The artificial sweetener acesulfame-K inhibits multi-drug resistant pathogens and potentiates antibiotic activity

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The antimicrobial resistance (AMR) crisis and new approaches to tackle it

1. Ace-K impacts the growth of multiple pathogens and produces membrane bulging

Ace-K inhibits growth of a range of clinically relevant pathogens which usually exhibit multi-drug resistance (Fig. 1A). Interestingly, this was partially alleviated by the addition of divalent cations, which have a positive effect on membrane stabilisation. In agreement with this, live cell microscopy imaging revealed morphological defects and bulge-mediated cell lysis after ace-K treatment (Fig. 1B,C). This is a similar mechanism to that described for antibiotics such as carbapenems.

2. Ace-K down-regulates important virulence factors in multi-drug resistant (MDR) Acinetobacter baumannii

Transcriptomic assays revealed that sub-inhibitory concentrations of ace-K down-regulate genes responsible for different virulence factors, which are important for infecting and gaining antibiotic resistances. This demonstrates that ace-K disables virulence (Fig. 2).

3. Ace-K re-sensitises MDR Acinetobacter baumannii to the last-resort antibiotics carbapenems

Carbapenems are highly efficient antibiotic used as a last resort to treat MDR bacteria. For this reason, the WHO has classified carbapenem-resistant (CR) A. baumannii as a top priority pathogen for which novel therapies are needed. In this regard, a sub-inhibitory concentration of ace-K could potentiate three different carbapenems against a CR A. baumannii isolate (Fig. 3), showing potential to be used in combination therapies against MDR pathogens.

4. Ace-K exhibits therapeutic potential in a pig skin ex vivo burn wound model

To show effectiveness of ace-K washes in treating A. baumannii infections, we set up an ex vivo burn wound model on pig skin (Fig. 4A). Ace-K washes resulted in a great reduction in bacterial numbers compared to a conventional chlorhexidine-based wash (Fig. 4B).

The sweet future of antimicrobial therapies

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