Institution: Robert Gordon University		
Unit of Assessment: 12. Engineering		
Title of case study: Environmental Engineering: Mitigating Blue-Green Algal Blooms and their Toxins		
Period when the underpinning research was undertaken: 2000 - present		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Linda A Lawton Christine Edwards	Professor Professor	1994 – to date 2004 – to date
Period when the claimed impact occurred: since 2015		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact (indicative maximum 100 words)

Research at Robert Gordon University has led to advancement in drinking water quality worldwide. Focussing on the ubiquitous problem of cyanobacteria (blue-green algae) and their highly toxic metabolites, cyanotoxins (toxins that contaminate drinking water and have both chronic and acute health effects), the research has supported the development of World Health Organisation (WHO) guidelines, underpinned international detection methods and water treatment strategies. Our in-house algal biotechnology generates the world's largest supply of cyanotoxins (17 individual toxins, c. 50 products) (transfer price>£2 million since 2009) used by stakeholders worldwide establishing and maintaining monitoring programmes, optimising water treatment and establishing health benefits.

2. Underpinning research (indicative maximum 500 words)

Cyanobacteria and their toxins in drinking water can affect animals and humans, potentially causing significant chronic diseases.

Lawton established RGU as a world-leader in developing effective solutions to the challenges of cyanotoxins in drinking water, being the first to employ novel technologies to mitigate the impact of these pollutants using advanced oxidative methods. The pioneering work was founded on successes in the large-scale biotechnological production of cyanotoxins and other bioactive compounds from cyanobacteria.

This research included innovative methods of detecting and eliminating toxins in drinking water and reservoirs using cutting-edge photocatalysis and nature-based solutions that benefitted single household supplies in Low and Middle Income Countries (LMICs). Combining elements from biotechnology, environmental biology and applied engineering, the team developed practical engineered solutions with low running costs and sustainable components.

Production and detection of cyanotoxins

RGU's state-of-the-art facilities for algal/cyanobacterial production, down-stream processing and supporting analytics are essential to facilitate research and sustainable revenue. The work resulted in the development of in-house large-scale production systems currently growing a range of toxic cyanobacterial strains (1200 L per month), with integrated harvesting and down-stream processing systems. The extraction of compounds from biomass has maximised the yield of a wide range of chemically diverse cyanotoxins[1]. Bioactive compounds such as the hepatotoxic microcystins are purified (95-99% purity) by high-performance flash chromatography and preparative high-performance liquid chromatography (HPLC). Throughout the production process, purity and concentration are determined by a suite of analytical methods[2]. These features allow the bespoke production of bulk purified compounds, key to developing cost-effective mitigation strategies (oxidative methods and biodegradation). An example of a prohibitively expensive alternative is the cyanotoxin cylindrospermopsin, which retails at £1,396 per mg. Without RGU's bespoke in-house production stream, the preliminary work on the understanding of photocatalytic microcystin removal from water would be impossible.

Advanced oxidation for cyanotoxin removal

The team pioneered the use of advanced oxidation processes using semi-conductor titanium dioxide (TiO_2) for the photocatalytic destruction of microcystins in water[3], thereby eliminating toxicity. TiO_2 acts as a catalyst of high-energy radicals, destroying organic compounds. The destruction of toxins ensures that they can neither be re-released (as seen with adsorptive technologies like granular activated carbon) and no toxic by-products are released (as seen with chlorination). By exploring the mechanisms involved in photocatalysis, the research confirmed the identity of the less toxic by-products produced and demonstrated their subsequent destruction[4], paving the way for engineering treatment systems deployed in Fortaleza, Brazil.

Nature-based cyanotoxin removal

Microbial remediation can also be an efficient, low-cost way of pollutant removal, and allows the use of a nature-based solution to address cyanotoxins in drinking water. Our work evidenced that microbial communities in all aquatic ecosystems were able to degrade microcystins[5]. Further studies led to isolation of novel biodegrading bacteria, highlighting broader microbial diversity than previously reported[6].

This expertise has led to new collaborations and funding, including £1,18 million (BBSRC/NERC Safe and Sustainable shellfish consortium grant) plus a further £250,000 from industry 2018-2021, and £160,000 from KTP with Scottish Bioenergy on valorisation of algal material 2018-2020.

3. **References to the research** (indicative maximum of six references)

[1] Optimization of intracellular microcystin extraction for their subsequent analysis by high-performance liquid chromatography
M Barco, LA Lawton, J Rivera, J Caixach - Journal of chromatography A, 2005 Cited by 101

[2] Purification of microcystins
LA Lawton, C Edwards - Journal of chromatography A, 2001
Cited by 145

[3] Hydrogen peroxide enhanced photocatalytic oxidation of microcystin-LR using titanium dioxide

BJPA Cornish, LA Lawton, PKJ Robertson - Applied Catalysis B: Environmental, 2000
Cited by 274

[4] Mechanistic studies of the photocatalytic oxidation of microcystin-LR: an investigation of byproducts of the decomposition process
I Liu, LA Lawton, PKJ Robertson - Environmental science & technology, 2003
Cited by 173

[5] Edwards, C., Graham, D., Fowler, N. and Lawton, L.A. (2008) Biodegradation of microcystins and nodularin in freshwaters. Chemosphere, 78, 1315-1321 -cited by 142.

[6] Isolation and identification of novel microcystin-degrading bacteriaIsolation and identification of novel microcystin-degrading bacteria
PM Manage, C Edwards, BK Singh, LA Lawton - Applied and Environmental Microbiology, 2009
Cited by 172

KEY FUNDING

- **£900,000 EU FW5** - Photocatalytic Destruction of Cyanotoxins and Pathogens, 2000-2003
- **£202,137 BBSRC** project - Molecular evolution approach for the affinity maturation of anti-microcystin antibodies from phage display libraries. 2001-2004
- **£250,000** Alexis Corporation, Switzerland. Isolation of cyanotoxins 2004-2009
- **£480,000** Enzo Life Sciences (formerly Alexis Corp), Switzerland. Isolation of Bioactive compounds from cyanobacteria 2009-2013

4. Details of the impact (indicative maximum 750 words)

Cyanobacteria and their toxins in water supplies pose a threat to human and animal health globally. Cyanobacterial blooms are on the increase due to eutrophication (nutrient enrichment, especially with nitrate and phosphate) and global warming. Studies have demonstrated that at least 50% of blooms produce cyanotoxins and their occurrence has been linked to ill-health and fatalities.

Compound production and analysis

RGU's in-house production of cyanotoxins has expanded the portfolio of commercially available bioactive compounds resulting in funding of £1.5 million from Enzo Life Sciences since 2013[S1,S2] .These compounds are used by regulators such as the US EPA, medical research and water treatment facilities worldwide. The extensive use of these cyanotoxins is evidenced by widespread literature. American Chemical Society Journals indicates 37% used cyanotoxins are from Enzo Life Sciences (or Alexis, as previous known) since 2013, and Science Direct indicated 30% product use.

The work with these high-value chemicals has underpinned successful KTP funded collaborations. The first, *Combined metabolomics-genomics workflow to enhance natural product discovery (*2016-19) with NCIMB[S3] aimed to enhance the value of the culture collection. The second, *Valorisation of algal biomass* (2019-21), with the biotech company ScotBio[S4], involved applying product analysis and composition. A further IBioIC funded collaboration linked the work of Xanthella, a leading biotech company, with the Scottish

Whisky industry to explore valorisation (transformation of waste into useful resource) of co-products for both algal growth and bioplastics.

Influencing policy and standards

This research has influenced guidelines, standards and good practice in managing cyanotoxin exposure. Lawton has worked with and advised the WHO in the publication of their "Toxic Cyanobacteria in Water - A Guide to their Public Health Consequences, Monitoring and Management" – both first (1999) and second edition (Feb 2021)[S5]. She has also supported the revision of WHO global guidelines on exposure to microcystins and other classes of cyanotoxins (hepatotoxin cylindrospermopsin, neurotoxins anatoxins and saxitoxins). Lawton is currently an expert advisor to the UK government's Centre for Environment, Fisheries and Aquaculture Science (CEFAS), sitting on their Scientific Advisory Committee with specific expertise for toxin analysis.

Working with the EU, the team has contributed to new standard methods for the analysis of cyanobacterial metabolites which cause problems through taste and odour.

Advanced oxidation for cyanotoxin removal

This pioneering research on the use TiO_2 for photocatalytic treatment of cyanotoxin contaminated water has benefitted global water treatment solutions with pilot treatment systems being evaluated by RGU researchers and others. Water resource managers and drinking water treatment providers are currently evaluating the efficacy of this technology at scale[S6,S7].

Building on the development and understanding of photocatalysis, Lawton secured £1.2 million[S9] in funding that resulted in the development and application of a novel photocatalytic rig for removal of cyanobacteria and their toxins at scale.

Nature-based cyanotoxin removal

The work on the biodegradation of cyanotoxins has informed practice both in water treatment and sample processing (as biodegradation will affect the quantity of toxin available).

Knowledge Transfer and Capacity Building

Collaboration with Pathmalal M. Manage, University of Sri Jayewadenpura, Sri Lanka, facilitated the development of a national centre of excellence as the Centre for Water Quality and Algae Research[S8], supporting the national water company.

Funded by the National Science Foundation the research investigated the role of cyanotoxins in chronic kidney disease, along with the publication of an easy to use training manual for analysis of cyanotoxins. This collaboration led to funding to translate research into a practical solution for safe water treatment in-line with the UN Sustainable Goal 6.1.

Further work by the RGU team proposed developing a scalable bio-based strategy for eliminating cyanotoxins in drinking water in Sri Lanka. Their Global Challenges Research Funding (GCRF) application was ranked top out of 31 projects submitted for funding.

The research addressed rising levels of kidney disease in Sri Lanka which were attributed to water contamination from significant cell densities of cyanobacteria and toxin concentrations in excess of WHO guidelines in drinking water suplly wells. RGU's research explored the link between the algal toxins in the well water and the kidney disease found in humans. The project also aimed to improve the quality of the well water, making it safer for consumption by removing harmful compounds. The team collaborated with the National Drainage Company in Sri Lanka to apply its work on a larger scale, which could improve the health and environment of other developing countries. Lawton and another RGU researcher were awarded fellowships from the University of Sri Jayewardenepura, in honour of their ongoing efforts to build research capacity, capability and quality in Sri Lanka.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[S1] Letter from industrial collaborators **Enzo Life Sciences**
[S2] Microcystin product listing - https://www.enzolifesciences.com/platforms/small-molecule-chemistry/natural-products-antibiotics/microcystins-toxins-from-cyanobacteria/
[S3] KTP with NCIMB https://www.ncimb.com/uncategorized/ncimb-and-rgu-kick-off-new-streptomyces-screening-project/
[S4] KTP Scotbio https://scotbio.com/academic-collaboration - Replace with letter from Polly if possible
[S5] Advising WHO on cyanotoxin analysis:
https://www.taylorfrancis.com/chapters/laboratory-analysis-cyanobacterial-toxins-bioassays-linda-lawton-james-metcalf-bojana-žegura-ralf-junek-martin-welker-andrea-törökné-luděk-bláha/e/10.1201/9781003081449-14?context=ubx&refId=acbb4fc7-79c2-445d-85d6-c138594bc66b
[S6] Letter from Water company Brazil
[S7] Letter from Reservoir Management company Brazil

[S8] Video: Our second training visit to Sri Lanka where we have supported the establishment of the centre for Water Quality and Algal Research.
http://research.sjp.ac.lk/cwar/projects/

[S9] https://gow.epsrc.ukri.org/NGBOViewGrant.aspx?GrantRef=EP/P029280/1