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Extended delivery of non-steroidal anti-inflammatory drugs through contact lenses loaded with Vitamin E and cationic surfactants

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ABSTRACT

The purpose of this study is to extend drug release from ACUVUE Oasys® and ACUVUE TruEye® silicone hydrogel contact lenses by incorporation of vitamin E in conjunction with a cationic surfactant. In ACUVUE Oasys® and ACUVUE TruEye®, the release of ketorolac tromethamine and flurbiprofen sodium is extended from hours to several days for 11% and 21% vitamin E, *(weight of vitamin E / weight of dry lens)* but with a considerable reduction in the amount of drug released. Cetalkonium chloride and stearylamine increased the drug loading capacity which was otherwise compromised by the addition of vitamin E in the contact lenses. In the case of diclofenac sodium, a sustained release over 150 h for both contact lenses can be achieved. It was found that the release-time-increase factor due to vitamin E has a linear dependence with the octanol-water partition coefficient of the drug in ACUVUE Oasys®. The results in this study show that contact lenses loaded with vitamin E in conjunction with cationic surfactants achieved sustained release of non-steroidal anti-inflammatory drugs (NSAIDs) within the therapeutic window.

1. Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are currently considered alternatives to topical corticosteroids in managing ocular inflammatory conditions because they are not burdened with possible increase in intraocular pressure (IOP) and risk of infection due to the suppression of the ocular immune system [1]. As a class of anti-inflammatory drugs that are often used topically in ophthalmologic surgery [2], NSAIDs work by inhibiting the cyclooxygenase enzymes that catalyze the formation of prostaglandins and thromboxanes [3].

Topical delivery *via* eye drops accounts for approximately 90% of all ophthalmic formulations [4] owing to simplicity of formulation development and production and general good acceptance by patients. However, eye drops are very inefficient, suffering from tear drainage in addition to corneal and sclera barriers. It is stated that eye drops could deliver only about 5% of functional ingredients contained in a burst dosage [4,5].

In order to address the limitations of eye drops, researchers have explored the use of therapeutic contact lenses [6–9]. When contact lenses containing ophthalmic drugs are placed on the eye, the drug diffuses through the lens matrix and enters the post-lens tear film, where drug molecules have a longer residence time and more direct path than eye drops [10]. However, a major limitation of contact lenses is that most of the drug absorbed is often released within the first few hours [4,5,11].

Several methods have recently been employed to increase the release duration of drugs, including nanoparticle-based contact lenses [12], biomimetic and imprinted contact lenses [13,14], and layer-structured contact lenses [15]. Recently, Chauhan and his group of researchers have developed an approach to extend the release of several hydrophilic drugs through the use of vitamin E lipophilic barriers [4,5,11–16]. Paradison et al. [10] demonstrated that hydrophilic antibiotics can be released from silicone-hydrogel contact lenses in days instead of hours. Vitamin E as a diffusion barrier has also been tested in poly-(2-hydroxy-ethyl methacrylate) hydrogel contact lenses (pHEMA) [17]; however, it improved the drug loading capacity but did not prolong the release duration.

Vitamin E (α-tocopherol) functions in humans as a fat-soluble antioxidant. In addition, *in vivo* studies have demonstrated its potential effect in inhibiting keratocyte apoptosis after surgery, retarding cataract development, and preventing glaucoma [4,18]. The safety and therapeutic efficacy of vitamin E loaded contact lenses have also been

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demonstrated through *in vivo* studies in Beagle dogs for the treatment of glaucoma [11].

To further explore the modifications of microenvironment in a contact lens to better control a drug's loading capacity and release rate, two cationic surfactants were incorporated in vitamin E-loaded contact lenses. Cetalkonium chloride (CKC) is a quaternary ammonium cationic surfactant with an alkyl group having a chain length of 16 carbons, and is often used in commercial ophthalmic solutions. It has been used in the development of stable oil-in-water nanoemulsions for topical ophthalmic drug delivery, proving to have additional benefits in the protection and restoration of a healthy tear film and corneal epithelium [19]. In pHEMA contact lenses, CKC increased both loading capacity and release duration of dexamethasone 21-disodium phosphate. In addition, CKC improved wettability, water content, and decreased protein absorption in the contact lenses [20]. Stearylamine is a primary amine cationic surfactant used in the fabrication of cationic lipid carriers for ocular drug delivery [21–23]. It prolonged the pre-corneal retention time of ibuprofen through nanostructured lipid carriers [23].

This paper systematically studies the integration of three NSAID drugs: ketorolac tromethamine, flurbiprofen sodium and diclofenac sodium into commercially available silicone hydrogel contact lenses. It is demonstrated that the release duration of the drugs from commercial silicone hydrogel contact lenses can be extended to several days and the extension factors are well correlated with the drugs' hydrophobic affinity, log *P* (partition coefficient in octanol and water). Furthermore, with the incorporation of cationic surfactants in vitamin E-loaded contact lenses, both loading capacity and drug release duration can be controlled. This study gives the option to design the modifications of a contact lens microenvironment for controlling a contact lens' drug delivery to be within an ideal time and therapeutic windows to treat ophthalmic diseases.

2. Materials and methods

2.1. Materials

Two commercial silicone hydrogel contact lenses (diopter -6.50) are used in this study: (ACUVUE Oasys® and ACUVUE TruEye®). ACUVUE Oasys® 1-week overnight and ACUVUE Oasys® 2-week were used. The information about these lenses is outlined in Table 1. Ketorolac tromethamine (KTH) secondary standard, diclofenac sodium salt (DFNa) analytical standard, vitamin E (α-tocopherol ≥ 95.5%), Dulbecco's phosphate buffered saline (PBS) and stearylamine (97%) were purchased from Sigma Aldrich (Sigma-Aldrich Corp, St. Louis, MO). Flurbiprofen sodium (FBNa) reference standard was purchased directly from the United States Pharmacopeia (USP, Rockville, MD). Ethanol (≥ 99.5) was purchased from Pharmco. Cetalkonium chloride was purchased from Toronto Research Chemicals.

2.2. Vitamin E loading into pure lenses

The commercial contact lenses were rinsed with deionized water and then air-dried before use. ACUVUE Oasys® 1-week overnight contact lenses were soaked in 3 mL of 25 mg/mL or 45 mg/mL vitamin E in ethanol. ACUVUE TruEye® contact lenses were soaked in 3 mL of 30 mg/mL or 49 mg/mL vitamin E in ethanol. The soaking duration was 24 h and at room temperature. Following the loading step, the contact lenses were taken out and excess vitamin E-ethanol solution was blotted out from the lens surface, and the lens was air-dried overnight. Based on prior work related to vitamin E-loaded contact lenses, it was assumed that after air-drying overnight, all the ethanol left in the contact lenses would be evaporated [4,5,10,24]. The loading amount of vitamin E was determined by weighing the dry lens before and after the vitamin E loading period using an analytical balance with 0.1 mg readability.

2.3. Vitamin E loading with cetalkonium chloride and stearylamine

Vitamin E was loaded in the silicone hydrogel contact lenses as described in Section 2.2, but this time two different amounts of surfactants were dissolved in the vitamin E-Ethanol solutions. ACUVUE Oasys® 2-week use contact lenses were soaked in 4 mL of 20 mg/mL or 50 mg/mL vitamin E/Ethanol solutions with either 2 or 4 mg of CKC or stearylamine. (0.05 or 0.1% w/v) ACUVUE TruEye® contact lenses were soaked in 4 mL of 25 mg/mL or 55 mg/mL vitamin E/Ethanol with the same amounts of CKC or stearylamine. Control silicone hydrogel contact lenses were soaked in the same vitamin E/Ethanol concentrations but without surfactants. The soaking duration was 24 h and at room temperature. After loading period, the lenses were gently blotted and dried overnight for the subsequent drug loading step.

2.4. Drug loading into pure lenses

The NSAIDs studied are summarized in Table 2. The effective dosages and solubility in PBS are different and therefore the concentrations of the loading reservoirs vary. Before use, the commercial contact lenses were rinsed with deionized water and air-dried overnight. KTH was loaded by soaking the lenses in 3 mL of a 1.2 mg/mL drug-PBS solution, DFNa was loaded by soaking the lenses in 3 mL of a 0.2 mg/mL drug-PBS solution and FBNa was loaded by soaking the lenses in 3 mL of a 0.2 mg/mL drug-PBS solution. The soaking duration of the pure lenses was for 24 h and at room temperature. Following the loading period, the lenses were taken out and excess drug solution on the surface was removed by blotting with filter paper.

2.5. Drug loading into Vitamin E loaded lenses

The three drugs were loaded in the vitamin E loaded lenses in 3 mL of drug-PBS solution for 7 days and at room temperature. The drug concentrations used in Section 2.4 were used in this section. Three contact lenses per case were used for the drug loading step in this section and in Section 2.4. After the drug loading step, lenses were tested in *in vitro* release experiments.

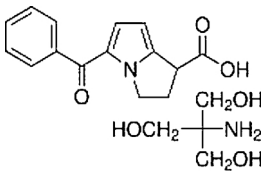
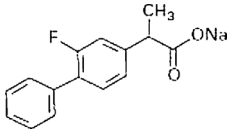
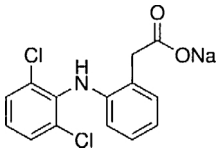
2.6. Drug release experiments

The drug release experiments were carried out by soaking the drug loaded lenses in 3 mL of Dulbecco PBS at pH 7.4 and at room temperature. During the release experiments, 1 mL of release sample was removed at predetermined time intervals, and 1 mL of fresh PBS was refilled into the release medium. The amount of drug released was calculated using a UV-Spectrophotometer (Varian Cary 50 Bio) at wavelengths of 322 nm for KTH, 276 nm for DFNa and 248 nm for FBNa.

Table 1
Contact lenses studied in this paper.

	ACUVUE Oasys®	ACUVUE TruEye®
Main component	Senofilcon A	Narafilcon A
Manufacturer	Johnson & Johnson Vision Care	Johnson & Johnson Vision Care
Intended use	1 week overnight or 2 weeks	1 day
Water Content	38%	46%
Oxygen Transmissibility Dk/t (10^{-9} (cm ml O_2)/(ml sec mmHg)).	147	118

Table 2
Water solubility and log P for each tested NSAID drug were obtained from DrugBank (water solubility from ALOGPS source and log P from ChemAxon source).

Drug	Chemical formula	Water solubility (mg/mL)	*log P*
Ketorolac tromethamine		0.861	2.28
Flurbiprofen sodium		0.013	3.94
Diclofenac sodium		0.00482	4.26

The drug release experiments were performed in triplicate for each different case.

3. Results

3.1. Vitamin E loading in contact lenses

For the silicone hydrogel contact lenses in this study, the amount of vitamin E loaded is linearly proportional to the vitamin E-ethanol soaking solution concentration. However, they showed different vitamin E absorption. Oasys® 1-week overnight has a slightly higher affinity for vitamin E than TruEye®. For Oasys®, soaking concentrations of 25 mg/mL and 45 mg/mL vitamin E-ethanol signified a vitamin E weight percent in the lenses of approximately 10.8% and 21.1% (wt. / wt. of dry lens) respectively; while for ACUVUE TruEye®, soaking concentrations of 30 mg/mL and 49 mg/mL vitamin E ethanol signify a vitamin E weight percent in the lenses of approximately 12.0% and 21.4% respectively.

3.2. Drug release from Vitamin E-loaded contact lenses

In order to evaluate the effect of the vitamin E loading on the release duration, two different vitamin E concentrations were used. Loadings of less than 10% of vitamin E were not used since these have been reported to have a negligible effect in prolonging release time [10]. ACUVUE Oasys® 1-week is a contact lens for overnight use and ACUVUE TruEye® is a daily disposable contact lens; this is amongst the most popular brands for daily wear.

Several authors have compared drug release durations when 70 or 90% of the loaded drugs have been released from the contact lenses [10,14,24]. In this study, "t_{80}" is defined as the time that it takes a contact lens to release 80% of the amount of drug loaded. Fig. 1 shows that Oasys® and TruEye® had a t_{80} of approximately 1.5 and 13 h respectively. Oasys® with 11% and 21% Vitamin E loading had a t_{80} of 30 h and 70 h respectively compared to 1.5 h from the control lenses. This indicates an increase in the release duration by factors of approximately 20 and 45. Additionally, the amount of drug delivered was influenced by the incorporation of vitamin E. It decreased from 133 µg for the control to 110 µg and 88 µg for 11% and 21% vitamin E respectively. In the case of TruEye®, with 12% and 21% vitamin E loadings, contact lenses had a t_{80} of 100 and 150 h respectively, compared to 13 h of the control lens. This is an increase in the release duration by a factor of approximately 8 and 11 respectively. Furthermore, the amount of KTH released was further compromised for TruEye® compared to Oasys®. It decreased from 129 µg for the control to 91 µg and 42 µg for 12% and 21% vitamin E loadings respectively.

From these findings, it was concluded that the effect of vitamin E on extending KTH release is more significant in Oasys® contact lenses than in TruEye® contact lenses, which agrees with the results from previous studies [10,24].

For the case of FBNa, contact lenses had a t_{80} of 6 and 20 h for Oasys® and TruEye® controls respectively. For Oasys®, t_{80} was approximately 30 h and 80 h for vitamin E loadings of 11% and 21% respectively. This signifies an increase in the release duration by factors of approximately 5 and 12 for each case. For TruEye®, t_{80} was 90 h and 110 h for 12% and 21% vitamin E respectively. This signifies an increase by a factor of 4.5 and 5.5 for each case respectively, but with a considerable difference in the amount of FBNa released between the two vitamin E loadings.

Regarding the amount of FBNa released in Oasys®, it decreased from 109 µg for the control to 100 µg and 89 µg for 11% and 21% vitamin E loading respectively. However, for TruEye®, it decreased from 99 µg for the control to 84 µg and 51 µg for 12% and 21% vitamin E loading respectively.

As in the case of KTH, the amount of drug delivered is more impacted in TruEye® than in Oasys®. The incorporation of vitamin E increases the hydrophobicity in the lens matrix, hence decreasing the solubility of all hydrophilic compounds with higher impact towards more hydrophilic drugs [24]. Therefore, a greater impact was expected

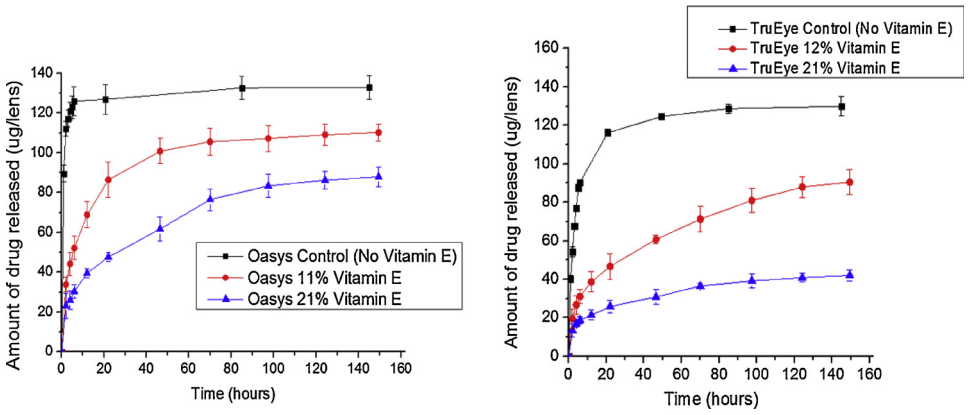


Fig. 1. Amount of KTH released from the commercial contact lenses under two different vitamin E loadings. 1-A (left) Oasys® and 1-B (right) TruEye®. Data are presented as mean ± SD with n = 3.

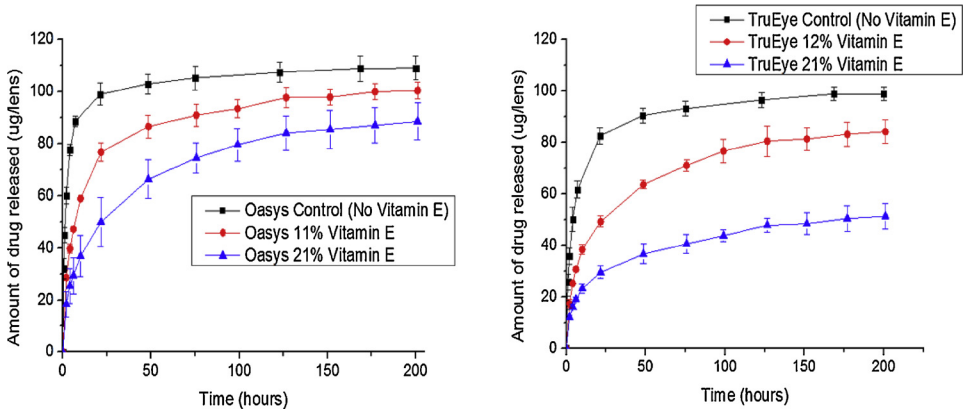


Fig. 2. Amount of FBNa released from the commercial contact lenses under two different vitamin E loadings. 2-A (left) Oasys® and 2-B (right) TruEye®. Data are presented as mean ± SD with n = 3.

Table 3
Amount of DFNa released from the commercial contact lenses under two different vitamin E loadings. Data are presented as mean ± SD with n = 3.

	% Vitamin E loading	Amount of drug released after 50 hours (μg/lens)	Amount of drug released after 100 hours (μg/lens)	Amount of drug released after 200 hours (μg/lens)
Oasys	0	168.3 ± 3.0	188.9 ± 6.2	209.7 ± 7.3
	11	128.9 ± 2.9	157.4 ± 4.8	179.2 ± 3.6
	21	106.4 ± 2.7	130.4 ± 3.1	157.3 ± 2.2
TruEye	0	119.4 ± 3.5	141.2 ± 0.2	161.4 ± 6.3
	12	100.5 ± 1.0	123.2 ± 1.4	153.1 ± 2.4
	21	73.6 ± 5.0	87.5 ± 2.2	107.2 ± 2.1

Table 4
Total amount of KTH released under different vitamin E and cationic surfactant loadings in ACUVUE Oasys® and TruEye®. Data are presented as mean ± SD with n = 3.

	% Vitamin E loading	Cationic surfactant concentration (%)	Total amount of drug released (μg/lens)
Oasys	0	0	111.8 ± 1.9
	8.5	0	107.3 ± 0.4
		0.05% CKC	122.9 ± 0.7
		0.1% CKC	135.5 ± 1.7
	23	0	98.9 ± 1.0
		0.05% CKC	124.7 ± 4.7
		0.1% CKC	146.0 ± 4.5
		0.05% stearylamine	129.2 ± 7.8
		0.1% stearylamine	164.1 ± 1.0
TruEye	0	0	126.6 ± 1.5
	10.5	0	84.4 ± 2.6
		0.05% CKC	111.7 ± 9.7
		0.1% CKC	147.6 ± 4.6
	26.5	0	48.9 ± 1.0
		0.05% CKC	70.0 ± 2.7
		0.1% CKC	92.5 ± 3.3
		0.05% stearylamine	95.1 ± 2.5
		0.1% stearylamine	144.9 ± 9.9

in KTH release duration since it is hydrophilic, unlike FBNa.

It should be noted that unlike Oasys®, TruEye® is a daily-disposable contact lens. For the case of Oasys®, the goal is to maintain a sustained release for at least 1 week. Figs. 1 and 2 show that this is only possible at high vitamin E loadings, which might affect critical lens properties. However, for the case of TruEye®, t_{80} for unmodified contact lenses is 13 and 20 for KTH and FBNa respectively. This means that only low vitamin E loadings should be necessary to achieve a controlled daily release of KTH or FBNa and meet the daily-disposable requirement of TruEye®.

Table 3 describes the drug release kinetics of DFNa. The sustained drug release time period is longer than with the two preceding drugs. It is hypothesized that interactions between the drug and the silicone gel matrix could be a factor in prolonging the release of DFNa. With DFNa, a sustained release over 150 h can be achieved which agrees with a study that evaluated the impact of sterilization methods in the release of DFNa from silicone hydrogel contact lenses [25]. Regarding the amount of DFNa released, there is equivalent influence of vitamin E in Oasys® to the delivery of DFNa compared to KTH and FBNa. In TruEye®, a vitamin E loading of 21% significantly decreases the amount of drug released compared to that of the control, which agrees with the trend

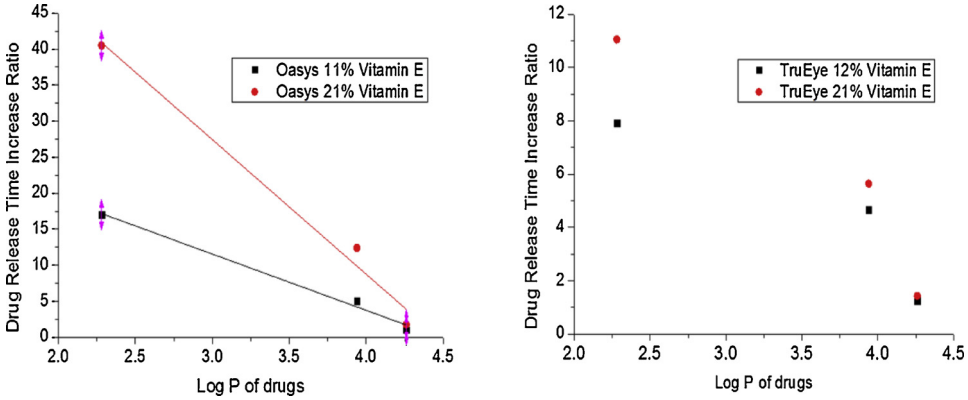


Fig. 3. Drug Release Time Increase Ratio plotted against the logarithm of the partition coefficient for each drug studied. 4-A (left) Oasys® and 4-B (right) TruEye®. Data are presented as mean ± SD with n = 3.

Table 5
Calculated therapeutic dosage for NSAID commercial clinical treatment considering a 50 µL drop size, a 5% bioavailability with topical eye drops and a 50% bioavailability with contact lenses.

Drug	Commercial brand	Treatment for	Therapeutic treatment	Calculated equivalent dosage rate from contact lens delivery (µg/hr)
Ketorolac Tromethamine	ACULAR LS (0.4 % ophthalmic solution	Ocular pain after corneal refractive surgery	One drop four times a day, for a period of 4 days. [27]	3.30
Diclofenac sodium	VOLTAREN (0.1 % ophthalmic solution	Postoperative inflammation after cataract surgery	One drop four times a day, for a period of 2 weeks [28]	0.80
Flurbiprofen sodium	OCUFEN (0.03 % ophthalmic solution	Postoperative inflammation after cataract surgery	One or two drops four times a day, for a period of 1-3 weeks [29]	0.25-0.5

discussed in previous sections.

3.3. Effect of Vitamin E diffusion barrier on different drugs

After observing differences in release time of each drug with the same loading concentration of the vitamin E barrier, an analysis was conducted to correlate the extended delivery of each drug with its respective solubility properties. The octanol-water partition coefficient (log *P*) was used for each drug, a widely utilized parameter in pharmaceutical studies, to distinguish its affinity with vitamin E.

The octanol-water partition coefficient has been a common parameter to study the lipophilic character of drug compounds and the correlation of lipophilicity to pharmacokinetics and pharmacodynamics [26]. Log *P* is extensively used in pharmaceutical industries to understand how well a drug performs in human trials. A hydrophobic drug, having a higher log *P*, is expected to be released from a lens to the PBS media slower than a hydrophilic drug, which agrees with the obtained experimental results.

Fig. 3 describes an analysis based on the drug-release-time-increase factor, which is the ratio of the drug release time period under a specific vitamin E loading, over the drug release time period without any vitamin E. For Oasys®, a linear relationship was found between the drug-release-time-increase factor against the log *P* of the three studied drugs. However, for TruEye®, linear relationships were not observed for the Vitamin E loadings described.

3.4. Ketorolac tromethamine release from Vitamin E-surfactant loaded contact lenses

As discussed in previous sections, the total amount of drug released is compromised by the increasing weight percent of vitamin E, especially for ACUVUE TruEye®. Paradiso et al [10] utilized vitamin E loaded commercial silicone hydrogel lenses to extend drug release of levofloxacin and chlorhexidine and found that higher amounts of vitamin E significantly reduced the loading capacity of chlorhexidine. Hsu et al. [24] found that vitamin E loaded commercial silicone hydrogel lenses extended the release of dexpanthenol and betaine with either a moderate or a significant decrease in the loading of these therapeutic agents due to vitamin E addition.

To overcome this limitation, cationic surfactants were incorporated with vitamin E to compensate for the reduced drug loading capacity due to the presence of vitamin E barrier layers. Two different surfactant loadings were studied to evaluate the effects of the surfactant concentration on drug's loading capacity and release duration. The obtained results showed that the increase in the amount of drug delivered is directly proportional to the amount of surfactant added to the lenses. Cetalkonium chloride is a cationic surfactant that when used in conjunction with an anionic drug, proved to increase the drug loading capacity and release duration in pHEMA contact lenses due to the electrostatic interaction of the head group of the surfactant with the drug [20]. In this study, it is shown that CKC can be used to increase the amount of KTH delivered in silicone hydrogel contact lenses when drug loading capacity is compromised by the duration-prolonging vitamin E.

From Table 4, for Oasys® 2-week under 8.5% vitamin E loadings, the amount of KTH released can be increased by approximately 15 and 25% for 0.05% and 0.1% CKC respectively.

There is a greater effect of the surfactant inclusion in TruEye®. Drug loading capacity lost due to addition of the vitamin E diffusion barriers can be overcome by increasing the amount of KTH released from 84 µg to 112 µg and 148 µg with inclusion of 0.05% and 0.1% CKC respectively.

Under higher loadings of vitamin E, the effect of CKC can be even more beneficial to increase the drug loading capacity. For Oasys® 2-week under 23% vitamin E, the amount of KTH released can be increased by approximately 25 and 45% for 0.05% and 0.1% CKC respectively. For TruEye® under 26.5% vitamin E, the total amount of

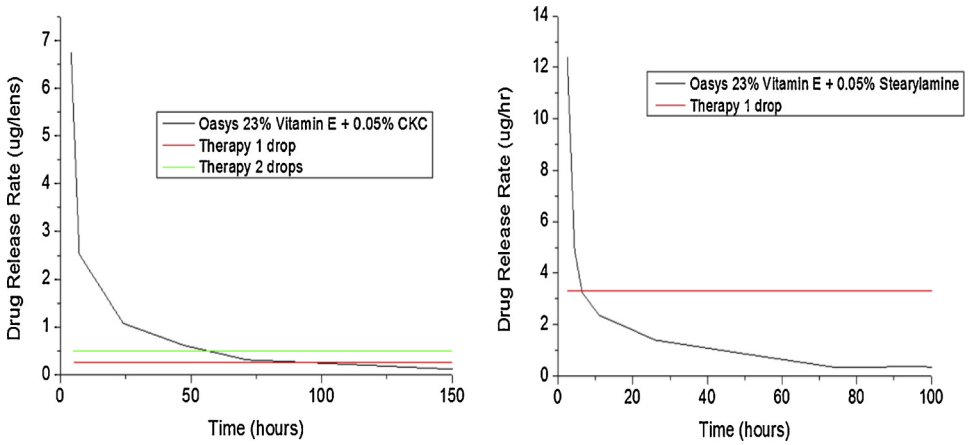


Fig. 4. FBNa (left) and KTH (right) release rate per lens compared to therapeutic dosages calculated. Data are presented as mean ± SD with n = 3.

KTH released increases from 49 μg to 70 μg and 93 μg with inclusion of 0.05% and 0.1% CKC respectively. It is hypothesized that the higher loading capacity is due to the increase in the affinity of the drug to the lens matrix caused by the hydrophobic interactions of the surfactant and the silicone material.

Furthermore, the increase in the drug loading capacity also depends on the type of surfactant used. In Oasys® and TruEye®, the amount of KTH released using stearylamine is higher than by using CKC. Stearylamine, as compared to CKC, is a primary amine with an 18-unit methylene tail. It is believed that the electrostatic interactions between the surfactant and the drug are stronger for primary amines than for quaternary ammoniums. From the obtained results, the loadings of vitamin E and surfactants can be adjusted to achieve drug release rates that meet the respective therapeutic window of each drug.

3.5. Drug release rate for therapeutic use

With controlled loading schemes of vitamin E and surfactants, the approach in this study proved to be successful in extending drug delivery rate and controlling its dosage. Table 5 summarizes the clinical treatment for each NSAID drug for a specific ophthalmic disease.

The goal is to load a sufficient amount of drug, vitamin E and surfactant in the contact lenses to control the drug release within the therapeutic window. For estimation of ketotifen therapeutic dose through contact lenses delivery [30], the calculation is based on assuming a 5% bioavailability of 50 μL eye drop volume, and 50% bioavailability of sustained contact lens deliveries. ACUVUE Oasys® contact lenses are intended for one or two weeks wear. Therefore, a one-week lens delivery period of therapeutic treatment was targeted. A contact lens designed for therapeutic treatment should release drugs within the calculated, equivalent therapeutic window during most time of the delivery period. Fig. 4 shows FBNa and KTH release rates from Oasys® contact lenses. The release rate was compared to the calculated release rate requirement for each drug. Except for the first four hours, the release rate of FBNa lies either close to or right within the therapeutic window in the first 3 days. For the last 4 days, the release rate lies either in the lower boundary or below the therapeutic window.

For the case of KTH, the release rate is within the therapeutic window for most of the 4-day treatment period, except for the fourth day where the release rate has leveled off.

For clinical consideration, the mentioned approach has some limitations that would need to be evaluated. One limitation is that the combined use of vitamin E and cationic surfactants may have adverse effects on the contact lens wettability, water content, material modulus, base curve, power or diameter. Therefore, future *in vitro* evaluations need to measure these parameters to avoid failure at a clinical stage. Another limitation is that the *in vitro* release experiments were carried at room temperature. Future work needs to conduct release experiments at eye temperature since contact lenses change size between room and eye temperature. Additionally, because release kinetic studies were performed without the sterilization of the contact lenses, future work should also evaluate the impact of different sterilization methods in the release kinetics of the drugs. Some of the sterilization methods that could be tested are autoclaving, gamma radiation and steam heat. Since sterilized commercial contact lenses have been used in this study as starting materials, re-sterilization should be required before performing *in vivo* or clinical studies.

Furthermore, *in vivo* studies need to evaluate any risks related to ocular toxicity or ocular irritation associated with the combined use of vitamin E and cationic surfactants.

4. Conclusions

This paper studied the effect of vitamin E into commercially available contact lenses on the drug release profile of three NSAIDs currently available as eye drops. Controlled release of the NSAIDs was achieved from the contact lenses for several days. It was further demonstrated that there is a linear relationship between the octanol-water partition coefficient and the drug-release-time-increase from vitamin E incorporation for ACUVUE Oasys®. Based on the obtained release kinetic results, it is believed that ACUVUE TruEye® could be the most effective lens for short-term drug delivery. With the inclusion of cationic surfactants in the vitamin E-loaded silicone hydrogel contact lenses, this study can additionally optimize the drug loading capacity and achieve drug delivery dosages by a contact lens in the desired therapeutic window. Before any possibility of moving to advanced clinical stages, the outcomes from this paper need to be supported by critical lens properties evaluation, *in vitro* release studies carried at eye temperature, and *in vivo* studies using contact lenses that meet regulatory requirements of sterility.

Conflict of interest

The authors declare no conflict of interest.

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