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RESEARCH ARTICLE

ADVANCES IN PREFILLED SYRINGES' TECHNOLOGY

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ABSTRACT

Prefilled syringes are a fast growing alternatives to vials for many drug products. Increased interest in prefilled syringes is largely driven by the advantages they offer relative to the vials. Currently, most prefilled syringes are made of glass, but plastic syringes are gaining popularity, particularly in applications for which glass is an unsuitable delivery system. Plastic has been an alternative to glass in prefilled syringes since the early 1990's. Earliest plastics were, however, made of polypropylene which did not offer the clarity of glass, many of its barrier properties or ease of sterilization. Polypropylene plastics also presented more challenges regards to extractables and leachables than glass due to the lack of historic data. Polymers are considered to get weathered due to the direct or indirect impact of heat and ultraviolet light. The effectiveness of the stabilizers against weathering depends on solubility, ability to stabilize in different polymer matrix, the distribution in matrix, evaporation loss during processing and use. Various stabilizers used as stabilizers for polymers are antioxidants like benzofuranones, and UV absorbers like oxanilides for polyamides, benzophenones for PVC, benzotriazoles for polycarbonate are used. Manufacturers have developed a new polymer such as cyclo olefin copolymer that are able to hold against glass. Cyclic Olefin Copolymer (COC) is an amorphous polymer made by several polymer manufacturers. COC is a relatively new class of polymers when compared to polypropylene and polyethylene. An analysis done for the comparison of drug stability in glass versus plastic containers is also been covered in this paper.

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INTRODUCTION

Prefilled syringes are a fast growing alternatives to vials for many drug products. Increased interest in prefilled syringes is largely driven by the advantages they offer relative to vials. These include greater ease of use, reduced waste, improved dosing accuracy and enhanced product differentiation. Recent advances in syringe technology promise to further enhance the benefits of a prefilled syringes. Currently, most prefilled syringes are made of glass, but plastic syringes are gaining popularity, particularly in applications for which glass is an unsuitable delivery system. In the last decade, pharmaceutical protein and peptide drug products have been approved for use with prefilled plastic syringes. One example is a peptide drug product in a Daikyo Crystal Zenith (CZ) syringe. More products using plastic prefilled syringes are in various phases of drug development.

Stabilizers for polymers

Stabilizers for polymers are used directly or by combinations to prevent the various effects such as oxidation, chain scission and uncontrolled recombinations and cross-linking reactions that are caused by photo-oxidation of polymers.

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Polymers are considered to get weathered due to the direct or indirect impact of heat and ultraviolet light. The effectiveness of the stabilizers against weathering depends on solubility, ability to stabilize in different polymer matrix, the distribution in matrix, evaporation loss during processing and use. The effect on the viscosity is also an important concern for processing. Various stabilizers used for polymers are antioxidants like benzofuranones, and UV absorbers like oxanilides for polyamides, benzophenones for PVC, benzotriazoles for polycarbonate are used.

Comparison of drug stability in glass versus plastic containers

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 25^0C and 3^0C for a ten-day period. Analysis 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.

Table 1. pH changes in syringe contents after 10 days storage

		3 C			25 C		
		Initial	Final		Initial	Final	
Hydroxyzine HCl	Glass	5.18	5.25		5.16	5.17	
50 mg/mL		± 0.02	± 0.00		± 0.02	± 0.02	
	plastic	5.15	5.18		5.15	5.16	
		± 0.00	± 0.02		± 0.00	± 0.00	
Meperidine HCl	Glass	3.55	3.57		3.54	3.54	
50 mg/mL		± 0.00	± 0.02		± 0.00	± 0.02	
	plastic	3.55	3.57		3.5	3.47	
		± 0.00	± 0.03		± 0.02	± 0.04	
Atropine sulfate	Glass	5.1	5.3		5.09	5.2	
		± 0.00	± 0.02		± 0.00	± 0.00	
	plastic	5.09	5.25		5.08	5.17	
		± 0.01	± 0.03		± 0.00	± 0.03	
Sample 1	Glass	4.5	4.58		4.46	4.55	
		± 0.00	± 0.02		± 0.04	±0.02	
	plastic	4.5	4.54		4.5	4.45	
		± 0.00	± 0.06		± 0.00	± 0.02	
Sample 2	Glass	4.58	4.68		4.55	4.65	
		± 0.02	± 0.03		± 0.02	± 0.02	
	plastic	4.58	4.62		4.51	4.58	
		± 0.02	± 0.02		± 0.02	± 0.05	

Values shown are means ± 1 standard deviation
Sample 1 concentration: hydroxyzine HCl 50 mg and meperidine HCl 50 mg per 2.0 mL
Sample 2 concentration: hydroxyzine HCl 50 mg, meperidine HCl 50 mg, and atropine sulfate 0.4 mg per 2.5 mL

Table 2. Hydroxyzine Hydrochloride Concentration (µg/mL) and % variance in concentration in syringe mixture after 10 days

Hydroxyzine					% Variance in
Hydrochloride	Syringe	Temp ©	Absorbance	Concentration	Concentration
with meperidine HCl	Glass	25	1.02	24.2	-3.2
(Initial concn		3	0.98	23.3	-6.8
About 25 µg/mL)	plastic	25	1.01	23.9	-4.4
		3	1	23.7	-5.2
with meperidine HCl	Glass	25	0.79	19.2	-4
and atropine sulfate		3	0.77	18.7	-6.5
(Initial concn	plastic	25	0.79	19	-5
About 25 µg/mL)		3	0.78	18.8	-6

Table 4: Chemical resistance of TOPAS

pH < 7 (acidic/aqueous)	hydrochloric acid 36%	+
	sulfuric acid 40%	+
	nitric acid 65%	+
	acetic acid > 94%	+
pH = 7 (neutral/aqueous)	water	+
	aqueous solution of soap	+
	saline solution	+
pH > 7 (basic/aqueous)	sodium hydroxide 50%	+
	ammonia (aq. sol.) 35%	+
Polar organic solvents	ethanol, methanol, butanol, isopropanol (short chain alcohols)	+
	acetone, butanone (short chain ketones)	+
Aromatic solvents	benzaldehyde	o
	toluene	–
	benzene	–
	chlorinated solvents	–
Non-polar organic solvents	pentane, hexane, heptane etc. (alkanes)	–
	gasoline (petrol ether)	–
	norbornene	–
Other	oleic acid	–

+	o	–
resistant increase of weight < 3% or loss of weight < 0.5% elongation at break not substantially altered	limited resistance increase of weight 3 to 8% or loss of weight 0.5 to 5% elongation at break reduced by < 50%	not resistant increase of weight > 8% or loss of weight > 5% elongation at break reduced by > 50%

Thus storage of such preparations in glass versus plastic syringes yielded no significant differences in product stability. One of the purposes for drug combinations in a single syringe is in administering preanesthetic medication, often mixtures of antichlolinergics, hypnotics, opiates, antiemetics and tranquilizers.

Cyclo olefin copolymer for the preparation of prefilled syringes

Manufacturers have developed a new polymer such as cyclo olefin copolymer that are able to hold against glass. These plastics offer high heat resistance and low level of extractables and leachable and are less permeable to water. They are also more transparent, light weight and shatter-resistant, enhancing visibility and facilitating filling operations as well as ease of use.

Cyclic Olefin Copolymer (COC) is an amorphous polymer made by several polymer manufacturers. COC is a relatively new class of polymers when compared to polypropylene and polyethylene. This material is primarily used in applications requiring glass-like clarity including lenses, vials, monitors, and medical devices.

Cyclo Olefin Copolymers (COC) have come a long way in developing newer applications in the past few years. The characteristic features of COC are:

- Water vapor barrier effect
- Air permeability/transparency
- Rigidity
- Dimensional stability
- Thermoforming
- Heat resistance, depending on product variant from 80 to 180 °C
- Halogen-free

General discussion of COC

COC is recognized as a resin with optical properties comparable with PMMA (polymethyl methacrylate, acrylic resin), superior heat resistance to PC (polycarbonate), and superior dimensional stability to both PMMA and PC. COCs have a very high moisture barrier, low water absorption, good resistance to hydrolysis and chemical media, and low density. In addition, they typically offer high transparency extending into the UV range, low birefringence, adjustable heat deflection temperature and high rigidity.

Advantages of COC prefilled syringes over glass prefilled syringes

1. Good drug compatibility
   a. No ion release
   b. No metal trace
   c. Reduced free silicon oil

2. Hydrophobic surfaces
   a. Less adsorption
   b. Easy emptying

3. High design flexibility
   a. syringes
   b. vials, cartridges
   c. less weight

Chemical resistance of Cyclo Olefin Copolymer

Conclusion

Pre-filled syringes offer advantages in the delivery of injectable biopharmaceutical products, including increased user-convenience and decreased product wastage. Demand for cyclic olefin copolymers (COC) is growing rapidly. The continous expansion of global production capacities testifies to the high interest in this new material.

REFERENCES

http://www.plastemart.com/upload/literature/288_art_cocpolymer.asp

http://www.iptonline.com/articles/public/IPT_24_p73nonprint.pdf

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