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Study of anti-resistance and anti-virulence effects of two antimicrobial molecules on Gram positive pathogens

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Introduction and objectives

Enterococci and Staphylococci are responsible for many healthcare associated infections¹. These microorganisms harbor different antibiotic resistances, including vancomycin. These Enterococci and Staphylococci are respectively called VRE and VRSA. Patients infected with VRE or VRSA are left with few treatment options. In this context, two molecules with anti-resistance and anti-virulence effect to vancomycin on VRE and VRSA are studied. Our goal is to investigate the efficacy of these molecules as a potential treatment to cure VRE and VRSA infections.

Results

Anti-resistance properties

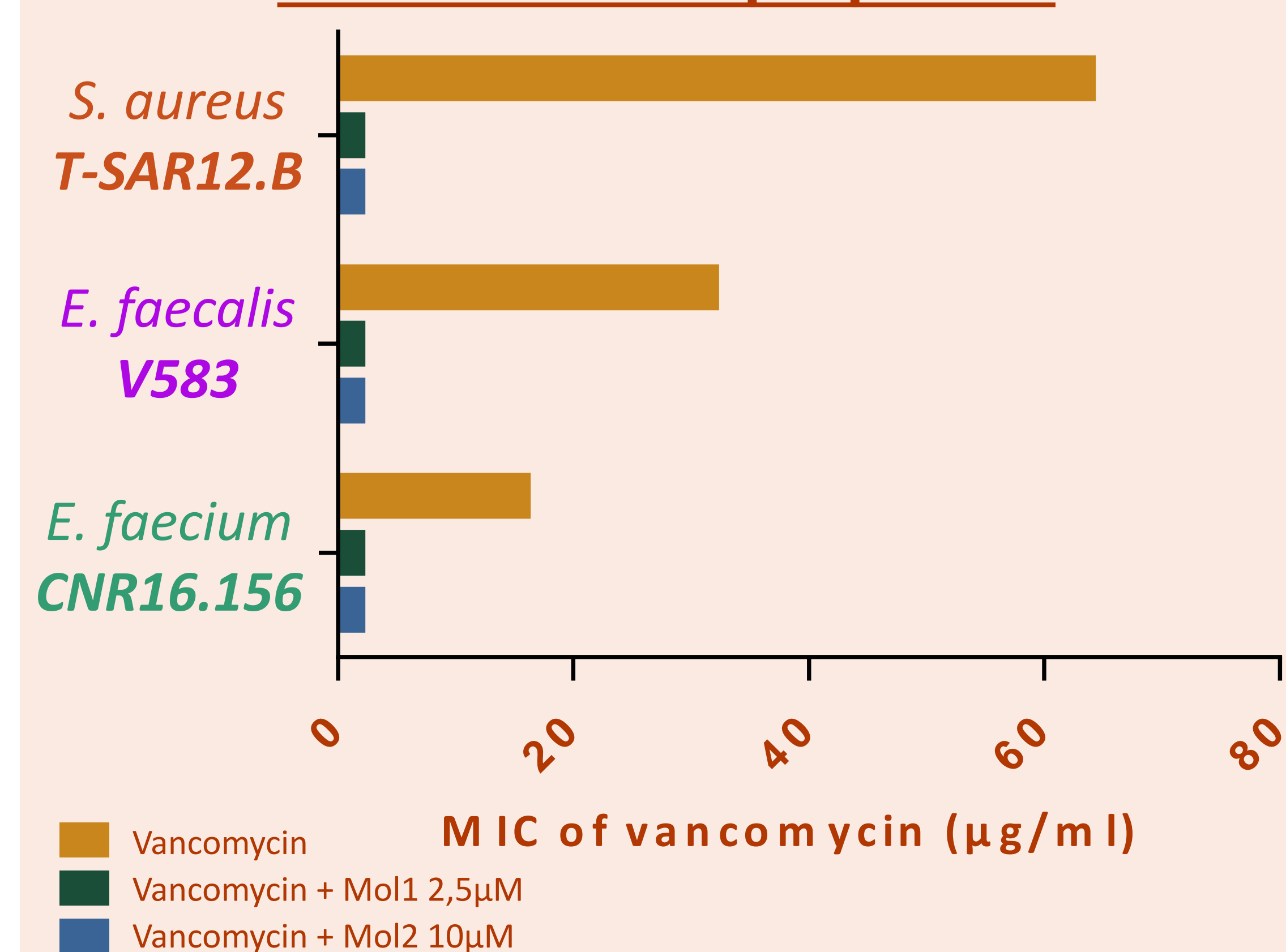


Fig 1 : Molecule 1 and 2 are capable of resensitising vancomycin-resistant pathogens to vancomycin. (MIC ≤ 4 µg/ml)²

Combinatory treatment efficiency

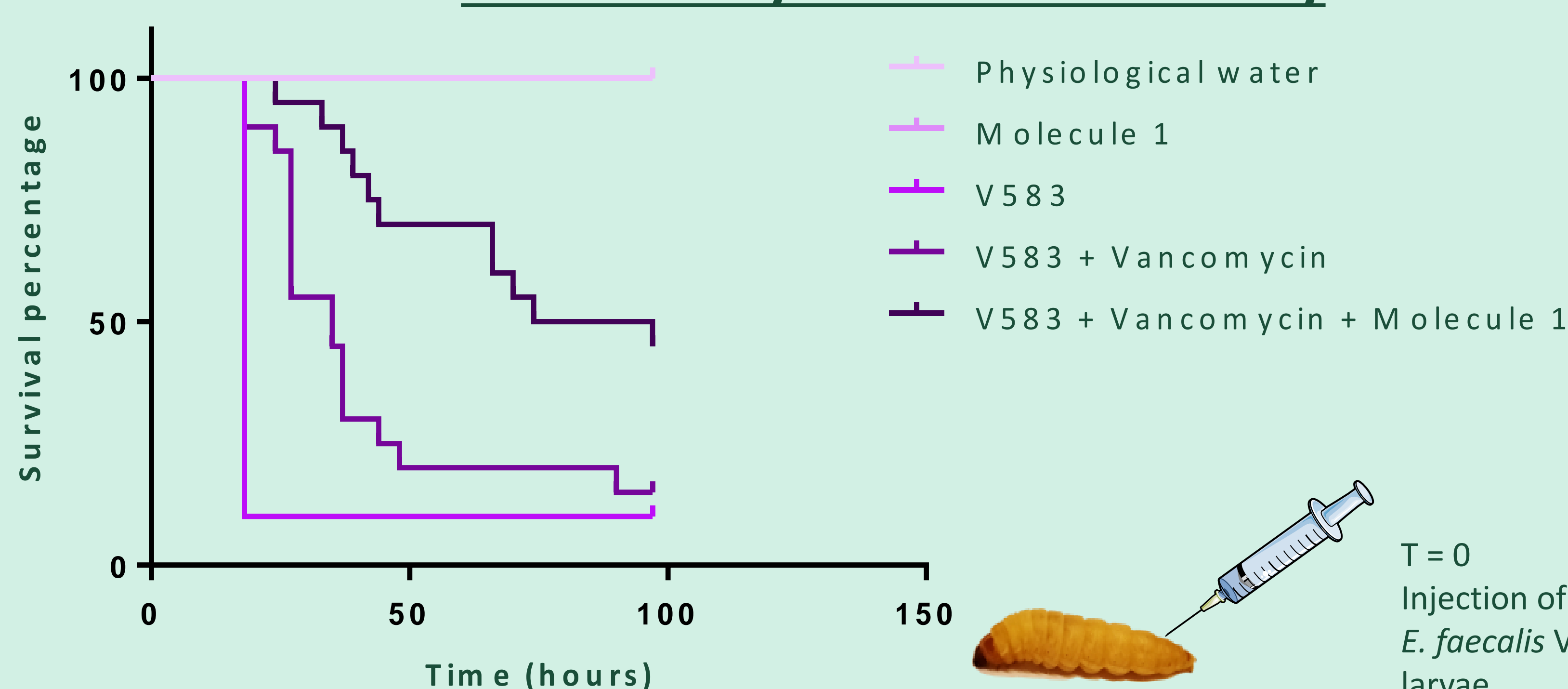


Fig 3 : Survival is increased in *Galleria mellonella* larvae infected with *Enterococcus faecalis* V583 then treated with vancomycin in combination with molecule 1 compared to vancomycin alone or non treated.

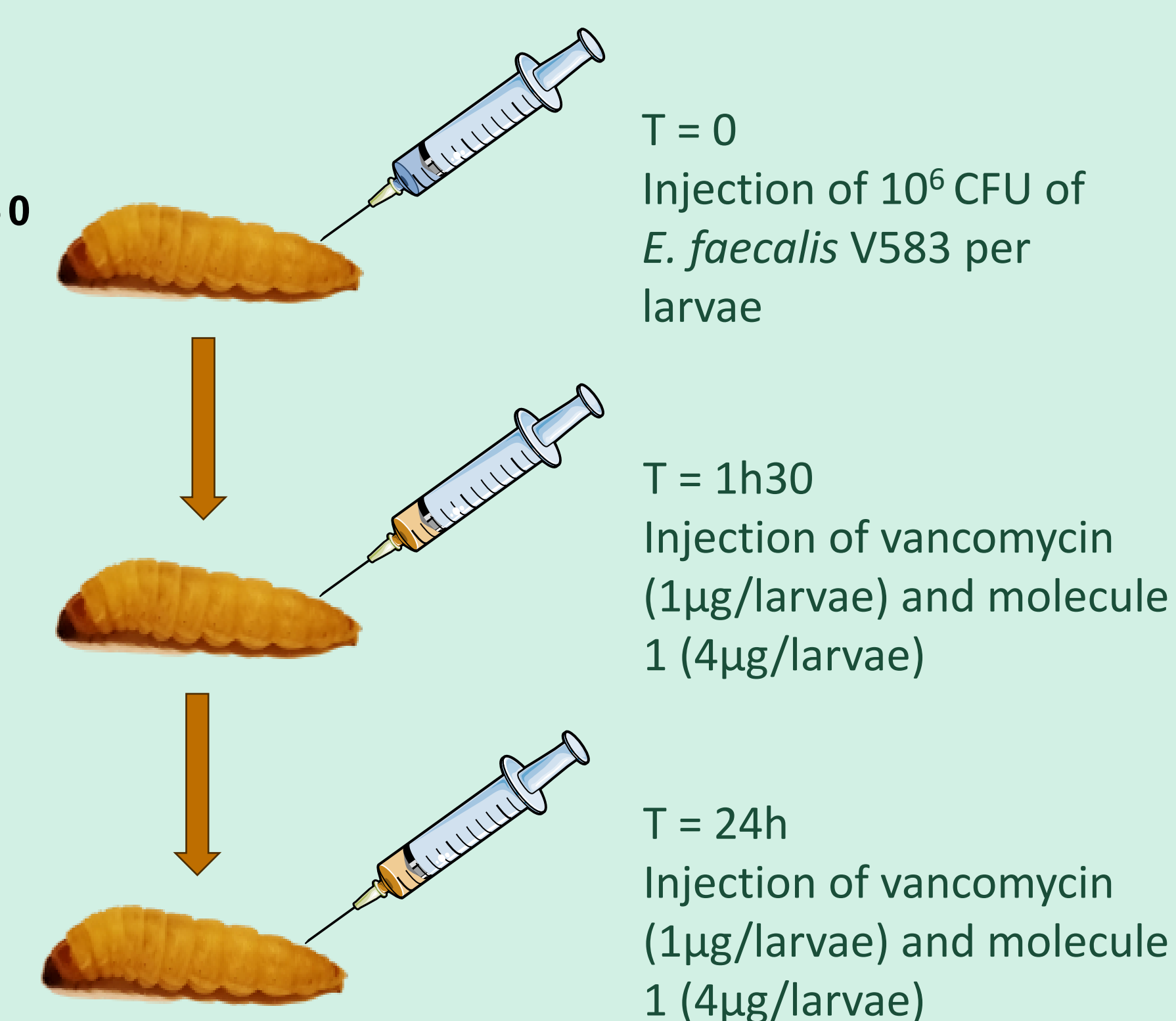


Fig 4 : Infection and treatment protocol of *Galleria mellonella* larvae.

Anti-bacterial properties

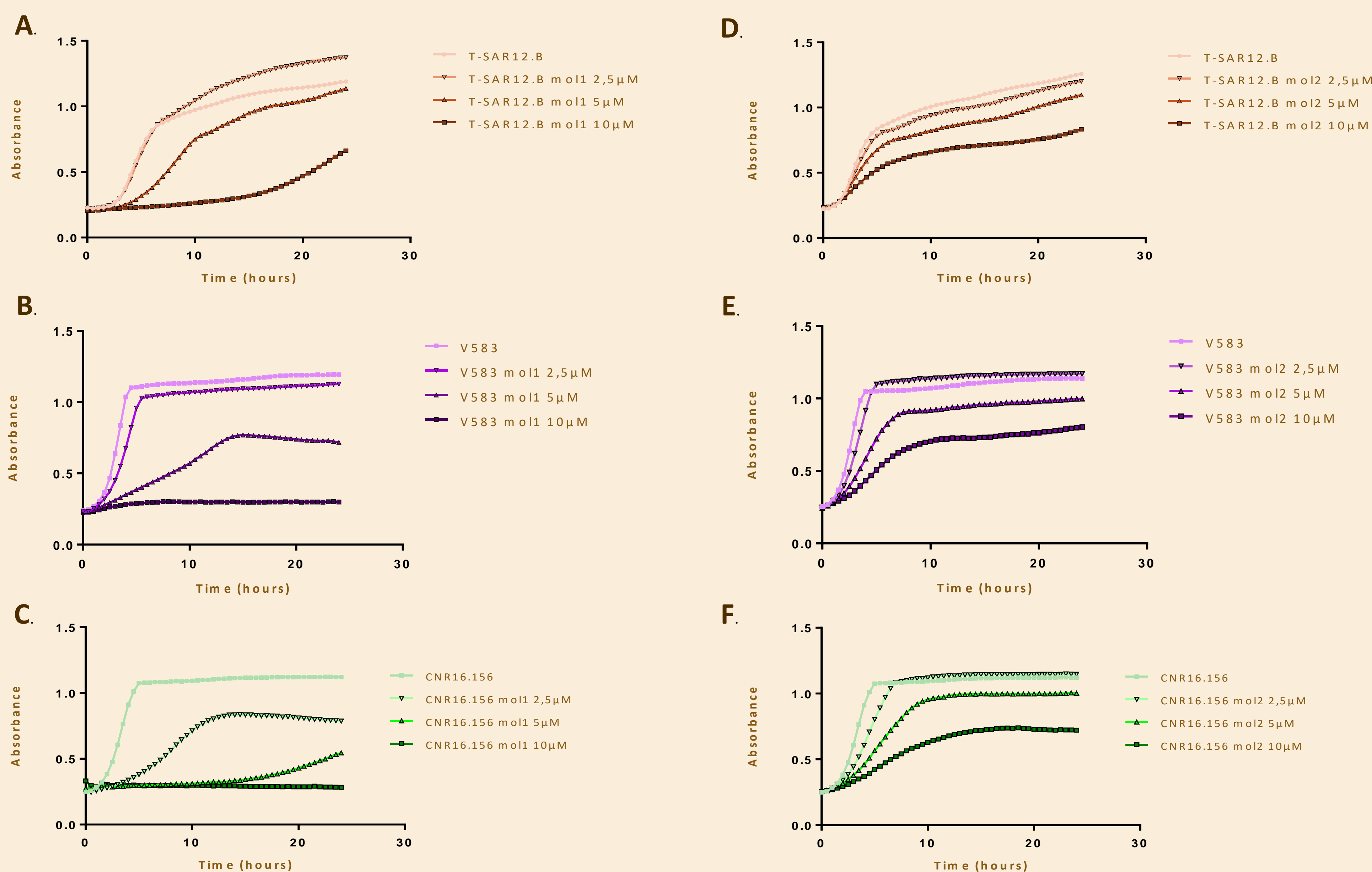


Fig 2 : Molecule 1 inhibits growth of Enterococci at 10 µM and reduces growth starting from 2,5 µM while Staphylococci are not inhibited by molecule 1 at 10 µM and growth is altered starting from 5 µM. On the other hand, molecule 2 does not inhibit growth of these bacteria at 10 µM for any strains but reduces their growth starting from 5 µM.

Anti-virulence properties

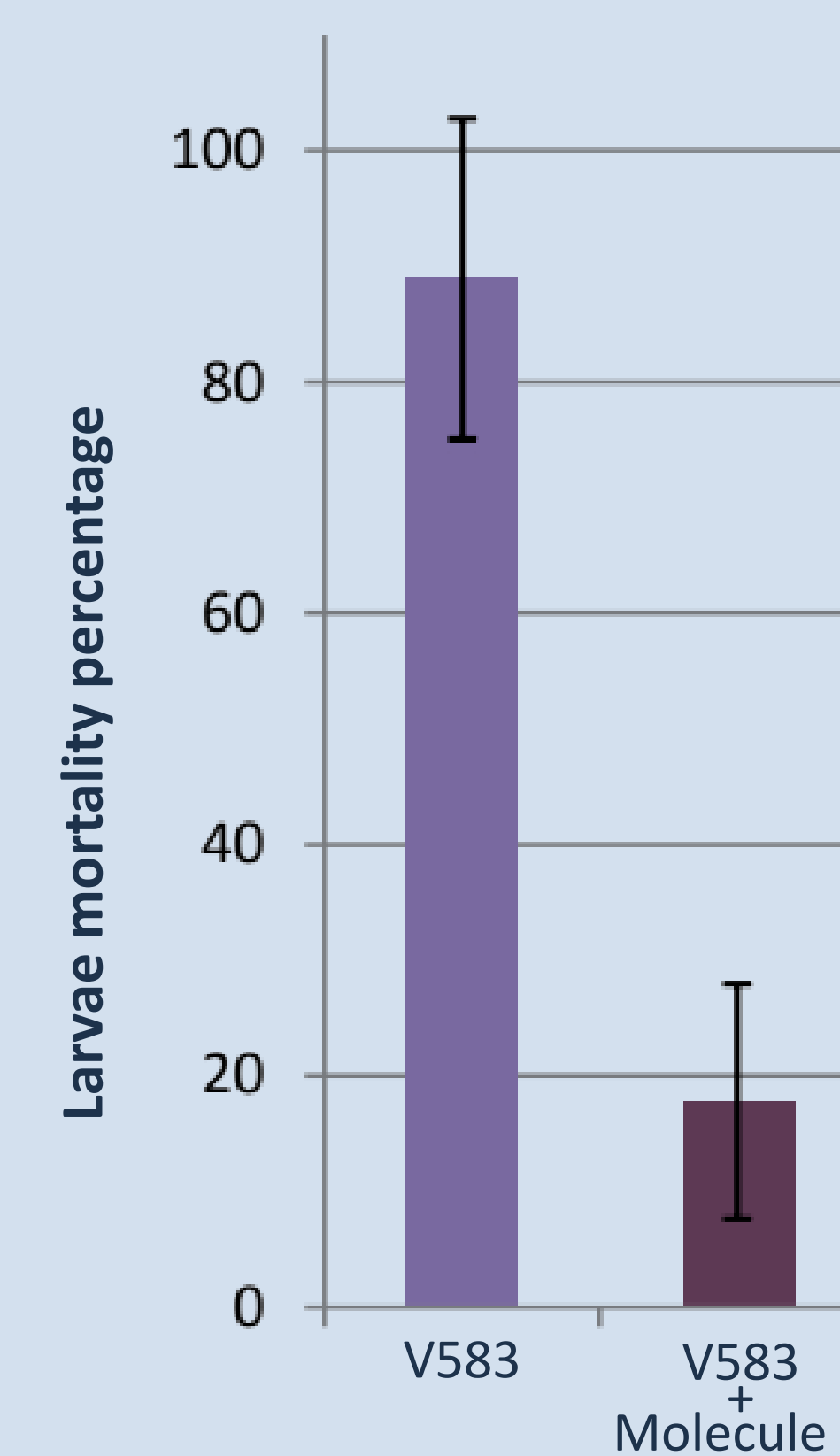


Fig 5 : Mortality of *G. mellonella* larvae infected with *Enterococcus faecalis* V583 is greatly reduced when treated with molecule 2.

Conclusion

Molecules 1 and 2 have shown their efficacy to resensitize VRE and VRSA to vancomycin *in vitro* and *in vivo* in a *Galleria mellonella* larvae model. These molecules decrease growth of VRE and VRSA and only molecule 1 totally inhibits growth at high concentration. This low bactericidal action prevents a high selection of resistant bacteria, allowing them to be used as anti-virulence treatment. Further analysis need to be done on these molecules to unravel their mode of action and use them as an alternative treatment to conventional antibiotics.