ABSTRACT

Isothermal Flow Microcalorimetric Investigation of Biological Activity and Determination of Thermokinetic Parameters for Two Novel Surfactant Series Containing Cobalt Cage Head Group

Amelia Trudy Boland

The continued emergence of resistant strains of microorganisms to antimicrobial agents in current use is a major concern to world health. Thus, there has been heightened interest in the discovery of new classes of antimicrobial agents and the development of fast reliable screening methods. In this study, the usefulness of flow through isothermal microcalorimetry (flow through IMC) to provide both biological activity and thermokinetic data, in the elucidation of the mechanism of action of potential antimicrobial agents, was investigated. Biological activity against *Saccharomyces cerevisiae* NCYC 239 and *Streptococcus mutans* NCTC 10832 of two novel homologous series of functionalized cobalt cage surfactants and two precursors in the synthetic route of the novel surfactants via flow through IMC is reported. The two homologous series of novel surfactants (C_{12} to C_{18}) tested against the microorganisms showed a parabolic relationship of activity vs. acyl chain length. The single acyl chain and the gemini novel surfactants, displayed optimum activity against the bacteria C_{14} and against the yeast C_{16} and $C_{14,}$ respectively. The two precursor series containing a benzyl group and a free amine group showed optimum activity against the yeast at C_{16}; against the bacteria at C_{16} and C_{18}, respectively. MIC vs LDR gradient map of the four series showed clustering of activity for the geminal surfactants in the bacterial membrane system. Clustering supports an identical mechanism for the members of the geminal surfactant series against the bacteria. Calibration of the flow-through IMC set up for the Setaram micro DSC III was successfully undertaken using the base-catalyzed hydrolysis of methyl paraben with ΔH = -48.8 ± 2.0 kJ mol-1 and k = 3.22 ± 0.35 x 10-4 s^{-1} showing good agreement with literature values. Thermo-kinetic treatment of the flow through IMC outputs of the biological activity of the metabolic modifiers with microorganisms showed the best fit kinetic model to be A → B→ C via residual plot analysis as opposed to simple A→B mechanism as previously reported. Thermokinetic data indicate non-detergent like behavior for the two series of Co-cage surfactants.

Keywords: biological activity, isothermal microcalorimetry, MIC, surfactants, *Saccharomyces cerevisiae*, *Streptococcus mutans*, Setaram microDSC III, methyl paraben, kinetic, thermodynamic