

## Impact of moisture and plasticizer properties on polymer–plasticizer physical mixing performance

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**ABSTRACT:** The ability for polymers and additives to physically mix in many industrial applications is dictated by a combination of kinetic and thermodynamic factors. The presence of moisture may complicate the mixing performance as water can interact at various degrees with each of the components; this depends on the hydrophilicity of the materials. In this study, the physical mixing behavior of a ternary system consisting of a hygroscopic polymer (copovidone), a plasticizer, and water was examined. Three different liquid plasticizers with a range of hydrophilic–lipophilic properties and viscosities were evaluated for their physical mixing performance and the impact of their water content. Inverse gas chromatography was introduced as a new method for measuring the surface characteristics of the physical mixtures to quantify the mixing performance. Through the application of the Flory–Huggins model to understand the thermodynamic behavior of the system, it was shown that mixing was less effective in a system of high water content for a hydrophobic plasticizer. However, the underlying thermodynamic unfavorability of such a system could be overcome by kinetic influence to provide a good mixing performance. Specifically, as the viscosity of the plasticizer decreased, the influence of the thermodynamic characteristics was found to become less apparent. © 2014 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* **2015**, *132*, 41679.

**KEYWORDS:** copolymers; phase behavior; plasticizer; surfaces and interfaces; theory and modeling

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### INTRODUCTION

The physical mixing of the polymers and additives are an inevitable part of manufacturing and industrial processes; this yields end products with desirable material and performance characteristics.<sup>1–5</sup> Additives such as plasticizers (e.g., surfactants) are important for reducing the glass-transition temperature and melt viscosity of polymers; they enable further processing to be carried out successfully.<sup>2,3</sup> In the pharmaceutical industry, for example, the ability to operate at lower processing temperatures is often crucial to the minimization of drug degradation. The mixing process typically begins with the formation of a blend of polymer powder and additives under shear, where the liquid additive is slowly absorbed by the porous solid polymer particles.<sup>4,6</sup> The ability of these components to mix uniformly is governed by a combination of thermodynamic interactions and kinetic input. Thermodynamic analysis is essential for understanding the intrinsic favorability for the components to mix and whether the system is ultimately stable (i.e., no demixing occurs). Both kinetic and thermodynamic effects can be qualitatively assessed through direct mixing experiments and through the understanding of the material properties of the components. As a result, these analyses offer a means for helping industries

appropriately screen their materials and achieve the expected processing results.

The physical mixing of polymer and plasticizer can be complicated by the introduction of a third component, water. Water may participate via purposefully targeted water addition or involuntary sources, such as background humidity, feed materials, and residual water from an upstream unit operation. Water has been shown to significantly impact the melt rheology and phase behavior of the system by providing a plasticization effect, as evident by changes in the moduli and thermal transitions.<sup>7–9</sup> The presence of unwanted water has also been reported to cause processing issues, such as gassing and foaming, and the deterioration of polymer properties, such as a reduced mechanical strength and increased brittleness, particularly in the case of hygroscopic polymers.<sup>7,9</sup> Thus, the role of water in influencing the polymer–plasticizer mixing performance via, for example, alteration of the interfacial interactions and wetting behavior between the polymer and plasticizer is of high interest. For industrial applications, it is desirable to have a straightforward predictive thermodynamic calculation to examine the favorability and strength of the interactions between each pair of

components in the ternary system (i.e., water–polymer, water–plasticizer, polymer–plasticizer) and to determine the Gibbs free energy of mixing ( $\Delta G_{\text{mix}}$ ) as a quantitative performance indicator at different moisture levels.

In this study, the physical mixing performance of a system consisting of a model polymer, various candidates of plasticizers, and water was evaluated with both experimental and theoretical approaches. Copovidone, a copolymer of vinyl pyrrolidone [poly(vinyl pyrrolidone)] and vinyl acetate, was selected as the model polymer because of its hygroscopicity. Three different types of nonionic plasticizers with various hydrophobicities and viscosities were used, namely, Lauroglycol FCC (propylene glycol monolaurate type I), Span 20 (sorbitan monolaurate), and Tween 80 (PEG-20 sorbitan monooleate).

From a thermodynamic perspective, we hypothesized that the quality of the copovidone–plasticizer mixing performance would decrease with increasing moisture when a hydrophobic plasticizer was used, whereas the quality would increase when a hydrophilic plasticizer was used. In this study, inverse gas chromatography (IGC), which was a physicochemical surface characterization technique, was introduced to measure the surface characteristics of the physical mixtures and the pure single components; this provided a direct means for quantifying the solid–liquid mixing performance. The theoretical understanding of the thermodynamic mixing behavior of the polymer–plasticizer–water ternary system was obtained by the application of the well-known Flory–Huggins model for polymer solutions. The binary Flory–Huggins interaction parameters (water–polymer, water–plasticizer, and polymer–plasticizer) were empirically determined with the water sorption isotherms of the individual components and mixtures. Subsequently, these parameters were used in the calculation of the Gibbs free energy given as a function of the composition for each of the three components. The results highlight the significant effects of water on the mixing performance in the systems containing plasticizers with various hydrophobicities and viscosities.

## EXPERIMENTAL

### Materials

Span 20 (sorbitan monolaurate, Croda, Snaith, United Kingdom), Tween 80 (PEG-20 sorbitan monooleate, Amresco, Solon, OH), and Lauroglycol FCC (Gattefosse, Saint-Priest, France) were used as model plasticizers. Copovidone (Kollidon VA64, BASF, Ludwigshafen, Germany) was used as the model polymer. Magnesium chloride (J. T. Baker, Center Valley, PA) and sodium bromide (J. T. Baker, Center Valley, PA) were used to generate controlled humidities to equilibrate the materials to the desired water content.

### Physical Mixture Preparation

The copovidone was equilibrated at room temperature over a saturated magnesium chloride solution [providing  $\sim 33\%$  relative humidity (RH)] and a sodium bromide solution ( $\sim 58\%$  RH) for more than 1 week to ensure that equilibrium was reached. To control the plasticizer water content, the plasticizers were also equilibrated over a saturated magnesium chloride solution at room temperature for at least 1 week. After moisture

equilibration, each plasticizer was physically mixed with copovidone at a 1:10 w/w ratio with a mortar and pestle for approximately 20 min with precautions that the amount of force applied was gentle and remained roughly consistent. The mixture was then immediately stored in sealed amber glass bottles before further characterization.

### Plasticizer Viscosity

The viscosities of the model plasticizers were measured at 25°C with an AR2000 rheometer (TA Instruments, New Castle, DE) equipped with a cone-and-plate geometry. A continuous flow test was performed to capture the relationship between the shear stress and shear rate. The plasticizers were confirmed to behave as Newtonian fluids. Accordingly, the viscosity was extracted from the slope of the shear stress versus the shear rate curve.

### Copovidone True Density

The true density of copovidone was determined with a pycnometer (Ultrapycnometer 1000, Quantachrome, Boynton Beach, FL). Helium gas was used as the displacement medium.

### Copovidone Molecular Weight

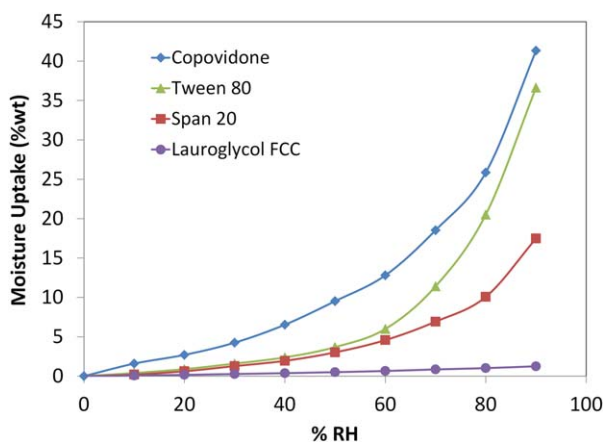
The molecular weight of copovidone was determined with size exclusion chromatography with multiangle light scattering. The high-performance liquid chromatography (HPLC) system (Agilent 1100, Agilent Technologies, Waldbronn, Germany) was used in conjunction with MALS (DAWN EOS, Wyatt Technology, Santa Barbara, CA) and refractive index (Optilab rEX, Wyatt Technology, Santa Barbara, CA) detectors. The mobile phase consisted of a 10 mM phosphate buffered saline solution at pH 7.4. The size exclusion chromatography column used was a Shodex OHpak SB-804 HQ ( $8 \times 300$  mm). Other parameters included a flow rate of 0.75 mL/min, column temperature of 35°C, injection volume of 50  $\mu\text{L}$ , acquisition run time of 30 min, and detector wavelength of 690 nm.

### Dynamic Vapor Sorption (DVS)

The moisture sorption profiles of the pure plasticizers, copovidone, and copovidone–plasticizer physical mixtures were measured by DVS (Advantage-1, Surface Measurement Systems, London, United Kingdom) at 25°C. The samples were first dried under a continuous flow of dry air (RH < 0.5%) for 360 min to establish the dry mass. The samples were then exposed to the following partial pressure profile: 0, 10, 20, 30, 40, 50, 60, 70, 80, and 90% RH. The equilibrium moisture uptake was obtained at each RH step when the mass change reached a plateau, with an equilibration criterion defined as less than a 0.002-mg change in 5 min.

### Thermogravimetric Analysis (TGA)

TGA was used to confirm the water content in samples after moisture equilibration at 33 and 58% RH through the measurement of the weight change from the loss of water as the samples were heated. Approximately 20–30 mg of sample was weighed in a platinum sample pan. The weight loss on heating was monitored with a thermogravimetric analyzer (Q50, TA Instruments, New Castle, DE). Each sample was heated at a constant rate (5°C/min) from room temperature to decomposition under a nitrogen purge (60 mL/min). The method end point was set



**Figure 1.** Water sorption isotherms for copovidone, Tween 80, Span 20, and Lauroglycol FCC at 25°C. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

at 400°C. The data were analyzed with TA Universal Analysis 2000 software (version 4.5A, TA Instruments).

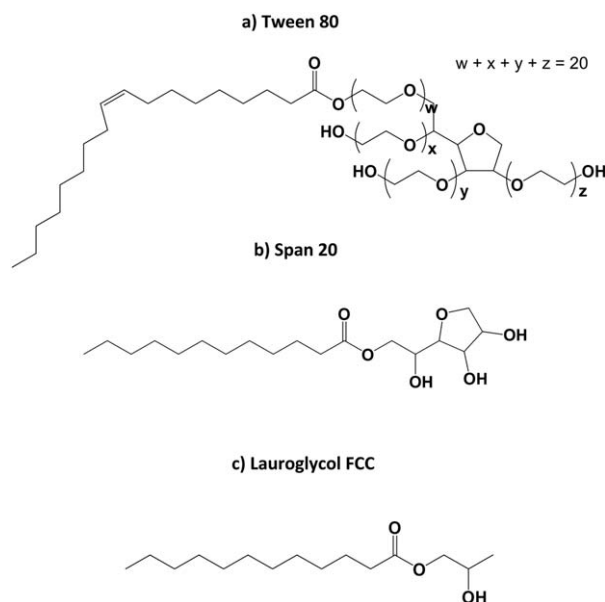
### IGC

The surface properties of the pure plasticizers, copovidone, and copovidone–plasticizer physical mixtures were measured by IGC (iGC 2000, Surface Measurement Systems, London, United Kingdom) at a finite concentration. For copovidone and the physical mixtures, approximately 0.5 g of materials was packed into standard presilanized columns (300 length  $\times$  4 mm inner diameter) with silanized glass wool at each end to prevent powder movement. The plasticizers were first coated on silanized glass wool, which acted as inert support, before being packed into the column. Vapor probes were injected at a ratio of the partial vapor pressure of moisture to the saturated vapor pressure ( $p/p_0$ ; i.e., RH %) of 0.20 with decane, nonane, octane, heptane, ethyl acetate, 1,4-dioxane, acetone, and dichloromethane (HPLC grade, Sigma-Aldrich, Poole, United Kingdom). Methane (99.99%, SGA, Toledo, OH), injected at 0.10  $p/p_0$ , was used to determine the column dead time. Helium at a flow rate of 10 sccm was used as the carrier gas for all injections. To determine the effect of the moisture content on the surface properties of the pure copovidone, separate experiments were conducted at background RHs of 0, 30, and 60%; these corresponded to copovidone moisture levels of 0, 5, and 11% w/w, respectively. For all other experiments, the samples were conditioned *in situ* in the IGC with a helium purge at 20 sccm for 2 h at 30°C to remove the physisorbed water. The dispersive surface energies ( $\gamma^{ds}$ ) were determined according to the method of Schultz, and the ratio of the Gutmann base ( $K_B$ ) to the acid number ( $K_A$ ) were determined as described previously.<sup>10</sup> All of the results are the average of identical experiments conducted in triplicate.

## RESULTS AND DISCUSSION

### Materials' Physical Properties

The moisture sorption profiles of the Span 20, Tween 80, Lauroglycol FCC, and copovidone are shown in Figure 1, and their chemical structures are provided in Figure 2. Copovidone was a hygroscopic copolymer, sorbing more than 41% w/w of water at

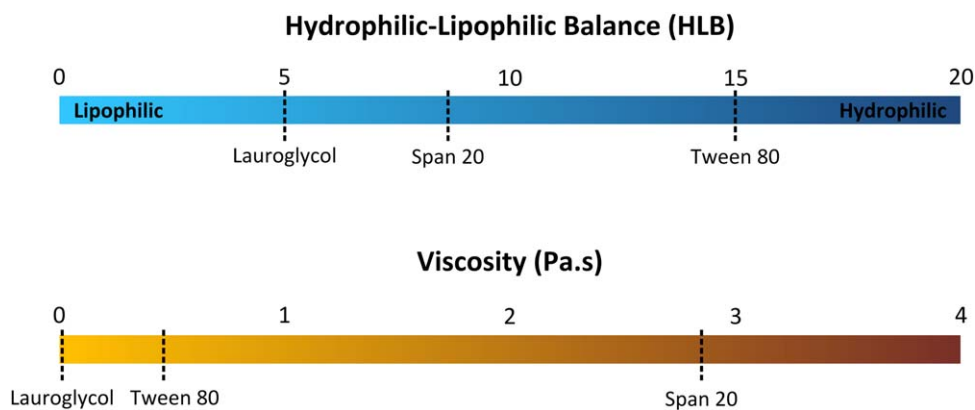


**Figure 2.** Chemical structures of (a) Tween 80, (b) Span 20, and (c) Lauroglycol FCC.

90% RH. For the model plasticizers, Tween 80 was more hygroscopic than Span 20 at an equivalent percentage RH, and Lauroglycol FCC was the least hygroscopic plasticizer. The hygroscopicity of the plasticizer was closely related to the strength and number of hydrophilic functional groups of the plasticizer molecule. With the concept of hydrophilic–lipophilic balance (HLB),<sup>11</sup> we observed that the hygroscopicity of Tween 80, Span 20, and Lauroglycol FCC trended positively with its HLB value, as shown in Figure 3. The moisture uptake of the plasticizers at 90% RH highly correlated with the HLB values. In terms of viscosity, Span 20 was the most viscous of the three plasticizers at 25°C (Figure 3), and it was approximately seven times more viscous than Tween 80. Lauroglycol FCC, which had the lowest viscosity among the three model plasticizers, had a viscosity approximately 20 times lower than Tween 80. The sorption and viscosity results highlight the differences in the material properties among the various plasticizers used in this study.

### Quantification of the Mixing Performance by IGC

In this study, we introduced an approach for quantifying the polymer–plasticizer mixing performance directly through the characterization of the surface of each moisture-equilibrated primary component (polymer and plasticizers) and polymer–plasticizer binary mixtures with IGC. In a liquid and solid binary system, the mixing performance can be quantified by the extent to which the liquid phase is able to spread over the solid phase. For a perfectly mixed system, the liquid phase would cover the solid phase completely (total wetting, or zero contact angle at the liquid–solid interface), provided that an adequate quantity of the liquid phase is present in the system for complete wetting to occur (Figure 4). Consequently, for a well-mixed system, the surface properties of the physical mixture are expected to be dominated by the properties of the liquid. In contrast to a well-mixed system, one would expect a



**Figure 3.** HLB and viscosity values at 25°C of the model plasticizers (the HLB values are referenced from the manufacturers' information; the viscosity values were obtained from the experimental measurements). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

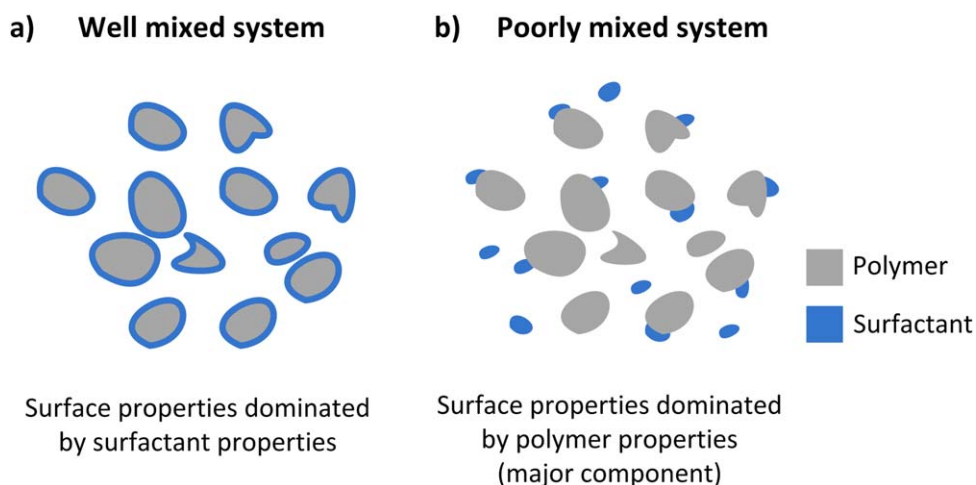
nonuniform coating of liquid on the solids throughout the mixture of a poorly mixed system. The surface properties of a poorly mixed solid–liquid system would be dominated by the major component in the mixture. According to this principle, the mixing performance can, in practice, be determined by the quantification of the surface properties of the physical mixtures and by a comparison of the surface properties to their constituent components.

IGC is a characterization technique frequently applied to study surface properties of solids.<sup>10</sup> In this study, the technique was used to characterize the surface properties of liquid (plasticizer) and binary liquid–solid (polymer–plasticizer) systems. To prevent the preferential characterization of hot spots or surface-active sites at infinite dilution, the IGC experiments were conducted at a finite concentration to achieve adequate probe surface coverage such that the average surface properties of the samples were measured. The dispersive component of the surface energy, which describes the extent of surface van der Waal's interactions of the materials, was obtained with a series of *n*-alkanes following the approach of Schultz.<sup>12</sup> The surface polarity of the materials was characterized by the acid

and base numbers,  $K_A$  and  $K_B$ , after the modified Gutmann approach<sup>13,14</sup> with four different polar probes with various degrees of electron donor (basic) and acceptor (acidic) properties.

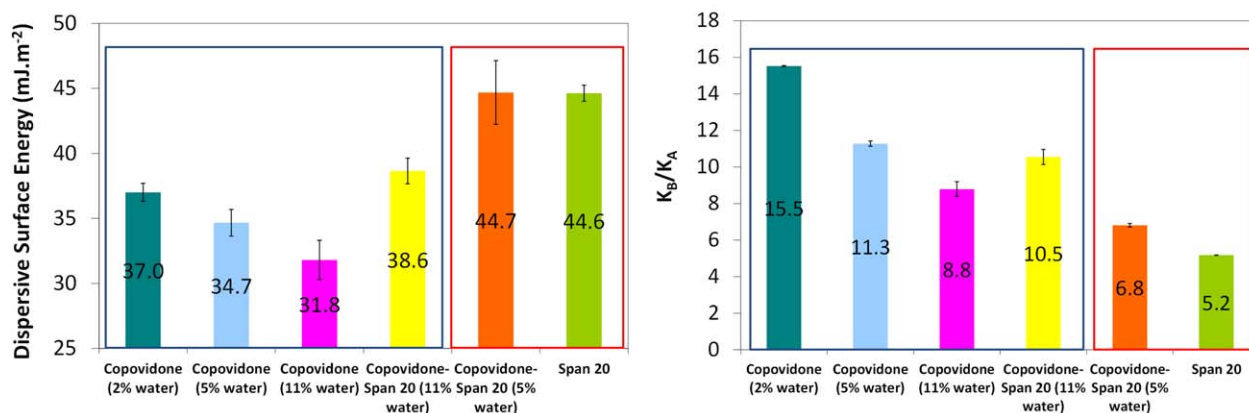
The properties of the plasticizer, such as the structure, ionic/nonionic distribution, flexibility, moisture sensitivity, rheology behavior, and solubility, may impact its physical mixing behavior. In this study, the influence of moisture and the extent of the plasticizer hydrophobicity to mixing were specifically evaluated. The copovidone was first equilibrated under 33 and 58% RH to achieve a moisture content of 5 and 11% w/w, respectively. The moisture content values of the copovidone measured by TGA were confirmed by the corresponding DVS moisture uptake values at 33 and 58% RH, as shown in Figure 1. After moisture equilibration, the copovidone was then physically mixed with the plasticizers to create various combinations of copovidone–plasticizer mixtures with two different initial copovidone moisture contents.

The  $\gamma^d$  values and ratio of  $K_B$  to  $K_A$  for all of the pure plasticizers, copovidone, and plasticizer–copovidone physical mixtures are displayed in Figure 5. An increase in the moisture content

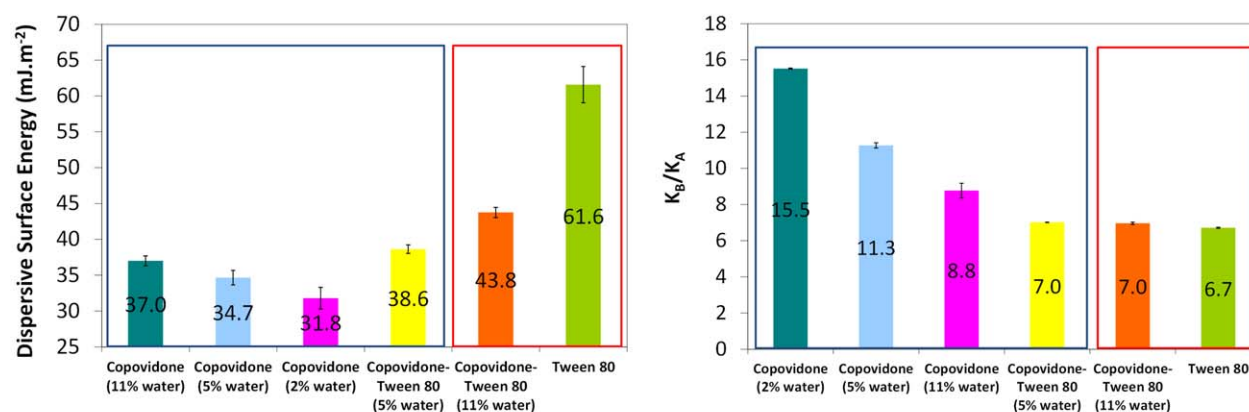


**Figure 4.** Differentiation of the surface properties of (a) a physically well mixed and (b) a poorly mixed systems of the binary polymer–plasticizer mixture. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

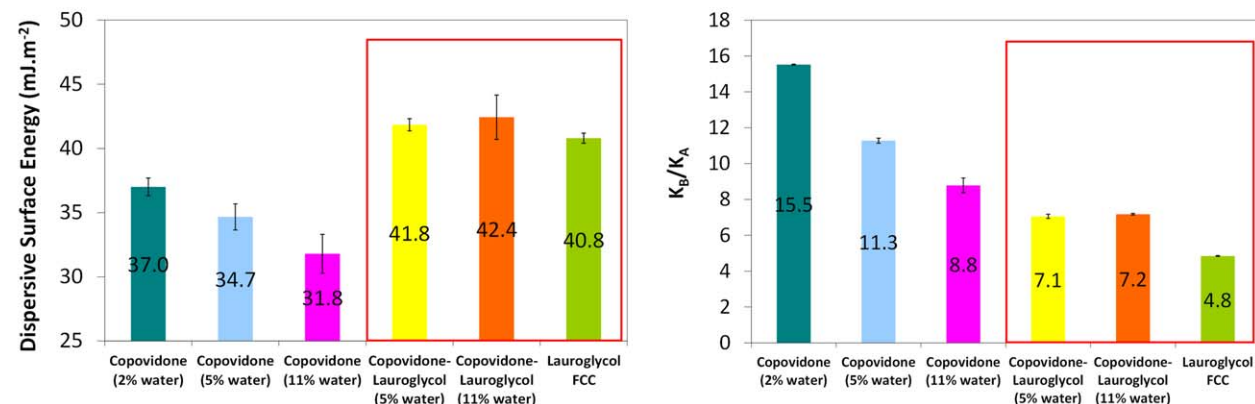
## Span 20 - Lower moisture level in copovidone promotes mixing



## Tween 80 - Higher moisture level in copovidone promotes mixing



## Lauroglycol FCC - Mixing is independent of moisture level in copovidone



**Figure 5.** Surface properties of the model plasticizers, copovidone at various moisture levels, and their physical mixtures. The blue box indicates that the physical mixture surface properties were similar to those of copovidone. The red box indicates that the physical mixture surface properties were similar to those of the surfactant. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

in copovidone caused  $\gamma^d$  and  $K_B/K_A$  to decrease. This was attributed to the increase in surface water. Siboni and Volpe<sup>15</sup> argued that water is primarily an electron acceptor, and an increase in the surface acidity, represented by  $K_A$ , as the copovidone moisture level increases is consistent with their observation. The plasticizer HLB values are also related to  $\gamma^d$  and  $K_B/K_A$ , both of

which increase as the hydrophilic content of the plasticizer increases. For Tween 80, the larger  $\gamma^d$  may have been due to its longer carbon chain length, compared to Span 20 and Lauroglycol FCC (Figure 2). Tween 80 was expected to be more basic (or electron-donating/activating) because of its large ratio of ether (basic) to hydroxyl (both acidic and basic) groups. For

**Table I.** Material Parameters for Input into the Flory–Huggins Model

Material	Density (g/cm <sup>3</sup> )	Molecular weight (g/mol)	Molecular volume (cm <sup>3</sup> /molecule)
Span 20 <sup>1</sup>	1.03	346.5	5.6 × 10 <sup>-22</sup>
Tween 80 <sup>1</sup>	1.08	1310	2.0 × 10 <sup>-21</sup>
Lauroglycol FCC <sup>2</sup>	0.93	258.4	4.6 × 10 <sup>-22</sup>
Copovidone	1.21	39,800	5.5 × 10 <sup>-20</sup>
Water	1.00	18.0	3.0 × 10 <sup>-23</sup>

<sup>1</sup>Gangolli, S. The Dictionary of Substances and Their Effects: Volume 6 O-S, 2nd ed.; Royal Society of Chemistry: Cambridge, U.K., 1999.

<sup>2</sup>Gattefosse Technical Data Sheet: Lauroglycol FCC, Specification number 3219 / 5 2010.

Span 20 and Lauroglycol FCC, their lower  $K_B/K_A$  ratios were due to the presence of moderately acidic ester groups; this made the molecule comparatively more acidic.

When the IGC results of the moisture-equilibrated physical mixtures of the polymer–plasticizer were compared, it was obvious that the copovidone moisture content influenced the mixing performance differently; this depended on the hydrophobicity of the plasticizer and the initial moisture content of copovidone. For Span 20, both  $\gamma^d$  and  $K_B/K_A$  of the physical mixture containing a 5% w/w copovidone–water content were similar to those of the pure plasticizer, and this indicated that the surface of the 5% w/w mixture was well coated by plasticizer. This result for Span 20 implied a good spreading of the plasticizer in the absence of moisture. For this hydrophobic plasticizer, mixing was favored in an environment of diminished water. For Tween 80 (a hydrophilic surfactant), the opposite behavior was observed, whereby the  $\gamma^d$  and  $K_B/K_A$  of the mixture prepared at an 11% w/w polymer water content were similar to those of the pure Tween 80. This indicated that spreading/mixing was favored in an environment with the presence of water. Interestingly, for Lauroglycol FCC (the most hydrophobic among the three model plasticizers), both mixtures showed equivalent  $\gamma^d$  and  $K_B/K_A$  values; these were similar to the pure Lauroglycol FCC. This suggested that good mixing could occur independently from the influence of water.

### Thermodynamic Considerations for the Underlying Mixing Behavior

To rationalize the difference in the mixing behavior of the plasticizers under different moisture levels, the thermodynamic behavior under the experimental mixing conditions was considered. The application of Young's equation and spreading coefficients (relating to the work of adhesion and cohesion) to study the thermodynamics of wetting and spreading of a liquid phase on a solid surface was well established from the surface energy data. However, for a system of three components (copovidone, plasticizer, and water), it was useful to explore the component interactions via modeling with the Flory–Huggins theory for a ternary system. Although the Flory–Huggins theory was developed to understand the thermodynamics of polymer solutions, it has been widely applied to study the component interactions and phase behavior of supercooled liquids in the solid state, such as amorphous solid dispersions.<sup>16,17</sup> The theory is based on a mean-field approximation and assumes that the system is generally uniform in composition with no large regions of pure solvent. Because the amount

of plasticizer and water distributed in this system was relatively small compared to the amount of copovidone present, it was reasonable to apply this theory in this study. Because of the high concentration of copovidone, it is important to note that the Flory–Huggins theory is used to understand and applicable only in the interfacial regions of the physical mixture, where the formation of a single-phase system and thermodynamic interactions between the components are possible.

$\Delta G_{\text{mix}}$  is a quantitative measure of the mixing tendency among different components. A negative  $\Delta G_{\text{mix}}$  would imply thermodynamic favorability where spontaneous mixing occurs and is a necessary condition for system stability. In the application of the ternary Flory–Huggins model,  $\Delta G_{\text{mix}}$  is made up of entropic and enthalpic terms as given by eq. (1):

$$\frac{\Delta G_{\text{mix}}}{RT} = n_1 \ln \phi_1 + n_2 \ln \phi_2 + n_3 \ln \phi_3 + n_1 \phi_2 \chi_{12} + n_1 \phi_3 \chi_{13} + n_2 \phi_3 \chi_{23} \quad (1)$$

where  $n$  is the molar fraction,  $\phi$  is the volume fraction,  $\chi_{xy}$  is the binary Flory–Huggins interaction parameter between the components  $x$  and  $y$ ,  $R$  is the universal gas constant, and  $T$  is the temperature. The subscripts 1, 2, and 3 denote the components of water, plasticizer, and copovidone, respectively. To calculate  $\Delta G_{\text{mix}}$  among water, plasticizer, and copovidone, the binary Flory–Huggins interaction parameters involving the three individual components must first be determined. In this study, these binary interaction parameters were derived from the moisture sorption isotherms of the pure components and the binary plasticizer–copovidone mixtures.

According to previously reported methods,<sup>18,19</sup> the DVS moisture sorption isotherms of the individual components (copovidone, Span 20, Tween 80, and Lauroglycol FCC) were used to evaluate and understand the existence of thermodynamic interactions between the water and individual components. The underlying expression describing the moisture sorption of the individual components is given by eq. (2);<sup>20,21</sup> this assumes that the absorption of water into the polymer or plasticizer can be treated as a dissolution process:

$$\ln \left( \frac{p}{p_0} \right) = \ln \phi_1 + \left( 1 - \frac{1}{x_{1k}} \right) \phi_k + \chi_{1k} \phi_k^2 \quad (2)$$

where the subscripts 1 and  $k$  refer to the water and individual component (copovidone, Span 20, Tween 80, or Lauroglycol FCC), respectively, and  $\phi_k$  is the volume fraction of component  $k$ . The term  $\chi_{1k}$  is the binary Flory–Huggins interaction

**Table II.** Flory–Huggins Interaction Parameters Determined from the Moisture Sorption Isotherms

System	Estimated interaction parameter
Copovidone–water	0.8
Tween 80–water	1.0
Span 20–water	1.5
Lauroglycol FCC–water	3.6

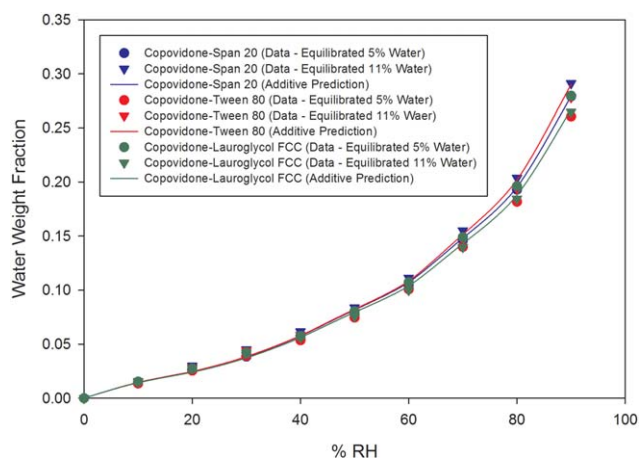
parameter dictating the strength of the interaction between the water and component  $k$ .  $x_{1k}$  is the relative molecular volume between the water and component  $k$ . Equation (2) can be used to predict the moisture sorption behavior of the individual component. In a comparison of this prediction against the experimental moisture sorption data, estimates of the strength of different interactions (i.e.,  $\chi_{1k}$ ) can be obtained. Table I provides a list of relevant parameters that were used in this study.

The application of the Flory–Huggins model is most appropriate at high relative humidities where the moisture is able to plasticize the sample significantly enough that its glass-transition temperature is near or falls below the experimental temperature (25°C). As a reasonable assumption, the focus was therefore placed on the moisture sorption results at 80 and 90% RH to estimate the interaction parameter. Using these two data points and solving for the water–copovidone interaction parameter, we obtained an estimated value of around 0.8. This value, being slightly larger than the critical value of 0.5 for polymer solutions,<sup>22</sup> suggested that the mixing of copovidone with water was slightly unfavorable. This result could be compared to the previously reported  $\chi$  value of 0.36 for the pure hydrophilic poly(vinyl pyrrolidone); this indicated slightly better mixing favorability with water.<sup>18</sup> Thus, we assumed that the hydrophobic portion of copovidone, poly(vinyl acetate), may have been the main contributor to the overall unfavorable interaction of copovidone with water.

With the same approach, the interaction parameters were estimated for the individual plasticizers with respect to water. The estimated binary water–plasticizer interaction parameters are tabulated in Table II. As expected, with increasing hydrophobicity of the plasticizers (in the order Tween 80, Span 20, and Lauroglycol FCC), the interaction parameter increased. This was due to the decreasing ability of the material to sorb moisture, as seen in the DVS isotherms. The positive binary interaction parameters with all of the plasticizers indicated their generally unfavorable mixing tendency with water.

For a ternary system of water, plasticizer, and copovidone and with the assumption that the water–copovidone and water–plasticizer interactions in the ternary system are the same as those in the binary systems, the Flory–Huggins model [eq. (2)] can be extended to a ternary form,<sup>18</sup> whereby the moisture sorption profile of the plasticizer–copovidone mixture can be described by the following equation:

$$\ln\left(\frac{p}{p_0}\right) = \ln\phi_1 + (\phi_2 + \phi_3) - \frac{\phi_2}{x_{12}} - \frac{\phi_3}{x_{13}} + (\chi_{12}\phi_2 + \chi_{13}\phi_3)(\phi_2 + \phi_3) - \chi_{23} \frac{\phi_2\phi_3}{x_{12}} \quad (3)$$



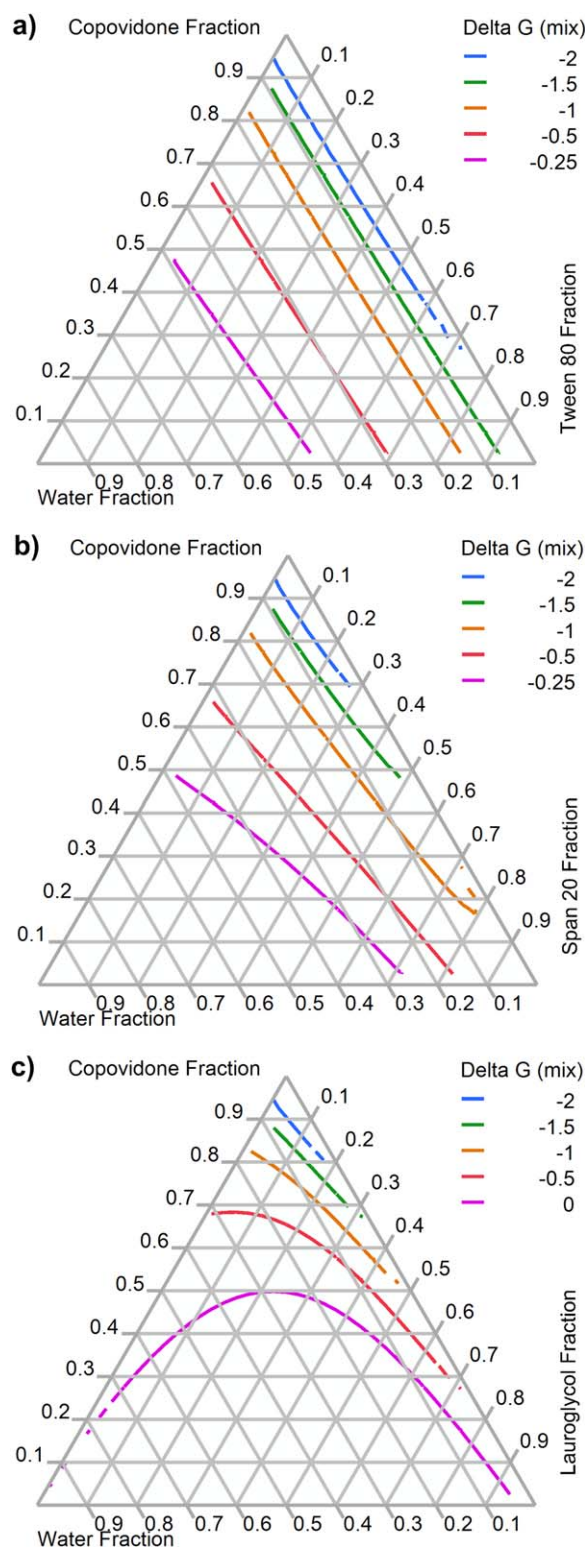
**Figure 6.** Experimental and calculated moisture sorption isotherms (on the basis of the additive approach) for the physical mixtures of copovidone with Span 20, Tween 80, and Lauroglycol FCC. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

The subscripts 1, 2, and 3 refer to water, plasticizer (Span 20, Tween 80, or Lauroglycol FCC), and copovidone, respectively as defined previously.  $\chi_{23}$  is the binary Flory–Huggins interaction parameter dictating the strength of the interaction between the plasticizer and copovidone. When the binary interaction parameters between the water and individual components were known,  $\chi_{23}$  could be predicted from the moisture sorption profile of the binary plasticizer–copovidone mixture with eq. (3).

As a first step to confirming the presence of the copovidone–plasticizer interactions and whether eq. (3) was required for the determination of  $\chi_{23}$ , the experimental moisture sorption data of the copovidone–plasticizer mixtures were used as follows. First, an additive approach was performed where the isotherms for the individual components were summed, weighted by their weight fractions in the physical mixture. Second, the calculated isotherm was then compared against the experimental moisture sorption isotherm as determined by DVS. We expected that the presence of copovidone–plasticizer interactions would lead to a deviation in the moisture uptake profile compared to the theoretical profile on the basis of their weight/weight summation.

Figure 6 compares the calculated isotherms with experimental isotherms for 10:1 w/w physical mixtures of copovidone (pre-equilibrated to achieve water contents of 5 and 11% w/w) with each of the three plasticizers (Span 20, Tween 80, and Lauroglycol FCC). As shown, for all three mixtures, there is a general overlap of the experimental and theoretical curves; this suggested that the water uptake properties of the individual components were not altered in the physical mixtures, and no significant interaction between the copovidone and plasticizer (i.e.,  $\chi_{23} \approx 0$ ) existed. This result was consistent with reported literature<sup>19</sup> for physical mixtures that exhibited no binary chemical interactions.

With the assumption that  $\chi_{12}$  and  $\chi_{13}$  played a dominant role in the mixing behavior and that there was no significant interaction between copovidone and each of the plasticizers ( $\chi_{23} \approx 0$ ), the last enthalpic term of the Gibbs free energy [eq. (1)] was now reduced to zero. With the binary interaction parameters



**Figure 7.** Ternary diagrams showing the contour lines of  $\Delta G_{\text{mix}}$  for the ternary systems of the copovidone, plasticizer, and water. The different plasticizers are (a) Tween 80, (b) Span 20, and (c) Lauroglycol FCC. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

( $\chi_{12}$ ) obtained from moisture sorption isotherms in Table II,  $\Delta G_{\text{mix}}$  was calculated as a function of the copovidone, plasticizer, and water composition via eq. (1). The resulting  $\Delta G_{\text{mix}}$  is shown as ternary diagrams in Figure 7. The overall trend for all three of these systems appeared to be qualitatively similar, but subtle differences in their thermodynamic mixing favorability were deduced: The lowest free energies were achieved when the water composition was low; this indicated that mixing between the copovidone and plasticizer was more favorable when the moisture was minimized. However, in a comparison of the three diagrams, the free energy contour lines in the system involving Tween 80 were less dependent on the copovidone and plasticizer compositions than in the systems involving Span 20 and, especially, Lauroglycol FCC. This was a reflection of the relatively similar interaction parameters between water–copovidone ( $\chi_{13} = 0.8$ ) and water–Tween 80 ( $\chi_{12} = 1.0$ ). Thus, from a mixing perspective, the thermodynamic favorability for physical mixing was most sensitive to the copovidone and plasticizer compositions in the case of Lauroglycol FCC and least sensitive for Tween 80. Our results also show that a more hydrophobic plasticizer (with a lower HLB value) resulted in decreased mixing favorability with increasing presence of water.

#### Kinetic Considerations to the Underlying Mixing Behavior

On the basis of thermodynamics of mixing, one would expect Tween 80 to have the best mixing performance with copovidone in the presence of water, followed by Span 20 and Lauroglycol FCC. In a comparison of the theoretical mixing performance to the IGC results, it was obvious that the underlying physical mixing behavior did not seem to be solely influenced by thermodynamic factors, as Lauroglycol FCC displayed the best mixing performance regardless of the presence of water. With Span 20 being relatively hydrophobic and Tween 80 being relatively hydrophilic, it was likely that the thermodynamic interactions of these plasticizers with water were of different strengths; this reflected the differences in the IGC observations. However, for Lauroglycol FCC, it was reasonable to assume that the kinetic barrier to mixing was low, as the viscosity of Lauroglycol FCC was one and two orders of magnitude less than those of Tween 80 and Span 20, respectively. The relatively low viscosity of this plasticizer allowed it to be easily incorporated into the copovidone regardless of the amount of water present and rendered this a purely kinetic effect. It was also interesting to note that even though Tween 80 was relatively nonviscous (i.e., the kinetic barrier to mixing was low), its mixing performance was still dictated by its more favorable interactions with water. Our study showed that for a viscous plasticizer, which had a high kinetic barrier to mixing, the impact of mixing as dictated by its underlying thermodynamic characteristics became more apparent.

#### CONCLUSIONS

This study showed that the mixing of polymers and additives in the presence of water was dictated by a combination of kinetic and thermodynamic factors; this may have arisen from the individual material physical properties, such as the viscosity, hydrophobicity (surface properties), and moisture-uptake behavior. An approach that consisted of the determination of the surface



properties of the mixtures with IGC was introduced to evaluate the mixing performance of solid–liquid mixtures. The Flory–Huggins model was also applied to understand the thermodynamic behavior of the system, where the plasticizer HLB was determined to be an important indicator for the mixing efficiency. For a hydrophobic plasticizer, mixing was more thermodynamically favorable for the system of low water content, whereas the opposite was true for the hydrophilic plasticizer. Nevertheless, the mixing kinetics may have assisted and overcome the underlying thermodynamic unfavorability of the physical mixing, as demonstrated in the case of Lauroglycol FCC. As the viscosity of the components decreased in the system, the influence of the thermodynamic characteristics became less important. Our study showed that the utility of the Flory–Huggins model and  $\Delta G_{\text{mix}}$  calculations can provide a quick and quantitative estimation of the mixing performance between a polymer and surfactant at different water contents. The observations and understanding derived from this work will provide important implications toward the selection and design of polymer–plasticizer combinations targeted for better compatibility and mixing efficiency under the influence of moisture-induced effects.

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