Solution-related *in Vitro* Dewetting Behavior of Various Daily Disposable Contact Lenses

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**SIGNIFICANCE:** The dewetting process of contact lenses (CLs) is a result of material and solution properties as well as environmental factors. This article describes an investigational approach to observe and describe dewetting characteristics of different CL material and solution combinations.

**PURPOSE:** This study aimed to determine the *in vitro* dewetting characteristics of various daily disposable CLs that were assessed using a noninvasive keratograph dewetting procedure (noninvasive keratograph dry-up time). *In vitro* dewetting data of the same CL materials soaked in saline solution and artificial tear solution (ATS) were measured to determine additional dewetting characteristics.

**METHODS:** Noninvasive keratograph dry-up time was measured for six different soft CL materials and three different test conditions, in their specific blister solution, after exposure to saline and an ATS. Twenty CLs of each solution/material combination were assessed after an 8-hour soaking, during a 180-second dewetting observation, and the results were expressed by area under the curve values.

**RESULTS:** Fastest dewetting occurred for all materials when measured out of saline, indicated by the highest averaged area under the curve value of 9243.3 ± 38.3 over all lens materials. Slower dewetting was detected for all materials when measured out of their specific blister solution (7755.9 ± 37.1) and out of ATS (7988.8 ± 40.0). Intragroup results were statistically significantly different for all solutions showing the smallest differences within the ATS group (P < .001; Kruskal-Wallis test).

**CONCLUSIONS:** A pure saline thin film is not an ideal representation of a complex tear film layer of a healthy human because it lacks any evaporative protection by a lipid layer. The use of an ATS, which more likely mimics the natural tear film, allowed in this experimental *in vitro* project to decrease the gap to the *in vivo* field. *In vitro* dewetting information in connection with the blister solution allows only a theoretical conclusion about the initial lens wear after lens insertion.

Comfortable contact lens wear is essentially connected to the hydrophilic surface of a contact lens material.1 The term *wettability* is widely used in this matter, and various methods were established that determine *in vitro* wettability on contact lenses and include the sessile drop2–4 and captive bubble method,5–7 or the Wilhelmy plate method.8–10 These tests assess the tendency of a solution to spread over the surface when exposed to a solid object.11 Typical test solutions that have been used for soaking procedures before wettability measurements are phosphate-buffered saline,9 contact lens care solutions,12 blister solutions,13 or artificial tear solutions.11,13,14

Besides investigating *in vitro* wettability,10,15,16 researchers explored the sustainability of a wetted lens surface over time. This topic is of special interest because a liquid film on a solid substrate does not behave consistently.17 The phenomenon is caused by the thermodynamics of the surface free energy minimization and kinetically mediated by the hydrodynamics of the liquid.18 The so-called surface dewetting considers the existing kinetic effect over time, which the traditionally used sessile drop or captive bubble methods do not consider. Every method addresses the wettability but under different environmental conditions. The time-related stability of a thin liquid film is clinically relevant because instability can cause a negative impact on vision.19 In addition to vision, comfort plays an important role. A dewetted surface would cause higher friction during the blink. Hence, a better lubricated surface provides potentially better wearing comfort and can positively contribute to better vision.20

Although the link between the *in vitro* wettability of a contact lens and its clinical performance seems to be theoretical, there is little literature available.21 Although it is known that *in vivo* results do not necessarily predict real-life performance, researchers attempt to create models to approach possible predictions.22,23 Compared with *in vivo* trials, *in vitro* studies have better cost and time efficiency and use predetermined conditions, which are controllable. Therefore, the aim should be to improve every experimental setup to incorporate real-life conditions such as the eye temperature or the properties of a test solution. The wetting- and dewetting-related outcome of combinations of solutions and materials may be important for clinical considerations. On the other hand, they can be clinically less relevant when phosphate-buffered saline solution is considered as the standard test solution, which is different from the tear film. However, an attempt was made to decrease the gap between *in vitro*-based
dewetting results and on-eye dewetting in the presence of artificial tear solutions assessed using ring mires. The purpose of this study was to determine the \textit{in vitro} dewetting characteristic curves of different daily disposable contact lenses that were measured out of their specific blister solutions using the noninvasive keratograph dewetting procedure to determine the dewetting characteristics.

The secondary objective was to measure the \textit{in vitro} dewetting characteristic curves of the same lenses soaked in saline solution (control) and an artificial tear solution to determine the dewetting characteristics.

**METHODS**

A modified Keratograph 5M (OCULUS Optikgeräte GmbH, Wetzlar, Germany) displayed in Fig. 1 was used to determine \textit{in vitro} contact lens surface dewetting characteristics. The dewetting assessment is based on the projection of an illuminated Placido ring pattern onto the contact lens surface and its reflection from it. The wettability of a contact lens surface is considered stable and homogeneous if the reflection of the Placido ring pattern is uniform at the beginning of the measurement. When the dewetting process becomes visible, the Placido ring pattern will show signs of surface drying, that is, distortions and gaps of the ring pattern but also interference phenomena. An inbuilt camera captures the reflected image over the assessment time.

Dewetting videos, each 180 seconds long, were captured for six different contact lens materials, including nelfilcon A, delefilcon A, senofilcon A, stenfilcon A, somofilcon A, and narafilcon A. Each contact lens had a back vertex power of $-3.0$ D. All materials were silicone hydrogel materials, except for nelfilcon A, which was a hydrogel contact lens with a releasing wetting agent. A duration of 180 seconds is needed to allow the surface to fully dewet in this \textit{in vitro} situation. On-eye dewetting can occur faster than \textit{in vitro} dewetting, with a consequence that a contact lens wearer would blink before the lens dries up because visual quality would be decreased.

The following procedure was carried out to prepare the lenses for the measurements: three measurement sequences related to three solutions (blister solution, saline solution, and artificial tear solution) were planned. A total of 60 original packed lenses per lens type were allocated to the three measurement sequences. A high number of 20 lenses per material were measured because the process involved manual handling, which potentially impacts the thickness of the thin fluid film on the lens because of the speed or angle of placing the lens on the measurement stage. Manual handling steps may not but could increase the variation of results. Before the lenses were measured in the saline or artificial tear solution sequence, contact lenses were prepared to remove most of the blister pack solution. Those lenses were removed from the blister with forceps and rinsed for 10 seconds in saline. However, the surface wettability at the point of contact with the forceps may alter, and therefore, close attention was paid to touch the lenses only at the very edge.

Two milliliters of either saline or artificial tear solution was filled in every well of a 12-well plate, and one lens was placed into one respective well. The well plates were placed on an orbital shaker, which gently agitated the solution by 15° tilting movement for 8 hours with 15 cycles per minute at room temperature (Muya L et al. IOVS 2016;57:ARVO E-Abstract 1463).

After 8 hours, the well plates were removed from the orbital shaker. One by one, lenses were removed out of the wells by forceps paying attention not to touch the lens area of interest, which was the central 10 mm, for the dewetting measurement. A first masked investigator placed the lens on a cornea-simulated measurement stage, and the capture session started immediately to avoid changes of the contact lens surface due to extensive handling time. A 180-second video was captured using the \textquotedblleftnoninvasive keratograph-breakup time\textquotedblright mode of the measurement instrument using the Keratograph Tear Film Scan (Oculus Optikgeräte GmbH, Wetzlar, Germany) software, released by the manufacturer. The lens was removed from the stage and disposed after capturing the video. Captured videos were overlain with a grid consisting of 192 segments using the editing option within the software. A second masked and trained investigator evaluated each video in steps of 1 second and marked segments that showed a dewetted area of

![FIGURE 1. Horizontally mounted measurement device without housing (left) and a close-up of a soft contact lens on the stage below the Placido disc (right). (1) Horizontally mounted Keratograph 5M (climate housing not shown), (2) adjustable x-y-z platform, (3) measurement stage, (4) contact lens, and (5) white illuminated ring mires.](image-url)
the soft contact lens if it was not automatically detected.\textsuperscript{19} This was performed to keep a possible time-related offset bias between detected and real dewetting as low as possible. The investigator marked second-wise segments that showed dewetted surface areas, visible by either a clear border of the thin film or reaching a base gray level. The analysis software plotted the number of marked segments over time starting from the time point of the first distortion.

Statistical Analysis

The edited dewetting measurements were exported from the experimental topographer as an Excel (Microsoft Inc., Redmond, WA) file. Every averaged measurement set consisting of 20 single measurements was transferred to SPSS version 21 for statistical analysis (SPSS, Chicago, IL). Based on the Kolmogorov-Smirnov test results, the Kruskal-Wallis test was performed to investigate if the nonnormally distributed, independent measurement sets were statistically different. The six different daily disposable contact lens materials were grouped for blister solution, saline solution, and artificial tear solution. A post hoc analysis was performed for every contact lens material group related to the soaking solution using the Dunn-Bonferroni test. The post hoc data tables are shown in the Appendix, available at http://links.lww.com/OPX/A578. All materials were pairwise compared for three end points. The end points are graphically explained in Fig. 2.

1) Area under the curve: it takes the dynamics of dewetting over the measurement period into account. In the analysis, numerical integration is used for calculating the numerical value of the integral, because the integrand $f(x)$ is known only at certain points, as obtained by sampling.\textsuperscript{28}

2) Time at 25\% dewetted surface\textsuperscript{25}: it is the time from starting the measurement directly after placing the lens onto the stage until the time in seconds at which 25\% of all segments show dewetting.

3) Time at 50\% dewetted surface: it is the time from starting the measurement directly after placing the lens onto the stage until the time in seconds at which 50\% of all segments show dewetting.

RESULTS

The mean areas under the curve were 9243.3 ± 38.3 for saline solution, 7755.9 ± 37.1 for blister solution, and 7988.8 ± 40.0 for artificial tear solution.

Intragroup results (Table 1) show that the lens materials were statistically significantly different regarding its dewetting behavior ($P < .001$, Kruskal-Wallis test) for saline and blister solution. Intragroup differences were not only smaller for artificial tear solution but also statistically significant ($P < .001$, Kruskal-Wallis test). The mean times to reach 25\% dewetted surface were 63 ± 21 seconds for saline solution, 86 ± 16 seconds for blister solution, and 86 ± 22 seconds for artificial tear solution. The mean times to reach 50\% dewetting were 93 ± 23 seconds for saline solution, 97 ± 25 seconds for blister solution, and 103 ± 25 seconds for artificial tear solution.

The dewetting characteristics differed most for the contact lens materials when they were measured out of their specific blister pack solution or soaked in saline solution (Figs. 3, 4). In comparison, Fig. 5 shows more narrow dewetting curves for all tested contact lens materials, except for delefilcon A. The majority of all test materials showed a faster dewetting when soaked in saline in comparison with artificial tear solution.

DISCUSSION

The dewetting curves, which were collected from lenses pre-soaked in blister solution, show a wide range of results depending on the lens material. Although the dewetting starts within the first 10 seconds for all materials, there is little difference until the time point of 30 seconds, indicating the presence of a sufficient thin film and a similar rate of evaporation. The speed of dewetting is different after this time point. The slowest dewetting was achieved for neofilcon A, and its original blister solution was represented by the smallest mean area under the curve value of 3168. The fastest dewetting was seen in neofilcon A out of saline solution expressed...
by the highest mean area under the curve value of 11,091, which is more than tripled. The investigator observed a full dewetting of all lens materials after 180 seconds, with an exception of the combination nelfilcon A and its blister solution, which still showed a partially wetted surface at this time point. Investigator-related observations after placing the lens on the stage include the impression that a certain slow and uncontrolled drainage of the thin film from the center toward the edge was visible at least in the first 15 seconds of the measurement, when the thin film had its thickest appearance. This slow flow of the thin film was primarily forced by gravitation because the stage had a base curvature of 8.5 mm with an eccentricity of zero. A contact lens material- or solution-related difference cannot be reported by this subjective impression. However, the thin film thickness cannot be controlled, and it can be supposed that the thickness varied depending on contact lens material and soaking solution. Furthermore, it can be assumed that, because it was not measured, the thin film achieved in this in vitro setup is thicker than the natural tear film. Most of the dewetting curves of a specific lens material differed between the test solutions. However, somofilcon A and stenfilcon A showed a similar dewetting behavior between saline and blister solution measurements. It is illustrated by an almost identical area under the curve value for somofilcon A of 10,762 for its blister solution and 10,910 for saline. Respectively, stenfilcon A revealed a mean area under the curve of 9225 regarding the dewetting in connection with its blister solution and 9236 regarding saline solution.

### TABLE 1. Numerical results for solution-related end points (NIK-DUT)

| Lens material                  | Blister solution | Saline solution | Artificial tear solution |
|--------------------------------|------------------|----------------|-------------------------|
|                                | AUC, mean ± SD   | AUC, mean ± SD | AUC, mean ± SD          |
| nelfilcon A, Dailies Aqua      | 3161.04 ± 15.86  | Not reached    | 8857.55 ± 43.62         | Comfort Plus                   |
| deleficon A, Dailies Total 1   | 6166.38 ± 33.54  | 96 ± 17        | 5532.60 ± 31.61         |                                |
| senofilcon A, Acuvue Oasys     | 9398.20 ± 51.57  | 90.00 ± 28     | 8248.62 ± 42.19         | 1 Day                           |
| stenfilcon A, MyDay            | 9225.63 ± 39.74  | 91 ± 21        | 8812.99 ± 42.01         |                                |
| naranfilcon A, 1 Day Acuvue    | 7821.98 ± 41.09  | 107 ± 30       | 8435.34 ± 40.67         | TruEye                          |
| somofilcon A, Clariti 1 Day    | 10,762.47 ± 40.73| 76 ± 22        | 8045.44 ± 39.76         |                                |

Dailies Aqua Comfort Plus (Alcon, Geneva, Switzerland); Dailies Total 1 (Alcon, Geneva, Switzerland); Acuvue Oasys 1 Day (Johnson and Johnson ACUVUE, Jacksonville, FL); MyDay (CooperVision, San Ramon, CA); 1 Day Acuvue TruEye (Johnson and Johnson ACUVUE, Jacksonville, FL); Clariti 1 Day (CooperVision, San Ramon, CA). AUC = area under the curve; NIK-DUT = noninvasive keratograph dry-up time; SD = standard deviation.

**FIGURE 3.** In vitro dewetting curves of various lenses (n = 20 per material) pre-soaked in blister solution during a period of 180 seconds.
The results of the secondary end points were similar as well and are displayed in Table 1. This indicates either a more solution-independent dewetting behavior or similar property of the specific blister solutions of these lenses.

The assessments of all materials using an artificial tear solution in comparison with the control solution, which was unpreserved saline, showed an improvement regarding all end points when using artificial tear solution. However, differences in the area under the curve, which have been present in saline investigations, almost disappeared when using artificial tear solution. The only exception is the dewetting behavior of delefilcon A, which seems to dewet slower when soaked in artificial tear solution in terms of achieving the lowest area under the curve value. This may be the results of the unique water gradient technology used in that material. The surface water content of this material is greater than 80%29 with the aim to mimic the surface characteristics of the corneal epithelium and the tear film. It can be speculated if this is the result of a higher water gradient surface interaction with artificial tear solution than with other lens surfaces or if delefilcon A could mask a possible dewetting by its water gradient technology. This cannot be clearly answered because we see, on the one hand, that delefilcon A performs very well in vivo,30,31 but on the other hand, it shows in vitro...

![Graph 4](image1.png)

**FIGURE 4.** In vitro dewetting curves of various lenses (n = 20 per material) pre-soaked in saline solution during a period of 180 seconds. Neofilcon A material showed a partial drop formation at the start, which led to an early exposure of the surface to some extent.

![Graph 5](image2.png)

**FIGURE 5.** In vitro dewetting curves of various lenses (n = 20 per material) pre-soaked in artificial tear solution during a period of 180 seconds. All materials dewet in a similar way, except for delefilcon A.
the least change regarding the ring distortions between the fully wetted and dewetted surface.

Overall, it was observed that the dewetting occurred faster when the materials were pre-soaked in saline. The mean area under the curve value of all materials measured out of saline solution was 9244 in comparison with blister solution with 7756 and artificial tear solution with 7988. These findings were supported by the secondary end points as well. The mean time at 25% dewetted surface was 23 seconds shorter for saline in comparison with blister solution and artificial tear solution. The mean time to reach 50% dewetting was 10 seconds shorter. All intergroup comparisons with saline were significant ($P < .001$, Wilcoxon signed rank test). The wettability of a contact lens should be more seen as a kinetic dewetting process. The data on the area under the curve represent most sufficiently that the dewetting of a thin film is a dynamic process and therefore could describe in vitro wettability better than a single time point, such as the time to reach a specific dewetting.

These solution-dependent results have also been described in previous literature. Muya et al. (Muya L et al. IOVS 2016;57:ARVO E-Abstract 1463) reported that the sessile drop angle and coefficient of friction decreased when wetting-enhancing substances were added to a saline solution. Bhamla et al. reported partially similar investigations. Their experiments showed a complete dewetting of silicone hydrogel material after 194 seconds. In contrast, Bhamla et al. reported a fast complete dewetting of saline solution after occurrence of an initial breakup. The used drainage system may be responsible for the accelerated dewetting in comparison with the captured results presented in this article. Havuz and Gokmen observed dewetting patterns of different soft contact lenses at 30-second time intervals using in vitro videokeratoscopy. The technical difference of their measurement setup was mainly the vertically positioned stage in combination with the use of a medical sponge positioned at the inferior part. In addition, gravity and hydrodynamic drainage were different, but also some similarities were reported. The investigated dewetting behavior of seven soft contact lens materials differed significantly when pre-soaked for 4 hours in saline solution. A total measurement time of 180 seconds was analyzed, and a small standard deviation was calculated for the dewetted area at the specific time intervals. Havuz and Gokmen concluded that the lens materials with their specific surfaces were responsible for the differences seen at out-of-saline measurements. The limitation to saline does not allow for a conclusion how those materials would dewet when using other solutions.

The overall dewetting process has multifactorial impact factors such as surface structure, temperature, humidity, or gravity. However, there are three primary factors including adhesive forces, cohesive forces, and the surface tension. Van der Waals forces are cohesive forces between nonconnected atoms or molecules. These forces are lower when temperature is rising; however, they are higher when molecular surface is bigger. For this study, all measurements were conducted at a room temperature of 21°C and 45% humidity, which was also reported in similar investigations. The cohesive forces were constant for the saline solution and artificial tear solution measurements but were different for the blister solution measurements because the blister solution of the different manufacturers varied.

Intramolecular cohesive forces of the saline solution are weaker in comparison with the forces of the blister solution or artificial tear solution, which might lead to a faster evaporation. It could also be expected that the adhesive forces are lower. The entire dewetting process is also connected with evaporation, which leads to localized thinning. Assuming that every lens material can initially sustain a thicker thin film, the thinning can occur because of a flow of the fluid away from the possible region of break in connection with evaporation. This thinning is then followed by breakup of the ridges, separating holes into drops when the cohesive force is higher. No drops were visible when adhesive forces are higher.

Adhesive forces between molecules of the solution and the contact lens surface play a key role. The achievable adhesion is determined by the work of adhesion and can be described by Dupré’s equation. The dewetting process occurs when adhesive forces are smaller than cohesive forces. If the difference between the forces were big, the liquid would pull itself together into the shape of a droplet. This may be the reason for the initial dewetting phase of the saline solution that was experienced over the nelfilcon A lens material. This effect could be triggered by the impression point of the forceps, which were used to transfer the lens from the solution toward the measurement stage. However, surface tension impacts the dewetting process as well. Lin and Svitova stated already that the surface tension of the aqueous medium should be brought into contact with a lens surface concerning wettability measurements. The surface tension decreases when additives were mixed into saline. The result is seen in the dewetting process. The formation of droplets was observed in dewetting measurements with pure saline solution, which was also detected in this study. The observed dewetting pattern for lens materials pre-soaked in artificial tear solution was a thinning of the film until breakups occurred.

Walther et al. observed a reduction of the artificial tear solution layer on different daily disposable contact lenses too. They used a model blink cell, placed in a temperature-controlled glove box, which allowed to rewet the contact lens surface in cycles. Walther et al. determined the noninvasive breakup time of five different daily disposable materials at different time points for up to 16 hours after incubation in the blink cell using an artificial tear solution. The intention to mimic in vivo conditions can be concluded because they performed the measurements at 34°C and 50% humidity. This contrasts with our study design, in which the measurements were performed at 21°C and 45% humidity. The end point differed as well. Whereas Walther et al. focused on the clinically relevant noninvasive breakup time end point (16 hours of simulated lens wear), this study concentrated more on the dynamic dewetting over time until an almost complete dewetting was reached after 180 seconds. This time span was consciously selected, knowing that it is much more than a usual interblink period. When Walther et al. compared their in vitro noninvasive breakup time results with in vivo data from studies investigating the same contact lens materials on the eye, they found that the in vitro results were two times longer. A potential reason could have been the use of a larger amount of artificial tear solution in comparison with the physiological levels of tears. In addition, they found significant reduction of the noninvasive breakup time over the course of the 16-hour lens cycle study using their model blink cell. Artificial tear solution components such as lipids and proteins can deposit similar to in vivo situations and may affect the dewetting of a contact lens surface. Differences between lens materials, found after the first cycle, disappeared after the 16-hour measurement. Results from our study with artificial tear solution are the averaged area under the curves of 20 single contact lenses of a specific material, which have been measured once. The captured dewetting curves were very similar between the materials, with an exception for delefilcon A.

Limitations of this study setup include that the measurements were conducted at room temperature and not at 35°C eye temperature. A higher temperature would lead to increased evaporation, and the dewetting process would get accelerated. It furthermore includes the fact that it cannot be ensured that all blister solution molecules were removed before saline or artificial tear solution soaking. This is a possible bias for all lens materials depending on the surface...
tension or viscosity of the blister fluid formulation and how quickly its components can be rinsed off.

In addition, manual handling of lenses in comparison with automated processes may lead to a greater variety of thin film thicknesses. However, the standard deviation achieved in this experimental setup showed that this impact is low.

CONCLUSIONS

A pure saline thin film is not an ideal representation of a complex tear film layer of a healthy human because it lacks any evaporative protection by a lipid layer. The use of artificial tear solution, which likely better simulates natural tears than saline or blister pack solutions, allowed for a better comparison with the on-eye situation than past studies, although a true human-based study is still needed to confirm the results of the current study.

In vitro dewetting information in connection with the blister solution allows only a theoretical conclusion about the initial lens wear after lens insertion. However, blister solutions showed benefits in delayed dewetting in comparison with saline solution. Therefore, the optimized blister pack solution should not be rinsed off before lens insertion by the contact lens wearer.

ARTICLE INFORMATION

Supplemental Digital Content: Appendix Table A1, available at http://links.lww.com/OPX/A578; Post hoc analysis for all lens materials pre-soaked in blister solution. P values below .05 indicate differences between the materials. It must be stated that the blister solutions were not identical. The different endpoints were color-wise highlighted. AUC = area under curve; NIK-DUT_S25% = time to reach 25% dewetted surface; NIK-DUT_S50% = time to reach 50% dewetted surface.

Appendix Table A2, available at http://links.lww.com/OPX/A578; Post hoc analysis for all lens materials pre-soaked in saline solution. P values below .05 indicate differences between the materials. The different endpoints were color-wise highlighted. ATS = artificial tear solution; AUC = area under curve; NIK-DUT_S25% = time to reach 25% dewetted surface; NIK-DUT_S50% = time to reach 50% dewetted surface.

Appendix Table A3, available at http://links.lww.com/OPX/A578; Post hoc analysis for all lens materials pre-soaked in ATS. P values below .05 indicate differences between the materials. The different endpoints were color-wise highlighted. ATS = artificial tear solution; AUC = area under curve; NIK-DUT_S25% = time to reach 25% dewetted surface; NIK-DUT_S50% = time to reach 50% dewetted surface.

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