Review

Current practices and future directions of stability testing in parenteral nutrition: A scoping review

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Background and Objectives: Parenteral nutrition (PN) provides nutrition intravenously, often as two-in-one (TIO) or all-in-one (AIO) solutions. These solutions are complex, containing around 50 chemical components, which can affect the admixture stability. While there is substantial data on stability tests for PN solutions, the methodologies and acceptance criteria are not well-defined in current literature. This scoping review aimed to identify and summarise the current tests and methods used to assess the stability of AIO solutions in hospital settings. **Methods and Study Design:** Comprehensive searches on stability tests and parenteral nutrition were conducted in Web of Science (WoS), PubMed, and Scopus on 11 January 2024, updated on 4 April 2025. Searches were limited to articles published in English from January 2010 to March 2025. Data extraction was done on the included studies for descriptive analysis. **Results:** 33 articles met the inclusion criteria, 25 focused on AIO solutions, six included both AIO and TIO, and one was on lipid emulsion only. Eleven stability tests were identified and classified into physical, chemical, and microbiological categories. The suggested core set of tests for assessing AIO solution stability includes visual inspection, pH measurement, particle size distribution using dynamic light scattering and light obstruction, zeta potential measurement, lipid peroxidation using the thiobarbituric acid reactive substances (TBARS) assay, and sterility testing via membrane filtration. **Conclusions:** This review identifies a suggested core set of stability tests essential for evaluating AIO solutions in hospital settings. Adoption of these standardised methods can enhance the reliability and consistency of stability assessments.

Key Words: stability tests, parenteral nutrition, parenteral nutrition solutions, all-in-one solutions, lipid emulsions

INTRODUCTION

Parenteral nutrition (PN) is a form of nutritional therapy involving essential nutrients delivered via an intravenous route. The essential nutrients are amino acids, carbohydrates, lipids, electrolytes, vitamins, and trace elements. The two-in-one (TIO) PN solution refers to a formulation that combines amino acids, glucose, electrolytes, vitamins, and trace elements into a single aqueous mixture, but excludes the lipid emulsion. This type of preparation is typically used when the inclusion of lipids compromises the stability of the formulation or when lipid administration is not clinically indicated.[1] In contrast, the all-in-one (AIO) PN solution, also known as a total nutrient admixture (TNA), incorporates both the aqueous components (amino acids, glucose, electrolytes, vitamins, and trace elements) and the lipid emulsion into a single infusion bag. This allows for the simultaneous administration of all nutrients, offering greater convenience and reduced risk of contamination from multiple infusions.

PN is widely recognised as a highly complex admixture comprising over 50 chemical entities, hence, PN stability is a concern and can be easily compromised.[2] PN solution may exhibit physical manifestations of instability, such as crystallisation and broken emulsion, as well as chemical manifestations, such as hydrolysis and oxidation.[2,3] Physical and chemical degradation from instability can impact a substance's pharmacological action or pharmaceutical properties, leading to reduced drug efficacy and potential therapeutic failures, toxicity, or adverse events.[4]

At present, there are no specific, standardised, and complete guidelines or protocols that clearly describe the essential stability tests for PN formulations. This is particularly important for in-house or hospital-compounded PN formulations, as they lack the manufacturer-established stability data typically available for commercially prepared products, making the determination of their stability critical to ensure patient safety and therapeutic efficacy. International Conference of Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Q1A(R2),[5] ASEAN Guidelines on Stability Study on Drug Product,[6] Food and

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Drug Administration (FDA)'s Guidance on Stability Testing on New Drug Substances and Products,[7] and European Medicine Agency (EMA)'s Guideline on Stability Testing[8] provided general guidance on the stability testing of new drug substances and products, but they do not include any specific information or sections addressing PN formulations. Additionally, the Yellow Cover Document published by the National Health Service (NHS) in 2016[2] only provides basic tests such as visual inspection, pH measurement, and assessment of degradation products. The document also focuses solely on the practices in the United Kingdom and does not describe the test methods or acceptance criteria in detail.

The existing guideline documents mentioned above were found to be vague, incomplete, or nonspecific in establishing the stability profiles of PN solutions. This highlights a significant gap in the literature and underscores the need for more comprehensive and practical guidance. This scoping review aims to identify and consolidate the current stability tests performed on AIO PN solutions, including the methods and acceptance criteria reported in the literature for stability assessment of these solutions in hospital settings. By synthesising evidence on physical, chemical, and microbiological stability assessments, this review aims to propose a comprehensive list of suggested stability tests specific to AIO PN formulations in hospital settings. The collated data will serve as a reference to guide future stability studies and support standardisation of stability testing practices.

This review focuses on PN stability testing of AIO solutions compounded for adult patients. While most earlier studies assessed formulations containing older lipid emulsions such as Intralipid, the introduction of newer lipid emulsions with distinct physicochemical properties necessitates updated stability evaluations. This is especially critical in hospital settings where PN is compounded in-house rather than sourced commercially. Defining appropriate stability tests for these formulations is essential to ensure safe and effective adult PN therapy and to promote standardised testing practices across institutions.

METHODS

For this scoping review, Joanna Briggs Institute (JBI) guide was used,[9] and the reporting was guided by the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist.[10] No review protocol was published prior to this review.

Eligibility criteria

This scoping review included experimental studies evaluating the stability of PN formulations intended for human use. Eligible publications reported physical, chemical, or microbiological stability tests performed on PN solutions. As the review specifically focuses on AIO PN solutions, studies involving TIO solutions only were excluded. Only full-text articles published in English from January 2010 to March 2025 were considered to ensure the inclusion of up-to-date and clinically relevant methodologies and to exclude outdated technologies.

Studies involving infusion or simulated infusion in patients were excluded. To maintain focus on established testing practices, studies comparing different methods for the same stability test or describing the development of new analytical methods were not included. Similarly, compatibility studies such as interactions between PN components or co-administered drugs were excluded. However, in studies that reported both compatibility and stability data, only the stability results were extracted. Articles reporting stability studies as part of new product development or routine quality control/assurance were also excluded.

Non-primary literature, including review articles, guideline documents, expert opinions, and letters to the editor, was excluded due to the absence of primary data. The inclusion and exclusion criteria were structured based on the Population, Concept, Context (PCC) framework, and are summarised and presented in Supplementary Table 1.

Search strategy

The search for relevant studies began with preliminary searches in PubMed and Google Scholar conducted by the first reviewer (NA). From this initial exploration, keywords and Medical Subject Headings (MeSH) terms were extracted from the titles and abstracts. Eight "gold standard" articles were identified to help inform and refine the final search strategy. Keywords were categorised into two core concepts; "stability tests" and "parenteral nutrition", including relevant synonyms. The refined search strategy was validated by a second reviewer (CM) and systematically applied to three electronic databases: Web of Science (WoS), PubMed, and Scopus using Boolean operators ("OR" for expansion, "AND" for narrowing). The search was performed on the selected databases on 11 January 2024, with an update on 4 April 2025. The full search strategy applied to PubMed was as follows:

(Stability test*[MeSH Terms]) OR (Stability assessment[Text Word])) OR (Galenic stability[Text Word])) OR (Precipitation test[MeSH Terms])) OR (Physicochemical stability[Text Word])) OR (Stability study*[Text Word])) OR (Integrity test[Text Word])) OR (Degradation test[MeSH Terms])) OR (Shelf-life test[MeSH Terms])) OR (Stability-indicating method study[Text Word])) OR (Physicochemical stability[Text Word])) OR (Kinetic stability[Text Word])) OR (Chemical interactions[Text Word])) OR (Drug stability[MeSH Terms])) OR (emulsion stability[Text Word])) AND (Parenteral nutrition[MeSH Terms]) OR (Parenteral nutrition formulation*[Text Word])) OR (Parenteral nutrition solution*[MeSH Terms])) OR (Parenteral nutrition solution*[Text Word])) OR (Parenteral nutrition emulsion*[MeSH Terms])) OR (Total Parenteral Nutrition[MeSH Terms])) OR (TPN[Text Word])) OR (Intravenous feeding[MeSH Terms])) OR (Intravenous nutrition[MeSH Terms])) OR (Parenteral feeding[MeSH Terms])) OR (Peripheral PN[Text Word])) OR (peripheral parenteral nutrition[MeSH Terms])) OR (Total nutrient admixture*[Text Word])) OR (Total nutrition admixture*[Text Word])) OR (Central PN[Text Word])) OR (central parenteral nutrition[MeSH Terms])) OR (Parenteral solution*[MeSH Terms])) OR (Parenteral hyperalimentation[MeSH Terms])) OR (Intravenous hyperalimentation[MeSH Terms])).

The search was limited to articles published in English from January 2010 to March 2025. Search results were cross-checked to confirm the retrieval of all the pre-identified "gold standard" articles. The complete search strategies used in all three databases are documented in Supplementary Table 2.

Study selection

All results obtained were exported to EndNote 21 to remove duplication. Following the removal of duplicates, the remaining articles were screened for relevance based on titles and abstracts regarding their potential relevance using Rayyan systematic review software. Full-text articles of the potentially eligible studies were then assessed against the predefined inclusion and exclusion criteria. All screening steps were performed by the first reviewer (NA) and independently verified by the second reviewer (CM). Any discrepancies were to be resolved through consultation with a third reviewer (BK or MM).

Data extraction and charting

Key data relevant to the research objectives were extracted from the included studies using a Microsoft Excel data extraction template developed by the first reviewer (NA) with input from the second reviewer (CM). The data extracted included (a) study details (authors, title, and year of publication); (b) study objectives; (c) type of PN solutions; (d) variables in the PN solutions being studied (compositions, packaging, storage conditions etc.); (e) details of the stability tests (type of test, test methods, time points and study duration); and (f) acceptance limits for the tests and the references. Extraction was conducted by NA and reviewed by CM. The full data extraction results are presented in Supplementary Table 3.

Data synthesis

The included studies were grouped for descriptive analysis to evaluate the distribution of study characteristics, including the country of origin. The types of PN solutions addressed in each study were identified, specifically as AIO, TIO, both, or lipid emulsions. Additionally, the stability tests mentioned or described in each study were listed and compiled into a table. Subsequently, a narrative synthesis was conducted to rank the stability tests and their methods based on the clinical relevance of each parameter, its reliability in detecting (in)stability, practicality, and potential clinical impact. Test methods were also assessed based on accuracy, sensitivity, feasibility, and cost-effectiveness. This approach enabled a critical review of the findings to identify and propose the essential tests required to establish AIO PN stability.

RESULTS

The electronic database search yielded a total of 1180 articles. After removing 290 duplicates using EndNote and Rayyan software, 890 articles were screened by title and abstract, resulting in the exclusion of 811 articles. The remaining 79 articles were searched for full-text, and only 76 full-text articles were obtained and assessed for eligibility. A total of 33 articles met the inclusion criteria and were included in this scoping review. The results of the screening process using the PRISMA extension for scoping reviews are shown in Figure 1.

Characteristics of included articles

The included studies were predominantly conducted in Europe, particularly in Poland (n = 8), Spain (n = 4), France (n = 3), and Italy (n = 3), with contributions from Asia, including Indonesia (n = 2) and China (n = 2). Out of the 33 included studies, 25 focused on AIO solutions, six studies examined both AIO and TIO solutions, one studied AIO solutions and lipid emulsions, and one was conducted solely on lipid emulsions. From these studies, 11 stability tests were identified and classified into physical, chemical, and microbiological tests. A summary of the tests conducted by each study is presented in Table 1.

Physical tests

Visual inspection was commonly conducted (included in 25 studies), following European Pharmacopoeia (EP) guidelines. The method involved two different trained personnel examining the AIO solutions against black and white backgrounds to detect signs of physical instability, such as creaming, coalescence, phase separation, and the presence of free oil droplets.[11,12] A total of 23 studies conducted pH measurement tests, typically performed using calibrated pH meters at room temperature with buffer solutions at pH 4, 7, and 9.[13-19] pH values <5.0 or deviations exceeding ±0.2–0.5 units were often considered indicative of instability.[20,21]

Particle size analysis was assessed in 28 studies based on the United States Pharmacopoeia (USP) <729> guidelines, which describe two main methods. Method I, dynamic light scattering (DLS) or laser diffraction, was most used (n = 27), while Method II, single-particle optical sensing (SPOS) or light obscuration (LO), was used in six studies to quantify the proportion of fat in droplets exceeding 5 µm, known as PFAT5. Four studies utilised both methods to achieve more accurate results. Additionally, optical microscopy was used in nine studies to assess droplet size. The USP recommends the mean droplet diameter (MDD) should not exceed 0.5 µm and PFAT5 should be less than 0.05%.[22]

Zeta potential, which reflects the electrostatic stability of emulsions, was assessed in 13 studies using Laser Doppler electrophoresis via DLS instruments.[13,23] The tests were conducted at 25 ± 1°C after diluting samples with sterile water.[13,20,24-26] Studies suggested a zeta potential in the range of –20 to –50 mV was considered ideal for ensuring emulsion stability due to sufficient electrostatic repulsion between droplets.[13,14,23,25] Five studies assessed osmolarity using osmometers that operate on the principle of freeze point depression, also known as cryoscopic osmometry. The osmometers were calibrated with standard solutions at 200 and 500 mosmol/kg.[15] Measurements were reported in osmolality and converted to osmolarity. Although most studies did not specify acceptance limits, one mentioned that a ±5% deviation from the initial value was acceptable.[20]

Only one study[23] measured surface tension using a computer-controlled tensiometer via the Wilhelmy plate method at 25 ± 0.5°C. Although no specific acceptance limits were established, consistent surface tension values

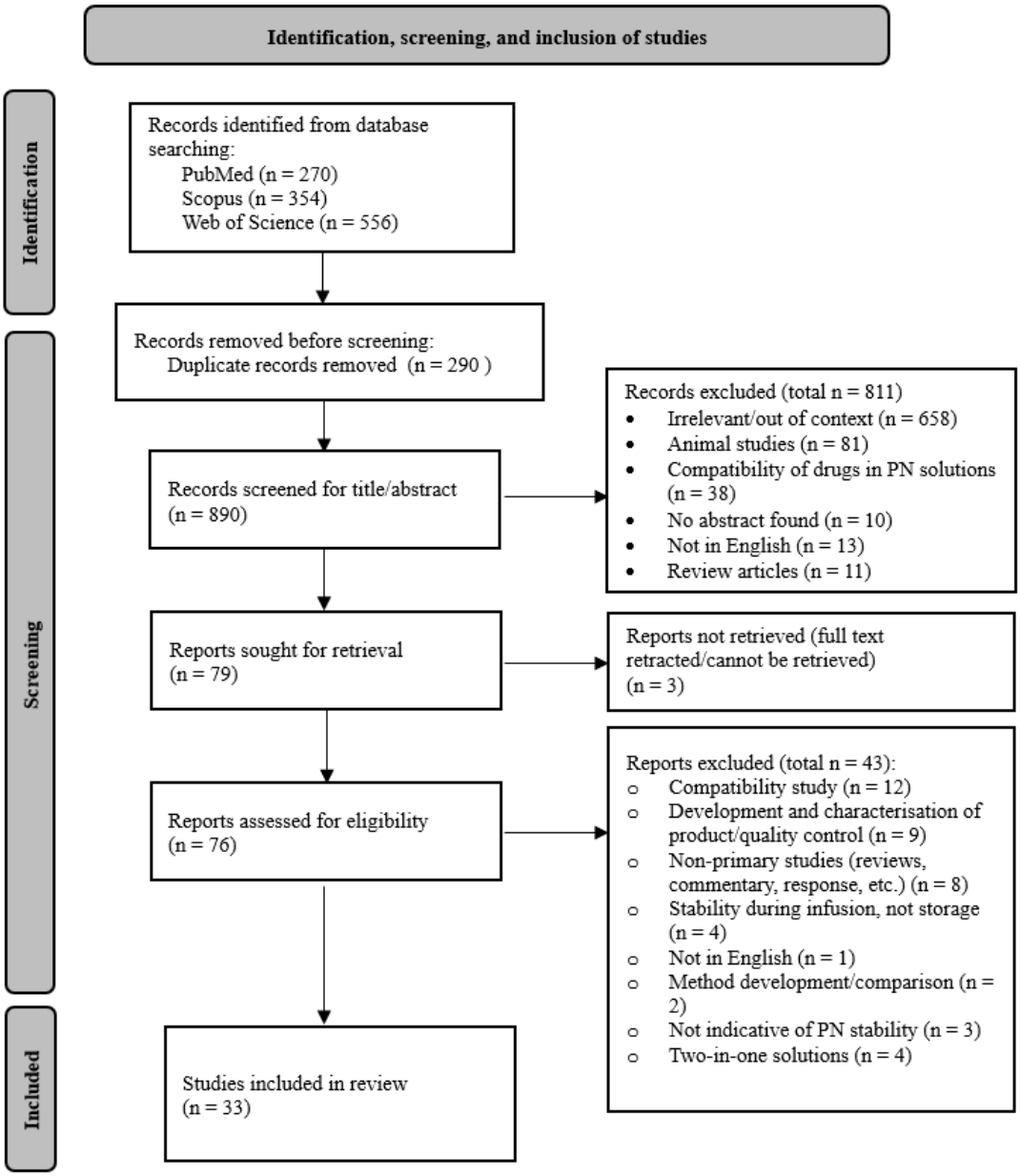

Figure 1. PRISMA flow diagram for study identification, screening, and inclusion[49]

over time were associated with a stable interfacial structure, whereas declining values suggested reduced stability.[23] Density and viscosity measurements were documented in two studies.[19,27] Density was determined using vibrating tube oscillation meters with internal temperature control and standard fluid calibration. Viscosity was measured using viscometers equipped with circulation baths to maintain constant temperature, and the instruments were calibrated with standard liquids. However, none of the studies mentioned specific acceptance criteria for these parameters.[19,27]

Chemical tests

Chemical stability assessment of AIO solutions mainly focused on lipid peroxidation and micronutrient analysis. Lipid peroxidation test was reported in seven studies using various analytical techniques. These included spectrophotometry at 560 nm using the FOX (ferrous oxidation of xylenol) assay,[28] iodometric titration with 1% starch as a colourimetric indicator,[14,29] potentiometric titration, and the thiobarbituric acid reactive substances (TBARS) assay, which was used in three studies.[16,30,31] One study also used liquid chromatography-mass spectrometry (LC-MS) to measure malondialdehyde (MDA),[32] a byproduct of polyunsaturated fatty acid peroxidation. However, no official pharmacopoeial acceptance limits for peroxide values were identified. Micronutrient analysis, reported in five studies, focused on vitamins A, C, and E. The most commonly used method was reversed-phase high-performance liquid chromatography (RP-HPLC).[26,28] One study applied electrospray ionisation tandem mass spectrometry (ESI-MS/MS) specifically for the detection of vitamin C.[33]

Microbiological tests

Microbiological stability was conducted in six studies, primarily through sterility testing in accordance with the British Pharmacopoeia (BP) guidelines. Two standard sterility testing methods were identified: membrane filtration and direct inoculation. Membrane filtration, used in

Table 1. Summary of stability tests conducted by each study

No	Author, Year	AIO/ BOTH/ LE	Visual inspection	Particle size	pH	Osmolarity	Vitamin assay
1	Hanifah et al. (2019)[11]	BOTH	X (B)	X (AIO)	X (B)	X (B)	
2	Gostynska et al. (2021)[20]	AIO	X	X	X	X	
3	Janu et al. (2011)[50]	AIO	X	X	X	X	
4	Forchielli et al. (2019)[51]	AIO		X			
5	Turmezei et al. (2015)[33]	AIO		X			X
6	Watrobska-Swietlikowska & Macloughlin (2019)[13]	AIO	X	X	X		X
7	Watrobska-Swietlikowska et al. (2015)[52]	BOTH	X (B)	X (AIO)	X (B)		
8	Watrobska-Swietlikowska et al. (2014)[53]	BOTH	X (B)	X (AIO)	X (B)		
9	Silva et al. (2015)[30]	AIO	X	X			
10	Lobo et al. (2018)[14]	AIO	X	X	X	X	
11	Gonyon et al. (2013)[54]	AIO		X			
12	Jalabert et al. (2011)[32]	AIO					
13	Giorgia et al. (2023)[31]	BOTH	X (B)	X (AIO)	X (B)		
14	Forchielli et al. (2014)[55]	AIO		X			
15	Bourcier & Poullain-Termeau (2015)[25]	AIO	X	X	X		

No	Author, Year	Zeta potential	Dynamic surface tension	Peroxide value	Sterility	Density	Viscosity
1	Hanifah et al. (2019)[11]						
2	Gostynska et al. (2021)[20]	X					
3	Janu et al. (2011)[50]				X		
4	Forchielli et al. (2019)[51]						
5	Turmezei et al. (2015)[33]	X			X		
6	Watrobska-Swietlikowska & Macloughlin (2019)[13]	X					
7	Watrobska-Swietlikowska et al. (2015)[52]	X					
8	Watrobska-Swietlikowska et al. (2014)[53]						
9	Silva et al. (2015)[30]			X	X		
10	Lobo et al. (2018)[14]	X		X	X		
11	Gonyon et al. (2013)[54]						
12	Jalabert et al. (2011)[32]			X			
13	Giorgia et al. (2023)[31]			X (AIO)			
14	Forchielli et al. (2014)[55]						
15	Bourcier & Poullain-Termeau (2015)[25]	X					

AIO: All-in-one solution; TIO: Two-in-one solution; BOTH: Both all-in-solution and two-in-one solution are studied; LE: Lipid emulsion; B: BOTH.

Table 1. Summary of stability tests conducted by each study (cont.)

No	Author, Year	AIO/ BOTH/ LE	Visual inspection	Particle size	pH	Osmolarity	Vitamin assay
16	Gao et al. (2021)[35]	AIO	X	X	X		
17	Zhao et al. (2021)[15]	AIO	X	X	X	X	
18	Riera et al. (2018)[12]	BOTH	X (B)	X (AIO)	X (TIO)	X (TIO)	
19	Skouroliakou et al. (2012)[28]	AIO	X	X	X		X
20	Tovsen et al. (2015)[16]	AIO/LE		X	X		
21	De Cloet et al. (2018)[29]	BOTH	X (B)	X (AIO)	X (B)		
22	Watrobska-Swietlikowska et al. (2018)[17]	AIO	X	X	X		
23	Hanifah et al. (2021)[21]	AIO	X	X	X		
24	Mirković et al. (2013)[36]	AIO	X	X			
25	Télessy et al. (2011)[23]	AIO	X	X			
26	Watrobska-Swietlikowska (2019)[22]	LE	X	X	X		
27	Driscoll et al. (2010)[18]	AIO		X	X		
28	Stawny et al. (2020)[26]	AIO	X	X	X		X
29	Sayed et al. (2021)[24]	AIO	X	X			
30	Pietka et al. (2015)[56]	AIO	X	X	X		
31	Escuder-Vieco et al. (2024)[57]	AIO		X	X		
32	Otero-Millán at al. (2024)[27]	AIO	X	X	X		
33	Otero-Millán at al. (2024)[19]	AIO	X	X	X		

No	Author, Year	Zeta potential	Dynamic surface tension	Peroxide value	Sterility	Density	Viscosity
16	Gao et al. (2021)[35]						
17	Zhao et al. (2021)[15]						
18	Riera et al. (2018)[12]				X (TIO)		
19	Skouroliakou et al. (2012)[28]			X			
20	Tovsen et al. (2015)[16]	X		X			
21	De Cloet et al. (2018)[29]			X (AIO)			
22	Watrobska-Swietlikowska et al. (2018)[17]	X					
23	Hanifah et al. (2021)[21]				X		
24	Mirković et al. (2013)[36]						
25	Télessy et al. (2011)[23]	X	X				
26	Watrobska-Swietlikowska (2019)[22]	X					
27	Driscoll et al. (2010)[18]						
28	Stawny et al. (2020)[26]	X					
29	Sayed et al. (2021)[24]	X					
30	Pietka et al. (2015)[56]	X			X		
31	Escuder-Vieco et al. (2024)[57]						
32	Otero-Millán at al. (2024)[27]					X	X
33	Otero-Millán at al. (2024)[19]					X	X

AIO: All-in-one solution; TIO: Two-in-one solution; BOTH: Both all-in-solution and two-in-one solution are studied; LE: Lipid emulsion; B: BOTH.

one study,[21] involved passing the sample through a 0.45 µm membrane, followed by incubation on nutrient pads for seven days. Direct inoculation, used in two studies, required 5–10 mL of the sample to be directly introduced into culture media and incubated at 37°C for 14 days.[14,33] One study used a depth spreading method,[30] while two studies did not specify the method used. Across all methods, the accepted criterion for sterility was the absence of microbial growth in the culture medium.

Suggested stability tests for AIO solutions

A key outcome of this scoping review is the suggested list of essential stability tests for assessing the physical, chemical, and microbiological stability of AIO PN formulations, particularly those compounded in hospital settings. Based on the tests identified from the included studies, each test was ranked according to its level of importance, categorised as high, intermediate, or low in determining the overall stability of AIO PN solutions. Additionally, where multiple methods were available for a particular test, these were further categorised based on the relevance, practicality, and analytical value to guide researchers in selecting the most appropriate approach. A summary of the suggested core tests and corresponding rankings is presented in Table 2.

The physical tests presumed most critical include visual inspection, particle size analysis, pH measurement, and zeta potential measurement. Among the available methods for particle size analysis, both Method I (DLS) and Method II (SPOS) as described in the USP <729> are proposed to be the most relevant. These methods are complementary, with Method I providing MDD data and Method II offering information on the proportion of large droplets (PFAT5), both of which are critical indicators of emulsion stability. For chemical stability, lipid peroxidation assessment via the TBARS assay is proposed as the most suitable method due to its sensitivity and widespread use. In terms of microbiological stability, sterility testing using the membrane filtration technique is suggested.

This compilation represents a novel contribution of the present review and provides a foundational framework for standardising stability evaluation protocols, especially for in-house hospital-compounded AIO PN formulations.

DISCUSSION

Over the past 15 years, there has been no significant increase or trend in the number of stability tests conducted on PN formulations; this number has remained relatively constant. However, it is noteworthy that while North America was reported as the largest global PN market in 2023,[34] the majority of recent stability studies were carried out in Europe, followed by countries in Asia, particularly the Asia Pacific region. This area is experiencing rapid growth in the global PN market, likely driven by an ageing population and a rising incidence of chronic diseases.[34]

As noted earlier, this review revealed a geographical disparity in the conduct of PN stability studies, with a clear dominance of high-resource or advanced countries. The majority of the included studies originated from European countries such as Spain, Poland, Italy, and France. Western and European countries currently account for an estimated 80–90% of published PN stability studies, indicating that the practice is well-established in these regions. In contrast, the current contribution of middle- and low-income countries to this field appears to be minimal. Only a few studies were identified from countries like Indonesia, China, Egypt, and Serbia, with just one or two publications from each. This limited representation from resource-constrained settings makes it difficult to perform meaningful cross-regional comparisons or to draw globally relevant conclusions.

Several factors may contribute to the underrepresentation of lower and middle-income countries in PN stability studies. High-resource countries seem to have better access to advanced analytical equipment, stronger research infrastructure, and more comprehensive regulatory guidelines or standards that encourage or mandate stability testing, such as the USP, BP, EP, and Japanese Pharmacopoeia (JP). These settings may also foster a greater awareness of the importance of PN stability studies and benefit from more robust financial support. In contrast, studies from middle- and low-income countries often focus on simpler, more cost-effective assessments, such as visual inspection, pH measurement, and particle size analysis.[11,15,21,24,35,36] More complex and resource-intensive stability tests, such as analyses of amino acids or vitamins, and microbiological tests, were scarcely reported. This scarcity can be attributed to limited access to advanced analytical technologies, high costs of reagents and skilled labour, and competing healthcare priorities.[37-39] Additionally, awareness of the importance of stability data in ensuring PN safety may be limited among healthcare providers.[37,38] Thus, it is hoped that this review can raise awareness of the feasibility and significance of PN stability testing in limited- or low-resource settings, ultimately encouraging broader participation from these countries and more inclusive research outputs that reflect a wider range of clinical and logistical contexts.

This scoping review aimed to identify and summarise current practices in the physical, chemical, and microbiological stability testing of AIO PN solutions in hospital settings. From the 33 included studies, we identified a wide array of tests used, with notable methodological inconsistencies and reporting standards. These discrepancies include variability in duration of study, instrument specifications, sample handling procedures, environmental testing conditions, and the acceptance criteria. Such discrepancies hinder reproducibility and limit the comparability of findings across studies.

Moreover, while existing guidelines, such as those from the ICH and NHS, provide general direction on stability-indicating parameters, they often lack detailed experimental methodologies tailored to PN solutions. This lack of clarity has led to procedural variability and lack of standardisation within the scientific community. Past reviews have also largely focused on individual stability domains, such as either physical or chemical aspects, rather than offering an integrated protocol. To address these challenges, we identified commonly used tests and evaluated their potential as standard components for a stability testing protocol for AIO PN formulations. The six suggested core tests; visual inspection, pH measurement,

Table 2. Summary of suggested stability tests and methods for AIO solutions

Test name	Category/ Rank of importance†	Method option	Category/ Rank of relevance†	Comment/ Remark
Physical				
Visual inspection (n = 25)	+++	Against a black and a white background to detect visual changes	+++	
Particle size analysis (n = 32)	+++	Method I: dynamic light scattering or laser diffraction	+++	-Provide essential data/parameter (MDD & PFAT5) -More accurate Expensive instrument
		Method II: light obscuration technique	+++	
		Optical microscopy	+	-Complement data -More accessible -Visualization & characterization -Poor statistics, lack accuracy
pH measurement (n = 23)	+++	Calibrated pH meter/potentiometry	+++	
Zeta Potential measurement (n = 13)	+++	Laser Doppler-electrophoresis or laser Doppler velocimetry	+++	
Osmolarity (n = 5)	++	Calibrated osmometer	+++	
Dynamic surface tension (n = 1)	+	Dynamic method; Du-Noüy ring and Wilhelmy plate operations of a computer-controlled tensiometer	+++	
Density (n = 2)	+	Mechanical oscillation density meter calibrated with standard fluids	+++	
Viscosity (n = 2)	+	Viscometer calibrated with standard fluids	+++	
Chemical				
Vitamin assay (n = 4)	++	HPLC	+++	-High sensitivity and specificity -Costly and requires expertise
		ESI/MS-MS	++	-Costly and requires expertise -Not easily accessible
Peroxide value (n = 7)	+++	FOX method	++	-Measures primary products (hydroperoxides)
		TBARS assay	+++	-Measures secondary oxidation products (MDA) -Suitable for complex matrices like PN
		HPLC or LC/MS	++	-High sensitivity and specificity -Costly and requires expertise
		Iodometric titration	+	Classic method, less sensitive
Microbiology				
Sterility tests (n = 6)	+++	Membrane filtration	+++	-Higher sensitivity -Costly and laborious sample preparation
		Direct inoculation	++	-Non-specific and less sensitive -Simpler, less costly

HPLC: High-performance liquid chromatography; ESI/MS-MS: Electrospray ionisation mass spectrometry; FOX: Ferrous oxidation; TBARS: Thiobarbituric Acid Reactive Substances; LC-MS: Liquid chromatography mass spectrometry; MDD: Mean droplet diameter; PFAT5: Percentage of fat residing in globules >5 µm values; MDA: Malondialdehyde; PN: Parenteral Nutrition

†+++: High, ++: Intermediate; +: Low

particle size analysis (via DLS or SPOS), zeta potential measurement, TBARS assay for lipid peroxidation, and sterility testing, were prioritised based on their recurrence in the literature, accessibility, and clinical relevance. These are the essential components of a suggested testing protocol for AIO PN stability evaluation.

Key findings and relevance

Visual inspection was nearly universally applied, serving as a basic yet important screening method to detect signs of instability in AIO solutions, including creaming, coalescence, and the presence of oil droplets.[13,14] Although this method is limited by human visual accuracy,[13] it provides a quick, straightforward, and cost-effective way to monitor early signs of physical changes, making it an appropriate routine physical test for assessing the stability of PN solutions.[40] pH monitoring, reported in over 80% of the included studies, is a simple yet sensitive marker for early chemical degradation or component incompatibilities, as significant fluctuations in pH can signify chemical degradation or interactions that may compromise the product's safety and efficacy.[19] A decrease in pH in AIO solutions may indicate the breakdown of lipids into fatty acids, resulting in increased acidity. Consequently, when the pH of the solutions falls below 5.0, the stability of the lipid emulsion is compromised, indicating substantial degradation of lipids into free fatty acids and the subsequent formation of larger lipid globules.[21,41]

Particle size analysis was one of the most employed methods to assess the physical stability of AIO PN formulations. The test monitors MDD and identifies larger droplets that may indicate aggregation, emulsion breakdown, and potential instability if these parameters exceed acceptable limits.[19] This test is also crucial to ensure that the lipid globules do not pose a risk of embolism by exceeding the 5-μm dimension threshold of human capillaries.[13,42]

USP <729> recommends two complementary methods for particle size analysis in PN solutions, which are Method I for measuring MDD and Method II for quantifying PFAT5. This method guarantees precise and dependable outcomes while enabling thorough characterisation of PN solutions.[20,27] Laser diffraction DLS are used for MDD (Method I), and when feasible, should be employed together, as laser diffraction is more effective for detecting larger globules, while DLS excels at identifying particles in the nanometer range.[14] Method II, which quantifies PFAT5 using light obstruction (SPOS), is critical for detecting large lipid globules (>5 μm), which must be kept below 0.05% to minimise the risk of embolism and other fatal complications.[14]

The final physical test proposed for assessing the stability of AIO solutions involves zeta potential measurements. Zeta potential is essential for indicating the stability of oil-in-water systems, such as AIO solutions, as it reflects the surface charge of lipid droplets. A high absolute value (–20 to –50 mV) signifies strong electrostatic repulsion between lipid droplets, preventing aggregation and coalescence.[13,23,41,43] It is particularly useful for detecting early signs of instability before visible changes occur.[23,33]

Chemical stability was primarily assessed via lipid peroxidation, with the TBARS assay identified as the most relevant method. TBARS quantifies malondialdehyde (MDA), a toxic byproduct of lipid oxidation[30,44] offering a simple, reproducible approach suitable for complex matrices such as PN solutions despite moderate sensitivity and specificity.[45]

Lastly, for microbiological stability, the only widely documented test for this category is the sterility test. Sterility testing assesses whether the PN solutions are free from microbial contamination and remain sterile throughout their intended shelf-life and storage conditions, to ensure patient safety during use.[12] Among the two methods outlined by BP, a study by Montejo et al.[46] mentioned that membrane filtration was preferred over direct inoculation as the former proved to be more effective and enabled better differentiation between accidental contamination and genuine bacterial growth. Membrane filtration is preferred for filterable pharmaceutical products as it isolates microorganisms more effectively, reducing interference from the product matrix and improving microbial recovery during incubation.[47,48] It also allows testing of larger sample volumes, increasing contamination detection.[47] However, it has drawbacks, including a potential 10% reduction in PN solution volume,[46] more complex sample preparation, and higher equipment costs.

Implications for clinical practice and policy

Given the complex, multicomponent nature of AIO PN formulations and their role in the care of especially critically ill patients, the implementation of a standardised and rational set of stability tests is crucial. This review proposes a stability testing protocol based on six suggested essential parameters: visual inspection, pH, particle size, zeta potential, lipid peroxidation, and sterility testing. Adoption of this protocol could help improve quality assurance in hospital pharmacies, facilitate regulatory compliance, and enhance patient safety. These suggestions are particularly relevant for low- and middle-income countries, where AIO PN solutions are often compounded in-house and may lack access to commercial testing infrastructure.

Strengths and limitations

While the review is strengthened by its systematic approach and focus on recent, clinically relevant practices, certain limitations must be acknowledged. Despite a broad search strategy, some relevant studies may have been missed due to language and database restrictions. The 15-year limit was selected to ensure technological and methodological relevance. Although expert consultation was not included, reliance on established guidelines and robust literature review enhances the reliability of our findings.

Conclusion

This scoping review systematically compiled and evaluated current practices in the stability testing of AIO PN solutions. Despite the availability of various analytical methods, significant heterogeneity and methodological gaps were observed across the literature, particularly in study design, test selection, and reporting standards.

These inconsistencies highlight the absence of a unified, evidence-based protocol for establishing AIO PN stability, especially in hospital settings. This review offers an overarching view of key stability tests that may be valuable in assessing the stability of compounded AIO solutions in hospital settings. These recommendations are not evidence-validated but rather represent a reasoned synthesis and opinion-based approach drawn from the reviewed literature. Six tests were proposed as essential components of a potential stability testing protocol for consideration: visual inspection, pH measurement, particle size analysis (using both DLS and SPOS/LO methods, including PFAT5 reporting), zeta potential, TBARS assay for lipid peroxidation, and sterility testing via membrane filtration. Ultimately, this review aims to serve as a practical guide for researchers, pharmacists, and clinicians, supporting more informed, reproducible, and standardised assessments of AIO PN solution stability. Future research should prioritise the development and validation of harmonised testing guidelines tailored for AIO PN, with collaborative efforts across disciplines and countries playing a crucial role in advancing safe and effective parenteral nutrition practices globally.

SUPPLEMENTARY MATERIALS

All supplementary materials are available upon request to the editorial office.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURES

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REFERENCES

1. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017;36:49-64. doi: 10.1016/j.clnu.2016.09.004.
2. NHS Pharmaceutical Quality Assurance Comittee. A Standard Protocol for Derivation and Assessment of Stability (Part 4 - Parenteral Nutrition). 2016 [cited 2023/08/11]; Available from: https://www.sps.nhs.uk/articles/a-standard-protocol-for-derivation-and-assessment-of-stability-part-4-parenteral-nutrition/
3. Boullata JI, Mirtallo JM, Sacks GS, Salman G, Gura K, Canada T, et al. Parenteral nutrition compatibility and stability: A comprehensive review. JPEN J Parenter Enteral Nutr. 2022;46:273-99. doi: 10.1002/jpen.2306.
4. de Villiers M. Compatibility and Stability of Drug Products and Preparations. In: Thompson JE, editor. A Practical Guide to Contemporary Pharmacy Practice. 3 ed: Philadelphia: Lippincott Williams & Wilkins; 2009. pp. 673 - 701.
5. ICH. Stability Testing Of New Drug Substances And Products Q1A(R2). Guidelines. Geneva: International Conference on Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use. 2003/02/06 [cited 2025/04/06]; Available from: https://www.ich.org/page/quality-guidelines
6. ASEAN. Asean Guideline on Stability Study of Drug Product (R1). 2013/05/15 [cited 2025/04/06]; Available from: https://asean.org/wp-content/uploads/2012/10/ASEAN-Guideline-on-Stability-Study-of-Drug-Product-R1-2013.pdf
7. FDA. Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products. Rockville, Maryland: Food and Drug Administration. 2003 [cited 2025/04/06]; Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q1ar2-stability-testing-new-drug-substances-and-products
8. EMA. Guideline on Stability Testing: Stability testing of existing active substances and related finished products. Revision 2 ed. Amsterdam: European Medicines Agency. 2023/02/17 [cited 2025/04/06]; Available from: https://www.ema.europa.eu/en/stability-testing-existing-active-substances-related-finished-products-scientific-guideline
9. Peters M, Godfrey C, McInerney P, Munn Z, Trico A, Khalil H. Chapter 11: Scoping Reviews. In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis. 2020 [cited 2023/11/08]; Available from: https://synthesismanual.jbi.global.
10. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169:467-73. doi: 10.7326/m18-0850.
11. Hanifah S, Maulidani Y, Nugroho BH, Sari CP. All-in-one versus lipid-free parenteral nutrition for premature infants: visual, pH, and particle size analyses. Nutr Hosp. 2019;36:1237-40. doi: 10.20960/nh.02758.
12. Riera P, Garrido-Alejos G, Cardenete J, Moliner E, Zapico-Muñiz E, Cardona D, et al. Physicochemical Stability and Sterility of Standard Parenteral Nutrition Solutions and Simulated Y-Site Admixtures for Neonates. Nutr Clin Pract. 2018;33:694-700. doi: 10.1002/ncp.10013.
13. Watrobska-Swietlikowska D, MacLoughlin R. The effect of UV-protected ethylene vinyl acetate (EVA) bags on the physicochemical stability of pediatric parenteral nutrition admixtures. DARU, J Pharm Sci. 2019;27:255-64. doi: 10.1007/s40199-019-00270-7.
14. Lobo BW, da Veiga VF, Cabral LM, Michel RC, Volpato NM, de Sousa VP. Influence of the relative composition of trace elements and vitamins in physicochemical stability of total parenteral nutrition formulations for neonatal use. Nutr J. 2012;11:26. doi: 10.1186/1475-2891-11-26.
15. Zhao B, Gao RC, Jiao L, Zhang F, Wang B, Mei D. Physical Stability of Medium-Chain Triglyceride/Long-Chain Triglyceride Emulsion Injections From 5 Manufacturers in High-Concentration Electrolyte-Based Total Nutrient Admixtures. JPEN J Parenter Enteral Nutr. 2021;45:1275-84. doi: 10.1002/jpen.2009.
16. Tovsen ML, Smistad G, Bjerke TM, Tønnesen HH, Kristensen S. Physicochemical Stability of Emulsions and Admixtures for Parenteral Nutrition during Irradiation by Glass-Filtered Daylight at Standardized Conditions. PDA J Pharm Sci Technol. 2015;69:346-54. doi: 10.5731/pdajpst.2015.01036.
17. Watrobska-Swietlikowska D, MacLoughlin R, Szlagatys-Sidorkiewicz A. The presence of inorganic calcium in pediatric parenteral admixtures. Nutr Hosp. 2018;35:11-8. doi: 10.20960/nh.1340.
18. Driscoll DF, Silvestri AP, Bistrian BR. Stability of MCT/LCT-based total nutrient admixtures for neonatal use over 30 hours at room temperature: applying pharmacopeial

standards. JPEN J Parenter Enteral Nutr. 2010;34:305-12. doi: 10.1177/0148607109338215.
19. Otero-Millán L, Bea-Mascato B, Soto JLL, Martínez-López-De-Castro N, Lago-Rivero N. Physicochemical Stability of Hospital Parenteral Nutrition Solutions: Effect of Changes in Composition and Storage Protocol. Pharmaceutics. 2024;16. doi: 10.3390/pharmaceutics16050572.
20. Gostynska A, Starkowska J, Sobierajska P, Jelinska A, Stawny M. All-in-One Pediatric Parenteral Nutrition Admixtures with an Extended Shelf Life-Insight in Correlations between Composition and Physicochemical Parameters. Pharmaceutics. 2021;13. doi: 10.3390/pharmaceutics13071017.
21. Hanifah S, Maulidani Y, Nugroho BH, Sari CP. Provision of Standardized All-in-One Parenteral Nutrition (AIO-PN) for Very Preterm Neonates: Evaluation at Room and Cold Temperatures. J Pharm Bioallied Sci. 2021;13:26-30. doi: 10.4103/jpbs.JPBS_278_19.
22. Watrobska-Swietlikowska D. Stability of commercial parenteral lipid emulsions repacking to polypropylene syringes. Plos One. 2019;14. doi: 10.1371/journal.pone.0214451.
23. Télessy IG, Balogh J, Turmezei J, Dredán J, Zelkó R. Stability assessment of o/w parenteral nutrition emulsions in the presence of high glucose and calcium concentrations. J Pharm Biomed Anal. 2011;56:159-64. doi: 10.1016/j.jpba.2011.05.002.
24. Sayed OAA, Hassan SB, Abdelkader A, Elsabahy M, Abdelaziz NHR, El-Sayed AM. Stability Study and Clinical Evaluation of Lipid Injectable Emulsion in Parenteral Nutrition Admixtures Used for Preterm Neonates. Nutr Clin Pract. 2021;36:696-703. doi: 10.1002/ncp.10556.
25. Bourcier E, Poullain-Termeau S. Parenteral nutrition in a neonatal intensive care unit: galenic stability of four all-in-one admixtures. Eur J Hosp Pharm. 2015;22:285-90. doi: 10.1136/ejhpharm-2014-000625.
26. Stawny M, Gostynska A, Olijarczyk R, Dettlaff K, Jelinska A, Ogrodowczyk M. Stability studies of parenteral nutrition with a high dose of vitamin C. J Oncol Pharm Pract. 2020;26:1894-902. doi: 10.1177/1078155220904438.
27. Otero-Millán L, Bea-Mascato B, Soto JLL, Martínez-López-De-Castro N, Lago-Rivero N. Evaluation of the Stability of Newborn Hospital Parenteral Nutrition Solutions. Pharmaceutics. 2024;16. doi: 10.3390/pharmaceutics16030316.
28. Skouroliakou M, Kountouri AM, Hatziantoniou S, Koutri K, Chiou A. Physicochemical stability assessment of all-in-one parenteral emulsion for neonates containing SMOFlipid. Eur J Hosp Pharm. 2012;19:514-8. doi: 10.1136/ejhpharm-2012-000121.
29. De Cloet J, Van Biervliet S, Van Winckel M. Physicochemical stable standard all-in-one parenteral nutrition admixtures for infants and children in accordance with the ESPGHAN/ESPEN guidelines. Nutrition. 2018;49:41-7. doi: 10.1016/j.nut.2017.11.019.
30. Silva CB, De Vasconcelos Araújo TD, Vasconcelos PRL, De Paula HCB, Nogueira NAP, De Oliveira Lira CAB, et al. Gamma radiation as a method for sterilization of all-in-one admixtures bags for clinical use: A study of stability. Int J Pharm Pharm Sci. 2015;7:129-35. doi: N.A.
31. Giorgia Z, Barzan D, Marzaro G, Pigozzo S, Valenti A. One-chamber and two-chamber parenteral nutrition admixtures for pediatric and adult patients: An evaluation of physico-chemical stability at room and cold temperature. Nutrition. 2023;106:111891. doi: 10.1016/j.nut.2022.111891.
32. Jalabert A, Gr, A, Steghens JP, Barbotte E, Pigue C, et al. Lipid peroxidation in all-in-one admixtures for preterm neonates: impact of amount of lipid, type of lipid emulsion and delivery condition. Acta Paediatr. 2011;100:1200-5. doi: 10.1111/j.1651-2227.2011.02269.x.
33. Turmezei J, Jávorszky E, Szabó E, Dredán J, Kállai-Szabó B, Zelkó R. Effect of Storage Temperature on The Stability of Total Parenteral Nutrition Admixtures Prepared for Infants. Acta Pol Pharm. 2015;72(5):843-9. doi: N.A
34. Kanhere M. Parenteral Nutrition Market Report 2025 (Global Edition). 2025 [updated March 2025; cited 12 May 2025]; Available from: https://www.cognitivemarketresearch.com/parenteral-nutrition-market-report
35. Gao S, Fan J, Jia X, Li B, Li X, Li Z, et al. PFAT5 stability assessment of Lipovenoes MCT in total nutrient admixtures. Ann Palliat Med. 2021;10:12244-50. doi: 10.21037/apm-21-3353.
36. Mirković D, Ibrić S, Antunović M. Quality assessment of total parenteral nutrition admixtures by the use of fractional factorial design. Vojnosanit Pregl. 2013;70:374-9. doi: 10.2298/vsp1304374m.
37. Adams SH, Anthony JC, Carvajal R, Chae L, Khoo CSH, Latulippe ME, et al. Perspective: Guiding Principles for the Implementation of Personalized Nutrition Approaches That Benefit Health and Function. Adv Nutr. 2020;11:25-34. doi: 10.1093/advances/nmz086.
38. Wischmeyer PE, Klek S, Berger MM, Berlana D, Gray B, Ybarra J, et al. Parenteral nutrition in clinical practice: International challenges and strategies. Am J Health Syst Pharm. 2024;81:S89-S101. doi: 10.1093/ajhp/zxae079.
39. Narke E. Challenges and Solutions for the Stability Program of Drug Products during CMC Drug Development. 2024 [updated 7 August 2024; cited 14 June 2025]; Available from: https://www.linkedin.com/pulse/challenges-solutions-stability-program-drug-products-during-narke-wmwpe/
40. Mirtallo J, Canada T, Johnson D, Kumpf V, Petersen C, Sacks G, et al. Safe practices for parenteral nutrition. JPEN J Parenter Enteral Nutr. 2004;28:S39-70. doi: 10.1177/0148607104028006s39.
41. Pertkiewicz M, Cosslett A, Mühlebach S, Dudrick SJ. Basics in clinical nutrition: Stability of parenteral nutrition admixtures. e-SPEN, E Spen Eur E J Clin Nutr Metab. 2009;4:e117-e9. doi: 10.1016/j.eclnm.2009.01.010.
42. Driscoll DF, Silvestri AP, Bistrian BR, Mikrut BA. Stability of total nutrient admixtures with lipid injectable emulsions in glass versus plastic packaging. Am J Health Syst Pharm. 2007;64:396-403. doi: 10.2146/ajhp060062.
43. Ribeiro DO, Pinto DC, Lima L, Volpato NM, Cabral LM, de Sousa VP. Chemical stability study of vitamins thiamine, riboflavin, pyridoxine and ascorbic acid in parenteral nutrition for neonatal use. Nutr J. 2011;10. doi: 10.1186/1475-2891-10-47.
44. Ayala A, Munoz MF, Arguelles S. Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. Oxid Med Cell Longev. 2014;2014:360 - 438. doi: 10.1155/2014/360438.
45. Deng FM, Wang SR, Jing DY, Wang YF, Yang ZM, Huang Y, et al. Comparison of three methods for quantitative analysis of LPO in different biological samples. Sichuan Da Xue Xue Bao Yi Xue Ban. 2004;35:422-6. doi: N.A.
46. Montejo O, Cardona D, Sanchez F, Rigueira AI, Coll P, Bonal J. Microbiological Quality Control Study of 'All-in-One' Total Parenteral Nutrition Admixtures. JPEN J Parenter Enteral Nutr. 2000;24:183 - 6. doi: N.A
47. Sandle T. Sterility Testing – Overcoming Difficult Products. 2022 [cited 20 April 2025]; Available from: https://www.rssl.com/media/v3cbndvx/rssl-white-paper-

sterility-testing-overcoming-difficult-products-2022.pdf#:~:text=at%20least%20half%20the%20contents
48. Wertalik P. Sterility Testing Guide: Direct Inoculation vs. Membrane Filtration. 2024 [updated 30 September 2024; cited 20 April 2025]; Available from: https://outsource.contractlaboratory.com/sterility-testing/
49. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021. doi: 10.1136/bmj.n71.
50. Janů M, Brodská H, Vecka M, Masteiková R, Kotrlíková E, Lažauskas R, et al. Comparison of long-term stability of parenteral all-in-one admixtures containing new lipid emulsions prepared under hospital pharmacy conditions. Medicina. 2011;47:323-33. doi: 10.3390/medicina47060046
51. Forchielli ML, Bonoli A, Stancari A, Bruno LL, Piro F, Piazza G, et al. Do carnitine and extra trace elements change stability of paediatric parenteral nutrition admixtures? Clin Nutr. 2019;38:2369-74. doi: 10.1016/j.clnu.2018.10.016.
52. Watrobska-Swietlikowska D, Agnieszka SS, Luszkiewicz K. Evaluation of physical stability of all in one parenteral admixtures for pediatric home care with high electrolytes concentrations. Nutr Hosp. 2015;31:236-43. doi: 10.3305/nh.2015.31.1.7965.
53. Watrobska-Swietlikowska D, Kwidzynska A, Szlagatys-Sidorkiewicz A, Sznitowska M, Klek S. Finding new solutions in pediatric parenteral admixtures; how to improve quality and to deal with shortages. Nutr Hosp. 2014;30:84-93. doi: 10.3305/nh.2014.30.1.7500.
54. Gonyon T, Tomaso AE, Jr., Kotha P, Owen H, Patel D, Carter PW, et al. Interactions between Parenteral Lipid Emulsions and Container Surfaces. PDA J Pharm Sci Technol. 2013;67:247-54. doi: 10.5731/pdajpst.2013.00918.
55. Forchielli ML, Bonoli A, Preite I, Stancari A, Maselli S, Guarguaglini AM, et al. Parenteral nutrition admixtures for pediatric patients compounded with highly refined fish oil-based emulsion: assessment of physicochemical stability. Clin Nutr. 2014;33:1127-31. doi: 10.1016/j.clnu.2013.12.011.
56. Pietka M, Watrobska-Swietlikowska D, Szczepanek K, Szybinski P, Sznitowska M, Klek S. Nutritional Support Teams: the cooperation among physicians and pharmacists helps improve cost-effectiveness of home parenteral nutrition (HPN). Nutr Hosp. 2015;31:251-9. doi: 10.3305/nh.2015.31.1.8012.
57. Escuder-Vieco D, Gomis Munoz P, Hernandez Ramos JA, Bruni Montero MA, Bergon Sendin E, de la Cruz Bertolo J, et al. Stability of individualized neonatal parenteral nutrition admixtures with fish oil and high calcium content. Nutr Hosp. 2024;41:547-53. doi: 10.20960/nh.04931.