



NEW

Candioli Innovation



with



Exclusive formula
patent

Natural patented formula

LACTOFERRICIN B



GPI Glycero-phospho-inositol lysine



Verbascoside

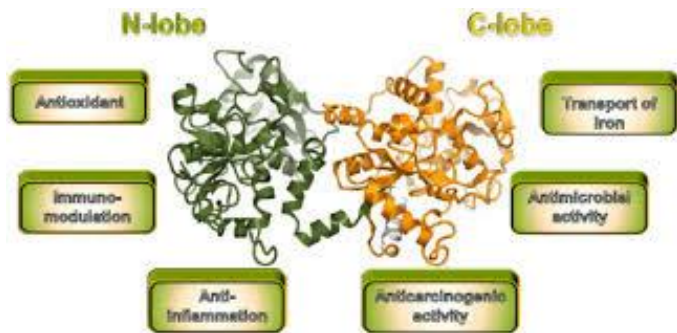


LACTOFERRICIN B

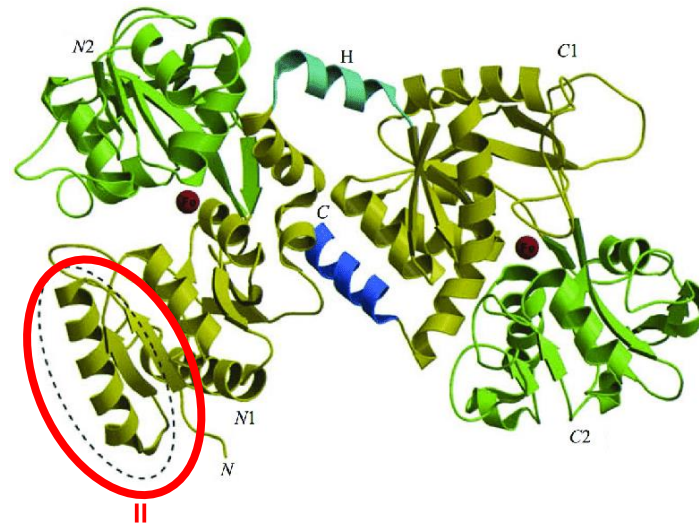


Lactoferricin B is a peptide fraction, derived from bovine lactoferrin, by acid hydrolysis thanks to pepsin activity. This peptide exerts a powerful bactericidal activity against gram + and gram – bacteria.

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

bactericidal effect

Inhibits the virus
binding to target
cells



IMMUNOLOGICAL ACTIVITIES

Modulates immune
system

Antigen-presenting
cells function

LACTOFERRICIN B

ANTIBACTERIAL ACTIVITY



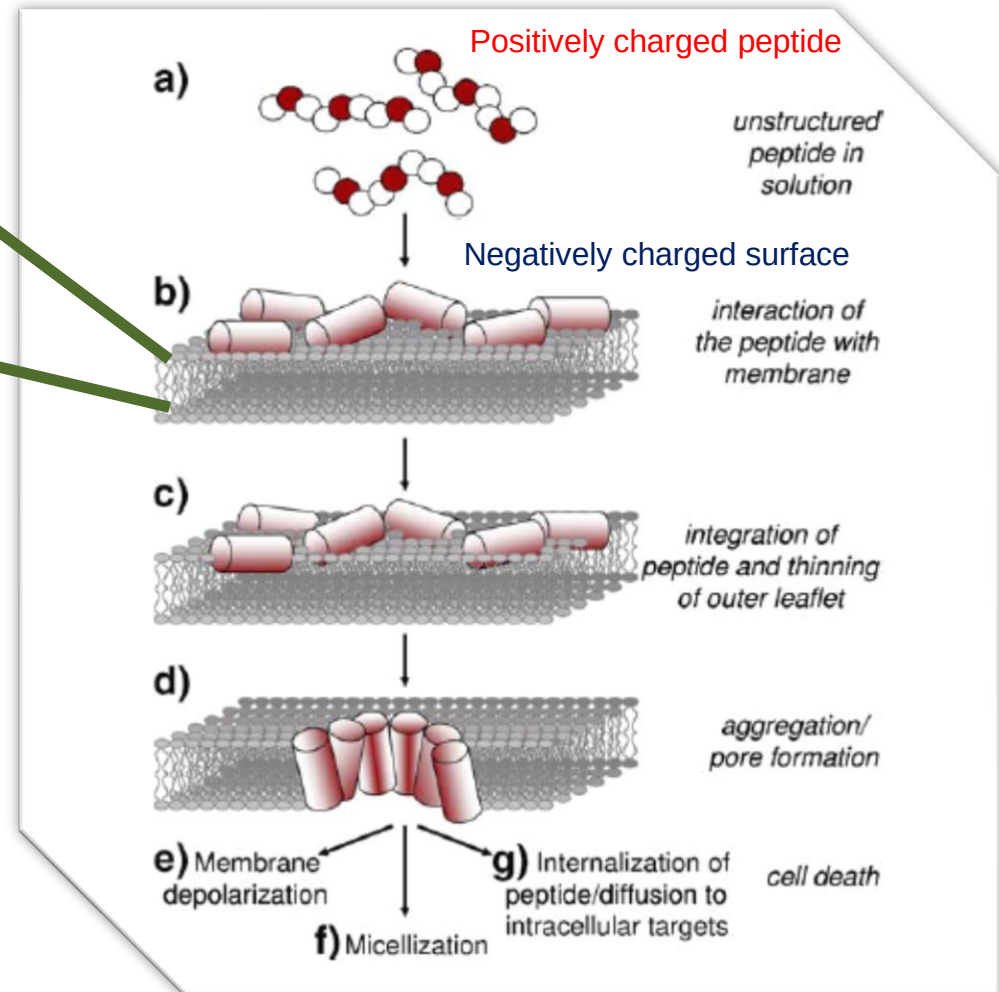
Teichoic acid layer surrounds cytoplasmic membrane

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

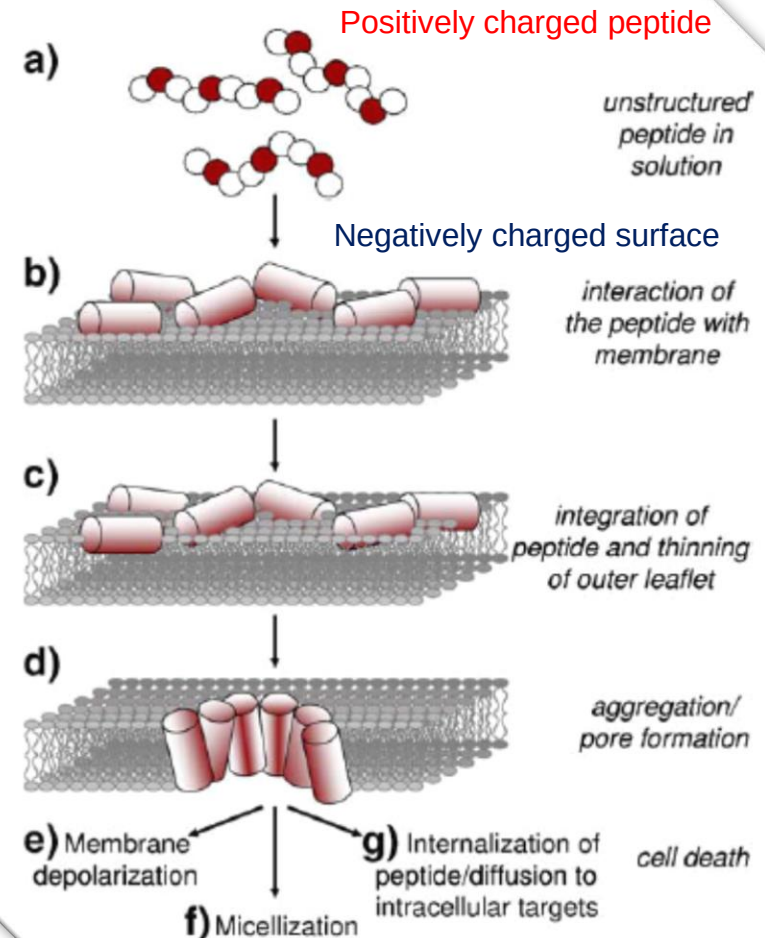
ANTIBACTERIAL ACTIVITY



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

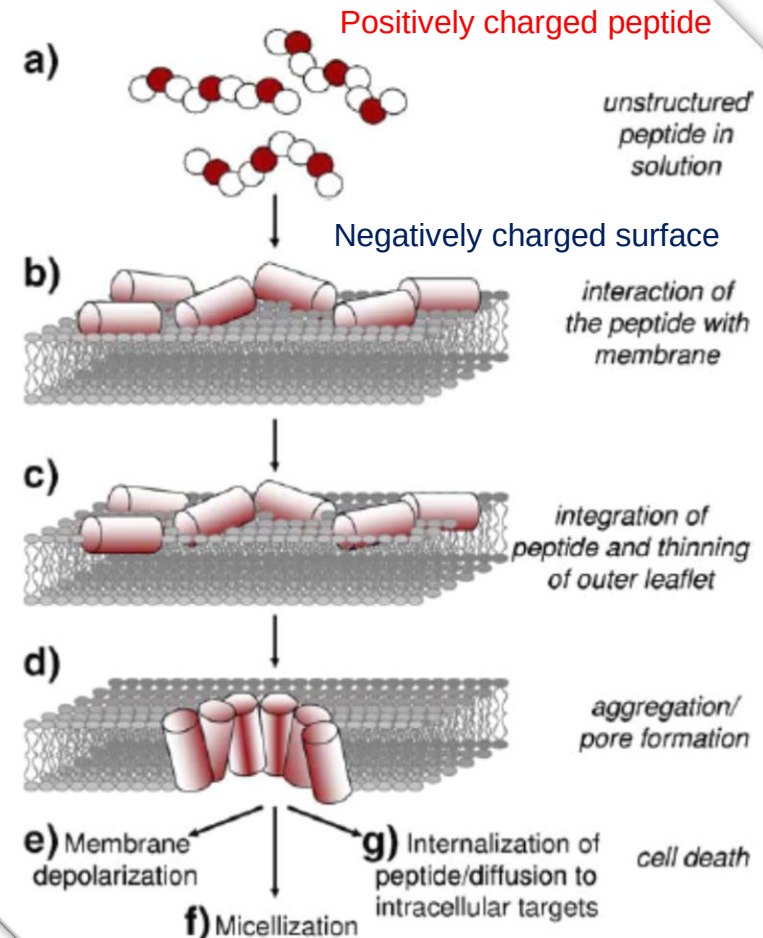


Lactoferricin B can enter the bacterial cell and act on intracellular target (DNA, RNA,...).

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

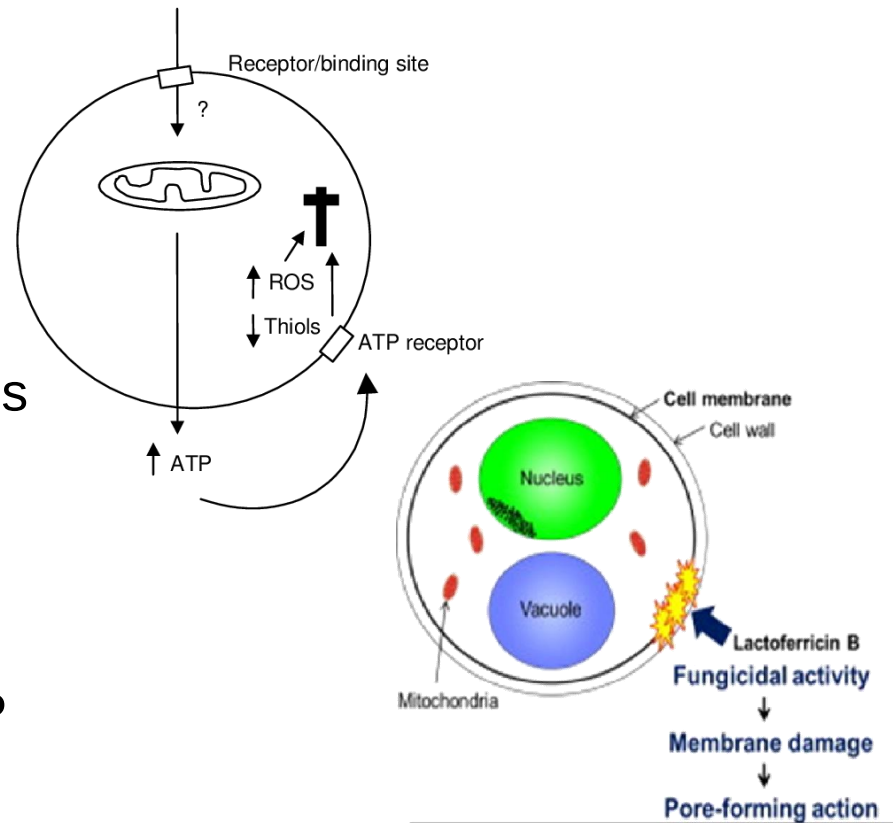
Direct fungicidal activity

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

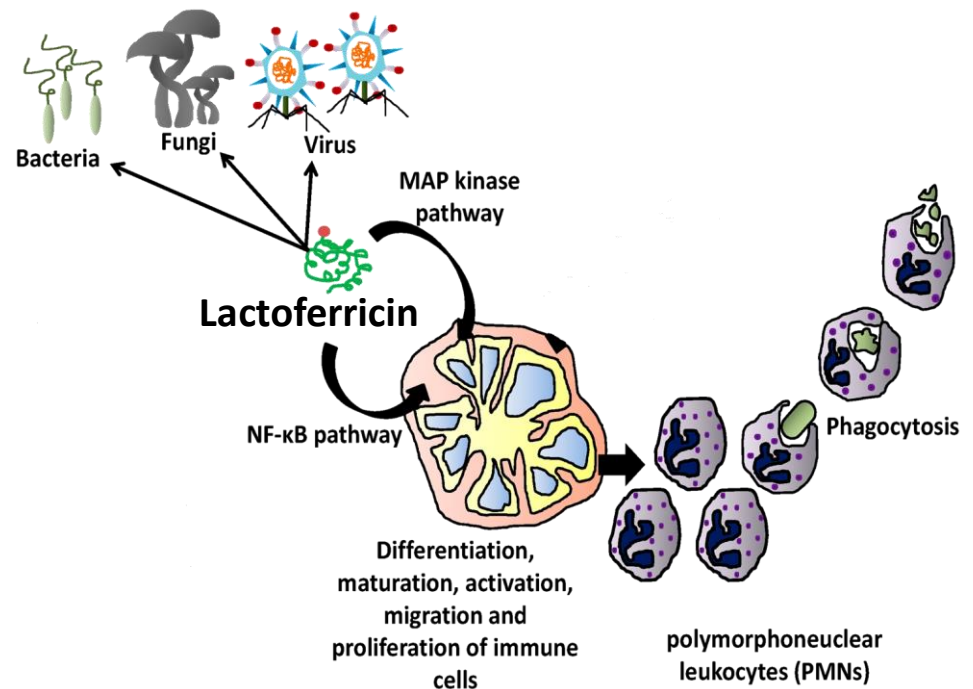
Direct fungicidal activity

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, mold and filamentous fungi

LACTOFERRICIN B



ANTIVIRAL ACTIVITY

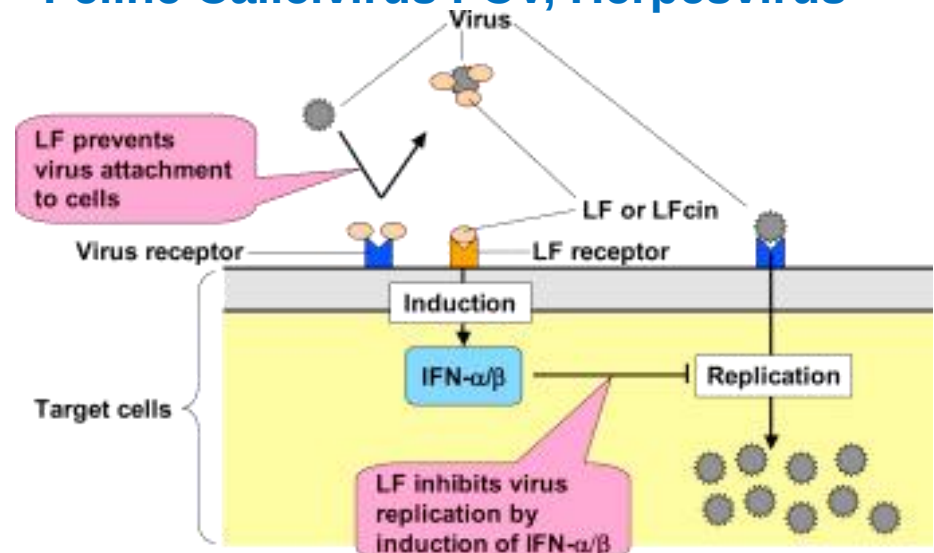
Binding site used by virus to enter into host cells as Heparin sulphate and GAGs

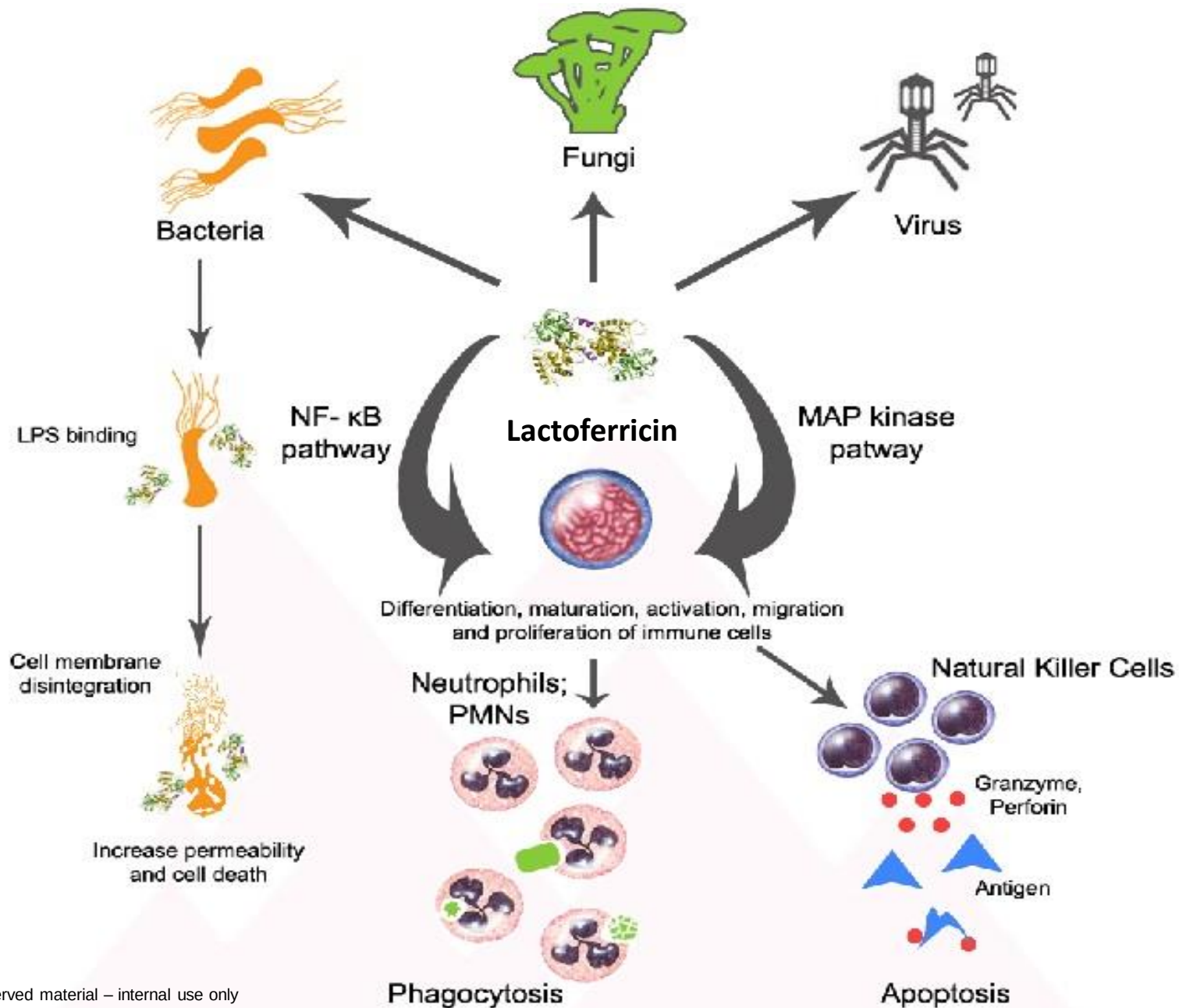
Directly inactivating virus particles. Lfcin B binds nuclear DNA and acts as transcription factor

Electrostatic attraction as for antibacterial activity

Upregulating host cell defence in response to viral attack

Feline Calicivirus FCV, Herpesvirus





LACTOFERRICIN B

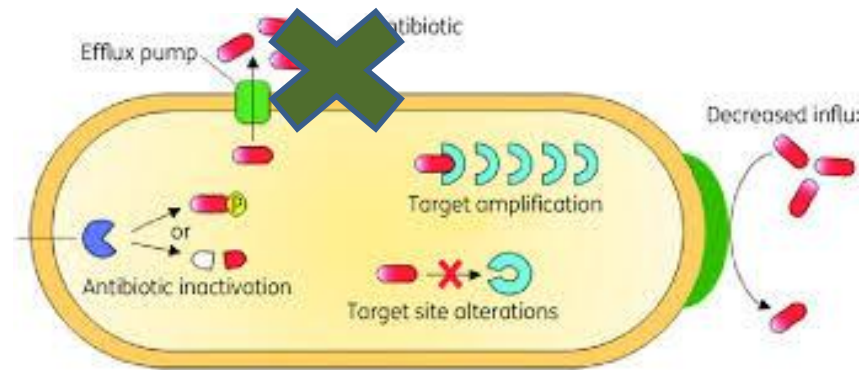
SYNERGISTIC ACTIVITY WITH ANTIBIOTICS AND ANTIFUNGAL AGENTS



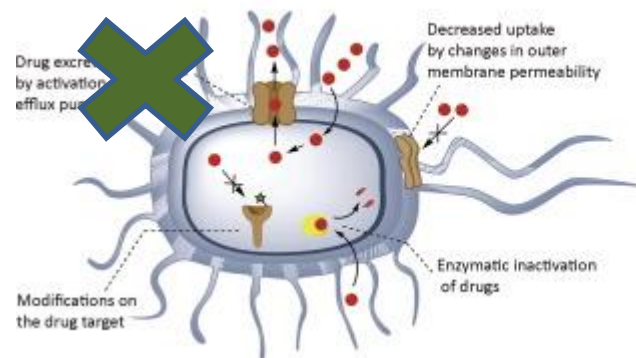
Lactoferricin B has been shown to be an effective synergistic agent when used in combination with antibiotics and antifungal agents.

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

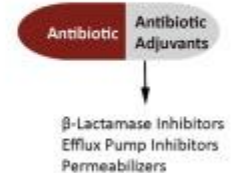
LACTOFERRICIN B



MECHANISMS OF BACTERIAL RESISTANCE TO ANTIBIOTICS



COMBINATION THERAPY STRATEGY TO UNLOCK INCREASING RESISTANCE



GPI Glycerophosphatidylcholine



What is it?

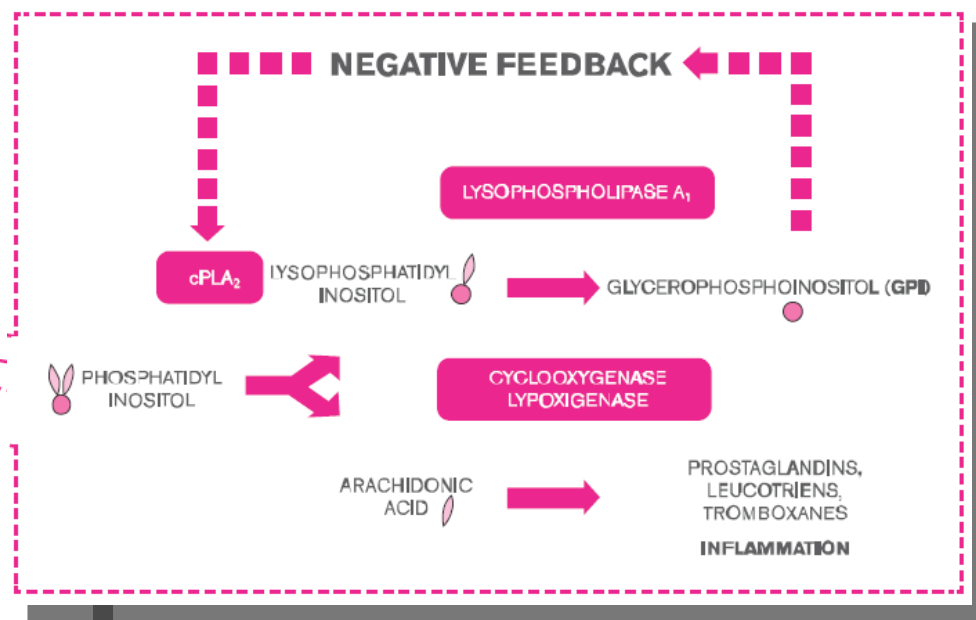
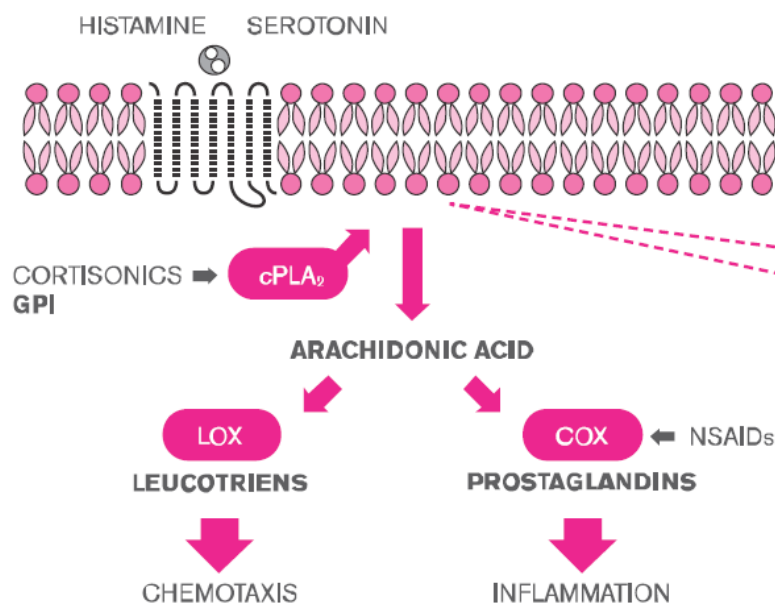
It is an **innovative** sunflower lecithin-derived **active ingredient** that acts upstream in the inflammatory cascade pathway. Its mechanism of action fits into an entirely physiological autoregulating system resulting very effective without side effects





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[™]) is obtained through a patented industrial HTN[™] 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

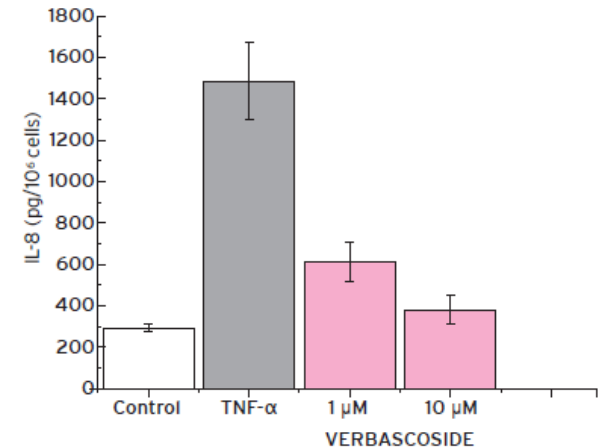


How does it work?

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 .

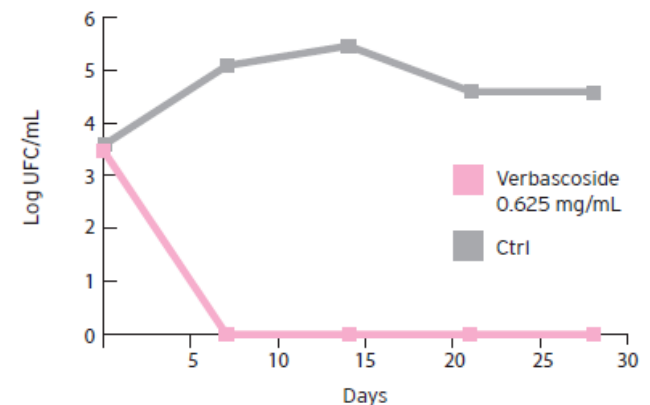
In a similar model using human keratinocytes (HaCaT) this significant anti-inflammatory activity is confirmed and verbascoside results to be superior to quercetin and rutin (Pastore et al. , 2009).



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



Exclusive formula
patent



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

- restoration to a normal skin structure
- exudative dermatitis of the skin fold (nose and groin)
- localized lesions in atopic dermatitis cases
- interdigital dermatitis
- skin characterized by excessive sebum production and unpleasant smell





Instructions of use

Apply a suitable amount of product (1 spray treats around 5 cm skin area), according to the skin surface to be treated, **twice** a day for at least **15 days**. Gently massage the skin to assure the product is adequately spread over and suitably penetrates the hydrolipidic film.

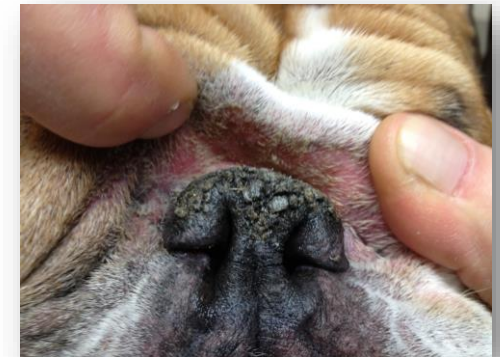


NO CHLOREXIDINE IN ACTEA DERM



PROVED EFFECTIVENESS

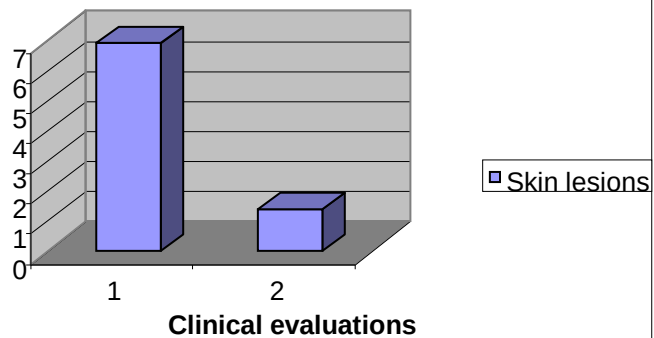
Pilot study in 10 dogs with erythematous localized dermatitis



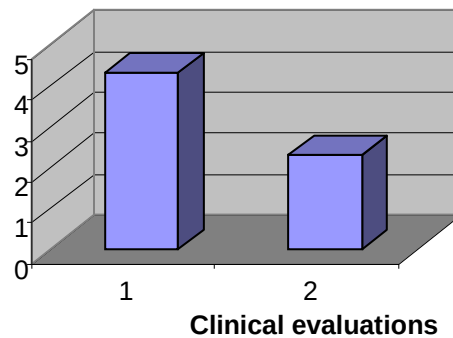
Objective of the study:

- ❖ To evaluate the clinical response, focused on the main dermatologic inflammatory symptoms reduction, after 15 days application of the product ACTEA™ DERM: erythema, excoriations, lichenification
- ❖ To evaluate if bacterial and Malassezia overgrowth is reduced
- ❖ To evaluate any appearance of side effects after application
- ❖ To evaluate ease of product application, based on the owner's opinion

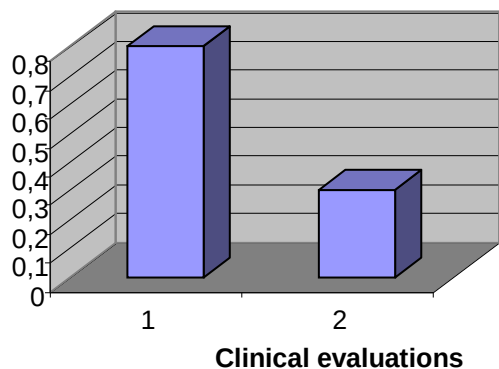
Skin lesions scores



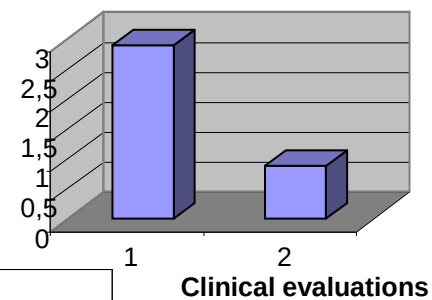
Visual Analogic Scale - Itching



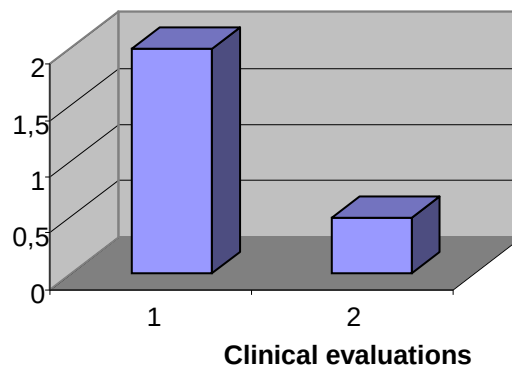
Cytology ■ Malassezia



Cytology ■ Corneocytes



Cytology ■ Bacteria





Before the
treatment V1



After the treatment
V15

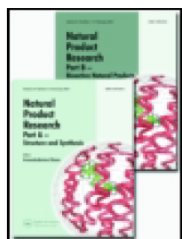






PROVED EFFECTIVENESS

Published clinical study in 38 dogs with atopic dermatitis



Natural Product Research
Formerly Natural Product Letters



ISSN: 1478-6419 (Print) 1478-6427 (Online) Journal homepage: <http://www.tandfonline.com/loi/gnpl20>

**Lactoferricin/verbascoside topical emulsion:
a possible alternative treatment for atopic
dermatitis in dogs**

Elena Biasibetti, Natascia Bruni, Mauro Bigliati & Maria Teresa Capucchio





PROVED EFFECTIVENESS

Published study in 38 dogs with atopic dermatitis

Objective: evaluate clinical response to topical lotion treatment containing Lactoferricin B, GPI and Verbascoside in dog affected by atopic dermatitis.

- 38 dogs with atopic dermatitis were treated for 15 days
- Evaluation of: CADESI score, itching score VAS and cytological analysis.

Results: after 15 days of treatment there was a significant difference in CADESI score, VAS and cytology; both cocci and Malassezia were decreased.

actea™

SHAMPOO

Candioli
PHARMA



Indication of use

- dermatological use shampoo for dogs and cats indicated for effective cleansing of coat and skin
- helps maintain the normal skin lipid film and contributes to limit itching, bacterial and fungal growth.
- regular and ongoing cleansing, in case of normal skin, puppies as well as for helping prevent and treat skin
- conditions of various origins in susceptible subjects



Thank you for your attention...

