



NEW

Candioli Innovation



with



Exclusive formula
patent

Natural patented formula

LACTOFERRICIN B



GPI Glycerophosphatidyl inositol lysine



Verbascoside

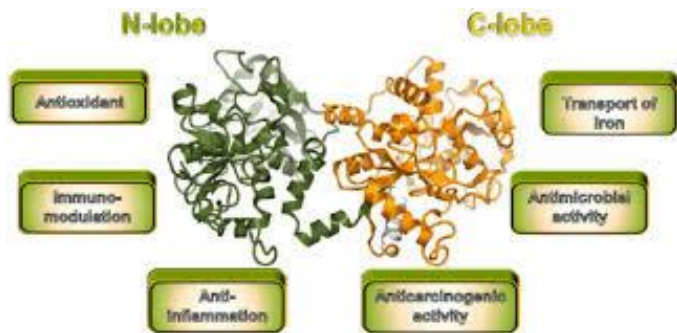


LACTOFERRICIN B

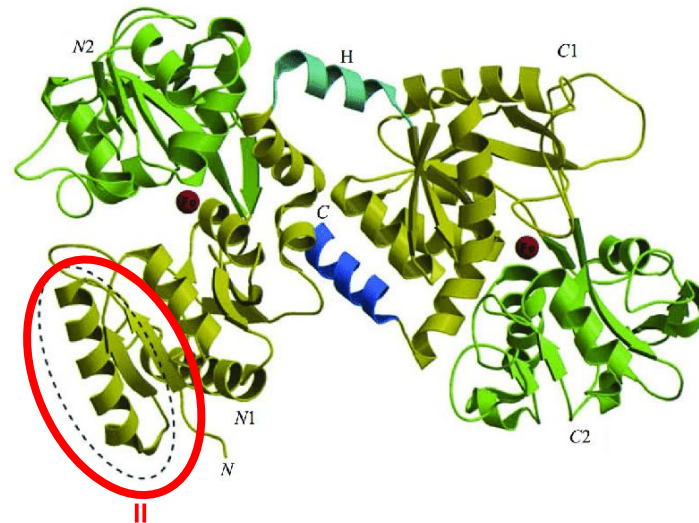


Lactoferricin B is a peptide fraction, derived from bovine lactoferrin, by acid hydrolysis thanks to pepsin activity. This peptide exerts a powerful bactericidal activity against gram + and gram – bacteria.

Lactoferricin B exerts also antifungal and antiviral activity.



Bovine Lactoferrin



Lactoferricin B

LACTOFERRICIN B



Lactoferricin B is more active than lactoferrin.

It has a double mechanism of action:

- antibacterial, antifungal and antiviral activity
- Immunomodulatory and anti-inflammatory activity

LACTOFERRICIN B



ANTIMICROBIAL ACTIVITIES

IMMUNOLOGICAL ACTIVITIES

bactericidal effect

Inhibits the virus
binding to target
cells

Modulates immune
system

Antigen-presenting
cells function

LACTOFERRICIN B

ANTIBACTERIAL ACTIVITY



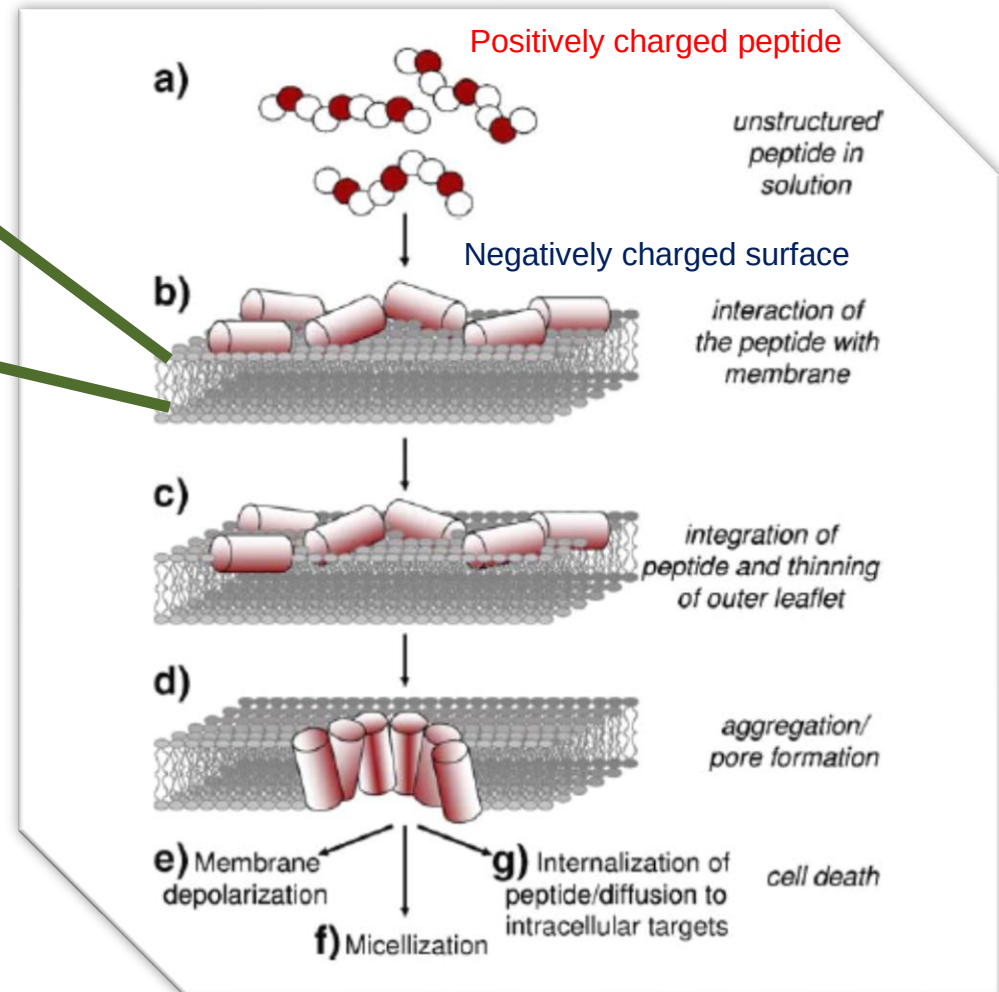
Teichoic acid layer surrounds cytoplasmic membrane

GRAM +

Lipopolysaccharide (LPS)-containing outer membrane

GRAM -

LACTOFERRICIN B



Lactoferricin B is a **cationic peptide** that first binds the outside of bacterial cell membrane thanks to **electrostatic attraction**

LACTOFERRICIN B

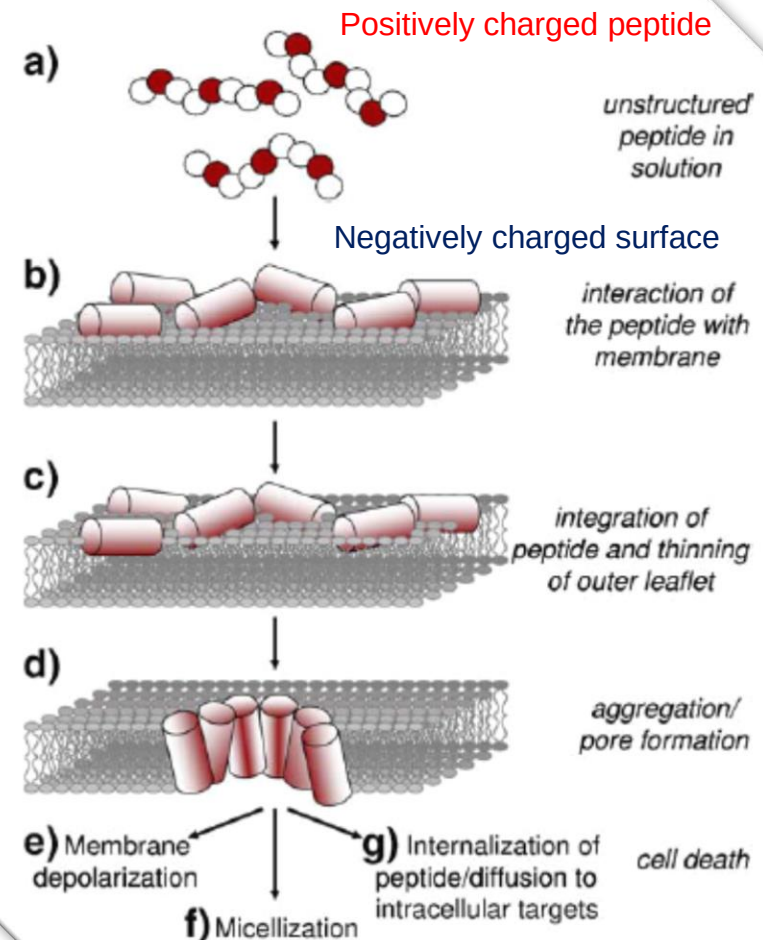
ANTIBACTERIAL ACTIVITY



After the **electrostatic attraction**, **Lactoferricin B** is able to become an amphiphile array, self-associating with LPS in an ordered manner.

When the polycationic surface of this array interacts with the polyanionic surface of the bacterial outer membrane, the fluidity of the membrane is disrupted, allowing the peptides to translocate across the cytoplasmic membrane

LACTOFERRINCIN B



LACTOFERRICIN B

ANTIBACTERIAL ACTIVITY

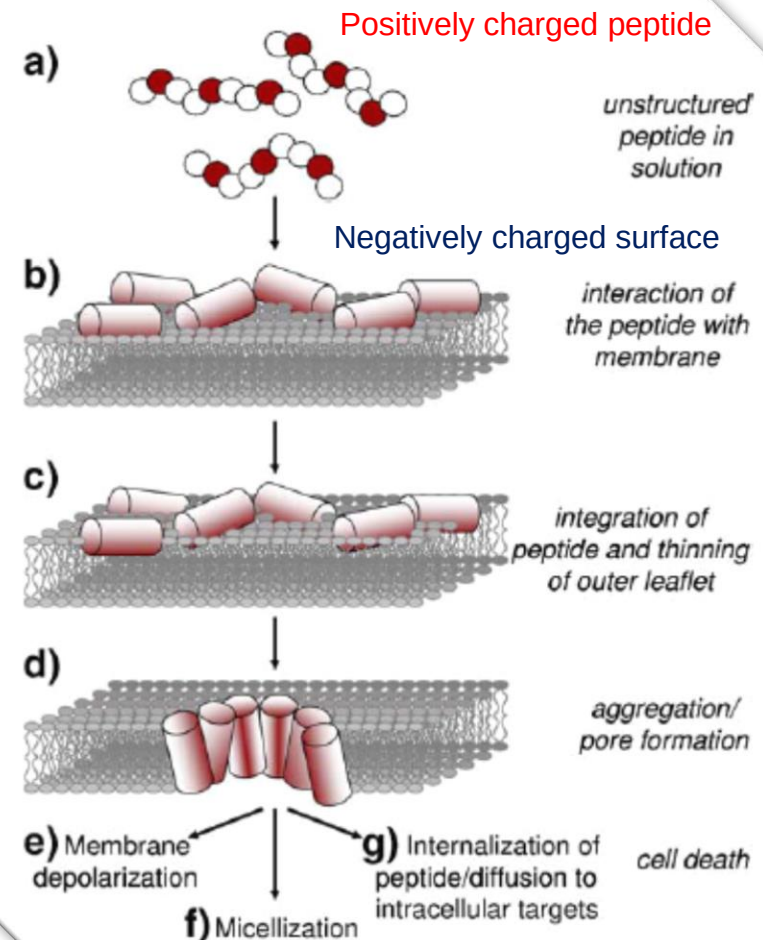


Lactoferricin B can enter the bacterial cell and act on intracellular target (DNA, RNA,...).

Lactoferricin B induces a compromise in membrane permeability, allowing the passage of small ions, and resulting in the loss of both the transmembrane electrochemical and pH gradients.

Lactoferricin B leads to a cell death due to membrane alterations and inhibition of protein synthesis.

LACTOFERRINCIN B



LACTOFERRICIN B

ANTIFUNGAL ACTIVITY

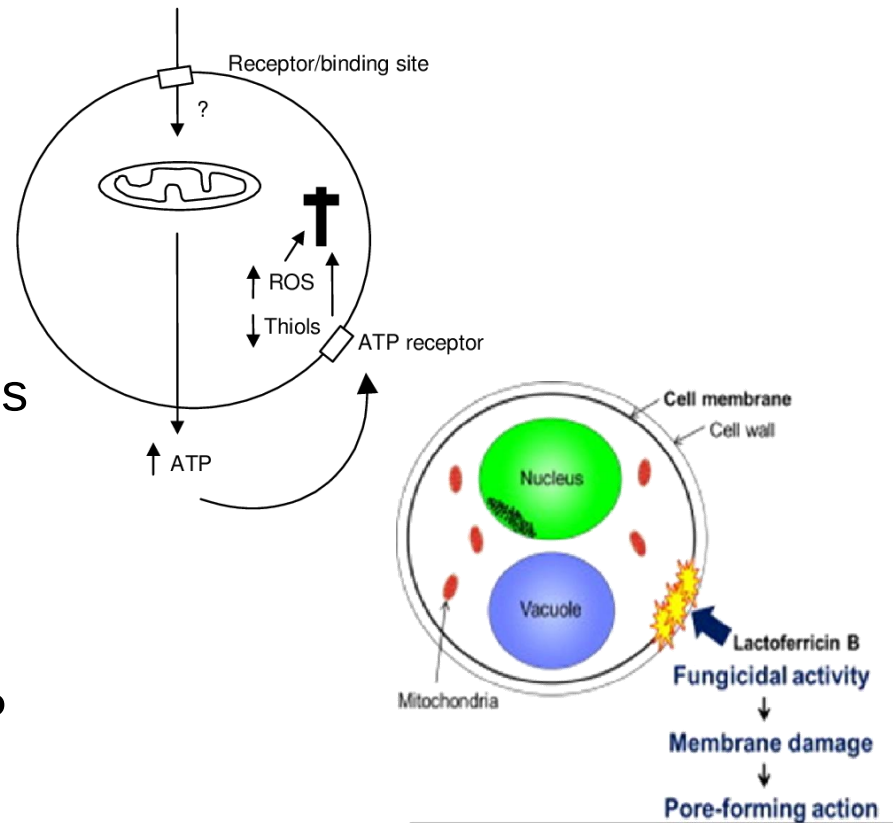
Direct fungicidal activity

Indirect fungicidal activity

Lactoferricin B interacts with fungal plasma membrane resulting in the dissipation of the proton gradient across the cell membrane. Lfcin B affects then the cytoplasm of fungal cell resulting in synthesis and secretion of ATP from mitochondria. This ATP is released extracellularly where interacts with ATP binding sites on plasma membrane giving rise to pore formation and cell death.



LACTOFERRINCIN B



Yeast, mold and filamentous fungi

LACTOFERRICIN B

ANTIFUNGAL EFFECT

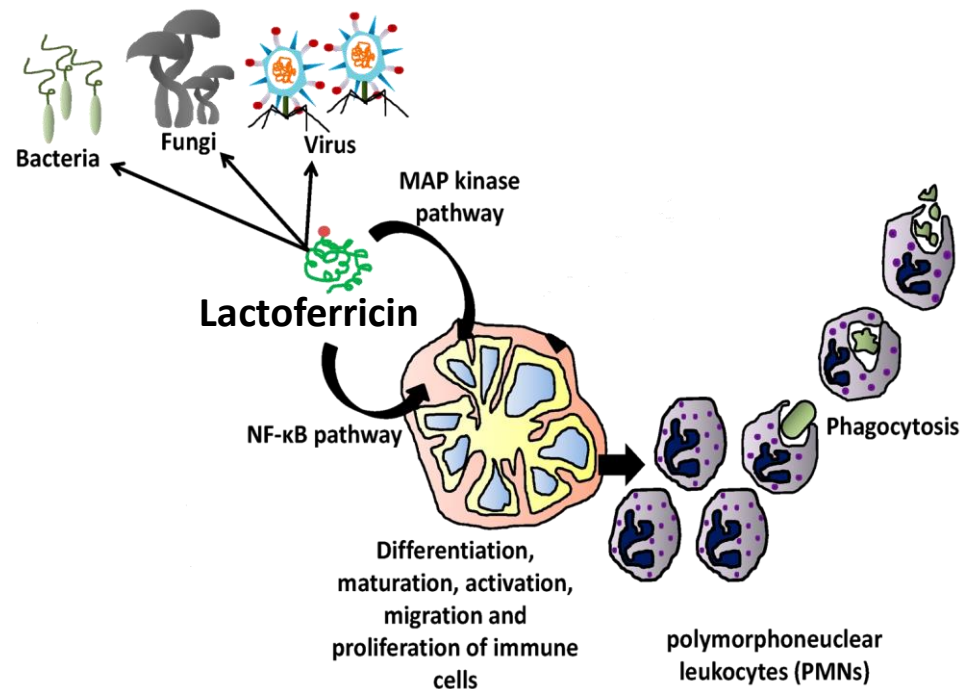
Direct fungicidal activity

Indirect fungicidal activity

Lactoferricin B upregulates fungal cell-killing activity of PMN leukocytes. These immune cells plays an important role in the inhibition of yeast (e.g. *Candida* and *Malassezia* spp.) growth and invasion



LACTOFERRINCIN B



Yeast, mould and filamentous fungi

LACTOFERRICIN B



ANTIVIRAL ACTIVITY

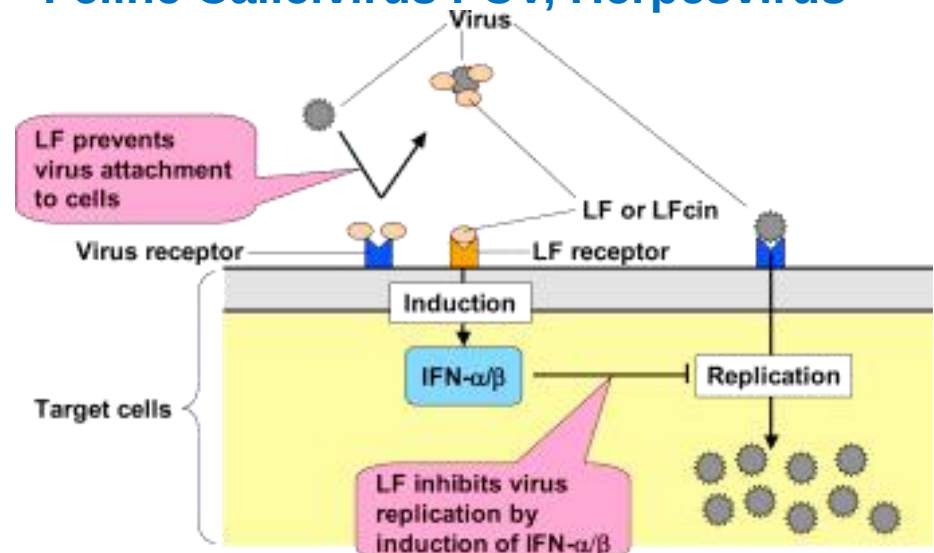
Binding site used by virus to enter into host cells as Heparin sulfate and GAGs

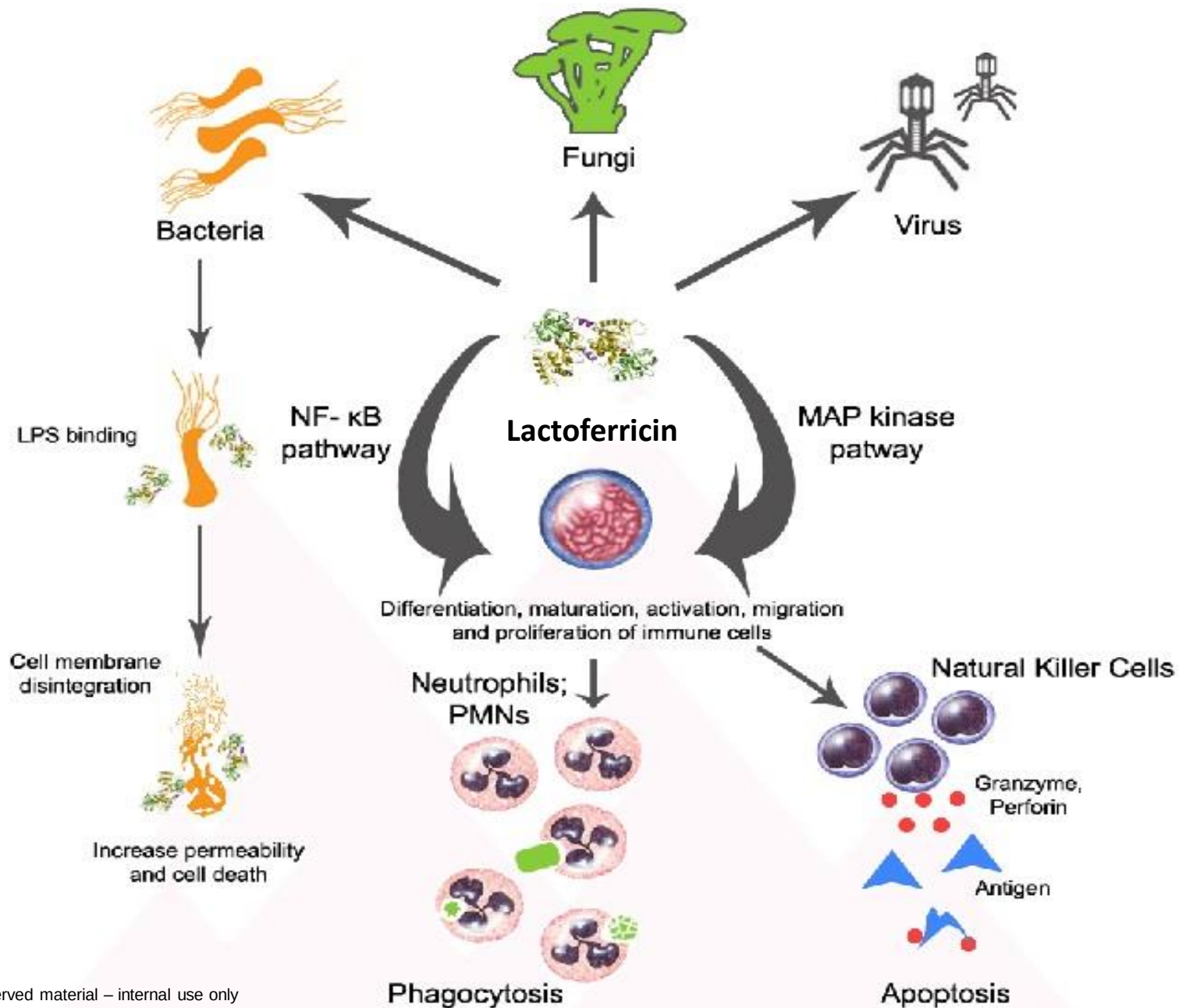
Directly inactivating virus particles. Lfcin B binds nuclear DNA and acts as transcription factor

Electrostatic attraction as for antibacterial activity

Upregulating host cell defense in response to viral attack

Feline Calicivirus FCV, Herpesvirus





LACTOFERRICIN B

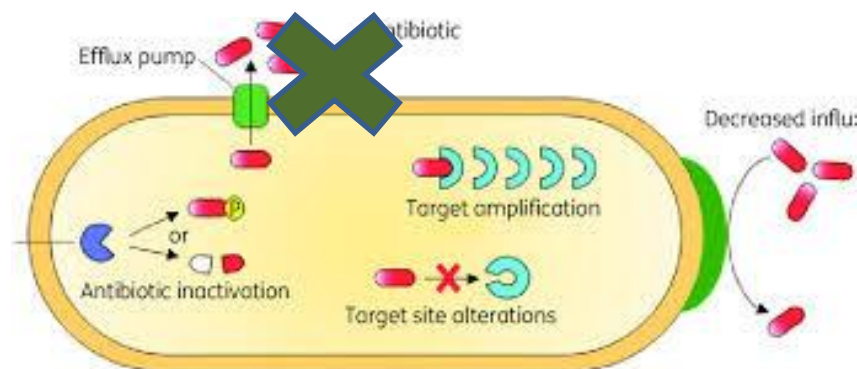
SYNERGISTIC ACTIVITY WITH ANTIBIOTICS AND ANTIFUNGAL AGENTS



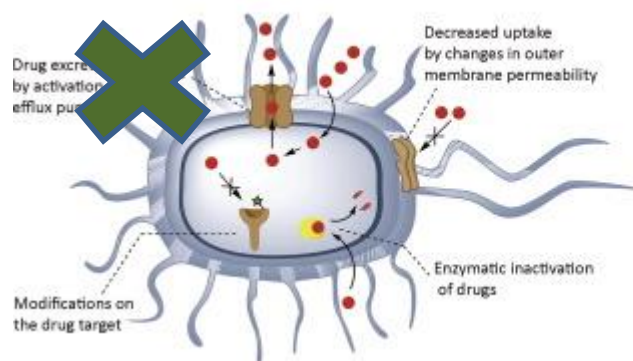
Lactoferricin B has been shown to be an effective synergistic agent when used in combination with antibiotics and antifungal agents.

This synergism is due to membrane-disorganizing nature of this peptide, which leads to increased permeability and to dissipation of the proton-motive force, resulting in decreased activity of ATP-dependent multi-drug efflux pump

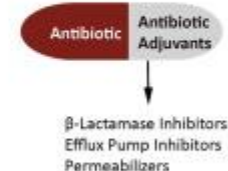
LACTOFERRICIN B



MECHANISMS OF BACTERIAL RESISTANCE TO ANTIBIOTICS



COMBINATION THERAPY STRATEGY TO UNLOCK INCREASING RESISTANCE



GPI Glycerophosphatidylcholine



What is it?

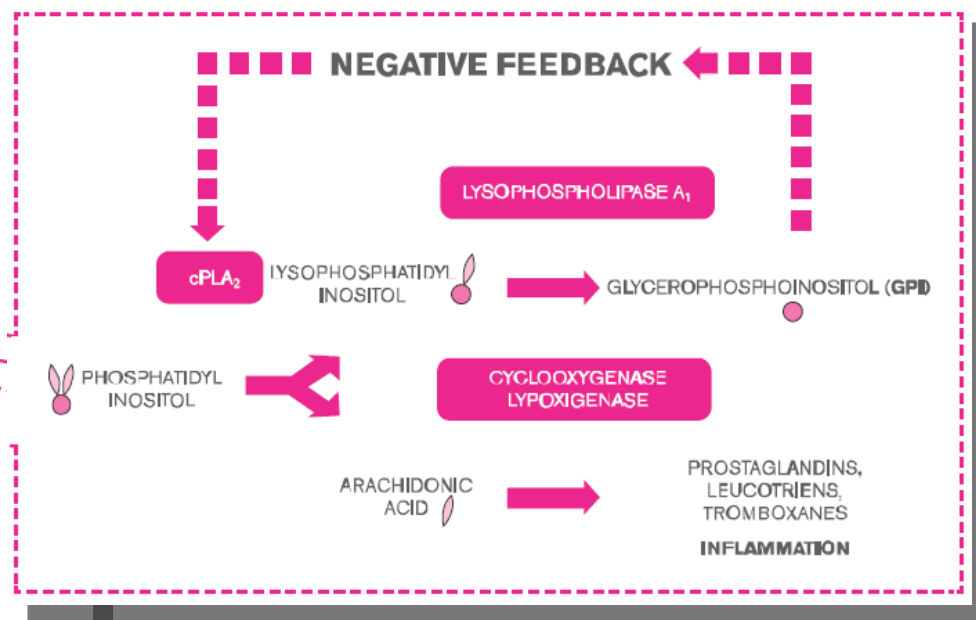
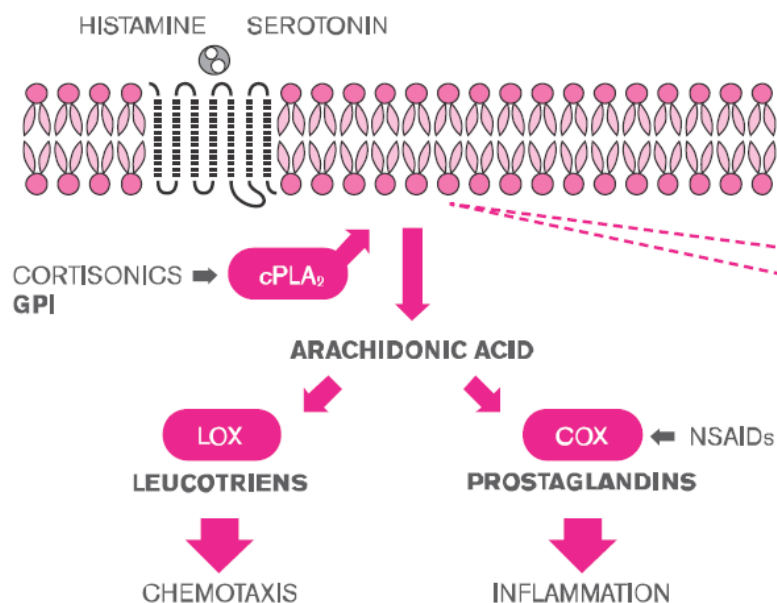
It is an **innovative** sunflower lecithin-derived **active ingredient** that acts upstream in the inflammatory cascade pathway. Its mechanism of action fits into an entirely physiological autoregulating system resulting very effective without side effects





How does it work?

GPI is able to **inhibit**, through negative feedback, the **cPAL2** (cytosolic phospholipase A2) **activity**. This enzyme is deeply involved in the inflammatory cascade as the main causal agent of arachidonic acid release





Safety and effectiveness

This natural mechanism of inflammation control is similar to that of corticosteroids, without any side or systemic secondary effects, because it selectively acts on the cPLA2 activity, with **no interaction on the hormonal balance**.

- No cyto-toxicity and sensitization in vitro and in vivo
- Optimal dermal compatibility, thus to be classified as not irritant
- Not mutagenic
- No oral acute toxicity
- LD50 for intravenous administration > 350 mg/kg

Verbascoside



What it is

Verbascoside (Dermasyr TM) is obtained through a patented industrial HTN TM technology from stem cells of some plants, (particularly *Syringa vulgaris*), with **anti-inflammatory, antioxidant, antibacterial and sebo-regulating properties**

Verbascoside exerts its **anti-inflammatory** effect reducing **TNF- α** and **IL-1 β** synthesis. In addition, it has antioxidant activity, decreases iNOS (inducible Nitric oxide synthases) activities and reduces NF-k β activation and nuclear traslocation, modulating inflammatory reactions.

Verbascoside promotes skin repair and ameliorate skin inflammation due to its **ROS scavenging**, antioxidant, iron chelating and GST-inducing (glutathione transferase) properties.

Verbascoside

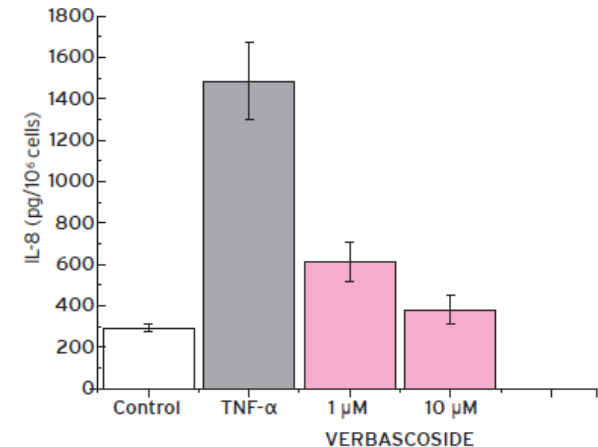


How does it work?

ANTI-INFLAMMATORY ACTIVITY

Verbascoside shows a strong anti-inflammatory activity since it induces a dose-dependent decrease of the expression of the pro-inflammatory chemokine IL-8 on primary cultures of human keratinocytes stimulated by TNF- α .

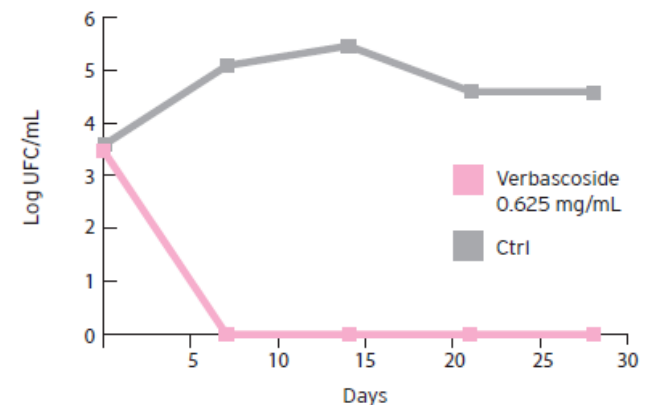
In a similar model using human keratinocytes (HaCaT) this significant anti-inflammatory activity is confirmed and verbascoside results to be superior to quercitin and rutin (Pastore et al. , 2009).



ANTI-MALASSEZIA FURFUR GROWTH

Malassezia furfur, also known as *Pityrosporum ovale*, is a yeast belonging to the resident skin flora which is associated with numerous skin infections, including pityriasis versicolor, seborrheic and atopic dermatitis, dandruff and folliculitis.

Verbascoside is a strong inhibitor of *Malassezia furfur* growth with a MIC of 0.625 mg/mL.



Verbascoside



Safety

- ✓ High dermatologic tolerability
- ✓ Not irritating on human epithelial cells
- ✓ Not mutagenic





Summary of effects



LACTOFERRICIN B

Antibacterial, antiviral,
antifungal activity

Immunomodulation



GPI (glycero-phospho-
inositol lysine)

Anti-inflammatory activity



VERBASCOSIDE

Anti-inflammatory activity

Seboregulatory activity

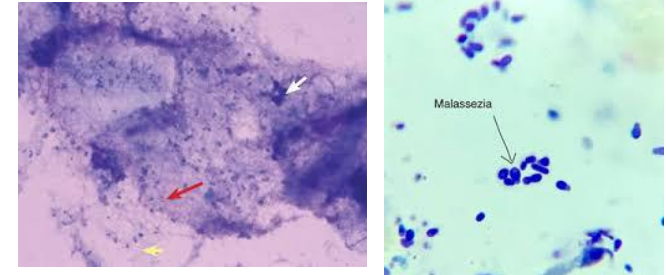
Control of:

Pain
Bacteria
Malassezia
Herpes and Calici virus
Sebo
Inflammation



Indication of use

- adjuvant in treatments of outer ear conditions characterized by itching, redness, bacteria and Malassezia overgrowth
- prevention of otitis of different origins in susceptible subjects
- all situations you need to restore the physiological status of the ear canal





Instructions for use:

Apply 4-8 drops, depending on pet size, into the ear canal **twice** a day for a minimum period of 15 days



NO CHLOREXIDINE IN ACTEA OTO

Apply 4-8 drops, depending on pet size, **once** a day to maintain physiological conditions in the ear canal





PROVED EFFECTIVENESS

Pilot study in 10 dogs as an adjuvant in the treatment of canine external otitis



Objective of the study were:

- ❖ Evaluating if during the use of product ACTEA™ OTO some changes in the ear bacterial and yeast colonization occur.
- ❖ Verifying, through owner's visual analogic scale, if there is reduction of auricular itching.
- ❖ Verifying, through clinical score, any objective modifications in erythema and lichenification of ear canal and pinna in dogs treated with ACTEA™ OTO



Materials and methods

The study was performed following the «good clinical practice», with owner's agreement

Inclusion criteria

- ❖ 10 dogs affected by erythematous and ceruminous otitis externa
- ❖ More than three otitis events in the last 18 months
- ❖ Otoscopic evaluation consistent with erythematous and ceruminous otitis
- ❖ Cytologic evidence of bacterial (> 10 /HPF) and Malassezia (> 10 /HPF) overgrowth, keratinocytes detection and lack of neutrophils and macrophages.

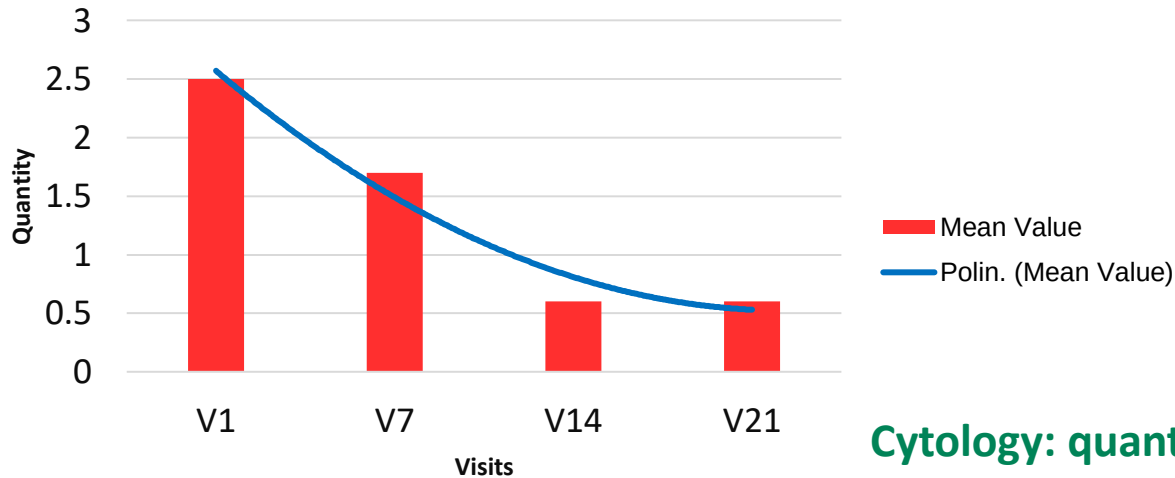
Exclusion criteria

- ❖ No antibiotic or antifungal topic therapies, ear cleaners included, were allowed in the 7 days before starting the study
- ❖ Otitis externa of different cause were excluded: parasitic, foreign bodies, neoplastic, suppurative

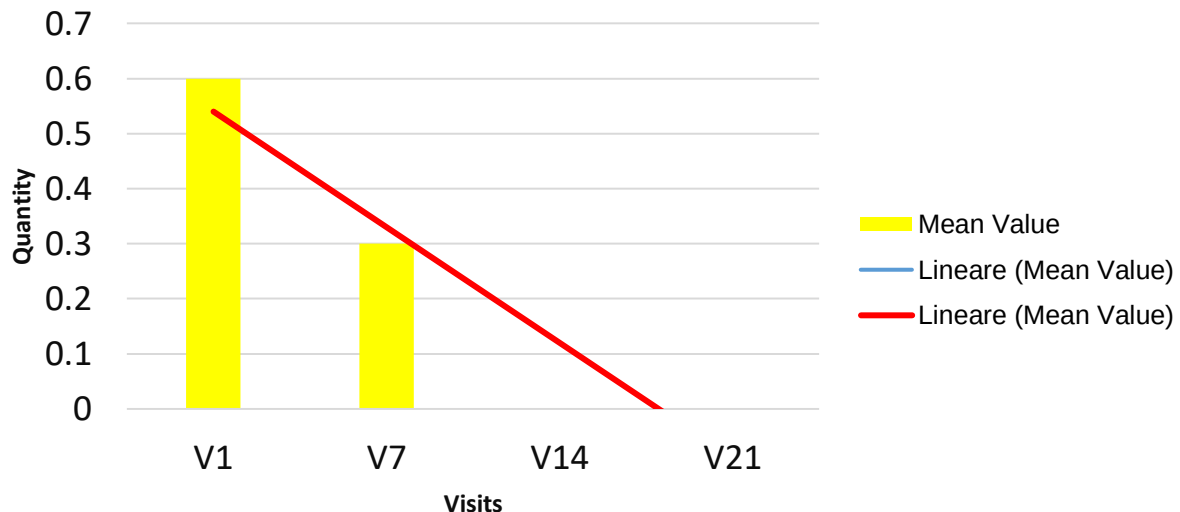
Pilot study results

dogs affected by chronic erythematous and ceruminous otitis externa

Cytology: Bacteria (cocci and rods)



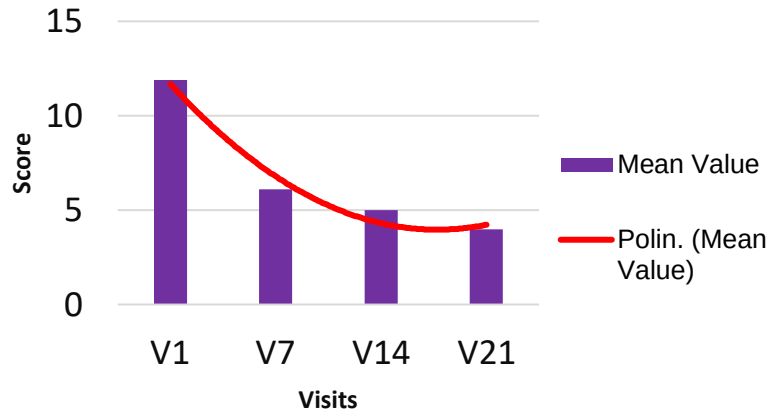
Cytology: quantity of Malassezia per HPF



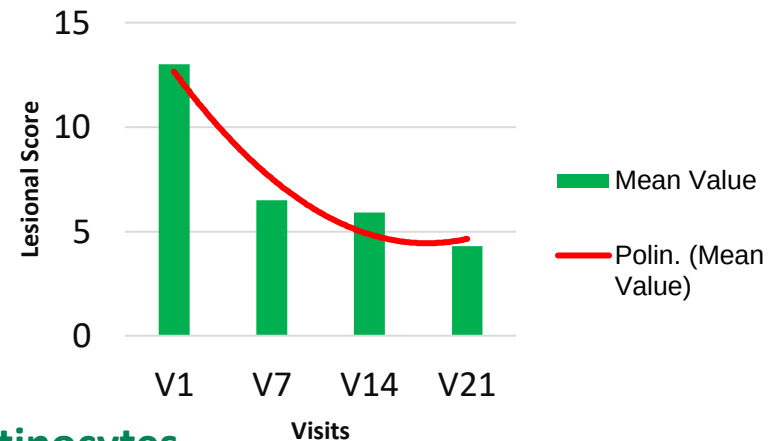
Pilot study results

dogs affected by chronic erythematous and ceruminous otitis externa

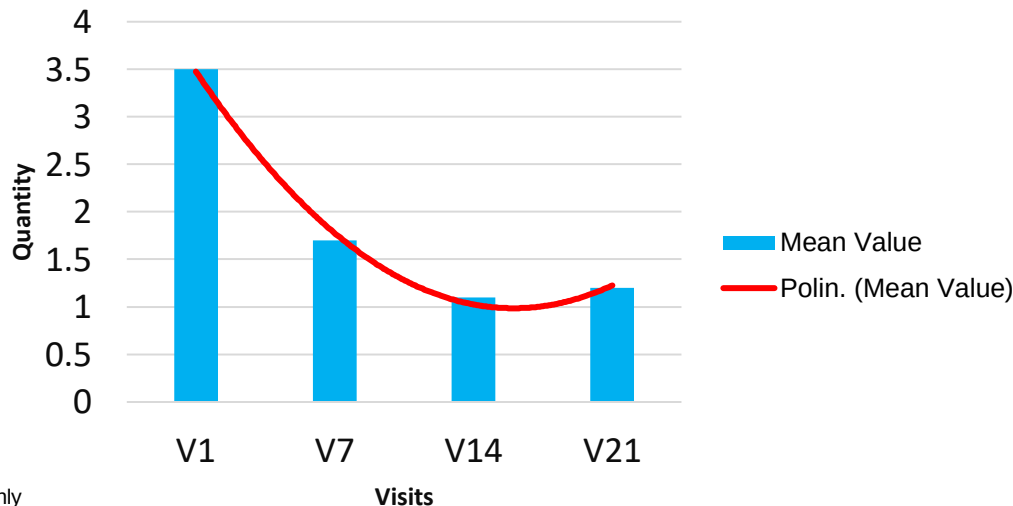
Mean Value - Ear Canal Lesions



Mean Value - Cadesi mod.



Cytology - Keratinocytes





Conclusion of the pilot study

A clear improvement of the ear canal lesions was observed after the first 7 days, with 50% score reduction. The improvement was maintained for up to 21 days (60% score reduction compared to V1).

These objective findings provide evidence of a very well cerumenolytic effect and of a fast and progressive improvement in all the evaluated parameters.





Other proven activity

The product showed great efficacy in earwax and cellular debridement removal from ear canal, few minutes after application.



BEFORE

AFTER few minutes from application



Conclusion of the pilot study

ACTEA™ OTO may be considered as an effective treatment for erythematous and ceruminous otitis externa due to bacterial overgrowth, particularly in recurrent otitis during atopic dermatitis, thus avoiding antibiotic, antifungal and anti-inflammatory topical therapies.

The use of **ACTEA™ OTO** did not show any side effect, and was rated by all the owners as practical and satisfactory about results.









Accomasso et al., Clin Dermatol Res J 2017, 2:1

Efficacy of a Topical Lotion Containing Lactoferricin, Glycerophosphoinositol Lysine and Verbascoside for External Otitis Due to Atopic Dermatitis

Lisa Accomasso^{1*}, Immacolata Miano², Tiziana Cocca², Mauro Bigliati¹, Silvia Arpicco³ and Alessandro Barge³

Abstract

Importance: Atopic dermatitis (AD) is a common skin disease in dogs with a great impact in quality of life, especially when ears are affected because of the difficult application of lotion due to the lesions localization.

Objective: This study is aimed to examine the effect of topical lotion containing lactoferricin, glycerophosphoinositol lysine and verbascoside on canine atopic dermatitis. The topical lotion must be easy to use in ears of dogs under treatment.

Methods: 21 dogs with external otitis due to atopic dermatitis were treated for 14 days and monitored from day 0 to day 14 to ascertain the effect of the treatment with different parameters such as CADESI score, lichenification, excoriation, alopecia, pruritus and cytological analysis.



Clinical Dermatology
Research Journal



Objective: efficacy evaluation of topical lotion containing Lactoferricin B, GPI and Verbascoside on canine atopic dermatitis.

- 21 Atopic dogs with external otitis were treated for 14 days
- Evaluation of: CADESI score, lichenification, excoriation, alopecia, itching and cytological analysis.

Results: a clear decreasing in clinical symptoms was observed, cytological analysis also confirms bacteria and *Malassezia* decrease.

Thank you for your attention...

