

Review

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Posted Date: 26 March 2026

doi: 10.20944/preprints202603.2150.v1

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Review

Beyond Antibiotics: The Emerging Role of Antiseptics in Veterinary Ophthalmology

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Simple Summary

The steady growth of bacterial resistance has encouraged the development of non-antibiotic therapeutic options to limit antibiotic dependence. Among these, topical ocular antiseptics have shown considerable promise as effective and safe agents for both preventive and therapeutic ophthalmic use. This study aimed to review the current literature on the use of antiseptics in veterinary ophthalmology, describing the main agents employed and analyzing their respective advantages and limitations. The study concludes that several antiseptic agents are available for clinical use in veterinary ophthalmology, and they can be effectively applied in cases of mild to moderate ocular disease severity. The study holds societal relevance by promoting rational therapeutic practices that can help decrease antibiotic dependence and, consequently, slow the development of antimicrobial resistance—an issue with implications for both animal and human health.

Abstract

The sustained increase in bacterial resistance has driven the search for therapeutic alternatives that may help reduce antibiotic use, particularly in empirical treatments. In this context, topical ophthalmic antiseptics have emerged as effective and safe tools, suitable for both perioperative prophylaxis and the management of mild or superficial ocular diseases. Their broad spectrum of activity -encompassing bacteria, fungi, viruses, and protozoa- together with the low likelihood of inducing resistance, establishes them as valuable partners in daily clinical practice. This article reviews the current evidence on the use of antiseptics in veterinary ophthalmology, focusing on their clinical applications, therapeutic benefits, and limitations. It also highlights the need for further studies to establish species-specific, disease-specific, and context-based protocols.

Keywords: infection; antibiotic; resistance; ocular surface; eye

1. Introduction

Antibiotic resistance is one of the major current challenges in both human and veterinary medicine. In ophthalmology, the empirical or indiscriminate use of topical antibiotics has contributed to the emergence of resistant strains such as *Staphylococcus pseudintermedius* and *Pseudomonas aeruginosa*, characterized by complex mechanisms of therapeutic evasion [1,2]. These resistances not only compromise treatment efficacy but may also lead to serious clinical consequences, including therapeutic failure and, in advanced cases, irreversible vision loss [3,4]. Additionally, excessive reliance on antibiotics has likely favored biofilm formation, whose heightened resistance to antimicrobial agents represents a significant obstacle to effective treatment.

To counteract this trend, several strategies have been proposed to promote the rational use of antimicrobials. These include: (1) restricting empirical antibiotic use, (2) encouraging treatments

guided by microbial culture or ocular cytology, (3) the use of antibiotic-potentiating agents, and (4) the incorporation of topical antiseptics when clinically feasible. Additionally, (5) antimicrobial stewardship programs aimed at monitoring and regulating antibiotic use are promoted [5]. In this context, ophthalmic antiseptics are emerging as a valuable complementary therapeutic tool. Unlike antibiotics, they act on multiple microbial structures through nonspecific mechanisms, significantly reducing the likelihood of resistance [6,7]. They also exhibit a broad spectrum of activity against Gram-positive and Gram-negative bacteria, fungi, viruses, certain protozoa and biofilms, making them highly versatile agents in diverse clinical scenarios [8]. Notably, bacterial biofilms are more resistant to both the immune system and antibiotic agents than their free-living planktonic counterparts; thus, infections related to biofilms are persistent, frequently recurrent and may lead to irreversible ocular damage.

The aim of this article is to critically review the role of antiseptics in veterinary ophthalmology by assessing their efficacy, safety and current clinical applications, as well as their potential to reduce dependence on topical antibiotics and improve the management of biofilm-associated infections. In addition, practical recommendations for their rational and integrated use are proposed, and priority areas for future research are identified.

2. Main Applications of Antiseptics in Veterinary Ophthalmology

The use of antiseptics is increasingly recognized as a valuable strategy for the management of mild ocular infectious diseases, as well as an adjunctive therapy in chronic or recurrent infections. However, although several antiseptics have shown clinical efficacy in the treatment or supportive management of specific ophthalmic conditions, the overall body of evidence remains limited. Consequently, prospective studies and controlled clinical trials are required to validate their therapeutic effectiveness in active ocular infections.

From our perspective, the use of ocular antiseptics is particularly relevant in four main settings: (1) perioperative antisepsis, (2) routine ocular surface hygiene, (3) management of mild ocular surface and adnexal disorders (e.g., tear film abnormalities, conjunctivitis, blepharitis, simple corneal ulcers), and (4) treatment of recurrent or chronic keratitis or keratoconjunctivitis. In our experience, ocular surface cytology is a rapid and effective diagnostic tool that supports an evidence-based selection of the initial therapeutic approach and helps determine whether the use of antiseptics, antibiotics, or a combination of both is most appropriate.

When no bacterial forms are observed cytologically, or when only scarce extracellular organisms are detected, the findings may correspond to normal flora or contamination [9], and therefore we opt for the exclusive use of antiseptics. In contrast, the presence of intracellular bacteria generally warrants the initiation of antibiotic therapy [10]. Nevertheless, if such intracellular forms are few in number, the use of antiseptics may be considered, reserving antibiotics for situations with a moderate to significant bacterial load. Finally, in chronic or recurrent lesions, in addition to performing bacterial culture, we combine antiseptics with antibiotic treatment to enhance the penetration of the latter and optimize the clinical response [11].

3. Main Antiseptics in Veterinary Ophthalmology

In both human and veterinary ophthalmology, various types of antiseptics have been used for prophylactic and therapeutic purposes. We describe below the main antiseptic agents used in the ophthalmic field, along with their mechanisms of action and key characteristics. Table 1 provides a practical comparative summary of the most relevant information on the antiseptics most used, including their mechanisms of action, antimicrobial spectrum, and clinical features. It also includes a list of veterinary products marketed in Europe and the USA, as well as selected human products that may be used off-label.

Povidone-Iodine

One of the most widely used antiseptics is iodopovidone, a complex of molecular iodine with a carrier polymer that acts by slowly and consistently releasing free iodine. This iodine penetrates microbial cell membranes and binds to proteins, lipids and nucleic acids, leading to their denaturation. It has a very broad antimicrobial spectrum, including Gram-positive and Gram-negative bacteria, fungi, viruses, protozoa, spores and biofilms [12]. When used in diluted concentrations (0.2–1%), it has been shown to be effective and well tolerated by the ocular surface [13], inhibiting biofilm formation and reducing the stability of established biofilms [14]. However, it may cause irritation if applied undiluted or if contact with the ocular surface is prolonged.

In veterinary ophthalmology, povidone-iodine-based formulations are frequently used off-label as safe and effective alternatives when ocular antisepsis is required [13,15], as well as in the management of conditions such as blepharitis, conjunctivitis, and superficial keratitis. As summarized in Table 1, there are currently no commercially available veterinary-specific ophthalmic products containing povidone-iodine in Europe or the United States. An exception is found in India, where a veterinary formulation (Visiotears®, Sava Vet) is available.

Polyhexanide

Polyhexanide is a broad-spectrum antiseptic that has gained increasing attention in ophthalmology due to its excellent safety profile and proven efficacy against Gram-positive and Gram-negative bacteria, fungi, protozoa and biofilms [13]. Its mechanism of action involves interaction with microbial cell membrane phospholipids, resulting in membrane disruption and subsequent cell death. In veterinary ophthalmology, polyhexanide has been incorporated into commercial formulations at very low concentrations (e.g., 0.0001%), in combination with other antiseptics, as part of the topical management of spontaneous chronic corneal epithelial defects (SCCED) [16]. In human medicine, it has been successfully used against *Acanthamoeba* spp. [17], although in veterinary medicine its use in this context is based primarily on extrapolation from that evidence.

Polyhexanide-containing ophthalmic formulations are commercially available in Europe; however, as outlined in Table 1, most are developed for human use rather than veterinary application. In contrast, veterinary-specific options are scarce, although Septostil® (Vetilea S.L, Spain) is commercially available in Europe, combining 0.0001% polyhexanide with other antiseptic compounds.

Hypochlorous Acid (HOCl)

Over the past few years, hypochlorous acid at low concentrations has emerged as a valuable antiseptic, recognized for its favorable safety profile and its broad antimicrobial spectrum, encompassing bacteria, fungi, viruses and biofilms [12,18]. This compound is naturally produced by neutrophils as part of the innate immune response and acts by inducing oxidative injury to microbial structures. Its high efficacy, combined with minimal toxicity, makes it a promising option for certain ophthalmic indications, provided it is used at concentrations of 0.01% [19,20]. In ophthalmology, its applications include eyelid hygiene in cases of blepharitis, management of conjunctivitis and superficial keratitis, and perioperative prophylaxis [19,20]. Although it does not replace antibiotics in severe infections, it represents a safe and effective alternative for reducing the use of topical antimicrobials and for treating ocular surface biofilms. It is worth noting that it is suitable for long-term use [19].

Hypochlorous acid-based ophthalmic formulations are currently available for veterinary use in both Europe and the United States, as summarized in Table 1. In Europe, Hypochlorine Eye Care® (JTPharma, Spain) represents a veterinary-specific product containing hypochlorous acid at the recommended concentration. In the United States, several veterinary formulations are also commercially available, including Vetericyn Plus® Antimicrobial Ophthalmic Gel (Innovacyn),

MicrocynAH® Ophthalmic Gel (Compana Pet Brands), and HICC Pet® Gentle Antimicrobial Eye Rinse for Dogs. These products provide species-specific options for ocular surface antiseptics and periocular hygiene in clinical practice.

Ethylenediaminetetraacetic Acid (EDTA)

EDTA is a chelating agent widely used in ophthalmology due to its ability to bind divalent cations such as calcium and zinc [21]. In veterinary medicine, EDTA has long been employed as an adjunctive treatment in complicated corneal ulcers, where it acts as an antiproteolytic agent at concentrations of 0.1–1% [22], and in calcific keratopathy, where it is used as a calcium chelator at 1–5% [23].

Although the antiseptic properties of EDTA have been recognized for more than 50 years [24], its application as an antiseptic and antibiotic adjuvant at concentrations of 0.05–0.1% is relatively recent. Its main value resides in its role as a therapeutic enhancer, potentiating and synergizing the activity of antibiotics [25]. Its mechanism of action involves destabilization of the bacterial outer membrane, thereby facilitating antibiotic penetration [26]. This effect is relevant against both Gram-positive and Gram-negative bacteria, but is particularly important in the latter, whose double membrane acts as a physical and functional barrier that limits the action of many antimicrobials [27]. Consequently, in chronic or persistent infections caused by Gram-negative bacteria such as *Pseudomonas* spp., *Chlamydia* spp., *Enterobacter* spp., *Bordetella bronchiseptica* or *Pasteurella multocida*, EDTA helps overcome this barrier and enhances antibiotic efficacy. Accordingly, it has recently been incorporated into ophthalmic formulations together with surfactants (such as polysorbate 80) or buffering agents (such as tromethamine) to potentiate the efficacy of topical antimicrobials in refractory or chronic conditions [25]. Although further clinical evidence is needed to establish standardized protocols, current experience supports the use of EDTA as a valuable adjunct in the management of refractory ocular infections.

As summarized in Table 1, several human ophthalmic formulations are available for periocular hygiene; however, veterinary-specific products are also commercially available in both Europe and the United States. In Europe, Optican Limpiador de Ojos® (Stangest, Spain) is indicated for routine periocular cleansing and tear stain management, while in the United States, I-LID 'N LASH VET® (I-MED Animal Health, Canada) is specifically formulated for eyelid hygiene and the management of blepharitis in companion animals.

Tromethamine (tris), also known as tris(hydroxymethyl)aminomethane, is a buffering agent incorporated into ophthalmic formulations for therapeutic purposes, particularly due to its ability to modulate pH and enhance the activity of other compounds. Although Tris does not have intrinsic antiseptic properties, it is frequently combined with agents such as EDTA and surfactants to promote disruption of the bacterial outer membrane, reducing inherent resistance and enhancing the penetration of topical antibiotics [26]. This synergistic interaction is especially valuable in biofilm-associated ocular infections, where bacteria assume a more treatment-resistant phenotype [27]. In veterinary medicine, Tris–EDTA solutions may be used as adjuvants for cleansing and preparing the ocular surface prior to antimicrobial application, particularly in chronic or refractory cases. Tris has demonstrated good tolerance by the ocular surface and represents a useful component in combined therapies to optimize treatment efficacy without increasing local toxicity.

In veterinary ophthalmology, products containing both Tris and EDTA such as ASTER® Trisoftal Wipes (VetNova, ES) are available in Europe while TrisOphtho® Eye Wipes (DermaZoo™ Pharma, USA) are available in the United States (Table 1).

Polysorbate 80, also known as Tween 80, is a nonionic surfactant widely used in ophthalmic pharmaceutical formulations due to its ability to solubilize lipophilic compounds and stabilize emulsions. Although it is not an antiseptic in the strict sense, it has been reported to reduce microbial load, primarily by altering bacterial cell membrane integrity and facilitating biofilm dispersion [28]. In veterinary ophthalmology, polysorbate 80 is mainly used as an excipient in eye drops and ophthalmic solutions and, in some cases, as an adjuvant in combination with antimicrobials,

enhancing their penetration and bioavailability. Although most of the available evidence derives from studies in human ophthalmology [29], this information is extrapolated to the veterinary field, where its use is considered particularly relevant in the management of chronic or recurrent ocular infections. In addition, its ocular safety profile is well established, showing good tolerance on the ocular surface [29].

In veterinary practice, a commercial formulation combining Tris, EDTA and polysorbate 80 is currently available (Ophthaprim®[®], Domes Pharma), which makes it an appealing option for use in small animals [30]. In addition to acting as an ocular cleansing solution, it prepares the ocular surface and enhances antibiotic activity. However, due to the surfactant effect of polysorbate 80, its use is generally limited to a maximum of 15 days. In patients with tear film disturbances, regular use of this combination may help reduce the proliferation of pathogenic microorganisms and maintain a controlled microbial load, thereby decreasing recurrence rates, improving ocular comfort, and limiting repeated antibiotic use. Similar combinations are commercially available in human ophthalmology in both Europe and the United States (see Table 1). In veterinary medicine, a comparable formulation is also available, such as Optixcare Eye Care® (CLC Medica, Canada), which combines polysorbate 80 with sodium citrate and disodium EDTA.

Sodium citrate, known primarily for its role as a mild chelating agent, may exert a synergistic effect when used as an adjuvant in combination with antibiotics or other antiseptics, such as EDTA or Tris-buffered formulations [31]. Although it is not as potent as EDTA, it is considered safer for chronic and daily administration [32]. Its mechanism of action is based on its ability to sequester divalent cations—primarily calcium—which are essential for the integrity of the bacterial outer membrane [33]. Similar to EDTA, it destabilizes the bacterial cell wall, thereby facilitating the penetration of other antimicrobial agents.

In veterinary ophthalmology, sodium citrate is available in Pet Hydra Drops® (Meraky by KF Srl, LU) in Europe. In human ophthalmology, sodium citrate is mainly used in artificial tears and lubricating emulsions with antioxidant and modulatory properties—such as Hyabak® (Laboratoires Théa, FR), Emustil® (SIFI, IT), Optive® Fusion and Refresh (Allergan, IRL) and Vismed® (Brudylab, ES) in Europe, Cationorm® (Santen, JP) in Asia and Systane® Hydration and Balance (Alcon, USA) and in the United States - where it acts as an adjunct in protecting the ocular surface and stabilizing the tear film.

Boric Acid

Boric acid is a traditional compound with mild antimicrobial properties, commonly used in ophthalmic solutions as an adjuvant or buffering vehicle. Its mechanism of action involves interference with microbial enzymatic metabolism, thereby limiting bacterial and fungal growth [34]. Although its antiseptic effect is weaker than that of other agents, its good ocular tolerance and soothing properties make it suitable for formulations used in mild conjunctivitis and routine ocular surface hygiene [32].

In veterinary medicine, some commercial products contain boric acid as a key ingredient (Ocryl®[®], Domes Pharma, FR; Siccostil Protect®[®], Vetilea, ES; Lavatears®[®], Santgar SA, USA; Angels' Eyes®[®], H&C Animal Health, USA). These formulations make use of the mild antimicrobial effect of boric acid for ocular hygiene, relief of mild irritations, and post-diagnostic rinsing. This compound is also incorporated into solutions aimed at managing tear staining syndrome. Its gentle antimicrobial activity [32] and its ability to modulate the periocular microenvironment—particularly through pH adjustment and reduction of the superficial bacterial load—help limit bacterial proliferation and the oxidation of tear components, which may contribute to reducing the intensity of reddish periocular staining. In human ophthalmology, boric acid is commonly included as a component of over-the-counter ocular formulations in both Europe and the United States (see Table 1).

Hexamidine

Hexamidine, in its salt form (hexamidine diisethionate), is an antiseptic with broad-spectrum antimicrobial activity, particularly effective against Gram-positive bacteria, some Gram-negative bacteria and certain protozoa such as *Acanthamoeba* spp. [8,35]. It exerts its effect by disrupting the microbial cell membrane, leading to cell lysis [32]. Hexamidine demonstrates good ocular tolerance when used at appropriate concentrations; however, it may cause irritation if applied in highly concentrated solutions or over prolonged periods. In veterinary ophthalmology, there are no specific studies supporting its use as an independent active ingredient; however, its application is based on extrapolation from human evidence and on its inclusion within combined commercial formulations [8,35,36].

In veterinary practice, a commercial formulation is available (Septostil[®], Vetilea, ES), containing hexamidine (0.05%), polyhexanide (0.0001%), EDTA (0.05%) and phosphates, providing an interesting profile for the treatment of mild ocular surface infections.

Ozone

Ozone has emerged as a promising agent in veterinary ocular antiseptics due to its strong oxidative potential [36]. In addition, it exhibits anti-inflammatory and wound-healing properties, further supporting its use as an adjuvant. In human medicine, low concentrations are recommended (<5 ppm in aqueous solutions, < 20 µg/mL in eye drops) to minimize topical irritation [37]. In veterinary medicine, no standardized concentrations have been established, and values are generally extrapolated from human protocols. In small animals, ozone is mainly administered as ozonated water for ocular surface cleansing and disinfection—particularly in cases of corneal ulcers or infectious keratitis—and as ozonated oils applied periocularly to promote wound healing and control infection [36,38]. However, clinical application requires caution, as high concentrations or improper formulations (non-buffered water or non-stabilized ozonated agents) may cause chemical keratitis [39]. Furthermore, repeated or uncontrolled exposure may induce chronic oxidative stress in epithelial and endothelial cells, impairing healing.

Despite encouraging preliminary results [40], scientific evidence in veterinary ophthalmology remains limited, and further controlled studies are needed to establish safe and effective treatment protocols. To the authors' knowledge, no veterinary-licensed ophthalmic ozone products are currently available, and its use relies on off-label formulations derived from human medicine, such as Ozonest[®] (Laboratorios Esteve, ES). Since the bactericidal effect of ozone has been shown to be less potent and slower in onset than 0.6% povidone-iodine, its perioperative application is not justified [7].

Biosecur[®]

Biosecur[®] is a patented plant-derived extract obtained from citrus (*Citrus aurantium*), rich in bioflavonoids and polyphenols, with antimicrobial activity against bacteria, fungi and viruses [41]. It has been incorporated into human ophthalmic formulations such as Oftasecur[®] (Offhealth, IT), demonstrating in vitro efficacy against *Candida albicans*, *C. auris* and even biofilms, according to available experimental studies and technical data [42]. However, to date, no veterinary-approved ophthalmic products containing Biosecur[®] are available. Therefore, any use in animals would constitute off-label administration and should be preceded by a critical evaluation of its safety and efficacy.

Although it does not replace broad-spectrum antiseptics such as polyhexanide or povidone-iodine, Biosecur[®] represents a useful option for ocular hygiene and is also marketed in wipe form for eyelid and conjunctival cleansing [43]. Its favorable tolerance allows for repeated use; however, its antimicrobial effect is limited compared with conventional ophthalmic antiseptics [8].

Ultraviolet (UV) Radiation

Ultraviolet (UV) radiation—particularly UV-C (wavelengths between 200 and 280 nm)—has been shown to be effective against bacteria, viruses and fungi. In veterinary ophthalmology, its use as an ocular antiseptic remains limited and experimental; however, it is gaining interest as a non-pharmacological tool for the management of resistant corneal infections [43]. Photodynamic therapy with UV-C, either alone or in combination with riboflavin (corneal cross-linking), has been used in cases of infectious keratitis in animals, particularly in horses and dogs, with the aim of reinforcing corneal structure and reducing microbial load [43,44]. In addition to its antimicrobial effect, this treatment can induce the formation of covalent cross-links within corneal collagen, contributing to stabilization of progressive ulcers. Nevertheless, its application must be performed under strictly controlled conditions, as inappropriate UV exposure can result in tissue damage and adverse effects on epithelial and endothelial cells. Despite its potential, further clinical studies in veterinary medicine are required to define its safety, efficacy and possible indications in routine practice.

Beyond the aforementioned antiseptics, several new agents are being investigated for potential application in veterinary ophthalmology. N-acetylcysteine has demonstrated significant *in vitro* activity against major pathogens responsible for infectious keratitis in dogs and cats, supporting its potential role as an ocular antiseptic [8,45]. However, *in vivo* studies are still needed to confirm its safety, clinical efficacy and dosage protocols in companion animals. Similarly, a recent study found that 0.1% polyquatonium-133 exhibits notable antiseptic activity against common ocular pathogens, even at low concentrations, suggesting a promising profile for future ophthalmic formulations [8].

4. Antiseptics with Limited Use in Veterinary Ophthalmology

Not all available antiseptic agents are suitable for ocular application, as some can induce toxicity to ocular structures or lack sufficient support in veterinary medicine. The antiseptics described below require restricted use or careful clinical consideration in veterinary ophthalmology.

Chlorhexidine

Chlorhexidine is one of the most widely used compounds for general disinfection. It is a cationic biguanide that exerts its antimicrobial effect by disrupting the bacterial cell membrane. At low concentrations, it acts as a bacteriostatic agent, whereas at higher concentrations it becomes bactericidal. Although its spectrum of activity primarily includes Gram-positive bacteria, it also shows some efficacy against Gram-negative bacteria, fungi and viruses. However, its ocular application requires caution, as concentrations above 0.05% may cause significant irritation to the cornea and conjunctiva [46]. For this reason, it is considered safe only in formulations specifically designed for ophthalmic use, such as certain chlorhexidine digluconate solutions $\leq 0.05\%$ as the Iryplus® ocular cleanser (Fatro, ES) and DROPSEPT® (Servimed Industrial, IT).

Hydrogen Peroxide (H₂O₂)

Despite its well-known antiseptic potency and ability to eliminate bacteria, viruses, fungi and spores through free radical formation, hydrogen peroxide is highly toxic to ocular tissues. Due to its cytotoxic effects on the cornea and conjunctiva, its direct use on the ocular surface is entirely contraindicated. Its application is restricted to instrument disinfection or contact lens cleaning systems, and only when followed by a neutralization step.

Tea Tree Oil (Melaleuca Alternifolia)

Tea tree oil possesses recognized antimicrobial, antifungal and anti-inflammatory properties [47]. However, its direct ocular application in veterinary ophthalmology is very limited due to its irritant and cytotoxic effects on ocular tissues, particularly in concentrated forms. Diluted or compounded formulations have been used for the treatment of blepharitis, palpebral demodicosis and other periocular conditions, mainly in dogs. Its efficacy against *Demodex* spp., Gram-positive

bacteria and some fungi makes it an interesting option for periocular antiseptics [48]. Nonetheless, its use requires extreme caution to avoid direct contact with the ocular surface, which can be challenging in clinical practice.

Silver compounds

Silver-based compounds, such as silver nitrate and silver nanoparticles, have demonstrated notable activity against multidrug-resistant microorganisms [49], leading to renewed interest in their medical use. However, their application in veterinary ophthalmology remains very limited and is largely confined to experimental settings. The high risk of ocular toxicity [32], limited clinical experience in animals and the absence of formulations specifically designed for ophthalmic use currently prevent their routine clinical application.

In summary, these considerations highlight the importance of carefully evaluating the safety and efficacy profile of each antiseptic prior to ocular use, always prioritizing agents with favorable clinical evidence and a low risk of toxicity.

5. Advantages and Limitations of Ocular Antiseptics

One of the main advantages of antiseptics is undoubtedly their (1) broad-spectrum activity [32]. This “multitarget” effect is due to nonspecific mechanisms of action—such as oxidation or microbial protein denaturation—which also means that (2) the likelihood of resistance development is extremely low or virtually negligible, even with repeated use. Another notable advantage is (3) their rapid onset of action and ability to significantly reduce microbial load without the need to await culture results [50]. This makes them ideal for use in the early phases of treatment, perioperative procedures or in patients with mild infections or unconfirmed etiologies. In addition, many antiseptics are (4) low-cost and (5) stable, which facilitates routine use both in clinical settings and at home. Furthermore, (6) some of these compounds enhance the penetration of antibiotics and other antiseptics [32] thereby potentiating clinical outcomes. This is particularly relevant in chronic or recurrent infections, where the combination with chelating or potentiating agents (such as EDTA) improves the penetration of antibiotics into Gram-negative bacteria, which are traditionally more refractory to treatment due to their double membrane and tendency to form biofilms.

Despite their advantages, ocular antiseptics also present several limitations that must be considered in veterinary practice. Firstly, (1) clinical evidence in animals remains scarce for many agents, particularly regarding controlled studies, ocular pharmacokinetics and species-specific protocol validation. Although extrapolating data from human medicine can be useful, it is not always appropriate due to anatomical and physiological differences among species. Another important consideration is (2) the potential irritative effect of certain antiseptics when used at inappropriate concentrations or in formulations not designed for ophthalmic use. Moreover, (3) their activity is not always selective for pathogens; prolonged or inappropriate use may delay healing or damage healthy tissues, underscoring the need for adherence to product guidelines. It should also be noted that many of these compounds (4) have poor penetration and thus are limited to external ocular surfaces (conjunctiva, eyelids, superficial cornea) and are ineffective in intraocular infections or deep keratitis. Finally, although antiseptics play a valuable role in reducing antibiotic use, (5) they should not be considered universal substitutes. In severe, progressive infections or deep corneal ulcers at risk of perforation, culture-based antibiotic therapy and sensitivity testing remain the clear standard of care.

6. Conclusion

The rational incorporation of antiseptics in ophthalmology not only supports ocular hygiene but also helps reduce the reliance on topical antibiotics, thereby contributing to the control of bacterial resistance. In addition, certain compounds—such as EDTA, Tris or specific surfactants—can enhance antibiotic penetration and efficacy when used concurrently, reinforcing their role as therapeutic adjuvants in selected cases. While the efficacy and safety of antiseptics are well established in human

medicine, available veterinary data support their use in specific clinical scenarios. However, further studies are still needed to establish standardized protocols according to species and disease type.

Overall, antiseptics represent a safe and effective option in the management of various ocular conditions, provided that formulations appropriate for the ocular surface are used and treatments are tailored to the clinical needs of each patient.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Table S1. Main antiseptics used in veterinary ophthalmology, their mechanisms of action, antimicrobial spectrum, and clinical considerations.

Author Contributions: Conceptualization, M.L.; methodology, M.L.; validation, M.L., R.V., L.G. and T.P.; formal analysis, M.L.; investigation, M.L.; resources, M.L. and T.P.; data curation, M.L.; writing—original draft preparation, M.L.; writing—review and editing, M.L., R.V., L.G. and T.P.; visualization, M.L.; supervision, M.L. and T.P.; project administration, M.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflicts of interest.

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