Novel Poly(vinylpyrrolidone)-Coated Silicone Contact Lenses to Improve Tear Volume During Lens Wear: In Vitro and In Vivo Studies

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ABSTRACT: Poly(vinylpyrrolidone) (PVP-K90) is widely used to manage dry eye syndrome (DES). The marketed eye drop solutions (high dose) need frequent instillation, affecting the routine lifestyle of patients. PVP-K90-laden contact lenses can be used to overcome the limitations of eye drop solutions (low bioavailability and frequent instillation). However, the conventional methods of PVP-K90 loading show poor loading capacity and short duration of effect. In the present study, we have developed PVP-K90-coated contact lenses via a short curing approach to increase the PVP-K90 loading capacity with a sustained release profile to manage dry eye syndrome. PVP-K90 was loaded by a soaking method (SM-PVP), direct loading (during fabrication, DL-PVP), a combination of soaking and direct loading (DL-SM-PVP), and a novel coating process (SM-PVP-C and DL-SM-PVP-C). The swelling studies suggested improvement in the water uptake (hydration) property of the contact lenses due to the presence of PVP-K90. The optical transparency was within an acceptable range. The in vitro release of PVP-K90 was in the following order: PVP-coated contact lens (168 h) > DL-SM-PVP (168 h) > DL-PVP (96 h) > SM-PVP (72−96 h). PVP-coated contact lenses showed a high burst effect (lubricating effect) and sustained release (3161−448 ng/h between 24 and 168 h) due to high PVP loading/coating in comparison to the uncoated respective contact lenses (964−113 ng/h between 24 and 96 h). In animal studies, the PVP-K90-coated contact lens showed higher tear volume in comparison to the respective uncoated contact lenses and an eye drop solution. This study demonstrates a novel approach of coating a high amount of PVP-K90 on contact lenses for sustained release to manage several ocular diseases like dry eye syndrome, conjunctivitis, and other ocular injuries.

1. INTRODUCTION

Dry eye syndrome (DES), also known as keratoconjunctivitis sicca, is a multifactorial ocular surface disease that leads to tear film instability, dryness, visual disturbance, irritation, itching, and light sensitivity due to inadequate lubrication of the eye.1,2 Currently, it is treated using artificial tears or tear substitutes containing lubricating/wetting agents, which increases the tear film stability by increasing the tear volume on the ocular surface.3,4 Artificial tears include polymers like poly(vinylpyrrolidone) (povidone), poly(vinyl alcohol), hyaluronic acid, cellulose esters, etc.5,6 The majority (>90%) of the artificial tears are available in the form of eye drop solutions, which show low ocular retention due to various factors like reflux tearing, blinking, nasolacrimal drainage, etc.7−9 To compensate for low ocular drug retention, ophthalmologists are forced to prescribe eye drops with frequent high doses, which affects the routine lifestyle of patients.10,11

Several novel drug delivery systems have been designed to improve the ocular drug retention time; however, each system has its own limitations.12 The contact lenses can bypass the issues related to eye drop therapy.13 However, the conventional soaking method, which is used to deliver polymers like poly(vinylpyrrolidone) (PVP-K90, lubricating agent or comfort agent), shows poor PVP-K90 loading and short duration of action. Winterton et al. first noted zero-order release kinetics of a lubricating agent (poly(vinyl alcohol)) from a Nellikon A contact lens (direct loading during fabrication). The contact lens showed sustained release for 20 h with improved wearing comfort.14 Johnson and Johnson’s Acuvue lenses have PVP (10−50 kDa) incorporated in the contact lens, which showed sustained release for 24 h.15 Yanez et al. fabricated contact lenses using hydroxyethyl methacrylate (HEMA) in the presence of PVP-K30, and the system showed sustained release of PVP for 2 days. They found molecular weight and water content as critical factors for comfort wear.16 Singh et al.
Table 1. Data for Swelling and Transmittance Study$^{a,b}$

| codes          | % swelling | $p$-value | % transmittance | $p$-value |
|----------------|------------|-----------|-----------------|-----------|
| control contact lens | 71.96 ± 09.13 | 0.892 | 99.10 ± 00.57 | 0.256 |
| 0.6-SM-PVP      | 72.77 ± 11.87 | 0.737 | 98.90 ± 00.67 | 0.952 |
| 1-SM-PVP        | 76.49 ± 09.06 | 0.171 | 99.07 ± 00.60 | 0.898 |
| 3-SM-PVP        | 78.19 ± 05.16 | 1.018 | 99.25 ± 00.44 | 0.315 |
| 1-DL-PVP        | 81.96 ± 06.01 | 0.160 | 97.20 ± 02.12 | 0.181 |
| 3-DL-PVP        | 81.30 ± 04.31 | 0.463 | 96.27 ± 03.23 | 0.163 |
| 3-DL-3-SM-PVP   | 81.63 ± 04.38 | 0.940 | 96.03 ± 02.97 | 0.163 |
| 3-SM-PVP-C      | 76.19 ± 03.24 | 0.395 | 99.10 ± 00.57 | 0.168 |
| 3-DL-3-SM-PVP-C | 81.81 ± 02.00 |          | 97.36 ± 01.86 |          |

“Values are shown as mean ± standard deviation ($n = 3$). $^a$SM: soaking method, DL: direct loading, and C: curing. The numbers in the prefix of each code indicate polymer concentration. $^b$indicates a significant difference ($p < 0.05$) with the control contact lens. $^{*}$indicates a very significant difference ($p < 0.01$) with the control contact lens.

Table 1. The data of percentage swelling are shown in Table 1. The soaked contact lenses (SM-PVP) showed a slight increase in percentage swelling with an increase in the PVP loading (i.e., increase in the PVP concentration in the packaging solution). However, statistically, it was insignificant ($p > 0.01$), due to a high deviation in the % swelling values. The small increase in the percentage swelling values was due to the presence of PVP-K90 on the surface of the contact lens. The molecular weight of PVP-K90 was > 6 x 10$^5$ Da, which restricts its entry in the aqueous channels of the contact lens matrix.

The direct-PVP-laden contact lenses (DL-PVP) showed an increase of 10 units in the percentage swelling values in comparison to the control contact lenses. The 1% PVP loading (200 μg PVP/lens, 1-DL-PVP) and 3% PVP loading (600 μg PVP/lens, 3-DL-PVP) did not show a significant difference in the percentage swelling. The improvement in the percentage swelling in comparison to the soaked contact lenses was due to the entrapment of PVP-K90 inside the contact lens matrix.

The PVP-K90-laden contact lenses prepared by soaking and direct loading (DL-SM-PVP) and PVP-coated contact lenses (3-SM-PVP-C and 3-DL-3-SM-PVP-C) also showed similar values of percentage swelling. The PVP-K90 coating on the 3-SM-PVP-C and 3-DL-3-SM-PVP-C batches did not show an increase in the swelling behavior in comparison to the respective uncoated contact lenses. Thus, the coating outside the contact lens did not take part significantly in the swelling behavior of the contact lens matrix.

2. RESULTS AND DISCUSSION

2.1. Swelling Studies. The percentage of swelling (water content) of a contact lens is one of the most critical parameters that decide its wearability. Alteration in the swelling behavior will affect the wettability (hydration) and oxygen and ion permeability of contact lenses.$^{24}$ In the present work, we have loaded PVP-K90 via a soaking method, by direct incorporation during fabrication of the contact lens, and by coating (short curing) on the surface of the contact lenses, with an expectation to improve the wettability of the contact lenses for comfort wear and for the treatment of various ocular injuries (lubrication property).

2.2. Transmittance Study. Optical transmittance of a contact lens should be greater than 95% for clear vision. As shown in Table 1, the % transmittance of the PVP-loaded contact lenses (for all of the batches, ranging from 99.25 to 96.72%) was not significantly ($p > 0.05$) altered in comparison to the control (blank) contact lenses. The values were >95% (acceptable range), assuring clear vision for users/patients.

2.3. In Vitro Flux of Soaked Contact Lenses (SM-PVP). Polymers can adhere to the surface of silicone contact lenses via interactions between the polymer and the surface of the lenses. The cumulative release ($μg$) and release rate (ng/h) of PVP-K90 from the soaked contact lenses are presented in Figures 1 and S1 (Supporting Information Part I), respectively. The uptake (based on the cumulative release data) of PVP-K90 during the soaking period (24 h) for batches 0.6-SM-PVP,
Thus, the data of direct-PVP-K90-laden lenses showed a
sustained release for 96 h, and the release rate profiles were
found to be better in comparison to those of the soaked
contact lenses.

2.5. In Vitro Flux of PVP-Laden Contact Lenses
(Soaking and Direct Loading, DL-SM-PVP). A single
batch combining the advantage of the soaking method (burst
release for initial comfort) and direct loading was fabricated
and coded as 3-DL-3-SM-PVP. The direct-PVP-K90-laden
contact lens (3-DL-PVP) was soaked in 3% w/v PVP-K90
soaking solution and tested by in vitro studies. The cumulative
release (μg) and release rate (ng/h) profiles of the 3-DL-3-SM-
PVP contact lenses are presented in Figures 2 and S2
(Supporting Information Part I), respectively. The 600 μg
PVP-K90-loaded (3-DL-PVP) contact lens when soaked in 3%
w/v PVP-K90 packaging solution showed unexpectedly very
high burst release (356 μg). The total cumulative release was
429 μg up to 96 h. The similarity factor (f2) value was <50 (3-
DL-PVP versus 3-DL-3-SM-PVP), which suggested significant
cumulative release from the 3-DL-3-SM-PVP contact lens.
Thus, the release rate profile of the 3-DL-3-SM-PVP batch was
improved in comparison to the individual soaking and direct
loading method.

2.6. In Vitro Flux of PVP-Coated Contact Lenses. To
further increase the PVP-K90 loading, we coated PVP-K90 on
the surface of the 3-SM-PVP and 3-DL-3-SM-PVP contact
lenses by short hit curing (30 s) and coded them as 3-SM-
PVP-C and 3-DL-3-SM-PVP-C batches, respectively. The
cumulative release (μg) and release rate (ng/h) profiles are
presented in Figures 2 and S2 (Supporting Information Part I),
respectively. The PVP-K90-coated contact lenses showed a
high burst release of 503 and 802 μg from 3-SM-PVP-C and
3-DL-3-SM-PVP-C batches, respectively, which will be bene-
cicial for initial lubrication of the eyes. Both the batches showed a
sustained release up to 168 h with high release rate (3161–448
ng/h between 24 and 168 h) profiles in comparison to uncoated
respective contact lenses (964–113 ng/h between 24 and
96 h). The statistical analysis (f2 < 50) indicates significant
improvement in the release rate profiles using coated contact
capes in comparison to uncoated contact lenses. Thus, the short hit curing process of the contact lens in
the soaking solution resulted in a strong interaction of PVP on
the surface of the contact lens, which was found to be
beneficial for high PVP-K90 loading and sustained release.
Further characterization studies are needed to investigate and

Figure 1. In vitro release of PVP-K90 from the contact lenses
prepared by soaking and direct loading techniques.

1-SM-PVP, and 3-SM-PVP was found to be 10.9 ± 3.5, 48.4 ±
7.5, and 80.27 ± 12.92 μg, respectively (72–96 h). The in vitro
flux data showed a high initial burst release (43.64–54.03%),
which indicated the release of adsorbed PVP-K90 from the
surface of the contact lenses, followed by a rapid decline in the
drug release rate profiles. The high burst release is beneficial in
producing an initial lubricating effect on the surface of the eye
for comfort wear. The burst release suggests the weak
interaction of PVP-K90 with the surface of the contact lens.
The PVP-K90 release profiles show that the release rate (ng/h)
increases with an increase in the PVP-K90 uptake (3-SM-PVP
> 1-SM-PVP > 0.6-SM-PVP), i.e., with an increase in the PVP-
K90 strength in the soaking solution (which leads to higher
uptake of PVP-K90).

2.4. In Vitro Flux of Direct-PVP-Laden Contact Lenses
(DL-PVP). The direct-PVP-K90-laden contact lenses were
treated for monomer extraction and the wet sterilization steps
(auto clave) prior to the in vitro release study. The direct-PVP-
K90-laden contact lenses (DL-PVP) did not show any
significant leaching (PVP-K90 was not detected by the
colorimetric method) during both treatments, which could be
due to the tight packaging and entrapment of high-
molecular-weight PVP-K90 in the matrix of the contact lens.
The cumulative release (μg) and release rate (ng/h) profiles
of the direct-PVP-K90-laden contact lenses post monomer
leaching and sterilization are presented in Figures 1 and S1
(Supporting Information Part I), respectively. The contact
lenses after the above treatment were shifted for the in vitro
release study where the cumulative PVP-K90 release was
found to be 74.25 ± 9.53 and 83.11 ± 6.50 μg for 1-DL-PVP
and 3-DL-PVP batches, respectively. The similarity factor (f2
= 71.2) value between 1-DL-PVP and 3-DL-PVP batches
indicated no added advantage of increasing the level of PVP
in the contact lens. The cumulative PVP-K90 release values
from the DL-PVP contact lenses were lower than the
theoretical loading (200 and 600 μg/lens for 1-DL-PVP and
3-DL-PVP batches, respectively), which indicated that the
major part of PVP-K90 was permanently entrapped inside the
matrix of the contact lens during the curing process
(fabrication), leading to polymerization of PVP-K90. The
release data showed a low burst release (in comparison to the
soaking method), followed by a sustained release up to 96 h.
The low burst release was due to the entrapment of PVP-K90
in the matrix of the contact lens, which resisted its liberation.
Thus, the data of direct-PVP-K90-laden lenses showed a

Figure 2. In vitro release of PVP-K90 from the contact lenses
prepared by a combination of soaking and direct loading techniques
and a coating technique.
understand the interaction of PVP-K90 on the surface of the contact lenses.

2.7. In Vivo Assessment of Tear Volume. The in vivo assessment of tear volume using a Schirmer strip (rabbit model) was performed to evaluate the tear production and the capability of the PVP-loaded contact lenses to stabilize the tear fluid volume in rabbit eyes in comparison to the eye drop solution.\textsuperscript{25,26} The selected contact lenses such as a control contact lens (without PVP-K90), 3-SM-PVP (80.2 μg), 3-DL-PVP (83.1 μg), 3-SM-PVP-C (923.6 μg), and 3-DL-3-SM-PVP-C (1399 μg) were placed on the rabbit eyes and the average reading (wetting of strip) in mm was noted and compared with the 0.6% w/v PVP eye drop solution (150 μg, 2 h study period). The control rabbit eyes (baseline, without any treatment) showed 13.2 ± 1.25 mm reading (study period 72 h, Figure 3). The control contact lenses (without PVP-K90) showed a reduction in the average value to 11.36 ± 2.21 mm, which was due to the inherent property of the contact lens leading to dry eyes (pink eyes). The eye drop group (1 drop = 150 μg) showed an improvement in the tear fluid volume (15.26 ± 2.11 mm), which was expected due to the hydration property of PVP-K90. The soaked (3-SM-PVP) and direct-PVP-K90-laden (3-DL-PVP) contact lenses showed 16.24 ± 3.22 and 17.44 ± 3.26 mm values, respectively, which indicated better performance in comparison to the eye drop group. The PVP-coated 3-SM-PVP-C and 3-DL-3-SM-PVP-C contact lenses showed 19.96 ± 3.26 and 19.82 ± 2.86 mm values, respectively, which was expected due to the high loading of PVP-K90.

During the Schirmer tear test study, the eyes were assessed on each day for protein adherence (see Supporting Information Part III). The 0.6% PVP-K90 eye drop study was conducted for 72 h (1 drop every 4 h). The data/scores clearly justified the Schirmer tear test results and confirmed the potential of the PVP-K90-coated contact lens (3-DL-3-SM-PVP-C) in comparison to the soaked and direct-laden contact lenses. Thus, the high retention of PVP-K90 on the ocular surface using contact lenses could be beneficial to treat many ocular diseases like dry eyes, conjunctivitis, and corneal wounds/injuries.

3. CONCLUSIONS

The study demonstrates the successful delivery of PVP-K90 from novel PVP-coated contact lenses to treat dry eye syndrome without altering the swelling and optical transmittance of the contact lenses. The ability of the system in sustaining the PVP-K90 release duration was found to be in the following order: PVP-coated contact lens (168 h) > PVP-laden contact lens (soaking and direct loading) (168 h) > direct-PVP-laden contact lenses (96 h) > soaked contact lenses (72–96 h). In the Schirmer strip study, PVP-K90-coated contact lenses showed higher tear volume in comparison to the respective uncoated contact lenses and eye drop solution. Thus, the novel approach of short curing justifies its scope of high PVP-K90 coating on the surface of the contact lens for prolonged release without affecting the optical and swelling properties. These lenses can be used to treat and manage many ocular diseases like dry eye syndrome, conjunctivitis, etc.

4. EXPERIMENTAL SECTION

4.1. Materials. Fabrication of the silicone contact lenses was accomplished with the following monomers: 2-hydroxyethyl methacrylate (HEMA), Irgacure (1-hydroxycyclohexyl phenyl ketone), ethylene glycol dimethacrylate (EGDMA), N,N-dimethyl acrylamide (DMA), N-vinyl pyrrolidone (NVP), and 3-[3(trimethylsiloxy)]silyl]propyl methacrylate (siloxane). All of the above monomers, poly(vinylpyrrolidone) K90, and other chemicals were purchased from Sigma-Aldrich (St. Louis).

4.2. Fabrication of the Contact Lenses for the Soaking Method (SM-PVP). The monomer mixture used to fabricate the contact lenses was composed of hydroxyethyl methacrylate (HEMA, up to 1 mL) as the basic contact lens material, dimethacrylic acid (DMA, 310 μL), ethylene glycol dimethacrylate (EGDMA, 10 μL) as a cross-linking agent that added dimensional stability, N-vinyl pyrrolidone (NVP, 10 μL) as a plasticizer for providing required flexibility, siloxane (2.5 μL) for increasing oxygen permeability, and Irgacure (20 mg) as a photoinitiator.\textsuperscript{27} The silicon contact lenses (diameter 14.2 mm and base curve 6.5 mm) were fabricated by a cast molding method using plastic polypropylene lens molds. The excess monomer mixture solution was added in the female mold and the male mold was kept over it, followed by exposing the assembly (molds) in an ultraviolet (UV) transilluminator (curing/polymerization) at 365–370 nm for 12 min.\textsuperscript{28} The silicone contact lenses were removed from the molds and stored in a desiccator at 45% humidity until further use.

Before the soaking procedure, the unreacted monomers were removed from the silicone contact lenses by boiling (100 °C) individual lens in water for 1 h.\textsuperscript{29} The PVP was loaded by soaking the contact lenses in the PVP packaging solution at varying concentrations of PVP (0.6, 1, and 3% w/v PVP in simulated tear fluid (STF) coded as 0.6-SM-PVP, 1-SM-PVP, and 3-SM-PVP, respectively), followed by sterilization using an autoclave (121 °C, 15 psi, 30 min). The soaking period was set to 24 h. STF was composed of 0.9% w/v NaCl and 0.015% w/v NaHCO₃ in deionized water. At the end of the soaking period, excess of the packaging solution adhered to the contact lens was removed using filter paper. The PVP concentration of the soaking solution was restricted to a maximum of 3% w/v, as the viscosity increased (>4.2 cP), for easy handling (packaging solution) and comfort wear.
4.3. Fabrication of Direct-PVP-Laden Contact Lenses (DL-PVP). The direct-PVP-laden contact lenses were fabricated using a monomer mixture (see Section 4.2) containing PVP in varying concentrations (1 and 3% w/v PVP in monomer solution coded as 1-DL-PVP and 3-DL-PVP batches, respectively). PVP was added into the monomer mixture and sonicated for 10 min to prepare a homogeneous PVP monomer solution. The direct-PVP-laden contact lenses were fabricated by the cast molding method as discussed in Section 4.24.2.

The level of PVP in the monomer solution was selected to load 200 and 600 μg of PVP per 20 mg of contact lens for 1-DL-PVP and 3-DL-PVP batches, respectively. The dose of PVP eye drop (0.6% w/v) is 4 times per day (50 μL = 300 μg × 4 times = 1200 μg) for dry eyes. Thus, considering 5% ocular bioavailability (60 μg/day) of the PVP eye drop solution, the required dose with contact lens (considering 50% bioavailability) will be 120 μg/day. The direct-PVP-laden contact lenses were extracted to remove the unreacted monomers, followed by sterilization using an autoclave. The amount of PVP leached during extraction and sterilization was quantified by the colorimetric method at 420 nm.30

4.4. Loading of PVP by the Soaking Method Using DL-PVP Contact Lenses. In this method, a combination of direct PVP and soaking methods was employed to improve PVP loading. The extracted direct-PVP-laden contact lens (3-DL-PVP) was soaked in 3% w/v PVP packaging solution followed by sterilization. At the end of the soaking period (24 h), the contact lenses (coded as 3-DL-3-SM-PVP) were removed and subjected to characterization.

4.5. Coating of PVP by Curing the Contact Lenses. In this technique, the PVP loading was further increased by coating PVP on the surface of the contact lenses (3-SM-PVP and 3-DL-3-SM-PVP) by short hit curing using UV light at 365–370 nm for 30 s (time was optimized in preliminary trials). The extracted and sterilized 3-SM-PVP and 3-DL-3-SM-PVP contact lenses after 24 h of the soaking period were shifted to an ultraviolet transilluminator for surface curing and coded as 3-SM-PVP-C and 3-DL-3-SM-PVP-C, respectively.

4.6. Swelling Study. A study of the percentage of swelling was performed to investigate the wettability of the contact lenses.31 The silicone contact lenses were de-molded and the weight was recorded as dry weight (Wd), followed by extraction, sterilization, and short curing, as discussed in the above sections. The PVP-loaded contact lenses were removed from their respective packaging solutions and the weight was recorded as Ws. The % swelling was calculated using the equation

\[
\% \text{ swelling} = \frac{W_s - W_d}{W_d} \times 100
\]

4.7. Optical Transmittance. The optical transmittance of the contact lenses should not be altered due to the presence of PVP. A study of the percentage of transmittance was carried out using a UV-visible spectrophotometer.52 The contact lenses were removed from the packaging solution and positioned inside a quartz cuvette, which was then placed in a UV-visible spectrophotometer and the transmittance was measured at 480 nm.

4.8. In Vitro Release Kinetics. The PVP-laden silicone contact lenses were kept individually in a glass vial containing 2 mL of STF at 34 °C in an incubator shaker at 100 rpm.53 To maintain the sink condition, the STF was replaced with the same volume of fresh STF media at regular time intervals until the PVP was detected. The amount of PVP released was quantified by a UV-visible spectrophotometer (colorimetric method) at 420 nm using citric acid and iodine–KI solution (for more details, see Supporting Information II). The release profile of PVP was evaluated by plotting the different graphs of cumulative PVP release versus time and release rate (ng/h) versus time. The experiments were carried out in triplicate.

4.9. In Vivo Assessment of Tear Volume. New Zealand white rabbits ranging from 3.5 to 4.0 kg in weight were housed individually in standard cages in a light-controlled room at 20 ± 1 °C and 50 ± 1% relative humidity (no restriction of food or water).34 During the study, the rabbits were placed in restraining boxes. They were allowed to move their heads freely, and their eye movements were not restricted. The animal protocol was approved by the Institutional Animal Ethical Committee (IAEC) (Protocol No. MPC/IAEC/03/2019) of Maliba Pharmacy College, Bardoli, India. The experiments were conducted according to the guidelines of the Committee for the Purpose of Control and Supervision of Experiment on Animals (CPCSEA). The animal studies were performed to compare the soaked contact lens (3-SM-PVP), direct-PVP-laden contact lens (3-DL-PVP), soaked direct-PVP-laden contact lens (3-DL-3-SM-PVP), soaked and cured PVP contact lenses (3-SM-PVP-C), and direct-PVP-laden soaked and cured contact lens (3-DL-3-SM-PVP-C) with conventional 0.6% w/v PVP eye drop (one drop = 50 μL = 150 μg of poly(vinylpyrrolidone), Tear plus).

The tear volume and tear film stability are important parameters in the treatment and management of dry eye syndrome.35 A test was conducted to evaluate tear production, which is an important parameter in the ocular investigation for corneal and conjunctival health. The in vivo assessment of tear volume was carried out to investigate the capability of the PVP-loaded contact lenses to stabilize the tear fluid volume in the rabbit eyes in comparison to the eye drop solution. The normal tear volume was measured on day 1 (baseline) before placing the contact lens or eye drop. The contact lens was inserted below the nictitating membrane on the cornea without local anesthesia (n = 6 rabbits, left eye control). In the eye drop group (n = 6), the right eye received a single drop (50 μL) of 0.6% w/v PVP solution and the left eye was kept as the control. At regular time intervals (up to 72 h), the strip paper was placed in the lower eyelid for 120 s and the wetted portion of the paper was noted in millimeter.

During the Schirmer tear test study, the eyes were assessed on each day for tearing, discharge, blepharospasm (twitchy and forceful blinking of the eyelids), ptosis (eyelid drooping), and conjunctival redness, which are all signs of ocular infection or discomfort. The eyes were also assessed on each day for protein adherence and scored: 0, no protein adherence; 1, slight protein adherence; 2, moderate protein adherence; 3, high protein adherence; and 4, very high protein adherence with discharge.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c01764.

In vitro release rate graphs; analytical method development for quantification of PVP; and protein adherence scores (PDF)
Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.0c01764

Notes
The authors declare no competing financial interest.

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