Fall 10-20-2015

What's in The Bag?

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Dissecting Multilayer Film Structures to Optimize Performance in Single-Use Bioprocessing Bags

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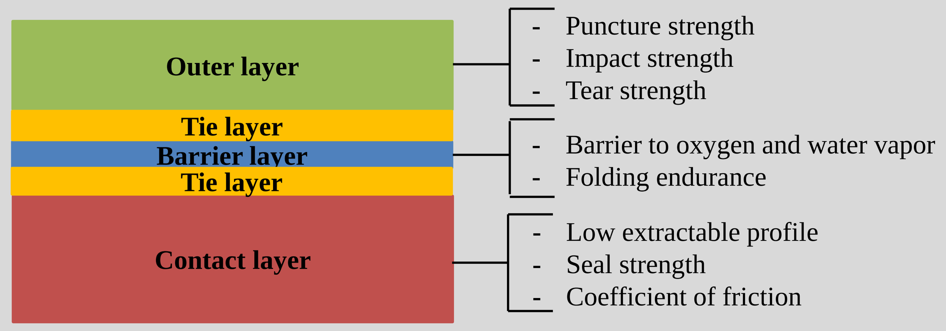
INTRODUCTION

Traditionally, the biopharmaceutical manufacturing industry has used stainless steel equipment for the production of biopharmaceuticals. More recently, the industry has shifted towards using single-use plastic bags for the production, storage, and transportation of biopharmaceuticals and other fluids necessary for manufacturing. The single-use plastic bags are made from multilayer film.



Each layer in the multilayer film structure serves a purpose. The contact layer is in direct contact with the contents of the bag and should be a "clean" polymeric material. The contact layer is also the material that is sealed to itself and to fitments during the bag converting process. The barrier layer serves to minimize oxygen and water vapor transmission through the film. The outer layer provides strength and toughness to the film to prevent failures due to puncture and abrasion. The tie layers function as adhesive layers to join the dissimilar materials of the overall structure.

The primary objective of this study is to demonstrate the differences between the extractable profiles of three different contact layer resins. A second objective of this study is to measure the physical properties such as tensile properties, tear strength, and puncture strength of various monolayer blown films. Knowledge of the monolayer film properties enables the design of a more optimized multilayer film structure for a given application.

MATERIALS AND METHODS

The polymer materials used to make the monolayer films for this study are described in Table 1.

Table 1. Physical characteristics of polymers in this study

Polymer	Composition	Density (g/cm³)	Melt Index (190°C/2.1 kg)	Melting Point (°C)
DuPont™ 20 Series DPE-20	LDPE	0.92	1.9	108
Commercially available ULDPE	ULDPE	0.902	1.0	99
DuPont™ Elvax® 3165	Ethylene – 18% vinyl acetate	0.94	0.7	89
Surlyn® 1857	Zinc ionomer	0.94	4.0	87
Surlyn® 8320	Sodium ionomer	0.95	1.0	70
EVAL™ F171[1]	32 mol % ethylene vinyl alcohol copolymer	1.19	1.8	183
SoarnoL™ DC3203F[2]	32 mol % ethylene vinyl alcohol copolymer	1.19	3.2	183

Monolayer nominal 2-mil blown film samples were made for most of the polymers listed in Table 1. The monolayer blown film samples were made on a three-layer 3" Brampton blown film line which includes three 1.25 inch extruders.

The monolayer blown film samples were sent to STERIS Isomedix Services in Libertyville, Illinois for gamma irradiation. The film samples were irradiated to 45.0-60.0 kGy. The average delivered dose was 50 kGy.

The physical properties of the monolayer blown film samples were measured using the appropriate ASTM standard and are listed along with the results.

DISSECT THE LAYERS

CONTACT LAYER

The contact layer in a bioprocessing container or reactor is arguably the most critical layer in the whole film because it is in direct contact with the contents of the container.

Extractable Screening

The DuPont™ 20 Series DPE-20, DuPont™ Elvax® 3165 and ULDPE irradiated film samples were sent to Eurofins Lancaster Laboratories, Inc. for extractables screening. The details of the extraction test conditions are described in Table 2. The method used in this study was an abbreviated version of the protocol described by Ding et al[3]. The methods used to identify and quantify the extractable compounds are methods commonly used in the industry.

Table 2. Extractable Screening Conditions

Extraction Condition	Condition Value
Test Films	DuPont™ 20 Series DPE-20 Elvax® 3165 ULDPE
Model Solvents	0.1 M H_3PO_4 0.5 N NaOH 50:50 Ethanol:Water
Surface Area of Extract Piece of Film	240 cm²
Solvent Final Volume	40 mL
Storage Temperature	40°C
Storage Time	21 days
Analyses	Direct injection GC/MS Headspace GC/MS Direct injection LC/MS

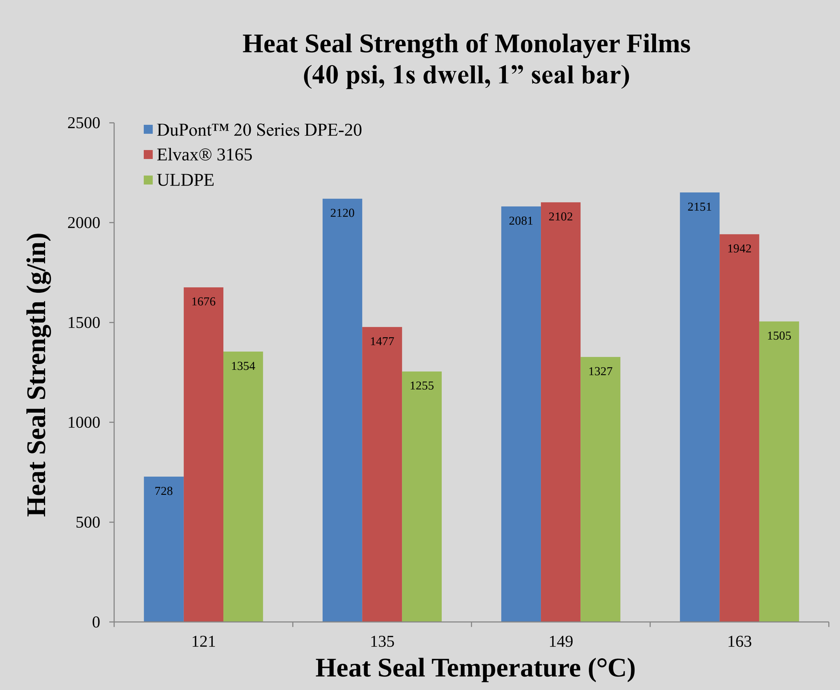
Table 3. Extractable analysis and compound detection

	DuPont™ 20 Series DPE-20	Elvax® 3165	ULDPE
Results from direct injection GC/MS analysis			
0.1 M H_3PO_4	ND	ND	ND
0.5 N NaOH	ND	ND	1 compound
50% Ethanol	ND	5 compounds	13 compounds
Results from headspace GC/MS analysis			
0.1 M H_3PO_4	ND	ND	ND
0.5 N NaOH	ND	ND	ND
50% Ethanol	ND	ND	ND
Results from direct injection LC/MS (MM+ and MM-) analysis			
0.1 M H_3PO_4	ND	ND	ND
0.5 N NaOH	ND	ND	8 compounds
50% Ethanol	ND	1 compound	9 compounds

'ND' indicates that no compound was detected above the 0.1 μg/mL reporting limit

Seal Strength

In addition to its extractable profile, the heat seal strength of the contact layer material is an important property to measure because it is the layer that is sealed together when the film is converted into bags.



Coefficient of Friction

The coefficient of friction (COF) is an indication of how easily the material can be processed. DuPont™ 20 Series DPE-20 has low COF without slip or antiblock, unlike other contact materials which require processing aids.

Table 4. Static Coefficient of Friction of Monolayer Films (ASTM D1894)

DuPont™ 20 Series DPE-20	Elvax® 3165	ULDPE
0.34	2.8	0.31

BARRIER LAYER

The barrier layer in a multilayer film structure minimizes oxygen and water vapor transmission through the film. The preferred barrier material for multilayer film used in the single use bioprocessing industry is ethylene vinyl alcohol (EVOH). EVOH is often the most brittle material in the film structure and most vulnerable to breakage from folding. The MIT Flex Test is a measurement of the endurance or strength of a film after repeated flexing.

Table 5. Oxygen Permeability at 20°C and 65% RH (cm³·mil/100in²·day·atm)

EVAL™ F171	SoarnoL™ DC3203F
0.020[1]	0.015[2]

Table 6. MIT Flex Results of EVOH film (ASTM D2176)

	EVAL™ F171	SoarnoL™ DC3203F
Average Number of Cycles	6,976	15,514

OUTER LAYER

It is important for the layers outside of the barrier layer to provide additional strength and toughness. Elmendorf tear, Spencer impact, and needle puncture were measured on three different monolayer films.

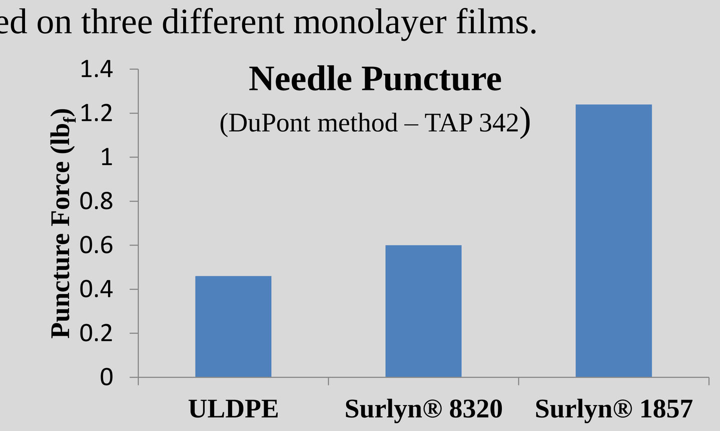


Table 7. Elmendorf Tear Strength, g/mil (ASTM D1922)

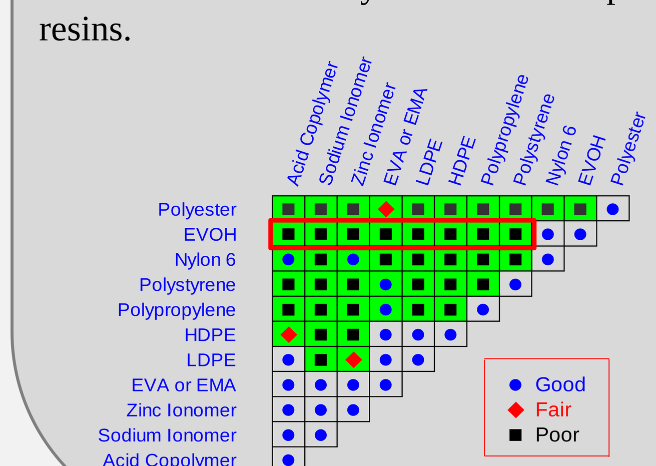
ULDPE	Surlyn® 8320	Surlyn® 1857
390	150	200

Table 8. Spencer Impact, g/mil (ASTM D3420)

ULDPE	Surlyn® 8320	Surlyn® 1857
1,830	1,230	810

TIE LAYER

Tie layer resins help join the dissimilar materials together in a multilayer structure. DuPont™ Bynel® is a broad portfolio of coextrudable tie layer resins.



Grades within the DuPont™ Bynel® 4100 and 4200 series are widely used as tie layer resins for EVOH-PE structures.

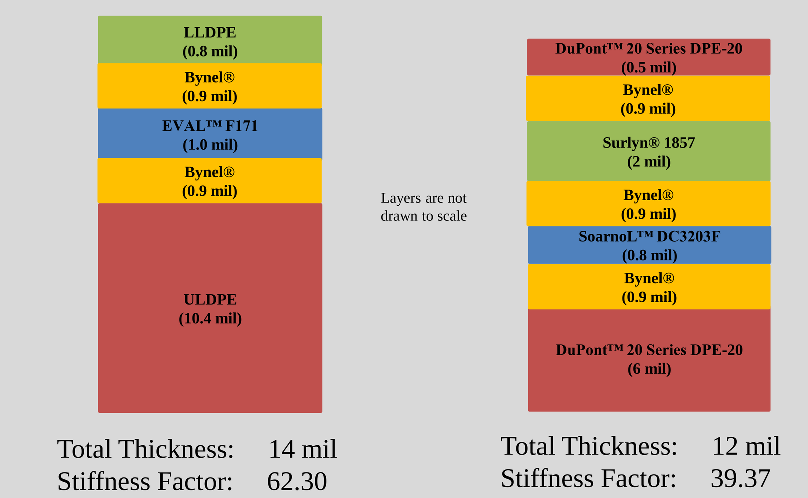
There are TNPP-free grades available.

SCOUTING MULTILAYER FILM

Understanding the properties of the materials in the individual layers allows one to design a more optimized multilayer film structure.

A computer model designed by DuPont helps predict the bending stiffness of a multilayer film[4]. The inputs for the model include layer thickness and modulus of each material. The output of the model is a stiffness factor that can be used for comparison of different multilayer structures.

Based on the results of the monolayer film property testing, multilayer film structures were entered into the model:



An optimized film structure would include a contact material that has a low extractable profile, such as DuPont™ 20 Series DPE-20, a more flexible EVOH such as SoarnoL™ DC3203F, and other tough layers such as Surlyn® 1857.

Although the model predicts that the 7-layer structure will be more flexible than the 5-layer structure, a next step would be to produce the film and measure physical properties such as puncture strength, tear strength, and the typical tensile properties.

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ACKNOWLEDGEMENTS

We would like to acknowledge STERIS Isomedix Services for their gamma irradiation services and Eurofins Lancaster Laboratories for conducting the extractable screening and analysis.

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