

Bath Monash Global PhD Programme in Sustainable Chemical Technologies

Project Title:	New bismuth-based biopolymer composites for challenging anti-microbial resistance
Supervisor at Bath:	Professor Toby Jenkins
Supervisors at Monash:	Professor Phil Andrews (lead) and Associate Professor Warren Bachelor
Home Institution:	Monash University
Indicative period at Host Institution:	12 months with exact dates to be confirmed

Project Summary

There is a steady and significant increase in microbial resistance to common antibiotics, and in fact many bacteria are now multi-drug resistant, for example *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. This is primarily of great concern in medical and healthcare environments where it impacts directly on human health. However, it also demands the continual development of effective bactericidal compounds capable of combating increasing antibiotic resistance.

Bismuth compounds show good antimicrobial activity, and are of low toxicity towards humans. This has led to increasing interest in bismuth and its potential applications in materials, medicine and bio-protective surfaces. Because of the way bacteria develop resistance, through mutation and evolution, it is easier for them to adapt to fully organic molecules than to those based on metals. There is no simple mechanism by which organisms can develop resistance to metal complexes. As such, there is great potential in the development of metal based antibiotics for both chemotherapeutic purposes and in generating antimicrobial materials.

The majority of antimicrobial polymers and materials currently used in healthcare facilities (silicones, plastics (eg polyurethane) or natural fibres e.g. linen (cellulose)) incorporate either Ag(I) ions or nanoparticulate silver (AgNPs). Other metals; Au, Cu, Ga, Sn and Zn, are components of current commercial antimicrobial products, and remain a major focus of ongoing research, particularly in nanotechnology where the formation of antibacterial nanoparticles and nanomaterials appears a promising strategy, and also in abiotic metal-impregnated surfaces.

The predominance of silver in broad-spectrum antimicrobial materials has generated significant interest recently, primarily over concerns around toxicity and environmental accumulation. Especially since little is known about the mechanism-of-action of silver ions and nanoparticles towards biological entities. There is also evidence that because of the long association of silver and human societies that bacterial strains resistant to silver are emerging and research is beginning to shed light on the adverse effects of increased exposure of humans and the environment to the large increase in the amount of bioavailable silver. Hence, opinion remains divided on whether silver antimicrobial products are generally safe and can be used into the future. This risk means the commercial market is actively looking at new and safer alternatives.

This project is focused on the development of bismuth impregnated materials which have the potential to be used as anti-infectives in wound management. It will involve the design and development of novel metal complexes which exhibit low micro- to nano-molar activity towards both Gram positive and Gram negative multi drug resistant bacteria. These complexes will be introduced into bio-compatible biopolymer matrices, for example nano-cellulose, silk, and soluble lignin, and will be used to fabricate or coat wound dressings and

implants. A second feature of the project will be to develop materials based on hydrogels (using for example cellulose or acrylamides) which can be used for securing a pathogen free environment around drivelines and skin openings.

At Monash the student will design, synthesise and fully characterize bismuth(III) complexes with a range of chemical and physical properties which allow them to be used as additives in polymer matrices and in hydrogels. The complexes and new materials will be studied for their antimicrobial activity, especially towards multi-drug resistant bacteria, using typical in vitro assays. These will be compared with routine toxicology assays on mammalian cell to establish selectivity indices.

The physical and biological properties of the composite materials will be studied for their suitability for application in wound dressing and management, and for coating of medicinal devices (e.g. catheters).

At Bath the student would make prototype wound dressings from materials made at Monash, and these would be tested on ex-vivo mixed species bacterial biofilm models, including pig skin and polycarbonate membrane systems. In addition, the student would look at integrating the infection diagnostic technology based on lipid vesicles (see <https://smartwound.co.uk/smartwound>) with the antimicrobial films to create a dressing prototype which alerts the patient / clinician to when the antimicrobial release system is no longer effectively controlling bacterial growth.