Quantitative Analysis of an Antibody Drug Conjugate using MSIA D.A.R.T.'S Technology, an Integral Part of the Universal Ligand Binding Mass Spectrometric Immunoassay (LB-MSIA) Workflow

Application Note

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Key Words
Q Exactive™ Plus, Antibody-Drug Conjugate, ADC, Deconvolution, HRAM, High Resolution/Accurate Mass, MSIA™, Mass Spectrometric Immunoassay, High -Throughput, Versette™, Streptavidin MSIA™ D.A.R.T.'S

Goal

To demonstrate the quantitative analyses of an ADC (antibody drug conjugate) using Thermo Scientific™ MSIA™ D.A.R.T.'S with the LB-MSIA™ workflow; a pre-clinical bioanalytical solution, based on mass spectrometric detection of an intact biotherapeutic.

Introduction

With the increase of biotherapeutic innovation and biological complexity, classic bioanalytical techniques for proteins such as LBAs (Ligand Binding Assays) are unable to meet the data needs for pharmacokinetics, biotransformation assessment, and antibody functional determination studies. The development of novel antibody therapeutics requires structural information such as variants, sites of glycosylation, and PTMs (post-translational modifications); necessary for drug safety, efficacy and stability. For example, an LBA would not provide the unique data requirements necessary for the establishment of DARs (Drug-Antibody Ratios) for Antibody-Drug Conjugates (ADCs). Many of these data requirements are met by the use of mass spectrometric (MS) based assays; an analytically robust and sensitive detection method that adds the specificity of identifying biomolecules by their intrinsic property of molecular mass.

The Ligand Binding-Mass Spectrometric Immunoassay (LB-MSIA) is a universal workflow solution for targeted pre-clinical analysis of biotherapeutics, such as ADCs, that combines the robust nature of traditional ligand binding assays with HRAM (High Resolution/Accurate Mass) mass spectrometric detection. By focusing on the enablement of preclinical discovery and development research the resultant automated and high throughput LB-MISA provides characterization data necessary to keep pace with new biotherapeutic innovation and increased biological complexity. This hybrid Immunoaffinity-LC/MS (IA-LC/MS) workflow is specifically enabled by Streptavidin MSIA D.A.R.T.'S; a unique pipette tip that contains molecular trapping microcolumns, covalently derivatized with streptavidin.

By mounting the Streptavidin MSIA D.A.R.T.'S onto a Thermo Scientific™ Versette™ automated liquid handler or a Thermo Scientific Finnpipette® Novus i Multichannel Electronic Pipette, the LB-MSIA workflow can be applied to high throughput sample processing for standardized routine applications. The functional design of the Streptavidin MSIA D.A.R.T.'S combined with the consistency of the Versette automated liquid handler or the Thermo Scientific Finnpipette Novus i Multichannel Electronic Pipette provides a high factor of ease-of-use and reproducibility that is not present in beads-based methodologies. When the Streptavidin MSIA D.A.R.T.'S are paired with a high affinity reagent, such as biotinylated anti-human IgG Fc affinity ligands, the workflow is enabled to selectively analyze for mAbs of a human IgG subclass.

Presented here is a study that utilized LB-MSIA to quantitatively measure the concentration of an ADC that was spiked into rodent plasma. While this study focuses on applications of intact analysis of an ADC, the LB-MSIA workflow has the potential to perform bottom up, middle down as well as intact analyses for comprehensive characterization of a biotherapeutic, as demonstrated in our previous application, "MSIA Workflow for Therapeutic Antibodies: Qualitative, Quantitative, and Functional Verification Data from HR/AM Detection of Intact, Reduced, and Peptide-level Forms of Adalimumab".

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The high biological complexity of an ADC mass spectra comes from the heterogeneous mixture of glycans and drug conjugates chemically linked to the monoclonal antibody. Two methods of data analysis were applied to the LB-MSIA performed in this study in order to demonstrate how the complexity of the MS data generated from the analysis of an ADC may be reduced in order to quantitate.

The first method is to deconvolve the MS data, reducing several peaks resulting from several charge states for each of the DAR species to a single peak representing each of the DAR species, which may then be summed to give the total ADC. The second method relies on the summation of the three most abundant charge states of each DAR species from the mass spectrum in order to achieve the AUC (area under the curve) for each DAR species. Similar to the deconvolved method, the summation of the AUCs for each of the DAR species was used to provide the AUC value for the total ADC. Both methods of data analysis when applied to this LB-MSIA were able to show reproducibility with CVs of less than 15% and within 20% accuracy.

Also shown is quantitation of a single DAR species of the ADC. By qualitatively profiling the ADC it is possible to determine the percentage each DAR species that is representative of the total ADC. Applying the appropriate percentage to the calibration curve resulted in an equation of the line that was then used to quantitate deconvolved peak intensities of the DAR3 species.

Materials

- Thermo Scientific™ Streptavidin MSIA™ D.A.R.T.'S, PN: 991STR12
- Thermo Scientific™ Versette™ Automated Liquid Handler
- Thermo Scientific™ Finnpipette™ F1 Adjustable-Volume Pipettes, PN: 4700850
- CaptureSelect™ Biotin Anti-IgG-Fc (Human) Conjugate, PN: 7103262100
- Antibody-Drug Conjugate (ADC) (Custom Made)
- Sigma-Aldrich® SILu™Lite SigmaMAb Universal Antibody Standard human, PN: MSQC4
- Mouse Plasma (K2 EDTA)
- Thermo Scientific™ BupH™ Modified Dulbecco's Phosphate Buffered Saline (PBS) Packs, PN: 28374
- MSIA™ Elution Buffer
- Fisher Chemical™ Optima™ LC/MS Grade Water, PN: W6
- Fisher Chemical™ Optima™ LC/MS Grade Formic Acid, PN: A117
- Fisher Chemical™ Optima™ LC/MS Grade Acetonitrile, PN: A955
- Thermo Scientific™ Nunc™ 500µL 96-Well Plates, Polypropylene, PN: 12-565-368
- Thermo Scientific™ ProSwift™ RP-4H Monolith Column, 1.0 x 250 mm, PN: 066640
- Thermo Scientific™ Vanquish™ UHPLC System
- Thermo Scientific™ Q Exactive™ Plus Hybrid Quadrupole-Orbitrap™ Mass Spectrometer
- Thermo Scientific™ Xcalibur™ Software, Version 3.0
- Thermo Scientific™ Protein Deconvolution Software, Version 4.0 with the ReSpect™ algorithm
- Thermo Scientific™ Protein Deconvolution Software, Version 4.0 with the ReSpect™ algorithm

Method

The LB-MSIA workflow for the bioanalysis of an ADC may be broken down into five major steps as illustrated in Figure 1. A Thermo Scientific™ Versette™ Automated Liquid Handler was used to provide the repetitive bi-directional pipetting (aspirating and dispensing cycles) necessary to pass solutions through the microcolumn housed within each of the Streptavidin MSIA D.A.R.T.S. The Streptavidin MSIA D.A.R.T.S are first derivatized with a biotin-conjugated anti-IgG Fc, an affinity ligand that specifically binds to the Fc portion of all four human IgG subclasses.

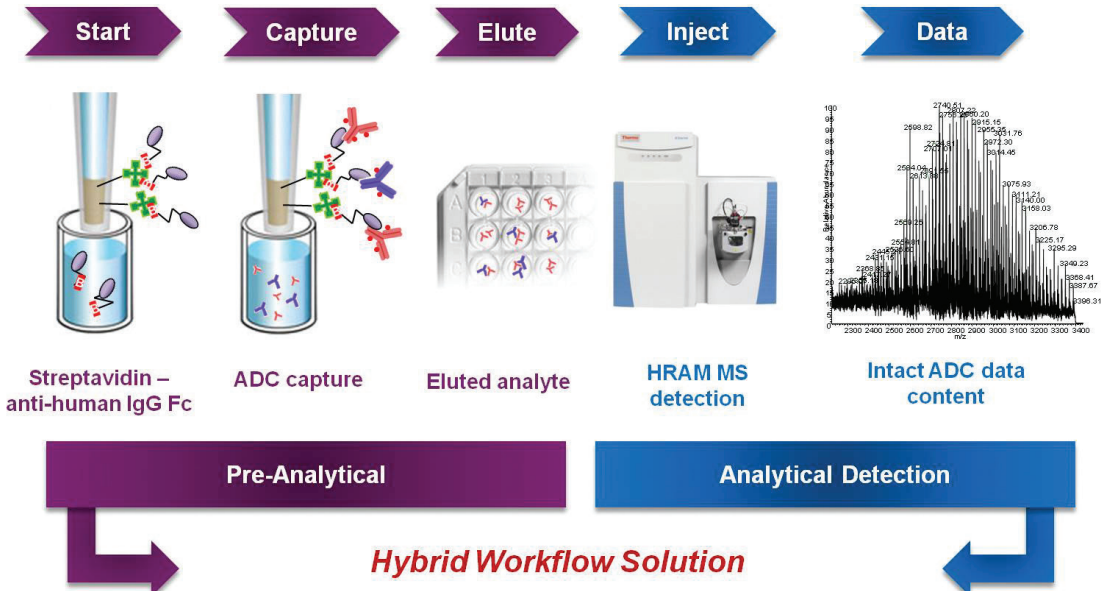


Figure 1. A schematic showing the five major steps of the LB-MSIA Workflow

The next step is to assay for the ADC from rodent plasma samples by incubating the samples with the anti-IgG-Fc-derivatized Streptavidin MSIA D.A.R.T.S. The affinity bound ADC is subsequently released from the D.A.R.T.S by treatment with the elution buffer. The ensuing eluate containing the ADC is then analyzed using LC-MS (HRAM). Utilizing Thermo Scientific's™ Xcalibur™ (Version 2.2) and Protein Deconvolution (Version 4.0) Software the resulting raw HRAM MS data is processed to provide high content quantitative data.

Pre-Analytical

Derivatization of Streptavidin MSIA D.A.R.T.'S with Affinity Ligand

To enable the Streptavidin MSIA D.A.R.T.'S to have a specific affinity for the Fc region of human IgG subclasses, each of the streptavidin derivatized microcolumns were loaded with 125 µL of 4 µg/mL CaptureSelect™ biotin anti-IgG-Fc (Human) conjugate, a single domain antibody (Life Technologies), prepared in PBS (BupH™ Modified Dulbecco's PBS). This was accomplished by following the steps provided in Table 1 utilizing a Thermo Scientific™ Versette™ Automated Liquid Handler equipped with Streptavidin MSIA D.A.R.T.'S.

	Assay Step	Assay Solution	Total Well Volume (µL)	Asp/Disp Volume (µL)	Asp/Disp Cycles	Syringe Speed (%)
1	Buffer Pre-Rinse	PBS	200	150	10x	100
2	Immobilization of anti-human IgG-Fc	Biotin anti-IgG Fc conjugate antibody	125	70	500x	100
3	Buffer Rinse	PBS	200	150	10x	100
4	Buffer Rinse	PBS	200	150	10x	100

Table 1 – Derivatization of Streptavidin MSIA D.A.R.T.'S with biotinylated anti-human IgG-Fc; Versette protocol in descending order

Sample Preparation

All samples prepared consisted of 20 µL of mouse plasma supplemented with varying concentrations of the ADC as referenced in Table 2. The ADC control sets were each prepared in replicates of five and the calibration curve was prepared in duplicate. Then, the curve and control sets were performed three times over three non-consecutive days.

ADC Samples	Concentration (µg/mL)
Dynamic Range	2.5-320
Control Set 1	5.0
Control Set 2	13.5
Control Set 3	53.5
Control Set 4	213.5

Table 2 – ADC Sample Concentrations. Each control set consisted of 5 replicate samples and each calibration curve was run in duplicate.

Prior to incubation of the samples with the anti-IgG-Fc-derivatized Streptavidin MSIA D.A.R.T.'S, each sample was further diluted with 80 µL of PBS supplemented with 0.7 µg of SILu™Lite SigmaMAb as an internal standard. Using the Versette Liquid Handler, the following steps outlined in Table 3 were performed to capture the ADC and internal standard from the samples.

	Assay Step	Assay Solution	Total Well Volume (µL)	Asp/Disp Volume (µL)	Asp/Disp Cycles	Syringe Speed (%)
1	ADC Capture*	Sample Solution	100	70	700x	50
2	Buffer Rinse	PBS	200	150	10x	100
3	Buffer Rinse	PBS	200	150	10x	100
4	Water Rinse	Water	200	150	10x	100
5	Water Rinse	Water	200	150	10x	100

**ADC Capture performed using Anti-human IgG-FC MSIA D.A.R.T.'S*

Table 3 – ADC Capture; Versette protocol in descending order

Sample Elution

Following the selective capture of the ADC with the anti-IgG-Fc-derivatized Streptavidin MSIA D.A.R.T.'S, each device was treated with 100 µL of the MSIA™ Elution Buffer liberating the ADC and internal standard. Reference Table 4 for the specifics of the repetitive pipetting used to elute the captured ADC from the D.A.R.T.'S. The intact ADC and internal standard were detected by LC-MS (HRAM).

	Assay Step	Assay Solution	Total Well Volume (µL)	Asp/Disp Volume (µL)	Asp/Disp Cycles	Syringe Speed (%)
1	Elution	Elution Buffer	100	30	20x	100

Table 4 - Versette protocol for elution of affinity-captured ADC from anti-IgG-Fc-derivatized D.A.R.T.'S. .

Analytical-Detection

Liquid Chromatography

The affinity-purified ADC eluates were separated on a Thermo Scientific™ Vanquish™ UHPLC system utilizing a Thermo Scientific™ ProSwift™ RP-4H (1 x 250 mm) column heated to 60 °C. Separation was performed utilizing a gradient of 10% - 48% of 0.2% formic acid in acetonitrile over 12 minutes at a flow rate of 200 µL/min.

Mass Spectrometry

For all samples, full-scan MS data were acquired over the range of m/z 2000-3400 m/z in positive-ion mode on a Thermo Scientific™ Q Exactive™ Plus Hybrid Quadrupole-Orbitrap mass spectrometer with a resolving power of 17,500 (FWHM) at m/z 200 and the AGC (Automatic Gain Control) set to a target value of 3.00E6.

Data Analysis

During this study, a comparison of two methods of data analysis was demonstrated for the quantitative analysis of the ADC. The LC-MS raw data utilized by both methodologies was collected using Thermo Scientific's Xcalibur™ Software, Version 3.0. Thermo Scientific's™ Protein Deconvolution™ Software Version 4.0 utilizing the Sliding-Window feature in the ReSpect™ algorithm was used to process the MS raw data as the first method of quantitation. The intensities of the deconvolved peaks were used to determine the peak intensity ratio (Sum of ADC peaks/SILuLite peaks) for each sample analyzed. The second method of data analysis, described here as the XIC Method, utilizes the raw MS data to generate an extracted ion chromatogram for the three most abundant charge states of each intact ADC DAR species, which were then integrated to obtain the AUC (Area Under the Curve) value for each sample analyzed. The same method was applied to the corresponding SILuLite internal standard (IS) allowing for the area ratio to be determined between each DAR species and the internal standard.

Results and Discussion

Normalization of the Samples

Quantification of the total ADC present in each sample requires the summation of the heterogeneous mixture of DAR (Drug to Antibody Ratio) species that is normalized by the use of the SILuLite IS (Figure 2). Referring back to the sample preparation of the pre-analytical section of the method, it should be noted that the SILuLite is added to each sample prior to the affinity capture. Upfront normalization of the affinity capture helps to increase sample analysis accuracy and reproducibility.

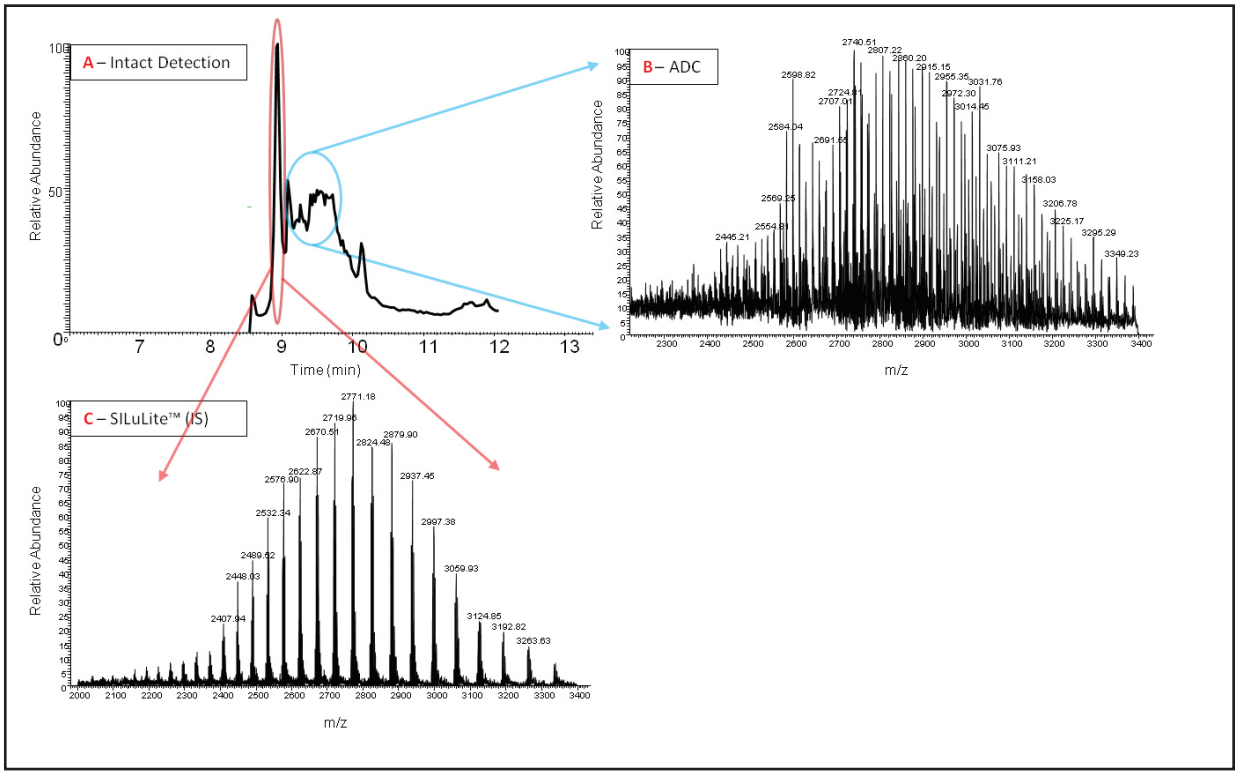


Figure 2. The results of the LB-MSIA workflow performed on a 20µL sample containing 53.5 µg/mL of the ADC and 35 µg/mL SILuLite™ from rodent plasma. A) Total ion chromatogram of the ADC sample showing the elution profile of the intact ADC and SILuLite IS. B) Mass spectrum of the several DAR species from the ADC sample. C) Mass Spectrum of the SILuLite IS from the ADC sample.

Deconvolution Method for the Quantitation of the ADC – Data Analysis Method 1

In this application, peak intensities obtained from deconvolved mass spectra were used for plotting the calibration curves for the ADC. The deconvolution software was applied to reduce the complexity in the raw MS data for the ADC (Figure 3A). The deconvolution data in Figure 3B shows multiple variants of the ADC ranging from DAR0 to DAR8. To generate the ADC calibration curve, a ratio between peak intensities of ADC and SILuLite IS was determined for each sample (that is, sum of DAR peak intensities/sum of SILuLite peak intensities) and plotted against the concentration of ADC as shown in Figure 4.

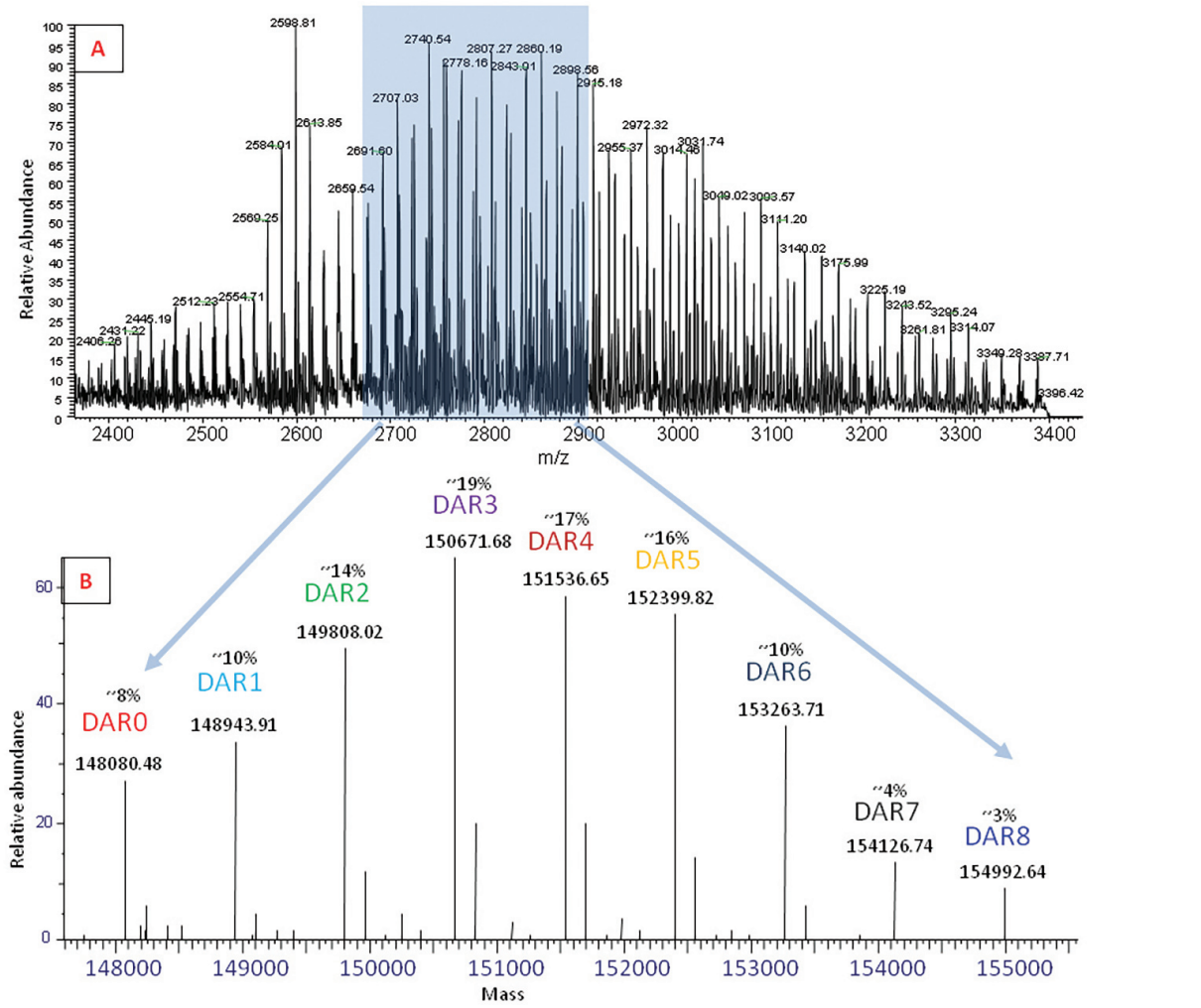
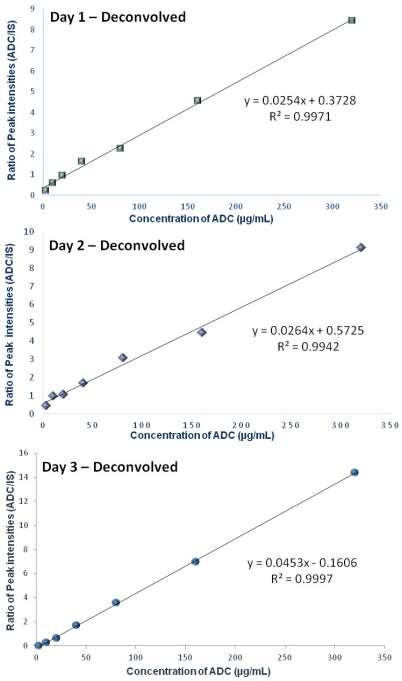


Figure 3. The results of the LB-MSIA workflow performed on a 20µL sample containing 53.5 µg/mL of the ADC from rodent plasma. A) Mass spectrum of numerous DAR species from the ADC sample. Each DAR species represents a different number of attached drug conjugates to the carrier antibody. B) Deconvolution of the mass spectrum from A resulting in the identification of a total of 9 DAR species. The intensities of all the DAR species were summed and the percentage of each DAR species was calculated based off of the total.

Following the calculation of the peak intensity ratio an average of duplicate samples was then used to generate the plots in Figure 4. The assay achieved a reproducible linear calibration curve ranging from 2.5-320 µg/mL for three curve sets generated on three separate non-consecutive days. The assay also showed CVs for most of the quintuplicate control samples below 15% and accuracy within 12%.



Controls

Sample Concentration (µg/mL)	Average concentration (µg/mL) (n=5)	% CV (n=5)	% Accuracy (n=5)
Day 1			
5.0	4.5	7.2	-10.7
13.5	14.2	5.9	5.2
53.5	53.4	5.0	-0.1
213.5	225.6	4.9	5.4
Day 2			
5.0	5.3	23.2	5.6
13.5	13.2	15.3	-2.6
53.5	52.4	8.3	-2
213.5	237.6	3.8	11.3
Day 3			
5.0	5.4	9.4	8.5
13.5	12.5	13.1	-7.5
53.5	59.5	13.7	11.2
213.5	238	8.0	11.5

Figure 4. Deconvolved Quantitation of an ADC analyzed with LB-MSIA from rodent plasma over a discontinuous period of 3 days: Calicbration Curve Range of 2.5-320 µg/mL.

XIC Method for the Quantitation of the ADC – Data Analysis Method 2

A comparative data analysis method, the XIC method, was also used to process the raw MS data obtained from each sample. In this method, the m/z values of the three most abundant charge states (+53, +54 and +55) for each ADC DAR species (Figure 5B) were combined to generate an extracted ion chromatogram. The ADC peak in the extracted ion chromatogram was then integrated to obtain AUC (area under the curve) value for each ADC sample. The same approach was also used to obtain the AUC value for the IS (SILuLite) in each sample. The ratios between the AUC values for ADC and IS (SILuLite) were determined and plotted against the concentrations of ADC as shown in Figure 6. Each calibration plot represents an average of two curves (n=2). The assay achieved a reproducible linear working curve ranging from 2.5-320 µg/mL for three curve sets. The assay also showed CVs of the quintuplicate below 15.8% and accuracy within 20%.

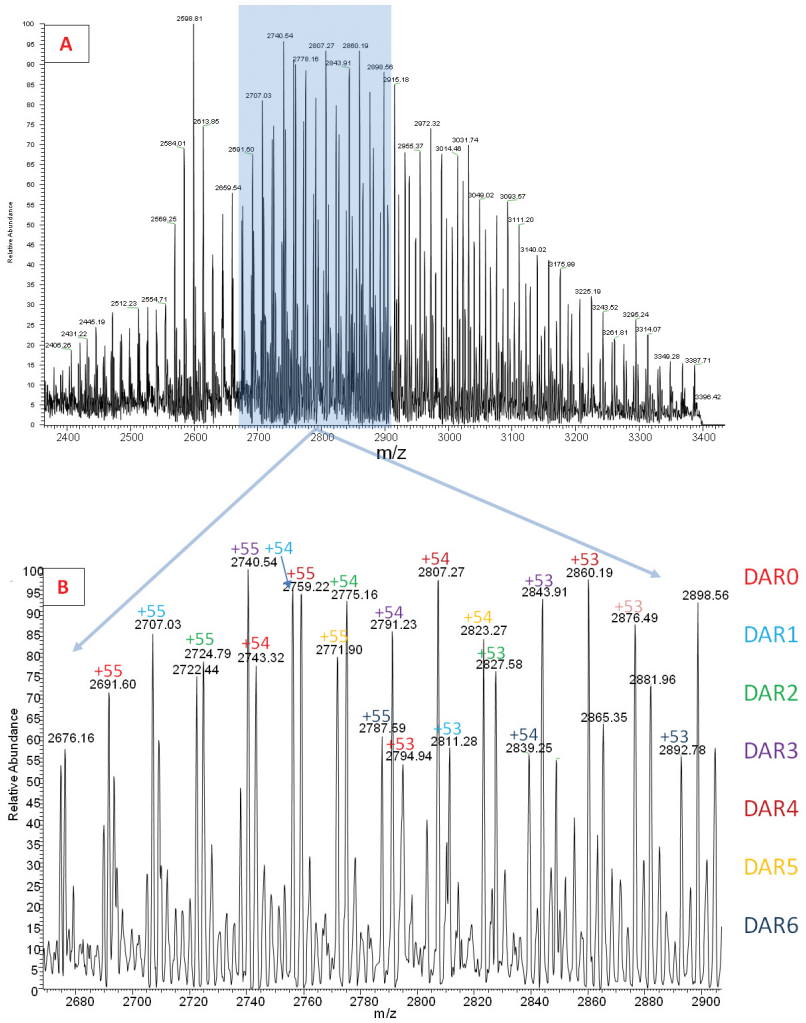
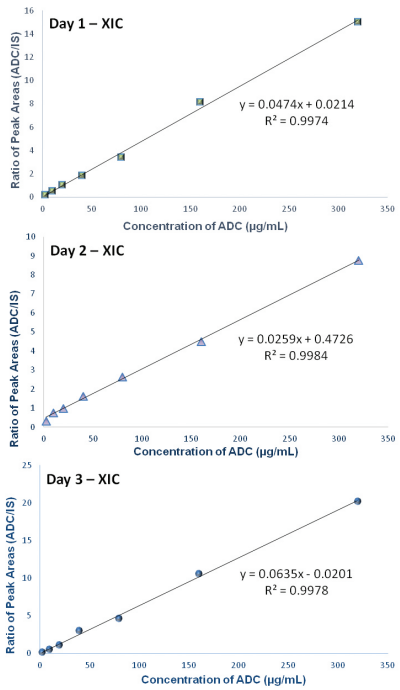


Figure 5. The results of the LB-MSIA workflow performed on a 20µL sample containing 53.5 µg/mL of the ADC from rodent plasma. A) Mass spectrum of numerous DAR species from the ADC sample. Each DAR species represents a different number of attached drug conjugates to the carrier antibody. B) Zoomed in image of A showing multiple charge states of DARo-DAR6 species.



Controls

Sample Concentration (µg/mL)	Average concentration (µg/mL) (n=5)	% CV (n=5)	% Accuracy (n=5)
Day 1			
5.0	5.1	15.0	2.9
13.5	14.2	15.8	6.9
53.5	53.4	8.2	7.2
213.5	219.4	7.1	2.8
Day 2			
5.0	6	12.4	19.3
13.5	10.8	10.7	-19.9
53.5	49.4	7.2	-7.7
213.5	208.7	8.2	11.3
Day 3			
5.0	4.5	7.2	-10.7
13.5	14.2	5.9	5.2
53.5	53.4	5.0	-0.1
213.5	225.6	4.9	5.4

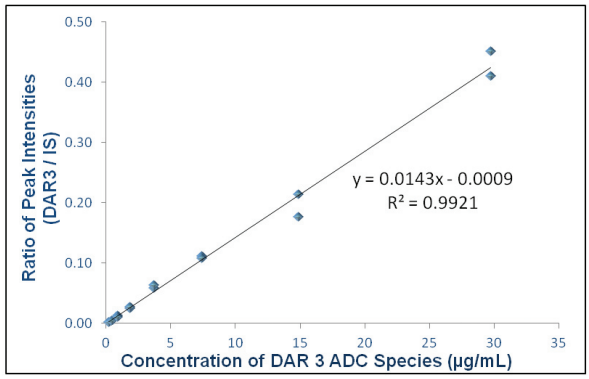
Figure 6 – XIC Quantitation of an ADC analyzed with LB-MSIA from rodent plasma over a discontinuous period of 3 days: Working Curve Range of 2.5-320 µg/mL.

Quantitation of an Individual DAR species of the ADC

A new study was performed in order to quantitate a single DAR species. The total ADC peak intensity was calculated by taking the summation of the deconvolved peak intensities from the nine ADC DAR species. The intensities for each individual DAR species were used to determine the percentage each contributed to the sum of their intensities listed in Table 5. Multiplying the percentage of each DAR species with the known concentration of the ADC stock, 225.6 µg/mL, the concentration for each DAR species was calculated and are listed in Table 5.

DAR Species	% Total	Concentration (µg/mL)
0	7.81	17.62
1	9.62	21.70
2	14.20	32.03
3	18.58	41.92
4	16.81	37.93
5	16.04	36.19
6	10.44	23.56
7	3.95	8.90
8	2.55	5.75

Table 5 -DAR Species Profile: The percentages of each DAR species were calculated by dividing the DAR species individual peak intensity by the total ADC. Then the percent contribution of each DAR species was multiplied by the stock concentration of the ADC, 225.6 µg/mL.



Controls

Total ADC Theoretical Sample Conc. (µg/mL)	DAR 3 Species % of Total ADC	DAR 3 Species Theoretical Conc. (µg/mL)	DAR 3 Species Peak Intensity	Avg. Dar 3 Species Experimental Conc. (µg/mL) (n = 5)	% CV (n=5)	% Accuracy (n=5)
2.50	18.58	0.47	5.249E-03	0.43	15.50	-8.3
5.00		0.93	1.369E-02	1.02	13.50	10.0
40.00		7.43	9.134E-02	6.45	3.35	-13.2
160.00		29.76	3.966E-01	27.80	4.80	-6.6

Figure 7 - A standard curve was created using the intensities of the DAR3 ADC species. The Total ADC dilution curve spanned a dynamic range from 1.25-160 µg/mL. In order to apply the dynamic range to the DAR3 ADC species the total ADC concentrations were multiplied by the DAR3 percentage listed in Table 5 (18.58%), reducing the dynamic range for the DAR3 ADC species to 0.23-29.73 µg/mL. The resultant equation of the line was within 15% accuracy for the controls (DAR3 Control Concentrations: 0.47, 0.93, 7.43, 29.76 µg/mL).

A control curve was generated using the DAR3 ADC peak intensity ratios (Figure 7). As seen in Table 5, the DAR 3 species represents 18.58% of the total ADC. By applying the same percentage to the curve concentrations for the Total ADC standard, the dynamic range is reduced from 1.25-160 ug/mL (Total ADC) to 0.23-29.73 µg/mL (DAR 3 ADC Species) resulting in an equation of the line that is specific for the DAR 3 ADC species (Figure 7). The MS data for the control samples were deconvolved and the peak intensities for the DAR 3 species were normalized by the SILuLite IS. The concentrations of the controls were then calculated from the equation of the line as represented in Figure 7.

Conclusion

The universal LB-MSIA utilizing Streptavidin MSIA D.A.R.T.'S demonstrated here, provided a sensitive, robust, and reproducible method for the quantitative analysis of an ADC. The high selectivity of the CaptureSelect™ biotin anti-IgG-Fc (human) conjugate combined with the molecular trapping technology of the MSIA D.A.R.T.'S created an ideal scenario to quantitatively assay a low abundant (µg/mL) intact ADC from rodent plasma with a dynamic range spanning two orders of magnitude. Furthermore, the workflow supported a high throughput application by performing the pre-analytical steps on the Thermo Scientific™ Versette™ automated liquid handler. As a hybrid approach, the use of the Q Exactive Plus for HRAM detection helped provide additional analytical flexibility and data content over other developing triple quadruple methods that are reliant on peptide analysis. The two methods of data analysis demonstrated here each help to reduce the biological complexity of the ADC MS. As shown, the combined benefits of the LB-MSIA enabled the quantitation of the total ADC and a single DAR species of the ADC with CVs that were less than 15% and accuracy that was within 20%.

Ordering Information

MSIA D.A.R.T.'S for Immunoaffinity Capture		
Compatible with the Thermo Scientific Versette Automated Liquid Handler and Thermo Scientific Finnpipette® Novus i Multichannel Electronic Pipette		
Cat. No.	**Description**	**Packaging**
991CUS02	300µl MSIA D.A.R.T.'S, Custom	Pack of 96 units
991PRT11	300µl MSIA D.A.R.T.'S, Protein A	Pack of 96 units
991PRT12	300µl MSIA D.A.R.T.'S, Protein A	Pack of 24 units
991PRT13	300µl MSIA D.A.R.T.'S, Protein G	Pack of 96 units
991PRT14	300µl MSIA D.A.R.T.'S, Protein G	Pack of 24 units
991PRT15	300µl MSIA D.A.R.T.'S, Protein A/G	Pack of 96 units
991PRT16	300µl MSIA D.A.R.T.'S, Protein A/G	Pack of 24 units
991STR11	300µl MSIA D.A.R.T.'S, Streptavidin	Pack of 96 units
991STR12	300µl MSIA D.A.R.T.'S, Streptavidin	Pack of 24 units
991001096	300µl MSIA D.A.R.T.'S, Insulin	Pack of 96 units
991001024	300µl MSIA D.A.R.T.'S, Insulin	Pack of 24 units
991R	300 µL MSIA D.A.R.T.'S, Reloadable Rack	1 reloadable rack, D.A.R.T.'S are not included

MSIA Streptavidin-EVO for Immunoaffinity Capture		
Compatible with the Tecan™ Freedom EVO® Liquid Handling Robotic Platform equipped with a MCA96 option		
Cat. No.	**Description**	**Packaging**
992STR96	500µl MSIA Streptavidin EVO microcolumns	Pack of 96 units

Automated Liquid Handling Platform	
Cat. No.	**Description**
650-MSIA	MSIA Versette Automated Liquid Handler

Multichannel Pipettes and Pipette Stand		
Cat. No.	**Description**	**Packaging**
991S	Finnpipette Novus i Adjustable Pipette Stand	1 pipette stand
991SP12	Finnpipette Novus i Electronic 12-Channel Pipette, 30-300µl and Pipette Stand	1 pipette and 1 pipette stand

Liquid Chromatography	
Cat. No.	**Description**
	Thermo Scientific™ Dionex™ UltiMate® 3000 UHPLC System
	Thermo Scientific™ Vanquish™ UHPLC System
066640	ProSwift™ RP-4H Monolith Column, 1.0 x 250 mm

Mass Spectrometry and Software
Description
Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap Mass Spectrometer
Thermo Scientific™ Q Exactive™ Plus Hybrid Quadrupole-Orbitrap™ Mass Spectrometer
Thermo Scientific™ Pinpoint Software
Thermo Scientific™ XCalibur™ Software
Thermo Scientific™ Protein Deconvolution Software, Version 4.0 with the ReSpect™ algorithm

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