STABILITY OF CYTOSTATIC DRUGS DILUTED IN POLYPROPYLENE INFUSION BAGS FLEBOFLEX®

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OBJECTIVES

For infusion solutions, plastic bags, in contrast with glass containers, are lightweight, less likely to break, and no air must enter the container to replace the fluid being administered. The main disadvantage comes from a possible drug-plastic interaction. Several cytostatic drugs include excipients such as cremophor in Paclitaxel or tween 80 in Etoposide which are incompatible with PVC.

In these cases the use of a non-PVC material such as polypropylene for dilution of the cytostatic drug, is recommended. Laboratorios Grifols has developed Fleboflex® infusion solutions in polypropylene bags.

The objective of the study was to study the behavior of three cytostatic drugs in polypropylene bags Fleboflex® and glass containers as non-interactive material. 5-Fu was also studied in PVC bags.

STUDY DESIGN

Three Cytostatic drugs were assayed: Paclitaxel, Etoposide and 5-Fluorouracil.

Polypropylene bags used in this study were Fleboflex® Normal Saline Grifols, PVC bags were Flebobag® Normal Saline Grifols and Glass solutions were Normal Saline Grifols. The volume of each was 100ml.

5-Fluorouracil, Etoposide and Paclitaxel were diluted in Fleboflex® and glass containers; 5-Fluorouracil was also diluted in PVC containers. All the units were prepared by trained personnel into biological safety cabinets. Final concentrations were as stated in table 1. Drug addition was verified by weight difference in all the units prepared.

All the units were tested for pH, drug assay and related compounds with HPLC-UV according to the USP monographs (if described). Additional tests not included in the pharmacopoeia were color, turbidity and weight loss. DEHP content was tested on PVC units at the end of the study.

Table 1 shows the diluent used and the concentration prepared for each drug.

Table 1

Drug	Initial concentration	Diluent	Final concentration
Paclitaxel	6 mg/ml	Normal Saline	0,3 mg/ml
Etoposide	20 mg/ml	Normal Saline	0,3 mg/ml
5-Fluorouracil	50 mg/ml	Normal Saline	3 mg/ml

Palcitaxel and 5-Fluorouracil were stored at 5°C and 25°C. Etoposide was stored only at 25°C, because precipitation at low temperatures is described in bibliography.

Controls were performed on samples once prepared and after 1, 2, 4, and 7 days. Etoposide and 5-Fluorouracil were also tested after 10 days and 5-Fluorouracil was tested after 15 and 30 days.

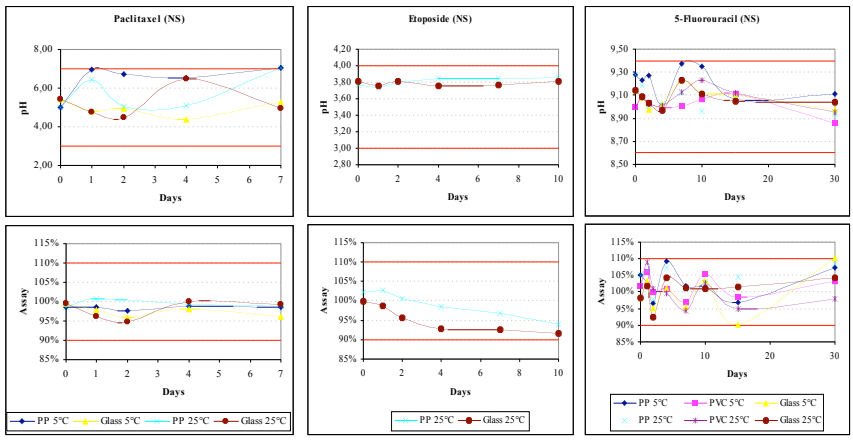
RESULTS

The results corresponding to color and turbidity show no differences between the materials. pH values are represented with the respective limits in red, and are based on the limits for undiluted solutions in the monograph.

Assay values are presented as % with respect to the theoretical value, calculated for each individually prepared unit. The limits, represented in red, are based on the limits for undiluted solutions in the monograph.

Related compounds in Paclitaxel and Etoposide evolved similarly for both materials, with results under the established limit at the end of the study.

DEHP content at the end of the stability was below the established limit (<5ppm) in all the PVC units:



DISCUSSION

All the drugs tested show the same behavior when diluted in glass or polypropylene containers. Drug content remains over the limit of 90% in all cases. Only Etoposide shows a decrease in concentration over time, but with values greater than 90% after 10 days.

5-Fluorouracil assay values show a great variability due to the difficulty in stabilizing the chromatographic system, although a USP method was used. Nevertheless, the results improved over time and were always within the established limits.

pH values depend on the pH of the infusion solution, which varies depending on the material and the effect of the drug when added. In all the cases the values were within the established limits, based on USP monographs for undiluted solutions.

No DEHP was found after 30 days in 5-Fu units.

REFERENCES

USP 28

Moorhatch, P., Chiou, W.L.: Interactions between drugs and plastic intravenous fluid bags, Part I, *Amer. J. Hosp. Pharm. 31:*72-78 (Jan.) 1974

Jobet-Hermelin I., Mallevais M.L., Jacquot C., Prognand J.L., Proposition d'une concentration limite acceptable du plastifiant libéré par le poly(chlorure de vinyle) dans les solutions injectables aqueuses. J. Pharm. Clin. 1996; 15:132-136.

Trissel. L. A., Handbook on Injectable Drugs 11th edition.

CONCLUSIONS

- Fleboflex® infusion solutions are suitable for the dilution of PVC-incompatible and compatible cytotoxic drugs.
- Drug solution behavior in Fleboflex® infusion containers is similar to those prepared in glass containers.

STATEMENT Conflict of interest: S. Jané, J. Menéndez and J. Girbau from Laboratorios Grifols, S.A.

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