

OBJECTIVES

Main **objectives** of this work are:

- To understand cyclosporine mechanism of action and pharmacokinetic parameters.
- To make an updated review of its use on feline dermatological conditions.
- To point out and discuss the main adverse reactions.
- To discuss new directions that research could take in the future.

MECHANISM OF ACTION

CsA + cyclophilin-1 → inhibition of calcineurin → stops the activation of NFAT

- Inhibition of IL-2, a T-cell growth promoter, is CsA's main mechanism of immunosuppression.
- In cats, CsA has been documented to suppress the transcription of IL-4, IFN-γ, TNF-α, GM-CSF and IL-10.
- CsA can also affect other cells, including B lymphocytes, antigen presenting cells, keratinocytes, basophils, mast cells, eosinophils and endothelial cells.

FELINE ATOPIC SYNDROME



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King et al. (2012): randomized, double-blinded placebo controlled study with n=100 cats. Mean TLS improved >50% in 70% of cats treated with 7.0mg/kg; compared with 47% in the 2.5mg/kg group and 23% in the placebo group.



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Roberts et al. (2016): randomized, double-blinded placebo controlled study with n=217 cats. Mean TLS reduction was 65.1% in the treated group compared with 9.2% in the placebo group. Owners considered a success in the clinical response in 78.6% cases in the CsA group vs 26.2% in the placebo group.

CHRONIC GINGIVOSTOMATITIS



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Vercelli et al. (2006): study with n=8 cats. 4 cats went into total remission, remaining cats showed an improvement of clinical signs (40-70%).

Lommer (2013): randomized, placebo-controlled, double-blinded clinical study with n=16 cats. 7 of 9 cats receiving CsA demonstrated a >40% of improvement vs 1 of 7 cats in the placebo group.

PLASMA CELL PODODERMATITIS



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CsA given at a dose of 7mg/kg/day seems a good alternative for those patients with an incorrect response to doxycycline.

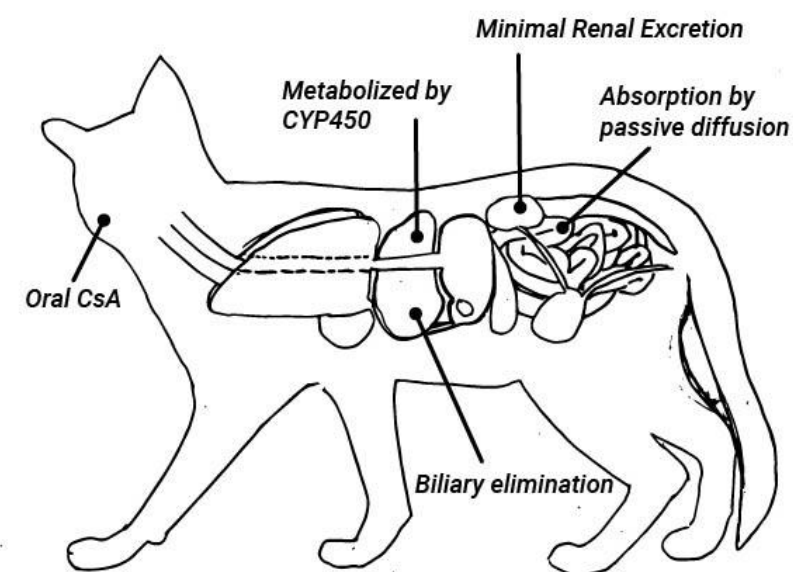
CONCLUSIONS

- CsA is a good option for the treatment of cats with Feline Atopic Syndrome.
- It seems a promising therapy for the treatment of several immune-mediated skin diseases, however, larger scale, randomized, double blinded and placebo-controlled studies are required.
- Monitoring of the patient during the treatment with CsA is highly advisable.
- Further research is also required in order to establish adverse effects associated with a long-term use of CsA.
- Development of other routes of administration could also be a good direction for future research, in order to make easier the administration to cats.

INTRODUCTION

Cyclosporine (CsA) is a lipophilic drug with powerful immunomodulatory and immunosuppressive properties that has been recently used in immune-mediated dermatological problems in cats. The licensed product (ATOPICA® for Cats), a modified version of cyclosporine, is approved for the treatment of feline allergic dermatitis as manifested by excoriations (including facial and neck), miliary dermatitis, eosinophilic plaques and self-induced alopecia. However, given its immunomodulatory activity, there has been much interest in using it in other immune-mediated and allergic dermatologic conditions in cats, although controlled clinical trials are very limited.

PHARMACOKINETICS



Absolute bioavailability: 23-29%.
Mean peak blood concentration: 1–2 h after oral administration.

Volume of distribution: 3.3 l/kg. CsA is widely distributed in the tissues due to its lipophilic character.

Blood levels of cyclosporine in field studies were highly variable, even among cats with similar clinical response.

EOSINOPHILIC GRANULOMA



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Guaguère & Prèlaud (2000): study with n=12 cats with EP, EG, IU. Complete regression was achieved in cats with EP and EG. Cats with IU only achieved partial regression.

Vercelli et al. (2004): retrospective study with n=7 cats with EP, IU and EG. After 30 days, all animals showed improvement. Complete remission was achieved after 60 days (5 cats) and after 90 days (2 cats).

PEMPHIGUS FOLIACEUS



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Irwin et al. (2012): retrospective study with n=15 cats with PF. All cats treated only with CsA were weaned off GC and scored a good response. One cat in the CsA group + one cat in the CsA+Chlorambucil group achieved remission of PF.

OTHER USES



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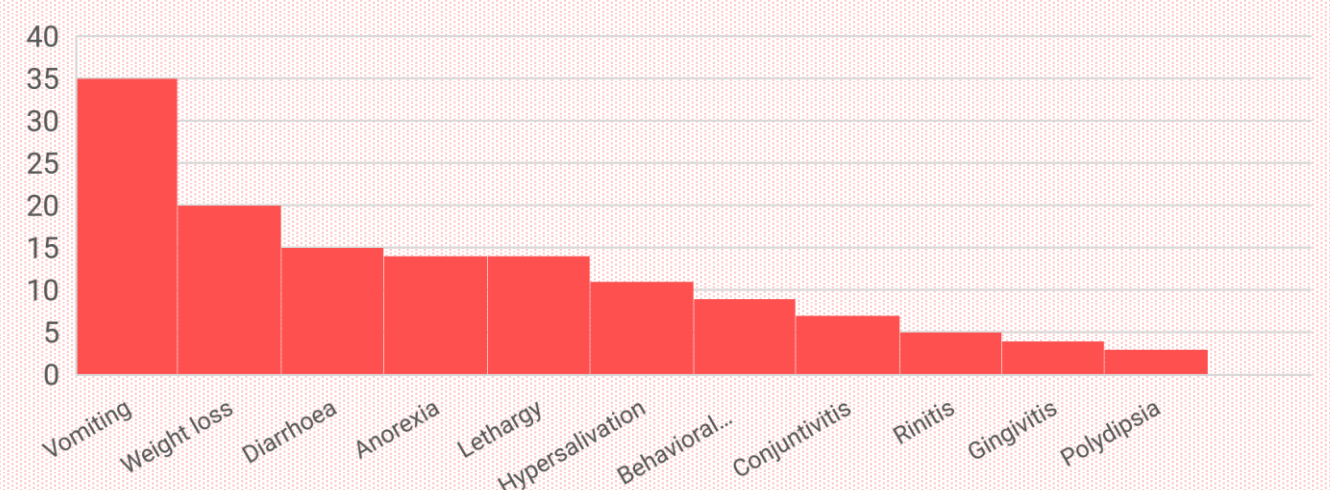
Olivry et al. (2000): report of the use of CsA to manage an immune-mediated folliculitis.

Fontaine & Heimann (2004): report of the use of CsA to manage 3 Persian cats with idiopathic facial dermatitis.

Guaguère & Fontaine (2004): report of the use of CsA to manage urticaria pigmentosa in two cats.

Noli & Toma (2006): report of the use of CsA to manage one cat with sebaceous adenitis.

SIDE EFFECTS



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