NACOTIL®

DERMATOLOGICAL **USABILITY STUDY** OF THE EAR CLEANER **NACOTIL®** IN VETERINARY MEDICINE

pharmadiet VETERINARIA
OPKO Health Europe

INTRODUCTION

Otitis is a common disease in canine veterinary medicine, and is characterized by inflammation of the epithelium of the external ear canal and of the pinna. **It is one of the most common diseases in veterinary clinics, and can affect up to 20% of the canine population and 6% of the feline population.** In the pathogenesis of otitis externa, a distinction is made between primary causative factors, predisposing factors, and factors that make it recurrent. The confluence of some of these factors is what determines how the clinical signs manifest.

In general, **the treatment should eliminate the primary cause, control opportunistic bacterial and fungal infections, and keep the ear canal clean and dry** with various treatment modalities depending on the severity of the condition.

Ceruminolytic cleaners and topical corticosteroids are used, and in severe cases it is necessary to clean the ear canal under general anesthesia. After cleaning, the ear should be treated according to which agent is acting: acaricides, antifungals or antibiotics.

In this study, we are not looking at the treatment of the cause, for which there are already several clinical efficacy and safety studies, **but at the cleaning pre-treatment that promotes the action of the active substances by acting as a cleaner, anti-septic and ceruminolytic and preventing the formation of adhesions and mucus.**

AIM

To determine the **level of veterinarian satisfaction with the Nacotil® coadjuvant treatment** as an ear cleaner in acute and chronic canine otitis.

MATERIAL AND METHODS

· **40 dogs** of different breeds aged 1–8 years.
· **18 participating veterinary centers** throughout Spain.

Groups:

Group A: 23 dogs with acute otitis with (bacterial or fungal) overgrowth.
Group B: 17 dogs with chronic or recurrent bacterial otitis.

Treatment:

Group A: 2-5 cc Nacotil® was administered, depending on the size of the animal, every 48 h for 21 days.
Group B: 2-5 cc Nacotil® was administered, depending on the size of the animal, every 24 h, 30 min before the use of concomitant treatment, for 21 days.

· **4 follow-up visits on days 0, 7, 14 and 21.**
· **1 additional visit after 30 days** to evaluate the residual effect of the treatment.

Evaluations:

· **Clinical** (presence of erythema, amount of cerumen/secretion, presence of ulcers, glandular hyperplasia) **and cytological evaluation** on days 0, 7, 14, 21 and 30.
· **Evaluations during the visit on day 30** (using the Likert scale): The animal's tolerance to the cleaning treatment, ease of use, product dosage, organoleptic characteristics of the product (smell, texture, color), satisfaction of the veterinarian and owner, owner's compliance with the treatment, and advantages of the product compared to other previously used cleaners.

Inclusion criteria:

· Species: canine, any breed.

· Age: 1–8 years.

· Two scenarios:
- Group A: acute otitis with (bacterial or fungal) overgrowth without severe pain preventing the correct application of the product.
- Group B: chronic or recurrent bacterial otitis, caused by Pseudomona spp as the main infectious agent (growth culture) or other bacteria that have not responded to the established treatment (based on the antibiogram).

· The culture must be recent, a maximum of 30 days before the start of the trial.

· There must be no signs of severe hyperplasia or stenosis of the ear canal that would prevent the evaluation of the ear canal and the collection of samples for cytology and/or culture, and there must be no pain that would impede the correct application of the product.

Exclusion criteria:

· Hyperplasia and/or stenosis of the ear canal that makes it difficult to evaluate the canal and collect the sample.

· Moderate or severe pain that impedes application of the product.

- In group A: no overgrowth.
- In group B: negative culture, or culture positive for other bacteria considered to be unusual ear pathogens.

· The application of new concomitant treatments that may interfere with the evaluation of the study product will not be accepted. Antibiotic, corticosteroid, or antifungal treatments will be accepted in chronic cases in which they were already being applied but without response. In the case of antibiotics and antifungals, these treatments should be based on the latest antibiogram (valid for one month as mentioned above).

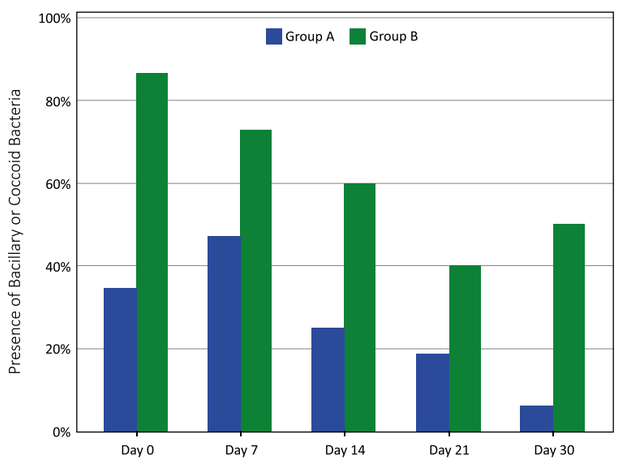
RESULTS

Demographic data

Characteristics of group A		Characteristics of group B	
Diagnosis of primary cause:	**Grupo A**	**Chronic process**	**Grupo B**
N	23	N	15
Allergy	2 (8,7%)	Chronic process (unresolved)	8 (53,3%)
Atopy	3 (13,0%)	Recurrent process	7 (46,7%)
Atopic dermatitis	7 (30,4%)		
Seborrheic dermatitis	1 (4,3%)	**Diagnosis of primary cause (if known):**	
Allergic otitis	1 (4,3%)	N	17
Atopic otitis	2 (8,7%)	Atopic	2 (11,8%)
Malassezia otitis	2 (8,7%)	Atopic dermatitis	8 (47,8%)
Otodectes	1 (4,3%)	Seborrheic dermatitis	1 (5,9%)
Not Know	3 (13,0%)	Otitis	3 (17,6%)
		Not Know	3 (17,6%)
Extension of the otitis:			
N	23	**Extension of the otitis:**	
External	21 (91,3%)	N	15
Middle ear	2 (8,7%)	External	9 (60,0%)
		Middle ear	4 (26,7%)
		Not Know	2 (13,3%)

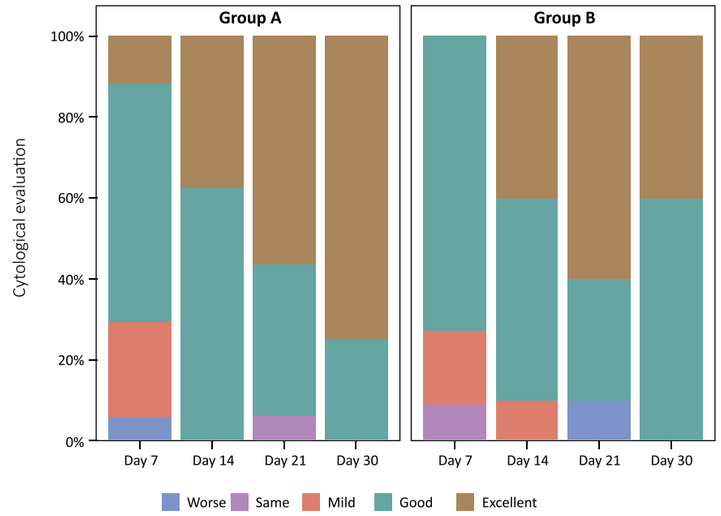
Presence of bacilli or cocci bacteria

On day 30 of follow-up, there is a decrease in the presence of bacilli and cocci bacteria, and this decrease is statistically significant **(p<0.005)** in all the cases studied, and more significant in the acute otitis group than in the chronic otitis group.



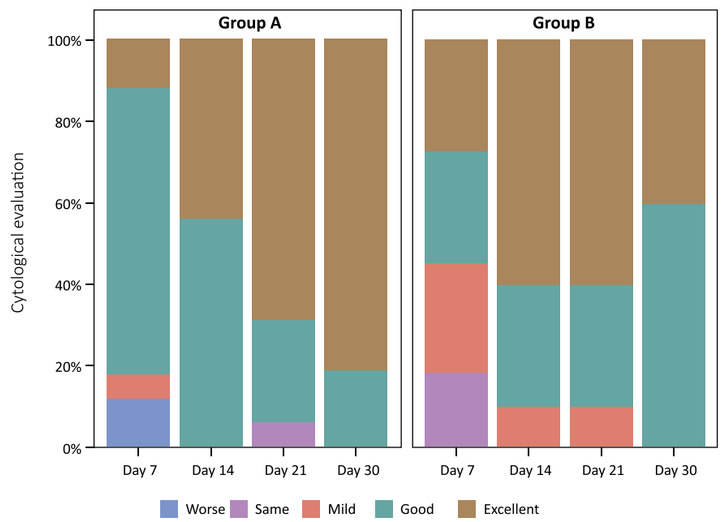
Clinical evaluation

The overall clinical evaluation, 30 days after the start of treatment, was good or excellent in all cases of both acute and chronic otitis, with it being considered excellent in 75% of acute cases compared to 40% of chronic cases ($p<0.05$).



Cytological evaluation

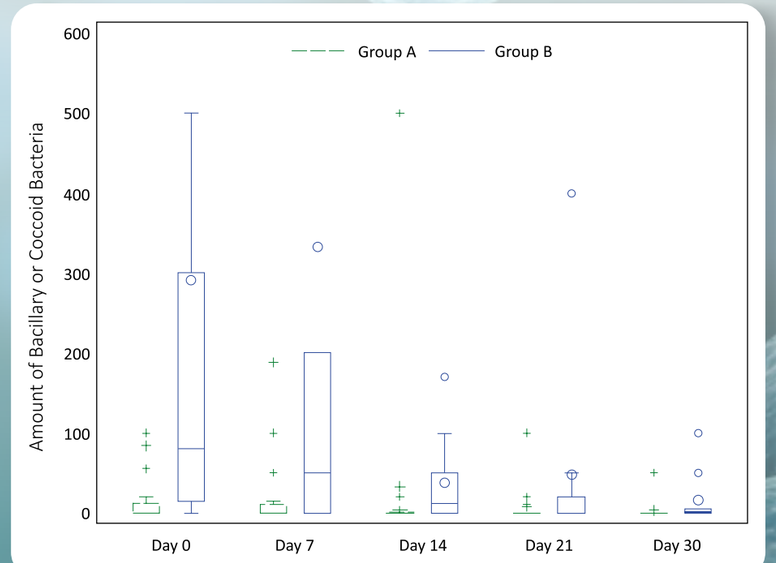
The cytological evaluation, 30 days after the start of treatment, was good or excellent in 100% of the cases of both acute and chronic otitis, with it being considered excellent in 81.3% of acute cases compared to 40% of chronic cases.



Quantity of bacilli or cocci bacteria (box plot)

When the **quantity of bacilli and cocci bacteria was quantified, a statistically significant decrease (p<0,0001) was observed** in all cases treated with Nacotil®, with the reduction being much **more pronounced in cases of chronic otitis** (in which both the presence and quantity of bacteria were much greater at the start of the treatment).

Taking into account that the patients had been treated for 21 days, we can observe how the **residual effect of the Nacotil®** treatment was maintained at the **additional visit on day 30.**



Quantity of bacilli or cocci bacteria (box plot)

	Group A	Group B	Total	P-Value
Baseline (Day 0)				
N	23	15	38	
Mean (SD)	83,8 (353,1)	291,1 (628,3)	165,2 (483,8)	
Median (Min/Max)	0,0 (0,0 ; 1.700,0)	80,0 (0,0 ; 2.500,0)	10,0 (0,0 ; 2.500,0)	0,0005 (a)
P25 ; P75	(0,0 ; 12,0)	15,0 ; 300,0)	(0,0 ; 80,0)	
Day 7				
N	17	11	28	
Mean (SD)	188,2 (725,0)	332,7 (887,6)	245,0 (780,1)	
Median (Min/Max)	0,0 (0,0 ; 3.000,0)	50,0 (0,0 ; 3.000,0)	10,0 (0,0 ; 3.000,0)	0,0469 (a)
P25 ; P75	(0,0 ; 10,0)	(0,0 ; 200,0)	(0,0 ; 50,0)	
P-value vs baseline (b)	0,8496	0,1875	0,2070	
Day 14				
N	16	10	26	
Mean (SD)	32,9 (124,7)	37,5 (56,4)	34,7 (102,3)	
Median (Min/Max)	0,0 (0,0 ; 500,0)	12,5 (0,0 ; 170,0)	0,0 (0,0 ; 500,0)	0,0542 (a)
P25 ; P75	(0,0 ; 1,5)	(0,0 ; 50,0)	(0,0 ; 20,0)	
P-value vs baseline (b)	0,0156	0,0078	<0,0001	
Day 21				
N	16	10	26	
Mean (SD)	8,1 (25,1)	48,0 (124,7)	23,5 (79,8)	
Median (Min/Max)	0,0 (0,0 ; 100,0)	0,0 (0,0 ; 400,0)	0,0 (0,0 ; 400,0)	0,2375 (a)
P25 ; P75	(0,0 , 0,0)	(0,0 ; 20,0)	(0,0 , 10,0)	
P-value vs baseline (b)	0,0313	0,0078	0,0002	
Day 30				
N	16	10	26	
Mean (SD)	3,1 (12,5)	16,3 (33,2)	8,2 (23,1)	
Median (Min/Max)	0,0 (0,0 ; 50,0)	1,5 (0,0 ; 100,0)	0,0 (0,0 ; 100,0)	0,0167 (a)
P25 ; P75	(0,0 ; 0,0)	(0,0 ; 5,0)	(0,0 ; 0,0)	
P-value vs baseline (b)	0,0156	0,0078	<0,0001	

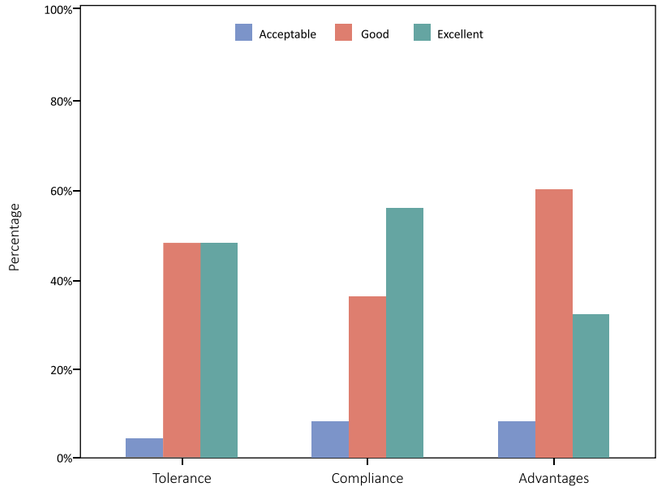
(a) Mann-Whitney U;
(b) Wilcoxon signed-rank test

Evaluation during the visit on day 30 (using the Likert scale)

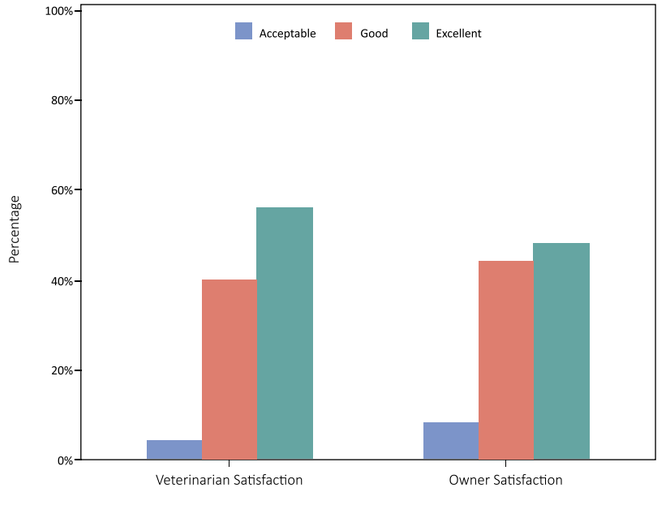
At the end of the follow-up, **treatment tolerability and compliance were good or excellent in 96.7% and 91.7% of cases, respectively.**

Veterinarian satisfaction at the end of treatment was evaluated as **good or excellent in 90% of cases and owner satisfaction was evaluated as good or excellent in 85%** of cases.

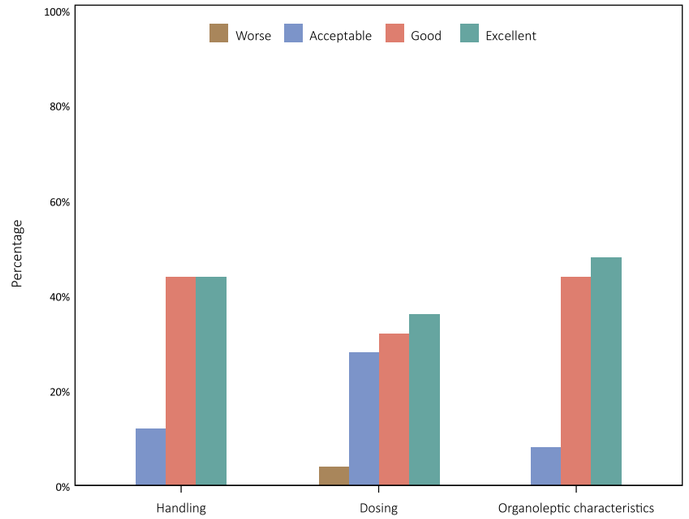
1. Animal's tolerance to the cleaning treatment, treatment compliance, advantages of the product compared to other previously used cleaners.



2. Veterinarian and owner satisfaction.



3. Ease of use of the product, dosage, organoleptic characteristics (smell, texture, color).



CONCLUSIONS

· **Nacotil®** has demonstrated that **it can help eliminate pathogens by acting as a cleaning agent, antioxidant and bacterial biofilm disruptor in canine otitis.**

· **Nacotil®** can be used as a **new coadjuvant cleaning treatment in both acute and chronic canine otitis externa,** particularly in cases diagnosed with presence of biofilms, with significant clinical benefits and clear owner and veterinarian satisfaction.

· **The use of Nacotil® daily for a minimum of 3 weeks is recommended.** In recurrent cases, consult your veterinarian about the maintenance regimen to be followed after that period.

· **No adverse effects have been reported.**

Ear cleaning solution for external use that helps with the antibacterial and antifungal treatment of chronic, acute, or recurrent otitis.

CONTAINS	*per 100 ml*
N-ACETYLCYSTEINE (NAC)	1.0 g
BORIC ACID	1.4 g
HYALURONIC ACID	200 mg
ZINC GLUCONATE	2,0 g
CITRUS LEMON (L.) ESSENTIAL OIL	100 mg

* Non-ototoxic

INSTRUCTIONS FOR USE

Position the ear canal as vertically as possible. Press the container to apply the quantity of NACOTIL® required to fill the canal according to its capacity. Lightly massage the base of the ear to allow the correct distribution of the product. If necessary, clean the inside of the auricle with sterile cotton wool or gauze.
After the procedure, allow 2-3 drops of the product to drip and clean the cannula externally with a clean gauze.
Container for individual use.

ADMINISTRATION REGIMEN

Use NACOTIL® for a minimum of 3 weeks. Use can be extended in line with instructions provided by the veterinarian.
When it is used for cleaning before the application of treatment in case of otitis externa, apply the cleaner first, 30 minutes in advance.

PACKAGING

Box containing a 125-mL bottle with silicone cannula cap and package leaflet.

SOLUTION STABLE AT ROOM TEMPERATURE ONCE OPENED (< 30°C)

RECONSTRUCTED FORMULA WITH SILICONE CANNULA

Dermatological Usability Study*

Ready-to-use Solution With Silicon Top

REFERENCES

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4. May ER, Conklin KA, Bemis DA. Antibacterial effect of N-acetylcysteine on common canine otitis externa isolates. Vet Dermatol 2016; 27: 188-e47.
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