Chemistry in New Zealand

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Carbohydrate catalysis:

The biochemistry of enzymes in honey

Photo credit: mostafa eissa on Pexels.com *(https://www.pexels.com/photo/swarm-of-bees-3424406/)*

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Chemistry in New Zealand

Volume 87, No.2, APRIL 2023

Articles and features

Other columns

Comment from the President

Tēnā koutou katoa.

As I write this, our news is filled with details of the ravages caused by Cyclone Gabrielle. To all our members who have been affected personally, professionally or through whanau, we send you our best wishes in recovering from the flooding, loss of electricity and trauma. Kia kaha! Certainly, evidence for climate change is all around us these days. As scientists, we are used to weighing up evidence, employing models to simplify the complexities of nature and factually communicating the outcomes resulting from our studies. It can be surprising if others are not on the same page. We need to address the challenges of these times in ways appropriate to our audience.

I also want to acknowledge chemists who have been impacted by job cuts. This causes great personal distress for those who have lost their jobs and affects those who remain, with fewer staff to maintain function. Job losses in STEM areas reduce our ability to function as a modern, educated, technologically underpinned society, which is sorely needed for the NZ economy to weather the current and future storms.

The emergence of ChatGPT, and other AI communication tools, is exercising those of us who are in the education sector. On the positive side, such functionality can help students and educators produce (generally) well-phrased written material in an efficienct manner. For example, this is what ChatGPT had to say when I asked about the benefits of AI tools for educators:

"*AI tools... can help to quickly generate ideas and content for educational materials, saving educators valuable time and effort. AI tools can assist in researching relevant literature and compiling data, which can be time-consuming if done manually. They can also assist with grammar and spelling checks, which can help ensure that educational materials are high-quality and professional. AI tools can be used to tailor educational materials to the needs of individual learners, including personalized feedback and assessments, as well as adaptive learning programs that adjust to individual learning styles and abilities. Additionally, AI tools can help to create more accessible educational materials, such as text-to-speech functions for visually impaired learners or translation functions for non-native speakers. Finally, AI tools can help create educational materials that are scalable and can be easily adapted to meet the needs of larger audiences, including the use of chatbots or virtual assistants to provide support and guidance to learners at scale.*"

"The emergence of ChatGPT, and other AI communication tools, is exercising those of us who are in the education sector."

ChatGPT produced this in a fraction of the time I would have taken to formulate those ideas and get them onto the page and, in my opinion, did a pretty good job. This was ChatGPT's second pass at the subject and might improve upon further refinement of my prompts.

There are significant ethical problems arising when using this tool to produce written work that we claim as our own. For education, this is creating challenges for assessment of written work (and other creative exercises), leading educators around the world to test out new ways of assessing work, including embracing the positive aspects of AI tools. In the research arena, journals are developing different approaches to AI content, from those forbidding any use of AI to those allowing writing that has AI input as long as the extent is described and acknowledged. Journalism, legal and other sectors are also grappling with the implications of this technology.

On the horizon for NZIC, we have a new-look online format for our journal *Chemistry in New Zealand* under development. A working group headed by Vyacheslav Filichev (Manawatu) has been planning the transition to a fully online journal with click-through and interactive functionality. We hope it will be in place by the end of this year and look forward to engaging more strongly with the community through this.

For your calendars, please note that the next NZIC conference will be in 2024, hosted by Otago Branch. Exact dates and location are under discussion so watch this space! Additionally, Pacifichem will be back as a fully in-person congress in Hawaii in December 2025 – there are some further details in this issue. Pacifichem runs as a series of overlapping symposia, most on highly specific areas of chemistry, and the scientific programme for each is organised by a team from at least three different chemical societies. Now is the time to be considering whether you could co-organise a symposium and/or be a topic reviewer. Mark Waterland, our Pacifichem rep, is on the lookout for reviewers. Having New Zealand-based symposium co-organisers is likely to attract more NZIC members and raise our profile. NZIC benefits financially from any members who attend, so the more, the merrier!

A reminder that NZIC also benefits financially from members publishing in the Royal Society of Chemistry journal *Phys. Chem. Chem. Phys.* and the Asian Chemical Editorial Society (ACES)/Wiley journals *Chemistry – an Asian Journal*, *Asian Journal of Organic Chemistry* and *ChemNanoMat*. Do consider submitting research articles to these quality international journals.

Finally, we are seeking a new Treasurer for NZIC. Our current treasurer, Hamish McDonald (Hon. FNZIC), has indicated his intention to retire from this position. We are incredibly fortunate to have benefitted from his financial expertise, wisdom and initiative over the past 4+ years. He led our transition to Xero's financial service and improvement in our accounting and auditing compliance, as well as delivering vision, insight and experience to the Executive group of NZIC, while also maintaining the accounts. Hamish has done all this voluntarily and from Australia – immense gratitude and thanks for such commitment to NZIC! We are looking for someone to fill this important role moving forward. Please get in contact with Samantha at nzic.office@gmail.com if you would like to know more, register your interest, or nominate someone.

Nāku noa, nā
Joanne

Letter to the editor

Vyacheslav Filichev's article, Chemistry in New Zealand at your fingertips: results of a reader survey and future direction of the journal *(Chemistry in New Zealand*, **2022**, *86(4), 178-181)*, took me back nearly 50 years to when an Auckland school teacher asked me if the NZIC could help teachers by making available information on chemical processes in New Zealand.

The result of this was the production of *Chemical Processes in New Zealand* in 1978, followed by a second smaller volume in 1988, and then a second two volume edition with 101 articles in 1998 (this is still on the NZIC website and the master copy from which this was printed is in the NZIC archives). A 1940 NZIC publication, *Chemistry in the Development of New Zealand Industry 1940*, is the last article of the 2nd edition.

It is now 25 years since this 2nd edition was produced. I think from memory we managed to give a copy of this 2nd edition to every secondary school in New Zealand. From a historical viewpoint it is the most comprehensive account of New Zealand's chemical history.

I would like to suggest that SCENZ consider whether starting on a 3rd edition would be a good idea. Most of the 122 contributors to the second edition will have either retired or died so a new team would have to be found! New or revised articles could be published on the NZIC website as they are produced.

John Packer
Editor, *Chemical Processes in New Zealand*, 1978-98
(email: j.packer384@gmail.com)

NEWS

CANTERBURY

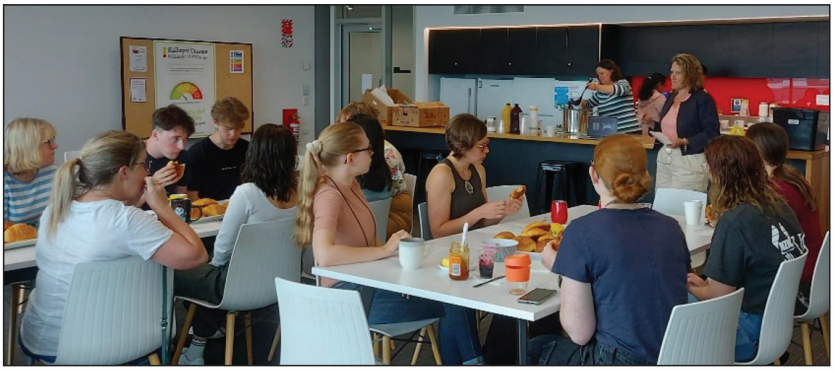
NEWS

The Canterbury branch has been playing catch up with events that were postponed due to Covid in 2022. Canterbury was particularly affected in November and December last year.

The 2022 AGM was finally held on 8 December and, as part of the proceedings, we were delighted to have Professor Dame Juliet Gerrard give her talk, "A front row seat – science advice in emergencies" which had been postponed numerous times during the year.

On 2 February we were able to host Associate Professor Michael Mucalo in person to give his 2022 President's talk.

14 February saw 31 attendees at the IUPAC Global Women's Breakfast. Professor Richard Hartshorn welcomed everyone by zoom from Auckland where he was stranded by Cyclone Gabrielle. The cyclone also meant that we were unable to liaise with any other branches for this event. Professor Catherine Moran, Deputy Vice-Chancellor - Academic, talked about her journey in science which was entertaining and thought provoking and engendered a good discussion.



Professor Catherine Moran addresses the Global Women's Breakfast event.

Chemistry Prize Winners 2022	
NZIC Prize (best overall 200-level grades)	Emily Tobbell and Adam Nolan
Haydon Prize – Chemistry (outstanding 300-level grades)	Finlay Player
Ralph H Earle Jnr Seminar Prize (best 2nd year PhD seminar)	Brooke Matthews
C E Fenwick Prizes in Chemistry (outstanding 400 grades)	Daniel Chong
C E Fenwick Prizes in Chemistry (best 400-level demonstrator)	Jude Kalan
Cuth J Wilkins Prize (top MSc thesis student)	Michael Hutton
Dr Gregory S C Hii Prize in Organic Chemistry	Toby McDonald
Jack Fergusson Prize (excellence in 300-level chemistry laboratories)	Finlay Player
Professor Jim Coxon Graduate Prize in Chemistry	Alexandra Aves

CONGRATULATIONS

■ We are delighted that Sarah Masters was promoted to Professor at the end of 2022.

■ **Congratulations to the following on their successful PhD completions:**

Lily Hermanspahn: "Synthesis of functionalised supramolecular assemblies" supervised by Professor Paul Kruger.

Nathan Harvey-Reid: "Design and synthesis of novel hybrid ultramicroporous materials for selective gas capture and separation" supervised by Professor Paul Kruger.

Pratik Solanki: "Lanthanide-doped potassium yttrium fluoride nanoparticles: spectroscopy, thermometry and crystal field analyses" supervised by Professor Jon-Paul Wells and Professor Mike Reid.

Sarah Masters.

Zach Stueven: "Synthesis and biological applications of anti-tuberculosis compounds" supervised by Professor Rudi Marquez.

■ Congratulations to Michele Klein (supervised by Dr Jodie Johnston) who won the student communicator prize at the recent New Zealand Institute of Chemistry conference in Auckland.

■ Congratulations to Rifana Irfan (supervised by Professor Sarah Masters) and Joel Schuurman (supervised by Dr Paula Brooksby) who won prizes at the Materials Cluster conference held at the University of Canterbury in December 2022. This is a particular achievement for Rifana who is an offshore doctoral student and presented remotely at the conference.

■ MANAWATU

NEWS

In staffing news, we welcome a new lecturer in chemistry, Dr Tyson Dais. Tyson will be working with magnetic materials having recently completed his PhD.

We also would like to acknowledge the departure of Professor Paul Plieger and Dr Karen Lyons. Paul has resigned to take up a management position at the Fonterra Research and Development centre while Karen, following 19 years of service to Massey University, has earned herself a well-deserved retirement.

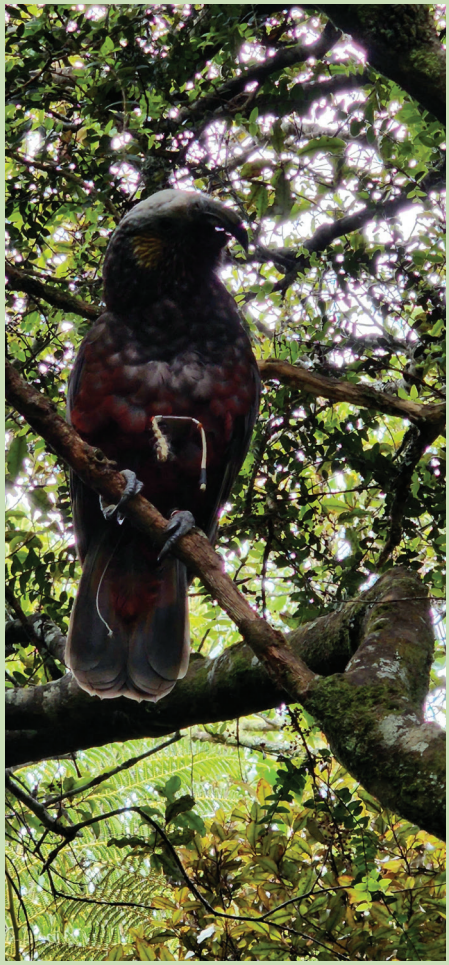
■ Shivangi Chourasia has joined the Whitby group as a PhD student and will be working on a project entitled, "Reconfigurable Pickering emulsions."

■ Mohana Arul has joined the Telfer group as a PhD student and will be working on multicomponent metal-organic frameworks (MOFs).

■ Victoria-Jayne Scott has completed her MSc entitled, "Isophthalic acid derivative metal-organic frameworks for gas capture and separation" supervised by Professor Shane Telfer.

Between 21-24 November 2022 six members of the Manawatū branch attended the NZIC conference held in Auckland. Attendees included members from the Filichev, Plieger, Rowlands and Whitby groups.

On behalf of the Nucleic Acid Chemical Biology group working on APOBEC3 inhibitors, Emeritus Professor Geoffrey B. Jameson was invited to present at the 4th International Conference on Base Editing Enzymes and Applications - Deaminet 2023 held in Palm Springs, California (22-24 January 2023). The talk was devoted to "Structural basis of modified DNA inhibitors that competitively restrict DNA-editing activity of APOBEC3A."



UNIVERSITY OF OTAGO, DEPARTMENT OF CHEMISTRY

Plant & Food Research (PFR) is running nationwide networking for early Natural products chemistry at Orokonui.

Nigel Perry presented to science teachers attending the Otago University Advanced School Sciences Academy on "Taonga natural products: mātauranga Māori and chemistry."

This was run at Orokonui Ecosanctuary in combination with a walk to look at the plants mentioned and others, led by the excellent science communicator Taylor Davies-Colley. A highlight for Nigel was seeing the many kaka there up close – one is photographed here, shedding a tracking device!

■ OTAGO

UNIVERSITY OF OTAGO, DEPARTMENT OF CHEMISTRY

NEWS

Gordon Group

■ Congratulations to Fatema Ahmmed who graduated with her PhD in December 2022 and is now working with the Riddet Institute in Palmerston North. Fatema's PhD covered analytical spectroscopy including data fusion-based chemometrics on aquaculture samples.

■ Sara Fraser, Sam Harris and Keith Gordon attended the NZIC conference in Auckland. Sam presented

his Honours work on twisted excited states which he published late last year (https://doi.org/10.1021/acs.jpca.2c03380). Sara talked about her work on detecting disease using multimodal spectroscopic techniques (https://doi.org/10.1021/acs.analchem.0c04963) and shared Fatema's research project on detecting adulteration of marine derived edible oils (https://doi.org/10.3390/molecules27144534). Keith presented a talk on spatially offset low frequency Raman spectroscopy in which subsample materials may be analysed non-destructively (https://doi.org/10.1021/acs.cgd.1c01401) and also presented some work on long-lived excited states.

Sara was presented with the ACES Early Career Award from the NZIC recognising her excellent research record.

■ Jeremy Rooney presented the work from his postdoc at the cyber marine science excellence advisory group meeting. Jeremy recently published some of his work in Aquaculture Research (https://doi.org/10.1111/are.16120) with Daniel Killeen from Plant and Food Research.

■ Peter Remoto, Sam Harris and Keith Gordon attended the 10th Advanced Materials and Nanotechnology conference (AMN-10) in February. Keith talked on excited state spectroscopy, Sam presented a poster on new donor-acceptor compounds and Peter gave a poster on dehydration kinetics in materials as probed by low frequency Raman spectroscopy. This work from his BSc (Hons) was published last year (https://doi.org/10.1021/acs.cgd.2c00121).

■ Working with a team in Marine Science led by Bridie Allen, Sara, Peter, Fatema and Keith contributed to a paper highlighting the issues of microplastics in fish species published in Marine Pollution Bulletin (https://doi.org/10.1016/j.marpolbul.2022.114121). This is part of the new Ki uta ki tai Plastic Pollution Research Theme started at Otago in 2022.

■ Summer students Lia Heremia and Samer Naji have been conducting work on a variety of projects. Lia has been working on formulating hydrogels to be used in assessing penetration depths for spatially offset Raman spectroscopy as part of Sara Miller's Marsden and MBIE projects. Samer, having looked at rat brain composition as a function of diet, has also been helping researchers in zoology look at microplastics in waterways and aquatic species.

■ Amir Sohail, MJ Punzalan and Mitchell Chambers started their PhD journeys in March.

■ Peter Remoto has submitted his MSc thesis.

Fatema Ahmmed with her daughter Maryam and supervisors Sara Miller and Keith Gordon

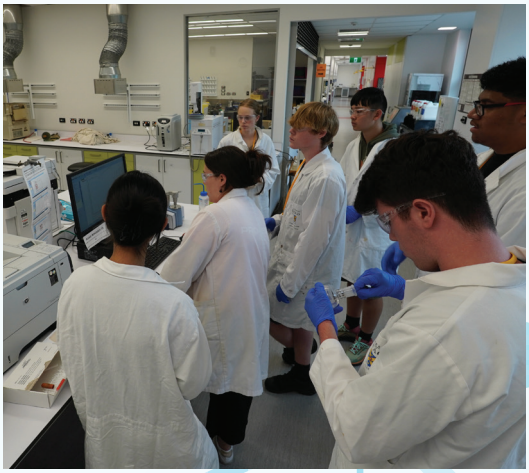
WELCOME

We welcomed visitors and new colleagues to the Gordon-Miller lab in February. Elina Harju and Teemu Temburg from the Univeristy of Helsinki (pictured) are visiting the lab to undertake Raman measurements on cells. Georgina Shillito (University of Jena) is visiting to use the time-resolved experiments to investigate new photocatalysts.

Hands On at Otago

After a year off due to COVID, the chemistry department was again involved in Otago's Hands On at Otago programme (which is now in its 33rd year). About 400 Year 12 and 13 students spent a week on campus, taking part in extended project groups each morning during the week, and then having 'tasters' of other subjects in the afternoons. The chemistry department runs two project groups, one studying natural products chemistry, using caffeine as a case study, and the other exploring the synthesis and properties of silver nanoparticles. Along with around 30 students who were in the project groups, another 90 took part in the taster sessions, where they made and studied [Co(PPh3)2Cl2].

Hands On at Otago provides a fantastic opportunity to introduce students to what chemistry is actually like as a subject and for them to spend time with academics and postgraduate students.



WAIKATO

NEWS

Congratulations to Brendan Gill (Fonterra) on being elected as a Fellow of the NZIC.

Michael Mucalo gave his Presidential address to the branch late last year, which was well attended.

A small but enthusiastic contingent from Waikato attended the NZIC conference in Auckland in November. The branch was ably represented by Lauren Gris in the student oral paper competition with her talk, "A chemical study of the predator-prey relationships in nudibranchs."

As part of the IUPAC Global Women's Breakfast event on 14 February for female chemists and supporters, a very enjoyable breakfast was held at Jack's Coffee Lounge in Hamilton. This was one of nearly 400 events held in over 70 countries and we were one of the very first breakfasts to launch.

The Waikato contingent at the conference dinner. From left: Michael Mucalo, Michèle Prinsep, Matthew Risi, Simon Winship and Lauren Gris. Absent: Sara Farahani, Jing Xu.

UNIVERSITY OF WAIKATO

Daniel Reason successfully defended his PhD on Process optimization for the manufacture of medicinal cannabis products. Daniel's research was supervised by Megan Grainger and Joseph Lane and was carried out for Cannasouth where Daniel is now employed full time.

Brittany Jaine and Edie Thomas (both supervised by Megan Grainger) completed their MSc(Research) work. Their theses were entitled, "Effects of toxic heavy metals on European honeybee (Apis Mellifera) neuronal cells" and "Characterisation of the aroma profiles of New Zealand monofloral honeys" respectively.

Megan Grainger, along with Dr Cathy Buntting (Director of Wilf Malcom Institute of Educational Research) and Dr Brent Wagner (School of Education) spent Terms 3 and 4 in 2022 working with a group of students and teacher Whaea Oriana Tauranga to learn more about honeybees. This was part of a joint venture with Professor Les Bailie (Cardiff University) and Ysgol Pen Rhos School students and teacher Jo Cudd (Llanelli, Wales). The spot-a-bee app (http://www.spotabee.buzz/) was modified for inclusion of New Zealand native flora to track the movement of bees. One of the highlights for the students was spending a day working with the university's portable SEM, dissection microscopes and light microscopes.

After many years of valuable service, both Bill Henderson and Merilyn Manley-Harris retired from the

The Waikato NZIC branch committee for 2023 is as follows:

Chairperson: Michael Mucalo

Secretary: Brendan Gill

Treasurer/Chemistry Education representative: Martina Pietsch Brown

Council delegate/Branch editor: Michèle Prinsep

Student representative: Amber Bell

Committee members: Megan Grainger, Lauren Gris, Kavitha Ranaweera, Matthew Risi, Simon Winship

Hamilton Global Women's breakfast attendees

WELLINGTON

VICTORIA UNIVERSITY OF WELLINGTON – SCHOOL OF CHEMICAL AND PHYSICAL SCIENCES

NEWS

Dynamic Science Wellington

The School of Chemical and Physical Sciences held a 2-day event called 'Dynamic Science Wellington' for Year 12 and 13 high school students who are passionate about chemistry and physics.

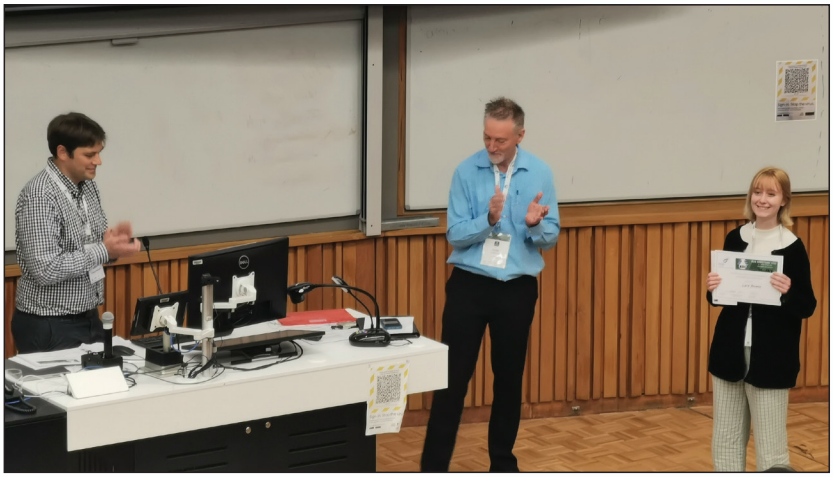
The first day included a series of engaging activities in the research labs where the students gained hands-on experience and insight into the cutting-edge research within SCPS, finishing with some inspiring talks from founders of start-up companies, who are using their scientific expertise to address global societal topics.

The second day started with a trip to the Robinson Research Institute and Ferrier Institute where the students learned about where science has a place in industry. They gained an understanding of how chemistry and physics can contribute to New Zealand's large scientific community allowing them to see where a degree in chemistry and physics can take them. They also interacted with current undergraduate science students, who shared some of their experience at University. The day ended with a fun and challenging chemistry and physics escape room, where the students had to use the knowledge they gained throughout the past two days to solve puzzles and clues in order to break out of the lab.

Dynamic Science Wellington was a successful event that inspired the students and got them excited to further their studies in chemistry and physics at Te Herenga Waka – Victoria University of Wellington.

High school students attending the Dynamic Science Wellington event

2023 Wellington Branch NZIC committee



Lara Brown receiving her best student poster prize at the NZIC 2022 conference

Lucy Hughes with her VUW 3MT certificate

Wellington NZIC Branch news

In December 2022, the NZIC President, Associate Professor Michael Mucalo, gave his NZIC Presidential Seminar to the Wellington NZIC branch. This was followed by the Wellington branch AGM with the election of the new branch committee, and a handing over of the baton to our new NZIC president Associate Professor Joanne Harvey.

Student successes

Congratulations to Victoria University of Wellington students who have won prizes at recent conferences:

- Lara Brown - best overall student poster prize at the NZIC 2022 conference.
- Aditi Kumar - best student poster at AMN-10, February 2023.
- Jake Hardy and Calum Gordon - best student talk at AMN-10, February 2023.
- Emily Stephens and Andrea O'Reilly - best poster at the MacDiarmid Symposium.

After winning the Victoria University of Wellington - Te Herenga Waka 3 Minute Thesis Competition, PhD student Lucy Hughes qualified for the 3M Asia-Pacific competition where she finished in the top ten.

PhD completions

Congratulations to Ferrier students who have recently successfully completed their PhD examinations in 2022: Rudy Bundela, Mitchell Ganley, Parastoo Khajeaian, Rose McLellan, Michael Meijlink, Charlotte Page and Yoan Preux.

Rose McLellan's exceptional PhD thesis was selected for the Dean's list.

PhD student Sarah Draper demonstrating at the opening of Te Pā Harakeke

TE KĀURU - FERRIER RESEARCH INSTITUTE

New lab facilities opened at Gracefield

Last year Minister Dr Ayesha Verrall (then Minister of Science) opened Te Pā Harakeke at the Gracefield Innovation Quarter. These new labs are occupied by some of Ferrier's researchers who welcomed the opportunity to give her a tour.

Callaghan Innovation - Te Kāuru joint NMR facility

Callaghan Innovation and Ferrier Research Institute have purchased two cutting-edge NMR spectrometers, with one in use and the other being installed soon. These 500 MHz spectrometers are equipped with the latest technology, being up to 100 times faster for some experiments compared to previous generations due to advances in instrument sensitivity and the use of cryo-probe technology.

New NMR suite at Gracefield Innovation Quarter

New Te Kāuru - Ferrier Research Institute Director appointed

On 1 February 2023 Professor Gary Evans became the new director of The Ferrier Research Institute. Professor Richard Furneaux has been leading the group that is now the Ferrier Research Institute for the past 40 years, building the Institute up to the powerhouse it is today. Richard will still be part of the Institute, but with much more time to spend on the science that he loves including delivery of research solutions to clients.

Gary completed his PhD at Otago and a postdoc at Oxford, UK, before joining the Institute as a FRST Postdoctoral Fellow. For the past 4.5 years he has been the Chief Science Advisor at MBIE. Gary's impressive publication and patent record along with his recent experience in government Ministry circles sets the Ferrier up well for the future.

Professor Gary Evans is the new director of Te Kāuru - Ferrier Research Institute

Pictured, Students and staff at Victoria University of Wellington celebrating the IUPAC Global Women's Breakfast on 14 February.

Article

Carbohydrate catalysis - the biochemistry of enzymes in honey

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Keywords: *honey, enzymes, biochemistry*

Introduction

Over millions of years, honeybees have mastered the art of creating their own food that can be stored for long periods of time. This is done through a series of complex biochemical reactions, where nectar and pollen are transformed into the sweet and sticky mixture that we call honey.

Honeybees have some capability to digest starches and oligosaccharides such as sucrose and maltose, which make up a significant portion of nectar composition. To make the honey product more compatible for consumption, they naturally produce a cocktail of enzymes in their salivary glands. This concoction is added to the pre-honey mixture as the bees collect nectar through their proboscis, the honeybee's equivalent of a mouth. After collection, the nectar enzyme mixture is stored in the honey stomach, a separate storage organ in front of the actual stomach. Here, the enzymes get to work converting the nectar into something that more closely resembles the honey we are used to.

Back at the hive, the worker bees will regurgitate the mixture and pass it to one another, aiding in the digestion of sugars in the nectar. At this stage, the pre-honey is 70% water and risks fermenting if stored in its current state. Bees employ a drying process by spreading the honey out in cells in the warm hive (Fig. 1.) and beating their wings to encourage evaporation. When it reaches 17-20% water, cells are capped in the honeycomb ready for consumption over the winter months. The initial additions of enzymes ensure that the honey can be stored indefinitely without going off or being tainted by bacterial growth.[1]

Fig. 1. "Inside the Bee Hive" Photo credit: Jean Beaufort *(CC BY 2.0) (https://www.publicdomainpictures.net/en/view-image.php?image=160442&picture=inside-the-bee-hive)*

"While they have a significant biological role in producing honey, the benefit to humans of these enzymes continues beyond the production process itself."

Honey is predominantly comprised of sugar and water, with a small fraction of 0.1-0.5% being made up of proteins and enzymes.[2] Despite their low quantity, they play a significant role in the production of honey. The main classes of enzymes found in honey are amylases to convert starch into maltose, invertases to break down sucrose, glucose oxidases to produce hydrogen peroxide and catalase to regulate hydrogen peroxide.[3] Most enzymatic activity is derived from the hypopharyngeal gland of the honeybee, but catalase has been shown to originate from pollen. Royal jelly proteins are also produced by the salivary glands. These proteins are typically included in royal jelly, which is fed to larvae to encourage growth, but often end up in honey.[2,4] While the structure of these enzymes have been deduced in many other organisms, those derived from honeybees are largely unknown. However, utilising machine learning, the program *Alphafold* can predict structures based on their amino acid sequence and similarity to other enzymes in an exhaustive database.[5]

While they have a significant biological role in producing honey, the benefit to humans of these enzymes continues beyond the production process itself. Due to their sensitivity to temperature and pH, as well as eventual degradation over time, measuring the activity of these enzymes can be used to indicate the quality of the honey. Fresher honey will have higher enzymatic activity.

Commercial assays for these enzymes use a variety of techniques. The Phadebas test for the detection of alpha amylase activity uses colorimetric measurements to determine quality. It incorporates a starch tablet that is cross-linked to a blue dye. As the enzyme in the honey breaks down the starch, the blue dye is released into the solution and its absorbance can be measured and correlated to a quality indicator.[6]

Invertase assays directly measure the reducing sugars produced by invertase: fructose and glucose. The assay utilises a modified Fehling's test where aldehydes such as glucose react with Cu^{2+} in an alkaline solution. The level of reduced copper is measured by titration of sodium thiosulfate.[7]

Assays for glucose oxidase are performed using fluorescence detection of a red dye. When the dye encounters hydrogen peroxide in the presence of the enzyme, horseradish peroxidase, a highly colored product, is formed and its fluorescence can be measured and related to the activity of glucose oxidase.[8]

Catalase activity can be measured using UV spectrophotometry. When a cobalt-bicarbonate reagent is added to a solution containing hydrogen peroxide, the cobalt is oxidised from Co^{2+} to Co^{3+}, which reacts with carbonate to form an intensely green solution. The absorbance of this solution is measured and is inversely proportional to the catalase activity. If there is high activity, there will be less hydrogen peroxide and a lighter green colour.[9]

Amylases

Nectar contains between 1%-20% starch,[10] with the branched amylopectin predominating over the linear amylose. Bees cannot utilise these complex carbohydrates, so they use amylase to break starch down into more manageable maltose units.

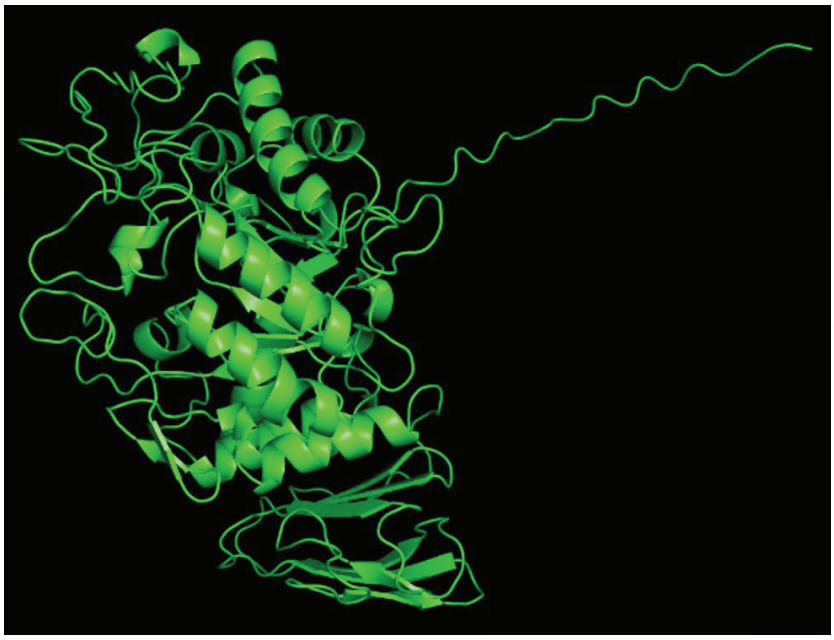

Fig. 2. Predicted structure of alpha amylase from honeybee

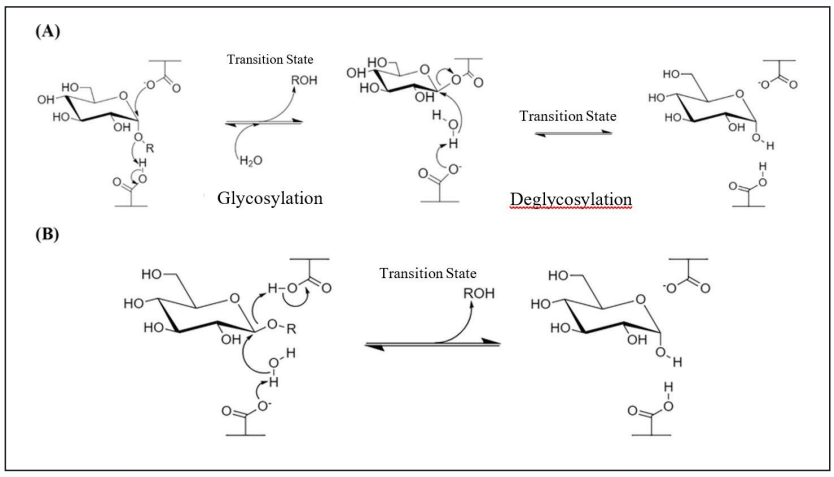

Fig. 3. Proposed reaction mechanism for the hydrolysis of starch in (A) alpha amylases and (B) beta amylases. Reproduced from reference 12 under a Creative Commons CC BY 4.0 License

The term diastase refers to alpha and beta amylases collectively, with alpha amylase being the predominant species. The predicted structure of alpha amylase from the honeybee[11] is shown in Fig. 2.

The proposed reaction mechanisms for the hydrolysis of starch by alpha and beta amylases are shown in Figs. 3A and 3B respectively.[12] They involve acidic glutamate and aspartate residues which each play a role as a nucleophile, proton donor and transition state stabiliser. Firstly, the anomeric carbon undergoes nucleophilic attack from the conjugate base of one of the acids to form a stabilised intermediate and a shortened oligosaccharide. Then, through the addition of water acting as a weak nucleophile, the acid detaches and another acid residue in its conjugate basic form procures a proton from the water, leaving a complete sugar unit as the final product and the acidic amino acids intact.

Alpha amylases operate on alpha sugars, featuring the nucleophile above and the proton donor below, whereas in beta amylases the locations of the nucleophile and proton donor are reversed to enable action on beta sugars.[12]

Amylases have been extensively studied in humans, with their 3-dimensional structures characterised in many situations alongside substrates, ligands and inhibitors.[13-14] However, structural characteristics of amylases produced by the honeybee (*Apis mellifera*) are those predicted by the artificial intelligence modelling system, *Alphafold*,[5] based on the existing structures of other amylases.[11] We know that calcium and chloride play a significant role in the overall structure of the enzyme.[15] From human models, it has been determined that amylases can be classified as metalloenzymes with calcium being key to their stability. They bind to a combination of carbonyl oxygens, an acid residue and water molecules in an 8-coordinate geometry.[16] The allosteric binding of chlorine has been shown to encourage calcium binding. Additionally, it induces changes to the conformation of the active site, allowing it to accept substrate. In particular, chlorine attaches to three basic amino acids, which become positively charged under the correct conditions. This induces glutamate to move into the active site so it can participate in the hydrolysis of starch. For these reasons, the activity of amylase is heavily dependent on chlorine concentration.[17]

Invertase

One of the primary components of nectar is sucrose. This is split into individual glucose and fructose units by invertase. The structure of honeybee invertase has not been determined but a plant invertase, determined by X-ray crystallography,[18] is given in Fig. 4.

The suggested reaction mechanism for the hydrolysis of sucrose by invertase is shown in Fig. 5.[18-19]

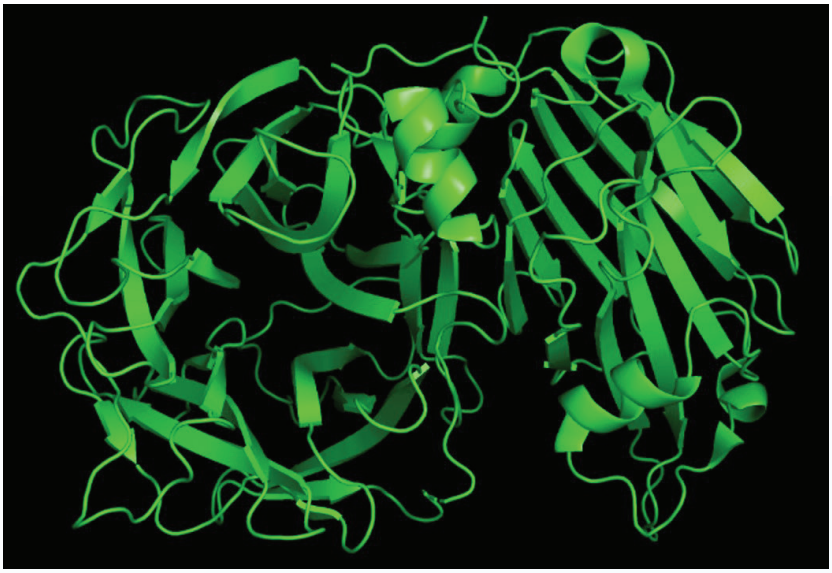

Fig. 4. Determined structure of invertase from Arabidopsis thaliana

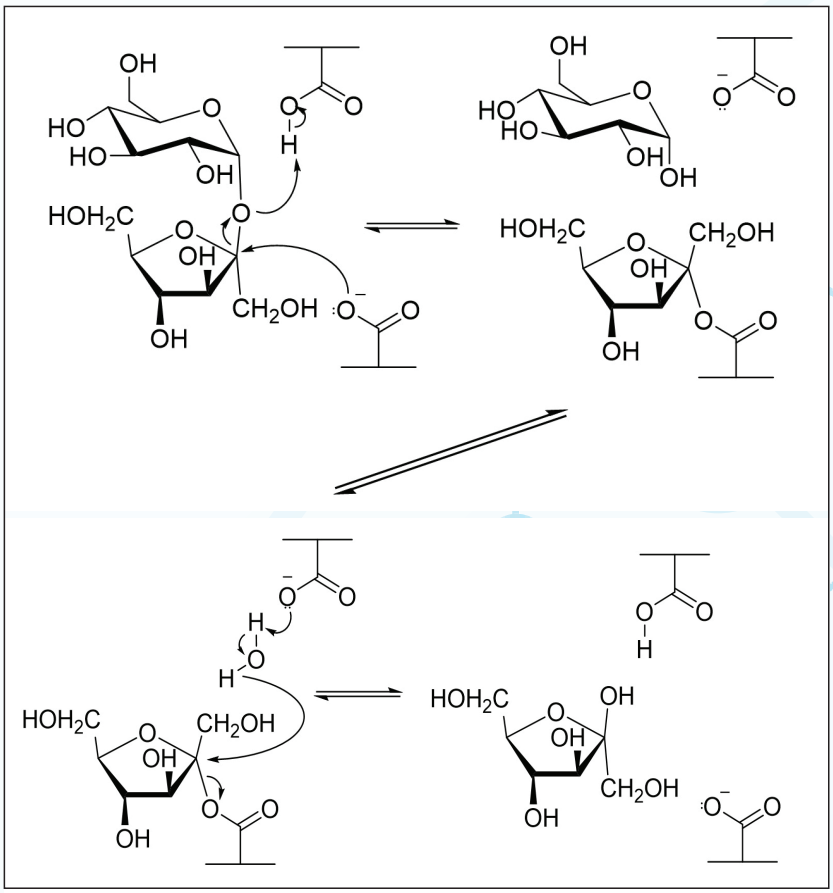

Fig. 5. Proposed reaction mechanism for the hydrolysis of sucrose in invertase

Like amylases, amino acids with acidic side chains facilitate this reaction as nucleophiles and proton donors. The conjugate base of an acidic amino acid is presumed to act as a nucleophile and attacks the anomeric carbon of the fructose subunit. The nucleophilic attack pushes electrons to the oxygen in the glycosidic bond.

The oxygen attacks the hydrogen on one of the acidic residues, creating a molecule of glucose and a transition state of fructose bound to the enzyme. Water is deprotonated by the resultant negatively charged acid group. The newly created nucleophile attacks the anomeric carbon of the bound fructose, breaking the bond between the enzyme and the fructose.[18-19] Related to invertases are sucrases but what distinguishes these is that sucrases break the C1-O bond to glucose, leaving the glucose bound to the enzyme, rather than the O-C2 bond to fructose.[20]

Proteins are comprised of various substructures, from helical secondary structures to molecular assemblies of quaternary structures. Invertase is an example of an 8-subunit quaternary structure classed as a tetramer of dimers. To produce the oligomer, the enzyme's monomer undergoes a two-fold rotation to create a dimer and this dimer undergoes a four-fold rotation creating a tetramer of dimers. These protein aggregates are stabilised by hydrogen bonding, disulfide bonds between cysteine residues and interactions between residues of similar hydrophobicity or hydrophilicity.[18,21]

Glucose oxidase

Many compounds have bactericidal properties. The most well-known of these is hydrogen peroxide, which oxidises the cell wall, destroying the structural integrity of the cell. Additionally, acidity prevents bacterial growth. For these reasons, bees utilise an enzyme that facilitates the production of peroxide and gluconic acid from glucose, available in abundance in honey. This prevents bacterial growth and aids in the maintenance of quality in the honey.[22-23] The predicted structure of glucose oxidase from the honeybee[24] is shown in Fig. 6. The predicted mechanism for the oxidation of glucose by glucose oxidase is shown in Fig. 7.[22-23,25]

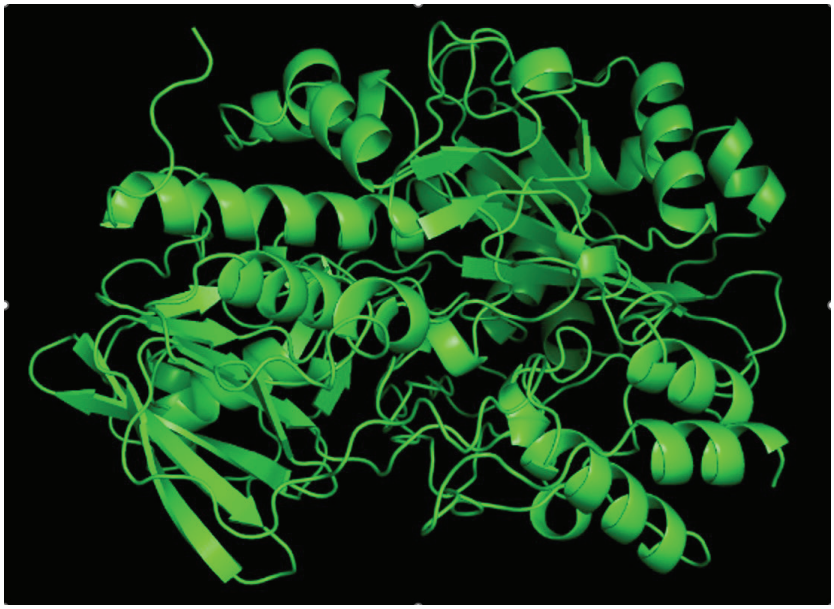

Fig. 6. Predicted structure of glucose oxidase from honeybee

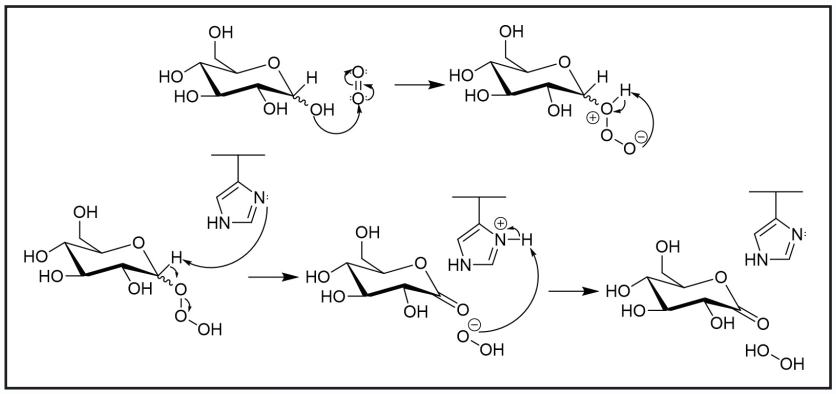

Fig. 7. Proposed reaction mechanism for the oxidation of glucose in glucose oxidase

In this reaction, the anomeric hydroxyl attacks an oxygen molecule. This creates a trioxide intermediate. The outermost oxygen, carrying a negative charge, bonds to the H of the anomeric hydroxyl restoring electron density to the positively charged anomeric oxygen. Nitrogen, from a histidine residue located in the enzyme's active site, removes the anomeric hydrogen and thus becomes positively charged. The electrons from the bond that was broken shift to form a double bond to the anomeric oxygen, liberating peroxide ion. The newly formed oxygen nucleophile removes the hydrogen on the positively charged nitrogen in histidine. The result of this reaction is glucono-1,5-lactone and hydrogen peroxide. The lactone product is in equilibrium with gluconic acid. In the dehydrating honey environment, the equilibrium favours the lactone, only forming gluconic acid upon dilution.[22-23,25]

For every oxidation reaction, there is a converse reduction reaction. The oxidation of glucose is supported by a molecule called flavin adenine dinucleotide (FAD). It features the double purine ring, adenosine attached to a ribose sugar linked to a flavonoid via a diphosphate. FAD is a coenzyme utilised for its reducing potential and its ability to accept electrons in the form of hydride.[26] Alongside glucose

oxidase, it has been reported that a small amount of glucose dehydrogenase exists in honey. Instead of using oxygen for its oxidoreduction reaction, it makes use of natural electron acceptors such as pyrroloquinoline quinone (PQQ).[27]

Catalase

Many organisms utilise chemical signalling as an indicator of environmental stress. One such example is hydrogen peroxide. The enzyme catalase is able to break down hydrogen peroxide into water and oxygen, to regulate levels in response to cellular stress.[28] As hydrogen peroxide is useful in preventing bacterial growth in honey, catalase is not deliberately added to honey by bees. However, it ends up in the final mixture due to a major component in the honey's composition - pollen.[2-3]

Each pollen grain produces catalase to regulate hydrogen peroxide as a means of responding to external pressures in order to protect the cell which is required for reproduction.[27] As a result, catalase ends up in honey as an unavoidable side effect of incorporating pollen into the mixture. While levels differ depending on floral origin, catalase activity has not been observed to be high enough to significantly reduce the amounts of hydrogen peroxide produced by glucose oxidase.[29] The predicted structure of catalase from honeybee[30] is shown in Fig. 8. The proposed reaction mechanism for catalase is shown in Fig. 9.[31]

At the centre of the active site sits a heme group consisting of iron 4-coordinate to a protoporphyrin ring. The iron is in a 3+ oxidation state. One of the oxygens in hydrogen peroxide attacks the iron forming a peroxyl intermediate with iron now in a 4+ oxidation state. Through the movement of hydrogen, a water leaving group is formed and removed, leaving an oxygen double bonded to the iron. The oxygen attacks one of the hydrogens in another molecule of hydrogen peroxide. This results in a hydroperoxyl and the iron complex in resonance between 4+ and 5+ oxidation states.

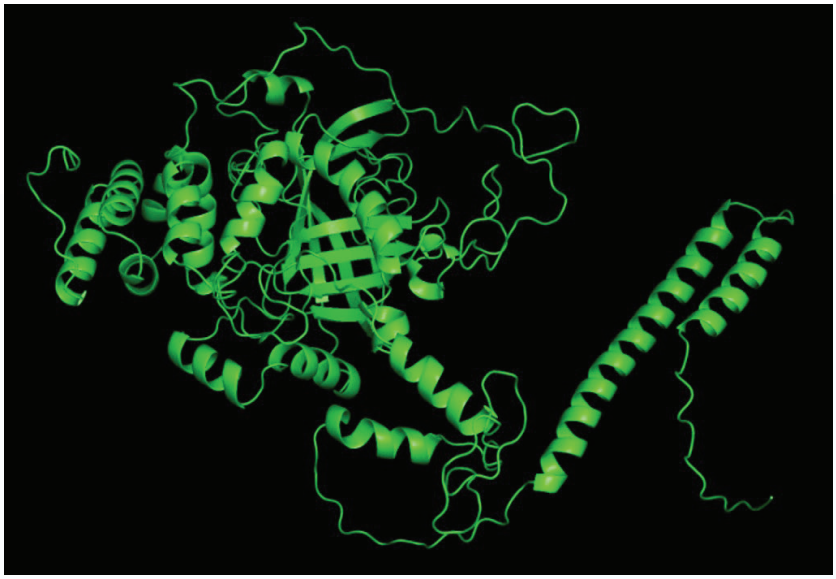

Fig. 8. Predicted structure of catalase from honeybee

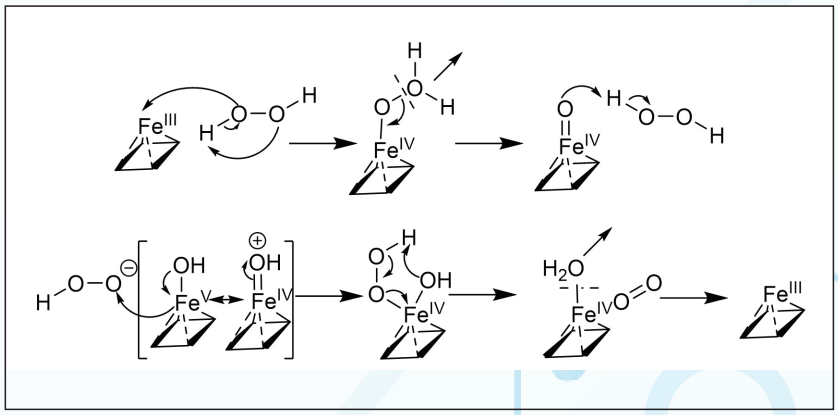

Fig. 9. Proposed reaction mechanism for the decomposition of hydrogen peroxide by catalase

The oxygen of the hydroperoxyl is attacked by the iron forming a pseudo-5-membered ring intermediate. This rearranges to give water, which leaves, oxygen, in its typical diatomic form, and the heme group with iron back in the 3+ oxidation state. The overall net product of this reaction is one oxygen and two water molecules for every two molecules of peroxide. It is interesting to note that the quaternary structure of the enzyme is a tetramer with, essentially, four active sites accounting for efficient activity.[31-32]

Conclusions

The addition of enzymes is essential to making honey nutritional for bees and storable for long periods of time. Each enzyme plays one of a wide variety of biochemical roles from the hydrolysis of oligosaccharides to the production and removal of hydrogen peroxide. They utilise metals, electron carriers and structural features to facilitate important reactions in the production of the bee's food. Even though we cannot see or taste them, without these biological catalysts, we would not have the sweet and sticky treat we call honey.

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Article

Metallodrugs: a brief overview

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Keywords: *metallodrugs, pharmaceuticals, cancer, coordination chemistry, platinum*

Introduction

Cisplatin **(1)** is a simple square–planar metal complex which contains two labile chlorine atoms and two ammonia molecules coordinated to a central platinum(II) atom in a *cis* configuration (Fig. 1). While cisplatin was discovered in 1845, it was not until its discovery as a cytotoxic agent by Rosenberg *et al.* in 1965[1] that the complex gained prominence, soon becoming the premier metallic based pharmaceutical drug in the treatment of a variety of cancers. In 1990, the implementation of cisplatin as a medication was linked to an increased cancer cure rate of 75%, up from 10% prior to implementation of the drug.[2]

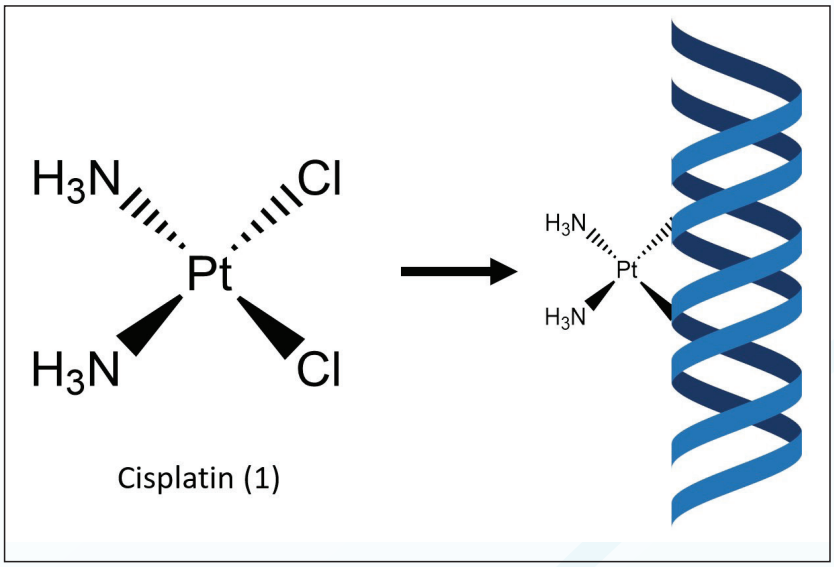

Fig. 1. Cisplatin and its binding to DNA

Cisplatin works in part by binding to guanine and adenine residues on DNA,[3] therefore inhibiting its replication[3] (Fig. 1). This mode of action primarily targets fast replicating cells such as cancer cells but also the stomach lining and hair follicles, leading to the common side effects of hair loss and nausea. Other common side effects include bone marrow suppression, kidney damage, numbness, electrolyte issues and heart disease.[4] Cisplatin has also been shown to harm the developing fetus during pregnancy.

While potent toxicity is advantageous for the treatment of cancer, the non-selective nature of cisplatin has created a desire for the development of the next generation of metallodrugs. Research in this area now spans the entire transition metal block of the periodic table, in the hope of finding treatments not only for cancer but other diseases as well. This review will give a brief overview on metallodrugs, including their history and current research areas.

Versatility of metallodrugs

Metallodrugs contain three main features of tailorability: the ligands coordinating the metal, the metal centre itself and its corresponding oxidation state. These three features contribute to the vast degree of variation and versatility of the compounds, making them much more tailorable than their organic counterparts. They also provide easy modulation for specific targeting and delivery mechanisms.

Ligands

Ligands are arguably the most important aspect of the metallodrug structure. The coordination mode, the geometry and the chemical properties of the ligand dictate not only the macro physicochemical properties of the resulting complex, but also the mode of action and potential biological targets.[5] Ligands also provide the simplest and most robust route for tailoring the chemistry of the resulting complex. The case of *cis*- and *trans*-platin is a good example of the importance of the ligand's geometry. Both isomers contain labile chlorine atoms which can undergo exchange within the cell, allowing the metal to coordinate as a bridge to the guanine residues on DNA. The *trans* isomer, however, is limited by steric constraint, preventing it from creating bridged complexation and therefore lowering its overall toxicity to sub therapeutically active concentrations.[6-7]

Metals

Due to the success of initial platinum based compounds, the majority of early examples of metallodrugs are based on platinum(II) with the primary mode of action being based on

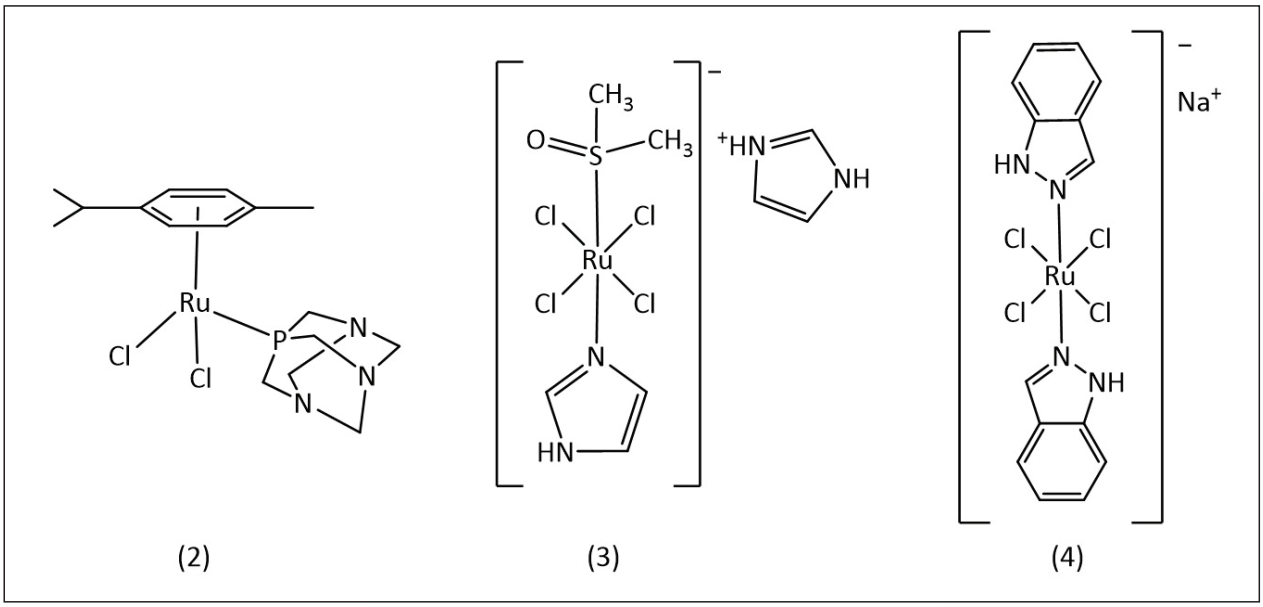

Fig. 2. Structures of RAPTA-C (2), NAMI-A (3) and BOLD-100 (4)

DNA binding. These complexes contain a high amount of unfavourable side effects which in most cases outweigh the high efficiency and cytotoxicity of the drugs.[8] Due to this low selectivity, non-platinum metals have been extensively researched of late in attempts to find more selective acting drugs with reduced side effects while maintaining cytotoxic efficiency.

Commonly studied metals include Ti, Fe, Cu, Ru, Pd, Ag, Os, Ir and Au. Chief among these is ruthenium since the discovery of the biological activity of the ruthenium complexes RAPTA-C (**2**), NAMI-A (**3**) and BOLD-100 (**4**) among others (Fig. 2).[9-11]

Oxidation state

The oxidation state of the central metal atom plays an important role in not only the types of ligands that can coordinate to the metal but also in the geometry they occupy. Both aspects have significant effects on the chemistry of the complex, especially when considering the importance of the ligands, as discussed previously. The ability of transition metals to undergo redox related reactions between stable oxidation states has prompted research into metallic based prodrugs.[12-13] These prodrugs

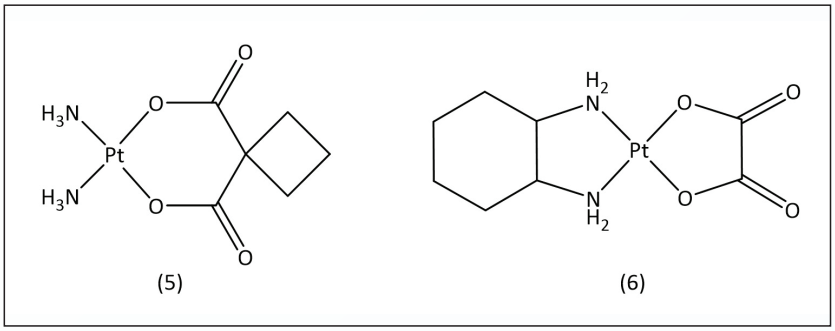

Fig. 3. Structures of carboplatin (5) and oxaliplatin (6)

are able to be activated by redox processes within the cell or by mechanisms specific to the target which allows the switching between oxidation states and therefore the changing of the coordination environment.[14] The ultimate goal of manipulating the oxidation state is to increase the overall selectivity of the drug or by increasing its variation by the implementation of new ligand binding sites.[15]

Platinum(II) and platinum(IV) based metallodrugs

Besides cisplatin, other early platinum(II) based metallodrugs such as carboplatin[16] (**5**) and oxaliplatin[17] (**6**) (Fig. 3) have seen clinical success against ovarian cancer and colon cancer respectively. Both carboplatin and oxaliplatin are considered second generation platinum drugs,[18] which have aimed to improve toxicological profiles and are often used in combination therapy with other drugs.

While slightly more selective than cisplatin and with fewer side effects, these second generation drugs suffer from increased drug resistance, which third generation drugs aim to overcome.[16] The key structural characteristics of platinum(II) compounds are the archetypal square-planar structure, the *cis* configuration of the labile ligands and the presence of at least one N-H group; the latter is important due to the hydrogen-bond donor properties.[7] Platinum(IV) is also an attractive contender for metallodrugs[19] as they often offer greater stability allowing for a great proportion of the drug to reach the target intact. Satraplatin[20]

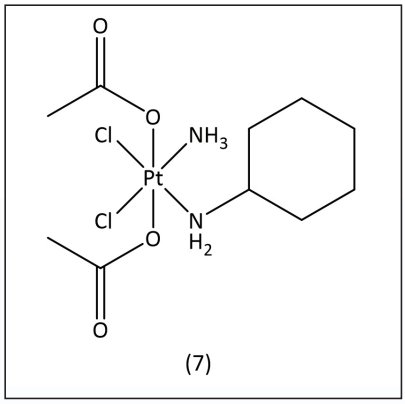

Fig. 4. Structure of satraplatin (7)

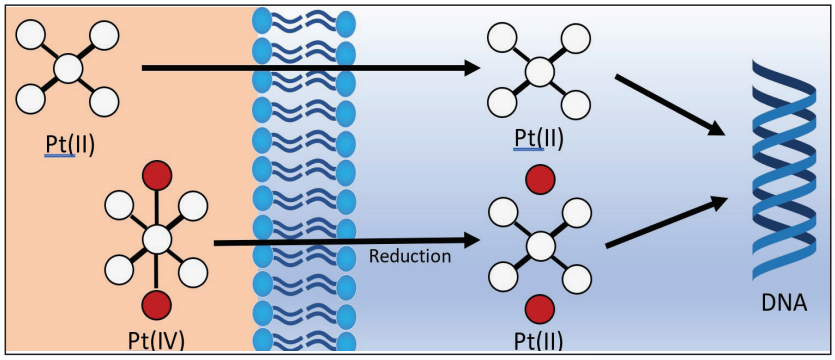

Fig. 5. Post cell transfer payload (red) release via reduction of the platinum(IV) prodrug to platinum(II)

(**7**) (Fig. 4), a platinum(IV) metallodrug, has been known since 1993 but is yet to receive FDA approval.

More recently, platinum(IV) compounds have been investigated as potential prodrugs.[12,21] Traditionally, platinum(IV) prodrugs are synthesised from their platinum(II) precursors by oxidative reactions followed by additional ligands coordinating to the newly available axial positions on the octahedral platinum metal centre. These newly introduced ligands are often seen as the "payload" which are released upon the inevitable reduction of platinum(IV) to platinum(II) (Fig. 5). This process has the added benefit of stabilising the complex until it has reached the target as well as introducing the payload ligands which increase the diversity of treatment.

Non platinum metallodrugs

There is no doubt that platinum based metallodrugs have had a profound impact on the treatment of cancer by chemotherapy, yet they possess significant drawbacks. To overcome these shortcomings, non-platinum based compounds are being investigated[22] and are already in use or in clinical trials.[23]

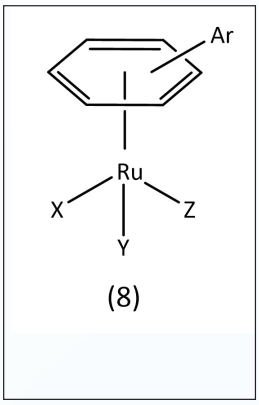

Fig. 6. Generic ruthenium piano stool structure (8)

"Ruthenium metallodrugs are attractive alternatives to platinum due to the different modes of action against cancer cells."

Ruthenium(III)

Ruthenium octahedral complexes are a potential candidate for non-platinum drugs. Known examples include NAMI-A and KP1019 which are both currently in clinical trials.[24]

Ruthenium piano stool structures (**8**) (Fig. 6) are of considerable interest with many reviews being conducted on their applications as metallodrugs.[25-27]

For example, the RAPTA class of metallodrugs (Fig. 2),[28] bearing arene "seats", water soluble phosphines and labile chlorines, provide extensive room for variation. Ruthenium metallodrugs are attractive alternatives to platinum due to the different modes of action against cancer cells. While ruthenium based compounds have been shown to bind to DNA,[28] they have also been shown to interact with proteins,[29] opening avenues for future drug discovery.

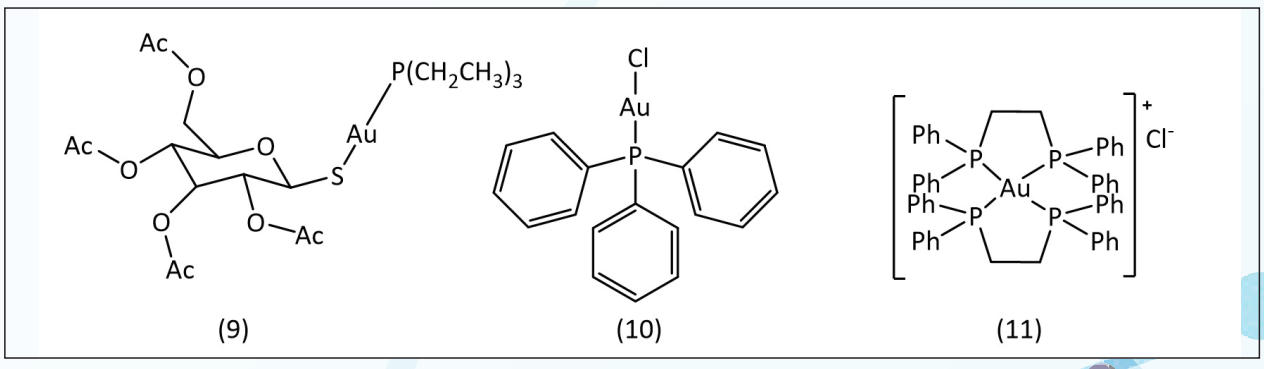

Fig. 7. Structures of auranofin (9), chloro(triethylphosphine)gold (10) and bis(diphenylphosphino)ethane (11)

Gold(I)

Gold compounds are also attractive avenues for metallodrug research. Auranofin (**9**) (Fig. 7) is a clinical drug used in the treatment of rheumatoid arthritis[30] and has also shown promising results in the treatment of HIV, cancer[31] and tuberculosis. Most recently it has shown potential to inhibit the SARS-CoV-2 virus replication.[32]

Other gold phosphine complexes have also been examined, such as the chlorine analogue of auranofin, chloro(triethylphosphine)gold[33] (**10**) and also the gold complex of bis(diphenylphosphino)ethane[34] ($[Au(dppe)_2]^+Cl^-$) (**11**) (Fig. 7). It is thought that these gold complexes act on DNA, RNA and protein synthesis,[35] with some studies suggesting mitochondria or enzymes to be the target.[36] Gold(I) as well as gold(III) continue to show potential for the development of novel metallodrugs.

Alternative delivery mechanisms

Due to the large degree of structural variation that metallodrugs possess, many drugs have been produced thus far for the treatment for a large array of diseases. However, as these metallodrugs suffer from poor targeting, poor bioaccumulation or unpleasant side effects, the most obvious remedy to these drawbacks is the alteration of metallodrug structure. This will not only give the opportunity to impart the desired properties, but it will also allow for the maintaining of the desired efficiency and cytotoxic effects. An alternative approach is to use compounds or structural motifs that are already proven to be effective with a different delivery system which can bypass the issue of poor targeting and potentially reduce unwanted side effects.

Lipid based nanoparticles

One such example of an alternative delivery mechanism is the employment of lipid based nanoparticles,[37-38] a technique that has most recently been used for the transport of mRNA in COVID-19 vaccines. Liposomes, consisting of bilayer spherical vesicles comprised of phospholipids, hold an internal hydrophilic core. This core can be used to contain payloads such as metallodrugs.

These lipid nanoparticles have the advantage of biocompatibility allowing the drug to easily traverse the body to reach the targeted area while keeping the compound inside stable. It also allows for the transport of more hydrophobic drugs, increasing the range of diversity. Some lipid based encapsulation methods have already seen some clinical success, such as the cancer drug liposome-encapsulated doxorubicin.[39]

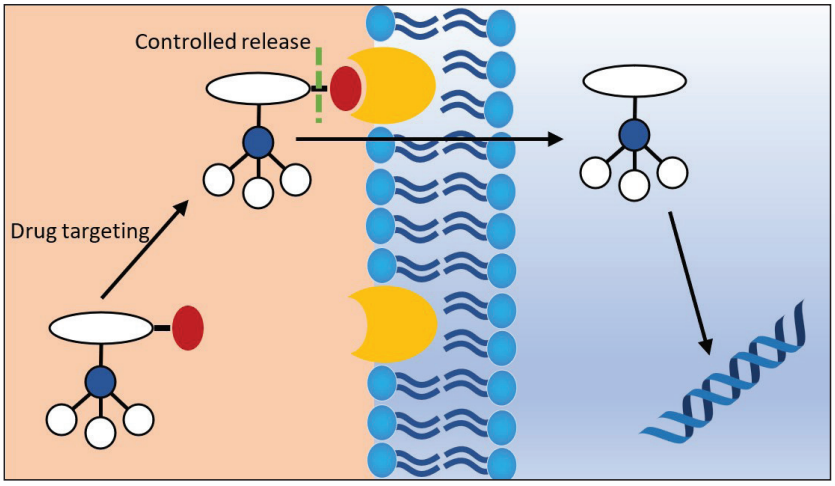

Fig. 8. Drug targeting via a carrier molecule

"These lipid nanoparticles have the advantage of biocompatibility allowing the drug to easily traverse the body to reach the targeted area while keeping the compound inside stable."

Smart delivery systems

Another potential method for overcoming the limitations of metallodrugs is the employment of smart delivery systems. This method involves the use of a carrier molecule, such as a peptide, protein, antibody or hormone.[40] These carrier molecules are usually attached to the target drug by a linkage molecule which is separated by external stimuli, such as ion concentration changes, protein docking or even by ultrasound (Fig. 8). While proven success is limited, the use of smart delivery systems for the transport of metallodrugs is in its early stages of research and represents a promising direction for the field.

Conclusions

Metallodrugs continue to be an active and important research field in inorganic chemistry. These versatile metal complexes have the potential for an array of biological functions, with compounds such as cisplatin demonstrating their importance in medicine. While metallodrugs suffer from numerous downsides such as unpleasant side effects and poor selectivity, their versatility allows for active research to overcome these challenges.

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Article

Rare earth element separations: a brief overview of some green methods

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Keywords: *ionic liquids, biosorption, supercritical liquids, green chemistry, rare earth elements*

Introduction

The rare earth elements (REEs) are a series of 17 elements consisting of the 14 lanthanide elements, lanthanum (La), cerium (Ce), praseodymium (Pr), neodymium (Nd), promethium (Pm), samarium (Sm), europium (Eu), gadolinium (Gd), terbium (Tb), dysprosium (Dy), holmium (Ho), erbium (Er), thulium (Th), and ytterbium (Yb), as well as scandium (Sc) and yttrium (Y).[1] The d-block element, lutetium (Lu) is also included in the lanthanide series and classified as a REE.

The lanthanide elements, typically defined by the gradual filling of the 4f electron shell across the series, are generally most stable in their 3^+ oxidation state, although for some elements, 2^+ and 4^+ are also common.[2] Many of these elements are vital components in much of our modern-day technology, found in smart phones, TV screens and more. They are also essential in green energy technology, such as wind turbines, solar panels and rechargeable batteries used in electric vehicles.[1]

The extraction and separation of these elements has long been a challenge due to the similar chemical and physical properties of neighbouring elements, as well as their abundance in the earth's crust. Despite their name, these elements are quite commonly found within the earth's crust but at such low concentrations that the mining of these elements requires the processing of large quantities of material and produces large volumes of waste.[3]

"The US Department of Energy, the European Commission, and the British Geological Society have all recognised the REEs as critical elements for the future."

For most of their uses, REEs are needed as single pure elements so the separation processes are of high importance. Traditionally, pyrometallurgical and hydrometallurgical methods have been used for these extractions. However, pyrometallurgical methods are energy intensive and result in poor separations, while hydrometallurgical methods often require many separation steps with large amounts of volatile organic solvents and the production of harmful acidic waste.[4]

Due to their technological importance, as well as their high supply risk and the difficulty involved in processing these elements, the REEs are frequently listed on reports of critical elements, or element risk lists. In fact, the US Department of Energy, the European Commission, and the British Geological Society have all recognised the REEs as critical elements for the future.[5-7] These lists account for the production and recycling rate, as well as the governance of the elements (i.e. production rates and the reserve size countries have of certain elements).

With the growing demand for the REEs, there is an increasing interest in creating and testing greener methods for their separation. In chemistry, "green" methods refer to those which follow some or all of the 12 Principles of Green Chemistry which help the method become safer and more environmentally friendly. Some of the principles most relevant to the separation methods discussed in this article include the reduction or prevention of waste, use of safer chemicals, design of methods which are energy efficient, use of chemicals which are derived from renewable feedstocks (such as plant-based sources) and the prevention of pollution.[8]

In REE separations, green methods may be designed by avoiding the need for large amounts of solvents, particularly harmful organic solvents, and using extractants which are easily recycled, and which originate from renewable and natural sources. In this article, a small selection of green separation processes which are being explored for the separation of the rare earth elements will be discussed. The discussion will include a brief overview of the use of ionic liquids, biosorbents, and supercritical liquids in REE separations.

Ionic liquids

Ionic liquids (ILs) are defined as being pure salts with a melting point below 100°C. However, it is typically those which are liquid at room temperature (aptly named room temperature ionic liquids) that are of more interest and use.[9] ILs have

been praised as green alternatives to harmful organic solvents due to their unique properties including their low volatility, low flammability, negligible vapour pressure as well as their recyclability. It should be noted that while these qualities are common in ILs, they are not characteristic of all ILs, with properties varying greatly depending on the cation and anion making up the IL, and the way these interact with each other.[10]

ILs can be designed and created for specific applications through the careful selection and functionalisation of the ions present in the IL.[9] Functionalisation can be used to alter the properties of ILs such as their viscosity, melting point and hydrophobicity. This offers many advantages and allows for a wider range of potential applications of these unique liquids, including uses as catalysts,[11] electrolytes,[12] corrosion inhibitors[13] and as solvents and extractants in separation methods.[14]

For the separation of REEs using IL extractants, liquid-liquid extractions are one of the most common methods used. Liquid-liquid extractions are often simple to carry out, involving the mixing or shaking of an aqueous REE-containing layer and the organic layer containing the IL. In some cases, it is possible to use a neat IL, but an organic solvent is often required to improve the ease of mixing of the two layers due to the viscous nature of many ILs.

In the creation of ILs for REE separations, organophosphorus extractants currently used in industrial separation methods can be used. For example, 2-ethylhexyl phosphonic acid mono(2-ethylhexyl) ester (P507) is widely used in China to achieve high purity REEs.[15] This success has seen it used in a range of ILs for the same purpose. For example, Shen *et al*. tested the IL [N1888][P507] (Fig. 1) in a sulfuric acid medium, achieving separations of trivalent Tm, Yb, Lu and Y from the lighter La, Gd and Tb elements.[16] Xu *et al*. also achieved promising results using the same IL mixed with a trialkyl phosphine oxide mixture (TRPO), resulting in good selectivity and extraction efficiencies for some of the heavy REEs including Yb and Lu which achieved extraction efficiencies greater than 96%.[17] These results, and many more, show the potential ILs have in REE separations, although difficulty is often faced with the separation of neighbouring REEs.

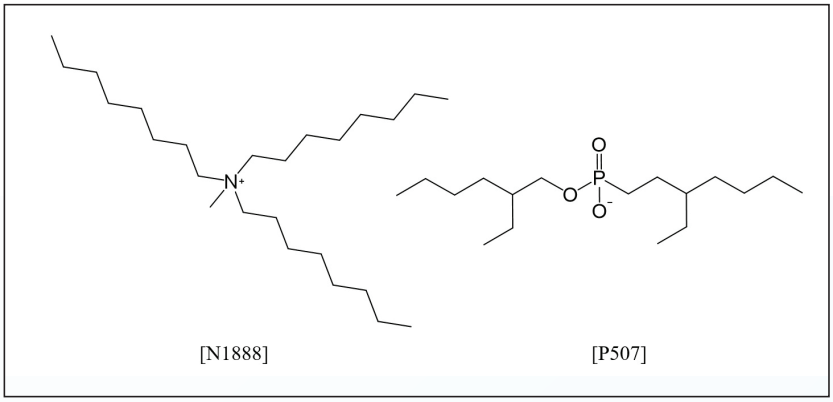

Fig. 1. Structure of cation [N1888] and anion [P507] used for REE separations

"ILs can be designed and created for specific applications through the careful selection and functionalisation of the ions present in the IL.9."

While liquid-liquid extractions appear to be the most common method for REE separations using ILs, the immobilisation of ILs on solid supports to create supported ionic liquids (SILs) is also popular in separations. SILs offer some advantages over those used in liquid-liquid extractions. For example, SILs often maintain the properties of the unsupported IL which are important for separations, while also reducing the leaching of the IL into the aqueous phase and requiring smaller volumes of IL to complete extractions.[18] In some cases, the addition of a support has been reported to improve metal separation.[19]

Common supports used to create SILs include polymer supports, silica supports and metal organic frameworks, with different separation methods applied. In a column chromatographic method aiming to separate the REEs from other metals present in NdFeB and SmCo magnets, Avdibegovic and Binnemans used a SIL phase, betainium sulfonyl(tri-fluoromethanesulfonylimide) poly(styrene-co-divinylbenzene).[20] This method achieved extraction recoveries of 82% and 90% for Nd and Sm respectively, as well as high selectivities towards the trivalent lanthanide elements over the divalent iron and copper also present in the spent magnet leachate.

Biosorbents

Biosorbents offer another opportunity for green separations of the REEs. These are naturally occurring sorbents, which are derived from a range of natural sources including plants, fungi, algae and animals.[21] Typically considered for the removal of heavy metals and other contaminants from wastewater, biosorption refers to processes which remove metal ions through passive binding to biomass materials in aque-

ous solutions.[22] With the trivalent lanthanides generally behaving as strong Lewis acids, they are found to bind to groups with basic properties. For example, Ln(III) ions can strongly bind to the electron donating oxygen groups present in many biosorbents, and may bind weakly to P and S ion donor groups.[21]

In recent years, biosorption methods have been developed for the separation of the REEs from nuclear and electronic waste. These methods offer advantages of being affordable, simple and environmentally friendly, and often result in high extraction efficiencies and ease of recycling.[21] These sorbents are also generally widely available and can be considered green due to their natural origin, as well as largely being biodegradable. Furthermore, much like ionic liquids, biosorbents can also be immobilised to offer similar advantages to SILs.

Extraction and separation using biosorbents typically involve a variety of processes including absorption, adsorption, ion exchange, complexation, chelation, electrostatic interactions and precipitation.[22] These occur between the REE ion in solution, and the functional groups found bonded to the cell walls of bio sorbents. In fact, one of the advantages of the use of biosorbents for separations are the functional groups which are naturally found bonded to cell walls, some of which are shown in Fig. 2.[21]

One of the drawbacks often observed in biosorbents for metal separations is their low selectivity towards metals, owing to the range of functional groups which are capable of extracting a large range of metals.[21] However, similar to ILs, biosorbents are able to be modified and functionalised to improve their separation ability.[23] In some cases, modification is required to stabilise the biosorbent to ensure it can withstand the conditions used throughout separation experiments. In other cases, biosorbents are modified to improve separation performance and ease of removal following the extraction step.

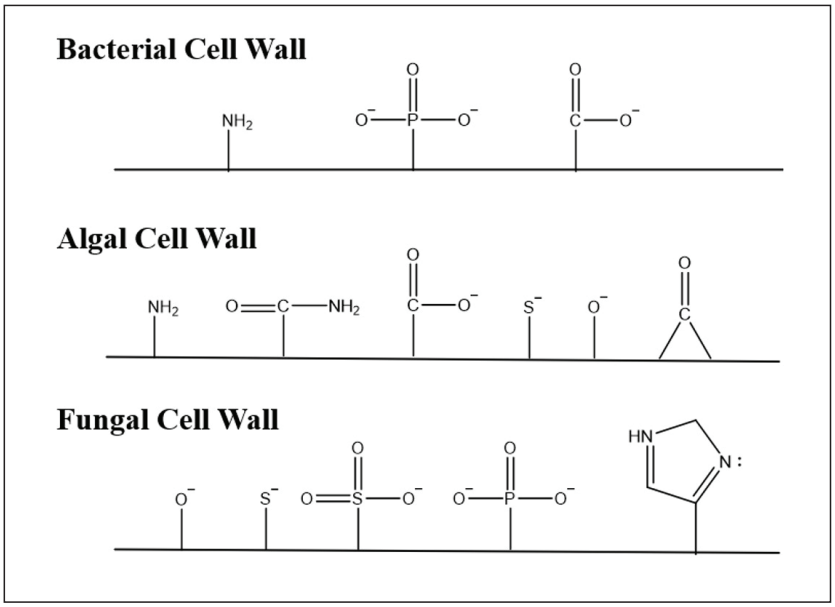

Fig. 2. Functional groups found on some common biosorbents sources

"These methods offer advantages of being affordable, simple and environmentally friendly, and often result in high extraction efficiencies and ease of recycling"

Many examples of biosorbent modification can be found, particularly those involving the modification of chitosan. Chitosan (poly-β-(1→4)-2-amino-2-deoxy-d-glucose) is a common biosorbent as it is abundant, inexpensive, biodegradable, and has low toxicity.[23] Due to the nitrogen and hydroxyl groups found in the structure, it is also a good contender for the separation of heavy metals, including the REEs, as it acts an effective chelating agent. However, modification is often required to improve the stability of chitosan in acidic solutions.

Further chemical and physical modifications can also be carried out to achieve better separations and improve selectivity. For example, Roosen and Binnemans created functionalised chitosan polymers with ethylenediaminetetraacetic acid (EDTA) and diethylenetriaminepentaacetic acid (DTPA).[24] The goal of this functionalisation was to decrease the solubility of the chitosan in acidic aqueous solution, as well as improve separation performance, as both EDTA and DTPA have shown good binding abilities with the lanthanide elements. The structures of the EDTA- and DTPA- chitosan are shown in Fig. 3.

Other methods of REE separations using biosorbents have also shown promising results. For example, Dong *et al*. tested the performance of spores of *Bacillus subtilis* PS533 and PS4150 for the removal of low concentrations of Tb(III) from wastewater.[25] Results showed 94% Tb(III) removed within 30 minutes using PS4150 spores with the amino, hydroxyl, methyl and phosphate func-

tional groups all playing a role in the extraction. High adsorptions of other lanthanide elements were also observed, indicating the potential of the PS4150 spores for the wider applications of rare earth extractions.

In another application of biosorbents for REE separation, Mohammadi *et al*. tested the biomass, *Magnetospirillum magneticum* AMB-1, for the separation of La(III) from aqueous solution.[26] This bacterium naturally possesses magnetic qualities enabling easy removal of the biosorbent following extraction using an external magnet. This biosorbent achieved adsorption efficiencies as high as 98.7% for Sc, with over 90% of all other REEs adsorbed. While biosorbents appear to show promising results for REE separations, the main drawback appears to be their low selectivity observed in many applications including the examples discussed here.

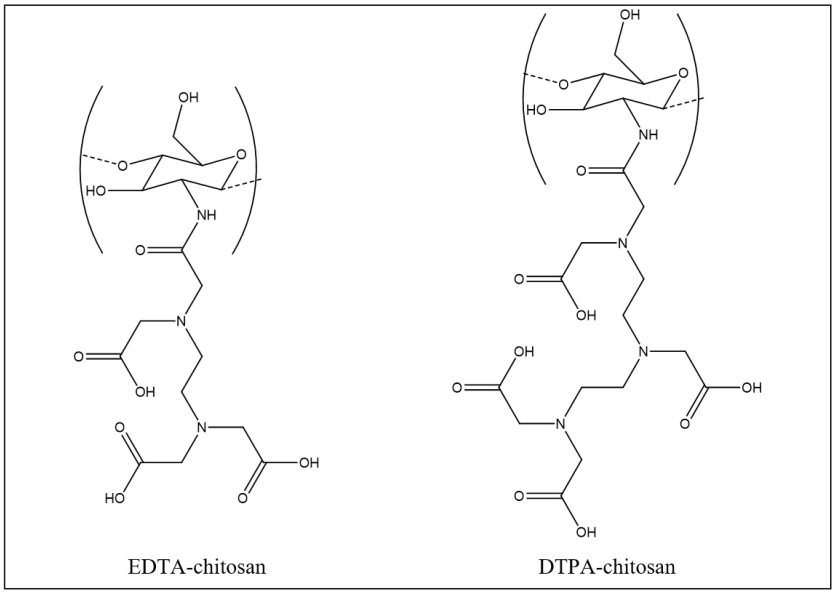

Fig. 3. Structure of chitosan modified with EDTA and DTPA

"While methods of SCF extractions are showing promising results, it appears there is still work to be done to improve their use in REE separations. "

Supercritical fluids

Supercritical fluid (SCF) extraction utilises fluids which have reached supercritical temperature, that is to say, they have been heated and compressed above their critical temperature and pressure to a point where they possess both liquid- and gas-like properties.[27] The use of supercritical fluids for the separation of REEs has been offered as another alternative greener method to traditional separation methods. SCFs offer many advantages including their low viscosity, fast mass transfer and ease of removal of separated elements from the SCF following extraction.[28] These properties can help increase the rate of extraction compared to alternative liquid extractants. Carbon dioxide (CO_2) is one of the most used SCFs as it is known to be inert, inexpensive, renewable and abundant. Furthermore, it does not require extreme temperature and pressure to reach critical conditions (T_c = 31□, P_c = 7.38 MPa).[29]

Due to its structure, supercritical CO_2 alone is a poor extractant for polar compounds and metal ions, including the REEs. However, the addition of CO_2-soluble complex-forming agents, such as tributyl phosphate (TBP) in nitric acid, can produce good extractions for the REEs as well as simple back-extraction and recyclability of the CO_2.[29]

Much like ionic liquids made for REE separations, SCF extractions often include the addition of common REE organophosphorus extractants to improve separations, with tributyl phosphate being one of the most widely reported. In many methods involving the use of sc-CO_2, extraction occurs through the mixing of the sc-CO_2 complex with lanthanide oxides. The dissolving of the lanthanide oxides and extraction of the lanthanides into the sc-CO_2-TBP phase in nitric acid can be described by Eq. 1 and 2 whereby the Ln^{3+} ions are extracted through the formation of a TBP complex as described by Yao *et al*.[30]:

$$Ln_2O_3 + 6HNO_3 \longrightarrow 2Ln^{3+} + 6NO_3^- + 3H_2O$$

(Eq. 1)

$$Ln^{3+} + 3NO_3^- + nTBP \longrightarrow Ln(NO_3)_3(TBP)_n$$

(Eq. 2)

Following extraction, the removal of the hydrophobic lanthanide complex formed with TBP can be simply achieved through the gasification of CO_2 at atmospheric pressure which results in the newly formed complex being precipitated out. Following this step, the CO_2 can be easily recycled for further extraction cycles. Methods like this have achieved promising results, with Shimuzu et al. reporting extraction efficiencies as high as 99% for the separation of Y and Eu from waste fluorescent lamps.[29] However, in a more recent study considering the recycling of REEs from fluores-

cent lamps, Zhang et al. discovered that these results may only be viable in synthetic mixtures due to competition between the REEs and Al^{3+} and Ca^{2+} ions commonly found in these waste materials.[31] Therefore, while methods of SCF extractions are showing promising results, it appears there is still work to be done to improve their use in REE separations.

Conclusions

The rare earth elements are vital components in much of our everyday and green-energy technology, but due to similarities in their physical and chemical properties, the separation of these elements can be challenging to achieve. The development of greener separation methods is important as demand for these elements grow. In this article, green REE separation methods involving the use of ionic liquids, biosorbents and supercritical fluids were briefly discussed to show their potential in the separation of the REEs.

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Article

Chemistry in New Zealand at your fingertips: results of a teacher survey and suggestions to consider

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Introduction

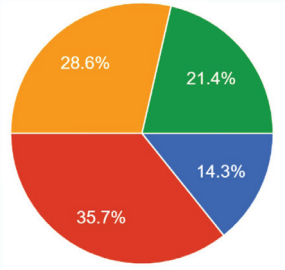
The October issue of *Chemistry in New Zealand* introduced the initiative 'Chemistry in New Zealand at your fingertips' (*Chemistry in New Zealand*, **2022**, *86(4)*, 178-181). This aims to transform the current quarterly publication into an online platform and has spurred motivation to expand the audience to the wider public. Teachers and students at secondary schools across the motu are one such group that could benefit from access to chemistry research conducted in Aotearoa New Zealand, to inform or be informed of the options in our own backyard but also to improve teaching practice. Being able to 'see' yourself in particular professions can motivate students, not only to engage with learning, but hopefully to pursue careers in chemistry.

To focus our efforts on material that is both well received and useful, a survey was conducted in August 2022. The survey was sent out via email to members of the Secondary Chemistry Educators of NZ (SCENZ), with approximately 10% of participants responding (28 of ~290). While acknowledging the low response rate, the information gathered still provides useful guidance as to the direction for this platform to go in the school space. The survey results are summarised in Table 1.

Table 1. Survey responses to *Chemistry in New Zealand* as an online platform for teachers

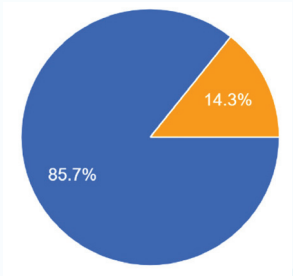
How familiar is *Chemistry in New Zealand (CiNZ)* to you?

(28 responses)



Would a SCENZ section within CiNZ be attractive to teachers?

(28 responses)

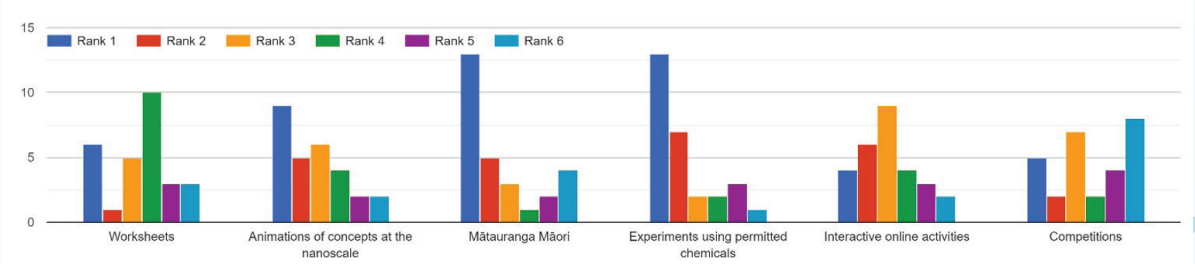


Chemistry in New Zealand was recognised by 64% of those surveyed. Around half of the high school teachers surveyed are at least familiar with CiNZ. The participants agreed (85.7%) that having a SCENZ section on the CiNZ website would be attractive to teachers. With 21.4% of participants not having heard of CiNZ, there is an opportunity for more engagement, and advertising to an extent, if we provide a space for secondary school content. Over-

Table 1 (cont). Survey responses to *Chemistry in New Zealand* as an online platform for teachers

What do you think would be most valuable to Teachers in a SCENZ section
(Rank 1 – highest priority; Rank 6 – lowest priority)

(28 responses)



all, there is support for CiNZ to be a chemistry hub for educators, or at least for one to exist.

When asked to rank a number of suggestions that may be valuable to each teacher surveyed, three out of six suggestions were preferred over the others. To process these results, for each suggestion the scores were weighted in each option by dividing the population of each Rank (1 – 6) by the rank number, and an average score was calculated.

For example, for 'Worksheets': $(\frac{6}{1}+\frac{1}{2}+\frac{5}{3}+\frac{10}{4}+\frac{3}{5}+\frac{3}{6})$ / 6 = 1.96

The suggestions and their corresponding scores are as follows:

Experiments using permitted chemicals:	**3.07**
Mātauranga Māori	**2.97**
Animations of concepts	**2.54**
Online interactive activities	**1.99**
Worksheets	**1.96**
Competitions	**1.82**

Therefore, a bank of experiments using chemicals permitted in secondary schools, followed by knowledge or resources on Mātauranga Māori are the two most valuable.

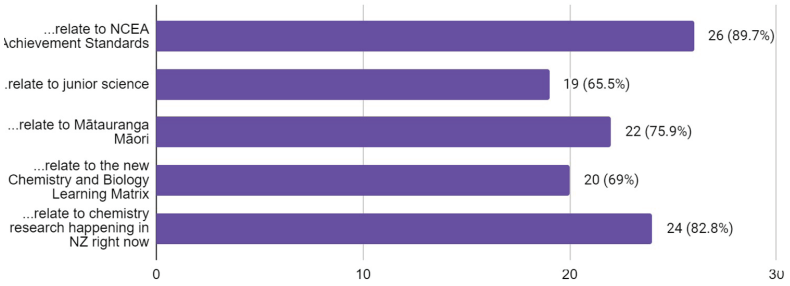
A need for resources on experiments could be due to a shortage of chemistry-trained technicians and the recent implementation of the *Safety and Science/Pūtaiao* document. This document details lists of chemicals that are 'forbidden' e.g. aromatic amines and phenolic compounds, in contradiction to the permitted chemicals phenolphthalein and fuchsine; those with 'a greater hazardous nature than educational utility' e.g. silver nitrate and potassium dichromate, which are virtually essential for teaching redox and precipitation reactions (osmium tetroxide, chromium trioxide and hydrofluoric acid are also on this list that are recognised as having 'some educational use'); and lastly those with 'a hazardous nature but with potential educational utility' e.g. glucose. The point being raised in this explanation is that for inexperienced chemistry teachers and technicians, adapting to this document requires some guidance and this could provide an opportunity for CiNZ.

As part of the NCEA change package currently underway, Change 2 'Mana Ōrite mō te Mātauranga Māori' or 'Equal status of Mātauranga Māori' will be embedded as part of the revised changes of the National Certificate in Education Achievement (NCEA) but to what extent it will appear in the science curriculum is still to be decided. The high score of Mātauranga Māori probably indicates a lack of exposure to Mātauranga Māori by many educators, and/or the implementation of the revised achievement standards in chemistry and biology starting in 2024. Having an online resource may provide educators with the confidence to prepare lessons in this space, noting of course that this would require consultation with

Table 1 (cont). Survey responses to *Chemistry in New Zealand* as an online platform for teachers

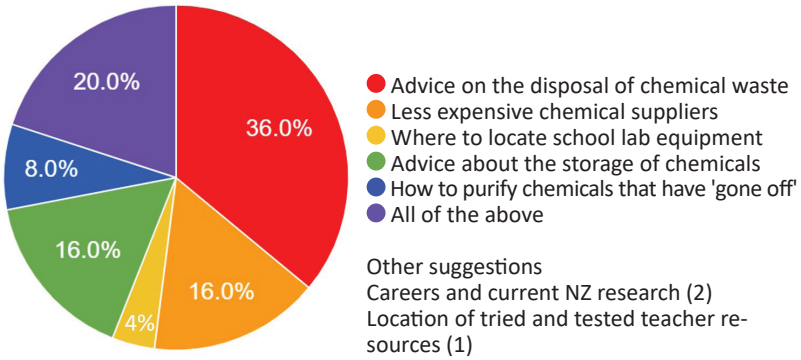
In terms of the focus of these resources, would you like them to… (tick all that apply)

(28 responses)



Aside from curriculum learning, what other areas of need would be useful if there was SCENZ section on this proposed CiNZ website? There are a few ideas below (5), but please feel free to add others.

(28 responses)



Other suggestions
Careers and current NZ research (2)
Location of tried and tested teacher resources (1)
Advice around implementing and complying with the Safety in Science document (1)

Mātauranga experts from iwi and hapū.

Animations illustrating concepts at the sub-micro scale, such as polarity, or the attractive forces between particles is also valuable. StudyPass® started to release visually appealing graphical content to explain some concepts but due to lack of funding and interest in what was a busy year for teachers, this project will not continue. Content like this, or links published onto the website, could be useful in helping students 'see the unseeable' and grasp the concepts at NCEA Levels 2 and 3.

When asked for a preference on what the focus of resources should be for an online CiNZ, all the options provided were favourable. However, there was a higher preference for those pertaining to the senior students (NCEA Achievement standards). What was pleasing is that there is a preference for NZ chemistry research, which aligns with our work tailoring CiNZ articles for secondary school students. Mātauranga Māori was also highlighted once again.

The teachers were then asked what other non-curriculum areas of need would be useful and five suggestions were provided. Advice on the disposable of chemical waste was popular, as the high costs of removal, particularly for forbidden chemicals or others such as lead and organic residues, make it difficult for schools. This can lead to the storage and buildup of these chemicals over years. Five teachers chose 'All of the above' suggesting that teachers need professional development or at least resources relating the handling, storage, treatment, and disposal of chemicals, as well as where to purchase less expensive chemicals.

Other than the pre-prepared suggestions, those surveyed also suggested highlights of research from recent graduates and chemistry academics within NZ, information linking chemistry to various career pathways, information about upcoming professional development and tailoring content from Education in Chemistry (RSC) to NCEA such as addressing misconceptions, relevant practical experiments and having a simple and user-friendly experience. CiNZ online has the potential to bridge secondary school science learning to tertiary and beyond.

Chemistry in New Zealand is a recognisable platform and the survey results indicate that an online version could be attractive as a resource to help and educate teachers and students alike. CiNZ would have an edge if it included in-demand aspects such as experiments using school compliant chemicals, approved content relating to Mātauranga Māori and animations to explain concepts at the sub-microscale.

It would be beneficial to teachers and students if CiNZ had content on the work of recent graduates and NZ research in general that is easy to read for students and relates to the curriculum. This could enable students to see what's available if they pursue chemistry further. CiNZ at your fingertips also has an opportunity to provide information on how to handle, store, dispose and possibly reuse chemicals for science technicians. Lastly, by engaging the public, chemistry within Aotearoa New Zealand can literally be *at their fingertips*.