Journal of Pharmaceutical Investigation
https://doi.org/10.1007/s40005-017-0364-2

Online ISSN 2093-6214
Print ISSN 2093-5552

ORIGINAL ARTICLE

Evaluation of nitroglycerin and cyclosporin A sorption to polyvinylchloride- and non-polyvinylchloride-based tubes in administration sets

Su-Eon Jin[1,2] · Jung Woo Park[3] · Hong Baek[3] · Seungho Jeon[4] · Sang Wook Park[3] · Sung-Joo Hwang[1,5]

Received: 16 August 2017 / Accepted: 26 October 2017

Abstract

We report the sorption evaluation method for injectable drugs administered using set tubes to evaluate the quality of the administration sets. The evaluation method using a peristaltic pump, so called pump method, was used for the kinetic sorption study. Nitroglycerin (NTG) and cyclosporin A (CSA) were selected as model drugs. The parameters of drug-diluted concentrations and flow rates were adapted to the clinically relevant values. Polyvinylchloride (PVC)- and non-PVC (PU and PO)-based tubes were cut to a fixed length of 1 m after removing the accessories in the administration sets. NTG and CSA were analyzed using high-performance liquid chromatography (HPLC) methods with ultraviolet (UV) detection. After the drug analyses, NTG and CSA sorption levels were calculated from the percentage values of the subtracted drug concentrations in samples from those in the diluted solutions. The average sorption levels and each sorption level at each sampling point were considered to compare the sorption levels in all administration set tubes. Both drugs showed high sorption levels in PVC- and PU-based administration set tubes. However, the drugs showed a minimum sorption potential of < 10% on PO-based tubes, which could be clinically acceptable. This suggests that the sorption evaluation methods for NTG and CSA could be promising standards for endorsing administration set tubes and for evaluating newly developed or designed polymeric alternatives. Additionally, PO could be an alternative and next-generation polymeric material for manufacturing administration set tubes.

Keywords Sorption evaluation · Administration set tube · PVC · Non-PVC · Nitroglycerin · Cyclosporin A

Introduction

Drug sorption to administration set tubes is defined as the adsorption of a drug to the surface and absorption in the matrix of administration set tubes (Jin et al. 2016; Treleano et al. 2009). This phenomenon causes additional and unpredicted drug loss, which leads to ineffective drug responses after administration of injectable drugs. Sorptive drugs are generally charged such as nitroglycerin (NTG, a medication for heart failure-related conditions such as angina and hypertension, Fig. 1a) or hydrophobic drugs, per the biopharmaceutical classification system (BCS) class II or IV, such as cyclosporin A (CSA, an immunosuppressive drug, Fig. 1b), diazepam (a sedative), and tacrolimus (an immunosuppressant for organ transplantation) (Jin et al. 2016, 2017a; Shibata et al. 2000; Tamura et al. 2002; Treleano et al. 2009). These agents interact with polymeric materials such as polyvinylchloride (PVC) and non-PVC in administration set tubes,

Su-Eon Jin and Jung Woo Park have contributed to this work equally.

✉ Sang Wook Park
safety@ktr.or.kr

✉ Sung-Joo Hwang
sjh11@yonsei.ac.kr

1 College of Pharmacy, Yonsei University, 85 Songdogwahak-ro, Yeonsu-gu, Incheon 21983, Republic of Korea

2 College of Medicine, Yonsei University, Seoul 03722, Republic of Korea

3 Korea Testing and Research Institute, 98, Gyoyukwon-ro, Gwacheon-si, Gyeonggido 13810, Republic of Korea

4 Polyscientech Co. Ltd, Anseong 17508, Republic of Korea

5 Yonsei Institute of Pharmaceutical Sciences, Incheon 21983, Republic of Korea

Published online: 28 November 2017

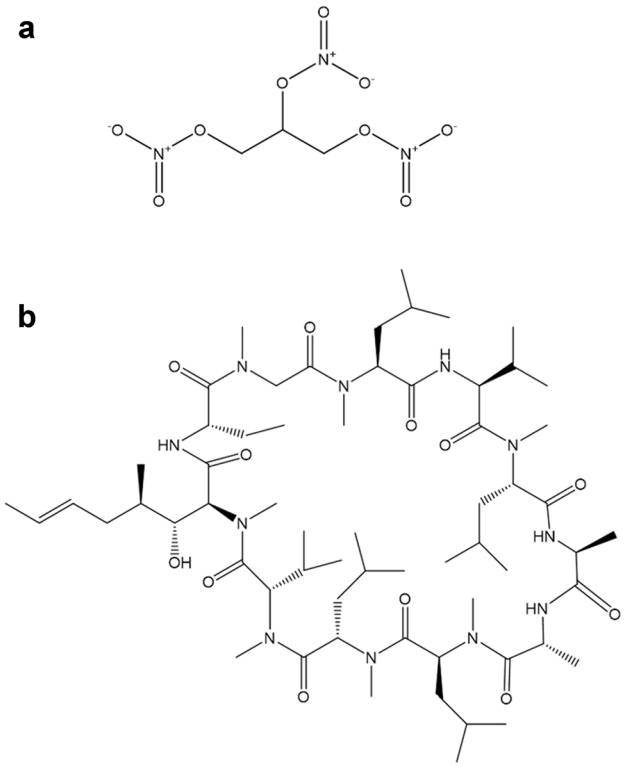

Fig. 1 Chemical structures of **a** nitroglycerin (NTG) and **b** cyclosporin A (CSA)

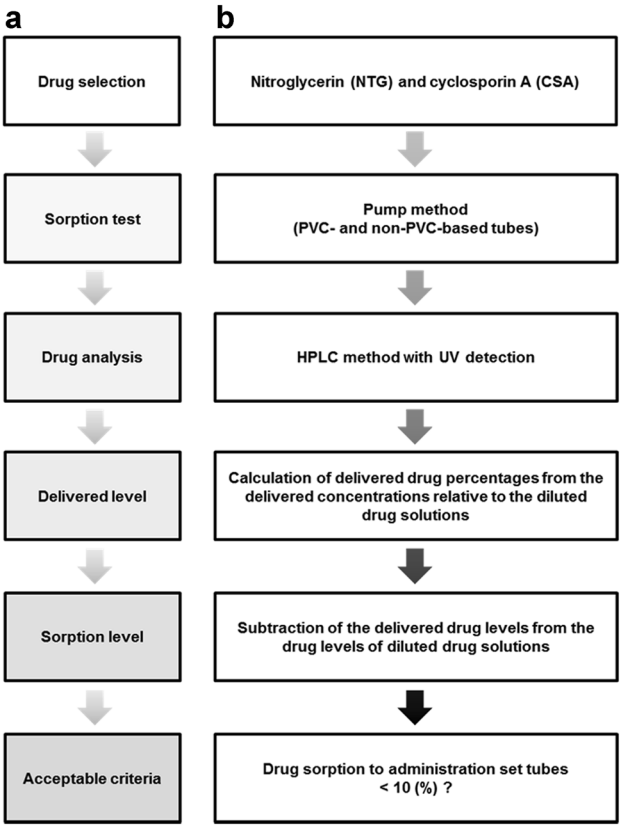

Fig. 2 Schematic diagrams of **a** sorption evaluation procedure and **b** evaluation conditions in this study

based on the physicochemical properties of the drugs and polymers. Thus, drug sorption to administration set tubes should be estimated to evaluate the quality of administration set tubes and ensure the safety and efficacy of injectable drugs. Furthermore, standard methods and procedures for evaluating drug sorption to administration set tubes should be considered and recommended.

Sorption evaluation techniques such as the pump and drip methods have been studied to confirm the sorption potential of polymeric bags or administration set tubes (Jin et al. 2016, 2017a, b). Pump and drip methods are extensively used for the administration of large-volume injections via infusion using administration sets. Since a peristaltic pump is used to regulate the flow rate precisely, the pump method can be used to determine low flow rates and low drug concentration conditions (Jin et al. 2017a; Shibata et al. 2000; Treleano et al. 2009). The drip method is also widely used to control the flow rate of large-volume injections (Kawano et al. 1992). In the drip method, a flow regulator or clamp is usually attached to the administration set tube for flow rate control. Compared with the drip method, the pump method enables relatively accurate flow rate control at low concentrations of diluted solutions for injectable drugs (Kawano et al. 1992; Jin et al. 2017a, b). It can be used for evaluating drug sorption to administration set tubes.

The standard procedure for sorption evaluation of drugs to administration set tubes is highlighted from the drug selection to determination of sorption levels after the drug solutions pass through the tubes (Fig. 2a) (Jin et al. 2017b). Highly sorptive drugs are usually selected to evaluate the sorption in tubes of administration sets, and kinetic sorption tests are performed using the pump method. For example, the highly sorptive drugs, NTG and CSA, can be used to evaluate drug sorption to administration set tubes (Fig. 2b). The clinically used administration conditions for injectable drugs, such as drug concentration and flow rate, are mimicked for the kinetic sorption test. After drug analyses, high-performance liquid chromatography (HPLC) methods are used to determine the sorption levels at each sampling point and the average sorption levels of drugs are calculated from their delivery levels after passing through the tubes of the administration sets relative to the diluted drug solutions (Jin et al. 2017b; Krzek et al. 2003; Szerkus et al. 2014). The acceptable criteria for drug sorption to administration set tubes can be determined based on the drug content specified in the pharmacopeia, which is generally < 10% (Jin et al. 2017b; Morar-Mitrica et al. 2015).

In this study, we evaluated the sorption of NTG and CSA (used as model drugs with high sorption levels) to

administration set tubes. The standard pump method was used to determine the flow rate control in the kinetic sorption study. PVC- and non-PVC (PU and PO)-based tubes were selected for the quality evaluation as 1-m long tubes without accessories. NTG and CSA levels were analyzed using HPLC methods with ultraviolet (UV) detection. Sorption levels were calculated as the drug percentages of remaining after the solution passed through the tubes, which were divided by the diluted drug concentrations in the bottles. The acceptable criteria for the calculated sorption values in tubes of administration sets were determined for this study.

Materials and methods

Chemicals

NTG was purchased from Sigma-Aldrich (St. Louis, MO, USA) and CSA was provided by Chong Kun Dang, Co., Ltd., (Seoul, Korea). NTG injection (0.5 mg/mL, Nitrolingua®), CSA injection (50 mg/mL, Cypol®, both Company, Region, Nation), and 5% dextrose solution (Daehan Pharmaceutical, Co., Ltd., Seoul, Korea) were purchased from Woori Pharm. Inc. (Incheon, Korea). For the administration sets, PVC-, PU-, and PO-based tubes were obtained from Polyscientech Co., Ltd., (Anseong, Gyunggi, Korea). Acetonitrile and methanol were purchased from Burdick and Jackson Co., Ltd., (MI, USA). Water was purified by a Milli-Q system (Millipore Corp., Bedford, MA, USA). All other chemicals and solvents were of analytical reagent grade.

Preparation of standard solutions for NTG and CSA

NTG and CSA were dissolved in methanol and acetonitrile using 100 mL-volumetric flasks after precisely weighing, respectively. The standard solutions of NTG and CSA were at the concentrations of 3, 10, 20, 40, and 194 µg/mL for NTG and 5, 10, 50, 100, 200, and 1000 µg/mL for CSA as standards.

HPLC analyses

NTG was analyzed using an HPLC method (Agilent, USA) with a UV detector connected to a C_{18} column (250 × 4.6 mm, 5-µm, Capcell Pak, Sheido, Japan) at 40 °C. The mobile phase was a mixture of methanol and water (5:5, v/v) run at a flow rate of 1 mL/min. Ten microliter standards and samples were directly injected into the HPLC system and detected at 205 nm. For the detection of CSA, an HPLC method with UV detection was used. Two-microliter standards and samples were directly injected into the HPLC system connected to a C_{18} column (150 × 2.1 mm, 2-µm, Shimadzu, Japan). The column oven temperature was 60 °C. The mobile phase was a mixture of acetonitrile and water (7:3, v/v). The flow rate was fixed at 0.3 mL/min, and the detection wavelength was 210 nm. The peaks of the standards and drug samples were monitored in the chromatograms by comparing them with the peaks of blank solutions. The limit of quantification (LOQ) was confirmed at 3 µg/mL for NTG and 5 µg/mL for CSA. The linearity was determined at ranges of 3–194 µg/mL for NTG and 5–1000 µg/mL for CSA. The calibration curves were constructed by plotting the average peak areas versus their respective concentrations.

Kinetic sorption test

PVC-, PU- and PO-based tubes were used for the sorption kinetic study. After all detachable accessories such as the connectors and needle covers were removed, and then the tubes were cut 1-m long using a sharp razor. The NTG and CSA injections were diluted with 5% dextrose solution to 100 and 50 µg/mL for NTG and CSA, respectively. After the diluted drug solutions had been gently mixed without creating bubbles, they were transferred into amber vials (10-mL). A glass bottle was used to minimize any additional drug sorption onto the plastics. Table 1 shows the sorption evaluation conditions for NTG and CSA. Briefly, each drug solution was diluted with 5% dextrose, purged, and then preloaded into the tubes of the administration sets using a peristaltic pump (Terumo infusion pump, Terumo Medical Corp., USA). The tubes were filled with the diluted drug solution, which was then delivered through at flow rates of 1 mL/min for NTG and 20 mL/h for CSA. The sorption kinetics of drugs were evaluated according to types of polymers using PVC-, PU-, and PO-based tubes. Samples were collected into amber vials at various time points. The sample at 0 h refers to the diluted drug solution in the glass bottle. Ten-microliter samples were directly injected into the HPLC system, and the drugs were analyzed as described in "HPLC analyses". To estimate the drug sorption levels of tubes in the administration sets, we subtracted the concentrations of drugs passing through the tubes from that of the diluted drug solution of injections in the bottle and then calculated the percentage of the subtracted values relative to the concentrations of the diluted drug solution in the bottle. Negative

Table 1 Experimental conditions for kinetic sorption study using nitroglycerin (NTG) and cyclosporin A (CSA)

	NTG	CSA
Concentration	100 µg/mL	50 µg/mL
Diluent	5% dextrose	5% dextrose
Flow rate	1 mL/min	20 mL/h
Sampling point	0, 0.17, 1.17, 2.17, 3.17, and 4.17 h	0, 0.5, 1.5, 2.5, 3.5, and 4.5 h

sorption levels were set at "0" and the average sorption level of the drugs at each time point was defined as the drug sorption level.

Statistical analysis

All the results are expressed as the mean ± standard deviation (SD). The statistical analysis was performed using the Student's *t* test and an analysis of variance (ANOVA). A p value < 0.05 was considered significant.

Results

Specificity and sensitivity

NTG

Figure 3 shows the representative chromatograms of NTG after the HPLC analysis. Compared with the blank (Fig. 3a), NTG was detected at 7.0 min in the chromatogram (Fig. 3b–d). The LOQ was determined at 3 μg/mL of NTG (Fig. 3b). No interference peaks were detected for the NTG peak in the chromatograms.

CSA

Figure 4 shows the representative HPLC chromatograms of CSA. There was no CSA peak in the blank sample (Fig. 4a). The retention time of CSA was 9.8 min compared with that of the blank (Fig. 4b–d). CSA was detected at up to 5 μg/mL as the LOQ over the signal-to-noise (S/N) ratio of 10 (Fig. 4b). The CSA peak was not overlapped by other interfering peaks.

Linearity for NTG and CSA

For the calibration of NTG, the linearity was evaluated (Fig. 5a). The calibration curves were constructed using a concentration ranged from 3 to 194 μg/mL. The linear regression equation of the average calibration curve was $y = 20069.78\ (\pm 102.60)x - 22318.17\ (\pm 9147.41)$ with an r^2 value of 0.99. Figure 5b shows the calibration curves of CSA in the range of 5–1000 μg/mL. The average calibration curve was calculated using linear regression, and the equation was $y = 14418.19\ (\pm 19.56)x - 5527.42\ (\pm 8193.98)$ with an r^2 value of 1.00. The samples for NTG and CSA were detected without further dilution at the calibration ranges.

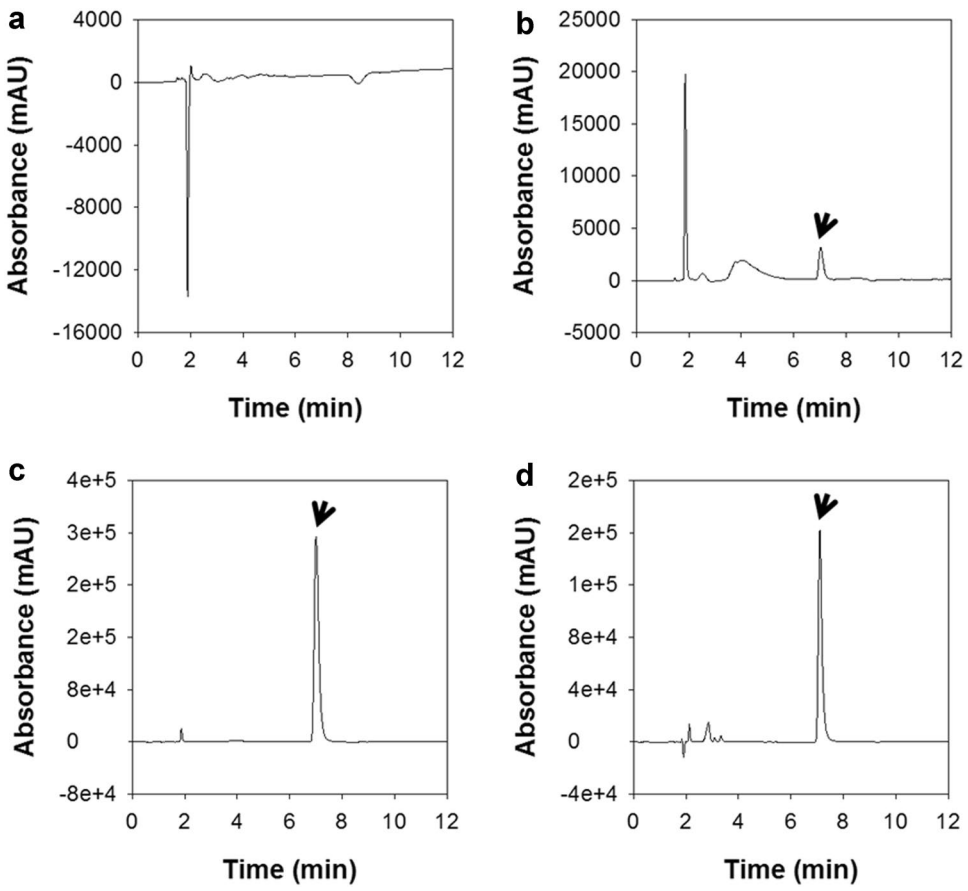

Fig. 3 Representative chromatograms of nitroglycerin (NTG): **a** blank, **b** 3 μg/mL as limit of quantification (LOQ), **c** 194 μg/mL as highest concentration, and **d** samples (PO-based tubes). Arrow indicates NTG peak in chromatograms

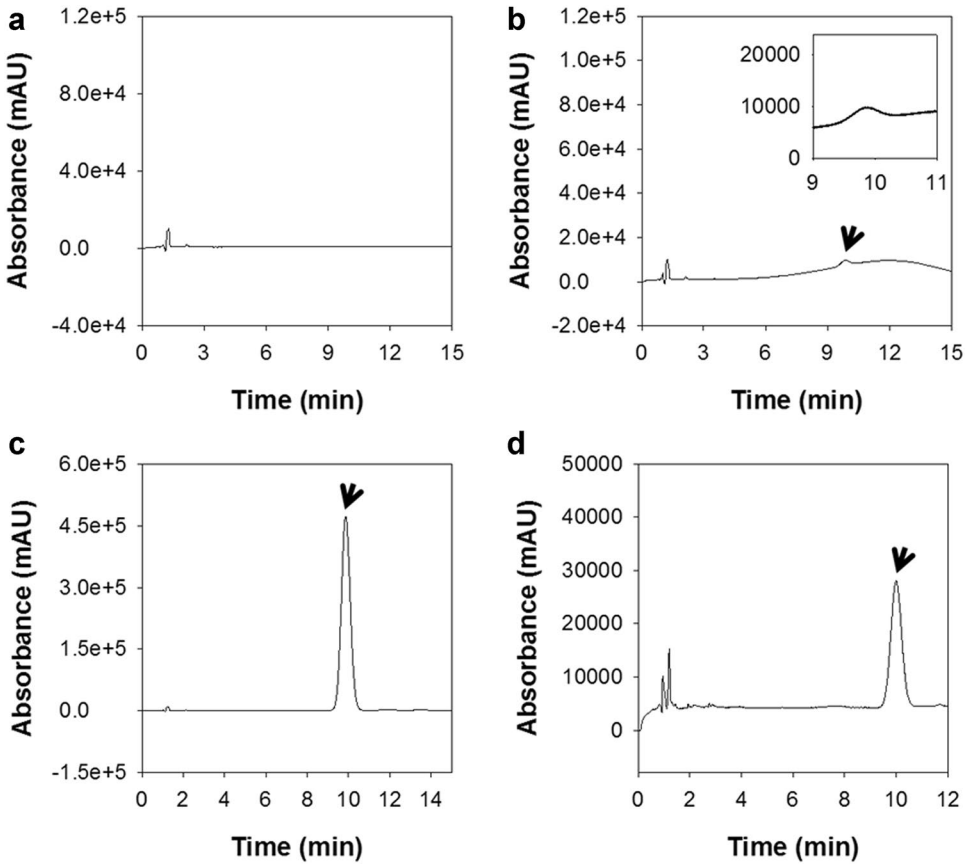

Fig. 4 Representative chromatograms of cyclosporin A (CSA): **a** blank, **b** 5 µg/mL as limit of quantification (LOQ), **c** 1000 µg/mL as highest concentration, and **d** samples (PO-based tubes). Arrow represents CSA peak in chromatograms

Drug sorption levels to administration set tubes

To compare sorption levels of the drugs to the administration set tubes, average sorption levels and sorption levels at each sampling point were calculated. Table 2 lists the sorption results of NTG and CSA to the administration set tubes. The average sorption results of NTG were 15.1 ± 9.4, 29.1 ± 3.9, and 1.4 ± 1.4% for PVC-, PU-, and PO-based tubes, respectively. In the case of CSA, average sorption results were 16.6 ± 9.0% for PVC-, 12.4 ± 6.6% for PU-, and 0.2 ± 0.4% for PO-based tubes in administration sets. NTG sorption levels were similar to CSA sorption levels in PVC- and PO-based tubes of the administration set. However, in the PU-based administration set tubes, NTG was more sorptive than CSA was. The NTG sorption levels in the PU-based tubes were higher than they were in PVC-based tubes (sorption level for NTG, PU < PVC < PO; and for CSA, PVC < PU < PO).

NTG sorption to administration set tubes

NTG was previously reported as a highly sorptive drug in administration set tubes as mentioned above. Figure 6a shows the delivery levels of NTG after the drug solution was passed through the tubes. In the initial phase of the kinetic sorption study, the PVC- and PU-based tubes showed higher sorption levels than the PO-based tubes did. The PO-based tubes had minimum sorption levels < 10%. Although drugs in the PU-based tubes showed lower sorption levels than those in PVC-based tubes did, NTG in the PU-based tubes showed higher sorption levels than it did in the PVC-based tubes. After the initial time point, high sorption levels of NTG were maintained in the PU-based tubes.

CSA sorption to administration set tubes

Figure 6b shows the CSA delivery levels in PVC- and non-PVC-based tubes. CSA showed the highest sorption levels in PVC-based tubes. Sorption levels of CSA in PU-based tubes were also high and comparable to those in the PVC-based administration set tubes. However, the PO-based tubes had minimum sorption levels at each sampling point (< 10%). The CSA sorption results in PO-based tubes were comparable to those of NTG. The sorption profiles of CSA were similar to those of NTG in the administration set tubes, which showed sorption phases in the early phase of the kinetic sorption study and reached the sorption equilibria.

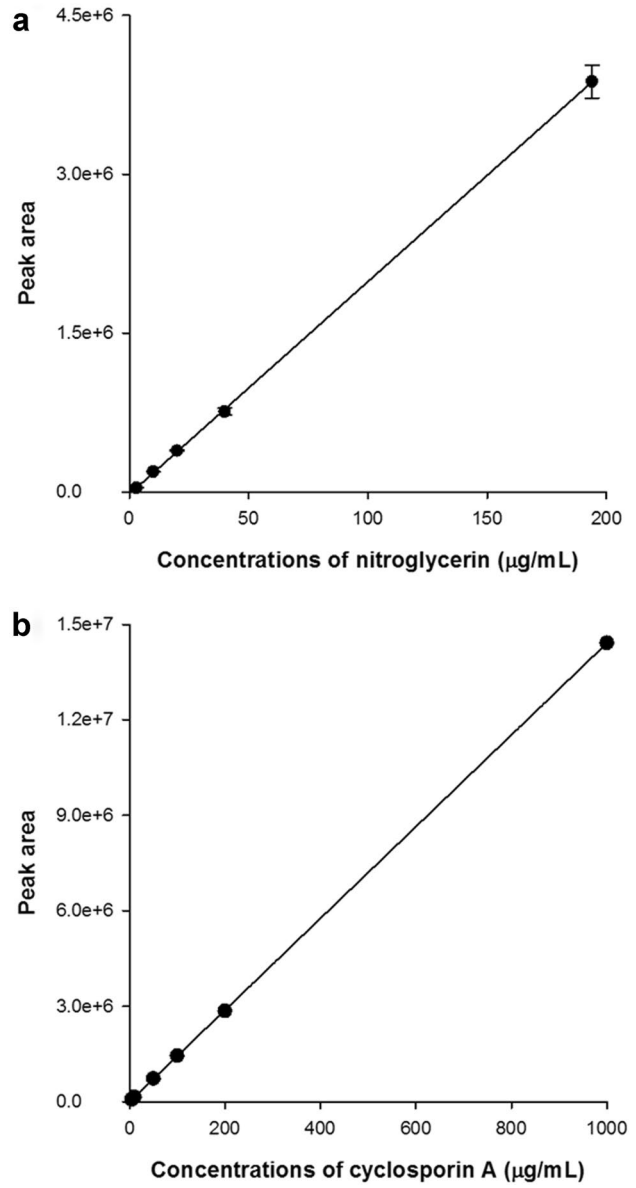

Fig. 5 Average calibration curves of **a** nitroglycerin (NTG) and **b** cyclosporin A (CSA)

Table 2 Average sorption levels of drugs to administration set tubes: nitroglycerin (NTG) and cyclosporin A (CSA)

Injectable drug	Sorption level after passing through tubes (%)		
	PVC	PU	PO
NTG	15.1 ± 9.4	29.1 ± 3.9	1.4 ± 1.4
CSA	16.6 ± 9.0	12.4 ± 6.6	0.2 ± 0.4

PVC polyvinylchloride, *PU* polyurethane, *PO* polyolefin

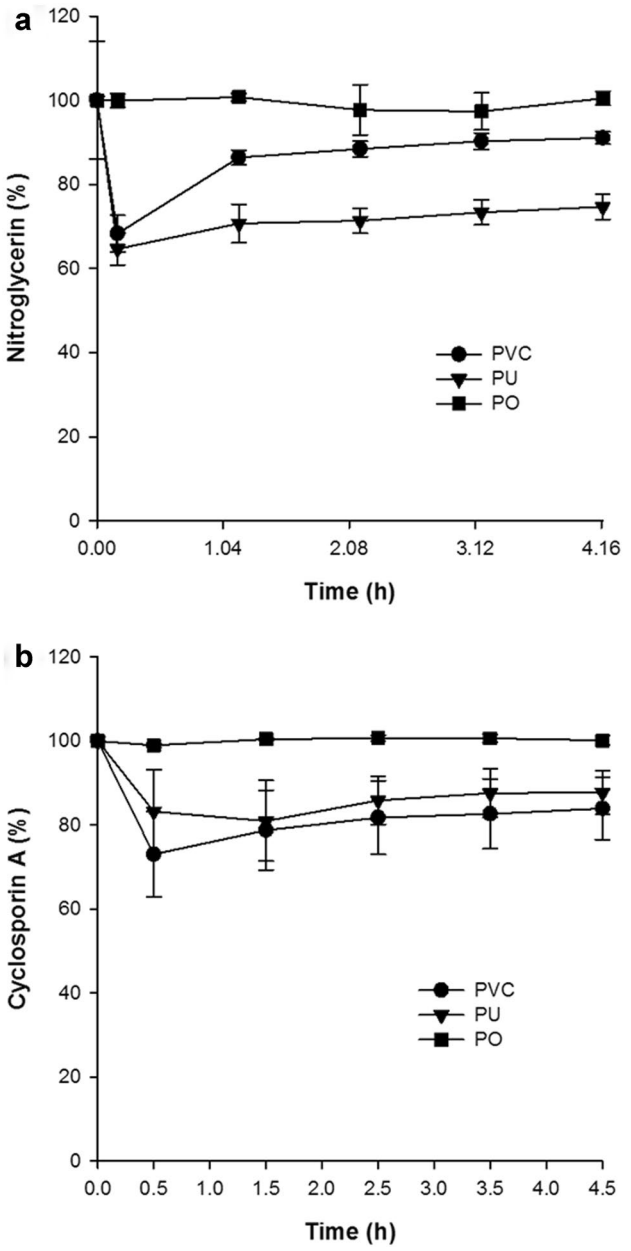

Fig. 6 Profiles of drug delivery (%) versus time (h) after passing through tubes: **a** nitroglycerin (NTG) and **b** cyclosporin A (CSA)

Discussion

Although the sorption potential of each injectable drug to the polymeric material was analyzed, the sorption evaluation standard of the administration set tubes was not recommended based on the quality evaluation of the administration set tubes. Here, we report "pump method" to evaluate drug sorption to administration set tubes using a peristaltic pump (Jin et al. 2017a, b). The kinetic sorption tests were performed based on the mimicked clinically relevant conditions. Then, drug concentrations before/after passing through the

tubes were quantitatively determined using HPLC methods with UV detection. Their sorption levels were calculated from the delivered drug concentrations relative to the diluted drug concentrations in solution (Jin et al. 2017b).

Sorption of NTG and CSA to polymeric materials has been studied for several decades (Kowaluk et al. 1986; Ritschel et al. 1989; Schaber et al. 1985). Their high sorption potentials to polymeric materials in administration set tubes, specifically PVC, were previously reported (Kambia et al. 2005; Roberts et al. 1991; Shibata et al. 2000; Treleano et al. 2009) although their administration amounts should be controlled precisely in emergency cases. NTG and CSA at 80 and 1000 µg/mL showed 18–43 and 40–50% sorption in PVC-based tubes at flow rates of 1.0 mL/min and 10 mL/h, respectively (Shibata et al. 2000; Treleano et al. 2009). Therefore, among injectable drugs, NTG and CSA were selected as model drugs due to their high sorption potentials to screen the drug sorption levels in PVC- and non-PVC-based tubes of administration sets.

Drug sorption was evaluated as a kinetic determinant of the delivered drug concentration relative to the diluted drug concentration using the pump method, from the model drug selection to determining the acceptable sorption criteria (Fig. 2a) (Jin et al. 2017a, b). The steps of the evaluation of drug sorption to the administration set tubes were as follows: (1) model drug selection, (2) kinetic sorption test, (3) drug analysis, (4) calculation of drug delivery and sorption levels, and (5) confirmation that drug sorption levels were within the acceptable criteria. NTG and CSA were used as representative drugs for the sorption study (Martens et al. 1990; Treleano et al. 2009). The pump methods were used to precisely regulate the flow rate of NTG and CSA. Clinically relevant parameters were used to mimic the clinical administration conditions of injectable drugs such as the flow rate and diluted drug concentration (Table 1). For the drug analyses, the HPLC method with UV detection recommended after the simple validation, successfully determined NTG and CSA (Krzek et al. 2003; Ritschel et al. 1989). The sorption level of the drugs on the administration set tubes was calculated by subtracting the drug concentrations of the solution after it passed through the tube from the diluted drug concentration, which should be $< 10\%$ to meet the acceptable criteria (Jin et al. 2017b; Morar-Mitrica et al. 2015).

For the kinetic sorption study, NTG and CSA were quantitatively determined using HPLC analyses (Schaber et al. 1985; Treleano et al. 2009). The pre-validations performed for the HPLC methods for NTG and CSA were the specificity, sensitivity (Figs. 3, 4), and linearity (Fig. 5) (Jin et al. 2017b; Krzek et al. 2003; Sruthi et al. 2013; Szerkus et al. 2014). Compared with the blanks (Figs. 3a, 4a), the LOQs of NTG and CSA were detected at 3 µg/mL (Fig. 3b) and 5 µg/mL (Fig. 4b). The LOQ values (Figs. 3b, 4b) and standards (Figs. 3c, 4c) were available for the determination of drugs in the samples after the kinetic sorption study (Figs. 3d, 4d). The linearity of NTG and CSA was confirmed at the ranges of 3–194 µg/mL for NTG (Fig. 5a) and 5–1000 µg/mL for CSA (Fig. 5b), respectively. For NTG, the calibration standards can be checked to shift to other concentration ranges such as 5–200 µg/mL which are within a range less than 15% relative standard deviation (RSD) of the highest concentration (194–200 µg/mL) and 20% RSD of the LOQ (3–5 µg/mL). The HPLC methods for the NTG and CSA analyses were successfully developed to determine the drugs in the samples.

High sorption potentials of NTG (Fig. 6a) and CSA (Fig. 6b) to the administration set tubes were confirmed in PVC- and PU-based tubes except in PO-based tubes (Schaber et al. 1985; Shibata et al. 2000; Treleano et al. 2009). The sorption levels of NTG and CSA to the PU- and the PVC-based tubes were highest in all tubes ($29.1 \pm 3.9\%$ in PU-based tubes for NTG and $16.6 \pm 9.0\%$ in PVC-based tubes for CSA), respectively (Table 1). In particular, NTG showed a higher sorption potential in the PU-based tubes than it did the in PVC-based tubes. This suggests that the hardness, elasticity, and other physicochemical properties of the PU-based tubes in study environments (e.g. temperature) possibly enhanced the sorption of NTG. Although NTG and CSA had the high sorption potentials in PVC- and PU-based tubes, they had low sorption potentials in the PO-based tubes ($< 10\%$), which could be acceptable for clinical uses based on their injectable drug content specified in the pharmacopoeia (Jin et al. 2017b; Morar-Mitrica et al. 2015).

For the mechanism of drug sorption to administration set tubes, the interactions between the drugs and polymeric materials (e.g., partition and diffusion) continuously occurred before the sorption equilibria were achieved (Jin et al. 2017b; Roberts 1996). Their sorption was one of physical incompatibilities caused by the physicochemical properties of the respective materials of polymers in the administration set tubes and drugs (Arruda et al. 1989; Jenke 1993a, b). NTG is a charged and slightly soluble drug in water (Fig. 1a), and CSA is a hydrophobic drug with a high log p value (4.3, Fig. 1b) (Cheng et al. 2006), categorized as BCS Class II. They can be partitioned to polymeric materials of PVC and PU in the liquid (diluted drug solution)—solid (administration set tubes) interfaces. NTG and CSA were highly adsorbed to PVC- and PU-based tubes except PO-based tubes in the initial phase of the kinetic sorption study. Thus, PO-based materials and layer-by-layer designs can be alternatives to reduce the drug sorption in administration set (Jin et al. 2016, 2017a, b; Trissel et al. 2006). This method can also be applied for the standardized evaluation methods of drug sorption to administration set tubes in clinical drug uses.

Conclusion

Sorption evaluation method using pump was developed for the quality evaluation of the administration set with regard to drug sorption to administration set tubes. NTG and CSA were selected as the model drugs based on their reported high sorption potentials. PVC- and non-PVC-based tubes were used at a fixed length of 1 m. The sorption of NTG and CSA to the administration set tubes was kinetically evaluated using the pump method. The flow rate and diluted drug concentration were used as the clinically relevant test parameters. While the PVC- and PU-based tubes showed high sorption levels of NTG and CSA, the PO-based tubes had the lowest sorption potential of $< 10\%$ in the kinetic sorption study, which could be acceptable for use. The standard procedure for sorption evaluation can be used for the guidelines of evaluation methods of drug sorption to administration set tubes. In addition, PO could be a new alternative as a tube material for minimizing drug sorption to administration set tubes and for improving the quality of administration sets.

Acknowledgements This work was supported by the Korea Ministry of Environment through "The Advancement of Scientific Research and Technological Development in Environmental Science Program" (E315-00015-0414-2).

Author contributions SEJ designed the study and wrote the paper, JWP performed the experiments and analyzed the data, HB and SWP designed the study and provided comments, SJ designed the study and provided the administration sets, and SJH designed the study as a principal investigator and confirmed the written paper.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Research involving human and animal rights This article does not contain any studies with human and animal subjects performed by any of the authors.

References

Arruda WO, Brito Filho D, Rosa SL et al (1989) Factors affecting diazepam availability from intravenous admixture solutions. Arq Neuropsiquiatr 47:291–294

Cheng WP, Gray AI, Tetley L et al (2006) Polyelectrolyte nanoparticles with high drug loading enhance the oral uptake of hydrophobic compounds. Biomacromolecules 7:1509–1520

Jenke DR (1993a) Evaluation of various solvent systems for modeling solute sorption with plasticized polyvinyl chloride materials. J Pharm Sci 82:617–621

Jenke DR (1993b) Modeling of solute sorption by polyvinyl chloride plastic infusion bags. J Pharm Sci 82:1134–1139

Jin SE, You S, Jeon S et al (2016) Diazepam sorption to PVC- and non-PVC-based tubes in administration sets with quantitative determination using a high-performance liquid chromatographic method. Int J Pharm 506:414–419

Jin SE, Jeon S, Byon HJ et al (2017a) Evaluation of tacrolimus sorption to PVC- and non-PVC-based tubes in administration sets: pump method vs. drip method. Int J Pharm 528:172–179

Jin SE, You S, Jeon S et al. (2017b) Evaluation of drug sorption to PVC- and non-PVC-based tubes in administration sets using a pump. J Vis Exp 121

Kambia NK, Dine T, Dupin-Spriet T et al (2005) Compatibility of nitroglycerin, diazepam and chlorpromazine with a new multilayer material for infusion containers. J Pharm Biomed Anal 37:259–264

Kawano K, Tsubouchi R, Nakajima S (1992) The effect of the drip condition (container materials, concentration, drip Rate) on the sorption of nicardipine hydrochloride from injection to the intravenous infusion set. Jpn J Hosp Pharm 18:491–495

Kowaluk EA, Roberts MS, Polack AE (1986) Kinetics of sorption of ionizable solutes by plastic infusion bags. J Pharm Sci 75:562–570

Krzek J, Moniczewska M, Zabierowska-Ślusarczyk G (2003) The HPLC determination of propane-1,2,3-triyl trinitrite and impurities: (2RS)-3-hydroxypropane-1,2-diyl dinitrate and 2-hydroxypropane-1,3-diyl dinitrate in ointment. J Pharm Biomed Anal 33:403–409

Martens HJ, De Goede PN, Van Loenen AC (1990) Sorption of various drugs in polyvinyl chloride, glass, and polyethylene-lined infusion containers. Am J Hosp Pharm 47:369–373

Morar-Mitrica S, Puri M, Beumer Sassi A et al (2015) Development of a stable low-dose aglycosylated antibody formulation to minimize protein loss during intravenous administration. mAbs 7:792–803

Ritschel WA, Ritschel GB, Sabouni A et al (1989) Study on the peroral absorption of the endekapeptide cyclosporine A. Methods Find Exp Clin Pharmacol 11:281–287

Roberts MS (1996) Modeling solute sorption into plastic tubing during organ perfusion and intravenous infusions. J Pharm Sci 85:655–665

Roberts MS, Kowaluk EA, Polack AE (1991) Prediction of solute sorption by polyvinyl chloride plastic infusion bags. J Pharm Sci 80:449–455

Schaber DE, Uden DL, McCoy HG (1985) Nitroglycerin adsorption to a combination polyvinyl chloride, polyethylene intravenous administration set. Drug Intell Clin Pharm 19:572–575

Shibata N, Ikuno Y, Tsubakimoto Y et al (2000) Adsorption and pharmacokinetics of cyclosporin A in relation to mode of infusion in bone marrow transplant patients. Bone Marrow Transplant 25:633–638

Sruthi A, Tejaswi P, Thanuja N et al (2013) Simple RP-HPLC method for estimation of diazepam in tablet dosage form. J Pharm Res 6:140–144

Szerkus O, Wolska E, Struck-Lewicka W et al (2014) Development and validation of UHPLC method for the determination of cyclosporine A in biological samples. Biomed Chromatogr 28:802–809

Tamura S, Ohike A, Ibuki R et al (2002) Tacrolimus is a class II low-solubility high-permeability drug: the effect of P-glycoprotein efflux on regional permeability of tacrolimus in rats. J Pharm Sci 91:719–729

Treleano A, Wolz G, Brandsch R et al (2009) Investigation into the sorption of nitroglycerin and diazepam into PVC tubes and alternative tube materials during application. Int J Pharm 369:30–37

Trissel LA, Xu QA, Baker M (2006) Drug compatibility with new polyolefin infusion solution containers. Am J Health Syst Pharm 63:2379–2382