ANALYSIS FOR EXTRACTABLE AND LEACHABLE COMPOUNDS FROM POLYMERIC MATERIALS

Gordon Fujimoto¹, Sarah Dowd¹, Baiba Cabovska², Marian Twohig² ¹Waters Corporation, Beverly, MA, USA; ²Waters Corporation, Milford, MA, USA

INTRODUCTION

Extractable and leachable compounds, which are potentially harmful to human health, are of great concern to manufacturing industries, particularly manufacturers of food contact materials and of materials intended for use in the pharmaceutical industry or in medical devices. Recent changes in regulatory requirements[1] have resulted in an increased need for the accurate analysis of these compounds.

This study focused on a group of 24 polymer additives (e.g. Irganox® 1010, Ethanox® 330, et.al.) that would be of interest in analyses for extractables and leachables. The method was developed for MRM analysis and analyses were performed for extractable and leachable compounds using two different tandem quadrupole systems. An electrospray based ion source was compared against UniSpray[™], an ion source based on surface enhanced ionization to determine the best ionization scheme for compounds in this area. To test the applicability of the method, samples of polymeric materials were extracted with isopropanol and analyzed.

METHODS

UPLC Method Conditions

UPLC system:	ACQUITY UPLC I-Class
Column:	UPLC BEH C ₁₈ , 2.1 x 50 mm,
	1.7 μm
Column temp.:	40 °C
Injection volume:	3 μL
Flow rate:	0.5 mL/min
Mobile phase A:	Water - 20 µM Ammonium Formate
Mobile phase B:	Methanol - 20 µM Ammonium
	Formate

Gradient Conditions

0 min 10% B 4 min 99%B 0.5 min 10%B 6.5 min 99% B 1 min 60% B (Curve 3) 6.6 - 8.3 min 10%B

Standards: Waters Extractables & Leachables Screening Standard [Part No. 186008063] (mix of 18 compounds). Additional compounds were obtained from AccuStandard (New Haven, CT, USA).

MS Conditions

MS systems:	Xevo® TQ-S and Xevo® TQ-XS
Ionization mode:	ESI Positive and Negative
Capillary voltage:	2.5 kV
Desolvation temp:	600 °C
Source temp.:	150 °C
Cone gas flow:	150 L/hr
Desolvation gas:	1000 L/hr
Source:	ESI and UniSpray on Xevo TQ-XS
Software:	MassLynx

Sample Preparation

Samples of polymeric material were extracted with isopropanol at 37 °C for one hour.



UniSpray is a novel ionization technique that works by having a collimated, high velocity spray from a grounded pneumatic nebulizer aimed at a 1.6mm polished, stainless steel rod target typically held at 1-3kV. Signal is optimized when the impact point on the target is off-center. Under these conditions, the downstream gas flow from the nebulizer follows the curvature of the target and is directed towards the inlet orifice (Coanda Effect) leading to enhanced desolvation.



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MRM TRANSITIONS

Compound	<u>Use</u>	Mode	<u>RT</u>	Prec	Prod	<u>CV</u>	<u>CE</u>	Prod 2	<u>CE 2</u>	Prod 3	<u>CE 3</u>
Dibutyl Sebacate	Plasticizer	ES +	3.64	315.25	241.18	42	9	185.12	13	139.11	19
Diethyl Phthalate	Plasticizer	ES +	1.74	223.10	149.02	15	16	121.03	28	177.06	7
Diphenyl Phthalate	Plasticizer	ES +	2.51	319.09	225.06	20	10	77.04	30	197.06	30
Erucamide	Slip agent	ES +	4.44	338.34	135.12	100	17	303.31	14	321.32	14
Ethanox 330	Antioxidant	ES +	4.87	792.63	219.17	30	32	203.18	70		
Irgafos 168	Processing stabilizer	ES +	5.64	647.46	235.05	100	50	291.12	43	441.29	36
Irgafos 168 Oxide	Degradant	ES +	4.95	663.45	495.27	100	35	607.39	20	551.33	37
Irganox 1010	Antioxidant	ES +	4.72	1194.82	841.42	80	32	785.35	32	897.48	32
Irganox 1076	Antioxidant	ES +	5.31	548.50	419.35	50	14	107.05	20	149.06	17
Irganox 1098	Antioxidant	ES +	3.57	637.49	321.25	40	42	100.11	64	581.43	22
Irganox 245	Antioxidant	ES +	3.21	604.38	263.16	40	22	207.10	22	177.13	48
Irganox 3114	Antioxidant	ES +	4.42	801.55	219.17	40	33				
Octabenzone	UV stabilizer	ES +	4.09	327.20	137.02	45	28	215.07	19	105.03	28
TCP	Plasticizer	ES +	3.26	369.13	165.20	30	50	91.00	50	107.00	30
Tinuvin 327	UV stabilizer	ES +	4.65	358.17	302.11	30	24	57.07	24	41.01	56
Tinuvin 360	UV stabilizer	ES +	5.81	659.41	336.21	80	28	224.08	34	58.00	60
Tinuvin P	UV stabilizer	ES +	3.00	226.10	120.06	40	18	107.05	18	79.05	25
Uvinul 3030	UV stabilizer	ES +	3.67	1078.38	232.11	30	30	350.10	30	581.21	30
Uvitex OB	Brightening agent	ES +	4.50	431.18	415.20	30	40	400.10	60	105.10	70
Antioxidant 2246	Antioxidant	ES -	3.79	339.23	163.11	35	30				
Antioxidant 425	Antioxidant	ES -	4.00	367.26	177.15	35	30				
BHT	Antioxidant	ES -	4.42	219.17	163.10	30	28	203.11	26		
Cyasorb 2908	UV stabilizer	ES -	5.05	473.40	204.30	30	50	429.30	50		
Ethanox 330	Antioxidant	ES -	4.88	773.59	205.18	96	70	717.47	48	701.47	66
Irganox 1010	Antioxidant	ES -	4.72	1175.78	521.28	100	55	739.44	50	957.61	40
Irganox 1098	Antioxidant	ES -	3.58	635.48	417.30	40	40	199.12	50	57.96	62
Irganox 245	Antioxidant	ES -	3.23	585.34	367.21	80	26	409.22	26	235.13	28
Methylparaben	Preservative	ES -	1.36	151.04	92.03	45	19	136.02	14		
Propylparaben	Preservative	ES -	1.70	179.07	92.03	45	21	137.02	15	93.03	21
Tinuvin 327	UV stabilizer	ES -	4.65	356.15	340.12	30	34	305.15	30	152.00	48
Tinuvin 360	UV stabilizer	ES -	5.81	657.39	322.10	100	42	250.10	75	251.10	60
Tinuvin P	UV stabilizer	ES -	3.00	224.08	118.04	45	28	163.08	28		
Vitamin E	Plasticizer	ES-	4.78	429.37	163.08	60	28				

Example MRM Chromatograms for 1.5 ng/mL Standard

10: MRM of 3 Channels ES+ EL_065

548.5 > 419.35 (Irganox 1076)

EL_065

100

EL_065

100-

EL_065

1003

EL_065

1003

EL_065

1003

EL_065

100-

EL_065

100-

EL_065

100-

EL_065

2.00

2.00

2.00

2.00

2.00

2.00

2.00

2.00

2.00

S+ 10) 3e6	EL_065		28: MRM 473.4 > 204	of 2 Channels ES- I.3 (Cyasorb 2908 8.45es
	-	2.00	4.00	6.00
ES- ien) 2e6	EL_065		29: MRM 585.34 > 36	of 3 Channels ES- 7.21 (Irganox 245 5.21e5
	•	2.00	4.00	6.00
S- en) 4e6	EL_065		30: MRM 635.48 > 41	of 3 Channels ES- 7.3 (Irganox 1098 1.02e6
	U Fri	2.00	4.00	6.00
ES- HT) 9e4	EL_065		31: MRM 657.39 > 3	of 3 Channels ES- 322.1 (Tinuvin 360 1.52e7
	• • • •	2.00	4.00	6.00
S- n P) 9e4	EL_065		32: MRM 773.59 > 20	of 3 Channels ES- 5.18 (Ethanox 330 1.02e6
	••••	2.00	4.00	6.00
S- 46) 3e6	EL_065		33: MRM 1175.78 > 521	of 3 Channels ES- .28 (Irganox 1010 1.07e6
	0	2.00	4.00	6.00
S- 27)	внт	and	Vitamin E c	hromatogram

Standard

ionization.

5.62e6	100		
6.00	0	2.00	4.00
Channels ES-	EL_065		30: MRM
Propylparaben) 4.54e6	100		635.48 > 4
6.00	• • • • •	2.00	4.00
Channels ES-	EL_065		31: MRM
> 163.1 (BHT) 1.19e4	100		657.39 >
6.00	•	2.00	4.00
1 Channel ES-	EL_065		32: MRM
8.04 (Tinuvin P) 6.09e4	100		773.59 > 20
6.00	• • • •	2.00	4.00
1 Channel ES-	EL_065		33: MRM
tioxidant 2246) 4.18e6	100		1175.78 > 52
6.00	07	2.00	4.00
Channels ES- 12 (Tinuvin 327) 1.08e6 6.00	BHT are	and from a	Vitamin E d a 5 ng/mL S
1 Channel ES- antioxidant 425) 3.36e6			

19: MRM of 3 Channels E

1194.82 > 841.42 (Irganox 10

	0.2	ceo	2			4.0000
)	4.00 6.00		•••	2.00	4.00	6.00
	11: MRM of 3 Channels E	S+ E	EL_065		20: MRM	I of 2 Channels ES-
3	3.21 604.38 > 263.16 (Irganox 2	245)	100 - ^{1.3}	36	151.04 > 92	2.03 (Methylparaben
	1.3	se/	8 	L		0.0200
ָרָ ס	4.00 6.00			2.00	4.00	6.00
	12: MRM of 3 Channels E	S+ E	EL_065		21: MRN	I of 3 Channels ES-
	637.49 > 321.25 (Irganox 10	J98) '207	100	1.69	179.07 > 92	2.03 (Propylparaben
		561	ŏ1_	. .		4.5460
)	4.00 6.00			2.00	4.00	6.00
	13: MRM of 3 Channels E	ES+ E	EL_067		22: MRN	A of 2 Channels ES-
	6 5 6 5 6 5 6 5 6 6 5 6 6 5 6 6 5 6 6 5 6 6 5 6 6 5 6 6 5	00) 8e6	100		2	1 19.17 > 103.1 (DH1
	·····	000	õ]		<u>,, k,, k, </u>	4
)	4.00 6.00			2.00	4.00	6.00
	14: MRM of 3 Channels E 659 41 > 336 21 (Tipuvin 1	284 E	L_005		2 00 224 08	M of 1 Channel ES-
	1.0	5e8	100		2.55 224.00	6.09e4
			ŏ‡			
J	4.00 6.00		-1 065	2.00	4.00 24: MB	6.00 M of 1 Channel ES
(663.45 > 495.27 (Irgafos 168 Ox	ide)	_L_005		339.232 > 163.1	1 (Antioxidant 2246)
	3.5	0e7	100		1	4.18e6
<u> </u>	4.00 6.00		04	200	·····	6.00
,	16 [°] MRM of 2 Channels F	S+ F	EL 065	2.00	25' MRN	A of 3 Channels ES-
	792.63 > 219.17 (Ethanox 3	330)	100-		356.15 >	340.12 (Tinuvin 327)
	2.0	8e7	100 8			1.08e6
)	4 00 6.00		04	2.00	4.00	6.00
	17: MRM of 1 Channel E	S+ E	EL 065		26: MR	M of 1 Channel ES-
	801.55 > 219.17 (Irganox 31	14)	100-		367.264 > 177.	15 (Antioxidant 425
	/.3	0e5	%			3.36et
ן ו	4.00 6.00		•	2.00	4.00	6.00
	18: MRM of 3 Channels E	S+ E	EL_067		27: MR	M of 1 Channel ES-
	1078.38 > 232.11 (Uvinul 30	J30)	100		429.37 >	• 163.08 (Vitamin E
		me	Ů 81.			Time
)	4.00 6.00			2.00	4.00	6.00

EL_065 100 ₃	1.74	223.	1: MRI 1 > 149.	M of 3 Channels ES+ 02 (Diethyl Phthalate)
8				3.11e/
- 1 -	2.00		4.00	6.00
EL_065		2.99	2: MRI 226.1	M of 3 Channels ES+ 1 > 120.06 (Tinuvin P)
8				0.9867
	2.00		4.00	6.00
EL_065		315.2	3: MRI	M of 3 Channels ES+
100		515.2	J ~ 241.	1.10e7
• + •	2.00		4.00	6.00
EL_065	0.50		4: MRI	I of 3 Channels ES+
100	2.50	319.09	> 225.06	6 (Diphenyl Phthalate) 1.61e6
0	2.00		4.00	6.00
EL_065			5: MRI	I of 3 Channels ES+
100		3	327.2 > 1	37.02 (Octabenzone) 3.01e7
0	2.00		4.00	6.00
EL_065			6: MRI	I of 3 Channels ES+
100			338.34 >	135.12 (Erucamide) 1.78e6
0-1	2.00		4.00	6.00
EL_065			7: MRI	I of 3 Channels ES+
100			358.17 >	302.11 (Tinuvin 327) 3.01e7
• +-	2.00		4.00	6.00
EL_065		0.0	8: MRI	M of 3 Channels ES+
100		3.2	o :	3.00e7
0	2.00		4.00	6.00
EL_065			9: MRI	I of 3 Channels ES+
100 ■			431.1	8 > 415.2 (Uvitex OB) 5.81e7
0-1	2.00		4.00	6.00

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XEVO TQ-XS

Using the new Xevo TQ-XS tandem quadrupole instru ment, the observed signal to noise and peak areas were higher compared to the Xevo TQ-S for the compounds of interest. Most compounds showed an increase of 2-3x in both S/N and peak area with the greatest gain in peak area seen with the fragile diethyl phthalate ion.



Example traces detected with the Xevo TQ-S and Xevo TQ-XS tandem mass spectrometers for ethanox 330 (left) and antioxidant 2246 (right). Both compounds were detected with higher signal with the Xevo TQ-XS.

IONIZATION COMPARISON

UniSpray combines the benefits of electrospray and atmospheric pressure chemical ionization to increase compound detection. Due to the diversity of the compounds of interest, both electrospray and UniSpray were investigated to determine which ionization provides the best coverage for the compounds tested. The results were mixed for compounds detected as positive ions. UniSpray showed greater peak areas for only a few compounds. In contrast, compounds detected as negative ions show an almost universal increase in the detected peak area with UniSpray ionization.



Bar graphs comparing the normalized peak areas for the compounds of interest with electrospray and UniSpray

SAMPLE ANALYSIS

To test the applicability of the developed method to unknown samples, heated isopropanol extractions were performed with a nitrile glove, vial screw caps and a plastic pipette tip. Only a few of the tested compounds were detected in the extracts with two of them highlighted below.



MRM chromatograms for Irganox 1010 and Irganox 3114 acquired from samples of extracts of a nitrile glove, a vial screw cap and a plastic pipette tip.

MRM Method for the analysis of extractable and leachable compounds.



CONCLUSIONS

- A highly sensitive and selective method for low level quantitation of extractable and leachable compounds on a tandem quadrupole mass spectrometer was developed.
- The method was tested on two different tandem quadrupoles with the Xevo TQ-XS showed increased sensitivity compared to the Xevo TQ-S.
- The novel ionization technique, UniSpray, was tested with these compounds and an increase in peak area was observed for negative ions.

REFERENCES

[1] Summarized in "Non-Targeted Screening Analysis of Packaging Extracts Using the UNIFI Scientific Information System", Baiba Cabovska, Waters, Application Note: 720005326EN.