The practical stability of anticancer drugs: SFPO and ESOP recommendations

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The publication of European recommendations for the storage conditions of reconstituted and diluted solutions of oncology drugs as they are used in practice is a major achievement. These recommendations will be referred to frequently by hospital and oncology pharmacists.

Introduction

It is critical for hospital pharmacists to have well-documented data about the real stability of an opened drug formulation, after reconstitution of a lyophilised product or after dilution in various vehicles. This is even more important for anticancer drugs, which are frequently used at their maximum tolerated dose, have a tightly defined therapeutic range and are very toxic [1]. Unfortunately, these data are not always available or the published results are old, contradictory, limited to a particular vehicle or a specific bag. Moreover, the manufacturers frequently quote stability after dilution as being 'stable for eight or 12 hours', but not for valid reasons. These short times reflect application of the 'care principle' considering possible bacterial contamination or the fact that stability tests were only conducted over a very short period.

However, in most countries, anticancer drugs are prepared by the pharmacy in centralised units under strict aseptic techniques. Therefore, the only relevant issue is the real chemical stability, which should take into account the various drug concentrations, vehicles and containers used in clinical situations. An advantage of knowing true stability limits is that the centralised units can optimise the workload, the opening hours and the cost balance. Doses prepared in advance can limit the need to work antisocial hours such as at the weekend. The implementation of a dose-banding strategy is strongly dependent on the stability data. Finally, extending the stability limits of costly drugs such as biologicals would be extremely helpful both for practical and financial reasons. In summary, hospitals pharmacists need to have available the stability data pertinent to their needs in real life situations. This is what is meant by the in-use (or 'practical') stability of drugs. From the authors' point of view, the term 'practical stability' should be primarily chosen.

Considering the need to have consensual recommendations of in-use stability of anticancer drugs, the French Society of Oncology Pharmacy (SFPO) decided to set up a working group to analyse all published data relating their stability. This SFPO stability group was made up of pharmacists with strong expertise in drug stability and analytical chemistry and followed a strict methodology of meta-analysis (levels of evidence).

The SFPO stability group's recommendations were initially included in the sixth edition of *Anticancéreux*, published in 2008 by the *Centre National Hospitalier d'Information sur le Médicament*, CNHIM–National Information Centre on Hospital Drugs, a non-profit organisation started 25 years ago by French hospital pharmacists [2], and have now been endorsed at European level by ESOP during the 2010 Delegate Annual General Meeting in Hamburg, Germany.

Methodology

General methodology

The group investigated thoroughly all the published physico-chemical stability data of parenteral anticancer drugs prepared by reconstitution of a lyophilised powder or dilution. Studies dealing with mixtures of anticancer drugs have not been considered. Non-injectable pharmaceutical forms were excluded.

The drugs were divided by pharmacological class, e.g. alkalyting drugs, anti-metabolites; or by chemical class, e.g. platinum derivatives, anthracyclines; and assigned to several subgroups of two or three experts who evaluated the corresponding publications. Following the standardised methodology described later, each subgroup assigned an evidence level from A to D for each publication using a method adapted from the recommendations of the Oxford Centre for Evidence-based Medicine [3].

At each working session, one or more subgroups presented the pooled results of the evaluation for each drug and subsequently an initial proposal for a recommendation. These were fully discussed by the entire expert group. Finally, the consensual recommendation was established and validated by the full group. If the evaluated studies did not meet the quality requirements, no specific recommendation was proposed and the stability data indicated by the manufacturer were adopted, i.e. the summary of product characteristics (SmPC) which corresponds to the stability limits supplied in the marketing authorisation. A table summarising the SFPO/ESOP recommendations for the stability of oncology drug infusions follows this article.

If several well-designed studies suggested different stability limits for a particular drug, the most favourable was recommended. The relevant bibliography is indicated for each drug. If several concentration ranges were tested in relevant studies, recommendations were made for each range. If the available studies were limited to a single concentration, the recommendations were based on this concentration. However, in some cases, the recommendations were extended if relevant data were available (expert opinion or closely-related data such as several concentrations tested for a particular dilution vehicle and only one for another).

Evaluation of publications

Relevant publications were searched on several databases using keywords such as the chemical and generic name or the international nonproprietary name of the anticancer drug and relevant terms: 'stability', 'instability', 'degradation'. The Stabilis database was particularly helpful [4]. A critical analysis of each publication was then performed using, as essential criterion, the quality of the evidence. A standardised evaluation sheet was filled in for each publication. The topics checked included the following:

– Well-described stability-indicating analytical methods; in general chromatographic methods such as HPLC, GC or capillary electrophoresis. The material and method section had to be sufficiently descriptive: column type, mobile phase, detection etc, or referenced to published methods. The method had to be validated according to the allowed recommendations [5-9].

– Well-described methodology which had to include:
  - generic name (and speciality names)
  - final concentration of drug
  - reconstitution or vehicle dilution
  - precise description of containers (type of plastic, volume, etc.)
  - conditions of exposure: temperature, light
  - length of stability assays
  - search for degradation products

– Relevant analysis of the results

The standardised evaluation sheet also contained items related to analytical method, global quality of the study design and interpretation of experimental results.

The global quality of the study required that the assays undertaken were relevant to what we were investigating. For example, the number of samples per condition tested had to be sufficient to enable an accurate statistical evaluation, and the vehicles tested had to be types used in usual clinical practice. However, a limited number of replicates were accepted if the drug tested was very expensive or if no previous independent data were available.

Other potential pitfalls included poorly defined temperature conditions such as 'room temperature' or 'fridge temperature' or poor data for physical stability limited to colour change or visual examination. Moreover, for several products, the published studies, even using well-validated HPLC methods and appropriate experimental design, were relatively old and had not used modern analytical instruments such as diode array or mass spectrometry detectors. Stressed conditions were not investigated, making it difficult to reach unambiguous conclusions.

It was not easy to set standards for quality of the interpretation of the stability results and a consensus decision was often required [9]. Indeed, the vast majority of publications analysed did not contain all the items we considered relevant. Moreover, the stability limit proposed by the authors was generally based on the time for the concentration to decline to 90% of the initial concentration. The relevance of this criterion is debatable for drugs with narrow therapeutic ranges; nevertheless we decided to use it in coming to our recommendations since it is widely accepted for pharmaceuticals by authorising agencies and takes into account the pharmacological variability of clinical response.

Table 1: Outline of the evaluations used for publications

Criterion	What was checked	Details of the check	Method
Physical stability	Visual appearance	Precipitate Colour changes Visible particles	Visual examination under optimal conditions
	Sub-visual appearance	Global size distribution	Turbidimetry Particle count Microscopic analysis
Chemical stability	Separation methods (HPLC, GC, CE)	Validation of the method ('Stability indicating') Description of materials Number of standards Intra-series repeatability Inter-series repeatability Interfering substances	
		Detection	UV/Vis Diode Array MS Other
		Degradation products	Identification Quantification
		Number of repeats per condition tested	
	Non-separating methods		UV FT-IR TLC Immunoanalysis Other
	Other tests	pH Osmolality Other	
	Conditions tested	Temperature Agitation Light Concentration Vehicle	
Experimental design	Suitability for our purposes	Number of batches tested Stressed conditions Different vehicles/containers Different concentrations	

Conditions for use of recommendations

The decision to recommend stability limits was taken without regard to current practices in

centralised units or the usual modalities of administration, but based only on the best stability data validated by the group. As an example, our recommended stability limit for carboplatin (0.70–2.15 mg per mL in dextrose conditioned in PVC or polyethylene bags) is 84 days. This limit is obviously higher than requested by the majority of cases in daily practice, since an in-use stability of seven days is usually enough. However, our recommendation makes it clear that carboplatin could be kept safely for longer periods if needed, for example for dose banding.

The recommendations assume that aseptic techniques are fully validated and respected in practice. If not, extemporaneous reconstitution and dilution should be the common rule.

Only the articles validated for establishing the recommendations are listed.

Monoclonal antibodies

Monoclonal antibodies were not considered in these recommendations since only a few preliminary results have been published on their extended stability limits [10, 11]. However, in the light of their very high cost, several review papers on the stability of monoclonal antibodies as raw material [12-14] and several preliminary results, we suggest some general rules.

Thermal stability

Monoclonal antibodies in solution at 4°C and 25°C seem stable for several days. It is possible that some currently used antibodies such as rituximab are stable for months. Few data are available on stability after freezing so freezing should be avoided.

In practice, for short-term interruption of the cold chain and exposure to ambient temperatures (1–2 days), antibodies in their primary containers can be considered as stable.

For partially used primary vials or diluted solutions in bags, storage for 2–3 days at 4°C–8°C is possible, if the sterility can be guaranteed and they have not been exposed to possibly harmful mechanical stresses such as shaking.

Physical stability

Monoclonal antibodies are, in general, sensitive to exposure to solid or gas hydrophobic surfaces. The consequence is aggregation. Therefore, it is useful to minimise anything that might cause the formation of a gas/liquid interface: shaking, introduction of bubbles during transferring, purging or withdrawal operations with syringes. Filtration should also be avoided. Complete filling of containers without obvious residual head space should minimise the gas/liquid interface and also reduce the possibility of oxidation [11].

Chemical stability

Desamidation, which is the main cause of chemical instability for antibodies, strongly depends on the pH. Since antibodies are formulated at their best pH, minimise pH change during dilution by using a neutral vehicle such as isotonic saline.

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References

1. Astier A. The stability of anticancer drugs. Eur J Hosp Pharm Prac. 2007;13(1):21-3.
2. Husson MC, editor. Dossier du CNIMH. Anticancéreux: utilisation pratique. 6th ed. XXIX, 5-6. Paris: CNIMH; 2008.
3. Greenhalgh T. How to read a paper: assessing the methodological quality of published papers. BMJ. 1997;315:305-8.
4. Stabilis database. Stability and compatibility of injectable drugs. V. 4.0. Available from: www.stabilis.org
5. Vigneron J. Stability studies: ten pieces of advice. Eur J Hosp Pharm Prac. 2008;14(1):2.
6. Williams LA, Hasting MB. Identifying the criteria of a valid stability study. IJPC. 2009;13(1):32-6.
7. United States Pharmacopeia (USP). (1191) Stability considerations in dispensing practice. In: USP 26-NF 21. RockviIIe, Maryland: UPS Convention, Inc.; 2003:2414.
8. de Lemos ML, Hamata L. Stability issues of parenteral chemotherapy drugs. J Oncol Pharm Pract. 2007;13(1):27-31.
9. Q2(R1): Validation of analytical procedures: text and methodology. ICH guidelines. Available from: www.ich.org
10. Paul M, Lahlou A, Carvalho M, Blanchet B, Astier A. Thermal stability of two monoclonal antibodies: cetuximab and bevacizumab. Eur J Oncol Pharm. 2008;2(1):37.
11. Lahlou L, Blanchet B, Carvalho M, Paul M, Astier A. Mechanically-induced aggregation of the monoclonal antibody cetuximab. Ann Pharm Fr. 2009;67(5):340-52.
12. Wang W. Instability, stabilization, and formulation of liquid protein pharmaceuticals. Int J Pharm. 1999;185:129-88.
13. Chang W, Singh S, Zeng DL, King K, Nema S. Antibody structure, instability, and formulation. J Pharm Sci. 2006;96:1-26.
14. Wang W. Protein aggregation and its inhibition in biopharmaceutics. Int J Pharm. 2005;289(1-2):1-30.

SFPO and ESOP recommendations for the practical stability of anticancer drugs

These recommendations for storage conditions of anticancer drugs are the result of the deliberations of the SFPO (French Society for Oncology Pharmacy) stability group. The data were published in 2008 by the *Centre National Hospitalier d'Information sur le Médicament*, CNHIM–National Information Centre on Hospital Drugs. The stability group comprised Arnaud P, Astier A, Bellanger A, Bonan B, Breilh D, Burnel S, Daouphars M, Ferrio AL, Havard L, Helvig A, Husson MC, Pinguet F, Poisson N, Sarrut B, Vigneron J. These recommendations were adopted as the European standard by ESOP in 2010.

SFPO and ESOP recommendations for the practical stability of anticancer drugs

Product	Container	Vehicle	Concentration	Recommended storage conditions	Reference
AMIFOSTINE (ETHYOL)				Follow SmPC	
BLEOMYCIN				Follow SmPC	
BORTEZOMIB	Glass - polypropylene syringes	NaCl 0.9%	Reconstituted: 1 mg/mL	5 days at room temperature	1
BUSULFAN Never freeze busulfan	Original syringes		Non-diluted solution: 6 mg/mL	28 days at 2°C–8°C or at room temperature	2
	Polypropylene or glass	NaCl 0.9%	0.5 mg/mL	51 hours at 2°C–8°C protected from light	
	Polypropylene or glass	NaCl 0.9%	0.5 mg/mL	36 hours at 13°C–15°C protected from light	
CALCIUM FOLINATE	Glass	Dextrose 5% or NaCl 0.9%	Reconstituted: 20 mg/mL	4 days at 4°C or 25°C protected from light	26
	Glass or PVC	Dextrose 5% or NaCl 0.9%	0.1–0.5 mg/mL	24 hours at 4°C or 25°C (absorption on PVC at low concentrations)	
	Glass or PVC	Dextrose 5% or NaCl 0.9%	1–1.5 mg/mL	4 days at 4°C or 25°C in the light	
CALCIUM LEVOFOLINATE				Follow SmPC	
CARBOPLATIN	PVC - polyethylene	Dextrose 5%	0.70–2.15 mg/mL	84 days at 4°C or 84 days, of which 83 days at 4°C and 1 day at room temperature protected from light	3, 4, 5
	Polyethylene - polypropylene	Dextrose 5%	3.2 mg/mL	30 days at room temperature protected from light	
CARMUSTINE - never use PVC - preferably use protected from light	Glass - polyethylene	Dextrose 5%	0.2 mg/mL	48 hours at 4°C, 2.5 hours in glass polyethylene at room temperature protected from light	6, 7
	Polyethylene	Dextrose 5%	0.1– 0.5 mg/mL	4 hours at 25°C in the light and 48 hours at 4°C	
	Polyethylene	Dextrose 5%	1 mg/mL	4 hours at 25°C and 24 hours at 4°C	
CHLORMETHINE				Follow SmPC	
CISPLATIN	Ethyl vinyl acetate - polyethylene	NaCl 0.9%	0.5–0.9 mg/mL	28 days at room temperature protected from light	8, 9
CLADRIBINE	PVC, polyethylene	NaCl 0.9%	0.016 mg/mL	30 days at 4°C and at 18°C	32
CYCLOPHOSPHAMIDE	PVC	Dextrose 5% or NaCl 0.9%	1 mg/mL	7 days at 4°C and at room temperature protected from light	10, 11
CYTARABINE	Polypropylene syringes	Dextrose 5%	10 mg/mL	14 days at room temperature in the light and at 4°C	12
	Bags without PVC	Dextrose 5%	0.1–1 mg/mL	14 days at room temperature in the light and at 4°C	

DACARBAZINE - toxic products are formed - must be administered protected from light (bag + tubing)	Amber glass	Dextrose 5%	Reconstituted: 11 mg/mL	7 days at 4°C and 4 days at room temperature protected from light	13
	PVC	Dextrose 5%	1.5 mg/mL	7 days at 4°C and 3 days at room temperature protected from light	
	PVC - polyethylene	NaCl 0.9%	0.640 mg/mL	2 days at room temperature in the light and at 4°C	
DACTINOMYCIN	PVC	Dextrose 5%	0.01 mg/mL	24 hours in the light and at room temperature	14
DAUNORUBICIN At concentrations > 0.5 mg/mL daunorubicin is not sensitive to light for at least 7 days	PVC	Dextrose 5% or NaCl 0.9%	0.1 mg/mL	43 days at -20°C, 4°C and 25°C	15, 16
	Polypropylene	WFI	2 mg/mL	43 days at 4°C	
DAUNOXOME				Follow SmPC	
DEXRAZOXANE	PVC	Ringer Lactate	4 and 8 mg/mL	8 hours at 25°C in the light	17
	Polyethylene	Ringer Lactate	8 mg/mL	8 hours at 25°C in the light	
	Polyethylene	Ringer Lactate	4 mg/mL	4 hours at 25°C in the light	
DOCETAXEL Avoid PVC containers	Glass	Special solvent	Reconstituted: 10 mg/mL	28 days at 2°C–8°C and at 25°C	18
	Propylene - polyethylene	NaCl 0.9% or dextrose 5%	0.3–0.9 mg/mL	28 days at 25°C protected from light	
DOXORUBICIN (CAELYX)				Follow SmPC	
DOXORUBICIN (MYOCET)				Follow SmPC	
DOXORUBICIN At concentrations > 0.5 mg/mL doxorubicin is not sensitive to light for at least 7 days	Polypropylene	NaCl 0.9%	1–2 mg/mL	124 days at 4°C and 23°C	19
	PVC	Dextrose 5% or NaCl 0.9%	0.1 mg/mL	24 days at 25°C and 43 days at 4°C or -20°C	20, 21
EPIRUBICIN At concentrations > 0.5 mg/mL epirubicin is not sensitive to light for at least 7 days	Polypropylene	NaCl 0.9%	1–2 mg/mL	150 days at 23°C and at 4°C	22
	PVC	Dextrose 5% or NaCl 0.9%	0.1 mg/mL	20 days at 25°C and 43 days at 4°C or -20°C	20, 21
ETOPOSIDE PHOSPHATE	Glass	WFI	Reconstituted: 10 and 20 mg/mL	31 days at 23°C and 4°C	24
	PVC	NaCl 0.9% or dextrose 5%	0.1–10 mg/mL	31 days at 23°C and at 4°C	
ETOPOSIDE	Polypropylene	NaCl 0.9%	0.2 mg/mL	96 hours at < 25°C in the light	23
	Polypropylene	NaCl 0.9%	0.4 mg/mL	24 hours at < 25°C in the light	
FLUOROURACIL	Glass or PVC	NaCl 0.9% or dextrose 5%	1.5 mg/mL	8 weeks at room temperature in the light	25
FOTEMUSTINE	PVC	Dextrose 5%	0.2–2 mg/mL	2 days at 4°C and 8 hours at room temperature protected from light	27, 28
GEMCITABINE	Polypropylene syringes	NaCl 0.9%	Reconstituted: 38 mg/mL	35 days at room temperature.	29
	PVC	NaCl 0.9% or Dextrose 5%	1–10 mg/mL	35 days at 4°C and 7 days at 23°C–32°C	
IDARUBICIN	Polypropylene	Dextrose 5% or NaCl 0.9%	0.1 mg/mL	28 days at ≤ 25°C protected from light	30
IFOSFAMIDE	PVC	Dextrose 5% or NaCl 0.9%	30 mg/mL	30 days at 4°C protected from light	28
	PVC	Dextrose 5% or NaCl 0.9%	0.6–40 mg/mL	4 days at 4°C or room temperature protected from light	
INTERLEUKIN 2				Follow SmPC	
IRINOTECAN	Glass	Dextrose 5%	0.02 mg/mL	24 hours at room temperature	31
L-ASPARAGINASE				Follow SmPC	
MELPHALAN - never use serum glucose - the degradation of melphalan increases with the temperature	PVC	NaCl 3%	0.2 mg/mL	48 hours at 4°C and 3 hours at 26°C in the light	33
	PVC, polyethylene	NaCl 0.9%	0.06 mg/mL	24 hours at 4°C and 8 hours at room temperature protected from light	

METHOTREXATE	Polypropylene syringes	NaCl 0.9%	2.5 mg/mL	7 days at room temperature and at 4°C protected from light	34
	PVC	NaCl 0.9% or dextrose 5%	0.225–24 mg/mL	30 days at 4°C protected from light	35
MITOGUAZONE	PVC	Dextrose 5% or NaCl 0.9%	1.3–3.3 mg/mL	14 days at 4°C and at 20°C	36
MITOMYCIN (AMETYCIN)				Follow SmPC	
MITOXANTRONE	Glass bottle	Ready-to-use solution	2 mg/mL	42 days at 4°C– 23°C	37
	PVC	NaCl 0.9% or Dextrose 5%	0.04–0.4 mg/mL	7 days at 4°C and at 23°C protected from light	38
OXALIPLATIN	Polyolefin bags	Dextrose 5%	0.7 mg/mL	30 days at room temperature protected from light	39
PACLITAXEL - exclude PVC containing DEHP - is less stable at increasing concentration or temperature due to increased risk of precipitation	Polypropylene	NaCl 0.9% or dextrose 5%	0.3–1.2 mg/mL	4 days at 25°C and 12 days at 5°C protected from light	40, 41
	Polyethylene	NaCl 0.9% or dextrose 5%	0.3 mg/mL	13 days at 2°C–8°C protected from light	
	Polyethylene	NaCl 0.9% or dextrose 5%	1.2 mg/mL	9 days at 2°C–8°C protected from light	
PEMETREXED If stored at 4°C microparticles might form, a 0.22 µm in-line filter has to be used	Polypropylene syringes	NaCl 0.9% or dextrose 5%	25 mg/mL	2 days at room temperature and 31 days at 4°C protected from light	42, 43
	PVC bags	NaCl 0.9%	5 mg/mL	28 days at 4°C protected from light	
PENTOSTATIN	Glass	NaCl 0.9%	Reconstituted: 2 mg/mL	3 days	44
	PVC	NaCl 0.9%	0.002–0.02 mg/mL	48 hours at 23°C	
STREPTOZOCIN				Follow SmPC	
THEPRUBICIN (pirarubicin)				Follow SmPC	
THIOTEPA	PVC, polyolefin	Dextrose 5%	5 mg/mL	3 days at 4°C and at room temperature in the light	45, 46
	PVC	NaCl 0.9%	0.5–3 mg/mL	2 days at 8°C and 1 day at room temperature in the light	
TOPOTECAN	PVC elastomer diffuser	NaCl 0.9% or dextrose 5%	0.01, 0.025, 0.05 mg/mL	28 days at 4°C and at room temperature protected from light	47
	Polypropylene	NaCl 0.9%	0.01 mg/mL	7 days at room temperature in the light	
VINBLASTINE	Glass	WFI	Reconstituted: 1 mg/mL	21 days at 4°C protected from light	48, 49
	Polypropylene	NaCl 0.9% or dextrose 5%	0.02 mg/mL	21 days at 4°C and at 25°C protected from light	
	PVC	NaCl 0.9% or dextrose 5%	0.1 mg/mL	7 days at 4°C protected from light	
VINCRISTINE	Polypropylene	NaCl 0.9% or dextrose 5%	0.02 mg/mL	21 days at 4°C and at 25°C protected from light	48, 50, 51
	PVC polypropylene	NaCl 0.9%	0.01–0.15 mg/mL	7 days at 4°C protected from light	
VINDESINE	Glass	WFI	Reconstituted: 1 mg/mL	21 days at 4°C protected from light	48
	Polypropylene	NaCl 0.9% or dextrose 5%	0.02 mg/mL	21 days at 4°C and at 25°C protected from light	
VINORELBINE	PVC, polyethylene	NaCl 0.9%	0.385 mg/mL	7 days at 23°C	49, 52
	PVC	Dextrose 5%	0.5 mg/mL	7 days at 4°C	

Concentration without specific comment refers to dilution in the vehicle. SPC: Summary of product characteristics.

Disclaimer

References

1. Andre P, Cisternino S, Chiadmi F, Toledano A, Schlatter J, Fain O, Fontan JE. Stability of bortezomib 1 mg/mL solution in plastic syringe and glass vial. Ann Pharmacother. 2005;39:1462-6.
2. Karstens A, Krämer I. Untersuchungen zur Stabilität der Busulfan-Stammlösung (Busilvex®, BusulfexTM) in B/Braun Injekt® Einmalspritzen. Pharmazie. 2006;61:845-50.
3. Vivekanandan K, Swamy MG, Prasad S, Maikap GC, Mukherjee R, Butman AC. Identification of degradation products from aqueous carboplatin injection samples by electrospray mass spectrometry. Int J Pharm. 2006;313(1-2):214-21.
4. Kaestner S, Sewell G. A sequential temperature cycling study for the investigation of carboplatin infusion stability to facilitate 'dose-banding'. J Oncol Pharm Prac. 2007;13:119-26.
5. Prat J, Pujol M, Girona V, Muñoz M, Solé LA. Stability of carboplatin in 5% dextrose solutions in glass, polyethylene and polypropylene containers. J Pharma Biomed Anal. 1994;12(1):81-4.
6. Favier M, De Cazanove F, Coste A, Cherti N, Bressolle F. Stability of carmustine in polyvinyl chloride bags and polyethylene-lined trilayer plastic containers. J Health- Syst Pharm. 2001;58(3):238-41.
7. Beitz C, Bertsch T, Hannak D, Schrammel W, Einberger C, Wehling M. Compatibility of plastics with cytotoxic drug solutions-comparison of polyethylene with other container materials. Int J Pharmaceutics. 1999;185(1):113-21.
8. Benaji B, Dine T, Luyckx M, Brunet C, Goudaliez F, Mallevais ML, et al. Stability and compatibility of cisplatin and carboplatin with PVC infusion bags. J Clin Pharm Ther. 1994;19(2):95-100.
9. Rochard E, Barthes D, Courtois P. Stability of cisplatin in ethylene vinylacetate portable infusion-pump reservoirs. J Clin Pharm Ther. 1992; 17(5):315-8.
10. Beijnen JH, Van Gijn R, Challa EE, Kaijser GP, Underberg WJ. Chemical stability of two sterile, parenteral stimulations of cyclophosphamide (Endoxan) after reconstitution and diluted in commonly used infusion fluids. J Parenter Sci Technol. 1992;46(4):111-6.
11. Menard C, Bourguignon C, Schlatter J, Vermerie N. Stability of cyclophosphamide and mesna admixtures in polyethylene infusion bags. Ann Pharmacother. 2003;37(12):1789-92.
12. Coulon S, Havard L, AM J. Stability of cytarabine solutions in parenteral preparations. J Health Syst Pharm. (In press).
13. El Aatmani M, Poujol S, Astre C, Malosse F, Pinguet F. Stability of dacarbazine in amber glass vials and polyvinyl chloride bags. J Health Syst Pharm. 2002;59(14):1351-6.
14. Benvenuto JA, Anderson RW, Kerkof K, Smith RG, Loo TL. Stability and compatibility of antitumor agents in glass and plastic containers. Am J Hosp Pharm.1981;38(12):1914-8.
15. Wood MJ, Irwin WJ, Scott DK. Stability of doxorubicin, daunorubicin, and epirubicin in plastic syringes and minibags. J Clin Pharm Ther. 1990;15(14):279-89.
16. Wood MJ, Irwin WJ, Scott DK. Photodegradation of doxorubicin, daunorubicin and epirubicin measured by high-performance liquid chromatography. J Clin Pharm Ther. 1990;15(4):291-300.
17. Kaiser JD, Vigneron J, Zenier H, May I, Demoré B. Chemical and physical stability of dexrazoxane diluted with Ringer's lactate solution, in polyvinyl and polyethylene containers. Eur J Hosp Pharm Prac. 2007;13(3):55-9.
18. Thiesen J, Krämer I. Physico-chemical stability of docetaxel premix solution and docetaxel infusion solutions in PVC bags and polyolefine containers. Pharm World Sci. 1999;21(3):137-41.
19. Walkers SE, Lau DWC, DeAngelis C, Iazetta J, Coons C. Doxorubicin stability in syringes and glass vials and evaluation of chemical contamination. Can J Hosp Pharm.1991;44:71-88.
20. Wood MJ, Irwin WJ, Scott DK. Stability of doxorubicin, daunorubicin, and epirubicin in plastic syringes and minibags. J Clin Pharm Ther. 1990;15(4):279-89.
21. Wood MJ, Irwin WJ, Scott DK. Photodegradation of doxorubicin, daunorubicin and epirubicin measured by high-performance liquid chromatography. J Clin Pharm Ther. 1990;15(4):291-300.
22. Walker SE, Lau DWC, DeAngelis C, Iazetta J, Coons C. Epirubicin stability in syringes and glass vials and evaluation of chemical contamination. Can J Hosp Pharm. 1990;43:265-72.
23. Barthes DM, Rochard EB, Pouliquen IJ, Rabouan SM, Courtois PY. Stability and compatibility of etoposide in 0.9% sodium chloride injection in three containers. Am J Hosp Pharm. 1994;51(21):2706-9.
24. Zang Y, Trissel LA. Physical and chemical stability of etoposide phosphate solutions. J Pharm Assoc (Wash). 1999;39(2):146-50.
25. Biondy L, Nairm C. Stability of 5-FU and fluorocytosine in parenteral solutions. Can J Hosp Pharm. 1986;39(3).
26. Lecompte D, Bousselet M, Gayrard D, Poitou P. Stability study of reconstituted and dilute solutions of calcium folinate. Pharm Ind. 1991; 53(1):90-4.
27. Dine T, Khalfi T, Gressier B, Luyckx M, Brunet C, Ballester L, et al. Stability study of fotemustine in PVC infusion bags and sets under various conditions using a stability- indicating high-performance liquid chromatographic assay. J Pharm Biomed Anal. 1998;18(3):373-81.
28. Dine T, Lebegue S, Benaji B, Gressier B, Segard V, Goudaliez F, et al. Stability and compatibility studies of four cytostatic agents (fluorouracil, dacarbazine, cyclophosphamide and ifosfamide) with PVC infusion bags. Pharm Sci Com. 1994;4:97-101.
29. Xu Q, Zhang Y, Trissel LA. Physical and chemical stability of gemcitabine solutions. J Am Pharm Assoc (Wash). 1999;39(4):509-13.
30. Beijnen JH, Rosing H, de Vries PA, Underberg WJ. Stability of anthracycline antitumor agents in infusions fluids. J Parenter Sci Technol. 1985;39(6):220-2.
31. Li WY, Koda RT. Stability of irinotecan hydrochloride in aqueous solutions. Am J Health Syst Pharm. 2002;59(6):539-44.
32. Daouphars M, Vigneron J, Perrin A, Hoffman MA, Hoffman M. Stability of cladribine in either polyethylene containers or polyvinyl chloride bags. Eur J Hosp Pharm Prac.1997;3(4):154-6.
33. Pinguet F, Martel P, Rouanet P, Fabbro M, Astre C. Effect of sodium chloride concentration and temperature on melphalan stability during storage and use. Am J Hosp Pharm. 1994;51(21):2701-4.
34. Benajii B, Dine T, Goudaliez F, Luyckx M, Brunet C, Mallevais ML, et al. Compatibility study of methotrexate with PVC bags after repackaging into two types of infusions admixtures. Int J Pharm. 1994;105:83-7.
35. Jacolot A, Arnaud P, Lecompte D. Stability and compatibility of 2.5 mg/ml methotrexate solution in plastic syringes with 7 days. Int J Pharm. 1996; 128:283-6.
36. Kleinberg ML, Oberdier J, Muller RJ, Duafala M, Boylan JC. Stability of gallium nitrate and mitoguazone dihydrochloride in commonly used intravenous fluids. Hosp Pharm.1989;24:929-34.
37. Walker SE, Lau DWC, DeAngelis C, Iazetta J, Coons C. Mitoxantrone stability in syringes and glass vials and evaluation of chemical contamination. Can J Hosp Pharm.1991;44:143-51.
38. Lecompte D, Bousselet M, Magnam J. Stabilité des solutions diluées de mitoxantrone (Novantrone®) en poches de PVC pour perfusions. J Pharm Clin. 1990;9(3):159-65.
39. André P, Cisternino S, Roy AL, Chiadmi F, Schlatter J, Agranat P, et al. Stability of oxaliplatin in infusion bags containing 5% dextrose injection. Am J Health Syst Pharm. 2007;64(18):1950-4.
40. Donyai P, Sewell GJ. Physical and chemical stability of paclitaxel infusions in different container types. J Oncol Pharm Prac. 2006;12(4):211-22.
41. Kattige A. Long-term physical and chemical stability of a generic paclitaxel infusion under simulated storage and clinical-use conditions. Eur J Hosp Pharm Sci. 2006;12(6):129-34.
42. Rondelot L, Serrurier C, Vigneron J, Zenier H, May I, Demoré B. Stability of pemetrexed 25 mg/mL in a glass vial and 5 mg/mL stored in a PVC container after storage for one month at 2-8°C. Eur J Hosp Pharm Sci. 2007;13(1):14-6.
43. Zhang Y, Trissel LA. Physical and chemical stability of pemetrexed solutions in plastic syringes. Ann Pharmacother. 2005;39(12):2026-8.
44. Razzak LA, Benedetti AE, Waugh WN, Stella VJ. Chemical stability of pentostatin (NSC-218321) a cytotoxic and immunosuppressant agent. Pharm Res. 1990;7(5):452-60.
45. Xu QA, Trissel LA, Zhang Y, Martinez JF, Gilbert DL. Stability of thiotepa (lyophilized) in 5% dextrose injection at 4 and 23°C. Am J Health Syst Pharm. 1996;53(22):2728-30.
46. Murray KM, Erkkila D, Gombotz WR, Pankey S. Stability of thiotepa (lyophilized) in 0.9% sodium chloride injection. Am J Health Syst Pharm. 1997;54(22):2588-91.
47. Krämer I, Thiesen J. Pharmazeutiche aspekte von topotecan infusionen. Pharmazeutische Zeitung. 1997;142(31):30-3.
48. Beijnen JH, Vendrig DE, Underberg WJ. Stability of vinca alkaloid anticancer drugs in three commonly used infusion fluids. J Parenter Sci Technol. 1989;43(2):84-7.
49. Dine T, Luyckx M, Cazin JC, Brunet C, Cazin M, Goudaliez F, Mallevais ML. Stability and compatibility studies of vinblastine, vincristine, vindesine and vinorelbine with PVC infusion bags. Int J Pharm. 1991;77(2-3): 279-85.
50. Lieu CL, Chin A, Gill MA. Five-day stability of vinorelbine in 5% dextrose injection and in 0.9% sodium chloride injection at room temperature. Int J Pharm Compound. 1999;3:67-8.
51. Trissel LA, Zhang Y, Cohen MR. The stability of diluted vincristine sulfate used as a deterrent to inadvertent intrathecal injection. Hosp Pharm. 2001;36(7):740-5.
52. Beitz C, Bertsch T, Hannak D, Schrammel W, Einberger C, Wehling M. Compatibility of plastics with cytotoxic drug solutions-comparison of polyethylene with other container materials. Int J Pharm. 1999;185(1): 113-21.