Heat flow calorimetry experiments were carried out with a Series 7 DSC calorimeter (Perkin-Elmer) in pressure-resistant stainless steel capsules. In order to evaluate the *T_g* of the pure polymers, the dried samples were first preheated to 185°C (zein-containing samples) and 200°C (ec-containing samples) respectively, kept for 10 min at this temperature, cooled rapidly to 30°C at a rate of 100°C/min, and reheated at a rate of 10°C/min, thereby allowing *T_g* to be determined. *T_g* is indicated by a discontinuity in the heat capacity (*C_p*) and was evaluated as the maximum of the first derivative of the *C_p* curve. Samples containing water were conditioned at defined water activities (*a_w*) in open capsules for 3 weeks at 25°C before the capsules were sealed and measurements made.

2.2.6. Sorption isotherms

The sorption isotherms were recorded by the isopiestic method at 25°C. Saturated solutions of salts and mixtures of sulphuric acid and water were used to establish the desired water activities in the sample containers (Beck and Tomka, 1996). The water activity (*a_w*) was taken as the water vapour pressure of the solutions normalized by the vapour pressure of pure water. The milled samples were dried to constant weight over P₂O₅ at 40°C in a vacuum oven and then kept in desiccators for 3–4 weeks at the required water vapour pressures. The desiccators were stored in a thermostatic chamber at 25 ± 0.1°C and the water uptake was determined gravimetrically. The vol-

ume fraction (ϕ) of sorbed water was calculated from the weight fractions (w) and densities (ρ) of the pure components assuming a linear relationship between composition and density:

$$\phi(\text{H}_2\text{O}) = \frac{w(\text{H}_2\text{O})/\rho(\text{H}_2\text{O})}{w(\text{H}_2\text{O})/\rho(\text{H}_2\text{O}) + w(\text{ec})/\rho(\text{ec})} \quad (1)$$

2.2.7. Permeation measurements

The water vapour transmission rate was determined according to ASTM F-1249. The oxygen permeability as a function of relative humidity was performed according to ASTM-3985.

3. Results and discussion

3.1. Thermal analysis and volumetric properties of zein

The heat flow calorimetry experiment performed on non-pretreated Zein F 4000 provided two endothermic transitions during the first step of the temperature program at 139.7°C ($\Delta H \sim 8.2$ J/g) and at 186°C (less pronounced). By rapidly cooling and reheating the sample, these transitions disappear and a distinct glass transition is instead indicated at 136°C ($\Delta C_p \sim 0.40$ J/g per K).

The latter transition is confirmed by a discontinuity of the thermal expansivity, α ($\alpha = (\partial \ln V / \partial T)_P$), and the compressibility, κ ($\kappa = -(\partial \ln V / \partial P)_T$), at 139.4°C (Fig. 1) detected by the pressure–volume–temperature analysis of a zein sample that was previously plasticized with water, compression moulded and subsequently dried again. The pressure dependence of the glass transition, dT_g/dP , in the range 10–100 MPa yielded a linear slope of 0.18 K/MPa (Fig. 2). This value is noticeably lower than that of ethyl cellulose (ec-2.5: $T_g = 125.5^\circ\text{C}$, $dT_g/dP = 0.30$ K/MPa and ec-2.1: $T_g = 143.6^\circ\text{C}$, $dT_g/dP = 0.26$) and reflects the low compressibility of zein melts.

The equation of state derived by Simha and Somcynsky (1969) relates the compressibility of polymers at temperatures above T_g to the fraction of unoccupied volume occurring in the materials. This quantity is of considerable interest since its magnitude and distribution affect the gas barrier

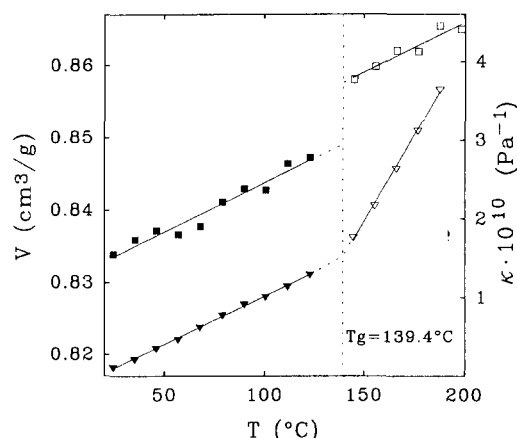


Fig. 1. Specific volume, V , (\blacktriangledown , \triangledown) and compressibility, κ , (\blacksquare , \square) of zein vs. temperature, T ($P = 1$ atm).

properties towards slightly soluble and small permeants like oxygen, nitrogen or the inert gases. It is commonly supposed that the molecular transport of these penetrants is enabled by microvoids or 'holes' in the polymer lattice that have a volume exceeding a certain critical volume (for example the volume of the diffusing gas molecule). In this context, it has previously been shown that the distribution of the unoccupied volume as a func-

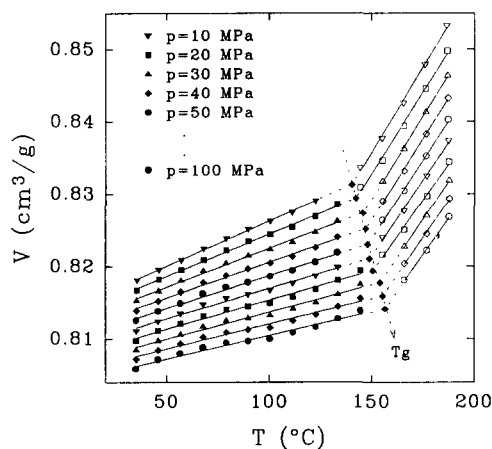


Fig. 2. Isobars of the specific volume, V , of zein vs. temperature, T (pressure as indicated). Filled (hollowed) symbols mark the data below (above) the glass transition temperature, T_g . (\blacklozenge), T_g ; (—), linear fits.

Table 1

Density in the glassy (ρ_g) and the rubbery (ρ_m) state, respectively, and internal pressure (P_i) of ethyl cellulose and zein ($P = 1$ atm). P_i calculated according to Eq. (2)

Compound	ρ_g (g/cm ³) ($T = 25^\circ\text{C}$)	ρ_m (g/cm ³) ($T = 175^\circ\text{C}$)	P_i (MPa) ($T = 175^\circ\text{C}$)
EC (DS = 2.5)	1.114	1.032	362
EC (DS = 2.1)	1.152	1.084	370
EC (DS = 1.9)	1.167	1.105	387
EC (DS = 1.7)	1.186	1.127	421
Zein	1.222	1.176	608

tion of the volume of the individual molecular holes (v_h) can be modelled by assuming an exponential dependence according to the Boltzmann distribution function. In so doing, the probability $P(v_h)$ of finding a hole of volume v_h at a given temperature T is proportional to $\exp(-v_h \cdot E_{\text{coh}}/T)$ (Beck and Tomka, 1996). Therefore, an increased value of E_{coh} leads to a significantly reduced accessible fraction of the unoccupied volume towards a penetrant of a given molecular volume and finally causes a markedly smaller diffusion coefficient of the penetrant. In the case of zein, this concept predicts outstanding barrier properties compared to ethyl cellulose which is confirmed by direct measurements discussed in the last section.

At low pressures, the compressibility is inversely proportional to the internal pressure (P_i) Eq. (2). U and α denote the internal energy and the thermal expansivity, respectively.

$$P_i = \left(\frac{\partial U}{\partial V} \right)_T = T \left(\frac{\partial P}{\partial T} \right)_V - P \cong T \frac{\alpha}{\kappa} \quad (2)$$

P_i is closely related to the cohesive energy density (E_{coh}) of the systems. Curro (1974) introduced an empirical proportionality factor n , where $n = P_i/E_{\text{coh}}$. Depending on the coordination number and the assumed potential energy function between the segments of the modelled quasi-lattice, n is found to be in the range 0.81–1.15. For simple liquids and polymer melts, E_{coh} may be directly obtained by fitting suitable equations of state to the measured PVT data. Unfortunately, zein and ethyl cellulose exhibit very few isotherms in the range between T_g and temperatures causing thermal decomposition. Therefore,

the numerical evaluation does not provide physically significant parameters for the pure polymers and, consequently, is restricted to plasticized mixtures that show a T_g below approximately 110°C (Beck and Tomka, 1996). However, at this point it is sufficient to obtain a qualitative impression of E_{coh} by calculating P_i with the help of the compressibility and volume expansivity data measured above T_g . Table 1 and Fig. 3 display the internal pressure and the volumetric properties of zein versus ethyl cellulose. Density, compressibility and thermal expansivity show values for zein which may correspondingly be expected for ethyl cellulose in the substitution range 1.1–1.3.

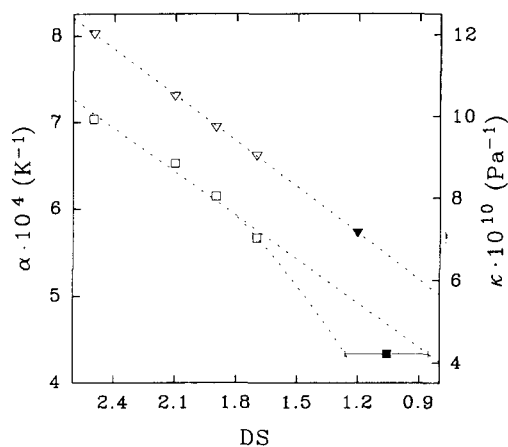


Fig. 3. Thermal expansivity, α , ($T > T_g$; ∇) and compressibility, κ , ($T = 175^\circ\text{C}$; \square) of ethyl cellulose vs. DS. (---), Extrapolation of EC-data vs. DS; (\blacktriangledown , \blacksquare), corresponding values for zein.

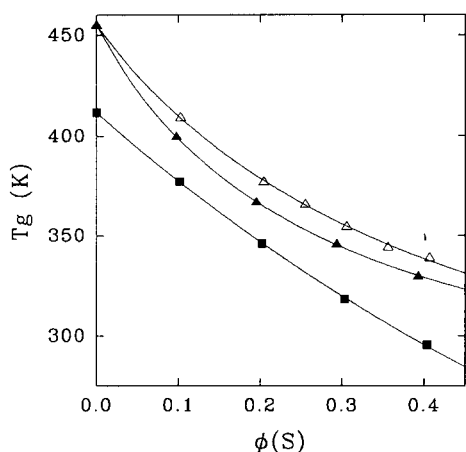


Fig. 4. Thermomechanical glass transition temperature, T_g , of binary polymer–plasticizer mixtures as a function of the volume fraction of the plasticizer, $\phi(S)$ fitted according to Eq. (3). (Δ), EC (DS = 1.9)–TEC: $T_g(P) = 454.9$ K, $k_1 = 3.23$, $k_2 = 284.4$ K; (\blacktriangle), EC (DS = 1.9)–DET: $T_g(P) = 454.9$ K, $k_1 = 4.60$, $k_2 = 288.1$ K; (\blacksquare), zein–DET (shifted by -40 K), $T_g(P) = 451.9$ K, $k_1 = 1.66$, $k_2 = 275.4$ K.

3.2. Plasticization of zein and low substituted ethyl cellulose

With the objective of investigating the actual T_g -depression of zein by different plasticizing compounds, dynamic–mechanical measurements were performed on compression-moulded samples. Figs. 4 and 5 illustrate the plasticizing efficiency of different plasticizers on zein and low substituted ethyl cellulose. Although the thermomechanical spectrum reflects primarily the long time relaxation modes and, hence, is not capable of providing direct information regarding the thermodynamic state of the material, its results may empirically be correlated with data from volumetric or calorimetric analysis. Thereby, the ‘true’ glass transition temperature, as defined by a discontinuity in C_p , α and κ , is obtained by shifting the temperature of the maximum loss tangent downward by approximately 30 K (Beck and Tomka, 1996). In contrast to DMTA, the signals of differential scanning calorimetry (DSC) and PVT measurements successively broadened with increasing plasticizer content creating difficulty in accurately evaluating T_g directly.

Numerous efforts have been made to describe the concentration dependence of the T_g of binary mixtures (Kelley and Bueche, 1961; Gordon et al., 1977; Couchman and Karasz, 1978). The respective theories either rely on the additivity of the free volume or on the loss of the configurational entropy at T_g and may generally be expressed by the following analytical relationship:

$$T_g = \frac{[1 - \phi(S)] \cdot T_g(P) + k_1 \cdot \phi(S) \cdot k_2}{[1 - \phi(S)] + k_1 \cdot \phi(S)} \quad (3)$$

$T_g(P)$ denotes the T_g of the pure polymer and $\phi(P) = 1 - \phi(S)$ and $\phi(S)$ are the volume fractions of the polymer and the solvent. However, it has to be stated that random molecular miscibility of the components is necessarily required to ascribe physical significance to the parameters k_1 and k_2 . Otherwise, they serve rather to empirically fit the measured T_g data than being particularly useful in a predictive manner.

Useful plasticizers for zein show a narrow range. With the exception of extremely polar solvents such as glycerol and sorbitol and the cyclic ester (CLON) and amide (CLAM), which may achieve internal plasticization by chemically reacting with the polymer, a marked dependence on hydrogen bond formation capability of the plasti-

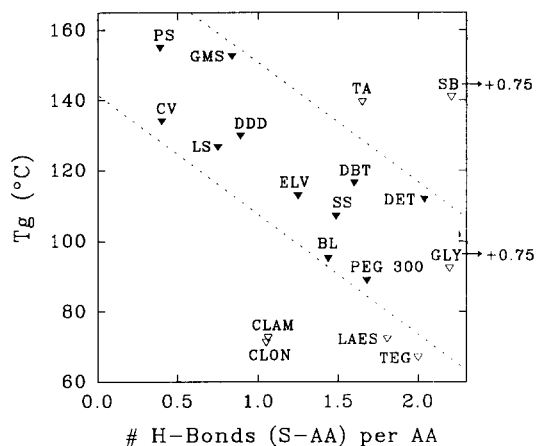


Fig. 5. Thermomechanical glass transition, T_g , of zein–plasticizer mixtures at a weight fraction, $w(S)$, of the plasticizer of 0.20 ($\#$ is the theoretical number of H-bonds between an amino acid of the protein and the plasticizer molecules in the mixture; see text).

cizer is indicated (Fig. 5). The x -axis displays the number of potential intermolecular H-bonds between an average-sized amino acid ($M(\text{AA}) \sim 120$ g/mol) of the protein chains and the plasticizer molecules. In order to obtain this value, the total number of H-bonds (S-AA) is summarized according to the chemical structure of the plasticizer molecules and subsequently divided by the number of average-sized amino acid monomers. As acceptors, the oxygen (nitrogen) atoms are expected to form 2(1) H-bond(s). Additional single (donor) H-bonds are ascribed to X-H units, where X = oxygen (nitrogen). Thermoplasticization of zein with esters of citric acid or polyethylene glycols ($M > 1000$ g/mol) could not be achieved.

3.3. Thermodynamic properties of plasticized mixtures of zein

The striking effect of diethyl tartrate as the plasticizer is recorded in Fig. 6. The isothermic plot demonstrates the basic change in PVT properties of zein at temperatures below 130°C when mixed with the low molecular weight component. Due to the increased mobility of the protein chains caused by the dissolution of interpolymer hydrogen bonds, the glassy solidification of the system takes place at a significantly reduced temperature. As a result of the larger thermal expansivity in the rubbery as compared to the glassy state, the isotherms are successively shifted downward, thereby increasing the PVT surface.

The compressibility (κ) of zein-plasticizer mixtures is markedly smaller compared to plasticized ethyl cellulose ($\text{DS} = 2.1$) as shown in Fig. 7. It can be seen that the compressibility exhibits a discontinuity with concentration thereby indicating the volumetric glass transition of the mixtures. Thus, thoroughly dried cast films of zein containing less than 30% diethyl tartrate are rigid and brittle at 25°C , whereas a plasticizer concentration of 35% is already sufficient to provide an elasticity to a point that allows easy handling of the films. Due to the lack of crystalline domains, materials that contain more than 35% of the plasticizer are increasingly viscous and tend to stick together.

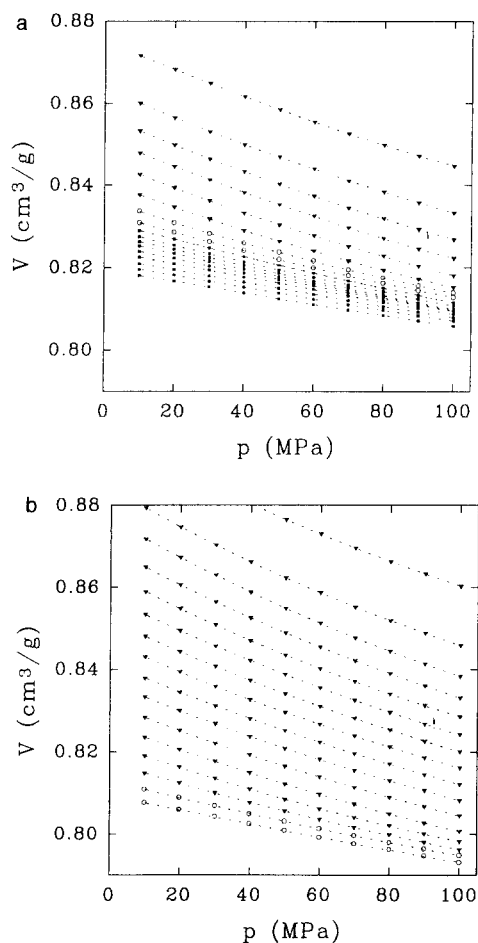


Fig. 6. (a) Equidistant isotherms ($\Delta T \sim 11^\circ\text{C}$) of the specific volume, V , of zein vs. pressure. (\blacktriangledown), $155\text{--}209^\circ\text{C}$ ($T > T_g$); (\circ), $134\text{--}145^\circ\text{C}$ ($T \sim T_g$); (\blacksquare), $35\text{--}123^\circ\text{C}$ ($T < T_g$); (---), third-order polynomial fits. Thermal decomposition takes place at $T > 200^\circ\text{C}$. (b) Equidistant isotherms ($\Delta T \sim 11^\circ\text{C}$) of the specific volume, V , of a zein-DET mixture ($w(\text{DET}) = 0.30$) vs. pressure. (\blacktriangledown), $57\text{--}198^\circ\text{C}$ ($T > T_g$); (\circ), $35\text{--}46^\circ\text{C}$ ($T \sim T_g$); (---), third-order polynomial fits. Thermal decomposition takes place at $T > 190^\circ\text{C}$.

Taking advantage of the principle of corresponding states, extended PVT data are reduced by the determination of three characteristic scaling parameters according to suitable equations of state for liquids and polymer melts. As an example, the hole theory of Simha and Somcynsky for multicomponent systems (Jain and Simha, 1980) was applied (see Appendix). The underlying the-

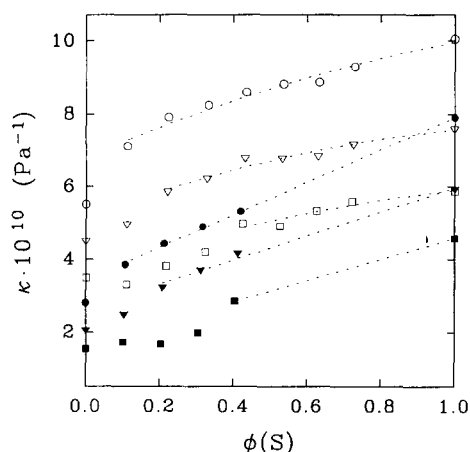


Fig. 7. Compressibility, κ , of polymer-plasticizer mixtures (filled symbols: zein-DET; hollowed symbols: EC (DS = 2.1)-TBC) vs. volume fraction, $\phi(S)$, of the plasticizer. (■, □), 25°C; (▼, ▽), 75°C; (●, ○), 125°C; (- - -), $T > T_g$.

ory and formalisms are described elsewhere in detail (Jain and Simha, 1980; Beck and Tomka, 1996) and we restrict ourselves to summarizing the results for mixtures of zein and diethyl tartrate in Table 2. The theory allows the calculation of the cohesive energy density of the plasticized systems which is compared with different ethyl cellulose-plasticizer mixtures and unsubstituted starch plasticized by glycerol in Table 3. Once again, it was found that the cohesive properties of zein are comparable with that of ethyl cellulose with a DS of approximately 1.3.

3.4. Water sorption of zein

For many applications, the most important

Table 3

Cohesive energy density (E_{coh}) at 25°C of polymer-plasticizer mixtures with differing polarity according to the Simha-Somcynsky equation of state (Jain and Simha, 1980) at a weight fraction of the plasticizer of 0.30. The equation for the calculation of E_{coh} is listed in the Appendix.

Polymer	Plasticizer	E_{coh}^a (J/cm ³)	Reference
EC (DS = 2.5)	TB	458	b
EC (DS = 2.1)	TBC	530	b
EC (DS = 1.7)	DET	633	b
Zein	DET	760	c
Starch	GLY	1300	d

^a As discussed in Section 3.1, E_{coh} is calculated based on the scaling parameters P^* , V^* and T^* evaluated in the temperature range above the glass transition temperature, T_g . At temperatures below T_g , E_{coh} may be obtained by using extrapolated values for the occupied volume fraction (ν) at $T < T_g$.

^b Beck and Tomka (1996).

^c See Table 2.

^d Sala and Tomka (1993).

functional characteristic of a coating is its resistance to the sorption and transport of water. The glass transition temperature as well as the permeation rates of water molecules in the polymer lattice are highly dependent on the equilibrium water sorption of the film. Sorbed water acts as a plasticizer by lowering the glass transition temperature of the polymer and enhancing the diffusional processes involved in drug release. The striking plasticizing efficiency of water on zein (Fig. 8) may be utilized to control the extrusion temperature in the case of encapsulations of

Table 2

Density (ρ) at $T = 25^\circ\text{C}$, scaling parameters (P^* , V^* , T^*) and cohesive energy density (E_{coh}) at $T = 125^\circ\text{C}$ of mixtures of zein and diethyl tartrate according to Jain and Simha (1980) as a function of the weight fraction (w) of diethyl tartrate. The underlying equation of state is listed in the Appendix. The accuracy of the fit is given by the average absolute deviation in pressure ΔP (Beck and Tomka, 1996)

w (DET)	ρ (g/cm ³)	T (°C)	$\langle r \rangle$	P^* (MPa)	V^* (cm ³ /g)	T^* (K)	ΔP (MPa)	E_{coh} (J/cm ³)
0.10	1.231	120–175	32.7	1167.6	0.8063	12541	2.4	787
0.20	1.239	95–175	16.9	1110.0	0.8050	11950	3.8	703
0.30	1.244	65–175	11.6	1114.7	0.8035	11071	3.2	687
0.40	1.244	45–175	9.0	1074.9	0.8010	10501	1.7	655
1.00	1.203	25–175	4.2	997.9	0.7981	8281	1.5	537

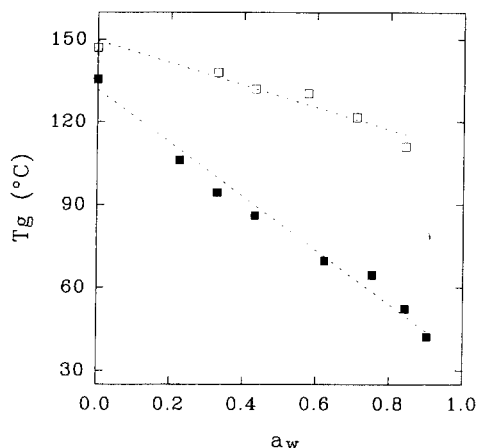


Fig. 8. Glass transition temperature, T_g , of zein (■) and ethyl cellulose (DS = 1.9) (□) vs. water activity, a_w (T_g measured by heat flow calorimetry).

thermo-sensitive agents and to keep the amount of organic plasticizers at the necessary minimum. Hydrophilic plasticizers like glycerol or the ethyleneglycols typically increase the water sorption of zein as shown in Table 4.

Fig. 9 indicates that the amounts of water sorbed by zein are comparable to those of ethyl cellulose with a DS in the range 1.2–1.5, which is in fair agreement to the results discussed in the preceding sections. However, it is worth noting

Table 4

Water uptake (in g/100 g of dry mixture) of zein–plasticizer mixtures (weight fraction of the plasticizer $w(S) = 0.20$) at a water activity (a_w) of 0.753 ($T = 25^\circ\text{C}$).

Plasticizer	Water content (g/100 g)
GLY	20.4
TEG	16.4
SB	15.6
PEG 300	13.9
CLAM	11.0
LAES	10.9
Pure zein	10.5
GMS	9.4
DDD	9.1
DET	8.9
TA	8.4
SS	7.7
DBT	7.5

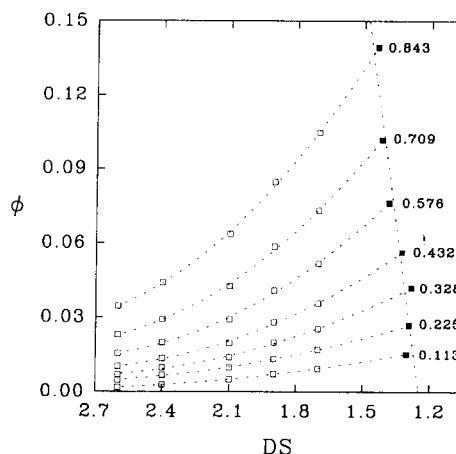


Fig. 9. Volume fraction, ϕ , of sorbed water in ethyl cellulose (□) vs. DS at 25°C and at water activities as indicated. (---), Second-order polynomial extrapolation of EC-data; (■), corresponding values for zein.

that the sorption mechanisms of water in ethyl cellulose differ from typical Flory-type sorption (Flory, 1942) by showing non-random distribution or ‘clustering’ of the sorbed water predominantly at high water activities (Beck and Tomka, 1996). This provides justification for the assumption that the comparison of the sorption behaviour of zein and ethyl cellulose is physically more significant at low water activities.

3.5. Gas barrier properties of zein

3.5.1. Water vapour

The water vapour transmission coefficient of plasticized zein and ethyl cellulose was measured at an activity gradient of $\Delta a_w = 0.30$ $\Delta P(\text{H}_2\text{O})_{25^\circ\text{C}} = 950$ Pa; the low pressure side of the film was kept at $a_w = 0$. The diffusion coefficient (D) was determined according to Eq. (4), where P and S are the permeability and the solubility coefficient, respectively.

$$D = P/S \quad (4)$$

In the case of highly soluble permeants such as water, the diffusion coefficient is typically dependent on the concentration, and neither Fick’s first law of diffusion nor Henry’s law of linearly increasing solubility with increasing permeant va-

Table 5

Permeability (P), solubility (S) and diffusivity (D) of water vapour in various (plasticized) polymers at 25°C measured at a pressure gradient of $\Delta P(\text{H}_2\text{O}) = 950$ Pa. The obtained values for ethyl cellulose and zein are compared with those of widely used pharmaceutical film coatings such as Pharmacoat and Eudragit (List and Kassis, 1982a).

System	$P \cdot 10^{10}$ ($\text{cm}^2/(\text{Pa} \cdot \text{s})$)	$S \cdot 10^3$ ($\text{cm}^3/(\text{cm}^3 \cdot \text{Pa})$)	$D \cdot 10^6$ (cm^2/s)
EC (DS = 2.5)	23.0	11.8	0.195
EC (DS = 1.7)	17.1	35.2	0.049
EC (DS = 1.7)–DET ^a	18.3	21.8	0.084
Zein–DET ^b	2.75	34.0	0.008
Pharmacoat 603	10–12	–	–
Eudragit L,S-TA ^c	1–2	–	–

^a $w(\text{DET}) = 0.30$.

^b $w(\text{DET}) = 0.35$.

^c $w(\text{TA}) = 0.09$.

pour pressure is applicable. However, at comparatively low activities, Eq. (4) may still serve to approximate D within reasonable error limits. From the results displayed in Table 5, it can be seen that although the diffusivity of water sharply decreases with increasing polarity of the film-forming compounds, the simultaneously increasing solubility compensates for the effect of D on the permeability of the cellulose derivatives. In contrast, a reduction of P of almost an order of magnitude compared to ethyl cellulose is found for plasticized films of zein due to the low diffusion coefficient.

3.5.2. Oxygen

As indicated by the volumetric properties, zein films provide an excellent gas barrier towards oxygen at low water contents. Upon comparing zein with highly substituted ethyl cellulose (DS ~ 2.5), it was found that dry zein exhibits an oxygen permeability coefficient that is about two orders of magnitude less (Fig. 10). With the objective of assessing the effect of increasing water activity on the oxygen permeability, experiments were performed that required the preceding conditioning of the samples and the maintenance of the desired water activity on either side of the film during the measurement. Fig. 10 shows that the oxygen permeability of plasticized zein is scarcely influenced up to an activity of about 0.60. In the range of higher activities, the permeability is sharply increased while the mechanical resistance breaks

down. The film becomes increasingly viscous and successively loses its elastic properties. At room temperature, a water content of more than 10–15% ($a_w > 0.8$) in addition to the original amount of the plasticizer ($w(\text{DET}) = 0.35$) causes the materials transition into a free flowing melt.

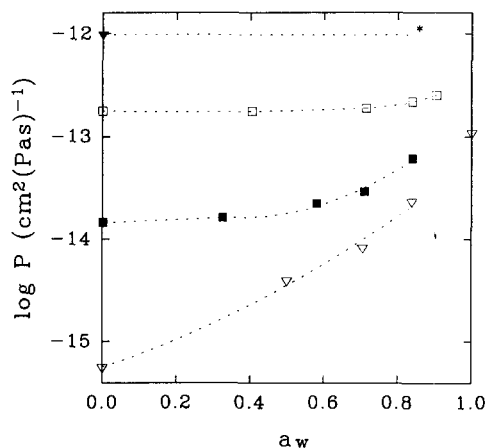


Fig. 10. Permeability coefficient, P , of oxygen at 25°C vs. water activity, a_w , in plasticized films of zein ($w(\text{DET}) = 0.35$) (■), EC (DS = 1.7; $w(\text{DET}) = 0.30$) (□) and EC (DS = 2.5; $w(\text{TB}) = 0.30$) (▼) compared with data of Pilar (1960) for pure regenerated cellulose (DS = 0.0) (▽). $P_0 \equiv$ permeability at $a_w = 0$; P_0 (EC (DS = 2.5)–TB) = $9.74 \cdot 10^{-13}$ $\text{cm}^2/(\text{Pa} \cdot \text{s})$, $w(\text{TB}) = 0.30$; P_0 (EC (DS = 1.7)–DET) = $1.77 \cdot 10^{-13}$ $\text{cm}^2/(\text{Pa} \cdot \text{s})$, $w(\text{DET}) = 0.30$; P_0 (zein–DET) = $0.145 \cdot 10^{-13}$ $\text{cm}^2/(\text{Pa} \cdot \text{s})$, $w(\text{DET}) = 0.35$; P_0 (regenerated cellulose) = $0.0056 \cdot 10^{-13}$ $\text{cm}^2/(\text{Pa} \cdot \text{s})$ (averaged value according Pauly (1989)).

* $P(\text{EC (DS = 2.5)–TB})$ is assumed to be less influenced by a_w than $P(\text{EC (DS = 1.7)–DET})$.

4. Conclusions

In conclusion, the discussed results revealed that zein generally exhibits volumetric, water sorption and gas barrier properties, which are similar to partially etherified celluloses in the DS range of 1.1–1.4. According to this tendency, the glass transition temperature of zein is comparatively low, which is a noticeable advantage considering the processing conditions and the final mechanical properties of zein-based materials. In contrast to films of highly substituted cellulose, zein provides an excellent resistance to oxygen permeation and, hence, is most useful for protecting encapsulated ingredients from oxidative degradation.

Suitable plasticizers for zein were shown to exhibit an appropriate polarity by means of hydrogen bonding capacity. Thus, it turned out that commonly employed plasticizers like the esters of citric acid, their acetylated derivatives, polyethylene glycols of a high molecular weight ($M > 1000$ g/mol) and di- or triesters of glycerol show a reduced miscibility with zein and, therefore, are only of limited use with respect to glass transition depression. As effective and non-toxic plasticizers, the esters of tartaric and lactic acid have to be mentioned in particular. Unfortunately, the latter were found to have a partial vapour pressure in mixtures with zein that is, even at 25°C, still sufficiently high to cause measurable weight losses by migration and evaporation of the plasticizer molecules. Free levulinic acid and particularly glycerol cause a marked increase in hygroscopicity of the mixtures compared to pure zein and are therefore assumed to reduce the shelf life of encapsulated agents.

The dependence of the glass transition temperature of zein towards absorbed water allows extrusion at low temperatures and facilitates the release of the active ingredients at high relative humidity. It has been pointed out that zein—in contrast to chemically modified polyacrylates for instance—is evidently not capable of providing retarded release and, hence, is limited to pharmaceutical applications that require fast disintegration of the coating (e.g. taste masking). In addition, film coatings for the prevention of at-

trition or dust formation during the handling of tablets in manufacturing plants may be a potential field of application. In this context, dispersions or emulsions of zein for spray-coating processes are necessary and, in particular, systematic investigations of highly concentrated aqueous systems might be a goal for the future.

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Appendix: Equation of state for multicomponent systems (Jain and Simha, 1980)

The reduced variables of state (designated by a tilde), are defined by the scaling parameters P^* , V^* and T^* which are computed by adjusting the equation of state (Eqs. (A2) and (A3)) to experimental volume data.

$$\tilde{P} = \frac{P}{P^*} \quad \tilde{V} = \frac{V}{V^*} \quad \tilde{T} = \frac{T}{T^*} \quad (\text{A1})$$

The Simha–Somcynsky equation of state assumes the form

$$\frac{\tilde{P}\tilde{V}}{\tilde{T}} = \frac{1}{1-\eta} + \frac{2y}{\tilde{T}(y\tilde{V})^2} \left(\frac{A}{(y\tilde{V})^2} - \frac{B}{2} \right) \quad (\text{A2})$$

where $A = 1.011$ and $B = 2.409$. The assumed quasi-lattice consists of a canonical ensemble of interacting sites occupied by the segments of the molecules. A molecule is characterized by the number of segments, r , and the number of external degrees of freedom, $3c$ (high polymers: $r \rightarrow \infty$ and $3c = r$; consistent analogue for oligomers: $3c = r + 3$). The volume fractions of occupied (y) and unoccupied ($1 - y$) lattice sites are found by minimizing the Helmholtz free energy with respect

to y , which leads to a transcendental equation for y :

$$\frac{\langle r \rangle}{3\langle c \rangle} \left[\frac{\langle r \rangle - 1}{\langle r \rangle} + \frac{1}{y} \ln(1 - y) \right] = \frac{\eta - 1/3}{1 - \eta} + \frac{y}{6\bar{V}(y\bar{V})^2} \left(B - \frac{3A}{(y\bar{V})^2} \right) \quad (\text{A3})$$

where $\eta = 2^{-1/6}y(y\bar{V})^{-1/3}$

In the case of multicomponent systems, defined by the component mole fractions (x_i), the scaled equation of state is formally identical to that of a homogenous fluid and the average values for $\langle c \rangle$ and $\langle r \rangle$ are defined explicitly by $\langle c \rangle = \sum x_i \cdot c_i$ and $\langle r \rangle = \sum x_i \cdot r_i$.

The cohesive energy density (E_{coh}) of the system becomes

$$E_{\text{coh}} = \frac{yP^*}{2\bar{V}} \left(\frac{B}{(y\bar{V})^2} - \frac{A}{(y\bar{V})^4} \right) \quad (\text{A4})$$

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