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Preliminary study of the stability of dexamethasone when added to commercial veterinary ear cleaners over a 90 day period

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Background – Topical corticosteroids are commonly used in the management of allergic otitis externa to diminish inflammation. A common strategy is to make compounded solutions of dexamethasone in ear cleaner.

Hypothesis/Objectives – The objective of this study was to determine the stability of dexamethasone when added to four commercial ear cleaners (ec): designated ecA, ecB, ecC and ecD.

Methods and Materials – Two concentrations (0.1 and 0.25 mg/mL) of dexamethasone were formulated for each cleaner solution from a 2 mg/mL solution and stored in the original manufacturers' bottles at two temperatures: room (22 °C) and refrigerated (4 °C). Samples were evaluated in triplicate, using liquid chromatography-tandem mass spectrometry at 10 time points over 90 days. The mean and standard deviation were calculated for each time point.

Results – A solution was considered stable if the dexamethasone value remained >90% of the target concentration. All dexamethasone solution values were stable to 90 days, except two solutions for ecA; the 0.25 mg/mL dexamethasone concentration was only stable to 14 (4 °C) and 21 days (22 °C).

Conclusions and clinical importance – These results provide preliminary evidence in support of pharmaceutical stability data for dexamethasone when included in the above compounded solutions at the noted concentrations and temperatures.

Introduction

Canine otitis externa (OE) is a very common presentation to the veterinarian.[1] Chronic OE often occurs when underlying primary causes are not identified and addressed. The most common primary cause for OE is allergic skin disease [atopic dermatitis (AD) and/or cutaneous adverse food reaction].[2] Managing the underlying primary risk factors is crucial to control chronic OE especially in dogs with allergic dermatitis.[2] Topical therapy is used to help control flares by removing allergens from the skin surface, minimizing overgrowth of bacteria and/or yeast, and reducing ceruminous debris in the ears.[2] When topical management of OE requires ongoing anti-inflammatory therapy, especially for ears that have chronic changes, topical corticosteroids are commonly used as they are efficacious in decreasing otic canal inflammation. In clinical practice, corticosteroids are added to various ear cleaners for maintenance of topical therapy and these compounded solutions can both clean the ear and deliver an anti-inflammatory corticosteroid. Anecdotally, topical corticosteroids have been used successfully as single agent products following ear cleaning, yet a combination product is easier for pet owners and may improve compliance when treating the animal. A prior study has shown that pulse topical corticosteroid therapy with hydrocortisone aceponate decreased the incidence between OE flares in allergic patients.[3]

To the best of the investigators' knowledge, there are no pharmaceutical studies that have evaluated long-term stability of injectable dexamethasone when it is added to commonly prescribed veterinary ear cleaners. This study had two objectives: the first was to evaluate the stability of dexamethasone when added to four commercial ear cleaners. The secondary objective was to monitor the compounded solutions via pH, gross inspection for any discoloration, precipitation or abnormal odour changes over 90 days. The response for dexamethasone was

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linear and gave correlation coefficients of 0.99 or better. Chemical stability as set forth by the guidelines of the *United States Pharmacopeia* (USP) mandates that dexamethasone needs to be 90–110% of the stated potency [from Day (D)0].[4] These study objectives would provide preliminary information on stability of these compounded solutions that are used in the management of OE.

Methods and materials

Compounded dexamethasone ear cleaner solutions

Four commercial veterinary ear cleaners (ec) were used: Triz-ULTRA + KETO Flush (Dechra Veterinary Products; Overland Park, KS, USA) (ecA); MAL-A-KET Plus TrizEDTA Flush (Dechra) (ecB); Epi-Otic Advanced (Virbac Animal Health; Fort Worth, TX, USA) (ecC); and Douxo Micellar Solution (Ceva Animal Health; Lenexa, KS, USA) (ecD).

The compounded solutions were formulated with manufacturers' bottles of 118 mL (4 oz) for Triz-ULTRA + KETO Flush, MAL-A-KET Plus TrizEDTA Flush and Epi-Otic Advanced, and 124 mL (4.2 oz) for Douxo Micellar Solution.

The composition, batch number and expiration for each of the four ear cleaners is as follows.

1. ecA: Triz-ULTRA + KETO Flush. Active ingredients: 0.15% ketoconazole, TrizEDTA (tromethamine USP, disodium EDTA dihydrate). Other ingredients: deionized water, carbopol aqua (lot 171190, expiration 10/19, store at room temperature).
2. ecB: MAL-A-KET Plus TrizEDTA Flush. Active ingredients: 0.15% chlorhexidine gluconate, 0.15% ketoconazole, TrizEDTA (tromethamine USP, disodium EDTA dihydrate). Other ingredients: deionized water, carbopol aqua, hydantoin and glycolic acid (lot 171056, expiration 09/19, store at room temperature).
3. ecC: Epi-Otic Advanced. Active ingredient: salicylic acid 0.2%. Other ingredients: disodium EDTA, docusate sodium, PCMX, a monosaccharide complex (L-rhamnose, D-galactose, D-mannose) and FD&C Blue #1 (lot 160550, expiration 11/2018).
4. ecD: Douxo Micellar Solution. Active ingredient: phytosphingosine HCl 0.02%. Other ingredients: water, polysorbate 80, alcohol denatured, propylene glycol, laureth-9, poloxamer 184, biosaccharide Gum-2, imidazolidinyl urea, phenoxyethanol, potassium sorbate, citric acid and fragrance (lot 170585A, expiration 02/06/19, store at room temperature).

The corticosteroid used was injectable dexamethasone (Vet One, Sparhawk Laboratories; Lenexa, KS, USA) (2 mg/mL) (lot 180217, expiration 2/20, store at 20–25 °C, protect from freezing). Each mL contains 2 mg dexamethasone, 500 mg polyethylene glycol 400, 9 mg benzyl alcohol, 1.8 mg methylparaben and 0.2 mg propylparaben as preservatives, 4.75% alcohol, HCl to adjust pH to approximately 4.9, water for injection q.s.). Two dexamethasone concentrations (0.25 and 0.1 mg/mL) were formulated for each cleaner. These two concentrations were chosen based on the previous clinical experience of the primary author. The same calculated volumes of ear cleaner were removed, and dexamethasone was added to create the two concentrations for each ear cleaner. For the MAL-A-KET Plus TrizEDTA Flush, Triz-ULTRA + KETO Flush and Epi-Otic Advanced, 0.1 mg/mL (5.9 mL of dexamethasone 2 mg/mL) and 0.25 mg/mL (14.8 mL of dexamethasone 2 mg/mL) were added. For the Douxo Micellar Solution 0.1 mg/mL (6.2 mL of dexamethasone 2 mg/mL) and the 0.25 mg/mL (15.5 mL of dexamethasone 2 mg/mL) were added. The volume for the Douxo Micellar Solution bottles was 6 mL greater than the other products' bottles, necessitating the addition of a greater volume of dexamethasone to achieve the desired concentrations. After each concentration was made, the bottles were hand-rocked by the primary author six times to mix the compounded solution.

Storage

One bottle of each concentration was stored at room temperature (22 °C) and a second duplicate bottle in the refrigerator (4 °C) in the laboratory. The room temperature was continually set to a standard (22 °C) which represents the average household temperature at which the bottles would most likely be stored by owners. The refrigerator (4 °C) was verified to be set to this temperature throughout the trial. Ambient humidity of the room where the bottles were stored was not measured in this study.

Analysis of stability and pH analysis

A standard protocol for recording observations for each bottle involved a gross inspection by the primary author at each of the ten time points (D0, D7, D14, D21, D28, D42, D56, D70, D84 and D90). All 16 bottles were examined for any visible changes in colour or clarity or odour change. Changes (if noted) were assessed subjectively as no change, mild or severe. After mixing, an aliquot was obtained for pH measurement using a Corning (Corning, NY, USA) pH Meter 445, at all ten time points. The initial pH of the dexamethasone before being added to any of the tested ear cleaners was 4.4. The pH of the ear cleaners with the added dexamethasone was measured at D0. This value was used as the reference pH and all ten time point measurements were recorded as a positive (+) or negative (–) change in comparison with the reference pH. After hand-mixing the compounded solutions, samples of each solution also were taken for dexamethasone analysis.

The analytical reference standard for dexamethasone was obtained from Cerilliant (Round Rock, TX, USA) as a 1 mg/mL solution. The dexamethasone working standard solution was prepared by dilution of the analytical reference standard solution with methanol to a concentration of 100 ng/μL.

Calibrators were prepared by dilution of the working standard solution with 100 μL water containing 2 ng/μL of the internal standard (Deuterated D5-dexamethasone, Toronto Research Chemicals; Toronto, Canada) and brought to a volume of 1 mL with a solution of 1% polyethylene glycol in 10% control (dexamethasone free) ear solution. Calibration curves were prepared fresh for each quantitative assay. The calibrators ranged between 1 and 40 ng/μL. To avoid differences in extraction recovery, the ear solutions were not extracted and instead simply diluted 10-fold in water containing internal standard. Diluted ear solutions were quantitated using a calibration curve prepared in the control ear solution spanning the range of nominal ear solution concentration. Refrigerated ear solution concentrations were compared to room temperature concentrations over 90 days. Before analysis, and in triplicate, 100 μL of each ear solution was diluted with 800 μL water and 100 μL internal standard. The inclusion of a deuterated internal standard was used to adjust for any matrix differences between each brand of ear solution. The ratio of dexamethasone to deuterated D5-dexamethasone was used as is done routinely in normal analytical determinations to account/correct for potential ion suppression.

The samples were vortexed briefly to mix them and 20 μL samples were injected into the liquid chromatography tandem-mass spectrometry (LC-MS/MS) system. The analysis was performed on a TSQ Vantage triple quadrupole mass spectrometer (Thermo Scientific; San Jose, CA, USA) with a 1100 series liquid chromatography system (Agilent Technologies; Palo Alto, CA). The spray voltage was 4,000 V, the vaporizer temperature was 300 °C, and the sheath and auxiliary gas were 45 and 30 AU (arbitrary units), respectively. Detection and quantification were conducted using selective reaction monitoring (SRM) of initial precursor ions for dexamethasone [mass: charge ratio (m/z) = 393] and the internal standard (m/z = 398). The response for the product ions for dexamethasone (m/z = 337, 355, 373) and the internal standard (m/z = 282, 360, 378) were plotted and peaks at the proper retention time (within ±0.1 min from the retention time of the dexamethasone standard) integrated using QUANBROWSER software (Thermo Scientific). QUANBROWSER was used to generate calibration curves and quantitate dexamethasone in all samples by linear regression analysis. A weighting factor of 1/*X* was used

for all calibration curves. Product masses and collision energies of each analyte were optimized by infusing the standards into the mass spectrometer. Chromatography employed an ACE 3 C18 10 cm x 2.1 mm, 3 μm inner diameter column (Mac-Mod Analytical; Chadds Ford, PA, USA). Mobile phase A was water with 0.2% formic acid and mobile phase B was acetonitrile with 0.2% formic acid. The high-performance liquid chromatography utilized a linear gradient of acetonitrile in water with a constant 0.2% formic acid at a flow rate of 0.35 mL/min. The initial acetonitrile concentration was held at 5% for 0.5 min, ramped to 90% over 5.0 min, and held at that concentration for 0.25 min before re-equilibrating for 3.7 min at initial conditions. The response for dexamethasone was linear and gave correlation coefficients of ≥0.99.

Results

Ear cleaner visual observations

On gross examination of the samples, there was no obvious formation of precipitates and only one solution had a mild change in colour. The D0 colours for each solution: Epi-Otic Advanced, dilute white/blue; Douxo Micellar Solution, clear; MAL-A-KET Plus TrizEDTA Flush, dilute pink; and Triz-ULTRA + KETO Flush, milky (white) blue. Sample colour was unaffected for Epi-Otic Advanced, Douxo Micellar Solution and Triz-ULTRA + KETO Flush during the entire 90 day trial. MAL-A-KET Plus TrizEDTA developed a slightly darker colour (pink to more golden over time) from D14 that appeared static thereafter.

pH measurements

There were no appreciable changes in the pH of any compounded solution (Table S1).

Dexamethasone measurements

The mean was taken of samples run in triplicate replicate samples and thus there was some variability in the concentration between individual samples, which accounts for some percentages being >100% (Table S2). There were no percentages above the USP 110% cut-off. The results showed that the Triz-ULTRA + KETO Flush 0.25 mg/mL solutions were stable, when refrigerated (4 °C) until D14 and at room temperature (22 °C) until D21 (Figure 1). All other dexamethasone compounded solutions were considered stable until D90 by the USP guidelines.

Data analysis

In total, three samples for each compounded ear cleaner and dexamethasone solution were analysed for each of the time points (n = 480); the mean and SD for the samples at the 10 time points of the study are provided in Table S2.

Discussion

Otitis externa is a very common presenting complaint in small animal practice and most often occurs as a manifestation of underlying allergic skin disease; both AD and cutaneous adverse food reactions predispose dogs and cats to developing OE. The use of a commercial ear flush regimen is a common and recommended practice in both the treatment and management of OE.[2,5] Commercial ear flushes contain active ingredients that function as ceruminolytics, drying agents or moisturizers, or produce synergistic effects with other medications to help treat secondary otic infections.[2,6]

For patients with chronic ear disease, it is common to utilize topical corticosteroid medications to decrease inflammation in the ear canal, as the inflamed canal often favours the development of secondary infections with either bacteria or yeast. In various clinical situations, injectable 2 mg/mL dexamethasone or 4 mg/mL dexamethasone sodium phosphate (Dex SP) is added to commercial ear flushes, so that a single prescribed topical product can be used for both ear flushing and for an anti-inflammatory effect. A single-use product is often easier for owners and may improve compliance and patient acceptance of the treatment. Responsible prescribing practices should include a scientifically validated beyond-use date on prescribed medications to note the time period during which they are chemically stable.

The use of compounded products is controversial in both human and veterinary medicine because of the lack of stability and efficacy study trials. However, in the absence of a commercially available, reasonably priced product, these in-house compounded medicated solutions often are used. The method and concentrations chosen for this study were based on formulations used previously by the primary author. Many other "recipes" may be found on the Veterinary Information Network (VIN; Davis, CA, USA) and similar sources. Normally, these compounded solutions are stored at the owners' homes after being prescribed. A previous study using dexamethasone 2 mg/mL paste noted that products were more stable after 30 days when refrigerated.[7] That study had a large temperature range from –20 to 80 °C, and only those products stored at 80 °C were unstable.[7] Although dexamethasone has been shown to be thermally stabile up 200 °C,[8] there is very limited information on how its stability is affected when mixed with the known ear cleaner ingredients. Consequently, in this study an objective was to determine if storage temperature, concentration of dexamethasone or the mixture of the solutions itself would influence stability over a longer period.

The results showed that dexamethasone stability (i.e. dexamethasone value remaining >90%) was not influenced by concentration or storage temperature for any solution except Triz-ULTRA + KETO Flush at 0.25 mg/mL. The compounded solution of dexamethasone with Triz-ULTRA + KETO Flush at 0.25 mg/mL was stable for only 14 days when refrigerated (4°C) temperature and 21 days at room temperature (22°C). The room temperature bottles may be more stable because the manufacturers' recommendations per the bottle instructions from Douxo and Dechra were to store the bottles at room temperature and not be refrigerated. The Virbac bottles did not include storage information on the label.

The reason as to why the higher concentration dexamethasone solutions appeared to degrade more rapidly for the Triz-ULTRA + KETO Flush 0.25 mg/mL dexamethasone concentration cannot be determined from the current study. However, the authors theorize, based on the physiochemical properties of the drug, that solubility may decrease at higher concentrations leading to precipitation

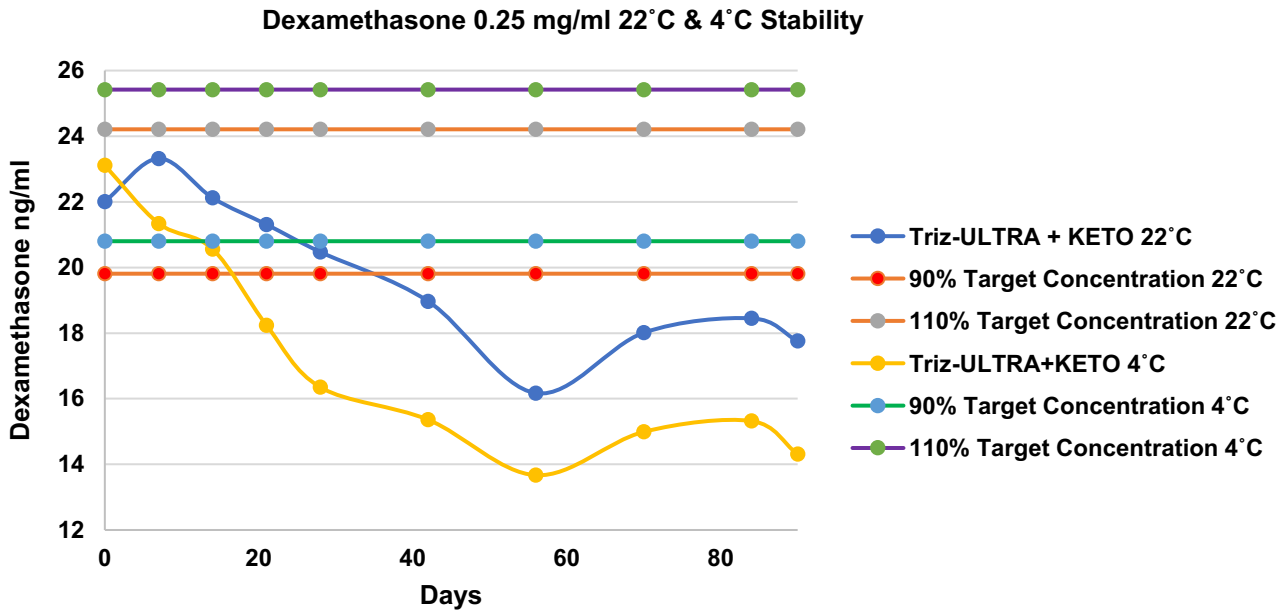

Figure 1. Stability of dexamethasone over time and at different temperatures when compounded with Triz-ULTRA + KETO Flush ear cleaner. Triz-ULTRA + KETO Flush ear cleaner with 0.25 mg/mL (2 mg/mL) dexamethasone is only stable until Day 21 at room temperature (22 °C) and until Day 14 at refrigerator temperature (4 °C).

of the drug. Although every effort was made to ensure that a homogenously mixed sample was taken for determination of dexamethasone concentrations, there is always the possibility that the aliquot which was analysed was not completely homogenous or that settling of the sample occurred before analysis. In addition, drug precipitation ultimately may have led to drug degradation. In basic chemistry, sometimes the temperature and concentration of a solution affects the rate of the reaction based on the collision theory. Increasing the temperature and concentration could increase the ability of molecules to collide, affecting the rate of degradation.[9]

A second possible explanation for the increased rate of degradation at higher (0.25 mg/mL) concentrations is the alteration in pH that occurred following addition of dexamethasone to the Triz-ULTRA + KETO Flush. As stated above, physiochemical properties can greatly influence solubility. Alterations in pH may lead to changes in the ratio of unionized to ionized drug affecting solubility and potentially leading to degradation. Over a longer storage time, this effect may increase, leading to continual degradation.

The pH of the injectable dexamethasone 2 mg/mL solution used in this study was acidic (4.4) while the average pH at D0 for the compounded 0.25 mg/mL solutions was alkaline (8.18). These Triz-ULTRA + KETO Flush compounded solutions stayed alkaline, as shown by the fact that on D90, their average pH was 8.15. Thus, compounding the acidic dexamethasone solution into an alkaline solution such as Triz-ULTRA + KETO Flush could have affected its stability. The difference in pH and the collision theory could explain why the 0.25 mg/mL Triz-ULTRA + KETO Flush solutions were not stable and the 0.1 mg/mL were. The authors could not find any stability studies in which dexamethasone with an acidic pH was compounded with alkaline solutions. To the best of the authors' knowledge, there are no prior stability studies investigating effects on the ear products' active ingredients when mixed with dexamethasone. Consequently, it is difficult to state how or if any of the active ingredients of the ear cleaners themselves could be influenced by the addition of dexamethasone. There was one stability study that investigated ear cleaner solutions compounded with the antibiotic Baytril (enrofloxacin, Bayer; Shawnee Mission, KS, USA) with four ear cleaners [Triz-EDTA and Triz-Chlor (Dermapet now Dechra) and Epi-Otic and Epi-Otic Advanced (Virbac)]. It showed that the bactericidal efficacy of TrizChlor decreased between D0 and D14.[10] The decrease in efficacy was suspected to have resulted from the difference in pH from the enrofloxacin-compounded TrizChlor (pH 9.2) and normal chlorhexidine (pH 5.0–7.0). This illustrates the importance of taking into account the pH of constituent components of a compounded solution. Further studies would be necessary to determine definitively the reason for the apparent decreased stability over time of the higher concentration solutions in this study.

The pH results did not deviate significantly from any of the bottles' baseline values from D0 to D90. The gross examination did not document any major changes over the 90 day study period, except for the mild colour change in the MAL-A-KET Plus TrizEDTA Flush solution at D14. This is a change the primary author has noted before when using these compounded solutions of dexamethasone with MAL-A-KET Plus TrizEDTA Flush, with either 2 or 4 mg/mL dexamethasone concentrations.

A limitation of the study is that although triplicate samples were run for each solution at each time point, having multiple bottles of each solution at each storage temperature and concentration was cost- and time-prohibitive. This preliminary stability study evaluating the addition of 2 mg/mL dexamethasone to four different ear cleaners at specific temperatures and concentrations, provides initial

data on the stability of these solutions. Future stability studies with other ear cleaners, a variety of dexamethasone concentrations and other formulations would be helpful.

In conclusion, this study showed that dexamethasone 2 mg/mL with pH 4.4 when compounded into a solution with four ear cleaners was stable at room (22 °C) and refrigerated (4 °C) storage temperatures and at 0.25 and 0.1 mg/mL concentrations for MAL-A-KET Plus TrizEDTA Flush, Epi-Otic Advanced and Douxo Micellar Solution over a 90 day period. Dexamethasone was stable at both storage temperatures for 0.1 mg/mL concentrations of Triz-ULTRA + KETO Flush. It is important to recognize that these results establish only introductory evidence of pharmaceutical stability data and only for the concentrations of 0.25 and 0.1 mg/mL, when stored at room or refrigerated temperatures, and only over a 90 day length of time. This study only offers preliminary data because only one batch of compounded solution was studied; these stability data may not be able to predict the stability of other formulations of dexamethasone or differing concentrations of dexamethasone, nor other products that might be used in compounded otic topical medication "recipes" using dexamethasone. Furthermore, this study does not provide any evidence for efficacy *in vitro* or *in vivo,* or information about possible adverse effects from the use of these solutions *in vivo*. However, this study does offer veterinarians and pharmacists introductory information on these compounded medications' stability when prescribed for management and prevention of chronic OE.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1. Day 0 pH of the four ear cleaners showing the range of variation (+ and -) over the 90 days of the study

RÉSUMÉ

Contexte – Les corticoïdes topiques sont fréquemment utilisés dans la gestion des otites chroniques externes pour diminuer l'inflammation. Une stratégie fréquente consiste à réaliser des préparations composées de déxaméthasone dans une solution de nettoyage.

Hypothèses/Objectifs – L'objectif de cette étude a été de déterminer la stabilité de déxaméthasone quand ajoutée à quatre solutions de nettoyant auriculaire commerciales (ec) : ecA, ecB, ecC et ecD.

Matériel et méthodes – Deux concentrations (0,1 et 0,25 mg/mL) de déxaméthasone ont été formulées pour chaque solution nettoyante à partir d'une solution de 2 mg/mL et conservées dans les bouteilles du fabricant à deux températures : ambiante (22°)et réfrigérée (4°C). Les échantillons ont été évalués en triple, à l'aide de spectrométrie de masse en chromatographie liquide tandème à 10 moments sur 90 jours. La déviation moyenne et standard ont été calculées pour chaque moment.

Résultats – Une solution a été considérée stable si la valeur de déxaméthasone restait >90% de la concentration cible. Toutes les valeurs de solution de déxaméthasone étaient stables à 90 jours, sauf deux solutions pour ecA ; la concentration de déxaméthasone de 0,25 mg/mL était stable uniquement à 14 (4°C) et 21 jours (22°C).

Conclusions et importance clinique – Ces résultats fournissent des preuves préliminaires de données de stabilité pharmaceutique pour la déxaméthasone quand ajoutée à des solutions composées aux concentrations et températures notées.

RESUMEN

Introducción – los corticosteroides tópicos se usan comúnmente en el tratamiento de la otitis externa alérgica para disminuir la inflamación. Una estrategia común es preparar soluciones compuestas de dexametasona en un limpiador de oídos.

Hipótesis/Objetivos – el objetivo de este estudio fue determinar la estabilidad de la dexametasona cuando se agrega a cuatro limpiadores de oídos comerciales (ec): denominados ecA, ecB, ecC y ecD.
Métodos y materiales – se formularon dos concentraciones (0,1 y 0,25 mg/ml) de dexametasona para cada solución limpiadora a partir de una solución de 2 mg/ml y se almacenaron en los frascos originales del fabricante a dos temperaturas: ambiente (22˚C) y refrigerado (4˚C). Las muestras se evaluaron por triplicado, utilizando cromatografía líquida-espectrometría de masas en tándem en 10 puntos de tiempo durante 90 días. Se calcularon la media y la desviación estándar para cada tiempo.
Resultados – una solución se consideró estable si el valor de dexametasona permanecía>90% de la concentración objetivo. Todos los valores de la solución de dexametasona se mantuvieron estables durante 90 días, excepto dos soluciones para la ecA; la concentración de 0,25 mg/ml de dexametasona solo fue estable hasta los 14 (4˚C) y 21 días (22˚C).
Conclusiones e importancia clínica – estos resultados proporcionan evidencia preliminar que respalda los datos de estabilidad farmacéutica de la dexametasona cuando se incluye en las soluciones compuestas anteriores a las concentraciones y temperaturas indicadas.

Zusammenfassung
Hintergrund – Topisch verabreichte Cortikosteroide werden häufig beim Management von allergischer Otitis externa eingesetzt, um die Entzündung abzuschwächen. Eine häufige Strategie besteht darin, gemischte Lösungen von Dexamethason im Ohrreiniger herzustellen.
Hypothese/Ziele – Das objektive Ziel dieser Studie war es, die Stabilität von Dexamethason zu bestimmen, wenn es zu vier kommerziellen Ohrreinigern (ec) zugesetzt wurde: ecA, ecB, ecC und ecD.
Methoden und Materialien – Zwei Konzentrationen (0,2 und 0,25 mg/mL) an Dexamethason wurden für jeden Ohrreiniger aus einer 2 mg/mL Lösung gemischt und in der Originalflasche des Herstellers bei zwei Temperaturen gelagert: Raumtemperatur (22° C) und gekühlt (4° C). Proben wurden im Triplet evaluiert, wobei die Flüssigkeitschromatografie im Tandem mit Massenspektrometrie zu 10 Zeitpunkten über einen Zeitraum von 90 Tagen zum Einsatz kam. Die durchschnittliche und Standardabweichung wurde für jeden Zeitpunkt kalkuliert.
Ergebnisse – Eine Lösung wurde als stabil betrachtet, wenn der Wert des Dexamethasons bei >90% der Zielkonzentration blieb. Alle Dexamethason-Lösungen waren 90 Tage lang stabil, außer zweier Lösungen für ecA; die 0,25 mg/mL Dexamethason Konzentration war nur stabil bis 14 (4° C) und 21 Tage (22° C).
Schlussfolgerungen und klinische Bedeutung – Diese Ergebnisse zeigten eine vorläufige Evidenz zur Unterstützung der Daten der pharmazeutischen Stabilität für Dexamethason, wenn es in die oben genannten gemischten Lösungen zu den genannten Konzentrationen und Temperaturen inkludiert wurde.

要約
背景 – 外用コルチコステロイド製剤は炎症を軽減するため、アレルギー性外耳炎の管理に一般的に使用されている。一般的な戦略は、イヤークリーナーでデキサメタゾンの配合溶液を作ることである。
仮説/目的 – 本研究の目的は、4つの市販イヤークリーナー (ec) (ecA、ecB、ecC、およびecDと指定) に添加した場合のデキサメタゾンの安定性を判断することであった。
材料と方法 – mg / mL溶液から各クリーナー溶液に対して2つの濃度(0.1および0.25 mg / mL)のデキサメタゾンを処方し、元のメーカーのボトルに2つの温度 (室内(22℃)と冷蔵(4℃)で保管した。液体クロマトグラフィー-タンデム質量解析を使用して、90日間にわたって10の時点でサンプルを3回評価した。各時点の平均および標準偏差を計算した。
結果 – デキサメタゾン値がターゲット濃度の> 90%のままである場合、溶液は安定していると見なした。ecAの2つの溶液を除いて、すべてのデキサメタゾン溶液の値は90日まで安定していた。 0.25 mg / mLのデキサメタゾン濃度は14日(4℃)および21日 (22℃)までしか安定しなかった。
結論と臨床的重要性 – これらの結果は、上記の濃度および温度で上記の配合溶液に含まれる場合のデキサメタゾンの医薬品安定性データを裏付ける予備的な証拠を提供している。

概要
背景 — 外用皮质类固醇通常用于治疗过敏性外耳炎，以减少炎症。种常见的策略是地塞米松加入洗耳水中，制备出复方溶液。
假设/目的 — 本研究目的是确定地塞米松加入四种市售洗耳水(ec)中的稳定性：指定为ecA、ecB、ecC和ecD。
方法和材料 — 使用原装2 mg/mL溶液与每种洗耳水溶液配制出两种浓度 (0.1和0.25 mg/mL) 的地塞米松，并在两种温度下储存：室温(22°C)和冷藏(4°C)。使用液相色谱-串联质谱法在90天内的10个时间点对样本进行一式三份评价。计算每个时间点的平均值和标准差。
结果 — 如果地塞米松值保持>目标浓度的90%，则认为溶液稳定。除两种ecA溶液外，所有地塞米松溶液值均可稳定储存90天；0.25 mg/mL地塞米松浓度仅可稳定储存14天(4°C)和21天(22 °C)。
结论和临床重要性 — 按照所述浓度和温度配制上述溶液，结果提供了初步数据，支持了地塞米松的药物稳定性。

Resumo

Contexto – O teste alérgico intradérmico (IDT) geralmente requer sedação. A lidocaína tópica pode ser utilizada de forma adjunta ou alternativa à sedação.

Hipótese/Objetivos – A nossa hipótese foi de que a aplicação de lidocaína tópica poderia reduzir significativamente as reações às injeções intradérmicas e que cães atópicos tratados com lidocaína tópica demonstrariam resultados semelhantes no IDT aos de cães atópicos testados sem lidocaína tópica.

Animais – Quinze cães atópicos de clientes.

Métodos – Na Parte I, um adesivo de lidocaína a 5%, um creme de lidocaína a 5% e um controle sem ingredientes ativos foram comparados. O escore de dor mais baixo durante a injeção intradérmica foi estabelecido em seis cães atópicos. Quinze cães atópicos foram selecionados na Parte II, e o creme de lidocaína (considerado o mais eficaz) foi aplicado aleatoriamente em um lado do tórax. Realizou-se um IDT em cada lado do peito. Escores objetivos e subjetivos do controle e tratamento com lidocaína foram comparados em 15 e 30 minutos pós-injeção.

Resultados – O creme de lidocaína a 5% apresentou a maior redução no escore de dor associada à injeção intradérmica. Não houve diferenças significativas no diâmetro médio da pápula para nenhum dos alérgenos avaliados em nenhum tempo experimental entre o lado controle e o lado tratado com lidocaína. Houve uma alta concordância entre os dois grupos quando avaliado o escore subjetivo para todos, exceto um alérgeno.

Conclusões e importância clínica – A lidocaína tópica pode ser utilizada como analgesia adjunta durante o IDT com cautela na interpretação do escore subjetivo para poeira doméstica. O creme de lidocaína aparentemente reduziu o escore de dor e pode permitir redução na sedação concomitante.

