Calcium/Phosphate Solubility Curves for Premasol and Trophamine Pediatric Parenteral Nutrition Formulations

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OBJECTIVES Calcium and phosphate incompatibility in parenteral nutrition formulations remains a critical concern for patient safety. This study examined calcium phosphate solubility for 2-in-1 admixtures prepared using 2 commercially available pediatric amino acid solutions (Premasol, Baxter Healthcare Corp; or Trophamine, B. Braun Medical Inc), applying identical test methods, storage conditions, and acceptance criteria.

METHODS Parenteral 2-in-1 admixtures included amino acid; dextrose; static concentrations of sodium, potassium, and magnesium, and varying concentrations of calcium (0–60 mEq/L), phosphate (15–50 mmol/L), and cysteine. Three replicate samples were stored for 48 hours at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and then visually inspected for particulate matter, evaluated for subvisible particulate matter, when particulate matter was noted, microscopic examination was performed to confirm the presence of calcium phosphate crystals. Pass criteria were: all replicates free of visible particulate matter related to calcium phosphate crystals and particle counts below US Pharmacopeia <788> limits.

RESULTS Premasol and Trophamine generated identical calcium phosphate curves for 2% amino acid formulations containing 20% dextrose with/without cysteine, and similar curves for the 1% or 3% amino acid formulations containing 10% or 20% dextrose with/without cysteine. Calcium phosphate particles were identified in failed samples by scanning electron microscopy/energy dispersive X-ray spectroscopy. Calcium phosphate solubility was higher in formulations containing cysteine 40 mg/g amino acid vs. cysteine 20 mg/g amino acid and in cysteine 20 mg/g amino acid vs. no cysteine.

CONCLUSIONS Admixtures made with 1%, 2%, or 3% Premasol or Trophamine have essentially equivalent calcium phosphate solubility curves when tested with identical methods, storage conditions, and acceptance criteria.

ABBREVIATIONS NMT, not more than; PN, parenteral nutrition; SEM, scanning electron microscopy; USP, US Pharmacopeia

KEYWORDS compatibility; parenteral nutrition; Premasol; solubility; Trophamine

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Introduction

Calcium and phosphate precipitation in parenteral nutrition (PN) formulations is a critical concern for patient safety. There have been numerous reported cases of precipitates of calcium phosphate causing a variety of conditions, such as pulmonary emboli and respiratory distress, and in some cases even death.^{1,2} This concern is especially critical for pediatric and neonatal populations, where high concentrations of calcium and inorganic phosphates are needed. Whether calcium and phosphate in solution will form insoluble calcium phosphate precipitate is complicated and is dependent on many conditions, including pH, amount of cysteine, amino acid type and concentration, calcium salt, phosphate type, temperature, and order of mixing.^{3–9} Hospital pharmacies and compounding centers rely

on manufacturer-supplied or published compatibility curves for various amino acid solutions when preparing products to meet patients' needs.³ It is vitally important that clinicians make decisions based on the most current and scientifically robust data; however, because there is no standard method for determining compatibility curves, each curve may have been generated using different test methods and acceptance criteria,¹⁰ making it difficult for clinicians to compare products.

Premasol (Baxter Healthcare Corp, Deerfield, IL)¹¹ or Trophamine (B. Braun Medical Inc, Irvine, CA)¹² are pediatric amino acid solutions that are bioequivalent and therapeutically equivalent (Table 1). Both are sterile, nonpyrogenic, hypertonic solutions that comprise a mixture of essential and nonessential amino acids, as well as taurine and a soluble form of tyrosine, *N*-acetyl-L-tyrosine. However, there are a few

Table 1. Comparison of Premasol and Trophamine Amino Acid Solutions^{11,12}

Components*	Premasol		Trophamine	
	6%	10%	6%	10%
Essential AA, g/100 mL				
Leucine	0.84	1.40	0.84	1.40
Isoleucine	0.49	0.82	0.49	0.82
Lysine (lysine acetate)	0.49	0.82	0.49	0.82
Valine	0.47	0.78	0.47	0.78
Histidine	0.29	0.48	0.29	0.48
Phenylalanine	0.29	0.48	0.29	0.48
Threonine	0.25	0.42	0.25	0.42
Methionine	0.20	0.34	0.20	0.34
Tyrosine (tyrosine + NALT)	0.14	0.24	0.14	0.24
Tryptophan	0.12	0.20	0.12	0.20
Cysteine (cysteine HCl H ₂ O)	<0.014	<0.016	<0.014	<0.016
Nonessential AA, g/100 mL				
Arginine	0.73	1.20	0.73	1.20
Proline	0.41	0.68	0.41	0.68
Alanine	0.32	0.54	0.32	0.54
Glutamic acid	0.30	0.50	0.30	0.50
Serine	0.23	0.38	0.23	0.38
Glycine	0.22	0.36	0.22	0.36
Aspartic acid	0.19	0.32	0.19	0.32
Taurine	0.015	0.025	0.015	0.025
Target pH (range)*	5.5 (5.0–6.0)	5.5 (5.0–6.0)	5.5 (5.0–6.0)	5.5 (5.0–6.0)
Osmolarity, mOsmol/L†	520	865	525	875
Total AA, g/100 mL‡	6	10	6	10
Total nitrogen, g/100 mL‡	0.93	1.55	0.93	1.55
Acetate (CH ₃ COO ⁻), mEq/L§	57.0	94.0	54.4	97.0
Chloride, mEq/L	<3	<3	<3	<3

AA, amino acid; NALT, N-acetyl-L-tyrosine

* All amino acids are added as the “L”-isomer except for glycine and taurine, which do not have isomers.

† pH adjusted with glacial acetic acid US Pharmacopeia.

‡ Calculated values.

§ Provided as acetic acid and lysine acetate.

minor differences between the solutions. Premasol is manufactured in polyvinyl chloride plastic containers, whereas Trophamine is manufactured in glass containers. Unlike Premasol, which is sulfite free, Trophamine contains sodium metabisulfite as an antioxidant. Given the therapeutic similarities between Premasol and Trophamine, it is expected that the calcium phosphate solubility curves of admixtures based on these amino acid solutions would be identical. This is supported by Huston et al,¹³ who demonstrated minor differences in calcium phosphate solubility when calcium chloride and potassium phosphate were added to Premasol- or Trophamine-containing PN solutions.

Manufacturer-supplied compatibility curves are currently available for 2-in-1 admixtures containing Premasol¹⁴ or Trophamine.¹⁵ These formulations comprise amino acids, dextrose, static concentrations of sodium, potassium, and magnesium, varying concentrations of calcium and phosphate, and varying amounts of cysteine. However, the methods used to generate these curves varied markedly (Table 2).

For Trophamine admixtures, dextrose, Trophamine, and sterile water were prepared using an automated HyperFormer compounder. Electrolytes, including different concentrations of calcium and phosphates, were manually added via syringe to 250-mL sterile evacuated

Table 2. Comparison of Trophamine¹⁵ and Premasol Test Criteria¹⁴

Test	Trophamine	Premasol	Current Study
Storage conditions	48 hr at 40°C	24 hr at 25°C followed by 24 hr at 40°C	48 hr at 40°C
Particulate matter test	Instrumental particle counter	Filtration then enumeration with optical microscope	Instrumental particle counter
Particulate matter limits	NMT 25 particles/mL $\geq 10 \mu\text{m}$ NMT 3 particles/mL $\geq 25 \mu\text{m}$	NMT 6 particles/mL $\geq 10 \mu\text{m}$ NMT 1 particle/mL $\geq 25 \mu\text{m}$	NMT 25 particles/mL $\geq 10 \mu\text{m}$ NMT 3 particles/mL $\geq 25 \mu\text{m}$
Visible particulate	Presence of precipitation according to B. Braun specifications and procedure	No visible particulate matter observed	No visible particulate matter observed
pH	Not mentioned	No limits applied	No limits applied
Containers	250-mL glass bottles	100-mL glass bottles	250-mL EVA containers
Compounding	Automated compounding and manual additions	Manual additions	Automated compounding
Replicates	2	1	3

EVA, ethyl vinyl acetate; NMT, not more than

glass containers. The samples were stored for 48 hours at 40°C and then visually inspected for the presence of precipitation; samples without visible precipitation were tested with an instrumental particle counter to enumerate subvisible particulate matter. The US Pharmacopeia (USP) <788> particulate matter limits¹⁶ for large-volume injections are not more than (NMT) 25 particles/mL $\geq 10 \mu\text{m}$ and NMT 3 particles/mL $\geq 25 \mu\text{m}$ using the light obscuration particle-counting test and were included within the acceptance criteria.

Premasol admixtures, dextrose, Premasol, sterile water, and electrolytes including different concentrations of calcium and phosphates were manually added to 100-mL glass containers. The samples were stored for 24 hours at 25°C, followed by 24 hours at 40°C before being visually inspected for precipitation. The samples were then filtered through a 0.8- μm retention filter, and the isolated particulate matter was enumerated with a light microscope; 50% of the USP <788> microscopic particulate matter limits¹⁶ for large-volume injections are NMT 6 particles/mL $\geq 10 \mu\text{m}$ and NMT 1 particle/mL $\geq 25 \mu\text{m}$, and were included within the acceptance criteria. For both amino acid solutions, the highest concentration of calcium for a given phosphate concentration that consistently met each manufacturer's acceptance criteria was supplied as the maximum acceptable concentrations of calcium and phosphate to be used for each PN formulation. It should be noted that USP <788> describes 2 different procedures for determining particle counts: a light obscuration particle count test (an instrumental test), which is the preferred method, and a microscopic particle count test, which involves filtering the solution and counting particles using a light microscope.

Direct comparison of the current manufacturer-supplied compatibility curves for PN formulations containing Premasol or Trophamine is not possible because

of the differences in test conditions and acceptance criteria. The aim of this study was to compare the calcium phosphate solubility points for 2-in-1 admixtures prepared using Premasol or Trophamine by applying identical test methods, storage conditions, and acceptance criteria to all tested admixtures. In addition, this study evaluated the impact of lower concentrations of cysteine on calcium phosphate solubility.

Materials and Methods

PN Solutions. Amino acids consisted of 10% Premasol-sulfite-free (Amino Acid) Injection (lots: P327080 expiration December 2016; P341735 expiration October 2017; Baxter Healthcare Corp) in 500-mL flexible containers, and Trophamine 10% (lots: J5L451 expiration March 2017, J6H458 expiration December 2017; J6K452 expiration February 2018; B. Braun Medical Inc) in 500-mL glass bottles. The target concentrations of the various additives for the six 2-in-1 admixtures were prepared as follows: 1% amino acid and 10% dextrose, 2% amino acid and 20% dextrose, and 3% amino acid and 20% dextrose. Each concentration was prepared with cysteine 40 mg/g amino acid and without cysteine. One formulation, Premasol at 3%, was also prepared with a cysteine concentration of 20 mg/g amino acid in light of recommendations by ASPEN to use lower cysteine levels during shortages.¹⁷ Formulations contained target concentrations of sodium (80 mEq/L), potassium (55 mEq/L), and magnesium (8 mEq/L), and varying concentrations of calcium (0–60 mEq/L) and phosphate (15–50 mmol/L).

The formulations as well as calcium and phosphate concentrations were selected based on the manufacturer-supplied Trophamine curve.¹⁵ Points along the solubility curve were selected for the initial testing, but if any of the points failed, lower concentrations of

calcium and phosphate were tested until formulations with both amino acids passed.

The preparation, test methods, data points, storage conditions, and acceptance criteria were chosen to closely match the published Trophamine solubility data and were based primarily on the B. Braun test methods and acceptance criteria (Table 2).

Preparation of Admixtures. All samples were prepared in 250-mL ethyl vinyl acetate containers using an automated compounder (Exactamix 2400,¹⁸ Baxter Healthcare Corp). Preparations were made in a laboratory environment within an ISO Class 5 laminar flow hood. The order of addition of components, although different from previous studies, was consistent across all admixtures and was therefore not expected to influence the study outcomes. The order of addition for this study was sodium chloride, potassium chloride, sodium phosphate, amino acid, dextrose, cysteine, magnesium sulfate, sterile water, calcium gluconate, and a final addition of sterile water. The order of additions is based on the standard recommended setup for the ExactaMix 2400 Compounder, which is consistent with the instructions from ASPEN when using automated compounding.¹⁹

Three replicate admixtures were prepared at each calcium/phosphate concentration, recording the order of addition and the actual volumes. Negative control articles were prepared in the same manner but without the addition of calcium gluconate. After preparation, samples were inverted 10 times to mix the contents and then stored for 48 hours at 40°C ± 2°C. After storage, samples were removed for testing and remained under general laboratory environmental room temperature conditions for a minimum of 2 hours and a maximum of 6 hours prior to testing.

Visual Inspection Test. All test and control samples were visually inspected for the presence of particulate matter, such as precipitates, crystals, flakes, flocules, fibers, etc, solution turbidity or cloudiness, and any significant discoloration, using a black/white visual inspection booth at a minimum illumination of 500-foot candles or 5400 lux within the “visual inspection zone” of the booth.²⁰ When a large amount of visible particulate matter was observed in the test samples, no further particle testing was performed, and the subvisible particle test was assumed to fail the acceptance criteria. For all samples with visible particulate matter, a portion of the remaining solution from the test sample was filtered through a 0.8-µm filter, and the retentate was assessed for the presence of calcium phosphate crystals by light and scanning electron microscopy (SEM).

Subvisible Particulate Matter Test. Testing was conducted on samples with no visible particulate matter and on samples identified as having only a few visible crystals. The subvisible particle concentration of all test and control samples was determined using a calibrated

instrumental particle counter.¹⁶ The instrument was a Hiac Model 9703 (Beckman Coulter, Brea, CA) light obscuration particle counter with a volumetric sampler calibrated with National Institute of Standards and Technology traceable particle size standards per USP <1788>.²¹ For test samples with particle counts that were close to or exceeding the USP <788> light obscuration limits, a portion of the remaining solution was filtered through a 0.8-µm filter, and the retentate was further characterized by microscopy as described above.

Confirmation of Calcium Phosphate Crystals. The elemental composition of particles in a subgroup of samples with visible particulate matter and elevated particle counts was assessed by SEM coupled with energy dispersive X-ray (SEM/EDX; ThermoFisher/FEI Quanta 650 FEG SEM [Waltham, MA], with Oxford Instruments X-Max EDX detector [Concord, MA]) spectroscopy.

pH. The pH of the test and control samples was measured using a calibrated pH meter.²² These data were collected for information purposes because pH is known to influence precipitation of calcium phosphate; however, there were no acceptance criteria for pH.

Acceptance Criteria. The current USP <788> particulate matter limits¹⁶ for large-volume injections were used as follows: NMT 25 particles/mL ≥ 10 µm and NMT 3 particles/mL ≥ 25 µm. It is important to note that the instrumental light obscuration particle counts include calcium phosphate crystals as well as extraneous environmental particulate matter, which may increase the particle count concentration. Samples without visible crystalline particulate matter were acceptable. All 3 replicate samples had to pass the acceptance criteria for all tests for a given formulation. If a single replicate contained visible particulate matter or exceeded the current USP <788> particulate matter limits,¹⁶ it was recorded as failed.

When a formulation did not meet the acceptance criteria, additional testing was performed with lower concentrations of calcium or phosphate. Iterations of testing were performed until a pass result was observed for both amino acids at specific concentrations of calcium and phosphate. Calcium phosphate solubility curves were determined using data for the highest concentrations of calcium and phosphate at which all replicates passed.

Results

Calcium Phosphate Solubility. Using identical methods and acceptance criteria, this study showed that calcium phosphate solubility was very similar for the six 2-in-1 admixtures made with Premasol or Trophamine, with and without the addition of L-cysteine (Tables 3 and 4). The concentrations indicated in Tables 3 and 4 indicate the highest concentrations of calcium and phosphate that produced passing results. The calcium phosphate solubility curve boundary points were identi-

Table 3. Calcium Phosphate Data Points for 2-in-1 Admixtures Made With Premasol

1% Premasol 10% Dextrose		2% Premasol 20% Dextrose		3% Premasol 20% Dextrose		3% Premasol 20% Dextrose		1% Premasol 10% Dextrose		2% Premasol 20% Dextrose		3% Premasol 20% Dextrose	
Cys 40 mg/g AA		Cys 40 mg/g AA		Cys 40 mg/g AA		Cys 20 mg/g AA							
Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻
45	18	35	30	60	30	60	20	37	9	30	19	50	14
25	23	31	31	45	32	45	26	35	11	25	21	40	17
21	26	18	41	36	36	36	31	17	17	22	22	17	25
8	35	12	50	15	50	15	40	5	35	18	25	15	40
6	45	NA	NA	NA	NA	NA	NA	3	45	10	35	9	50

AA, amino acid; Ca²⁺, calcium ion (mEq/L); Cys, L-cysteine; NA, not applicable; PO₄³⁻, phosphate ion (mmol/L)

cal for Premasol and Trophamine formulations containing 2% amino acid and were very similar for formulations containing 1% and 3% amino acid (Figure 1).

Calcium phosphate solubility was higher in formulations with cysteine at a concentration of 40 mg/g amino acid than in formulations without cysteine (Figure 1). For all formulations, addition of cysteine 40 mg/g amino acid shifted the solubility curves to higher concentrations of calcium and phosphate that could be added compared with no addition of cysteine.

When examining the effect of varying cysteine concentration on calcium phosphate solubility, the results as shown in Figure 2 indicated that higher amounts of calcium and phosphate can be added with increasing concentrations of cysteine (0 mg/g vs. 20 mg/g vs. 40 mg/g). Although the addition of cysteine at 20 mg/g amino acid did allow higher amounts of calcium and phosphorus to be added compared with formulations without the addition of cysteine, the effect was not as great compared with cysteine at 40 mg/g amino acid (Figure 2).

Particle Identification. Every solution was visually inspected for presence of visible particulate matter. Most samples did not contain visible particulate matter or only contained a few particles and required instrumental analysis for subvisible particulate matter. For solutions that contained large amounts of visible par-

ticulate matter or elevated instrumental particle counts, all were filtered and examined by light microscopy. Representative samples were further characterized by SEM/energy dispersive X-ray and were determined to be calcium phosphate based on the presence of Ca, P, and O in the recorded spectra. If the particulate matter was not identified as calcium phosphate, the sample was recorded as a passing result. Samples containing visible particulate matter, such as a fiber or other extraneous material, that were not consistent with calcium phosphate morphology were not further characterized. Because these visible particles were not the result of precipitation of calcium phosphate, these samples were considered a passing result.

pH. The pH was measured for all samples and ranged from 5.23 to 6.17. According to a review of the pH values and the samples with high amounts of particulate matter, there was no direct correlation between pH and the presence of particulate matter. The addition of cysteine at 40 mg/g amino acid to the formulations lowered the solution pH by approximately 0.2 to 0.3 pH units compared with formulations without cysteine. The addition of cysteine at 20 mg/g amino acid lowered the pH by approximately 0.25 pH units for the 3% amino acid formulations when compared with formulas without cysteine. The pH of 3% amino acid solutions was lower than the pH of 1% amino acid formulations

Table 4. Calcium Phosphate Data Points for 2-in-1 Admixtures Made With Trophamine

1% Trophamine 10% Dextrose		2% Trophamine 20% Dextrose		3% Trophamine 20% Dextrose		1% Trophamine 10% Dextrose		2% Trophamine 20% Dextrose		3% Trophamine 20% Dextrose	
Cys 40 mg/g AA		Cys 40 mg/g AA		Cys 40 mg/g AA							
Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻	Ca ²⁺	PO ₄ ³⁻
45	18	35	30	60	30	40	9	30	19	50	14
25	21	31	31	45	32	35	11	25	21	40	17
15	23	18	41	36	36	17	17	22	22	25	25
8	35	12	50	20	50	5	35	18	25	10	40
6	45	NA	NA	NA	NA	5	45	10	35	9	50

AA, amino acid; Ca²⁺, calcium ion (mEq/L); Cys, L-cysteine; NA, not applicable; PO₄³⁻, phosphate ion (mmol/L)

Figure 1. Calcium/phosphate solubility curves for six 2-in-1 admixtures made with Premasol and Trophamine.

(A) Curves for admixtures with L-cysteine 40 mg/g amino acid. (B) Curves for admixtures without L-cysteine.

○ 1% Troph + 10% D; □ 2% Troph + 20% D; △ 3% Troph + 20% D; ● 1% Prem + 10% D; ■ 2% Prem + 20% D; + 3% Prem + 20% D
D, dextrose; Prem, Premasol; Troph, Trophamine.

by approximately 0.2 to 0.3 pH units regardless of cysteine addition.

Discussion

In clinical practice, it is vitally important that health care professionals make decisions based on the most current and scientifically robust data available. New data generated in this study demonstrate that calcium phosphate compatibility curves are essentially equivalent for 2 pediatric amino acid solutions (Premasol and Trophamine) with identically prepared formulations when the test methods and acceptance criteria are the same. The small differences in the solubility curves observed between the 2 products are likely because some of the calcium and phosphate concentrations were very close to the solubility limits of the samples tested, and precipitation close to the line is not always predictable. Overall, the compatibility data for most concentrations tested and the similarities in composition between the 2 amino acid solutions suggest that PN formulations made with these solutions have nearly identical calcium phosphate solubilities.

In the current study, the acceptance criteria used to generate the compatibility curves were aligned with USP <788> light obscuration particulate matter limits of NMT 25 particles/mL $\geq 10 \mu\text{m}$ and NMT 3 particles/mL $\geq 25 \mu\text{m}$ rather than with the acceptance criteria previously used for Premasol, which were 50% of USP <788> microscopic particulate matter limits of NMT 6 particles/mL $\geq 10 \mu\text{m}$ and NMT 1 particle/mL $\geq 25 \mu\text{m}$. Comparing data from both previous and current Premasol solubility studies shows that higher amounts of calcium and phos-

phorus can be added to PN formulations made with Premasol without exceeding the current USP <788> limits. This finding is not surprising given that changes in test methods, storage conditions, and acceptance criteria in particular will greatly affect the outcome and are most likely the reason for the previous lower and more conservative compatibility curves.

Although the test conditions and acceptance criteria used to generate the compatibility curves in this study were similar to those previously used by B. Braun for Trophamine, some concentrations of calcium and phosphate that previously passed in B. Braun's evaluation did not pass in this study. The reason for this is unclear, but it is important to note that even though the study design mimicked the test conditions and acceptance criteria previously used for Trophamine, compatibility results on or near the solubility limit are often unpredictable. In the current study, the absence of visible particulate matter was required for a sample to pass, and 3 rather than 2 replicates had to meet the acceptance criteria (Table 2). In some concentrations, the samples had numerous particles and were clearly incompatible, whereas in others there were very few particulates, which may have passed previously but did not pass in the current study. In addition, the ethyl vinyl acetate container used in this study was not the same as the glass containers that were used previously. Container choice is not expected to influence the calcium phosphate solubility curves, but the ethyl vinyl acetate containers were chosen because they are widely used in the compounding of PN solutions.

Findings from this study have confirmed the posi-

Figure 2. Calcium/phosphate solubility curve for 3% Premasol + 20% dextrose with and without added L-cysteine.

tive benefits of adding cysteine 40 mg/g amino acid on calcium phosphate solubility in PN formulations.⁸ The addition of cysteine lowers the pH of the solution, allowing for higher concentrations of calcium and phosphate to be added to the solution without precipitation. However, it has become increasingly common for formulation ingredients, including cysteine, to be in short supply.^{17,23} Hence, clinicians often must decide on the best approach for their patient when using a dose lower than cysteine 40 mg/g amino acid. Because compatibility curves with lower concentrations of cysteine are not typically available, clinicians are sometimes forced to base their decision on the compatibility curve that contains no cysteine. The current study shows that even the presence of low amounts of cysteine, such as 20 mg/g amino acid, can affect calcium phosphate solubility such that half the normal dose of cysteine allows more calcium and phosphate to be added to the 2-in-1 admixture compared with no cysteine added. It should be noted that the effect of low amounts of cysteine was studied at only one concentration of 3% amino acid and may not be representative of other formulations.

In summary, the 2-in-1 admixtures made with 1%, 2%, or 3% Premasol or Trophamine demonstrated essentially equivalent calcium phosphate solubility curves when tested under the same conditions with identical methods and acceptance criteria. The previously published Trophamine curve was confirmed at some concentrations but showed incompatibility at other concentrations of calcium and phosphate. Addition of cysteine 20 mg/g amino acid shifted the solubility curves to lower concentrations of calcium and phosphate that could be added compared with cysteine 40 mg/g amino acid, but to higher concentrations of calcium and phosphate that could be added compared with no added cysteine.

The new compatibility curves for Premasol and Trophamine generated in this study can be used to update clinicians' databases and improve patient care. As with any compatibility curve, care should be taken when formulating to avoid putting the patient at risk. These studies show that slight changes in formulation components can greatly impact calcium phosphate solubility; it is therefore recommended that all solutions be visually inspected upon production as well as before use, and administered through an appropriately sized inline filter.

Conclusions

Pharmacists rely on published literature or manufacturer-supplied calcium phosphate compatibility curves when preparing parenteral solutions to meet the nutritional needs of patients. The currently available calcium phosphate solubility curves for 2 therapeutically and bioequivalent pediatric amino acid solutions (Premasol, Trophamine) were generated using different formulations, test methods, and compatibility acceptance criteria. This study has demonstrated that when identical formulations, test methods, and acceptance criteria are used, the solubility curves for these 2 pediatric amino acid solutions are essentially equivalent.

ARTICLE INFORMATION

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