Clinical effect of four different ointment bases on healthy cat eyes

Réka Eördögh,* Ilse Schwendenwein,† Alexander Tichy,‡ Igor Loncaric†,§ and Barbara Nell*  
*Department for Companion Animals and Horses, University of Veterinary Medicine Vienna, Vienna, Austria; †Department for Pathobiology, Clinical Pathology, University of Veterinary Medicine Vienna, Vienna, Austria; ‡Department of Biomedical Sciences, University of Veterinary Medicine Vienna, Vienna, Austria; and §Department for Pathobiology, Institute of Bacteriology, Mycology and Hygiene, University of Veterinary Medicine Vienna, Vienna, Austria

Abstract

Objective To describe the effects of long-term treatment with four different eye ointment bases (OBs) in cats.

Animals studied Ten healthy cats.

Procedures The study was performed in two periods. Four different OBs were tested. Hundred grams of OB contained the following: OB-A: 35.17 g liquid paraffin (lp), 64.83 g white petrolatum (wp); OB-B: 10.03 g lp, 84.95 g wp 5.02 g lanolin; OB-C: 18.34 g lp, 51.40 g wp, 25.00 mg KH2PO4, 57.00 mg K2HPO4, 18.90 g eucerinum anhydricum, 11.28 g water for injections; and OB-D: 70 g unguentum lanalcoli, 20 g lp, 10 g aqua conservans. One eye was treated, and the other served as a negative control. Cats received the OBs TID for 28 days. The two study periods were separated by a 4-month washout phase. Samples for conjunctival impression cytology, swabs for bacteriologic and mycologic examination, and cytobrush samples for FHV-1 and Chlamyphila felis PCR detection were obtained. Both eyes were examined daily.

Severity of ocular symptoms was scored using a modified Draize eye irritation test. A total of five eyes were treated with OB-A, five with OB-B, four with OB-C, and five with OB-D.

Results Treated eyes had significantly higher clinical scores. Eyes receiving OB-A had the highest overall clinical score. The results of bacteriologic and mycologic examination concur with the previously published data. All samples tested were negative for FHV-1 and Chlamyphila felis. There was no significant difference between treated and control eyes upon cytological examination.

Conclusion The application of OBs resulted in clinical symptoms in treated eyes. The long-term use of ointments is not well tolerated in cats and may lead to ocular irritation.

Key Words: cat, eye, impression cytology, ocular irritation, ointment base, petrolatum

INTRODUCTION

Topical therapy is the preferred method of drug administration in ophthalmology. Therapeutic levels are achieved in the target tissue with minimal systemic absorption. The clinician may choose between eye drops and ointments. The choice depends on several factors, patient compliance being of utmost importance. Frequent topical therapy is particularly difficult in cats. Therefore, ointments are preferred, as their prolonged contact time provides a depot of the drug, thus increasing its bioavailability. On the other hand, longer contact time may result in mucosal irritation. Observations in cats indicate that the long-term use of eye ointments is not well tolerated in this species. We hypothesize that this effect is caused by the base of the ointments. Ointment bases (OBs) are divided into two categories. Simple bases provide a continuous ointment phase and are usually composed of white petrolatum and liquid paraffin. The latter contributes to ointment melting upon reaching conjunctival temperature. Compound (or biphasic) bases are emulsions, consisting of a mixture of water and oil, and may be further subdivided, based on the component of the continuous phase: (1) oil in water (o/w; oil dispersed in water), or (2) water in oil (w/o; oil forms the continuous phase).
The latter is more commonly used as it is less irritating than the o/w type.\textsuperscript{3,5} To enhance water absorption, lanolin, cetylstearyl alcohol, or eucerinum anhydricum is used.\textsuperscript{3,6} Although w/o bases tend to be more comfortable for the eyes, a higher risk of contamination is reported, as microbes may multiply and disseminate in a medium containing water.\textsuperscript{3} To avoid contamination, preservatives—such as benzalkonium chloride, or benzalkonium chloride plus EDTA—are used.\textsuperscript{7,8} Another way to avoid contamination is water-free production. Upon contact with the tear film, the ointment forms the final emulsion.\textsuperscript{2,6}

This study describes the long-term use of different OBs on healthy cat eyes. The aim of this trial was to determine which ointment base (OB) results in the least ocular irritation during long-term treatment in cats.

**MATERIALS AND METHODS**

The study protocol was approved by the institutional ethics committee and by the Austrian government. Ten university-owned cats of various ages (median age=19 ± 11.5 months), genders (2 males, 6 neutered males, and 2 spayed females), and breeds (9 Domestic Short-haired cats and 1 Ragdoll) were included in the study. The cats were healthy and devoid of signs of ocular disease upon ophthalmic examination. The trial was performed in two periods. Each period was 28 days long.

**Study design**

Four different OBs were studied (Table 1). OBs were assigned to the cats using a Latin square. In the first period, cats received OBs in the right eye (OD); the left eye (OS) served as a negative (untreated) control. In the second period, OS was treated, whereas OD remained untreated. Cats received one of the OBs three times daily: between 7 and 8 a.m., 2 and 3 p.m., and 9 and 10 p.m. for 28 days. Each time an amount of approximately 0.01-0.02 g (0.5 cm) of OB was instilled into the lower conjunctival fornix. The two study periods were separated by a 4-month washout period. OBs were packed identically by the manufacturer and coded (A-D), to mask the first examiner (RE). After obtainment of all data, the codes were revealed. In the second study period, one cat was excluded from further investigation due to systemic illness. Therefore, a total of five eyes were treated with OB-A, five with OB-B, four with OB-C, and five with OB-D.

**Ophthalmic examination**

Seven days prior to and immediately after each period (at the 29th day), a complete ophthalmic examination of each cat was performed using slit-lamp biomicroscopy (Kowa Portable Slit-Lamp SL-14; CR Medical, Linz, Austria), direct and indirect ophthalmoscopy (Heine Omega 2C; Heine Optotechnik GmbH & Co. KG, Herrsching, Germany), rebound tonometry (TonoVet, TV01; Dioptrix, Toulouse, France), and fluorescein staining (Fluorescein...
Sodium Ophthalmic Strips USP; Eickemeyer KG, Tuttlingen, Germany) of the cornea by a board-certified ophthalmologist (BN). Schirmer tear test 1 (STT; Schirmer-Tränentest; Essex Pharma GmbH, Munich, Germany) and TFBUT (tear-film breakup time) values were recorded. Furthermore, samples for cytologic, bacteriologic, mycologic, and virologic workup were obtained.

Every morning from day 1 to day 29, cats received an ophthalmic examination using slit-lamp biomicroscopy prior to the first daily treatment. The severity of ocular symptoms was scored using a previously described scoring system (modified Draize eye irritation test) with minor modifications (Table 2).9 Ocular examination findings were recorded on examination sheets and later listed on an Excel spreadsheet for the further statistical analysis. Examinations were always performed by the same examiner (RE).

### Table 2. The evaluation of the clinical scores based on the Modified Draize Eye Irritation Scale

<table>
<thead>
<tr>
<th>Palpebral and bulbar conjunctiva</th>
<th>Redness</th>
<th>Chemosis</th>
<th>Discharge</th>
<th>Third eyelid</th>
<th>Eyelid margin, eyelid skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessels normal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Some vessels definitely injected</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Diffuse, crimson red, individual vessels not easily discernible</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Diffuse, beefy red</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Any swelling above normal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Obvious swelling with partial eversion of lids</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Swellings with lids approximately half closed</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Swellings with lids more than half closed</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Discharge</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Any amount different from normal (does not include some small amount observed in inner canthus of normal animals)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Seromucous discharge with moistening of the lids and hairs just adjacent to lids</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Tenacious, seromucous discharge with moistening of the lids and hairs, and considerable area around the eye</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Vessels normal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Some vessels definitely injected</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Diffuse, crimson red, individual vessels not easily discernible</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Diffuse, beefy red</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Chemosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No swelling</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mild swelling</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moderate swelling</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Heavily swelling</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Redness</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No redness</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Redness</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hair loss</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No hair loss</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Sampling**

Cytological samples of the temporal area of the superior bulbar conjunctiva of each eye were obtained using the Biopore membrane device (BMD; Millicell-CM, PICM01250, Tullagreen, Ireland). Handling of the samples was previously described in detail.10 Briefly, one drop of 0.4% oxybuprocaine (Novain 0.4% Augentropfen; Agepha, Vienna, Austria) was instilled into the eye. After 1 min, a cotton swab was used to absorb the inferior tear pool and slightly dry the superior bulbar conjunctiva. Specimens were obtained by pressing the BMD onto the temporal superior bulbar conjunctiva. Samples were fixed and then stained using a Romanowsky-type quick stain (Hemaquick®; Biomed Labordiagnostik GmbH, Oberschleißheim, Germany).

Cytological evaluation was carried out immediately after sampling by a board-certified clinical pathologist (IS), who was unaware of the treatment and the treated site. Each sample was evaluated according to cellularity and quality.10 In case of low cellularity or inadequate quality, a second sample was obtained the following day. Assessment of the specimens was performed using light microscopy (Olympus Provis, AX70TRF, Japan) at 400× magnification. The following grading scale was used: 0 points were given in the absence of inflammatory cells, and 1 point was given in the presence of inflammatory cells.

**Bacteriologic and mycologic examinations**

Conjunctival swabs (Transwab, Medical Wire & Equipment, Wiltshire, UK) of both eyes were obtained individually and cultured for bacteria and fungi. Cytobrush samples (Celletta brush cell collector; Engelbrecht Medizin- und Labortechnik GmBH, Edermünde, Germany) from both eyes were obtained under local anesthesia, pooled, and tested for Chlamydophila felis via polymerase chain reaction (PCR) as described elsewhere.11 For bacteriologic and mycological isolation, samples were incubated on BD™ Columbia Agar III with 5% sheep blood under aerobic/microaerophilic (5% CO2)/anaerobic conditions, BD™ Columbia CNA Agar with 5% sheep blood, Improved II, and BD™ Mac Conkey II at 37 °C for 24–48 h, and on BBL™ Sabouraud dextrose agar with gentamicin and chloramphenicol (all from Becton Dickinson, Heidelberg, Germany) at 28 °C for 5 days. Samples were also incubated in thioglycollate medium, enriched with vitamin K1 and hemin (Becton Dickinson).

**Virologic examination**

Conjunctival cytobrush swabs were obtained under topical anesthesia from both eyes, pooled, and submitted for feline herpesvirus Type 1 (FHV-1) PCR.12

**Statistical analysis**

For each ocular symptom, the given score was normalized by dividing the given score by the number of choices for that particular symptom. The total clinical score for each
eye at each time point was derived from the sum of these normalized results. Higher values indicated more severe symptoms. The effect of the different OBs on treated eyes and the difference between the treated and control eyes were analyzed using linear mixed models. Paired-samples t-tests were used to compare the clinical scores between the treated and control eyes of each treatment group on each day. Differences in clinical scores among the four different treatments were examined using Sidak’s post hoc test. Differences between treated and control eyes in mean STT, IOP (intra-ocular pressure), and TFBUT and changes in mean values prior to and after the study within each group (i.e., control and treated) were analyzed using paired-samples t-tests. Diversities in these values among different treatments were identified using one-way ANOVA. To compare the cytology results and changes in cytology between the treated and control eyes, Fisher’s exact test was used. For all analyses, $P < 0.05$ was considered significant.

RESULTS

Prior to each period, the clinical score was 0 or close to 0 in each eye of all cats. All OBs had a significant effect ($P < 0.001$) on treated eyes compared to untreated controls (Fig. 1). A significant difference among the OBs was found (Fig. 2). OB-A resulted in significantly higher clinical scores (more severe symptoms, Fig. 3) compared with OB-B ($P = 0.002$) and OB-C ($P = 0.020$). The lowest clinical score was achieved in eyes treated with OB-B (Fig. 4); however, results were not statistically different from OB-C ($P = 0.998$) or OB-D ($P = 0.871$). Although OB-A resulted in the highest mean clinical score, there was no significant difference compared to OB-D ($P = 0.062$). No other significant differences between OBs were detected.

STT, IOP, and TFBUT values are illustrated in Table 3. There was no significant difference between results of control and treated eyes prior to and after the study. Furthermore, there was no statistical difference between values prior to and after the challenge in either group.

Prior to treatment, 14/19 of the control eyes had a normal cytology (i.e., score 0), whereas in 5/19 eyes single inflammatory cells, mainly neutrophil granulocytes and small lymphocytes, were present (i.e., score 1). After the study, 5/14 eyes remained normal, whereas 9/14 eyes revealed the presence of inflammatory cells. Three of five samples with signs of inflammation prior to the study remained unchanged, and 2/5 had no cytological signs of inflammation after completion of the study. Prior to treatment, 14/19 of the treated eyes had no sign of inflammation, whereas 5/19 eyes had cytological signs of an

Figure 1. Graphs represent the effect of the OBs on the treated eyes compared with untreated controls. Note the significant difference in clinical score among the control and the treated eyes. Difference became constantly significant for OB-A from day 13, OB-B day 15, OB-C day 22, and for OB-D day 10.
inflammation prior to treatment. Seven of 14 eyes had cytological signs of inflammation after treatment, whereas 7/14 remained normal. Regarding samples with cytological signs of inflammation prior to the study, 4/5 remained positive, whereas 1/5 was negative for signs of inflammation upon cytology after the trial. No epithelial metaplasia was recognized in any sample. None of the cytological samples contained intra- or extracellular bacteria. There was no significant difference between the control and the treated eyes prior to ($P = 1$) and after ($P = 0.740$) the trial. Comparing the rate of the cytological changes between the treated and the control eyes, no significant differences ($P = 0.743$) were detected. The differences between various treatments could not be statistically analyzed due to the low sample size.

All eyes tested were negative for FHV-1 prior to and after treatment. All eyes tested were negative for *Chlamydia felis* prior to and after the challenge. Detailed results of the bacteriologic and mycologic examinations of conjunctival swabs are summarized in Tables 4–5. Results are presented descriptively due to the low number of positive results.

**DISCUSSION**

Merely one report of severe local reaction to topical ointment in cats exists, to the authors’ knowledge. The ointment used in that report was cyclosporin. In our clinic, we also experienced ocular irritation in cats, following topical treatment with various ointments, not only those...
containing cyclosporine. Therefore, the long-term effect of various OBs on the cat eye was tested.

The results of the current study suggest that long-term treatment with ocular ointments is generally not well tolerated in cats. All treated eyes had a significantly higher clinical score compared to the untreated controls. The severity of reaction depended on the type of the OB. OB-A caused the most severe reactions.

Ocular OBs are primarily composed of white petrolatum and liquid paraffin. Upon application, ointments rapidly transform into an oily state, dispersing into the preocular tear film. Petrolatum-based ointments have a prolonged contact time compared with eye drops due to their larger molecules that delay ointment removal via the nasolacrimal drainage system. Another contributing factor is that oil droplets tend to be caught by mucus and form a mucus thread alongside the lower conjunctival fornix. Unfortunately, their prolonged contact time can result in mucosal irritation.

OB-A was the only simple base used in the study, created by a mixture of white petrolatum and liquid paraffin. Upon application, ointments rapidly transform into an oily state, dispersing into the preocular tear film. Petrolatum-based ointments have a prolonged contact time compared with eye drops due to their larger molecules that delay ointment removal via the nasolacrimal drainage system. Another contributing factor is that oil droplets tend to be caught by mucus and form a mucus thread alongside the lower conjunctival fornix. Unfortunately, their prolonged contact time can result in mucosal irritation.

OB-A was the only simple base used in the study, created by a mixture of white petrolatum and liquid paraffin. As it does not contain any emulgor, its miscibility with tear fluid is slow, resulting in even longer contact time, thus leading to more ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.

Testing of ocular irritation is difficult due to the involvement of several anatomic structures. The Draize rabbit eye irritation test was developed in 1944, and since then, it has been the gold standard in the assessment of ocular irritation of cosmetical products and ingredients. The initial grading scale was modified by Gupta et al. in 1976 to detect very low levels of ocular irritation. Emulsion-type OBs (i.e., compound bases) have better mixing properties.
Eyes treated with OB-A—which is a simple base—had the highest clinical score in our study. However, there was no significant difference among each treatment regarding TFBUT values. A wide range of TFBUT values was noticed, as reflected by the high standard deviation, and TFBUT values obtained in this study were lower than those previously reported. Davis et al. investigated TFBUT in healthy cats and also reported a wide variation. The authors suggested that the difference in distribution of TFBUT values in their study compared to other studies may have been influenced by the number of subsequent TFBUT measurements. A high interindividual variation between animals may be a further explanation for the difference of reported TFBUT values. The latter theory is supported by the results of another study, in which significant differences among cats were found. To the authors’ knowledge, there is no standardized method of TFBUT measurement to date. In our study, a single measurement was obtained at each examination period. The values of each examination were subsequently compared. The lack of a significant difference between TFBUT values suggests that goblet cell function was not affected by the 4-week treatment period.

Ocular irritation generated by topical treatment is described in human ophthalmology. It may be diagnosed by increased numbers of eosinophils upon impression cytology or in conjunctival biopsy samples. However, cytological evaluation in the current study did not reveal differences between treated and control eyes. This was not surprising as several studies showed that cats with apparent signs of conjunctivitis had normal cytology findings. Conjunctival cytology is commonly used as an additional diagnostic technique to diagnose various ocular surface anomalies. However, its diagnostic value is considered limited unless infectious agents or tumor cells are detected. Furthermore, the type of inflammation, which may be specified by cytology (e.g., suppurative vs. eosinophilic), is usually not predictive of its cause and duration. Allergy is considered an infrequent cause of conjunctivitis in cats, but an intolerance against various topical medications is described. According to Jégou et al., the cytological sign of allergic conjunctivitis is the presence of eosinophils and occasionally mast cells. However, in a case report of two cats with allergic conjunctivitis, cytology and conjunctival biopsy revealed the presence of lymphocytes. The diagnostic hallmark of allergic conjunctivitis is the cessation of clinical signs upon removal of the antigen. The improvement of clinical symptoms upon completion of the trial indicates contact allergy and local irritation, despite the lack of scientific evidence.

The second most irritating OB in our study was OB-D, containing 0.002% benzalkonium chloride (BAC). BAC is the most commonly used and studied preservative in ocular preparations. Several studies reported its effects on the ocular surface. Furthermore, its toxicity is

<table>
<thead>
<tr>
<th>Cat</th>
<th>Eye</th>
<th>Time</th>
<th>Bacillus spp.</th>
<th>CoNS</th>
<th>Streptomyces sp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OS</td>
<td>b</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>OD</td>
<td>b</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>OD</td>
<td>a</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>OS</td>
<td>a</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>OD</td>
<td>b</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>OD</td>
<td>a</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>OS</td>
<td>b</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>OD</td>
<td>a</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>OD</td>
<td>b</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>OS</td>
<td>a</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Table 5. The results of bacteriological and mycological examination in the second period.
dose-dependent. In a study on rabbit eyes, treated with 0.1% BAC solution twice daily for 14 days, depletion of goblet cells and squamous metaplasia was detected. In our study, no signs of squamous metaplasia were detected upon cytology, neither with OB-D, nor with the other OBs. A possible reason for this result may be the significantly lower BAC concentration in the current study. According to Epstein et al., lower concentration may cause adverse reaction over long periods. Further studies are warranted to test this hypothesis on the feline eye.

Long-term conjunctival irritation may induce submucosal infiltration by inflammatory cells. A study showed that submucosal inflammation is also associated with squamous metaplasia and decreased goblet cell density in cats. Submucosal changes may be readily demonstrated by histopathology; however, impression cytology is inappropriate as it merely allows the investigation of the superficial 2–3 epithelial layers. Conjunctival biopsy was not performed in this study, due to the degree of invasiveness and a likely negative effect on the clinical scores.

Despite the plethora of studies on bacterial conjunctivitis, limited information on the normal conjunctival bacterial and fungal flora of clinically healthy cats is available. In the present study, predominantly Gram-positive bacteria were identified, which is in accordance with previously published studies on normal conjunctival microbiota. In addition, none of the cytological samples revealed a high amount of neutrophils and intra- or extracellular bacteria. Limitations of the study include the small group size to identify statistically significant differences between control and treated eyes.

CONCLUSION

The results of this study indicate that eye ointments are not well tolerated in cats as they can cause severe local reaction in healthy eyes. Therefore, they should be used with caution in diseased eyes.

ACKNOWLEDGMENTS

The study was supported by the ESVO Research Grant (2013) and by the Austrian Cats United. The authors would like to thank James Rushton for proofreading the manuscript.

REFERENCES


