

Synergistic antibacterial activity of CATH-2 and D-Arginine for treatment of mastitis

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THE CHALLENGE

The overuse and misuse of antibiotics in veterinary medicine have contributed to the rise of antibiotic-resistant bacterial strains, creating a global issue that requires urgent action and innovative solutions. Mastitis, an inflammatory condition of the udder tissue is one of the most significant diseases in dairy cows, leading to reduced milk production and economic losses, resulting in annual damages exceeding €100 million for the cattle sector in the Netherlands alone. Antibiotic resistance is a growing concern in the treatment of mastitis in dairy cows, complicating management strategies and threatening animal welfare. As a result, alternatives to antibiotics, such as the one described here, are urgently needed.

THE TECHNOLOGY

Researchers at the Faculty of Veterinary Medicine at Utrecht University have discovered that the combination of an antimicrobial peptide with a positively charged D-amino acid (D-AA) effectively kills bacteria, whereas these compounds individually have limited antibacterial effect (Fig. 1). These compounds effectively eradicate mastitis-causing *Staphylococcus aureus* (and other bacterial strains) in the physiologically challenging environment of raw cow's milk (Fig. 2), while they are not toxic for eukaryotic cells (Fig. 3). The bactericidal activity of CATH-2 and D-Arg is fast, 3-Log reductions in 30 min and maintained in anaerobic conditions. These novel synergistically working antibacterial compounds offer promising potential for treating bacterial infections, particularly those caused by antibiotic-resistant strains and moves us nearer to combating the global threat of antibiotic resistance.

TECHNOLOGY READINESS LEVEL

The technology is currently at the TRL4.

NEAR FUTURE DEVELOPMENT PLANS

- Injection of our product *in vivo* in the udder of cows suffering from mastitis.
- Determine development of resistance against the combined product.
- Determine exact mode of action and optimal ratio's of AMP/D-Arg combinations

MODE OF APPLICATION

Our synergistic combination product could be a standalone application for treatment of mastitis in cows or goats. The envisioned route of administration would be intramammary infusion.

ADVANTAGES

- This product is a real alternative for antibiotics with a different mechanism of action.
- The product is bactericidal against multi-resistant bacterial strains.
- Platform potential for novel Amp- D-AA beyond mastitis
- Scalable production of compounds

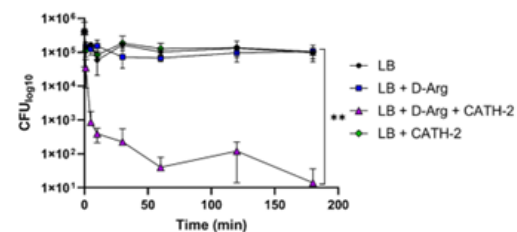


Figure 1. The bactericidal activity of CATH-2 and D-Arg is fast and maintained in anaerobic conditions.

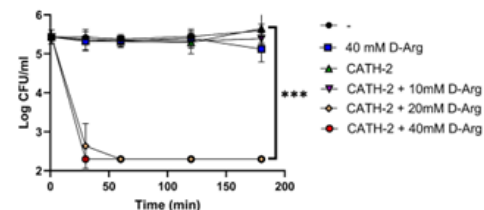


Figure 2. *S. aureus* is efficiently killed in raw cow milk only by the CATH-2 and D-Arg combination, while each component individually does not have a bactericidal effect.

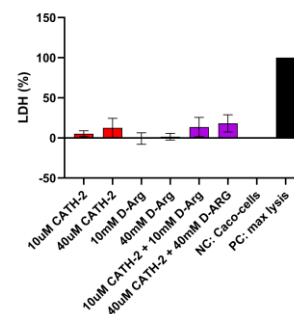


Figure 3. CATH-2 + D-Arg are not toxic to Caco-2 cells at the concentrations required for bacterial killing.

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