CONTROLLED EXTRACTION STUDY ON POLYPROPYLENE TEST ARTICLE

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ABSTRACT

A qualitative and quantitative study was performed following PQRI's Leachable and Extractable Working Group's Experimental Protocol for Controlled Extraction Studies on Plastic Test Articles. The Working Group obtained a polypropylene resin of known ingredients for the purpose of this study. The project entailed three phases:

- 1) Qualitative Controlled Extraction (Profile) 2) Quantitative Controlled Extraction
- 3) Validation

Phase one included an analytical survey to determine the following: if the known ingredients could be detected, if other species not predicted would be extracted, and if the analytical techniques were appropriate. The second phase of the study was the quantitative controlled extraction. Three target analytes were selected to be analyzed by High Performance Liquid Chromatography (HPLC) based on the results obtained in the profile study (qualitative). The third phase, validation of the HPLC method, was performed using a specific validation procedure.

This presentation summarizes results for both qualitative and quantitative extractables from the polypropylene test article

PROFILE METHODOLOGY

Solvents

Solvents were selected by the Working Group to represent a range of polarities and boiling points 2-Propanol Heyane

Methylene Chloride

Extraction Techniques

Extractions were accomplished using typical laboratory equipment. Soxhlet Sonication Reflux

Analytical Techniques

A variety of analytical techniques were used to detect a wide range of analytes. High Performance Liquid Chromatography (HPLC) Liquid Chromatography/Mass Spectrometry (LC/MS) Gas Chromatography/Mass Spectrometry (GC/MS) Non-volatile residue (NVR) Fourier Transform Infrared Spectroscopy (FTIR) Optical Microscopy/Electron Microprobe (OM/EM)

SYSTEM SUITABILITY

The Working Group recommended standard reference materials to be used with certain analytical techniques to ensure system suitability. The reference materials and concentrations are listed in Table 1.

Constraint	Telepar	Target Executivation particular
Forme	35 mil (234)	1 1000
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Polypropylene Test Article

The Working Group obtained a polypropylene test article to perform qualitative and quantitative extraction studles. The known polymer formulation ingredients are listed in Table 2.

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Extraction Conditions

The extraction conditions used for the three solvents are listed in Table 3. The resulting extracts were evaluated by the six analytical techniques.

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Initial HPLC/UV Chromatographic Conditons

Eluent A: Acetonitrile Eluent B: Water

LIGENT A. ACC	contrine	LIGENT D. Water	
Gradier	t (Linear)	Flow Rate: 1.0mL/min
Time, min	%A	%B	Injection Volume: 10µL
0	50	50	Column Temp: 60°C
11.00	100	0	Column: Vydac, C18, 150mm x 4.6mm P/N# 201TP5415
19.00	100	0	Detector: Diode Array Detector (DAD)
Post Gradient	Time: 5	minutes	Signals: 200nm, Bandwidth 4nm; 220nm, Bandwidth 4nm

Reference Signal: 550nm, Bandwidth 100nm

Qualitative Results

Qualitative results from all analytical techniques and solvents are summarized in Table 4.

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Profile Evaluation

Profile data was evaluated for potential leachables. A majority of the known polymer formulation ingredients were observed by HPLC/UV. Peaks in the HPLC/UV chromatograms were associated with Extractables A, B and C. Figures 1, 2 and 3 show HPLC/UV chromatograms from all solvents and extraction techniques. The peaks were compared to those of corresponding reference materials and were found at the highest concentrations in the 2-propanol reflux extract. The 2-propanol reflux extract also produced a significant amount of non-volatile residue (7200µg/g) compared to that produced by sonication (<0.1µg/g) in 2-propanol. The amount of NVR produced by soxhlet (7700µg/g) in 2-propanol was similar to the reflux technique.

Extractables D and E were not observed in the 2-propanol reflux extract HPLC/UV chromatograms. However, D was identified from the presence of stearic acid in LC/MS data and calcium in microprobe data, and E was identified in GC/MS data.

Reflux in 2-propoanol with measurement of three analytes (A, B and C) by HPLC/UV was determined to be the preferred technique for the controlled extraction study and subsequent material control method.

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Quantitative Controlled Extraction Preferred Technique

Reflux was the technique selected for the polypropylene controlled extraction study based on the results of the profile study. A method was optimized for material control to measure Extractables A, B and C by HPLC/UV

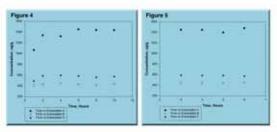
Method Optimization

In order to improve separation, the column and mobile phase composition was changed from the initial conditions. During the profile phase, it was determined that some of the reference materials were only partially soluble in 2-propanol. Several different solvents were explored in order to completely dissolve the materials. A 50:50 (v/v) solvent mixture of 2-propanol:tetrahydrofuran (THF) was successful and then used for sample extraction and standard preparation.

The sample to solvent ratio was evaluated by performing an extraction of polypropylene sample using 100cm2 (2 grams) in 50mL solvent compared to 50cm2 (1 gram) in 25mL solvent. The ratio of 50cm2 (1 gram) in 25mL solvent was ultimately chosen. Two extraction time studies were then carried out using the selected sample to solvent ratio to determine the optimal length of reflux extraction. Table 5 lists results from a broad range time study and Table 6 lists results from a narrow range time study. Visual representation of the time studies are shown in Figures 4 and 5.

	10 Acres 6490	Component µg/g	
Time, hours	Extractable A	Extractable B*	Extractable (
distant and a second	\$100	410	490
2	3300	430	590
4	\$300	450	600
-	\$500	430	890
. 8	1400	410	560
30	1400	440	570

		Component µg/g	
Time, hours	Extractable A	Extractable 8"	Extractable 0
3	1400	440	590
4	1400	440	550
5	1400	440	560
4	1500	450	570



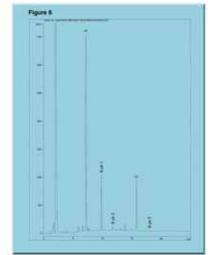
Final Sample Preparation and Analysis Conditions

Solvent: 50:50 2-propanol:THF Sample/Solvent Ratio: 50cm2/25mL Reflux Time: 3 hours HPLC/LIV Conditions

Eluent A: Acetonitrile

Eluent E	3: Wate	3r
Gradient (Linear)		
Time, min	%A	% B
0	30	70
12.00	100	0
25.00	100	0
Post Gradier	nt Time	: 5 minute
Flow Rate:		1.0mL/m
Injection Volu	ume:	10µL
Column Tem	p:	60°C
Column:		Columbu
Detector:		Diode An
Signals:		200nm, E
Deference Si	anal	550nm B

A chromatogram of the polypropylene test article extracted and analyzed using the final sample preparation and analysis conditions is shown in Figure 6.



Acknowledgements

Resin supplied by Chevron-Phillips. Resin molded by Owens-Illinois Closure Division. Data acquired by West Monarch Analytical Laboratories and Cardinal Health.