The selective glucocorticoid receptor agonist mapracorat displays a favourable safety–efficacy ratio for the topical treatment of inflammatory skin diseases in dogs

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Introduction

Canine atopic dermatitis (CAD) is defined as a genetically predisposed inflammatory and pruritic skin disease with characteristic clinical features. In most cases CAD is associated with IgE antibodies directed at environmental allergens.¹ Dogs are frequently treated with immune modulators such as glucocorticoids and the calcineurin-inhibitor ciclosporin; the Janus kinase inhibitor oclacitinib has been shown to have comparable efficacy to ciclosporin.² Glucocorticoids are used frequently in the treatment of pruritus and CAD as they are effective and inexpensive. They are, however, associated with adverse effects including polyphagia and polyuria, diabetes mellitus, growth retardation, enhanced risk of infections and – especially when administered by the topical route – the potential for cutaneous atrophy.³,⁴ Many efforts have been made in recent years to identify specific glucocorticoid receptor ligands with a dissociated profile: maintenance of the potent anti-inflammatory effects but reduced potential for adverse effects.⁵ Common adverse effects such as diabetes mellitus, dyslipidaemia, glaucoma induction, muscle atrophy and skin thinning are partly or even mainly dependent on glucocorticoid...
receptor mediated activation of gene expression (transactivation). By contrast, many of the immunosuppressive and anti-inflammatory effects of glucocorticoids are due to glucocorticoid receptor mediated suppression of cytokine and chemokine synthesis, and expression of adhesion molecules and enzymes. This phenomenon is referred to as transrepression. In best cases, dissociated glucocorticoid receptor ligands such as the nonsteroidal family of Selective Glucocorticoid Receptor Agonists (SEGRA) show less transactivation compared to classical glucocorticoids. Mapracorat was also tested in a rabbit dry eye model, where it had comparable anti-inflammatory immunomodulatory potential of the nonsteroidal SEGRA treatment of atopic dermatitis in humans are underway

Mapracorat in dogs and to assess its potential for promoting skin atrophy as compared to the topical glucocorticoid triamcinolone acetonide.

**Material and methods**

**Animals**

All procedures involving animals were carried out in agreement with the current version of the German Law on the Protection of Animals. The animal experiments were registered by Bezirksregierung Hanover, Germany (AZ 33.9-42502-04-11/063).

Six laboratory beagles (three male, three female, aged between 3 and 5 years, weighing between 8.8 and 16.7 kg) were group housed in rooms at 20–22°C. Water was offered ad libitum and a standard diet (Altromin; Lage/Lippe, Germany) was offered twice daily. All dogs were neutered, vaccinated (Virbagen SHAP, LT; Virbac Tierarzneimittel GmbH; Bad Oldesloe, Germany) and regularly dewormed (Milbemax, Novartis Tiersgesundheit GmbH; München, Germany). The dogs had access to a courtyard and were taken for a walk once daily for approximately 30 min. The dogs did not receive any medication within 30 days before blood samples were taken or in vivo experiments were performed.

Female BALB/c mice (Charles River; Sulzfeld, Germany), aged between 8 and 12 weeks, were housed in groups at 22°C with a 12 h light/dark cycle. Water and a standard diet (Altromin) were available ad libitum.

**Generation of canine peripheral blood derived mononuclear cells (PBMC)**

Blood samples (8 to 9 ml) were taken from the jugular vein by means of a vacuum container with heparin (BD Vacutainer, NIH 170 l.U.; Plymouth, UK). The following steps were carried out in a class 1 safety cabinet. In an appropriate plastic tube, 9 ml blood were diluted with approximately 10 ml phosphate buffered saline (PBS) and underlain with 15 ml histopaque 1077 (Sigma; Steinheim, Germany). Samples were centrifuged at 1200 g, 19°C for 35 min with the brakes turned off. The peripheral blood mononuclear cells (PBMC) were removed from the interface between the layers and cells were washed two times by the addition of phosphate buffered saline (PBS) (1000 g for 10 min, 4°C, brakes activated). Following the final washing step, the cell pellet was resuspended in an appropriate volume of tissue culture medium (RPMI 1640 + 10% fetal calf serum, both Biochrom; Berlin, Germany) and viable cells were counted with trypan blue staining. The cells were used directly for the experiments.

**Generation of murine bone marrow derived dendritic cells (BMDC)**

Large numbers of highly pure BMDC were generated according to a standard protocol. Briefly, bone marrow was flushed from femurs of the hind limbs of drug-naive mice with ice cold PBS and taken into RPMI 1640 + 10% fetal calf serum (Biochrom) with 50 μM 2-mercaptoethanol (Sigma) added. Cells, 2 x 10^6, were seeded in 10 ml medium on a petri dish (Cell+; Sarstedt; Nürnberg, Germany). The medium contained 20 ng/ml granulocyte macrophage colony stimulating factor (GM-CSF) (R&D systems; Wiesbaden, Germany). On Day 3, 10 ml fresh medium supplemented with 200 ng GM-CSF was added. At days 6 and 8, 50% of the medium was collected, centrifuged and the cell pellet re-suspended in 10 ml fresh medium containing 200 ng GM-CSF. Flow cytometry analysis of the Day 10 cell suspension demonstrated a high yield of CD 11c and major histocompatibility complex II positive cells. 

**In vitro test incubation protocol**

The compound stock solutions of mapracorat in acetone (Bayer Animal Health GmbH; Leverkusen, Germany) and mometasone furoate [10 mg/ml in dimethyl sulfoxide (DMSO), Sigma] were serially diluted to the final concentrations tested; the vehicle was spiked with the highest possible DMSO concentration used for the drugs (0.001%). The mapracorat concentration ranged from 0.1 to 100 nmol/L and mometasone furoate from 0.01 to 1 nmol/L. Compound (mometasone furoate) and concentration selection were performed according to published data. For PBMC, 200,000 cells in 200 μl were treated with each concentration at least in duplicate in three to four independent settings (i.e. cells from the blood of three to four different dogs). For murine BMDC, 200,000 cells in 200 μl were treated with each concentration at least in duplicate in two independent settings (i.e. cells from the bone marrow of two mice).

A pilot study was conducted to determine the best conditions for in vitro stimulation of canine PBMC. From this study it was concluded that 1 μg/ml lipopolysaccharide (LPS) was better than 10 μg/ml LPS. After 30 min of pre-incubation with the test compounds, cells were stimulated with 1 μg/ml LPS (from E. coli, O127:B8, Sigma). Twenty four hours after LPS stimulation cells were centrifuged (500 g, 10 min, 4°C) and the cell culture supernatant was frozen at −20°C until determination of TNFα (canine and murine Dusset ELISA, R&D systems; Wiesbaden, Germany).

**In vivo experiments: Topical application of glucocorticoid agonists, injection of compound 48/80 and determination of wheal reaction as well as erythema**

The skin of the abdomen (mainly nonpigmented) was shaved with an electric hair clipper at three different sites of about 100 cm² each. At least 15 cm space was left between each application site. All dogs received vehicle (500 µl acetone), mapracorat (500 µL 0.1% in acetone) and triamcinolone acetonide (500 µl 0.015% in acetone, Sigma) at one of the shaved areas one day after skin preparation. The doses were chosen according to a licensed product (Genesis spray, Virbac; Fort Worth, TX, USA, 0.015% triamcinolone acetonide) or in vivo data in mice (80% reduction of ear swelling in a mouse model of allergic dermatitis with a 0.1% solution for mapracorat). The topical administration was repeated 24 h after first application and again at 48 and 72 h. The administration of test compounds was performed in a blinded fashion (substance “A” to “C”) and were varied from dog to dog to be equally distributed across the test items. One hour after the last (fourth) application of substances, compound 48/80 (50 µg/50 µL) was injected intradermally (30 gauge needle) into the centre of each of the three shaved areas. Wheal and erythema reactions were assessed by means of planimetry at 10, 30 and 60 min after injection of compound 48/80.
Determination of skin thinning potential
The same dogs were used for this experimental protocol. They had not received any medication or other experimental treatment within 30 days prior to this part of the study. The skin of the lateral thorax (left and right side) and flank (left and right side) were shaved with an electric hair clipper and the skin thickness was determined by means of a cutimeter (model 7309, Mitotoyo; Neuss, Germany). For determination of the baseline value, the mean of three independent thickness measurements (performed on days –3, –2 and –1) was used. All dogs received vehicle (50 µL acetone), mapracorat (50 µL 0.1% in acetone) and triamcinolone acetonide (50 µL 0.015% in acetone), once daily over 14 days on an area of approximately 9 cm². The treatment areas were varied from dog to dog to be distributed equally across the test items. However, the skin areas allocated to the respective treatments remained the same in each individual dog over the entire treatment phase. The skin fold thickness was determined three times a week for each area, directly before the next scheduled application of test item. The skin was shaved again 11 days after first treatment. This had no impact on determination of skin fold thickness (evaluated before and after shaving).

Statistical evaluation
For the in vitro experiments, results are presented as mean % inhibition of two determinations at each tested concentration, each investigated in duplicate or triplicate. The concentrations which led to 50% inhibition (IC50s) were determined directly from the graphs.
For the in vivo compound 48/80 study, time courses are presented as mean (±SEM). For statistical analysis of wheal and erythema areas, a two-way repeated measures ANOVA with the fixed factors pre-treatment, time and the pre-treatment by time interaction was performed. Analysis was performed with SigmaPlot (version 12.5, Systat Software Inc.; San Jose, CA, USA) followed by a post hoc test (All Pairwise Multiple Comparison Procedure, Holm–Sidak method) when the difference in the mean values among the different levels of pre-treatment or time was greater than would be expected by chance.
Skin thickness results are presented as mean (±SEM) for the determination of skin fold thickness by means of a cutimeter. The different treatment groups were checked at all time points for significant differences against vehicle treatment by means of a one-way ANOVA followed by a post hoc test (Dunnett’s). P values <0.05 were considered to be statistically significant for all comparisons.

Results
Modulation of TNFα secretion of murine BMDC
A mean concentration of TNFα of 7,500–9,500 pg/mL was recovered in the supernatant of vehicle-treated murine BMDC 24 h after LPS stimulation (these values had

![Figure 1](image-url)
been set as 100%; see Figure 1). Mapracorat and mometasone furoate concentration-dependently inhibited the LPS-induced TNFα secretion. However, the maximal effect achieved by all tested glucocorticoid agonists was approximately 40% inhibition (Figure 1); this value was set as the maximal effect. IC50s determined directly from graphs were approximately 0.5 nmol/L for mapracorat and 0.05 nmol/L for mometasone furoate.

**Modulation of TNFα secretion of canine PBMC**

A mean concentration of TNFα of 100–250 pg/mL was determined in the supernatant of vehicle-treated canine PBMC 24 h after LPS stimulation (these values had been set as 100%; see Figure 1), whereas the TNFα concentration of non-LPS stimulated PBMC was below the limit of detection. Mapracorat and mometasone furoate concentration-dependently inhibited the TNFα secretion (Figure 1c and d). IC50s determined directly from graphs were approximately 0.2 nmol/L for mapracorat and 0.04 nmol/L for mometasone furoate.

**Compound 48/80 induced inflammation and oedema**

Intradermal injection of compound 48/80 resulted in a significant wheal and erythema reaction over the 60 min observation period in vehicle-treated areas (Factor Time \( P < 0.001 \); Figure 2). There was a significant overall effect of pre-treatment on this reaction (\( P = 0.005 \) for wheal and 0.012 for erythema, respectively). Post hoc testing confirmed that mapracorat and triamcinolone acetonide significantly reduced wheal and erythema reaction to compound 48/80 compared to sites pre-treated with vehicle. Pairwise comparisons further revealed that the SEGRA compound mapracorat and the classical glucocorticoid did not differ in their efficacy and potency, neither overall nor at any specific observation time point.

**Skin thickness evaluation**

Topical treatment with vehicle or mapracorat (0.1%) had no obvious impact on skin fold thickness within the 14 days of consecutive treatment. However, triamcinolone acetonide (0.015%) reduced skin fold thickness significantly from Day 7 onwards (Figure 3).

**Discussion**

This study has demonstrated that mapracorat exerts in vitro inhibitory effects on activated canine and murine immune cells with comparable efficacy to mometasone furoate. Mapracorat has also been shown to have anti-inflammatory efficacy similar to topical triamcinolone acetonide – with less thinning of the skin – at equipotent concentrations. The better safety profile might be explained by the dissociative profile of the SEGRA. Whereas transrepression and reduction of the expression of enzymes involved in inflammation are comparable between SEGRAs and classical glucocorticoids, the transactivation potential of SEGRAs is reduced.\(^5\) Several adverse effects such as glaucoma induction, muscle atrophy and skin atrophy previously have been shown to be less pronounced with SEGRAs.\(^6,7\) As such, this new class of glucocorticoid agonists holds promise for long-term treatment of atopic dermatitis patients.
Results of this study, which show a concentration-dependent inhibition of TNFα secretion from activated canine PBMC and murine BMDC in vitro that is similar in efficacy to mometasone furoate, is consistent with reports from prior studies that used similar cell culture systems. However, the potency of mapracorat was higher in the present study.

The observation that glucocorticoids mediate only a partial inhibition of LPS-induced cytokine release from murine BMDC is corroborated by former findings, where the highly potent topical steroid (WHO class 1) diflorasone diacetate was tested in the same system, leading to similar maximal inhibitory potential.

The in vitro results of the present study indicate that the novel SEGRA mapracorat is able to stimulate canine glucocorticoid receptors as effectively as murine glucocorticoid receptors. Hence, it can be reasonably assumed that mapracorat will display similar anti-inflammatory/ immunomodulatory potential in dogs as that observed in mice if provided in a suitable formulation for topical administration.

The in vivo inflammation study indicated that the intracutaneous compound 48/80 injection model is a robust, reproducible and fast system with which to study skin inflammation in dogs and to test the possible anti-inflammatory effects of steroidal and nonsteroidal glucocorticoid receptor agonists. Compound 48/80 is a basic secretagogue which induces mast cell degranulation followed by liberation of histamine and other pro-inflammatory mediators such as cytokines, proteases and prostaglandins. A recent study indicated that compound 48/80-induced mast cell degranulation is mediated by activation of the Mas-related G protein-coupled receptor X2 (MrgrpX2) in humans and mice. Corroborating studies in dogs have not yet been published, although mRNA of MrgrpX2 has been identified in canine mastocytoma cells in pilot studies conducted by the authors (unpublished data).

The intradermal injection compound 48/80 has been studied as a positive control for the intradermal allergen test in dogs and also as a test system to evaluate glucocorticoid action in an immediate type hypersensitivity model. It was shown that a 0.015% topical triamcinolone acetonide solution inhibited the “reaction area” induced by compound 48/80. We applied the topical test solutions (triamcinolone acetonide and mapracorat) four times in order to obtain a reliable anti-inflammatory response. A pilot study had determined that two applications (24 h and 1 h prior to compound 48/80 challenge) resulted only in marginal reduction of erythema and wheal reaction for both compounds (data not shown). Although compound 48/80 provoked distinct wheal and flare reactions, it did not induce pruritic behaviours in the dogs tested. Therefore, we were unable to evaluate the topical test solutions for any anti-pruritic effects. Of note, the inflammatory response to compound 48/80 in vehicle treated areas was visible for at least 2 weeks, so it should be kept in mind that long inter-study periods might be necessary for a full reconstitution of degranulated mast cells in skin when using this compound in vivo.

Given that cutaneous atrophy during use of topical glucocorticoids is a major concern, we addressed this potential adverse effect in a separate experiment. The progressive reduction of skin fold thickness observed with triamcinolone acetonide, which had already achieved statistical significance after 7 days of treatment, is consistent with a study in human subjects where daily administration of 0.01% triamcinolone acetonide led to a reduction of skin thickness by roughly 10% within 10 days. A similar approach has been used in mice where skin thickness was observed over a period of 19 days, where mapracorat led to a significant reduction in skin fold thickness, although the effect was less pronounced than with an equipotent concentration of mometasone furoate.

Results of the study reported here have demonstrated the safety advantage of the SEGRA mapracorat over a conventional topical steroid when applied in the same vehicle formulation. However, bioavailability of topical administered drugs is strongly dependent on the physicochemical characteristics of the pharmaceutical formulation, so results of this study must be interpreted with care. The true safety advantage of a SEGRA for veterinary use over licensed benchmark steroidal glucocorticoid should be determined using both the respective final formulations and the therapeutically recommended dose volumes.

In conclusion, the experiments described here demonstrate that the SEGRA mapracorat exerts in vitro inhibitory effects on activated canine immune cells with comparable efficacy to mometasone furoate and provides comparable in vivo anti-inflammatory activity to topical triamcinolone acetonide with less cutaneous atrophy at equipotent concentrations. Future studies should assess the clinical efficacy and safety profiles of mapracorat in controlled clinical trials of dogs with atopic dermatitis using an approved pharmaceutical formulation.

References

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**Resumen**

**Contexto** – Mapracorat es un agonista selectivo de receptores glucocorticoides no esteroide (SEGRA) supuesto être un meilleur index thérapeutique que les glucocorticoides classiques.

**Objetivos** – Comparer l’efficacité et la sécurité du mapracorat avec les corticoïdes classiques utilisés pour le traitement des dermatoses allergiques du chien.

**Sujet** – Six beagles de laboratoire.

**Méthodes** – L’effet du mapracorat sur la sécrétion de TNFα induit par les lipopolysaccharides à partir de cellules mononucléées (PBMC) du sang périphérique de chien a été testé. *In vivo*, le mapracorat a été comparé à l’acétonide de triamcinolone sur un modèle d’inflammation cutanée. L’épaisseur du pli cutané a été déterminée après une administration quotidienne de mapracorat et d’acétonide de triamcinolone sur 14 jours.

**Résultats** – La concentration de mapracorat inhibe indépendamment la sécrétion de TNFα de PBMC canin activé avec une valeur de concentration minimale inhibitrice (IC50) d’approximativement 0,2 nmol/L. L’injection intradermique de composition 48/80 (50 μg dans 50 μL de saline) a résulté en une plaque claire et surélevée au cours de la période d’observation de 60 min. Le pré-traitement topique au mapracorat (0,1%) et l’acétonide de triamcinolone (0,015%) a mené à une diminution significative des plaques en diamètre et volume, comparé au véhicule (acétone) sur les zones traitées. Cependant, une application par jour d’acétonide de triamcinolone a significativement réduit l’épaisseur du pli cutané du jour 8 à 14 tandis qu’aucune diminution n’a été observée pour le mapracorat.

**Conclusion** – Ces résultats démontrent que le mapracorat a un effet anti-inflammatoire comparable aux glucocorticoides stéroïdiens classiques sous ces conditions expérimentales et le maintien de l’épaisseur du pli cutané indique un meilleur profil de sécurité comparé à l’acétonide de triamcinolone à concentrations équivalentes. Ces résultats suggèrent que les SEGRAs sont prometteurs dans la gestion des dermatoses prurigineuses et inflammatoires du chien.

**Resumen**

**Introducción** – Mapracorat es un agonista selectivo de receptores glucocorticoides no esteroideo (SEGRA) que presumiblemente tiene un índice terapéutico mejor comparado con los glucocorticoides clásicos.

**Objetivos** – comparar la eficacia y seguridad de Mapracorat con glucocorticoides clásicos utilizados para el tratamiento de enfermedades alérgicas en perros.

**Animales** – seis perros de raza Beagle de laboratorio.

**Métodos** – se probó el efecto de mapracorat en la secreción de TNFα inducida por lipopolisacárido en células mononucleares derivadas de sangre periférica (PBMC). *In vivo*, mapracorat se comparó con acetonido de triamcinolona utilizando un modelo de inflamación de la piel. Se determinó el grosor de pliegues de la piel tras la administración diaria de acetonido de triamcinolona durante 14 días.

**Resultados** – hubo una inhibición dependiente de concentración de mapracorat en la secreción de TNFα en PBMC con valor de la mitad de la concentración máxima inhibitrice (IC50) de aproximadamente 0,2 nmol/L. La administración intradermica del compuesto 48/80 (50 μg en 50 μL de suero salino) resultó en la creación de una ampolla con líquido claro y una reacción de enrojecimiento durante los 60 minutos del periodo de observación. La aplicación tópica previa al tratamiento con mapracorat (0,1%) y acetonido de triamcinolona (0,015%) produjo una reducción significativa en las respuestas de formación de ampolla inflamatoria y enrojecimiento comparado con el vehículo (acetona) en las áreas tratadas. Sin embargo, la aplicación tópica una vez al día de acetonido de triamcinolona redujo significativamente el grosor de los pliegues de la piel del día ocho al día 14, mientras no se observó tal reducción con mapracorat.
**Zusammenfassung**

**Hintergrund** – Mapracorat ist ein nichtsteroidaler selektiver Glucocorticoid Agonist (SEGRA), von dem angenommen wird, dass er einen besseren therapeutischen Index im Vergleich zu klassischen Glucocorticoiden aufweist.

**Ziele** – Ein Vergleich der Wirksamkeit und Sicherheit von Mapracorat und klassischen Glucocorticoiden bei der Behandlung allergischer Hauterkrankungen von Hunden.


**Ergebnisse** – Mapracorat Konzentrationen verhinderten die TNFα Sekretion aus aktivierten PBMC der Hunde mit einer halben maximalen inhibitorischen Konzentration (IC50) von etwa 0,2 nmo/l. Eine intradermale Injektion von Compound 48/80 (50 µg in 50 µl Kochsalzlösung) ergab eine deutliche Urticaria Reaktion über den Verlauf der 60 minütigen Beobachtungsperioden. Eine topische Vorbehandlung mit Mapracorat (0,1%) und Triamcinolon Acetonid (0,015%) führte zu einer signifikanten Reduzierung der Urticaria-Reaktion im Vergleich zu Hautstellen, die nur mit dem Trägermolekül (Aceton) behandelt worden waren. Eine einmal tägliche topische Anwendung von Triamcinolon Acetonid reduzierte die Hautfaltendicke von Tag 8 bis 14signifikant, während keine derartige Verbesserung bei der Anwendung von Mapracorat beobachtet werden konnte.

**Schlussfolgerung** – Diese Ergebnisse zeigen, dass Mapracorat in diesen experimentellen Settings eine vergleichbare enzündungshemmende Wirksamkeit wie klassische steroidale Glucocorticoiden aufweist. Außerdem weist die Erhaltung der Hautfaltendicke im Vergleich zu Hautstellen, die nur mit dem Trägermolekül (Aceton) behandelt worden waren, die gleiche Wirksamkeit wie klassische steroidale Glucocorticoiden auf.

**Summary**

**Background** – Mapracorat is a nonsteroidal selective glucocorticoid agonist (SEGRA), which is believed to have a better therapeutic index compared to classical glucocorticoids.

**Objectives** – A comparison of the efficacy and safety of Mapracorat and classical glucocorticoids in the treatment of allergic skin diseases in dogs.

**Methods** – The effect of Mapracorat on the TNFα secretion from activated PBMC of dogs at half-maximal inhibitory concentration (IC50) of about 0.2 nmol/L. Intradermal injection of Compound 48/80 (50 µg in 50 µl saline) induced a significant Urticaria reaction for 60 minutes. Topical pretreatment with Mapracorat (0.1%) and triamcinolone acetonide (0.015%) resulted in a significant reduction in the Urticaria reaction compared to skin areas treated only with the carrier molecule (Aceton). A once-daily topical application of triamcinolone acetonide reduced the skin fold thickness from Day 8 to 14 significantly, whereas no such improvement was observed with the use of Mapracorat.

**Conclusions** – These results show that Mapracorat in these experimental settings has a comparable anti-inflammatory efficacy to classical steroidal glucocorticoids. Moreover, the maintenance of skin fold thickness compared to skin areas treated only with the carrier molecule (Aceton) showed the same efficacy as classical steroidal glucocorticoids.

**Supporting Information**

**Background** – Mapracorat is a nonsteroidal selective glucocorticoid agonist (SEGRA), which is believed to have a better therapeutic index compared to classical glucocorticoids.

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**Methods** – The effect of Mapracorat on the TNFα secretion from activated PBMC of dogs at half-maximal inhibitory concentration (IC50) of about 0.2 nmol/L. Intradermal injection of Compound 48/80 (50 µg in 50 µl saline) induced a significant Urticaria reaction for 60 minutes. Topical pretreatment with Mapracorat (0.1%) and triamcinolone acetonide (0.015%) resulted in a significant reduction in the Urticaria reaction compared to skin areas treated only with the carrier molecule (Aceton). A once-daily topical application of triamcinolone acetonide reduced the skin fold thickness from Day 8 to 14 significantly, whereas no such improvement was observed with the use of Mapracorat.

**Conclusions** – These results show that Mapracorat in these experimental settings has a comparable anti-inflammatory efficacy to classical steroidal glucocorticoids. Moreover, the maintenance of skin fold thickness compared to skin areas treated only with the carrier molecule (Aceton) showed the same efficacy as classical steroidal glucocorticoids.
结果 — Mapracorat为浓度依赖性抑制犬活化PBMC分泌TNFα，其半抑制浓度(IC50)约为0.2 nmol/L。皮内注射化合物后，48/80（50 μL 生理盐水中含有50 μg）在60分钟内诱发清晰的风团。和赋形剂(丙酮)相比，预先在治疗区域使用mapracorat (0.1%)和曲安耐德(0.015%)，风团有明显的减小。每天局部使用曲安耐德，皮褶厚度在第8-14天有明显降低，但是在使用mapracorat时，无明显变化。

总结 — 这些结果证明在相同浓度下，mapracorat与传统甾体类皮质激素相比，在以上实验条件下抗炎效果相似。皮褶厚度表明，mapracorat比曲安耐德安全性更好。以上从侧面显示出SEGRAs在管理犬炎症性和瘙痒性皮肤病方面具有良好前景。