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Initial screening of marine bacterial extracts for antibiotic activity against a range of human pathogenic bacteria

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Introduction

As the number of bacterial human pathogens developing resistance to known antibiotics increases, it has become increasingly recognised that the marine environment may provide a new and richer source of chemical diversity with applications in drug discovery including new natural antibiotics and chemical leads. A screening programme was therefore initiated to assess the prevalence of antibiotic-like activity in the PML marine bacterial culture collection testing against a range of bacterial strains associated with human pathogenicity.

Methods

Plymouth Marine Laboratory houses an extensive collection of bacterial strains isolated from a variety of marine habitats, including the rocky shore, sediment samples and the water column. Initially 400 strains were grown for 5 and 15 days, then the bacterial cells were removed and concentrated extracts were produced from the spent media, using ion-exchange resin capture and solvent extraction. Each extract was tested for activity using a simple antibiotic disc diffusion test except for the organism *Mycobacterium marinum* which was screened against using liquid cultures. Extracts demonstrating antibiotic activity are being purified by HPLC and initial structural information is being determined by LC-MS analysis.



Fig 1: Zone of clearance in *A. iwoffii* lawn

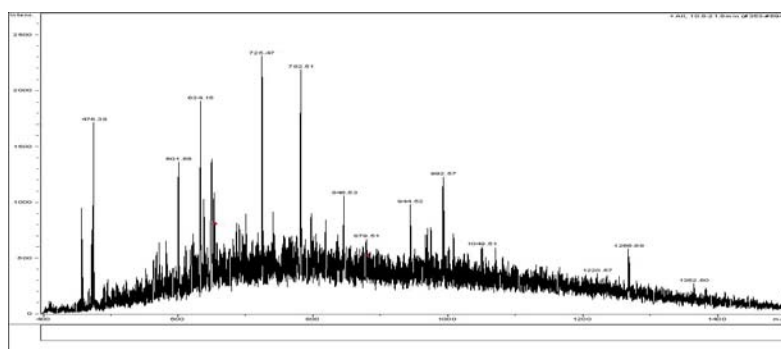


Fig 2: Early LC-MS analysis of an extract shown to exhibit antibiotic activity against a number of pathogens.

	R. S	Act 9	26	109	140	142	143	147	148	149	155	158	242b	572
<i>S. Aureus</i>	X		X		X	X	X	X	X	X	X	X	X	
<i>B. Cenocepacia</i>														
<i>B. Multivorans</i>														X
<i>S. Enterica</i>														
<i>A. iwoffii</i>										X				
<i>S. Pyogenes</i>														
<i>S. maltiphilia</i>	X		X		X	X	X	X	X	X		X		
<i>L. monocytogenes</i>														
<i>B. cereus</i>	X	X	X	X	X		X	X	X	X	X	X		
<i>M. marinum</i>					X		X					X		
<i>C. albicans</i>														

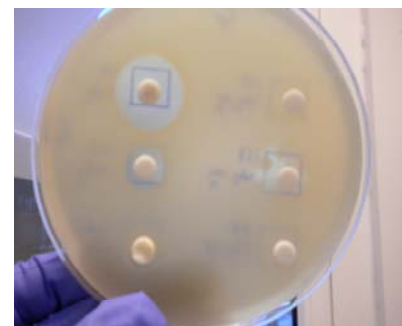


Fig 4: Testing a variety of compounds against *S. aureus* in order to determine which have antibiotic activity.

Fig 3: Table showing positive antibiotic results from Gram positive and Gram negative human pathogenic bacteria plus *Mycobacterium marinum*.

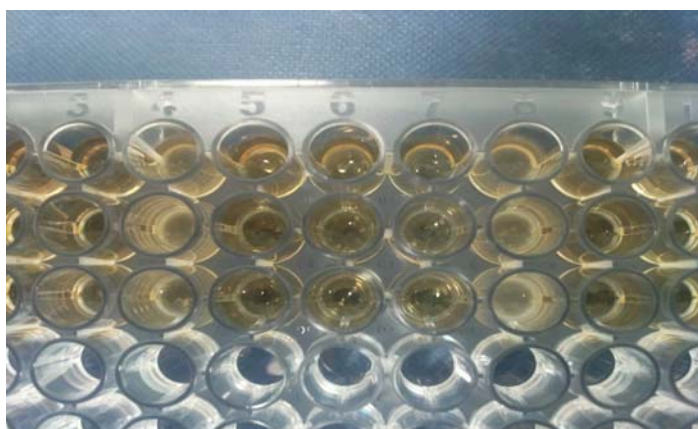


Fig 5: 96 well plate showing effect of increasing extract concentration on cultures of *M. marinum*. Complete inhibition of growth was observed at the higher concentrations.

Conclusion

Our initial results show there are numerous marine strains of bacteria (mainly *Streptomyces*) which have the ability to produce antibiotic compounds active against a range of bacteria but no anti-fungal activity (against *C. albicans*) has been detected to date. Table 1 shows that the most prevalent activities (9 extracts) are against the Gram positive strains *S. aureus* and *B. cereus* and the Gram negative strain *S. maltiphilia*. Interestingly, 3 of these extracts also show activity against the marine organism *Mycobacterium marinum*, a potential model organism for the discovery of anti-tuberculosis drugs. Further analysis to determine the full spectrum of activity against these model organisms using purified compounds is planned.