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# A Trojan Horse strategy for the delivery of biologicals

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**Background:** Glycoside hydrolases have emerged as potent, novel therapeutics that can disrupt biofilms, thereby increasing the susceptibility of the residing bacteria to co-administered antibiotics. The broader clinical use of glycoside hydrolases such as alginate lyase (AL) is limited due to challenges in maintaining enzyme stability, adequate delivery and release of the enzyme at the site of infection. Herein, we present a Trojan horse carrier for AL using environment-sensing lyotropic liquid crystalline gels (LLC).

**Aim:** The aim of this study was to design a LLC-gel carrier based on the lipid glycerol monooleate to protect, deliver and release AL in combination with the antibiotic gentamicin (GENT) as a novel anti-biofilm strategy.

**Methods:** The effect of *Pseudomonas* lipase on the release of AL/GENT from LLC-gels was evaluated and the efficacy of the gel was determined over 1 week *in vitro* against biofilms formed by alginate producing P. aeruginosa (clinical isolate) and compared to an unformulated simple drug solution. Finally, the stability of AL after fabrication of the LLC gel was assessed.

**Results:** GENT and AL were released at different rates and extent from the LLC-gels (10% AL over nine days; 60% GENT over two days, respectively). Addition of Pseudomonas lipase increased AL release >2-fold (20-30% within two days). The LLC-gel demonstrated similar anti-biofilm activity (2.5 log reduction in CFU) compared to unformulated solution, confirming preservation of AL activity in the LLC-gels. Interestingly the antimicrobial effect could not be sustained over extended period (>2 days) which was attributed to a gradual loss of AL activity from prolonged exposure to 37°C during the assay, rather than short exposure to higher temperatures (60°C) during LLC-gel fabrication.

## Biography

Nicky Thomas is an NHMRC Research Fellow at the School of Pharmacy and Medical Sciences, University of South Australia and is working in the Professor Clive Prestige's group. He is a trained Pharmacist with several years of experience in both hospital and community pharmacies. In 2012, he has been awarded his PhD in Pharmaceutical Sciences from the University of Otago, New Zealand. His PhD research was concerned with the development and *in vitro* and *in vivo* characterization of nano emulsions for drug delivery. He has joined UniSA in 2012 to work on novel treatments against bacterial biofilms. Building on his expertise in nanomedicine-based drug delivery systems he has been awarded an NHMRC Early Career Researcher Fellowship in 2014 for the investigation on the interaction of antimicrobial therapies with bacterial biofilms. In 2017, he established the Adelaide Biofilm Test Facility at UniSA's Sansom Institute for Health Research, SA's first facility dedicated to test antimicrobials and pharmaceutical products in a range of *in vitro* and *in vivo* biofilm models. His main area of research is anti-infective treatment options against biofilms; oral drug delivery and lipid-based drug delivery.

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