# CLINICAL EFFICACY OF L-THEANINE TABLETS TO REDUCE ANXIETY-RELATED EMOTIONAL DISORDERS IN CATS: A PILOT OPEN-LABEL CLINICAL TRIAL

**V. DRAMARD [1], L. KERN [2], J. HOFMANS [3], C. HALSBERGHE [4], C.A. RÈME [5]**

[1]Referral Behaviour Veterinary Clinic, Lyon, France; [2]Referral Behaviour Veterinary Clinic, Paris, France;
[3]Veterinary Clinic, Fléron, Belgium; [4]Veterinary Clinic, Kortrijk, Belgium; [5]Medical Department Virbac SA, Carros, France

## BACKGROUND

L-theanine ($\gamma$-ethylamino-L-glutamic acid) is a structural analogue of glutamate that is absorbed in the gut and can cross the blood-brain barrier. L-theanine binds to glutamate receptors, thereby countering the stimulatory activity of this excitatory neurotransmitter in the brain.

In humans, L-theanine promotes mental and physical relaxation, and reduces stress and anxiety without causing drowsiness. Forty minutes after the absorption of L-theanine, alpha waves (indicative of a relaxed and calm state) begin to appear on the electroencephalogram around the occipital regions. The amplitude of the alpha-waves are dose-dependent. Subjects report a relaxed feeling.

## OBJECTIVES

The present study evaluates whether a veterinary L-theanine based nutritional supplement (Anxitane® tablets, Virbac) can attenuate symptoms of anxiety in cats under field conditions.

## MATERIALS & METHODS

**Animals:**
- 33 cats, gender: 14 females / 19 males, age: 5 months to 16 years, size: 2 to 10 kg, breeds: 29 Europeans, 2 Persians, 1 Siamese, 1 Somali.
- Inclusion criteria: occurrence for at least one month of one or more of the following manifestations of anxiety: inappropriate urination / defecation, aggressiveness (from fear), hypervigilance / tenseness, inhibition, cohabitation problems, fear of humans, physical manifestations of anxiety (digestive problems, hypersalivation, body licking, bulimia).
- Exclusion criteria: life-threatening disease, use of psychotropic drugs or pheromones in the preceding week.

**Treatment:**
- Half a 50mg L-theanine tablet (**Anxitane® S**) BID for **1 month**.
- No other behaviour treatment.
- Unrestricted access to food.
- Litter changed every week.

**Concurrent medications:**
- None (32 cases).
- Fipronil spot-on, milbemycine oxyme tablet (1 case).

**Evaluation:**
- Clinical & behavioural evaluation before (D0), during (D15) and after treatment (D30).
- 20-item grid of autonomic, behavioural, emotional & physical signs of anxiety (table 2). Each symptom graded 0-3 according to intensity. All 20 scores added together to calculate **the global clinical score of anxiety**.
- Perceived improvement of dominant problem(s) as estimated subjectively by investigators (relative % severity scale: baseline being rated 100% = reference pre-treatment state).
- Owner satisfaction on treatment outcome and tablet palatability.

## RESULTS

Table 1. History of the cats in relation to anxiety at baseline (D0)

| History | Breakdown (number of cats) |
| --- | --- |
| Age at adoption | ≤ 2.5 months (17), 3-8 months (11), > 8 months (5) |
| Origin | found in street (11), relatives (11), cattery (7), other (4) |
| Dominant signs of anxiety *(several possible /cat)* | hypervigilance/tenseness/fears (26), inappropriate urination/defecation (15), aggressiveness (8), organic manifestations (7) |
| Age at onset of signs | < 8 months (13), 8 months-3 years (13), > 3 years (7) |
| Evolution of signs | improving slowly (1), steady (15), aggravating (14) |
| Associated signs | hyperactivity (4), recurrent cystitis (2), panic reactions (1), sleep disturbance (1), rolling skin syndrome (1), clothe sucking (2), obesity (5), constipation (1), gingivitis (1) |

Table 2. Items used for scoring manifestations of anxiety in cats

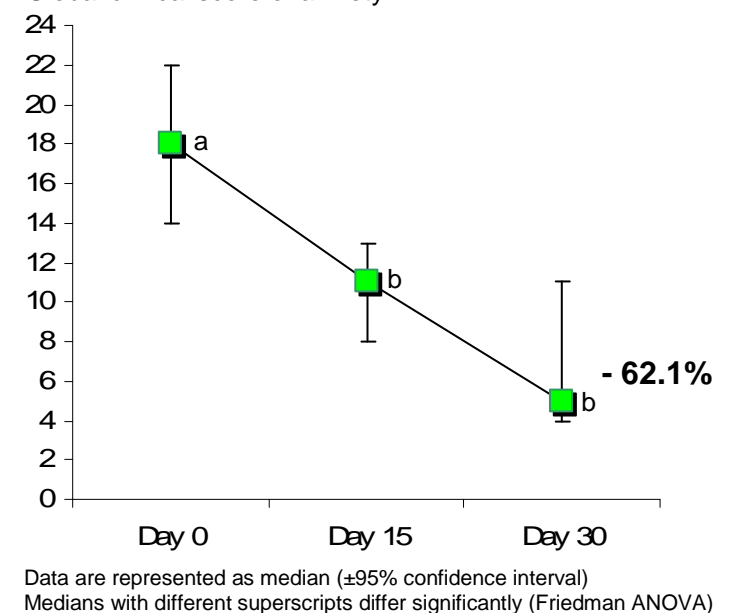| Category | Items scored according to severity |
| --- | --- |
| Neurovegetative signs | polypnea, shivering, mydriasis, piloerection, rolling skin, vomiting, diarrhea, hypersalivation, fear-induced urination or defecation |
| Behavioural signs | meowing, excessive demands for attention, threats (hiss) or even bites because of irritation (when patted or while playing with the owner), threats (hiss) or even attacks when surprised or because of fear, aggression redirected against people / objects / furniture / tail, avoidance behaviour |
| Emotional state and associated postures | inhibition with flattened ears / tendency to crouch, agitation, hypervigilance and hyperaesthesia, tendency to panic / run away or hide, inhibition with licking / stereotypical behaviour |



Global clinical score of anxiety

- 62.1%

Data are represented as median (±95% confidence interval)
Medians with different superscripts differ significantly (Friedman ANOVA)

Figure 1. Global clinical score of anxiety during treatment



Number of cats

% reduction of the global clinical score of anxiety on D30
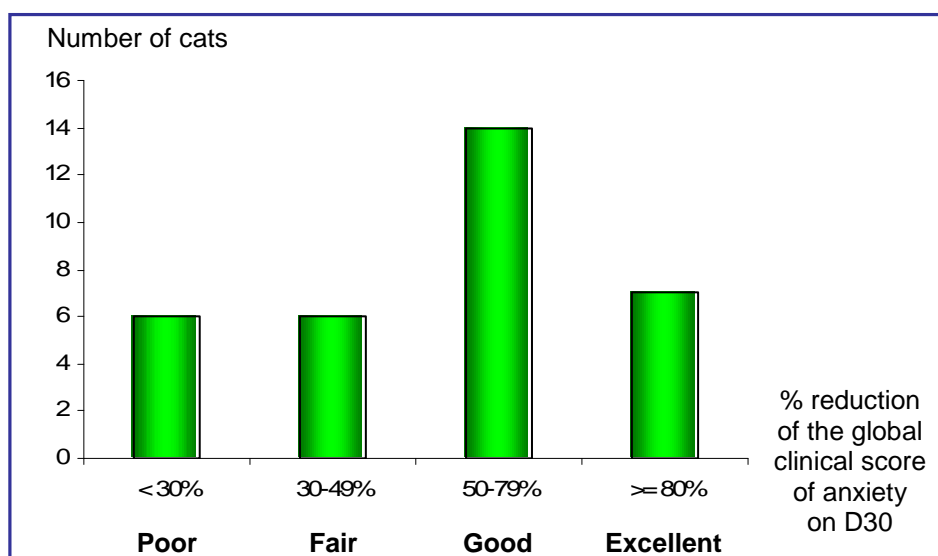
Figure 2. Breakdown of the response to treatment after 1 month



Relative severity

Baseline reference level (D0)

- Inappropriate urination/defecation
- Aggressiveness
- Hypervigilance/tenseness
- Physical manifestations

Data are represented as mean
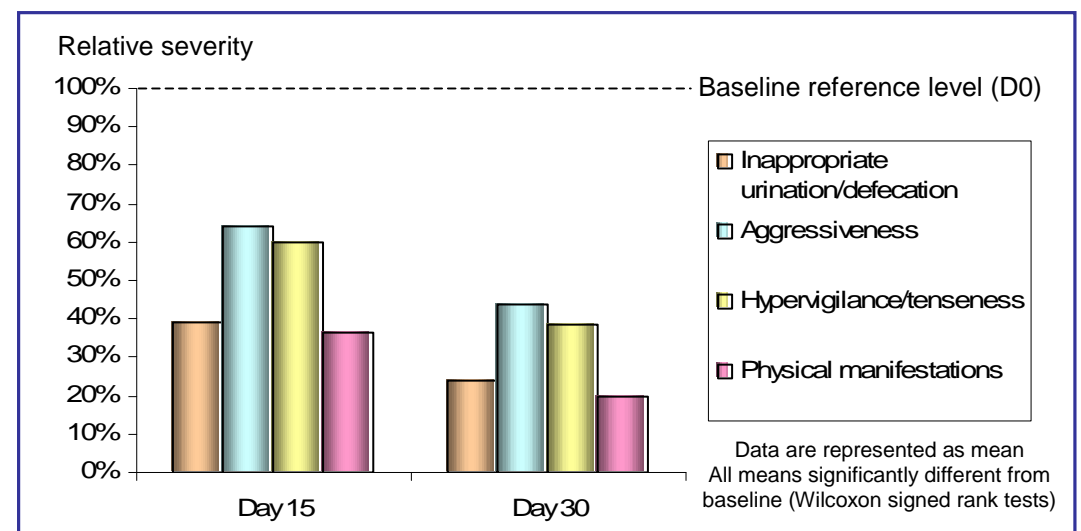All means significantly different from baseline (Wilcoxon signed rank tests)

Figure 3. Relative rating by investigators of the severity of the major manifestations of anxiety as compared to pre-treatment condition

- Most owners (27/33) were satisfied with treatment efficacy.
- Tablet palatability was judged good in 93.9% of cases with spontaneous intake by cats from hand or on food.
- No side effects were reported.

## CONCLUSIONS

This clinical trial points up **the value of L-theanine supplementation to mitigate symptoms of anxiety in cats**.
The magnitude of effects as measured by scores place the efficacy of the supplement beyond the typical response seen with placebo.
L-theanine seemed particularly effective on organic manifestations of anxiety and cohabitation problems in cats.