New applications for veterinary dermatology from the ICF laboratories

A. Romani¹, C.S. Cabassi², N. Milanesi³, N. Confortini⁴, T. Della Mura⁵, P. Lupi⁶

¹Fellowship Researcher in Azienda Ospedaliera di Parma,
²DVM Dipartimento Scienze Medico Veterinarie Università di Parma,
³Dottore in CTF: R&D Responsible ICF Laboratory,
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Premise
Antibiotic resistance is becoming a pressing issue in the field of veterinary medicine. Moreover, there is also a need for rapidly effective products with low environmental impact, that are safe for both the owner and the pet.

Scope
Research and develop formulations:
1. innovative and that doesn’t give resistance;
2. active towards the most common pathogens of dog and cat skin (gram +/gram -/ Malassezia / Candida);
3. rapidly effective to encourage the owner’s compliance;
4. alternative to conventional therapies;
5. with a high degree of tolerability;
6. with a very low environmental impact;
7. easy to use.

Research method
Starting from the premise, we assessed the various antimicrobial agents and ruled out:
• inorganic oxidising agents (hypochlorites, …)
• aldehydes
• iodophors (pvp-iodine)
• natural antimicrobial peptides
• quaternary ammonium salts
• Triclosan
because they do not correspond to our safety and efficacy standards, and have a high environmental impact,
and we included:
• alcohols
• Chloramine T
• Chlorhexidine Diacetate
• Chlorhexidine Digluconate
• synthetic antimicrobial peptide because they potentially correspond, based on scientific evidence, to our safety, efficacy and tolerability standards.

Choice of components
The result of our studies over the past 10 years, based as on assessing bibliographical references as on detailed and precise laboratory and on field tests, has led, among the active ingredients included, to the choice of APM 2041, Chlorhexidine digluconate and Tris-EDTA.
For our formulations these active ingredients are the only ones that fully meet our safety, efficacy and tolerability standards we’ve requested.

AMP2041
AMP2041 is an ICF patented synthesised antimicrobial peptide. It is an innovative molecule, whose action disturbs and perforates the bacterial membrane, selective against prokaryotic cells.

Chlorhexidine Digluconate
Chlorhexidine digluconate, even at low doses, keeps its indisputable properties and contributes to speed up antimicrobial activity of AMP2041.
Tris-EDTA
Tris-EDTA acts by destabilising and enhancing the permeability of the bacterial membrane. The association of these molecules, AMP2041, Chlorhexidine digluconate, Tris-EDTA, at low doses, has allowed us to obtain effective formulations, safe, highly selective and well tolerated. These innovative and original formulations were made possible by the combination of active principles not antagonists but synergistic between them.

Results
The results of the efficacy tests conducted in vitro are summarised in the plots below, where the term “MIX” designates the association between AMP 2041, chlorhexidine digluconated and Tris-EDTA:

Assessment of antimicrobial activity on selected strains*
*(Professoressa C.S. Cabassi/ Dipartimento di Scienze Mediche e Veterinarie, Università degli Studi di Parma)

- E. coli
- Pseudomonas aeruginosa
- Proteus mirabilis
- Staph. pseudintermedius
- Strept. Agalactiae
- MRSA
- Candida albicans
- Malassezia

![E. coli](image-url)
Comments on MIX activity toward Gram negative bacteria:
The activity of the MIX on E. coli, Pseudomonas ATCC and Proteus mirabilis is particularly interesting. On these bacteria, MIX causes the total destruction of CFUs in 1 min.
Comments on MIX activity toward Gram positive bacteria:
MIX is effective as it reduces to zero the bacterial load in 30 seconds-3 minutes in all Gram positive bacteria. On Staph. Pseudintermedius, MIX is particularly effective already at 30 seconds.
Comments on yeasts
The activity of MIX on *Candida albicans ATCC* is high already at 30 seconds. The activity of MIX on *Malassezia* (clinical isolate) is high with total destruction of CFUs in 3 and 5 min.

Conclusions
The scope sought and reached has led to the improvement of formulations containing a MIX of AMP2041, Chlorhexidine digluconate and Tris-EDTA.
AMP2041, thanks to its particular amino acid sequence and high degree of hydrosolubility, makes a unique synergy possible with other components of MIX.
This has allowed to create formulations with:
• broad spectrum action
• rapid activity at low doses
• safe use
• low environmental impact.
These results have been confirmed by studies conducted by the laboratory of the Department of Medical and Veterinary Sciences, University of Parma, studies in vitro presented like poster at World Veterinarian Dermatological Congress in Bordeaux (31 May- 4 June 2016), and from in vivo trial.
Our MIX of molecules has allowed us to create new products directed to veterinary dermatology which represent, once again, another milestone in evolution of knowledge!