

# COMPARISON OF DRUG STABILITY IN GLASS VERSUS PLASTIC CONTAINERS: ANALYSIS OF PREFILLED SYRINGE ADMIXTURES

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A commonly prescribed drug combination, (hydroxyzine hydrochloride, meperidine hydrochloride, and atropine sulfate), utilized as a preanesthetic medication, was studied to compare possible differences in stability between mixtures stored in glass and plastic containers. Combinations of drugs were stored in both glass and plastic syringes at 25 C and 3 C for a ten-day period. Analyses were performed at intervals throughout the time period utilizing visual examination, pH determination, ultraviolet absorption spectra, and gas chromatography. No significant degradation of the syringe contents nor appearance of additional constituents were detected in any of the admixture preparations. Thus storage of such preparations in glass versus plastic syringes yielded no significant differences in product stability.

## INTRODUCTION

Use of prepackaged syringes in the hospital setting is increasing due to the advantages offered by their use (1) and the current interest in unit-dose medication. Since all the various dosages and combinations prescribed are not commercially available, many hospital pharmacies are developing or operating a centralized parenteral admixture program. Such packaging requires consideration of the sterility and particulate matter content of single-syringe injections as well as compatibility between drugs and with the syringe components (1, 2).

Plastic syringes are usually constructed from either polyethylene or polypropylene plastic (3). Sterilization after packaging is done with either ethylene oxide or radiation. There are a number of advantages for plastic syringe packaging including breakage reduction, lighter weight, simplified disposal, ease of manipulation, and economy in space during storage (4). On the other hand, contact between plastic containers and drugs can present a number of problems including leaching, sorption, permeation, chemical reactivity of the plastic polymer, and alteration in physical properties of the plastic (5, 6). These problems have to be considered for plastic used as a packaging material, especially for solutions, as evidenced in recent studies in the literature (4, 5, 7, 8).

Glass disposable syringes, although less expensive than those which are reusable, have a higher cost than those made from plastic. Their advantage is in possessing the handling and physical characteristics associated with glass (3). Additionally, drugs stored in glass may be subject to fewer compatibility and administration problems than those stored in plastic (4-9).

Previous studies on interactions between drugs and plastic containers have largely been confined to large-volume bottles and bags (4, 9), as have comparative studies on contamination of drugs in glass versus plastic containers (7, 10-15).

## OBJECTIVES

One of the purposes for drug combinations in a single syringe is in administering preanesthetic medication, often mixtures of anticholinergics, hypnotics, opiates, antiemetics and tranquilizers. Although a great deal of information is not yet available on the compatibility of multiple drugs in the same syringe, reports are emerging in the literature (2, 3, 16, 17) describing the stability of standardized preanesthetic medications in prefilled syringes.

Previous studies (16) have reported the stability of hydroxyzine hydrochloride and atropine sulfate mixtures in prefilled syringes; many of the same procedures were utilized in the present study. The additional data obtained from these studies regarding the stability and therapeutic availability of the studied mixtures of prepackaged preanesthetic medications should assist in eval-

\*Glass syringes, standard hospital stock, manufactured by MPL Inc., Chicago, Ill.; plastic syringes, standard hospital stock, manufactured by JELCO Laboratories, Raritan, N.J.

uating any differences in product stability resulting from storage in glass versus plastic syringes.

The purpose of this study was to develop a method of obtaining data relating to physical and chemical stability of a preanesthetic drug mixture in glass and plastic syringes. The methodology utilized was designed to: 1) include procedures available in the clinical setting; 2) determine the feasibility of prefilling syringe units in the hospital pharmacy; and 3) detect any differences in drug mixtures stored in glass versus plastic syringes at room temperature and under refrigeration.

### MATERIALS AND METHODS

Selected preanesthetic mixtures of hydroxyzine hydrochloride, meperidine hydrochloride, and atropine sulfate were studied over a ten-day period utilizing the Fisher Accument Model 320 expanded-scale research pH meter, the Beckman ACTA III spectrophotometer and the Varian Aerograph Series 1200 gas chromatograph.

All samples for analysis were obtained from a 30-ml vial of previously prepared stock solution and introduced into 3-mL syringes. Control contents were transferred directly from the manufacturer's ampule or vial into glass or plastic syringes\* identical to those containing sample solutions.

Triplicate samples of each stock solution were prepared for storage under the following conditions: a) glass syringes at 25 C; b) glass syringes at 3 C; c) plastic syringes at 25 C; and d) plastic syringes at 3 C. Controls consisted of two samples of each drug in each storage category.

Analysis with the pH meter was performed at time intervals of 0, 1, 4, 12, 24, 48, 72 and 240 hr after admixture preparation.

Prior to obtaining ultraviolet absorption spectra, the solutions were diluted to comply with limits for range of measurement by the instrument, using sterile water in both the samples and reference solution. A Beer-Lambert curve was plotted for each drug for reference in determining loss in absorbance, hence possible loss of activity. The same dilution procedure was used at time intervals of 0, 1, 4, 12, 24, 48, 72 and 240 hr after admixture preparation.

Gas chromatographic analysis was utilized to detect any internal change in the components of the syringe admixtures following the storage period of ten days. Three refrigerated and room temperature samples stored for 10 days in both the glass and plastic syringes were compared with three freshly prepared controls. The analysis results of the syringe admixture were obtained by determining the peak and retention time. Any changes in retention time or the appearance of any additional peaks as compared to controls were used to monitor any occurrence of chemical interaction.

### RESULTS AND DISCUSSION

Prior to instrument analysis of each admixture, the syringe contents were examined visually at each time interval to detect physical evidence of incompatibility (e.g., color change, precipitate formation, haze, cloudiness). Initial examination of the drug mixtures indicated no physical change had occurred over the ten-day period in either the glass or plastic containers.

Triplicate analyses of each solution utilizing the pH meter indicated no significant changes in pH of sample and control solutions in either glass or plastic syringes at room temperature (25 C) or refrigeration (3 C) within a ten-day period (see Table 1).

The ultraviolet spectrophotometric absorbance of hydroxyzine hydrochloride solutions ranging in concentration from 10  $\mu\text{g/mL}$  to 50  $\mu\text{g/mL}$  was plotted on a graph to obtain a Beer's plot. This was used to determine the concentration of hydroxyzine hydrochloride in the sample syringes at the wavelength of maximum absorbance (231 nm). Final concentration of the mixture of hydroxyzine hydrochloride and meperidine hydrochloride did not vary significantly from the original 25  $\mu\text{g/mL}$  concentration in either glass or plastic syringes at either storage temperature. Similar results were noted with the mixture of hydroxyzine hydrochloride, meperidine hydrochloride, and atropine sulfate (see Table 2).

The retention time of control solutions and the separation of the admixture of hydroxyzine hydrochloride, meperidine hydrochloride, and atropine sulfate were also studied by gas chromatography. No significant difference was observed between sam-

TABLE 1. pH Changes in Syringe Contents After 10 Days Storage

		3 C		25 C	
		Initial	Final	Initial	Final
hydroxyzine HCl 50 mg/mL	glass	5.18 ±0.02	5.25 ±0.00	5.16 ±0.02	5.17 ±0.02
	plastic	5.15 ±0.00	5.18 ±0.02	5.15 ±0.00	5.16 ±0.00
meperidine HCl 50 mg/mL	glass	3.55 ±0.02	3.57 ±0.02	3.54 ±0.00	3.54 ±0.02
	plastic	3.55 ±0.00	3.57 ±0.03	3.50 ±0.02	3.47 ±0.04
atropine sulfate	glass	5.10 ±0.00	5.30 ±0.02	5.09 ±0.00	5.20 ±0.00
	plastic	5.09 ±0.01	5.25 ±0.03	5.08 ±0.00	5.17 ±0.03
Sample <sup>a</sup>	glass	4.50 ±0.00	4.58 ±0.02	4.46 ±0.04	4.55 ±0.02
	plastic	4.50 ±0.00	4.54 ±0.06	4.50 ±0.00	4.45 ±0.02
Sample <sup>b</sup>	glass	4.58 ±0.02	4.68 ±0.03	4.55 ±0.02	4.65 ±0.02
	plastic	4.58 ±0.02	4.62 ±0.05	4.51 ±0.02	4.58 ±0.05

Values shown are means ± 1 standard deviation

<sup>a</sup>Sample concentration: hydroxyzine HCl 50 mg and meperidine HCl 50 mg per 2.0 mL

<sup>b</sup>Sample concentration: hydroxyzine HCl 50 mg, meperidine HCl 50 mg, and atropine sulfate 0.4 mg per 2.5 mL

TABLE 2. Hydroxyzine Hydrochloride Concentration ( $\mu\text{g/mL}$ ) and % Variance in Concentration in Syringe Mixture After 10 Days

Hydroxyzine hydrochloride	Syringe	Temp (C)	Absorbance <sup>a</sup>	Concentration	% Variance in Concentration
with meperidine HCl (initial concn. about 25 $\mu\text{g/mL}$ )	glass	25	1.02	24.2	-3.2
		3	0.98	23.3	-6.8
	plastic	25	1.01	23.9	-4.4
with meperidine HCl and atropine sulfate (initial concn. about 25 $\mu\text{g/mL}$ )	glass	25	0.79	19.2	-4.0
		3	0.77	18.7	-6.5
	plastic	25	0.79	19.0	-5.0
		3	0.78	18.8	-6.0

<sup>a</sup>in sterile water for injection, USP; 3 determinations for each mean value

ples after ten days storage and freshly prepared controls, nor were differences detected between contents stored at either 3 C or 25 C in glass or plastic syringes. No additional peaks were observed on the chromatographs which would have indicated the occurrence of some specific chemical interaction within the admixture.

### CONCLUSION

It is concluded that the drug combination studied is appropriate for prepackaging in the hospital pharmacy up to ten days prior to use when study parameters are followed regarding selection of containers and storage conditions.

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