Stability of Ibuprofen Solutions in Normal Saline or 5% Dextrose in Water

Scott E Walker, Julie Choudhury, Shirley Law, and John Iazzetta

ABSTRACT

Background: A shortage of the standard medication for treatment of patent ductus arteriosus has necessitated use of parenteral ibuprofen, which is equally efficacious for this indication. The beyond-use date recommended by the manufacturer is very short and has implications for resource allocation and wastage.

Objective: To evaluate the stability of ibuprofen (undiluted or diluted in either 0.9% sodium chloride [normal saline; NS] or 5% dextrose in water [D5W]) with storage for up to 21 days under refrigeration or at room temperature in glass vials or polypropylene syringes.

Methods: Six glass vials, each containing undiluted ibuprofen (5 mg/mL), were prepared. In addition, ibuprofen was diluted to 2.5 mg/mL in NS or D5W, and 6 syringes were prepared for each diluent (total of 12 syringes). Finally, 6 extension tubes were each primed with 1 mL of ibuprofen (duplicates of undiluted solution and solutions diluted to 2.5 mg/mL in NS or D5W). Half of the vials, syringes, and tubes were stored under refrigeration (4°C) and the other half at room temperature (23°C). The concentration of ibuprofen was determined by a validated, stability-indicating liquid chromatographic method on study days 0, 1, 2, 3, 6, 8, 10, 13, 17, and 21 for samples stored in vials and syringes, or at time 0, 6, 24, and 30 h for samples stored in tubes.

Results: Analysis of variance showed differences in the percentage of ibuprofen remaining due to study day (p < 0.001) and diluent (p < 0.005), but no differences due to concentration (p = 0.06) or temperature (p = 0.12). All solutions of ibuprofen were stable throughout the study period, retaining at least 90% of their initial concentration.

Conclusions: Undiluted ibuprofen (5 mg/mL) stored in glass vials and ibuprofen diluted to 2.5 mg/mL with either NS or D5W and stored in polypropylene syringes will retain more than 90% of its initial concentration with storage for up to 14 days at 4°C. A beyond-use date of 14 days would allow for up to 24 h storage at 23°C during this 14-day period. Storage of ibuprofen solutions in extension tubing should not exceed 29 h at 4°C or 17 h at 23°C. Beyond-use dates should be applied only after consideration of US Pharmacopoeia Revised General Chapter <797> guidelines for compounding of sterile preparations.

Key words: ibuprofen, drug stability
INTRODUCTION

Patent ductus arteriosus affects 1 in 3 preterm infants. Because of hypoperfusion of vital organs, this condition may lead to other comorbidities such as bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular hemorrhage, and renal failure. Indomethacin, a nonselective cyclooxygenase (COX) inhibitor, is effective in closure of patent ductus arteriosus and is the gold standard for medical management of this condition. However, recent trials have shown that ibuprofen, another nonselective COX inhibitor, is equally efficacious and has fewer renal adverse effects.

At the time this study was undertaken, in 2010, a temporary manufacturer’s shortage of indomethacin in Canada had halted its use for closure of patent ductus arteriosus. As a result, neonatal patient care units were required to use ibuprofen as an alternative agent for this therapy. The drug was accessible through Health Canada’s Special Access Programme as ibuprofen–THAM (Pedea, Orphan Europe, Puteaux, France). The Pedea monograph states that the product should be used immediately and that unused portions of the vial contents should be discarded. This beyond-use date has implications for neonatal intensive care units (NICUs) in terms of staffing, equipment, and wastage, and for patients in terms of effectiveness and time to administration. Volonté and others previously evaluated the stability of ibuprofen solutions, but they used a product containing ibuprofen lysinate, a different salt with a different formulation from that of Pedea, which contains ibuprofen in aqueous solution, with tris(hydroxymethyl) aminomethane (THAM or trometamol) as a buffer.

The beyond-use dates of medications intended for IV administration following reconstitution or dilution are often limited to about 24 h, even when data on extended stability exist, because of the potential for breaks in sterility and contamination of the product. However, when reconstitution and dilution are carried out in a sterile environment, based on the guidance of US Pharmacopoeia Revised General Chapter <797>, it is entirely reasonable to assign beyond-use dates of up to 14 days for low-risk compounded sterile products if stored with refrigeration. Extending the beyond-use date for many drugs might facilitate admixing in the pharmacy, reduce wastage, and lead to substantial cost savings.

The objective of this study was to evaluate the stability of ibuprofen-THAM, both undiluted (5 mg/mL) and diluted to 2.5 mg/mL with either 0.9% sodium chloride (normal saline; NS) or 5% dextrose in water (D5W), in glass vials and polypropylene syringes. Because of the precision required for delivering small volumes of medication, extension tubing (each 152 cm long, holding 1 mL of solution) is attached to IV medication syringes in the NICU at the authors’ hospital and is primed with the solution before administration. Therefore, the stability of the various ibuprofen solutions in extension tubing was also evaluated. Test solutions were stored under refrigeration or at room temperature for up to 21 days. All of the concentrations, containers, and storage conditions used in the study reflected practice conditions in the authors’ institution at the time of the study.

METHODS

Liquid Chromatographic Method

The liquid chromatographic system consisted of an isocratic solvent delivery pump (model P4000, Thermo Separation Products, San Jose, California), which pumped a mixture of methanol (OmniSolv, EMD Chemicals Inc, Gibbstown, New Jersey) and 0.05 mol/L phosphoric acid (catalogue no. P286, Fisher Scientific, Toronto, Ontario) through a 15 cm × 4.6 mm reversed-phase C18, 3-µm column (Supelcosil ABZ+Plus, catalogue no. 59194, Supelco, Oakville, Ontario) at 1.0 mL/min. The ratio of methanol to 0.05 mol/L phosphoric acid (68:32) was held constant during each chromatographic run. The samples were introduced into the liquid chromatographic system using an autoinjector (WISP 717-Plus, Waters Scientific, Toronto, Ontario).

The column effluent was monitored with a variable-wavelength ultraviolet (UV) detector (UV6000, Thermo Separation Products) at 225 nm. A signal from the detector was inte-
grated and recorded with a chromatography data system (ChromQuest, version 5.0, ThermoFisher Scientific Inc). The area under the ibuprofen peak was subjected to least-squares linear regression, and the actual ibuprofen concentration in each sample was determined by interpolation from the standard curve.

**Assay Validation**

Following development of the chromatographic system for ibuprofen, the suitability of this method for use as a stability-indicating assay was tested by analysis of ibuprofen samples subjected to accelerated degradation. A 10-mg sample of ibuprofen (4-isobutyl-α-methylphenylacetic acid; catalogue no. 375160-1G, Sigma-Aldrich Co, St. Louis, Missouri; lot MKBC5901, expiry November 2012) was diluted in 10 mL of distilled water to prepare a 1 mg/mL solution. This stock solution was divided into 3 portions. First, 2 mL was placed directly into an empty, sterile 2-mL vial (Allergy Laboratory Inc, Oklahoma City, Oklahoma; lot SEV100209). A second portion was adjusted to pH 1.85 with 3 mol/L hydrochloric acid (Fisher Scientific, Nepean, Ontario; lot 112713, expiry May 2013), and the third portion was adjusted to pH 10.4 with 5 mol/L sodium hydroxide (ACP Chemicals Inc, Montréal, Quebec; lot 108307, expiry January 2013). A sample was drawn immediately from each of the vials, and all 3 vials were then placed in a water bath at 85°C. Additional samples were drawn at 5 different times over a 21.6-h period from the pH-adjusted solutions or over a 72-h period from the unadjusted sample of ibuprofen in water. These samples (1.0 µL each) were injected directly into the chromatographic system with the autoinjector. Chromatograms were inspected for the appearance of additional peaks, and the ibuprofen peak was compared with a fresh, undegraded sample in terms of changes in concentration, retention time, peak shape, and UV spectral purity (over the wavelength range 200–320 nm).

Following this first phase of evaluation and validation, the accuracy and reproducibility of standard curves were tested over 5 days, and system suitability criteria (theoretical plates, tailing, and retention time) were developed to ensure consistent chromatographic performance, according to accepted analytical guidelines. Standard curves were prepared daily by measuring out 15 mg of an ibuprofen standard (4-isobutyl-α-methylphenylacetic acid, catalogue no. 375160-1G, Sigma-Aldrich Co; lot MKBC5901) and diluting this quantity of drug in 10 mL of a solution consisting of equal parts distilled water and methanol. This stock solution of 1500 mg/L was further diluted with distilled water to prepare additional standards with final concentrations of 150.0, 100.0, 50.0, 25.0, and 18.8 mg/L. When combined with a blank, these standards served to construct a standard curve. A 4-µL portion of each sample was chromatographed in duplicate. Also, 2 quality control samples of ibuprofen (concentrations 37.5 and 75 mg/L) were chromatographed in duplicate each day, and their concentrations were determined and compared with the known concentrations. Intraday errors of reproducibility were assessed by the coefficients of variation of the peak areas of both the quality control samples and the standards. Accuracy was assessed each day on the basis of deviation from known concentration and was expressed as percent deviation. During the validation period, interday errors of reproducibility were assessed by determining the coefficients of variation of the determined concentrations of quality control samples, prepared on day 1 and re-analyzed on each study day. During the study period, interday errors of reproducibility were assessed by the standard deviation of regression, expressed as a percentage relative to the concentration.

**Stability Study: Glass Vials and Polypropylene Syringes**

On study day 0, the contents of six 2-mL ampoules of ibuprofen-THAM (Pedea 5 mg/mL solution for injection, Orphan Europe SARL, Puteaux, France; lot IBJ0909, expiry July 2013) were withdrawn. The contents of each vial were transferred into an empty sterile 10-mL vial (Allergy Laboratories Inc) to prepare 6 vials each containing 2 mL of ibuprofen 5 mg/mL. On the same day (study day 0), multiple 1-mL samples of ibuprofen solution were withdrawn from an ampoule into 3-mL polypropylene syringes with Luer-Lok tip (BD, Franklin Lakes, New Jersey) and diluted with either 1 mL of NS (0.9% sodium chloride for injection USP in 10-mL vial, Hospira, Saint-Laurent, Quebec) or 1 mL of D5W (5% dextrose for injection USP in 50-mL polyvinylchloride bag, Baxter Healthcare Corp, Deerfield, Illinois; lot P247353, expiry July 2011) to prepare 6 syringes containing ibuprofen 2.5 mg/mL diluted in NS and 6 syringes containing ibuprofen 2.5 mg/mL diluted in D5W.

For each combination of concentration and diluent, 3 containers were stored under refrigeration (4°C) and 3 were stored at room temperature (23°C). The samples were not protected from light. On study days 0, 1, 2, 3, 6, 8, 10, 13, 17, and 21, the concentration of ibuprofen was determined in duplicate, and visual inspection was performed. Solutions stored in glass vials were inspected directly, whereas samples stored in syringes were transferred to glass test tubes for inspection. Inspection was performed with the naked eye, against a white background and a black background.

On each study day, a 0.1-mL sample was drawn from each container. The pipette tip used to withdraw the sample was rinsed with 0.1 mL of distilled water, and the mixture was then diluted further with distilled water (3 mL for solutions with concentration 2.5 mg/mL; 5 mL for solutions with concentration 5 mg/mL). Each sample was then vortexed, and duplicate 4-µL samples were injected directly into the chromatographic system.
**Stability Study: Extension Tubing**

On study day 0, the contents of a 2-mL ampoule of ibuprofen-THAM (Pedea 5 mg/mL solution for injection) were withdrawn, and a 1-mL volume was transferred into each of two 152-cm lengths of sterile extension tubing (catalogue no. BC576, Codan US Corporation, Santa Ana, California). Also on study day 0, a 1-mL volume of undiluted ibuprofen (5 mg/mL) was withdrawn from another ampoule and diluted with 1 mL of NS. Approximately 1 mL of this diluted solution was transferred into each of two 152-cm lengths of sterile extension tubing, one of which was stored at 4°C and the other of which was stored at 23°C. This process was repeated using D5W as the diluent.

After 0, 6, 24, and 30 h, a 0.1-mL sample was drawn from each container. The pipette tip used to withdraw each sample was rinsed with 0.1 mL of distilled water, and the mixture was then diluted further with distilled water (3 mL for solutions with concentration 2.5 mg/mL; 5 mL for solutions with concentration 5 mg/mL). Each sample was then vortexed, and duplicate 4-µL samples were injected directly into the chromatographic system.

**Data Reduction and Statistical Analysis**

After the coefficient of variation of replicate determinations of concentration for an assay was determined, a power calculation indicated that 2 replicates would be required to ensure that the analytical method could distinguish between concentrations that differed by at least 10%. Means were calculated for replicate analyses and are reported in the summary tables. Mean results from different days for each test were compared statistically (by linear regression) to determine if there was an association between the observed result and time. Analysis of variance was used to test differences in degradation rate between various temperature–diluent–concentration combinations. The 5% level was used as the a priori cut-off for significance. The concentration of a solution on a particular day was considered “acceptable” or “within acceptable limits” if it was greater than 90% of the initial concentration (as determined on day 0) and the amount found on that day, with 95% confidence, exceeded 90% of the initial concentration.

**RESULTS**

**Accelerated Degradation and Assay Validation**

Application of heat (85°C) and acid (pH 1.85) led to degradation of ibuprofen to 30% of the initial concentration within 21 h. A single degradation product was observed (Figure 1), as previously reported. Application of heat and base (pH 10.40) resulted in no noticeable degradation over 21 h. Similarly, incubation at 85°C for 72 h without application of acid or base resulted in no noticeable degradation. Nevertheless, as a result of consistent degradation of ibuprofen with acid and heat, the separation of ibuprofen and the observed degradation product, and the similarity of the UV spectrum (200–320 nm) between a fresh ibuprofen sample and ibuprofen in the degraded acidic sample, it was concluded that this analytical method was stability-indicating.

Assay validation demonstrated that absolute deviation from the known concentration for quality control samples on any day averaged 2.6% for the quality control samples at 37.5 mg/L and 3.5% for those at 75 mg/L. The error of replicate analysis within a day averaged less than 1.9% for the standards, 3.5% for the quality control samples at 37.5 mg/L, and 1.5% for those at 75 mg/L.

The analysis of accuracy based on the means of duplicate determinations of standards over the study period showed less than 3.2% absolute deviation from the expected concentration. The error of replicate analysis within a day (as measured by the coefficient of variation) averaged less than 2.0% for the standards. Interday variation, as measured by the observed standard deviation of regression for percent remaining, was 4.08%. This value indicates that differences of 10% or more could be confidently detected with acceptable error rates, with duplicate analysis. System suitability criteria were based on daily calculations of theoretical plates, tailing, retention time, and accuracy during the validation period and were used to
ensure continued chromatographic performance during the study period. On each day, the mobile phase was prepared to ensure a retention time for ibuprofen between 6.2 and 7.9 min.

### Stability of Ibuprofen in Glass Vials and Polypropylene Syringes

During the 21-day study period, there was no apparent loss of concentration in ibuprofen solutions stored in glass vials or polypropylene syringes (Table 1). Similarly, no degradation products were observed in any sample after storage for up to 21 days (Figure 2).

Multiple linear regression revealed differences in the percent remaining due to study day ($p = 0.005$) and container ($p = 0.010$), but detected no differences due to temperature ($p = 0.22$), nominal concentration ($p = 0.50$), or diluent ($p = 0.70$). Analysis of variance revealed differences in percent remaining due to study day ($p < 0.001$) and diluent ($p = 0.005$), but detected no differences due to concentration ($p = 0.06$) or temperature ($p = 0.12$). Although the differences due to diluent were statistically significant, the differences due to temperature, concentration, diluent, and container were all less than 3% and thus clinically unimportant.

The data were also analyzed by linear regression, and the time for the concentration to decline to 90% of initial concentration (T-90) was calculated for each container–temperature–diluent combination. When the 95% confidence limits for the degradation rates were used to estimate T-90, a beyond-use date of 18 days or longer was calculated for all containers at all temperatures, regardless of concentration (Table 1). However, the 95% confidence limits of the degradation rate spanned a degradation rate of 0%/day.

#### Table 1. Percent of Ibuprofen Remaining* after Storage in Vials or Syringes

<table>
<thead>
<tr>
<th>Study Day</th>
<th>Solution; Storage Temperature</th>
<th>Mean % of Initial Concentration Remaining ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Original (Undiluted)</td>
<td>Diluted in NS</td>
</tr>
<tr>
<td></td>
<td>23°C</td>
<td>4°C</td>
</tr>
<tr>
<td>Initial concentration, observed (mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4.64 ± 0.02</td>
<td>4.55 ± 0.03</td>
</tr>
<tr>
<td>1</td>
<td>100.1 ± 0.5</td>
<td>100.0 ± 0.6</td>
</tr>
<tr>
<td>2</td>
<td>104.4 ± 0.6</td>
<td>106.3 ± 1.2</td>
</tr>
<tr>
<td>3</td>
<td>100.1 ± 1.6</td>
<td>98.4 ± 2.0</td>
</tr>
<tr>
<td>4</td>
<td>98.8 ± 0.5</td>
<td>99.5 ± 2.6</td>
</tr>
<tr>
<td>5</td>
<td>95.4 ± 2.4</td>
<td>97.4 ± 2.1</td>
</tr>
<tr>
<td>6</td>
<td>107.6 ± 0.6</td>
<td>102.5 ± 8.7</td>
</tr>
<tr>
<td>7</td>
<td>101.1 ± 0.6</td>
<td>106.4 ± 4.8</td>
</tr>
<tr>
<td>8</td>
<td>103.0 ± 2.5</td>
<td>106.0 ± 2.7</td>
</tr>
<tr>
<td>9</td>
<td>99.6 ± 3.3</td>
<td>110.4 ± 0.5</td>
</tr>
<tr>
<td>10</td>
<td>97.2 ± 2.0</td>
<td>101.6 ± 6.2</td>
</tr>
</tbody>
</table>

$SD = \text{standard deviation}$

*Each value is based on duplicate determination of 3 samples. The percent remaining is based on designation of initial concentration (day 0) as 100%.

†$S_y$ is the standard deviation describing the distribution of data about the regression line.

†‡The degradation rate was determined by linear regression of the percent remaining on each study day.

§The 95% confidence interval was determined from the lower limit of the 95% confidence interval of the slope determined by linear regression.

¶T-90 = time for the concentration to decline by 10%, to 90% of initial concentration.

**Calculated from the fastest degradation rate, determined from the lower limit of the 95% confidence interval of the slope determined by linear regression.

††Poor chromatography results for at least one of the replicate samples created an apparently divergent result. Rather than discard the results altogether or re-do the assay, the divergent results of the single replicate or analysis is shown. The inclusion of divergent results increases the variability in observed results (as indicated by the increase in SD from the regression). This ultimately widens the confidence intervals and shortens expiration times and T-90s.
Stability of Ibuprofen in Extension Tubing

During the 30-h study period, there was no apparent loss of concentration in samples stored in the extension tubing (Table 2). No degradation products were observed in any sample (chromatograms not shown) obtained over the 30-h study period.

Analysis of variance revealed differences in percent remaining due to temperature ($p = 0.021$) but not time ($p = 0.08$) or diluent ($p = 0.34$). Although the difference for temperature was statistically significant, the observed difference was only 1.36%, which would not be clinically significant.

The data were also analyzed by linear regression, and T-90 was calculated for each temperature–diluent combination. When the 95% confidence limits for the degradation rates were used to estimate T-90, a beyond-use date of 17 h or longer was calculated for solutions stored in extension tubing at both temperatures, regardless of concentration (Table 2). However, the 95% confidence limits of the degradation rate spanned a degradation rate of 0%/day.

DISCUSSION

We determined that ibuprofen, either undiluted (5 mg/mL) and stored in glass vials or diluted with NS or D5W to a concentration of 2.5 mg/mL and stored in polypropylene syringes, would retain more than 92% of its initial concentration when stored for 14 days at 4°C. During this storage period, the containers may be held at 23°C for up to 24 h, with solutions retaining more than 90% of their initial concentration with 95% confidence (Table 1).

Similarly, solutions of ibuprofen retained more than 90% of initial concentration during storage in extension tubing for 30 h at 4°C. The construction of 95% confidence intervals around T-90 showed that these solutions will retain more than 90% of initial concentration for more than 29 h (Table 2). With storage at 23°C, solutions of ibuprofen stored in extension tubing retained more than 90% of initial concentration over 30 h. The construction of 95% confidence intervals around T-90 for these solutions showed that they will retain more than 90% of initial concentration for more than 17 h (Table 2).

The analytical method used in this study was judged accurate and reproducible. Furthermore, during accelerated degradation with heat and acid, a single degradation product was observed, as previously reported by Farmer and others. As a result of the separation of ibuprofen from its degradation product, consistent degradation of ibuprofen with application of acid and heat, and the similarity of the UV spectrum (200–320 nm) between a fresh ibuprofen sample and the ibuprofen in a degraded acidic sample, the method was judged to be stability-indicating.

We are unaware of any previous stability studies reporting the stability of ibuprofen–THAM after dilution in NS or D5W. Volonté and others evaluated the stability of an ibuprofen lysinate formulation at concentrations of 1.0 and 4.0 mg/mL, diluted in NS, D5W, or sterile water, protected and unprotected from light. These authors reported a loss of about 7% for a 27.5 mg/mL solution diluted in sterile water and stored at 23°C for 360 h without protection from light. However, they did not determine beyond-use dates using 95% confidence intervals. Even though the formulation evaluated by Volonté and others and the Pedea product analyzed in the study reported here are different formulations, the results of the 2 studies are in agreement.

CONCLUSIONS

A 14-day beyond-use date is reasonable for undiluted (5 mg/mL) solutions of ibuprofen stored in glass vials and for 2.5 mg/mL solutions, diluted in either NS or D5W and stored in polypropylene syringes at 4°C. This beyond-use date allows for up to 24 h storage at 23°C. Notably, ibuprofen (either
undiluted, at 5 mg/mL, or diluted to 2.5 mg/mL with NS or D5W) was stable in extension tubing for up to 29 h at 4°C or 17 h at 23°C. If recommendations are limited to evidence-based evaluation of conditions in this study, solutions may be drawn into a glass vial or polypropylene syringe and stored for up to 13 days at 4°C. Once dispensed, the extension tubing may be attached to a syringe and primed with solution under sterile conditions. Under these circumstances, the syringe with primed tubing would retain the initial concentration for up to 29 h at 4°C or 17 h at 23°C. The beyond-use dates presented here should be applied only after consideration of US Pharmacopeia Revised General Chapter <797> guidelines.

References

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Table 2. Percent of Ibuprofen Remaining* after Storage in Extension Tubing

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Solution; Storage Temperature; Mean % of Initial Concentration Remaining ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Original (Undiluted)</td>
</tr>
<tr>
<td></td>
<td>23°C</td>
</tr>
<tr>
<td>Initial concentration, observed (mg/L)</td>
<td>4.99 ± 0.07</td>
</tr>
<tr>
<td>0</td>
<td>100.0 ± 0.5</td>
</tr>
<tr>
<td>6</td>
<td>100.9 ± 1.9</td>
</tr>
<tr>
<td>24</td>
<td>101.3 ± 0.8</td>
</tr>
<tr>
<td>30</td>
<td>103.6 ± 1.8</td>
</tr>
<tr>
<td>SD from regression (S95)</td>
<td>0.898</td>
</tr>
<tr>
<td>Degradation rate based on 95% CI (%/h)</td>
<td>-0.0618</td>
</tr>
<tr>
<td>T-90 (hours)</td>
<td>161.70</td>
</tr>
<tr>
<td>% remaining</td>
<td>100.0 ± 0.5</td>
</tr>
<tr>
<td>At 24 h, by linear regression</td>
<td>102.26</td>
</tr>
<tr>
<td>At 24 h, by 95% CI for linear regression</td>
<td>98.52</td>
</tr>
<tr>
<td>At 12 h, by 95% CI for linear regression</td>
<td>99.26</td>
</tr>
</tbody>
</table>

Cl = confidence interval, D5W = 5% dextrose in water, NS = normal saline (0.9% sodium chloride), SD = standard deviation.

*Each value is based on duplicate determination of one sample assayed twice (4 chromatographic runs). The percent remaining is based on designation of initial concentration (day 0) as 100%.

**S95** is the standard deviation describing the distribution of data about the regression line.

†The degradation rate was determined by linear regression of the percent remaining on each study day.

‡The 95% CI was determined from the lower limit of the 95% CI of the slope determined by linear regression.

¶T-90 = time for the concentration to decline by 10%, to 90% of initial concentration.
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