Title

Multipurpose Lens Care Systems and Silicone Hydrogel Contact Lens Wettability: A Systematic Review

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Abstract

Purpose: To provide a current perspective on the relationship between materials developed for silicone hydrogel contact lenses and multipurpose care solutions to identify improvements in wettability patterns.

Methods: This systematic review was completed according to the updated PRISMA 2020 statement recommendations and followed the explanation and elaboration guidelines. The PubMed, Web of Science, and Scopus scientific literature databases were searched from January 2000 to November 2021.

Results: A total of five clinical trials published between 2006 and 2017 were included in this investigation. All included studies were randomized clinical trials. The success of contact lenses is related to the comfort of their use and therefore to the stability of the tear film and the wettability of its surface. The relationship between these parameters and changes in the ocular surface and inflammatory and infectious processes has been demonstrated.

Conclusion: Hyaluronan and propylene glycol multipurpose solution wetting agents achieved slightly higher pre-lens noninvasive break-up times than poloxamine. Polyquaternium-1 achieved better wettability and patient comfort than polyhexamethylene biguanide in medium-term studies. Short-term studies did not demonstrate differences between multipurpose solutions in their effect on contact lens wettability.

Keywords

Pre-lens tear film stability; Wettability; Dewetting; Multipurpose solution; Contact lens care.

Introduction

Wettability is defined as the balance of adhesive and cohesive forces on the surface of the contact lens (CL) [1,2]. The biomaterial wettability calculation is measured with the contact angle between the liquid and the CL surface within the Young equation. The smaller the contact angle is, the greater the CL wettability degree [3]. A lack of CL wettability is associated with the interruption and discomfort of stability of use, a lack of tear film stability, changes in the ocular surface, and the interaction of areas with CL movement [4]. When a CL is inserted on the ocular surface, it partitions the tear film layer into two interfaces, the precontact and postcontact phases, which induces changes in tear film stability. Mostly in the precontact phase, there can be thinning and greater mechanical friction of the eyelid [5].

Silicone hydrogels (SiHy) are compounded with a silicone-rich core, with hydrophobic properties and high oxygen permeability, and on the surface is a hydrophilic monomer [6–8]. Its composition and material balance are essential for stabilization of the precontact layer, improving wettability and lubrication [9,10]. CL surface wettability does not play a corneal role due to its lack of mucinic and hydrophilic patterns [11]. Maintenance of CLs requires certain care for their hygiene, decontamination, and conservation to be able to prevent specific microorganisms and improve their comfort [12].

Multipurpose solutions (MPSs) generally contain systems to maintain pH, chelating agents to fix metal ions, antimicrobial agents such as biguanides for disinfection and preservation, or the use of multiple biocides that also perform preservative functions and osmotic agents for adjustment of osmolarity [13]. MPS solutions can vary the physical and mechanical parameters of the properties of contact lenses and the ocular surface, and this interaction compromises patient comfort [14]. MPS usually induces corneal desiccation compatible with increased corneal inflammation [15], which is improved by incorporating wetting agents into its composition, such as viscous polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), hydroxypropyl methylcellulose (HPMC), and polyethylene glycol (PEG) [16,17]. The combination of different materials and the incorporation of wetting agents into MPS has been shown to maintain the degree of wetting for longer periods on the contact lens surface and a greater degree of extended release

[18]. Some of the factors that affect wettability are the interaction between the contact lens material, multipurpose solutions, and the final fit of CL [19].

The purpose of this systematic review is to study the relationship between the materials used for the manufacture of silicone hydrogel contact lenses and multipurpose solutions with the aim of identifying what improves the wettability patterns.

Methods

This systematic review was completed according to the updated PRISMA 2020 statement recommendations [20] and followed the explanation and elaboration guidelines [21]. The PubMed, Web of Science, and Scopus scientific literature databases were searched from January 2000 to November 2021. The following search strategy was used within the three databases: *"(Pre-Lens Tear Film Stability OR Pre-Lens Tear Film OR Wettability OR Dewetting OR Drying-Up Time OR Non-Invasive Drying-Up Time OR Non-Invasive Dry-Up Time OR Break-Up Time OR Non-Invasive Break-Up Time) AND (Solution Care OR Contact Lens Care OR Contact Lens Solution Care OR Lens-Care Solution OR Silicone Hydrogel Contact Lens Care)"*. The filter limitations on the search strategy were publication after 2000, only human studies, and exclusion of reviews.

Two authors (M-J. B-LL. and J-M. S-G.) identified and evaluated the selected articles according to title and abstract in a first identification round. Only articles on the influence of the contact lens care solution on silicone hydrogel and conventional hydrogel contact lenses went through the second phase. At this point, these two reviewers evaluated duplicate articles. In the second phase, articles were again analysed and excluded for the following reasons: (1) non-English publication, (2) non-Journal Citation Reports index publication, (3) in vitro study, and (4) case report or case series articles. Both reviewers worked blinded to each other. In case of disagreement, the third author (R. C-P.) made the tiebreaker decision.

Regarding the extraction and selection of the studies, the Mendeley platform was used. The authors designed the tables to extract the study data.

Systematic review records were obtained that were consistent with the characteristics of the research and the main outcome procedures. For the first part, the extracted data items comprised (1) authors and publication year; (2) study design (randomization, blind study); (3) declaration of conflicts of interest (yes or no; which, if yes); (4) subject inclusion criteria; (5) subject exclusion criteria; (6) study duration (in weeks); (7) mean age and standard deviation (minimum to maximum, range); (8) gender distribution; (9) number of subjects; (10) number of eyes involved; (11) multipurpose contact lens care solution (name and manufacturer) and (12) contact lens material (name and manufacturer). Among the outcome measures, the following data items were reported: (13) pre-lens noninvasive break time (PLNIBUT), reporting the PLNIBUT measuring instrument, endpoint criteria and break time value (expressed in seconds) and (14) ocular surface sign, reporting the sign measurement instrument, classification or scale criteria and value (expressed in score scale or comparable). In addition to these measurements, information on contact lens material (brand, permeability, water content, FDA group, modulus, and information on wettability agent) and multipurpose contact lens care solution (brand, preservative, and wetting agent) was extracted from studies.

To determine the risk of bias of individual studies, this systematic review followed the standards of Cochrane Reviewers' Handbook version 5.4.1, and the quality of the included methodologies was evaluated [22]. The standards mainly included the following conditions: (1) whether the random method was appropriate; (2) whether it was hidden by the allocation plans; (3) whether blinding was applied to the patient and the researchers; (4) whether blinding was applied to the evaluators of outcome measures; (5) whether bias was caused by missing data; (6) whether bias was caused by selective information; and (7) whether there were other types of bias. On this basis, each index was assessed by the risks or ambiguity of low and high bias (relative information missing or inexplicit bias). Two evaluators review the literature (M-J. B-LL. and R. C-P.) for independent determination, and the resulting data were

checked repeatedly. For comparing the results, a third researcher (J-M. S-G.) also resolved any disagreement, and secondary analysis and evaluation were performed to reach the final decision.

Results

The systematic review selection process is presented in a flow chart (Figure 1). A total of five clinical trials [13,16,18,23,24] published between 2006 and 2017 were included in this investigation. All included studies [13,16,18,23,24] were randomized clinical trials (RCTs). None of the studies presented conflicts of interest; however, two [18,23] RCTs were sponsored by Alcon, and Martin et al. [24] was sponsored by Disop. Contact lens users were included in three of the studies[18,23,24], while the other two RCTs [13,16] included only noncontact lens wearers. Within the exclusion criteria, almost all studies excluded patients with MPS intolerance, topical ocular medications, dry eye disease, giant papillary conjunctivitis, corneal opacities, or any ocular surgery or disease. Regarding the duration of the study, we can differentiate two types: long-term studies [18,23,24] between four and twelve weeks and short-term studies [13,16] between 10 and 15 minutes. The mean age of the included patients was 28.7 ± 6.86 years. The sex distribution was 39.8% male patients and 60.2% female patients. In all, the RCTs included 570 subjects, and the mean number per article was 112.2 ± 140.65 patients. The detailed characteristics of the RCTs are presented in Table 1.

Outcome measurement variables related to wettability and signs and symptoms of the ocular surface are presented in Table 2. A wide range of MPS was analysed in the studies. To clarify cleaning, preservative, buffer and wetting agents, a summary of the MPS data sheet is presented in Table 3. Four of the five studies examined only one or two CL materials, except for Stiegemeier et al.[23] that included several CL materials (Etafilcon A and Ocufilcon D, among other Group IV high water and ionic hydrogel polymers). The method used, the criteria, and the values achieved for wettability and the signs and symptoms of the ocular surface are summarized in Table 2.

The specific assessment of the risk of bias within the studies is presented in Figures 2 and 3. Regarding the risk of bias assessment of the included studies in the systematic review, it should be noted that in the study by Guillon et al.[18], patients already wore contact lenses and knew which lenses they were wearing. Lau et al.[16] used the same procedures that were performed for each presoaked lens on the same day, with a rest period of twenty minutes between each pair of lenses. This means that the result cannot be the same with respect to the PLNBUT in the first contact lens used, compared with the last one, after having changed it five times.

Regarding the clinical trial by Martin et al.[24], the use of a single CL is a significant limitation of this study, as the manufacturer provided specific recommendations on which CL was compatible with the MPS tested in this clinical trial. Finally, Stiegemeier et al. [23] considered the use of rewetting drops during the month prior to the study acceptable, being able to influence the state of the participant's tear film and therefore the wettability of the CL and the measurement of PLNBUT.

Discussion

The success of contact lenses is related to the comfort of their use and therefore to the stability of the tear film and the wettability of its surface. The relationship between these parameters and changes in the ocular surface and inflammatory and infectious processes has been demonstrated [25–28]. In this review, we studied the relationship between the materials used for the manufacture of SiHy CLs and MPSs with the aim of identifying what improves the wettability patterns.

New advances in the industry of MPS and CL solutions bring with them a series of changes in concepts such as ocular wettability and biocompatibility to improve possible signs at the inflammatory level [29]. In short-term studies (10 to 15 minutes), Kitamata et al. [13] found no significant differences between MPS solutions in terms of PLNIBUT (between 3.4 ± 0.5 and 4.2 ± 0.6 seconds) and ocular signs and symptoms (with a maximum of 91 ± 12 and a minimum of 88 ± 12 on a subjective comfort scale of 0 to 100), and even reported greater comfort with a saline solution. These changes justify possible

modifications in the pH, although the pH of higher acidity obtained in saline solutions should have resulted in the opposite effect.

Lau et al. [16] also obtained short-term PLNIBUT results (between 2.78 (0.80-57.75) and 3.08 (0.43-28.90)), in this case lower than Kitamata et al. [13], and without symptomatic correlation, although it should be noted that they did not use preservative-free saline solutions in their composition, which could also modify the results. This result may be justified by the methodology used; the six MPSs were assessed on the same day in short intervals of time so that the simple fact of removing and applying the CL would alter the tear film. According to Gonzalez-Méijome et al. [30], the stability of the tear film may depend more on the subject than on the MPS. The effects of MPS on tear film stability are likely to occur during the initial period of CL use, while tear film composition plays an increasingly important role as MPS leaks out of the CL.

Marx et al.[31] observed statistically significant changes in the wettability of the CL when it incorporates the Hydraglyde® matrix in its composition due to its moisturizing function. In the medium-term results, Martin et al. [24] used two PHMB-based (polyhexamethylene biguanide) care systems and a single type of CL to not vary in vivo behaviour, and the research team did not find significant changes in terms of safety, subjective ocular signs and symptoms, or ocular surface comfort within a month. Similar studies were carried out by Guillon et al. [18] and Stiegemeier et al. [23], where the CL care system was changed from a PHMB solution to a solution based on hydrogen peroxide or polyquaternium-1 (PQ-1). This research was carried out if they obtained significant improvements in performance and wettability with three months of follow-up, although both studies were sponsored by the laboratory that manufactures the MPS used, and their composition included low concentrations of hydrogen peroxide or PQ-1. Furthermore, Stiegemeier et al. [23] use a subjective measurement scale with different CLs and regular users of them; this could explain the result, since the MPS used was similar, but typical CL users may be more sensitive to changes in comfort.

Guillon et al. [18] reported the trial that lasted the longest, although its participants knew what CL they were using and had symptoms. The cleanliness of the CL was evaluated, and improvement with

hydrogen peroxide significantly enhanced the wettability. This could support the theory that comfort is given by the relationship between the CL and therefore its composition and its relationship with the tear film of the user, which were justified as modifications of the corneal morphology. In addition, the same author in later studies also associated the lack of wettability with the act of prolonged visual tasks and low wettability environmental conditions, factors that again affect the user's tear film [19,32].

Limitations and Strengths

To the best of our knowledge, this is the first systematic review of the influence of MPS on silicone hydrogel material based on the available scientific literature. The recently updated PRISMA method improves the level of evidence available to date. Regarding limitations, only five studies could participate in this review; there is a lack of literature on randomized clinical trials comparing the same contact lens material with different comparable MPSs. The methodology design of the present study was nonstandardized, and for this reason, a meta-analysis could not be performed. In the same way, there is great heterogeneity in the follow-up results, and therefore, the design should be standardized. Furthermore, three studies [18,23,24] that reported the best results among the articles included in this review have risks of bias. For instance, Alcon (Fort Worth, Texas, USA) and Disop (Alcobendas, Madrid, Spain) financially sponsored the research. Therefore, we allow the readers to weigh the results and conclusions of this systematic review. In addition, the low validity of the tests used, all with a large subjective component on the part of the observer, creates deficits of repeatability, sensitivity, and specificity, which would be solved with the use of standardized tests and with a more objective observer.

Future research lines

Regarding this issue, the scientific literature needs long-term studies, with more than three months of follow-up, to report the influence of MPS on the silicone hydrogel and the conventional hydrogel contact lenses on the signs and symptoms of the ocular surface. There is a lack of in vivo studies that analyse SiHy CL wettability within noninvasive PLNIBUT measurements.

In conclusion, this systematic review did not reveal statistically significant differences in PLNIBUT with the different MPSs used in the reviewed works. However, slightly higher PLNIBUT was found in those that incorporated a wetting agent such as hyaluronan and propylene glycol. There were no studies that evaluated the effects for more than six months that would help us to have a better vision of the modifications on the wettability parameters, using different MPS maintenance systems and treatments that improve wettability in the CL.

Declarations statements

Ethics

Study approval: non-required due systematic review

Data Availability

All data were included in this article. Further inquiries can be directed to the corresponding author.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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Authors Contribution

All the authors contributed to the study concept and design, data collection and analysis, as well as the preparation of the material. All the authors read and approved the final version of the manuscript.

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Figure Legends

Figure 1 – Systematic review flowchart diagram

Figure 2 – Risk of bias summary panel assessment using Cochrane risk of bias tool showing review author's judgment about each risk of bias item for each included study.

Figure 3 – Risk of bias bar graph showing review author's judgment about each risk of bias item presented as percentages across all included studies.

Table 1. Study characteristics

Authors & Year	Study Design	Conflict of Interest	Inclusion Criteria	Exclusion Criteria	Duration	Mean Age ± SD	Gender (%) M / F	Subjects
Stiegemeier et al.[1] (2006)	RCT	Alcon Sponsored	CL users	MPS Intolerance, Eye topical medication,	4 weeks	36 ± NR	23 / 77	362
Martin et al.[2] (2011)	RCT	Disop Sponsored	Lotrafilcon B Daily	DED, GPC Corneal Opacities, Ocular Medication	4 weeks	27.9 ± 5.7	24 / 76	54
Guillon et al.[3] (2015)	RCT	Alcon Sponsored	Senofilcon A Balafilcon A	NR	12 weeks	35.5 ± 10.1	62 / 38	74
Lau et al.[4] (2016)	RCT	No	No CL users	DED, Ocular medication or disease	15 min	22.1 ± 0.2	50 / 50	30
Kitamata-Wong et al.[5] (2017)	RCT	No	No CL users	DED, ocular disease, surgery, or medication	10 min	22.0 ± 3.0	40 / 60	40
SD: Standard Deviation, M: Male, F: Female, RCT: Randomized Clinical Trial, CL: Contact Lens, MPS: Multipurpose Solution, DED: Dry Eye Disease, GPC: Giant Conjunctivitis Papillary, NR: Not Reported								

Table 2. Wettability and ocular surface signs and symptoms

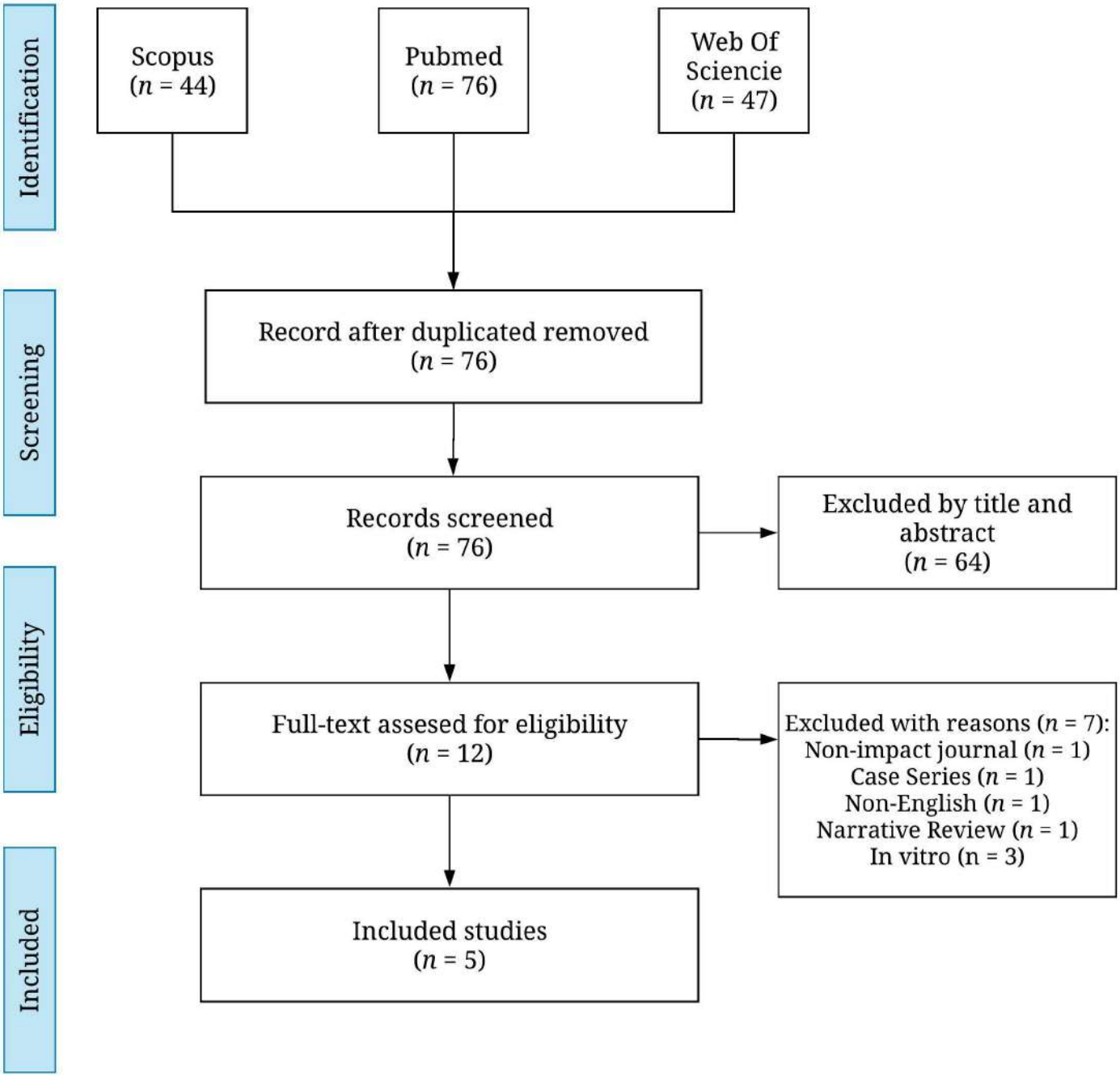
Authors & Year	Multipurpose Solution	Contact Lens Material	Wettability			Ocular Surface Signs & Symptoms		
			Method	Criterion	Value	Method	Criterion	Value
Stiegemeier et al.[1] (2006)	Opti-Free Replenish ReNu MultiPlus	Mixed CL	Front surface score	From absence to severe	Lower Higher	MPS Surface Comfort	Likert Scale (0 – 5)	3.7* 3.3*
Martin et al.[2] (2011)	Solo Care Aqua Hidro Health Solution	Lotrafilcon B	Subjective Score Scale	0 = Uniform Surface 3 = Non – wettable	0.8 ± 0.9 0.9 ± 0.8	Corneal Oedema	0 = None 4 = Severe	0.08 ± 0.3 0.10 ± 0.5
Guillon et al.[3] (2015)	Clear Care ReNu Fresh	Senofilcon A and Balafilcon A	PLNIBUT (Tearscope)	First dark spot (sec)	5.7 ± 4.5* 4.2 ± 2.1*	Percentage Scale	% Mucus Free Surface	95% 87%
Lau et al.[4] (2016)	Opti-Free PureMoist Opti-Free Replenish Complete Biotrue ReNu Fresh Sensitive Eyes	Senofilcon A	PLNIBUT (Topographer)	First Placido disk disturbance (sec)	2.84 (0.50-36.20) 2.93 (0.73-43.35) 2.84 (1.05-12.98) 3.08 (0.43-28.90) 3.04 (0.53-8.15) 2.78 (0.80-57.75)	NR	NR	NR
Kitamata-Wong et al.[5] (2017)	Opti-Free PureMoist Biotrue Clear Care RevitaLens OcuTec	Etafilcon A	PLNIBUT (Topographer)	First Placido disk disturbance (sec)	3.9 ± 0.6 3.5 ± 0.5 3.4 ± 0.5 4.2 ± 0.6	Comfort Subjective Scale	0 = Intolerable 100 = Excellent	89 ± 17 91 ± 12 91 ±12 88 ± 12

CL: Contact Lens, PLNIBUT: Pre-lens Non-Invasive Break Up Time *Statistically significant differences within $P < 0.05$

Table 3. Multipurpose contact lens care solution characteristics

Brand	MPS Solution	Disinfections and Preservative	Buffers and Saline	Wetting Agent and Lubricants
Alcon	Opti-Free Replenish	0.001 % Polyquad 0.0005 % Aldox	Sodium borate Sodium saline	Poloxamine Propylene glycol
Alcon	Opti-Free PureMoist	0.001 % Polyquad 0.0006 % Aldox	Sodium chloride	Poloxamine Polyoxyethylene Polyoxybutylene
Alcon	Solo Care Aqua	0.0001 % PHMB Disodium EDTA	Sodium Phosphate Tromethamine	Poloxamine
Alcon	Clear Care	3% Hydrogen Peroxide	Sodium chloride	Poloxamine
AMO	Complete Easy Rub	0.0001 % PHMB	Sodium chloride	Poloxamine
AMO	RevitaLens OcuTec	0.00016% Alexidine Dihydrochloride 0.0003% PQ1	Sodium Citrate Sodium Chloride	-
Bausch & Lomb	ReNu MultiPlus	0.0001 % PHMB 0.03 % Hydroxyalkylphosphonate	Sodium Chloride Sodium Borate	Poloxamine
Bausch & Lomb	ReNu Fresh	0.0001 % PHMB 0.03 % Hydroxyalkylphosphonate	Sodium Chloride Sodium Borate	Poloxamine
Bausch & Lomb	Biotrue	0.00013 % PHMB 0.0001 % PQ1	Sodium Chloride Sodium Borate	Hyaluronan Poloxamine
Bausch & Lomb	Sensitive Eyes Plus	0.00003 % PHMB Disodium EDTA	Sodium Chloride Sodium Borate	-
Disop	Hidro Health	0.0001 % PHMB	Sodium chloride	Hyaluronan

MPS: Multipurpose Solution, PHMB: Polyhexamethylene biguanide, EDTA: Ethylenediamine tetraacetic acid, PQ1: Polyquaternium-1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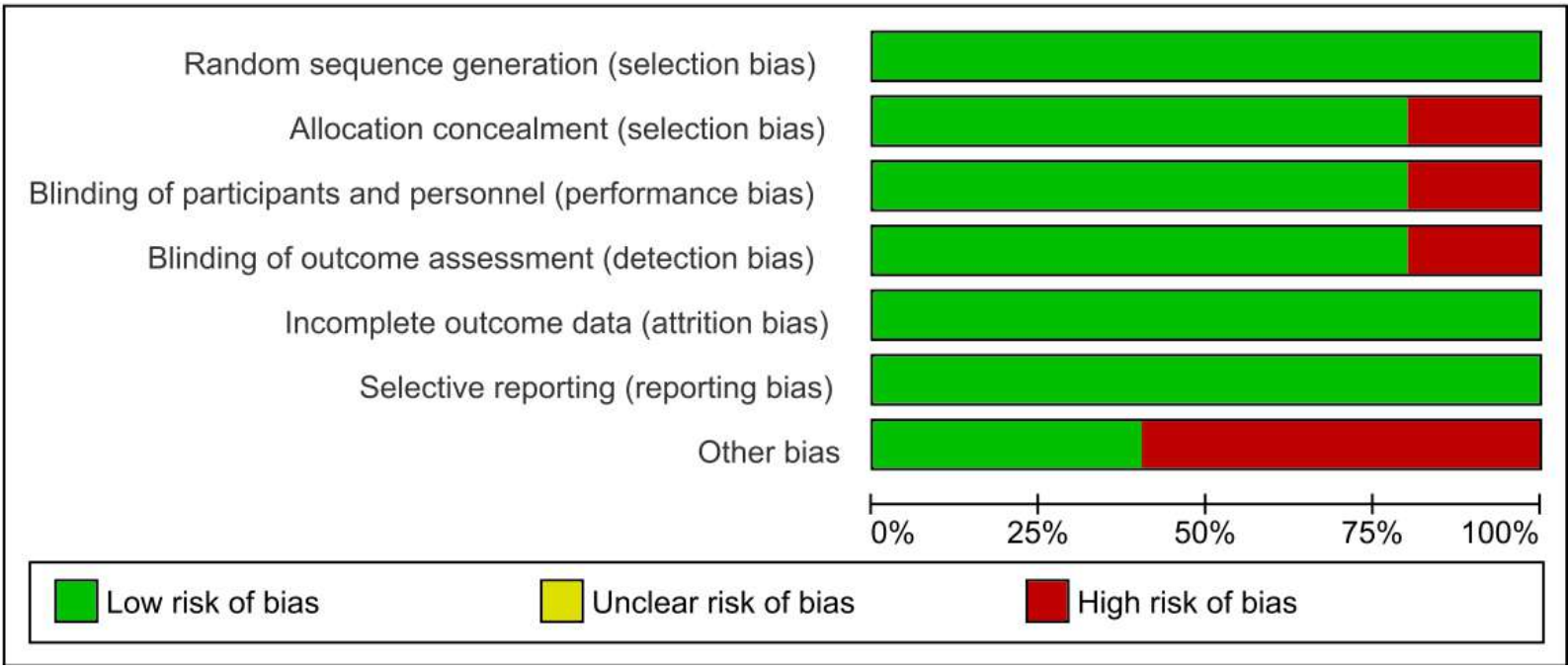
(n = 47)
Record after duplicated removed
(n = 76)
Records screened
(n = 76)
Excluded by title and
abstract
(n = 64)
Full-text assesed for eligibility
(n = 12)
Excluded with reasons (n = 7):
Non-impact journal (n = 1)
Case Series (n = 1)
Non-English (n = 1)
Narrative Review (n = 1)
In vitro (n = 3)
Included studies
(n = 5)

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Guillon M. et al. 2015
Kitamamta-Wong B. et al. 2017
Lau J. et al. 2016
Martin R. et al. 2011
Stiegemeier MJ et al. 2006


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias