International Journal of Pharmaceutics 528 (2017) 172–179

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Evaluation of tacrolimus sorption to PVC- and non-PVC-based tubes in administration sets: Pump method vs. drip method

Su-Eon Jin[a,b,c], Seungho Jeon[d], Hyo-Jin Byon[b], Sung-Joo Hwang[a,c,*]

[a] College of Pharmacy, Yonsei University, Incheon, 21983, Republic of Korea
[b] College of Medicine, Yonsei University, Seoul, 03722, Republic of Korea
[c] Yonsei Institute of Pharmaceutical Sciences, Incheon, 21983, Republic of Korea
[d] Polyscientech Co. Ltd, Anseong, 17508, Republic of Korea

ARTICLE INFO

Article history:
Received 24 February 2017
Received in revised form 16 May 2017
Accepted 18 May 2017
Available online 23 May 2017

Keywords:
Tacrolimus
Sorption
PVC
Non-PVC
Administration set
Pump

ABSTRACT

Tacrolimus sorption to tubes was evaluated using pump and drip methods For tubes, polyvinylchloride (PVC)- and non-PVC-based (polyurethane [PU] and polyolefin [PO]) tubes were used. First, inner surface properties of tubes were analyzed using field emission scanning electron microscopy and X-ray photoelectron spectroscopy. Tacrolimus was quantitatively analyzed using high-performance liquid chromatography with UV detection. For kinetic sorption analysis, diluted tacrolimus to 10 μg/mL was passed through 1-m-long tubes at 10 mL/h. Samples were collected at 1–4 h. The inner surface of PO-based tubes was relatively smooth and soft compared with those of PVC- and PU-based tubes. Atomic compositions of tubes matched chemical formulas of polymers excluding low-level impurity in PVC-based tubes. Tacrolimus was successfully analyzed and linearly determined at 2.5–20 μg/mL. From both methods, PVC- and PO-based tubes exhibited the highest and the lowest (<10%) sorption levels to tacrolimus, respectively. Tacrolimus was stably delivered using the pump method. Results suggested that the pump method can estimate tacrolimus sorption in administration set tubes and evaluate other sorptional drugs used at low concentrations. PO-based tubes also have promising potential as an alternative for administration set tubes.

1. Introduction

Drug sorption involves the adsorption and absorption of drugs to polymeric materials on the inner surface and in the matrix of tubes of administration sets (Jin et al., 2016; Treleano et al., 2009). This phenomenon causes unpredicted drug loss in tubes before sorptional equilibrium. Physicochemical properties of injectable drugs (e.g., hydrophobicity, and charge), infusion conditions (e.g., concentration of drugs, flow rate, and time), and polymeric materials of tubes [polyvinylchloride (PVC) and non-PVC] generally affect drug sorption to tubes of administration sets (Jenke, 2011; Roberts, 1996; Jin et al., 2016, 2017). Drug sorption levels in administration sets should be evaluated for the quality control of administration sets and minimized to ensure drug safety and efficacy.

Tacrolimus (Fig. 1) is an immunosuppressant used to prevent rejection following organ transplantation (Coilly et al., 2015; Diehl et al., 2016). Some studies have previously reported tacrolimus sorption (Suzuki et al., 2000; Taormina et al., 1992) based on the drug properties. It is a hydrophobic drug categorized as class 2 in the biopharmaceutical classification system (Tamura et al., 2002). The concentration of tacrolimus is monitored clinically because of its narrow therapeutic index; its sorption leads to urgent situations such as graft rejection and other adverse events (Lancia et al., 2015). Sorption evaluation of tacrolimus is necessary to predict tacrolimus delivery levels in the body and to minimize sorption by the tubes of administration sets. It can be selected as a model drug for sorption evaluation.

In evaluations of drug sorption, pump (Fig. 2a) (Jin et al., 2016, 2017) and drip methods (Fig. 2b) (Kawano et al., 1992) have been used to control flow rate, which is one of the critical factors in kinetic sorption analysis as it extensively affects drug sorption (Arruda et al., 1989; Jenke, 1993; Mason et al., 1981; Treleano et al., 2009). A pump or flow regulator is used to quantitatively control

Abbreviations: PVC, polyvinylchloride; PU, polyurethane; PO, polyolefin; FE-SEM, field emission-scanning electron microscopy; XPS, X-ray photoelectron spectroscopy; HPLC, high-performance liquid chromatography; UV–Vis, ultraviolet–visible; LOQ, limit of quantification.

* Corresponding author at: College of Pharmacy, Yonsei University, 85 Songdogwahak-ro, Yeonsu-gu, Incheon, 21983, Republic of Korea.
E-mail address: sjh11@yonsei.ac.kr (S.-J. Hwang).

http://dx.doi.org/10.1016/j.ijpharm.2017.05.040
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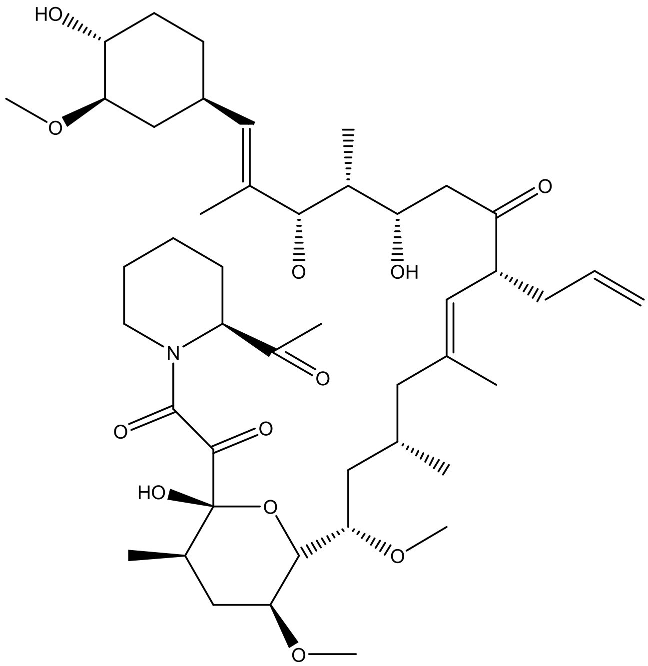

Fig. 1. Chemical structure of tacrolimus.

the flow rate and transfer the drug through the tubes. In the clinic, both techniques are widely used to deliver large-volume solutions of injectable drugs via infusion. To mimic clinically relevant systems, researchers have developed methods for kinetic sorption analysis (Jin et al., 2016, 2017; Suzuki et al., 2000).

In the present study, we reported the evaluation of tacrolimus sorption to the tubes of administration sets using pump and drip methods. Tacrolimus was selected as a model drug that should be monitored in the clinic. PVC- and non-PVC-based tubes (polyurethane [PU] and polyolefin [PO]) were used to clarify the sorption potential of tacrolimus. Inner surface properties of the tubes were evaluated using field emission- scanning electron microscopy (FE-SEM) and X-ray photoelectron spectroscopy (XPS). Tacrolimus was analyzed using high-performance liquid chromatography (HPLC). For kinetic sorption analysis, clinically used factors for tacrolimus infusion were mimicked (e.g., concentration, and flow rate). The tube length was fixed at 1 m to enable sorption levels to be easily determined. Sorption profiles were computed after subtracting the tacrolimus concentration that passed through the tubes from that in the bottle. Then, average sorption levels were then calculated.

2. Materials and methods

2.1. Chemicals

Tacrolimus (Teva Czech Industries, Czech Republic) was provided by Chong Kun Dang, Co. Ltd. (Seoul, Korea). Tacrolimus injections (5 mg/mL, total 1 mL; Tacrobel injection®, Chong Kun Dang, Co. Ltd.) and 5% dextrose solutions (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 using a Milli-Q system (Millipore Corp., Bedford, MA, USA). All other chemicals and solvents were of analytical reagent grade.

2.2. FE-SEM

The inner surface morphology of PVC- and non-PVC-based tubes was monitored using an FE-SEM (S-4200SE, Hitachi Ltd., Japan) operated at an acceleration voltage of 15.0 kV. Magnifications ranged from ×500 to ×4,000. Samples were investigated after platinum coating.

2.3. XPS

The atomic compositions of inner surface of tubes were determined using an XPS (K-Alpha, Thermo Scientific, Thermo Fisher Scientific Inc., USA) with a source of monochromated Al K-alpha. A flood gun was used for charge compensation.

2.4. Preparation of tacrolimus stock solution

Tacrolimus was weighed and dissolved in acetonitrile at a concentration of 1 mg/mL as a stock solution.

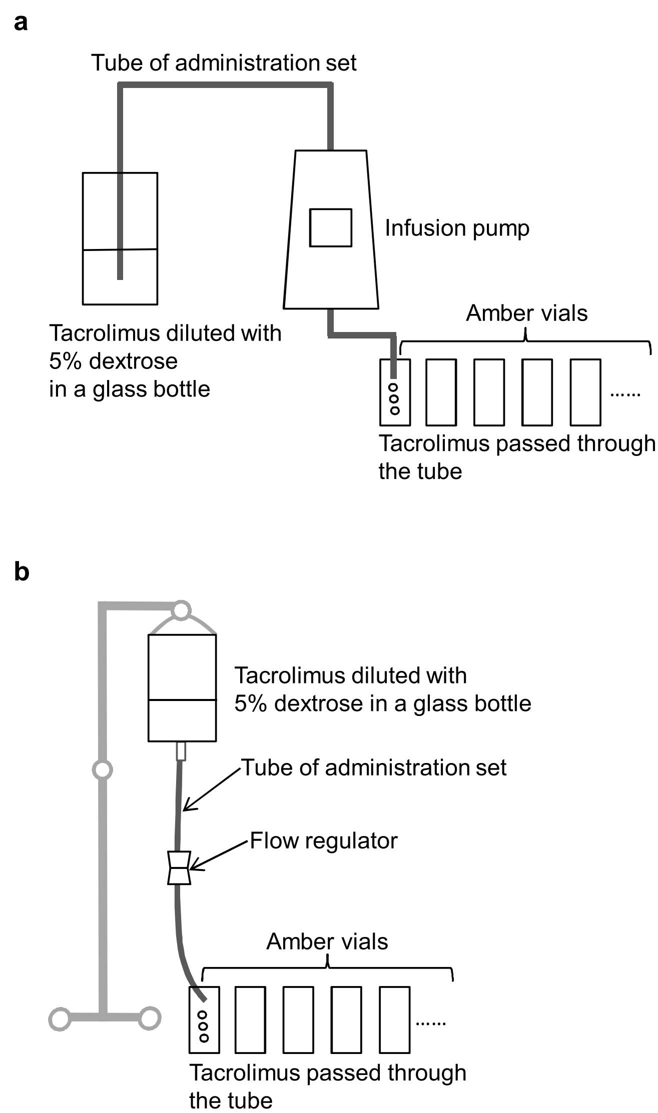

Fig. 2. Schematics of the kinetic sorption tests: (a) pump and (b) drip methods.

2.5. Determination of tacrolimus

2.5.1. Ultraviolet–visible (UV–Vis) spectroscopy

To confirm the maximum absorption wavelength of tacrolimus, the optical absorption of tacrolimus was analyzed using UV–Vis spectroscopy. Tacrolimus (0.5 mg/mL) was prepared in acetonitrile and transferred into standard cuvettes. The UV–Vis absorption spectra of the solutions were then obtained. Acetonitrile was used as a blank control. Samples were scanned at room temperature in the wavelength range of 200–800 nm. UV–Vis spectrophotometer (Cary 100 Conc, Varian, Agilent, Santa Clara, CA, USA) was used in conjunction with Cary scan application software.

2.5.2. HPLC analysis with UV detection

We previously reported an analytical method for tacrolimus (Jin et al., 2017). Briefly, tacrolimus was analyzed using an HPLC method with UV detection (Agilent 1260, Agilent). The tacrolimus stock solution was diluted to 20 μg/mL with 5% dextrose as a standard and then further diluted with 5% dextrose solution to 2.5 μg/mL. Furthermore, 10 μL of the blank (acetonitrile with 5% dextrose) and standard solutions (2.5, 5.0, 10.0, 15.0, and 20.0 μg/mL) were directly injected into the HPLC system equipped with a C_{18} column (1.5 $\times$ 250 mm, 5 μm, Shiseido, Japan) at 20°C. The mobile phase was 100% acetonitrile at a flow rate of 0.1 mL/min. Tacrolimus was detected at 213 nm. The retention time and average peak areas were recorded and analyzed using ChemStation software (Rev.B.04.03, Agilent). The run time was 10 min for each sample.

2.5.3. Specificity and sensitivity

The peak of tacrolimus was monitored to determine whether it was separated from other peaks in the chromatogram. The limit of quantification (LOQ) of tacrolimus was determined by comparison with 5% dextrose solution as a blank.

2.5.4. Linearity

Calibration standards for tacrolimus were prepared at 2.5–20.0 μg/mL. The calibration curves were constructed by plotting average peak areas vs. concentrations. A regression equation was computed.

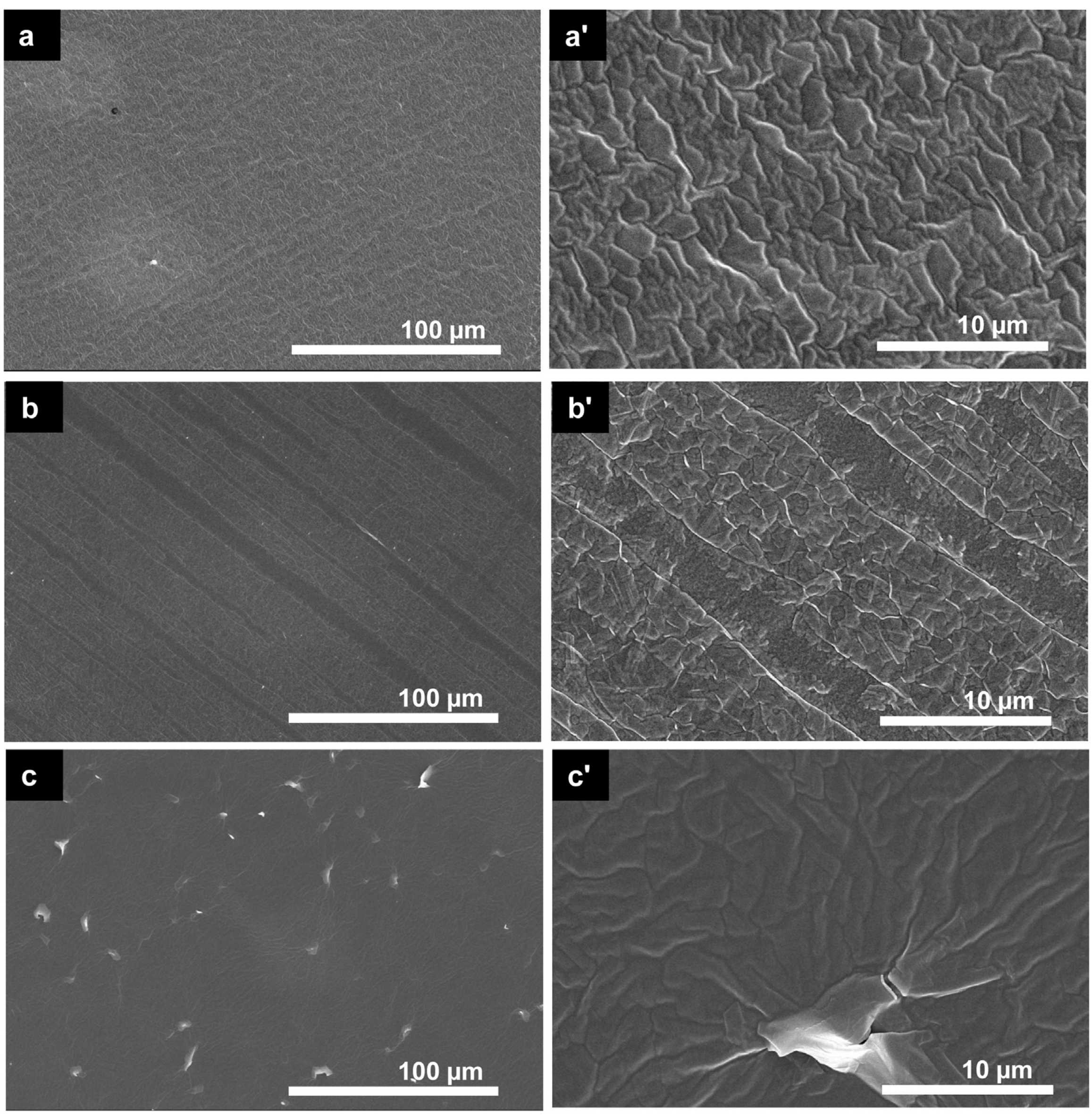

Fig. 3. FE-SEM images of the inner surface of tubes in administration sets: (aa′) PVC-, (bb′) PU-, and (cc′) PO-based tubes. The magnification ranged from $\times$ 500 (abc) to $\times$ 4,000 (a′b′c′).

2.6. Kinetic sorption study

To compare sorption evaluation methods, we determined sorption levels of tacrolimus to PVC- and non-PVC-based tubes using the peristaltic pump and drip methods. We used clinically relevant infusion factors in the kinetic sorption study (e.g., drug concentration, and flow rate). Tacrolimus sorption to administration set tubes was kinetically monitored at room temperature. All sorption materials except the tubes were removed during the study to minimize additional drug sorption.

2.6.1. Preparation of tubes of administration sets

PVC- and non-PVC-based (PU and PO) tubes were used. The inner diameters of PVC-, PU-, and PO-based tubes were 2.768, 2.699, and 2.701 mm, respectively. In the pump method, we prepared administration set tubes by removing other accessories included in the administration sets and cutting the tubes to 1 m in length using a sharp razor. In the drip method, we prepared the administration sets using 1-m tubes accessorized with a spike, air vent cap, drip chamber, and flow regulator. Flow regulators (not a roller clamp) were used to accurately control flow rates during the administration of the drug solution.

2.6.2. Preparation of diluted solution of tacrolimus

Tacrolimus injections (5 mg/mL) were diluted with 5% dextrose solution to 10 μg/mL. In this step, a glass bottle was used to prevent the additional sorption of tacrolimus in the kinetic sorption study.

2.6.3. Pump method

In each test set, a tacrolimus solution diluted in 5% dextrose was purged and preloaded into the administration set tube using a peristaltic pump (Terumo infusion pump, Terumo Medical Corp., USA), which moved fluid through a tube via intermittent squeezing. After the tube was filled with diluted tacrolimus solution, the solution was delivered through the tubes at 10 mL/h. The PVC-, PU-, and PO-based tubes were used to compare the sorption kinetics of tacrolimus according to polymer type. Samples (10 mL) were collected into amber vials at 0, 1, 2, 3, and 4 h. The sample at 0 h refers to the diluted solution of tacrolimus in the glass bottle described in Section 2.6.2. Ten-microliter samples were directly injected into the HPLC system. Analysis of tacrolimus was conducted as mentioned in Section 2.5.2.

Table 1
Atomic compositions of the inner surface of PVC- and non-PVC-based tubes in administration sets.

	Atomic composition (%)		
	PVC	PU	PO
Cl 2p	2.15	–	–
C 1s	86.21	89.39	92.84
N 1s	2.59	4.80	2.79
O 1s	8.54	5.82	4.37
Zn 2p	0.52	–	–

PVC, polyvinylchloride; PU, polyurethane; PO, polyolefin.

2.6.4. Drip method

A glass bottle containing diluted tacrolimus solution was inversely fixed and connected to one end of each tube using a spike in the administration set. The diluted tacrolimus solution was passed through the tube at 10 mL/h under the control of a flow regulator. Samples (10 mL) were immediately collected after dilution and at 1, 2, 3, and 4 h. Tacrolimus concentrations in samples were determined using the HPLC method with UV detection, as mentioned in Section 2.5.2.

2.6.5. Calculation of sorption levels

To estimate sorption levels of tubes in administration sets, we subtracted the concentrations of tacrolimus passed through the tubes from those of the diluted solution of tacrolimus injections in the bottle and then calculated percentages of the subtracted values relative to the concentrations of diluted tacrolimus solution in the bottle. The average value of the sorption level at each time point was defined as the sorption level of tacrolimus.

2.7. Statistical analysis

All results are expressed as the mean ± SD. Statistical analysis was performed using Student's *t*-test and analysis of variance. A *p*-value of <0.05 was considered significant.

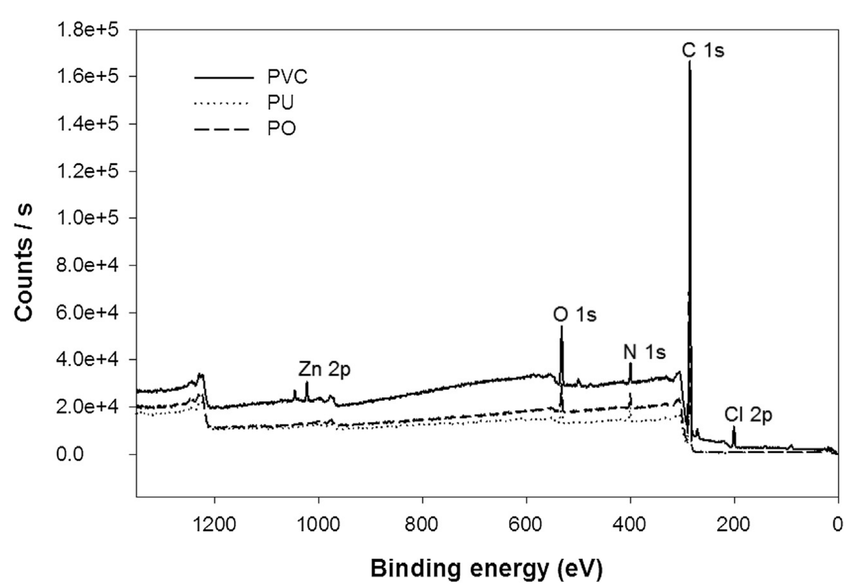

Fig. 4. XPS spectra of the inner surface of tubes in administration sets.

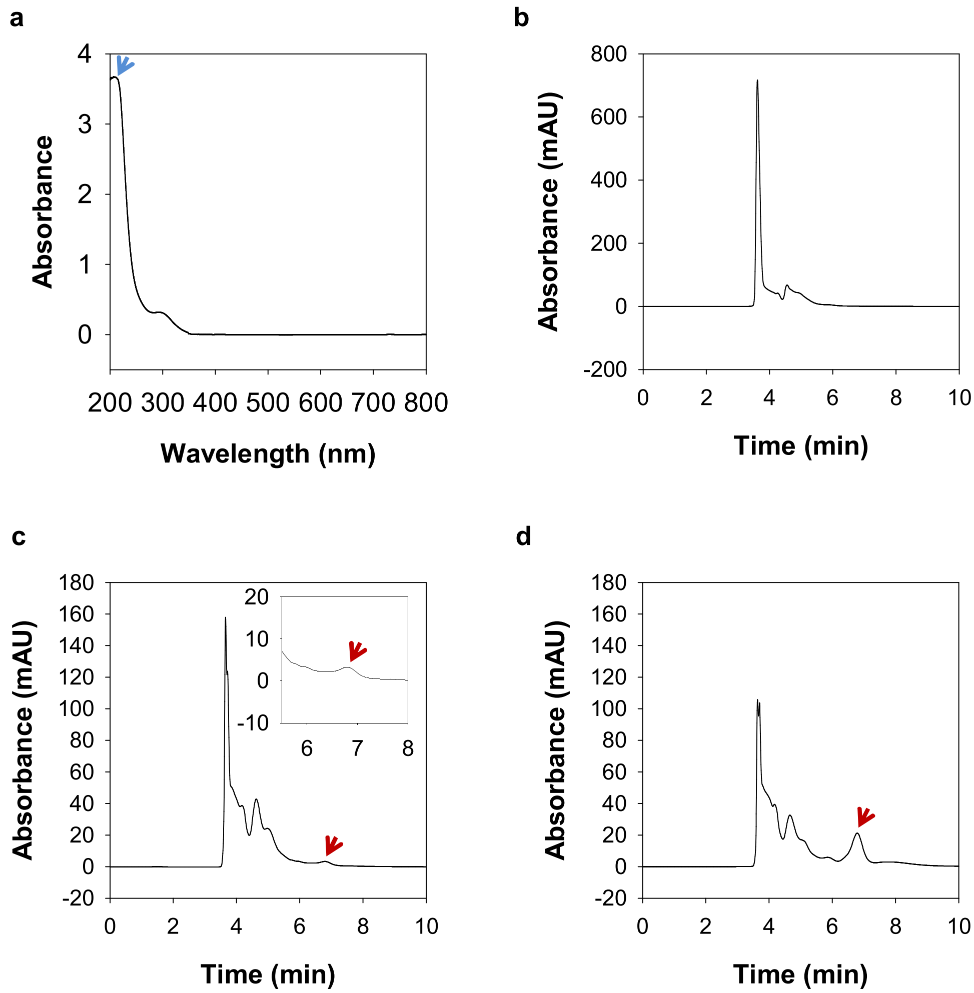

Fig. 5. Qualitative and quantitative analyses of tacrolimus: (a) UV–Vis absorption spectrum of tacrolimus at 0.5 mg/mL in acetonitrile, representative chromatograms of (b) blank and (c) tacrolimus standards at 2.5 μg/mL as the LOQ, and (d) sample (tacrolimus passed through a PO-based tube). The blue and red arrows represent λ_{max} at 213 nm and the peaks of tacrolimus at 6.8 min, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3. Results

3.1. Surface characteristics of tubes in administration sets

3.1.1. Morphology of inner surface of tubes

Fig. 3 shows FE-SEM images of inner surface of administration set tubes. Inner surface of all tubes had micrometric irregular structures that were homogeneously distributed. PVC- (Fig. 3aa′) and PU-based tubes (Fig. 3bb′) had a relatively rough and striped surface, respectively. However, PO-based tubes (Fig. 3cc′) had a smooth and soft surface with small bleb-like bumps.

3.1.2. Atomic composition of the inner surface of tubes

Fig. 4 shows the XPS spectra of the inner surfaces of tubes and Table 1 lists the atomic composition levels of the inner surfaces of tubes. In the XPS spectra, the binding energy peaks for Cl 2p, C 1s, N 1s, O 1s, and Zn 2p were located at 200, 285, 399, 531, and 1,022 eV, respectively. In PVC-based tubes, Cl 2p, C 1s, N 1s, O 1s, and Zn 2p comprised 2.15%, 86.21%, 2.59%, 8.54%, and 0.52%, respectively, of the polymer. Zn 2p was detected as a low-level impurity in PVC-based tubes. Conversely, in PU- and PO-based tubes, peaks for Cl 2p and Zn 2p were not detected. Peak levels of C 1s, N 1s, and O 1 s in PU-based tubes were 89.39%, 4.80%, and 5.82%, respectively. In PO-based tubes, C 1s, N 1s, and O 1 s were detected at levels of 92.84%, 2.79%, and 4.37%, respectively. The O 1 s peaks of the inner surface

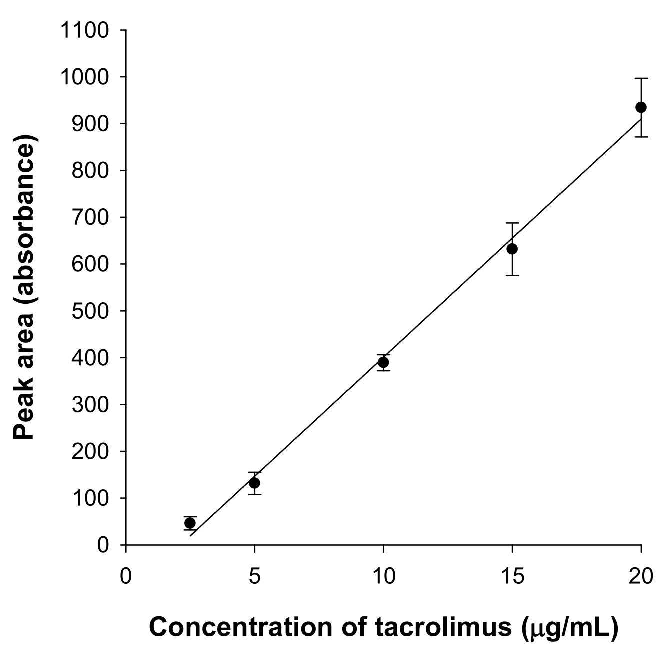

Fig. 6. The mean calibration curve of tacrolimus ranged from 2.5 to 20 μg/mL: $y = -107.75\ (\pm 23.478) + 50.875\ (\pm 1.9090)x$, $r^2 = 0.996$.

Table 2
Average sorption levels of tacrolimus passing through PVC- and non-PVC-based tubes in administration sets for 4 h.

	Average sorption level (%)		
	PVC	PU	PO
Pump method	16.5 ± 2.0	10.8 ± 2.0	1.1 ± 1.2
Drip method	24.8 ± 6.2	5.0 ± 2.0	3.0 ± 2.6

PVC, polyvinylchloride; PU, polyurethane; PO, polyolefin.

of all tubes were considered to denote surface oxidation by environmental oxygen, although the polymers were pure materials in tubes.

3.2. Tacrolimus analysis

3.2.1. Absorption spectrum

Tacrolimus displayed absorption in the wavelength range of 200–350 nm (absorption = 3.65 at λ = 200 nm; absorption = 0.01 at λ = 350 nm) (Fig. 5a). The wavelength range of maximum absorption (λ_{max}) was 200–213 nm (absorption = 3.65 at λ_{max} = 200–213 nm).

3.2.2. Specificity and sensitivity

Compared with peaks in the chromatogram of the blank sample (Fig. 5b), the peak of tacrolimus, which was detected at a retention time of 6.8 min, was successfully separated (Fig. 5c–d). LOQ was 2.5 μg/mL, corresponding to a signal-to-noise ratio exceeding 10 (Fig. 5c). No peaks overlapped that of tacrolimus in the chromatogram (Fig. 5d).

3.2.3. Linearity

The absorbance of tacrolimus was linear over the concentration range of 2.5–20 μg/mL (Fig. 6). The average calibration curve for tacrolimus was $y = -107.7488\ (\pm\ 23.4779) + 50.8751\ (\pm\ 1.9090)x$, with $r^2 = 0.996$.

3.3. Sorption evaluation of tacrolimus: pump method vs. drip method

Both pump and drip methods were used to monitor sorption levels of tacrolimus, and results were compared. Table 2 lists the average sorption levels at 4 h determined using both methods. In PVC-based tubes, sorption levels determined by the pump method were lower than those determined by the drip method. However, in PU-based tubes, sorption levels determined by the pump method were higher than those determined by the drip method. PO-based tubes exhibited sorption levels of less than 10%. In particular, in PO-based tubes, all sorption levels at 1–4 h determined using the pump method were < 5.0%. From results using both methods, average sorption levels were the highest in PVC-based tubes and the lowest in PO-based tubes. Results are comparable to the roughness of tubes in administration sets from FE-SEM results.

3.3.1. Pump method

Tacrolimus sorption in PVC- and non-PVC-based tubes was evaluated at 1–4 h using the pump method (Fig. 7a). Levels of tacrolimus delivered after passing through PVC- and PU-based tubes were 81–85% and 87–91%, respectively. However, tacrolimus sorption levels in PO-based tubes ranged 0.7–1.8%, which were negligible.

3.3.2. Drip method

Tacrolimus sorption was also evaluated using the drip method (Fig. 7b). In PVC-based tubes, the delivered amounts of tacrolimus were 61–89%. After 1 h in the kinetic sorption test, which

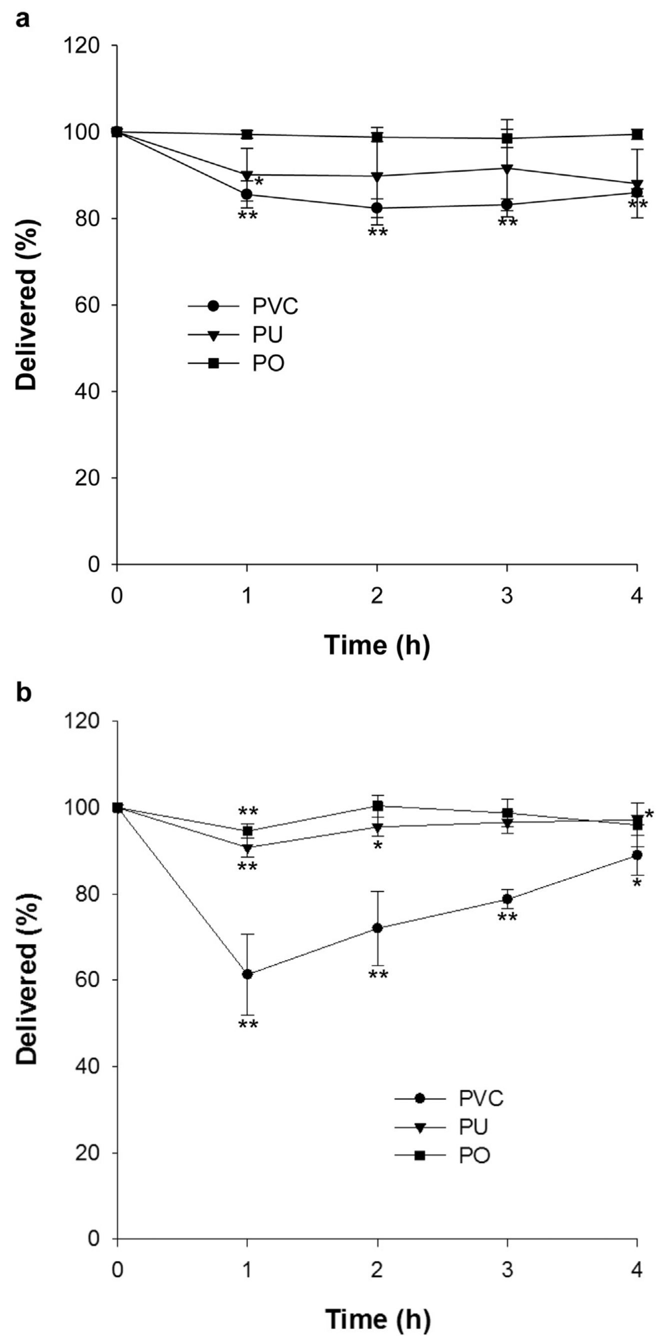

Fig. 7. Tacrolimus levels in administration set tubes, as evaluated using (a) the pump and (b) drip methods ($p < 0.05$, *; $p < 0.01$, **).

represents the early phase of the sorption study, sorption levels in PVC-based tubes were as high as 39%, which was the highest among the three tube types. By contrast, non-PVC-based tubes (PU, 9.3%; PO, 5.5%) had lower sorption levels than PVC-based tubes at 1 h. Sorption levels in PU- and PO-based tubes were 2.8–9.3% and 0.7–5.5%, respectively.

4. Discussion

Drug sorption results in drug partitioning on polymeric materials of tubes in administration sets via both adsorption and absorption, which can cause additional and unpredicted drug loss in the clinic (Treleano et al., 2009). Its occurrence depends on various factors including the properties of drugs and polymeric materials. First, sorption can be explained on the basis of the physicochemical properties of drugs such as their hydrophobicity (log *P*) and partition coefficient (Jin et al., 2016). Polymeric materials in administration set tubes also affect drug sorption behavior (Aloumanis et al., 2009; Treleano et al., 2009; Trissel et al., 2006). PVC-based materials used in administration sets (Roberts, 1996; Treleano et al., 2009) and plastic bags (Aloumanis et al., 2009; Jenke, 1993; Kambia et al., 2005; Martens et al., 1990; Roberts et al., 1991) have been reported to exhibit high sorption potential. However, in administration sets, non-PVC-based materials such as PO generally exhibit low sorption potential compared with PVC materials (Aloumanis et al., 2009; Jin et al., 2016; Treleano et al., 2009; Trissel et al., 2006). Thus, drug sorption to administration set tubes should be evaluated and minimized using an alternative material or design. In this study, we investigated drug sorption in administration set tubes using pump and drip methods.

Tacrolimus (Fig. 1) was selected as a model drug for sorption evaluation (Suzuki et al., 2000). It is an immunosuppressive drug for organ transplantation with a narrow therapeutic index, and it is infused at low concentrations in the clinic (Diehl et al., 2016; Lancia et al., 2015; Lei et al., 2013). Because tacrolimus concentration must be accurately and precisely monitored, its sorptional loss to the tubes can cause problems related to drug safety and efficacy (Shibata et al., 2000). Based on previous reports, after passing through a 1-m-long PVC-based tube at 5.0 mL/h, diluted tacrolimus solution from Prograf® (Astellas Pharma, USA) at 50 μg/mL was delivered up to 76% and di-2-ethylhexyl phthalate (DEHP) was leached at 12 μg/mL/h because of polyoxyethylated castor oil 60 (HCO60), a surfactant in the formulation (Suzuki et al., 2000). Continuous drip infusion was used to evaluate tacrolimus sorption using Prograf®.

Using pump (Jin et al., 2016) and drip methods (Kawano et al., 1992) (Fig. 2), we evaluated drug sorption to tubes under clinically relevant conditions. Pump (Fig. 2a) and drip methods (Fig. 2b) are widely used infusion techniques. In general, the pump method is recommended for tacrolimus infusion in the clinic because the clinically used infusion rate of tacrolimus, 10 mL/h, is relatively low (Shibata et al., 2000). The drip method is also performed at medium to high flow rates without a pump (Kawano et al., 1992). In the drip method, a flow regulator can be used (instead of a screw clamp) as a quantitative controller in administration sets. Tacrolimus sorption to other accessories of administration sets such as spikes and drip chambers should be minimized in both methods.

The interaction between a drug and the inner surface of a tube is an essential factor that explains drug sorption to tube of administration set. Regarding the physicochemical properties of polymeric materials, the inner surface properties of tubes were determined and clarified using FE-SEM (Zhou et al., 2016) and XPS (Awaja et al., 2013). FE-SEM images reflect the morphology and roughness of the inner surfaces of tubes (Fig. 3). Roughness levels of the inner surfaces were in the order of PVC > PU > PO, suggesting their interaction levels with drugs and their sorption potential. In the XPS spectra, inner surfaces of PVC-based tubes were composed of Cl 2p, C 1s, N 1s, O 1s, and Zn 2p, compared with C 1s, N 1s, and O 1 s for PU- and PO-based tubes (Fig. 4). The atomic compositions of the inner surfaces of tubes matched the chemical formula with the responses by environmental gases (Plackowski et al., 2014) and without impurities excluding PVC-based tubes (Table 1).

Tacrolimus was analyzed using HPLC with UV detection (Jin et al., 2017; Taormina et al., 1992). On the basis of the UV–Vis spectrum of tacrolimus, the maximum absorption wavelength of 213 nm was selected for the HPLC analysis of tacrolimus to enhance specificity and sensitivity (Fig. 5a). Before analyzing tacrolimus in samples, we conducted a simple validation based on specificity, sensitivity, and linearity. The developed method was specific and sensitive for tacrolimus (Fig. 5b–d), which was detected at 2.5 μg/mL as LOQ with no interfering peaks. Although the column was not heated to 70°C, LOQ was similar to that for a previously reported HPLC method (Taormina et al., 1992). The calibration curve for tacrolimus was confirmed to be linear over the concentration range of 2.5–20 μg/mL (r^2 = 0.996) (Fig. 6). Tacrolimus in samples was analyzed within the concentration range of the calibration curve without further dilution.

In the kinetic sorption study, sorption levels in PVC- and non-PVC-based tubes (i.e., PU- and PO-based tubes) were estimated using the pump method (Fig. 7a) (Jin et al., 2016, 2017) and drip methods (Fig. 7b) (Kawano et al., 1992). Results for both methods illustrated tacrolimus sorption to all tube types of administration sets (PVC > PU > PO) (Table 2). In the drip experiments, tacrolimus was highly sorptive to PVC-based tubes (24.8 ± 6.2%), in line with the previously reported sorption result for tacrolimus at a concentration of 50 μg/mL and flow rate of 5.0 mL/h (24%) (Suzuki et al., 2000). Tacrolimus sorption was also detected in non-PVC-based tubes (PU, 5.0 ± 2.0%; PO, 3.0 ± 2.6%) using the drip method, although sorption levels were much lower than those in PVC-based tubes. Compared with the drip method, the pump method more effectively transferred drug solution (PVC, 16.5 ± 2.0%; PU, 10.8 ± 2.0%; PO, 1.1 ± 1.2%). Specifically, in PVC-based tubes, sorption levels determined by the drip method were higher than those determined by the pump method in the early phase of the kinetic sorption study. Sorption levels of PO-based tubes were also negligible from the pump method (Table 2).

Tacrolimus is generally administered at low concentrations to patients, as the drug has a narrow therapeutic index as previously mentioned (Diehl et al., 2016; Lancia et al., 2015). In this case, tacrolimus sorption to administration set tubes can extensively affect drug safety and efficacy based on its sorptional loss. Consequently, tacrolimus sorption to the tubes should be evaluated to qualify and endorse the administration sets (Jin et al., 2017). In the present work, clinically used simple infusion using the pump and drip methods were mimicked to evaluate tacrolimus sorption to administration set tubes. Several factors such as tube length and flow rate were fixed to minimize conditional variation in the experiments. Sorption levels of tube materials (e.g., PVC, PU, and PO) were successfully evaluated using our developed method (Jin et al., 2016, 2017). Newly developed components or designs for the tubes included in administration sets could also be evaluated using the present methods (Aloumanis et al., 2009; Kambia et al., 2005).

5. Conclusion

We evaluated tacrolimus sorption to administration set tubes using the pump and drip methods. The pump method was found to be advantageous over the drip method because of a low flow rate of tacrolimus. Using both methods, the results indicated that sorption levels in PVC-based tubes were higher than those in non-PVC-based tubes. Among the tubes, the PO-based tubes showed the lowest sorption levels (< 10.0%). Results suggested that the pump method can be adopted to evaluate the compatibility of polymeric materials in administration set tubes. In addition, PO, as an alternative tube material, has strong potential to minimize drug sorption to tubes of administration sets.

Funding

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).

Conflict of interest

The authors declare no conflicts of interest.

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