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Original Article

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# Assessment of contamination in ophthalmic drops and the development of preventive measures and detection methods for nosocomial infections arising from the use of ophthalmic drops in hospital settings

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## ABSTRACT

**Objectives:** This research aims to assess the prevalence of microbial contamination related to the usage of eye drops in hospital settings and identify strategies to manage such undesirable incidents. **Research Methodology:** A systematic literature review was conducted, followed by a planned analysis to see if sufficient data were available. Subsequently, research and development were undertaken to innovate a solution for detecting or preventing microbial contamination of eye drops before usage. Research **Findings:** Six selected studies met the inclusion criteria, displaying internal validity and practical applicability. However, there is a moderate to low level of bias present. The studies collectively suggest that current management practices in hospitals lack effective measures to address the microbial contamination risks associated with eye drops. Contamination can occur both externally in the packaging and within the eye drop solution, leading to ongoing risks during continuous usage. Analytical challenges arise due to the substantial methodological differences and biases in each study, preventing comprehensive data synthesis. In the research and development phase, it was found that determining whether eye drops are contaminated before use is more beneficial than using them without this knowledge. A simple chemical method involving a reaction between silver nanoparticles and microorganisms, resulting in a visible color change, was proposed for contamination detection. **Conclusion:** This research provides insights into the prevalence of microbial contamination in eye drops, indicating a continual risk. The lack of standardized methodologies and biases in existing studies hinder comprehensive analysis. The innovation introduced involves a straightforward method for detecting contamination before eye drop usage, offering a practical preventive measure for undesirable incidents.

**Key words:** Innovation, meta-analysis, ophthalmic solution contamination, systematic review

## INTRODUCTION

In the complex realm of hospital ophthalmology departments, where patients undergo a variety of eye-related treatments, the widespread necessity for various types of eye drops before and after procedures is evident.[1-3] Examining medical evidence throughout historical periods uncovers a consistent pattern in the administration of eye drops among inpatients in ophthalmology wards and outpatient settings.[1-3] This common practice places the responsibility of self-administration on patients with normal or assisted vision.

Notably, the evidence emphasizes a significant absence of standardized procedures governing the storage of ophthalmic

medications, particularly those housed in refrigerators.[4] Despite potential risks stopping from the contamination of ophthalmic solutions due to improper storage practices, the existing literature lacks systematic approaches to prevent microbial contamination, especially in cases involving refrigerated storage.[5-7] Compounding this concern are documented instances of microbial contamination infiltrating dissolved drug solutions, posing substantial risks such as infections, antimicrobial resistance, and various adverse effects.[7-10] These complications necessitate intensified management efforts, heightening the vulnerability of patients and escalating overall health-care costs.[11]

Driven by the urgency of these challenges, our research aims to examine the current prevalence and incidence of nosocomial infections or complications linked to the contamination of ophthalmic solutions. Furthermore, our study aspires to unveil correlations between suboptimal usage and storage practices and the emergence of adverse outcomes.[12-15] By shedding light on these issues, our research seeks to offer not only corrective measures for addressing incidents but also preventive strategies to forestall future complications.

As a pivotal step, we formulate research questions to guide an in-depth and systematic literature review and analysis. This thorough examination aims to expose the true underlying issues perpetuating these challenges. Our main goal is to provide insightful revelations that can guide the formulation of robust management protocols, ultimately minimizing the occurrence of undesirable events. Moreover, this research lays the groundwork for innovation in the field, sparking the exploration of novel interventions crafted with the singular purpose of fortifying patient safety and contributing to the reduction of unwarranted health-care expenditures.

The inadequacy of prevailing systems or methodologies to address and prevent such issues serves as the driving force for our pursuit of groundbreaking solutions. The objective of this research is to undertake a thorough systematic review (SR) and meta-analysis (MA), concentrating on the administration, storage, and potential contamination of ophthalmic solutions within hospital environments. By accurately exploring a range of literature sources, spanning historical to contemporary perspectives, the study aims to distill crucial insights regarding current practices, variations, and challenges related to the management of ophthalmic solutions. Through the synthesis and consolidation of this accumulated evidence, the research endeavors to pinpoint innovative and practical solutions geared toward enhancing patient safety, reducing contamination risks, and optimizing the utilization of resources.

Beyond establishing a robust knowledge foundation for future investigations, this initiative is poised to guide evidence-based practices in ophthalmic care. The goal is to contribute to the formulation of standardized protocols that elevate the overall quality of patient care.

# METHODOLOGY

## SR

*Literature searching*

The research methodology initiates with an exhaustive literature review, employing electronic databases like PubMed, Scopus, Web of Science, Embase, Cochrane Library, Ovid MEDLINE, and ClinicalTrials.gov. This survey aims to pinpoint relevant articles concerning the administration, storage, and contamination of ophthalmic solutions in hospital settings. Inclusion and exclusion criteria are meticulously outlined, encompassing factors such as publication date, study design, and relevance. The SR methodology explores differences in administration procedures, frequencies, and patient responsibilities, while the subsequent MA quantitatively synthesizes the extracted data for a comprehensive overview.

The literature review encompasses gray literature, including conference proceedings, theses, and reports, ensuring a holistic understanding of current practices. Summarizing the findings, the study emphasizes common practices, challenges, and potential improvements. Innovative solutions are identified based on analyzed evidence, proposing practical strategies to enhance patient safety and optimize health-care resource utilization. The research concludes with a knowledge translation plan, disseminating findings to health-care stakeholders for informed protocol development and evidence-based practices in ophthalmic solution management. In systematically reviewing and meta-analyzing literature concerning the administration, storage, and contamination of ophthalmic solutions in hospital settings, a refined search strategy using Mesh terms and Boolean logic is devised.

Mesh terms and Boolean logic include “Ophthalmic Solutions/administration and dosage,” “Eye Drops/administration and dosage,” “Ophthalmic Solutions/storage,” “Drug Storage,” “Ophthalmic Solutions/contamination,” “Drug Contamination,” “Hospitals,” and “Hospital Units.” The Boolean logic combines these terms to form a comprehensive search query: (“Ophthalmic Solutions/administration and dosage” OR “Eye Drops/administration and dosage”) AND (“Ophthalmic Solutions/storage” OR “Drug Storage”) AND (“Ophthalmic Solutions/contamination” OR “Drug Contamination”) AND (“Hospitals” OR “Hospital Units”).

## Inclusion Criteria

*Publication date*

Articles published within the specified timeframe are relevant to the current state of ophthalmic solution management.

*Study design*

Rigorous study designs include randomized controlled trials (RCTs), observational studies, and SRs.

*Relevance*

Articles directly address the administration, storage, and contamination of ophthalmic solutions in hospital settings.

*Gray literature*

Conference proceedings, theses, and reports provide additional insights into current practices.

## Exclusion Criteria

1. Study Design: studies with insufficient rigor, such as case reports or anecdotal evidence.
2. Irrelevance: articles not directly related to the

administration, storage, and contamination of ophthalmic solutions in hospital settings.

## The Process of Critiquing the Evidence

This structured approach ensures a focused yet inclusive exploration of relevant literature, aligning with specific research objectives and facilitating a thorough analysis of practices within hospital ophthalmology departments. RCTs were critically evaluated for factors such as randomization methods, blinding, and participant characteristics. A systematic assessment of the risk of bias[16] was conducted to ensure high internal validity. Observational studies underwent scrutiny for their study design, control of confounding variables, and statistical analyses. The Newcastle-Ottawa Scale[17] was employed to evaluate the quality of observational studies. In cases of conflicts during study selection or critique, a consensus-based approach was adopted. Two independent reviewers assessed the studies, and disagreements were resolved through discussion or the involvement of a third reviewer if needed.

## Data Synthesis

In the data synthesis and analysis phase, a meticulous approach rooted in SR and MA methodologies is employed. Initial data extraction utilizes a standardized form designed to capture pertinent details regarding the administration, storage, and contamination of ophthalmic solutions in hospital settings. Rigorous quality assessments, conducted in adherence to established criteria, ensure the inclusion of high-quality evidence. For studies with comparable outcomes, a quantitative synthesis (MA) is conducted using appropriate computer software. This process provides a quantitative overview of the combined evidence, incorporating effect sizes, confidence intervals, and heterogeneity statistics. Subgroup analyses and sensitivity analyses contribute to the interpretation by considering variations across study characteristics. In instances of heterogeneity or limited data, a narrative synthesis approach is applied. In addition, an assessment of publication bias is conducted to gauge the potential impact of selective publication on the findings. The comprehensive interpretation of the synthesized results offers valuable insights into ophthalmic care practices in hospital settings, guiding evidence-based improvements and identifying avenues for future research.

## Evidence Synthesis

This process provides a quantitative overview of the combined evidence, incorporating effect sizes, confidence intervals, and heterogeneity statistics. Subgroup analyses and sensitivity analyses contribute to the interpretation by considering variations across study characteristics. In instances of heterogeneity or limited data, a narrative synthesis approach is applied. In addition, an assessment of publication bias is conducted to gauge the potential impact of selective publication on the findings. The comprehensive interpretation of the synthesized results offers valuable insights into ophthalmic care practices in hospital settings, guiding evidence-based improvements and identifying avenues for future research. Following the SR and MA of literature on the administration, storage, and contamination of ophthalmic solutions in hospital settings, the reporting phase strictly adheres to the Preferred Reporting Items for SRs and Meta-Analyses (PRISMA) guidelines[18] for transparent and comprehensive reporting.

The report meticulously details the search strategy, including databases and terms, utilizing a flowchart to illustrate the selection process, and outlining the number of studies at each stage. The characteristics of the included studies, such as design, sample size, and outcomes, are systematically presented. MA results, including effect sizes and heterogeneity statistics, are reported, with subgroup and sensitivity analyses providing insights into variations. A narrative synthesis complements quantitative findings by discussing patterns and disparities. The report delves into quality assessment, acknowledges limitations, and interprets the findings' implications for ophthalmic care. This thorough reporting contributes significantly to evidence-based ophthalmic solution management.

## Research and Development Methodology

The study employs a systematic thinking approach, constructing a conceptual framework for innovation domains. Parameters such as relevance and feasibility are defined, integrating diverse team brainstorming and design thinking principles. Innovations, identified through SWOT analysis, are strategically aligned with SR findings to address gaps. Scenario planning envisions real-world implementation, expert consultation validates feasibility, and systematic documentation guides prioritization for pilot testing methodologies. When contemplating an innovation, the efficacy, safety, and economic viability of the innovation will be subject to testing in the research and development part, contingent upon the characteristics of the newly conceived innovation. However, the various tests, as previously mentioned, will employ scientific research methodologies that uphold high internal and external validity, aiming to analyze and yield objective data with minimal bias.

## Statistical Analysis Methodology

*SR and MA*

The statistical analysis methodology for the SR/MA adhered to rigorous and established approaches. Initial data extraction employed a standardized form to capture essential details regarding the administration, storage, and contamination of ophthalmic solutions in hospital settings. Stringent quality assessments were conducted based on predefined criteria to ensure the inclusion of high-quality evidence. For studies with comparable outcomes, a quantitative synthesis (MA) was conducted using appropriate statistical software. This process offered a quantitative overview, including effect sizes, confidence intervals, and heterogeneity statistics. Subgroup analyses and sensitivity analyses were applied to interpret variations across study characteristics, and a narrative synthesis approach addressed instances of heterogeneity or limited data. An assessment of publication bias was carried out to evaluate the potential selective publication impact.

*Research and development*

In the context of research analysis, the statistical methodology employed hinges upon the determination of which interventions are to be synthesized in a SR/MA. Such an

endeavor necessitates the meticulous design and development of research protocols that are aptly tailored to address the research questions at hand. Regardless, the metric of measurement revolves around the general characteristics of the interventions under scrutiny, and their representation is based on central tendencies during data presentation. The efficacy of the interventions is quantified employing the relative risk with a corresponding 95% confidence interval. Subsequently, these values are utilized in the computation of absolute risk reduction and the determination of the number needed to treat.

# RESULTS

## Results from Evidence Synthesis

This SR synthesizes evidence from six diverse studies[19-21] investigating microbial contamination in ophthalmic solutions. The PRISMA flow and the obtained evidence are illustrated in Figure 1 and Table 1. Among the significant findings, the study by Kim *et al*. revealed a 2.4% contamination rate in preservative-free artificial tears, identifying advanced age and fingertip touch as key risk factors. Chua *et al*. observed a substantial 30% contamination rate in multi-user preserved ophthalmic drops (POD), with variations over time. Daehn *et al*. highlighted a 2% contamination rate in multi-dose ophthalmic solutions in the operating theater, emphasizing the importance of dropper tip hygiene. Garcia *et al*. underscored the effectiveness of manual occlusion in minimizing breath contamination during eye drop administration. Lee *et al*. reported a significantly higher microbial contamination risk (45%) when fingertips touched vial tips compared to no touch (0%) and lid margin touch (10%). Here are crucial points from the results of SR.

*Contamination rate*

The study found a notable 30% microbial contamination rate in multi-user PODs.

*Duration and drop type impact*

Significant differences in contamination rates were identified between 14 and 30 days, with proparacaine displaying higher contamination at 14 days compared to tropicamide.

*Contaminating organisms*

Coagulase-negative Staphylococcus species constituted the majority (89%) of contaminants, underscoring the importance of dropper tip hygiene.

*Data gaps and limitations*

The study lacks crucial information on eye drop use duration, patient patterns, and time to expire. The inability to link contamination to factors like preservatives or cap types hampers comprehensive understanding. Specific limitations include the exclusion of artificial tears with preservatives, a focus on a 10-h period, and culture materials obtained only from the dropper.

While the internal validity of the evidence varied across studies, with moderate levels of bias mainly associated with sample size and data gaps, the collective findings stress the importance of addressing microbial contamination risks. Limitations include the exclusion of eye drops with preservatives in some studies, insufficient information on interventions, and a potential underestimation of contamination risk. Nevertheless, these results provide valuable insights for enhancing hygiene practices during eye drop administration. The evidence, though diverse, contributes to a comprehensive understanding of microbial contamination risks associated with different eye drop usage scenarios. The implications for practice suggest heightened awareness and adherence to sterility guidelines, especially in specific settings, with a recommendation for the cautious use of single-dose eye drops.

The synthesis of a MA from the provided dataset faced challenges due to inherent heterogeneity among diverse

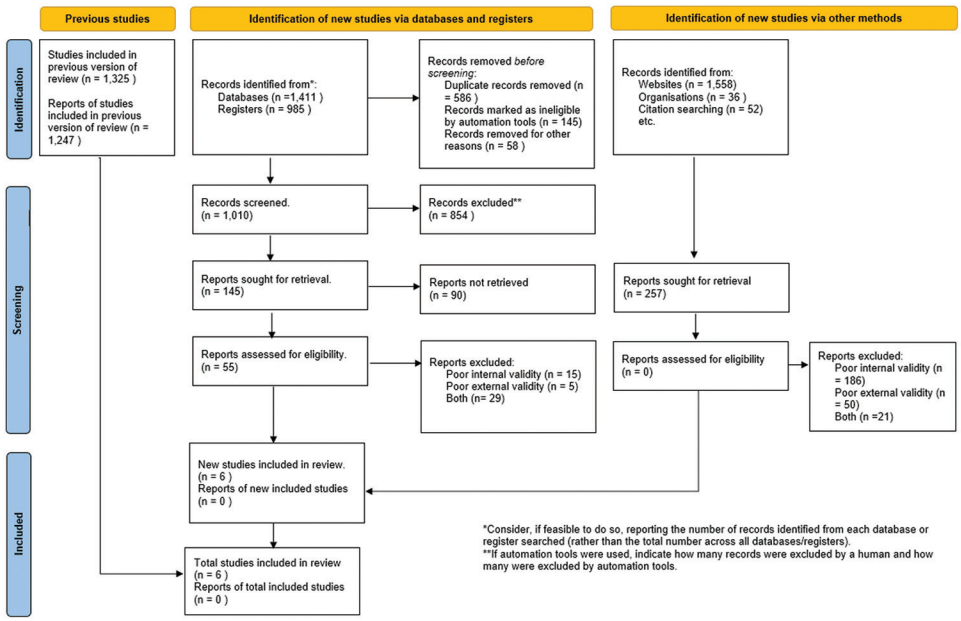


**Figure 1:** Preferred reporting items for systematic reviews and meta-analyses flow

**Table 1:** The characteristics of the studies

| Details | Kim *et al.*, 2008[19] | Chua *et al.*, 2021[8] | Daehn *et al.*, 2021[7] | Garcia *et al.*, 2021[20] | Chantra *et al.*, 2022[5] | Lee *et al.*, 2022[21] |
|---|---|---|---|---|---|---|
| Study design | A prospective observational study | Cross-sectional study | Cross-sectional study | Cross-sectional study | Cross-sectional study | Descriptive study |
| Participants | Users of preservative-free artificial tears in reclosable containers face a microbial contamination risk, particularly with factors such as advanced age and fingertip touch being significant contributors, especially in daily and multiple-use situations. | Individuals using multi-user POD at the Ophthalmology Outpatient Clinic (OOC) of Universiti Kebangsaan Malaysia Medical Center, Malaysia, with a focus on 140 out of 149 extended-use POD bottles. | Participants who use multi-dose ophthalmic solutions in the University Eye Hospital Hamburg-Eppendorf operating theatre. | Ophthalmologists and patients in an academic ophthalmology center are investigating the potential contact of redirected exhaled air, passing through the superior mask gap, with multiuse eye drop bottles. | Study participants using hospital-made preservative-free eye drops were divided into two groups: Group 1 (hospital setting) and Group 2 (home use), with a total of 295 eye drop containers. | Participants aged 20–40 years. |
| Intervention or exposure | The use of preservative-free artificial tears in re-closable containers. | No data | No data | No data | No data | No data |
| Comparator or non-exposure | Abstaining from the use of these artificial tears or opting for artificial tears containing a preservative. | No data | No data | No data | No data | No data |
| Outcomes | Microbial contamination in reused preservative-free artificial tears in daily re-closable containers. | Evaluating the prevalence of microbial contamination, specifically focusing on contamination rates at the dropper tip and within the residual contents of Multi-user POD bottles. | Contamination rate, emphasizing the extent of contamination at the dropper tip. | The potential contact of redirected exhaled air through the superior mask gap with multiuse eye drop bottles during administration, considering microbial contamination. | Microbial Contamination | The incidence of microbial contamination in preservative-free artificial tears based on instillation techniques, emphasizing varied methods of touching the vial tip during its initial use. |
| Main results | In 242 eye-drop bottles, 2.0% had bacterial contamination. Group 1: 3.9%, Group 2: 1.0%, Group 3: None. Advanced age and fingertip touch were significant risk factors ($P<0.05$). | Extended use POD bottles: 30% contamination (19% at T14, 11% at T30). Higher contamination with Proparacaine and Tropicamide at T14. Dropper tips had higher contamination than residual contents, not statistically significant. Frequent contaminants: 89% coagulase-negative Staphylococcus species. | A 2% contamination rate was observed in multi-dose ophthalmic solutions from the operating theatre, with contamination specifically occurring on dropper tips. | Breath plume height (275.5±16.3 mm) was significantly greater than bottle height (13.9±4.7 mm). Manual occlusion of the superior mask gap effectively reduced plume height, minimizing breath contamination during eye drop administration. | Contamination rate: 24.06% in diverse eye drops, with Vancomycin most affected. Primary pathogens: 42.98% molds. Higher tip contamination than in residual fluid. Users with up to 2 eye drops had 42.8% contamination, while those with at least 3 had 22.18% | In a study with 60 unit-dose vials, touching the vial tip with fingertips resulted in a higher microbial contamination rate (45%) compared to no touch (0%) and lid margin touch (10%). |
| Prevalence | 2.00%. | 30.00% | 2.00% | Not mention | 24.07% | Not mention |
| Incidence | No data | No data | No data | No data | No data | The overall incidence of microbial contamination in preservative-free artificial tears was 18%, with the highest incidence observed when the vial tip was touched by fingertips (45%). |

*(Contd...)*

**Table 1:** ***(Continued)***

| Details | Kim *et al.*, 2008[19] | Chua *et al.*, 2021[8] | Daehn *et al.*, 2021[7] | Garcia *et al.*, 2021[20] | Chantra *et al.*, 2022[5] | Lee *et al.*, 2022[21] |
|---|---|---|---|---|---|---|
| Odds ratio | Group 1 (preservative-free artificial tears): OR = 2.80 (95% CI: 0.25–30.68)<br>Age over 50 years: OR = 8.23 (95% CI: 1.01–67.44)<br>Cilia or globe touch: OR = 2.99 (95% CI: 0.28–32.49)<br>Fingertip touch: OR = 9.86 (95% CI: 1.07–90.75) | 3.97 (95% CI: 0.22, 0.99) | Calculation is not feasible due to the absence of sufficient data. | No data | 2.29 (95% CI:1.12, 4.69) | No data |
| Relative risk | No data | No data | No data | No data | No data | Cannot be calculated |
| Extracted key contents | The study found a 2.4% contamination rate in reused preservative-free tears, with advanced age and fingertip touch as significant risk factors in daily and multiple-use situations. | Microbial contamination in multi-user POD at the clinic was 30%, peaking at 14 days, particularly for propacaine and tropicamide. | The study revealed a 2% contamination rate in surgery dropper tips. To reduce risks, it recommends using single-dose eye drops in pre- and intraoperative settings. | The study used imaging to reveal exhaled air reaching eye drop bottles during administration. Manual occlusion is crucial for patient safety, especially during COVID-19. | Preservative-free eye drops have high contamination, especially with more drops per person. Emphasizes the need to follow sterility guidelines, especially for patients. | The study found higher contamination risk in preservative-free eye drops when fingertips touched the vial mouth. Emphasizes the need for proper instillation techniques to prevent contamination. |
| Major limitation and details | The study may not fully apply to preserved artificial tears and could underestimate contamination risk, as only dropper cultures were considered. | The study found 30% contamination in multi-use eye drops, higher in proparacaine at 14 days. Emphasizes the need for dropper tip hygiene (89% Coagulase-negative Staphylococcus). | The study lacks key information on eye drop use and contamination links, limiting its applicability to specific settings. | Limited data on interventions, small sample size, and no exploration of environmental factors or respiratory pathogen presence on multiuse eye drop bottles. | The study identified a 24.07% contamination rate in eye drop bottles, emphasizing the need for targeted interventions based on user groups and usage frequency. | Small sample size, no hand hygiene consideration, no bacterial load measurements, short duration between vial opening and culturing, impacting contamination rates. |
| Assessable bias level | Moderate | Moderate | Low | Moderate | Moderate | Moderate |

POD: Preserved ophthalmic drops

studies. Variations in study designs, including prospective observational studies, cross-sectional investigations, and descriptive analyses, introduced methodological differences. Populations differed, encompassing users of various eye drops, from preservative-free tears to multi-user POD. The lack of uniformity in interventions, comparators, and outcome measures hindered standardized quantitative synthesis. Reporting discrepancies and missing numerical details in some instances prevented comprehensive aggregation. Varied bias levels across studies indicated differences in internal validity. Challenges, such as insufficient data for odds ratios or relative risk calculation and substantial heterogeneity, highlighted the complexity of synthesizing the data into a cohesive MA. Thus, a nuanced SR focusing on significant results, internal validity, generalizability, and an executive summary of the evidence seems more appropriate. Future research standardization may prompt reconsideration of a MA for a more cohesive dataset.

## Results from Research and Development

The systematic literature review identified contamination issues in managing ophthalmic medications in hospitals, emphasizing a high incidence and the potential for undesirable events, especially eye infections. Recommendations focused on educating patients about proper administration but overlooked mitigating the consequences of medication solution contamination. In response, the research team proposed a systematic thinking approach, advocating for redesigned vials and educational initiatives to prevent contamination in eye drop administration. This holistic strategy aims to

comprehensively reduce risks, considering both packaging and medication solution contamination. Derived principles underscore the importance of methodologies or innovations to detect microbial contamination before administering eye drops. The emphasis on end-user abilities, efficiency, safety, and cost-effectiveness is crucial. The research team also explored chemical reactions as an innovative solution, aiming to provide a tangible indication of contamination visible to users. This aligns with the limited methodology framework, offering a potential means to address microbial contamination concerns effectively.

Researchers propose a diagnostic tool inspired by cost-effective chemical principles for SAR-CoV2 detection. This tool utilizes a color-changing solution upon contact with microbes, offering a user-friendly and efficient method for detecting contamination. The procedure entails swabbing the medication bottle using a fingertip and a thumb-cover-encased swab, with the swab then placed in tubes containing silver nanoparticles. The interaction between silver nanoparticles (AgNP) and microorganisms, including viruses, bacteria, and fungi, involves various mechanisms primarily associated with the antimicrobial properties of silver.[22,23]

Silver nanoparticles (AgNPs) possess notable antimicrobial properties, positioning them as promising candidates for diverse applications in biomedical and environmental domains. The intricacies of their antimicrobial efficacy involve multifaceted processes. Upon encountering microorganisms, AgNPs initiate the generation of reactive oxygen species (ROS), including superoxide and hydroxyl radicals, inducing oxidative stress in microbial cells and resulting in the degradation of lipids, proteins, and nucleic acids. Interactions with the microbial cell membrane lead to destabilization and disruption, altering membrane permeability and causing the release of cellular contents, ultimately leading to cell death. AgNPs also exhibit the capacity to bind to microbial DNA, disrupting crucial replication and transcription processes, thereby impeding microbial growth. Interaction with microbial proteins further contributes to antimicrobial effects, affecting their structural integrity and essential enzymatic activities. The release of silver ions ($Ag^+$) from AgNPs is pivotal in their antimicrobial activity, penetrating microbial cells and interfering with cellular functions, influenced by factors such as pH and temperature. Additionally, AgNPs may engage in electron transfer reactions within microbial cells, disrupting redox processes and compromising energy metabolism. Notably, in specific instances, AgNPs have been reported to induce apoptosis-like processes in microbial cells, providing a programmed cell death mechanism for effective microbial elimination. Understanding these complex mechanisms is imperative for the judicious design and optimization of silver nanoparticles for robust antimicrobial applications while minimizing potential cytotoxicity to human cells.[22,23]

## Silver Nanoparticle Dissolution

$AgNP \rightarrow Ag^+ + e^-$ This represents the release of silver ions ($Ag^+$) from the surface of silver nanoparticles.

## Interaction with Microbial Cell Membrane

$Ag^+$ + Microbial Cell Membrane → Disruption of Cell Membrane Integrity Silver ions can interact with the microbial cell membrane, leading to disruption of its integrity and compromising its structural stability.

## Inhibition of Cellular Processes

$Ag^+$+Cellular Processes → Inhibition of Vital Functions Silver ions can interfere with essential cellular processes within the microorganism, leading to the inhibition of vital functions required for survival.

## For Specific Types of Microorganisms

**Bacteria:** $Ag^+$+Bacterial Cell Components →Inhibition of Metabolism and DNA Replication

**Virus:** $Ag^+$+Viral Envelope/Proteins → Inactivation of Viral Structure and Proteins

**Fungi:** $Ag^+$+Fungal Cell Components → Disruption of Fungal Cell Integrity

In this study, we meticulously examine the efficacy and precision of a novel tool designed for the detection of microbial contamination in eye drops. The method is grounded in the observation of discernible color changes, offering a visual indicator for contamination and thereby facilitating targeted corrective interventions. The robustness of microbial identification is achieved through culturing, ensuring a rigorous assessment of accuracy, precision, and reproducibility. Employing silver nanoparticle solutions, acknowledged for their potent antimicrobial properties, the tool selectively interacts with a broad spectrum of microorganisms, thereby enhancing its sensitivity and detection capabilities. The application of this innovative tool is exemplified in Figure 2, illustrating its utility in the pre-use evaluation of eye drops. A preliminary *in vitro* investigation substantiates its performance, revealing 100% contamination in a meticulously chosen sample of 100 instances. These samples, originating from the ophthalmology ward and scrutinized by trained health-care professionals, represent a critical medication for patients at an elevated risk of microbial contamination. Furthermore, the categorization of eye drops into two distinct groups, those with preservatives and preservative-free formulations, each consisting of 50 samples, enables a nuanced exploration of the tool's sensitivity across various formulations. In summary, this study underscores the versatility, affordability, and user-friendly attributes of the tool, positioning it as a promising solution to enhance safety and quality in ophthalmic care, particularly in hospital settings.

# DISCUSSION

The SR synthesized evidence from six diverse studies[19-21] investigating microbial contamination in ophthalmic solutions, providing valuable insights into the risks associated with different eye drop usage scenarios. Key findings highlighted a range of contamination rates, with significant risk factors identified, such as advanced age and fingertip touch. While the internal validity of the evidence varied across studies, with moderate levels of bias mainly associated with sample size and data gaps, the collective results underscored the importance of addressing microbial contamination risks in eye drop administration.[19-21]

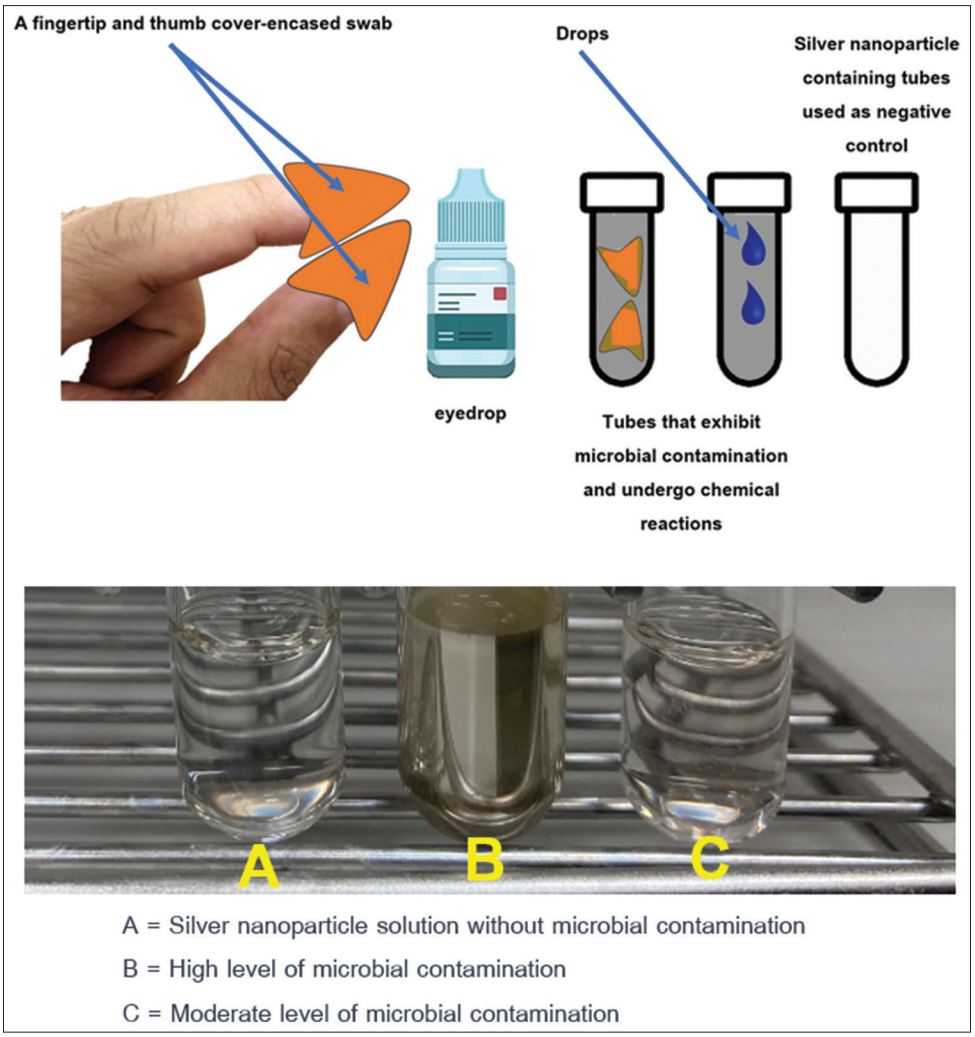


**Figure 2:** The innovation from the research and development. Note: In cases where microbial contamination is identified, a discernible change in the color of the solution from transparent to turbid may be observed. If microbial contamination is found specifically within the confines of the packaging, cleaning procedures can be employed, and eye drops may be administered. However, should microbial contamination originating from the medication droplets be detected, it is recommended to discard the affected medication

The internal validity of the studies was subject to moderate levels of bias, particularly concerning sample size and data gaps. Variability in study designs, populations, and interventions introduced methodological challenges. Limitations included the exclusion of eye drops with preservatives in some studies, insufficient information on interventions, and a potential underestimation of contamination risk. Despite these limitations, the diverse evidence contributed to a comprehensive understanding of microbial contamination risks. The generalizability of the study findings is crucial for informing practice. The heterogeneity among studies, encompassing different eye drop types and usage scenarios, presents challenges in creating universally applicable recommendations. Nevertheless, the results suggest heightened awareness and adherence to sterility guidelines, particularly in specific settings, with a cautious approach recommended for single-dose eye drops.

The innovative solution proposed,[22,23] rooted in systematic thinking, involves the redesign of eye drop vials with advanced dispensing mechanisms and targeted educational initiatives. This holistic approach aims to systematically reduce contamination risks in eye drop usage. While innovation holds promise, it comes with pros and cons. On the positive side, it addresses a pressing issue in eye care, offering a user-friendly and efficient diagnostic tool. However, challenges may arise in the widespread adoption of the proposed changes, considering the need for a shift in dispensing mechanisms and comprehensive educational initiatives.

The integration of silver nanoparticles for early detection of microorganism contamination in eye drops presents a promising approach in ophthalmic care.[24] The proposed diagnostic tool utilizes the antimicrobial properties of silver nanoparticles, triggering a color change upon contact with microbes. This user-friendly method involves swabbing the medication bottle and culturing the swab in silver nanoparticle-containing tubes, demonstrating 100% contamination detection in a preliminary *in vitro* investigation. The versatility, cost-effectiveness, and ease of use make this tool applicable in diverse health-care settings, particularly hospitals. While further research is needed to establish standardized protocols and validate their

effectiveness, this innovation holds potential for rapid and precise identification of microbial contamination in eye drops, contributing to enhanced safety and quality in ophthalmic care.

Based on our setting, some expensive eye drops include Cyclosporine 2%, Dexamethasone sodium phosphate, + Neomycin sulfate, Natamycin, Dorzolamide hydrochloride, + and Timolol maleate. The indirect health costs associated with work interruption, financial loss due to missed working days, missed opportunities, and reduced quality of life further underscore the health impact of early detection and prevention using silver nanoparticles. While the initial investment in the detection tool is a consideration, the potential health benefits and savings in health-care management costs position the use of silver nanoparticles as a health-effective strategy for enhancing the safety and quality of ophthalmic care. The economic analysis of incorporating silver nanoparticles for the early detection of microorganism contamination in eye drops reveals a compelling case for cost-effectiveness. With a fixed cost of 100 baht per test for the detection tool, the initial investment is justifiable. Considering the average cost of eye drops at 500 baht, the health significance of averting contamination becomes evident, potentially preventing additional medical expenses. Moreover, the range of management costs in hospital settings, estimated between 5,000 and 10,000 baht, underscores the long-term health benefits. By preventing contamination-related complications and subsequent hospitalization, the potential cost savings could be substantial. For instance, preventing just 10 hospitalizations could result in savings of 75,000 baht. This analysis suggests that the proactive use of silver nanoparticles not only contributes to economic savings but also enhances overall health-care efficiency and patient well-being.

Silver nanoparticles not only serve as efficient biological contamination traps but also exhibit documented antimicrobial properties, effectively eliminating viruses,[24-27] bacteria, and fungi without harming dermal cells[28] or causing corrosive effects. This versatile capability, demonstrated through various medical studies, highlights silver's potential as a multifunctional agent with applications in both contamination prevention and medical disinfection.[29]

The limitations of this study include the inherent heterogeneity among the diverse studies, which prevents the synthesis of a MA. Challenges in standardizing methodologies, outcome measures, and reporting formats across studies hindered comprehensive aggregation. In addition, insufficient data for odds ratios or relative risk calculations and substantial heterogeneity emphasized the complexity of synthesizing the data into a cohesive MA.

Future clinical studies should aim for standardized methodologies, outcome measures, and reporting formats to facilitate quantitative synthesis. Addressing the limitations, such as the exclusion of eye drops with preservatives and data gaps, will enhance the robustness of future research. Moreover, longitudinal studies assessing the long-term effectiveness of the proposed changes and the real-world impact on contamination rates are essential. Collaborative efforts to standardize eye drop packaging and usage guidelines across health-care settings could further contribute to reducing microbial contamination risks and improving patient safety in ophthalmic care.

## CONCLUSION

This SR of six studies on microbial contamination in ophthalmic solutions reveals key risk factors, such as fingertip touch and advanced age, contributing to contamination rates. Despite variations in internal validity, the collective evidence underscores the importance of addressing microbial risks during eye drop administration. The proposed innovative solution, driven by systematic thinking, involves a simple chemical method involving a reaction between silver and microorganisms, inducing a color change from clear to turbid. This alteration enables the detection of microbial contamination, providing a means to capture instances of biological impurities.

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