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ARTICLE

Melamine Detection in Infant Formula Powder Using Near- and Mid-Infrared Spectroscopy

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Near- and mid-infrared spectroscopy methods (NIR, FTIR-ATR, FTIR-DRIFT) were evaluated for the detection and quantification of melamine in infant formula powder. Partial least-squares (PLS) models were established for correlating spectral data to melamine concentration: $R^2 > 0.99$, RMSECV ≤ 0.9, and RPD ≥ 12. Factorization analysis of spectra was able to differentiate unadulterated infant formula powder from samples containing 1 ppm melamine with no misclassifications, a confidence level of 99.99%, and selectivity > 2. These nondestructive methods require little or no sample preparation. The NIR method has an assay time of 1 min, and a 2 min total time to detection. The FTIR methods require up to 5 min for melamine detection. Therefore, NIR and FTIR methods enable rapid detection of 1 ppm melamine in infant formula powder.

KEYWORDS: Melamine detection; infant formula powder; infrared spectroscopy

INTRODUCTION

Recent recalls involving pet food and milk products contaminated with melamine (2,4,6-triamino-1,3,5-triazine) have created a widespread food safety scare. Melamine contamination has been reported in products such as milk, infant formula, frozen yogurt, pet food, biscuits, candy, and coffee drinks (*1*). Melamine is commonly used industrially in the production of plastics, glues, and laminates and as a fertilizer (*2*). It was previously considered as a nonprotein nitrogen (NPN) source for cattle feed supplementation, but its use in cattle feed has been discontinued due to its incomplete hydrolysis (*3*). A driving force for the adulteration of a food product with melamine is that its high nitrogen content increases the apparent protein content measured by standard protein analysis tests, such as Kjeldahl or Dumas, that measure total nitrogen content as an indication of protein levels (*4*).

In 2007, pet food adulteration with melamine resulted in the illness and death of animals that consumed the contaminated product (*5*). The more recent incident of contamination of milk with melamine in China likely caused 300,000 cases of renal complications in children, and at least 6 child deaths, directly resulting from consumption of tainted product (*4*, *6*). Toxic effects associated with melamine consumption occur only following high doses (*7*). The oral 50% lethal dose (LD_{50}) has been reported as approximately 3 g/kg of body weight (*8*). It is thought that simultaneous ingestion of melamine and one of its analogues, cyanuric acid, may result in the formation of crystals in the kidney (*7*), as was the case in the pet food incident (*9*). To ensure the U.S. food supply is not affected by melamine-containing products, the Food and Drug Administration (FDA) has taken proactive steps, such as confirming that U.S. manufacturers of infant formula do not use milk-based ingredients from China, and increasing sampling and testing of milk-derived ingredients and finished products from Chinese sources (*10*). The FDA has currently stated that a level of up to 2.5 ppm melamine and its analogues in foods (not including infant formula) does not raise public concern. Recently, a threshold of 1 ppm for melamine in infant formula was set by the FDA (*11*).

In 2008, brands of infant formula produced and sold in the United States were found to contain low levels of melamine (*12*). Due to the serious health concerns associated with melamine consumption and the extensive scope of affected products, rapid and sensitive methods to detect melamine's presence are essential. This is especially true for infant formula because formula is the major calorie and nutrient source for infants, the kidney function of infants is immature, and the product would be consumed for an extended period of time. Therefore, detection of 1 ppm melamine in infant formula is critical (*9*).

The detection limits and total time to detection for a variety of melamine detection methods are summarized in **Table 1**. The applicability of the majority of these methods for infant formula analysis has not been reported, and others may not be useable for high-throughput analysis due to sample pretreatment requirements. The complexity of the infant formula matrix may complicate detection efforts. Currently, the FDA uses a liquid chromatography−triple-quadrupole tandem mass spectrometry (LC-MS/MS) method to detect residues of melamine in dry infant formula (*13*). Although this method provides limits of detection as low as 250 ppb, the sample preparation and cleanup procedures are time-consuming and labor-intensive. Therefore, the use of this method as a screening tool for a large number of samples is not practical or cost-effective. A recently developed rapid method using a low-temperature plasma probe in combination with tandem mass spectrometry (LTP-MS/MS)

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Table 1. Summary of Published Methods for Detecting Melamine in Food Products[a]

method of melamine detection	food product	assay time	total time to detection	detection limit	ref
UPLC-ESI-MS/MS	animal feeds		3+ h[b]	10 ppb	*25*
HPLC-DAD	plant origin protein powders		3+ h[b]	10 ppm	*26*
HPLC-MS/MS	plant origin protein powders		3+ h[b]	500 ppb	*26*
HPLC	rice, wheat, corn flours		3+ h[b]	5 ppm	*27*
ELISA	solution/buffer		1.5 h[b]	9 ppb	*28*
	dog food		1.5 h[b]	1 ppm	*28*
SERS	aqueous solutions[c]		0.5−1 h	33 ppb	*29*
ZIC-HILIC	animal feed		2+ h[b]	500 ppb	*30*
LTP-MS/MS	milk powder	25 s		6 ppb	*14*
EIA	pet food		1.5 h[b]	20 ppb	*31*
HPLC-DAD	pet food	15 min	3+ h[b]	100 ppb	*31*
SERS	wheat gluten		0.5−1 h	1000 ppm	*24*
	chicken feed		0.5−1 h	500 ppm	*24*
	cake		0.5−1 h	500 ppm	*24*
	noodles		0.5−1 h	700 ppm	*24*
HPLC	animal feed powdered rice protein	8 min	3+ h[b]	75 ppm	*32*
LC-MS/MS	dry infant formula	14 min	3+ h[b]	250 ppb	*13*
MS-DART	pet food	1−1.5 min	10 min	1 ppm	*33*
LC-MS	catfish, pork, chicken, pet food		30 min[b]	10 ppb	*34*

[a] UPLC-ESI-MS/MS, ultraperformance liquid chromatography coupled with electrospray ionization quadrupole tandem mass spectrometry; HPLC-DAD, high-performance liquid chromatography with diode array detection; HPLC-MS/MS, high-performance liquid chromatography−tandem mass spectrometry; HPLC, high-performance liquid chromatography; ELISA, enzyme-linked immunosorbent assay; SERS, surface-enhanced Raman spectroscopy; ZIC-HILIC, zwitterionic hydrophilic interaction chromatography; LTP-MS/MS, low-temperature plasma probe combined with tandem mass spectrometry; EIA, enzyme immunoassay; LC-MS/MS, liquid chromatography−triple-quadrupole tandem mass spectrometry; MS-DART, mass spectrometry using soft ionizaiton by direct analysis in real time; LC-MS, liquid chromatography−mass spectrometry. [b] Estimated total time to detection. [c] Better performing Klarite nanosubstrate used with SERS.

is reported to have a 6 ppb detection limit in milk powder (*14*), but equipment may not be widely available or exportable for international adoption of the method. Thus, there is still a need for a rapid, high-throughput, widely available, cost-effective method for detecting melamine in infant formula. Rapid infrared spectroscopy methods have been successfully used in adulteration detection for a wide range of complex food products, including oils, carbohydrate powders, juices, honey, coffee, milk, vinegar, crab meat, and wheat (*15*−*20*). The objective of this study was to evaluate the ability of near- and mid-infrared techniques to quantify and detect melamine in infant formula powders.

MATERIALS AND METHODS

Sample Preparation. Two powder infant formula products were provided by Mead Johnson Nutritionals (Evansville, IN) and mixed in a 1:1 w/w ratio to prepare the unadulterated infant formula blend. A stock powder blend of a 1:1 w/w ratio of melamine (Alfa Aesar, Ward Hill, MA) and the infant formula mixture was prepared. This blend was further diluted to 40, 30, 20, 10, 5, 4, 3, 2, 1, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, and 0.1% melamine by geometric mixing of equal mass ratios of stock and the infant formula blend to a final mass of 5 g. Lower concentrations of melamine in infant formula (0.075, 0.05, 0.025, 0.01, 0.005% w/w) were prepared by geometrically mixing a 1% w/w melamine stock powder with the infant formula blend. Similarly, a 0.1% w/w melamine stock powder was diluted to achieve melamine levels of 0.001 and 0.00025% w/w. The sample with the lowest concentration of melamine was prepared by diluting a 0.05% w/w melamine stock powder to a melamine level of 0.0001% w/w (1 ppm). All samples were prepared in duplicate and stored in sealed glass vials at room temperature prior to analysis, and all dilutions were analyzed.

Mid-Infrared Spectroscopy Methods. Spectra of samples in the mid-infrared region (4000−650 cm^{-1}) were collected using a Thermo-Nicolet Nexus 670 FTIR equipped with a mercury cadmium telluride A (MCTA) detector and KBr beam splitter (ThermoNicolet Analytical Instruments, Madison, WI). Two sampling techniques were used to collect spectra: diffuse reflectance (DRIFT) spectroscopy and multi-bounce attenuated total reflectance (ATR). For the FTIR-DRIFT method, samples were mixed with KBr in a 1:1 ratio prior to spectral acquisition using an Avatar Diffuse Reflectance Smart Accessory (ThermoElectron Corp., Madison, WI). A pure KBr background was collected and subtracted from all sample spectra prior to statistical analysis. For the FTIR-ATR method, spectra were collected without the addition of KBr using a Smart Orbit ATR accessory with a diamond crystal (ThermoElectron Corp.). An air background spectrum was collected and subtracted from all sample spectra in the OMNIC software program (ThermoElectron Corp.) prior to statistical analysis. Spectra were collected in triplicate from duplicate samples prepared for each concentration of melamine tested, and samples of unadulterated infant formula and melamine were separately analyzed. A total of 256 scans at 4 cm^{-1} resolution were co-added for each spectrum collected.

Near-Infrared Spectroscopy Method. A Multiple Purpose Analyzer (MPA) NIR spectrometer (Bruker Optics Inc., Madison, WI) with a 30-position sample rotation wheel in combination with an integrating sphere module with RT-PbS (external) detector was used to collect the spectra. An internal, computer-controlled reference wheel was utilized for an automatic background spectrum acquisition. Glass vials 15 mm in diameter (Bruker Optics Inc.) were filled with 5 g of sample and placed into vial holders on the rotation wheel. Reflectance spectra were collected using 64 scans at 2 cm^{-1} resolution in the 12500−3500 cm^{-1} spectral range. Triplicate measurements were carried out on each sample. Samples were prepared and analyzed in duplicate, and six replications, collected following rotation of the glass vials between each replication, were averaged for each sample. The spectra were collected and analyzed using OPUS 6.5 software (Bruker Optics Inc.).

Spectral Analysis. All spectra were analyzed using OPUS 6.5 software (Bruker Optics Inc.). The spectra acquired by FTIR-DRIFT and -ATR methods using OMNIC software were converted into 1D OPUS files before analysis using the OPUS 6.5 software was carried out. Partial least-squares analysis (PLS) was utilized to build quantitative models, and cross-validation (internal validation) was performed to evaluate the prediction power of the model (*21*). For cross-validation, an individual sample was taken from the calibration data set and a chemometric (calibration) model was established using the remaining samples. This model was then applied to the sample that had been removed. The error of analysis for this sample was calculated as $Y_i^{meas} - Y_i^{pred}$ where Y_i^{meas} is a measured melamine concentration in sample i and Y_i^{pred} is a predicted melamine concentration in sample i.

The sample was returned to the data set, a new sample was removed and analyzed, and the procedure was repeated until all samples were

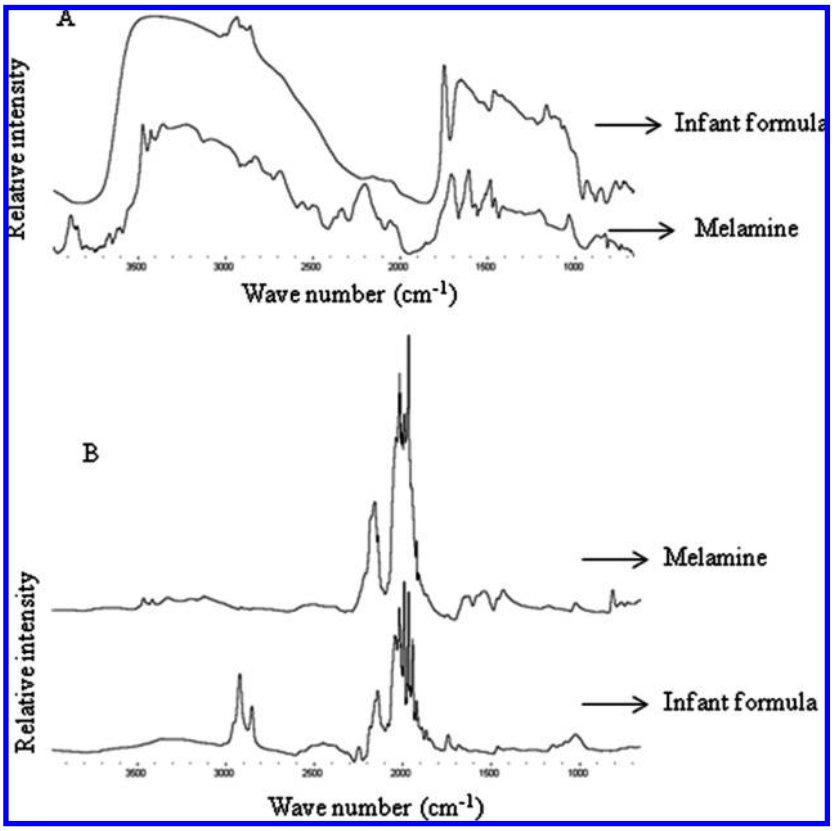

Figure 1. FTIR spectra of melamine and infant formula collected using (**A**) DRIFT method and (**B**) ATR method after automatic baseline correction and smoothing.

analyzed. Extracting samples before establishing a calibration data set guaranteed that the samples were independent. The root mean square error of prediction (RMSECV) was calculated as

$$\mathrm{RMSECV} = \sqrt{\frac{1}{M} \times \sum_{i=1}^{M} (Y_1{}^{\mathrm{meas}} - Y_1{}^{\mathrm{pred}})^2}$$

with M denoting total number of samples analyzed. For the analysis error of the calibration samples, the root mean square error of estimation (RMSEE) was calculated as

$$\mathrm{RMSEE} = \sqrt{\frac{\mathrm{SEE}}{M - R - 1}}$$

with SEE denoting standard error of estimation, and R is the sample correlation coefficient between the outcomes and their predicted values (*21*). To evaluate the quality of a validation, calculating the residual prediction deviation (RPD) is more meaningful than only looking at the error of prediction. RPD is a qualitative measure for the assessment of the validation results, and higher RPD values indicate better calibrations. The RPD value is the quotient of the standard deviation of the reference values (SD) and the bias-corrected mean error of prediction of the validation ($\mathrm{SEP_{bias}}$) (*21*):

$$\mathrm{RPD} = \frac{\mathrm{SD}}{\mathrm{SEP_{bias}}}$$

The spectral preprocessing techniques and wavenumber regions selected for the PLS models were based on the highest correlation coefficients for the calibration and validation models, the lowest RMSEE and RMSECV, and the lowest number of PLS factors as well as the highest RPD value compared to other preprocessing steps.

To determine if the NIR and FTIR methods could detect 1 ppm melamine in infant formula powder, the factorization method in the Opus Ident software package was used (Bruker Optics Inc.). Spectral preprocessing techniques were selected on the basis of best performance, and then factorization was performed on average spectra of the respective groups (pure infant formula and 0.0001% melamine). For each group, two samples in six replications were used for the analysis. Factorization breaks apart the spectral data into the most common spectral variations (factors, loadings, principal components) and the corresponding scaling coefficients (scores). The advantages of factorization are data compression and noise suppression. Factorization was based on calculation of the Mahalanobis distance (D_{M}):

$$\mathrm{D_M} = \sqrt{\sum_i (T_{\mathrm{sample},i} - T_{\mathrm{ref},i})^2}$$

where T_i is a score of the ith factor. The ability of the method to uniquely identify each group (cluster) was judged by the selectivity (S) (*21*). Selectivity was calculated as the ratio of the distance (D) between average spectra to the sum of threshold values T_1 and T_2 (cluster radii): $S = D/(T_1 + T_2)$. When $S < 1$, the two groups overlap, and when $S > 1$, the two clusters are separated and can be uniquely identified (*21*).

RESULTS AND DISCUSSION

Quantification of Melamine in Infant Formula Powders. Representative FTIR-ATR and FTIR-DRIFT absorbance spectra collected from unadulterated infant formula powder and melamine are shown in **Figure 1**. The wavenumber positions of absorbance peaks, peak intensities, and peak widths are useful for functional group and sample identification. Wavenumber positions of absorbance bands are specific to the functional groups in a sample; thus, each sample has a unique "fingerprint" absorbance spectrum. Thus, structural differences between melamine and the complex mixture of ingredients present in infant formula are evident as differences in the spectra (**Figure 1**).

Table 2. Partial Least-Squares Analysis of FTIR and NIR Spectra for Quantifying Melamine in Infant Formula Powders[a]

				calibration			validation		
method	spectrum range (cm^{-1})	melamine concn (% w/w)	no. of PLS factors	R^2	RMSEE	RPD	R^2	RMSECV	RPD
FTIR-ATR	3330−2993 1321−983.5	50−0.0001	10	0.995	0.80	14.1	0.9931	0.90	12
FTIR-DRIFT	3665−1989 1655−1319	40−0.0001	6	0.9933	0.80	10.9	0.9916	0.89	12.3
NIR	12497−6098 5450−4248.5	50−0.0001	6	0.9995	0.475	46	0.9992	0.616	35

[a] RMSEE, root mean square error of estimation; RMSECV, root mean square error of prediction; RPD, residual prediction deviation.

The mid-IR absorption peaks at 3500−3000 and 1700−1300 cm^{-1} in the melamine spectra (**Figure 1**) are attributed to the stretching and bending vibrations of amino groups present in the melamine. The absorption band present at 1650 cm^{-1} results from the stretching vibrations of >C═N bonds present in the triazine ring of melamine (*22*). These peaks are relatively weaker in the spectra of infant formula powder. The 1300−910 cm^{-1} region is considered to be the fingerprint region: absorption in this region includes contributions from complex interacting vibrations, giving rise to the generally unique fingerprint for each compound.

For quantitative spectral analysis, Beer's law defines the concentration of the sample in terms of the path length, absorptivity, and concentration. The intensity of the absorbance peaks varies with concentration, and standard curves can be generated to correlate absorbance to concentration. Chemometrics enable the interpretation of molecular structural information and correlation to sample composition by processing and interpreting complex spectra using multivariate statistical tools. To develop PLS models from FTIR-ATR spectra, multiplicative scatter correction and first-derivative preprocessing steps were selected for analyzing spectral regions 3330.5−2993 and 1321−983.5 cm^{-1} (encompassing stretching vibrations of amino group and the fingerprint spectral region). The multiplicative scatter correction corrects spectra for spectral noise and background effects, which cause baseline shifting and tilting. Powders usually display scattering variation, due to variation in particle size or shape or in the powder density, and this can be reduced by using the multiplicative scatter correction for preprocessing the spectra (*23*). First-derivative preprocessing emphasizes the steep edges of a peak and pronounces small features over a broad background. PLS for validation of the FTIR-ATR method established a linear relationship between the actual content of melamine and the predicted content of melamine in infant formula powder with an R^2 of 0.9931 (**Table 2**). The PLS model developed for quantifying melamine in infant formula powder using FTIR-ATR spectra meets the following criteria for valid PLS models (*21*): $R^2 \geq 0.95$; RMSEE and RMSECV ≤ 1; number of PLS factors ≤ 10; RPD > 8.

To develop PLS models from FTIR-DRIFT spectra, min−max normalization preprocessing and spectral regions 3665−1989 and 1655−1319 cm^{-1} (encompassing the stretching and bending vibrations of amino groups present in the melamine) were used. Min−max normalization scales the spectrum intensities and reduces the differences between each measurement of the same sample. The FTIR-DRIFT PLS model (**Table 2**) also met the criteria for valid PLS models. There were differences in the number of PLS factors used for the PLS models of FTIR-ATR and DRIFT spectra; however, validation parameters were similar between these two techniques.

Representative NIR absorbance spectra (after automatic baseline correction and smoothing in the 12500−3800 cm^{-1} spectral region) collected from unadulterated infant formula powder, melamine, and adulterated infant formula powders are shown in **Figures 2** and **3**. Absorbance peaks related to the first, second, and combination overtones of the NH_2 group can be clearly identified in the melamine spectrum, and differences between the spectra of melamine and infant formula powder are evident. The peaks near 6580−6490 and 6670−6580 cm^{-1} are due to the first overtone of NH_2 symmetric and antisymmetric stretching, respectively (*21*). The second overtones of NH_2 symmetric and antisymmetric stretching are located at 9800−962 and 1000−9800 cm^{-1}, respectively (*21*). The peak attributed to NH stretching plus NH bending at 5080−4980 cm^{-1} is also present (**Figure 2**). The first visual difference between unadulterated and adulterated infant formula samples occurred at 6900−6780 cm^{-1} (**Figure 3**), attributed to aromatic amine structures (*21*), which also showed the highest absorption in the spectra of pure melamine (**Figure 2**). Increases in the absorption in this region were notable as the melamine concentration was increased.

It is more difficult to assign specific spectral features to specific functional groups in NIR spectra than in FTIR spectra. The molecular overtones and combination bands present in NIR spectra are very broad in comparison to absorbance peaks in the mid-IR region; however, quantitative analysis is still possible using NIR spectra. For calibrating the PLS model for the NIR method, the NIR spectra were preprocessed with min−max normalization. The two spectral regions selected for the calibration were 12497−6098 and 5450−4248.5 cm^{-1} (encompassing the overtone absorbances of NH_2 stretching and bending). The correlation coefficients ($R^2 > 0.999$) and other calibration and validation parameters (**Table 2**) met the criteria for valid PLS models.

A comparison of the calibration and validation performances of the PLS models reported in **Table 2** indicates that the NIR method may perform better than the FTIR methods for quantifying melamine in infant formula powder (higher R^2 and RPD and lower RMSEE and RMSECV). Although the types of values reported for the quality of the quantitative methods summarized in **Table 1** vary, the calibration and validation analyses reported for the FTIR and NIR methods (**Table 2**) are within the range previously reported. For example, the SERS method (*24*) had $R = 0.90$ and RMSEP = 0.33, and for the LTP-MS/MS method (*14*), R^2 was >0.99 in milk powder.

Detection Limit of Melamine in Infant Formula Powder. A threshold of 1 ppm for melamine in infant formula has been set by the FDA (*11*). Therefore, the ability to differentiate between unadulterated infant formula samples and those containing 1 ppm melamine is needed. Spectra of pure infant formula powder

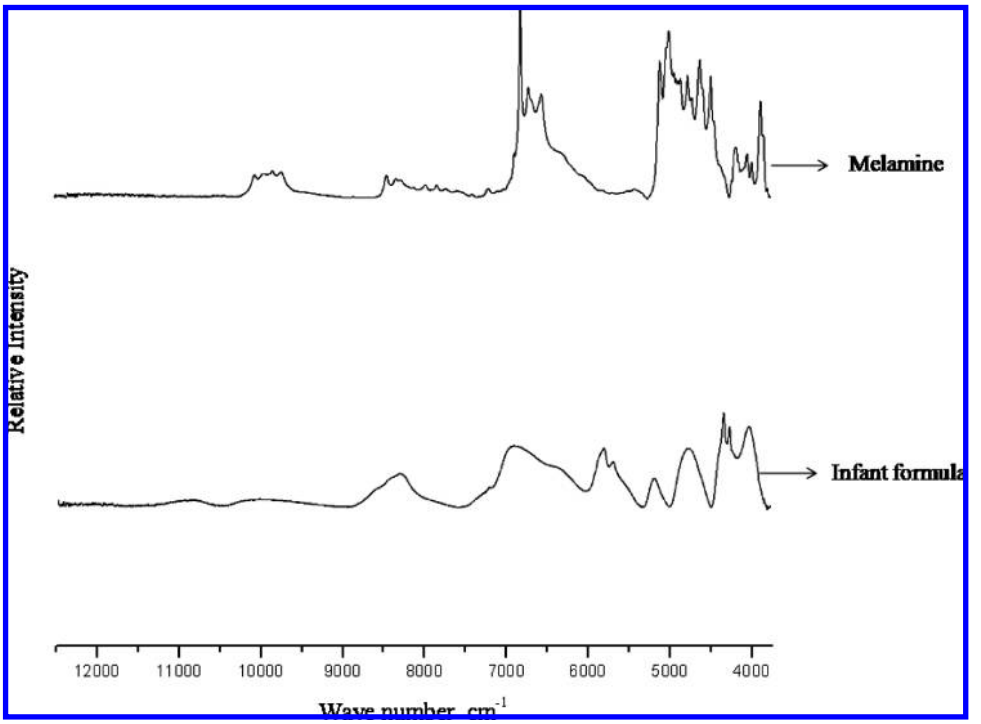

Figure 2. NIR absorption spectra of melamine and infant formula powder collected after automatic baseline correction and smoothing.

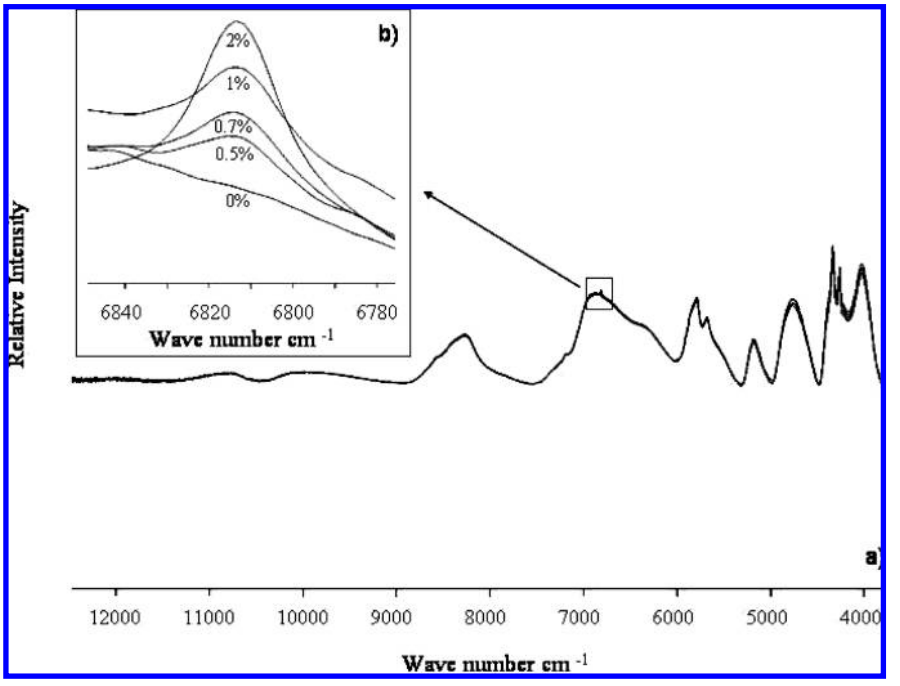

Figure 3. NIR absorption spectra, after automatic baseline correction and smoothing, of infant formula powder and infant formula adulterated with melamine at 0.5, 0.7, 1, and 2% w/w: (**a**) entire NIR spectral region (12500−3500 cm^{-1}) with a peak appearing at 6900−6780 cm^{-1}, attributed to $ArNH_2$, identified as the smallest visual spectral difference between unadulterated infant formula and infant formula adulterated with melamine: (**b**) magnified image of the peak at 6900−6780 cm^{-1} region, where spectra with 0, 0.5, 0.7, 1, and 2% w/w melamine can be clearly differentiated.

and infant formula powder containing 0.0001% w/w (1 ppm) melamine were collected using FTIR-ATR, FTIR-DRIFT, and NIR methods and analyzed using the Opus Ident test method (based on factorization and calculation of the Mahalanobis distances). First-derivative preprocessing of FTIR-ATR spectra (3999−650 cm^{-1}) after vector normalization and FTIR-DRIFT spectra (3999−650 cm^{-1}) without preprocessing were used for factorization. NIR spectra (11733.4−3747.2 cm^{-1}) were preprocessed with first-derivative and vector normalization prior to factorization. Results are presented in **Table 3**. All three methods were able to distinguish between adulterated (1 ppm melamine) and unadulterated infant formula powders (selectivity > 2), with no misclassifications, in a short period of time. The NIR method took the least amount of time: powder samples were placed directly into glass vials, spectra were collected of the powders in the vials, and the spectra were analyzed in < 2 min. The spectral collection time for the FTIR methods was slightly longer (~3 min): the ATR method used powder placed directly on

Table 3. Melamine Detection Limits and Times to Detection from Infant Formula Powder for FTIR and NIR Methods

method of melamine detection	assay time (min)	total time to detection (min)	detection limit (ppm)	confidence level (%)	selectivity
FTIR-ATR	3	4	1	99.99	2.09
FTIR-DRIFT	3	4	1	99.99	2.44
NIR	1	2	1	99.99	2.4

the ATR crystal, and the DRIFT method required a blending step with KBr prior to spectral collection, leading to a total time to detection of ~5 min.

The 1 ppm melamine detection limit for NIR and FTIR methods is more sensitive than some previously published methods and less sensitive than others (**Table 1**). The assay times and total times to detection for the spectroscopy methods (**Table 3**) are less than most of the previous methods (**Table 1**), increasing the potential usefulness of these methods for high-throughput analyses. The current FDA LC-MS/MS method has a detection limit of 250 ppb in infant formula powder, but the total time to detection is >3 h (*13*). The recent LTP-MS/MS method reports a 6 ppb detection limit with an assay time of 25 s (*14*). Whereas both of these methods are more sensitive than the spectroscopy methods presented here, we propose that the NIR or FTIR methods could be useful for screening infant formula powders for the presence of 1 ppm melamine, the threshold set by the U.S. FDA.

There is an obvious need for melamine detection methods applicable to infant formula powders. The ideal method would have high sensitivity; specificity for melamine; high throughput; rapid detection; matrix independence; simple, rugged, and reliable instrumentation; and quantitative accuracy (*14*). Most available detection methods do not meet all of these criteria. The NIR and FTIR spectroscopy methods described are more rapid (taking only minutes) than most published methods with an acceptable 1 ppm detection limit, and the instrumentation is widely available. However, the developed PLS and factorization models are not matrix independent. New calibration models are required for application to different brands or formulations of infant formula powders or other food products. It is expected that the analytical approach for quantifying or detecting melamine using NIR or FTIR spectroscopy would be applicable to other products. The NIR and FTIR methods meet the need for a rapid, simple, and available technique for detecting 1 ppm melamine in infant formula powder.

ABBREVIATIONS USED

ATR, attenuated total reflectance; DRIFT, diffuse reflectance; EIA, enzyme immunoassy; ELISA, enzyme-linked immunosorbent assay; FDA, U.S. Food and Drug Administriation; FTIR, Fourier transform infraref spectroscopy; HPLC, high-performance liquid chromatography; HPLC-DAD, high-performance liquid chromatography with dioade array detection; HPLC-MS/MS, high performance liquid chromatography tandem mass spectrometry; LC-MS, liquid chromatography−mass spectrometry; LC-MS/MS, liquid chromatography−triple-quadrupole tandem mass spectrometry; LTP-MS/MS, low-temperature plasma probe combined with tandem mass spectrometry; MS-DART, mass spectrometry using soft ionizaiton by direct analysis in real time; NIR, near-infrared spectroscopy; PLS, partial least-squares analysis; RMSEE, root mean square error of estimation; RMSECV; root mean square errror of prediction; RPD, residual prediction deviation; SEE, standard error of estimation; UPLC-ESI-MS/MS, ultraperformance liquid chromatography coupled with electrospray ionization quadrupole tandem mass spectrometry; ZIC-HILIC, zwitterionic hydrophilic interaction chromatography.

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