

# Ultratrace Aluminum Analysis of Nutritional Intravenous Solution Components in 1-Propanol Using GFAAS

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The ultratrace aluminum analysis of two nutritional intravenous solution components with limited water solubility can be performed by GFAAS with dissolution in 1-propanol. Use of this solvent allows aqueous aluminum stock standards and nitric acid–magnesium nitrate matrix modification as in the analysis of aqueous solutions.

The FDA final rule on aluminum levels (*21 CFR Part 201*, January 26, 2000) states that certain components of nutritional intravenous solutions, also known as total parenteral nutrition (TPN) solutions, shall contain no more than 25 ppb of aluminum. The requirements were added by FDA to characterize such solutions to address concerns from the medical community (1).

Baxter Healthcare (Deerfield, IL), a major manufacturer of TPN solutions, complies with this rule by monitoring TPN final product and by screening raw materials for aluminum content using graphite furnace atomic absorption spectroscopy (GFAAS). The screening of raw materials of slight or no water solubility for aluminum content creates an analytical challenge. Two examples of such materials include the nonessential amino acid L-tyrosine, and the lipid raw material soybean oil. L-Tyrosine has a solubility in water of approximately 0.05 wt %, whereas soybean oil is practically insoluble in water (2).

Wet ashing, microwave digestion, and muffler furnace combustion are widely accepted means of preparing water-insoluble specimens for elemental analysis. However, it was desirable to develop a GFAAS method fundamentally consistent with the *U.S. Pharmacopeia (USP)* 206 aluminum procedure (3) for testing water-soluble raw materials. We have determined that 1-propanol acidified with nitric acid is a suitable solvent system for the analysis of aluminum in these two TPN components.

## EXPERIMENTAL

The instrument used for these analyses was a PerkinElmer Instruments (Norwalk, CT) AAnalyst 600 graphite furnace atomic absorption spectrometer using Zeeman-effect background correction and configured with a model AS-800 autosampler running version 3.9 of PerkinElmer Instruments' AAWinLab software. The testing methodology used for L-tyrosine and soybean oil was fundamentally consistent with *USP* 206 (3). The specific experimental parameters are listed in Table I. Three replicate injections were made of each calibration and sample solution.

Unspiked samples were prepared by accurately weighing 0.5 g of L-tyrosine (Aldrich, Milwaukee, WI) or 2.5 g of soybean oil (Aldrich) into separate 25-mL nitric acid-washed polymethylpentene volumetric flasks. Five separate unspiked sample replicates of each material were prepared. Approximately 10 mL of 1-propanol and 0.5 mL of nitric acid were slowly added to each flask. When adding the nitric acid to the 1-propanol in this manner, no noticeable heat was generated. (Utmost caution should always be exercised when adding strong acids to alcoholic solutions.) Each flask was swirled thoroughly to mix the contents. The flask



**Table I.** Experimental parameters.

Spectrophotometer (AAAnalyst 600)		Graphite Furnace				
Element	Al	Step No.	Temp. (°C)	Ramp (s)	Hold (s)	Ar (cc/min)
Lamp	Hollow cathode	1	90	5	10	250
Current	Recommended on lamp	2	110	10	20	250
Wavelength (nm)	309.3	3	130	10	25	250
Slit (nm)	0.7	4	400	10	30	250
Signal type	AA-BG	5	1300	10	20	250
Signal measurement	Peak area	6	1300	1	3	0
Read time (s)	3	7	2300	0	4	0
Read delay (s)	0.0	8	2450	1	3	250
BOC time (s)	1	Fume extractor engaged for furnace program				
Tube type	THGA, End Capped	Sample volume (μL)				20
Read step	7	Matrix modifier volume (μL)				10
Calibration program	Linear, calculated intercept	Diluent volume (μL)				5

**Table II.** Accuracy and precision results.\*

Sample Identification	Al Conc. (ng/g) (Avg. Conc. of Five Replicates)	% RSD (Five Replicates)	% Recovery	
			Manual Spike (Avg. of Five Recoveries)	Autosampler Spike (Avg. of Three Recoveries)
L-Tyrosine	135	3.7	110	104
Soybean Oil	16	4.9	94	99

\*L-Tyrosine specimens were manually spiked with aqueous aluminum intermediate (1.00 μg/mL) standard and spiked via the autosampler using the 20-ng/mL aluminum working standard. Manual and autosampler spike concentration: 5.0 ng/mL. Soybean oil specimens were manually spiked with an organometallic aluminum standard and spiked via the autosampler using the 20-ng/mL aluminum working standard. Manual spike concentration: 10 ng/mL; autosampler spike concentration: 5.0 ng/mL.

**Table III.** Regression statistic for aluminum standard in 1-propanol.

Statistical Parameter	L-Tyrosine	Soybean Oil
Correlation coefficient ( <i>R</i> )	0.99905	0.99825
Slope	0.00455	0.00451
<i>y</i> intercept	0.0001	0.0003
Blank standard deviation ( <i>n</i> = 6)	0.000259	0.000335
Method limit of detection (MLOD) 3σ (ng/g)	8.6	2.2

The method limit of detection was calculated from the standard deviation of six blank responses and the slope of the linear regression calibration curve as follows:

$$\text{LOD(ppb)} = \frac{3 \times \text{SD of the blank (abs units)}}{\text{Slope of the regression line (abs / ng / mL units)}} \times \frac{\text{Volume (mL)}}{\text{Test article weight (g)}}$$

containing soybean oil was diluted to the volume 25 mL with HPLC-grade 1-propanol (Aldrich). An additional 0.5 mL of nitric acid was slowly added to the flasks containing L-tyrosine before dilution to volume with 1-propanol. Each flask was capped and inverted to mix. The contents in each flask were transferred immediately into separate acid-washed 30-

mL tetrafluoroethylene bottles. L-Tyrosine was prepared at the 2 wt % level in 4% (v/v) Ultrex II grade nitric acid (J.T. Baker, Phillipsburg, NJ) in 1-propanol. Soybean oil was prepared at the 10 wt % level in 2% (v/v) nitric acid in 1-propanol.

We were unable to locate analogous standard reference materials for these two samples. Therefore, accuracy and

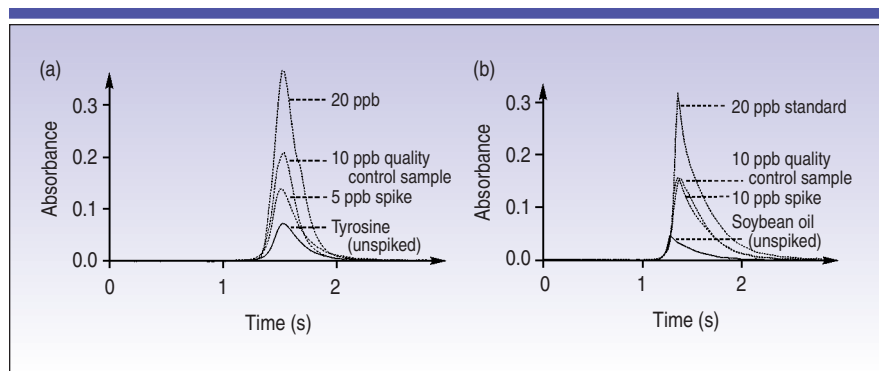
precision of the method were determined by performing a series of spiking experiments. Manually spiked L-tyrosine samples were prepared by transferring 125 μL of an aqueous 1.00-μg/mL aluminum quality assurance standard prepared from an aqueous 1000-μg/mL aluminum stock standard (High Purity Standards, Charleston, SC) to five separate L-tyrosine sample preparations before dilution to volume with 1-propanol. This resulted in a 5.0-ng/mL aluminum spike of each L-tyrosine sample preparation. Manually spiked soybean oil samples were prepared by accurately weighing approximately 0.1 g of an approximately 2.5-μg/g organometallic aluminum standard (High Purity Standards) into each of five separate soybean oil preparations before dilution to volume with 1-propanol.

This resulted in an approximately 10-ng/mL organometallic aluminum spike of each of the soybean oil sample preparations. In addition to the manually spiked samples, the AS-800 autosampler was used to automatically spike one of each of the unspiked L-tyrosine and soybean oil sample solutions in triplicate at the 5.0 ng/mL level using a portion of the 20-ng/mL calibration standard.

Individual aluminum calibration working standards were prepared in 2% (v/v) nitric acid–1-propanol at blank, 2.0, 10, and 20 ng/mL from an aqueous 1000-μg/mL aluminum stock standard (Ricca Chemical Company, Arlington, TX). The AS-800 autosampler automatically prepared a 5.0-ng/mL working calibration standard using a portion of the 20-ng/mL aluminum working standard.

Quality assurance check standards were prepared from an aqueous 1000-μg/mL aluminum stock standard of a different manufacturer than used to prepare the calibration standards (High Purity Standards) in 2% (v/v) nitric acid–





**Figure 1.** Aluminum peak profiles for (a) L-tyrosine and (b) soybean oil.

1-propanol at 10 ng/mL. The check standard was analyzed after every five auto-sampler locations to monitor instrument drift throughout the analysis.

A matrix modifier solution of 0.5-mg/mL magnesium nitrate (Perkin-Elmer) in 10% (v/v) nitric acid was prepared in 1-propanol and stored in a 30-mL acid-washed tetrafluoroethylene bottle.

An autosampler rinse solution of 1:1 1-propanol-ethanol (HPLC-grade

[Aldrich]) was used throughout the analyses.

#### DISCUSSION

The analytical accuracy and precision results are shown in Table II. The regression statistics for aluminum calibration standards are shown in Table III.

The intermediate polarity of 1-propanol allowed complete dissolution of the two materials while allowing for the use of

aqueous aluminum stock standards and magnesium nitrate-nitric acid matrix modification. The solvent also has a slow rate of evaporation, is relatively nontoxic, and is free of an offensive odor. Several lots of HPLC-grade 1-propanol proved to be of sufficiently low aluminum content to be used without the requirement of further cleanup.

L-Tyrosine and soybean oil sample analyses were completed within 4 h. The practical time limit for analysis of samples prepared in this manner is approximately 8 h. Table II shows the precision and accuracy results for five replicate analyses.

The average of five soybean oil manual spike recoveries of 10-ng/mL organo-metallic aluminum standard was compared with the average of three 5.0 ng/mL spikes prepared by the autosampler with the aluminum standard. The purpose of this experiment was to demonstrate that the furnace temperature program, matrix modification, and solvent system would produce accurate results regardless of the molecular species of

aluminum in the sample. The other consideration was to establish that the positive displacement pump of the AS-800 autosampler would meter the 1-propanolic sample preparations with the same relative accuracy as we have experienced with aqueous sample preparations.

The average of five L-tyrosine manual 10-ng/mL spike recoveries of water-based aluminum standard was compared with the average of three 5.0-ng/mL spikes prepared by the autosampler using the 20-ng/mL aluminum working standard.

The percent recoveries for manually spiked and autosampler-spiked soybean oil and L-tyrosine test solutions were all within 10% of theoretical, which is considered acceptable accuracy by our laboratory.

Figures 1a and 1b show aluminum peak profiles for L-tyrosine and soybean oil. A new tube was used for the L-tyrosine sample analysis (Figure 1a); the same tube was used for the analysis of the soybean samples (Figure 1b). Note

that the tube had approximately 300 firings before the analysis of the soybean oil samples. The difference in peak shapes from Figure 1a and Figure 1b may be due to the relative aging of the tube. However, accuracy and precision for the soybean oil analysis was equivalent to that for the L-tyrosine analysis. In our experience, this is typical of tube lifetime when aqueous solutions are analyzed by GFAAS.

#### CONCLUSION

The use of an organic solvent of intermediate polarity proved to be a successful matrix for the GFAAS analysis of these test articles. Analytical parameters and matrix modification as suggested by the instrument manufacturer and USP 206 for the analysis of aluminum in aqueous solutions were essentially maintained. Accuracy, precision, and sensitivity of the methodology are characteristic of GFAAS for ultratrace aluminum analysis as experienced in this laboratory.

Due to evaporation of the 1-propanol from the GFAAS autosampler cups, the

practical time limit for conducting an analysis is more restricted than for an analysis of aqueous solutions. However, the use of an organic solvent for GFAAS analysis of these types of insoluble compounds has proven to be a practical alternative to digestion.

#### REFERENCES

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- (3) *United States Pharmacopeia 24. NF 19*, Aluminum <206>, 1856 (Rockville, MD: U.S. Pharmacopeial Convention, 1999).

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