Lubrizol LifeSciences

Polymers | Formulation | Manufacturing

Compatibility of Thermoplastic Polyurethanes with Drugs for IV Sets

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Purpose

Compatibility between medications and intravascular (IV) administration sets is important for assuring predictable delivery of the drug dose, safety and efficacy. Potential interactions include sorption, permeation of the drug into the administration set, leaching of the set material components into the drug solution. The use of thermoplastic polyurethanes (TPU) for IV sets has seen a recent increase, however a comprehensive testing had not been conducted to evaluate their compatibility with drugs. The purpose of this study was to evaluate in vitro compatibility of IV sets of thermoplastic polyurethanes with an array of drugs with different properties.

Methodology

Materials – Three types of infusions sets (Jiangsu Suyun Medical Materials Co., Ltd., China) were tested: thermoplastic polyurethane set made from material supplied by Lubrizol Advanced Materials, Inc (USA), styrene butadiene thermoplastic elastomer set (TPE) and polyvinyl chloride (PVC) set (standard PVC with diethylhexyl phthalate). All sets had similar tube design: OD 4 mm, ID 2.4mm, length 1.6 m (Fig. 1-3).

The following commercial drugs were used in the study: Levofloxacin hydrochloride injection 100 mg/2ml (Jiangsu Ruinian Qianjin Pharmaceutical Co., Ltd., China), Docetaxel injection 20 mg/0.5ml (Jiangsu Hengrui Medicine Co.,Ltd., China), Furosemide injection 20 mg/2ml (Tianjin Tianyao Pharmaceuticals Co., Ltd., China), Ranitidine hydrochloride injection 50 mg/2ml (Hangzhou Minsheng Pharmaceutical Group Co., Ltd., China), Moxifloxacin hydrochloride in sodium chloride injection 400 mg/250ml (Bayer Healthcare, Germany), Metronidazole injection 500 mg/250 ml and Pantoprazole sodium for injection 40 mg (Cisen Pharmaceutical Co., Ltd., China).

Figure 1. TPU IV set

Figure 2. TPE IV set

Figure 3. PVC IV set

Methods – The study included seven commonly IV drugs, to cover different properties (aqueous solubility and log P) and therapeutic classes – Table 1. Commercially approved drug products were tested. The study parameters (drug dose, volume, concentration, flow rate, administration time) were designed to simulate the clinical administration (Table 1).

The concentration of drug in the solution circulated through the IV sets was quantified at different time intervals by high-performance liquid chromatography with UV detection, using reference standards. The impurity level, pH of the solution and particulates were measured before and after circulation in the IV sets. IV sets based on TPE and PVC were also evaluated for comparison.

Table 1. Drugs properties and study parameters

Drug	Levofloxacin hydrochloride	Moxifloxacin hydrochloride	Metronidazole	Docetaxel	Furosemide	Ranitidine hydrochloride	Pantoprazole sodium
Class	Antibacterial Fluoroquinolone	Antibacterial Fluoroquinolone	Antibacterial Nitroimidazole	Antineoplastic Antimicrotubular	Loop diuretic	H2 antagonist	Proton pump inhibitor
log P	2.10	2.90	-0.02	2.40	2.03	0.27	0.50
Solubility in water (USP/NF*)	Sparingly soluble	Sparingly soluble	Sparingly soluble	Practically insoluble	Practically insoluble	Very soluble	Freely soluble
Daily dose (mg)	400	400	1000	120	400	100	160
Volume (ml)	80	250	500	134	140	404	220
Concentration (mg/ml)	5	1.6	2	0.9	2.86	0.25	0.73
Administration time (h)	1.0	1.5	1.0	1.0	1.67	2.0	0.25
Administration rate (ml/h)	80	167	500	134	84	200	880
Recirculation time (h)	24	24	24	6	24	24	4

Results

- TPU sets did not affect the pH, impurity and particulates of the drug products tested.
- For all tested drugs, independent of their aqueous solubility and logP, the TPU sets showed very low drug sorption during infusion for the recommended administration time, delivering more than 90% of the dose. Further recirculation of the solution in the sets beyond the recommended administration time did not result in an increased drug absorption (for up to 4 – 24 hours) - Fig. 4.
- TPU based IV sets performed similar or better than TPE or PVC – Fig 5, 6.
- In the case of pantoprazole sodium, TPU IV sets performed slightly better, having lower initial sorption compared to TPE and PVC – Fig. 7.

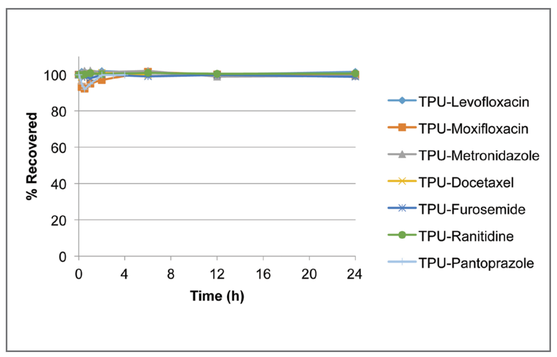

Figure 4. Drug recovery following circulation through TPU IV sets.

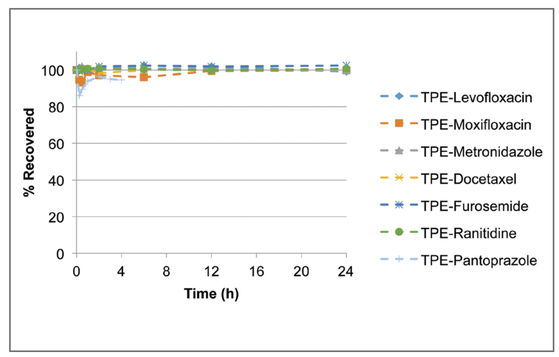

Figure 5. Drug recovery following circulation through TPE IV sets.

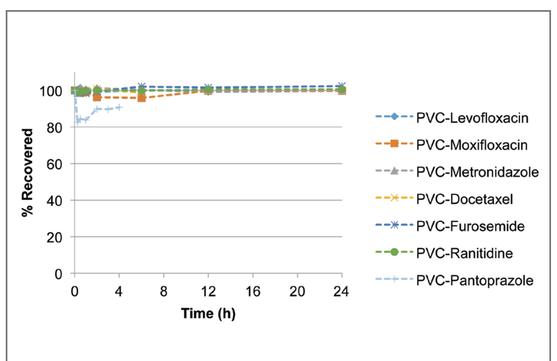

Figure 6. Drug recovery following circulation through PVC IV sets.

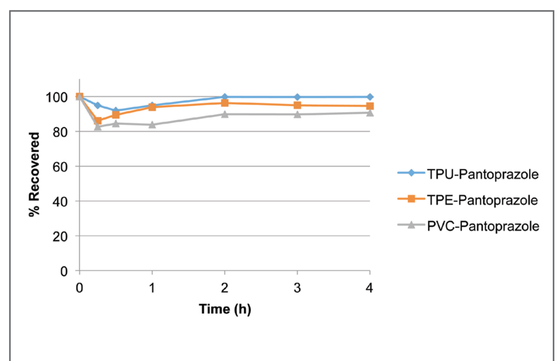

Figure 7. Pantoprazole recovery following circulation through TPU, TPE and PVC IV sets.

Conclusion

TPU based IV sets performed similar or better than TPE or PVC, showing very low sorption for drug of different properties:

- Levofloxacin hydrochloride
- Moxifloxacin hydrochloride
- Metronidazole
- Docetaxel
- Furosemide
- Ranitidine hydrochloride
- Pantoprazole sodium

In the case of pantoprazole, TPU IV sets performed slightly better, having lower sorption compared to TPE (initial stage) and PVC (entire duration). The TPU properties and their compatibility with drugs, make them suitable for use in intravascular administration sets.

Reference: *The United States Pharmacopeia and The National Formulary (USP–NF) USP 39–NF 34, United States Pharmacopeial Convention, Rockville, Maryland, 2016.