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Evaluation of Alternative Plasticizers for Surelease®, an Aqueous Ethylcellulose Dispersion for Modified Release Film-Coating

Charles F. Vesey, Thomas Farrell, Ali R. Rajabi-Siahboomi
New Product Development, Colorcon, West Point, PA 19486
E.mail: modified_release@colorcon.com

Introduction

Ethylcellulose, a water-insoluble polymeric film-forming material, has been formulated into aqueous latexes (Surelease) for modified released film coating in the pharmaceutical industry. Because the glass transition temperature (Tg) of ethylcellulose is 130-133°C, [1] plasticizer must be added to the polymer to impart the requisite melt-flow properties needed to thermally process into a stable latex. The polymer-plasticizer combination must also be compatible, possess the desired thermal properties, such as Tg and minimum film-forming temperature, and mechanical properties, such as tensile strength and modulus of elasticity.

The purpose of this study was to examine the effects of various plasticizers, possessing different known and experimentally determined solubility parameters [2-3], on the thermal and physical properties of ethylcellulose.

Methodology

The required amount of ethylcellulose (Ethocel* 20cP Standard Premium, Dow Chemical Company, Midland, Michigan) and plasticizer (15%, 20% and 25% w/w) diethyl phthalate (DEP), dibutyl phthalate (DBP), Eastman Chemical Company, Kingsport, TN; polyethylene glycol 400 (PEG), Clariant, Charlotte, NC; trietyl citrate (TEC), dibutyl sebacate (DBS), Morflex Chemical Co., Greensboro, NC; medium chain triglycerides (MCT), Abitec Corporation, Janesville, WI; oleic acid, Croda Inc, Edison, NJ; or triacetin, Tessenderlo group, UK) were weighed. Polymer and plasticizer were mixed in Patterson-Kelly 16-qt V-Blender (Patterson-Kelley, East Stroudsburg, PA). Each polymer and plasticizer blend was then hot-melt extruded in a Randcastle Taskmaster 1000 (36:1) extruder equipped with a 0.375-inch (9.525mm) diameter die.

The glass transition temperature (Tg) of each extrudate was determined using a TA Instruments TMA 2940 Thermomechanical Analyzer (TMA) equipped with an expansion probe to measure thermal coefficient of expansion and glass transition. Samples were tested (n=3) under a nitrogen atmosphere (100ml/min) at a heating rate of 10°C/min. The temperature range evaluated was 25 to 180°C.

Free films of all formulations were prepared from dispersions of 10% solids content in 80:20 toluene:ethanol using a draw-knife (Gardner Casting Knife, Silver Spring, MD) casting technique onto glass plates. Casting knife settings were kept constant to control the thickness of the wet film in order to obtain the desired film thickness after drying. Cast films were allowed to dry and equilibrate, for a minimum of 24 hours, in a controlled environment laboratory (23°C/55%RH) prior to testing.

The mechanical properties of cast films were determined using a tensile testing instrument (Instron Mini 44 equipped with a Series IX data acquisition and analysis software). Test strips of film were cut into rectangular strips of 10mm x 100mm. The extension rate was 1mm/min. The average (n=10) tensile strength and modulus of elasticity was determined for each formulation from the stress-strain curve.

The Hansen solubility parameters of polymer and plasticizers were calculated from the chemical structure, group contribution method, using the approaches of Hoftyzer and VanKrevelen [4].

$$\delta^2 = \delta_d^2 + \delta_p^2 + \delta_h^2$$

Where σ_d is the component due to dispersion forces, σ_d the component due to dipole interactions, and σ_d the component due to hydrogen bonding.

The units of the solubility parameter are $MPa^{0.5}$

Results and Discussions

Pure ethylcellulose has a glass transition temperature of approximately 130°C. The tensile strength and modulus of elasticity of ethylcellulose films were experimentally determined as 43±1 MPa and 1350±60 MPa, respectively.

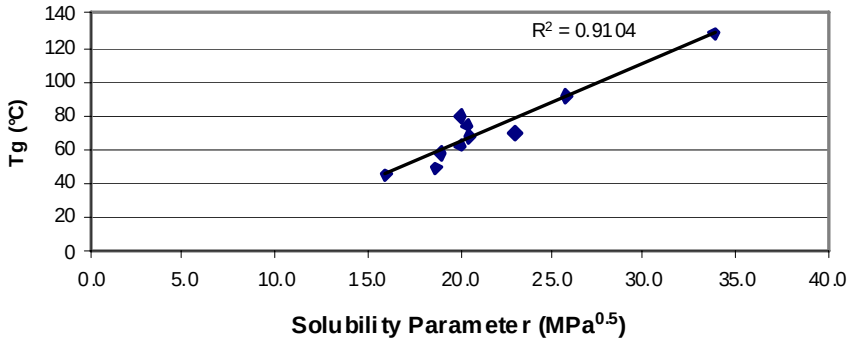
Compatibility between ethylcellulose and plasticizers were qualitatively assessed. Incompatibilities were evidenced by cloudy films and distinct phase separation of polymer and plasticizer. All plasticizers, except glycerin, polyethylene glycol 400, and propylene glycol, were compatible with the ethylcellulose polymer.

Table 1 shows the solubility parameters and the influence of plasticizer (25%*w/w*) addition on the Tg of ethylcellulose. The plasticizers of similar solubility parameter to that of ethylcellulose (20 $MPa^{0.5}$) had a greater effect on Tg suppression with good correlation between solubility parameters and Tg (figure 1).

Table 1. Tg (°C) and Solubility Parameters

Plasticizer	Tg (°C)	Solubility Parameter ($MPa^{0.5}$)
Oleic Acid	45.2	16.0
DBS	49.6	18.8
DBP	58.1	19.0
MCT	62.0	20.0
DEP	67.7	20.5
PEG 400	70.0	23.0
TEC	74.4	20.4
Triacetin	79.6	20.0
Propylene Glycol	91.1	25.8
Glycerin	128.5	33.8
Ethylcellulose	130.0	20.0

Figure 1. Effect of Plasticizer on Ethylcellulose Tg (°C)
(Tg versus Solubility Parameter)



While increasing plasticizer concentration did result in a lowering of tensile strength and modulus of elasticity (Fig.s 2 & 4), as expected, the correlation with solubility parameter was not as strong as noted with the thermal properties (Fig.s 3 & 5).

Tensile Strength

Figure 2. Plasticized Ethycellulose Films: Tensile Strength Tensile Strength (MPa) versus Plasticizer Concentration

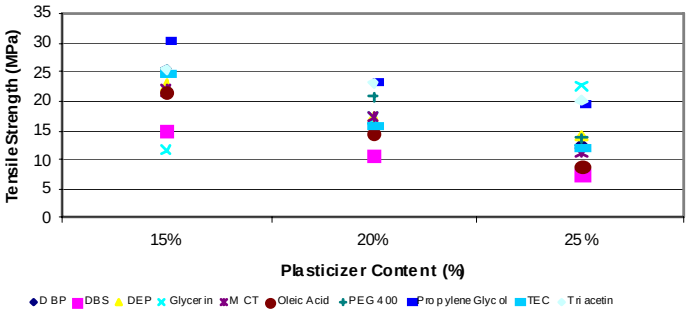
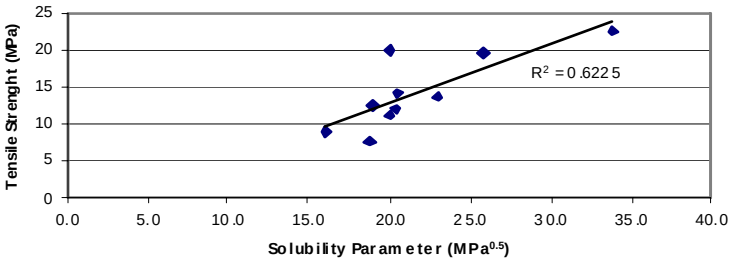


Figure 3. Effect of Plasticizer (25% w/w) on Ethylcellulose Tensile Strength versus Solubility Parameter



Modulus of Elasticity

Figure 4. Plasticized Ethylcellulose Films: Modulus of Elasticity Modulus of Elasticity (MPa) versus Plasticizer Concentration

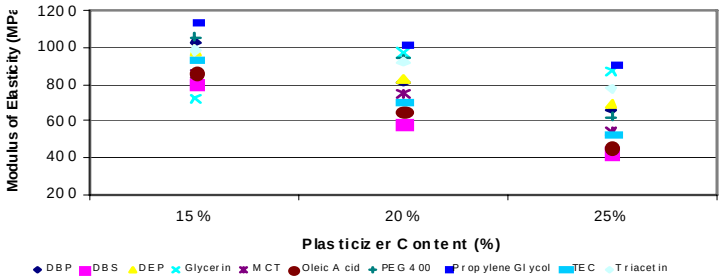
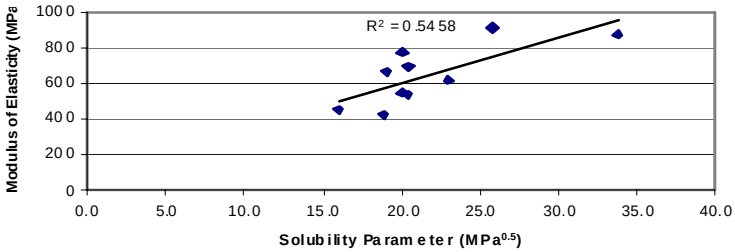


Figure 5. Effect of Plasticizer (25% w/w) on Ethylcellulose Modulus of Elasticity versus Solubility Parameter



Conclusions

Thermal properties of plasticized ethylcellulose polymer correlated well with solubility parameters for polymer and plasticizer combinations.

Of the plasticizers studied here, some represent excellent choices for optimizing the thermal behavior such as glass transition temperature and mechanical properties of ethylcellulose in fully formulated systems. Based on these data and the increasing popularity of multi-particulate formulations new grades of Surelease are currently being evaluated.

References

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World Headquarters
Colorcon
415 Moyer Blvd., P.O. Box 24, West Point, PA 19486-0024
Tel: 215-699-7733 Fax: 215-661-2605 Website: www.colorcon.com e-mail: info@colorcon.com

Locations	Telephone	Facsimile
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