Stereoisomerism of antimicrobial agents and risks to freshwater ecosystems

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This project is one of a number that are in competition for funding from the NERC Centre for Doctoral Training in Freshwater Biosciences and Sustainability (GW4 FRESH CDT) which is offering 12 studentships for entry in September/October 2019.

Full Project Description

This FRESH CDT studentship will focus on understanding of the impact stereoisomerism of AAs might have on biological effects linked with ecotoxicity and the development of AMR in freshwater ecosystems. We will focus on two critical hotspots linking human activities with the environment: (i) wastewater treatment (incl. activated sludge, trickling filters as well as anaerobic digestion to account for different process related physicochemical conditions as well as prevalence of certain microbial communities, and (ii) receiving aqueous environment. The project will address above via the three main objectives:

Objective 1. To understand the mechanisms of transformation of chiral antimicrobial agents in the environment at both nanocosm, microcosm and macrocosm scale.

Objective 2. To verify how stereoselective processes of AAs in the environment are associated with the higher prevalence of specific resistant strains of bacteria.

Objective 3. To undertake environmental risk assessment of AAs in the Avon Catchment.

We will study (stereoselective) transformation of selected antibiotics, antifungal agents (incl.synthetic quinolones, β-lactams, and carbapenems, azole antifungal agents as individual stereoisomers and in mixtures) in wastewater and receiving waters at both nanocosm (lab-based experiments) and macrocosm (the Avon Catchment, sites identified by Wessex Water) scale with the usage of state-of-the-art chiral liquid chromatography coupled with (high resolution) tandem mass spectrometry (chiral-LCMS): sensitive triple quadrupole (Xevo TQD, Waters) for targeted analysis or accurate QTOF (Bruker) for screening of unknowns. (Resistant) bacterial taxa will be identified (before and after exposure to individual stereoisomers and their mixtures) with the usage of dPCR and sequencing. We will focus mainly on sludge and river water derived microorganisms. Both isolated strains exposed to different stereoisomers of AAs as well as mixed communities in WWTP and river microcosms will be studied.

The research student will receive training in a range of modern analytical and bioanalytical techniques including state-of-the-art chromatography coupled with tandem mass spectrometry techniques, digital PCR technology and bioassays. In addition, he/she will work with the leading water utility company in the UK, Wessex Water as well as leading pharmaceutical company, Astra Zeneca. Furthermore, he/she will join interdisciplinary teams at the University of Bath, and Exeter with substantial research expertise in the area and excellent research infrastructure. Experience of academic / industrial research, interdisciplinary and international working and development of legislation and water policy, will provide an exciting opportunity for further professional development.

Real Life challenges this project will address

Water security, deteriorating ecosystem health and population growth/urbanisation affecting the natural environment. Stricter regulation of antibiotics in the environment is envisaged. The European Commission has recently proposed an inclusion of antibiotics on the Watch List under the Water Framework Directive. Antibiotics are also key targets within UKWIR National Chemical Investigation Programme. A full understanding of the fate and effects of antibiotics is therefore of crucial importance to the water and pharmaceutical sectors represented in this project by Wessex Water and Astra Zeneca.

What you should know about this project

Water pollution is a problem of multi-dimensional nature and here we establish an interdisciplinary studentship project proposal interfacing with environmental/water science, chemistry, microbial ecology, bioanalytical science and water engineering to understand the role antimicrobial agents play in freshwater ecosystems. All academic and industrial supervisors are experienced researchers with skills required to effectively guide the project

What expertise you will develop

1. Expertise in advanced bioanalytical techniques
2. Skills in ecotoxicology, microbial ecology, environmental and water sciences
3. Operational understanding of the UK water industry and regulatory systems.

Why this project is novel

The risk of promotion of antibiotic resistant bacteria is the greatest human health concern with regards to medicinal products. The continuous introduction of sub-inhibitory quantities of antimicrobial agents (AAs) to the environment is directly linked with antimicrobial resistance (AMR). Unfortunately, there is little understanding of mechanisms due to the multi-dimensional nature of the AMR problem. Surprisingly, the environmental fate and biological effects of AAs are assessed without considering their stereoisomeric forms (this is despite our knowledge on isomer dependent toxicity, taking thalidomide as a prime example). Such an approach leads to the incorrect verification of biological effects of AAs and direct risk to the environment and human health. This FRESH DTP studentship proposal emerged from our NERC 'AMR in the real world' pump priming project (NE/N019261/1) with Wessex Water (WW) and Environment Agency as Project Partners and existing collaboration with Astra Zeneca. NE/N019261/1 aimed to understand the impact of stereoisomerism of antimicrobial agents (AAs) in their environmental cycle on mechanisms behind the development of antimicrobial resistance (AMR) in environmental hotspots. It confirmed our hypothesis that different stereoisomers of AAs have different environmental fate, hence potentially different ability to impact the development of AMR, a phenomenon that has never been the subject of investigation before. Therefore, the role of stereochemistry of antimicrobial agents in the aquatic environment in the context of their biological potency and risks to freshwater ecosystems requires urgent attention and further study.

Funding

Studentships cover Home tuition fees, training support grant and stipend (£14,777 p/a, 2018/19 rate) for a period of 3.5 years and are open to UK/EU applicants who have been resident in the UK since September 2016.

Applications

Applicants must have obtained, or be about to obtain, a First or Upper Second Class Honours degree, or the equivalent qualifications gained outside the UK, in an area appropriate to the skills requirements of the project.

Applications should be made direct to the CDT using their online application form. See http://www.gw4fresh.co.uk/how-to-apply/doctoral-students/.

APPLICATIONS CLOSE AT 09:00 ON 17 DECEMBER 2018.

You do NOT need to apply to the University of Bath at this stage – only those applicants who are successful in obtaining an offer of funding from the CDT will be required to submit an application to study at Bath.