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Effects of halichlorine and pinnaic acid structural analogues on the enhancement of phagocytosis of methicillin resistant *Staphylococcus aureus* (MRSA) *via* U937 macrophages *in vitro*

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Inappropriate use of antibiotics has caused a global crisis in antibiotic resistance. Last line antibiotics are now becoming ineffective, resulting in inappropriate hospital stays and resource pressures. There is limited desire by pharmaceutical companies to develop new therapies due to the rapid rate of resistance. Natural marine environments are said to be an untouched reserve of medicinal products. Halichlorine and Pinnaic acid (HPA) have demonstrated anti-inflammatory properties however, their effect on phagocytosis is not yet known. Three structural analogues of HPA were assessed by an *in vitro* model of phagocytosis. Each HPA analogue differed in its structural composition and was identified using a unique coding system (HPA 17, 43, 44). Analogues were tested at two concentrations (10-4 M) and (10-5 M). U937 macrophages were treated with HPA analogues with (experiment 1) and without (experiment 2) inflammatory mediators (IFN-ɣ and LPS). A phagocytosis assay was used to assess the phagocytosis of MRSA colonies over a 3 hour period at 37°C. Bacterial recovery was determined by culturing samples onto nutrient agar. HPA analogues were found to significantly reduce MRSA recovery, suggesting enhanced phagocytosis in the presence (P=<0.015) and absence (P=<0.001) of inflammatory mediators. HPA analogue 43 was found to be the most effective at enhancing phagocytosis; demonstrating complete clearance of MRSA. To conclude, results suggests HPA analogues (particularly HPA 43) may be potential therapeutic alternatives to antibiotics in addressing the global crisis of antibiotic resistance. Replication of these results in animal/human clinical trials may lead to new therapeutic strategies that mediate the natural host response as an alternative to traditional antibiotics.

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