



# Marine antimicrobials for the food industry

The MabS project is investigating the antimicrobial potential and genetic aspects of the biosynthesis of tropodithietic acid and other metabolites in marine-derived *Pseudovibrio* species to develop antibacterial agents for the meat industry.

Food is an essential means for humans and other animals to acquire the necessary elements needed for survival. However, it is also a transport vehicle for food-borne pathogens, which can pose a threat to human health as well as to the food industry. Antibiotics are typically used to tackle these pathogens and enhance the human health system; however, selective pressure among bacteria allows the development of antibiotic resistance. Thus, the emerging antibiotic resistance among pathogenic microorganisms is a matter of great concern (Lucera *et al.*, 2012). Unfortunately, progress in the discovery and development of new antibiotics that may be used to tackle these pathogens has lagged behind the pace with which resistance has developed. Recently, marine ecological niches have been established as promising sources for new antimicrobials to combat antibiotic-resistant strains of pathogenic microorganisms. Marine bacteria, fungi, cyanobacteria, sponges and other organisms produce a number of pharmaceutically useful compounds possessing antibacterial, antifungal and antimycobacterial activities. With the efforts of researchers around the world, the total number of approved drugs from the marine environment has risen from four in 2010 to seven in 2014 (Choudhary *et al.*, 2017).

### Antimicrobial potential of *Pseudovibrio* genus

*Pseudovibrio* species are ubiquitous in the marine environment and, in particular, in communities within marine sponges. After being first isolated and described from seawater in Taiwan in 2004, they have been isolated from ascidians, tunicates, algae, coral, tube worms, and from a plethora of marine sponges. Our group has isolated and identified a number of *Pseudovibrio* species from Irish marine sponges with anti-*Salmonella* activities. Infections caused by food-

borne pathogens, such as *Salmonella* spp., are a major public health problem worldwide and the consumption of pork products containing salmonellae is a major source of food poisoning. Thus, there is a clear need to identify novel products to control the threat both to human health and the pig industry in Ireland. Antimicrobial activity within *Pseudovibrio* spp. has previously been reported in different biological assay systems owing to the production of various bioactive secondary metabolites. *Pseudovibrio* species are known to produce specific bioactive compounds, such as heptyl prodigiosin and tropodithietic acid (TDA). TDA (Figure 1) is a sulphur-containing compound with a unique structure consisting of a dithiete moiety fused to tropone-2-carboxylic acid, which is believed to co-exist with its tautomer, thiotropocin, previously identified in *Pseudomonas* spp. TDA has been shown to have a strong inhibitory activity against a range of marine bacteria, such as *Proteobacteria*, *Actinobacteria*, *Firmicutes* and *Bacteroidetes*, the fish pathogens *Vibrio anguillarum* and *Vibrio splendidus*, as well as marine algae and a range of human pathogenic bacteria (Harrington *et al.*, 2014). Moreover, in a recent study, we have been able to detect and characterise a unique analogue of TDA, namely methyl-TDA, and a number of cholic acid derivatives together with amino diols and triols in the *Pseudovibrio* W64 strain. These metabolites have previously been reported to possess antimicrobial activity.

### Understanding biosynthesis of TDA

In genomic 'mining' studies, the *tdaA* and *tdaB* genes were found to be involved in the production of TDA, and further studies confirmed that these genes are expressed from between 24 and 48 hours of growth. The comparative analysis of various strains has indicated that

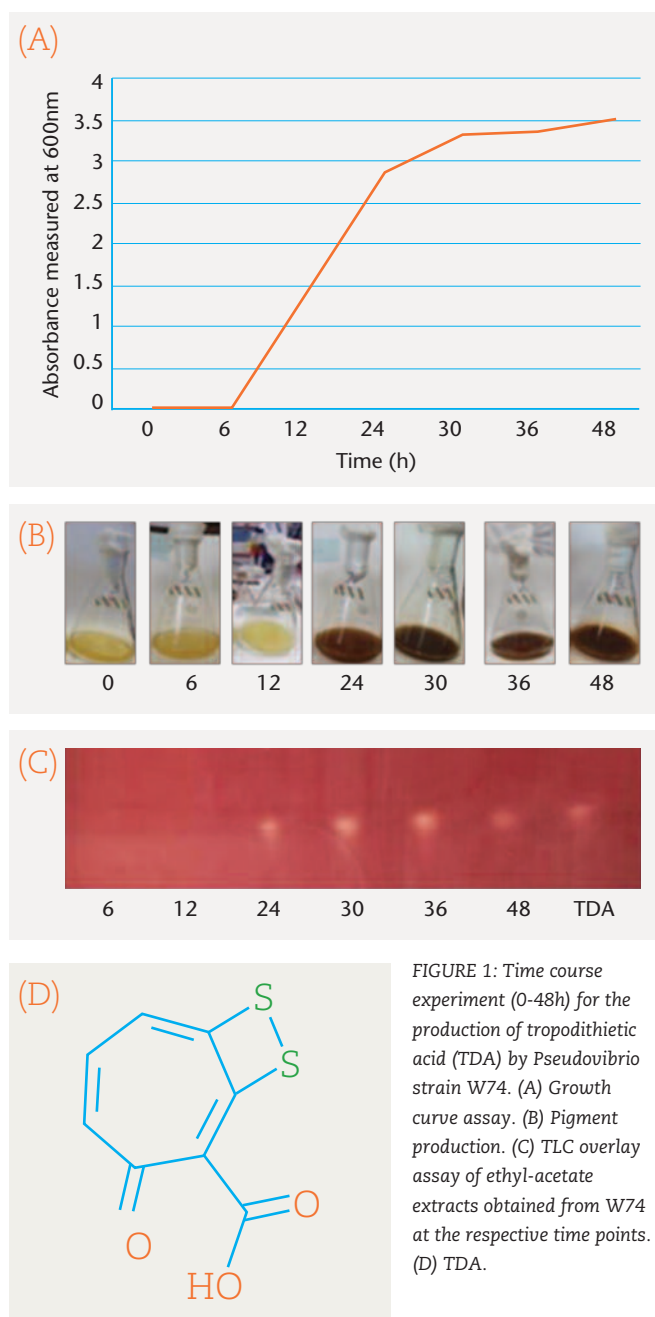


FIGURE 1: Time course experiment (0-48h) for the production of tropodithietic acid (TDA) by *Pseudovibrio* strain W74. (A) Growth curve assay. (B) Pigment production. (C) TLC overlay assay of ethyl-acetate extracts obtained from W74 at the respective time points. (D) TDA.

the *tda* genes show a high degree of homology in most of the marine *Pseudovibrio* isolates (>94% of similarity). Moreover, higher levels of TDA production in some isolates appears to be due to differences in the regulation or production of TDA among marine isolates, and is also independent of any growth effects (Harrington *et al.*, 2014).

### Future prospects

In recent years, because of a greater degree of consumer awareness and concern regarding health risks of synthetic chemical additives, foods preserved with natural additives have become popular. To inhibit growth of undesirable microorganisms in food, the antimicrobials can be directly added into the product formulation, coated on its surface or incorporated into the packaging material. As our search for new antibiotics continues, TDA, or some of its analogues produced by marine sponge-derived *Pseudovibrio* isolates, has the potential to be a template for clinical development. Indeed, synthetic modification focussing on structure-activity relationships

resulting in analogues with enhanced antimicrobial activity, can result in the discovery of new antibiotic-like molecules, thereby helping to combat the emergence of bacteria resistant to common antibiotics. These studies clearly indicate that the *Pseudovibrio* genus holds the potential to be a source of new antimicrobial compounds other than TDA. The metabolites from *Pseudovibrio* can be evaluated as antibacterial agents either as single molecules, or in combination, to observe their synergistic effects. Hence, these compounds may find application as antibacterial agents for use against various food-borne pathogens such as *Salmonella*, to help control the microbiological and physicochemical shelf life of food products and, in particular, porcine-based products.

### Acknowledgements

The MabS project is funded by the Irish Department of Agriculture, Food and the Marine under the Food Institutional Research Measure (FIRM 11/F/009). Contributions of Elaine Lawton and Lynn Naughton to the MabS project are acknowledged.

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