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Novel daily disposable therapeutic contact lenses based on chitosan and regenerated silk fibroin for the ophthalmic delivery of diclofenac sodium

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ABSTRACT

The aim of this study was to investigate the possibility of chitosan and regenerated silk fibroin (CS/RSF) blended films as novel biomaterials for daily disposable therapeutic contact lenses based ophthalmic drug delivery system. Diclofenac sodium (DS), a hydrophilic anti-inflammatory agent, was loaded into CS/RSF films by a soaking method. The best conditions of DS loading manifested the loading time of 2 h and pH 6.5 of drug solution. The drug loading capacity and the drug release profile could be controlled by varying the film RSF content. With increasing the film RSF content from 0 to 30%, the amount of loaded DS increased from 12 to 23 μg. Furthermore, the prolong drug released within therapeutic level was obtained with increasing the film RSF content. Consequently, a fast released characteristic within a therapeutic level up to 3 h was observed with the 100CS/0RSF film. On the other hand, the 70CS/30RSF film demonstrated a significant prolonged drug release within therapeutic level up to 11 h. In conclusion, the CS/RSF films are promising as novel biomaterials for daily disposable therapeutic contact lenses-based ophthalmic delivery.

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1. Introduction

Topical eye drops in the form of solutions and suspensions are a common approach to treat ocular disorders because of their convenient and noninvasive application (Lang, 1995; Bourlais et al., 1998; Ali & Byrne, 2008). However, a rapid drug clearance induced by a blink action leads to poor drug bioavailability with less than 5% of administered drugs entering the intraocular tissues (Deshpande & Shirolkar, 1989; Lang, 1995; Geroski & Edelhauser, 2000; Hyun & Anuj, 2012). Therefore, to maintain sustained therapeutic drug levels, frequent administration or large doses of eye drops are commonly required. However, this may reduce patient compliance, increase local and systemic side effects (Winfield et al., 1990; Lang, 1995; Lin & Sung, 2000; Barbu et al., 2006).

To overcome these limitations, daily disposable contact lenses could be an interesting alternative approach (Gulsen & Chauhan, 2005; Xinming et al., 2008; Tieppo et al., 2012; Guzman-Aranguez et al., 2013; Maulvi et al., 2016). The daily disposable therapeutic contact lenses could increase the residence time of the drug leading to improved drug bioavailability, ~50%, and minimized drug side effects. In addition, they can be administered without surgery. Therefore, the platform of therapeutic contact lenses is considered as a noninvasive application that could enhance the patient compliance by elimination of multiple drug administrations (McDermott & Chandler, 1989; Karlgard et al., 2003; Guzman-Aranguez et al., 2013; Lee et al., 2016).

Generally, most conventional hydrogel contact lenses based on poly (2-hydroxyethyl methacrylate) (pHEMA) was examined to deliver the hydrophilic ophthalmic drug by soaking the contact lenses in drug solution before insertion into the eyes (Peng et al., 2010; Sharma & Majumar, 2011; Hsu et al., 2013; Lee et al., 2016). Although, more effective than eye drops in theory, but in practice, the conventional contact lenses have some limitations including low drug loading and a fast release characteristic within 1–3 h. Therefore, developing a new daily disposable contact lenses to effectively deliver the hydrophilic drug in a prolonged drug release pattern is still a challenging task.

In previous study, we successfully developed a novel chitosan/regenerated silk fibroin (CS/RSF) blended films as the sustainable biomaterials for daily disposable contact lenses. The films have met material standards for daily disposable contact lenses (Jeencham et al., 2019). We propose that the incorporation of RSF into CS/RSF films with increasing amorphous portion of the films would enhance the drug loading capacity and prolong the drugs release time. To test this hypothesis, diclofenac sodium (DS), a non-steroidal anti-inflammatory drug, was used as a hydrophilic model drug.

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DS is commonly used, as 0.1% eye drops, to prevent post-operative inflammation in surgery and reduce the inflammation from corneal ulcer.

The aim of this study was to investigate the possibility of CS/RSF films as biomaterials for contact lenses based ophthalmic delivery for hydrophilic drug, DS. The effects of drug loading parameters on drug loading capacity were studied. The effects of the film RSF content and the loaded drug content on drug release characteristics of the films were observed. Moreover, the effects of DS loading on intrinsic contact lens properties, such as optical transparency and mechanical property, were also investigated.

2. Materials and methods

2.1. Materials

Chitosan shrimp (CS, >90% deacetylation with mean molecular weight of 250 kDa) was obtained from Marine Bio Resources Co., Ltd (Samutsakhon, Thailand). *Bombyx mori* raw silk yarns were purchased from Badin Thai-Silk Korat Co., Ltd (Nakhon Ratchasima, Thailand). Polyethylene glycol 400 (PEG400) was purchased from Merck KGaA, (Darmstadt, Germany). Snakeskin pleated dialysis tube with MWCO at 10,000 Daltons was obtained from Thermo Fisher Scientific, Inc. (Illinois, USA). Diclofenac sodium (DS) was purchased from Sigma-Aldrich Co., Ltd (MO, USA.). All other chemicals and solvents were of analytical grade.

2.2. Preparation of RSF

RSF was prepared according to Yamada et al. (2001) and Akiyoshi (1998), Yamada et al. (2001). Briefly, raw silk yarns of Bombyx mori were degummed twice by boiling in a 0.5% (w/v) sodium carbonate solution for one hour to remove sericin. Then, the silk yarns were washed three times with warm reverse osmosis (RO) water and dried overnight at 40 °C. The resulting degummed silk yarns were heated at 85–90 °C in a solution of $CaCl_2$:H_2O:$Ca(NO_3)_2$:EtOH at 30:5:45:20 weigh ratio until a gel-like solution was formed. Next, the resultant gel is dialyzed (using a snakeskin pleated dialysis tube having a 10,000 MWCO) against RO water at room temperature for 3 days to remove residual salts, then centrifuged at 15300 g for 30 min to remove aggregates. The RSF solution was lyophilized and kept in sealed plastic bags at −20 °C until use.

2.3. Preparation of CS/RSF films

CS/RSF films were prepared according to the optimum condition in our previous study (Jeencham et al., 2019). The films were prepared by a casting method. Briefly, 2% (w/v) of CS solution in acetic acid, 2% (w/v) of RSF aqueous solution in deionize water and PEG400 25% (w/w) of polymer matrix were mixed using magnetic stirrer at 200 rpm for 30 min. The CS/RSF ratios were varied as 100/0, 90/10, 80/20 and 70/30 (w/w). The mixtures were then poured onto the polystyrene plates and dried in an oven at 60 °C. The dried films were immersed in 1 M NaOH solution for 15 min, and then repeatedly rinsed with deionize water until the neutral pH was obtained. The films were then soaked in 0.01 M phosphate buffer saline (PBS) solution, pH 7.4 for 24 h and autoclaved at 121 °C and 15 psi for 20 min.

2.4. Drug loading by soaking method

DS solution was prepared by dissolving in 0.01 M PBS. The DS solution was sterilized by filtration method using cellulose acetate membrane filter (pore size 0.22 μm). Then the autoclaved film ($10 \times 10 \times 0.1\ mm^3$) was soaked in 1 mL of DS solution for a predetermined time at room temperature in a laminar flow hood through UV light disinfection. After film soaking, the amount of free drug remaining in the DS solution was determined using UV-VIS spectrophotometer at 276 nm. Then, the amount of DS loading into the films was determined from the difference between the amount of initial drug and drug remaining in solution after film soaking. The loading parameters were varied as follows: the loading time was varied from 1 to 24 h; the pH of drug solution was varied from 6.5 to 8.5; and the concentration of initial DS solution was varied from 62.5 to 250 μg/mL.

To confirm drug loading into the films, the morphology of the surface and cross-section of the DS loaded CS/RSF films were examined by a scanning electron microscope (SEM, Carl Zeiss AURIGA®, Thuringia, Germany). The samples were sputter-coated with platinum using a plasma sputter coater in order to obtain fine images via minimize electron charging on the surface (Figure 1).

2.5. *In vitro* drug release studies

In vitro drug release studies were carried out at 34 ± 1 °C. The DS loaded CS/RSF film ($10 \times 10 \times 0.1\ mm^3$) was placed into a micropipette tip, which fluid cavity of 30 μl. Then, the micropipette tip was inserted into a microtube and subjected to stimulated tear fluid (STF), pH 7.4, at a flow rate of 10 μl/min (Figure 2). The compositions of STF were sodium chloride 0.67 g, sodium bicarbonate 0.2 g, calcium chloride·$2H_2O$ 0.008 g, and deionized water added to 100 g. At predetermined time intervals, the microtube was taken and replaced with a new microtube. The amount of DS released in microtube was then determined using UV-VIS spectrophotometer at 276 nm (Maulvi, 2016). The release profile of DS was evaluated by plotting graphs of cumulative drug release (μg)

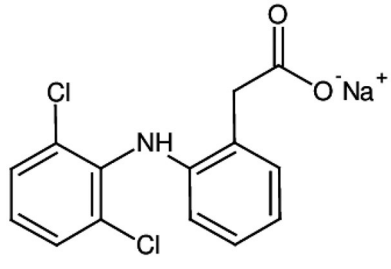

Figure 1. Chemical structures of diclofenac sodium.

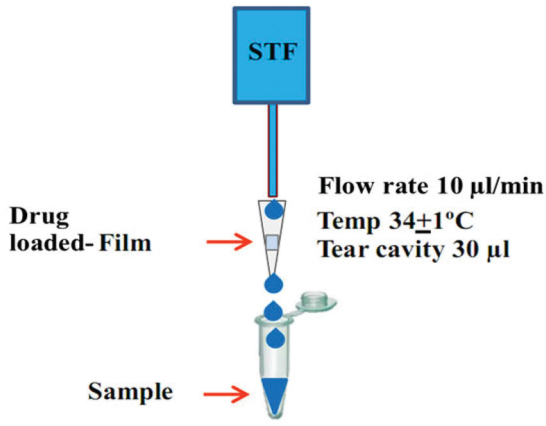

Figure 2. *In vitro* drug release testing.

versus time and drug release rate (ng/h) versus time. All the experiments were carried out in triplicates.

2.6. Mathematical model for release kinetics and diffusion coefficient

The *in vitro* drug release results were fitted with different kinetic models, such as zero order, first order, and Higuchi, to understand the kinetics and mechanism of drug release. The plots of above models were analyzed by regression analysis and the regression coefficient (R^2) values were calculated for the obtained linear curve (Higuchi, 1963; Lapidus & Lordi, 1966; Brazel & Peppas, 2000).

Diffusion coefficient (D) of DS into CS/RSF films was observed by using Fickian diffusion model. Theoretical model was applied to determine diffusion of drug from the films. We considered the case in which the films are shaped like slab. The aspect ratio of the exposed surface diameter to the thickness is greater than 10, so we can assume diffusion is occurring in one dimension. The films immersed in an aqueous environment, the concentration of the diffusing drug is negligible in the bulk fluid outside the contact lens. The diffusion of drug from soaked films can be calculated according to Equation (1) (Piringer & Baner, 2008; Rungchang et al., 2013).

$$M = 2AC_{p,o}\sqrt{Dt/\pi} \quad (1)$$

In these equations, M is the mass of drug leached from film to STF medium (µg), A represents the area of films in contact with liquid (cm^2), Cp,o is the initial concentration of drug in the film (µg/cm^3), D is the diffusion coefficient of the drug from film to STF medium (cm^2/s) and t is the migration time (s).

2.7. Estimation of therapeutic dose

The estimated therapeutic dose of DS was calculated based on Maulvi et al. (2016). DS eye drop solution (0.1% w/v) commonly recommended dose is one drop four times a day (Bodaghi, 2008). Considering 1 drop ≈ 50 µl, thus the daily DS eye drop dose is 200 µg (Maulvi et al., 2016). However, the ocular bioavailability through eye drop therapy is only ~1%, which suggests that the therapeutic requirement is ~2 µg/day (Kearns & Williams, 2009). Nevertheless, many scientific studies have proved that the bioavailability of drug to target tissue is more than 50% through contact lenses (Li & Chauhan, 2006; Bengani & Chauhan, 2012; Jung et al., 2013). Assuming 50% bioavailability, the therapeutic requirement of DS from contact lens is 4 µg/day or 166 ng/h.

2.8. Physical properties of DS loaded CS/RSF films

The film thickness was measured with a thickness gauge (Holex Digital Micrometer, Munich, Germany). The measurement was taken at the center and at four positions around the perimeter of the hydrated films and then the average thickness was calculated (Kim et al., 2006).

The light transparency of the films were determined using UV-VIS spectrophotometer (Genesys 10S, Thermo scientific, Wisconsin, USA). The hydrated film with an average thickness of 100 µm was mounted on the outer surface of a quartz cuvette. The cuvette was placed in the spectrophotometer and the visible light transparency was measured at 381–780 nm (Peng et al., 2010).

The Young's modulus and elongation at break of the films with width of 3 mm and thickness of 0.1 mm were determined according to ASTM D882-12 using a universal testing machine (Zwick/Roell Z2.5, Ulm, Germany) with a load cell of 2 kg, a crosshead speed of 20 mm/min, and a gauge length of 10 mm (Tranoudis & Efron, 2004).

The water content of the films was determined by measurement the weight of initial hydrated films (W_{wet}). Then, the films were allowed to dry at 105 °C until weight constant (W_{dried}) (Jung et al., 2013). The water content of CS/RSF films were calculated according to Equation (2)

$$\text{Watercontent}(\%) = [(W_{wet} - W_{dried})/W_{wet}] \times 100 \quad (2)$$

The water content of drug loaded film was determined by measurement the weight of hydrated film after drying at 105° C until constant weight (W_{dried}). The amount of drug loaded films was obtained from drug loading study (W_{drug}). The hydrated drug loaded films was weighed for its initial weight (W_{wet}) (Jung et al., 2013). The water content of drug loaded film was calculated as shown in the following Equation (3)

$$\text{Watercontent}(\%) = \left[(W_{wet} - W_{dried} - W_{drug})/W_{wet}\right] \times 100 \quad (3)$$

2.9. Statistical analysis

The results were expressed as mean ± standard deviation (SD). For all comparisons, statistical significant differences were analyzed with paired t-test or one-way ANOVA followed by Tukey's post hoc test, and $p < .05$ was considered statistically significant.

3. Results and discussion

The CS/RSF films were prepared following the optimum condition in our previous study (Jeencham et al., 2019). The resulting CS/RSF films have met the material standards for daily disposable contact lenses requirement. The films possessed smooth surface with a high visible light transparency (> 90%) and high water content (59–65% by weight). They were also easy to handle with Young's modulus and elongation at break in the range of 6.4–7.2 MPa and 70–100%, respectively, and showed no degradation in STF containing lysozyme for 24 h. The films also showed high ion permeability of 11×10^{-3} mm^2/min and oxygen permeability of 22–26 Barrers. Thus we further explored the possibility of using CS/RSF films as biomaterials for contact lenses based ophthalmic delivery of diclofenac sodium.

3.1. Drug loading capacity

One of the most conventional ways of loading a therapeutic drug into the contact lenses is the soaking method due to its cost-effectiveness and simplicity (Peterson et al., 2006; Bengani et al., 2013). To this end, the preformed contact lenses are immersed in the drug solution and the drug molecules can be adsorbed into the lenses surfaces and/or inner core. The drug loading capacity depends on the drug loading time, pH of drug solution and concentration of initial drug solution (Xinming et al., 2008).

To study the effect of drug loading time, the films were soaked in 125 μg/mL of DS solution, pH 6.5, with varying soaking time from 1 to 24 h. Table 1 illustrated that the amount of DS loading increased with increasing soaking time from 1 to 2 h and reached equilibrium at 2 h for all films ratios. Thus, the short drug loading time of 2 h suggesting its benefit for manufacturing process, comparing to conventional contact lenses which require drug loading time of 12–24 h (Maulvi et al., 2015; Lee et al., 2016).

To investigate the effect of the drug solution pH on drug loading capacity, the films were soaked in 125 μg/mL of DS solution with varying pH at 6.5, 7.4 and 8.5 for 2 h. When increasing the drug solution pH, the DS loading capacity was decreased (Table 2). All film ratios showed maximum drug loading at pH 6.5 and the minimum drug loading at pH 8.5. This could be explained by the pKa of DS. With increasing the DS solution pH from 6.5 to 8.5 (≫ pKa of DS = 4.15), the drug becomes more ionize from DS carboxylic acid groups leading to drug favors to diffuse from the films to aqueous solution.

The results indicated that DS can be loaded in all ratios of CS/RSF films. This could be explained by the intermolecular interaction, possible via hydrogen bonding and ionic interaction, between DS and CS or RSF. However, the amount of DS loading was increased with increasing the film RSF content. The 100CS/0RSF film gave the lowest DS loading capacity. On the other hand, the 70CS/30RSF film showed the highest DS loading capacity, which could be a result from its higher amorphous portion than 100CS/0RSF film, confirmed by DSC as discussed in our previous study (Jeencham et al., 2019). Thus, the high amorphous portion provides more space in the film, which could enhance drug adsorption in the film. This result was also correlated well with SEM micrographs, Figure 3. From SEM micrographs, DS was only illustrated on the outer surface of 100CS/0RSF, while DS was observed both outer surface and inner core of CS/RSF blended films. Notably, the higher ratios of RSF resulted in higher drug found in the inner core of films.

Therefore, the 70CS/30RSF film was selected to study the effect of drug concentration on drug loading capacity. The 70CS/30RSF film was soaked in three different DS concentrations (62.50, 125 and 250 μg/mL), pH 6.5, for 2 h. It can be seen that the drug loading capacity significantly increased proportionally with increasing the initial drug concentration, Table 3.

3.2. *In vitro* drug release studies

From the drug loading study, the best conditions of DS loading parameters were chosen. Therefore, all films were soaked in 125 μg/mL of DS solution, pH 6.5, for 2 h before performing the *in vitro* drug release studies.

Figure 4 illustrated that the 100CS/0RSF film showed a fast release characteristics with nearly 100% released within 3 h. On the contrary, a prolonged drug release characteristics was observed with increasing the film RSF content. The 90CS/10RSF, 80CS/20RSF, and 70CS/30RSF films showed a fast release during initial hours followed by a prolonged drug release up to 6, 9 and 11 h, respectively. Nevertheless, the drug release profiles of all tested CS/RSF films were best fitted to the Higuchi's model with regression coefficient = 0.93–0.99, Table 4. This implies that the DS released from the films by a diffusion controlled mechanism. As expected, the 100CS/0RSF film manifested the highest diffusion coefficient of 1.63×10^{-8}, Table 4. Thus, the released DS was maintained within therapeutic level, 166 ng/h, for only 3 h, Figure 5. This short acting time, although better than the eye drops, was not significantly different comparing to the conventional contact lenses. On the other hand, 90CS/10RSF, 80CS/20RSF, and 70CS/30RSF films showed a lower diffusion coefficient of 0.50×10^{-8}, 0.20×10^{-8} and 0.15×10^{-8} cm^2/s, respectively, Table 4. Consequently, their drug therapeutic level was extended to 5, 9 and 11 h, respectively, Figure 5. To explain

Table 1. Effect of drug loading time on drug loading capacity.

Mass ratio of CS/RSF (w/w)	Drug loading (μg)/10 mm^3 of film			
	1h	2h	3h	24h
100/0	8.72 ± 0.63	11.82 ± 0.66	11.32 ± 0.42	11.85 ± 0.48
90/10	10.36 ± 1.71	14.92 ± 1.55	14.70 ± 1.46	14.42 ± 1.33
80/20	16.84 ± 1.79	18.69 ± 1.97	18.51 ± 1.80	18.30 ± 1.21
70/30	16.91 ± 2.01	23.46 ± 0.57	23.46 ± 0.35	23.35 ± 1.04

Condition: DS solution pH6.5; SD: standard deviation; $n = 3$.

Table 2. Effect of pH of drug solution on drug loading capacity.

Mass ratio of CS/RSF (w/w)	Drug loading (μg)/10 mm^3 of film		
	pH6.5	pH7.4	pH8.5
100/0	11.82 ± 0.66	5.84 ± 1.54	4.91 ± 1.10
90/10	14.92 ± 1.55	9.57 ± 1.25	5.70 ± 0.64
80/20	18.69 ± 1.97	10.61 ± 1.11	6.34 ± 0.91
70/30	23.46 ± 0.57	14.38 ± 2.12	10.68 ± 0.65

Condition: loading time 2 h; SD: standard deviation; $n = 3$.

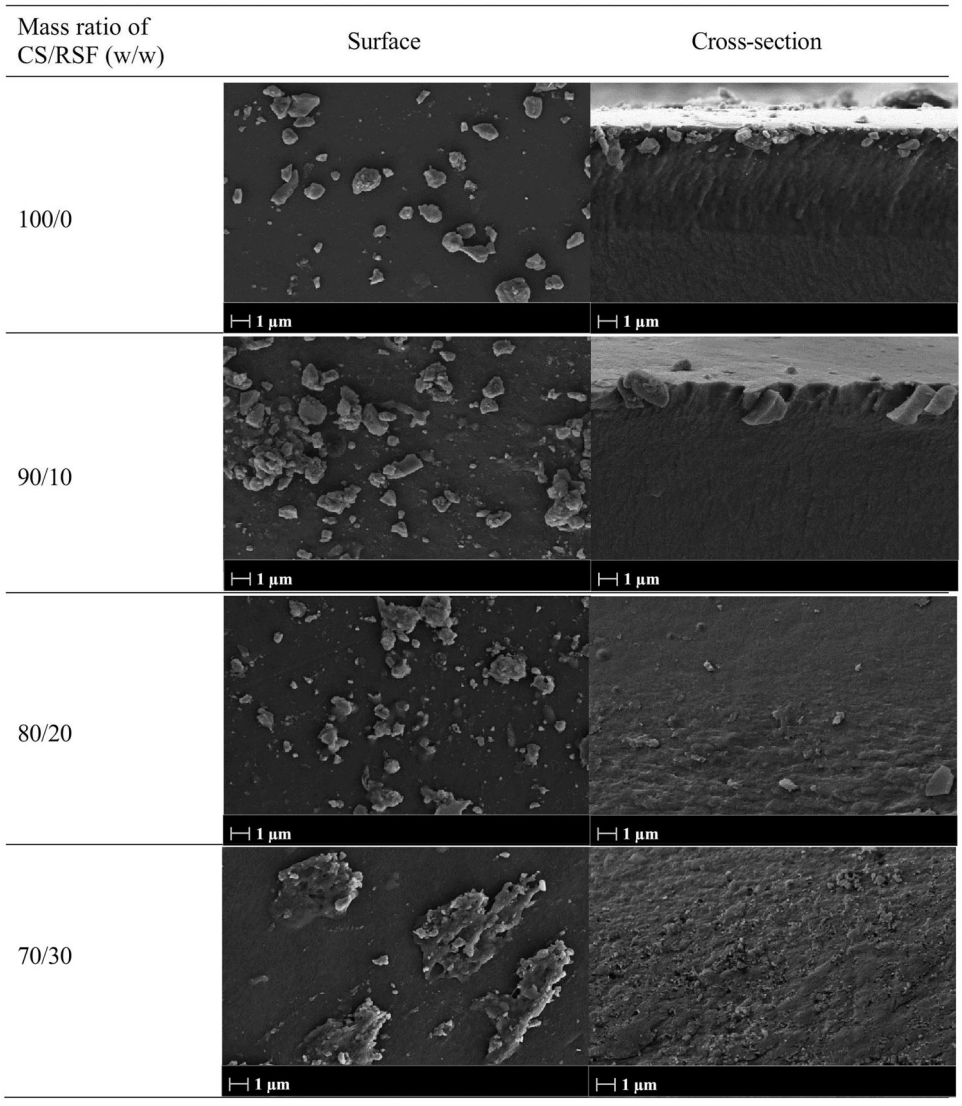

Figure 3. SEM micrographs of the surface and cross-section of DS loaded CS/RSF films, soaking in 125 µg/mL of DS solution, pH 6.5, for 2 h (×5000 magnification).

Table 3. Effect of concentration of initial drug solution on drug loading capacity.

Concentration of DS solution (µg/mL)	Drug loading (µg)/10 mm^3 of film
62.5	10.75 ± 1.33
125.0	23.46 ± 0.57
250.0	45.64 ± 0.67

Condition: DS solution pH6.5; loading time 2 h, $n = 3$.

this phenomenon, the adsorbed drug locations effected the drug release profile significantly. Obviously, the drug located on the film surface immediately release into the media, contributing to the fast release phase. On the other hand, drug stayed in the inner core used longer time for dissolving and diffusion to outer surface, consequently attributed to the prolong release phase. These results correlated well with the film SEM micrographs, Figure 3. Thus, the higher RSF content resulted in an increased drug amount in the film inner core, hence, prolonging the drug release time.

To further extend the drug release duration, we hypothesized that it could be achieved by increasing the loaded drug content in the film. Thus, the 70CS/30RSF film was selected to study the effect of different amount of loaded drug, ~11, 24 and 46 µg, on the drug release profile. All films displayed similar drug release profiles, Figure 6. Accordingly, their diffusion coefficient of DS from the films was not significantly different, 0.14–0.16 × 10^{-8} cm^2/s, Table 5. These results suggested that the drug release duration was not extended with increasing amount of loaded drug in the film. Nevertheless, the amount of drug release increased with increasing loaded drug content, Figure 7. The film with 11 µg of DS showed prolonged drug release within the therapeutic window of only 8 h, whereas both films with 23 and 46 µg of DS showed prolonged drug release within the therapeutic window of 11 h. This result was in agreement with the Maulvi et al. They reported that the drug release duration within the therapeutic window of pHEMA-hydrogel contact lenses showed no significant enhancement with increasing amount of timolol maleate into the lenses (Maulvi et al., 2015).

3.3. Physical properties of DS loaded CS/RSF films

According to the drug release results, 70CS/30RSF film soaking in125 µg/mL of DS solution, pH 6.5 for 2 h was selected

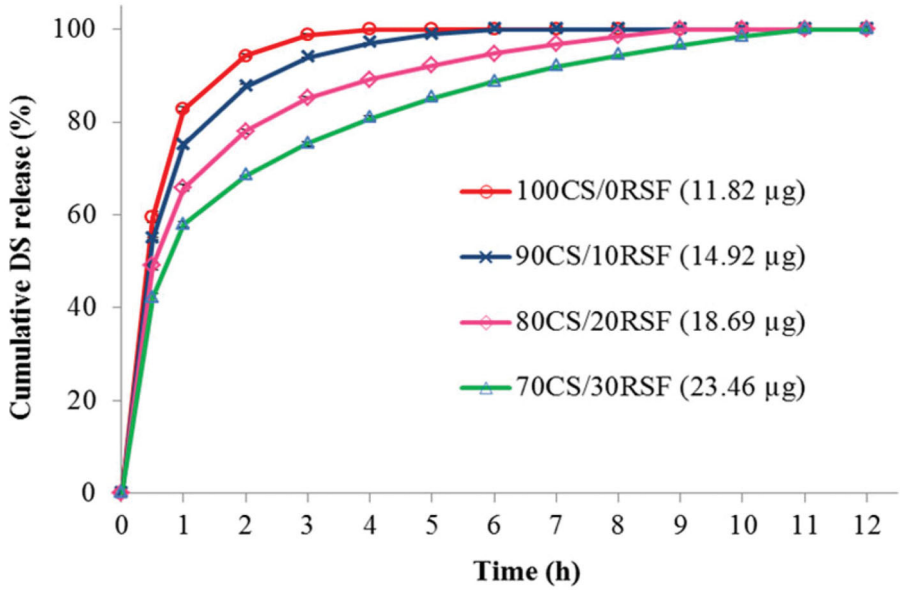

Figure 4. Cumulative DS release from CS/RSF films.

Table 4. Drug release kinetic data of DS loaded CS/RSF films.

Mass ratio CS/RSF (w/w)	Release time within therapeutic level (h)	Diffusion coefficient ($\times 10^{-8}$ cm^2/s)	Regression coefficient, R^2
100/0	3	1.63	0.93
90/10	5	0.50	0.94
80/20	9	0.20	0.97
70/30	11	0.15	0.99

SD: standard deviation, $n = 3$.

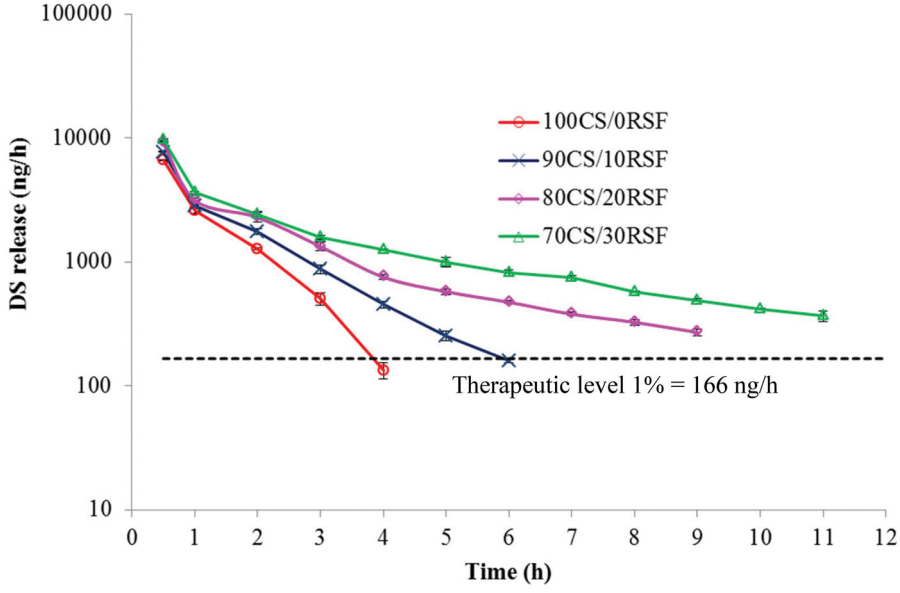

Figure 5. DS release from CS/RSF films compared with therapeutic level.

to further study the effect of drug loading on physical properties of films. The physical properties of the film and DS loaded-film showed no significant difference, Table 6. They manifest similar thickness of 100 ± 10 µm, which comply with typical commercial contact lenses having thickness of 50–200 µm (Gonzalez-Meijome et al., 2008; Lee et al., 2015). They showed high visible light transparency of $>$ 90% which meet the visual requirement (Lai et al., 2018). They possessed Young's modulus of $>$ 1.5 Mpa and the elongation at break of $>$ 50% satisfying the stiffness and flexibility requirement of contact lens (Tranoudis & Efron, 2004; Horst et al., 2012; Selby et al., 2014). According to FDA's classification (Reynalyn, 2017), they showed high water content implying that these films could promote the comfort for wearing. In summary, DS loading did not affect the intrinsic contact lens physical properties. Thus, the developed DS loaded CS/RSF

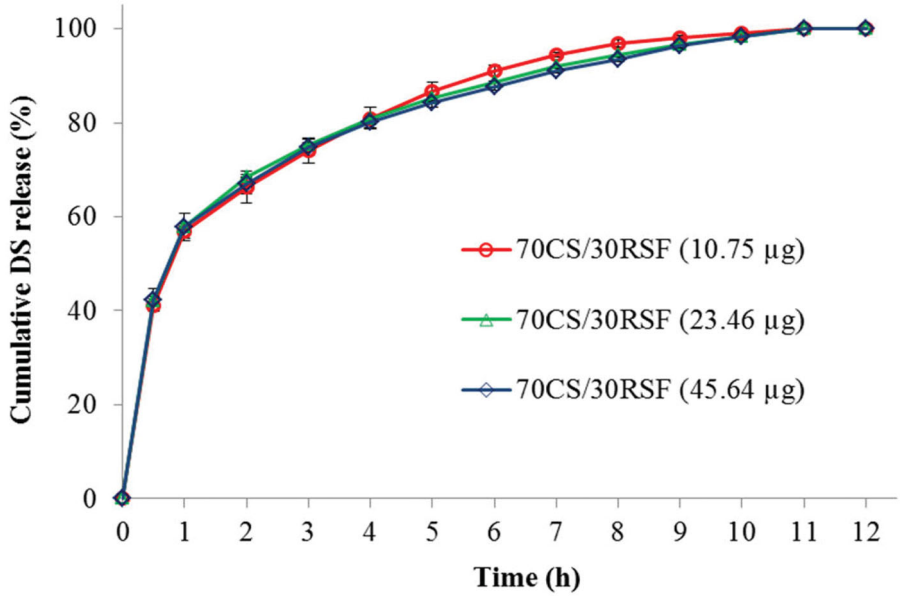

Figure 6. Cumulative DS release from 30CS/70RSF films with different loaded DS content.

Table 5. Drug release kinetic data of 30CS/70RSF films with different loaded DS content.

DS (µg/mL)	Release time within therapeutic level (h)	Drug loading (µg)/10 mm^3 of film ± SD	Diffusion coefficient ($\times 10^{-8}$ cm^2/s)	Regression coefficient, R^2
62.50	8	10.75 ± 1.33	0.16	0.95
125	11	23.46 ± 0.57	0.15	0.99
250	11	45.64 ± 0.67	0.14	0.99

SD: standard deviation, $n = 3$.

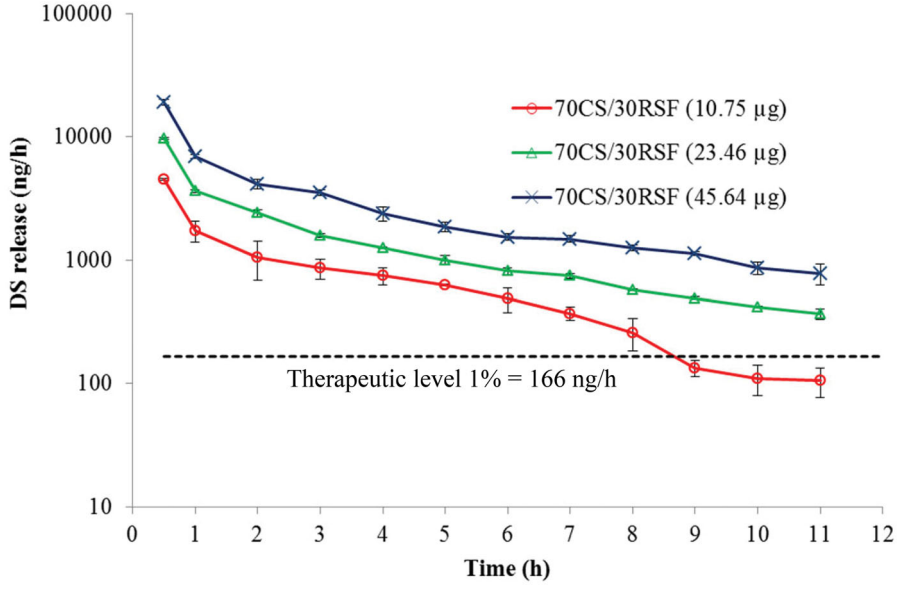

Figure 7. DS release from 70CS/30RSF films with different loaded DS content compared with therapeutic level.

Table 6. Physical properties of 30CS/70RSF films and DS-loaded 30CS/70RSF films.

Formulation	Thickness (µm) ± SD	Light transparency (%) ± SD	Young's Modulus (Mpa) ± SD	Elongation at break (%) ± SD	Water content (%) ± SD
70CS/30RSF	100 ± 10	93 ± 2	6.43 ± 1.00	72 ± 14	58 ± 1
DS loaded 70CS/30RSF	100 ± 10	92 ± 0	6.52 ± 1.00	72 ± 18	58 ± 1

SD: standard deviation, $n = 3$.

films comply with the requirements for daily disposable contact lenses.

4. Conclusion

DS as a hydrophilic model drug could be successfully loaded in the prepared CS/RSF films by the soaking method with a short drug loading time of 2 h. The DS loading did not affect the intrinsic contact lens properties of CS/RSF films. Essentially, the drug loading capacity and the drug released profile could be altered favorable by varying the film RSF content. The drug loading capacity was increased with increasing the film RSF content. As the film RSF content increased, the more DS could be found in the inner core of the film. Consequently, a fast released characteristic within a therapeutic level up to 3 h was observed with the 100CS/0RSF film. On the contrary, the 70CS/30RSF film demonstrated a significant prolonged drug release within therapeutic level up to 11 h. In conclusion, the developed CS/RSF films are promising novel biomaterial for daily disposable contact lenses-based ophthalmic delivery, which is beneficial for reducing drug side effects and administration frequency as compared to conventional contact lenses.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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